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A REVIEW ON USE OF HERBAL PLANT SOURCES IN ADHESIVE BANDAGES FOR WOUND HEALING PROCESS

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ABSTRACT

Wound is an anatomical and functional disruption of the skin which leads to an injury. In response to such injuries, wound healing is a complex process resulting in tissue repair or remodeling. In the present times, there are different types of pharmaceutical products such as synthetic adhesive/ non-adhesive bandages developed for economical, sustainable, stable, and effective delivery system for the treatment of wounds but may lead to side effects. Hence in order to overcome such problems, plant or plant derived products can be used. Historically, plants and plant derived constituents were been extensively utilized for the treatment and management of different types of wounds. The whole study gives precise data of such plants, by making them use in preparation of organic bandages and patches for treatment of wounds. The utilization of these plant derived extract can be more beneficial and effective which can be administered for injuries due to wounds either chronic or acute. Making appropriate use of herbal plants may lower the risk of adverse effects of synthetic forms and may also increase its mechanism of action for efficient tissue remodeling. The compiled data aims to provide the researchers/scientists a directional view in understanding the role and importance of plant-based formulations for the treatment and management of wounds and moving towards natural form of bandages for more efficiency and potency.

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INTRODUCTION

Skin is the largest organ of our body and which is made up of several different parts, including water, lipids, proteins and minerals, which keeps on regenerating approximately after every 27 days. Skin consist of three distinctive layers- first the outer layer called **Epidermis**: which acts as a guard for protection from external environment and are hosts for keratinocytes, melanocytes and langerhans cell. Second is the **Dermis**, the center layer of the skin, which contains a variable measure of fat, and furthermore collagen and elastin strands which give strength and adaptability to the skin. It consists of blood vessel, nerve cells and hair follicle which are helpful in protection and maintaining the change from the environment. The last and deepest layer called the **Hypodermis** (subcutaneous fats) which acts as energy source for body and helps to insulate body against changes in the outside temperature.

But what happens if the skin get's damage?

A **wound** is a disruption of living tissue's cellular, anatomical and functional integrity caused by physical, chemical, electrical or microbial threats to the tissue i.e. injury formed on the body tissues. These injuries can be minor or major depending on how deep the wound is. These wounds are caused due to breakage of skin due to accidents, cuts, scrapes and starches etc. In order to protect and heal such wounds, adhesive bandages are used. These are also termed as sticking plaster or clinical mortar along with "Band-aids" as a brand name term. As this bandage binds at the junction of wound, it leads to protection from bacterial or fungal infection which might be caused due to environment. The bandage's keeps the healing process of the wound less disturbed and hence acts as first aid. So this bandage acts as antiseptic, antibiotic, and analgesic.

Bandages are used globally as a quick remedy for wounds, as no direction or professionals are required for its administration of application. Bandages are also primary first aid products and more than thousands of such adhesive bandages are sold every day. But as these bandages are synthetically formulated with drugs, it consists of limitations and adverse effect which might sometime caused unsatisfactory and non-beneficial effect on the skin. The required effectiveness and efficacy are sometime cureless due to poor active ingredient drug release or poor penetration or permeability of the drugs. It may sometime lead to microbial growth which might cause fungal or bacterial infection to skins. Hence in order, to mark such effects and show more modulation in wound healing, decreasing bacterial count, improving collagen deposition, increasing fibroblasts and collagen etc., organic adhesive bandages consisting medicinal plants can be used. Medicinal plants would not just promote wound healing and blood clotting but at the same time would have anti-bacterial, anti-fungal, anti-inflammatory activity also. As plants or plant derived products consist of no adverse side effects or less side effects in comparison to such synthetic forms and this herbal formulated products are found to be more effective and efficient. Whether be topical creams or transdermal patches, herbal forms of products are capturing the market and are better alternative to synthetic forms. The main outcome of the review is to provide better and more effective alternative products for wound healings in order to minimize the adverse effects and more healthful products for treatment of wounds. The paper also includes certain patents related herbal form of products for wound healing property.

History:

In different time interval, various methods and substances were used for healing the wounds. The following are given below: 1500 BC: Ancient Egyptians used honey to protect wounds that served as an antibiotic barrier [1].By the different time use of vinegar, alcohol, turmeric, ginger paste was made used. But the first ever actual adhesive bandage was prepared by Earle Deckson in the year 1920 for his wife. He made the Band-Aid model for her by putting a little piece of bandage on top of a portion of tape. Then, at that point, he covered the encompassing tacky parts with crinoline, a hardened texture. This kept the dressing sterile and kept the cement from adhering to itself. By 1921 Johnson-Johnsons began setting up these gauzes and gave the name "bandages", and by 1924 machines were created for large scale manufacturing. By 1940 and with spending year it turned into a piece of First-help, which the local people groups could administer with no direction.

The use of organic natural and biodegradable bandages got initiated because of its beneficial effects, such as use of *Curcuma longa, Aloe vera, Bambusa vulgaris etc.*

Wound healing process:

After the onset of lesion the process of tissue regeneration and repair occurs. External and internal stimuli can cause lesion and this can result in damage to specific organelles or to cells as a whole [2]. It might take days to months for healing of the injured region depending on how the wound is. Some of them are given below:

Acute type injury: Wound or injury which normally proceed through an orderly and timely reparative process that results in sustained restoration of anatomic and functional integrity [3]. It might be caused due to cuts and surgical incision which if failed to heal may lead to development of chronic wounds. It almost takes few weeks for healing process.

Chronic wound:

Wound which fails to progress and follow normal stages of healing and hence enters a state of pathologic inflammation, which do not heal within few weeks but requires few months to heal. It may be caused due to various serious physical disabilities [4].

Open wound:

It is the breakage of the skin tissue, which leads to an injury causing blood flow outside the body i.e. bleeding. It may be of different types according to object or condition causing damage.

1) Incision: The injury or damage caused due to sharp object such as blade, knife or razor. The tissues are not loss or minimum tissues loss. The recovery can take up to 2 weeks, depending on how serious the injury was. Sometime serious or deep incision wound repairs the tissue but scars of injury remains.

2) Lacerations: It is an irregular or blunt breaking or tearing of soft tissues causing nonsurgical injury due to certain accidents, resulting in tissue damage. Healing is almost done within 5-7 days but sometime may require more time for remodeling.

3) Abrasion: Wound injury caused due to scraping the skin on a rough surface such as roads, grounds, tree barks, walls etc and sometime due to frictional integrity of skin with smooth surface such as slides. The topmost layer i.e. epidermis of skin gets scraped off. It can heal within 3-5 days but remodeling takes time, but might increase if damage is large.

4) Puncture: The wound caused by pointed objects such as needle or nail; which can cause a small hole in the tissue of the skin. The injury can be serious depending on how deep the object is penetrated. Minor punctures may heal within 4-6 days. But they can get infected easily due to dirt or infectious agents.

5) Minor Avulsion: These can be minor injury caused by animal bites or scratches due to forcible claws can cause tearing which may lead to damage of tissues. Such injuries might take several weeks to heal.

Depending on skin injuries Biochemical events and cell healing process are divided into 3 stages which are:

- Inflammatory reaction
- Cell proliferation
- Remodeling stage

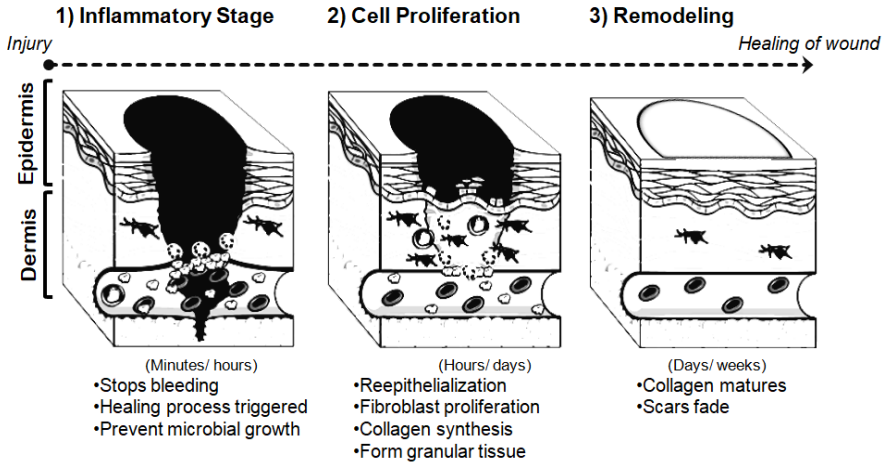

Figure 1: Stages of wound healing process.

These stages make up the extracellular matrix and the posterior period which is called as remodeling.

INFLAMMATORY STAGE

Contraction of lesioned blood vessels and the leaked blood coagulates are a part of vascular inflammatory response and also contribute to the maintenance of its integrity. Aggregation of thrombocytes and platelets in fibrin network which relies on the action of specific factors through the activation and aggregation of cells is called coagulation [5]. The network of fibrin reestablishes homeostasis and forms a barrier against invasion of microorganisms and helps to restore the function of skin as a protective barrier. Influx of leukocytes is a very quick response and is simultaneously followed with the key signs of inflammation. The occurrence of a lesion causes inflammation which is a localized and protective tissue response. An important role in wound healing is played by the inflammatory cells which release lysosomal enzymes and reactive oxygen species and also help to dispose of various cell debris [6]. According to Burkley the interaction of leukocytes and stromal cells during an acute inflammatory response resolves around the inflammatory focus [7]. The activation of complement system, platelet degranulation and bacterial degradation products causes the active recruitment of neutrophil as a result of inflammatory response [8]. Neutrophils help to dispose a tissue and play an important role in the death of invading agents as they are the primary activated and recruited cells. Macrophages are activated through chemokine signaling act as present antigens and help neutrophils in phagocytosis. These macrophages are recruited from blood in response to chemo tactic products and can be seen in extracellular matrix protein fragments. They carry out phagocytosis of muscular debris and help to produce and release cytokines and pro-angiogenic, inflammatory and fibrogenic factors, and free of radicals [9].

PROLIFERATIVE STAGE

To diminish the lesioned tissue area by contraction and fibroplasia and establishing a viable thelial barrier to activate keratinocytes is the main aim of this stage. The closure of lesion begins in the micro environ of the lesion within the first 48 hours and can last upto the 14th day after the onset of lesion [10].Angiogenis is important for diverse physiological and pathological conditions which includes embryogenesis, tumor growth and metastasis. The microvasculature that is recently formed makes it possible to transport fluid, oxygen, nutrients and immune-competent cells to the stroma [11]. The endothelial, lymphocyte appears as solitary entities and share the basal membrane of blood vessel and endothelial cells. The pericyte makes focal contact with endothelium through specialized junctures that stretch and surround the endothelial tube [12]. Pericytes which run continuously along the endothelial basal membrane are the mural cells of Micro-blood vessels involved in the basal membrane. Tissue granulation begins approximately 4 days after lesion formation. The mechanism involves increase in fibroblastic proliferation; collagenous and elastic biosynthesis and production of chemotactic factors and IFN-beta by fibroblasts [13]. Fibroblasts which produce collagen are recruited from the dermis of border of wound to synthesize protein. During the initial stage of repair type III collagen is found in large amounts which is synthesized by fibroblasts in the granulation tissue .The combination of proliferative stage with the migration of cells near the lesion causes reepithelialization of a wound by keratinocytes. When migration stops due to inhibition caused by contact the keratinocytes reconnect to the substrate and reconstruct the basal membrane.

REMODELING STAGE

This stage begins two to three weeks after the onset of lesion and can last for a long time. To achieve maximum tensile strength through degradation, reorganization and resynthesis of the extracellular matrix is the core aim of this particular stage. Elements mature and deep changes occur in the extracellular matrix and resolution of initial inflammation. Deposition of matrix and subsequent change in composition occurs at this stage [10]. As the wound closes type III collagen degrades and synthesis of type I collagen increases. Thicker collagen fibres are placed in parallel which results in an enhanced tensile strength for the tissue during this stage [14]. This stage is essential for restoration of function and "normal" appearance of the injured tissue. Vitronectin contributes to the contraction of tissue mediated by collagen produced by fibroblasts.

Factors that may cause adverse effect and may lead to improper and impaired wound healing can include both endogenous and exogenous factors. Especially disorders such as diabetes, immunosuppression, venous stasis, corticotherapy, smoking etc. along with factors such as improper diet, infection on wound site, insufficient oxygen supply, age and contamination with the external environment.

Adhesive bandages on wounds:

Basically adhesive bandages (bandaids) are used for minor or acute wounds. These bandages functions by adhering and stop the loss of blood. Hence it protects the tissue to lose blood due to bleeding. It seal's the area to prevent from getting rubbed or touched. The bandages provide a protection barrier for the wound preserving it from getting contaminated by bacterial, fungal and other infectious agents due to dirt and water. Keeps the wound dry and hence provide thermal and mechanical protection to the wound, as if the wound gets wet it may lead to bacterial attack. Medicated bandages with certain antiseptic formulation or fibers containing certain medicaments if use can be helpful for more effective in wound healing and increase healing property. Povidone iodine a bactericidal, it aids in healing a range of acute and chronic wounds [15]. Certain pain relieving medicaments are:

TABLE 1: Johnson & Johnson band-aid® hurt-free® first aid antiseptic pain relieving liquid [16]**.**

Active ingredients	Purpose
Benzalkonium Cl 0.13%	First aid antiseptic
Lidocaine HCl 2% w/w	Topical analgesic

A moist environment is maintained which is effective for wound healing purpose. A moist environment has been proven to facilitate the healing process of the wound by preventing dehydration and enhancing angiogenesis and collagen synthesis together with increased breakdown of dead tissue and fibrin [17]. These band aids remain harmless to the wounds and hence can be used majorly without any professional direction for immediate action. It is easy to carry, easy to handle and use. It is cheap and hence is important part of first aid kits.

Use of natural organic resources (medicinal plants) for healing wounds:

It is been observed that plants were used as first line therapy for inflammation, wounds etc from prehistoric period. These plants consist of various organic bioactive properties for healing, remodeling and regeneration of skins and other body tissues. The study of plant in ayurveda is termed as "Rig-Veda". Plants consist of properties like antimicrobial, anti-inflammatory, antioxidant, antipruritic, hypotensive, proliferative, hypoglycemic, and analgesic which can be a key to wound healing[18]. Recently, WHO (World Health Organization) estimated that 80 percent of people worldwide rely on herbal medicines for some aspect of their primary health care needs. According to WHO, around 21,000 plant species have the potential for being used as medicinal plants. Natural Ingredients are more effective in comparison to synthetic, as natural sources includes various healing as well as pharmacological factors which may be directly or indirectly benefit the skin. Some of the natural medicinal plants along with its properties are given below:

Aloe vera

Aloe vera (L.) Burm. f. (Asphodelaceae) is a xerophytic plant commonly found in the arid regions of Africa, Europe, the Americas and Asia. In Ayurveda, it is termed as "kumari". In India, it is cultivated in Rajasthan, Andhra Pradesh, Gujarat, Maharashtra and Tamil Nadu [19]. The leaves of *Aloe vera* are used for medicinal purpose. Acemannan, β-(1,4)-acetylated polymannose, is the major component of *Aloe vera*, which exerts an immunostimulative effect by activating macrophages [20]. It consist of Vitamins: vitamins A (beta-carotene), C and E, which are antioxidants, It contains 8 enzymes: aliiase, alkaline phosphatase, amylase, bradykinase, carboxypeptidase, catalase, cellulase, lipase, and peroxidase which helps to decrease excessive inflammation when applied to the skin topically, while others help in the breakdown of sugars and fats. It consist of 12 anthraquinones, which are phenolic compounds traditionally known as laxatives e.g. Aloin and emodin which act as analgesics, antibacterials and antivirals [21]. There are 4 plant steroids; cholesterol, campesterol, β-sisosterol and lupeol and all these have anti-inflammatory action while lupeol possesses antiseptic and analgesic properties. Auxin and gibberellin hormones help in wound healing and have anti-inflammatory action [22]. These are all beneficial for healing the injury and may also protect from other environmental factors, from infection, dirt, germs, etc. The formulations are basically in gel form.

Curcuma longa (Turmeric) [23, 24].

Turmeric is a rhizomatous herbaceous perennial plant belonging to the ginger family Zingiberaceae, which is mostly grown in regions of India, China, Taiwan, Indonesia, Sri Lanka, Java, Brazil, Peru, along with many parts of Africa and Australia. It is used in **Ayurveda** to balance **vata, pitta, and kapha.** Curcuma also has variety of names along with its historical features such as:haldi in Hindi, *jayanti* (one that wins over diseases), *krimighni* or *kashpa* (killer of worms), *varna datri* (enhancer of body complexion), *vishagni* (killer of poison) etc. It consists of curcumin, demethoxycurcumin and bis-demethoxycurcumin. **Curcumin** (1,7-bis(4-hydroxy-3-methoxyphenyl)-1,6-heptadiene-3,5-dione) also called **diferuloylmethane**, is the main natural polyphenol found in the rhizome of *Curcuma longa* (turmeric) and in other *Curcuma spp* [25]. Curcumin shows various effects such antioxidant, antiaging, anti-inflammatory, immunomodulatory, wound healing, antitumoral and antipsoriatic effects [26]. Oxidative conditions may lead to slow wound healing, which may cause chronic effect and hence oxidative properties can be used. The main activity is to target the ROS (reactive oxygen species) responsible for chronic wounds and eradication of this ROS may increase healing and remoduling of the wound. Refined curcumin combined with honey in the form of gels, collagen films, alginate foams can enhance by acting on the inflammatory proliferative and maturation phases of wound healing [27].

Arctium lappa (Greater burdock)

Arctium lappa also called burdock belonging to the family Asteraceae. These are mostly found in regions of Nothern America, Europe, and many parts of Asia which can be used to treat skin injuries such as wounds, rashes, burns etc. Leaves and roots of the plants are used for extraction of active ingredients. The major active ingredients isolated from this herb are: tannin, arctigenin, arctin, beta-eudesmol, caffeic acid, chlorogenic acid, inulin, trachelogenin 4, sitosterol-beta-D-glucopyranoside, lappaol and diarctigenin. Arctigenin and diarctigenin show anti- inflammatory action by inhibiting the nitric oxide production required for inflammatory diseases [28]. Lyophilized extract of the leaves of burdock along with other leaf extracted ingredients show anti-bacterial properties along with skin problems and injuries [29]. The root extract have significantly enhanced dermal extracellular matrix metabolism, affecting glycosaminoglycan and controlling wrinkles in human skin [30]. It also regulate cell adhesion and gene expression in canine dermal fibroblasts, affecting the Wnt/ β-catenin signalling pathway, for wound healing [31].

Ocimum tenuiflorum (Tulsi)

Tulsi is an aromatic shrub in the basil family Lamiaceae, which are mostly found in Indian countries along with throughout the Southeast Asian tropics. It is also named with different terms such as: Manjari, Krishna Tulsi, Trittavu, Tulshi, while in English it is termed as "Holy basil". It is effective for numerous numbers of diseases such as fever, cold, flu, diarrhea, dysentery, hemorrhage and dyspepsia, glucoma, cataract along with properties of antioxidant, anti-fungal, anti-bacterial, anti-microbial infection, antifungal, anticancer, arthritis, hepatoprotective, antispasmodic, analgesic, antiemetic and cardio protective [32, 33]. The active constituents present in the volatile oil are: eugenol (1-hydroxy-2-methoxy-4-allylbenzene), euginal(eugenic acid), urosolic acid (2,3,4,5,6,6a,7,8,8a,10,11,12,13,14btetradecahydro-1H-picene-4a-carboxylicacid), carvacrol (5-isopropyl-2-methylphenol), linalool (3,7-dimethylocta-1,6-dien-3-ol), limatrol, caryophyllene (4,11,11-trimethyl-8-methylene-bicyclo[7.2.0] undec-4-ene), methyl carvicol (also called Estragol) (1-allyl-4-methoxybenzene) [34].

During a study evaluated by *Gautam et al.* and *Goel et al.*, it was observed that the antioxidative properties of beta-carotene of tulsi along with superoxide dismutase, SOD and reduced glutathione, GSH; free radicals- lipid peroxidation, LPO and nitric oxide (NO) and acute inflammatory marker myeloperoxidase (MPO) were used and protein were estimated in wet granulation tissue homogenates which revealed that the active constituents of tulsi had significant antioxidant activity and reducing MPO and free radicals stress and helped to prevent inflammation and oxidative damage and promote the healing process [35].

Ethanolic extract of leaves of tulsi was researched for normal wound healing and dexamethasone-depressed healing. The extract consisted of 75g of dried Tulsi and 700ml of 95% ethanol in soxhelt apparatus. The extract increased wound breaking strength, with increased wound contraction and wound epithelializes fast along with increase in wet and dry granulation tissue weight and granulation tissue breaking strength [36].

Azadirachta indica (Neem)

Azadirachta indica also called as neem, nimtree or Indian lilac, belonging to the family of Meliaceae, mostly native to Indian countries and some parts of Africa. The chemical constituents found in the leaves of neem nimbin, nimbanene, 6-desacetylnimbinene, nimban-diol, nimbolide, ascorbic acid, n-hexacosanol and aminoacid, 7-desacetyl-7-benzoylazadiradione, and nimbio [37]. It consist of the biological and pharmacological actions such as, antibacterial, antipyretic, antifungal, antiseptic, anti-inflammatory antiviral and antiparalitic uses. During investigation of "Effect of Neem Leaves Extract (*Azadirachta indica*) on Wound Healing" neem leave extract were made by 1kg of neem leaves and the extracted powder was macerated in 10litres of 96% ethanol. Neem showed effects of anti-microbial, anti-oxidant and anti-inflammatory which accelerated the healing process by preventing the infection. The neem extract speeds up the proliferation phase in entire wound healing phase [38]. *Maan et al.* investigated on the Wound Healing Activity from the stem bark, for which 100 g plant material was macerated separately with water, ethanol and ethanol-water. The stem bark showed significant wound healing effects along with wound contraction and breaking strength effects [39].

Mentha piperita (peppermint)

Mentha piperita belonging to the family of Lamiacea, found in various regions of Europe, Asia along with Middle east countries. Pepper- mint essential oil (PEO) contains many compounds, including menthol, menthon, isomenthol, limonene, cineol, men-thyl acetate, beta-caryophyllene, menthofuran, terpinene, caron, pinene, Sabinene, β-pinene, tannin etc. PEO has antimicrobial, antiviral, and antifungal activities [40], along with anti-inflammatory activity to inhibit nitric oxide and prostaglandin E2 effects [41]. ***Modaressi et al***. evaluated the eff ects of topical administration of ointment containing PEO (*M. piperita*) on the infected wounds by evaluating mRNA expression for inflammation, collagen synthesis, as well as remodeling and regeneration of epithelial tissue after tissue injury [42]. The extract menthol (39.80%), mentone (19.55%), neomenthol (8.82%), menthyl acetate (8.64%), 1,8-cineole (5.81%), Trans-beta caryophyllene (2.76%), germacrene-d (2.73%), limonene (1.12%) and beta-pinene (0.92%) were the main compounds in peppermint oil. It was observed that peppermint extract not only increased rate of fibro-blasts, collagen production and secretion, regeneration of epithelial tissue and downregulation of inflammatory cytokines but they also control infiltration of immune cells into the wound region and inflammation of the tissue showing anti-bacterial property.

Allium sativum (Garlic)

Garlic is a species of bulbous flowering plant belonging to the family of Amaryllidaceae. Mostly found in Central Asian countries along with European and North American countries. *A. sativum* contains alliin, allyl disulfide, allyl cysteine and allicin, which consist of antioxidant property [43]. Anti-inflammatory properties are also effective for wound healing purpose, results in rapid action of the proliferative stage and well-formed cellularity including antiplatelet, and antifibrinolytic effects [44]. Faad et al. combined 1 part crushed garlic with 2 parts Vaseline, leading to release of Allicin the active constituent. The observation made was garlic ointment increases proliferation of fibroblasts and thus leading to increase in wound healing. The benefit of allicin ointment was find to be a decreased risk of surgical site infection due to both rapid wound healing and antimicrobial properties [45].

While investigating "Hydroethanolic *Allium sativum* extract accelerates excision wound healing", 50g of garlic powder was suspended in 1000 ml of hydroethanolic solution, then filtered and tested with Wistar rats. *A. sativum* reduced the inflammation-induced degenerative impacts and it also accelerated the healing process significantly by reducing inflammatory reaction along with enhancing mast-cell distribution and promoting angiogenesis [44].

Aegle marmelos (Indian Bael)

Aegle marmelos belonging to the family of Rutaceae, commonly known as bael, also Bengal quince, golden apple, Japanese bitter orange mostly found in India, Bangladesh, Sri Lanka, Nepal and various other parts of Asia. It consists of Alkaloids like: Aegeline, Aegelinosides A and B, Ethyl cinnamamide, Ethyl cinnamate, Fragrine showing Antidiabetic, antibacterial, anti-inflammatory, and anticancerous properties. Coumarins like: Imperatorin, Alloimperatorin, Isoimperatorin, Marmelide etc showing antioxidant, anti-inflammatory activities [46].

The extracts show antibacterial, antiviral and antifungal activities. Antibacterial effect was shown on pathogenic *Shigella dysenteriae* and the inhibitory activity was obtained from coumarin compounds [47]. Antifungal activity were obtained against pathogenic strains of Aspergillus species and *Candida albicans* [48].

A. marmelos was seen to promote wound healing by enhancing connective tissue formation and antioxidants showed a decrease in free radicals and myeloperoxidase having tissue damaging effects. *R. K. Goel* performed Excision, Incision, and Dead Space Wound Models for determining the potential of *A. marmelos* extracting 50% ethanol extract of AM (AME) was prepared by adding 1 liter of ethanol and water (1: 1) in 200 g of dried fine powder of AM. 50% ethanol extract of bael fruit pulp decreased free radical and myeloperoxidase generated tissue damage, promoting effects on antioxidant status, faster collagen deposition was evidenced by increase in collagen determinants and decrease in inflammation confirmed [49].

Centella asiatica (Indian pennywort) [50]

It is a perennial herbaceous creeper belonging to the family *Apiceae found mostly in India and other parts of wetland in Asia.* Primary active constituents found are saponins i.e. triterpenoids including asiaticosides linked to the aglycone asiatic acid, madecassoside and madasiatic acid. Triterpene saponins and their sapogenins are liable for the wound healing process and vascular effects which inhibits the production of collagen at the wound site [51]. Wound healing are the increasing the property of this natural resources [52]. Formulations i.e. ointment, cream and gel of aqueous extract of *C. asiatica*, when applied topically, 3 times daily for 24 days on the open wounds in rats it increased the cellular proliferation and collagen synthesis at the wound area and was evidenced by increase in collagen content and tensile strength. The treated wounds was found to epithelialised faster and compared to rate of wound control, the rate of contraction was higher [53].

When extract of 0.2% solution of asiaticoside applied topically in guinea pig it produced 56% increase in hydroxyproline, 57% increase in tensile strength along with increased collagen content with better epithelisation rate. When 0.4% solution of asiaticoside applied in streptozotocin diabetic rats, where healing is delayed, increased hydroxyproline content along with tensile strength, collagen content and epithelisation. These results indicated that asiaticoside were demonstrating wound healing activity in normal as well as delayed healing models and is the main active constituent of *Centella asiatica* [54]. Another study of alcoholic extract of *C. asiatica* performed on rat. The extract not only increased the cellular proliferation but also collagen synthesis at the wound site, which exhibited DNA, protein and collagen content for granulation tissues and it was found that extract treated wounds epithelialise faster and the rate of wound contraction was higher [55].

Glycyrrhiza glabra (Liquorice/ Licorice)

Glycyrrhiza glabra a flowering plant of the bean family Fabaceae, herbaceous perennial legume native to Western Asia, southern Europe and North Africa. Licorice root contains glycyrrhizin, which is also called glycyrrhizic acid: a triterpenoid saponin. Major flavonoids such as isoliquiritigenin (2′,4,4′- trihydroxychalcone), such as liquiritin, isoliquiritin and liquiritigenin (4′,7- dihydroxyflavanone) are present**.** The roots of licorice show antifungal, antimicrobial [56] along with antioxidant property and anti-inflammatory property [57]. It also shows wound healing property for internal wound performed on rabbit [58].

In a study powdered liquorice was mixed with water and was applied on the wound of 45 male Spragne-Dawley rats, Licorice extract was applied once in a day for 7 days. The extract caused a significant increase in the number of fibroblasts and capillary buds, collagen contents and tensile strength of the wounds. It was concluded that licorice were effective herbal remedy in wound healing [59]. In a study, wound healing potential and the mechanism of licorice alcoholic extract were effective against cutaneous wound healing through immune, antioxidant, histopathological, immunohistochemical (IHC) studies and it was observed that licorice were effective as a herbal drug for wounds [60].

Allium cepa (Onion)

Allium cepa, a bulb onion or common onion, is a vegetable belonging to the family of Amaryllidaceae. Its species differs according to regional areas, along with China and India the top producers. The chemical constituents present are Alliinase, sulphur containing compounds such as amino acids cysteine and methionine, the S-alk(en)yl-substituted cysteine sulphoxides and the γ-glutamyl peptides. It contains anthocyanins and flavonoids quercetin along with kaempferol. Saponins such as tropeoside A and B and ascalonicoside A and B. It shows antimicrobial [61], antioxidant and anti-inflammatory effects [62].

Extracts of *A. cepa* were applied on burned bodies 32 rats and it was observed that *A. cepa* showed hyperemic chorion in the Control group, fibroblasts, and collagen in the Standard group, and dermis composed of a reticular stratum of fibroblasts, collagen, and few blood vessels in the Experimental group, hence revealing wound healing activity [63]. In a study while investigating wound healing activity of *A. cepa*, the alcoholic extract of tubers of *Allium cepa* has significant effect due to free radical scavenging action and the antibacterial property due to tannins and flavonoids present in it which either due to their individual or additive effect fastens the process of wound healing [64].

Table 2: Medicinal Plants with Wound Healing Activity.

Medicinal plant	Plant part used	Extract	Active ingredient	Uses	Ref.
Calotropis gigantean (Giant calotrope)	stem bark and latex	shade-dried and powdered plant material (200 g of each) was extracted with 1000 mL of hexane for 10 h with further process for ointment preparation	polyphenols, teriterpene glycosides, flavonoids, steroids, tannins, coumarins, anthraquinones, saponins, cardiac glycosides, sterols, and alkaloids	effective for inhibition of bacterial pathogens and can be used as antibacterial materials	[65]
Morinda Citrifolia (Indian Mulberry)	Leaves and fruits	180 g of the powder was suspended in 200 ml of ethanol for 20 h at room temperature.	phenols, alkaloids, triterpenoids, steroids and carboxylic acids	Wound healing activity for excision wounds possible.	[66]
Catharanthus roseus *(*Madagascar Periwinkle/ Vinca rosea)	Leaves	Fresh leaves, shade dried and ground into a powder (120 g), macerated in 200 ml of EtOH and filtered, were dried at 40 °C.	phenols, tannins, alkaloids, saponin and flavonoids	Wound contraction, increased tensile strength and increased hydroxyproline content	[67, 68]
Datura alba (Indian Thornapple)	flower part	*Datura metel Linn*., plants were shade dried at room temperature, pulverized by a mechanical grinder, sieved through 40-size sieve mesh. 500g of fine flower powder were suspended in 1500ml of ethanol for 24 hours at room temperature.	saponin, tannin, glycosides, flavanoid, terpenoides, steroids	Significant increase in wound closure rate, tensile strength, dry granuloma weight, wet granuloma weight and decrease in epithelization period	[69]
Euphorbia Neriifolia (Indian Spurge Tree)	milky latex and leaves	shade dried leaves were powdered, soxhlet extracted with 70% ethanol and vacuum concentrated to dryness under reduced pressure	flavanoids, sugar, tannins, triterpenoidal saponin, alkaloid and cardiac glycosides	enhanced epithelization and promoted wound contraction	[70, 71]
Ficus Racemosa (Cluster fig/ goolar)	all parts (leaves, fruits, bark, latex and sap of root)	dried and coarsely powdered roots of *F. racemosa* were extracted with 90% v/v ethanol in Soxhlet apparatus for 36 hours	campesterol, hentriacontane, hentricontano l, kaempferol, stigmasterol, methyl ellagic acid	enhanced collagen synthesis which increased the breaking strength	[72]
Cynodon dactylon L. (Indian doab)	whole plant	rhizomes of *C. dactylon* were grounded using a Kenwood CG100 grinder and then mixed with methanol at a ratio of 1:10	phenolic acid, alcoholic extract and flavanoids	used as hemostatic and wound healing agent from ethnopharm acological point of view	[73–75]
Ficus bengalensis (Indian banyan)	leaves	leave powders were extracted along with ethanolic, hydroalcoholic and petroleum extract prepared using soxhlet apparatus	bengalenosides, flavanoids, leucocyanidin, campestrol, sigmasterol and α & β Amyrins, tannins, amino acids, piperine, piperlongumine	A significant increase in the breaking strength was observed along with affectivity on burn wounds	[76, 77]
Pterocarpus santalinuss Linn. (Red sandalwood)	powder made from the wood of *P. santalinus* tree	extracted both ethanol and blackish brown residue was obtained and percentage yield was found to be 15% w/w	alkaloids, steroids, phenols, tannins, flavanoids, glycosides, saponins, marsupin, pterosupin, liquiritigenin, isoliquiritigenin, carpusin	punch and burn wound healing and also effective for skin diseases	[78]

Advantages of Natural Band-aids:

1. Hypoallergenic

Some people experience allergic skin reactions to materials commonly used in wound dressings. Natural bandages utilize normal materials that are hypoallergenic. Conveying normal bandages with you consistently guarantees that regardless of who needs a bandage, you can give one without agonizing over setting off their skin hypersensitivities.

2. Reduced Skin Irritation

Wound dressings that have strong, artificial adhesives can cause a lot of skin irritation when you try to remove them. Commercial glues bond strongly to skin and hair, which means that pulling off a band-aid, is often a very painful experience. Conversely, normal natural bandages can be made with regular glues which cause fewer disturbances and are simpler to eliminate.

3. Breathable

Skin wounds require oxygen to allow the healing process to progress normally. However, many mainstream brands of band-aids are made from non-breathable materials, such as various forms of plastic. Covering a wound with these materials can slow down healing so that you have to suffer the annoyance of having a cut or graze on your skin for longer. Natural band-aids, in contrast, are breathable. They allow oxygen to pass through the dressing to reach the wound, where it can assist in healing.

Oxygen is likewise useful for the skin that encompasses the cut, which here and there becomes touchy, delicate, and wrinkly under a bandage. Natural band-aids help to keep this skin healthy while the wound heals.

4. Compostable

Many individuals pick natural bandages over standard brands since they need to be ecologically cognizant. As natural band-aids contain only materials that are found in nature, they break down much more quickly and easily than the typical plastic-filled band-aid, which can hang around in landfill for decades or even longer. In a world where litter and plastic waste are both huge topics of concern, eco-friendly options are more important than ever.

Some natural band-aids can even be composted at home, in a garden compost pile or countertop composter. Check the packaging to find out if you have the facilities to compost your natural band-aids at home.

5. The Band-aids Will Not Cause You Allergies

A many individuals are oversensitive to the synthetic compounds and additives used to make standard bandages. When they use them to dress their wounds, the inflammation level increases, and the wounds take longer to heal than they should. Inflammation also leads to swelling and pain, and if the cut or other injury is on a limb, this limits your mobility for a long time before you recover. The natural bandages will assist you with keeping away from this large number of confusions since they are hypoallergenic.

6. The Band-aids Fight Off Bacteria

An open wound is at a higher risk of bacterial infection than when your skin is healthy Assuming a physical issue comes into contact with microbes and you don't treat it on schedule, it may putrefy and prompt extreme conditions like sepsis. The most ideal way to keep this from happening is by covering the injury constantly. Natural bandages are made of herbal materials which is a characteristic enemy of bacterial

7. The Adhesives Do Not Irritate the Skin

The glues used to make the ordinary bandages append to the skin quick.. Removing them can be painful, and it might even worsen the wound by opening bleeding. Natural band-aids are made using natural adhesives. You can remove the dressing without the fear that it will irritate you or cause you any discomfort.

Different advantages that you get from natural bandages are that most are brimming with cancer prevention agents, minerals, and amino acids that support your skin all through the recuperation time frame. Consider changing from counterfeit bandages to regular options since they advance better recuperation from wounds.

Patents on herbal formulation for wound healing:

1) A flexible dressing for direct application to a wound for absorbing exudates where the dressing comprised of an alginate fiber sheet having honey fully impregnated through the fiber sheet such that the dressing has moist surfaces, and on application to the wound, the dressing becomes gel-like as exudate is absorbed which will have a gel like effect on the wound. It was patented by *Phillip Roy Caskey*, **US7714183B2** [79].

2) "Novel herbal composition for the treatment of wound healing" was patented by *Suresh Balakrishnan*, **US8709509B2**. Petition was done on 2013, the patent comprises of the summation of herbal composition. Composition of herbal extract produced new product which is effective on Wound healing, containing curcuma longa, glycyrrhiza glabra, Hamil tonia suaveolens, Tipha angustifolia and Azadirachta indica which is chemical constitute of certain herbal component [80].

3) *Michael Koganov* was inventor of "Bioactive compositions from theacea plants for the treatment of wounds and cuts" year of patent was 2013, **US20050181079A1**. The patent is related to bioactive topical formulation containing the bioactive constitute of theacea plants. Bioactive compound of theaceae plants produces antiinflammatory effect on skin and cure skin damage and tissue injury [81].

4) Patent "**WO2014147638**- Multifunctional natural wound healing matrix" was introduced by *Parveen Walia*. This patent includes a sheet hydrophilic cotton fabric coated with zwitterionic low molecular weight chitosan and organically synthesise silver nanoparticles is line on it. Curcumin and tulsi extracts are used to improve the healing property by the principal constitute they contain and they all together produces synergistic effect for healing of wound [82].

5) "Process for preparing curcumin encapsulated chitosan alginate sponge useful for wound healing"- **US20130171215A1** patented by *Sanjeeb Kumar* and *Mohanty Chandanna*. It consist of curcumin which is mixed with oleic acid fluid and the resultant mixture is goes under emulsification process with chitosan solution and then again it is emulsify with alginate solution and on the last stage lyophilization of resulted product is done and produce curcumin loaded AC sponge [83].

6) "Herbal composition for cuts, burns and wounds"- **WO2004056383A1** patented by *Pushpangadan Palpu*. A novel herbal composition for treatment of cuts, burns and wounds, the composition comprising plant material selected from *Utleria solicifolia, Jatropha curcas, Clerodendrum infortunatum*, and *Centella asiatica* [84].

7) "Herbal formulation for wound healing"- **US20100178367A1** patented by *Manish Saxena*. Herbal formulation has highly potent wound healing properties, in humans and animals. The composition consists of aqueous extracts of *Azadirachta indica*, in a mixture of natural oils along with herbs *viz. Berberis aristata, Curcuma longa, Glycyrrhiza glabra, Jasminum officinale, Picrorhiza kurrooa, Pongamia pinnata, Rubia folia, Saussurea lappa, Terminalia chebula, Trichosanthes dioica, Capsicum and Stellata* wild in well-defined ratios [85].

CONCLUSION

Wound healing is a complex process which involves inflammatory, proliferative and remodeling stage. If any misleading to this stages it may lead to development of chronic wound which might take several months to heal. Wound healing not only needs time but also requires proper care, Hence natural herbal ingredients are the best sources for curing such wounds caused due to various factors. Medicinal plants are used since from pre-historic ages, and its benefits are known to all. In this review article the wound healing property of various plants are studied and concluded. The modern development with such traditional plants may show various benefactor and therapeutic effect for human body. The use of natural products and modern knowledge might lead to better development of drugs for treatment of such adhesive bandages. Adhesive bandages (band-aids) are the primary or quick form of treatment which is administered during wound injury; hence its better and productive effect for inflammatory, proliferative and remodeling stage is quite necessary. Hence, for protective treatment of such injuries plant derived products can be favourable. With advancement of nanotechnology and availability of novel materials, wound management is becoming more effective and patient-centric. More up to date advancements like 3D printing are likewise giving profitable choices to create different medication conveyance frameworks for treating wounds. Tissue engineering and regenerative medicines are the modern perspective on innovations for creating wound recuperating frameworks. Better quality control methods for recognizable proof, screening, and evaluation herbal components along with well-designed pre-clinical and clinical studies will open new exploration entryways in injury care management.

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The authors declare no conflict of interest.

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