World Journal of Advanced Pharmaceutical and Medical Research

Journal homepage: https://zealjournals.com/wjapmr/

ISSN: 2799-0656 (Online)

(Review Article)

Check for updates

The efficacy and safety of medicinal plants documented by clinical trials (part 1)

Ali Esmail Al-Snafi *

Department of Pharmacology, College of Medicine, University of Thi-Qar, Thi-Qar, 64001, Iraq.

World Journal of Advanced Pharmaceutical and Medical Research, 2022, 03(01), 030–077

Publication history: Received on 27 July 2022; revised on 01 September 2022; accepted on 03 September 2022

Article DOI: https://doi.org/10.53346/wjapmr.2022.3.1.0036

Abstract

Plants are a valuable source of a wide range of secondary metabolites, which are used as pharmaceuticals, agrochemicals, flavours, fragrances, colours, biopesticides and food additives. In the current review, PubMed, Web Science, Science Direct, Researchgate, Academia. edu and Scopus were searched to determinethe medicinal plantswhich pass the clinical trials with documented efficacy and safety.

Keywords: Medicinal plants; Pharmacology; Therapeutics; Clinical trial

1. Introduction

Medicinal plants have been a resource for healing in local communities around the world for thousands of years. Still it remains of contemporary importance as a primary healthcare mode for approximately 85% of the world's population. Herbal preparations are complex mixtures, and any assessment of efficacyand safety must rely on an adequate pharmaceutical documentation. Data relating only to *in vitro* pharmacology or experimental *in vivo* pharmacology,will not deliver sufficient supportive evidence to establish evidence of efficacy and safetythat would be acceptable for marketing authorization [1]. The current review discuss the medicinal plants which showed bebefical effect and safety in clinical trials.

2. Medicinal plants

2.1. *Agrimonia eupatoria*

A compound herb preparation containing agrimony has been used to treat 35 patients suffering from chronic gastroduodenitis. After 25 days of therapy, 75% of patients claimed to be free from pain, 95% from dyspeptic symptoms and 76% from palpitation pains. Gastroscopy indicated that previous erosion and haemorrhagic mucous changes had healed [2]. A successful treatment of cutaneous porphyria in a group of 20 patients receiving agrimony infusions has been described. An improvement in skin eruptions together with a decrease in serum iron concentrations in urinary porphyrins was noted [3-4].

2.2. *Agropyron repens [Elymus repens]*

A post-marketing surveillance was designed to investigate the efficacy and tolerability of a fluid extract of *Agropyron repens* [*Elymus repens*] (Acorus drops) in patients with urinary tract infections or irritable bladder. Data for 313 patients with urinary tract infections or irritable bladder were analysed. The patients were treated on average for twelve days with 50-60 drops 3 times a day. The primary efficacy criterion was the change of urological symptoms during the course of therapy. Between 69% and 91% of the urological symptoms initially documented were relieved in the course of

*Corresponding author: Ali Esmail Al-Snafi; Email:aboahmad61@yahoo.com
Department of Pharmacology, College of Medicine, University of Thi-Qar, Thi-Qar, Iraq.

therapy. Depending on the underlying urological diagnosis, between 32% and 53% of the patients were completely free of symptoms following treatment. Acorus drops were tolerated very well. No adverse drug reactions occurred [5].

In an open clinical trial in 99 patients with micturition disorders (12 female and 87 male), a 20% ethanol fluid extract of Agropyron repens was administered for 28-31 days (60 drops 3 times daily). The complaints of urge incontinence, dysuria, nycturia and tenesmus due to adenoma of prostate, prostatitis and cystitis were significantly reduced in 44. 4-100% of patients. Laboratory markers of inflammation (protein, epithelia, leucocytes and erythrocytes in urine) were also normalized. 96% of patients mentioned that the treatment is good or very good. Adverse effects were not recorded. The effect of single and repeated oral administration of the lyophilized aqueous extract of rhizomes of Agropyron repens (20 mg/kg) on lipid metabolism was studied in normal and streptozotocin-induced diabetic rats. In normal rats, the aqueous extract induced a significant decrease in the plasma triglycerides concentrations 4 days and 1 week after repeated oral administration. This reduction was abolished 2 weeks after once daily repeated oral administration. A significant decrease of plasma cholesterol levels was observed only 1 week after repeated oral administration. In diabetic rats, the treatment caused a significant decrease in plasma cholesterol after a single and repeated oral administration. A strong decrease in cholesterol levels was observed 6 hours after a single oral administration of the extract. Four days after the repeated oral administration of the extract, the plasma cholesterol level was significantly decreased and remained still diminished after 2 weeks. Repeated oral administration of the aqueous extract of Agropyron repens rhizome caused a significant decrease in body weight 2 weeks after oral treatment. In severely hyperglycaemic rats, Agropyron repens extract treatment induced reduction of lipid levels and body weight [6-7].

2.3. *Allium cepa*

In assessment of hypoglycemic activity of *Allium cepa* in type 1 and type 2 diabetic patients, ingestion of crude *Allium cepa* (100 g) caused a considerable reduction in fasting blood glucose levels by about 89 mg/dl in relation to insulin (145 mg/dl) in type 1 diabetic patients and it reduced fasting blood glucose levels by 40 mg/dl, compared to glibenclamide (81 mg/dl) in type 2 diabetic patients, 4 hours later. The same dose of crude *Allium cepa* produced a significant reduction in the induced hyperglycemia (GTT) by about 120 mg/dl compared to water (77 mg/dl) and insulin (153 mg/dl) in type 1 diabetic patients and considerably reduced GTT by 159 mg/dl in relation to water (55 mg/dl) and glibenclamide (114 mg/dl) in type 2 diabetic patients, after 4 hours [8].

2.4. *Allium sativum*

Eating of 10 g fresh garlic per day for 2 months significantly decreases (15%-28. 5%) serum cholesterol levels among hypercholesterolemic patients [9]. Garlic oil caused a steady decrease in LDL and VLDL levels with concomitant increase in HDL levels[910-11]. Intake of enteric-coated garlic powder (equal to 400 mg garlic, 1mg allicin) twice daily in hyperlipidemic patients has significantly reduced total cholesterol, LDL-cholesterol and triglyceride and increased HDL-cholesterol [12]. The level of cholesterol, triglyceride, phospholipids and ß- lipoproteins were significantly declined in the individuals consuming 10-50 g of garlic /week. These results indicate that routine consumption of garlic in the diet has a beneficial effect in maintaining the serum lipids at low or normal levels [13]. In a placebo-controlled trial of patients with stage II peripheral arterial occlusive disease, garlic powder supplements, 800 mg daily were associated with a significant increase in walking distance by 46 meters; the improvement started after the fifth week of treatment [14]. Patients treated with 900 mg daily of standardized garlic powder showed 9-18% reduction in plaque volume, a 4% decrease in LDL levels, an 8% increase in HDL concentrations, and a 7% decrease in blood pressure [15]. Clinical studies showed that garlic produced hypotensive effects. Garlic induced significant reduction in systolic and diastolic blood pressure**.** The authors postulated that the hypotensive action of garlic is due to a direct relaxant effect on smooth muscles [16-23]. On the other hand, oral administration of garlic powder (800mg/day) to 120 patients for 4 weeks in a double-blind, placebo-controlled study decreased the average blood glucose by 11. 6 % [24]. The therapeutic efficacy of (garlic 10% in petrolatum) was compared with (sulphur l0% in petrolatum) in 106 patients with scabies in three primary health care centers. It was found that the efficacy of sulphur 10% in petrolatum was (100%), while the efficacy of garlic 10% in petrolatum was (83. 33 %.) [25-26].

2.5. *Aloe vera*

A significantly faster healing time and a higher number of healed lesions than the placebo was recorded in a randomized, controlled double blind clinical trial of 60 men suffering from an initial episode of Herpes simplex infection, treated with an *Aloe vera* extract (0. 5%) in a hydrophilic cream [27]. A clinical study showed that *Aloe vera* gel might be helpful in treating patients with duodenal ulcers [28-29]. Five thousand patients of atheromatous heart disease, presented as anginapectoris, were studied over a period of five years. After adding the (Husk of Isabgol) and *(Aloe vera*) (an indigenous plant known as ghee-guar-ka-paththa) to the diet, a marked reduction in total serum cholesterol, serum triglycerides, fasting and postprandial blood sugar level in diabetic patients, reduction of total lipids and an increase in

HDL were noted. Simultaneously the clinical profile of these patients showed reduction in the frequency of anginal attacks [30]. Orally administered *Aloe gel* (1-2 tablespoons twice daily) enhanced the hypoglycemic effect of glibenclamide [31-33].

2.6. *Alpinia galanga*

In a randomized double-blind placebo controlled study, patients with osteoarthritis of the knee and moderate-to severe pain, the concentrated extract has been found significantly reduce symptoms of osteoarthritis [34-35].

2.7. *Althaea officinalis*

In a double blind clinical study, Rouhi and Ganji used *Althaea officinalis* in patients with hypertension who had been developed cough during taking of angiotensin converting enzyme inhibitors. The patients received 40mg of *Althaea officinalis* three times daily as 20 drops for four weeks. The Mean scores of the severity of the cough in the group which have been treated by *Althaea officinalis* had a significant change from the score of 2/66+0. 958 (to) 1/23+1. 006. Eight patient in the *Althaea officinalis* group showed almost complete cough abolition [36-37].

2.8. *Ammi majus*

Numerous studies have assessed the efficacy of Fructus *Ammi majus* and xanthotoxin for the treatment of vitiligo, psoriasis, and hypopigmentation tinea versicolor [38-47]. Experimentation with *Ammi majus* extracts was started in Egypt by El Mofti [40, 47]. This followed by the work of Sidi and Bourgeois who used *Ammi majus* Linn, in six patients with vitiligo, five men and one woman. Their ages were from 30 to 50 years. *Ammi majus* Linn was used (a) by oral administration, (b) by local topical application at the affected sites followed by sun or ultraviolet lamp exposure, or, (c) by a combination of (a) and (b). Three of patients were subjected to the combined treatment, two only to topical treatment and one to treatment by mouth for 5 months, and then to the combined treatment. The repigmentation appeared in allpatients as pigmented minute macules with hair follicles in their center. These macules were distributed over the leukodermic plaques and increased progressively in size until they joined, forming larger islands. This was particularly distinct in the lesions on the trunk and on the extremities. On the face the repigmentation developed more rapidly and appeared to be progressing more from the periphery towards the center [48].

Many clinical trials were carried out to investigate the efficacy of *Ammi majus* in vitiligo, Patient with leukodermis took oral *Ammi majus* powderd fruits with exposing the affected patches to direct sunlight for 1 hour developed symptoms of itching, redness, oedema, vesiculation and oozing in the leukodermic patches. Within few days, the affected skin gradually started to display deep brown pigmentation [49].

In two small group of patients (eight patients each) with leukoderma treated with oral (0. 05 g of *Ammi majus* three time daily) or liniment 1 g/100 ml, applied to the skin, with daily exposure of leukodermic areas to the sun for 0. 5 hour or to UV light for 2 minutes, gradually increasing to 10 minutes, the leukodermic skin areas were inflamed and vesiculated, and the leukodermic areas began to show normal pigmentation [50].

However *Ammi majus* and its furanocoumarins constituents showed good results in many other clinical studies, 70% of the patients treated with an oral dose of 0. 6 mg/kg bw of xanthotoxin 2 hours before exposure to sunlight three times per week with calcipotriol ointment in a randomized double-blind study, showed significant improvement [51].

Xanthotoxin with exposure to either UV-A or UV-B radiation for the treatment of plaque psoriasis in 100 patients appeared effective in reducing the number of plaques [120]. Oral administration of 0. 6 mg/kg BW of xanthotoxin with two UV-A radiation dosage regimens was used for treatment of patients with moderate–severe chronic plaque psoriasis. 42% of patients were clear 1 year after treatment and the treatment regimens were well tolerated [52]. Many other similar results were obtained in assessment of *Ammi majus* and its furanocoumarins in the treatment of psoriasis, vitiligo and tinea versicolor by many authors [39, 46, 53-54].

2.9. *Ammi visnaga*

A clinical trial of khellin in 38 cases of angina pectoris and in 8 cases ofcoronary thrombosis was performed. Continuous treatment, by the oral or intramuscular routes or by both, gave favourable results in 35 out of 38 cases of angina pectoris. Continuously administration of khellin for several weeks to eight patients after coronary thrombosis appeared favourable [55]. A clinical study was carried out on 20 non-obese, normolipaemic male subjects to determine the effects of orally administered 50 mg khellin four times daily for 4 weeks on the plasma lipids. Plasma total cholesterol and triglyceride remained unchanged, but high-density-lipoprotein cholesterol concentration was significantly elevated

during the treatment and till one week after cessation of treatment [56]. In a comparison with glyceryl trinitrate, khellin (3 ml. containing 150 mg. of khellin, alcoholic extract standardized to contain 50 mg/ml) was used in twelve patients for prevention of angina of effort and the electrocardiographic changes that may accompany it. Khellin was less potent but longer acting than glyceryl trinitrate, and it did not cause any unpleasant side effects [57]. A double-blind, placebo-controlled study of 60 people indicated that the combination of oral khellin (which is the main constituent of *Ammi visnaga*) and natural sun exposure caused repigmentation in 76. 6% of the treatment group, in comparison, no improvement was seen in the control group receiving sunlight plus placebo [58]. A subsequent placebo-controlled study of 36 patients of vitiligo, showed that a topical khellin gel plus UVA caused repigmentation in 86. 1% of the treated cases, as opposed to 66. 6% in the placebo group [59-60].

2.10. *Anthemis nobilis*

In an open clinical study carried out on 54 patients with chronic bronchial asthma, *A. nobilis* showed antiasthmatic effects, it caused significant elevation in the values of forced expiratory volume in first second (FEV1%) and forced volume capacity (FVC) with marked reduction in asthmatic attacks [61-62].

2.11. *Arctium lappa*

Silver *et al* investigated the effect of burdock powder on normal and diabetic patients, and found out that burdock root possess hypoglycemic effects. The antidiabetic effects of burdock root was related to polysaccharides, the main component of the root. Root extract maintained the blood glucose level constant, therefore improving the tolerance to high glucose level [63-64].

2.12. *Avena sativa*

In overweight patients, beta glucan from oats has been shown to decrease hypertension. Avenanthramide is an oat polyphenol that has been shown to enhance production of nitric oxide, a potent vasodilator, and to inhibit thickening of vascular smooth muscle. Both actions are preventative to developing atherosclerosis [65-66].

A clinical trial was carried out to confirm the anti- obesity effect of oat. Subjects with BMI ≥27 and aged 18-65, were randomly divided into a control (n=18) and an oat-treated (n=16) group, taking a placebo or beta glucan-containing oat cereal, respectively, for 12 weeks. The result showed that consumption of oat reduced body weight, BMI, body fat and the waist-to-hip ratio. Profiles of hepatic function, including AST and ALT showed decrements in patients with oat consumption. Nevertheless, anatomic changes were not observed by ultrasonic image analysis. Ingestion of oat was well tolerated and there was no adverse effect during the trial [67-68].

2.13. *Bacopa monnieri*

A clinical trial was carried out to assess the effects of 12-weeks administration of *Bacopa monnieri* (300mg/day) on memory performance in people over the age of 55-years. Bacopa significantly improved memory acquisition and retention in olderpersons [69]. Significant cognitive enhancing benefits have been demonstrated with chronic administration of Bacopa extracts. A double-blind, placebo-controlled, 12-week trial utilizing the same patient selection criteria and the same dose of Bacopa extract (300 mg daily) containing 55% combined bacosides, was carried out. Forty-six healthy volunteers (ages 18-60) were randomly and evenly divided into treatment and placebo groups. The same series of tests administered in the acute dosage trial were administered at baseline, five, and 12 weeks after treatment began. At the end of the 12-week study, results indicated a significant improvement in verbal learning, memory consolidation, and speed of early information processing in the treatment group compared to placebo. These effects were not observed at baseline or at five weeks [70].

The Bacopa supplement was commercially available as KeenMind™ (Flordis). This product is manufactured from the stems, leaves and roots of Bacopa and is extracted with 50% ethanol. It is standardized to contain active bacosides at levels of 55% ± 5%. KeenMind™ help develop novel preventative health practices and nutritional/ pharmacological targets in the elderly for cognitive and brain health. Bacopa appeared to have multiple modes of action in the brain, all of which may be useful in ameliorating cognitive decline in the elderly. These include: direct pro-cholinergic action; anti-oxidant (flavonoid) activity; metal chelation; anti-inflammatory effects; improved blood circulation; adaptogenic activity; and removal of b-amyloid deposits [71]. However, in a double-blind randomized, placebo control study performed on 76 adults aged between 40 and 65 years, in which various memory functions were tested and levels of anxiety was measured, the rate of learning was unaffected by *Bacopa monnieri* suggesting that *Bacopa monnieri* decreases the rate of forgetting of newly acquired information. Tasks assessing attention, verbal and visual short-term memory and the retrieval of pre-experimental knowledge were unaffected. Questionnaire measures of everyday memory function and anxiety levels were also unaffected [72].

A double-blind, randomized, placebo controlled trial of 169 patients with irritable bowel syndrome, effects of an Ayurvedic preparation containing *Bacopa monniera* and *Aegle marmelos* was compared with standard therapy (clidinium bromide, chlordiazepoxide, and psyllium). Subjects were randomly assigned to standard drug treatment, botanical treatment, or placebo for six weeks. Treatment was administered orally as drug, botanical, or placebo three times daily. Ayurvedic therapy was superior to placebo, however, the two botanicals were not given separately, and the benefit could not link specifically to the Bacopa portion of the Ayurvedic preparation [73-74].

2.14. *Bellis perennis*

The effect of *Bellis perennis* on postpartum blood loss was studied by double blind, placebo-controlled, randomized, clinical trial. At 72 h postpartum, mean Hb levels remained similar after treatment with homeopathic remedies (12. 7 versus 12. 4) as compared to a significant decrease in Hb levels in the placebo group (12. 7 versus 11. 6; p<0. 05), in spite of less favorable initial characteristics of the treatment group. The mean difference in Hb levels at 72 h postpartum was -0. 29 (95% CI -1. 09; 0. 52) in the treatment group and -1. 18 (95% CI -1. 82; -0. 54) in the placebo group (p<0. 05) [75]. *Bellis perennis* showed haemolytic activity. It has been found that the haemolytic activity of the drug changes in dependence on the time of collection of capitula during the year; it is lowest in March, then it increases, reaching the maximum in summer months (June, July, August), and then it decreases again. In two placebo-controlled studies, Traumeel injections, (which contains *Bellis perennis*) was used in patients with hemarthrosis. It showed that Traumeel injections improved joint and mobility, and decreased intensity of pain and effusion [76-78].

2.15. *Benincasa hispida*

Salad was prepared by using 100gm of ash gourd (*Benincasa hispida*) and one gram of curry leaves (10 curry leaves) and five grams of skimmed milk powder (made into curd) and pepper and salt are added for taste. This salad was freshly prepared every day and given to hyperlipidemic diabetic patients in mid morning for a period of three months to find out the therapeutic effect of supplementation of ash gourd and curry leaves. Supplementation of ash gourd and curry leaves had significant hypoglycemic and hypolidemic effect and it reduced the blood glucose level (both fasting and post prandial), within the period of three months [79-80].

2.16. *Bidens tripartitus*

500 patients with dysentery, 65 with acute enteritis and 248 with chronic enteritis were used the aerial parts of the plant. Several different dosage forms of the herb were used: 200 g of fresh whole herb and 100 g of dried herb in decoctions (in three divided doses per day); granules containing 5 g of dried aqueous extract, three times daily; 0. 5 g tablets of dried aqueous extract, 10 tablets each time three times daily; and injection, 2 ml per injection (dose not stated), 2–3 times daily. The herbal preparations were administered for 3–10 days to patients who already had diarrhoea. 387 of the 500 patients with chronic dysentery were reported to have been cured, 13 had not responded within 3 days. All 313 patients with enteritis were reported to have been cured [81].

Clinically, 70% ethanol extract of the aerial parts of the plant and an ointment containing 2. 5% of the extract were used by 53 patients with psoriasis. After one week of oral administration of the extract (20 drops three times daily) with application of the ointment to the affected areas of the skin once a day, desquamation of the skin was decreased, and a decoloration of the psoriatic plaques was observed. 29 of the patients were clinically recovered, 22 patients were clinically improved and failure of the therapy was recorded in 2 patients [82-83].

2.17. *Bryophyllum calycinum*

A prospective double-blind trial with orally applied Bryophyllum versus placebo was carried out. Thirty-two patients divided into two groups, 15 patients received Bryophyllum and 17 received the placebo. The time of delivery did not differ between the groups. In both groups the mean time of birth was in the 35 week of gestation. The mean birth weight was slightly higher in the placebo group (2192g) compared to the Bryophyllum group (1948g). A transition to the intensive care unit was slightly higher in the placebo groupcompared to the Bryophyllum group [84-85].

2.18. *Calendula officinalis*

The therapeutic efficacy of marigold (*Calendula officinalis* ointment) was investigated in the epithelialization of lower leg venous ulcers. Twenty-one patients with 33 venous ulcers out of 34 patients were treated with (which applied twice a day for 3 weeks. The second group was a control group that consisted of 13 patients with 22 venous ulcers. In the control group, saline solution dressings were applied to ulcers for the same period. In the experimental group the total surface of all the ulcers at the beginning of the therapy was 67,544 mm. After the third week the total surface of all the ulcers was 39,373 mm (a decrease of 41. 71%). In seven patients, complete epithelialization was achieved. In the control

group the total surface of all the ulcers at the beginning of the therapy was 69,722 mm. After the third week the total surface of all the ulcers was 58,743 mm2 (a decrease of 14. 52%). In four patients, complete epithelialization was achieved. There was a statistically significant acceleration of wound healing in the experimental group ($p < 0.05$) [86].

The effect of *Calendula officinalis* flowers extract mouthwash as oral gel (by maceration in ethanol 70% for a 72 hour period) was evaluated in radiation-induced oropharyngeal mucositis (OM) in patients with head-and-neck cancer. Forty patients with neck and head cancers under radiotherapy or concurrent chemoradiotherapy protocols were receive either 2% calendula extract mouthwash or placebo. Patients were treated with telecobalt radiotherapy at conventional fractionation (200 cGy/fraction, five fractions weekly, 30–35 fractions within 4–7 weeks). The oropharyngeal mucositis was evaluated by the oral mucositis assessment scale (OMAS). Calendula mouthwash significantly decreased the intensity of OM compared to placebo at week 2 (score: 5. 5 vs. 6. 8, $p = 0.019$), week 3 (score: 8. 25 vs. 10. 95, $p < 0.0001$) and week 6 (score: 11. 4 vs. 13. 35, $p = 0.031$) [87].

170 patients with duodenal ulcers and/or gastroduodenitis, treated with a herbal combination containing calendula showed improvement of symptoms in 90%. 24 adults with non-specific colitis treated with herbal tea included calendula, showed improved symptoms in 96% of the patients within two weeks [88-89].

2.19. *Calotropis procera*

Topical preparation of *C. procera* was used for the treatment of eczema in 94 patients. The trials were conducted for nine months. The result was found encouraging, complete cure of all the signs and symptoms have been noted in 14 (14. 89%) patients, excellent response was noted in 24 (25. 53%) patients, good response in 33 (35. 10%) patients, and fair response in 10 (10. 63%) patients. Two (2. 12%) patients showed poor response to the treatment and 2 (2. 12%) patients exhibited worsened condition [90-91].

2.20. *Carthamus tinctorius*

The therapeutic and preventive effects of Safflower Injection (Al) in vascular crisis after free flap transplantation was studied clinically. Sixty patients undergoing free flap transplantation were randomly assigned to the treatment group and control group, thirty in each. Free flap transplantation was performed on all patients, and medication was given 0. 5h before flap vascular anastomosis, 1-7 days after surgery. Twenty ml Al was intravenously dripped to patients in the treatment group after adding in 250 ml 5% glucose injection, while Dextran-40 was intravenously dripped to patients in the control group. The medication was conducted once per day. The hemorheology and four indices of blood coagulation [prothrombin time, international normalized ratio, activated partial thromboplastin time, fibrinogen] were compared between the two groups before operation (TO), during operation (T1), 24 h after operation (T2), three days after operation (T3), and seven days after operation (T4). Meanwhile, flaps were observed and adverse reaction recorded. The clinical efficacy and safety were compared. Better result was obtained in the treatment group when compared their clinical efficacy (86. 67% vs 60. 00%, $P<0.05$). The whole blood high and low viscosity, plasma viscosity, red blood cell volume, RBC aggregation index all decreased, and RBC deformed index increased in the two groups at T4, showing statistical difference when compared with those at T3 ($P<0.05$, $P<0.01$). There was no statistical significance in the four indices of blood coagulation when compared with any time point in the same group ($P>0.05$). There was no statistical significance in hemorheology and the four indices of blood coagulation between the two groups at the same time point ($P>0.05$). The adverse reaction rate in the treatment group was lower than that in the control group, showing statistical difference (13. 33% vs 30. 00%, $P<0.05$) [92].

The effects of long-term supplementation with Safflower seed extract (SSE) on arterial stiffness in human subjects were evaluated in a double blind clinical trial. 77 males (35-65 years) and 15 postmenopausal females (55-65 years) with high-normal blood pressure or mild hypertension who were not undergoing treatment received SSE (70 mg/day as serotonin derivatives) or placebo for 12 weeks, and pulse wave measurements, ie, second derivative of photoplethysmogram (SDPTG), augmentation index, and brachial-ankle pulse wave velocity (baPWV) were conducted at baseline, and at weeks 4, 8, and 12. Vascular age estimated by SDPTG aging index, improved in the SSE-supplemented group when compared with the placebo group at four ($P=0.0368$) and 12 weeks ($P=0.0927$). The trend of augmentation index reduction ($P=0.072$ versus baseline) was observed in the SSE-supplemented group, but reduction of baPWV by SSE supplementation was not observed. The SSE-supplemented group also showed a trend towards a lower malondialdehyde-modified-LDL autoantibody titer at 12 weeks from baseline [93-94].

2.21. *Carum carvi*

The effect of the *Carum carvi* plant on resumption of bowel motility after Cesarean section was investigated by a randomized controlled pilot study conducted on 20 women undergoing elective Caesarean section under general

anesthesia. The patients were randomly divided into two groups. The intervention group drank 10 ml of *Carum carvi* syrup containing 2 g of *Carum carvi* in 20 ml of syrup at 8 to $8_{1/2}$ hours after surgery. The control group was given 10 ml of the placebo syrup at 8 to $8_{1/2}$ hours after surgery. Demographic characteristics, time of first peristaltic, first gas passage, first bowel movement, and time until hospital discharge were compared for the two groups. The results showed that compared to the control group, the intervention group had significantly shorter mean interval of the first intestinal sounds (10. 0 ± 2. 03 h vs. 19. 28 ± 3. 95 h); mean time to first passage of flatus (15. 91 ± 3. 73 h vs. 26. 82 ± 5. 83 h), mean time to first bowel movement (20. 31 ± 4. 63 h vs. 31. 7 ± 10. 2 h) and mean length of hospitalization (31. 71 ± 7. 57 h vs. 50. 6 ± 16. 49 h) ($p < 0.05$). There were no serious side effects associated with consumption of the syrup. Accordingly, the use of *Carum carvi* after caesarean section can speed the resumption of post-operative bowel motility [(95)].

The efficacy and safety of a herbal preparation STW 5-II containing extracts from bitter candy tuft, matricaria flower, peppermint leaves, caraway, licorice root and lemon balm was investigated in the treatment of 120 patients with functional dyspepsia. During the first 4 weeks, the gastrointestinal symptom score (GIS) was significantly decreased in subjects on active treatment compared to the placebo ($p < 0.001$). During the second 4-week period, symptoms further improved in subjects who continued on active treatment or who switched to the active treatment ($p < 0.001$), while symptoms deteriorated in subjects who switched to placebo. After 8 weeks 43. 3% on active treatment and 3. 3% on placebo reported complete relief of symptoms. ($p < 0.001$ vs. placebo) [(96)].

Carum carvi elevated TSH level, high TSH levels was recorded in few patients with thyroid cancer who receiving *Carum carvi* despite being on suppressive dose of levothyroxin. TSH level returned to normal after discontinuation of the *Carum carvi* [(97-98)].

2.22. *Cichorium intybus*

A placebo-controlled, double-blind, dose-escalating trial, was conducted to determine the safety and tolerability of a proprietary bioactive extract of chicory root in patients with osteoarthritis (OA). The results of the pilot study suggested that a proprietary bioactive extract of chicory root has a potential role in the management of OA. Only one patient treated with the highest dose of chicory discontinued treatment due to an adverse effects [(99-100)].

2.23. *Cistanche tubulosa*

The efficacy and safety of *Cistanche tubulosa* glycoside capsules (CTG capsule, Memoregain®) for treating Alzheimer's disease (AD) were studied clinically. A total of 18 patients with AD administered with Memoregain® for 48 weeks were assessed for drug efficacy by Alzheimer's disease assessment scale–cognitive subscale (ADAS-cog), mini-mental state examination (MMSE), activities of daily living (ADLs), blessed behavioral scale, and clinical global impression (CGI) scales. The MMSE score was 14. 78 ± 2. 51 at baseline and 14. 06 ± 4. 26 at study completion. While changes in ADAS-cog score before and after 48 weeks of treatment were statistically insignificant, the score improved, deteriorated, and remained unchanged in 10, 7, and 1 patients, respectively. The ADL and CGI scores showed no significant difference from baseline. All adverse reactions were mild. After Memoregain® treatment, patients with AD showed no obvious aggravation of cognitive function, independent living ability, and overall conditions but were stable throughout the study. Comparison with other long-term medications,acetylcholinesterase inhibitors suggests that Memoregain® has a potential to be a possible treatment option for mild to moderate AD [(101-102)].

Cistanche tubulosa extract was studied indouble-blinded, placebo-controlled clinical trial, to investige its efficacy in promoting hair health in patients with mild to moderate patterned hair loss. The density and diameter of hairswas compared with that in patients receiving a placebo at baseline, 8 and 16 weeks of the study. In order to determine the efficacy of treatment on dandruff and scalp inflammation, investigator's visual assessment score and patient's subjective score were also performed. A statistically significant increase in the hair density and hair diameter of the test group was recordedafter 16 weeks. There were also significant outcomes regarding the investigator's visual assessment and patient's subjective score of dandruff and scalp inflammation in the test group compared to those in control group. Based on the results of this clinical study, the authors conclude that *Cistanche tubulosa* extract *is a*promising substances for promoting health of the scalp and hair [(103-104)].

2.24. *Citrullus colocynthis*

Theefficacy of*Citrullus colocynthis* (L.) Schrad fruitin2 months clinical trial was conducted in 50 type II diabetic patients. Two groups of 25 each under standard antidiabetic therapy, received 100 mg *Citrullus colocynthis*fruit capsules or placebos three times a day, respectively. The patients were visited monthly and glycosylated hemoglobin (HbA1c), fasting blood glucose, total cholesterol, LDL, HDL, triglyceride, aspartate transaminase, alanine transaminase, alkaline

phosphatase, urea and creatinine levels were determined at the beginning and after 2 months. The results showed a significant decrease in HbA1c and fasting blood glucose levels in *C. colocynthis* treated patients. Other serological parameters levels in bothgroups did not change significantly. No notable gastrointestinal side effect was observed in either group [105].

A double-blind randomized placebo-controlled clinical trial using a parallel design was carried out to examine the safety and efficacy of*Citrullus colocynthis*topical formulation in patients with painful diabetic neuropathy. Sixty patients with painful diabetic polyneuropathy (PDPN) were randomly allocated to receive the topical formulation of *Citrullus colocynthis* (1:1 allocation ratio) or placebo for three months. The patients were evaluated before and after the intervention in terms of Neuropathic Pain Scale, electrodiagnostic findings, World Health Organization BREF quality of life scores and reported adverse events. The mean change in pain score was significantly higher in the *Citrullus colocynthis*group 3. 89 than in the placebo group 2. 28 (P<0. 001). The mean changes in nerve conduction velocity of the tibial nerve, distal latency of the superficial peroneal nerve and sural nerve, as well as sensory amplitude of the sural nerve in the intervention group were significantly higher than in the placebo group (P<0. 001). No significant differences were observed between the mean changes in other nerve conduction values. World Health Organization BREF quality of life scores, only showed significant improvement of the physical domain [106].

The hypolipidemic effect of*Citrullus colocynthis*was studied clinically. One hundred dislipidemic patients were randomly divided into two treated and placebo groups. They weretreated daily with powdered seeds of *Citrullus colocynthis* (300 mg) and placebo for 6 weeks. Lipid profile, SGOT and SGPT were measured at the beginning and the end of the treatment period. Significant differences within and between treated and placebo groups was recorded in TG andcholesterol (p<0. 05). A daily intake of 300 mg/ day of powdered seeds of *Citrullus colocynthis*can lower the triglyceride and cholesterol concentration significantly in nondiabetic hyperlipidemic patients [107-108].

2.25. *Citrus species*

Four-week consumption of orange juice in healthy middle-aged, normal-weight men reduced diastolic blood pressure (DBP) [109]. However, the effects of four-week intake of natural and commercial orange (*Citrus sinensis*) juice (CSJ)on blood pressure was evaluatedin healthy volunteers. 22 healthy subjectswere included and randomly divided into two groups. Group A consumed commercial CSJ during the first four-week period. After a two-week washout period, they consumed natural CSJ for another four weeks. The procedure was reversed in group B. The participants were asked to drink 500 ml/day of either natural or commercial CSJ twice a day with breakfast and dinner. After drinking commercial CSJ, diastolic and systolic blood pressure were significantly decreased (5. 13%; P = 0. 03 and -5. 91%; P = 0. 003, respectively). However, consumption of natural CSJ did not have significant effects on either diastolic or systolic blood pressure. Higher flavonoid, pectin, and essential oils content of concentrated products compared to natural juice might have been responsible for thiseffect [110].

To compare the efficacy and safety of two routes of administration (nasal spray versus subcutaneous injections) of Citrus/Cydonia in seasonal allergic rhinitis, a randomised, comparative clinical trial with two parallel groups was carried out. After a one- or two-week wash-out period, 23 patients were randomized, to a 6-week treatment period and the immunological and symptom severity changes and safety were evaluated. Both routes of administration were safe,they demonstrate therapeutic immunological and clinical effects [111-112].

2.26. *Colchicum balansae*

Colchicine was antigout agent, produced noanalgesic effect, not a uricosuric, and will not prevent progression of gout to chronic gouty arthritis. Its mechanisms of action involved reducing inflammatory response to the deposited crystals, diminishing phagocytosis and suppressing monosodium urate crystal-induced NACHT-LRR-PYD-containing protein-3 (NALP3) inflammasome-driven caspase-1 activation, IL-1b processing and release, and L-selectin expression on neutrophils. Its prophylactic, suppressive effect helped reduce the incidence of acute attack. It was a good alternative to NSAIDs, and probably as effective. It was of value in patients with heart failure since unlike NSAIDs it did not induce fluid retention, also it can be given to patients receiving anticoagulants [113-114].

Colchicine was effective and safe for the treatment and prevention of recurrent pericarditis and might ultimately serve as the initial mode of treatment, especially in idiopathic cases. Colchicine plus conventional therapy led to a clinically important and statistically significant benefit over conventional treatment, decreasing the recurrence rate in patients with a first episode of acute pericarditis [115].

Inthe treatment of dermatological diseases, colchicineshowed effectiveness in psoriasisin many clinical trials [116-121]. Sweet's syndrome also improvedwith a daily dose of 1. 5 mg colchicines [122]. Colchicinealso used at the dose of 1. 2-1. 8

mg/day to treat patients with dermatitis herpetiformis, it appeared as a good alternative in those who could not take sulfonamides [123]. It appeared that colchicinealso asuccessful treatment of epidermolysis bullosa acquisita [124],and inchronic bullous dermatosis of childhood with G6PD deficiency [125]. It was also beneficial in leucocytoclastic vasculitis and urticarial vasculitis [126], scleroderma and amyloidosis [127-128].

Many other dermatological diseases were also treatedwith colchicines including erythema nodosum leprosum, pyoderma gangrenosum,severe cystic acne, calcinosis cutis,keloids, sarcoid, condyloma acuminata,fibromatosis,relapsing polychondritis, primary anetoderma, subcorneal pustular dermatosis, erythema nodosum,scleredema,and actinic keratosis. It also possessed other pharmacological effects including,decrease of the corporal temperature, depression of the respiratory center, increased response to sympathomimetic agents, contraction of blood vessels, hypertension by central vasomotor stimulation, and alteration of the neuromuscular function [129].

Colchicine was the gold standard and indeed the only recommended drug for treating familial Mediterranean fever (FMF). It was thought to primarily concentrated in neutrophils and inhibit their increased chemotactic activity during FMF attacks [130].

It was an effective drug for eliminating the attacks and preventing the development of amyloidosis in patients with familial Mediterranean fever (FMF) [1311].

Colchicine should be administered orally once the diagnosis of FMF is confirmed (or as a therapeutic trial in establishing the diagnosis). Adult dosing is 1. 2–2. 4 mg/day, whereas children usually start at 0. 3–1. 2 mg/day according to age and weight and can increase sequentially up to 2 mg/day depending on how effectively the attacks were regulated [132-133].

2.27. *Coriandrum sativum*

A polyherbal ayurvedic formulation from an ancient authentic classical text of ayurveda was evaluated for its activity against inflammatory bowel disease (IBD). The polyherbal formulation contained four different drugs viz. , Bilwa (*Aegle marmeloes*), Dhanyak (*Coriandrum sativum*), Musta (*Cyperus rotundus*) and Vala (*Vetiveria zinzanioids*). The formulation has been tried in clinical practice and was found to be useful in certain number of cases of IBD. Accordingly, the same form, decoction (aqueous extract)was evaluated in experimental animals. The formulation was tried on two different experimental animal models of inflammatory bowel disease (acetic acid-induced colitis in mice and indomethacin-induced enterocolitis in rats). Prednisolone was used as the standard drug for comparison. The formulation showed significant inhibitory activity against inflammatory bowel disease induced in these experimental animal models. The activity was comparable with the standard drug prednisolone. The results obtained established the efficacy of this polyherbal formulation against inflammatory bowel diseases [134].

The hypoglycemic effect of *Coriandrum sativum* was studied clinically in patients withtype-2 diabetes mellitus. After assaying fasting plasma and urinary glucose, 10 patients of type-2 diabetes mellitus with no previous medication, 10 patients of type-2 diabetes mellitus taking oral hypoglycemic agents with history of inadequate control and six control subjects were given low (2. 5 g tid) and high (4. 5 g tid) doses of aqueousand alcoholic extracts of *Coriandrum sativum* for 14 days. On 15th day, blood and urine samples were taken for glucose estimation. *Coriandrum sativum* has significant hypoglycemic activity in high dose and can be successfully combined with oral hypoglycemic agents in type-2 diabetic patients whose diabetes was not controlled by oral hypoglycemic drugalone [135-136].

Ina randomized, double-blinded clinical trial, performed in Isfahan dental school in 2012, a new herbal medicament containing combined extracts from *Q. brantii* and *Coriandrum sativum* was formulated in the gel form for subgingival application. Following scaling and root planing (SRP), both herbal and placebo gels were delivered at the experimental and control sites, respectively. Periodontal pocket depth, clinical attachment level, papilla bleeding index, and plaque index were measured at baseline, 1 month and 3 months later. Both groups indicated statistically significant improvements in the periodontal indices ($p<0. 05$) [137-138].

2.28. *Crocus sativus*

The efficacy of hydroalcoholic extract of*Crocus sativus* (stigma) in comparison with fluoxetine in the treatment of mild to moderate depression was studiedin a 6-week double-blind, randomized trial. Forty adult outpatients who met the Diagnostic and Statistical Manual of Mental Disorders, fourth edition for major depression based on the structured clinical interview for DSM-IV and with mild to moderate depression wereparticipated in the trial. Patients were randomly assigned to receive capsules of saffron 30 mg/day (BD) (Group 1) and capsule of fluoxetine 20 mg/day (BD) (Group 2) for a 6-week study. Saffron at this dose was found to be effective similar to fluoxetine in the treatment of mild

to moderate depression (F = 0. 13, D. F. = 1, P = 0. 71). There were no significant differences between the two groups in terms of observed side effects [139].

The efficacy of petal of *Crocus sativus* was compared with fluoxetine in the treatment of depressed outpatients in an 8-week pilot double-blind randomized trial. Forty adult outpatients who met the DSM- IV criteria for major depression based on the structured clinical interview for DSM- IVwere participated in the trial. Patients have a baseline Hamilton Rating Scale for Depression score of at least 18. In this double-blind and randomized trial, patients were randomly assigned to receive either capsule of petal of *Crocus sativus* 15 mg bid (morning and evening) or fluoxetine 10 mg bid (morning and evening) for a 8-week. At the end of trial, petal of *Crocus sativus* was found to be effective similar to fluoxetine in the treatment of mild to moderate depression (F=0. 03, d. f. =1, P=0. 84). In addition, in the both treatments, the remission rate was 25%. There were no significant differences in the two groups in terms of observed side effects [140].

In a randomized, double-blind study, 30 mg of saffron extract (in capsules) given for 6 weeks resulted in significant alleviation of depression compared to placebgroup, andno side effects were recorded. Many follow-up double blind trials carried outon saffron preparation compared withimipramine andfluoxetine; showed that saffron possessed antidepressant effects [141-143].

The efficacy of *Crocus sativus* was studiedin the treatment of patients with mild-to-moderate Alzheimer's disease. Fifty-four Persian adults, 55 years of age or older were participatedin a 22-week, double-blind study of parallel groups of patients with AD. The main efficacy measures were the change in the Alzheimer's Disease Assessment Scale-cognitive subscale and Clinical Dementia Rating Scale-Sums of Boxes scores compared with baseline. Adverse events (AEs). Participants were randomly assigned to receive a capsule saffron 30 mg/day (15 mg twice per day) or donepezil 10 mg/day (5 mg twice per day). Saffron at this dose was found to be effective similar to donepezil in the treatment of mild-to-moderate AD after 22 weeks. The frequency of AEs was similar between saffron extract and donepezil groups with the exception of vomiting, which occurred significantly more frequently in the donepezil group [144].

Fifty milligrams of saffron dissolved in 100 ml of milk was administered twice a day to human subjects,the significant decrease in lipoprotein oxidation susceptibility in patients with coronary artery disease (CAD) indicated the potential of saffron as an antioxidant [145].

A randomized, parallel-group, double-blind, placebo-controlled trialwas designed to investigate the effects of *Crocus sativus*gel on erectile dysfunction in diabetic men. Patients were randomly allocated to 2 equal groups (with 25 patients each). The intervention group was treated with topical saffron, and the control received a similar treatment with placebo. The 2 groups were assessed using the international index of erectile function questionnaire before the intervention and 1 month after the intervention. Compared to placebo, the prepared saffron gelsignificantly improved erectile dysfunction in diabetic patients (P < . 001) [146-147].

2.29. *Cuminum cyminum*

The effect of cumin powder on body composition and lipid profilewas studied in overweight and obese women in a randomized clinical trial. 88 overweight/obese women were randomly assigned into two groups. The experimental group wasgiven 3 g/day cumin powder with yogurt at two meals for 3 months. The same amount of yogurt without cumin powder was prescribed for the control group. All patients received nutrition counseling for weight loss in a similar manner. Anthropometric and biochemical parameters were determined before and after the intervention. Cumin powder reduced serum levels of fasting cholesterol, triglyceride, and LDL and increased HDL. Weight, BMI, waist circumference, and fat masswere alsosignificantly reduced. However, it exertedno effect on FBS and fat-free mass [148].

The effects of cumin extract supplementation on oxLDL, paraoxanase 1 activity, FBS, total cholesterol, triglycerides, High density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C), apolipoprotein A1 (Apo A1), and apolipoprotein B (Apo B) were studied in the patients with hypercholesterolemia. The results demonstrated that there was a significant decrease in the level of oxLDL after receiving cumin. Paraoxonase and arylesterase activities increased in serum after taking cumin extract. Paraoxanase 1 (PON1) played a protective role against the oxidative modification of plasma lipoproteins and hydrolyzes lipid peroxides in human atherosclerotic lesions [149].

Theeffects of *Cuminum cyminum*intake on weight loss and metabolic profiles among overweight subjects was studied by arandomized double-blind placebo-controlled clinical trial which conducted among 78 overweight subjects (male, n = 18; female, n = 60) aged 18-60 years old. Participants were randomly assigned into three groups to receive: (1) *Cuminum cyminum*capsule (n = 26); (2) orlistat 120 capsule (n = 26) and (3) placebo (n = 26) three times a day for 8

weeks. Anthropometric measures and fasting blood samples were taken at baseline and after 8 weeks of intervention. Consumption of the *Cuminum cyminum*and orlistat120 resulted in a similar significant decrease in weight (-1. 1 ± 1. 2 and -0. 9 ± 1. 5 compared with placebo 0. 2 ± 1. 5 kg, respectively, p = 0. 002) and BMI (-0. 4 ± 0. 5 and -0. 4 ± 0. 6 compared with placebo 0. 1 ± 0. 6 kg/m (2), respectively, p = 0. 003). In addition,*Cuminum cyminum*L. , compared with orlistat and placebo, led to a significant reduction in serum insulin levels (-1. 4 ± 4. 5 vs. 1. 3 ± 3. 3 and 0. 3 ± 2. 2 μIU/ml, respectively, p = 0. 02), HOMA-B (-5. 4 ± 18. 9 vs. 5. 8 ± 13. 3 and 1. 0 ± 11. 0, respectively, p = 0. 02) and a significant rise in QUICKI (0. 01 ± 0. 01 vs. -0. 005 ± 0. 01 and -0. 004 ± 0. 01, respectively, p = 0. 02) [150-151].

2.30. *Cuscuta planiflora*

The effects of *Cuscuta planiflora* (500mg capsules) were evaluatedin patients with major depression bya randomized triple-blind controlled clinical trial. Patients were taken the treatment for 8 weeks. Depression was measured before and after the study by Beck depression inventory and Hamilton depression inventory. There was a significant decrease in mean scores of Beck and Hamilton depression inventories in the group treated by *Cuscuta planiflora* (p<0. 01) compared with control [152-153].

2.31. *Cydonia oblonga*

To compare the efficacy and safety of two routes of administration (nasal spray versus subcutaneous injections) of Citrus/Cydonia in seasonal allergic rhinitis, a randomised, comparative clinical trial with two parallel groups was carried out. After a one- or two-week wash-out period, 23 patients were randomized, to a 6-week treatment period and the immunological and symptom severity changes and safety were evaluated. Both routes of administration were safe,they demonstrate immunological and clinical effects, with larger inflammatory and innate immunological effects of the nasal spray route and larger allergen-specific clinical effects of the subcutaneous route [154-155].

2.32. *Cyperus rotundus*

Clinical studies with 2% aqueous extract of*Cyperus rotundus* showed anti-inflammatory activity in conjunctivitisin human [156].

A double blind trial of crude powder of *Cyperus rotundus*, *Withania somnifera* and their combination (1:1) was carried out in 200 patients suffering from rheumatoid arthritis. Each patient received 500 mg capsule three times a day for three months. Duringthis period biweekly general assessment based onglobal criteria (duration of morning stiffness, grip strength, articular index, consumption of escape analgesic, erythrocyte sedimentation rate, haemoglobin, rheumatoid factor titre, x-ray findings) was carried out. *Cyperus rotundus* was more effective than*Withania somnifera*, and when both drugs were combined, the response was better than the response of single drug [157].

Theefficacy of topical*Cyperus rotundus* oilto decrease hair growth, was evaluated byan open-label pilot study. Eligible participants (n=65) with unwanted axillary hair were assigned randomly to3 study groups: topical *Cyperus rotundus* oil (group 1), saline (group 2), and Alexandrite laser (group 3). Three methods were used to evaluate the results: hair counts, observations of independent professionals, and patient self-assessments. Overall results did not differ significantly between *Cyperus rotundus* oil and the Alexandrite laser (p>0. 05). However, statistically significant differences were noted with respect to decrease of growth of whitehair (p<0. 05), favoring the oil. This finding was evident by all 3 methods (hair counts, observations of independent professionals, and patient self-assessments)of assessment. No side effects were detected [158-159].

2.33. *Datura stramonium*

The specific airway resistance (sRaw) of twelveasthmatic patients with mild airway was measuredafterinhaling the smoke of one *Datura stramonium* cigarette. In 11 patients sRaw decreased substantially after the cigarette, the mean maximal decrease being 40% at the 30th minute. In seven patients the subsequent inhalation of 200 micrograms salbutamol caused no further decrease in sRaw. In the remaining four patients salbutamol induced a larger decrease in sRaw than the cigarette smoke. The inhalation, however, of a synthetic anticholinergic agent (SCH 1000, 600 micrograms) proved as effective as salbutamol in these patients. In one patient the cigarette smoke and SCH 1000 produced only a negligible amount of bronchodilatation whereas [160].

Digoxintherapy was indicated in patients with severe heart failurewith reduced ejection fractionafter initiation of ACE inhibitor, β-blocker, and diuretic therapy. A low serum drug concentration of digoxin (0. 5 to 0. 8 ng/ml) was beneficial in heart failurewith reduced ejection fraction and reducedheart failureadmissions, along with improved survival. At higher serum drug concentrations, admissions are prevented, but mortality likely increased. Digoxinwas not indicated in patients with diastolic or right sided heart failureunless the patient has concomitant atrial fibrillation or flutter.

Electrophysiological effects:The major effect on cardiac rhythm of digitalis preparations was believed to be due to inhibition of the sodium pump. However, cells in various parts of the heart showed differing sensitivities to digitalis, and both direct and neurally mediated effects were occured. Indeed, at therapeutic levels, these drugs decreased automaticity and increased maximum diastolic potential, effects that can be blocked by atropine, whereas higher (toxic) concentrations decreased diastolic potentials and increased automaticity. Similarly, the toxic arrhythmogenic effects of the cardiac glycosides were due to a combination of direct effects on the myocardium and neurally mediated increases in autonomic activity. Both systolic and diastolic [Ca^{+2}]i increased during digitalis-induced arrhythmias, increases that leading to the idea that intracellular (Ca^{+2} overload)contributes to the observed arrhythmogenic effects. Spontaneous cycles of Ca^{+2} release and reuptake then ensued, resulting in after depolarizations and after contractions. The after depolarization was the result of aCa^{+2}-activated transient inward currentand was thought to be the macroscopic manifestation of Ca^{+2}-activated nonspecific cation channels, plus Na^{+}-Ca^{-2} exchange current [161-162].

2.34. *Ephedra species*

2.34.1. Cardiovascular effects

The effect of ephedrine administered intravenously to experimental animalswas similar to that ofepinephrine. The arterial pressure, systolic, diastolic, and mean pressurerised and vagal slowing occured. In comparisonwith epinephrine, the pressor response to ephedrine occured somewhat more slowly and lasted about ten times longer. In addition, it required more ephedrine than epinephrine to obtain an equivalent pressor response. It was commonly accepted that it required about 250 times more ephedrine than epinephrine to achieve equipressor responses. The pressor response to ephedrine is due in part to peripheral constriction and in part to myocardial stimulation. Vasoconstriction can be demonstrated by intra-arterial injection, but compared to epinephrine, ephedrine was only about one thousandth as active. This would imply that the cardiac effect was predominant in increasing the arterial pressure.

In humans, ephedrine increases the arterial pressure both by peripheralvasoconstriction and by cardiac stimulation. The heart rate was usually increased, as was the pulse pressure, both suggesting an increased cardiac output. However, the hypotension that commonly occured during surgery under spinal anesthesia was practically always prevented by ephedrine. As a conclusion, it appeared thatephedrine activated the same adrenergic receptors as epinephrine but was less potent and has a longer duration of action.

In complete heart block with Stokes–Adams syncope, ephedrineprovedof valueto increase ventricular rate and prevent ventricular asystole, an initial dose of about 8 mg of ephedrine sulfate orally may be tried, thenthe doseincreased to 25 mg three or four times daily. Syncope due to ventricular tachycardia can also be prevented in some cases with ephedrine [5,36].

2.34.2. Bronchodilitation

The smooth muscle of the bronchial tree was relaxed by ephedrine. Compared with epinephrine, the action of ephedrine was slow in onset, completedan hour or more after administration. Ephedrine alsopreventedhistamine-induced broncho-constrictionin patients with asthma [5].

2.34.3. Nasal decongestion:

Because ofvasoconstrictiveeffectof ephedrine, it was utilizedas a decongestantsolutions applied topically to the mucous membranes of thenose. Similar to epinephrine, ephedrine often produced a secondary congestive response [163-164].

2.34.4. Mydriasis

Ephedrine produced mydriasis when applied locally to the conjunctiva, as well as upon systemic absorption.

2.34.5. Nocturnal enuresis

Ephedrine hydrochloridetabletswere used in many trialsto control nocturnal enuresis. It was appeared thatephedrine hydrochloride improvedinternal sphincter tone, thus preventing uncontrolled urination [164-165].

2.34.6. Spinal anesthesia

Ephedrinewas used to prevent occurance of hypotension during surgery under spinal anesthesia. The usual dose of ephedrine employed to treat, rather than prevent, the hypotension was 50 mg intramuscularly or 15 mg intravenously.

The central stimulant action of ephedrine, which may be objectionable, was controlled by adequate preanesthetic sedation or the concomitant use of a short acting Barbiturate [163].

2.34.7. CNS stimulation

Ephedrinewas acorticomedullary stimulants. Depending on the dose, this stimulant action in humans results in feelings of anxiety, tremor, insomnia and mental alertness, and increased respiration. When ephedrine was used for its adrenergic effects, the central stimulation was considered as a side effect. However, ephedrine was used previouslyas a useful central stimulant in narcolepsy and depressant poisoning, but amphetamine and methamphetamine were commonlyused today [163].

2.34.8. Weight lost

Today, *Ephedra* wasapplicated for enhancing performance, appetite suppression and weight lost [39]. Several studies have found that ephedrine/caffeine combinations were modestly effective for short- and long-term weight loss [40-43]. Furthermore, ephedrine stimulant effect caused an increase in basal metabolic rate that contributes to weight loss [166-168].

2.35. *Equisetum arvense*

The effectiveness of topical application of *Equisetum arvense* ointment 3% in wound healing, reduction of inflammation and pain relief after episiotomy was studied in nulliparous mothers. A double-blind clinical trial was performed on 108 postpartum nulliparous mothers (54 women in horsetail group and 54 women in placebo group). About 5 ± 1 and 10 ± 1 days after the childbirth, the primary outcomes of episiotomy (wound healing and pain intensity) were assessed based on redness, edema, ecchymosis, discharge and approximation of the edges scale and a visual analogue scale (VAS). The number of used painkillers and the adverse events during the 10-daytreatment periodwere also recorded. The mean scores were significantly lower in the treatedgroup than the control group. The adjusted pain score difference after 5 ± 1 and 10 ± 1 days was -2. 3 (95% CI: -3. 2 to -1. 3) and 3. 8 (95% CI: -4. 7 to -3. 0), respectively. The mean numbers of acetaminophen pills used in the control andtreatedgroupduring the 10-day period of the study were 6. 8 ± 4. 4 and 11. 6 ± 7. 1, respectively (P < 0. 001). Accordingly,3% *Equisetum arvense* ointment promoted wound healing and relieved pain during the 10-day period after episiotomy [169].

The HPCH (Hydroxypropyl-Chitosan nail lacquer: a medical device intended to relieve symptoms and signs of nail dystrophy contained hydroxypropyl-chitosan (HPCH), *Equisetum arvense* and methylsulphonyl-methane) was evaluated inbrittle nailcompared to another nail lacquer (P-09-005) with identical composition, except for the presence of insoluble chitosan instead of HPCH. Thirty-four healthy women with onychoschizia of the fingernails were included. Both products were applied by all subjects once daily on the affected fingernails of either hand at random, for 4 weeks. The severity of nail signs was assessed using a 0-3 scale. Nail surface profilometry was assessed by morphometrical analysis of nail grooves on nail casts. Visual score of onychoschizia improved at T4 in 74% of volunteers with HPCH nail lacquer and in 52% with P-09-005 (Wilcoxon test P< 0. 05 between treatments). Severe onychoschizia, present in 35% of patients at baseline, improvedin 80% of subjects with HPCH nail lacquer and in 42% with P-09-005. On the morphometrical analysis a significant reduction of rugosity of the longitudinal nail grooves was noticed 19% for HPCH nail lacquer and 16% for P-09-005 (not significant between treatments). Both products were well tolerated [170].

The diuretic effect of EADE was assessed clinically by monitoring the volunteers' water balance over a 24 h period. The dried extract of *Equisetum arvense* (900mg/day)produced a diuretic effect that was stronger than that of the negative control and was equivalent to that of hydrochlorothiazide without causing significant changes in the elimination of electrolytes. Only rare minor adverse events were reported [171-172].

2.36. *Eschscholzia californica*

A multicenter, double-blind, randomized, placebo-controlled study was carried out in general practice offices in Paris, France and the Paris area. Men and women (N = 264) with mild to moderate generalized anxiety disorder as diagnosed according to the DSMIII- R criteria were participated in the study. Patients received either 2 tablets of placebo or Sympathyl® (Laboratoire Innotech International, Arcueil, France) twice daily for 3 months. Sympathyl contains 75 mg of dry hydroalcoholic extract of the flowering head of hawthorn, 20 mg of dry aqueous extract of California poppy, and 75 mg of elemental magnesium. Efficacy was assessed by change in Hamilton anxiety scale total and somatic scores, change in patient self-assessment, number and percentage of responsive subjects (reduction of at least 50% in Hamilton or self-assessment score)and the physician's clinical global impression. Treatment produced a rapid and progressive fall in anxiety. There was a significant improvement in the total anxiety score (P = 0. 005), somatic score (P = 0. 054), and self-assessment (P = 0. 005) in patients taking Sympathyl for 3 months [173-174].

2.37. *Eucalyptus species*

The effect of chewing gum containing Eucalyptus extract on periodontal health was investigatedin a double-masked, randomized, controlled trial. Healthy humans with gingivitis but not deep periodontal pockets were randomly assigned to the following groups: high-concentration group (n=32): use of 0. 6% Eucalyptus extract chewing gum for 12 weeks (90 mg/day); low-concentration group (n=32): use of 0. 4% Eucalyptus extract chewing gum for 12 weeks (60 mg/day); and placebo group (n=33): use of chewing gum without Eucalyptus extract for the same period. Plaque accumulation (PLA), gingival index (GI), bleeding on probing (BOP), periodontal probing depth (PD), and clinical attachment level (CAL) were measured at weeks 0, 4, 8, 12, and 14. The interaction between the effects of Eucalyptus extract chewing gum and the intake period was statistically significant for PLA, GI, BOP, and PD, but not for CAL. The low- and high-concentration groups exhibited statistically significant (P< 0. 05) improvements compared to the placebo group for PLA, GI, BOP, and PD [175-176].

2.38. *Euphorbia hirta*

The effect of herbal water of *Euphorbia hirta* on flu like symptoms and blood biochemical parameters especially thrombocytopenia was studied in patients with Dengue fever. Blood samples were collected on the day of enrollment and subsequently after*Euphorbia hirta* therapy. Before the treatment,platelet countinmale patients was < 25000, and in females >50000. Hematocrit values) were >40% in males and less than 30-40% in females. Total leukocyte count (TLC) was observed in a range of 4000-11000/mm^3 in both male and female subjects. IgMhaemagglutination antibody titer values greater than 1:160 were observed in 71% females and 50% males. AST level was found to be >40 IU/L in 38% female and 36% males while ALT level was >40 IU/L in 9% females and 12% males. Platelet count and TLC were increased non significantly after treatment,while HCT value was non significantly decreased after herbal use. Over 70% patients had slight recovery of platelet count and increased retrieval of leukopenia after herbal therapy along with recovery from fever and flu like symptoms [177-178].

2.38.1. Fagopyrum esculentum

Sixty-seven male and female patients (22–74 years) with chronic venous insufficiency (CVI) were randomly divided into two groups. They received either buckwheat herb tea (*Fagopyrum esculentum*) or a placebo tea for a period of 3 months. The main outcome measure was the lower leg volume determined by ultrasound. Subjective symptoms were assessed by a clinical symptom score system. The femoral vein diameters were measured by B-scan sonography. In a subgroup of patients, capillary permeability was determined by cutaneous fluorescence angiography. Although the mean partial leg volume did not change in the treatment group (from 2041 to 2073 ml), but it increased in the placebo group by 110 ml (from 1972 to 2082 ml). The subjective clinical symptoms were significantly reduced in both groups. The mean diameters of the femoral veins were reduced and capillary permeability was improved, but the canges werestatistically insignificant. No drug-related adverse effects were observed [179-180].

2.39. *Ficus carica*

The hypoglycemic effect of a decoction of leaves of*Ficus carica*, as a supplement to breakfast, on diabetes control was studied in insulin-dependent diabetes mellitus patients. The patients were managed with their usual diabetes diet and their twice-daily insulin injection. During the first month, patients were given a decoction of leaves of *Ficus carica* and during the next month a non-sweet commercial tea. Post-prandial glycemia was significantly lower during supplementation with a decoction of leaves of *Ficus carica* 156. 6 ± 75. 9 mg/dl versus non-sweet commercial tea 293. 7 ± 45. 0 mg/dl (P < 0. 001). Medium average capillary profiles were also lower in patients during *Ficus carica* therapy versus non-sweet commercial tea. Average insulin dose was 12% lower during*Ficus carica*therapy in the total group [181].

A prospective, open right/left comparativeanti- warts trial, of fig tree latex therapy vs. local standard of cryotherapy was carried out ontwenty-five patients. The patients were instructed in self-application of fig tree latex to warts on one side of the body. The wart on the opposite side was treated using standard cryotherapy. A 6-month follow-up study was planned. In 11 (44%) of the 25 patients, complete resolution of fig tree latex-treated warts was observed. The remaining 14 patients (56%) had a complete cure following cryotherapy. Two patients had complete remission on both sides [182-183].

2.40. *Ficus religiosa*

A clinical trial on 44 patients of erectile dysfunction (ED)were divided into two main groups: diabetic and non-diabetic, and were further divided into two subgroups as trial group and placebo group. In the trial group, Ashvatthaprepared with 10 g powder of Ficus relegiosa root bark, stem bark, fruit and tender leaf buds, was given twice a day. In both the

diabetic and the non-diabetic subjects, Ashvattha provided encouraging results on ED as well as on seminal parameters in comparison to the placebo [184-185].

2.41. *Foeniculum vulgare*

The laxative effect of a phytotherapic compound containing (*Pimpinella anisum* L. , *Foeniculum vulgare* Miller, *Sambucus nigra* L. , and Cassia *augustifolia*)wasevaluated by a randomized, crossover, placebo-controlled, single-blinded trial included 20 patients with chronic constipation. Half of the subjects were received the phytotherapic compound for a 5-day period, whereas the other half received placebo for the same period. Both treatment periods were separated by a 9-day washout period followed by the reverse treatment for another 5-day period. Mean colonic transit time assessed by X ray was 15. 7 hours (95%CI 11. 1-20. 2) in the active treatment period and 42. 3 hours (95%CI 33. 5-51. 1) during the placebo treatment ($p < 0. 001$). Number of evacuations per day increased during the use of active tea; significant differences were observed as of the second day of treatment ($p < 0. 001$). Patient perception of bowel function was improved ($p < 0. 01$), but quality of life did not show significant differences among the study periods. The findings of the randomized controlled trial revealedthat the phytotherapic compound exerted laxative effects and is a safe alternative option for the treatment of constipation [186].

The clinically efficacyoffennelextract was compared with echinophora-platyloba in the primary dysmenorrhea. The clinical trial was carried out in sixty unmarried students with mild and moderate dysmenorrhea in Shahrekord University of medical sciences. The severity of pain was detected by the visual analogue scale during two cycles before and two cycles after the intervention. There was no significant difference in the mean of dysmenorrhea severity during the two cycles before the intervention between the two groups, but during the two cycles after the intervention, both drugs could reduce the severity of dysmenorrheal but fennel extract showed moresignificantly ($P<0. 001$) reduction [187].

The effects of *Foeniculumvulgare*extractin reduction of pain and other systemic symptoms accompanying primary dysmenorrhea were studied using double-blind clinical trial carried out on female students [90 (46 cases and 44 controls)] at Shahid Beheshti University, Iran. Five capsules containing 46 mg of *Foeniculum vulgare* and identical placebos were provided to be taken daily by the case and control groups respectively, during the first three days following the onset of dysmenorrheal pain whenever they needed the medications. The severity of pain in the treated group with *Foeniculum vulgare* extract, showed a significant difference ($p<0. 001$) in comparison with the placebo group, in addition tosignificant differences in systemic symptoms [188].

The response of idiopathic hirsutism to topical *Foeniculum vulgare* extractcream was evaluated clinically in a double blind study. 38 patients were treated with creams containing 1%, 2% of*Foeniculum vulgare* extract and placebo. Hair diameter and rate of growth were evaluated. The efficacy of treatment with the cream containing 2% *Foeniculum vulgare* was better than the cream containing 1% *Foeniculum vulgare* and these two were more potent than placebo. The mean values of hair diameter reduction was 7. 8%, 18. 3% and -0. 5% for patients receiving the creams containing 1%, 2% and 0% (placebo) respectively [189].

The effect of fennel topical gel on mild to moderate idiopathic hirsutism was studied by randomized, double-blind, placebo-controlled clinical trial using forty four women with mild to moderate idiopathic hirsutism. The case group received fennel gel 3% and the control group received placebo. The effect of fennel gel 3% was defined as reduction of thickness of facial hair in micrometer by microscope in comparison with placebo. Measurements were performed at zero time and 24 weeks after treatment. Hair thickness was similar between the two groups before intervention. The hair thickness reduced from 97. 9±31. 5 to 75. 6±26. 7 micron in patients receiving fennel gel after 24 weeks ($P<0. 001$). Four patients complained of itching (3 in case group) and 4 patients complained of irritation and itching (3 in case group). However, this difference was not statistically significant [190-191].

2.42. *Fumaria officinalis*

However, in a comprehensive study of patients with cholecystopathies, the extract had an improvement in 70% of the treatment group, and further over 80% improvement of the symptoms of concomitant biliary dyskinesia [192-194].

Adouble blind placebo clinical trial was performed in a group of 30 patients (20 women, 10 men of 26-57 years old) with different biliary disorders (dyskinesia, cholocystitis, hepatopathy, chololithiasis, and post-operation cholocystectomy syndrome). Patients were taking 3 tablets of (Fumaria-Nebulisat) (water extract 4-6:1) 250 mg daily (two before meals and the thirdbefore sleep), for 28 days. The results weresuccessful, especially against the symptoms of fullness and flatulence. The tratment was tolerated and safe [195].

The efficacy of two herbal remedies used in the treatment of irritable bowel syndrome was assessed clinically using a randomized, double-blind, placebo-controlled trial, IBS patients were randomly assigned to one of three treatment groups: *Curcuma xanthorriza* 60 mg daily (curcuma group), *Fumaria officinalis* 1500 mg daily (fumitory group)and placebo. The study treatment was applied three times a day for 18 weeks. IBS-related painwas decreased by −0. 9±11. 5 (mm±SD) in the fumitory group, IBS-related distension was increased by 0. 3±9. 3 in the fumitory group. Additionally, the global assessment of changes in IBS symptoms and psychological stress due to IBS did not differ significantly among the three treatment groups [196-197].

2.43. *Fumaria parviflora*

The efficacy of *Fumaria parviflora*for reducing uremic pruritus severity among hemodialysispatients was investigated by randomized, double-blind, placebo-controlled trial. A total of 79 hemodialysis patients with pruritus were randomly assigned to receive either *Fumaria parviflora* (2 X 500-mgplant powder capsules/ day)or a placebo (2X 500 mg Wheat flour capsule/ day)for eight weeks. The visual analogue scale (VAS), the Duo score for calculating pruritus score, serum interferon- (IFN-α) level, interleukin-4 (IL-4), and high-sensitivity C-reactive protein were measured in the patients before and after treatment. At the end of the treatment phase, the pruritus score decreased in both groups (P < 0. 001); however, the mean reduction in pruritus scores was significantly higher in the *Fumaria parviflora*group than the placebo group according to VAS (-6. 15±2. 12 vs. -2. 25±2. 46, P <0. 001) and Duo scores (-22. 03±9. 64 vs. -8. 38±6. 28, P < 0. 001). Mean serum IFN-α levels in the *Fumaria parviflora* group significantly decreased (P< 0. 001), but there was no significant change in these levels in the placebo group (P = 0. 604). The elevation of the mean serum IL-4 level was significant in the *Fumaria parviflora* group (P = 0. 028) but not in the placebo group (p = 0. 100). The authors concluded that*Fumaria parviflora* can significantly decrease the severity of uremic pruritus in hemodialysis patients [198].

In a randomized double-blind, placebo-controlled study, 44 patients with hand eczema were randomly assigned to apply 4% cream of *Fumaria parviflora* or vehicle cream to hand twice daily for 4 weeks. The reduction of eczema area and severity index score before and two weeks after therapy was statistically significant between vehicles treated and4% cream Fumaria parvifloratreated patients. Only one patient showed side (erythema and population) [199-200].

2.44. *Glycyrrhiza glabra*

Glycyrrhizinwas investigated as a therapy ofhuman immuno-deficiency virus (HIV) in 42 hemophilia patients with HIV-1 infection. Patients showed improvement in their clinical symptoms (oral candidiasis, lymph node swelling and rash), immunological functions and liver functions [201].

The bronchorelaxant effect of*Glycyrrhiza glabra*was studied in a clinical trial (54 patients)in comparison with Boswellia carterii (Olibanum) and prednisolone (18 patients each group) for 21 days. After clinical assessment, estimation of pulmonary function tests and serum electrolytes: calcium, magnesium, potassium and selenium were done before and after the study. The results showed that the tested plants had significant elevation in the values of forced expiratory volume in first second (FEV1%) as (72. 45±5. 83 vs 61. 33±6. 04 and 81. 10±11. 07 vs 62. 30±7. 22) for olibanum and licorice respectively. Also, elevation in the values of forced volume capacity (FVC) with marked reduction in asthmatic attacks as (2. 63±0. 82 vs 0. 72±0. 16, 3. 60±0. 02 vs 1. 08±0. 08, and 2. 25±0. 16 vs 1. 05± 0. 15) for olibanum licorice and prednisolone respectively, withbetter symptomatic improvement in licorice group as compared to olibanum. Glycyrrhiza glabra was significantlyelevatedMg: from0. 66±0. 17to 1. 02±0. 10, Se: from28. 19±3. 72 to51. 70±8. 63, Ca: from1. 90±0. 06 2 to . 30±0. 08 and K: from3. 60±0. 03to 4. 10±0. 12 [202].

The efficacy of intravenous glycyrrhizin in decreasing alanine aminotransferase level in the early stage of acute onset acute onset autoimmune hepatitis was studied clinically. Thirty-one patients defined as acute onset of autoimmune hepatitis based on a uniform criteria, were enrolled in study. 17 patients were treated with (100 ml/day) of intravenous glycyrrhizin at an early stage and14patients of severe disease were treatedwith intravenous glycyrrhizin and corticosteroids. Treatment response,clinical and biochemical parameters were evaluated. The alanine aminotransferase level could be controlled at an early stage using intravenous glycyrrhizin with no significant difference compared with glycyrrhizin and corticosteroids. Recovery rate was higher in the intravenous glycyrrhizin group than in the glycyrrhizin and corticosteroids group. The authors concluded that introduction of sufficient doses of intravenous glycyrrhizin might prevent disease progression in patients with acute onset autoimmune hepatitis [203].

Carbenoxolonea glycyrrhizate analog waseffective in clinical trials in the treatment of gastric and duodenal ulcer at the medium dose of 100 mg three times a day. Liquorice can raise the concentration of prostaglandins in the digestive system that promote mucus secretion from the stomach, it was also prolonged the life span of surface cells in the stomach and has an anti-pepsin effects [204-208].

In a trial of 40 patients receiving either 3. 0 or 4. 5 g Deglycyrrhizinated licorice (DGL) daily for eight weeks. Patients were assessed for relief from epigastric pain, nausea, vomiting, x-ray of ulcer craters to determine changes in size, and frequency of relapse. All patients showed significant improvement after 5-7 days [209].

Inmore largertrial carried out on 874 patients with chronic duodenal ulcers. Patients were received DGL, cimetidine, or antacids. No differences were recorded among groups in the rate of ulcer healing, but patients in the DGL group showed less occurance ofrelapses [210].

In a double-blind, placebo-controlled trial, 24 patients with recurrent aphthous ulcers were randomly allocated to consume 2 g glycyrrhizin (carbenoxolone sodium) in 30 ml of warm water three times daily following meals for four weeks. Oral licorice mouthwash significantly reduced the average number of ulcers per day, pain scores, and the development of new ulcers compared with placebo. In another trial,20 patients used DGL mouthwash four times daily, 50-75 percent clinical improvementwas recorded in 15 patients after only one day, with complete healing of canker sores after three days [211-212].

In an open clinical trial, 17 hepatitis C positive patients with oral lichen planus (an inflammatory disease characterized by lymphocytic hyperkeratosis of the oral mucosa)were given either routine dental care or 40 ml iv glycyrrhizin daily for one month. 66. 7% of patientsnotedgeneral clinical improvement, decreased redness, fewer white papules, and less erosion of the mucosa [213-214].

2.45. *Gossypium hirsutum*

Cotton honeydew extract is composed of a unique combination of oligosaccharides, including fructose, glucose, inositol, melezitose, saccharose, trehalose and trehalulose. Studies have shown that these oligosaccharides exhibit a protective effect. Furthermore, the effect of these oligosaccharideswas studiedin normal and damaged human hair. Both clinical and scanning electron microscopy (SEM) studies were performed. Standardized human hair samples were used to determine the effect of a rinse-off mask with 1% cotton honeydew extract on the ultrastructure of hair. In addition, hair samples were submitted to different aggressions, following various experimental protocols. SEM showed that, without extra aggression, the cuticle scales appeared to lie more smoothly in the hair in cotton honeydew extract-treated samples than in untreated samples. The extract-treated hair samples were also less prone to chipping. In a clinical study, 15 volunteers had half of their hair treated with a formula with 1% honeydew extract and the other half was left untreated as a control. Pictures and visual evaluation of the hair showed that the honeydew extract formula left the hair with a smoothness and this result was confirmed by SEM. In addition, mRNA studies on epidermal cells were confirmed the stimulating effect of honeydew extract on keratin synthesis [215].

Using of 20 mg/day of racemic gossypol for 2-3 months followed by a maintenance dose of 40 mg/week for 4-5 months in women with endometriosis, uterine myomas and functional uterine bleeding, resulted in amenomania and atrophy of the endometrium. Examination of uterine biopsies showed a local cytotoxic effect on the uterus together with a systemic effect on the ovarian function [216-218].

Furthermore, gossypol affectedmale and female gametogenesis and causedembryo toxicities [219].

The efficacy of oral gossypol as a treatment for adrenal cancer in humans was studied. Twenty-one patients with metastatic adrenal cancer received oral gossypol at doses of 30-70 mg/day. Eighteen patients completed at least 6 weeks of gossypol treatment. 13 patients had disease progression. The side effects of gossypol were generally well tolerated; the only serious side effect was abdominal ileus that resolved when the drug was temporarily withheld and restarted at a lower dose [220-221].

2.46. *Hedera helix*

A double blind, placebo-controlled, randomized cross-over study was carried out on 30 children suffering from partial or uncontrolled mild persistent allergic asthma. Patients either received ivy leaves dry extract for four weeks in addition to their inhaled corticosteroid therapy or placebo, followed by a wash-out phase before switching to the other treatment arm. There was a significant improvement of MEF (75-25), MEF25 and VC after treatment with ivy leaves dry extract (MEF (75-25) change in the mean 0. 115 l/s, p=0. 044; MEF25 change in the mean 0. 086 l/s, p=0. 041; VC change in the mean 0. 052 l, p=0. 044), but not after treatment with placebo. For the primary outcome parameters (relative change of FEV1 and MEF (75-25) before bronchodilation) no treatment effect could be detected in the cross-over analysis (FEV1 p=0. 6763 and MEF (75-25) p=0. 6953) [222].

The efficacy ofthe extracts from dried ivy leaves (Hedera helix L.) intreatment of chronic airway obstruction was studiedin children suffering from bronchial asthma. Drops containing ivy leaf extract were significantly superior to placebo in reducing airway resistance (P=0. 04). Syrup and suppositories showed non-inferiority in comparison with drops. The trials indicated that ivy leaf extract preparations have effects with respect to an improvement of respiratory functions of children with chronic bronchial asthma [223].

9657 patients (5181 children) with bronchitis (acute or chronic bronchial inflammatory disease) were treated with a syrup containing dried ivy leaf extract. After 7 days of therapy, 95% of the patients showed improvement or healing of their symptoms. The safety of the therapy was very good with an overall incidence of adverse events of 2. 1% (mainly gastrointestinal disorders with 1. 5%). The additional application of antibiotics had no benefit respective to efficacyofsyrup of dried ivy leaf extract alone, but did increase the relative risk for the occurrence of side effects by 26% [224].

Two formulations of an ivy herbal extract, syrup and cough drops, were tested for their efficacy and safety in the paediatric treatment of cough and bronchitis in two independent open, non-interventional studies with identical design. Two-hundred and sixty-eight children aged 0-12 yr were treated with one of the two preparations for up to 14 days. The effects on cough-related symptoms were addressed on a verbal rating scale. At the end of the study the major symptoms rhinitis, cough and viscous mucus, were found to be only mildly expressed or absent in 93, 94. 2 and 97. 7% of cases. The global effect was rated as 'good' or 'very good' in 96. 5% of cases. Tolerability and compliance were found 'good' to 'very good' in 99% (syrup) and 100% (drops) of patients on completion of the study. A subgroup analysis according to four different age and dosing groups did not reveal differences in treatment response [225].

The changes in the symptoms of cough after treatment with a combined herbal preparation containing dry ivy leaf extract as main active ingredient, decoction of thyme and aniseed, and mucilage of marshmallow rootand its tolerability were investigated in an open clinical trial. The study was carried out on 62 patients. The results showed that at the final visit, all symptom scores showed an improvement as compared to baseline. Doctors and patients assessed efficacy as good or very good in 86% and 90% of the cases, respectively. Tolerability was assessed as good or very good by 97% of the doctors and patients [226].

A double-blind, randomized study was conducted to assess the efficacy and tolerability of ivy leaves soft extract with another ivy leaves extract. The study was carried out on 590 patients with acute bronchitis. They were treated with test or comparator for 7 days (±1). The Bronchitis Severity Score (BSS) decreased gradually and to a similar extent from Day 1 to Day 7 in both treatment groups. Starting from values of 6. 2-6. 3±1. 2, the BSS decreased by approximately 4. 7-4. 9 points until Day 7, so that patients left the study with a mean BSS of 1. 4-1. 6. The BSS subscales cough, sputum, rhales/rhonchi, chest pain during coughing, and dyspnoea improved to a similar extent in both treatment groups. Overall, 2. 7% of patients (per group and overall) experienced an adverse event, all of which were non-serious. Fewer patients younger than ten years had adverse events than would have been expected from their share of the study population [227].

The efficacy and tolerability of a fixed fluid extract combination of thyme and ivy leaves (5. 4 ml three times daily, 11-day treatment) were evaluated by double-blind, placebo controlled, multicentre study, performed on 361 outpatients suffering from acute bronchitis with productive cough. The efficacy of the treatment was evaluated by the patient's daily counting of coughing fits during the daytime (manual counter), assessment of acute bronchitis related symptoms and by the investigator's assessment of the most important symptoms of acute bronchitis using the Bronchitis Severity Score (BSS). The mean reduction in coughing fits on days 7 to 9 relative to baseline was 68. 7 % under thyme-ivy combination compared to 47. 6 % under placebo ($p < 0.0001$). In the thyme-ivy combination group, a 50 % reduction in coughing fits from baseline was reached 2 days earlier compared to the placebo group. Treatment was well tolerated with no difference in the frequency or severity of adverse events between thyme-ivy combination and placebo groups. Severe or serious adverse events were not reported. Accordingly, the authors concluded that the oral treatment of acute bronchitis with thyme-ivy combination for about 11 days was superior to placebo in terms of efficacy. The treatment was safe and well tolerated [228-229].

2.47. *Helianthus annuus*

The effect of topical application of sunflower seed oil 3 times daily to preterm infants <34 weeks gestational,on skin condition, rates of nosocomial infections and mortality was studied in Kasr El-Aini neonatal intensive care unit at Cairo University. Treatment with sunflower seed oilresulted in a significant improvement in skin condition (P = 0. 037) and a highly significant reduction in the incidence of nosocomial infections (adjusted incidence ratio, 0. 46; 95% confidence

interval, 0. 26-0. 81; P = 0. 007) compared with infants not receiving topical prophylaxis. No adverse events were recorded as a result of topical therapy [230-231].

2.48. *Hibiscus Rosa sinensis*

The antidiabetic effect of *Hibiscus Rosa sinensis* flower powder was studied in type II diabetic patients. 2g flower powder of*Hibiscus rosa sinensis* ,daily for 60 day significantlydecrease level,mean fasting blood glucose,post prandial blood glucose level,mean glycosylated Hb level , mean total cholesterol, triglyceride level, total LDL and total VLDL cholesterol Level [232-233].

2.49. *Hibiscus sabdariffa*

A controlled and randomized clinical trial was carried out to compare the antihypertensive effectiveness and tolerability of a standardized extract from *Hibiscus sabdariffa*with captopril. Patients with diagnosed hypertension and without antihypertensive treatment for at least 1 month were included, they were recieved eitheran infusion prepared with 10 g of dry calyx from H. sabdariffa (9. 6 mg anthocyanins content), daily before breakfast, or captopril 25 mg twice a day, for 4 weeks. The results showed that H. sabdariffa was able to decrease the systolic blood pressure (BP) from 139. 05 to 123. 73mm Hg ($p < 0. 03$) and the diastolic BP from 90. 81 to 79. 52mm Hg ($p< 0. 06$). At the end of the study, there were no significant differences between the BP detected in both treatment groups ($p > 0. 25$). The rates of therapeutic effectiveness were 0. 7895 and 0. 8438 with *Hibiscus sabdariffa*and captopril, respectively ($p> 0. 560$), whilst the tolerability was 100% for both treatments [234].

The daily consumption of extract of Hibiscus sepals significantly decreases systolic blood pressure (SBP) and diastolic blood pressure (DBP) in adults with pre to moderate essential hypertension and type 2 diabetes. The results revealed that the effectiveness of extract was equivalent to captropril, but less effective than Lisinopril [235].

A randomized, double-blind, placebo-controlled clinical trial was conductedto determinethe antihypertensive effects of *Hibiscus sabdariffa*tea consumption on 65 pre- and mildly hypertensive adults with no blood pressure-lowering medications. They usedeither three 240-ml servings/day of brewed hibiscus tea or placebo beverage for 6 wk. At 6 wk, hibiscus tea lowered systolic BP (SBP) compared with placebo. Diastolic BP was also lower, although this change did not differ from placebo. The change in mean arterial pressure was of borderline significance compared with placebo. Participants with higher SBP at baseline showed a greater response to hibiscus treatment [236].

Polyphenols from *Hibiscus sabdariffa* calices were administered to patients with metabolic syndrome (125 mg/kg/day for 4 wk) and spontaneously hypertensive rats (125 or 60 mg/kg in a single dose or daily for 1 wk). H. sabdariffa extract improved metabolism, displayed potent anti-inflammatory and antioxidant activities, and significantly reduced blood pressure in both humans and rats [237].

Clinical trials confirmed the antihypertensive effect using watery infusions. The results showed that the treatment decreased blood pressure (BP) from 146. 48/97. 77 to 129. 89/85. 96 mmHg, reaching an absolute reduction of 17. 14/11. 97 mmHg (11. 58/12. 21%, $p < 0. 05$). The treatment showed therapeutic effectiveness of 65. 12 % as well as tolerability and safety of 100 %. BP reductions and therapeutic effectiveness were lower than those obtained with lisinopril ($p < 0. 05$) [238].

The cholesterol-lowering potential of *H. sabdariffa* extract (HSE) was investigated in human subjects, a clinical study was conducted using an oral preparation of HSE capsules. The study consisted of 42 volunteerswith a cholesterol level of 175 to 327 mg/dl. They were randomly divided into 3 groups: group I (1 capsule of HSE during each meal), group II (2 capsules), and group III (3 capsules). HSE causedsignificant decrease in serum cholesterol level in subjects from groups I and II after 4 weeks. HSEafter2 weeks, decreasedserum cholesterol levels in all groups ($P < . 05$ for groups I-III) compared with baseline values by 7. 8% to 8. 2%, while, a reduction in serum cholesterol level by 8. 3% to 14. 4%,was recorded after 4 weeks. The serum cholesterol level for 71% of group II volunteers was significantly lowered with a mean reduction of 12% ($P < . 05$) [239].

In a sequential randomized controlled clinical trial, 60 patients with diabetes were randomly assigned into two groups: sour tea (*Hibiscus sabdariffa*, ST) and black tea (BT). They were instructed to consume sour tea or black tea two times a day for 1 month to investigate the hypolipidemic effects of sour tea in patients with diabetes and compare them with black tea. In the *Hibiscus sabdariffa* group, the mean of high-density lipoprotein-cholesterol (HDLc) increased significantly ($p = 0. 002$) at the end of the study, whereas changes in apolipoprotein-A1, and lipoprotein (a) were not significant. Also, a significant decrease in the mean of total cholesterol, low density lipoprotein-cholesterol,

triglycerides, and Apo-B100 were seen in this group. In the BT group, only HDLc showed significant change (p = 0. 002) at the end of the study, while, the changes in the other measures were not statistically significant [240].

A triple blind randomized placebo-controlled clinical trialwas carried out to determineeffects of *Hibiscus sabdariffa* (HS) calices on controlling dyslipidemia in 72 obese adolescents. They received 2 grams of fine powdered calices of *Hibiscus sabdariffa* per day for one month, while controls received placebo powder with the same dietary and physical activity recommendations and duration of exposure. Full lipid profile and fasting blood sugarwere measured before and after the trial. In the *Hibiscus sabdariffa* calyces treated group, serum total cholesterol, low density lipoprotein cholesterol and serum triglyceride showed a significant decrease but high density lipoprotein cholesterol level was not changed significantly [241].

A clinical trialwas carried out to confirm the metabolic-regulating and liver-protectingeffect of *Hibiscus sabdariffa* extracts (HSE). Subjects with a BMI ≧ 27 and aged 18–65, were randomly divided into control and HSE-treated groups, for 12 weeks. the results revealedthat consumption of HSE reduced body weight, BMI, body fat and the waist-to-hip ratio. Serum free fatty acids were also lowered by HSE. Anatomic changes revealed that HSE improved the illness of liver steatosis. Ingestion of HSE was well tolerated and there was no adverse effect during the trial [242].

A total daily dose of 100 mg of Hibiscus sabdariffa extract powder (HSEP)was orally administered in capsules for one month to determine its effect on lipid profiles of individuals with dyslipidemiaassociated with metabolic syndrome (MeSy). The MeSy patients treated with HSEP had significantly reduced glucose and total cholesterol levels, increased HDL-c levels, and an improved TAG/HDL-c ratio, a marker of insulin resistance (p<0. 05). Furthermore, a triglyceride-lowering effect was observed in MeSy patients treated with HSEP plus diet, and in individuals without MeSy treated with HSEP. Significant differences in total cholesterol, HDL-c, and the TAG/HDL-c ratio were found when the means of absolute differences among treatments were compared (p<0. 02) [243].

In a double blind, placebo controlled, randomized trial, sixty subjects with serum LDL values in the range of 130-190 mg/dl and with no history of coronary heart disease were randomized into experimental and placebo groups. The experimental group received 1 gm of the extract for 90 days,while the placebo received a similar amount of maltodextrin in addition to dietary and physical activity advice for the control of their blood lipids. Body weight, serum LDL cholesterol and triglyceride levels decreased in both groups, there were no significant differences between the experimental and placebo group. At a dose of 1 gm/day, hibiscus sabdariffa leaf extract did not appear to have a blood lipid lowering effect [244].

The health benefit effects of *Hibiscus sabdariffa* Lin (*H. sabdariffa* L.) dried calyces beverage on some clinical, biochemical and hematological parameters were investigated in humans. A drink was prepared a Drin for 32 male volunteers. Each participant consumed 500 ml twice a day (in the morning and in the evening) as supplement beverage for two weeks. The anthropometrics (age, height, weight, body mass index (BMI)), clinical (systolic and diastolic blood pressure), hematological (RBC, Hb, PCV, MCV, MCH, MCHC, WBC, Lymphocytes, MID cells, Granulocytes, platelet and MPV) and biochemical (TC, HDL-C, LDL-C, TG, serum iron, blood glucose, creatinine, urea, ASAT and ALAT) parameters were determined in the blood on days 0 and at the end of each week. A significant increase of RBC, Hb, PCV, MPV, HDL-C, TG and creatinine and a significant decrease of WBC, MID cells, LDL-C and TC (p < 0. 05) were observed during the study period. Furthermore, there was no significant change on BMI, MCV, MCH, MCHC, lymphocyte, granulocyte, platelet, serum iron, blood glucose, and ASAT, ALAT and urea levels. The authors concluded that *H. Sabdariffa* L. dried calyces drink can be safely used. It also revealed good cholesterol lowering potential. No hepatoxicity and no kidney damage have been observed [245-246].

2.50. *Jasminum sambac*

The efficacy of *Jasminum sambac* flowers applied to the breasts to suppress puerperal lactation was comparedtobromocriptine. Effectiveness of both regimens was monitored by serum prolactin levels, clinical evaluation of the degree of breast engorgement and milk production and the analgesic intake. While both bromocriptine and Jasmine flowers brought about a significant reduction in serum prolactin, the decrease was significantly greater with bromocriptine. However, clinical parameters such as breast engorgement, milk production and analgesic intake showed that both treatments wereequally effective. The failure rates of the two treatments to suppress lactation were similar, rebound lactation occurred in a small proportion of women treated with bromocriptine [247-248].

2.51. *Juglans regia*

Diet supplemented with walnuts possessedbeneficial effect on blood lipids, lowering blood cholesterol and lowering the ratio of serum concentrations of low density lipoprotein: high densitylipoprotein by 12% [249]. In cross-sectional

surveys, it appeared that high levels of HDL cholesterol and apo A1 were associated with a high amount of walnut consumption (oil and kernel) in the regular diet [250].

A randomized, double blind case-control study was conducted to evaluate the lipid-lowering effect of Persian walnut oil (encapsulated in 500 mg capsules, 3 g/day, for 45 days) in the population of southern Iran. Lipid profiles were checked before; on days 15, 30, and 45 after the beginning; and 15 days after termination of the study. Plasma TG concentrations decreased by 19% to 33% of baseline (p value < 0. 05). No statistically significant change was observed in other measured parameters [251].

In a randomized, double-blind, placebo-controlled clinical trial, consumption of walnut oil by type 2 hyperlipidemic diabetic patients (15 ml Persian walnut oil)resulted in a significant decrease in total cholesterol levels (treatment difference (TD)=-30. 04, P<0. 001), triglyceride level (TD=-15. 04, P=0. 021), low-density lipoprotein level (TD=-30. 44, P<0. 001) and total cholesterol to high-density lipoprotein ratio (TD=-0. 72, P<0. 001) compared to the control group. There was a increase in the HDL level with consumption of walnut oil (TD=2. 28, P=0. 06). Frequency of patients reaching a LDL level below 100 was higher in the case group (20 vs 0%) [252].

The effects of the Juglans regia leaf extract on hyperglycemia lipid profiles in type II diabetic patients were investigated clinically using 61 patients, suffering from type II diabetes with fasting blood glucose (FBG) between 150 and 200mg/dl, glycated hemoglobin (HbA1c) between 7% and 9%. First group received 100mg Juglans regia leaf extract in capsules form two times a day for 3 months and other group received 100mg placebo capsule with the same dosage. The standard anti-diabetic therapy (metformin and glibenclamide, and nutritional regimen) was continued in both groups. The results indicated that FBG, HbA1c, total cholesterol and triglyceride levels in Juglans regia treated patientssignificantly decreasedafter 3 months compared with the baseline and with placebo group. Patients in Juglans regia group were significantly satisfied with Juglans regia treatment compared with the placebo group. No liver, kidney and other side effects were observed in the groups, except more GI events (specially a mild diarrhea) associated with extract treatment at the beginning of the study [253].

Fifty eight Iranian male and female patients with type 2 diabetes were enrolled in a clinical trial,received J. regia leaves extract for two months for determination of HbA1c and blood glucose level as a main outcome and insulin, SGOT, SGPT, and ALP level as secondary outcome. The results revealedthat serum fasting HbA1C and blood glucose levels were significantly decreased and the insulin level was increased in patients in the J. regia group [254].

A pilot study was carried out to determine the efficacy and safety of walnut hydrosol (WH) in patients with type 1 diabetes. Eight patients with diabetes mellitus (DM) type 1 were enrolled in the study. They were advised to drink 250 ml WH after meals twice a day for four weeks. WH can control the glycemic level in people with diabetes, but it may be associated with minor and major side effects. The average daily blood sugar level and insulin dose decreased in seven subjects. Two subjects developed generalized pruritic erythematous skin rash. One patient presented hypoglycemic coma [255].

2% and 3% concentration of petrol-ether and ether fractions in propylene glycol and 2% water soluble extract of the bark of Juglans regia were testedagainst developing plaque. All the preparations were applied twice a day on 20 subjects for 3 days. *Juglans regia* exhibited antiplaque activity in all the preparations tried. Ether extracts and aqueous extracts showed promising results as compared to petroleum extracts. 2% and 3% ether fraction of *Juglans regia* showed the antiplaque activity of 32. 12% and 31. 56% respectively. 2% aqueous solution of *Juglans regia* inhibited 30. 32% plaque; 2% and 3% petroleum ether fraction showed 17. 62% and 19. 45% of plaque inhibitions respectively [256].

The effect of acetone and aqueous extracts of *J. regia*was studied by testing on salivary samples of patients suffering from dental carries. Antimicrobial assay was carried out using disc diffusion method. Acetone extract was found to be effective as anti-cariogenic medicine [257-258].

2.52. *Lagerstroemia speciosa*

The antidiabetic activity of the leaves extract of*Lagerstroemia speciosa* [standardized to 1% corosolic acid (Glucosol)] was studiedin a randomized clinical trial in Type II diabetics. Glucosol at daily dosages of 32 and 48mg for 2 weeks inducedsignificant reduction in the blood glucose levels. Glucosol in a soft gel capsule formulation showed a 30% decrease in blood glucose levels compared to a 20% drop in hard gelatin capsule formulation (P<0. 001), suggesting that the soft gel formulation has a better bioavailability than a dry-powder formulation [259].

A randomized, double-blind, placebo-controlled clinical trial was carried out in 24 patients with metabolic syndrome. 12 patients received *Lagerstroemia speciosa*, 500 mg twice daily before meals during 3 months, and12 patients received placebo with the same prescription and for the same period. Area under the curve of glucose and insulin, total insulin secretion (insulinogenic index), first-phase of insulin secretion (Stumvoll index) and insulin sensitivity (Matsuda index) were determined. *Lagerstroemia speciosa* has shown evidenceof beneficial modification of the metabolic syndrome, insulin sensitivity and insulin secretion [260].

A randomized,placebo-controlled, double-blind, parallel group study conducted over 14weeks (including a 2-week run-in phase) was designedto investigate the efficacy and safety of IQP-GC-101 (a standardized extracts of *Garcinia cambogia*, *Camellia sinensis*, unroasted *Coffea arabica*, and *Lagerstroemia speciosa*)in reducing body weight and body fat mass in overweight Caucasian adults. Subjects took three IQP-GC-101 or placebo tablets, twice a day, 30 min before main meals. All subjects also adhered to a 500 kcal/day energy deficit diet with 30% of energy from fat. After 12-week intervention, IQP-GC-101 resulted in a mean (±SD) weight loss of 2. 26 ± 2. 37 kg compared with 0. 56 ± 2. 34 kg for placebo (p< = 0. 002). There was also significantly more reduction in body fat mass, waist circumference, and hip circumference in the IQP-GC-101 group. No serious adverse events were reported [261].

DLBS3233, a combined bioactive fraction of *Cinnamomum burmanii* and *Lagerstroemiaspeciosa*, possessed beneficial effects on glucose and lipid metabolism through the upregulation of insulin-signal transduction. The clinical efficacy of DLBS3233 was evaluated in type-2 diabetes mellitus subjects inadequately controlled by metformin and other oral anti-diabetic drugs. DLBS3233 was given orally at the dose of 100 mg once daily for 12 weeks of therapy in addition to their baseline oral anti-diabetic medication. After 12 weeks of treatment, the HbA1c level was reduced by 0. 65±1. 58 % (p=0. 001) from baseline (9. 67±2. 11 %); while the 1h- postprandial glucose level was reduced by -1. 45±3. 89 mmol/l (p=0. 021) from baseline (15. 29±4. 49 mmol/l). Insulin sensitivity, lipid profile and adiponectin level were improved to a considerable extent. DLBS3233 did not adversely affect body weight, liver, and renal function. Most adverse events observed were mild and they all had been resolved by the end of the study [262].

In other study, after 12 weeks, DLBS3233 improved insulin resistance better than placebo as reflected by a reduced homeostatic model- assessed insulin resistance (HOMA-IR) (-27. 04%±29. 41% vs -4. 90%±41. 27%, P=0. 013). The improvement of the first- and second-phase insulin secretion was consistently greater in DLBS3233 group than placebo group (-144. 78±194. 06 vs -71. 21±157. 19, P=0. 022, and-455. 03 ±487. 56 vs -269. 49±467. 77, P=0. 033, respectively). Furthermore, DLBS3233 also significantly better improved oral disposition index than placebo. No serious hypoglycemia, edema, or cardiovascular- related adverse events were found in either groups [263-264].

2.53. *Lantana camara*

The anti–hemorrhoidal activity of *Lantana camara* was studied in 20 patients suffering from 1st and 2nd degree hemorrhoids, using capsules prepared from dry aqueous extract of *Lantana camara* 500mg/kg and Lactose 100mg/kg. The results revealed significant reduction in signs and symptoms of acute hemorrhoidal attack (bleeding, anal discomfort, anal discharge, swelling and pain at prolapse and proctitis) at last week (on 28th day). No significant adverse effects were reported [265-266].

2.54. *Lawsonia inermis*

The antifungal effect of ethanolic extract of crude lawsone was tested in comparison with listerine mouth wash in diabeticswearing dentures. Each subject was given distilled water at baseline and Colony Forming Units (CFU) of candidal species was determined. Post therapeutic samples were then collected 1hr and 1week following drug usage and they were further advised to use given mouth washes twice daily with volume of 5 ml/ rinse for 30 seconds and CFU was evaluated. Crude lawsone mouthwash showed superior antifungal activity when compared to listerine mouthwash. Lawsone was appeared more effective in reducing CFU, at 1 hr and 1 week of using the mouth wash (p< 0. 01). Subjective symptoms like taste and smell were determined by Chi square test, good taste was felt for lawsone and olfactory satisfaction was good with listerine (p< 0. 01). Burning sensation was found to be more with listerine mouth wash [267].

The cooling and protecting effects of henna on prevention of decubitus ulcers were investigated in a randomized clinical trial conducted on 80 patients hospitalized in intensive care units. Patients were randomly allocated into 2 groups of control and intervention. For the intervention group, henna was applied with 15 cm extent on the patients' sacrum. At the end of the study, 1 patient in the intervention group (2. 7% male) and 6 patients in the control group (14. 29% male, 2. 85% female) had developed decubitus ulcers; this difference was significant (p = . 001) [268].

Theeffect of *Lawsonia inermis* leaves infusion in gingivitis healing was studied clincally. Sixty three gingivitis patients were instructed to rinse with 3 concentrations (50000, 10000 and5000 µg/ml) of *Lawsonia inermis*leaves infusion, 0. 1% hexetidine solution, and placebo as control. Bleeding index was decreasedin *Lawsonia inermis* leaves infusion at 10000 µg/ml concentratation (80%), more than hexetidine 0. 1% (76%) [269-270].

2.55. *Lepidium sativum*

The anti asthmatic effectof *Lepidium sativum* seed powder (1 gm thrice a day orally)was investigated in patients of mild to moderate bronchial asthma. The respiratory functions (FVC, FEV1, FEF25-75% and MVV) were assessed using a spirometer prior to, and after 4 weeks of treatment. Efficacy of the drug in improving clinical symptoms and severity of asthmatic attacks was evaluated by interviewing the patient and by physical and hematological examination at the end of the treatment. Four weeks treatment with the drug showed significant improvement in pulmonary functions andin clinical symptoms and severity of asthmatic attacks. None of the patient showed any adverse effect with *Lepidium sativum* [271].

In a clinical trial , the seeds (6 gm divided in two doses daily, orally) were evaluated for the management of osteoarthritis. The patients were subjected to the evaluation of cardinal sign and symptoms on the basis of scores according to their severity, frequency and duration before and after treatment. Seeds showed considerable improvements in cardinal signs and symptoms like pain in joint, swelling, stiffness, crepitus, tenderness and difficulty in movement (30% complete remission, 37. 5% marked improvement, 25% moderate improvement, and only 7. 5% didn't improve) [272].

The effects of dietary flaxseed on plasma cholesterol were studied in patients with clinically significant mild biomarkers of cardiovascular disease (CVD) and in those administered cholesterol-lowering medications, statins. Dietary flaxseed (foods that contained30 g of milled flaxseed) resulted in a 15% reduction in circulating LDL cholesterol as early as 1 month into the trial (P= 0. 05). The concentration in the flaxseed group (2. 1 ± 0. 10 mmol/l) tended to be less than in the placebo group (2. 5 ± 0. 2 mmol/l) at 6 months (P= 0. 12), but not at 12 months (P = 0. 33). Total cholesterol also tended to be lower in the flaxseed group than in the placebo group at 1 month (11%, P= 0. 05) and 6 months (11%, P = 0. 07), but not at 12 months (P= 0. 24). In a subgroup of patients taking flaxseed and statins, LDL-cholesterol concentrations were lowered by 8. 5% ± 3. 0% compared with baseline after 12 months, which differed from LDL-cholesterol concentrationsin the placebo + statins subgroup, which increased by 3. 0% ± 4. 4% (P= 0. 030) [273].

A randomized double-blind placebo controlled study was carried out to assess the effects of flaxseed lignan complex supplementation (543 mg/day)during exercise training on a metabolic syndrome composite score and osteoporosis risk in older adults. Males taking the flaxseed lignan complex reduced metabolic syndrome score relative to men taking placebo, but a similar trend was not seen in females. Flaxseed lignan had no effect on bone mineral density or content, body composition, lipoproteins, glucose, or inflammation [274].

The hypoglycemic and hypotensive effectsof (a standardized *Linum usitatissimum*lignan enriched product, 543 mg)were studied in healthy older adults as an aspect of safety. After 6 months of treatment, no incidents of hypoglycemia or hypotension were observed during flaxseed treatment, suggesting that 543 mg below the concentrationsproduced observable adverse effect level [275].

An 8-week, randomised, double-blind, placebo-controlled study was conducted in hypercholesterolaemic subjects, using treatments of 0 (placebo), 300 or 600 mg/day of dietary secoisolariciresinol diglucoside (SDG) from flaxseed extract to determine the effect on plasma lipids and fasting glucose levels. SDG significantlydecreased total cholesterol (TC), LDL-cholesterol (LDL-C) and glucose concentrations (p< 0. 05 to p< 0. 001). At weeks 6 and 8 in the 600 mg SDG group, the decreases of TC and LDL-C concentrations were in the range from 22. 0 to 24. 38 % respectively (p< 0. 005 for all compared with placebo). For the 300 mg SDG group, only significant differences from baseline were observed for decreases of TC and LDL-C. A substantial effect on lowering concentrations of fasting plasma glucose was also noted in the 600 mg SDG group at weeks 6 and 8, especially in the subjects with baseline glucose concentrations > or = 5. 83 mmol/l (lowered 25. 56 and 24. 96 %; p= 0. 015 and p= 0. 012 compared with placebo, respectively) [276].

The efficacy and safety of dietary flaxseed supplementation was studied in the management of hypercholesterolemia in children. The use of dietary flaxseed supplementation, was associated with adverse changes in the lipid profile of children with hypercholesterolemia, although a potential benefit of low-density lipoprotein cholesterol lowering could not be excluded. The use of flaxseed supplementation in children with hypercholesterolemia might not be a viable option for lipid management, although it was safe [277].

The effects of flaxseed dietary fibers (a diet with flaxseed fiber drink 3/day, and flaxseed fiber bread (3/day) on blood lipids and fecal excretion of fat and energywere studied in a double-blind randomized crossover study. Compared to control, Flax drink lowered fasting total-cholesterol and LDL-cholesterol by 12 and 15%, respectively (p< 0. 01), whereas Flax bread only produced a reduction of 7 and 9%, respectively (p< 0. 05). Fecal fat and energy excretion increased by 50 and 23% with Flax drink consumption compared to control (p< 0. 05), but only fecal fat excretion was increased with Flax bread compared to control (p< 0. 05) [278].

The effect of increased alpha-linolenic acid intake (12-week dietary supplementation with flaxseed oil, rich in alpha-linolenic acid,8 g/day) on blood pressure was examined in dyslipidaemic patients. Supplementation with alpha-linolenic acid resulted in significantly lower systolic and diastolic blood pressure levels (p=0. 016 and p=0. 011, respectively [279].

The effects of daily ingestion of flaxseed on systolic and diastolic blood pressure were studiedin peripheral artery disease patients (ingested foodscontained 30 g of milled flaxseed or placebo each day over 6 months). Plasma levels of the ω-3 fatty acid α-linolenic acid and enterolignans increased 2- to 50 fold in the flaxseed-fed group but did not increase significantly in the placebo group. Systolic blood pressure was ≈10 mm Hg lowered, and blood pressure was ≈7 mm Hg lowered in the flaxseed group compared with placebo after 6 months. Patients who entered the trial with a SBP ≥140 mm Hg at baseline obtained a significant reduction of 15 mm Hg in SBP and 7 mm Hg in DBP from flaxseed ingestion [280].

A randomized, double-blind, placebo-controlled clinical trial was carried outonone hundred patients (155 hands) with idiopathic mild to moderate carpal tunnel syndrome. They were randomized in two parallel groups andwere treated during 4 weeks with topical placebo and linseed oil. Symptomatic severity and functional status were measured using Boston Carpal Tunnel Questionnaire. In addition, median sensory nerve conduction velocity, motor distal latency, sensory distal latency and compound latency as electrodiagnostic parameters were measured at baseline and after the intervention period. After the treatment period, significant improvement was observed regarding Boston Carpal Tunnel Questionnaire symptomatic severity and functional status mean differences (p< 0. 001) in the linseed oil group compared with those in the placebo group. Furthermore, a significant improvement of nerve conduction velocity of the median nerve was seen in the linseed oil group by a value of 2. 38 m/sec (p< 0. 05). However, motor distal latency and sensory distal latency of the median nerve showed no significant changes (p= 0. 14 for both items) between-groups. No significant adverse events were reported from using linseed oil [281].

The efficacy of flax seedsupplementation was investigated in type 2 diabetic's patients,they treated with diet supplemented with 10 g of flax seedpowder daily for a period of 1 month. The control group received no supplementation or placebo. During the study, diet and drug intake of the subjects remained unaltered. Supplementationwith flax seedreduced fasting blood glucose by 19. 7% and glycated hemoglobin by 15. 6%. A favorable reduction in total cholesterol (14. 3%), triglycerides (17. 5%), low-density lipoprotein cholesterol (21. 8%), and apolipoprotein B and an increase in high-density lipoprotein cholesterol (11. 9%) were also noticed [282].

A randomized, double-blind, placebo-controlled clinical trial was carried out, patients with benign prostatic hyperplasia were treated with 300, or 600 mg/day secoisolariciresinol diglucoside (SDG) for 4 months, to evaluatetheability of SDGto alleviate lower urinary tract symptoms in patients with benign prostate hyperplasia. For the 0, 300, and 600 mg/day SDG groups, respectively, the International Prostate Symptom Score (IPSS) decreased -3. 67 ± 1. 56, -7. 33 ± 1. 18, and -6. 88 ± 1. 43 (p= 0. 100, < 0. 001, and < 0. 001 compared to baseline), the Quality of Life scoreimproved by -0. 71 ±0. 23, -1. 48 ± 0. 24, and -1. 75 ±0. 25 (p= 0. 163 and 0. 012 compared to placebo and p= 0. 103, < 0. 001, and < 0. 001 compared to baseline), and the number of subjects whose LUTS grade changed from moderate/severe to mildincreased by three, six, and 10 (p= 0. 188, 0. 032, and 0. 012 compared to baseline). Maximum urinary flows insignificantly increased 0. 43 ± 1. 57, 1. 86 ± 1. 08, and 2. 7 ± 1. 93 ml/second, and postvoiding urine volume decreased insignificantly by -29. 4 ±20. 46, -19. 2 ±16. 91, and -55. 62 ± 36. 45 ml. Plasma concentrations of secoisolariciresinol, enterodiol, and enterolactone were significantly raised after the supplementation [283].

Flaxseed, the richest source of mammalian lignan precursors, has previously been shown to reduce the growth of tumors in rats. However, in a randomized double-blind placebo-controlled clinical trial in comparison with placebo,flaxseed caused reductions in Ki-67 labeling index (34. 2%; p= 0. 001) and in c-erbB2 expression (71. 0%; p= 0. 003) and an increase in apoptosis (30. 7%; p= 0. 007). No significant differences in caloric and macronutrient intake were seen between groups and between pre- and post-treatment periods. A significant increase in mean urinary lignan excretion was observed in the flaxseed group (1,300%; p< 0. 01) compared with placebo controls [284].

A pilot study was carried out to study the effects of flaxseed-supplemented, fat-restricted diet (30 g/day) on the prostate cancer growth. Flaxseed-supplemented, fat-restricted diet significant decreases PSA (8. 47 ±3. 82 to 5. 72 ± 3. 16 ng/ml; p= 0. 0002) and cholesterol (241. 1 ± 30. 8 to 213. 3 ±51. 2 mg/dl; p= 0. 012). No statistically significant change was seen in total testosterone (434. 5 ± 143. 6 to 428. 3 ± 92. 5 ng/dl). The proliferation rates in the benign epithelium decreased significantly from 0. 022 ±0. 027 at baseline to 0. 007 ±0. 014 at 6 months of followup (p= 0. 0168). [285]

A double-blind, placebo-controlled, randomized clinical trial was performed to study the therapeutic effects of daily intake of bread produced with partially defatted ground flaxseed [2 slices of bread containing 25 g of flaxseed (46 mg lignans), or wheat bran (<1 mg lignans) every day for 12 consecutive weeks]in the climacteric symptoms and endometrial thickness of postmenopausal women. Both treatments showedsignificant, but similar, reductions in hot flashes and Kupperman Menopausal Index (KMI), after 3 monthsof treatment. Moreover, endometrial thickness was not affected in either group. Accordingly,although flaxseed was safe, but itsconsumption at this level (46 mg lignans/day) was not more effective than placebo for reducing hot flashes and KMI [286].

The efficacy of flaxseed meal and flaxseed extract was tested for reducing climacteric symptoms of menopausal women. Both the flaxseed extract (P=. 007) and the flaxseed meal (p=0. 005) were effective in reducing the menopausal symptoms when compared with the placebo control (p=0. 082) ([287].

A randomized, double-blind study was performed to study theeffects of flaxseed incorporation in the diet of healthy menopausal women. Flaxseed reduced serum total cholesterol concentrations (-0. 20 ± 0. 51 mmol/liter; p= 0. 012) and high-density lipoprotein cholesterol concentrations (-0. 08 ±0. 24 mmol/liter; p= 0. 031) compared with wheat germ placebo. BMD did not differ significantly between the two groups (flaxseed and wheat germ) . Both flaxseed and wheat germ reduced (p< 0. 0001) the severity scores of menopausal symptoms, but no statistical difference was found between the two groups [288].

An open randomised controlled trialwas carried out to study the clinical effectiveness ofwhole linseeds and ground linseeds in the management of irritable bowel syndrome. The improvement in symptom severity did not reach statistical significance for whole linseedsversus ground linseeds (p= 0. 62), whole linseeds versus controls (p= 0. 12) and ground linseeds versus controls (p= 0. 10). There were no significant changes in stool frequency or stool consistency for any of the groups [289-290].

2.56. *Lithospermum officinale*

The effects of the freeze-dried extracts of*Lithospermum officinale*, were studied on the binding and biological action of Graves'-IgG, the thyroid-stimulating immunoglobulin G (IgG), whichfound in the blood of patients with Graves' disease (Graves'-IgG) and which resemble TSH in their ability to bind to the thyroid plasma membrane, probably at the TSH receptor, and to activate the gland. The extractand their auto-oxidized constituents also inhibited the biological responses to Graves'-IgG [291-292].

2.57. *Lycium barbarum*

The effects of *Lycium barbarum* fruit (goji) intake was studied on general well-being in a randomized, double-blind, placebo- controlled 30 day intervention trial. *Lycium barbarum* intake significantly attenuated the increases in plasma DHEA and cortisol concentrations produced by a short and intense exercise challenge. In comparison with the placebo, tiredness and overall health were significantly improved in the *Lycium barbarum* group. Cortisol, DHEA and lactic acid levels were significantly increased by the exercise for the pre-intervention. At the post-intervention, *Lycium barbarum* intake significantly attenuated cortisol and DHEA levels. Lactic acid levels were comparable for both groups, and glucose and BUN levels were not altered [293].

The standardized *Lycium barbarum* fruit juice (GoChi®, Free Life International, Phoenix, AZ, USA) at 120 ml/day (equivalent to at least 150 g of fresh fruit), was studied for 30 days in a randomized, double-blind, placebo-controlled clinical study in 60 older healthy adults to determine its effects on general well-being, and safety. GoChi group showed a significant increase in general feelings of well-being, such as fatigue and sleep, and showed a tendency for increased short-term memory and focus between pre- and post-intervention. No adverse reactions, abnormal symptoms, or changes in body weight, blood pressure, pulse, visual acuity, urine, stool, or blood biochemistry were recorded [294].

A randomized, double-blind, placebo-controlled clinical trial was carried out to examined the general effects of the orally consumed*Lycium barbarum*, as a standardized juice (GoChi) to healthy adults for 14 days. Significant differences between day 1 and day 15 were found in the GoChi group in increased ratings for energy level, athletic performance, quality of sleep, ease of awakening, ability to focus on activities, mental acuity, calmness, and feelings of health,

contentment, and happiness. GoChi also significantly reduced fatigue and stress, and improved regularity of gastrointestinal function [295].

Two separate randomized, double-blind, placebo-controlled, small clinical studies were conductedto determine the effects of *Lycium barbarum* consumption on caloric expenditure and changes in morphometric parameters (waist circumference) in healthy human adults. A single bolus of *Lycium barbarum* intake increased postprandial energy expenditure1 through 4 hours post-intake over the baseline level in a dose-dependent manner and was significantly higher than the placebo group by 10% at 1 hour post-intake of 120 ml (p< 0. 05). In a 14-day intervention trial, *Lycium barbarum*significantly decreased waist circumference by 5. 5 ± 0. 8 cm compared with the preintervention measurements and placebo group at postintervention day 15 (p< 0. 01). Accordingly, *Lycium barbarum* consumption increases metabolic rate and reduced the waist circumference, relative to placebo treated control subjects [296].

The effect of *Lycium barbarum* polysaccharide (LBP, 300 mg/day bw), for the treatment of various diseases with the symptoms of frequent drinking and urination was investigated using a randomized, controlled clinical trial carried out on67patients with type 2 diabetes (30 in control group and 37 in LBP group). LBP possessed remarkable protective effect in patients with type 2 diabetes. Serum glucose was found to be significantly decreased and insulinogenic index increased after 3 months administration of LBP. LBP also increased HDL levels in patients with type 2 diabetes. It showed more obvious hypoglycemic efficacy for those people who did not take anyhypoglycemic medicine compared to patients takinghypoglycemicmedicines [297].

The preventive effects of LBP-standardized *Lycium barbarum* preparation on oxidant stress-related conditions in humans were studiedin a 30-day randomized, double-blind, placebo-controlled clinical study carried out on50 Chinese healthy adults. In LBP-standardizedtreated group, antioxidant markers significantly increased by 8. 4% for SOD and 9. 9% for GSH-Px between the preintervention and postintervention measurements, whereas MDA were significantly decreased by 8. 7%. The SOD, GSH-Px, and MDA levels in the LBP-group were significantly different from those in the placebo group at the postintervention time point, with increases of 8. 1% and 9. 0% and a decrease of 6. 0%, respectively [298].

Seventy nine advanced cancer patients in a clinical trial were treated with LAK/IL-2 combining with *Lycium barbarum* polysaccharides (LBP). Thetreatmentof75evaluablepatients revealed that objective regression of cancer was achieved in patients with malignant melanoma, renal cell carcinoma, colorectal carcinoma, lung cancer, nasopharyngeal carcinoma, malignant hydrothorax. The response rate of patients treated with LAK/IL-2 plus LBP was 40. 9% while that of patients treated with LAK/IL-2 was 16. 1% (p< 0. 05). The mean remission in patients treated with LAK/IL-2 plus LBP also lasted significantly longer. LAK/IL-2 plus LBP treatmentled to more marked increase in NK and LAK cell activity than LAK/IL-2 without LBP [299].

The anthropometric and biochemical parameters in patients with metabolic syndrome were investigated after the consumption of goji berry. After 45 days of supplementation with goji berry a significant reduction in transaminases as well as an improvement in lipid profile was observed. A significant reduction in the waist circumference was also recorded with anincreased glutathione and catalase levels associated with a reduction of lipid peroxidation [300].

The effects of flaxseed oil consumption on serum lipids and lipoproteins wereinvestigated in 34 hemodialysis patients using a randomized double-blinded controlled trial. The patients in the flaxseed oil group received 6 g/day of flaxseed oil for 8 weeks, whereas the control group received 6 g/day of medium chain triglycerides oil. Serum triglyceride concentration decreased significantly up to 23% in the flaxseed oil group at the end of week 8 compared to baseline, and the reduction was significant in comparison with the medium chain triglycerides oil group (p< 0. 01). There were no significant differences between the two groups in the mean changes of serum total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, and lipoprotein (a) [301].

The standardized *Lycium barbarum* fruit juice (GoChi®, FreeLife International, Phoenix, AZ, USA) at 120 ml/day (equivalent to at least 150 g of fresh fruit), was studied for 30 days in a randomized, double-blind, placebo-controlled clinical study in 60 older healthy adults to determine its effects on immune function. The GoChi group showed a statistically significant increase in the number of lymphocytes and levels of interleukin-2 and immunoglobulin G compared to pre-intervention and the placebo group, whereas the number of CD4, CD8, and natural killer cells or levels of interleukin-4 and immunoglobulin A, were not significantly altered [294].

2.58. *Lycopus europaeus*

An open post-marketing surveillance study consisting of (a prolective assessment in patients receiving Thyreogutt® mono for 4 weeks, a retrolective documentation of data from patients who had received at least one course (4 weeks) of Thyreogutt® mono therapy during the previous 2 years, and a control cohort receiving no drug treatment) was carried outon four hundred and three patients with mild symptomatic hyperthyroidism, to assess the effects and safety of an extractof*Lycopuseuropaeus* (Thyreogutt® mono tablets or drops). The extract of*Lycopuseuropaeus* was well tolerated and associated with a statistically significant and clinically relevantimprovement of the symptoms in mild hyperthyroidism [302].

A prospective two-armed open study wascarried out (patients with a basal TSH <1. 0 mU/l and hyperthyroidism-associated symptoms) to study the effect of *Lycopuseuropaeus* on thyroid function and on associated symptoms during a 3-month follow up phase. Symptoms specific to the thyroid gland were diminished (the increased heart rate in the morning). The *Lycopuseuropaeus* preparation showed a good tolerance. The urinary T4 excretion was significantly increased in *Lycopuseuropaeus* - treated patients [303-30].

2.59. *Mangifera indica*

The possible therapeutic effects and the safety of *Mangifera indica* extract (Vimang tablets, 900 mg/ day) combined with methotrexate (MTX) on reducing disease activity in rheumatoid arthritis (RA) were studied clinically. Only the patients of MTX-Vimang group revealed statistically significant improvement in disease activity score-28 (DAS 28) parameters with respect baseline data but no differences were observed between groups. American college of rheumatology (ACR) criteria showed80%improvements only in MTX-Vimang group at the 90 days (p< 0. 001). In MTX-Vimang group, 100% of patients decreased NSAIDs administration (p< 0. 01) and 70% of those eradicated gastrointestinal side effects (p<0. 01) ensuing of the preceding treatment. Other adverse effects were not reported [305-306].

2.60. *Marrubium vulgare*

The antidiabetic effect of the aqueous extract of *Marrubium vulgare*was studied intype 2 non-controlled diabetic patients. Patients received a prepared infusion of the dry leaves of the plant treatment for 21 days. *Marrubium vulgare* treatmentdecreased the plasma glucose level by 0. 64% and cholesterol and triglycerides by 4. 16% and 5. 78%, respectively [307].

A randomized, double-blind, and controlled clinical trial was conducted to evaluate the clinical effect of theaqueous extract on type 2 non-controlled diabetes mellitus. The product consisted of fresh *Marrubium vulgare* leaves that were dried underenvironmental temperatures and protected from direct light and then milled. Patients had to prepare the treatment immediately before administration. *Marrubium vulgare* extract was administered three times a day, before every meal. The study was carried out for 21 days. Prior to infusion administration, every seven days and after the clinical trial, the fasting glucose, cholesterol, triglycerides, urea, creatinine, and uric acid in blood were determined. Theeffectiveness was considered as a decrease in the basal concentration of glucose, cholesterol, or triglycerides by at least 25%. *Marrubium vulgare* caused that effect in only two of the 21 patients (9. 52%). The mean of plasma glucose level was reduced by 0. 64%, and that of cholesterol and triglycerides by 4. 16% and 5. 78%, respectively [308-309].

2.61. *Matricaria chamomilla*

Many experimental and clinical trials showed that formulationsof *Matricaria chamomilla* [contained aqueous extracts, alcoholic extracts, hydroalcoholic cream, ointment containing α-bisabolol and chamazulene (Kamillosan)] wereeffective inacute skin reactions due to physical, chemical andimmunological causes. Chamomile extract 1%, effectivelyreduced the ultraviolet erythema, but0. 1% betamethasone was more effective in reducing erythema after 24 and 48 hrs [310].

Theefficacy of hydroalcoholic cream chamomile extract 10% compared to placebo cosmetic cream was evaluated inpityriasis alba and eczema lesions. 36%of the patients were cured and 45. 5% wereimproved [311].

The effects of aqueous extract of German chamomile applicationwas comparedwith thetopical corticosteroids in the management of peristomal lesions in patients with colostomy. Healing of the lesions was significantly faster in camomile treated group (8. 89 ±4. 89 days) than the hydrocortisone treated group (14. 53 ±7. 6 days) (P = 0. 001) [312].

The clinical efficacy of two formulations containing extracts enriched with *C. recutita*, (a liposomal and non-liposomal) were studiedin treating contact dermatitis. The cream samples, 2 mg /cm^2 doses were applied to the affected areas of

skin three times daily over a period of 2 weeks. The liposomal cream was more effective than non-liposomal formulations [313].

The efficacy of cream containing 2% ethanol extract of chamomile flowers (Kamillosan [R]) was studied in comparison with hydrocortisone cream in patients with atopic eczema. The difference between the average scores showed that Kamillosan was superior to hydrocortisone [314].

Effect of Kamillosan was evaluated in patients undergoing radiation therapy presented radiodermatitis. There was delay in the onset of the reactionstreated withKamillosan (occurred between 5th and 7th week) [315].

The effect ofchamomile extract (standardized to 3 mg of chamazulene and 50 mg of α-bisabolol) in healing of injuries from the tattoo dermabrasion was studied after 3 applications a day. The reduction of the wound area and the reduction of secretions by chamomile were statistically significant [316].

The efficacy of Kamillosan®, compared with hydrocortisone, fluocortin and bufexamac in maintenance therapy of eczema was studied in 161 patients with eczema in hands, forearms and legs. Kamillosan® showed the same efficacy ofhydrocortisone at 0. 25% (22% vs. 18%) and was superior to the fluocortin 0. 75% (25. 5% vs. 2. 2%) and the bufexamac (53, 6% vs. 14. 3%) [317].

The hands of health care workers were the primary routes of transmission of nasocomial infection to patients, which represented a critical issue in hospital care utcome, resulting in substantial morbidity and mortality. The antimicrobial activity of the prepared chamomilehand wash was investigated against skin pathogens using disc diffusion method. Its efficacy was checked and compared with the commercial ones. Results revealed that chamomile soap formulation was more efficient in reducing the number of organisms from hands than the commercial antiseptic soaps thus it can be used as an antiseptic soap with less or no side effects [318].

The efficiency of chamomile (*Matricaria chamomilla*) extract on reduction of dysmenorrhea and premenstrual syndrome (PMS)was evaluated clinically, women with PMS symptoms was studied for two monthly menstrual cycles, the first cycle without chamomile extract and the second cycle with administration of the chamomile extract before menstruation. Chamomile extract was effective in reduction PMS symptoms. The most prominent effect of chamomile extract was on the reduction of severity of anxiety and retention symptoms [319].

The effects of *Matricaria chamomilla* extract and mefenamic acid on the severity of premenstrual syndrome symptoms were carried out ina randomized double-blind clinical trial. Particepants received one 100 mg capsule of *Matricaria chamomilla*or or 250 mg mefenamic acid three times daily from day 21 of menstrual cycle till the beginning of the menstruation. The reduction of symptoms was significantly greater among *Matricaria chamomilla* extract users (25±13. 8 and 28±14. 5%) than that among mefenamic acid users (14. 8±18. 5 and 16. 2±18. 2%) after the first and second cycles (P<0. 05). Severity of emotional symptoms was significantly higher among *Matricaria chamomilla* extract users (30. 1±26. 6 and 33. 4±25. 3%) than that among mefenamic acid-users (11. 6±25. 7 and 10. 7±26. 8%) after two cycles intervention (P>0. 05). Reduction of physical symptoms was not significantly different between the two groups [320].

The effects of chamomile tea consumption (3 g/150 ml hot water, three times per day immediately after meals for 8 weeks) on glycemic control and serumlipidprofilewere studied inpatients with type 2 diabetes mellitus (T2DM) in a single-blind randomized controlled clinical trial. Chamomile tea significantly decreased the concentration of HbA1C (P = 0. 03), serum insulin levels (P < 0. 001), insulin resistance (P < 0. 001), total cholesterol (P = 0. 001), triglyceride (P < 0. 001), and low-density lipoprotein cholesterol (P = 0. 05) compared with control group, while, itcausednosignificant changes in serum HDL levels [321].

The long-term *Matricaria chamomilla*usewas evaluated for prevention of generalized anxiety disorder relapse by clinically study included two-phase, during Phase 1, eligible participants received 12 weeks of open-label therapy with chamomile pharmaceutical grade extract 1500mg (500mg capsule 3 times daily), while, during Phase 2, treatment responders were randomized to either 26 weeks of continuation chamomile therapy or placebo in a double-blinded, placebo-substitution design. The primary outcome was time to relapse during continuation therapy andthe secondary outcomes included the proportion who relapsed, treatment-emergent adverse events, and vital sign changes. Long-term chamomile was safe and significantly reduced moderate-to-severe generalized anxiety disorder, but did not significantly reduce the rate of relapse [322].

A randomized double-blind placebo-controlled trialwas carried out to investigate the antidepressant effect of *Matricaria chamomilla*extract (1500 mg daily for 8 weeks)in subjects with generalized anxiety disorder with and

without comorbid depression. *Matricaria chamomilla* produced clinically meaningful antidepressant effects in addition to its anxiolytic activity in subjects with generalized anxiety disorderand comorbid depression [323].

A randomized, double-blind, placebo-controlled efficacy and tolerability trial was carried out to determined the effect of *Matricaria recutita* extract therapy in mild to moderate generalized anxiety disorder using Hamilton anxiety rating scores. Chamomile possessedmodest anxiolytic activity, a significantly greater reduction in mean total Hamilton anxiety rating scores during chamomile versus placebo therapy (P = 0. 047) was recorded [324].

The efficacy of topical use of *Matricaria recutita*oil in the treatment of enuresis was studied in children. Eighty patients diagnosed as monosymptomatic nocturnal or daytime enuresis were receive *Matricaria recutita* oil or placebo topically for 6 weeks in a double-blind randomized placebo-controlled trial. Patients were evaluated prior to and following 8 weeks of the intervention in terms of frequency of enuresis and any observed adverse effects. The mean frequency of enuresis at the first, second, and third 2 weeks was lower in *Matricaria recutita* oil treatedgroup compared with the placebo group (P< . 001, P ¼ . 03, and P< . 001, respectively). There was no report of any adverse effects in the study groups [325].

2.62. *Medicago sativa*

Fifteen patients with hyperlipoproteinemiatypes IIA, IIB and IV were given 40 g of heat prepared alfalfa seeds 3 times daily at meal times for 8 weeks with otherwise unchanged diet. Body weight increased slightly during the first 4 weeks of alfalfa treatmentprobably because of the caloric content in the alfalfa seeds. However, the treatment significantly decrease thetotaland LDL cholesterol [326].

In a clinical trials carried out on volunteers, the application of alfalfa leaves extract cream resulted in human body hair diameter reduction with no side effects. The rate of hairgrowth was reduced in the three groups treated with 1%, 2% and 5% of Alfalfa cream compared to group which received placebo (P< 0. 05). The actual mechanism behind this effect could be attributed to the high concentration of estrogenic components in alfalfa [327-328].

2.63. *Melilotus officinalis*

The therapeutic activity of cumarinic extract of *Melilotus officinalis* was studied clinically in fourteen patients with chronic upper arm lymphedema due to post-lymphadenectomy of the axilla for breast cancer. Patients were receive 400 mg of cumarinic extractcontaining 8 mg of cumarine in a sole daily administration for 6 months. Ofthe fourteen treated patients, 11 patients (52. 3%) showed reduction of the circumference of the affected arm of 5% with respect to base values. Three patients (14. 2%) had no change. In 12 patients (57. 1%), thesymptoms were improved. Regarding tolerability: 3 patients (14. 2%) had transitory gastrointestinal side effects. The authors concluded that cumarinic extract of *Melilotus officinalis* was effective in reducing lymphedema in 79% of the patients treated for a period of six months [329].

The therapeutic efficacy of oral use of a combination of [desmin (300 mg/day) and troxerutin (300 mg/day) with *Centella asiatica* (30 mg/die) and *Melilotus officinalis* (160 mg/die) for 14 months] was evaluated indiabetic patients with diabetic cystoid macular edema without macular thickening. The orally administered combinationpreserved retinal sensitivity in diabetic patients [330].

Melilotus officinalis was introduced as a component of a new drug by trade name of Semilil (Angipars). The effects of Angipars (ip, 5, 10, and 20mg/kg for 2 weeks) on nerve conduction velocity, histological alterations, and behavioral indices were investigated in streptozotocin (STZ) induced diabetic rats. Intraperitoneal injection of Angipars, significantly improved nerve conduction velocity in neuropathic rats. It also reduced the physiologic symptoms and improved sciatic morphological injuries in neuropathic rats [331].

Furthermore, the investigations also revealed that Semilil (Angipars)was safe withtherapeutic efficacy in focal cerebral ischemia in rats, wound healing in rodents, human diabetic foot ulcer and pressure ulcers [332-335].

The therapeutic efficacy and the clinical tolerabilityof an association of alphatocopherol, rutin, *Melilotus officinalis*, and *Centella asiatica* was evaluated in patients with chronic venous insufficiencyafter 15 and 30 days treatment. A significant improvement of the clinical simptomatology was obtained, characterised by a diminution of the soprafascial edema after the treatment period [336-337].

2.64. *Melissa officinalis*

A double blind randomized placebo-controlled clinical trial was carried out to evaluate the efficacy and safety of lyophilized aqueous extract of *Melissa officinalis*leaves (500 mg twice a day, for 14 day)on adults suffering from benign palpitations. *Melissa officinalis*leavesextract reduced the frequency of palpitation episodes and significantly reduced the number of anxious patients in comparison to the placebo. The extract showed no serious side effects [338].

A randomized, double-blind, placebo-controlled clinical trial was performedto investigate the effects of oral administration of powdered *Melissa officinalis* (3 g/day, for eight weeks)on biomarkers of oxidative stress, inflammation, and lipid profile in patients with chronic stable angina. The mean serum concentrations of triglycerides, total-cholesterol, LDL-cholesterol, malondialdehyde, and high sensitive C-reactive protein were lower in the treated group compared with placebo (P<0. 01). Moreover, the mean serum concentration of paraxonase 1 (PNO1) and HDL-c were higher (p<0. 001) in the treated compared with the control group [339].

The anxiolytic and antidepressant effectsof *Melissa officinalis* tea were studied in burn patients. The serum levels of antioxidants were measured once before the intervention and at 20 days after the intervention. Depression, anxiety, and insomnia levels were measured by questionnaires. The percentages of those experiencing anxiety and depression were significantly less in *Melissa officinalis* treated patients than those in control group. Sleep quality in *Melissa officinalis* treated increased significantly. However, the mean serum antioxidant levels were not significantly changed by *Melissa officinalis* [340].

The cognitive and mood effects of single doses of the most cholinergically active *Melissa officinalis* dried leaf (600, 1000, and 1600 mg of encapsulated dried leaf, at 7-day intervals) were assessed in a randomized, placebo-controlled, double-blind. Cognitive performance and mood were assessed before intiation ofthe treatmentand at 1, 3, and 6 h posttreatment. The most notable cognitive and mood effects were included improvement memory performance and increase (calmness) at all post treatment time points for the highest (1600 mg) dose. However, decrements in the speed of timed memory task performance and on a rapid visual information-processing task increased with decreasing dose [341].

A placebo-controlled, double-blind, balanced-crossover studywas performed to determine the effects of *Melissa officinalis*[single doses of 300, 600 and 900 mg of a standardised extractof *Melissa officinalis* (Pharmaton)] on cognition and mood in healthy humans. Melissa extract causedtime- and dose-specific reductions in both secondary memory and working memory factors. Self-rated (calmness),was elevated at the earliest time points by the lowest dose, whilst, alertness was significantly reduced at all time points following the highest dose. Both nicotinic and muscarinic binding were found to be low [342].

Four month, parallel group, placebo controlled trialwas carried outto evaluate the efficacy and safety of *Melissa officinalis*extract (60 drops/day) in patients with mild to moderate Alzheimer's disease. *Melissa officinalis*extract produced a significantly better outcome on cognitive function than placebo [Alzheimer's disease assessment scale (ADAS-cog):P = 0. 01 andclinical dementia rating (CDR): P< 0. 0001]. There were no significant differences in the side effects except agitation, which was more common in the placebo group (P = 0. 03) [343].

2.65. *Mentha longifolia*

Eight weeks administration of a polyherbal formula remedy contained (*Mentha longifolia, Cyperus rotundus* and *Zingiber officinale*) topatients with irritable bowel syndromeexhibited improvement of all irritable bowel symptoms, the therapeutic efficacy of the polyherbal therapy was comparable to mebeverine [344].

A double-blind, randomized clinical trial was performed to study the efficacy of *Mentha longifolia* (capsules, three times daily for four weeks) on relieving the symptoms and improving the quality of life of patients with postprandial distress syndrome. At the end of treatment period, the *Mentha longifolia* group showed more significant improvement in the mean severity scales of symptoms than the placebo group (P< 0. 001). *Mentha longifolia*, significantlyimproved the scores of quality of the life (general health, role-physical, social functioning, bodily pain, vitality, and mental health) [345].

A pilot studywas performed on seven amenorrheic women with premature ovarian failure to study the effect of *Mentha longifolia* (a cup of herbal tea three times a day for 2 weeks in 3 menstural cycles) on serum FSH level in premature ovarian failure. After treatment with herbal teas, there was a significant decrease in FSH (79. 39 ± 19. 17 to 27. 83 ±16. 14 mIU/ml, P< 0. 001). All patient except four (14. 81%) had mensturation after taking the herbal medicine. Patients showed no decrease in FSH level,achieved regular monthly bleeding when followed for three cycles [346].

The effect of *Mentha longifolia* (tea for two consecutive cycles from two days before until the first three days of menstruation) on severe dysmenorrheal was carried out on ten female students with severe dysmenorrhea. Pain intensity was reduced from severe to low in 9 patients and it reduced from severe to moderate in one patient [347].

The efficacy of *Mentha longifolia* (oral syrup, 15 ml three times a day for 2 weeks) in secondary amenorrheawas investigated in a double-blind, randomized, placebo-controlled, multicenter study on women with secondary amenorrhea and oligomenorrhea. The drug and placebo were repeated in three cycles of menstruation. Bleeding was documented by the patient on diary cards. The number of women with bleeding during the first cycle were higher in the drug group compared with placebo group (68. 3% vs. 13. 6%; p < 0. 001). The regularity of bleeding throughout the study was markedly better in the drug group compared with those receivedplacebo (33. 3% vs. 3. 3%; P< 0. 001). No notable complicationand side effects were reported in relation to *Mentha longifolia*syrup [348].

2.66. *Momordica charantia*

The effects of*Momordica charantia*in reducing pain was studied inprimary knee osteoarthritis patients. The patients with primary knee osteoarthritis were used*Momordica charantia* (500 mg capsule thrice daily, for 3 months). Pain and symptoms throughout the *Momordica charantia*supplementation period were assessed using knee injury and osteoarthritis outcome score. After 3 months supplementation period, body weight, body mass index, and fasting blood glucose were reduced significantly in the *Momordica charantia*group. There were also significant improvements in knee injury and osteoarthritis outcome score subscales and EQ-5D-3L dimension score, and reduction in analgesic score [349].

Many studies were carried out to investigate the clinical hypoglycemic effects of *Momordica charantia*. The effects of *Momordica charantia*, on fasting and post prandial (2 hours after 75 gm oral glucose intake) serum glucose levels were studied in 100 patients of moderate non-insulin dependent diabetic subjects. Drinking of the aqueous homogenized suspension of the vegetable pulp led to significant reduction (P < 0. 001) of both fasting and post-prandial serum glucose levels. The hypoglycaemic action was observed in 86 (86%) of the patients [350].

*Momordica charantias*oft extract was used orally in a dose of 200 mg twice daily in 15 patients with non-insulin dependent diabetic patient. It was observed that the extract plus half doses of metformin or glibenclamide or both caused hypoglycemia greater than that caused by full doses of the oral hypoglycemic drugs,with 7 days treatment. The extract possessed synergism with oral hypoglycemics and potentiates their hypoglycemia in non-insulin dependent diabetic patient [351].

The effect of powdered fruit was investigated in eight patients with uncomplicated maturity-onset diabetes. The patients were instructed to take the, powdered drug in milk twice daily at the rate of 50 mg/kg body weight, to continue on the carbohydrate deficient diet as before, and not to take any other medication. The results revealedthat the powdered fruit possessedhypoglycaeimic effect in all the patients [352].

A randomised clinical study was carried out to determine the effect of driedfruits of *Momordica charantia* intype 2 diabetes. Dried*Momordica charantia*fruit was administered at a dose of 2 g three times daily, and riboflavin was employed as placebo. All subjects were instructed to maintain their pre-existing oral hypoglycaemic treatment and dietary patterns. Fasting blood sugar and postprandial sugar levels were measured with fructosamine levels at baseline before treatment, at 2 weeks, and at 4 weeks post-treatment. Results revealed nostatistically significant therapeutic effects [353].

On another study,Bitter melon had a modest hypoglycemic effect and significantly reduced fructosamine levels from baseline among patients with type 2 diabetes who received 2g/day. However, the hypoglycemic effect of bitter melon was less than metformin 1g/day [354].

A randomized, double-blind, placebo-controlled trial was conducted to determine the effect of*Momordica charantia*capsules on glycosylated hemoglobin (hemoglobin A1C or HbA1c) levels in diabetic patients with poor sugar control. The difference in mean change in A1C between the two groups was 0. 22% in favor of*Momordica charantia* (95% CI: -0. 40 to 0. 84,P=0. 4825). Furthermore, *Momordica charantia*causedno significant effect on mean fasting blood sugar, total cholesterol, weight, and on serum creatinine, ALT, AST, sodium, and potassium [355].

3. Conclusion

The World Health Organization (WHO) estimates that 4 billion people, 80 percent of the world population, presently use herbal medicine for some aspect of primary health care. Many medicinal plants possessed effective therapeutic

effects with high degree of safety. This review presented a comprehensive overview of the medicinal plantswhich pass the clinical trials with documented efficacy and safety.

Compliance with ethical standards

Acknowledgments

We would like to thank the college of medicine, University of Thi-Qar for support.

References

[1] Govindaraghavan S and Sucher NJ. Quality assessment of medicinal herbs and their extracts: Criteria and prerequisites for consistent safety and efficacy of herbal medicines. Epilepsy Behav 2015;52 (Pt B):363-371.

[2] Chakarski I. Clinical study of a herb combination consisting of A*grimonia eupatoria, Hipericum perforatum, Plantago major, Mentha piperita, Matricaria chamomila* for the treatment of patients with chronic gastroduodenitis. Probl Vatr Med 1982; 10:78-84.

[3] Patrascu V and Chebac PI. Rezultate terapeutice favorabile in porfiria cutanata cu *Agrimonia eupatoria*. Dermato-venerologia 1984; 29: 153-157.

[4] Al-Snafi AE. The pharmacological and therapeutic importance of *Agrimonia eupatoria*- A review. Asian Journal of Pharmaceutical Science and Technology 2015; 5 (2):112-117.

[5] Hautmann C. and Scheithe K. Fluid extract of *Agropyron repens* for the treatment of urinary tract infections or irritable bladder. Results of multicentric post-marketing surveillance. Zeitschrift für Phytotherapie 2000; 21 (5):252-255.

[6] An agency of the European Union. Assessment report on Agropyron repens (L.) P. Beauv. , rhizome,

[7] Al-Snafi AE. Chemical constituents and pharmacological importance of *Agropyronrepens* – A review. Research Journal of Pharmacology and Toxicology2015; 1 (2): 37-41.

[8] Taj Eldin IM , Ahmed EM, and Abd Elwahab HM. Preliminary study of the clinical hypoglycemic effects of *Allium cepa* (Red Onion) in type 1 and type 2 diabetic patients. Environmental Health Insights 2010; 4:71-77.

[9] Bhushan S, Sharma SP, Singh SP *et al.* Study of the hypocholesterolemic effect of onion (*Allium cepa*) on normal human beings. Indian Med Gaz 1979; 16, 249-251.

[10] Jain RC. Effect of garlic on serum lipids, coagulability and fibrinolytic activity of blood. Am J Clin Nutr 1977; 30:1380-1381.

[11] Bordia A. Effect of garlic and blood lipids in patients with coronary heart disease. Am J Clin Nutr 1981; 34: 2100-2103.

[12] Kojuri J, Vosoughi AR and Akrami M. Effects of *Anethum graveolens* and garlic on lipid profile in hyperlipidemic patients. Lipids Health Dis 2007; 6: 5.

[13] Sainani GS, Desai DB, Gorhe NH *et al.* Effect of dietary garlic and onion on serum lipid profile in jain community. Indian J Med Res 1979; 69:776-780.

[14] Kiesewetter H, Jung F, Jung EM *et al*. Effects of garlic coated tablets in peripheral arterial occlusive disease. Clin Investig 1993; 71: 383-386.

[15] Siegel G, Walter A, Engel S *et al.* Pleiotropic effects of garlic. Wien Med Wochenschr 1999; 149: 217-224.

[16] Bordia AK, Joshi HK, Sanadhya YK and Bhu N. Effect of essential oil of garlic on serum fibrinolytic activity in patients with coronary heart disease. Atherosclerosis 1977; 28: 155-159.

[17] Harenberg J, Giese C, and Zimmermann R. Effect of dried garlic on blood coagulation, fibrinolysis, platelet aggregation and serum cholesterol levels in patient with hyperlipoproteinemia. Atherosclerosis 1988; 74: 247-249.

[18] Jung F, Jung EM, Pundir G and Kiesewetter H. Effect of different garlic preparations on the fluidity of blood, fibrinolytic activity and peripheral microcirculation in comparison with placebo. Planta Med 1990; 56: 668.

[19] Lawson LD. Bioactive organosulfur compound of garlic and garlic products: role in reducing blood lipids. In: Kinghorn AD, Balandrin MF, editors. Human medicinal agents from plants. Washington. American Chemical Society 1993; 306-330.

[20] Srivastava KC and Tyagi OD. Effects of a garlic derived principle (ajoene) on aggregation and arachidonic acid metabolism in human blood platelets. Prostaglandins Leukot Essent Fatty Acids 1993; 49: 587-595.

[21] Silagy CA and Neil HA. A meta-analysis of the effect of garlic on blood pressure. J Hypertens 1994; 12: 463-468.

[22] Bolton S, Null G and Troetel WM. The medical uses of garlic-fact and fiction. Am Pharmacol 1982; 22: 40-43.

[23] Srivastava KC, Bordia A and Verma SK. Garlic (*Allium sativum*) for disease prevention. South Afr J Sci 1995; 91: 68-77.

[24] Kiesewetter H, Jung F, Wolf S *et al.* Effect of garlic on thrombocyte aggregation, microcirculation, and other risk factors. International Journal of Clinical pharmacology, Therapy and Toxicology 1991;29:151-155.

[25] Kadir MA, Al-Snafi AE and Farman NA. Comparison between the efficacy of sulpher and garlic in treatment of scabies. Med J Tikrit Univ 1999; 5:122-125.

[26] Al-Snafi AE. Pharmacological effects of *Allium* species grown in Iraq. An overview. International Journal of Pharmaceutical and health care Research2013;1 (4):132-147.

[27] Syed T, Afzal M, Ashfax A, Holt A, Ali A and Ahmad S. Management of genital herpes in men with 0. 5% *Aloe vera* extract in a hydrophilic cream: a placebo-controlled double blind study. Journal of Dermatological Treatment 1997; 8:99-102.

[28] Wang H, Chung J, Ho C, Wu L and Chang S. *Aloe*-emodin effects on arylamin N-acetyltransferase activity in the bacteriaum Helicobacter pylori. Planta Medica 1998;64:176-178.

[29] Blitz J, Smith J and Gerard J. *Aloe vera* gel in peptic ulcer therapy: preliminary report. J American Osteopathic Association 1963; 62:731-735.

[30] Agarwal OP. Prevention of atheromatous heart disease. Angiolog 1985;36: (8). Presented at the 31st Annual Meeting, American College of Angiology and 26th Annual Meeting, International College of Angiology, November 5, 1984 .

[31] Bunyapraphatsara N, Yongchaiyudha S and Rungpitarangsi V. Antidiabetic activity of *Aloe vera L* juice II. Clinical trial in diabetes mellitus patients in combination with glibenclamide. Phytomed 1996; 3:245-248.

[32] Yongchaiyudha S, Rungpitarangsi V, Bunyapraphatsara N and Chokechaijaroenporn O. Antidiabetic activity of *Aloe vera L* juice. I. Clinical trial in new cases of diabetes mellitus. Phytomed 1996; 3: 241-243.

[33] Al-Snafi AE. The pharmacological importance of *Aloe vera*- A review. InternationalJournal of Phytopharmacy Research 2015; 6 (1) : 28-33.

[34] Altman RD and Marcussen KC. Effects of a ginger extract on knee pain in patients with osteoarthritis arthritis. Rheumatism 2001; 44 (11):2531-2538.

[35] Al-Snafi AE. The pharmacological activities of *Alpinia galangal* - A review. International Journal for Pharmaceutical Research Scholars 2014; 3 (1-1): 607-614.

[36] Rouhi H and Ganji H. Effect of *Althaea officinalis* on cough associated with ACE inhibitors. Pakistan Journal of Nutrition 2007; 6 (3): 256-258.

[37] Al-Snafi AE. The Pharmaceutical importance of *Althaea officinalis* and *Althaea rosea*: A Review. Int J Pharm Tech Res 2013; 5 (3):1387-1385.

[38] El-Mofty AM. A preliminary clinical report on the treatment of leucodermia with *Ammi majus* Linn. J Egypt Med Assoc 1948; 31: 651–665.

[39] Fahmy IR and Abu-Shady H. The isolation and properties of ammoidin, ammidin and majudin and their effect in the treatment of leukodermia. Q J Pharm Pharmacol 1984; 21: 499-503.

[40] El-Mofty AM. Further study on treatment of leucodermia with *Ammi majus* Linn. J R Egypt Med Assoc 1952; 35: 1-19.

[41] Selim YA, and Ouf NH. Anti-inflammatory new coumarin from the *Ammi majus* L. Medicinal Chemistry Letters 2012; 2: 1-4.

[42] Ubramanian P, Rajan S and Kumar S. Physico-chemical profile of *Ammi majus* . Ancient Science of Life. 1996; XVI: 142 -147.

[43] El-Mofty AM. A preliminary clinical report on the treatment of leucodermia with *Ammi majus* Linn. J Egypt Med Assoc 1984; 31: 651–665.

[44] Parrish JA. Photochemotherapy of psoriasis with oral methoxsalen and long wave ultraviolet light. N Engl J Med 1974; 291:1207-1211.

[45] El-Mofty AM and El-Mofty M. Psoralen photochemotherapy in contrast to chemotherapy of psoriasis. Med J Cairo Univ 1980; 48:71-83.

[46] El-Mofty AM, El-Sawalhy H and El-Mofty M. Clinical study of a new preparation of 8-methoxypsoralen in photochemotherapy. Int J Dermatol 1994; 33: 588-592.

[47] El-Mofty AM, El-Sawalhy H and El-Mofty M. Photochemotherapy in the treatment of post tinea versicolor hypopigmentation. Med J Cairo Univ 1995; 61 (4), 632–637.

[48] Sidi E, and Bourgeois J. The treatment of vitiligo with *Ammi majus* Linn. J Invest Dermatology 1951;391-395.

[49] Hakim RE. Rediscovery of a treatment for vitiligo. Clio Medica 1969; 4: 277-289.

[50] Parsad D, Saini R and Verma N. Combination of PUVAsol and topical calcipotriol in vitiligo. Dermatology 1998; 197:167-170.

[51] De Berker D A *et al.* Comparison of psoralen-UVB and psoralen UVA photochemotherapy in the treatment of psoriasis. Journal of the American Academy of Dermatology 1997; 36: 577-581.

[52] Collins P *et al.* 8-MOP PUVA for psoriasis: a comparison of minimal phototoxic dose-based regimen with a skin-type approach. British Journal of Dermatology 1996;135: 248-254.

[53] Kavli G and Volden G. Phytophotodermatitis. Photodermatology 1984; 1: 65-75.

[54] Becker SW. Psoralen phototherapeutic agents. Journal of the American Medical Association 1967; 202: 422-424.

[55] Galal EE, Kandil A and Latif MA. Evaluation of cardiac inotropism of *Ammi visnaga* principles by the intra-ventricular technique. Journal of Drug Research of Egypt 1975; 7: 45-57.

[56] Harvengt C and Desager JP. HDL-cholesterol increase in normolipaemic subjects on khellin: a pilot study. International Journal of Clinical Pharmacology Research 1983; 3: 363-366.

[57] Dewar HA and Grimson TA. Khellin in the treatment of angina of effort. Br Heart J 1950; 12: 54-60.

[58] Abdel-Fattah A, Aboul-Enein M N, Wassel GM *et al.* An approach to the treatment of vitiligo by khellin. Dermatologicia 1982; 165:136-140.

[59] Orecchia G, Sangalli ME, Gazzaniga A *et al.* Topical photochemotherapy of vitiligo with a new khellin formulation: preliminary clinical results. J Dermatol Treat 1998; 9: 65-69.

[60] Al-Snafi AE. Chemical constituents and pharmacological activities of *Ammi majus* and *Ammi visnaga*. A review. International Journal of Pharmacy and Industrial Research 2013; 3 (3):257-265.

[61] Al-Jawad FH, Al-Razzuqi RAM, Hashim , HM and Ismael AH. Broncho-relaxant activity of *Nigella sativa* versus *Anthemis nobilis* in chronic bronchial asthma; a comparative study of efficacy. IOSR Journal of Pharmacy 2012; 2 (4): 81-83.

[62] Al-Snafi AE. Medical importance of *Anthemis nobilis* (*Chamaemelum nobilis*)- A review. Asian Journal of Pharmaceutical Science& Technology 2016; 6 (2): 89-95.

[63] Silver AA and Krantz JC. The effect of the ingestion of burdock root on normal and diabetic individuals, a preliminary report. Ann Int Med 1931; 5: 274-284.

[64] Al-Snafi AE. The Pharmacological importance and chemical constituents of *Arctium Lappa*. A review. International Journal for Pharmaceutical Research Scholars 2014; 3 (1-1): 663-670.

[65] Maki KC, Galant R, Samuel P, Tesser J, Witchger MS, Ribaya-Mercado JD, Blumberg JB and Geohas J. Effects of consuming foods containing oat beta- glucan on blood pressure, carbohydrate metabolism and biomarkers of oxidative stress in men and women with elevated blood pressure. Eur J Clin Nutr 2007; 61 (6):786-795.

[66] Nie L, Wise ML, Peterson DM and Meydani M. Avenanthramide, a polyphenol from oats, inhibits vascular smooth muscle cell proliferation and enhances nitric oxide production. Atherosclerosis 2006; 186 (2):260-266.

[67] Chang HC, Huang CN, Yeh DM, Wang SJ, Peng CH and Wang CJ. Oat prevents obesity and abdominal fat distribution, and improves liver function in humans. Plant Foods Hum Nutr 2013; 68 (1):18-23.

[68] Al-Snafi AE. The nutritional and therapeutic importance of*Avena sativa* - An Overview. InternationalJournalof Phytotherapy 2015; 5 (1): 48-56.

[69] Morgan A, and Stevens J. Does *Bacopa monnieri* improve memory performance in older persons? Results of a randomized, placebo-controlled, double-blind trial. The Journal of Alternative and Complementary Medicine 2010;16 (7):753-759.

[70] Stough C, Lloyd J, Clarke J, *et al.* The chronic effects of an extract of *Bacopa monniera* (Brahmi) on cognitive function in healthy human subjects. Psychopharmacology 2001;156:481-484.

[71] Stough CK, Pase MP, Cropley V, Myers S *et al.* A randomized controlled trial investigating the effect of Pycnogenol and Bacopa CDRI08 herbal medicines on cognitive, cardiovascular, and biochemical functioning in cognitively healthy elderly people: The Australian Research Council Longevity Intervention (ARCLI) study protocol (ANZCTR12611000487910). Nutrition Journal 2012;11 (11):2-9.

[72] Roodenrys S, Booth D, Bulzomi S, Phipps A, Micallef C, and Smoker J. Chronic effects of Brahmi (*Bacopa monnieri*) on human memory. Neuropsychopharmacology 2002;27 (2):279-281.

[73] Yadav SK, Jain AK, Tripathi SN and Gupta JP. Irritable bowel syndrome: therapeutic evaluation of indigenous drugs. Indian J Med Res 2003;90:496-503.

[74] Al-Snafi AE. The pharmacology of *Bacopa monniera*. A review. International Journal of Pharma Sciences and Research 2013; 4 (12): 154-159.

[75] Siatka T and Kasparová M. Seasonal changes in the hemolytic effects of the head of *Bellis perennis* L. Ceska Slov Farm 2003;52 (1):39-41.

[76] Thiel W and Borho B. Die Therapie von frischen, traumatischen Blutergüssen der Kniegelenke (Hämarthros) mit Traumeel N Injektionslösung. Biologische Med 1991;20:506-515.

[77] Kunt T. Traumatische Ergüsse des Kniegelenks (Hämarthros und Hydrarthros) und deren Behandlung mit intraartikulären Traumeel-Injektionen. Biologische Med 1983; 12: 344-347.

[78] Al-Snafi AE. The Pharmacological importance of *Bellis perennis* - Areview. InternationalJournalof Phytotherapy 2015; 5 (2): 63-69.

[79] Amirthaveni M and Priya V. Hypoglycemic and hypolipidemic effect of ash gourd (*Benincasa hispida)* and curry leaves (*Murraya koenigii*). International Journal of Current Research 2011; 3 (8):37-42.

[80] Al-Snafi AE. The Pharmacological Importance of *Benincasa hispida*. A review. Int Journal of Pharma Sciences and Research 2013; 4 (12): 165-170.

[81] Shoutai Z. Treatment of 500 cases of dysentery with *Bidens tripartita.* Shandong Journal of Traditional Chinese Medicine 1989; 8:11–12.

[82] Sokolov SJ and Zamotaev IP. Spravocznik po lekarstvennym rastenijam. Moscow, Meditsina. 1990.

[83] Al-Snafi AE. Chemical constituents and pharmacological importance of *Bidens tripartitus* - A review. Ind J of Pharm Sci & Res 2015; 5 (4): 257-263.

[84] Lapaire O, Ramos M, Manegold G, zanetti-Daellenbach R, Birkenmaier A, Holzgreve W and Hoesli I. The impact of the prophylactic or therapeutic application of Bryophyllum (*Bryophyllum calycinum*) on preterm delivery- A prospective study. European Journal of Integrative Medicine 2008; 1 (1): 28.

[85] Al-Snafi AE. The Chemical constituents and pharmacological effects of *Bryophyllum calycinum*-A review. Journal of Pharma Sciences and Research 2013; 4 (12): 171-176.

[86] Duran V, Matic M, Jovanovć M, Mimica N, Gajinov Z, Poljacki M and Boza P. Results of the clinical examination of an ointment with marigold (*Calendula officinalis*) extract in the treatment of venous leg ulcers 2005;27 (3):101-106.

[87] Babaee N, Moslemi D, Khalilpour M, Vejdani F, Moghadamnia Y,Bijani A, Baradaran M, Kazemi MT, Khalilpour A, Pouramir M and Moghadamnia AA. Antioxidant capacity of *Calendula officinalis* flowers extract and prevention of radiation induced oropharyngeal mucositis in patients with head and neck cancers: arandomized controlled clinical study. DARU Journal of Pharmaceutical Sciences 2013; 21:18-24.

[88] Chakurski I, Matev M, Koichev A, Angelova I and Stefanov G. Treatment of chronic colitis with an herbal combination of *Taraxacum officinale, Hipericum perforatum, Melissa officinaliss*, *Calendula officinalis* and *Foeniculum vulgare*. Vutr Boles 1981; 20: 51-54.

[89] Al-Snafi AE. The Chemical constituents and pharmacological effects of *Bryophyllum calycinum*-A review. Journal of Pharma Sciences and Research 2013; 4 (12): 171-176.

[90] Falguni S and Minoo P. Use of *Calotropis procera* (Ait.) R. Br. in treatment of eczema: A pilot study. International Journal of Drug Discovery and Herbal Research (IJDDHR) 2012; 2 (4): 493-498.

[91] Al-Snafi AE. The constituents and pharmacological properties of *Calotropis procera*- An Overview. International Journal of Pharmacy Review & Research 2015; 5 (3): 259-275.

[92] Shi NN, Cheng CS,Zha ZQ, Zhongguo Zhong Xi et al. Clinical study of safflower injection in treating and preventing the vascular crisis after free flap transplantation 2011; 31 (10): 1322-1327.

[93] Suzuki K, Tsubaki S, Fujita M, Koyama N, Takahashi M,Takazawa K. Effects of safflower seed extract on arterial stiffness. Vasc Health Risk Manag 2014; 6:1007-1014.

[94] Al-Snafi AE. The chemical constituents andpharmacological importance of *Carthamus tinctorius* - An overview. Journal of Pharmaceutical Biology 2015; 5 (3): 143-166.

[95] Yosefi SS, Sadeghpour O, Sohrabvand F, Atarod Z, Askarfarashah M, Ateni TR and Yekta NH. Effectiveness of *Carum carvi* on early return of bowel motility after caesarean section. Euro J Exp Bio 2014; 4 (3):258-262.

[96] Madisch A, Holtmann G, Mayr G, Vinson B, Hotz J. Treatment of functional dyspepsia with a herbal preparation. A double-blind, randomized, placebo-controlled, multicenter trial 2004;69 (1);45-52.

[97] Mashhad University of Medical Sciences. Effect of *Carum carvi* on thyroid hormones and TSH level, http://clinicaltrials. gov/ct2/home

[98] Al-Snafi AE. The chemical constituents and pharmacological effects of*Carum carvi* - A review. IndianJournalof Pharmaceutical ScienceandResearch 2015; 5 (2): 72-82.

[99] Olsen NJ,Branch VK,Jonnala G, Seskar M andCooper M. Phase 1, placebo-controlled, dose escalation trial of chicory root extract in patients with osteoarthritis of the hip or knee. BMC Musculoskeletal Disorders 2010; 11, article 156.

[100] Al-Snafi AE. Medical importance of *Cichorium intybus* – A reviewIOSR Journal of Pharmacy 2016; 6 (3): 41-56.

[101] Guo Q, Zhou Y, Wang CJ, Huang YM, Lee YT, Su MH andLu J. An open-label, nonplacebo-controlled studyon*Cistanche tubulosa* glycoside capsules (Memoregain®) for treating moderate Alzheimer's Disease. Am J Alzheimers Dis Other Demen 2013;28 (4):363-370.

[102] Health supplement herbal food Memoregain, http://www. taiwantrade. com. tw/EP/ sinphar/products-detail/en-US/520667/Health-Supplement-herbal-food- Memoregain/

[103] Seok J, Kim TS, Kwon HJ, Lee SP, Kang MH, Kim BJ and Kim MN. Efficacy of *Cistanche tubulosa* and *Laminaria japonica* extracts (MK-R7) supplement in preventing patterned hair loss and promoting scalp health. Clin Nutr Res 2015; 4 (2): 124-131.

[104] Al-Snafi AE. Bioactive metabolites and pharmacology of *Cistanche tubulosa*- A review. IOSR Journal of Pharmacy 2020; 10 (1): 37-46.

[105] Huseini H, Darvishzadeh F, Heshmat R, Jafariazar Z, Raza M and Larijani B. The clinical investigation of *Citrullus colocynthis* (L.) Schrad fruit in treatment of Type II diabetic patients: a randomized, double blind, placebo-controlled clinical trial. Phytotherapy Research 2009;23 (8): 1186-1189.

[106] Heydari M, Homayouni K, Hashempur MH andShams M. Topical*Citrullus colocynthis* in painful diabetic neuropathy: a double-blind randomized placebo-controlled clinical trial. J Diabetes 2015;doi: 10. 1111/1753-0407. 12287.

[107] Rahbar AR and Nabipour I. The hypolipidemic effect of *Citrullus colocynthis* on patients with hyperlipidemia. Pak J Biol Sci2010; 13 (24):1202-1207.

[108] Al-Snafi AE. Chemical constituents and pharmacological effects of *Citrullus colocynthis* - A review. IOSR Journal of Pharmacy 2016; 6 (3): 57-67.

[109] ReshefN, Hayari Y, Goren C, Boaz M, Madar Z andKnobler H. Antihypertensive effect of sweetie fruit in patients with stage I hypertension. AmJ Hypertens2005; 18 (10): 1360-1363.

[110] Asgary S and Keshvari M. Effects of *Citrus sinensis* juice on blood pressure. ARYA Atheroscler2013; 9 (1): 98-101.

[111] Baars EW,Jong M, Nierop AFM,Boers I andSavelkoul FHJ. Citrus/Cydonia compositum subcutaneous injections versus nasal spray for seasonal allergic rhinitis: A randomized controlled trial on efficacy and afety. ISRN Allergy 2011;doi:10. 5402/2011/836051

[112] Al-Snafi AE. Nutritional value and pharmacological importance of citrus species grown in Iraq. IOSR Journal of Pharmacy 2016; 6 (8): 76-108.

[113] Tripathi KD. Essential of medical pharmacology, 5th ed. Jaypee BrothersMedical Publications, New Delhi 2003.

[114] Nuki G. Colchicine: Its mechanism of action and efficacy in crystal-induced inflammation. Curr Rheumatol Rep 2008;10:218-227.

[115] Imazio M, Bobbio M, MD; Cecchi E, Demarie D, Demichelis B, Pomari F, Moratti M, GaschinoG, Giammaria M, Ghisio A, Belli R and Trinchero R. Colchicine in Addition to Conventional Therapy for Acute Pericarditis: Results of the colchicine for acute pericarditis (COPE) trial. Circulation 2005; 112: 2012-2016.

[116] Wahba A and Cohen H. Therapeutics trials with oral colchicines in psoriasis. Acta Derm Venereol 1980;60:515-520.

[117] Kaidbey KH, Petrozzi JW and Kligman AM. Topical colchicine therapy for recalcitrant psoriasis. Arch Dermatol 1975;111:33-36.

[118] Horiguchi M, Takigawa M and Imamura S. Treatment of generalized pustular psoriasis with methotrexate and colchicine. Arch Dermatol 1981;117:760.

[119] Zachariae H, Kragballe K and Herlin T. Colchicine in generalized pustular psoriasis: clinical response and antibody-dependent cytotoxicity by monocytes and neutrophils. Arch Dermatol Res 1982;274:327-333.

[120] Mori S, Hino K, Izumi H and Hino H. Clinical manifestations and treatment of pustulosis palmaris et plantaris. J Dermatol 1976;86:671.

[121] Seideman P, Fjellner B and Johannesson A. Psoriatic arthritis treated with oral colchicine. J Rheumatol 1987;14:777-779.

[122] Suehisa S and Tagami H. Treatment of acute febrile neutrophilic dermatosis (Sweet's syndrome) with colchicine. Br J Dermatol 1981;105:483.

[123] Silvers DN, Juhlin EA, Berczeller PH and McSorley J. Treatment of dermatitis herpetiformis with colchicine. Arch Dermatol 1980;116:1373-1374.

[124] Megahed M and Scharffetter-Kochanek K. Epidermolysis bullosa acquisita: Successful treatment with colchicine. Arch Dermatol Res 1994;286:35-46.

[125] Zeharia A, Hodak E, Mukamel M, Danziger Y and Mimouni M. Successful treatment of chronic bullous dermatosis of childhood with colchicine. J Am Acad Dermatol 1994;30:660-661.

[126] Wiles JC, Hansen RC and Lynch PJ. Urticarial vasculitis treated with colchicine. Arch Dermatol 1985;121:802-805.

[127] Bibas R, Gaspar NK and Ramos-e-Silva M. Colchicine for dermatological diseases. J Drugs Dermatol 2005;4:196-204.

[128] Zemer D, Pras M, Sohar E, Modan M, Cabili S and Gafni J. Colchicine in the prevention and treatment of the amyloidosis of familial Mediterranean fever. N Engl J Med 1986;314:1001-1005.

[129] Konda C and Rao AG. Colchicine in dermatology. IJDVL2010;76 (2):201-205.

[130] Ben-Chetrit E and Levy M. Familial Mediterranean fever. Lancet 1998;351:659-664.

[131] Ozkaya Nand Yalçinkaya F. Colchicine treatment in children with familial Mediterranean fever. Clin Rheumatol 2003;22 (4-5):314-317.

[132] Zadeh N, Getzug T and Grody W. Diagnosis and management of familial Mediterranean fever: Integrating medical genetics in a dedicated interdisciplinary clinic. Genetics in Medicine 2011; 13: 263-269.

[133] Al-Snafi AE. Medicinal importance of *Colchicum candidum*- A review. The Pharmaceutical and Chemical Journal 2016;3 (2):111-117.

[134] Jagtap AG, Shirke SS andPhadke AS. A polyherbal formulation compares favorably to prednisolone in experimental models of inflammatory bowel diseases. Reprod Toxicol 2007 ;23 (2):182-191.

[135] Waheed A, Miana GA, Ahmad SI and Khan MA. Clinical investigationof hypoglycemic effect of *Coriandrum sativum* in type-2 (NIDDM) diabetic patients. Pakistan Journal of Pharmacology 2006; 23 (1): 7-11.

[136] Naquvi KJ, Ali M and Ahamad J. Antidiabeticactivity of aqueous extract of *Coriandrum sativum* L. fruits in streptozotocin induced rats. Int J Pharm Pharm Sci 2012; 4 (Suppl 1): 239-240.

[137] Yaghini J, Shahabooei M, Aslani A, Zadeh MR, Kiani S and Naghsh N. Efficacy of a local-drug delivery gel containing extracts of *Quercus brantii* and *Coriandrum sativum*as an adjunct to scaling and root planing in moderate chronic periodontitis patients. J Res Pharm Pract2014; 3 (2): 67-71.

[138] Al-Snafi AE. A review on chemical constituents andpharmacological activities ofCoriandrum sativum. IOSR Journal of Pharmacy 2016; 6 (7): 17-42.

[139] Noorbala AA, Akhondzadeh S, Tahmacebi-Pour N andJamshidi AH. Hydro-alcoholicextract of*Crocus sativus* L. versus fluoxetine in the treatment of mild to moderatedepression: a double-blind, randomized pilot trial. J Ethnopharmacol2005; 97 (2):281-284.

[140] Basti AA, Moshiri E, Noorbala A, Jamshidi A,Abbasi SH and Akhondzadeh S. Comparison of petal of *Crocus sativus* L. and fluoxetine in the treatment of depressed outpatients: A pilot double-blind randomized trial. Progress in Neuro-Psychopharmacology & Biological Psychiatry 2007; 31: 439-442.

[141] Akhondzadeh S, Tahmacebi-Pour N, Noorbala AA, Amini H, Fallah-Pour H, Jamshidi AH and Khani M. *Crocus sativus* L. in the treatment of mild to moderate depression: a double-blind, randomized and placebocontrolled trial. Phytother Res. 2005; 19: 148 -1 51.

[142] Moshiri E, Basti AA, Noorbala AA, Jamshidi AH, Hesameddin Abbasi S, Akhondzadeh S. *Crocus sativus* L. (petal) in the treatment of mild-to-moderate depression: a double-blind, randomized and placebo controlled trial. Phytomedicine 2006; 13: 607- 611.

[143] Akhondzadeh Basti A, Moshiri E, Noorbala AA, Jamshidi AH, Abbasi SH and Akhondzadeh S. Comparison of petal of *Crocus sativus* L. and fluoxetine in the treatment of depressed outpatients: a pilot double-blind randomized trial. Prog. Neuropsychopharmacol Biol. Psychiatry 2007; 31: 439 -442.

[144] Akhondzadeh S, Shafiee Sabet M, Harirchian MH, Togha M, Cheraghmakani H, Razeghi S, Hejazi SS, Yousefi MH, Alimardani R, Jamshidi A,Rezazadeh SA,Yousefi A, Zare F, Moradi A and Vossoughi A. A 22-week, multicenter, randomized, double-blind controlled trial of*Crocus sativus* in the treatment of mild-to-moderate Alzheimer's disease. Psychopharmacology (Berl)2010; 207 (4): 637-643.

[145] Verma SK andBordia A. Antioxidant property of saffron in man. Indian J Med Sci1998; 52: 205-207.

[146] Mohammadzadeh-Moghadam H, Nazari SM, Shamsa A,Kamalinejad M,Esmaeeli H, Asadpour AA andKhajavi A. Effects of a topical saffron (*Crocus sativus* L) gel on erectile dysfunction in diabetics: A randomized, parallel-group, double-blind, placebo-controlled trial. J Evid Based Complementary Altern Med 2015,doi:10. 1177/2156587215583756

[147] Al-Snafi AE. The pharmacology of *Crocus sativus*- A review. IOSR Journal of Pharmacy 2016; 6 (6): 8-38.

[148] Zare R, Heshmati F, Fallahzadeh H and Nadjarzadeh A. Effect of cumin powder on body composition and lipid profile in overweight and obese women. Complement Ther Clin Pract 2014; 20 (4): 297-301.

[149] Samani KG and Farrokhi E. Effects of cumin extract on oxLDL, paraoxanase 1 activity, FBS, total cholesterol, triglycerides, HDL-C, LDL-C, Apo A1, and Apo B in in the patients with hypercholesterolemia. Int J Health Sci (Qassim) 2014; 8 (1):39-43.

[150] Taghizadeh M, Memarzadeh MR, Asemi Z andEsmaillzadeh A. Effect of the *Cuminum cyminum* L intake on weight loss, metabolic profiles and biomarkers of oxidative stress in overweight subjects: A randomized double-blind placebo-controlled clinical trial. Ann Nutr Metab 2015; 66 (2-3):117-124.

[151] Al-Snafi AE. The pharmacological activities of *Cuminum cyminum* - A review. IOSR Journal of Pharmacy 2016; 6 (6): 46-65.

[152] Firoozabadi A,Zarshenas MM,Salehi A,Jahanbin S andMohagheghzadeh A . Effectiveness ofCuscuta planiflora Ten. and Nepeta menthoides Boiss. & Buhse in major depression: a triple-blind randomized controlled trial study. Journal of Evidence-Based Complementary & Alternative Medicine 2015; 20 (2): 94-97.

[153] Al-Snafi AE. Traditional uses, constituents and pharmacological effects of *Cuscuta planiflora* . The Pharmaceutical and Chemical Journal 2016; 3 (4): 215-219.

[154] Baars EW,Jong M, Nierop AFM,Boers I andSavelkoul FHJ. Citrus/Cydonia compositum subcutaneous injections versus nasal spray for seasonal allergic rhinitis: A randomized controlled trial on efficacy and afety. ISRN Allergy 2011;doi:10. 5402/2011/836051

[155] Al-Snafi AE. The medical importance of *Cydonia oblonga*- A review. IOSR Journal of Pharmacy 2016; 6 (6): 87-99.

[156] Saxena RC, Punhami, Palit TK, Garg KC, Singh N andKohli RP. Preliminary report on the anti-inflammatory activity of *Cyperus rotundus* in cojunctivities (in human subjects). Indian J Pharm 1971; 3: 9.

[157] Singh N, Singh SP, Dixit KS, Saxena RC and Kohli RP. A placebo controlled clinical trial of *Cyperus rotundus*, *Withania somnifera* and their combination in cases ofrheumatoid arthritis. Proc International Seminar on Clinical Pharmacology in Developing Countries, Lucknow, India 1986; 2:18-21.

[158] Mohammed A and Ghada F. Topical*Cyperus rotundus* oil: a new therapeutic modality with comparableefficacy to Alexandrite laser photo-epilation. Aesthet Surg J2014; 34 (2): 298-305.

[159] Al-Snafi AE. A review on *Cyperus rotundus* A potential medicinal plant. IOSR Journal of Pharmacy 2016; 6 (7):32-48.

[160] Lindholm P, Gullbo J, Claeson P, Göransson U, Johansson S, Backlund A, Larsson R andBohlin L. Selective cytotoxicity evaluation in anticancer drug screening of fractionated plant extracts. J Biomol Screen2002; 7 (4): 333-340.

[161] Hauptman PJandKelly RA. Cardiovascular drugs, Digitalis. *Circulation* 1999; 99: 1265-1270.

[162] Al-Snafi AE. Medical importance of *Datura fastuosa* (syn: *Datura metel*) and *Datura stramonium* - A review. IOSR Journal of Pharmacy 2017;7 (2):43-58.

[163] Ebadi M. Pharmacodynamic basis ofherbal medicine. 2nd ed. CRC Press, Taylor & Francis Group 2007: 311-318.

[164] Abula T, Rao SA, Mengistu A,Worku S,Legesse E andAberra M. Pharmacology. University of Gondar 2004: 46.

[165] El Hemaly AK. Nocturnal enuresis: pathogenesis and treatment. Int Urogynecol J Pelvic Floor Dysfunct 1998; 9 (3): 129-131.

[166] Rudolf G M. The ephedrine treatment of nocturnal enuresis. The British Journal of Psychiatry1948; 94 (396): 629-640.

[167] Shekelle PG, Hardy ML, Morton SC, *et al*. Efficacy and safety of ephedra and ephedrine for weight loss and athletic performance. A meta-analysis. JAMA 2003; 289:1537-1545.

[168] Al-Snafi AE. Therapeutic importance of*Ephedraalata*and *Ephedrafoliata*- A review. Indo Am J P Sci 2017; 4 (02): 399-406.

[169] Asgharikhatooni A, Bani S,Hasanpoor S,Alizade SM, andJavadzadeh Y. The effect of *Equisetum arvense* (horse tail) ointment on wound healing and pain intensity after episiotomy: A randomized placebo-controlled trial. Iran Red Crescent Med J 2015; 17 (3): e25637. doi: 10. 5812/ircmj. 25637

[170] Sparavigna A,Caserini M,Tenconi1 B,Ponti1 ID and Palmieri R. Effects of a novel nail lacquer based on hydroxypropyl-chitosan (HPCH) in subjects with fingernail onychoschizia. J Dermatolog Clin Res 2014; 2 (2): 1013.

[171] Carneiro DM,Freire RC, Honório TC, Zoghaib I, Cardoso FFS, Tresvenzol LMF,Paula JR,Sousa ALL,Jardim PCBV andCunha LC. Randomized, double-blind clinical trial to assess the acute diuretic effect of *Equisetum arvense* (field horsetail) in healthy volunteers. Evidence-Based Complementary and Alternative Medicine 2014, http://dx. doi. org/10. 1155/2014/760683

[172] Al-Snafi AE. The pharmacology of *Equisetum arvense*- A review. IOSR Journal of Pharmacy 2017;7 (2):31-42.

[173] Hanus M,Lafon J and Mathieu M. Double-blind, randomised, placebo-controlled study to evaluate the efficacy and safety of a fixed combination containing two plant extracts (*Crataegus oxyacantha* and *Eschscholtzia californica*) andmagnesium in mild-to-moderate anxiety disorders. Current Medical Research and Opinion 2004; 20 (1): 63–71.

[174] Al-Snafi AE. *Eschscholzia californica*: A phytochemical and pharmacological review. Indo Am J P Sci 2017; 4 (02): 257-263.

[175] Nagata H, Inagaki Y, Tanaka M, Ojima M, Kataoka K, Kuboniwa M, Nishida N, Shimizu K, Osawa K andShizukuishi S. Effect of Eucalyptus extract chewing gum on periodontal health: a double-masked, randomized trial. J Periodontol2008; 79 (8): 1378-1385.

[176] Al-Snafi AE. The pharmacological and therapeutic importance of *Eucalyptus* species grown in Iraq. IOSR Journal ofPharmacy 2017; 7 (3): 72-91.

[177] Khurshid R, Saleem M, Karim S and Mir M. Antipyretic, antiviral and antithrombotic properties of*Euphorbia hirta*against Dengue fever. Pharmacia 2013;60 (3): 8.

[178] Al-Snafi AE. Pharmacology and therapeutic potential of*Euphorbia hirta* (Syn: *Euphorbiapilulifera*) - A review. IOSR Journal of Pharmacy 2017;7 (3): 7-20.

[179] Ihme N, Kiesewetter F, Jung F, Hoffmann KH, Birk A, Muller A and Grutzner KI. Leg oedema protection from a buckwheat herb tea in patients with chronic venous insuffenciency: a single, randomized. double blind, placebo-controlled clinical trial. Eur J Clin Pharmocol 1996; 50: 443-447.

[180] Al-Snafi AE. A review on*Fagopyrumesculentum*:A potential medicinal plant. IOSR Journal of Pharmacy 2017;7 (3): 21-32.

[181] Serraclara A, Hawkins F, Pérez C, Domínguez E, Campillo JE and Torres MD. Hypoglycemic action of an oral fig-leaf decoction in type-I diabetic patients. Diabetes Res Clin Pract 1998; 39 (1): 19-22.

[182] Bohlooli S, Mohebipoor A, Mohammadi S, Kouhnavard M and Pashapoor S. Comparative study of fig tree efficacy in the treatment of common warts (Verruca vulgaris) vs. cryotherapy. Int J Dermatol 2007; 46 (5): 524-526.

[183] Al-Snafi AE. Nutritional and pharmacological importance of*Ficus carica* - A review. IOSR Journal ofPharmacy 2017;7 (3):33-48.

[184] Virani NV, Chandola HM, Vyas SN and Jadeja DB. Clinical study on erectile dysfunction in diabetic and non-diabetic subjects and its management with *Ficus relegiosa* Linn. Ayu 2010;31 (3):272-279.

[185] Al-Snafi AE. Pharmacology of *Ficus religiosa*- A review. IOSR Journal ofPharmacy 2017; 7 (3): 49-60.

[186] Picon PD, Picon RV, Costa AF, Sander GB, Amaral KM, Aboy AL and Henriques AT. Randomized clinical trial of a phytotherapic compound containing *Pimpinella anisum*, *Foeniculum vulgare*, *Sambucus nigra*, and *Cassia augustifolia* for chronic constipation. *BMC Complementary and Alternative Medicine* 2010, 10:17, http://www. biomedcentral. com/1472-6882/10/17

[187] Delaram M andSadeghian, Z. The comparison of Echinophora platyloba and Fennel effects on the primary dysmenorrhea. Sci J Hamadan Univ Med Sci 2011;18 (1):42-47.

[188] Torkzahrani Sh, Akhavan-Amjadi M, Mojab F, Alavimajd H. Clinical effects of *Foeniculumvulgare* extract on primary dysmenorrhea. J Reprod Infertil. 2007; 8 (1):45-51.

[189] Javidnia K, Dastgheib L, Mohammadi Samani S andNasiri A. Antihirsutism activity of Fennel (fruits of Foeniculum vulgare) extract. A double-blind placebo controlled study. Phytomedicine 2003;10 (6-7):455-458.

[190] Akha O, Rabiei K,Kashi Z, Bahar A, Zaeif-Khorasani E, Kosaryan M, Saeedi M, Ebrahimzadeh MA and Emadian O. The effect of fennel (*Foeniculum vulgare*) gel 3% in decreasing hair thickness in idiopathic mild to moderate hirsutism, A randomized placebo controlled clinical trial. Caspian J Intern Med 2014; 5 (1): 26-29.

[191] Al-SnafiAE. The chemical constituents and pharmacological effects of *Foeniculum vulgare* - A review. IOSR Journal ofPharmacy 2018; 8 (5):81-96.

[192] Reynier M, LagrangenE,Haring J, VigourouxnM. Effet du nebulisat de Fumeterre, de la Protopine et de la Papaverine sur la secretion biliaire du rat en hypocholerese . Travaux de la Societe de Pharmacie de Montpellier 1977, 37 (2): 73-84.

[193] Fablet J, Coluin R and Geffroy Y. Action therapeutiques du Fumaria officinalis dans le syndrome hepatobiliaires et les migraines. Actualite Therap 1968: 3376-3379.

[194] Hunold W. Klinische erfahrungen mit dem amphocholeretikum oddibil bei primar und sekundar organischen sowie funktionellen cholezysto- und cholangiohepatopathien. Zeitschrift fur Allgemeinmedizin 1975; 51 (5): 237-241.

[195] Kopp H. Choleretische Wirkung und Vertraeglichkeit von Chol-Kugeletten® bei Cholezystopathien. *Therapiewoche* 1979, 29: 5645-5655.

[196] Brinkhaus B, Hentschel C, Hentschel C, Von Keudell C, Schindler G et al. Herbal medicine with curcuma and fumitory in the treatment of irritable bowel syndrome: A randomized, placebo-controlled, double-blind clinical trial. Scandinavian Journal of Gastroenterology 2005;40 (8):936- 943.

[197] Al-Snafi AE. Constituents and pharmacology of *Fumaria officinalis*- A review. IOSRJournal of Pharmacy 2020; 10 (1):17-25.

[198] Akrami R, Hashempur MH, Tavakoli A, Nimrouzi M,Sayadi M, Roodaki M, Roozbeh J and Faridi P. Effects of *Fumaria parviflora* L on uremic pruritus in hemodialysis patients: A randomized, double-blind, placebo-controlled trial. Jundishapur J Nat Pharm Prod 2016 doi: 10. 17795/jjnpp-39744.

[199] Jowkar F, Jamshidzadeh A, Mirzadeh Yazdi A and Pasalar M. The effects of *Fumaria parviflora* L extract on chronic hand eczema: a randomized double-blind placebo controlled clinical trial. Iran Red Crescent Med J 2011;13 (11):824-828.

[200] Al-Snafi AE. *Fumaria parviflora*- A review. Indo Am J P Sc 2018; 5 (3): 1728-1738.

[201] Mori K, Sakai H, Suzuki S, et al. Effects of glycyrrhizin (SNMC: *Stronger neo minophagenin* hemophilia patients with HIV-1 infection. Tohoku JExp Med 1990; 162 (2): 183-193.

[202] Jawad FH, Al-Razzuqi RAM, Hashim HM andAl-Bayati NJM. *Glycyrrhiza glabra* versus Boswellia carterii in chronic bronchial asthma: A comparative study of efficacy. Indian Journal of Allergy, Asthma and Immunology 2012; 26 (1): 6-8.

[203] Yasui S, Fujiwara K, Tawada A, Fukuda Y, Nakano M and Yokosuka O. Efficacy of intravenous glycyrrhizin in the early stage of acute onset autoimmune hepatitis. Dig Dis Sci 2011;56 (12):3638-3647.

[204] Adel M, Alousi LA and Salem HA. Licorice: A possible anti-inflammatory and anti-ulcer drug. AAPS Pharm Sci Tech2005; 6: 74-82.

[205] Horwich L andGalloway R. Treatment of gastric ulceration with carbenoxolone sodium: clinical and radiological evaluation. Br Med J 1965; 2: 1274-1277.

[206] Fraser PM, Doll R, Langman MJ, Misiewicz JJ andShawdon HH. Clinical trial of a new carbenoxolone analogue (BX24), zinc sulphate, and vitamin A in the treatment of gastric ulcer. Gut1972;13: 459-463.

[207] Montgomery RD, Lawrence IH, Manton DJ, Mendl K and Rowe P. A controlled trial of carbenoxolone sodium capsules in the treatment of duodenal ulcer. Gut1968, 9: 704-706.

[208] Doll R, Langman MJS andShawdon HH. Treatment of gastric ulcer with carbenoxolone: antagonistic effect of spironolactone. Gut1968; 9: 42-45.

[209] Tewari SN, Wilson AK. Deglycyrrhizinated liquorice in duodenal ulcer. Practitioner 1973; 210:820-823.

[210] Kassir ZA. Endoscopic controlled trial of four drug regimens in the treatment of chronic duodenal ulceration. Ir Med J1985;78:153-156.

[211] Poswillo D andPartridge M. Management of recurrent aphthous ulcers. BrDent J 1984;157:55-57.

[212] Das SK, Das V, Gulati AK andSingh VP. Deglycyrrhizinated liquorice in apthous ulcers. J Assoc Physicians India 1989; 37:647.

[213] Da Nagao Y, Sata M, Suzuki H, *et al*. Effectiveness of glycyrrhizin for oral lichen planus in patients with chronic HCV infection. J Gastroenterol 1996;31:691-695.

[214] Al-SnafiAE. *Glycyrrhiza glabra*: A phytochemical and pharmacological review. IOSR Journal ofPharmacy 2018;8 (6): 1-17.

[215] Oberto G, Bauza E, Berghi A, Portolan F, Botto JM, Peyronel D, Dal Farra C and Domloge N. Cotton honeydew (*Gossypium hirsutum* L.) extract offers very interesting properties for hair cosmetics and care products. Drugs Exp Clin Res 2005; 31 (4):131-140.

[216] Zhu PD. Electron microscopic observations on the effect of gossypol on the human endometrium. Zhonghua Fu Chan Ke. Za Zhi 1984; 19: 246-249.

[217] Wu D. An overview of the clinical pharmacology and therapeutic potential of gossypol as a male contraceptive agent in gynaecological disease. Drugs 1989; 38: 333-341.

[218] Randel RD, Chase CC and Wyse SJ. Effects of gossypol and cottonseed products on reproduction of mammals. J Anim Sci 1992; 70 (5), 1628-1638.

[219] Gadelha ICN,do Nascimento Rangel AH, Silva AR and Soto-Blanco B. Efeitos do gossipol na reproduc¸˜ao animal. Acta Veterinaria Brasilica 2011;5 (2): 129–135.

[220] Flack MR, Pyle RG, Mullen NM, Lorenzo B, Wu YW, Knazek RA, Nisula BC and Reidenberg MM. Oral gossypol in the treatment of metastatic adrenal cancer. J Clin Endocrinol Metab 1993; 76 (4): 1019-1024.

[221] Al-SnafiAE. Chemical constituents and pharmacological activities of*Gossypium herbaceum* and*Gossypiumhirsutum* - A review. IOSR Journal ofPharmacy 2018; 8 (5):64-80.

[222] Zeil S, Schwanebeck U andVogelberg C. Tolerance and effect of an add-on treatment with a cough medicine containing ivy leaves dry extract on lung function in children with bronchial asthma. Phytomedicine 2014;21 (10):1216-1220.

[223] Hofmann D, Hecker M andVölp A. Efficacy of dry extract of ivy leaves in children with bronchial asthma-a review of randomized controlled trials. Phytomedicine2003; 10 (2-3):213-220.

[224] Fazio S, Pouso J, Dolinsky D, Fernandez A, Hernandez M, Clavier G andHecker M. Tolerance,safety and efficacy of Hedera helix extract in inflammatory bronchial diseasesunder clinical practice conditions: a prospective, open, multicentre postmarketingstudy in 9657 patients. Phytomedicine 2009;16 (1):17-24.

[225] Schmidt M, Thomsen M and Schmidt U. Suitability of ivy extract for the treatment of paediatric cough. Phytother Res 2012;26 (12):1942-1947.

[226] Büechi S, Vögelin R, von Eiff MM, Ramos M and Melzer J. Open trial to assess aspects of safety and efficacy of a combined herbal cough syrup with ivy and thyme. Forsch Komplementarmed Klass Naturheilkd 2005;12 (6):328-332.

[227] Cwientzek U, Ottillinger B and Arenberger P. Acute bronchitis therapy with ivy leaves extracts in a two-arm study. A double-blind, randomised study vs. another ivy leaves extract. Phytomedicine 2011;18 (13):1105-1109.

[228] Kemmerich B, Eberhardt R and Stammer H. Efficacy and tolerability of a fluid extract combination of thyme herb and ivy leaves and matched placebo in adults suffering from acute bronchitis with productive cough: A prospective, double-blind, placebo-controlled clinical trial. Arzneim. -Forsch/Drug Res 2006; 56 (9): 652−660.

[229] Al-SnafiAE. Pharmacological and therapeutic activities of*Hedera helix*- A reviewIOSR Journal ofPharmacy 2018; 8 (5): 41-53.

[230] Darmstadt GL, Badrawi N, Law PA, Ahmed S, Bashir M, Iskander I, Al Said D, El Kholy A, Husein MH, Alam A, Winch PJ, Gipson R andSantosham M. Topically applied sunflower seed oil prevents invasive bacterial infections in preterm infants in Egypt: a randomized, controlled clinical trial. Pediatr Infect Dis J 2004; 23 (8):719-725.

[231] Al-Snafi AE. The pharmacological effects of *Helianthus annuus*- A review. Indo Am J P Sc 2018; 5 (3):1745-1756.

[232] Sharma K,Pareek A andChauhan ES. Evaluation of hyperglycemic and hyperlipidemic mitigating impact of *Hibiscus rosa sinensis* (Gudhal) flower in type II diabetes mellitus subjects. International Journal of Applied Biology and Pharmaceutical Technology 2016; 7 (2): 223-228.

[233] Al-Snafi AE. Chemical constituents, pharmacological effects and therapeutic importance of *Hibiscus rosa-sinensis*-A review. IOSR Journal of Pharmacy 2018; 8 (7): 101-119.

[234] Harera-Arellano A, Flores-Romero S, Chavez-Soto MA and Tortoriello J. Effectiveness and tolerability of a standardized extract from Hibiscus sabdariffa in patients with mild to moderate hypertension: A controlled and randomized clinical trial. Phytomedicine 2004; 11 (5): 375-382.

[235] Sudan P, Behl T, Sharma S and Sabharwa S. Treatment of hypertension with *Hibiscus sabdariffa* in Diabetes type-II patients. The Pharmaceutical and Chemical Journal2014; 1 (3):25-27.

[236] McKay DL,Chen O, Saltzman E andBlumberg JB. Hibiscus Sabdariffa L. Tea (Tisane)lowers blood pressure in prehypertensive and mildly hypertensive adults. J Nutr2010; 140: 298–303.

[237] Joven J, March I, Espinel E, Fernández-Arroyo S, Rodríguez-Gallego E, Aragonès G, Beltrán-Debón R, Alonso-Villaverde C, Rios L, Martin-Paredero V, Menendez JA, Micol V, Segura-Carretero A and Camps J. Hibiscus sabdariffa extract lowers blood pressure and improves endothelial function. Mol Nutr Food Res 2014;58 (6):1374-1378.

[238] Clinical effects produced by a standardized herbal medicinal product of Hibiscussabdariffa on patients with hypertension. A randomized, double-blind, lisinopril-controlled clinical trial. Planta Med 2007;73 (1):6-12.

[239] Lin T, Lin H, Chen C and Chou MC. Hibiscus sabdariffa extract reduces serum cholesterolin men and women. Nutr Res 2007; 27:140-145.

[240] Mzaffari-Khosravi H, Jalali-Khanabadi BA, Afkhami-Ardekani M and Fatehi F. Effects of sour tea (*Hibiscus sabdariffa*) on lipid profile and lipoproteins in patients with type II diabetes . The Journal of Alternative and Complementary Medicine 2009; 15 (8): 899-903.

[241] Sabzghabaee AM, Ataei E, Kelishadi R, Ghannadi A, Soltani R, Badri S, and Shirani S. Effect of *Hibiscus sabdariffa* calices on dyslipidemia in obese adolescents: A triple-masked randomized controlled trial. Mater Sociomed 2013; 25 (2): 76–79.

[242] Chang HC, Peng CH, Yeh DM, KaoES and Wang CJ. *Hibiscus sabdariffa* extract inhibits obesity and fat accumulation, and improves liver steatosis in humans. Food Funct2014; 5: 734-739.

[243] Gurrola-Díaz CM, García-López PM, Sánchez-Enríquez S, Troyo-Sanromán R, Andrade- González I andGómez-Leyva JF. Effects of Hibiscussabdariffaextract powder and preventive treatment (diet) on the lipid profiles of patients with metabolic syndrome (MeSy). Phytomedicine 2010;17 (7):500-505.

[244] Kuriyan R, Kumar DR, R R and Kurpad AV. An evaluation of the hypolipidemic effectof an extract of Hibiscus Sabdariffa leaves in hyperlipidemic Indians: a double blind, placebo controlled trial. BMC Complement Altern Med. 2010;10:27. doi: 10. 1186 / 1472-6882-10-27.

[245] Maffo Tazoho G, Gouado I, Ndomou M, Tchuandom Bonsi S, Mbaduet Wamba Y and Agbor EE. Clinical, hematological and biochemical health benefit effects of *Hibiscus sabdariffa* Lin dried calyces beverage in human. Food and Nutrition Sciences 2002;**7**: 383-395.

[246] Al-Snafi AE. Pharmacological and therapeutic importance of*Hibiscus sabdariffa*- A review. International Journal of Pharmaceutical Research 2018; 10 (3): 451-475.

[247] Shrivastav P, George K, Balasubramaniam N, Jasper MP, Thomas M and Kanagasabhapathy AS. Suppression of puerperal lactation using jasmine flowers (*Jasminum sambac*). Aust N Z J Obstet Gynaecol 1988;28 (1):68-71.

[248] Al-Snafi AE. Pharmacological and therapeutic effects of *Jasminum sambac*- A review. Indo Am J P Sc 2018; 5 (3): 1766-1778.

[249] Sabaté J, Fraser GE, Burke K, Knutsen SF, Bennett H andLinstead KD. Effects of walnuts on serum lipid levels and blood pressure in normal men. New Engl J Med 1993; 329: 603-660.

[250] Lavedrine F, Zmirou D, Ravel A, Balducci F and Alary J. Blood cholesterol and walnut consumption: A cross-sectional survey in France. Prev Med 1999; 28: 333-339.

[251] Zibaeenezhad MJ, Rezaiezadeh M, Mowla A, Ayatollahi SM and Panjehshahin MR. Antihypertriglyceridemic effect of walnut oil. Angiology 2003;54 (4):411-414.

[252] Zibaeenezhad MJ, Farhadi P, Attar A, Mosleh A, Amirmoezi F and Azimi A. Effects of walnut oil on lipid profiles in hyperlipidemic type 2 diabetic patients: a randomized,double-blind, placebo-controlled trial. Nutr Diabetes 2017;7 (4):e259. doi: 10. 1038/nutd. 2017. 8.

[253] Hosseini S, Jamshidi L, Mehrzadi S, Mohammad K, Najmizadeh AR, Alimoradi H and Huseini HF. Effects of Juglans regia L. leaf extract on hyperglycemia and lipid profiles in type two diabetic patients: a randomized double-blind, placebo-controlled clinical trial. J Ethnopharmacol 2014;152 (3):451-456.

[254] Hosseini S, Huseini HF, Larijani B, Mohammad K, Najmizadeh A, Nourijelyani K andJamshidi L. The hypoglycemic effect of Juglans regia leaves aqueous extractin diabetic patients: A first human trial. Daru 2014;22 (1):19. doi: 10. 1186/2008-2231-22-19.

[255] Moravej H, Salehi A, Razavi Z, Moein MR,Etemadfard H,Karami F andGhahremani F. Chemical composition and the effect of walnut hydrosol on glycemic control of patients with type 1 diabetes. Int J Endocrinol Metab. 2016; 14 (1):e34726. doi: 10. 5812/ijem. 34726.

[256] Saimbi CS,Shubh N, Kapoor KK andKaushal S. Clinical effect Of *Juglans regia* on developing dental plaque. JICDRO 2009; 1 (3): 1-4.

[257] Deshpande RR, Kale AA,Ruikar A, Panvalkar PS, Kulkarni AA,Deshpande NR andSalvekarJP. Antimicrobial activity of differentextracts ofagainst oral microflora. Int J Pharm Pharm Sci 2011; 3 (2): 200-201.

[258] Al-SnafiAE. Chemical constituents, nutritional, pharmacological and therapeutic importance of *Juglans regia*- A review. IOSR Journal of Pharmacy 2018; 8 (11): 1-21.

[259] Judy WV, Hari SP, Stogsdill WW, Judy JS, Naguib YM and Passwater R. Antidiabeticactivity of a standardized extract (Glucosol) from *Lagerstroemia speciosa*leaves in Type II diabetics. A dose-dependence study. J Ethnopharmacol2003; 87 (1):115-117.

[260] Ortiz MG. Effect of banaba (*Lagerstroemia speciosa*) on metabolic syndrome, insulin secretion and insulin sensitivity. University of Guadalajara 2017; https://clinicaltrials. gov/ct2/show/NCT02767869

[261] Chong P, Beah Z, Grube B and Riede L. IQP-GC-101 reduces body weight and body fat mass: A randomized, double-blind, placebo-controlled study. PhytotherRes 2014;28: 1520–1526.

[262] Tjokroprawiro A, Murtiwi S and Tjandrawinata RR. DLBS3233, a combined bioactive fraction of *Cinnamomum burmanii* and *Lagerstroemia speciosa*, in type-2 diabetes mellitus patients inadequately controlled by metformin and other oral antidiabetic agents. J Complement Integr Med 2016; 13 (4):413-420.

[263] Manaf A, Tjandrawinata RR and Malinda D. Insulin sensitizer in prediabetes: a clinical study with DLBS3233, a combined bioactive fraction of *Cinnamomum burmanii* and *Lagerstroemia speciosa*. Drug Des Devel Ther2016; 10:1279-1289.

[264] Al-Snafi AE. Medicinal value of *Lagerstroemia speciosa*: An updatedreview. International Journal of Current Pharmaceutical Research 2019; 11 (5):18-26.

[265] Gidwani BK, Bhargava S,Rao SP, Majoomdar A,Pawar DP and Alaspure RN. Analgesic, anti–inflammatory and anti–hemorrhoidal activity of aqueous extract of *Lantana camara* Linn. Research JPharm and Tech 2009;2 (2): 378-381.

[266] Al-Snafi AE. Chemical constituents and pharmacological activities of*Lantana camara*- A review. Asian J Pharm Clin Res 2019; 12912):10-20.

[267] Sujanamulk B, Chintamaneni R, Chennupati A, Nahar P,Chaluvadi RS, Vemugunta R and Prabhat MV. Evaluation of antifungal efficacy of ethanolic crude lawsone and listerine mouthwash in onc ontrolled diabetics and denture wearers - A randomized clinical trial. J Clin Diagn Res 2016; 10 (6): ZC90-95.

[268] Hekmatpou D, Ahmadian F, Eghbali M and Farsaei S. Henna (*Lawsonia inermis*) as an inexpensive method to prevent decubitus ulcers in critical care units: A randomized clinical trial. J Evid Based Integr Med 2018;23:2515690 X18772807. doi: 10. 1177/2515690X18772807.

[269] ZubardiahL, Mustaqimah DN andAuerkari EI. Effectiveness of *Lawsonia inermis* Linneaus leaves infusion in gingivitis healing. Dentika Dental J 2012; 17 (2): 105.

[270] Al-Snafi AE. A review on *Lawsonia inermis*:A potential medicinal plant. International Journal of Current Pharmaceutical Research 2019; 11 (5):1-13.

[271] Paranjape AN and Mehta A. A study on clinical efficacy of *Lepidium sativum* seeds in treatment of bronchial asthma. Iranian Journal of Pharmacology and Therapeutics 2006; 5 (1): 55-59.

[272] Raval ND and Pandya TN. Clinical trial of *Lepidium sativum* Linn (Chandrashura)in the management of sandhivata (osteoarthritis). An International Quarterly Journal ofResearch in Ayurveda 2009; 30 (2): 153-157.

[273] Edel AL, Rodriguez-Leyva D, Maddaford TG, Caligiuri SP, Austria JA, Weighell W, Guzman R, Aliani M and Pierce GN. Dietary flaxseed independently lowers circulating cholesterol and lowers it beyond the effects of cholesterol-lowering medications alone in patients with peripheral artery disease. J Nutr 2015; 145: 749-757.

[274] Cornish SM, Chilibeck PD, Paus-Jennsen L, Biem HJ, Khozani T, Senanayake V, Vatanparast H, Little JP, Whiting SJ and Pahwa P. A randomized controlled trial of the effects of flaxseed lignan complex on metabolic syndrome composite score and bone mineral in older adults. Appl Physiol NutrMetab 2009; 34: 89-98.

[275] Billinsky J, Glew RA, Cornish SM, Whiting SJ, Thorpe LU, Alcorn J, Paus-Jenssen L, Hadjistavropoulos T and Chilibeck PD. No evidence of hypoglycemia or hypotension in older adults during 6 months of flax lignan supplementation in a randomized controlled trial: a safety evaluation. Pharm Biol 2013; 51: 778-782.

[276] Zhang W, Wang X, Liu Y, Tian H, Flickinger B, Empie MW and Sun SZ. Dietaryflaxseedligninextractlowersplasmacholesterolandglucoseconcentrations in hypercholesterolaemic subj ects. Br J Nutr 2008; 99 (6): 1301-1309.

[277] Wong H, Chahal N, Manlhiot C, Niedra E and McCrindle BW. Flaxseed in pediatric hyperlipidemia: a placebo-controlled, blinded, randomized clinical trial of dietary flaxseed supplementation for children and adolescents with hypercholester olemia. JAMA Pediatr 2013; 167 (8): 708-713.

[278] Kristensen M, Jensen MG, Aarestrup J, Petersen KE, Søndergaard L, Mikkelsen MS and Astrup A. Flaxseed dietary fibers lower cholesterol and increase fecal fat excretion, but magnitude of effect depend on food type. Nutr Metab (Lond) 2012; 9: 8. doi:10. 1186/1743-7075-9-8.

[279] Paschos GK, Magkos F, Panagiotakos DB, Votteas V andZampelas A. Dietary supplementation with flaxseed oil lowers blood pressure in dyslipidaemic patients. Eur J Clin Nutr 2007;61: 1201-1206.

[280] Rodriguez-Leyva D, Weighell W, Edel AL, LaVallee R, Dibrov E, Pinneker R, Maddaford TG, Ramjiawan B, Aliani M, Guzman R and Pierce GN. Potent antihypertensive action of dietary flaxseed in hypertensive patients. Hypertension 2013; 62: 1081-1089.

[281] Hashempur MH, Homayouni K, Ashraf A, Salehi A, Taghizadeh M and Heydari M. Effect of *Linum usitatissimum* L. (linseed) oil on mild and moderate carpal tunnel syndrome: a randomized, double-blind, placebo-controlled clinical trial. DARU Journal of Pharmaceutical Sciences 2014; 22:43-51.

[282] Mani UV, Mani I, Biswas M and Kumar SN. An open-label study on theeffectof flax seed powder (*Linum usitatissimum*) supplementation in themanagementofdiabetes mellitus. J Diet Suppl 2011; 8 (3): 257-265.

[283] Zhang W, Wang X, Liu Y, Tian H, Flickinger B, Empie MW, *et al*. Effects of dietary flaxseed lignan extract on symptoms of benign prostatic hyperplasia. J Med Food 2008;11 (2):207-214.

[284] Thompson LU, Chen JM, Li T, Strasser-Weippl K and Goss PE. Dietaryflaxseedalters tumor biological markers in postmenopausal breast cancer. Clin Cancer Res 2005; 11 (10): 3828-3835.

[285] Demark-Wahnefried W, Robertson CN, Walther PJ, Polascik TJ, Paulson DF and Vollmer RT. Pilot study to explore effects of low-fat, flaxseed-supplementeddiet on proliferation of benign prostatic epithelium and prostate -specific antigen. Urology 2004; 63 (5): 900-904.

[286] Simbalista RL, Sauerbronn AV, Aldrighi JM and Arêas JA. Consumption of a flaxseed-rich food is not more effective than a placebo in alleviating theclimacteric symptoms of postmenopausal women. J Nutr 2010; 140 (2): 293-297.

[287] Colli MC, Bracht A, Soares AA, de Oliveira AL, Bôer CG, de Souza CG and Peralta RM. Evaluation ofthe efficacy of flaxseed meal and flaxseedextractinreducingmenopausal symptoms. J Med Food2012; 15 (9): 840-845.

[288] Dodin S, Lemay A, Jacques H, Légaré F, Forest JC and Mâsse B. Theeffectsof flaxseed dietary supplement on lipid profile, bone mineral density, andsymptomsinmenopausalwomen: a randomized, double-blind,wheat germ placebo-controlled clinical trial. J Clin Endocrinol Metab2005; 90 (3): 1390-1397.

[289] Cockerell KM, Watkins AS, Reeves LB, Goddard L and Lomer MC. Effectsof linseeds on the symptoms of irritable bowel syndrome:a pilot randomisedcontrolledtrial. J Hum Nutr Diet 2012; 25 (5): 435-443.

[290] Al-Snafi AE. Chemical constituents and pharmacological effects of *Lepidium sativum*- A review. International Journal of Current Pharmaceutical Research 2019; 11 (6):1-10.

[291] Aufmkolk M, Ingbar JC, Kubota K, Amir SM and Ingbar SH. Extracts and auto-oxidized constituents of certain plants inhibit the receptor-binding and the biological activity of Graves' immunoglobulins. Endocrinology1985; 116 (5): 1687-1693.

[292] Al-Snafi AE. Chemical constituents and pharmacological effects of *Lithospermum officinale*. IOSR Journal ofPharmacy 2019; 9 (8): 12-21.

[293] AmagaseH andNance DM. *Lycium barbarum* fruit (goji) attenuates the adrenal steroid response to an exercise challenge and the feeling of tiredness: A randomized, double-blind, placebo-controlled human clinical study. Journal of Food Research 2012; 2 (1): 3-12.

[294] Amagase H, Sun B and Nance DM . Immunomodulatory effects of a standardized *Lycium barbarum* fruit Juice in Chinese older healthy human subjects. Journal of Medicinal Food2009; 12 (5): https://doi. org/10. 1089/ jmf. 2008. 0300

[295] Amagase H and Nance DM. A randomized, double-blind, placebo-controlled, clinical study of the general effects of a standardized *Lycium barbarum* (goji) Juice, GoChi. J Altern Complement Med 2008;14 (4):403-412.

[296] Amagase H and Nance DM. *Lycium barbarum* increases caloric expenditure and decreases waist circumference in healthy overweight men and women: pilot study. J Am Coll Nut2011; 30 (5): 304–309.

[297] Cai H, Liu F, Zuo P, Huang G, Song Z, Wang T, Lu H, Guo F, Han C and Sun G. Practical application of antidiabetic efficacy of *Lycium barbarum* polysaccharide in patients with type 2 diabetes. Med Chem 2015; 11 (4): 383-390.

[298] Amagase H, Sun B and Borek C. *Lycium barbarum* (goji)juice*improvesinvivo*antioxidantbiomarkersin serum of healthy adults. Nutr Res2009; 29 (1): 19-25.

[299] Cao GW, Yang WG and Du P. Observation of the effects of LAK/IL- 2therapy combiningwith*Lycium barbarum* polysaccharides in thetreatmentof75cancer patients. Zhonghua Zhong Liu Za Zhi 1994; 16 (6): 428-431.

[300] Zanchet MZ, Nardi GM, Bratti LDS,Filippin-Monteiro FB andClaudriana L. *Lycium barbarum* reduces abdominal fat and improves lipid profile and antioxidant status in patients with metabolic syndrome. Oxidative Medicine and Cellular Longev 2017: 9763210, doi:10. 1155/2017/9763210.

[301] Mirfatahi M, Tabibi H, Nasrollahi A andHedayati M. Effects of flaxseed oil on serum lipids and lipoproteins in hemodialysis patients: a randomizedcontrolled Ttrial. Iranian journal of kidney diseases 2016 ;10 (6):405-412.

[302] Eiling R, Wieland V and Niestroj M. Improvement of symptoms in mild hyperthyroidism with an extract ofLycopus europaeus (Thyreogutt® mono). Wien Med Wochenschr 2013;163 (3-4):95-101.

[303] Beera AM, Wiebelitza KR andSchmidt-Gaykb H. Lycopus europaeus (gypsywort): Effects on the thyroidal parameters and symptoms associated with thyroid function. Phytomedicine 2008; 15:16–22.

[304] Al-Snafi AE. A review on Lycopus europaeus:A potential medicinal plant. IOSR Journal ofPharmacy 2019; 9 (7): 80-88.

[305] López Mantecón AM, Garrido G, Delgado-Hernández R and Garrido-Suárez BB. Combination of *Mangifera indica* L extract supplementation plus methotrexate in rheumatoid arthritis patients: a pilot study. Phytother Res 2014;28 (8):1163-1172.

[306] Al-Snafi AE, Ibraheemi ZAM, Talab TA. A review on components and pharmacology of *Mangifera indica*. International Journal of Pharmaceutical Research 2021; 13 (2): 3043- 3066.

[307] Herrera-Arellano A, Aguilar-Santamaría L, García-Hernández B, Nicasio-Torres P and Tortoriello J. Clinical trial of *Cecropia obtusifolia* and*Marrubiumvulgare* leaf extracts on blood glucose and serum lipids in type 2 diabetics. Phytomedicine 2004;11 (7-8): 561-566.

[308] Villanueva JR, ID Esteban JM and Villanueva LR. A reassessment of the *Marrubium vulgare* L herb's potential role in diabetes mellitus type 2: First results guide the investigation toward new horizons. Medicines 2017; 4: 57.

[309] Al-Snafi AE. Al-Saedy HA , Talab TA, Majid WJ, El-Saber BatihaG, Jafari-Sales Abolfazl. The bioactive ingredients and therapeutic effects of *Marrubium vulgare* - A review. International Journal of Biological and Pharmaceutical Sciences Archive 2021; 1 (2):9–21.

[310] Beikert FC, Schönfeld BS, Frank U, *et al*. Antiinflammatory potential of seven plant extracts in the ultraviolet erythema test. A randomized, placebo- controlled study. Hautarzt 2013; 64 (1): 40-46.

[311] Shimelis ND, Asticcioli S, Baraldo M, *et al*. Researching accessible and affordable treatment for common dermatological problems in developing countries. An Ethiopian experience. Int J Dermatol 2012; 51 (7):790-795.

[312] Charousaei F, Dabirian A and Mojab F. Usingchamomile solution or a 1% topical hydrocortisone ointment in the management of peristomal skin lesions in colostomy patients: results of a controlled clinical study. Ostomy Wound Manage 2011; 57 (5): 28-36.

[313] Arsić I,Tadić V, Vlaović D, *et al*. Preparation of novel apigenin-enriched, liposomal and non-liposomal, anti-inflammatory topical formulations as substitutes for corticosteroid therapy. Phytother Res 2011; 25 (2): 228-233.

[314] Patzelt-Wenczler R andPonce-Pöschl E. Proof of efficacy of Kamillosan (R) cream in atopic eczema. Eur J Med Res 2000; 5 (4): 171-175.

[315] Maiche AG, Gröhn P andMäki-Hokkonen H. Effect of chamomile cream and almond ointment on acute radiation skin reaction. Acta Oncol 1991; 30 (3): 395-396.

[316] Glowania HJ, Raulin C andSwoboda M. Effect of chamomile on wound healing-a clinical double- blind study. Z Hautkr 1987; 62 (17): 1267-1271.

[317] Aertgeerts P, Albring M, Klaschka F, *et al*. Comparative testing of Kamillosan cream and steroidal (0. 25% hydrocortisone, 0. 75% fluocortin butylester) and non-steroidal (5% bufexamac) dermatologic agents in maintenance therapy of eczematous diseases. Z Hautkr 1985; 60 (3): 270-277.

[318] Saad AH, Ahmed NG, Kadhim RB and Abdul Rasool BK. Formulation and evaluationof herbal handwash from *Matricaria chamomilla* flowers extract. International Journal of Research in Ayurveda and Pharmacy 2011; 2 (6):1811-1813.

[319] Dadfar F. Effectiveness of Chamomile (*Matricaria chamomilla*) extracts on the reduction of dysmenorrhea and premenstrual syndrome symptoms. Der Pharmacia Lettre 2015; 7 (12):454-458.

[320] Sharifi F, Simbar M, Mojab F and AlaviMajd H. A comparative study of the effects of *Matricaria chamomilla* extract and mefenamic acid on the severity of premenstrual syndrome symptoms. Arak Medical University Journal 2013; 16 (70): 71-78.

[321] Rafraf M, Zemestani M and Asghari-Jafarabadi M. Effectiveness of chamomile tea on glycemic control and serumlipidprofileinpatientswithtype 2 diabetes. J EndocrinolInvest2015; 38 (2): 163-170.

[322] Mao JJ, Xie SX, Keefe JR, Soeller I, Li QS and Amsterdam JD. Long-term chamomile (*Matricaria chamomilla* L.) treatment for generalized anxiety disorder: A randomizedclinical trial. Phytomedicine 2016; 23 (14):1735-1742.

[323] Amsterdam JD, Li QS, Xie SX and Mao JJ. Putative antidepressant effect of chamomile (*Matricaria chamomilla* L) oral extract in subjects with comorbid generalizedanxiety disorder and depression. J Altern Complement Med 2019; doi: 10. 1089/acm. 2019. 0252.

[324] Amsterdam JD, Li Y, Soeller I, Rockwell K, Mao JJ and Shults J. A randomized, double-blind, placebo-controlled trial of oral *Matricaria recutita* (chamomile) extract therapy for generalized anxiety disorder. J Clin Psychopharmacol 2009; 29: 378-382.

[325] Sharifi H, Minaie MB, Qasemzadeh MJ, Ataei N, Gharehbeglou M and Heydari M. Topical use of *Matricaria recutita* L (chamomile) oil in the treatment of monosymptomatic enuresis in children: A double-blind randomized controlled trial. Journal of Evidence-Based Complementary & Alternative Medicine 2017; 22 (1):12-17.

[326] Mölgaard J, von Schenck H and Olsson AG. Alfalfa seeds lower low density lipoprotein cholesterol and apolipoprotein B concentrations in patients with type II hyperlipoproteinemia. Atherosclerosis 1987; 65 (1-2): 173-179.

[327] Sargazi A, Sargazi A, Nadakkavukaran PK, Jim, SrgaziA, Aali N, Sargolzaeiaval F and Sepehri Z. Effect of alfalfa (*Medicago sativa* L) extract on undesired hair growth in human: A safe remedy for cosmetic procedures. Der Pharmacia Lettre 2016; 8 (19):351-356.

[328] Al-Snafi AE. Khadem HS, Al-Saedy HA, Alqahtani AM, El-Saber Batiha G. Jafari-Sales Abolfazl. A review on *Medicago sativa*: A potential medicinal plant. International Journal of Biological and Pharmaceutical Sciences Archive 2021; 1 (2):22-33.

[329] Pastura G, Mesiti M, Saitta M, Romeo D, Settineri N, Maisano R, Petix M and Giudice A. Lymphedema of the upper extremity in patients operated for carcinoma of the breast: clinicalexperience with coumarinic extract from *Melilotus officinalis*. Clin Ter1999; 150 (6): 403-408.

[330] Forte R, Cennamo G, Finelli ML, Bonavolontà P, de Crecchio G and Greco GM. Combination of flavonoids with Centella asiaticaandMelilotusfordiabeticcystoid macularedema without macular thickening. J Ocul Pharmacol Ther2011; 27 (2): 109-113.

[331] Zangiabadi N, Mohtashami H, Hojatipour M, Jafari M, Asadi-Shekaari M and Shabani M. The effect of angipars on diabetic neuropathy in STZ-induced diabetic male rats: A study on behavioral, electrophysiological, sciatic histological and ultrastructural Indices. Hindawi Publishing Corporation, The Scientific World Journal 2014, http:/dx. doi. org/10. 1155/2014/721547

[332] Heshmat R, Mohammad K, Mohajeri Tehrani MR,*et al*. Assessment of maximum tolerated dose of a new herbal drug, semelil (angipars) in patients with diabetic foot ulcer: A phase I clinical trial. Daru 2008;16 (1):25-30.

[333] Shamimi Nouri K, Karimian R, Nasli E,*et al*. Topical application of semelil (angipars) in treatment of pressure ulcers: A randomized clinical trial. Daru 2008; 16 (1): 54–57.

[334] Abdollahi M, Farzamfar B, Salari P, Khorram Khorshid HR, Larijani B, Farhadi M, *et al*. Evaluation of acute and sub-chronic toxicity of semelil (angipars), a new phytotherapeutic drug for wound healing in rodents. Daru J Pharm Sci 2008;16 (Suppl 1):7-14.

[335] Asadi-Shekaari M, Eftekhar Vaghefi H, Talakoub A and Khorram Khorshid HR. Effects of semelil (angipars) on focal cerebral ischemia in male rats. Daru 2010; 18:265-269.

[336] Cataldi A, Gasbarro V, Viaggi R, Soverini R, Gresta E and Mascoli F. Effectivenessof the combination of alpha tocopherol, rutin, melilotus, and centella asiatica in the treatment of patients with chronic venous insufficiency. Minerva Cardioangiol2001; 49 (2): 159-163.

[337] Al-Snafi AE. Chemical constituents and pharmacological effects of *Melilotus officinalis*- A review. IOSR Journal of Pharmacy 2020; 10 (1):26-36.

[338] Alijaniha F,Naseri M,Afsharypuor S,Fallahi F,Noorbala A,MosaddeghM,Faghihzadeh S and Sadrai S. Heart palpitation relief with *Melissa officinalis* leaf extract: double blind, randomized, placebo controlled trial of efficacy and safety. J Ethnopharmacol 2015;164:378-384.

[339] Javid AZ, HaybarH, Dehghan P,Haghighizadeh MH, Mohaghegh SM, Ravanbakhsh M, Mohammadzadeh A. The effects of *Melissa officinalis* (lemon balm) in chronic stable angina on serum biomarkers of oxidative stress, inflammation and lipid profile. Asia Pacific Journal of Clinical Nutrition 2018; 27 (4): 785-791.

[340] Chehroudi S, Fatemi MJ, Isfeedvajani MS, *et al*. Effects of *Melissa officinalis* L. on reducing stress, alleviating anxiety disorders, depression, and insomnia, and increasing total antioxidants in burn patients. Trauma Mon2016; 22 (4): e33630.

[341] Kennedy DO, Wake G, Savelev S, *et al*. Modulation of mood and cognitive performance following acute administration of single doses of *Melissa officinalis* (Lemon balm) with human CNS nicotinic and muscarinicreceptor-binding properties. Neuropsychopharmacology 2003; 28 (10): 1871-1881.

[342] Kennedy DO, Scholey AB, Tildesley NT, Perry EK and Wesnes KA. Modulation of mood and cognitive performance following acute administration of *Melissa officinalis* (lemon balm). Pharmacol Biochem Behav2002; 72 (4): 953-964.

[343] Akhondzadeh S, Noroozian M, Mohammadi M, *et al*. *Melissa officinalis* extract in the treatment of patients with mild to moderate Alzheimer's disease: a double blind, randomised, placebo controlled trial. J Neurol Neurosurg Psychiatry 2003; 74: 863-866.

[344] Sahib AS. Treatment of irritable bowel syndrome using a selected herbal combination of Iraqi folk medicines. J Ethnopharmacol 2013; 148 (3): 1008-1012.

[345] Babaeian M, Naseri M, Kamalinejad M, Ghaffari F, Emadi F, Feizi A, Rafiei R, Mazaheri M, Hasheminejad SA,Park JW andAdibi P. The efficacy of *Mentha longifolia* in the treatment of patients with postprandial distress syndrome: A double-blind, randomized clinical trial. Iran Red Crescent Med J 2017; 19 (2): e34538.

[346] Mokaberinejad R, Akhtari E, Tansaz M, Bioos S, Kamalinejad M, Zafarghandi N, Ghobadi A, Sohrabvand F and Akhbari A. Effect of *Mentha longifolia* on FSH serum level in premature ovarian failure. Open Journal of Obstetrics and Gynecology 2014; 4: 356-360.

[347] Shirooye P and Abdolhosseini S. Effect of *Mentha longifolia* on 10 patients with primarydysmenorrhea. Asian J Clin Case Rep Trad Alt Med 2017; 1 (1): 51-56.

[348] Mokaberinejad R, Zafarghandi N, Bioos S, Dabaghian FH, Naseri M, Kamalinejad M,Amin G, Ghobadi A, Tansaz M, Akhbari A and Hamiditabar M. *Menthalongifolia*syrup in secondary amenorrhea: a double-blind, placebo-controlled, randomizedtrials. Daru 2012; 20 (1): 97.

[349] Soo May L, Sanip Z, Ahmed Shokri A, Abdul Kadir A, Md Lazin MR. The effects of*Momordica charantia* (bitter melon) supplementation in patients with primary knee osteoarthritis: A single-blinded, randomized controlled trial. Complement Ther Clin Pract 2018; 32: 181-186.

[350] Ahmad N, Hassan MR, Halder H, Bennoor KS. Effect of*Momordica charantia* (Karolla) extracts on fasting and postprandial serum glucose in NIDDM patients. Bangladesh Med Res Counc Bull 1999; 25: 11-13.

[351] Tongia A, Tongia SK and Dave M. Phytochemical determination and extraction of*Momordica charantia*fruit and its hypoglycemic potentiation of oral hypoglycemic drugs in diabetes mellitus (NIDDM). Indian J Physiol Pharmacol2004; 48 (2): 241-244.

[352] Akhtar MS . Trial of*Momordica charantia*Linn (Karela) powder in patients with maturity-onset diabetes. J Pak Med Assoc 1982; 32: 106-107.

[353] John AJ, Cherian R, Subhash HS, *et al*. Evaluation of the efficacy of bitter gourd (*Momordica charantia*) as an oral hypoglycemic agent – a randomized controlled clinical trial. Indian J Physiol Pharmacol 2003; 47: 363-365.

[354] FuangchanA, Sonthisombat P, Seubnukarn T, Chanouan R, Chotchaisuwat P, Sirigulsatien V, Ingkaninan K, Plianbangchang P and Haines ST. Hypoglycemic effect of bitter melon compared with metformin in newly diagnosed type 2 diabetes atients. J Ethnopharmacol 2011; 134 (2): 422-428.

[355] Dans AM, Villarruz MV, Jimeno CA, Javelosa MA, Chua J, Bautista R andVelez GG. The effect of*Momordica charantia*capsule preparation on glycemiccontrol in type 2 diabetes mellitus needs further studies. J Clin Epidemiol 2007; 60 (6): 554-559