

Healing activity of many Tunisian medicinal plants on wounds and burns

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Abstract— Objectives: medicinal plants are the main ingredients in folk's medicine. This study evaluates ethnomedicinal plants and their effects, according to the literature article, analyses, field observations and comparisons, to investigate wound healing. Components act on the skin, which present the highest susceptibility to interact with the environment and therefore receive recurrent harm and damage. Wound healing is the process described as a fundamental connective tissue response.

Methods: A computer-based search of Medline was performed for this study. Researchers were contacted; bibliographies of relevant papers and previous meta-analyses were hand searched for additional references. Comparison was made with earlier standard literature of ethnomedicinal and medicinal plants.

Results: Through traditional knowledge, the herbal medicine was the basis of treatment of most diseases. The medicine was available via traditional health care practices such as the preparation of home-made herbal remedy. The traditional herbal medicine has survived and thrived in the trans-cultural environment with the mixture of ethnic traditions and beliefs. Of the showed medicinal plants assessed in the present work, many species showed an interesting capacity of wound healing.

Conclusions: Through the ages, traditional herbal medicine has been a primary means of health care. Therefore, further pharmacological evaluation of traditional herbal medicine deserves more attention.

Index Terms— wound healing, medicinal plant, proliferation, tissue healing, skin.

INTRODUCTION

The practice of herbal medicine continues, despite important cultural and economic changes through the last decades.

Pharmacopeia is still alive all around the world (1), in order to recognize the plants for their pharmacological investigation and therapeutic interest.

Primary therapeutic use of herbal remedies was for the respiratory system diseases; cold, cough, asthma and bronchitis. The second most frequent use was for the skin disorder treatment, bleeding, eczema,..., and finally, digestive disorder (2). Traditional medicine is known as a complementary medicine and always an important data to modern pharmaceutical company cost and less time.

Most common of all home cures are plants or derived. In ancient times, many plant derived remedies are proven treatments, such as Aloe Vera is believed to be effective in treating stomach ailments, gastrointestinal problems, skin diseases, constipation for radiation injury, as an anti-ulcer and diabetes(3), for sunburn. Ephedra is recommended for fatigue and weight loss, and garlic consumption shows results in lowered cholesterol, in deed, the Use of root extracts such as root oil is recorded to have been used by the Chinese for over two millennia, to aid in nausea, vomiting, and even memory loss. for wound healing and burns, As repair and regeneration of

new skin is nearing completion(4), Aloe vera was known for their anti-inflammatory effect, (3).

The definition of a wound is the loss or the breaking of cellular and anatomic or functional stability of the living tissue. Wound healing is a process depicted as a fundamental connective tissue response. The investigation on wound healing is focused on the whole skin, which presents the susceptibility to be in interaction with the environment and therefore receives constant harm and damage. The wound healing involves a complex series of events: chemotaxis, cell division, neovascularization, synthesis of new extracellular matrix, and remodeling of the scar tissue (5). By the way, these events are regulated by several mediators including platelets, inflammatory cells, cytokines and growth factors (5). These processes involve the four overlapping phases of hemostasis, inflammation, proliferation, and remodeling; finally, an avascular scar is the final stage of the wound healing process (5).

The first step is the inflammatory stage. Once a break has been sensed by the body, vasoconstriction immediately takes place to minimize blood loss, and is quickly followed by swelling. The inflammatory phase is the body's natural response to injury. After initial wounding, the blood vessels in the wound bed contract and a clot is formed.

Once hemostasis has been achieved, blood vessels then dilate to allow essential cells; antibodies, white blood cells, growth factors, enzymes and nutrients to reach the wounded area. At this stage the characteristic signs of inflammation can be seen; erythema, heat, oedema, pain and functional disturbance.

The proliferative phase comprises stages: angiogenesis, granulation, epithelialization, and contraction. In the first stage, new blood vessels grow from endothelial cells. In fibroplasia and granulation tissue formation, fibroblasts grow and form a new, provisional extracellular matrix by excreting collagen and fibronectin. At the epithelialization stage, epithelial cells cross the wound bed to cover it. In contraction, the wound is made smaller by the action of myofibroblasts by establishing a grip on the wound edges. The product of the proliferative stage is a scab: a temporary cover that protects the healing process occurring beneath it (4).

In the maturation and remodeling phases, collagen is remodeled and realigned along tension lines and cells that are no longer needed are removed by apoptosis. In fact, the inflammatory phase is followed by synthesis of collagen and other extracellular macromolecules that helps in the formation of a scar (6). Remodeling phase begins at about 2 to 3 weeks and can last up to 2 years. At this time, collagen synthesis and degradation reach equilibrium. Fibroblasts organize and cross-link the collagen, wound strength gradually increases, wound contraction occurs, and the wound loses its pink or purple color as capillary and fibroblast density decrease.(7)

The expertise in herbal medicine was documented in many publications in the popular literature. Medicinal plant preparations are used as tonics/ purgatives and emetics/ expectorants and demulcents, wound dressings and antiseptics, poultices, ophthalmic and oral preparations, as skin washes and as fumigants. Herbal preparations are used to prevent illness and promote health. Likewise, there is a strong emphasis in treatment of disease by purgatives or emetics/ which drive out the impurity or illness, leaving the body clean and ready for the return to normal body function (8). Knowledge about indigenous herbal medicine must include the propriety of all parts of the plant, the manner of extraction and may be the manner of preparation as infusions, or decoctions, or poultices. Often, different plant parts have had specific ethnomedic-

ample, the flowers, seeds and roots of Rhus and Epilobium were used as anti-hemorrhagic, dermatological aid, and for analgesic applications(9). Decoction was the most used method of preparation; it is eaten fresh for external use. Although a specific plant part might have a reported use, other parts of the plant and additional applications may remain uninvestigated or a plant may not have a recorded ethnomedical use.

Medicinal plants can present an important natural remedy for human health and nowadays, the majority of chemical drugs have their origin in natural plant sources. Many protocols are used to extract the active components from different parts of plants.

OBJECTIVES

The objective of the present work is to evaluate Tunisian herbal medicines in their capacity to treat wounds.

Data sources/search methods

A computer-based search of Medline was performed. Researches and bibliographies of relevant papers and previous meta-analyses were hand searched for additional references. The comparison was made with earlier standard literature of ethnomedicinal and medicinal plants.

Medicinal plants

Several plants were investigated in part or as a whole to treat some diseases. The active components were extracted and developed into different drug types. For this purpose, we took some Tunisian plants known for a healing effect on wound or burn. This table recapitulated the healing power of selected Tunisian plants and their effect on wound and burn.

Discussion

Folk medicine has given rise to the interest in the treatment of different diseases especially skin burns and inflammatory disorders. Healing requires the collaboration of physiological actions and responses of cells and tissues(25). Wound healing involves various phases which include granulation, collagenation, collagen maturation and scar maturation(37). The phenomenon includes a chain of well-orchestrated biochemical and cellular reactions that lead to the growth and regeneration of wounded tissue in such a specific manner.

The repair process requires the participation of various inflammatory cells which facilitate the healing process. These cells also promote the migration and proliferation of

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cal applications. All parts could be used: fruits, flowers, leaves, branches, seeds, roots and stems, bulbs and tuber (2). For ex-

endothelial cells, leading to neovascularization; of connective tissue cells which synthesize the extracellular matrices including collagen; and of keratinocytes leading to re-epithelization of the wounded tissue(38). Nevertheless, Collagen is one of the most dominant extracellular matrix proteins in the granulation tissue, which appears to be significantly high by the fifth day of wounding and after seventh day collagen productions is further advanced (39).

Tissue healing is a complex and dynamic system that enables effective repair of different damaged tissues. There is still a little doubt that appropriates some therapy that has the capacity to influence the process in the positive way. Qualitatively, During and after the formation of the platelet plug and the deposition of the fibrin matrix, neutrophils infiltrate the wound sites(40). After two-three days, monocytes appear in the wound, and differentiate into macrophages to coordinate the next phase of wound repair. Next step occurs two-ten days after injury and it is characterized by the cellular proliferation and the migration of keratinocytes over the injured dermis (15). Angiogenesis replaces the fibrin matrix and granulation tissue. Finally, remodeling begins two-three weeks after injury. Inflammatory response is down regulated and the dead cells are replaced by collagen and other extracellular matrix proteins (15).

For every plant, its therapeutic virtues are imperative to assure an effective treatment of point of view quality and duration. In fact, Aloe vera is reported to contain tannins, sterols, organic acids, enzymes, saponins, vitamins and minerals (3). This revealed the presence of many secondary metabolites in the leaves it confirmed that the plant extracts could be used for the treatment of various infections including skin infections (3). The Aloe vera gel increases epithelial cell migration, more rapid maturation of collagen and reduction in inflammation, increases synthesis of hyaluronic acid and dermal sulfate in the granulation tissue (15).

Calendula officinalis is used medicinally in Europe, China and India it was known as "African marigold", used especially for wound healing, jaundice, blood purification, and as an antispasmodic. Studies have underlined the presence of triterpenoids, flavonoids, coumarines, quinones, volatile oil, carotenoids and amino acids that have explored in phytochemistry and pharmacological activities in order to collate existing information on this plant as well as highlight its multi-activity properties as a medicinal agent (41). In fact, hexanolic and ethanolic extracts from *Calendula officinalis* are studied and both extracts of *Calendula officinalis* stimulated the proliferation and migration of fibroblasts at low concentrations (42).

Sesame oil is considered to be a health - promoting food, owing to the fact that it contains a higher proportion of

monounsaturated fatty acids than saturated ones, dominated by oleic (C18:1) and linoleic (C18:2) (43). Traditionally, sesame seeds are used in the treatment of wounds, especially burn wounds. It contains a water soluble base like carbopol containing paraben for gel local application (24).

Hypericum perforatum can be considered to be a rich source of water-soluble antioxidants and/or phenolic compounds as compared to studied foreign plants(44). These properties may contribute to the wound healing effect. In addition, Extracts of plants used in Phytotherapy for the treatment of inflammatory disorders were screened in vitro for antioxidant activity and phenolic compounds content.

For the *curcuma longa*, the study reveals that the wound contraction increases on increasing the herbal extract concentration (45). Curcuminoids are the main active compounds in turmeric. Usually, these polyphenols are present in 3-15% of turmeric rhizomes with curcumin (46).

The chemical composition of the three essential oils obtained by steam distillation of the mastic gum, leaves and twigs of *Pistacia lentiscus*, alpha-Pinene, myrcene, trans-caryophyllene and germacrene D were found to be the major components (47).

In another way, the use of antioxidant has been shown to promote wound healing: several natural compounds like flavonoids, terpenes, alkaloids and polyphenolic biomolecule might positively influence one or more phases of the healing process(25). Some of active secondary metabolites could have advantages on chronic diseases, others could enter body tissues by free diffusion and influence the membrane fluidity and permeability (40).

Some varieties are good sources of oxidants and carotenoids like For the *Artocarpus altalis*, (48), and may contribute to the wound healing effect. Phytochemical analysis of the extract and fractions indicate the presence of typical constituents such as alkaloids, saponins, sterols, terpenoids, carbohydrates, glycosides and tannins (49). α -pinene, one of the terpenoids, is known to possess anti-inflammatory activity(50) and may contribute to the wound healing activity by suppressing inflammatory reactions invoked by the injured tissues. In addition, there is a percentage of saponins and tannins in the leaves of this plant (51) implicating for these constituents in the activities of the leaf extracts, especially tannins, which have been implicated in the haemostatic activity of plants where they arrest bleeding from damaged or injured vessels by precipitating proteins to form vascular plugs (49). Okoli et al, proved the presence of the Riboflovin in *Aspilia africana* which makes it an important tool in herbal medicine and helps to account of its use in wound healing and treatment of skin disease (52).

As for beta-caryophyllene, it allows the exhibition of several biological properties such as anti-inflammatory antibiotic, antioxidant, anticarcinogenic activities and stimulates local anesthetic activities (40).

Therapeutic activity of the medicinal plants polyphenols (phenolic acid, lignans, tannins, flavonoids, coumarins and stilbenes), terpenes, sulfur containing compounds, carotenoids, saponins, alkaloids, polyphenols, sugars, fatty oils and phyosterols (15). Aloe vera contained a wide variety of bioactive constituents of different structures stands behind. The main effects of these active compounds are connected to their anti-microbial activity, antioxidant properties and their abilities to enhance cell proliferation collagen production. However, in many cases, the active molecules have not been identified yet (15).

Alkaloids have an important role in improving wound healing, it allows the acceleration of angiogenesis in small doses by stimulating intracellular processes; for example nicotine increases the intracellular level of calcium (53).

Flavonoids promote rapid wound healing due to the anti-microbial antioxidant and astringent properties (54), in fact, flavonoids enhance the proliferation and viability of human fibroblast cells and lead to subsequent faster wound healing. Terpenes promote wound healing stimulating collagen production and mitotic activity of embryonic fibroblasts (55) such as catalpol, borneol, thymol, alpha-bisabolol (56). Glycosides are beneficial to the pro-wound healing activity; it promotes re-epithelization of the skin wounds in animal models and can enhance collagen synthesis in skin fibroblasts. It inhibits inflammatory processes at the early phases of wound healing (57). Some metabolites like flavonoids were developed to control the release of Calendula officinalis flower extract and ensure polyphenol antioxidant activity throughout a time period that can match the in vivo remodeling stages of skin wounds (17).

The main antioxidants present in edible oils are vitamin E, mainly the tocopherols, and tocotrienols, such as sesaminol and sesamol in sesame oil (58).

There are multiple chemotypes based on essential oil composition characterized by germacrane D 14% as a major metabolite, alpha-pinene 5%, beta-caryophyllene 5%, caryophyllene oxide 4%, bicyclic germacrane 4%, dodecanol 5% and spathulenol 3% (40). Hypericum perforatum is used as a wound healing aid in France and Turkey. In fact, flavonoids were the active components. In Russia, this plant is called "means for the ninety-nine diseases".

All studies showed the importance of the antioxidant. Some vitamins may have synergy effect on wound

healing and the treatment of skin disease. We have the opportunity to evaluate the antioxidant effect, the effect of vitamins on the skin: healing, re-epithelization and production of collagen.

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Table: Medicinal Plants properties

Common name	Scientific name	Ethno medical uses	Mechanism	Part(s) used
Aloes	Aloe vera (Pedaliaceae)	Used to heal the wound properly (10, 11) Used to treat skin and subcutaneous diseases (12) Used for burn healing first and second degree burns (13) May shorten the time of healing by 8 days (14)	Increases epithelial cell migration rapid maturation of collagen Reduces inflammation increases synthesis of hyaluronic acid and dermal sulfate in the granulation tissue (15)	Gel(15)
Souci officinal	Calendula officinalis (Asteraceae)	Stimulates the physiological regeneration and the epithelialization(16) Used as remedies for burns, bruises, cuts and rashes(16) Used to treat wounds (17)	Hexanolic and ethanolic extracts stimulate the proliferation and migration of fibroblasts at low concentration (16)	Juice of leaves (18) Flower extracts (16)
St. John's wort	Hypericum perforatum (Hypericaceae)	Used traditionally to speed healing of burns and wounds, anti-inflammatory and analgesic activity (19)	Inhibits the protein kinase C activity and release the arachidonic acid and leukotriene B4 (LTB4) (20)	Leaves extracts (19)
Walnuts	Juglans regia (Pedaliaceae)	Used to treat scalp itching (21), as a remedy for dermal inflammation and superficial skin inflammations (21) Used for superficial burns (21)		
Sesame	Sesamum indicum (Pedaliaceae)	Seeds oil is deemed for burns and many other wounds (22) A nutritive source of natural oxidants (sesamin and sesamol) (23)	produced a significant increase in the breaking strength, dry weight and hydroxyproline content of the granulation tissue (24)	Oil seeds, Crops and leaves (25)
Mastic	Pistacia lentiscus (Anacardiaceae)	Signed as a anti-inflammatory (26) Used remedy burns and wounds (27)	Stimulates the maturation of scar by the production of type I collagen (28) decreases the inflammatory reaction and myofibroblasts production (28)	Oil fruit (28)
Apricot	Prunus armeniaca (Rosaceae)	Helps the skin to retain elasticity and supple-	Histological evaluation revealed an improved	fruit oil (29)

		ness (29)	collagen deposition and an increased fibroblast and vascular densities (29)	
Cocos	Cocos nucifera (Rosaceae)	Improving the methods of tissue repair and wound healing enhance the quality of trauma and burn (30) Anti-inflammatory activity could play a part in the burn wound healing (30)	A histopathological study showed an increase in fibroblast proliferation and neovascularization in treated wounds (31)	Seed oil (32)
Chamomile	Matricaria recutita (Asteraceae)	Used for the treatment of minor wounds (33)	Increased rate of wound contraction, together with the increased wound-breaking strength, hydroxyproline content (34)	Flower extracts(34)
Turmeric	Curcuma longa (Zingiberaceae)	Used to cure skin diseases	Excellent to increase the formation of collagen (35)	Rhizome (36)

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