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Review of selected herbal phytoconstituents for wound healing treatment

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Abstract
Wounds are an unavoidable part of life that can come through physical accidents that cause an opening or break in the skin, as well as chemical sources. Many invading organisms find the wound region to be an appropriate medium for manipulation. As a result, invasive microbial diseases can still invade the wounded skin. Wound healing is a complex process of tissue repair and remodelling that happens in the following of an injury. As a result, wound care's primary purpose is to prevent or reduce infection while also promoting healing. Antibacterial medicines, among other materials and procedures, are used. Phytochemicals are well-known for their ability to treat a variety of diseases and conditions. It also has a lot of potential for discovering and developing new medications for a variety of human illnesses. Plants and plant-derived elements have long been used to treat and manage many types of wounds. Plants and plant-derived elements have long been used to treat and manage many types of wounds. The purpose of this review is to compile a list of medicinal plants and phytoconstituents that have been shown to be beneficial in the treatment of wounds.

Keywords: Phytoconstituents, wound, wound healing, plants

Introduction
For thousands of years, plant-derived medicines have been used in human treatment [1]. A huge portion of the world's population relies on plant-based medicine because of its broad availability and lack of superior healthcare options. Many countries, including China, India, and much of Africa, have relied on plant-based medications or herbal remedies to cure a variety of ailments [2]. The treatment of diseases, wounds, and burns in many nations is aided by the use of plant extracts, mixes, decoctions, and pastes. For as long as anybody can remember, many medicinal herbs and plant-based approaches have been widely recognised for their beneficial effects on healing wounds and regenerating skin [2].
Wounds can be caused by both physical and chemical methods that open or break the skin [3]. It is estimated that wounds affect millions of people's bodily and mental health, and they are also a huge financial burden. Restrictions in physical activity can be caused by wounds. About 6 million people around the world are estimated to suffer from chronic wounds [4]. Numerous medicinal plants and their phytoconstituents have been reported to exhibit wound healing activity and to be useful for wound care and infection prevention.
There are a number of phytoconstituents that have antioxidant and antibacterial activities as well as the ability to trigger one or more reparative pathways in the body [5]. Wound healing has been improved by using a range of plant extracts as a result [6]. Antioxidant capabilities have been discovered in a variety of wound-healing medicinal plants. In other dimensions, various research conducted over the years have shown that plants have a tremendous potential for boosting wound healing due to their high antioxidant content. As a result, the purpose of this publication is to add to the current research on medicinal plants' wound-healing abilities and antioxidant capabilities.
The review article begins with a classification of wounds, then moves on to numerous elements that affect the wound healing process, as well as the mechanism, explained in detail.

Methodology
I used the accessible electronic databases as a source and search approach. The search was conducted with the help of a few well-known botanical names and keywords. Since 2001, published publications on wound healing and antioxidant capabilities have been consulted online.

This study focused on wound healing plants that had been treated with wound models and showed evidence of antioxidant capability. Researchers also looked at phytoconstituents from plants that have been found to heal wounds.

Literature review

Wound

Living tissue can be affected by a variety of physical, chemical, thermal, microbiological and immunological factors [7]. These factors can disrupt cellular, anatomical and functional continuity.

A wound is a harm to the skin or the underlying tissue or organ that results from this event. Wounds are described as injury to or disruption of normal anatomical structure and function [8, 9].

Types of wound

Acute wounds

In acute wounds, tissue damage/injury occurs, which normally follows an ordered and time-reparative phase that recovers anatomical and functional integrity over time. Cuts or surgical incisions are the most common causes of acute wounds [10].

Closed wounds

When a wound is closed, blood leaks out of the circulatory system, but remains inside the body. As a result, bruising is more obvious.

Wounds that have not healed Blood pours out of a cut and causes apparent bleeding. Depending on the origin of the wound, the open wound can be further subdivided into many categories.

Incised wounds

Only a small amount of tissue has been damaged in this incision, which shows no tissue loss. Sharp objects, such as a scalpel or knife, are the primary cause.

Tear or laceration wounds

Tissue loss and damage occur as a result of this non-surgical injury, which often occurs in conjunction with other forms of trauma.

Puncture wounds

These are the result of a nail or a needle puncturing the skin. Infection is a common occurrence because dirt can penetrate deep into the wound.

Abrasive or superficial wounds

Abrasion is caused by sliding on a rough surface. In this period, the epidermis is scraped off, exposing nerve endings, causing in pain and discomfort.

Penetration wounds

When a knife or other sharp item penetrates the skin, it leaves a penetrating wound.

Gunshot wounds

A gunshot or other object that penetrates or enters the body is the most common cause of these injuries.

Chronic wounds

Since they have not gone through the usual healing process, chronic wounds are in a state of pathological inflammation. [11] They take longer to heal.

Wound healing

The anatomical and functional structure and function of a wound are preserved during the healing process. Repair and regeneration of injured tissue is possible in all species, including humans. Factors such as the patient's health and immunity, the intensity and type of wounds they have, the patient's habits (such as smoking, drinking, etc.), as well as the disastrous nature of an assault-environment around a wound site, and the potential for serious microbial infection are all important to consider.

Mechanism/pathophysiology of wound healing

There are three steps of wound healing: allergic response, propagation, and remodelling. During the inflammatory process, the wound healing response propagates and blood clotting and coagulation factors occur. Examples of cellular activity include the infiltration of leukocytes and the release of antibiotics and cytokines. Epithelium covers the wound surface and granulation tissue forms to fill it in during the proliferative process. Granulation tissue is formed by the proliferation of fibroblasts, the deposition of collagen and other extracellular matrix, and the development of new blood vessels [14].

The remodelling process begins as soon as new tissue forms inside the wound, restoring the tissue's structural integrity and functional competency. Time-dependent rather than simple linear methods, the three stages of wound healing constitute a different storey. To describe acute wounds, such as a burn or a significant trauma or an open wound from surgery, we use the term "acute." Organized healing aims to produce tissues that are structurally and functionally comparable to the retained skin, but regeneration is a rare occurrence (with significant exceptions, such as early foetal healing). As a result, healing produces a physically and functionally competent but not identical product. Various growth factors and cytokines generated at the wound site tend to influence wound healing processes. Tissue damage and delayed recovery can occur when healing processes are disrupted [15].

Blood-borne cells including neutrophils, macrophages, and platelets play key roles in the healing process' coagulation and inflammation phases (A). For epidermal and dermal cell recruitment, these cells provide the growth factors and intermediate matrices that are required. The proliferative phase (B) begins roughly 3 days after damage when keratinocytes and fibroblasts respond to autocrine, juxtracrine, and paracrine growth factors with increased proliferation, migration, and ECM creation. This process also includes angiogenesis/neovascularization.

The granular appearance of the tissue is due to the involvement of blood vessels (granulation tissue). Extracellular matrix remodelling begins in the granulation tissue about 1 to 2 weeks after injury by differentiated fibroblastic cells (my fibroblasts). Acellular scar development is caused by extracellular matrix remodelling along with resident cell death [17, 18].

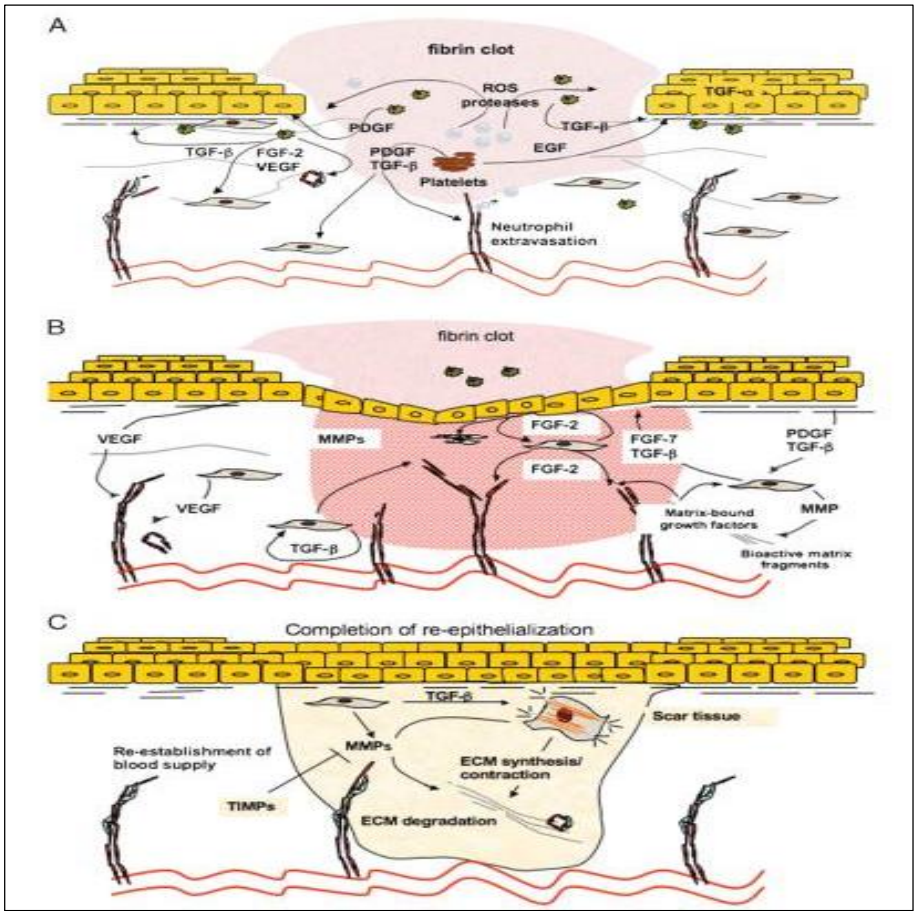

Fig 1: Mechanism of wound healing [16]

Treatment of wound

Wound care's main goal is to prevent or reduce infection while also promoting healing. Unfortunately, particular wound healing agents are not available in the allopathic medical system, only antibiotics, anti-inflammatory drugs, and analgesics are excepted from this general guideline. It is for this reason that scientists are working to find new ways to treat wounds. Wound healing treatments include topical antimicrobial therapy with commercial antibiotics. One of the most significant treatments for wound care is topical antibiotic therapy. Chloramphenicol, penicillin ointment, ampicillin and mebendazole are some of the most regularly prescribed antibiotics. Various compounds, which are routinely used as antimicrobials and disinfectants, are effective in combating these illnesses. Antimicrobial therapy's future effectiveness is, unfortunately, in question. Antimicrobial agents are becoming increasingly resistant to microorganisms, particularly bacteria. Furthermore, these chemical agents are costly and have negative effects.

Wound Healing Potency of Plants

A variety of plants and plant-derived items have been used to treat wounds for thousands of years. According to the literature, a wide range of plants can heal wounds in a variety of ways when tested in a variety of wound healing models. Based on data from phyto-extracts collected over the preceding two decades, an estimated 450 plant species have wound-healing characteristics [21]. To treat wound infections as demonstrated in Table 1, plants have been used in the scientific literature.

Table 1: List of plants used in treatment of wound

Plant	Part used	Phytoconstituents	Mode of application	Mechanism of action
Aloe vera (Liliaceae)	Liquid gel	Glycoproteins, vitamins, mineals	Gel is used locally	Creates a protective layer on the damaged areas, speeding up wound healing and lowering the risk of infection. Accelerates wound contraction, closure, and epithelization [22, 23].
Azadiracta indica (Meliaceae)	Oil	Hydrocarbons, phenolic compounds, terpenoids, alkaloids, glycosides	Local application	Suppress inflammation, allowing for faster wound healing and increased epithelization [24].
Calophyllum inophyllum Linn. Guttiferae or (Clusiaceae)	Seed oil, leaf	Flavonoids, tannins, saponins, steroids and triterpenes	Oil is used on burned wound	Increases tensile strength and hydroxyproline content while stimulating wound contraction and decreasing epithelialization time [25, 26].
Calotropis procera W. T. Aiton (Asclepiadaceae)	Leaf latex, stem bark	steroids, triterpenes, proteins flavonoids, polyphenolic hydrocarbons	Latex of leaf is used on fresh injury to stop bleeding	Collagen and epithelialization are increased, resulting in a significant reduction in wound area [27].
Catharanthus roseus L. (Apocynaceae)	Leaf or flower	Alkaloids, tannins	Leaf paste and flower extract are used on wound	Wound breaking strength, wound contraction, and epithelization were all improved [27, 28].
Chromolaena odorata (Compositae),	Leaf	Alkaloid, tannins, steroids, terpenoids, flavonoids and cardiac glycosides	Aqueous extract & decoction leaves are crushed and the decoction used in	Enhances hemostatic action, granulation tissue stimulation, and re-epithelialization processes [29].

			treating skin wounds	
Commelina diffusa Burn. F (Commelinaceae)	Leaf	Ascorbic acid, ß-carotene, tannins	Aqueous extract are used topically on the wound	Antioxidant and antifungal activities [30]
Pupalia lappacea (Amaranthaceae)	Leaf and fruit Juice	Steroids, glycosides, saponins, alkaloids, sugar, tannins, penol	Paste of leaf and juice of fruit is applied over the wound	Wound epithelization and wound contraction [31]
Spathodea campanulata Beav (Bignoniaceae)	Stem bark	Saponin, steroid, flavonoids, glycoside, alkaloids, phenol, tannin, terpenoids, phlobatanin and anthraquinone.	Paste or aqueous extract is used on the wound	↑ wound contraction [32, 33]
Tridax procumbens (Compositae	Leaf juice	Flavonoids, alkaloids, tannins, phytosterols,	Leaf juice is given i.p. route	Stops bleeding and promotes epithelialization and collagen synthesis [34].
Sida acuta (Malvaceae)	Leaf and root Juice	Alkaloids, phytosterols, tannins, flavonoids saponins,	Leaf decoction is used to clean the wound root juice applied on the wound	↑tensile strength, quicker epithelialization, and wound contraction rate [35, 36].
Heliotropium indicum L (Boraginaceae)	Leaf	Alkaloids, glycosides, tannins, flavonoids, saponins,	Paste of leaf over the affected area	↑ in the weight of granulation tissue and the amount of hydroxyproline [37]

Phytoconstituents in wound healing

Compounds extracted from plants known for their wound-healing capabilities have been used to help develop new pharmaceuticals. When it comes to treating wounds, traditional medicinal herbs have a unique perspective. These plant-derived compounds' therapeutic usefulness is based on their physiological impact on the human body. Alkaloids, essential oils, flavonoids, tannins, terpenoids, saponins, and phenolics are just some examples of these compounds [38-44]. There have been numerous research on plant-derived chemicals with antibacterial and antioxidant activities that aid wound healing and skin regeneration.

Table 2: Plant derived products in wound healing

SL. No.	Phytochemical class	Compounds
1.	Alkaloids	Berberine
2.	Cardinolides	Calotropine
3.	Coumarin	Cleomescosin A,B and C
4.	Cyanogenic glycosides	Acalyphin
5.	Flavonoids	Kaempferol, Quercetin
6.	Glycoside	Morindin, Rutin
7.	Polyphenol	Curcumin, Chlorogenic acid, Ferulic acid, Caffeic acid
8.	Sterol	ampesterol, ß-sitosterol and Stigmasterol
9.	Tannins	Gallic acid, Tannic acid
10.	Terpenes	Asiaticoside, Lupeol, Asiatic acid, Jasminol, Madecassic acid, Cleomeolide, Scabertopin, Salograviolide A, Ursolic acid

Asiaticoside

It is well known that Asiaticoside, a triterpene glycoside from Centella asiatica, has wound-healing characteristics, this has been examined in the healing of normal and diabetic wounds. Topically applying asiaticoside to the wound of streptozotocin-induced diabetic rats resulted in an increase in the strength of the wound's tissue, as well as an increase in the protein and epithelialization of the wound. Asiaticoside was applied topically to guinea pigs, resulting in increased hydroxyproline levels, increased strength, and quicker recovery. It was found that Asiaticoside stimulated angiogenesis at 40 g/disk in the model of the CAM (chick chorioallantoic membrane). Angiogenesis, collagen production, enhanced collagen matrix remodelling, and increased glycosaminoglycan synthesis have all been linked to Asiaticoside wound healing activities in wound chamber models [46, 47]. While Asiaticoside has been connected with angiogenesis and collagen creation in rat wound chamber models [46-47], it has also been linked to an enhanced glycosaminoglycan synthesis. Many researchers have studied the impact of asiaticoside on the level of antioxidants in wounds since antioxidants are critical to wound healing (Figure 2). After being applied topically to cutaneous wounds in rats, Antioxidants such glutathione peroxidase, superoxide dismutase and catalase, Vitamin E, and Vitamin C were enhanced by Asiaticoside (0.2 percent). While healing wounds, asiaticoside was found to help increase antioxidant levels in wounds at an early stage, according to studies. animal activity in an experimental rat wound chamber model [46, 47]. All of these studies show that asiaticoside has a considerable wound healing effect in both normal and delayed healing models [48].

Curcumin

Studies show that curcumin has wound-healing and antioxidant effects, as well as anti-inflammatory and antimutagenic qualities. It has also been shown to be anti-infective and anticoagulant. All of curcumin's wound-healing properties are assumed to be attributed to its anti-inflammatory, antioxidant, and anti-infectious properties, as well as the inhibition of STAT, TNF-, cyclin D1, COX-2, NFkB, IL (-1b, -6, -8), and MMP-8 production. Curcumin's ability to treat diabetic wounds has been demonstrated in various studies [53]. Collagen production, tissue remodelling, fibroblast proliferation, granulation tissue development, and vascular density are all promoted by curcumin [49]. Curcumin's antibacterial properties are attributed to its ability to alter the bacterial membrane. MRSA, *P. gingivalis*, *P. intermedia*, *F. nucleatum*, *T. denticola* [56], *B. cereus*, *E. coli* [57], *S. mutants*, *E. faecalis*, *P. aeruginosa*, and *B. subtilis* [54] were all inhibited by curcumin.

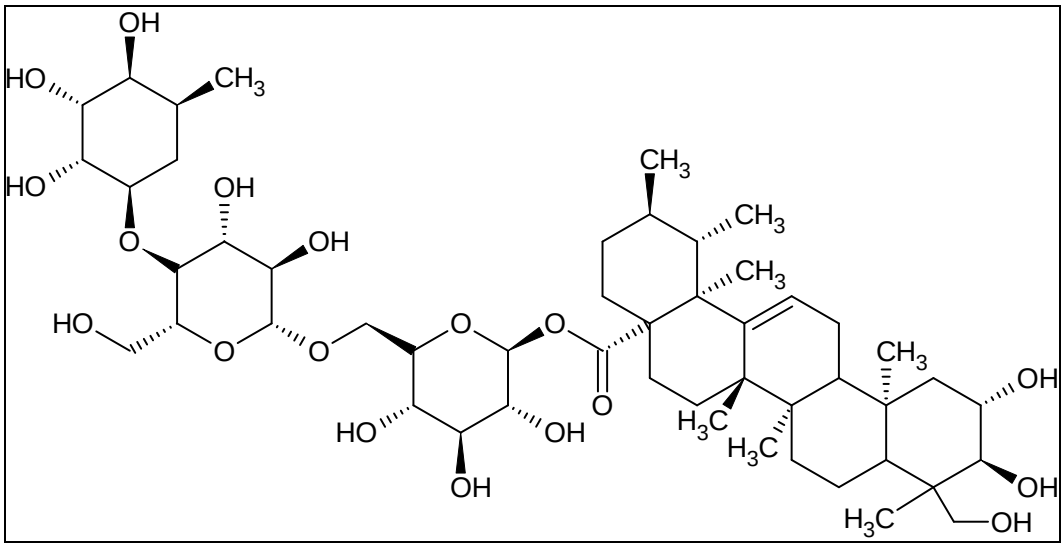

Fig 2: Structure of Asiaticoside

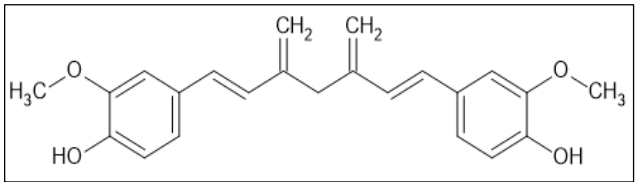

Fig 3: Structure of Curcumin

Chlorogenic acid

Is Chlorogenic acid one of the most commonly found polyphenolic molecules in our diet? As an antimicrobial indicator of quality control for traditional Chinese medicines, Chlorogenic acid is used in the majority of Chinese heat-clearing treatments [59]. Results from *in vitro* and *in vivo* investigations show that Chlorogenic acid has predominantly anti-oxidant and anti-carcinogenic characteristics compared with other polyphenols. When compared to controls, rats treated with Chlorogenic acid had significantly higher SOD, CAT, and GSH activity and lower TBARS levels in granulation tissue. As a result, Chlorogenic acid's antioxidant action may help to wound healing efficacy. Its antioxidative impact could potentially be responsible for its wound healing boosting activity in excision wounds Figure 4 illustrates this point. In the therapy of wound healing and the control of abnormal healing, Chlorogenic acid, which is found in many plants, may be a cost-effective therapeutic treatment [61]. Chlorogenic acid could be used as an example of an antioxidant wound healing method. The therapeutic benefits of Chlorogenic acid supplementation on wound healing have been studied [62]. Chlorogenic acid has antioxidant and free radical-scavenger effects on oxidative parameters and anti-inflammatory effects on MMPs in wound tissues in addition to improving capillary density and collagen synthesis.

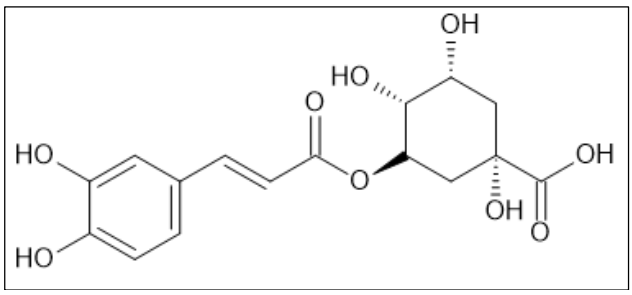

Fig 4: Structure of Chlorogenic acid

Quercetin

Quercetin is a flavonoid component found in most plants, Fruits and vegetables are included in this category. Anti-inflammatory, cancer-fighting, and antioxidant characteristics are attributed to quercetin. Enhances the synthesis of collagen and fibronectin, which aids wound healing. Studies have indicated that quercetin aids in the repair of nerve tissue damage in skin wounds, therefore it's possible that it can help with wound healing too. In comparison to the control group, animals treated with a collagenous matrix containing quercetin demonstrated improved wound healing, with increased cell proliferation and wound contraction. A collagen matrix containing quercetin has been shown to be an unique dressing material for cutaneous wound healing (Figure 5) [63]. A naturally occurring antifibrotic chemical called quercetin has been found to lessen the production of scar tissue. Studies on fibrosis and wound healing in mice and fibroblast cells found that quercetin reduced fibrosis, fibroblast cell surface integrin expression was found to be correlated with better wound healing. For those who received quercetin as a therapy, wound healing took 14 days. Since quercetin-treated animals showed less wound fibrosis, it's possible that quercetin regulates integrin expression to alter cell-extracellular matrix interactions and, hence, reduce wound fibrosis [64]. Another study found that quercetin had a significant impact on wound healing by influencing growth factors, cytokines, and cells involved in the process. There was a large time-dependent increase in wound closure, as well as considerable upregulation of VEGF and TGF-1 expression, while TNF levels were significantly lowered. Quercetin-treated male Wistar groups had higher levels of IL-10 and CD31 stained vessels, as well as increased micro vessel density, accelerated fibroblast proliferation, regular collagen deposition, and epithelialization compared to control groups [65].

Gallic acid

In addition to its anti-oxidant and anti-inflammatory effects, gallic acid also has anti-microbial, anti-cancer, and wound healing properties as a polyphenolic molecule derived from plants [66]. Internal haemorrhage is treated with it as an astringent. The antioxidant properties of gallic acid have been found to increase the expression of antioxidant genes, which in turn increase keratinocytes and fibroblasts cell migration in both normal and hyperglycemic conditions, leading to the

activation of wound-healing growth factors such as c-Jun N-terminal kinase (JNK), focal adhesion kinases (FAK), and extracellular signal regulated (Erk) growth factors [67]. Gallic acid can be utilised as a wound healing agent and as a treatment for wounds caused by metabolic problems, according to several research [67-69].

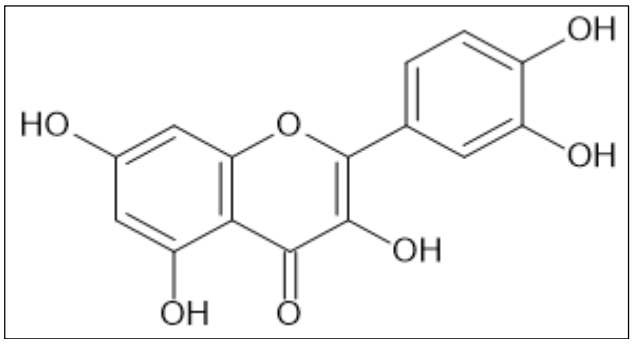

Fig 5: Structure of Quercetin

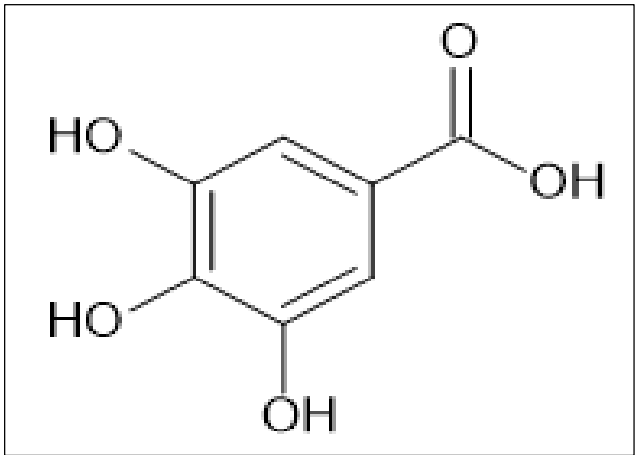

Fig 6: Structure of Gallic acid

Conclusion

Wound healing has been a difficult clinical issue for wound management since ancient times. Multiple cell types, Wound healing depends on the extracellular matrix and soluble mediators such as growth factors and cytokines. Wound care has received a lot of attention in Ayurveda, with a focus on innovative therapeutic procedures and the progress of acute and chronic wound therapy treatments (herbal). Researchers are testing new formulae, dressings, and medicinal plant compositions in the hopes of establishing a cost-effective, efficient, stable, and long-lasting wound management / treatment system. Wound treatment is becoming more effective and patient-centric as nanotechnology and innovative materials become available. Newer technologies, such as 3D printing, are also enabling the creation of new wound treatment drug delivery devices. In the future, improved wound healing systems may be achieved through the use of tissue engineering and regenerative medicine. Research in wound care management will be bolstered by improved quality control processes for identifying, screening and measuring herbal components as well as well-designed preclinical and clinical trials.

References

1. Balachandar R, Prakash SL, Kumar AK, Ragavi A, Gurumoorthy P. Antioxidant activity and wound healing potential of selected medicinal plants. Journal of Chemical and Pharmaceutical Sciences. 2014;2:100-103.
2. Amri B, Martino EID, Vitulo EID, Corana F, Kaâb BLB, Rui M, *et al*. *Marrubium vulgare* L. leave extract: Phytochemical composition, antioxidant and wound healing properties. Molecules. 2017;22:1851.
3. Wadankar GD, Malode SN, Sarambekar SL. Traditionally used medicinal plants for wound healing in the Washim District, Maharashtra (India). International Journal of PharmTech Research. 2011;3(4):2080-84.
4. Kumar B, Vijayakumar M, Govindarajan R, Pushpangadan P. Ethno pharmacological approaches to wound healing-exploring medicinal plants of India. J. Ethnopharmacol. 2007;114:103-13.
5. Somashekar Shetty B. Wound healing and indigenous drugs: Role as antioxidants: A review. Research and Reviews: Journal of Medical and Health Sciences. 2013;2(2):5-15.
6. Fikru A, Makonnen E, Eguale T, Debella A, Mekonnen GA. Evaluation of *in vivo* wound healing activity of methanol extract of *Achyranthes aspera* L. Journal of Ethnopharmacology. 2012;143:469-474
7. Ammar I, Bardaa S, Mzid M, Sahnoun Z, Rebaii T, Attia H, *et al*. Antioxidant, antibacterial land *in vivo* dermal wound healing effects of Opuntia flower extracts. International Journal of Biological Macromolecules. 2015;81:483-490.
8. Paarakh PM, Chansouria JPN, Khosa RL. Wound healing activity of *Annona muricata* extract. Journal of Pharmacy Research. 2009;2:404-406
9. Dixit V, Verma P, Agnihotri P, Paliwal AK, Rao CV, Husain T. Antimicrobial, antioxidant and wound healing properties of *Leucas lanata* Wall. ex Benth. The Journal of Phytopharmacology. 2015;4(1):9-16
10. Schultz GS. Molecular regulation of wound healing in: acute and chronic wounds: nur mngmt. Br, RA (Ed), 1999; 2nd edn, pp 413-429.
11. Nagori BP, Salonki R. Role of medicinal in wound healing. Res J Med Plant. 2011;5(4):392-405.
12. Ghosh PK, Gaba A. Phyto-extracts in wound healing. J Pharm Pharm Sci. 2013;16(5):760-820.
13. Vadivel V, Brindha P. Wound healing potential of *Ipomoea Carnea* Jacq. An Unexplored herb used in Indian traditional system of medicine. Glob J Pharmaceu Sci. 2017;3(1):555601.
14. Chen J, MD KR. Pathophysiology of acute wound healing. Clin Derm. 2007;25:9-18
15. Kirsner RS, Eaglstein WH. The wound healing process. Clin Derm. 1993;11:629-640
16. Demidova-Rice TN. Acute and impaired wound healing: pathophysiology and current methods for drug delivery. Part 1: Normal and Chronic Wounds: Biology Causes and Approaches to Care. Adv Skin Wound Care. 2012;25(7):304-314
17. Eming SA, Krieg T, Davidson JM. Inflammation in wound repair: molecular and cellular mechanisms. J Invt Derm. 2007;127:514-525
18. Humar R, Kiefer FN, Berns H, Resink TJ, Battegay EJ. Hypoxia enhances vascular cell proliferation and angiogenesis *in vitro* via rapamycin (mTOR) dependent signaling. FASEB J. 2002;16:771-780
19. Saha R. Unseen aspects of wound healing: An overview. International Journal of Pharma and Biosciences. 2011;2(4):275-285.
20. Esimone CO, Nworu CS, Jackson CL. Cutaneous wound healing activity of a herbal ointment containing the leaf extract of *Jatropha curcas* L. (Euphorbiaceae)

International Journal of Applied Research in Natural Products. 2009;1(4):01-04.
21. Ghosh PK, Gaba A. Phyto-extracts in wound healing. J Pharm Pharm Sci. 2013;16(5):760-820.
22. Yadav KCH, Kumar JR, Basha SI, Deshmukh GR, Gujjula R, Santhamma B. Wound healing activity of topical application of *Aloe vera* gel in experimental animal models. International Journal of Pharma and Bio Sciences. 2012;3(2):63-72.
23. Haesler E. Evidence Summary: Wound Management low resource communities *Aloe vera* for wound healing. Wound Practice and Research. 2017;25(2):115-17.
24. Nagesh HN, Basavanna PL, Kishore MS. Evaluation of wound healing activity of ethanolic extract of *Azadirachta Indica* leaves on incision and excision wound models in Wister Albino rats. Int J Basic Clin Pharmacol. 2015;4(6):1178-1182.
25. Jawaid T, Kamal M, Mallik T. Wound healing potential of methanolic extract of *Calophyllum inophyllum* Linn. Bark. Bull. Env. Pharmacol. Life Sci. 2016;5(4):27-32.
26. Nguyen VL, Truong CT, Nguyen BCQ, Vo TNV, Dao TT, Nguyen VD, Trinh DTT, Huynh HK, Bui CB. Anti-inflammatory and wound healing activities of calophyllolide isolated from *Calophyllum inophyllum* Linn. PLoS ONE. 2017;12(10):e0185674.
27. Agyare C, Boakye YD, Bekoe EO, Hensel A, Dapaah SO, Appiah T. Review: African medicinal plants with wound healing properties. Journal of Ethno-Pharmacology. 2016;177:85-100.
28. Nayak BS, Pinto Pereira LM. *Catharanthus roseus* flower has wound healing activity in sprague dawley rats. BMC Comp. Altern. Med. 2006;6(1):41.
29. Obi RK, Nwanebu FC, Ndubuisi-Nnaji UU, Onuoha LN, Nneamaka C. Ethanolic extraction and phytochemical screening of two Nigerian herbs on pathogens isolated from wound infections. Pharmacie Globale (IJCP). 2011;10(02).
30. Abraham Y M, Houghton PJ, Dickson RA, Fleischer TC, Heinrich M, Bremner P. *In vitro* evaluation of effects of two Ghanaian plants relevant to wound healing. Phytother. Res. 2006;20:941-944.
31. Udegbunam SO, Udegbunam RI, Muogbo, Anyanwu MU, Nwaehujor CO. Wound healing and antibacterial properties of methanolic extract of *Pupalia lappacea* Juss in rats. BMC Complementary and Alternative Medicine. 2014;14:157.
32. Ofori-Kwakye K, Kwapong AA, Adu F. Antimicrobial activity of extracts and topical products of the stem bark of *Spathodea campanulata* for wound healing. Afr. J. Trad. CAM. 2009;6(2):168-74.
33. Kulkarni M, Singhal RG, Bhise K. Study of wound healing activity of extracts of some Indian medicinal plants. Journal of Pharmacy Research. 2014;8(10):1375-79.
34. Yaduvanshi B, Mathur R, Mathur SR, Velpandian T. Evaluation of wound healing potential of topical formulation of leaf juice of *Tridax Procumbens* L. in mice. Indian Journal of Pharmaceutical Sciences. 2011;73(3):303-306.
35. Eluwa MA, Ofem PS, Asuquo R, Akpantah AO, Ekanem TB. Histological study of the effect of ethanolic leaf extract of *Sida acuta* on the cerebral cortex of adult Wistar rats M. IOSR Journal of Dental and Medical Sciences (IOSR-JDMS). 2013;8(5):60-63.
36. Tcheghebe OL, Seukep AJ, Tatong FN. Ethnomedicinal uses, phytochemical and pharmacological profiles, and toxicity of Sida acuta Burm F.: A review article. The Pharma Innovation Journal. 2017;6(6):01-06.
37. Dash GK, Murthy PN. Studies on wound healing activity of *Heliotropium indicum* Linn. Leaves on Rats, ISRN Pharmacol. 2011:847980.
38. Maenthaisong R, Chaiyakunapruk N, Niruntraporn S, Kongkaew C. The efficacy of Aloe vera used for burn wound healing: A systematic review. Burns. 2007;33(6):713-718.
39. Ribeiro MP, Morgado PI, Miguel SP, Coutinho P, Correia IJ. Dextran-based hydrogel containing chitosan microparticles loaded with growth factors to be used in wound healing. Mater Sci Eng C. 2013;33(5):2958-2966.
40. Cheppudira B, Fowler M, McGhee L, Greer A, Mares A, *et al*. Curcumin: A novel therapeutic for burn pain and wound healing. Expert Opin Investig Drugs. 2013;22(10):1295-1303.
41. Mosae Selvakumar P, Antonyraj CA, Babu R, Dakhsinamurthy A, Manikandan N, *et al*. Green synthesis and antimicrobial activity of monodispersed silver nanoparticles synthesized using lemon extract. Synth React Inorg Met Org Chem. 2016;46(2):291-294.
42. Mariselvam R, Ranjitsingh AJA, Nanthini AUR, Kalirajan K, Padmalatha C, *et al*. Green synthesis of silver nanoparticles from the extract of the inflorescence of Cocos nucifera (Family: Arecaceae) for enhanced antibacterial activity. Spectrochim Acta. 2014;129:537-541.
43. Kiruba KK, Joel JT, Lalitha S, Merrin S, Rajkumar RJS, *et al*. Efficacy and comparative evaluation of antimicrobial properties from the peel of citrus fruits used to treat diabetic foot ulcer. Asian Journal of Biochemical and Pharmaceutical Research. 2016;1(6):151-166.
44. Rajkumar RJS, Kuruppilakathmanikandan S, Nadar MMSA. Qualitative Phytoconstituents Profile of Lobelia trigona Roxb Extracts. Int J PharmTech Res. 2015;8(10):47-50.
45. Maquart FX, Chastang F, Simeon A, Birembaut P, Gillery P, *et al*. Triterpenes from Centella asiatica stimulate extracellular matrix accumulation in rat experimental wounds. Eur J Dermatol. 1999;9(4):289-296.
46. Rosen H, Blumenthal A, McCallum J. Effect of asiaticoside on wound healing in the rat. Proc Soc Exp Biol Med. 1967;125(1):279-280.
47. Liu M, Dai Y, Li Y, Luo Y, Huang F, *et al*. Madecassoside isolated from Centella asiatica herbs facilitates burn wound healing in mice. Planta Med. 2008;74(8):809-815.
48. Shukla A, Rasik AM, Dhawan BN. Asiaticoside-induced elevation of antioxidant levels in healing wounds. Phytother Res. 1999;13(1):50-54.
49. Mahmood K, Zia KM, Zuber M, Salman M, Anjum MN. Recent developments in curcumin and curcumin based polymeric materials for biomedical applications: A review. Int J Biol Macromol. 2015;81:877-90.
50. Naksuriya O, Okonogi S, Schiffelers RM, Hennink WE. Curcumin nanoformulations: A review of pharmaceutical properties and preclinical studies and clinical data related to cancer treatment. Biomaterials. 2014;35(10):3365-3383.
51. Jardim KV, Joanitti GA, Azevedo RB, Parize AL. Physico-chemical characterization and cytotoxicity

evaluation of curcumin loaded in chitosan/chondroitin sulfate nanoparticles. Mater Sci Eng C Mater Biol Appl. 2015;56:294-304.
52. Ghosh S, Banerjee S, Sil PC. The beneficial role of curcumin on inflammation, diabetes and neurodegenerative disease: a recent update. Food Chem Toxicol. 2015;83:111-124.
53. Ranjbar-Mohammadi M, Bahrami SH. Electrospun curcumin loaded poly(-caprolactone)/gum tragacanth-nanofibers for biomedical application. Int J Biol Macromol. 2016;84:448-456.
54. Tyagi P, Singh M, Kumari H, Kumari A, Mukhopadhyay K. Bactericidal activity of curcumin I is associated with damaging of bacterial membrane. PLoS One. 2015;10(3):e0121313.
55. Mun SH, Joung DK, Kim YS, Kang OH, Kim SB, *et al*. Synergistic antibacterial effect of curcumin against methicillin resistant Staphylococcus aureus. Phytomedicine. 2013;20(8-9):714-718.
56. Izui S, Sekine S, Maeda K, Kuboniwa M, Takada A, *et al*. Antibacterial activity of curcumin against periodontopathic bacteria. J Periodontol. 2016;87(1):83-90.
57. Wang X, Ip M, Leung AW, Yang Z, Wang P, *et al*. Sonodynamic action of curcumin on foodborne bacteria Bacillus cereus and Escherichia coli. Ultrasonics. 2015;62:75-79.
58. Wang Y, Ho CT. Polyphenolic chemistry of tea and coffee: a century of progress. J Agric Food Chem. 2009;57:8109-8114.
59. Huang X. Current status and prospect of the study of Lonicera japonica Thunb. Zhongguo Zhong Yao Za Zhi. 1997;22:247-249.
60. Xu JG, Hu QP, Liu Y. Antioxidant and DNA-protective activities of chlorogenic acid isomers. J Agric Food Chem. 2012;60:11625-11630.
61. Wei-Cheng Chen, Shorong-Shii Liou, Thing-Fong Tzeng, Shiow-Ling Lee, I-Min Liu. Effect of Topical Application of Chlorogenic Acid on Excision Wound Healing in Rats. Planta Med. 2013;79:616-621.
62. Bagdas D, Gul NY, Topal A, Tas S, Ozyigit MO, *et al*. Pharmacologic overview of systemic chlorogenic acid therapy on experimental wound healing. Naunyn-Schmiedeberg's Arch Pharmacol. 2014;387:1101-1116.
63. Gomathi K, Gopinath D, Ahmed MR, Jayakumar R. Quercetin incorporated collagen matrices for dermal wound healing processes in rat. Biomaterials. 2003;24(16):2767-2772.
64. Doersch KM, Newell-Rogers MK. The impact of quercetin on wound healing relates to changes in αV and β1 integrin expression. Exp Biol Med. 2017;242(14):1424-1431.
65. Gopalakrishnan A, Ram M, Kumawat S, Tandan SK, Kumar D. Quercetin accelerated cutaneous wound healing in rats by increasing levels of VEGF and TGF-β1. Indian J Exp Biol. 2016;54(3):187-195.
66. Bachrach U, Wang YC. Cancer therapy and prevention by green tea: Role of ornithine decarboxylase. Amino Acids. 2002;22(1):1-13.
67. Yang DJ, Moh SH, Son DH, You S, Kinyua AW, *et al*. Gallic acid promotes wound healing in normal and hyperglucidic conditions. Molecules. 2016;21(7): 899.
68. Kroes BH, Berg VDAJ, Ufford QVHC, Dijk VH, Labadie RP. Anti-inflammatory activity of gallic acid. Planta Med. 1992;58(6):499-504.
69. Kubo I, Xiao P, Fujita K. Antifungal activity of octyl gallate: Structural criteria and mode of action. Bioorg Med Chem Lett. 2001;11(3):347-350.