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Application of Essential Oils for Wound Healing and Drug Delivery Strategies: A Review

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ABSTRACT

The traditional Indian medicine – Ayurveda, describes various herbs, fats, oils and minerals for various diseases, including anti-aging and wound healing properties. Wounds are the result of injuries to the skin and disrupt the soft tissue. Wound healing can be referred as a complex dynamic process that results in the restoration of skin anatomic continuity and function. The exudative, proliferative and extracellular matrix remodeling stages are sequential events that happen through the integration of dynamic processes involving soluble mediators, living blood cells, parenchymal cells and tissues. Essential oils are volatile, lipid-soluble secondary metabolites of aromatic plants that can be synthesized from all whole plant or plant parts and are characterized by their odor, synthesis, physical and chemical properties. Basically, all essential oils have anti-inflammatory and anti-microbial activity. Wound healing of essential oils promotes the healing of wounds, tissue remodeling, cell regeneration and collagen formation, and promotion of the migration of fibroblast to the site of a wound. Essential oils to enhance the effectiveness of the wound healing process have been focused on boosting devices, preventing infections, promoting tissue regeneration and minimizing pain, discomfort and scar formation.

INTRODUCTION

Aromatherapy is a part of TCIM (Traditional, Complementary and Integrative Medicines) and is characterized by promoting healing and well-being through the use of essential oils, which are highly concentrated and volatile substances extracted from plants. Essential oils are produced by more than 17,500 aromatic plants and are stored in several structures of plants, such as flowers, buds, leaves, bark, roots, rhizomes, fruits and seeds.[1] Currently the possibility of using phytochemicals in the form of plant extracts and isolated phytoconstituents for the treatment of open skin wounds is gaining therapeutic importance. In particular, the essential oils extracted from different parts of plants contain many active compounds with anti-oxidant, anti-inflammatory and antimicrobial properties.[2] Essential oils are natural oils which are typically obtained by a different type of distillation and have the characteristics odor of the plant from which there are extracted. Indeed, many natural essentials as well as animal oils have been reported to improve healing in various preclinical models of animal wound healing and have shown strong anti-microbial effects against the most common pathogenic bacteria present in clinical acute and chronic wound infection.[3] Essential oils to enhance the effectiveness of the wound healing process have been focused on boosting devices, preventing infections, promoting tissue regeneration and minimizing pain, discomfort and scar formation.[4] This review aims to highlight the role of essential oils in skin wound healing with the intention of promoting novel and extensive studies to identify improved treatments.

Essential oils

Essential oils are composed of lipophilic and highly volatile-natured secondary plant metabolites, reaching a mass below a molecular weight of 300, that can be physically separated from plant parts or membranous tissues.[5] The respective main compounds are mainly derived from three biosynthetic pathways only, the mevalonate pathway leading to sesquiterpenes, the methyl erythritol pathway leading to mono and diterpenes and the shikimic acid pathway is an route to phenylpropenes.[6] Essential oils have been used as perfumes, flavors, and food and beverages or to heal both body and mind for thousands of years from the ancient systems of medicine.[7] Essential oils are enhancing the results in skin wound healing, by influencing the mechanism involved in the inflammatory, proliferative and remodeling phases.[8]

Extraction of essential oils

Essential oils present within plant cells are liberated through heat and pressure from various parts of plant matter, for an example, the leaves, buds, rhizomes, stem, flowers, fruit, grass, roots, wood bark, gums and blossom. The extraction of essential oils from plant materials can be achieved by various methods such as hydro-distillation, steam and water distillation. Other methods include solvent extraction, aqueous infusion, cold or hot pressing, enfleurage, supercritical fluid extraction and photonics process.[7]

Wounds

A wound may be defined as any disruption of the integrity of skin cells, mucous membranes, cartilage or collagen tissues. A distinction is made between simple wounds which are injury to the skin and complicated wounds that are deeper and also involve injury to muscles, nerves and blood vessels. Wounds can be caused by mechanical, thermal, pathogens, chemical and radiogenic trauma[9].

Wound healing

Wound healing is a complex process involving interactions between diverse immunological and biological system of human body. The various process involved in the acute tissue repair, which are triggered by tissue damage caused by different factors, may be united into a sequence of 4 time dependent phases: a) coagulation and haemostasis, beginning immediately after injury; b) inflammation, which begins shortly thereafter; c) proliferation, which starts within a days of the injury and encompasses the major healing processes; and iv) wound remodeling, in which scar tissue formation takes place and which may last up to a year or more[10].

Essential oils (EO) used for wound healing

***Chenopodium botrys* L. (Amaranthaceae)**

Essential oils were obtained from hydrodistillation using a modified Clevenger apparatus performed over 4 hours period. The results of GC-MS indicated that the most frequently found chemical constituents in *Chenopodium botrys* (CB) essential oil was α- eudesmol, epi-α-muurolol and cubenol. EO of CB was evaluated by cutaneous wound healing marker in Sprague-Dawley male rats. Rats are divided in four groups are untreated (control), treated with 1ml basal cream (placebo), treated with 1ml tetracycline (3%) and treated with 1ml CB

essential oil (6%) for 10 days. CB EO has healing tissue, re-epithelization, epithelial formation, decreased wound surface area, and a number of lymphocytes and neutrophils, increased number of blood vessels, and ratio of collagen and collagen cell, in comparison with control and basal cream groups.[11]

***Bursera morelensis* (Burseraceae)**

The essential oil was extracted by hydrodistillation from *Bursera morelensis* (BM) and chemical analysis was reported by Gas chromatography and Mass spectroscopy (GC-MS). The results showed that 18 terpenoid-type compounds were identified in the BM essential oil. The results of this study demonstrated that the EO was a pro-wound healing agent because it has good healing effectiveness with scars and good tensile strength with the accelerated repair. The probable mechanism of action of BM EO during the wound healing process, is the promotion of the migration of fibroblasts to the site of wound, making the active in the production of collagen and promoting the remodeling of their collagen tissues.[12]

***Croton adamantinus* (Euphorbiaceae)**

The Plant materials were collected and fresh leaves were immediately extracted by hydro distillation for 2 hours by utilization Clevenger type apparatus. Twenty constituents were identified in *Croton adamantinus* (CA) EO by GC-MS, 1H-NMR and 13C-NMR the major constituents being methyl-eugenol (14.81 %) and 1, 8-cineol (3.74 %). The wound healing was verified by using excisional wound animal models. Topical treatment of EO (1%) increased wound contraction from the third day of the treatment (compared with Nitrofurazone 0.2 %). While systemic treatment (50 mg/Kg/day) enhanced granulation tissue formation and reduced the water content. CA EO also showed antimicrobial activity against *Staphylococcus aureus* in disk diffusion method.[13]

***Teucrium polium* L. (Lamiaceae)**

Teucrium poliumis (TP) is widely used in Algerian folk medicine as to treat different types of wounds. The phytochemical composition was obtained by a combination of Gas Chromatography with Flame Ionization Detector (GC-FID) and GC-MS analyses. The main components were identified in this order: β-pinene, germacrene, α-pinene, myrcene, limonene, bicyclo germacrene, trans-β-guide, spathulenol and β-bourbonene. *In-vitro* anti-oxidant activity was done by DPPH method to show moderate antioxidant activity. *In-vivo* experiments showed that 10 % TP EO accelerated wound healing in comparison with

controls. This study provides a scientific evidence for the use of *T.polium* essential oil in the treatment of wounds.[14]

***Eucalyptus globulus* Labill. (Myrtaceae)**

Essential oil from *Eucalyptus globules* (EG) extracted from hydrodistillation, was characterized by GC-MS. Analysis of the essential oil showed that the main constituents are eucalyptol, alpha-phellandrene, beta-phellandrene, cymene, 4-terpineol, alpha-pinene, alpha-thujone, and alpha-terpinene. Linear incision, circular& excision wound models on rats were used for the evaluation of wound healing activity of the oil and acetic acid-induced increases in capillary permeability model in mice were used for the evaluation of the anti-inflammatory activity. The EG essential oil contains 53.67 % eucalyptol. It exhibited significant wound healing activity in the animal models and the essential oil revealed a significant inhibitory effect on inflammation. These findings add significant information to the wound healing and anti-inflammatory activities of essential oil *E.globulus*[15].

***Mentha piperita* L. (Lamiaceae)**

Twenty-three compounds were identified in the peppermint essential oil (PEO) with the main significant chemical compound as menthol (53.29 %). Also, PEO showed a high content of oxygenated monoterpene compounds. Topical application of PEO at doses of 200 and 20 µL/kg specifically reduced the acute ear oedema by 38.09 % and 36.50 %, respectively. The PEO reduced the nociceptive effect at all doses tested in the acetic acid-induced nociception test ($p<0.05$). *In-vivo* wound healing activity of cream prepared from PEO (0.5 % w/w) was assessed by circular excision animal wound model showed a significant decrease of unhealed wound area rate between the sixth and ninth days of treatment when compared with the vehicle and Madecassol 0.1 % cream. The PEO is a good promising candidate for use in skin care products with anti-inflammatory and wound healing properties[16].

***Mentha puligium* L. (Lamiaceae)**

Mentha puligium (MP) Essential oil was extracted by hydrodistillation procedure and its major compounds were pulegone (72.18 %), piperitenone (24.04 %), chrysanthenol (0.90%), menth-2-en-ol (0.3 %), α-pinene (0.6 %) and β-pinene (0.5 %). Gels prepared from *Mentha pulegium* EO (MPO) loaded into nanostructured lipid carriers (MPO-NLCs) might hasten the infected wound healing process. MPO-NLCs showed the most antibacterial activity against gram positive bacteria of *Staphylococcus epidermidis*, *Staphylococcus aureus* and *Listeria*

monocytogenes and also gram-negative bacteria of *Escherichia coli* and *Pseudomonas aeruginosa* (P<0.0). Topical administration of MPO-NLCs reduced the inflammatory phase and increased proliferative phase, increased the expressions of IL-10, TGF-β and b-FGF and also decreased the levels of NF-κB compared to the control group. The MPO-NLCs promoted and enhanced the healing of infected wounds by increasing antibacterial properties, decreasing the inflammatory phase and accelerating proliferation phase of wound healing process.[17]

***Origanum vulgare* L. (Lamiaceae)**

In this study, evaluated the anti-inflammatory, anti-oxidant activity as well as wound healing capacity of a well characterized *Origanum vulgare* essential oil (OEO) on human keratinocytes NCTC-2544 treated with interferon-gamma (IFN-γ), histamine (H) or subjected to a scratch test compared to untreated control, OEO revealed enhancing cell motility. The DNA damage was shown by the formation of 8-oxo-7,8-dihydro-2'-deoxyguanosine (8-OHdG) and activation of proliferating cell nuclear nitrogen (PCNA). The abnormal modification of extracellular matrix components was examined by determining matrix metalloproteinase (MMP)-1 and -12. OEO was proved useful to treat inflammation and enhancing cell motility during wound healing.[18]

***Eugenia dysenterica* DC (Myrtaceae)**

The *Eugenia dysenterica* leaf essential oil was composed mainly of sesquiterpenes (43.39 %), in which α-humulene (19.3 %) and caryophyllene (24.36 %) were identified as the major compounds analyzed by gas chromatography. Skin cytotoxicity assay was evaluated by using a fibroblast cell line (L929) by MTT assay. The chick chorioallantoic membrane (CAM) assay was used to evaluate the angiogenic activity and irritating potential of *E.dysenterica* essential oil. Essential oil of *E. dysenterica* DC leaves (OED) to stimulate *in-vitro* skin cell migration. OED induced skin cell migration on 542.2 µg/ml concentration. The inhibition of nitric oxide by OED and α-humulene has an anti-inflammatory effect. The CAM assay showed that treatment with OED≤292 µg/mL did not cause skin injury and it can promote angiogenesis *in-vivo* studies. The results indicate the feasibility of the essential oil of *Eugenia dysenterica* DC leaves to develop dermatological products capable of helping the body repair damaged tissue and heals skin wound.[19]

***Citrus reticulata* L. (Rutaceae)**

Citrus essential oil (CEO) was isolated by hydro-distillation of freshly collected peels of *C. reticulata*. Antioxidant activities were assessed by total phenolic content, DPPH scavenging activity and reducing power assay. Total flavonoid and phenolic contents were found to be 14.63±0.95 mg CE/g and 17.03±3.24 mg GAE/g respectively, while DPPH scavenging activity was found to be 73.32%. GC-MS analysis showed the presence of various components with the highest proportion of D-limonene (89.31%). CEO be revealed better antibacterial activity against *E.coli*. *In-vivo* studies showed the CEO significant reduction in wound diameter and enhance wound healing.[20]

***Rosmarinus officinalis* L. (Lamiaceae)**

Evaluated the efficiency of topical rosemary essential oil (REO) loaded into the nanostructured lipid carriers (NLCs) on *in-vitro* anti-bacterial activity and *in-vivo* infected wound healing process by using an animal model. Two circular full-thickness wounds were made on the back of each mouse and each wound was infected with a solution containing 10^7 CFU *Staphylococcus aureus* and *Pseudomonas aeruginosa*. Animals were divided into four groups including control, Mupirocin® and two treated groups with a gel containing REO and REO-NLCs. REO-NLCs exhibited antibacterial activity against *Staphylococcus epidermidis*, *Staphylococcus aureus*, *Listeria monocytogenes*, *Escherichia coli* and *Pseudomonas aeruginosa*. REO-NLCs would reduce the rate of tissue bacterial colonization and wound diameter, while they increased the vascularization, fibroblast infiltration, re-epithelialization, and collagen production, IL-3, IL-0, vascular endothelial growth factor (VEGF) and stromal-derived factor-1α (SDF-α) serum levels. REO-NLCs have antibacterial properties and enhanced infected wound healing confirming their potential clinical uses for the treatment of infected wounds.[21]

***Eugenia caryophyllata* L. (Myrtaceae)**

Optimized clove oil (CO) containing nanoemulsion presented significant wound healing effect in rats as compared to pure CO. Nano emulsion of clove oil was prepared by spontaneous emulsification method. Nanoemulsion as well as presented significant enhancement in leucine content (0.61 mg/g) as compared to pure CO (0.50 mg/g) and negative control (0.31 mg/g) and standard. Histopathological evaluation showed absence of

inflammatory cells and represented the capacity of nanoemulsion for oral delivery of CO for enhancing its wound healing effects.[22]

Developed and evaluated the natural Clove essential oil containing nanofiber (NF) mat with enhanced antibacterial activity, regenerative, non-cytotoxic and wound healing potential. Clove essential oil (CEO) encapsulated in chitosan (natural polymer) and poly-ethylene oxide (PEO) polymers to form NFs and their morphology was examined by using scanning electron microscopy (SEM) that confirmed the finest NFs prepared with a diameter of 54±35 nm. Prepared NF mat showed good antibacterial activity against *Staphylococcus aureus*, *Escherichia coli* and non-cytotoxic behaviour against human fibroblast cell lines and showed good wound healing potential[23].

***Lavandula stoechas* (Lamiaceae)**

This study was designed to evaluate the chemical composition of *Lavandula stoechas* essential oils (EOLS) also the *in-vivo* wound healing activity. Linalool was identified as the major chemical compound (24.87 %), followed by linalyl acetate (19.10 %) by the use of GC-MS analysis. EOLS expressed a high content of oxygenated compounds (63.54 %). The EOLS formulation cream (0.5 %v/w) showed the highest effect on animal wound models when compared to reference Madecassol® (Asiaticoside). On days 4, 11 and 16 wound contractions were 26.4 %, 78 % and 96.3 % for EOLS treated animals group and 8.5 %, 64 % and 86 % for the vehicle-treated animals group with the excisional experimental model. Animals treated with EOLS cream revealed a significant decrease in the epithelization period, wound area and scar thickness whereas the rate of wound contraction significantly increased[24].

***Commiphora gileadensis* L. (Burseraceae)**

Chloroform extract of fresh stem *Commiphora gileadensis* with reported antimicrobial activity was compared with the EO sample of the fresh stems for wound healing potential. Wound healing assay was assessed by 11 mm diameter full thickness of excision wound was made on the back of rats. The negative group I control was treated wa ith cream base. Group II was treated with 2% Fucidin cream, which served as a reference standard groupsroup III & IV were treated with 1% & 3% EO-containing cream respectively. Antimicrobial testing using Gram positive & Gram negative bacteria in addition to pathogenic fungus indicated that the EOs of the fresh & dry stems were equally active against microbial pathogens[25].

***Thymus vulgaris* (Lamiaceae)**

The present study evaluated encapsulated thyme essential oil in sodium caseinate (NaCAS) nano micelles and formulated a gelatin nanocomposite hydrogel. This was investigated as a drug delivery platform for *in-vitro* antibacterial activity and *in-vivo* wound healing potential. *Thymus vulgaris* essential oil (TEO) showed a sustained release pattern and exhibited a significantly higher antibacterial effect than free TEO. TEO-loaded composite hydrogel significantly promoted wound contraction, reduced interleukin-6, and increased transforming growth factor-β1 and vascular endothelial growth factor levels, versus control or blank hydrogel group[26].

***Ocimum gratissimum* L. (Lamiaceae)**

Ocimum gratissimum have mainly essential oil and non-phlorotannins (non-condensed tannins). The main constituents of *ocimum* oil are thymol (48.1 %) and p-cymene (12.5%) with traced amount of 40 other constituents. Evaluated the wound healing effects of *ocimum* oil and two antibacterial preparation such as Cicatrin (GlaxoWellcome) and Cetavlex (AstraZeneca), on the healing of full thickness excisional and incisional wounds, created under anesthesia on the back of test and control groups of adult albino rabbits. *Ocimum* oil was marked enhancement in the inflammatory and proliferative phases of wounds than the control and reference products. Cetavlex showed on sign of healing for eight days but responded to ocimum oil after a three day wash out period. The essential oil of *Ocimum gratissimum* can promote wound healing and showed local anaesthetic activity[27].

***Trachyspermum ammi* (Apiaceae)**

Trachyspermum ammi (Ajwain) essential oil (EO), as a potent and natural antimicrobial agent against microorganisms was incorporated into the core of nanofiber mats using coaxial electrospinning method. The *in-vitro* and *ex-vivo* release of Ajwain EO from the fabricated nanofiber mat corroborated a prolonged release profile. Furthermore, *in-vivo* anti-bacterial activity, wound closure and histomorphological examinations revealed the higher efficacy of the core shell/ EO mat in the treatment of *staphylococcus aureus* infected full thickness animal wounds compared to standard control treatment with gauze. These results exhibits the core-shell/ EO mats potential as a newly developed wound dressing for bacteria infected full thickness skin injuries[28].

***Cymbopogon nardus* (Poaceae)**

In traditional and ancient system of medicine like Ayurveda, essential oil extracted from leaves of *Cymbopogon nardus* L., (Poaceae) has been using for the treatment of microbial infections, inflammation and pain. EO of *C.nardus* was obtained through hydro-distillation and subjected to GC-MS analysis for chemical characterization. A total of 95 compounds were identified through GC-MS analysis, with major compounds are citral, 2,6-octadienal-, 3,7-dimethyl-, geranyl acetate, citronellal, geraniol and citronellol. *In-vitro* test results demonstrated strong anti-candida activity of essential oil of *Cymbopogon nardus* (EO-CN) with a Minimum inhibitory concentration (MIC) value of 25µg/ml against *Candida albicans*, 50µg/ml against *candida glebrata* and *Candida tropicalis*. EO-CN treatment resulted in significant reduction of candida infection load on diabetic wounds; simultaneously reduces the inflammation which leads to acceleration of the wound healing process[29].

***Clematis flammula* L. (Ranunculaceae)**

The essential oil was extracted by hydrodistillation and analyzed by GC-MS method. Anemonin was isolated and then incorporated as active in a cream for which the cytotoxicity was evaluated by methyl thiazolyl tetrazolium (MTT) based colorimetric assay. The GC-MS analysis revealed that the major compound was protoanemonin (86.74 %) which spontaneously dimerised in part to form the anemonin. The wound healing activity of anemonin cream exhibited a non-toxic potential of anemonin at a concentration of 25 µg/ml with a higher cell migration efficiency that leaches more than 80 % after 48 hours of treatment. Anti-oxidant activity was assessed by the malondialdehyde (MDA) rates and antioxidant enzymes (glutathione peroxidase (GPx) and catalase) determination. The histological examination showed complete wound closure. The results provided strong support for the effective wound healing activity of anemonin cream, making it a excellent promising candidate as a therapeutic agent in tissue repairing process and wound healing[30].

***Schinus molle* L. (Anacardiaceae)**

Schinus molle L., is an aromatic tree originated from South America but now it is cultivated in Mediterranean area. This study was evaluated the wound healing activity of fruit essential oil containing ointment 2, 10 and 15 % (w/w) essential oil and nanocapsules (2 %) was formulated and their wound healing activity was evaluated. Pharmaceutical forms was topically applied on the incision wound model that was created on the lumbar region of rats

and the wound length was measured daily until complete healing of skin wounds. Treatment the wound with nanocapsules 2 % or essential oils 10 % showed the best wound healing potential compared to negative control[31].

***Nigella sativa* L., (Ranunculaceae)**

The *Nigella sativa* essential oil (NSE) was isolated by hydrodistillation (seed materials in boiling water) using Clevenger's apparatus for 4 hours, Streptozotocin was given at a single dose of 60 mg/kg/i.p to animal models. The animals showing diabetes and blood glucose level >250 mg/dl will be choosed for wound groups MDA and glutathione (GSH) levels, GPx, superoxide dismutase (SOD) and catalase (CAT) activities were measured in plasma & wound tissues of the diabetic and treatment groups. GSH, GPx, SOD and CAT levels were increased in the NSE treatment compared to the diabetes group while NDA levels were decreased. NSE can play an important role of reducing lipid peroxidation, oxidative stress and associated complication and plays an excellent role in the treatment of diabetic wound[32].

***Cinnamon verum* J. (Lauraceae)**

Cinnamon essential oil is known to have antioxidant and antibacterial properties, which may accelerate skin wound healing. Cinnamic aldehyde (54 %), α-copaene (12.3 %), styrene, ethylene (7%) were the major constituents analyzed by GC-MS. A circular excisional infected wound model of 5 mm surface area was surgically created and inoculated with 10^7 CFU of each of two bacterial strains of *Staphylococcus aureus*, *Pseudomonas aeruginosa*. Animals were treated with yellow-paraffin (control) and ointments containing 2 % & 4 % *C.verum* remarkably shortened the inflammatory phase, increased fibroblast distribution, collagen deposition and accelerated cellular proliferation, re-epithelialization and keratin synthesis. Topical administration of *C.verum* essential oil increased antioxidant power & reduced MDA content in comparisons to control animals. The mRNA levels of insulin or insulin like growth factor (IGF-1), fibroblast growth factor (FGF-2), and vascular endothelial growth factor (VEGF) were significantly higher in *C.verum* treated groups[33].

***Artemisia absinthium* L. (Asteraceae)**

The essential oil was extracted by hydro distillation using a Clevenger type apparatus according to European Pharmacopoeia. The wound healing activity was evaluated by the excisional wound model of rats. The wounds were treated daily with an ointment prepared with two different concentrations (5 % and 10 %) of *Artemisia absinthium* essential oil. The

important component of *A.absinthium* essential oil was camphor (48 %) followed by chamazulene (10 %) which was responsible for the dark blue color of the essential oil. *A.absinthium* essential oil exhibited moderate antioxidant activity compared with BHT and Trolox. The 10% ointment enhances skin wound re-epithelialization and speeds up the wound healing process[34].

***Matricaria chamomilla* L. (Asteraceae)**

Chamomile oil (CM) is one of the most commonly used herbal oil on account of its anti-inflammatory, anti-bacterial, antioxidant and anti-irritant activities, in addition to its good occlusive effect via acting as a skin protective barrier. Furthermore, chamomile oil has crucial effect in enhancing the re-epithelization rate and stimulating collagen deposition. CM oil is poor skin membrane permeability and the degradation of chamomile oil after exposure to environmental oxygen to overcome this oil is encapsulated into lipid nanocarriers can protect it and enhance its therapeutic effect in wound healing. This study was to ameliorate CM healing effect by encapsulating it into solid lipid nanoparticles (SLN). The *in-vivo* involved 40 rats divided into 5 groups, Group I: was normal control, Group II: indicated wounded rats without treatment and Group III to V: were wounded rats treated with plain SLN, CM cream (Camisan) and CM-SLN, respectively. Topical administration of CM-SLN showed enhancement in restoring the normal integument architecture, wound contraction, transforming growth factor-β1 and collagen deposition, in addition to the reduction in the Interleukin-1β and metalloproteinases-9/tissue inhibitor metalloproteinase-1 ratio, as compared to other groups. This result showed that the encapsulation of Chamomile oil in SLN exhibited a significant wound repairing mechanism[35].

CONCLUSION

Currently, the topical treatment of bedsores, pressure ulcers, internal and external wounds are based on dressing and treatment medication contains antibiotics, and chemically synthesized antimicrobial active substances. This study explains a potential therapeutic benefit of application of essential oil in wound healing through mechanisms such as faster wound contraction, enhanced activity of proteins involved in the tissues remodeling process and increased expression of collagen and reduced pain. As regards their efficacy, a huge of preclinical studies has documented the biological activities of essential oils also elucidating their mechanism of action and pharmacological targets. In particular antimicrobial, wound healing, antioxidant, anti-inflammatory and anticancer activity have been demonstrated in a

number of cell line studies and animal model. However, the paucity of in human studies, compared with the *in-vitro*/*iv-vivo* ones limits the potential of essential oils as effective and safe phytotherapeutic agents through the efficacy of essential oils in human health care is well documented. Therefore, better designed clinical trials are needed in order to reach a high level of scientific evidence and as certain the real efficacy and safety of plant products which have accompanied human since ancient times.

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