

Effect of curcumin on wound healing: implications for health education in the SUS

ARTICLE

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Abstract

Chronic wounds represent a burden for the Unified Health System, and curcumin emerges as a cost-effective option in their treatment. The objective of the study is to analyze the evidence for the use of curcumin, alone or in combination with other medicinal active ingredients or biophysical agents in the healing of chronic wounds in adults. This is a narrative review from April to September 2023, employing structured search strategies based on PICO and MeSH Terms related to "curcumin," "chronic wounds," and "wound healing." Studies without restrictions on the year of publication were included, with participants over 18 years of age and with chronic wounds. Studies in Portuguese, Spanish or English were included. Of the 525 articles identified, six met the inclusion criteria. The study highlights promising results of curcumin in the healing of chronic wounds, especially in diabetic patients. However, the need for more clinical studies on the subject is highlighted.

Keywords: Curcuma Longa. Wound Healing. National Policy on Integrative and Complementary Practices. Public health.

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Efeito da curcumina na cicatrização de feridas: implicações para a educação em saúde no SUS

Resumo

Feridas crônicas representam um ônus para o Sistema Único de Saúde, e a curcumina emerge como uma opção custo-efetiva no seu tratamento. O objetivo do estudo foi analisar as evidências do uso da curcumina, isoladamente ou em combinação com outros ativos medicinais ou agentes biofísicos na cicatrização de feridas crônicas em adultos. Trata-se de uma revisão narrativa de abril a setembro de 2023, empregando estratégias de busca estruturada baseadas em PICO e MeSH Terms relacionados à "curcumin", "chronic wounds" e "wound healing". Foram incluídos estudos sem restrição de ano de publicação, com participantes com idade superior a 18 anos e que apresentassem feridas crônicas. Foram incluídos estudos em português, espanhol ou inglês. Dos 525 artigos identificados, seis atenderam aos critérios de inclusão. O estudo destaca resultados promissores da curcumina na cicatrização de feridas crônicas, principalmente em pacientes diabéticos, contudo, ressalta-se a necessidade de mais estudos clínicos sobre a temática.

Palavras-chave: Curcuma Longa. Cicatrização de Feridas. Política Nacional de Práticas Integrativas e Complementares. Saúde Pública

1 Introduction

Wound healing is a complex biological process that is fundamental to preserving the integrity and barrier function of the skin. However, it is susceptible to dysfunctions and pathologies that can have an adverse impact, compromising the effectiveness of the healing process and culminating in the formation of chronic wounds, which show an inability to heal properly. These chronic wounds are characterized by the absence of coordinated and punctual tissue repair over a period of more than three months, causing painful symptoms, physical and psychological discomfort, as well as a decrease in quality of life (WERDIN et al., 2008).

The ageing of the population and the increase in chronic diseases, such as hypertension and diabetes, have led to an increase in chronic wounds, especially on the lower extremities (AGALE, 2013; GREEN et al., 2014). The most common causes are venous, arterial and neuropathic, accounting for around 90% of cases (ABBADE, 2020). In addition, pressure ulcers are frequent in immobilized patients during prolonged hospitalizations. Studies in intensive care units in São Paulo and Rio Grande do Sul report





high incidences of pressure ulcers of 41.0% and 17%, respectively (ROGENSKI, 2012; BARON et al., 2016).

In the treatment of chronic wounds, debridement is the standard approach, involving the surgical or enzymatic removal of necrotic tissue to create an environment conducive to healing. Other therapeutic options include pressure relief, edema reduction, hyperbaric oxygen therapy, skin grafts, growth factors and vacuum closure. Wet occlusive dressings, such as semi-permeable films, gels, hydrocolloids, alginate dressings and foams, are the most commonly used (HAN; CEILLEY, 2017). In the midst of the variety of options, many with high costs, treatments have been investigated with a view to improving cost-effectiveness, with the use of herbal medicines standing out (ESTEVES et al., 2020).

Spices have historically been used to treat and prevent diseases (GOVINDARAJAN; STAHL, 2009). Medicinal plants, such as Turmeric (Cúrcuma longa), have received increasing attention due to the relationship between nutrition and health (JYOTIRMAYEE; MAHALIK, 2022). Turmeric, which originated in Southeast Asia, is an important spice due to its active biochemical properties (AYATI et al., 2019). Curcumin, the main component of turmeric, has anti-inflammatory, antioxidant, antitumor, antimicrobial and angiogenic properties, making it promising in wound healing (AGHARAZI et al., 2022).

Although turmeric has been used for millennia, evidence of its benefits in healing chronic wounds comes mainly from in vitro and animal studies, with a dearth of human research (AYATI et al., 2019). Recent focus from the scientific community involves the application of curcumin in nanomaterials to overcome limitations, such as its low bioavailability and solubility, and thus improve the delivery of the substance to the body (FAMIHIRAD et al., 2021). Molecular simulations show that curcumin accelerates healing stages and affects inflammatory signaling pathways (RESHAD et al., 2021). Studies in animal models confirm curcumin's efficacy in inhibiting pathogens and promoting wound healing (DONS et al., 2018).

Clinical evidence suggests that curcumin is widely used to promote skin health, treating conditions such as acne, alopecia, eczema, psoriasis, radiodermatitis and vitiligo (VAUGHN, 2016). In addition, the combination of curcumin with other herbal medicines and





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biophysical agents, such as phototherapy, has shown potential to increase tissue regeneration in adults (SANPINIT et al., 2020; SANTANA, 2021).

The aging of the population, the increase in chronic non-communicable diseases, antimicrobial resistance and biofilm formation have boosted the incidence of chronic wounds, generating significant costs for the Unified Health System (SUS) (CARTER, 2014). Current estimates indicate that costs related to the management of patients with chronic wounds may represent 1% to 3% of total health expenditure, although it is believed that these costs are underestimated (FRYKBERG, 2015; PHILLIPS, 2016). In Brazil, in Palliative Care units, the total average costs for treating PI can vary from R\$36,629.95 per month or R\$915.75 per patient per month, and can reach an annual figure of R\$445,664.38 in certain scenarios (COSTA, 2015).

Commercial curcumin, a combination of curcuminoids, has a more affordable cost, estimated at approximately R\$1.25 per 5 g, positioning itself as a viable alternative to the SUS when compared to industrialized dressings, and is in line with the promotion of phytotherapy promoted by the Ministry of Health's National Policy for Integrative and Complementary Practices (MASSIMINO, 2016; BRASIL, 2015). Therefore, there is an urgent need to seek effective treatments that reduce wound care costs and improve patients' quality of life (AUGUSTIN, 2014), as well as to provide continuing education for health professionals who treat this population.

The central objective of this research was to analyze the evidence currently available regarding the application of curcumin, either in isolation or in association with other active medicinal ingredients or biophysical agents, in the context of chronic wound healing in adult individuals.

2 Methodology

This study consists of a narrative review of the literature investigating the effects of curcumin on the healing of chronic wounds. The inclusion criteria considered included articles, dissertations or theses without limitation as to the year of publication, written in Portuguese, Spanish or English and encompassed studies carried out on human subjects





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aged 18 or over who had any type of chronic wound that had been treated with curcumin, either alone or in combination with other active medicinal ingredients or biophysical agents. In addition, studies initially conducted in vitro and subsequently applied to human beings were also incorporated into the analysis. Studies that were restricted to in vitro tests, animal research (pre-clinical studies), letters to the editor, books, book chapters and review studies were excluded from the review.

The search was carried out in various databases, including "Pubmed", "Scopus", "Web of Science", "Google Scholar", "Lilacs", "Virtual Health Library (VHL)", "Embase", "The Cochrane Central Register of Controlled Trials" and "WHO International Clinical Trials Registry". Specific descriptors such as "curcumin", "chronic wounds" and "wound healing" were used to identify the relevant studies. The selection of studies included only those that were aligned with the objective of this review and the results were discussed later.

The preparation of this article followed the guidelines established by the "Scale for the Assessment of Narrative Review Articles - SANRA" checklist in order to ensure the quality of the narrative review. It was not necessary to obtain approval from an ethics committee, as this work is a literature review and does not directly involve research with human beings or animals.

3 Results and Discussion

In the initial search of the databases, a total of 525 studies were identified. After the initial screening, only six studies met the established selection criteria and were therefore included for analysis and discussion in this study. The data relating to these studies is summarized in Table 1, which includes information on the title of the study, the authors and year of publication, the country of origin of the study, the type of research conducted and the journal in which the study was published.

Title	Author/year	Country	Type of study	Magazine/ Repository

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Effect of neem oil and haridra on non-healing wounds	Singh et al., 2014	India	Clinical trial	Ayu
Clinical study on doorvadi taila in management of dushta vrana	Ray et al., 2018	India	Randomized clinical trial	International Journal of Research in Ayurveda and Pharmacy
Antibacterial properties of Ya- Samarn-Phlae (YaSP): a pilot study on diabetic patients with chronic ulcers	Sanpinit et al., 2020	Tailândia	Randomized clinical trial	Journal of Herbal Medicine
Topical turmeric ointment in the treatment of diabetic foot ulcers: a randomized, placebo - controlled study	Agharazi et al., 2022	lrã	Randomized, double-blind, placebo- controlled study	The international Journal of Lower Extremity Wounds
Analysis of inflammation and oxidative stress in the tissue healing process after the combined use of liposomes with curcumin in natural latex biomembranes and led therapy for tissue regeneration in diabetic ulcer patients	Santana, 2021	Brazil	Controlled clinical trial	University of Brasilia Repository (dissertation)
Therapeutic effect of the combined use of natural latex biomembrane containing curcumin and LED therapy (Rapha® Therapeutic Device) in diabetic ulcer patients	Ferreira, 2021	Brazil	Double-blind comparative randomized clinical trial	University of Brasilia Repository (dissertation)

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The six studies included were published between 2014 and 2022, showing that the subject is still new in the field of clinical research. Of the studies, 2 (33.3%) were carried out in India, 2 (33.3%) in Brazil, 1 (16.7%) in Thailand and 1 (16.7%) in Iran. This shows that 4 (66.7%) of the studies were carried out in Asian countries. Since, in these countries, turmeric is a spice recognized for its biochemical properties and used for millennia in nutrition and health by these peoples (JYOTIRMAYEE; MAHALIK, 2022; AYATI et al., 2019). Of the six studies, all have a clinical trial design, showing greater methodological robustness in the conduct of the studies.

In the study conducted by Agharazi et al. (2022), the efficacy of curcumin ointment in the treatment of diabetic foot ulcers was investigated. The ointment contained 10% curcumin, while a placebo was used for comparison, both manufactured by Seagull Pharmaceutical & Healthcare Products. The trial involved 130 patients with grade 3 ulcers at a diabetic foot care center. Patients were excluded from the study if they had neuropathy, vasculopathy or used offloading methods. Patients were randomized into intervention and placebo groups using random allocation software, resulting in 67 participants in the intervention group and 63 in the placebo group. All patients were instructed to apply the curcumin ointment or the placebo twice a day, after irrigating the wounds with saline, applying a thin layer of the ointment of around 2 to 3 millimeters, for a period of 5 consecutive weeks. To assess the progression of the ulcers, the ulcers were measured using a ruler and photographs were taken at the start of the study (day 0) and after 5 weeks of treatment. Analysis of the area of the ulcers before and after treatment showed a significant improvement in the curcumin-treated group, while the placebo group showed no change in the area of the ulcers after 5 weeks (p < 0.001).

In the study carried out by Santana (2021), the therapeutic potential of Rapha® therapy for the healing of diabetic foot ulcers (DFUs) was investigated. This therapy combined LED therapy (Light Emitting Diode) with natural latex biomembrane (BLN), plus liposomes containing curcumin. The average age of the 15 participants was 59. In addition to diabetes, 67% were hypertensive, 33% obese, 7% smoked and 33% drank alcohol. Of the diabetics, 60% used insulin. The effectiveness of the treatment was assessed in 15 participants with UPD, divided into three groups: the control group (CG), which received





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the standard SUS treatment (calcium alginate dressings, hydrogel and activated charcoal with silver); experimental group 1 (EG1), which received Rapha® therapy with BLN and LED for 35 minutes; and experimental group 2 (EG2), which received Rapha® plus therapy with BLN, curcumin liposomes and LED for 35 minutes. The latex biomembrane with curcumin liposomes was produced with varying concentrations of curcumin (5 to 10 mg/mL). Participants in GE1 and GE2 interrupted the standard SUS treatment during the study and underwent the experimental treatment, including application of the latex biomembrane and exposure to LED. The wounds were measured using disposable rulers (length versus width) and photographed. All participants were evaluated for a total of 45 days. The results showed a notable improvement in the healing of the wounds treated with Rapha® therapy, particularly in GE2 (Rapha® plus), where all the ulcers showed a significant reduction in area of over 60%. The GE2 group achieved the highest healing percentages, with a rate four times higher than that of the CG and twice that of GE1.

Finally, the hematological and biochemical analyses, including parameters such as red blood cells, hemoglobin, hematocrit, VCM, HCM, CHCM, RDW, leukocytes, segmented leukocytes, eosinophils, basophils, lymphocytes, monocytes, platelets and mean platelet volume, together with the quantification of reactive oxygen species (ROS) on days 0, 22 and 45, showed no significant associations with the wound healing process. Furthermore, no relationship was observed between systemic inflammatory indicators such as leukocytes, C-reactive protein and ROS, and the healing of UPDs in the experimental groups. As no significant differences were found in inflammatory markers throughout the study, the authors suggest that future research should focus on the mechanisms of action of combined therapy (BLN with curcumin liposomes and LED) in the healing process of diabetic ulcers (SANTANA, 2021).

The study conducted by Ferreira (2021) evaluated the treatment of diabetic foot sufferers with a combination of natural latex biomembrane containing curcumin and LED therapy, known as Rapha® plus. The inclusion criteria required participants to have type I or II diabetes, lower limb ulcers of at least three weeks' duration, no latex allergy and the ability to photograph the wounds. Most of the participants had type II diabetes, with an average disease duration of 10 to 20 years. The sample was made up mainly of men (64%),





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with ages ranging from 50 to 75. Around 87.5% of the participants had hypertension and 75% had already undergone amputation. In addition, 75% had corns and dry skin and 50% had cracked feet. The participants were divided into two experimental groups: GE1 and GE2. GE1 received treatment with BLN and LED, while GE2 was treated with BLN containing curcumin and LED. The intervention consisted of daily application of the latex biomembrane, with or without curcumin, together with red wavelength LED phototherapy (636 ± 20 nm) for 35 minutes over 45 days. Clinical, sociodemographic and self-care assessments were carried out on days 0 (baseline), 15 and 30. Blood tests were carried out on days 0, 22 and 45 to assess toxicity, including blood count and biochemical analyses. Materials for changing the dressings included BLN with or without curcumin, gauze, saline solution, bandage, adhesive plaster, moisturizing cream, antibacterial soap and a measuring ruler.

Daily photographic records of the wounds were standardized with rulers and used to measure the length, width and depth of the ulcers on days 0, 22 and 45. The estimated wound area was calculated by multiplying the length by the width. The percentages of ulcer contraction were calculated to assess the effectiveness of the treatment on healing (NICHOLS, 2015). The results showed that GE2, which received treatment with BLN containing curcumin and LED, achieved an average healing of 70%, while GE1, which used BLN without curcumin, achieved an average healing of 46%. On the other hand, there were few alterations in the hematological and biochemical tests, which are related to the inflammatory process. In addition, attention to self-care proved to be effective in preventing foot injuries and re-ulceration (FERREIRA, 2021).

The study conducted by Sanpini et al. (2020) investigated the antibacterial and antibiofilm activity of Ya-Samarn-Phlae (YaSP) extracts against wound-associated pathogens and evaluated the effects of YaSP-infused oil in the treatment of diabetic foot ulcers. The YaSP preparation involved G. mangostana, C. longa, O. sativa and A. catechu in equal proportions, together with virgin coconut oil. The therapeutic potency of each component was assessed using the broth microdilution method. When used in combination, the therapeutic effects of the plant extracts increased due to the synergy between the components. The study included 14 patients aged between 44 and 77 with



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diabetic foot ulcers, who underwent a 4-week open pilot study. The patients had type II diabetes and Wagner grade 1 and 2 ulcers. The average size of the ulcers at the start of the study was 9.7 cm². The patients received treatment with YaSP and were followed up every 3 days. The treatment did not result in any adverse effects. In the second week, 93% of patients showed a reduction in ulcer size of 50%. After 4 weeks of treatment with YaSP, all the ulcers showed significant improvements, with an average reduction in size of 55.8%. The results suggest that the YaSP preparation is an effective and safe approach for treating diabetic foot ulcers.

The study conducted by Ray et al. (2018) aimed to evaluate the effect of Doorvadi Taila oil compared to Jatyadi Taila oil, used in Ayurvedic medicine, in the treatment of persistent ulcers (Dushta Vrana). Forty patients aged between 21 and 90 with diabetes mellitus and ulcers at least 7x7 cm in size were selected. The patients were divided into two groups: Group 1, consisting of 20 participants, used Doorvadi Taila containing ingredients such as Cynodon dactylon, Mallotus philippensis, Berberis aristata, Sesamum indicum, while Group 2, with another 20 patients, used Jatyadi Taila which contained Curcuma longa, among other ingredients such as Jasminum officinale, Azadirachta indica, Trichosanthes diocia, Pongamia pinnata, Adiantum caudatum, Madhuca indica, Saussurea lappa, Berberis aristata, Picrorhiza kurroa, Rubia cordifolia, Prunus cerasoides, Symplocos racemosa, Terminalia chebula, Nymphaea nouchali, Copper Sulphate, Hemidesmus indicus, Pongamia pinnata and Sesamum indicum. Both oils were applied once a day after cleansing the wound with normal saline solution, over 37 days. Symptoms such as pain, burning, itching, odor, color and presence of pus, as well as the size of the ulcer, were assessed before and after treatment. The results showed that Doorvadi Taila was effective in treating chronic ulcers, providing significant symptom relief and stimulating healing, with a substantial improvement and no adverse effects.

The study conducted by Singh et al. (2014) aimed to compare the effect of Neem oil (Azadirachta indica A. Juss) and Haridra (Curcuma longa linn), two Ayurvedic medicine plants, in the treatment of chronic non-healing wounds. 47 patients aged between 19 and 78 with persistent wounds (diabetic ulcers, leprosy lesions, venous ulcers and pressure ulcers) that had not healed for more than 6 weeks were recruited. Most of these wounds





were associated with diabetes. The patients were divided into three groups: Group I (n = 16), treated with topical Neem oil; Group II (n = 11), treated with Haridra capsules, 1 g, 3 times a day orally; Group III (n = 20), which received both topical Neem oil and Haridra orally. Dressings were changed daily, and the duration of treatment varied until the wound healed completely or until the 4th and 8th week, depending on progress. The results showed that, after 8 weeks, Group III (which received both treatments) had a significantly higher wound healing rate of 50% compared to the other groups. In addition, all groups showed an increase in angiogenesis after 4 weeks, and the concentration of deoxyribonucleic acid (DNA) in the wound tissues increased significantly in all groups. The study concluded that the isolated use of each drug showed efficacy in the treatment of chronic wounds, but the combined use of both drugs had a more significant effect, promoting vascular proliferation and increasing the concentration of DNA in the tissues. Therefore, both treatments showed angiogenic properties and the ability to stimulate tissue regeneration in non-healing wounds.

4 Final considerations

The aim of this research was to analyze the evidence currently available regarding the application of curcumin, either alone or in association with other active medicinal ingredients or biophysical agents, in the context of chronic wound healing in adult individuals.

In summary, the studies analyzed provide valuable information on the use of herbal products, such as curcumin and Ayurvedic formulations, in the treatment of chronic and persistent ulcers, especially in patients with diabetes. They highlight the effectiveness of these products in stimulating healing, reducing associated symptoms and, in some cases, increasing angiogenesis in the affected tissues.

The studies address a variety of therapeutic formulations, including ointments, oils and combined therapies, such as the application of natural latex biomembranes containing curcumin and LED therapy. The results suggest that these approaches are promising for the treatment of chronic ulcers, providing symptom relief, improved healing and, in some cases, faster healing rates. In addition, the absence of significant adverse effects in all the

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studies highlights the safety of these therapies, which is fundamental for the treatment of patients with chronic conditions such as diabetic foot ulcers.

Several limitations can be identified in the studies presented. In many of them, the main limitation is the small sample size, which makes it difficult to generalize the results to wider populations. In addition, the absence of control groups in some studies prevents adequate comparison of the effects of therapeutic interventions. Relatively short follow-up periods in some clinical trials also limit long-term understanding of treatments. The diversity of patients, with different types of ulcers and underlying medical conditions, can introduce variability into the results. In some studies, the therapeutic formulations were complex and non-standardized, making it difficult to isolate the effect of specific ingredients. In addition, the lack of detailed information on dosage and procedures can make it difficult for other researchers to replicate the studies. Finally, the heterogeneity of the results in relation to inflammatory and oxidative stress markers highlights the need for more comprehensive investigations to clarify these associations.

Furthermore, it is imperative to point out that, despite the widespread use of turmeric in Asian countries, there is still a lack of publications on the results of its application. In the Brazilian context, in particular, studies on the use of this herbal medicine are limited. Given this scenario, there is an urgent need to conduct more clinical research, with a view to confirming and expanding existing results. This endeavor aims to substantially improve the evidence base, making a significant contribution to the dissemination of more grounded knowledge in health, especially within the Unified Health System (SUS), in accordance with the Ministry of Health's National Policy for Integrative and Complementary Practices..

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