World Journal of
Biological and Pharmaceutical Research

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

ISSN: 2799-0338 (Online)

(REVIEW ARTICLE)

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Tannins: Natural plant-derived polyhydroxy phenolic compounds with potential for biotechnological and biomedical applications

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World Journal of Biology Pharmacy and Health Sciences, 2022, 02(01), 001–004

Publication history: Received on 01 August 2021; revised on 10 September 2021; accepted on 12 September 2021

Article DOI: https://doi.org/10.53346/wjbpr.2022.2.1.0127

Abstract

The difference between Tannin and Tannic Acid is that the term Tannin is used to name the group of organic compounds whereas Tannic acid is a type of tannin.

Members of the group of Tannins - all of them polyhydroxyphenolic compounds – are present in leaves and other nutrient-rich parts of a huge number of Angiosperm plants. In nature, Tannins play a significant role in the protection of the plants against herbivores. Tannins inactivate enzymes in the digestive tract of the herbivores, with respective consequences: the herbivores may die of starvation.

A well-known example for a technological application of Tannins is the process of leather production. Complex formation with collagen the denaturation of proteins - here in the animal skin - by the polyhydroxyphenol components of Tannin is their major function. Various biomedical applications are known, such as application of Tannins due to their adstringent property, production of tannate salts, antihistamines and antitussive drugs.

Recently, it was discovered that Tannic acid suppresses the virus SARS-CIY-2 as a dual inhibitor of the main viral protease and the cellular TMPRSS 2 protein, with the consequence that the virus cannot infect human cells.

Keywords: Tannins; Plant-derived origin; Function in Nature; Properties; Biotechnological and Biomedical applications; Outlook

1. Introduction

1.1. Tannins: Properties

Tannins are natural plant-derived compounds characterized by their content of polyhydroxyphenols [1-5] In nature, this property is involved in the function of Tannins in defense of plants against Herbivores [6]. This happens as follows: the Tannins form complexes with other macromolecules, especially with proteins. By doing so, they cover the protein surface. Due to the presence of polyhydroxyphenols, they are more hydrophobic than the surface of proteins, and they hinder water to have access to the protein. Hence, the protein is denatured by the lack of water. This situation is critical for the function of the proteins, and it leads to the loss of the protein functions. Herbivores would, in such a situation, suffer because the enzymes in their digestive tract would no longer work properly. It is observed that herbivores avoid feeding on plants that contain Tannins and Tannic Acid in their nutrient-rich leaves.

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2. Tannins: Occurrence and some applications

Besides a function in leather production [6], Tannins play further roles: red wine grapes have Tannins in their grape skin and their leaves [7]. These Tannins protect the grapes against decay by bacteria and yeasts the tannins end up in the red wine. There, they act for an improvement of the taste of the wine by denaturing fine dissolved particles (remnants of decaying bacteria and yeasts) in the early stages of wine processing. If the amount of Tannin in the grape skin is not sufficient, a simple biotechnological step takes place: extra Tannin is added. The consequence is a typical kind of the character of the red wine. Many people like this taste.

Tannins are also present in tea leaves, especialle in green tea, in coffee beans and in some berries [8-10]. Biomedical applications are listed in Data collections on Tannins [2,11] and in reviews such as „Tannins and human health: a review“[7]. Here is a quotation: "...The anticarcinogentic and antimutagenic potentials of tannins may be related to their antioxidative property which is important for protecting cellular oxidative damage, including lipid peroxidation..The generation of superoxide radicals was reported to be inhibited by tannins and related compounds".

Effects of Tannins in context with bacteria and viruses are also well documented [12,13]

2.1. Tannins: new ideas for biotechnological and biomedical applications

Tannins are natural plant-derived compounds with several remarkable propoerties. For a scientist interested in the use of these interesting properties, a wide variety of applications in biotechnology and in medicine may be considered.

Recently, several ideas have been proposed as far as biotechnology is concerned.

Examples: very simple (unpublished): Tannin solutions can be used to avoid unpleasant smell from the kitchen waste bin: just use a spray can for spraying tannin solution into the bin; the tannin will cover all surfaces of the biological waste, and kill microorganisms and fungi.

Next example: protection of wooden beams: Just place the material in a bath of tannin solution. The solution will penetrate into the outer layers of wooden beams and protect them against microorganisms and fungi [14,15].

One more - perhaps promising - example is the struggle against the bark beetle (unpublished, but submitted to the Government). By spraying of Tannic Acid on the lower part of the stems these areas of the stems can be impregnated with Tannin. The solution can be expected to penetrate the outer layers of the bark because the bark is already partly decomposed by the actions of the bark beetle. The larvae chew their way through the bark; after all, the bark is their food. However, due to the spraying with Tannic Acid the bark will be contaminated by Tannin. Hence, the larvae chew the bark and the contaminating Tannin. This Tannin will detroy the enzymes in the digestion tract of the larvae, and the larvae will die of starvation.

Further proposed ideas and tests are more complex. They deal with the Corona virus SARS-CoV-2 and its mutations

One project is the design of a mouthwash solution with Tannin as the acting component [16]. This approach is based on early publications describing the fact that Tannins can neutralize several kinds of viruses including Corona viruses [17,18]. The design of the solution has recently been completed and is ready for production. However, no company was found and willing to enter this project or, at least, carry out tests of the solution for efficacy. It is known that Corona viruses are present in high numbers in the mouth cavity (and the sputum) on their way into the lung. Viruses in this situation would be good targets for Tannin. Former publications on the denaturing activity of Tannin on viruses have been the instigation for the development of a mouthwash solution on the basis of Tannin. As mentioned, no Company was interested in such an approach. Probably, they did not know the facts.

A similar situation was experienced after the design of a special kind of mouth-nose mask was completed (unpublished). The idea behind the construction of such a mask was that an inlay made from absorbent cloth can reversibly be fixed to the inside of the mask Prototypes of such a kind of inlays were handmade. Before the inlay was fixed inside the mask, it had been impregnated with a suspension containing Tannin and a polysaccharide (Guaran). This mixture did cover the inlay similar to a lining. After drying, the inlay was mounted inside the mask. Now, when the mask was used, the polysaccharide started swelling due to the presence of humidity/water (microdroplets and aerosols set free by coughing, speaking or respiration) inside the mask. The Tannin attached to the network of wet polysaccharide got also wet. In this state, wet Tannin denatures proteins, also proteins present on the surface of the viruses that make contact with the lining. Hence, viruses possibly present in the microdroplets or aerosols inside the mask are neutralized.

In fact, such a mask controls any microdroplets and aerosols, both those entering the inside of the mask, and those created inside the mask and released to the outside. Viruses possibly present in the microdroplets and aerosols that are set free to the outside, are in a neutralized state and no longer dangerous for the people in immediate vicinity of an infected person. The used inlays can easily be removed and exchanged by new inlays. The design of the inlays was chosen in such a way that they can be transiently fixed inside nearly all usual mask types.

As mentioned above, no company was interested in the project – primarily due to the fact that they were happy with their own masks.

In early states of infection by the Corona virus SARS-CoV-2, a combination of the mouthwash solution described above and the Tannin-containing mouth-nose mask might be a helpful aid for the protection against Corona viruses and their mutants.

2.2. Tannins in general and Tannic Acid: Outlook

Ideas and proposals described above might be interesting and even promising for future developments in the use of Tannins. However, mere description and handmade prototypes are not sufficient to categorize them as subjects worth to be described in detail in an outlook.

The situation is different in case of an approach based on former experimental findings regarding processes of denaturation of proteins in general, and it is related to Tannic Acid [19]. The discovery is dealing with the process of propagation of the virus SARS-CoV-2 into human host cells.The publication of the findings and the description of their consequences are convincing. After all, the findings describe the involved processes at the molecular level in all details This is a situation not very common in former experiments related to the phenomenon of protein denaturation by Tannins.

Here is a quotation of parts of the Abstract of the respective publication. The Abstract describes the main observations and discusses possibilities for future research, but reading the full article is very much recommended.

„The cell surface protein TMPRSS2 (transmembrane protease serine 2) is an androgen-responsible serine protease... Besides its role in tumor biology, TMPRSS2 is also a key player in cellular entry by the SARS-CoV viruses.....effective cures are highly demanded.... The main protease (M^{pro}/$3CL^{pro}$) of SARS-CoV-2 is a critical enzyme for viral propagation in host cells and, like TMPRSS2, has been exploited for treatment on the infectous disease. Numerous natural compounds abundant in common fruits have been suggested with anti-coronavirus infection in the previous outbreaks of SARS-CoV-2....screening identified tannic acid a potent inhibitor...Molecular analysis demonstrated that tannic acid formed a thermodynamically stable complex with the two proteins.... Consistently functional assays....demonstrated that tannic acid suppressed viral entry into the cells. Thus, our results demonstrate that *t*annic acid has high potential of deveoping anti-COVID 19 therapeutics as a potent dual inhibitor of two independet enzymes essential for SARS-CoV-2 infection ". (End of quotation).

This is certainly a promising Outlook!

We are waiting for more discoveries and developments to come!

3. Conclusion

All members of the group of Tannins are polyhydoxyphenols. When Tannins form complexes with proteins, they cover the protein surface with polyhydroxyphenols. Polyhydroxyphenols are more hydrophobic than the surface of proteins, and they hinder water to have access to the proteins. Hence, the proteins are denatured by the lack of water. This situation is critical for the function of the proteins. Examples of this effect of Tannins on various proteins including exposed enzymes at the surface of the virus SARS-CoY-Z are described, and they demonstrate the consequences of the effect. Especially in the case of the virus SARS-CoV-2, the effect causes neutralization of the virus and is very convincing. This situation and the other described examples indicate that application of Tannins in future biotechnological and biomedical applications will benefit to the way forward and the society.

Compliance with ethical standards

Acknowledgments

Parts of the content of the article were discussed with Dr.Michael Hoppert, Georg-August-University Goettingen/Gennany, Institute of Microbiology and Genetics, The author is retired and did not have any financial supports.

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