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Tannins: Plant-Derived Polyphenols That Enhance Skin Healing

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ABSTRACT

In view of the healing process, factors such as depth, length and microorganisms infection can delay cicatrization, requiring the search for therapeutic alternatives, such as plant-derived metabolites. Tannins are secondary metabolites constituents of plants whose action on wounds is the most reported. The present work aims to do an exploratory descriptive literature review of tannins action as a therapeutic agent in wound healing through different mechanisms. Tannins work by forming a film on the lesion, creating an environment favorable to cell anticipation and extracellular matrix agents such as collagen and elastin, also having antioxidant and anti-inflammatory action. This polyphenol can adapt to different conditions according to their specificity and degree of aggression, thus proving to be superior to conventional means that have already been eliminated, leading to a brief discussion about these mechanisms that act synergistically during the healing process assisting in the development of new therapies.

Keywords: *Natural products, Healing, Polyphenols, Secondary metabolites*

INTRODUCTION

Skin is the largest organ of the human body serving as a primary barrier against biological agents such as viruses, bacteria and fungi, physical elements such as ultraviolet radiation and chemicals such as corrosive materials [37, 99]. In view of this, the skin tissue needs balance in response to stress or injury, and this process is then called healing, which is divided into 3 phases: inflammation, proliferative and remodelling, which are intrinsically correlated [6]. It is estimated that the annual expenditure on stitches for skin wounds reaches more than 28 billion dollars in many countries according to the world health organization (WHO), thus highlighting the importance of new treatments that are suitable

according to each clinical condition and its specificity, since particularities such as the presence of chronic and resistant diseases can make hospitalization imminent and treatment lasting, with greater expense, physical and emotional exhaustion [105].

According to the health insurance system in the United States of America (USA), Medcare, the value alone exceeds more than 40 billion annually in the outpatient service, which tends to increase as a result of hospitalizations and increased life expectancy [73]. In Brazil, public spending on treatments aimed at healing tends to increase with treatment time and the material used can reach approximately R$ 293.00/person in coverage granted in a short period of time, varying according to location, availability of resources, and people [13]. In an attempt to avoid costly public health spending on the treatment of wounds, which is sometimes ineffective, there are countless studies that aim to improve the healing process.

One of the many lines of research is the use of plant media, an age-old practice employed by many peoples, but which requires scientific proof of its efficacy and safety [12, 117]. Scientific research on medicinal plants is mainly focused on their constituents and control of action in healing, and one of the groups of secondary metabolites most associated with healing potential are the tannins that are part of the group of polyphenols [8, 88, 113, 81]. Tannins are found in several plants, and their relationship with healing in *Punica granatum* [43], *Terminalia arjuna* [103] has already been well elucidated and *Bauhinia ungulata* [95] which acts through all stages of tissue preparation by stimulating tissue cells, fibroblasts, collagen and neutrophils [67]

Tannins are divided according to their resistance or not to hydrolysis, thus being classified as condensed and hydrolysable, respectively. They have anti-inflammatory, antimicrobial, antioxidant and vasoconstrictor action already well reported in the literature. Condensed tannins are used therapeutically because of their easy binding to protein structures, conferring broad biological activity and greater permanence in the tissue [69, 45, 102]. These metabolites can be extracted from plant tissues by the most different methods of extraction methods by solvents such as methanol, ethyl acetate and ethanol [96, 44, 30]. The present work aims to gather and integrate information on the action of tannins during the healing process in cutaneous wounds, and/or locally depending on the route of administration, as well as to evaluate the current scenario of bioprospecting these as a new therapeutic alternative in the treatment of wounds.

METHODOLOGY

A literature review was carried out, with a descriptive and exploratory character. A literary survey of works published between the years 2003 - 2023 in Portuguese, Spanish and English, in the main databases of scientific works, Scielo, Google Scholar, Springerlink, Pubmed and Lilacs, being them: taninos (tannins/taninos), cicaytização (healing tannins/cicatrización), condensed tannins (condensed tannins/taninos condensados), fração rica em taninos na cicatrização (fraction rich in tannins in wound healing/fracción rica en taninos en cicatrización) and medicinal plants (medicinal plants /plantas medicinales). Emphasis was given to the direct action of tannins in all phases of healing, highlighting their influence and action pathways and those studies that do not prove this direct relationship are not included in this review.

ORIGIN, CHARACTERISTICS AND BIOLOGICAL ACTION OF TANNINS

Tannins are part of the large group of natural compounds, the polyphenols. In their structure, they have hydroxyls connected to aromatic rings and are subdivided into hydrolyzable and condensed (Figure 1) [2]. Condensed tannins, mainly, have the ability to easily bind to protein complexes and polysaccharides in mucous membranes and tissues through hydrogen bonds, which makes them widely used in the commercial in the production of wines and leather tanning, which is quite profitable in those obtained by its large-scale performance [36, 24]. Tannins have a high adhesion index and molecular weight, especially condensed ones, which add what adds astringency to wines improves their flavor and what also aids in the healing of deep or deep wounds [105,113].

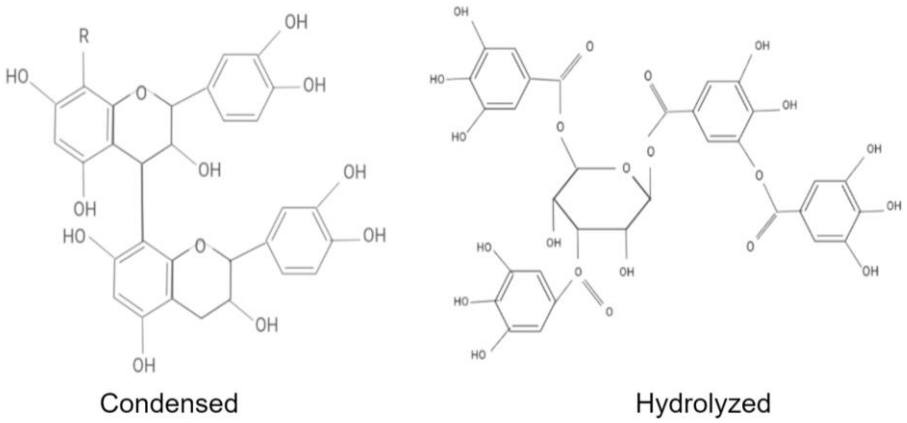


Figure 1. Representation of the structure of the main tannin groups

The synthesis of tannins occurs mainly in organelles derived from chloroplasts and are located in waxes that occur in plants and vacuoles [25]. Two pathways are responsible for its formation, namely the acid pathway, with the union of phosphoenolpyruvate with erythrose 4-phosphate which is divided into 3 phases: galloylation, generation of gallotannins and emission of galioid residues [86,104 , 16]. This union can generate gallic and ellagic acid with enzymatic action, having 2 main representatives of gallotannins and ellagitannins with influence on antioxidant activity and on the aging process by shortening telomeres [86,102].

The other is the acetate malonate route, highlighted in nutrition research, which is the precursor of flavan-3-ol, it has two phases for the formation of tannins, namely, glycosylation, where sugars are added to proteins and lipids forming glycoproteins structured and oligomerization with linkage of two or more polypeptide chains [104]. Tannins, in addition to originating from plants, can also be produced artificially using naphthalenes, crucibles and other superior hydrocarbons as primary ingredients [103, 113].

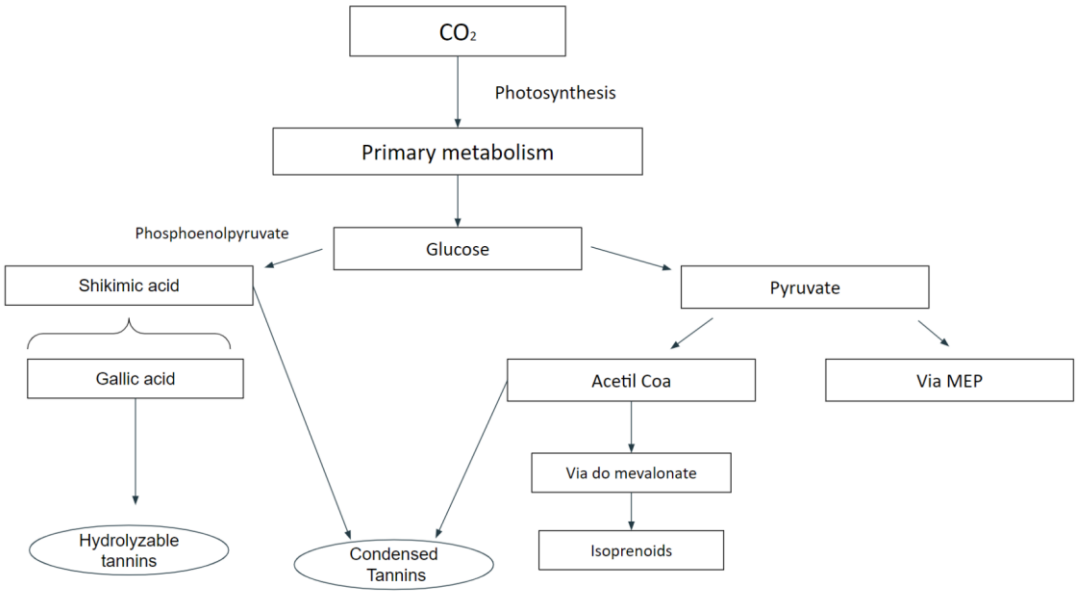


Figure 2. Reaction chain for the synthesis of hydrolyzable and condensed tannins.

Tannins can be found in various parts of plants such as roots, leaves, fruits with a greater proportion in the bark [86]. The secondary metabolites of plants, including tannins, can undergo changes due to changes in temperature, tension force and storage, however, it is seen in the literature that they do not change in their contents in order to survive the seasons of the year, but with greater ratio in protection and post storage [114]. Its ingestion takes place with the use of water or organic solvents such as methanol and ethanol, it is worth noting that the quality of the extract rich in tannins depends on factors such as the duration of the process and order of application of the solvents, since the constituents of the plant can interfere with the presence of high levels of tannins to be used in different clinical conceptions [25].

It is evidenced that the absorption of ingested tannins occurs normally despite its high molecular weight, being a dietary component metabolized by the intestinal microflora composed of bacteria whose reaction products are similarly phenyl valeric, phenylpropionic, phenylacetic and benzoic acid with systemic effect and subsequently excreted in the colon by two lactones conjugated by glucuronic acid [70]. It is observed that if consumed excessively, tannins form non-absorbable complexes with proteins, sugars, digestive enzymes, metal ions and vitamins (A, B12), which reduces their nutritional value [56] and increases the availability of oxidative and nutritive agents [111, 103].

The consumption of tannins also acts on internal lesions such as gastric ulcers by increasing the cytoprotection of the mucosa, however in deep gastric lesions beyond the epithelium, in the connective and smooth tissue, the time of use may be longer, adapting according to the state of patient's health, like those with chronic diseases [108, 104, 102, 57], however, it is worth mentioning that its safe dosage according to the American Federal Drug Administration (FDA) is 100 mg/kg a day with a minimum frequency of use, and cannot be used indiscriminately because it causes severe damage to the function of organs such as the liver [115].

In topical application, tannins can act by stimulating endogenous factors at all stages of healing [84]. These polyphenols act in the inflammatory phase, helping from homeostasis, with fibrin formation, to the recruitment of inflammatory mediators and growth factors such as tumor necrosis alpha (TNF-□), platelet-derived growth factor (PDGF), fibroblastic growth (FGF) and transforming growth factor (TGF). In this process there is also the activation of defence and elaborated cells such as monocytes, lymphocytes and keratinocytes in addition to essential proteins such as elastin, ordering the tissue to its initial state [89, 28]. Due to its astringent property, tannins form complexes with proteins or polysaccharides that also create a protective physical barrier under the lesion, protecting against bacteria, free radicals and possible cell that give rise to various neoplasms [67, 46].

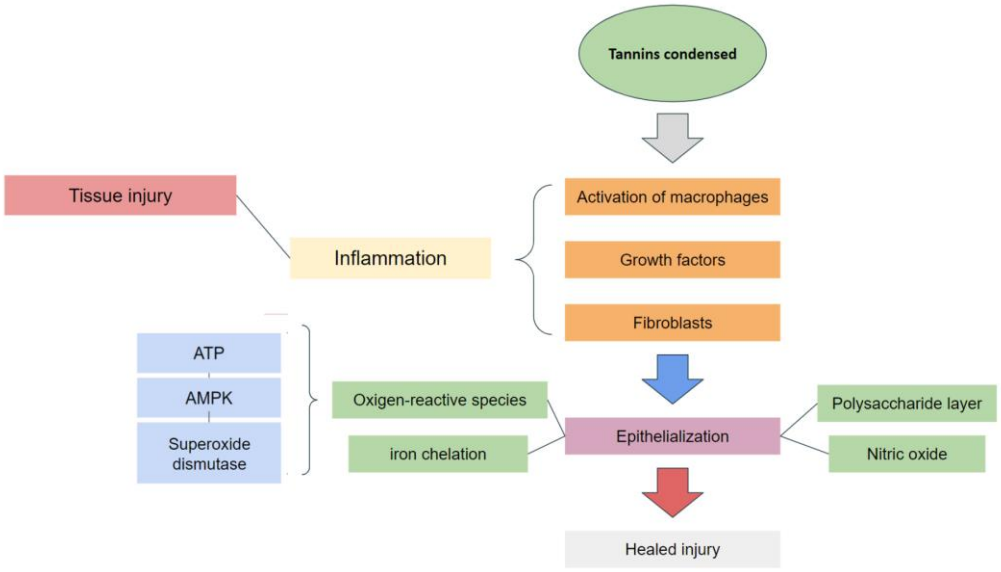


Figure 3. Tissue healing process using condensed tannins with representation of the main pathways of action.

In the proliferative phase of wound healing, tannins aid in the chemotaxis of growth factors, stimulating collagen and forming new blood vessels [81]. The action of tannins reaches a peak on the 7th day of tissue healing, which corresponds to a proliferative phase. However, wound characteristics such as: size, friction and amount of exudate can interfere with the closing time of its edges [102, 87]. Among the types of tannins available for consumption and administration (Figure 2) they are largely related to the healing process due to their resistance to hydrolysis, which in turn allows for a longer residence time and tissue response in addition to having low toxicity [95].

The non-use of topical formulations, hydrogels, creams and gels, with the addition of tannins is determinant that their physical/chemical characteristics provide a more accelerated permeation adapting to humidity, an essential factor in angiogenesis, a fundamental process for tissue oxygenation [61] . Its greatest use in the treatment of injuries concerns the use in spongy and gelatinous format for the membrane or in teas with the benefit of non-toxicity by the report of more traditional communities in the interior of Brazil, mainly in the Northeast [69]. In the use of hydrogels, tannic acid has been encouraged as it promotes stability in solutions that are crosslinked controlled, a factor that further drives its use in emulsions [66].

Tannins have vasoconstrictor, anti-inflammatory, antimicrobial properties, use in healing cuts or immunosuppressive diseases in traditional communities [88]. In view of its clinical potential, topical use at low concentrations has been highlighted for wound healing [76]. In addition to healing, research on affected problems has enormous prominence, such as combating the replication of the HIV virus [115] and diabetes [63].

TANNIN EXTRACTION METHODS

Due to their heterogeneous nature, the yield, purity and composition of these polyphenols are dependent on parameters such as: natural source, collection technique and environmental conditions so that there is a better inheritance of these plant constituents [45]. Several organic solvents are used to extract tannins from natural tissues such as twigs, leaves and bark, most of which are methanol (MEOH), dichloromethane petroleum ether (DCM), ethanol (ETOH) and ethyl acetate, which provided higher yields, but the use of n-hexane, ether and petroleum, which are non-polar, are also used along with chloroform [104,31].

In most works involving tannin plants, aqueous organic solvents are the most adopted due to their easy handling, with methanol and acetone being the main ones due to the degree of yield, however, other solvents show promise in practice, such as ethanol [74]. The principle to understand the application of these solvents is the eluotropic scale which consists of using polarity as a means of extracting the active principles of plants, being necessary to know the class of compounds to be reflected and their water, in addition to the material available for use and the plant in question. There is still no definitive consensus on choosing the best tannin inheritance method, therefore screening and interaction studies between these compounds and organic solvents are extremely important [106].

When using organic solvents, it is also necessary to pay attention to the fact that their stability decreases with increasing temperature and exposure to sunlight. A shelf extract exposure between 2 and 5 hours, depending on the degree of storage, affected the efficacy, given the choice of acetone or methanol [14]. The proportion of plant material/solvent and the transmission time can also interfere with the amount to be extracted [106]. In general, the temperature, the solvent and its proportion in relation to the plant material act interdependently [51].

Maceration is one of the most used techniques, being in accordance with a physical training that uses thermodynamics such as temperature and applied force. The time for ingestion can vary from 30 to 40 minutes, however what will define is the time for overcoming the surface membrane of the plant giving access to its constituents and their degree of conductivity together with the type of solvent that can be used, being usually ethanol, methanol and water [15].

Water is employed to extract polar substances particularly when it has experienced a temperature corresponding to its boiling, where components containing carboxylic acid and hydroxyl

groups are extracted through hydrogen bonds, however due to the polarity of organic solvents are still the best choice [75]. Water as a solvent in pediatrics requires temperatures between 60° to 120° C when used together with methanol or ethanol [25]. The concentration of aqueous solvents seems to be directly related to the absorbance value since between the use of methanol and acetone, the higher the concentration, the greater the decrease in absorbance. If acetone is not used in the sample, there is a decrease in absorbance and time, which is why it is chosen recurrently [74].

In some cases, ingestion process accelerators can be used, taking vanillin and phenolic aldehyde as an example to increase precision as additives for quantification of the crude extract, that is, to provide greater precision in the calculation of polyphenols together with sodium sulfite in a process called sulfitation to increase the total material, making it more evident [21]. The addition of enzymes ends up accelerating the processes within the cell membrane, which makes the guarantee even more effective [25].

In addition to traditional laboratory methods, it is possible to use distillable ionic liquid ingestion for large-scale production of plant-derived tannins that are used for commercial leather tanning. The infrared method increases efficiency according to the wavelength of the heater and the distance between the source and the solvent material. There are also other techniques such as supercritical, ionic, liquid-assisted and pressurized hot microwaves [25].

MEDICINAL PLANTS AND TANNINS IN WOUND HEALING

Among the plants that have a healing action with activity related to tannins, it is possible to highlight *Punica granatum*, which, based on the analysis of the bark by methanolic inheritance at 75% with the use of soxhlet, highlighted the increase in granulation tissue, mainly related to the isolated tannic of type A and B punicalagin, as well as gallic and ellagic acid [43] visited the wound area if applied in gel vehicle, corresponding to 55% [80] to 95% of the wound edge [82].

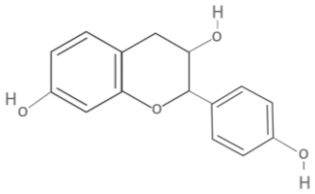
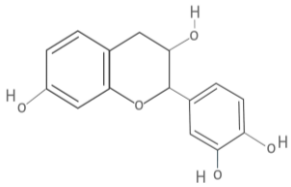
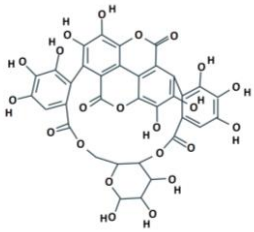
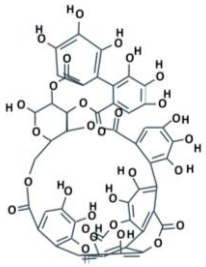
This potential is also studied for other solvents such as 70% ethanol in burn wounds [78] and for cuts, ethyl ether tested an absolute positive effect [91], its effect being similar to the role of ampicillin in combating infectious agents in the lesion [65], with collagen stimulation being the main means of promoting action [91]. The action and other tannic isolates are also highlighted with the use of methanolic extract, being punicalin and penecalagin with antioxidant activity as described in table 1 [83].

Mimosa *pudica* known as “sensitive plant” presents a healing effect as a methanolic extract after degreasing with total aqueous petroleum ether (extraction of the lipid recipe), being reported in addition to the ointment, evidencing the presence of alkaloids and mainly hydrolysable tannins, with a result on the fourth day and a peak on the eighth of the tissue, with the presence of hydroxyproline highlighted [54]. The use of this root based on the recommendation with methanol and chloroform solvent is related to the synthesis of growth factors [50]. Its effect on diabetic wounds is also reported [55].

Since the beginning of the 20th century, it has been possible to identify tannins from the phytochemistry of *Terminalia arjuna* [18], a factor responsible for increased migration and parenchyma trends from the hydroalcoholic recommendation with increased traction [20]. The use of ethanol solvent also demonstrating tannins has its effect related to the increase of hydroxyproline favoring the formation of type 1 collagen, mainly in the gel formulation [98]. It has in its aqueous extract action in a norepinephrine ring, mainly in the inflammatory phase and hypotensive effect [109] in addition to combating agents such as Propionibacterium *acnes* [112] and anti-inflammatory activity directly related to tannins [118] and induction of cancer cells [52].

The use of *Terminalia arjuna leaves* from the use of ethanol solvent demonstrates activity related to increased traction and collagen stimulation, helping in neovascularization [107, 66], and combating bacteria such as Staphylococcus *epidermidis, Staphylococcus subtilis* and *Staphylococcus aureus* [53], the presence of tannins [103] and the antioxidant activity promoted by it having already been demonstrated in phytochemistry, preventing the shortening of telomeres, a process responsible for the state of the skin causing aging [84].

Table 1 . Main tannic isolates with healing action reported in the literature.

Structure	Name	Formula	Reference
	guibourtinidol	$C_{15}H_{14}O_4$	[95]
	Fisetinidol	$C_{15}H_{14}O_5$	
	Punicalin	$C_{34}H_{22}O_{22}$	[83]
	punicalagin	$C_{48}H_{28}O_{30}$	[43]

It is seen that the tannins have about 14 isolates related to healing activity divided into 4 groups, the carboxylics, gallotannins, ellagitannins and without specifications for containing isolated particularities, both easily dissociated in high pH anions, some of which are found in the methanolic extract of *Terminalia chebula* [60] with identification by HPLC [55].

The use of methanolic extract from the bark of *Lafoensia pacari* is due to the presence of saponins, steroids and mainly pyrogallic tannins, with its anti-inflammatory activity also being evidenced by the intensified COX 1 and reduction of oxidative stress [34]. The 70% hydroethanolic extract of the leaves also demonstrates macrophage-promoting action in lesions, as well as in ulcers and gastritis [90].

Poincianella *pluviosa* has already demonstrated an effect on tissue processing in the optimization of keratinocytes and fibroblasts by brute, with polyphenols being the most related to this activity [10]. Condensed tannins together with triterpenes collaborate in the proliferative cascade by stimulating chemical mediation, with the best result coming from methanol inheritance in the formation of carboxy cellulose polymers on an injured area [40].

The ethanolic extract of *Psidum guajava leaves* has a healing effect on gingival cells related to its tannins and flavonoids [33, 93]. It has already been applied in formulation and gel with positive results in diabetic wounds [48]. Another plant already studied for this principle is *Stryphnodendron barbatiman* in formulations of 2.5 and 5% in cream [28, 33]. The use of its extract by ethyl acetate favored vasoconstriction and coagulation of proteins related to tannins [44] , having anti-inflammatory activity [92], being able to potentiate results from optimization [108] and applied in formulations for chronic deficiencies such as diabetes [5], as well as possible properties to try to be applied to the ethanolic extract of Cnidoscolus quercifolius [*37*] .

Plants such as *Bauhinia ungulata* show healing action with the use of its ethyl acetate extract where its tannic isolates such as Guiboutinialol and fisetinidol inhibit reactive oxygen species and cell migration from the beginning of proteins [95]. Quercus *infector* from its ethanolic extract of dried leaves showed antioxidant activity related to free radical scavenging and increased granulation and collagenization [110], as well as Blechnum orientale [92]. Types such as *Mimosa tenuiflora* with ethanolic extract and *Quercus persica* are also well explained [96,118]. The use of polyherbals tends to have positive effects if applied to harmful processes, an example being the use of leaves of *Psidium guajava* and *Mellaostoma malabatericum* from ethanolic therapy, where their tannins produced action on wounds [77, 74].

Table 2. *In vivo* studies using extracts with tannins for wound healing (cutaneous) using plant extracts and their respective inheritance methods.

plant species (Popular name)	part of the plant	Hospitalization/fraction/isolation processes	wound model	Tested groups	Formulation of cream	Performance	closing %	References
Research involving the use of tannins in healing without association with comorbidities								
Blechnum orientale Linn	sheets	Methanol	Excision in the dorsal region in a rodent	(-) creamy base (+) 10% povidone-iodine	1% and 2% extract cream respectively	6.5%	1% extract (95%) and 2% extract (100%) - 14 days	[62]
Terminalia chebula (Meleric Mirabolan)	immature fruit	Ethanol 95%,	The dorsal surface of the rodent	(-) Vaseline ointment 5 mg per wound (+) Erythromycin ointment 5 mg per wound	Extracts at a dosage of 5 mg + vaseline, per wound	without measurement	Significant difference to the control (P< 0.05) 100% before the 21st	[67]
terminalia arjuna *(Haritaki or arjuna bark)*	bark	Ethanol 50%	Incision in shaved skin and cutaneous muscles of rats	Untreated group; 100,300,10 mg/kg; 1.5 and 0.1%	Orally with 150 and 300 mg kg of extract day and another 10 mg/day. And they contain 1.5 and 0.1% processed	12%	Topical application of 0.1% tannins with 462 g pull 16 days of treatment	[98]
terminalia arjuna	bark	Ethanol 50%	6 cm incision	(-) No application (+)Betadine	Cream with addition of hydroalcoholic extract	Not mentioned	Fraction rich in tannins with traction of 719 g. 9th day of experiment	[18]

phaseoloid input (Saint Thomas)	bark	Ethanol 95%	back injury	(-) 5 mg vaseline ointment (+) 5 mg Bactroban	Formulation: Vaseline + 5 mg of extract.	do not measure .uproar	On the 14th day, the Test Wounds showed partial epithelialization without itching	[102]
Salarbio Corp (Cas 1401-55-4, HPLC ‡ 98%, China) .	Specific tannic acids	Tannins 2g/mL stock solutions	Incision in the dorsal region	White group: No application, left separately and test group	0.25 mL of TA were used at different concentrations of 1.5, 1.0 and 0.5g/mL, respectively	not measured	Model group of 98.43%; comparing the mice TA-treated with YB-treated rats, group YB after day 7 and almost healed on day 15.	[22]
Persian Quercus (Black Oak)	bark	Methanol	Incision 2.0 cm long and 0.2 cm deep	Ucerin-based ointment and untreated group	The experimental group was treated by daily application of 5% methanolic extract ointment.	No percentage measured	94.41±0.26 26 days after starting the application.	[7]
Bauhinia ungulata L *(Bovine leg).*	stem wood	hexane (4 × 10 L) and ethanol (4 × 10 L)	Incision in the back region	Base Formulation	Topically treated with 200µL of 0.5% FABU gel once daily for 5 days	80%	Significant repair on the 14th day of treatment	[95]
poincianella pluviosa (Sebipira)	bark	20L of EtOH-water (1:1 v/v)	*In vitro* cell culture	Positive control: cells treated with 5% FCS And the untreated negative	Mitochondrial activity was assessed by the MTT test, the rate of myogenic cell prospects by incorporation of BrdU	Not mentioned	Significant reduction in the 10th day (no reduction by area %)	[10]

					Assay and release of lactate dehydrogenase			
poincianella pluviosa (Sebipira)	stem bark	Ethanol 50%	Incision in the back region	not described	Polymer film added over wound	Not mentioned	Significant difference from 10th to 14th (without %)	[38]
Lafoensia pacari *(Foxglove)*	sheets	Extracted with 50% acetone/water in an ultrasonic bath for 30 min at a drug:solvent ratio of 10% (w/v).	Incision in the dorsocervical region	Negative control: Distilled water Positive Control: Base cream for days	10% *L. pacari* extract in distilled water	Not mentioned	Significant difference from the 7th to 14th day of treatment	[17]
Lafoensia pacari *(Foxglove)*	sheets	Maceration in 70% hydroethanolic solution (1:10, w/v) for 7 days at 25°C to obtain the aqueous ethanolic extract	6 cm incision up to the fascia in the craniocaudal direction in the dorso-lumbar region	Positive Control: Doxorubicin Negative control: No application	Not mentioned	Not mentioned	Complete re-epithelialization of the wound in 22.0 ± 1.5 ($p < 0.05$) and 21.7 ± 1.6 ($p < 0.01$) days	[90]

prudish mimosa (Do not touch me)	sheets	Acetone + Water (7:3) by the cold maceration method. Petroleum ether is added to this filtrate.	back injury	Negative control: Plain ointment (e.g. beeswax, cetostearyl alcohol, etc.), Positive control: 5% povidone iodide	*Mimosa pudica* and ointment applied 5%	Not mentioned	On the 19th day reduction in length of 0.69 mm and width of 1.17.	[19]
prudish mimosa (Do not touch me)	source	Total aqueous extract was prepared by decoction method with distilled water in the ratio of 1:5	Excision on the back in a circular shape (approx. 500 mm2)	Simple ointment blood control	Ointment containing 1% and 2% (no formula description) total aqueous extract	14.42%	1% of the extract (88.69%) 2% of the extract (97.34%)	[54]
Stryphnodendron adstrigens (Barbatimão)	Not mentioned	Not mentioned	Ovariohysterectomy injuries	placebo ointment	Manipulated ointment based on barbatimão in the percentage of 2.5 and 10%	Not mentioned	In 15 days it was obtained: 2.5% (2.5%); 10% (1.7%)	[28]
Rubia cordifolia L. (Indian madder)	roots	Ethanol (95%)	back of mice	flat base	A 0.2%, 0.5% and 1% gel	9%	Reduction of 4.7 mm in 7 days from the 1st application	[47]

Psidium guajava Linn (Guava)	sheets	Acetone (70% v/v)	mouse coast	Negative control: control (white gel without drug. Positive control: 0.8% formalin aqueous solution	5% and 10% gels.	Not mentioned	Reduction in 5% Gel (57.57 mm) and 10% Gel (103.62 mm) in 12 Days.	[48]
Psidium guajava Linn (Guava)	leaves and bark	Ethanol and solvents of increasing polarity such as petroleum ether, chloroform, ethanol and aqueous to produce its production	rodent coast	Negative Control: Plain ointment (eg, beeswax, cetostearyl alcohol Positive Control: 5% Povidin iodine ointment	5% of the extract in the ointment	Not mentioned	Contraction of 94.81% in 16 days of treatment	[93]
Psidium guajava Linn (Guava)	sheets	70% ethanol	On the tongue with a 3 mm diameter circular scalpel.	not described	Two applied applications of the swab-tested drug at 12-hour intervals throughout the experiment	Not mentioned	Significant repair on the 3rd to 14th Day (No percentage)	[33]

Mimosa *tenuiflora (Calumbi)*	husks	By maceration with ethanol for 72 h at room temperature	Double-blind clinical trial, randomized and placebo-controlled	Treated and untreated groups	hydrogel	Not mentioned	92% reduction in 21 days of treatment	[96]
Stryphnodendron adstringens (Barbatimão)	Not mentioned	Uninformed	back of rodents	Negative control: 0.9% regulatory solution Positive control: Formulated ointment	Barbatimão 10%	Not mentioned	100% on the 14th day of treatment	[102]
Pterolobium hexapetalum	sheets	Organic solvents (500 mL) such as petroleum ether, ethyl acetate and methanol in increasing order of their polarity	Excision wound on the back	Negative control: Ointment without actives Positive control: Neomycin 5%	2.5% and 5% of the ointment	Not mentioned	100% reduction in 21 days of treatment	[103]
Quercus infectoria	sheets	95% Ethanol	On the backs of rodents there were Two incisions for vertebral	Not mentioned	In acute toxicity: increasing doses (1, 2, 4 and 8 g / kg body weight)	270 g	Epithelialization of 98, 58 on the 14th day of treatment	[110]

					In the incision: 400 and 800 mg/kg			
Research involving polyherbal in wound healing								
malva sylvestris *Solanum nigrum* *damask rose*	sheets petal oil	Sesame oil as a solvent	15 mm deep circular burn on back	Negative control: No medication Positive control: 1% fadiazine silver sulfate (SS) cream	Aqueous extract of M. silvers and S. nigrum and 33% oil extract of R. damascena in a cream base including eucerin (25%), white vaseline (28%) and white beeswax (4%).	Not mentioned	54.8% better than the control on Day 14 of treatment	[30]

Table 3 . *In vivo* experimental research involving tannins in healing diabetic wounds.

plant species (Popular name)	**part of the plant**	**Hospitalization/ fraction/isolation processes**	**wound model**	**Tested groups**	**cream formulation**	**Performance**	**Wound Decrease**	**References**
butea gum	gum	Boiling water and sated brine solution	dead space	Not mentioned	Powdered substance, which has been treated with ether	42%	Formation of granulation tissue on the 8th day, (Not mentioned %)	[58]

Psidium guajava Linn (Guava)	sheets	Extracted with acetone (70% v/v) by the cold maceration method, this fraction was evaporated and used for the study.	A single dose of 84 mg/kg of alloxane monohydrate dissolved in saline mouse back	Negative control: control (white gel without drug Positive control: 0.8% formalin aqueous solution	5% and 10% gels	Not mentioned	5% gel fraction (76.27 for 18.70 mm) and 10% gel fraction (110.29 for 6.67 mm)	[52]
Research involving polyherbal								
Melastoma malabathricum L. *from Psidium guajava L.*	sheets	oven at ± 50EC and 70% ethanol	dorsal surface of the foot	5 groups in a hyperglycemic state, then the mice were induced using a 10 g alloxan monohydrate injection	Mixture of leaf extracts	Not mentioned	40 to 29.6 mm² in 5 days	[77]

Table 4 . *In vivo* experimental research involving the use of tannins in healing associated with burns

plant species (Popular name)	part of the plant	Hospitalization /fraction/isolation processes	wound model	Tested groups	cream formulation	Performance	Wound Decrease	References

punica granatum *(Pomegranate)*	flower	Aqueous ethanol (70%)	Supine position on box with back up	Saline Solution and Base Cream	Creams containing 5% And 10% extract It was mixed with liquid paraffin, stearyl alcohol, cetyl Alcohol and Span 80 to 70∘	26.8%.	Size of 1 cm² without 20° diameter	[85]
prudish mimosa (Do not touch me)	source	Chloroform and methanol	6 cm long straight paraspinal incisions	Group I, Untreated control; Group II, Simple Ointment	The methanolic extract formulation was prepared as 2.5% (w/w) and 5% (w/w) hydrophobic base as a simple ointment The chloroform extract was made at 2.5% (w/w) and 5% (w/w) in a hydrophilic base such as carbopol (1%) containing methyl paraben (0.01%) and propylparaben (0.1%) .	Not mentioned	50% reduction compared to the control group on the 10th day	[50]

MAIN CONTROL OF ACTION OF TANNINS IN WOUND HEALING

ANTIOXIDANT ACTION

Reactive oxygen species (ROS) are the main cause of damage to the surface of the skin and are present in the environment. These compounds are produced and acquired at all times, and it is up to the body to bring about a balance between oxidant and antioxidant agents [71]. The antioxidant activity of tannins is dependent on the structures of absorption, neutralization of radicals and peroxide compounds [11]. In view of this, they act by avoiding lipid peroxidation, balancing the creation and elimination of peroxides, thus not becoming an aggravating factor [2, 86]. This class of polyphenols works from three main pathways, which are the elimination of free radicals, the chelation and transcription of metals and the orientation of pro-oxidative enzymes [70].

The lipid peroxidation time is dependent on characteristics such as molecular weight, ring hydroxylation and antioxidant potential of the analyzed constituents. The mechanism of action occurs through the orientation of pro-oxidative enzymes that age in nitric oxide synthase, generating an effect on lipoxygenase (LOX), which then damages membrane lipids, with research into this effect contributing to the discovery of phlorotannins, which are a class tannins and which has been highlighted for its potential use as an antioxidant and anti-inflammatory agent. The chelation pathway of heavy metals occurs through the binding of cations of metals such as iron and copper, which are cofactors of antioxidant enzymes such as catalase and superoxide dismutase. The lipid peroxidation pathway occurs through the oxidative modification of low-density lipoproteins, the most common being LDL [3, 59, 70].

Tannins have a wide variety of types, which can often dictate their antioxidant effect depending on their structural organization, however there is a wide relationship with proanthocyanidins belonging to the group of condensed tannins that due to their complex structural and ecological diversity Physical chemistry bestows this potential in a more illuminating way. From different tests using different identification pathways against an effect reducer, either by the antioxidant capacity by trolox equivalence (TEAC), iron reduction (FRAP) and 2, 2-diphenyl-1-picrylhydrazyl-hydrate (DPPH), antioxidant potential is already seen [119].

ANTI-INFLAMMATORY ACTIVITY

Tannins relieve the pain threshold due to inflammatory hyperalgesia, where there is no continuous stimulation of inflammation during healing, which causes heating and other cardinal signs of inflammation, mainly edema, which would generate pain due to the release of endogenous mediators such as bradykinin and serotonin. In addition to this process, there is an increase in cyclooxygenase in the release of arachidonic acid by the biosynthesis of prostaglandins of the neurogenic phase, that is, there is a local psychological effect in prolonging the intensity of inflammation and this is due to the transition beyond the prostaglandin 2 (PGE) and enzymatic acceleration that are stimulated by the induction of carbon dioxide (CO 2) from the spinal cord and cyclooxygenase (COX-2). In addition, its effect may contribute to thermal, mechanical and muscular hyperalgesia pathways due to its high bioactivity in chronic pain, inhibiting chemical mediators such as TNF, IL 1 and PGE and decreasing nitric oxide responsible for great swelling, intensity and increased itching throughout the inflammatory phase in its extension of origin [27, 39, 91, 23, 101, 81), which would explain its potential against toothaches [94].

MICROBIOLOGICAL EFFECT

Faced with the high level of problems facing bacterial resistance to antibiotics in their indiscriminate use by the population, several alternatives have been studied as a possible treatment model, one of which is the use of tannins because they are of plant origin and have good distribution and low toxicity [29] . This action is related to several action pathways against gram positive and negative bacteria, the main ones being induced cell synthesis, combating the formation of biofilms,

enzyme induced and iron chelation where the o-dihydroxyphenyl groups are linked by ferric ions that unite at the molecular level [16].

The antibacterial effect of tannins is related to the surface components and their ability to non-covalently associate with proteins and other macromolecules which, if done successfully, causes bacterial susceptibility, this compound causes the lysis process and consequently the death of microorganisms which may delay healing by producing exudate [35]. Some analyzes have already been carried out on the class of bacteria that present this susceptibility, considering that species such as *Staphylococcus aureus*, *Staphylococcus luteus*, *Staphylococcus epidermidis*, *Proteus vulgaris*, *Escherichia coli*, *Salmonella typhi*, *Listeria innocua* and *Bacillus cereus* have also been shown to bacteriostatic action in these groups [61, 26, 11], also in the literature it is possible to find action in other less pathogenic types, such as Propionibacterium acnes [42] *and* having already experiments with formation of minimum inhibitory concentrations (MIC) higher than 1600 µg mL^{1} that are considered bactericidal [32].

Its action against fungal groups that can also disrupt tissue control is still little related, however, it is known that its mechanism of action depends on the destabilization and permeation of the cytoplasmic cell membrane, driven by extracellular membrane enzymes and direct actions on its metabolism, which consequently generates death to the infectious agent [11]. It is seen that the presence of carbohydrates in tannins reduces their antifungal efficiency [25].

In research carried out in groups of basidiomycetes, ascomycetes and mitospores (deuteromycetes) it was seen that tannins function with their own inhibitory effect from these previously mentioned pathways. Within the growth of the so-called brown subgroups in relation to the white and soft types, this designation referring to the factor of decay and destruction of the plant support of fungal groups dispersed in the environment, to which these classes were identified for the first time, it is seen the decay of their survival with a fungicidal character with the addition of copper impregnation, although not many cause resistance in humans, being more present in the commercial sphere, they observe the quality of export in wood [5].

PHYSICAL BARRIER

Tannins have as their main pathway in healing the formation of a layer on the surface of the epithelium that encourages the formation of collagen, elastin and components of the extracellular matrix that fight infectious agents, functioning as a mechanical barrier preventing physical particles (eg dust, pollen , etc) come into contact with the area that would be exposed [67]. This constipated layer of polysaccharide acts in the fight against free radicals and neoplasms by stimulating agents such as tissue factor (TF), which participates in an accompanying way in the cascade of coagulation and cytokine migration [46, 114].

It is the formation of this film that the healing phases are not negatively sustained by microbial agents that received exudate formation, mainly in the inflammatory and proliferative phase, with the action of chemotactic growth factors and overlapping of vascular connective tissue with re-epithelialization and vessel formation [56, 81]. Tannins thus end up increasing the number of cells continuously without affecting the migration of agents such as keratinocytes and essential proteins such as collagen and elastin during the last stages of epithelialization [89]. The use of tannic acid should still be boosted in the production of creams and cosmetics, as it aids in the stability of this formula with a high water content, with an emphasis on hydrogels increasing its crosslinking which even better seen in rheological analyzes increased its attraction and prospects cell according to the chosen property [66].

CLINICAL USE IN COMORBIDITIES

In the population with chronic diseases, secondary interferences such as hormonal, behavioral and chemical interaction factors can generate immense difficulty in the duration of the healing process, mainly in the formation of ulcers due to dermal xerosis of the lower limbs in diabetics with

uncompensated hyperglycemia [1, 100]. For the treatment to work properly, it is necessary to understand the entire pathological process in question for adequate traditional use together with the practice of scientific knowledge about what is present there and how it can interact to generate some kind of benefit in the short term. An example of type 2 diabetes where the use of free radical chelating products decreases the amount of reactive oxygen species and increases the formation of capillaries, generating oxygenation and stimulation of fibroblasts, thus being a great alternative to this problem [67].

With regard to tannins, they can be applied to the skin from a vehicle, helping to maintain a favorable microenvironment, which is humid, allowing and accelerating controls. Tannins are closely linked in the regulation of enzymatic activities, which configures an action in the fight against several pathologies that can be from diabetes mellitus to the rarest, acting in a systemic way from its consumption and topically in wound healing, being also seen that its functionality is related to non-damage to the membrane and combating neoplasms [41, 61] **.**

Despite this high potential for use, it is worth noting that the tannins had a limited effect due to their tendency to interact with other so-called substances, their low chemical stability, rapid metabolism and low availability, requiring the development of means that preserve them for a longer time compared to the its clinical use that can last for days, either this topic or systemically as an example of using the encapsulation process [68].

THERAPEUTIC POTENTIAL

The action of tannins in wound healing is evident, acting through multiple ways of action such as their antimicrobial action, as a physical barrier and stimulator of fibroblasts, neutrophils and macrophages, these of which interact and function at the same time in the cascade of processes of respectability. This efficiency is dependent on the minimum amount of these polyphenols in a given location or systemically with the formation of agents such as blood vessels by stimulating angiogenesis, which is one of the main precursors of tissue nutrition and inflammatory intensity [47, 30, 93, 28] .

It is evident that the tannins act by stimulating mainly the fibroblasts that continue to stimulate collagen and elastin, which are the main agents responsible for the reduction of the lesion. epidermis that has antibacterial activity [64, 17, 48, 101, 9, 7]. This pathway also stimulates keratinocytes, which are agents belonging to the dermal layer and have a pro-inflammatory action in stimulating cytokines [22].

Antioxidant activity is the main agent responsible for contributing to healing time, which is the main means of combating cells that may undergo the presentation process together with granulation agents [110]. It is clear to point out that tannins from these aforementioned routes have an enormous potential for clinical applicability, which is sometimes still unlikely in medical routine, due to the greater incentive for synthetic products [100, 95].

It is evident the contribution that this compound tends to bring to a population that often uses plants rich in tannins in food, being more evident in the preparation of teas. If tannins are applied, not only does it offer the convenience of being cheaper and more accessible to the population, but also for those who use it in healing, it is possible to observe the formation of crusts in a shorter time, absence of itching and better tissue organization, bringing elasticity and a better degree of of skin contraction [72].

CONCLUSION

Tannins are constituents of plants that received protection against predators, being reported in traditional medicine as a healing agent and acting in all phases of tissue reconstitution, mainly in inflammation and remodeling. In view of this, the present literary overview demonstrates that tannins act in an anti-radical, anti-inflammatory way, in the fight against bacterial and fungal microorganisms, as well as generating a physical barrier, elucidating the importance of looking for better ways to stabilize

and deliver this compound as a therapeutic model, which can be done mainly through creams and gels increasing their permanence time under the injured skin.

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REFERENCES

(1) Andrade, MG L et al. Evidence of changes in the healing process of burns in diabetic individuals: a summary review. **Rev Bras Queimaduras** . 2013; 12(1):42-8

(2) Andrade, JMM et al. Identification of compounds from nonpolar fractions of Blechnum spp and a multitarget approach involving enzymatic modulation and oxidative stress. **Journal of Pharmacy and Pharmacology** , 69 (2017), pp. 89–98

(3) Aziz et al. Inhibition of 15-lipoxygenase by Blechnum orientale leaves and their isolated flavonoid glycosides: in vitro and in silico studies. **HAYATI J Biosci** 355 Vol. 29 No. 3, May 2022

(4) Aguiar, PS et al. Benefits of Stryphnodendron adstringens when associated with hydrogel in wound healing in diabetic rats. **Clinical Phytoscience** (2021) 7:22; doi: https://doi.org/10.1186/s40816-021-00257-5

(5) Anttila, A.-K. and others (2013). Condensed tannins from conifers as antifungal agents in liquid culture. **Holzforschung**, *67(7)*. https://doi.org/10.1515/hf-2012-0154

(6) Aragão-Neto, AC et al. Combined therapy with low power laser and chitosan policaju hydrogel for wound healing. International Journal **of Biological Macromolecules** , p. 268-272, 2017.

(7) Akran, E. et al. Evaluation of the antibacterial and healing activity of Quercus persica. **Journal of Basic & Applied Sciences** , 2012, 8, 118-123

(8) Baptistel AC Coutinho, JMCP Neto-Lins, EMF Monteiro, JM Medicinal plants used in the Santo Antônio Community, Currais, southern Piauí: an ethnobotanical approach. **Rev. Bras. Pl. Med** ., Campinas, v.16, n.2, p.406-425, 2014.

(9) Bueno, FG et al. Hydrolyzable tannins from the hydroalcoholic extract of the stem bark of Poincianella pluviosa and its healing properties: phytochemical investigations and influence on in vitro cellular physiology of human keratinocytes and dermal fibroblasts. **Phytotherapy 99** (2014) 252–260.

(10) Bueno, FG et al. Skin Wound Healing Enhanced In Vivo by Standardized Crude Extract of Poincianella pluviosa. **PLOS ONE** | https://doi.org/10.1371/journal.pone.0149223 March 3, 2016

(11) Cano, A. et al. Use of tannins to improve the functional properties of protein-based films. **Food Hydrocolloids** 100 (2020) 105443.

(12) Castro, MR Figueiredo, FF Traditional knowledge, biodiversity, integrative and complementary practices: the use of medicinal plants in the SUS. **Hygeia** 15 (31): 56 - 70, March/2019.

(13) Cortez, DN et al. Costs of treating skin lesions in Primary Health Care. **ESTIMATE, Braz. J. Enterostomal Ther.** , São Paulo, v.17, and 2419, 2019.

(14) Cork, J. Krockenberger , AK Methods and pitfalls of transmission of condensed tannins and other plant phenolics: research insights in eucalyptus leaves. **J Chem Eco** . 1991 January;17(1):123-34. https://doi.org/10.1007/BF00994426

(15) Cuong, DX et al. Tannins: traction for plants. **Tannins: Structural Properties, Biological Properties and Current Knowledge.** p: 57-77, 2020

(16) Cruz, EH et al. Poly(vinyl alcohol)/cationic tannin blend films with antioxidant and antimicrobial activities. **Materials Science and Engineering** C 107 (2020) 110357

(17) Chaibud, BA et al. Pharmacognosy Investigation of the healing activity of the extract of the leaves of Lafoensia pacari (Lythraceae) cultivated in the state of Goiás, Brazil. **Pharmacognosy** , Rodriguésia 71 (2020). https://doi.org/10.1590/2175-7860202071058

(18) Chaudhari, M. Mengi, S. Evaluation of Terminalia arjuna Phytoconstituents for Wound Healing Activity in Rats. **Phytother** . Res. 20, 799–805 (2006)

(19) Chamakuri, SR et al. Different Fractions of Mimosa pudica by Healing Activity. **Journal of Chemical and Pharmaceutical Research** , 2019, 11(3): 14-21.

(20) Chopra, RN Ghosh, S. *Terminalia arjuna* . **The Indian Medical Journal** , p. 70-73, (February) 1929.

(21) Chavan, U., Shahidi, F., & Naczk, M. Extraction of condensed tannins from beach pea (Lathyrus maritimus L.) as affected by different solvents. **Food Chemistry** , 75(4), 509-512, (2001), https://doi.org/10.1016/s0308-8146(01)00234-5

(22) Chen, Y. et al., Tannic Acid Accelerates Cutaneous Wound Healing in Rats Via Activation of the ERK 1/2 Signaling Pathways. **Advances in wound care** , *wound.2018.0853–*. https://doi.org/10.1089/wound.2018.0853

(23) Chopade, AR et al. Pharmacological Aspects of Phyllanthus fraternus Standardized Extract (Rich in Lignans and Tannins) as a Pain Modulator. **The Open Pain Journal** , 2020, Volume 13.

(24) Dias, RAL et al. Drying and Total Tannin Extraction from Spearmint (Mentha x Vilosa Hudson). **Rev. agarian.** v.4, n.12, p.123-133, 2011.

(25) Das, AK et al. Review on tannins: extraction processes, applications and possibilities. **South African Journal of Botany** 135 (2020) 5870.

(26) Doss, A. et al. Antibacterial activity of tannins from *Solanum trilobatum Linn leaves* . **Indian Journal of Science and Technology** . Vol.2, pages 41-43, nº 2 (February 2009), ISSN: 0974-6846.

(27) Ebaid, R., Ahmed, OM Mahmoud, AM Ahmed, R. Limiting prolonged inflammation during the proliferation and remodeling phases of wound healing in streptozotocin-induced diabetic rats supplemented with undenatured camel whey protein. **Rev. BMC Immunology** , 2013.

(28) Fagundes, SK et al. Efficacy of barbatimão ointment (Stryphnodendron barbatiman) in the healing of iatrogenic scars in cats. **Archives of Veterinary Sciences and Zoology at UNIPAR** , Umuarama, v. 23, no. 2, count 2310, 2020.

(29) Farha, AK Tannins as an alternative to antibiotics. **Food Bioscience** 38 (2020) 100751

(30) Fahimi, S. et al. Wound healing activity of a traditionally used herbal product in a rat burn model. **Iran Red Crescent Med J.** 2015 September; 17(9): e19960

(31) Fawole, OA et al. Anti-inflammatory, anticholinesterase, antioxidant and phytochemical properties of medicinal plants used for pain-related diseases in South Africa. **Journal of Ethnopharmacology 127** (2010) 235–241.

(32) Fernandes, AFC et al. Antiproliferative, antileishmanial and antimicrobial studies in *Cnidoscolus quercifolius* Pohl (Euphorbiaceae) Antiproliferative, antileishmanial and antimicrobial studies in *Cnidoscolus quercifolius* Pohl (Euphorbiaceae). **NATURAL PRODUCTS RESEARCH** , 2020 Informa UK Limited, trading as Taylor & Francis Group

(33) Fernandes, KPS Healing and cytotoxic effects of Psidium guajava (Myrtaceae) leaf extracts. **Braz J Oral Sci** . 9(4):449-454

(34) Filho, PTetal. Evaluation of the antiulcer activity and mechanism of fractionation of methanol extracts from the stem bark of Lafoensia pacari A. St.-Hil. (Lytraceae) in experimental animals. Journal of **Ethnopharmacology** 144 (2012) 497–505

(35) Figueroa-Espinoza, Maria-Cruz & Ratisbonne-Zafimahova, Andrea & Maldonado Alvarado, Pedro & Dubreucq, Eric & Poncet-Legrand, Céline. (2015). Grape seed and apple tannins: emulsifying and antioxidant properties.

(36) Fonseca P. Librandi, APL Evaluation of the chemical, physical and phytochemical characteristics of different tinctures of barbatimão (Stryphnodendron barbatiman). **Brazilian Journal of Pharmaceutical Sciences** , v. 44, No. 2, 2008.

(37) Gomes, TB Bandeira, FPSF Use and diversity of medicinal plants in 23,533 ± 0.01a quilombola community in Raso da Catarina, Bahia. **Acta Botanica Brasilica** 26(4): 796-809. 2012.

(38) Guidi, ACS Poincianella pluviosa bark extract incorporated into polymeric film: Evaluation of wound healing and anti-staphylococcal activities. **Injury** 51 (2020) 840–849

(39) Gomes, LCS; Carmo, KF Effects of high power ultrasound in the treatment of localized lipodystrophy: Case report. **Health and science electronic magazine** , v. 5, no. 2, pg. 25-33, 2015.

(40) Gomes, LMA et al. Antinociceptive activity of the ethanolic extract of the bark and leaves of Cnidoscolus quercifolius (Euphorbiaceae) in mice. **Journal of Young Pharmacists** Vol 6 ● Issue 2 ● Apr-Jun 2014

(41) Gupta A. et al. Screening of the flavonoid-rich fraction of three Indian medicinal plants used for the treatment of liver diseases. **Rev. Brasileira de Framacognosia** , p. 485-490, 2015.

(42) Gurnig, K. et al. Determination of Total Tannins and Antibacterial Activities Ethanol Extraction Seri Leaves (Muntingia calabura L.). Journal **of Physics: Conference Series** , 1811 (2021) 012121, IOP Publishing, doi: 10.1088/1742-6596/1811/1/012121

(43) Hayouni, EA et al. Ointment based on hydroalcoholic extract of Punica granatum L. bark with greater in vivo healing potential in dermal wounds. **Phytomedicine** 18 (2011) 976– 984

(44) Hernandes, L. Evaluation of healing of Stryphnodendron adstringens ointment (barbatimão) in rat skin. Brazilian **Journal** of Pharmaceutical Sciences, 2010.

(45) Hoyos-Martínez, PL et al. Tannin extraction: Key point for its valorization and cleaner production. **Journal of Cleaner Production** 206 (2019) 1138e1155

(46) Jesus, NZT et al. Tannins, Peptic Ulcers and Related Mechanisms. **Int. J. Mol. science** . V.13, P. 3203-3228, 2012

(47) Karodi, R. et al. Evaluation of the healing activity of a crude extract of Rubia cordifolia L. (Indian redhead) in mice. International Journal **of Applied Research in Natural Products Vol. 2(2**), pp. June 12-18, 2009 Available online http://www.healthy-synergies.com ©2009 Healthy Synergies Publications.

(48) KumarI, SJ et al. Formulation and evaluation of herbal gel from the tannin-enriched fraction of Psidium guajava Linn. leaves for healing diabetic wounds. **International Journal of Green Pharmacy** • July-Sep 2018 (Suppl) • 12 (3) | S490

(49) Kumar, RS et al. Evaluation of Healing Activity of Diabetic Incisional Wounds of Mimosa pudica L. Leaf Ethanol Extract in Rats. International Journal of Pharmacognosy and Phytochemical Research 2017; 9(8); 1143-1147

(50) Paul. J. et al. Evaluation of wound healing of chloroform and methanolic extract of mimosa pudica roots in rats. **Int J Biol Med Res** . 2010; 1(4): 223-227

(51) Ping, L. et al. Extraction of condensed tannins from grape pomace: Characterization and use as wood adhesives for wood particleboards. **Crops and Industrial Products** , Volume 34, Issue 1 , July 2011, Pages 907-914.

(52) Kumari, SJ Formulation and evaluation of herbal gel from the tannin-enriched fraction of Psidium guajava Linn. leaves for healing diabetic wounds. International Journal **of Green Pharmacy** • July-Sep 2018 (Supl) • 12 (3) | S490

(53) Kannan, P. et al. Antibacterial activity of Terminalia chebula fruit extract. **African Journal of Microbiology Research** Vol. 3 (4) pp. 180-184 April 2009

(54) Kokane, DD et al. Evaluation of the healing activity of Mimosa pudica root. **Journal of Ethnopharmacology** 124 (2009) 311–315.

(55) Kumar, KJ et al. Effect of geographic variation on tannic acid, gallic acid, chebulinic acid and ethyl gallate contents in Terminalia Chebula fruits. **NPAIJ,** 2(3-4), 2006 [100-104].

(56) Kuo, PL, and others. Casuarinin from the terminalia arjuna bar induces apoptosis in human breast adenocarcinoma cell cycle arrest in MCF-7 cells. **Plant Med** 2005; 71: 237-243

(57) Kundu, A. et al. Wound healing activity of ethanol root extract and polyphenolic-rich fraction of Potentilla fulgens. **Taylor & Francis Group** , p. 1-12, 2015.

(58) Kuppan, D. et al., Wound healing potential of tannin in dead space wounds in diabetic rats. **World J Pharm Sci** 2021; 9(8): 110-113.

(59) Koleckar, V. et al. Condensed and hydrolyzable tannins as antioxidants influencing health. **Mini-Reviews in Medicinal Chemistry** , 2008, 8, 436-447.

(60) Juang, L, J. et al. Determination of hydrolyzable tannins in the fruit of Terminalia chebula Retz. by high performance liquid chromatography and capillary electrophoresis. **J. Sep. Sci** . 2004, 27, 718-724.

(61) Lai, HY et al. Blechnum Orientale Linn - a fern with potential as an antioxidant, anticancer and antibacterial agent. **Complementary and Alternative Medicine** 2010, 10:15 am

(62) Lai, HY et al. Dermal healing potential in Blechnum orientale Linn. **BMC Complementary and Alternative Medicine** 2011, 11:62

(63) Lai, JCY et al. Treatment for diabetic ulcers using a hydrogel formulation optimized with fern tannin with antibacterial and antioxidant properties. **Journal of Ethnopharmacology** 189 (2016) 277–289

(64) Lai, HY et al. Isolation and characterization of a proanthocyanidin with antioxidant, antibacterial and anticancer properties from Fern Blechnum orientale. **Revista Farmacognosia** , January-March 2017, Vol 13, Issue 49

(65) Lukiswanto, BS et al. Evaluation of the wound healing potential of whole pomegranate (Punica granatum) fruit extract on skin burns in rats (Rattus norvegicus). **J. Adv. Veterinarian. Animal Res.**, 6(2): 202–207, June 2019.

(66) Lee, HY et al. Improvement of biostability and mechanical properties of hyaluronic acid hydrogels by tannic acid treatment. **Carbohydrate Polymers** 186 (2018) 290–298.

(67) Li, K. et al. Tannin extracts from immature fruits of Terminalia chebula Fructus Retz. promote healing of skin wounds in mice. **BMC Complementary and Alternative Medicine** , p. 1-9, 2011.

(68) Liang, X. et al. Zein-pectin nanoparticles fortified with tannic acid: stability, properties, antioxidant activity and in vitro digestion. **Food Research International** 145 (2021) 110425

(69) Lu, B. et al. Skin wound healing with a chitosan-gelatin sponge loaded with tannins and platelet-rich plasma, **International Journal of Biological Macromolecules** , p. 1-10, 2015.

(70) Macákova, K. et al. Tannins and their influence on health. **Recent Advances in Medicinal Chemistry** , vol. 1, 2014, 159-208.

(71) Machado, PA et al. Molecular mechanisms of antioxidant action of resveratrol intrinsic intracellular pathways. **Biosfera Encyclopedia** , Knowing Scientific Center - Goiânia, v.13 n.23; pg. 750, 2016.

(72) Madhura, MR Mengi, SA Comparative effect of oral administration and topical application of alcoholic extract of Terminalia arjuna bark in incision and excision wounds in rats. **Phytotherapy 74** (2003) 553–558

(73) Medicare and Medicaid Services (USA). Available from: <https://www.cms.gov/search/cms?keys=healing> Accessed on: March 14, 2022.

(74) Makkar, HPS Becker, K. vanillin-hc1 method for condensed tannins: effect of organic solvents used for tannin extraction. **Journal of Chemical Ecology** , vol. 19, No. 4, 1993

(75) Markom, M. et al. Extraction of hydrolyzable tannins from Phyllanthus niruri Linn.: Effects of solvents and extraction methods. **Separation and Purification Technology** 52 (2007) 487–496

(76) Mekonnen A. et al. In vivo wound healing activity and phytochemical screening of crude extract and various leaf fractions of Kalanchoe petitiana A. rich (Crasulaceae) from a mouse. **jor. Ethnopharmacology** , pg. 638-646, 2013.

(77) Maigoda, TC Wound Healing and Blood Sugar Effect of Psidium guajava L. Leaves and Melastoma malabathricum L. Leaves in Rats with Diabetic Foot Ulcer. **j. Applied Sciences.** , 19(4); 287-294, 2019

(78) Ma, K. et al. Evaluation of the healing effect of Punica granatum L Peel Extract on deep second-degree burns in rats. **Trop J Pharm Res** , January 2015; 14(1): 73

(79) Mukherjee, PK Evaluation of the wound healing activity of some herbal formulations. **Fitoter. res** . 17, 265–268 (2003)

(80) Murthy, KN C et al. Study of the healing activity of Punica granatum peeling. **Journal of Medicinal Foods** VOL. 7, No. 2 | 2004.

(81) Moreski, DAB Leite-Melo, EVS Bueno, FG Healing action of medicinal plants: a review study. **Arch. Science Health UNIPAR** , Umuarama, v. 22, no. 1, pg. 63-69, Jan./Apr. 2018.

(82) Nayak. SB et al. Wound healing activity of the bark of Punica granatum fruit. **Journal of Medicinal Foods** , VOL. 16, No. 9 | 2013

(83) Nema, N. et al. Topical in vivo wound healing activity of Punica Granatum bark extract in rats. **AJPCT** , 1[2] [2013],195-200.

(84) Na, M. et al. Cytoprotective effect on oxidative stress and inhibitory effect on cellular aging of Terminalia chebula fruit. **Fitoter. Res.** 18, 737–741 (2004)

(85) Nasiri, E. et al. The effects of Punica granatum flower extract on burn-induced skin lesions in rats. **Hindawi Publishing Corporation Advances in Pharmacological Sciences** Volume 2017, Article ID 3059745, 8 pages http://dx.doi.org/10.1155/2017/3059745

(86) Nogueira, AJL et al. Tannins a review. **Rev. Integrated Topics of Botany,** Ed. Athena, p. 32-44, chap. 4, 2021.

(87) Olczyk, Mencner P., Komosinska-Vassev L., K. The role of extracellular matrix components in cutaneous wound healing. **BioMed Research International** , V. 2014, p. 1-8, 2014

(88) Passaretti, T. et al. Effective use of barbatimão (Stryphnodendron barbatiman) in the wound healing process: a literature review. **ABCS Health Science**, v. 41, 2016.

(89) Pellenz, NL et al. Healing activity of Stryphnodendron adstrigens (Mart.), a Brazilian species rich in tannins: literature review and case series. **Wound medicine** , v. 26, 2019.

(90) Pereira, LOM et al. Lafoensia pacari A. St.-Hil.: Healing activity and mechanism of action of standardized hydroethanolic leaf extract. **Journal of Ethnopharmacology** 219 (2018) 337–350.

(91) Pirbalout, AG et al. The wound healing activity of Punica granatum and Achillea Kellalensis flower extracts in Wistar rats. **Acta Poloniae Pharmaceutica – Drug Research** , vol. 67 No. 1 pp. 107-110, 2010

(92) Pinto, SCG et al. Stryphnodendron adstringens: Unraveling wound healing in streptozotocin-induced diabetic rats. **Plant Med** 2015; 81: 1090–1096

(93) Rao, CS Comparative Study of the Tannin Fraction of Psidium guajava Linn. Leaves and Bark for Healing Activity, **JPRPC** | Volume 3 | Edition 4 | December 2015.

(94) Ramakrishnan, K. and Krishnan, MRVTannin – classification, analysis and applications. **Ancient science of life** , 13 (3-4), 232, 1994.

(95) Rodrigues, RO et al. Antioxidant, anti-inflammatory and healing potential of the ethyl acetate fraction of Bauhinia ungulata L. (Fabaceae) in an in vitro and in vivo wound model. Molecular **Biology Reports** (2020) 47:2845–2859

(96) Rivera-Arce, E. et al. Therapeutic efficacy of an extract of Mimosa tenuiflora cortex in the treatment of venous leg ulceration. **Journal of Ethnopharmacology** 109 (2007) 523–528 Kokane, DD Evaluation of the wound healing activity of Mimosa pudica root. Journal of **Ethnopharmacology** 124 (2009) 311–315.

(97) Raja F. Júnior, JPP Preliminary phytochemical analysis and GC-MS of methanolic extract of Blechnum orientale L. collected in Kothiyar, Kanyakumari district, Tamil Nadu, India. **Journal of Drug Delivery & Therapeutics**. 2019; 9(4-A):587-590

(98) Rane, MM Mengi, SA Comparative effect of oral administration and topical application of alcoholic extract of Terminalia arjuna bark in incision and excision wounds in rats. **Phytotherapy** 74 (2003) 553–558

(99) Rente, SCC; Mejia, DPM Application of 3MHz ultrasound in the treatment of gynoid lipodystrophy. **Articles BIO CURSOS,** Articles on dermatofunctional physiotherapy, 2015. P.121-132.

(100) Rodrigues, D, F. et al. Barbatimão Bark Extract, Stryphnodendron Adstringens (Martius) Coville, In Wound Healing In Animals. **Biosphere Encyclopedia** , Knowing Scientific Center - Goiânia, v.9, N.16; pg. 2011584 3, 2013.

(101) Rodriguez, JAM et al. Evaluation of granulation capacity in surgical wounds with condensed tannins in tio2 matrices. **Herb tea. Res. Simple Society Proc** . Vol. 1479 © 2012 Materials Research Society https://doi.org/10.1557/opl.2012.1599

(102) Santos, AT Júnior, JM Cunha, GN Second intention healing of wounds in Wistar rats using Stryphnodendron adstringens. **Animal Science** , v.29, n.1, p.15-29, 2019.

(103) Sathyanarayanan, S. et al. Chemical profiling of Pterolobium hexapetalum leaves by HPLC analysis and their productive wound healing activities in rats. **Biomedicine and Pharmacotherapy** , Volume 95, November 2017, pages 287-297

(104) Sieniawska, E., Baj, T. (2017). Tannins.Pharmacognosy, 199–232. https://doi.org/10.1016/b978-0-12-802104-0.00010-x

(105) Silva, LL et al. Importance of the use of medicinal plants in the processes of xerosis, fissures and healing in diabetes mellitus. **Rev. Bras. Pl. Med.** , Campinas, v.17, n.4, suppl. I, p.827-835, 2015.

(101) Souza, SMC et al. Anti-inflammatory and anti-ulcer properties of Allemão Myracrodruon urundeuva (Anacardiaceae) tannins in rodents. **wiley interScience** , pg. 220-225. 2007.

(102) Su, X. et al. Healing effect of total tannins from Entada phaseoloides (L.) Merr. in mouse. **Elsevier** , 2016.

(103) Sharmaa, Kartik; Kumar, Vikas; Kaur, Jaspreet; Tanwar, Beenu; Goyal, Ankit; Sharma, Rakesh; Gat, Yogesh; Kumar, Ashwani (2019). *Health effects, sources, utilization and safety of tannins: a critical review.* ***Toxin Reviews****, (), 1–13.* https://doi.org/10.1080/15569543.2019.1662813

(104) Shukla, V. Bhatena, Z. Broad-spectrum antiquorum detection activity of tannin-rich crude extracts of Indian medicinal plants. **Hindawi Publishing Corporation Scientific** , 2016.

(105) Sharma, P. et al. Antiulcerogenic activity of Terminalia chebula fruit on experimentally induced ulcer in rats. **Pharmaceutical Biology** , 49:3, 262-268, 2011, DOI: https://doi.org/10.3109/13880209.2010.503709

(106) Shad, MN et al. (2012). Optimization of tannin extraction efficiency from Cichorium intybus L.: application of response surface methodology. J. Med. Plant Res. 6. 4467-4474.

(107) Saguna, L. et al. Influence of Terminalia chebula on the healing of dermal wounds in rats. **Fitoter.** Res. 16, 227–231 (2002)

(108) Souza, JN et al. Optimization of ultrasound-assisted extraction of polyphenols, tannins and epigallocatechin gallate from bark extracts of Stryphnodendron adstringens (Mart.) Coville. **Pharmacognosy Magazine** | April-June 2014 | Volume 10 | Issue 38 (Supplement 2).

(109) Takahashi, S. et al. Hypotensive effect in rats of hydrophilic Terminalia arjuna extract containing tannin-related compounds. **PHYTOTHERAPY RESEARCH**, VOL. 11, 424–427 (1997)

(110) Umachigi, SP et al. Studies on the healing properties of Quercus infectoria. **Tropical Journal of Pharmaceutical Research** , March 2008; 7(1): 913-919

(111) Vannuchi, H. et al. Role of Nutrients in Lipid Peroxidation and Antioxidant Defense System. Medicine, Ribeirão Preto, **Symposium: CLINICAL NUTRITION**, 31: 31-44, Jan./Mar. 1998

(112) Vijayalakshmi, A. et al. Development and Evaluation of Antiacne Products from Terminalia arjuna Bark. Int. **J. PharmTech Res** .2011.3(1).

(113) Vizzotto, M. Krolow, AC Weber, GEB Secondary Metabolites Found in Plants and their Importance. **Embrapa- Brazilian Agricultural Research Corporation**, p. 6-16, Pelotas-RS, 2010.

(114) Wolfe, RM Terril, TH Muir. JP Drying method and pattern source affect condensed tannin (CT) concentrations in perennial herbaceous legumes using simplified butanol-HCl CT analysis. **J. Sci Food Agric**, p. 1060–1067, 2008.

(115) Yang B. Liu. P. Composition and biological activities of hydrolysable tannins from Phyllanthus emblica fruits. **J. Agricultural and food chemistry**, p. 529-541, 2014.

(116) Yi Sun, Z. et al. A biocompatible bacterial cellulose/tannic acid compound with antibacterial and anti-biofilm activities for biomedical applications. **Materials Science and Engineering** C 106 (2020) 110249

(117) Zeni, ALB Use of medicinal plants as home remedies in Primary Care in Blumenau, Santa Catarina, **Brazil, Ciência & Saúde Coletiva** , 22(8):2703-2712, 2017.

(118) Zibanejad, S. et al. Healing effect of Quercus persica and Lawsonia inermis ointment on episiotomy wounds in primiparous women. **Res Med Sci** 2020;25:11

(119) Zhou, Ch. et al. Structural diversity and antioxidant activity of fractionated condensed tannins from mangosteen pericarp. **Food Chemistry** 129 (2011) 1710–1720

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