

Astringents and their advancement in the therapeutic uses – a literature review

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Received on: 17-06-2022; Revised and Accepted on: 14-11-2022

ABSTRACT

The use of astringents in medicine dates back to the period of Hippocrates. Ever since astringents have been known to be used in several health specialties widely ranging from dentistry to dermatology. Analysis of the literature data showed us that astringents due to its ability to coagulate proteins and vaso constrict is being used in surgical procedures such as in dentistry and otorhinolaryngology as well as in therapeutic management of several health issues. Various plants have been found to possess astringent properties and play a vital role in other indigenous and alternate systems of medicine such as Ayurveda and Chinese medicine as well.

Based on the available evidence, this article describes the basic understanding of the mechanism of action of astringent compounds and its classification and their uses in the medical field.

Keywords: Astringents, tannins, dentistry

INTRODUCTION

Latin/adstringere/means “to bind fast”. Astringents are substances capable of precipitating proteins and causing local vasoconstriction. They have very low cell permeability thus affecting only the superficial mucous layer. They abstract water from tissues thus causing shrinkage of local tissues. In view of its remarkable properties, it has a wide application.

The American Society for Testing and Materials (1991) defines Oral astringency as “the complex of sensations caused by the epithelium shrinking, drawing, or puckering as a result of exposure to chemicals such as alums or tannins” [1].

Accordingly, we define 'drying' as the “lack of lubrication, or friction between the surface of the mouth;” ‘roughing’ is felt as “a physical bumpiness of the tissues.” It is the polyphenols found in certain food substances such as certain fruits, tea that elicits puckering drying sensation in

mouth as a result of interaction between salivary proteins and polyphenols [2].

II. ASTRINGENTS THROUGH AGES AND CULTURES

Guido Majno, through his book “The Healing Hand: Man and Wound in the Ancient World” states in Mesopotamia, wounds were washed and dressed with Myrrh, a resin with astringent property obtained from Commiphora molmol. Egyptians introduced the usage of minerals into wound treatment. Green copper pigment obtained from malachite and chrysocolla had powerful astringent and antiseptic properties. Hippocrates (460-370 B.C) recommend the use of wine and vinegar in wound treatment which later proved to exhibit astringent properties. He also formulated a mouth rinse containing salt, vinegar and alum. Paulus Aegineta (625 – 690A.D.) was a 7th-century Byzantine Greek physician best known for writing the medical encyclopedia classified the substances according to its effects. He mentioned that copper ore, chimolian chalk, cold water, vinegar and wine were used as styptics and Myrrh, frankincense, sponge soaked in vinegar and wine acted as astringent [3][4].

Native Americans produced decoction by boiling the stems of witch hazel which was used to treat swellings, inflammations, and tumors [5].

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DOI: <https://doi.org/10.5281/zenodo.7319175>

An ointment made from the ground leaves of Acacia (senso latu) was used to treat haemorrhoids [6]. Astringents are found to play a vital part in Chinese medicine. Astringents are known as "Herbs to stabilise and bind". Accordingly, Astringent herbs reduce the loss of essence and body fluids via diarrhoea, sweating, vomiting, etc. by reducing the 'Qi'. Potassium alum is mentioned in the Ayurveda with the name phitkari or saurashtri which is also used in traditional Chinese medicine under the name mingfan [7][8].

III. CLASSIFICATION OF ASTRINGENTS

Joslyn and Goldstein (1964) classified astringent compounds into four main groups:

1. Polyphenols (e.g., tannic acid).
2. Salts of multivalent cations (e.g., aluminium salts),
3. Dehydrating agents (e.g., ethanol),
4. Mineral and organic acids (e.g., malic acid). [9]

IV. ASTRINGENT COMPOUNDS

1. POLYPHENOLS

They are the major source of astringent substances found in plants and their products. They regulate primary plant physiology such as pigmentation, reproduction and growth.

Polyphenols are naturally occurring organic substances containing several hydroxyl groups on aromatic rings. They range from simple molecules like phenolic acid to highly condensed compounds like tannins. Tannins, a specific class of polyphenols, are defined as compounds of intermediate to high molecular weight, capable of forming insoluble complexes with carbohydrates and protein. These compounds are used in the process of tanning which is the process of converting animal hide into leather and hence the name. Tannins are classified into 1. Hydrolysable (Tannic acid) 2. Non hydrolysable 3. phloro tannins. Tannins, bind salivary proteins and cause precipitation and aggregation [2] producing a rough, "sandpapery", or dry sensation in the mouth [10]

MECHANISM OF ACTION: Initially, several multi dentate polyphenols bind to multiple places on the protein, causing the previously randomly coiled protein to coil around the polyphenol and become denser.

The polyphenol components of the protein-phenol complex then create polyphenol bridges and protein dimers via cross-linking. Later, the dimers combine to form massive precipitating complexes. This process is thought to be initiated by the binding of the hydrophobic portion of the polyphenol's aromatic ring with the pyrrolidine ring of the protein's proline residues. [11]

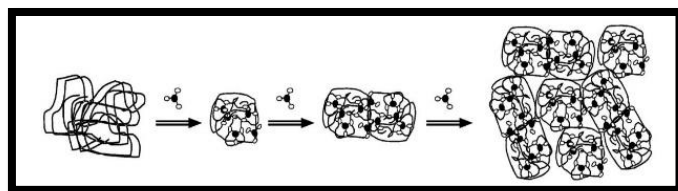


Fig 1: Molecular model of astringency produced by polyphenols [11]

USES: Tannins have been used for providing immediate relief to patients with sore throats, diarrhoea, dysentery, haemorrhaging, fatigue, skin ulcers. Tannins can cause regression of tumours, but if used excessively over time, they can cause new tumours in other healthy tissues. They have been also reported to have anti-viral antibacterial and antiparasitic effects. Poliovirus, HSV virus, and several enteric viruses are inactivated when incubated with red grape juice and red wines with a high content of condensed tannins. [13]

2. SALTS OF MULTIVALENT CATIONS (ALUMINIUM SALTS)

Aluminium sulphate (alum), a multivalent salt, is an extensively used ingredient in a variety of products including toothpastes, soaps, topical astringents, and antiperspirants. Alum is a hydrated double sulphate salt of aluminium. They are generally odourless, colourless crystalline solids that turn white in air. Alum occurs naturally in rocks that are located in areas where sulphide materials and potassium-bearing minerals.

General Formula $A_2(SO_4)_3 \cdot xH_2O$, where 'A' - monovalent cation (such as K^+ or NH_4^+), 'M' - trivalent metal ion (e.g. Al or Cr (III)). [15]

MECHANISM OF ACTION: The formation of alum ion neutralizes the charges on plasma proteins, causing the blood to coagulate.

It acts on the surface of cells and in the interstitial spaces. It has little chance of systemic absorption as it has very low permeability into cells. Potassium alum being a negatively charged particle, makes it unable to pass through the cell wall and not absorbed. In the setting of Antiperspirants, alum molecules form complexes with water, small scales of skin and lipids to create a protein mass which blocks the sweat glands. In this way the amount of sweat produced can be effectively but not permanently reduced.

Other examples include Zinc chloride ($ZnCl_2$), Zinc sulphate ($ZnSO_4$), Silver nitrate ($AgNO_3$), and Zinc oxide (ZnO).

USES: Food and Drug Administration (FDAs) has recommended alum as category I active ingredient in mouthwashes. Alum is used in many subunit vaccines as

an adjuvant which enhances the body's response to immunogens; such vaccines include hepatitis A, hepatitis B. In some parts of Nigeria, alum is also used to treat paediatric cough. It upregulates the expression of costimulatory molecules (CD80 and CD86) and intercellular adhesion molecule-1 (ICAM-1), thus promoting tight interactions between DCs and CD4+ T cells. This proves that Alum enhances humoral immunity. [17][18][19]

They are often employed as after shaving and to reduce bleeding in minor cuts and abrasions. A survey in Pakistan revealed the fact that almost 79% of barbers use alum after shave. Recent study in Pakistan suggested that most of HCV positive patients have history of facial/arm-pit shaving from barbers and it was found that frequent and continuous use of the same alum stone on different people paved way for the spread of HCV. It has been demonstrated that the virus remains infectious on the stone for an extended period of time, and that using the same stone to a normal person's shaving wounds is the definitive method of HCV transmission [20]. Potash Alum has a potent antifungal activity against *C. albicans* on acrylic resin. It may offer a cost-effective and safe alternative to commercial denture cleaning agents. [21]

3. DEHYDRATING AGENTS (ALCOHOLS)

Alcohol has one or more hydroxyl (–OH) groups attached to a carbon atom of an alkyl group. The general formula is $C_nH_{2n+1}OH$. Alcohols are good astringents at high concentration. Commercially available astringent compositions comprise high amounts of alcohol about 35-45% by weight, and are liquids having a low viscosity.

MECHANISM OF ACTION: Alcohol tends to augment the vasoconstriction caused by catecholamines and vasopressin and inhibits endothelium-dependent vasodilation. Endothelin and nitric oxide are involved in alcohol-induced vasoconstriction. [22] Soardo et al observed that alcohol increased the levels of endothelin-1, nitric oxide, plasminogen activator inhibitor-1 and oxidative stress both in vivo and in vitro. When you apply alcohol to the skin, it evaporates very quickly, stimulating the sensory nerve endings in the skin that constrict blood vessels. [23]

USES: Alcohol containing astringents are used topically over skin to treat oily skin. It also enhances its effect as antibacterial agent.

4. COCAINE

Cocaine is a tropane alkaloid extracted from the leaves of *Erythroxylum coca* and *Erythroxylum novogranatense*. [24] Cocaine has a short half-life of 0.7-1.5 hours and is metabolized by cholinesterase enzymes (primarily in the liver and plasma) and only about 1% is excreted unchanged in the urine [25].

MECHANISM OF ACTION: Cocaine binds to the dopamine, serotonin, and norepinephrine transport proteins and inhibits the re-uptake of dopamine, serotonin, and norepinephrine into pre-synaptic neurons and leads to accumulation of neurotransmitter in synaptic cleft. It binds and blocks the voltage-gated sodium channels in the neuronal cell membrane, inhibiting the initiation and conduction of nerve impulses and produces a local anaesthetic effect. [26]

USES: Cocaine has been extensively used in otorhinolaryngology surgery for its vasoconstrictive activity.

V. PLANTS WITH ASTRINGENCY

- *Geranium maculatum* (Cranesbill)
- *Croton lechleri* (Dragon's blood)
- *Salvia officinalis* (Sage)
- *Oak* (*Quercus*)
- *Acacia* (*Wattles*)
- *Achillea millefolium* (yarrow)
- *Hamamelis* (Witch-hazels)
- *Myrica*
- *Cabernet Sauvignon*
- *Merlot*
- *Aronia* (chokeberries)
- *Prunus virginiana* (bitter-berry)
- *Prunus padus* (Bird cherry)
- *Rheum rhabarbarum* (Rhubarb)
- *Cydonia oblonga* (quince)
- *Diospyros kaki* (Persimmon)
- *Prunus spinosa* (Blackthorn)

VI. THERAPEUTIC USES OF ASTRINGENTS

1. DENTISTRY

Astringents have numerous therapeutic applications in the realm of dentistry. Due to their local vasoconstricting and protein precipitating capabilities, astringents have become indispensable in dentistry. Astringents are commonly used in dental treatment to cleanse, tighten, and detoxify the gums, as well as to eliminate plaque from the teeth. [27]

GINGIVAL RETRACTION

Gingival retraction is done to a traumatically displace gingival soft tissue to allow access for impression material to record the finish line and provide sufficient thickness of gingival sulcus such that the impression doesn't tear off during removal. An ideal retraction agent should be effective and safe both locally and systemically. It should have a reversible short acting effect so that it leaves no permanent damage to tissues. [28][29]

The use of epinephrine in gingival retraction has become controversial due to its cardiovascular side effects. Epinephrine (0.1% & 8%) is used to saturate the retraction cord creates local vasoconstriction of the gingival tissues. One an inch of cord soaked with an 8% solution carries two to fifteen times the safe amount of epinephrine advised for outpatients. Though its use is found to be equally effective with nil systemic side effects, its inappropriate use could cause local tissue injury. [30] Recently invented thermally reversible gingival retracting gel compositions (polyvinyl alcohol, hydroxy aromatic gelling agent, aluminium chloride and water) stay on tissue until the completion of therapeutic purpose. [31]

ASTRINGENT MOUTHWASH

Astringent mouthwashes tend to remove excess mucous secretion of the oral cavity and research by Mitchel and butcher tends to prove that it replenishes palatal glandular activity. Recent research suggest that astringents tend to modify pellicle formation [32]. TiO₂ incorporated mouthwashes have enhanced antimicrobial activity [33].

Condensed extract derived from fruit persimmon (*Diospyros kaki*) which is rich in tannin is a common constituent of Japanese beverages and is proved to exhibit antibacterial activity against polymicrobial biofilm formed in the oral cavity. It is also known to have antiviral effect against norovirus [33].

GUM PAINT

Astringent being a constituent of gum paints along with antiseptics, it exerts a soothing and cooling effect. They are applied on edentulous ridges to strengthen its foundation [27].

Table 1: Astringents in dentistry

	ASTRINGENTS	TRADE NAME
GINGIVAL RETRACTION		
1	Aluminium sulphate gel (25%)	Gelcord/gel cord clear
2	15.5%FeSO ₄	Stat Gel
3	15%AlCl ₃	Taxodent/hemodent
GUMPAINTS		
1	2%ZnSO ₄	Zingisol
2	Tannic acid, Glycerine	Sensoform

	and KI	
3	Tannic acid 5% Choline salicylate 8% Cetrimide 0.01% Lignocaine 2% and Glycerine	Astradent
MOUTHWASH		
1	Alcohols, ZnCl, ZnSO ₄	Astradent

2. OTORHINOLARYNGOLOGY

Cocaine has been favoured for decades as the optimal agent for its long-lasting local vasoconstriction and profound sensory nerve inhibition properties. For nasal and sinus surgery in particular, topical vasoconstriction is essential to minimize bleeding for adequate visualization of anatomic landmarks and to prevent intraoperative haemorrhage. But its use is still a controversy due to its cardiotoxic effects. Procedures like nasal cauterization involve soaking cocaine in a ball of cotton wool, which is placed in the nostril for 10–15 minutes immediately before the procedure, which causes both numbing of the area to be cauterized, and vasoconstriction. [35]

'Moffett's Solution', a combination of cocaine, sodium bicarbonate and adrenaline is a standard solution in many rhinological procedures to provide local anaesthesia, vasoconstriction and decongestion [36].

Approved in Dec 2017, Cocaine hydrochloride (Goprelto) is indicated for the introduction of local anaesthesia of the mucous membranes for diagnostic procedures and surgeries on or through the nasal cavities of adults. [37]

However, research studies reveal there was no statistically significant event rate difference (major cardiac event and death) in the patients who were treated at institutions that used cocaine versus those that did not. Lidocaine (lignocaine) and tetracaine (pantocaine) in combination with epinephrine (adrenaline), naphazoline or oxymetazoline are better tolerated alternatives for cocaine. [38]

3. MELANOMA EXCISION

Studies have revealed that melanoma excision using 50% ZnCl increased the survival rate when compared to conventional surgeries. Zinc chloride deeply penetrates and kills the occult cells that are still present around the margins after excision which cannot be viewed under conventional microscopic examination and immune histochemical examination [39].

4. EYE DROPS

Over the counter eye drops for redness removal are available. Its active constituents include Tetrahydrozoline HCl 0.05% which is a sympathomimetic amine relieves

redness by vasoconstriction and Zinc sulphate 0.25% which is an astringent. This provides temporary relief of discomfort and redness of the eye due to minor eye irritations.

5. DIARRHOEL MANAGEMENT

Tannins bind to proteins on the bowel walls to alter the permeability and reduce water loss. Astringents are also effective in controlling diarrhoea by make the intestines more resistant to infections by reducing the binding of micro-organism and their enterotoxins to the bowel walls. Furthermore, astringents are used to stop internal bleeding associated with dysentery.

The tannin-rich roots of cranesbill help to reduce the permeability of the bowels. Although no research studies exist, studies show that tannins have antisecretory effects this is likely one of the mechanisms.

The oak tannins react with proteins on the surface of mucous membranes to decrease intestinal permeability and reduce bleeding. In particular, Gallo tannins possess antisecretory activity by inhibiting Ca²⁺ activated Chloride channel (CaCC).

Dragon's blood (*Croton lechleri*), a South American herb contains tannins and the active ingredient named crofeleamar, inhibits several intestinal chloride channels that cause secretory diarrhoea. The herbal extract is so effective that it was developed into an approved drug for HIV-drug induced diarrhoea. It is widely available as an herbal extract in Latin America but still is relatively difficult to find in North America.

6. SKIN CARE

Astringents are used under a variety of terms such as toners, clarifying lotions, controlling lotions, protection lotions, skin fresheners, toning lotions, T-zone tonics, etc. With its cooling effect, astringents reform the salt bonds of keratin which tighten the skin. Astringents remove excess sebum in the pores and cleanses the skin and reduces the incidence of acne in oily skin individual's especially. 2% salicylic acid and hazel which has keratolytic and drying effects can be used in acne patients. They are being used for effective removal of oily residues following the use of facial cosmetics. Astringents are also used in normal skin individuals to make their skin clean and fresh without causing dryness. Such formulations contain propylene glycol which acts as a humectant, a water attracting mild moisturizing agent. For dry or sensitive skin individuals, alcohol-free and light-weight occlusive moisturizers, such as silicone (dimethicone, cyclomethycaine) are used. In addition, soothing agents such as allantoin, guaiazulene, and quaternium-19 may be added. Modern astringents are those designed for photoaged skin containing salicylic acid (b-hydroxy acid) or glycolic acid (a-hydroxy acid) to aid in keratinocyte exfoliation and achieve smoother, more

evenly pigmented skin.[40] Calamine lotion which has zinc oxide as its active ingredient is astringent by nature. It elicits cooling effect and blocks broad spectrum sunlight and also has bactericidal action against *Staphylococcus aureus* and *Pseudomonas aeruginosa*. It is used in eczema, herpes zoster infection, pityriasis rosea, dermatitis herpetiformis, lichen planus, sunburn, urticaria, and acne vulgaris. [41]

ZnCl₂ which is an astringent along with deferoxamine is known to have protective and preventive action against burns and nuclear damage caused by nitrogen mustard (HN2) gas use during war. [42]

7. COVID CARE

Ministry of AYUSH, Government of India has stated that 20 herbs are found to be efficient in managing mild to moderate COVID-19 cases. Of which 7 herbs which include *Withania somnifera* (L.) Dunal, *Cinnamomum verum* Presl, *Azadirachta indica* A. Juss, *Justicia adhatoda* Medick, *Hedychium spicatum* Sm., *Inula racemosa* Hook.f, *Cymbopogon jwarancusa* (Jones) Schult are known to have astringent taste and action. [43]

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How to cite this article:

P.K. Sanjai Krishna; Astringents and their advancement in the therapeutic uses – a literature review. *J Pharm Res*, 2022; 11 (06): 59-65. DOI: <https://doi.org/10.5281/zenodo.7319175>

Conflict of interest: The authors have declared that no conflict of interest exists.

Source of support: Nil