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Effects of Phytomedicines on Wound Healing

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Abstract

The interrelationship between wound healing and phytomedicines is a long past concept that has been practiced since time immemorial and still is being considered as one of the most reliable sources of curing wounds. The process of wound healing is not a very quick process rather it is a matter of multiple steps that are involved in the process of wound healing like homeostasis and inflammation, proliferation and remodelling. A number of phytomedicines have been discovered since the primitive people were on hunt for wound cure, some of which are curcumins, picrolivs, arbenins, aloe vera etc. The beautiful science that is inducing these phytomedicines to the site of damage is something that is very fascinating. Phytomedicines are not only used in wound healing but also in numerous other treatments. Thus, phytomedicines are considered to be the future of medical aid because of the almost negligible side effects that it has in comparison to synthetic medicines.

Keywords: Phytomedicines; Wound healing; Treatment; Cure; Medicine

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Introduction

Use of medicinal plants, bioactive phytocompounds and scientific knowledge in combination gives rise to the study of phyto science. Phyto sciences majorly deal with the science of usage of plants as the pivotal source of any medicine. Large percentage of the world's population, especially the developing nations, despite the enhancement of pharmaceutical technology in the twentieth century, by combination of extensive drug moieties, still considers plant sources as the main source of medicinal aid [1].

Prevention and treatment of disease, for countable centuries, was dependent on plants for both traditional and popular sources of medicine. For more than 5000 years, "Ayurveda" was considered as a nature obtained system of treatment, with plants as their main element for cure and prevention of disease in India. For at least 3000 years, the Chinese traditional medicine was used throughout Eastern Asia, which engaged plants of various species [2].

Nonetheless, the World Health Organization (WHO) stated that phytomedicines has been nationwide considered as a possible alternative of synthetic therapeutics due to the unwanted side effects that it follows.

To uncover the antiquity of phytotherapy, one might uncover the history of mankind itself. Primitive people used plants as food and hence could learn about the process of ingestion and with time used these plants were considered as a source of medicines as an aid to wounds. During World War II, the injured were dependent on herbal plants for their wound healing. Thus, medicinal plants, in the nineteenth century, were surveyed as the sustained source of life.

Wound Healing is a physiological process of restoring the damaged tissue by reinstating the skin integrity. Wounds are caused due to the opening or rupture of skin which damage the skin anatomically and physiologically. Skin wounds result in the loss of consciousness of the epithelium with or without the loss of underlying connective tissue [3].

In modern science, the plant species which are used to cure diseases are considerably studied to identify the various active constituents and through which they develop new drugs. Various mechanisms of action and efficacy of the medicinal plant are studied to know about its pharmacological safety [4].

Considering the importance of the effects of plants and their components on the tissue, we had performed a systematic review to explore or inspect the effects of phytomedicines that can amplify or accelerating the wound repairing or skin regeneration and also about the pharmacological effect of medicinal plants on the process of healing of the wound [5].

Wound Healing and Angiogenesis

Wound healing is quite a lot more than just four simple phases of homeostasis and inflammation, proliferation, and remodeling.

With each passing year, a new mediator is discovered which

supposedly tends to affect the process of wound healing in either intrinsic or extrinsic fashion [6]. The long-ignored interest in wound healing developed when people became enthused to know about the Healing process of the human body [7].

The process of wound healing is independent of time, whereas dependent on the location of the wound. The conclusion about any wound and its healing is based on macroscopic examination.

Homeostasis and Inflammation

The presiding phase in wound healing is the homeostasis and the inflammatory phase [6]. When a certain part of the body is exposed to any kind of wound/injury, there is a significant disruption of the blood vessel which might lead to bleeding. The first and foremost commitment of the body mechanism is to stop the bleeding (homeostasis), in order to avoid death by excessive loss of blood [7]. The process of clot formation immediately takes place as soon as the collagen is released. This marks the starting of the inflammatory phase. Collagen, platelets, thrombin and fibronectins, initiates the process of inflammation formation, when cytokines and growth factors are released. Neutrophils, monocytes, fibroblasts and endothelial cells come together at the platform served by the fibrin clot. A signal is sent as soon as the clot formation takes place, to which neutrophils are the first responders. Accumulation of the mediators followed by the vasodilation of the blood vessels takes place due to the tangle formation of prostaglandins. With the help of Interleukin (IL)-1, Tumor Necrosis Factor (TNF)-α, Transforming Growth Factor (TGF-ß), Platelet Factor-4 (PF4) and bacterial product allows the entry of neutrophils at the injured site. Approximately 48-96 hours of injury, transformation of macrophages from monocytes takes place, after they are attracted to the site of injury from nearby tissue and blood. The synthesis of nitric oxide, fibroplasia and angiogenesis will be mediated by the activated macrophage in the proliferative phase and hence the conversion is considered important.

Macrophage is of great importance because of the numerous enzymes and cytokines it secretes. Stimulation of fibroblast (production of collagen) and promotion of angiogenesis are carried out by enzymes like ILs and TNF secreted by the macrophages, along with keratinocyte stimulation carried out by TGF.

Cells like neutrophils also release caustic proteolytic enzymes on entering the site of injury in order to digest the bacteria and clear the wound site [6].

Proliferation

The proliferative phase includes replacement of fibrin matrix with a new matrix of collagen fibres, proteoglycans, and fibronectin to reshape the structure and function of the tissue. Angiogenesis is a healing event in this proliferation phase, and other significant events in this phase of healing are the granulation tissue and epithelialization. Fibroblasts are the important cells in the proliferation phase of healing [8].

Proliferation is a major concept with the focus on covering the wound surface (i.e., re-epithelialization) restoring the vascular network and forming granulation tissue. Re-epithelialization requires migration and proliferation of keratinocytes. Within a few hours to 1 day after the injury, the existing wound keratinocytes started to migrate. It generates more cells to cover the wound, keratinocytes at the basal layer of the wound edge and epithelial stem cells from nearby hair follicles or sweat glands start proliferating in 2-3 days after injury [9].

Angiogenesis

During wound healing, angiogenic capillary sprouts invade the fibrin or fibronectin-rich wound clot. In a few days, the fibrin or fibronectin rich wound organizes into a microvascular network all over the granulation tissue. Accumulation of collagen fiber produces scars in the granulation tissue, also the density of blood vessels diminishes. A dynamic interaction occurs in between the endothelial cells, angiogenic cytokines, such as FGF, VEGF, TGF-β, angiopoietin, and mast cell tryptase, and the Extracellular Matrix (ECM) environment. wound healing repair endothelial cell ECM receptors are critical for the morphogenetic change in blood vessels [10].

Granulation

Granulation tissue is one of the main components in the wound healing process. The formation of granulation tissue is complex and requires an intricate interplay between the cell types at the wound site. The wound can heal by primary intention and secondary intention. In primary intention wound edges are approximately easily and in secondary intention, the edges of the wound do not approximate. The wound will heal by the granular matrix by the secondary intention [11].

Epithelization

A process of covering the denuded epithelial surface is called epithelialization. All dermal wounds heal by three mechanisms. And the mechanisms are contraction, connective tissue matrix deposition and epithelialization. Epithelialization has various processes which consist of epithelial cell detachment and there is a change in internal structure, epithelialization which causes migration, proliferation and differentiation of the tissue. During the healing process the growth factor such as Epidermal Growth Factor (EGF), keratinocytes growth factor, and TGF alpha is released, and they bind to the receptors on these epithelial cells which stimulate migration and proliferation. The binding of the growth factors with the receptors triggers the desmosomes and hemidesmosomes so that the cell can detach for migration. Then epithelial cell begins to migrate as a monolayer over the newly deposited granulation tissue. Once the network has been made the entire epithelial monolayer enters in a proliferative mode and the epidermis is re-established. The desmosomes and hemidesmosomes are attached to the new form basement for re-established [12].

Remodelling

Remodeling is also known as the maturation phase. The cells had been used to repair the wound after that the cells which are no longer needed are removed by apoptosis or cell death. The remodeling phase is when collagen is remodeled from type III to type I ratio and the wound fully closes.

During the remodeling phase, collagen fiber is aligned and the water which was present is reabsorbed so that the collagen fibers lie together and form a cross-link. The advantage of the cross-link is that it reduces the thickness of the scar and makes the skin area of the wound even stronger. Normally, remodeling starts about 21 days after an injury. Cross-linking makes the healed wound area weaker than uninjured skin.

The stages of wound healing are complex. Failure in the progress of the wound healing stages can lead to chronic wounds. Factors that can lead the chronic wound are diabetes, infection etc. wound care can speed the stage of wound healing by keeping the wounds moist, clean and protected from reinjury and infection.

Phytomedicines

Sources

Herbs/plants act as a base for any phytomedicine. All the Phytomedicines are derived from various useful parts of different plants. 121 pharmaceutical products were prepared with the knowledge of traditional medicine in the last century. A shift from synthetic to herbal drugs is being made for the purpose of repairing and strengthening bodily functions in the world today. The great contribution of the plants in the field of pharmacy was first noted in 1995, when the root of the Indian plant *Rauwolfia serpentina* was used in the treatment of blood pressure and hypertension. Owing to this, a number of such discoveries were made, 100 new plant-based drugs were recognized approximately within a period of 1950 to 1970, in the markets of the USA, which included plants derived from higher plants like deserpidine, rescinnamine, reserpine, vinblastine and vincristine.

In 1967, for the treatment of choriocarcinoma, Hodgkins, non-Hodgkin's lymphomas, leukemia in children, testicular and neck cancer, vinblastine isolated from the *Catharanthus roseus*. Vinblastine was also used in the treatment of acute lymphocytic leukemia in childhood, advanced stages of Hodgkins, lymphosarcoma, small cell lung, cervical and breast cancer. During the period of 1991 to 1995, 2% of drugs like paciltaxel, topotecan, gomishin, irinotecan etc. were developed [13].

Importance and advantage of phytomedicines

According to WHO, the population of developing countries depends upon traditional medicines, they mostly depend on plant drugs for primary health care needs. There is no doubt, modern medicines have tremendous advantages and their application [14]. People on all continents are using thousands of indigenous plants for the treatment of ailments. A gorilla species called lowland gorillas take approximately 90% of their diet from the fruits and the name of the fruit is *Aframomum melegueta*, which is useful for the treatment of the antiviral, antibacterial, antifungal, and anthelmintic properties which is the reason for the self-medication by a wild animal. The ginger plant is a potent antimicrobial that keeps shigellosis and similar infections at bay. Generally, two types of metabolites are produced by the plant primary metabolites and secondary metabolites. Plants produce a high diversity of secondary metabolites. The examples of secondary metabolites are alkaloids, terpenoids. Phytopreparation is applicable for treatment for severe disease. Phyto Preparation is also used as chemo-synthetic drugs. Phytomedicines have chemotherapeutic effects and no adverse effects. Many phyto preparations have no chemotherapeutic and adverse effect but achieve optimum efficacy after long treatment of the medication. Herbal drugs and plant derived products have major sources of anti-drugs cancers. A blend of against malignant growth drugs and polypharmacological plant-determined concentrates or mixtures may offer a huge benefit in sharpening the adequacy of monotherapy and defeating drug-incited obstruction in disease patients. Plant optional metabolites have incredible potential as a wellspring of viable antifungal specialist. As specific illustrations, plant-determined mixtures for example hydroquinones and naphthoquinones (*lapachol, juglone*), sesquiterpenes (*cinnamodial, capsidiol*), and alkaloids, for example berberine have shown assorted antimicrobial exercises including antifungal exercise.

Roles of phytomedicines

Since time immemorial, medicinal plants and its derivatives have been used for the treatment of various diseases in humans [15]. Treatment of ailments since prehistoric times, were dependent on hundreds and thousands of plants [13]. Phytomedicines is playing a game changing move in the discovery of new medicines, including antifungal/antiviral. Fungal diseases like Cladosporum cladosporioides were treated with the help of the bark of Butea monosperma (*Caesalpiniaceae*) extracted with petroleum and ethyl acetate. 80% of 4 billion population of the globe depends on plant and plant related aids for primary medical treatment. This includes teas to crude tablets. Red Lapacho, in 1960s, was considered as 'wonder drug' in Brazil and Argentina as two major bioactive components were extracted from *Tabebuia impetiginosa,* namely lapachol and beta lapachone, the main anti-tumor component and pro-apoptotic effects were seen *in-vitro*. Thus, the incoming of such sources made it easier of us to obtain treatment. Management of bacterial and fungal maladies using herbal plants is an art that is carried over a period of time. Long back as 600 BC, Indian physician Sushruta spoke about the importance of medicinally essential oils. Treatment of various infections in the moths, jaw, teeth was considered to be cured with the help of essential oils. Families such as *Asteraceae, Apiaceae, Lamiaceae, Fabaceae, Rutaceae, Zingiberaceae, Myrtaceae, Lauraceae, Cyperaceae*, are believed to have antimicrobial effects, when derived in oil base.

While the world is progressing with each passing day, the cure for diabetes is still questionable. Research indicates that food rich in phytomedicines, to a very large extent, helps in reducing the risk of diabetes. In the years 2008 and 2011, the World Health Organisation laid emphasis to begin an elaborative research on medicinal plants that is anti-diabetic and cardioprotective. For example fruit extract, aqueous seed, and leaf extract of *Aegle marmelos* (holy fruit tree) belonging to the family of *Rutaceae* having active ingredients like alkaloids, tannins, cardiac glycosides, and terpenoids helps in the management of diabetes. Other than this, *Aloe vera* (aloe), *Allium cepa* (onion), *Allium sativum* (garlic), *Eugenia jambolana* (jamun/black plum), *Lawsonia inermis* (henna), *Trigonella foenumgraecum* (fenugreek seeds), *Cynara cardunculus var. scolymus* (globe artichoke), *Cinnamomum tamala* (Malabar leaf), etc. also helps in the management of diabetes.

Rhodiola rosea is a medicinal plant that has a variety of medical uses. It is used to increase mental and physical performance, endurance and strength. Also, it is used to increase the body's nonspecific resistance. Cardiovascular disease, infection, impotence, high altitude sickness, and numerous gastrointestinal ailments are also controlled with the help of this plant [16].

Thus, the majority of the nation is dependent on phytomedicines for combating diseases such as diabetes, hypertension, cardiac diseases, anxiety etc. Traditional medicine continues to be the primary source of treatment for most of the developing nations. The role of phytomedicines is numerous in every aspect of pharmacy. Be it treating fungal infections, to controlling chronic diseases, to a wide range of research of developing new medicines, phytomedicines has always been a help.

Effects of phytomedicines on wound healing

The increasing use of phytochemicals for therapeutic effect and numerous researches helps us in understanding the interaction of the natural nutrient with the human genome and helps us in concluding the rapidity of effect of these medicines on humans [16].

Research on wound healing drugs and the plant constituents which are derived from plants is a developing area in modern biomedical sciences. More than 50% of all the drugs having a natural product origin show the importance of therapeutic effects. The product is generally accepted by its high acceptability and good toleration in the wound healing process. Much natural product has been claimed to have wound healing properties. Many plants and their extracts are investigated at present in this direction of wound healing. Natural products can induce its effect by various mechanisms. The primary challenge is to improve the supply of vascular wound healing. Products derived from the plant discussed below are known to have wound healing properties [17]. The main wound healing herbal medicines are mimosa, aloe vera, grape seed, echinacea, chamomile, papaya, oat, garlic, ginkgo, olive oil ocimum, ginseng, green tea, jojoba, tea tree oil, rosemary, lemon, soybean and comfrey.

Curcumins: For the past many centuries, Curcumin, a polyphenol derived from Indian dietary spice turmeric, has been extensively used to treat inflammation and other diseases. The curcumin structure present in the turmeric is diferuloylmethame-(1,7-bis (4-hydroxy-3-methoxyphenyl)-1,6-heptadiene-3,5-dione) is widely used for treating various skin disorders. Other than that, curcumin possesses anti-inflammatory, antioxidant and antiproliferative properties which are controlled/regulated by the growth factors, inflammatory cytokines, transcription factor, protein kinases and several other enzymes. The wound healing and skin regeneration properties of curcumin have shown to be of much effectiveness when several researches on rat and guinea pig were made. Wound healing with the help of curcumin begins to occur when a compact and well aligned collagen layer is formed. It enhances the wound healing mechanism by activating the anti-inflammatory and reactive oxygen species in the area of the wound.

Picrolivs: *Picrorhiza kurroa* is a plant whose roots and rhizomes form picroliv which is regarded to be of great importance in the field of pharmacy. Iridoid glycosides, picroside-1, and kutkoside in the ratio of 1:1:5 are the active components of picroliv. It is considered important since for ages it has been used to treat fever, asthma, allergies and other inflammatory conditions. Picroliv acts by not only repairing the endothelial cells but also enhances re-epithelization, neovascularization, and migration of multiple cells like the dermal fibroblast and the fibroblasts in the wounds. Although the exact mechanism is not yet known [18].

Arnebin: *Arnebia nobilis* (a member of the Boraginaceae genus) whose plant root is a naphthoquinone derivative. The chemical structure of arnebin is 1(5,8-dihydroxy-2-(1'-b,b-dimethylaroxy-4'-methyl-pent-3-enyl)-1.

The scientists noticed that on use of Arnebin on wound healing a huge decrease in the injury width and hole length was contrasted and controlled. It has likewise been accounted for that arnebin-1 treatment can incite cell expansion, movement, and vessel development to frame a thick granulation tissue and re-epithelialization of the wounds. The increment in the amalgamation of collagen, fibronectin, and TGF-1 was observed in arnebin-1-treated injuries contrasted and the untreated control. They proposed that arnebin-1 might actually upgrade the declaration of TGF-1 at both translational and transcriptional level, which may be liable for the improvement of wound healing. Taken together, these discoveries recommend that arnebin-1 can possibly be additionally concentrated as a strong helpful specialist for wound recuperating [19].

Panax ginseng: Panax ginseng (*Araliaceae* family) has been the most generally utilized natural medication in Eastern Asia for over 2000 years. Ginseng has multiple pharmacological activities for treating cardiovascular illnesses, rheumatoid joint inflammation, and in the maintenance of in-manageable skin ulcers of patients with diabetes mellitus [20].

Centella asiatica: The *Centella asiatica*, popularly known as the Indian Pennywort or Asiatic Pennywort, has been utilized for a very long time as a traditional herbal medication in a huge number of the Asiatic nations in the Asian sub-landmass, as a utilization in the wound recuperating interaction, and it has as of late acquired a lot of ubiquities in the western nations. The Plant species are known to discover their quality deepest tropical and subtropical nations, pertaining to their helpful development conditions, including the swampy regions. These parts incorporate most regions, including most regions in India, Pakistan, Madagascar, Sri-Lanka and South Africa, and South Pacific and Eastern pieces of Europe. *Centella asiatica* has a place with the family *Apiaceae*, however the various pieces of the plant, where the entire plant extricate is utilized in the evaluation techniques with creature wound models are pertinent in the extraction models in the ordinary just as the Sprague-Dawley rodents, rather than where the extraction, entry point and dead space in Wistar Albino rodents are utilized as the test creatures in the evaluation of the airborne pieces of the last. The viability of the *Centella asiatica* in their advancement of the injury recuperating measure was widely investigated both in-vitro and in-vivo and was found to advance entry point type wounds and open injuries as addressed by a more noteworthy collagen content and thickness of the epithelium [21].

Anana scomosus: Pineapple has been a section of traditional

people medication for long time and proceeds to be available in numerous home-grown arrangements. Bromelain has been known as a compound since1875, and from that point forward has been applied as a phytotherapeutic clinical specialist. The term bromelain was at first utilized as a replacement to describe a combination of proteolytic compounds and other non-enzymatic substances found in the *Bromeliaceae* species, especially in pineapple *(Anana Comosus L.)* and its different parts like the stem, natural products, and leaves [22].

Ocimum: Ocimum is a notable plant in Indian medication and has been one of the primary plants to be introduced into the treatment routine in the conventional medication framework. It displays distinctive restorative impacts, for example, fix properties and cytokine acceptance. The injury recuperating action was surveyed by the enlistment of the chilly fluid concentrate of Ocimum sanctum leaves alongside its effect on the Tumor Necrosis Factor-(TNF-)using the extraction model of twisted fix in wistar albino rodents. After use of the 10% concentrate of Ocimum sanctum in the oil jam demonstrated to be effective with an expanded pace of epithelialization and an expanded injury constriction. The concentrates of Ocimum sanctum may likewise be strong in the treatment of the administration of strange injury mending, for example, keloids and hypertrophic scars, inferable from its high cancer prevention agent movement. Right now, effective definitions, arranged by the fuse of improved Silver-Nanoparticles into the Carbopol gel base, trailed by in-vivo assessment utilizing the rodent model of skin wound mending, showed a 96.20% injury recuperating movement and the inhibitory proficiency of arranged nano gel was much the same as the business item against the *Staphylococcus aureus, E. coli and Pseudomonas aeruginosa* [23].

Comfrey: The underlying foundations of the Comfrey (*Symphytum officinale L.*) plant have been local to the European customary medication routine yet have likewise been extrapolated to certain pieces of Asia and South America. In the customary medication framework, comfrey roots are utilized topically, especially for wound therapy, joint issues, and wounds relating to the musculoskeletal framework, particularly caused due to pyrrolizidine alkaloids that have been connected to liver harmfulness (hepatotoxicity) and cancer formation (cancer-causing nature). A few cell instruments have been advanced to clarify their system of activity, especially the ones that object to diverse intracellular flagging pathways set off by NF-B, AP-1, PPAR, Nrf2, and MAPKs. The dynamic constituents have depicted the critical part in comfrey root, which fundamentally incorporate allantoin, adhesive polysaccharides, phenolic mixtures, for example rosmarinic corrosive, chlorogenic corrosive, caffeic corrosive, and their subordinates and salts, glycopeptides, and triterpene saponins. Comfrey likewise incorporates pyrrolizidine alkaloids in particular, 7-acetyl intermedine, 7-acetyl lycopsamine, intermidine, lycopsamine, and symphytine which are normally credited to their intrinsic hepatotoxic nature, and accordingly fresher restorative items use pyrrolizidine alkaloid-exhausted or missing concentrates as dynamic specialists. [24]

Aloe vera: Aloe vera is a useful herb which grows in hot and dry climates, and it is mainly grown in Asia, Africa and other tropical region. Worldwide more than 360 known species which are used in pharmaceutics and cosmetics industries. Aloe vera is very useful for the topical administration, on burn and other cutaneous injuries. Aloe vera contains anthraquinones, saccharides, vitamin E and C, Zinc, enzymes, acetyl salicylic and many more properties. Hydration, oxygenation, and removal of dead tissue is one of the major factors in the epithelialization process of wound healing. Aloe vera content 96% of water which prevent wound desiccation and increase migration of epithelial cells and microcirculation of wound is enhanced by aloe.

Mimosa pudica: The roots of mimosas are very useful for the wound healing process. Mimosa root contains phenol and tennis constituents which play an important role in healing. The roots of mimosa contain high content of tennis, which is responsible for wound healing activity, due to the astringent property of tennis.

Echinacea: Echinacea is used for phytotherapy for wound healing, pain relief and cold symptoms. Alcohol extract of echinacea inhibits inflammatory production. Alcohol extracts of echinacea have two classes of natural chemicals, lipophilic alkamides and water-soluble caffeic acid derivatives. Echinacea strengthening the immune system against microbial infection [25].

Conclusion

Phytomedicines have an excellent role within the wound healing process. Cutaneous healing may be a multistage process that depends on the activation of various cells including endothelial cells, inflammatory cells, keratinocytes and fibroblasts. Many fast-growing herbal drugs were utilized in the previous couple of decades which captured the eye of scientists for the plant investigation. Most developing countries depend upon the use of herbal therapies, and it's been assessed that 9.6-12.1% folks grown-up routinely use them. These are the drugs common marigold, *Centella asiatica*, *Angelica sinensis*, American wormseed and Polygonum gaining popularity in both developing countries and developed countries due to the low cost, low side fact, and natural origin. Active ingredients are described as constituents of herbal medicine with therapeutic activity and include carbohydrates, glycosides, lignanoids, alkaloids, amino acids, peptides, proteins and enzymes. Many studies have already mentioned the biological activities of natural preparations just like the induction of the immune system and anti-inflammatory, antioxidant, antimicrobial, antimutagenic, anticancer and antiulcer effects. Phytomedicines are widely used in the case of epilepsy, hypertension, diabetes mellitus. Numerous plants advance the skin's normal fix systems and have along these lines a colossal potential for remedial use in wound consideration. As our experience with natural extracts and disengages increases and keeping in mind that we utilize normally utilized logical philosophy to examine plants and their extracts from the physiological and pharmacological perspective, the quantity of home-grown items for wound treatment is consistently expanding. Clinical verifications of home grown item remedial impacts prompted the investigation of a lot more spices for their helpfulness. dynamic substances from plant extracts, which could likewise reveal compounds with better restorative worth. A combination of traditional and modern knowledge can create novels. drugs for wound healing altogether brought down undesirable results.

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