

The use of essential oils on wound healing

El uso de aceites esenciales en la curación de heridas

O uso dos óleos essenciais na cicatrização de feridas

ABSTRACT

In recent years, the search for active ingredients that help in the healing process have boosted the use of herbal medicines. Essential oils have different properties, including anti-inflammatory, bactericidal, antiseptic, moisturizing and healing effects. The objective was to identify the use of essential oils in wound healing. It is an integrative literature review indexed in the LILACS, Medline, PEDro, PubMed and SciELO databases. Data collection took place between May and June 2019. The sample consisted of 11 articles published between the years 2012 and 2017, all of which were carried out in rodents. In summary, this review achieved the objective of verifying essential oils as an effective and low-cost therapeutic alternative for the treatment of skin lesions, however, it is necessary to have a scientific basis to expand the practice in a safe and effective way.

DESCRIPTORS: Oils Volatile; Wound Healing; Wounds.

RESUMEN

En los últimos años, la búsqueda de ingredientes activos que ayuden en el proceso de curación han impulsado el uso de hierbas medicinales. Los aceites esenciales tienen diferentes propiedades, que incluyen efectos antiinflamatorios, bactericidas, antisépticos, hidratantes y curativos. El objetivo fue identificar el uso de aceites esenciales en la curación de heridas. Es una revisión de literatura integradora indexada en las bases de datos LILACS, Medline, PEDro, PubMed y SciELO. La recolección de datos tuvo lugar entre mayo y junio de 2019. La muestra consistió en 11 artículos publicados entre los años 2012 y 2017, todos los cuales se llevaron a cabo en roedores. En resumen, esta revisión ha logrado el objetivo de verificar los aceites esenciales como una alternativa terapéutica efectiva y de bajo costo para el tratamiento de lesiones cutáneas, sin embargo, es necesario tener una base científica para expandir la práctica de manera segura y efectiva.

DESCRIPTORES: Aceites Esenciales; Curación; Heridas.

RESUMO

Nos últimos anos a busca por princípios ativos que ajudem no processo de cicatrização impulsionam o uso de fitoterápicos. Os óleos essenciais apresentam diferentes propriedades, entre elas, efeitos antiinflamatório, bactericida, antisséptico, hidratante e cicatrizante. O objetivo foi identificar o uso de óleos essenciais na cicatrização de feridas. Trata-se de uma revisão integrativa de literatura indexadas nas bases de dados LILACS, Medline, PEDro, PubMed e SciELO. A coleta de dados ocorreu entre maio e junho de 2019. A amostra constituiu-se de 11 artigos publicados entre os anos 2012 e 2017, sendo todos realizados em roedores. Em suma, esta revisão atingiu o objetivo de constatar os óleos essenciais como alternativa terapêutica efetiva e de baixo custo para o tratamento de lesões cutâneas, no entanto, torna-se necessário embasamento científico para ampliação da prática de forma segura e eficaz.

DESCRITORES: Óleos Essenciais; Cicatrização; Feridas.

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INTRODUCTION

The skin is one of the largest organs in the human body, comprising 15% of body weight. It acts in the regulation of temperature, in the perception of sensory stimuli, as well as presenting itself as a barrier against aggressive internal and external agents, making it vulnerable to injuries⁽¹⁾.

The wound is characterized by the discontinuity of the tissue, this injury can reach beyond the skin, muscles, tendons and bones. They can be classified into acute and chronic^(2,3).

The healing mechanism is complex, as it depends on a series of events that results in tissue regeneration. This starts with an inflammatory response, with the recruitment of inflammatory mediators, followed by the proliferative phase where the process of neovascularization and reepithelization takes place and finally the tissue remodeling, in which the scar tissue matures^(4,5).

In recent years, the search for active ingredients that help in the healing process have boosted the use of herbal medicines. Essential oils (OE) have different properties, including anti-inflammatory, bactericidal, antiseptic, moisturizing and healing effects^(6,7).

In Brazil, wounds are a serious public health problem. They affect the population in general, regardless of age or sex, resulting in many people with injuries, demanding high financial costs for both health institutions and the individual affected.^(8,9)

The relevance of this study is in recognizing the positive effects of using essential oils that can contribute to wound healing therapy.

In this context, the present study aimed to identify the use of essential oils in the treatment of wounds. Knowledge about the biological effects of essential oils will contribute to guide

and highlight the potential topical use of essential oils as a therapeutic alternative in the wound healing process. So, one wonders, what are the effects of using essential oils on wounds?

METHODOLOGY

It was an integrative review study in articles from the electronic databases LILACS, Medline, PEDro, PubMed and SciELO during the months of May and June 2019. The search was performed according to the Health Sciences Descriptors (DeCS), using the following terms: "essential oils", "healing", "wounds" and "injuries" / "oils volatile", "wound healing" and "wounds" and "injuries" with Boolean operator "AND".

The following inclusion criteria were used: studies carried out on rodents, published in full between the years 2009 and 2019, in Portuguese and English, which addressed the topical application of essential oils to wounds. This study excluded: literature review articles, Course Conclusion Papers, monographs, theses, incomplete texts and duplicate papers.

During the research, the crossing was performed using the descriptors in each database. All articles were submitted to the evaluation stages: the first by reading the titles and abstracts and studies that did not include the inclusion criteria were excluded; in the second stage, the studies were analyzed and displayed in tables, ordered chronologically and then discussed.

RESULTS

This review consisted of analyzing 11 articles in full that met the established inclusion criteria. The selection of articles of interest took place in three phases: 1) research in the databases, 2) reading of the titles and abstracts of the selected publications; and 3) reading of the publications selected in the second phase.

In phase 1, the search was carried out in the LILACS, MedLine, PEDro, PubMed and SciELO databases, the articles that referred to the researched subject and/or had the descriptors in the title were selected. In this phase, of 410 articles selected by the databases, 376 articles were discarded.

Figure 1. Flowchart of the literature review. Fortaleza, CE, Brazil, 2019.

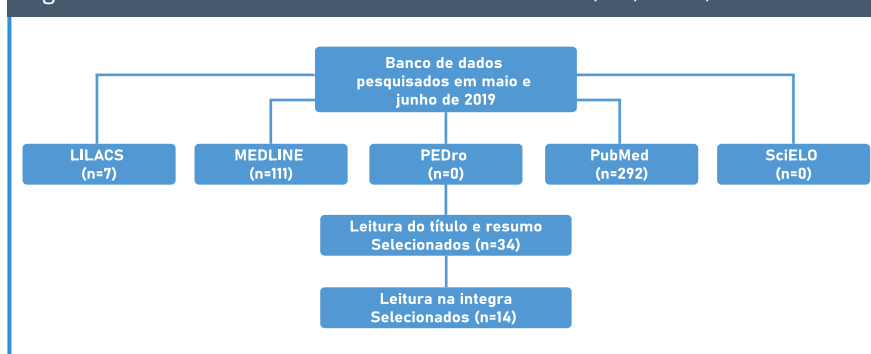


Chart 1. Description of articles included in the RIL, according to author, title, objective and result. Fortaleza, CE, Brazil, 2019.

AUTOR	TÍTULO	OBJETIVO	RESULTADOS
Estevão et al ⁽¹⁰⁾	Concentração de mastócitos e contração da pele em ratos tratado com óleo essencial de pimenta brasileira (<i>Schinus terebinthifolius</i> Raddi).	Avaliar a contração da ferida e a concentração de mastócitos em feridas cutâneas tratadas com pomada à base de óleo essencial de pimenta brasileira a 5% em ratos.	Avaliando-se a contração da ferida com o óleo lubrificante a 5%, observou-se que a partir do 7º dia de pós-operatório, as feridas estavam em processo de contração. Analisando as médias dos resultados percentuais, as feridas do grupo tratado contraíram mais do que as feridas do grupo controle no 14º dia e no 21º dia as feridas já estavam totalmente fechadas. O grupo controle apresentou alguns mastócitos dispersos próximos ao tecido de granulação ou ao redor dos capilares recém-formados, já o grupo tratado apresentou múltiplos agregados de mastócitos no tecido fibrovascular e apresentou maior quantidade no 7º dia de pós-operatório.
Bezerra; Barros; Coelho ⁽¹¹⁾	A ação do óleo de pequi (<i>Caryocar brasiliense</i>) no processo cicatricial de lesões cutâneas em ratos.	Analisar o efeito do óleo de pequi no processo cicatricial de lesões cutâneas em ratos.	No grupo tratado com o óleo essencial foi observado maior percentual de regressão das lesões. A partir da análise histológica foi possível detectar que nesse grupo houve menor número de células inflamatórias e maior número de fibroblastos em relação ao grupo não tratado nos diferentes tempos experimentais.
Lavasanijou et al ⁽¹²⁾	Efeitos da cicatrização de feridas em extratos de <i>Quercus Brantii</i> e <i>Pelargonium Graveolens</i> em ratos machos Wistar	Investigar os efeitos dos extratos de <i>Quercus Brantii</i> e <i>Pelargonium Graveolens</i> no processo de cicatrização em ratos.	De acordo com as avaliações histopatológicas a velocidade de contração da ferida e o processo de cicatrização da ferida foram significativamente mais rápidos no grupo tratado com pomada de óleo Q. brantii do que nos demais grupos, até mesmo o grupo tratado com pomada de nitrofurazona
Kittana et al ⁽¹³⁾	O extrato aquoso tópico de <i>Ephedra alata</i> pode melhorar a cicatrização de feridas em modelo animal.	Demonstrar se o extrato de <i>Ephedra alata</i> pode melhorar o processo de cicatrização de úlceras causadas por feridas profundas e queimaduras de espessura total.	Em comparação com pomada placebo, pomada de <i>E. alata</i> melhorou significativamente a cicatrização das úlceras da ferida, ao passo que não mostrou nenhuma vantagem sobre a qualidade da cicatrização de úlceras de queimadura.
Tumen et al ⁽¹⁴⁾	Efeitos colaterais da cicatrização de feridas e composição fitoquímica de óleos essenciais de cerne de <i>Juniperus virginiana</i> L., <i>Juniperus occidentalis</i> e <i>Juniperus ashei</i> J. Buchholz.	Avaliar o potencial cicatrizante e antiinflamatório de subextratos de óleos essenciais obtidos do <i>Juniperus virginiana</i> L., <i>Juniperus occidentalis</i> e <i>Juniperus ashei</i> J. Buchholz. em modelos animais.	O óleo essencial de <i>J. occidentalis</i> apresentou a maior atividade nos modelos de atividade biológica in vivo. Além disso, o óleo de <i>J. virginiana</i> mostrou-se altamente eficaz no método de atividade antiinflamatória. Os dados experimentais demonstraram que o óleo essencial de <i>J. occidentalis</i> exibia atividades de cura e antiinflamatória significativas.
Mori et al ⁽¹⁵⁾	Potencial de cicatrização de feridas do óleo de lavanda por aceleração da granulação e contração da ferida por indução de TGF- β em modelo de rato.	Investigou-se o efeito do óleo de lavanda em várias etapas da cicatrização de feridas e seu mecanismo molecular, com foco no fator de crescimento transformador- (TGF-).	A aplicação tópica de óleo de lavanda promove o fechamento da ferida, com uma redução na área da ferida, que o fechamento da ferida progrediu mais rapidamente com a aplicação tópica de óleo de lavanda. A área da ferida de ratos tratados com óleo de lavanda foi significativamente menor em comparação com ratos não tratados e ratos de controle aos 4, 6, 8 e 10 dias após o ferimento. Não houve diferença significativa no tamanho da ferida em 12 e 14 dias. Esses dados sugerem o potencial de cicatrização de feridas do óleo de lavanda na fase inicial.

Riella et al ⁽¹⁶⁾	Atividade antiinflamatória e cicatrizante do timol, um mono-terpeno de óleo essencial de <i>Lippia gracilis</i> , em roedores.	Avaliar as atividades anti-inflamatórias e cicatrizantes de timol em roedores.	O timol reduziu significativamente o edema, diminuiu o influxo de leucócitos para a área lesada, de acordo com a avaliação da atividade da MPO, contagem total de células e análise histológica. As feridas vestidas com os filmes COLTHY apresentaram taxas significativamente maiores de retração da ferida e melhoraram a reação de granulação, além de proporcionar melhor densidade e arranjo de colagenização durante a cicatrização da ferida. O timol é um composto promissor a ser utilizado no tratamento de processos inflamatórios, bem como na cicatrização de feridas. As ações farmacológicas de <i>Lippia gracilis</i> nas práticas de medicina popular podem estar relacionadas, pelo menos em parte, à presença de timol no óleo essencial.
Gebrehiwot et al ⁽¹⁷⁾	Avaliação da propriedade de cicatrização de feridas de <i>Commiphora guidottii</i> Chiov. ex. Guid.	Investigar o óleo essencial e a resina obtida de <i>C. guidottii</i> por suas potenciais propriedades de cicatrização de feridas.	As formulações de pomada, tanto do óleo como da resina, mostraram-se não irritantes nas concentrações utilizadas e mostraram aumento significativo na taxa de contração da ferida, menor tempo de epitelização e maior resistência à ruptura da pele em comparação com o controle negativo. No geral, as atividades antibacteriana e antifúngica do óleo e resina foram comparáveis com os antibióticos padrão ciprofloxacino e griseofulvina, respectivamente.
Ximenes et al ⁽¹⁸⁾	Atividade antinociceptiva e cicatrizante de <i>Croton adamantinus</i> Müll. Arg. óleo essencial.	Pesquisar as plantas usadas na medicina popular para tratar distúrbios inflamatórios e feridas cutâneas. E verificar as alegações populares sobre a atividade antinociceptiva e cicatrizante usando as folhas de <i>Croton adamantinus</i> Muüll. Arg.	Os resultados do estudo indicam que o tratamento tópico com OE de <i>C. adamantinus</i> 1% apresenta uma atividade de cicatrização de feridas significativa. Isto foi demonstrado pelo aumento da taxa de contração da ferida entre 3 e 7 dias de tratamento e aumento da epitelização da excisão (50 mg / kg / dia, i.p.). Além disso, uma redução na água do tecido de granulação foi observada. A análise histológica mostrou melhor epitelização, população de fibroblastos e deposição de colágeno em animais tratados com OE de <i>C. adamantinus</i> quando comparados aos tratados com veículo e nitrofurazona, após 7 e 14 dias de ferimento, respectivamente. A atividade antimicrobiana do óleo essencial foi avaliada contra bactérias Gram-positivas e Gram-negativas isoladas de áreas infectadas de pacientes de Recife, Brasil. OE puro foi ativo somente contra bactérias Gram-positivas; <i>Staphylococcus aureus</i> resistente à meticilina e teste D positivo <i>S. aureus</i> . <i>Pseudomonas aeruginosa</i> e <i>Enterobacter aerogenes</i> foram resistentes à atividade da suspensão pura e a 1% de OE. A atividade antimicrobiana é esperada de óleos essenciais e provavelmente contribui para a atividade de cicatrização de feridas.
Nagappan et al ⁽¹⁹⁾	Eficácia dos alcalóides de carbazol, óleo essencial e extrato de <i>Murraya koenigii</i> no aumento da cicatrização subcutânea de feridas em ratos.	Investigar o potencial cicatrizante dos alcalóides de carbazol, óleo essencial e extrato bruto de <i>M. koenigii</i> .	As taxas de contração da ferida foram evidentes no dia 4 para o grupo tratado com extrato (19,25%) e no grupo tratado com maimbimina (12,60%), enquanto a epitelização completa foi alcançada no dia 18 para todos os grupos de tratamento. Feridas tratadas com maimbimina (88,54%) e extrato de <i>M. koenigii</i> (91,78%) apresentaram a maior taxa de deposição de colágeno com bandas de colágeno bem organizadas, formação de fibroblastos, brotamento do folículo piloso e redução de células inflamatórias em relação às feridas tratado com mahanina, mahanimbina e óleo essencial. O estudo revelou o potencial da maimbimina e do extrato bruto de <i>M. koenigii</i> na facilitação e aceleração da cicatrização de feridas.

<p>Cavalcanti et al⁽²⁰⁾</p>	<p>O óleo essencial de Croton zehntneri e trans-anethole melhora a cicatrização de feridas cutâneas.</p>	<p>Investigar se o óleo essencial de Croton zehntneri e trans-anethole podem ser agentes de cura de feridas.</p>	<p>Nos 3 primeiros dias o OE de Croton zehntneri (OE Cz) e trans-anethole (trans-AT) não produziu qualquer melhoria significativa na cicatrização de feridas, comparados aos tratamentos controle e fibrinolisisina. Após 15 dias de uso observou-se uma grande redução na área da ferida dos camundongos tratados com 20% de OE Cz que foi similar àquela produzido pelo tratamento com fibrinolisisina, indicando um potencial de cicatrização da ferida do produto à base de plantas. Além disso, o tratamento com 20% de trans-AT induziu um fechamento significativamente melhorado da ferida. A aparência das áreas cicatrizadas nos ratos submetidos aos tratamentos de 20% de OE Cz e 20% de trans-AT foi reduzida em comparação com o grupo de controle e quase idêntica à dos ratinhos tratados com fibrinolisisina no 15 ° dia pós-ferimento.</p>
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In the next step, the 34 studies selected from the titles and abstracts were read and then useful publications were selected. In the sequence, 14 full papers were read, and at the end of the reading process, 11 selected articles were obtained. Of these articles, 02 were published in the LILACS database and 09 in MedLine. 03 of which were published in 2012, 02 in 2013, 03 in 2015, 02 in 2016 and 01 in 2017.

In Figure 1 we present, according to the flowchart of the review process, the results found. Next, an overview of the articles analyzed in Table 1 will be presented.

DISCUSSION

OE are characterized as secondary metabolites extracted from plants, with complex chemical composition. They are used since ancient Egypt for medicinal and aesthetic purposes and, until today, they are great allies in the pharmaceutical, agri-food, perfumery and cosmetics industries^(21,22).

This wide acceptance consists of a wide variety of therapeutic properties, among which the following stand out: antioxidant, microbial, larvicidal, fungicidal, analgesic, anti-inflammatory, anti-tumor, insecticidal, and healing action^(15,23-25).

Among the 11 studies included in this review, all analyzed the healing effectiveness of EO and used rodents as animal models. However, 07 mentioned

only the healing action of different OE, 02 addressed the anti-inflammatory effect, 01 analyzed the anti-inflammatory and microbial power and 01 highlighted the antinociceptive and antimicrobial properties.

Healing property

Cavalcanti and collaborators⁽²⁰⁾ investigated the essential oil of Croton Zehntneri and Trans-Anethole as wound healing agents. They reported a great reduction in the wound area of mice treated with 20% essential oil of Croton Zehntneri and 20% Trans-Anethole, the reduction was almost identical to that of mice treated with fibrinolysin on the 15th day after injury. Also in 2012, Nagappan and collaborators⁽¹⁹⁾ investigated the healing potential of carbazole alkaloids (mahanine, mahanimbicine, mahanimbine), essential oil and crude Murraya Koenigii extract.

The results revealed that M. Koenigii extract significantly accelerated the rate of repair and granulation of new tissue formation by increasing more collagen, fibroblasts and hair follicles from wounds and by reducing the number of inflammatory cells. The increase in the numbers of neutrophils and lymphocytes initiating the inflammatory phase through the release of histamine, bradykinin and other factors that are essential for remodeling tissue damage.

In bedsores, it was observed as early as the fifth day after the injury, decreased inflammation, rapid contraction of the edges and debridement of the wound⁽¹⁹⁾.

Authors⁽¹⁰⁾ used a 5% ointment based on Brazilian mastic essential oil in rats. In this study, the contraction of the wound and the concentration of mast cells in skin wounds treated with topical use of petroleum jelly and lanolin, and an ointment manipulated with anhydrous lanolin (30%), solid petroleum jelly (70%) and vitamin E (0, 5%) with the addition of Brazilian essential oil. It was observed that the group of rats that used the ointment with the addition of Brazilian mastic OE, on the 7th postoperative day, were in the process of contracting the wound and, on the 21st, the wounds were already completely closed.

The control group showed some mast cells scattered near the granulation tissue or around the newly formed capillaries; the treated group, on the other hand, had multiple aggregates of mast cells in the fibrovascular tissue and had a greater amount on the 7th postoperative day. During this period, a significant increase in the number of mast cells was observed in the treated group compared to the control group. However, no significant differences were observed on days 4, 14 and 21⁽¹⁰⁾.

Another study, carried out in 2015, ensures success using Brazilian mastic

oil and pequi oil respectively. In this study, authors⁽¹¹⁾ used 1 ml of pequi oil on the skin incision in rats every day for 14 days. The treated group showed a higher percentage of lesion regression. From the histological analysis it was possible to detect that in the treated group there were fewer inflammatory cells and more fibroblasts than the control group.

Study⁽¹²⁾ used *Quercus* and *Pelargonium Graveolens* extract to investigate the healing process of rats. In that study, 40 rats were divided into 4 groups, group A was treated with 200 mg/kg/day of *Q. brantii* ointment, group B was treated with 200 mg/kg/day of *P. graveolens* ointment, group C + received 200 mg/kg/day of nitrofurazone ointment as a positive control; and group C- was treated with 200 mg/kg/day of a simple Vaseline-based ointment as a negative control. During the first 6 days, the percentage of wound contraction (PCF) in group C + was significantly higher than in group A, however, after that, the speed of wound contraction (VCF) increases in this group becoming significantly more faster than the other 3 groups. During the first 6 days after wound induction, VCF in group B was significantly higher than in groups A and C +.

From day 9, the authors found an unpredictable reduction in VCF in group B. As a result, the rats in group B achieved complete healing after day 18, while groups A and C + were completely healed on days 12 and 15, respectively. According to histopathological assessments, VCF and the wound healing process in group A were significantly faster than the other 3 groups, even the positive control group. Group A showed VCF and the wound healing process significantly faster than the other 3 groups, even the positive control group⁽¹²⁾.

Another study that used *Ephedra Alata* extract found that it can improve the healing process of ulcers caused by deep wounds and full-thickness burns.

It was observed that the ulcers treated by the EA ointment heal faster than those in the control or with the treatment with placebo. All ulcers treated with EA ointment showed a higher degree of fibrosis when compared to the corresponding ulcer treated with placebo from the same animal⁽¹³⁾.

Authors⁽¹⁴⁾ observed the effects of sub-extracts of essential oils obtained from Red Cedar, Western Cedar and Mountain Cedar in which the animals of the vehicle group were treated only with base, while the animals of that group of medicines were treated with 0.5 g of Madecassol (Bayer). Indomethacin (10 mg/kg) in 0.5% (w/v) CMC was used as the reference medicine. The topical application of the western cedar essential oil ointment showed the best effect in the linear incision model of the incision. The essential oil obtained from western cedar proved to have potential for wound healing, with a contraction value of 39.75% and 52.44% for western cedar on days 10 and 12. On the other hand, the group treated with reference ointment it showed 71.31% and 100.00% of contraction on days 10 and 12. The other experimental groups did not have any significant effect on this model.

That same year, Mori and collaborators⁽¹⁵⁾ investigated the effect of lavender oil on various stages of wound healing and its molecular mechanism, focusing on the transforming growth factor- β (TGF- β). Topical application of lavender oil promotes wound closure, with a reduction in the wound area, and faster closure with wound topical application of lavender oil. The wound area of rats treated with lavender oil was significantly smaller compared to untreated rats and control rats at 4, 6, 8 and 10 days after injury. However, there was no significant difference in wound size at 12 and 14 days. These data point to sunflower oil as a powerful wound healing agent of lavender oil in the initial phase⁽¹⁴⁾.

Healing and anti-inflammatory properties

Authors tested the healing and anti-inflammatory activities of different essential oils. Riella and collaborators⁽¹⁶⁾ used thymol in rodents. Thymol was shown in collagen-based dressing films and a biological wound healing test was conducted. The wound retraction index and histological analysis were performed on the 3rd, 7th, 14th and 21st days, divided into three groups: naked wounds (CTR), dressed in collagen-based films (COL) and dressed with collagen containing films of thymol (COL-THY). Thymol significantly reduced edema and, in addition, decreased the influx of leukocytes to the injured area, according to the assessment of MPO activity, total cell count and histological analysis. Wounds dressed in COLTHY films showed significantly higher wound retraction rates and improved granulation reaction, in addition to providing better collagen density and arrangement during wound healing.

The skin healing process is complex, as it depends on a series of events that result in tissue regeneration. The healing process begins with an inflammatory response that begins immediately after the injury, at this stage the recruitment of inflammatory mediators occurs, followed by the proliferative phase that is responsible for the epidermal reconstruction, the process of neovascularization and re-epithelialization occurs, and Finally, the tissue remodeling process occurs, a phase characterized by the maturation of scar tissue^(5,13).

However, this process can suffer interferences, among which stand out nutritional status, age, diabetes mellitus, lupus, among other chronic and degenerative diseases, in addition to mechanical factors. In addition to these factors, there is also the infection, which can delay or even prevent healing^(17,26).

Healing, anti-inflammatory and bactericidal properties

Study⁽¹⁸⁾ investigated the antimicrobial activity in addition to the healing and anti-inflammatory properties of the essential oil and resin of *Commiphora Guidottii* Chiov. ex. Guid. The study compared ointments prepared from 4% fragrant myrrh OE, 5% resin ointment in the experimental groups, in the positive control treatment 0.2% nitrofurazone ointment and simple ointment in the negative. The samples showed significant wound contraction between day 8 and day 16 compared to the negative control, and the difference was insignificant with nitrofurazone. The time for complete epithelialization was significantly shorter in the test sample and in the groups treated with nitrofurazone compared to the negative control. However, there was no significant difference between nitrofurazone and resin, between nitrofurazone and oil, and between resin and oil. The levels of hydroxyproline in the granulation tissue of the groups treated with OE and resin ointment increased significantly compared to the group treated with simple ointment.

As for anti-inflammatory activity, standard drug (indomethacin 10 mg/kg) and resin in three dose levels (150, 300 and 600 mg/kg) were administered orally after the administration of carrageenan. The animals treated with resin and indomethacin showed a significant reduction in edema compared to the negative control. However, there was no significant difference with the standard drug indomethacin in any course of the study⁽¹⁸⁾.

Regarding antimicrobial activity, Gram-negative bacteria including all *E. Coli* and *V. Cholerae* strains, as well as *S. Typhi* Ty2 were the bacterial pathogens most inhibited by *C. Guidottii* oil and resin. The remaining Gram-negative bacterial strains, namely, all *Shigella* strains and the

The time for complete epithelialization was significantly shorter in the test sample and in the groups treated with nitrofurazone compared to the negative control. However, there was no significant difference between nitrofurazone and resin, between nitrofurazone and oil, and between resin and oil.

Gram-positive bacterial strains: *B. Pumilus* and *B. Subtilis* were moderately inhibited. The oil and resin also exhibited a good antibacterial effect against *S. Aureus*. Overall, both the oil and the resin were 68.8-88.9% as active as the standard griseofulvin antifungal agent⁽¹⁷⁾.

Healing, bactericidal and antinociceptive properties

In 2013, study⁽¹⁹⁾ evaluated the antinociceptive and healing effects, as well as the antimicrobial activity of the essential oil of *Croton Adamantinus* Müll. Arg. The antinociceptive action was evaluated by the formalin test and by the abdominal contortion test, the wound healing activity was verified through the experimental models: excisional wound and dead space, and the antimicrobial activity of the essential oil was evaluated against Gram-positive bacteria and Gram-negative. To assess pain, the essential oil of *C. Adamantinus* (50 and 100 mg/kg, i.p.), morphine (7.5 mg/kg, i.p.) or indomethacin (10 mg/kg) was applied. The EO decreased the licking time of both phases of the formalin test compared to the vehicle, but not to the morphine. In the abdominal contortion test, EO reduced the number of contortions compared to the vehicle and indomethacin

Regarding healing, topical treatment with OE (1%) increased wound contraction from the third day of treatment (compared with nitrofurazone at 0.2%), while systemic treatment (50 mg/kg/day) increased the formation of granular tissue and reduced the water content. Histological analysis showed better epithelialization, fibroblast population and collagen deposition in animals treated with *C. Adamantinus* OA when compared to those treated with vehicle and nitrofurazone, after 7 and 14 days of injury, respectively. Regarding the antimicrobial effect, pure EO was active

only against Gram-positive bacteria, Methicillin resistant *Staphylococcus Aureus* and *S. Aureus* positive D test. *Pseudomonas Aeruginosa* and *Enterobacter Aerogenes* were resistant to the activity of the pure suspension and to 1% EO⁽¹⁹⁾.

CONCLUSION

The present review allowed us to

observe the vast amount of plants that have medicinal properties. In short, this review achieved the proposed objective and contributes to the construction of knowledge within complementary health practices. However, the studies found were performed in animal models, with different oils and in different concentrations, thus, its adverse effects and its cytotoxic action are not known for

sure, since most studies do not present specific data.

Treating wounds, especially chronic injuries, requires specific care and requires the skills of a trained multidisciplinary team. And essential oils are an effective and low-cost therapeutic alternative for the treatment of skin lesions, however, it is necessary to have a scientific basis to expand the practice in a safe and effective way. ■

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