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VIRGIN COCONUT OIL ACCELERATES WOUND HEALING: A SYSTEMATIC REVIEW

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ABSTRACT
Virgin Coconut Oil (VCO) has been shown to have significant therapeutic benefits for skin wound healing, primarily due to its anti-inflammatory effects, ability to stimulate tissue regeneration, and potent antioxidant properties. This review analyzes the available research exploring the relationship between VCO and its impact on wound healing. A comprehensive search was conducted using the Medline database via PubMed and Scopus to identify relevant studies published between 1970 and March 2023. The main inclusion criteria were original articles written in English that evaluated wound healing in in vivo skin models using topically applied VCO. The search initially yielded 689 articles, but only 4 articles met these criteria. These studies addressed various types of wounds, including excisional, burn, and diabetic wounds. All four studies demonstrated positive outcomes, showing that VCO promotes skin wound healing. The oil's anti-inflammatory, antioxidant, and antibacterial properties were identified as key contributors to its role in enhancing the wound healing process.

Keywords: anti-inflammatory; topical; VCO; wound healing

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INTRODUCTION

Curing process of diabetic wound involves cellular and biochemical responses both locally and systemically. It is involving dynamic and complex processes of serial coordination including bleeding, coagulation, initiation of an acute inflammatory response immediately after trauma, regeneration, migration and proliferation of connective tissue and parenchymal cells, also extracellular matrix protein synthesis, parenchyma and connective tissue remodeling and collagen deposition (Arndt et al., 2013) . The most important role in all wound healing processes played by macrophage cells, which function to secrete pro-inflammatory and anti-inflammatory cytokines as well as growth factors, fibroblasts and their ability to synthesize collagen which affects the tensile strength of the wound and fills the wound tissue back to its original shape, followed by skin keratinocyte cells to divide and migrate to form re-epithelialization and cover the wound area (Faten et al., 2010).

Conventional treatment of diabetic wounds uses repeated dressings and debridement of necrotic tissue. However, the results of the treatment are not so significant with the incidence of 14-12% of amputations. The objectives of treatment continuously developed are to overcome the inflammatory response and growth factors involved (Hong et al., 2014). Complementary therapy as an alternative for wound care are continuously develop to overcome some of the limitations of modern medicine such as high cost, and antibiotic resistance. The availability of traditional-based treatment in wound management currently

provides a balanced condition for accelerating the healing process as an anti-inflammatory, accelerating growth factors and cell migration (Rubem and Paulo., 2013).

A nature ingredient as an alternative commonly used for wound healing is Virgin Coconut Oil (VCO). VCO produce from coconut milk through mechanical or natural, with or without heating, without chemical refining, bleaching, and coloring (Soorya et al., 2021). VCO is an unsaturated oil with medium chain fatty acids (MCFA = Medium Chain Fatty Acid) such as lauric acid which has antibacterial and anti-inflammatory activity (Arifin and Hasma., 2016). Besides, VCO also contains polyphenols which have anti-inflammatory and oxidative stress activities (Hayatullina et al., 2016).The main polyphenol identified in VCO is ferulic acid, which is reported as a strong molecule that has antioxidant and anti-inflammatory activity (Gerin et al., 2016). LC-MS analysis of VCO proves the presence of syringic acid which is also a natural phytochemical that has anti-inflammatory potential (Ham et al., 2016). Previous studies explained that VCO reduced inflammation caused by ethyl phenylpropionate in rats and carrageenan and arachidonic acid-induced leg edema in mice (Intahphuak et al., 2010). VCO shows an inhibitory effect on chronic inflammation by reducing granuloma formation and serum alkaline phosphatase activity (Vysakh et al., 2014). Another study demonstrated that administration of FVCO inhibited formalin-induced chronic inflammation and cyclophosphamide-induced systemic toxicity (CTX) in preclinical models (Nair et al., 2016). Recent studies have shown that FVCO supplementation reduces methotrexate-induced kidney toxicity in rats by its antioxidant and anti-inflammatory potential (Famurewa et al., 2017)

HVCO is effective for increasing cell proliferation and wound healing processes (Jansen et al., 2019). FVCO significantly increases the migration ability of CCD-18 and RGC-5 cells in wound healing (Ahamd et al., 2017). The results of other studies also showed that VCO and HVCO increased the expression of MMP-9, PDGF-BB, TGF beta proteins in wound healing. Increased expression of MMP 9, PDGF-BB, TGF beta will affect proliferation, migration, angiogenesis which play a role in the wound healing process. MMP 9 specifically breaks down type IV collagen which plays a role in facilitating vascular endothelial cells, PDGF-BB chemotactically attracts fibroblasts, neutrophils, monocytes, smooth muscle cells to the wound, activates macrophages to release growth factors while TGF beta acts as a powerful chemoattractant for macrophages, mitogens for fibroblasts, stimulate the proliferation of various cells and promote the formation of new tissue (Dian et al., 2019)In this review, a systematic search of the electronic databases, namely Medline via PubMed was conducted to identify published research articles regarding the positive effect of VCO towards skin wound healing. The findings were critically appraised and presented in terms of the wound healing outcome measures.

METHOD

Literature Review

Relevant studies reporting topical effect of VCO on skin wound were systematically obtained via an extensive search on the biomedical science-related databases, namely Medline via PubMed (published between 1970 to March 2023). The search approach included a combination of the following two sets of keywords (1) VCO OR *virgin coconut oil* AND (2) skin OR wound healing.

Selection of Research Articles

Records obtained from the keyword search were filtered under three different phases by three independent reviewers before the content was evaluated according to the inclusion and exclusion criteria of this review. First, the records were limited to primary literature with

abstracts written in English language. In the second phase, articles that falls within the category of secondary literature were excluded from the selection process. Finally, duplicate records were excluded.

Inclusion and Exclusion Criteria

For this review, article that reported the effect of VCO product on wound healing in an in vivo skin model were included. Articles must report the effects of at least one of these which were (1) wound size OR (2) gross appearance of wound area OR (3) histological analysis (4) Biological markers. Wound healing can occur in various skin conditions such as skin cancer, skin fibrosis, and embryonic development. These factors may hinder the role of VCO in wound healing. Therefore, for this systematic review, papers that reports the effect of VCO on wound healing of (1) skin cancer, (2) skin fibrosis, or (3) embryonic development were excluded from this review.

Data Extraction and Management

Following record screening, the titles of the articles were examined to exclude articles that were not relevant to the proposed inclusion criteria. It was followed by the abstract's evaluation prior to data extraction from a full paper read. Last but not least, the rest of papers were read carefully line by line, to exclude any articles that did not meet the inclusion criteria. These articles were read thoroughly by three independent reviewers, and the data collection standardization was made through the data extraction form (DEF). However, all the selected articles were agreed on by all reviewers to ensure their clarity and unbiasedness before the data extraction phase began. The details of DEF included the following information: (1) experimental model used; (2) form of VCO; (3) summary of methods used; (4) summary of results; and (5) final conclusions.

RESULT

The extensive literature search successfully identified 8050 potentially relevant records. Identification continued by using the tools available on PubMed so that it succeeded in deleting 7235 irrelevant articles. Then read the 696 articles to see the completeness of the articles according to the inclusion and exclusion criteria in order to obtain 4 articles that are relevant for the review process.

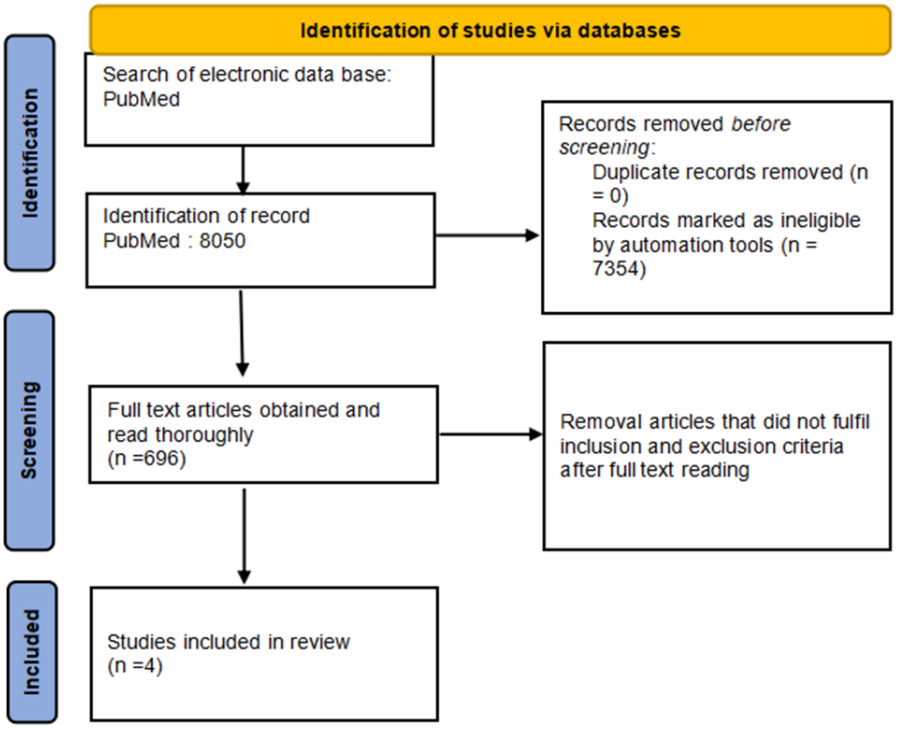

Table 1
Summary of virgn coconut oil (VCO) data

Table 1,
Article Analysis

Refences	Experimental model	Methods	Results	Conclusion
Ahmad et al, 2017	In vitro: cells ware cultured in medium containing different concentration of FVCO Animal model A full-thickness of the skin was excised to obtain a wound of circular area of approximately 150 mm^2 diameter and 2 mm depth along the markings using a tooth forceps, surgical blade and pointed scissors	Treatment groups 1. HUVEC 2. CCD-18 3. RGC-5 Parameter: 1. Proliferation 2. Migration 3. Morphological	Outcome 1. FVCO (6 and 12 ug/ml) improved the proliferation of HUVEC, CCD-18, RGC 5 2. FVCO 25 (ug/ml) increased the migration ability of CCD-18, RGC-5 FVCO did not affect cell morphology as indicated	Study confirms a high angiogenic and wound healing potency of FVCO that might be mediated by the regulation of VEGF signing pathway
K.G. Nevin and T. Rajamohan	Animals were anesthetized by sodium Pentothal injection and the skin on the dorsolateral flank was shaved. An excision wound of a size of 4 cm^2 was made by cutting out a 2 x 2-cm piece of skin from the shaven area	Treatment groups: 1. Control groups 2. Treated with 0,5 ml 3. Treated with 1 ml VCO Parameter: 1. The total Collagen 2. Collagen solubility patterns DNA levels	Outcome: 1. The total collagen content of VCO-treated wounds showed a significant increase compared to the control 2. The solubility pattern of collagen from the granulation tissue indicates higher levels of pepsin-	The beneficial effect of VCO can be attributed to the cumulative effect of various biologically active minor components present in it.

Refences	Experimental model	Methods	Results	Conclusion
			soluble collagen in the VCO treated group than in the control group DNA levels in wounds treated with 1 and 0.5 ml VCO showed a significant increase compared to the control wounds. Glycohydrolase, glucuronidase and N acetyl glycosaminidase were also found to be significantly increased in wounds treated with 1 ml VCO	
Dian et al, 2019	NIH-3T3 Cell	Treatment groups 1. Control groups 2. VCO 3. HVCO Parameter: 1. MMP-9 2. PDGF-BB TGF-beta 1	Outcome: 1. Percentage of MMP-9 expressions treated by VCO increased from 2.89 to 28.16, PDGF-BB from 28.11 to 48.53, TGF beta 1 from 4.19 to 18.41 Percentage of MMP-9 expressions treated by HVCO increased from 2.8 to 55.40, PDGF-BB 28.11 to 61.65, TGF-beta 1 from 4.19 to 36.35	VCO dan HVCO increase the expressions of MMP-9, PDGF-BB, TGF-Beta 1 in NIH3T3 cells.
Jansen et al, 2019	In vitro : NIH 3T3 cell	Treatment groups 1. Control HVCO	Outcome Effect of HVCO 62.5 ug/ml on cell proliferation after 24h, 48h, 72 h incubation found as viable cell are 109.24, 118.29 and 106.59 and expression of COX-2 increased from 1 to 1.83	The results suggest that HVCO is effective to increase cells proliferation and hence wound healing process

DISCUSSION

This study of systematic literature review revealed the current state of evidence regarding the effects of virgin coconut oil (VCO) on wound healing. Wound healing is a complicated and dynamic process including proliferation, differentiation, migration of keratocytes and their elaboration of the new extracellular matrix (ECM) (Galego et al., 2017). VCO contains more biological active constituent such as tocopherols, sterols, polyphenols, and squalene (Abujazia et al., 2021). Furthermore, VCO also contains lauric acid, which has antimicrobial, anti-viral,

anti-fungal and antibacterial properties Arifin et al., 2016)In vitro studies showed that FVCO (6 and 12 µg/mL) significantly promoted the proliferation of HUVEC, RGC5 and CCD18 cells as indicated by CKK assay. Moreover, wound scratching assay demonstrated that FVCO (25 µg/mL) also significantly enhanced the migration ability of RGC5 and CCD18 cells. This is the first study showing the beneficial effects of FVCO on the growth of HUVEC, RGC-5 and CCD-18 cells (15). Another study describe that treatment with VCO and HVCO on NIH 3T3 cells increase MMP-9, PDGF-BB, and TGF-β1expressions and hence play a role in the wound healing process (Dian et al., 2019)

HVCO increase cell proliferation after 24 hours incubation, constant at 48 hours, and decreased after 72 hours of incubation. Percentage of the wound closed at 48 hours incubation, closing up to 100%. HVCO is also able to increase COX-2 expression. HVCO increase cell proliferation, percent of the wound closed, and COX-2 expression, so HVCO is useful as wound healing (Jansen et al., 2019).A study showed that FVCO enhanced the length of blood vessels and promoted the blood vessel formation in rat aorta ring assay, indicating its angiogenesis effects (Ahmad et al., 2017). Possible reasons are the bioactive compound in coconut oil such as phenolic compound and medium chain fatty acids (MCFAs) might promote the proliferation of HUVEC through stimulating the production of VEGF, a signal protein secreted by cells that stimulates vasculogenesis and angiogenesis. VEGF is an angiogenic protein and is produced in large quantities by the epidermis during wound healing [Teng et al., 2008; johnson et al., 2014; Bao et al., 2009). The results indicate a significant beneficial effect of VCO on intracellular and extracellular matrix components and the antioxidant profile during cutaneous wound healing in animals treated (Nevin and Rajamoha et al., 2010).Wound healing is an important physiological process to maintain the integrity of skin after trauma, either by accident or by intent procedure. The normal wound healing involves three successive but overlapping phases, including hemostasis/inflammatory phase, proliferative phase, and remodeling phase (Peng et al., 2018)

Platelets release several growth factors, including the transforming growth factor-b (TGF-b), epidermal growth factor (EGF), insulin-like growth factor-1, and platelet-derived growth factor (PDGF), which are responsible for the activation of fibroblasts, endothelial cells, and macrophages in the surrounding environment (Groeber et al., 2011)Practices and compounds that arise from traditional medicine have been used to create the optimal conditions for the skin regeneration process and to prevent the failure of the healing process due to their therapeutic activities, availability, affordability, and relative low cost (Ruben and Paulo, 2013)

CONCLUSION

This review suggests that VCO have a significant role in accelerating wound healing, depending on the metabolic conditions. It is supported by four studies reporting the effect of VCO expedite recuperation of wound due to the anti-inflammatory, antioxidant, and antibacterial properties of its active constituent.

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