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SHORT REVIEW

Herbal Approach for Healing: A Comprehensive Guide to Natural Remedies for Wounds

Sunil Kardani*, Mit Bhatt, Ghanshyam Parmar, Nirmal Shah, Dipti Gohil, Chintan Aundhia, and Rajesh Maheshwari

Department of Pharmacy, Sumandeep Vidyapeeth Deemed to be University, Vadodara - 391760, Gujarat, India; sunilkardani@yahoo.co.in

Abstract

The pursuit of effective wound healing has prompted a resurgence in the investigation of the therapeutic properties of medicinal plants. This review comprehensively examines ten promising plants and their notable wound-healing attributes. Ranging from the Indian tree *Butea monosperma* to the common herb *Ribwort plantain*, each plant offers a distinct array of bioactivities, including antibacterial, antioxidant, and anti-inflammatory effects, all of which are pivotal in the intricate orchestration of the wound healing process. The in-depth exploration of these plants underscores their potential as safe and effective alternatives, or synergistic complements, to conventional wound care products and dressings. Furthermore, the review underscores the significance of standardization, rigorous scientific research, and personalized treatment plans to fully leverage the potential of nature for wound healing. By embracing the synergy between traditional knowledge and scientific rigour, a future where nature's resources become a cornerstone of wound care, providing accessible, cost-effective solutions for all, is within reach.

Major Findings: The use of herbal medicines and plant-based products for wound healing has grown significantly, with several medicinal plants, such as *B. monosperma* and *Calendula officinalis*, demonstrating effective wound-healing properties. Regulatory bodies, including the FDA and WHO, oversee the quality and safety of these herbal products, ensuring their efficacy through stringent guidelines and standards.

Keywords: Bioactivities, Medicinal Plants, Nature-based Wound Care, Wound Healing

1. Introduction

Over the past three decades, there has been a significant growth in the usage of herbal medicines and supplements, with at least 80% of individuals using them for some aspect of their primary healthcare. Although the efficacy of many herbal medications has been proved, treatments utilising these substances have shown remarkable promise[1,2]. This growing interest in plant-based medicines and natural cures has also been seen in wound healing in recent years. While Western medicine has access to a wide range of wound care treatment techniques, several plant-based products may also aid in wound healing[3,4].

Wound injuries are severe traumatic events that are frequently disregarded and can happen to anybody, at any time. The majority of wound injuries have a variety of causes, such as accidents, running into something, getting cut or scraped, underlying medical conditions, and surgery, skin ulcers from traumas or inadequate blood flow, and fire. Additionally, infections from wounds can result in sepsis, hypovolemia, hypothermia, respiratory problems, and scarring[5,6]. In response to an injury, wound healing is a multifaceted process of tissue remodelling or repair. Medicinal herbs and their constituents have long been employed in the management and treatment of many kinds of wounds[7]. Indeed, some medicinal plants have been shown to have wound-healing properties and are useful in the treatment of wounds. These include *Curcuma longa, Terminalia arjuna, Centella asiatica, Bidens pilosa, Aloe barbadensis, Rauwolfia serpentine*, etc. Research has also

*Author for correspondence

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been done on plant-based wound dressings to produce stable, cost-efficient, long-lasting, and effective delivery methods for wound care. The information gathered attempts to inform scientists and researchers about the function and significance of plant-based ingredients in the management and treatment of wounds. The uniformity and therapeutic efficacy of medicinal plants are guaranteed by standardisation. The identification (characterization), quality, and quality of the extracts included in herbal products are assessed because these factors are necessary to assess their medicinal efficacy, or the ability to demonstrate authenticity through pharmacological activity[4,8].

2. Wound Causes and Pathophysiological Healing Mechanism

The four unique stages of wound healing are haemostasis, inflammatory, proliferative, and remodelling. It is a very complex and dynamic process. Tissue damage causes the first stage of haemostasis, which activates platelets to start the clotting process. This stage is critical for controlling bleeding and preparing the body for later phases of recovery. Next comes the inflammatory phase, which is characterised by the elimination of germs and cell debris. Angiogenesis, thrombosis, and epithelialization are among the vital processes that are aided by inflammatory cells, which include neutrophils, cytokines, and mediators[9,10]. Cellular migration is promoted during this phase, which lasts for many days, while the wound starts to shut. Granulation tissue, neovascularization, and re-epithelialization all occur during the proliferative phase. This phase, which can last several weeks, is actively participated in by a variety of cell types, including macrophages, fibroblasts, endothelial cells, mast cells, B cells, and myofibroblasts. This step, which comes before the last stage, remodelling, which usually begins around week three, sets the groundwork for tissue repair and regeneration. However, several circumstances can impair the natural process of wound healing[6]. Among the many variables that contribute to delayed wound healing include a lack of oxygen or perfusion, metabolic abnormalities that change cellular responses, smoking, starvation, infections, altered pH, and oedema. It is critical to address these underlying issues to receive good therapy[11,12].

Global regulatory bodies, including the FDA, ICH, national regulatory agencies, pharmacopoeias, and the WHO, oversee the regulations governing herbs and herbal products. The World Health Organization (WHO) provides comprehensive guidelines addressing contaminants such as pesticides and heavy metals while emphasizing the importance of quality and safety. In the United States, the FDA enforces stringent regulations for herbal dietary supplements, focusing on Good Manufacturing Practices (GMPs) to ensure product quality and accurate labelling. The International Council for Harmonisation (ICH), through its pharmaceutical standards, indirectly impacts the regulation of herbal products. Many countries also have national regulatory bodies, such as Health Canada and the UK's MHRA, which establish specific requirements for the efficacy, quality, and safety of herbal goods. Additionally, the legislation on traditional medicine in several countries often takes into account the historical use of herbal remedies. Pharmacopoeias, such as the European Pharmacopoeia and the United States Pharmacopeia (USP), set quality standards to ensure the safety and efficacy of herbal products. Adhering to these regulations helps guarantee the safety and effectiveness of herbal supplements and products for both manufacturers and consumers.

3. Current Treatment Options and Their Limitations

3.1 Wound Care Products and Dressing

Debridement, or the removal of non-viable tissue, is crucial to the treatment of wounds. Both surgical and autolytic/enzymatic techniques can be used, albeit surgical debridement is more successful[13]. Bio-surgical debridement, which uses larvae or maggots and combines mechanical and enzymatic techniques, is a promising technique that still requires investigation. A moist environment is maintained by a variety of wound dressings to promote healing and re-epithelialization[14]. Alternatives to traditional dry gauze include foams, collagen products, hydrocolloids, hydrogels, alginate dressings, and low-adherent dressings[15,16]. Traditional dry gauze might impede healing. Recent developments have improved dressings' ability to control infections by including antibacterial substances like silver. To meet

the demands of each unique patient in this changing environment, personalised treatments are essential[17]. Although essential for treating different types of wounds, wound care treatments and dressings have their limits. Without regular wound washing and dressing changes, infections may arise. It's critical to maintain the proper moisture balance since either too much or too little moisture might impede recovery[18,19]. Options may be limited by allergic responses to bandages, and expensive treatments may make it difficult to get care, particularly for people without sufficient insurance. Specialised therapies, such as negative pressure therapy or surgery, may be necessary for complex wounds in addition to basic bandages[20,21]. Patient cooperation is crucial for wound care, including routine dressing changes; noncompliance can impede healing. Efforts are being made to address these issues to improve wound care products and increase their efficacy and accessibility[22].

3.2 Skin Substitutes

Developments in wound care have resulted in the creation of bioprosthetic skin replacements, which blend biological components with materials used for wound treatment. Research has demonstrated their cost effectiveness despite their high cost since they shorten hospital stays[23]. Alternative materials for mesh include Biobrane and Transcyte, fibroblast-derived Derma graft, and Apligraf, which improves blood flow in diabetic foot ulcers. By demonstrating a 50% improvement in wound closure rates, the FDA-approved Integra Dermal Regeneration Template (Omnigraft) shortened the time to closure by five weeks[24]. The majority of patients only required a single Omnigraft treatment, highlighting how effective it is in wound management[25]. Skin substitutes are less effective than natural skin grafts in deep wounds; they are more expensive and therefore less accessible[26]; they are less durable over the long term, increasing the risk of rejection or allergic reactions[27]; they are subject to strict regulatory procedures that delay their availability; and their results vary depending on the patient's health and the state of the wound[28]. Current studies are being conducted to overcome these constraints and increase the efficiency and availability of skin replacements in tissue regeneration and wound healing[29].

3.3 Negative Pressure Wound Therapy (NPWT)

Vacuum-assisted closure, another name for negative pressure wound therapy (NPWT), has garnered interest since its 1997 debut in the United States. These devices exert pressure, remove exudates, improve blood flow, and keep the wound moist to promote wound closure to address various aspects of chronic wounds[30]. Studies indicate a reduction in the incidence of infections and more convenient dressing changes. Standard NPWT components include an evacuation tube and a foam dressing; alternatives for acute care settings include complex machinery and portable home units. In difficult surgical wounds, NPWT has a new use where it can reduce wound volume and facilitate additional surgical repairs[31]. However, while it has its limits, Negative Pressure Wound Therapy (NPWT) is an effective method of managing wounds. When administered improperly, it can be expensive, uncomfortable for the patient, and less effective in wounds with significant necrosis[32-35]. Although bleeding complications are uncommon, they nevertheless need to be closely watched. NPWT has advantages, but as with any treatment, it should be customised for each patient's needs and wound state[36].

3.4 Hyperbaric Oxygen Therapy

Although hyperbaric oxygen treatment has been shown to have minimal practical value, it has generated debate since it aims to stimulate angiogenesis in wound healing, improve immunological function, and promote fibroblast development[37]. A Cochrane study found that this treatment, which is given in a hyperbaric oxygen chamber, has not significantly improved the healing of diabetic foot ulcers. Currently, only ischemic diabetic ulcers with hypoxic symptoms are eligible for its usage[38]. There are now clinical trials underway to evaluate its potential in avoiding amputations in non-healing diabetic ulcers due to recent research suggesting minimal effectiveness[39]. While some research points to favourable effects, especially in certain situations like diabetic ulcers, the findings are not always consistent. In addition, individuals pursuing this therapy option may encounter difficulties due to restricted accessibility to HBOT facilities. As such, the implementation of this approach frequently hinges on the meticulous

assessment of specific instances and the accessibility of specialised resources.

4. Medicinal Plants with Wound-healing Properties

4.1 *Butea monosperma*

Butea monosperma (BM) commonly known as flame tree, belongs to the subfamily *Caesalpinioideae*, family *Fabaceae* (formerly *Leguminosae*). In India, the plant is referred to as the Palash tree. It is *B. monosperma*, a tropical and subtropical tree that grows sporadically in India's drier parts in woodlands, open grasslands, and wastelands. When utilised as a medicinal plant in Ayurvedic medicine, BM has significant effects. Numerous research endeavours have examined the capacity of *B. monosperma* to promote wound healing. Research has demonstrated that the plant possesses antibacterial, wound-healing, and antioxidant properties[40]. In one study, bioactive fractions from *Butea monosperma* stem bark extract were evaluated for their ability to promote wound healing. The results showed that the extract shortened the time it took for the wound to heal, increased wound contraction, and increased the amount of hydroxyproline, granulation tissue weight, and tensile strength of the incision wound area. The effectiveness of topical *B. monosperma* extract administration on cutaneous wound healing in rats was shown in another investigation[41]. The plant was shown to have antioxidant qualities, which lower lipid peroxidation and the results demonstrated that the extract sped up the healing process for wounds. *B. monosperma* has been discovered to exhibit osteogenic and osteoprotective activity in its cajanin, along with other bioactive components such as tannins, flavonoids, and saponins, which are responsible for the wound healing benefits of the plant[42]. It is thought that these phytochemicals support the plant's antioxidant, antibacterial, and wound-healing abilities.

4.2 *Eucalyptus globulus*

The *eucalypti* are commonly known as gum trees or stringybark trees. Eucalyptus trees are prized for their quick growth and for the oil found in their leaves, which has a variety of practical and therapeutic uses, including treating wounds and providing essential oil for aromatherapy. It has been shown that eucalyptus essential oil promotes better wound healing for cold sores and ulcers. It may help reduce inflammation in arthritis sufferers. According to studies, eucalyptus alba leaves have the best wound-healing qualities and encourage cell proliferation when they are dried to a maximum temperature of 30°C and then extracted in ethanol[43]. It has been shown that the essential oil derived from *E. globulus* leaves has wound-healing properties. This suggests that Eucalyptus essential oil may accelerate the healing process for cold sores and ulcers[44]. Its many pharmacological characteristics, including antioxidant, antibacterial, and anti-inflammatory actions, which support healthy wound healing and reduce the risk of infection, are thought to be the mechanism of action of eucalyptus in wound healing. According to reports, eucalyptus alba is used to treat oxidative stress and wounds. Its extracts have been shown to inhibit α-glucosidase and stimulate cell proliferation, which helps to accelerate wound healing in diabetics[45].

4.3 *Anethum graveolens*

The plant species known as dill is *Anethum graveolens*. It is a native of North Africa, Iran, and the Arabian Peninsula. It is an annual plant of the celery family *Apiaceous*. Dill is a common plant that is used in cooking and medicine. In Indian traditional medicine, it has been used to treat "Vata," "kapha," ulcers, gastrointestinal discomfort, eye conditions, and uterine pain. It is also said to help with digestion[46]. Recent research has demonstrated the potential of *Anethum graveolens* (dill) in wound healing. Studies have shown that the application of *A. graveolens* extract on wounds induces significant wound contraction and accelerates the healing process in male rats[47]. Furthermore, it has been discovered that *A. graveolens* leaf extract reduces the area of the wound, increases the percentage of wound size reduction, and raises hydroxyproline and nitric oxide levels all of which are signs of better wound healing[48]. *A. graveolens* extract is a good option for local distribution via a drug delivery system to maximise its healing potential because of its anti-inflammatory and wound healing properties, which have been linked to its capacity to reduce inflammation and oxidative stress induced tissue damage[49]. Moreover, it has been



Figure 1. Plants with wound-healing properties.

demonstrated that *A. graveolens* essential oil is useful in lowering tissue bacterial counts and minimising the inflammatory phase of wounds, which speeds up the healing process[50].

4.4 *Calendula officinalis*

Calendula officinalis, commonly known as pot marigold, a member of the *Asteraceae* family, originates from southern Europe and the Eastern Mediterranean region. This versatile plant, functioning as an annual or short-lived perennial, has been utilized for both culinary and medicinal purposes throughout history. This plant, particularly exhibits significant wound healing activity by promoting collagen synthesis, increasing wound contraction, and influencing the levels of crucial factors like interleukin-6, Epidermal Growth Factor (EGF), Platelet Derived Factor (PDGF), and Tumor Necrosis Factor-alpha (TNF-α)[51,52]. Moreover, *C. officinalis* extract displays robust antibacterial properties, showcasing a remarkable 96% and 94% reduction in Gram-positive and Gram-negative bacteria, respectively. *In vitro* studies with fibroblast cells confirm heightened cell proliferation, growth, and attachment. Further, *in vivo* and histological analyses of rat wounds demonstrate the exceptional wound-healing abilities of CO dressings. This improvement is attributed to enhanced collagen synthesis, re-epithelization, and tissue remodelling[53]. The findings underscore the promising therapeutic potential of *C. officinalis* in promoting effective wound healing through diverse mechanisms.

4.5 *Morinda citrifolia* Linn

Morinda citrifolia Linn (*Rubiaceous*), Also referred to as Indian mulberry or noni, is a little evergreen tree. The oval-shaped, dark green, glossy leaves have prominent veins and are 8 to 10 inches in length. Parts of the plant were utilised by traditional Polynesian healers for a variety of ailments, including intestinal problems[54]. Noni extract demonstrated a significant enhancement in wound contraction rate, epithelialization rate, and granulation tissue weight. Granulation tissue, composed of fibroblasts, collagen, oedema, and new blood vessels, was notably increased in treated animals during the proliferative phase. The elevated content of dry granulation tissue implied a higher collagen presence, suggesting that the constituents in noni extract may promote collagen formation during the proliferative stage of wound healing[55]. The data demonstrate that noni leaf juice promotes wound healing by increasing the ligand bindings at the A_{2A} and PDGF receptors and also increasing the wound closure rate as its mechanism of action[56]. The antioxidant properties of NONI may thus also contribute to its antinociception and anti-inflammatory actions by preventing nuclear factor activation brought on by free radicals and the subsequent release of proinflammatory cytokines, which is a vicious cycle that feeds inflammation[57].

4.6 *Euphorbia hirta*

Euphorbia hirta, a fascinating herb nicknamed the "asthma plant," hails from the sun-soaked tropics of America. This member of the *Euphorbiaceous* family

holds a treasure trove of chemical compounds, many of which work wonders on our health. Studies reveal that *E. hirta* boasts a range of impressive properties: alleviating pain, curbing fever, easing anxiety, and even battling inflammation. Its potential doesn't stop there! In diabetic rats, oral administration of the plant's extract offered a sweet surprise: significantly lower blood glucose levels. While topical application didn't impact blood sugar, it might offer other benefits[58,59]. Researchers have diligently investigated this plant, uncovering a vibrant bouquet of active ingredients. Afzelin, quercitrin, and myricitrin, isolated from their extract, act as detoxifying agents, fight bacteria, bring down fevers, and even tame inflammation[60]. These properties suggest that *E. hirta* could aid in wound healing, reducing inflammation and swelling, ultimately promoting faster recovery and soothing pain[61,62].

4.7 *Pistacia atlantica*

The versatile *Pistacia atlantica*, not just an attractive tree in arid landscapes, possesses remarkable potential for wound healing. Hailing from western Asia and the Middle East, this resilient plant boasts a rich history of culinary, medicinal, and industrial uses. However, its recent exploration into healing wounds takes the spotlight. *P. atlantica* thrives in dry environments, but it flourishes in the realm of wound recovery[63]. *P. atlantica* extract accelerates wound healing by promoting skin cell growth, reducing inflammation, boosting collagen, improving blood vessel formation, and protecting cells from oxidative damage[64,65]. *P. atlantica* may work via receptors for PDGF, FGFRs (cell growth and collagen), and VEGFRs (new blood vessels)[64,66,67]. *Pistacia atlantica* contains various phytochemicals that contribute to its medicinal properties. These include fatty acids, phenolic compounds, and triterpenes, which exhibit anti-inflammatory, wound healing, antioxidant, and antimicrobial effects, respectively[68]. Research indicates its remarkable efficacy, both topically and orally, in speeding up wound closure in diabetic rats[69]. Studies reveal its ability to combat wound-infecting bacteria like *Staphylococcus aureus* and *Pseudomonas aeruginosa* while simultaneously calming inflammation, a crucial step in the healing process[70]. This anti-inflammatory action stems from the plant's influence on immune pathways, further showcasing its multifaceted healing process[68].

4.8 *Bidens pilosa*

Bidens pilosa is a plant species in the family *Asteraceae*, commonly known as beggar ticks, Spanish needle, or blackjack. It is native to the Americas but has spread to other parts of the world. In some places, it is considered a weed, while in others, it is used in traditional medicine. It shows promising potential in wound healing, but its exact mechanisms are still under investigation. *B. pilosa* extract has been found to promote reepithelialisation, reduce inflammation, stimulate collagen synthesis, and improve angiogenesis, all of which contribute to faster and more effective wound healing[71-73]. *B. pilosa* silences inflammatory talk via TNF and NF-kB receptors, turning down the heat on wound damage. It then dials up the healing volume on FGFRs, boosting collagen and cell growth for speedy repair. Overall, *B. pilosa* talks to a trio of receptors, whispering calm and shouting growth for faster, smoother healing[73,74]. *B. pilosa* contains flavonoids, terpenoids, and polysaccharides, which respectively combat oxidative stress and promote tissue regeneration, possess anti-inflammatory and antimicrobial properties, and play a role in cell signalling and wound repair, contributing to its potential for wound healing[71,75].

4.9 *Plantago lanceolata*

Ribwort plantain, also known as *Plantago lanceolata*, is a perennial herb that is commonly found in Europe, North America, and other temperate regions. It has been used in traditional medicine for various purposes, including as a remedy for coughs, wounds, and skin conditions. The leaves of the plant are often used in herbal preparations. Ribwort plantain helps wounds heal faster through multiple mechanisms. It fights inflammation with iridoid glycosides, reducing swelling and pain. Its antibacterial properties help prevent infections that slow healing. Astringent tannins shrink tissues, stop bleeding, and form a protective scab. Plantain also boosts collagen production and new blood vessel formation for optimal healing[76,77]. Ribwort plantain contains phytochemicals such as aucubin, catalpol, tannins, plantagoside C, acetonide, and vitamin C, which collectively contribute to its wound healing effects through anti-inflammatory, antibacterial, astringent, and collagen synthesis-promoting properties[77,78]. Ribwort plantain's wound healing action may involve interactions with specific

receptors, such as Toll-Like Receptors (TLRs) on immune cells, triggering anti-inflammatory and wound healing responses, and Fibroblast Growth Factor Receptors (FGFRs), which may be activated by compounds like aucubin and catalpol, stimulating fibroblast proliferation and collagen synthesis. Additionally, it has antioxidant qualities that lessen inflammation and promote rabbit wound contraction[76].

4.10 *Moltkia coerulea*

Moltkia coerulea, commonly known as the Himalayan Bluebell, is a flowering plant found in the high-altitude regions of the Himalayas. While it has been traditionally used in *Ayurvedic* medicine for various purposes, including wound healing, there is limited scientific evidence to support its efficacy and mechanism of action in this specific context[79]. *M. coerulea* contains active phytochemicals such as iridoids, phenolic acids, and flavonoids, which exhibit anti-inflammatory, antioxidant, and antibacterial properties. These compounds work together to stimulate fibroblast activity, reduce inflammation, combat infection, and enhance angiogenesis, ultimately promoting faster and more effective wound healing[80,81]. The active phytochemicals in *M. coerulea*, such as aucubin, moltkioside A, rosmarinic acid, caffeic acid, apigenin, and luteolin, are speculated to interact with key receptors and signalling pathways involved in inflammation and wound healing, including NF-κB, TLR4, PPARs, MAPK, and VEGF receptors. These interactions may contribute to the plant's anti-inflammatory, tissue regeneration, and angiogenic effects, ultimately promoting improved wound healing[82-84].

5. Risk Assessment in Herbal Medicine

The regulation of herbal medications is crucial to ensure their safety, quality, and efficacy. Challenges such as adverse reactions, inadequate safety monitoring, and varying definitions of herbal medicines among different countries have prompted the need for comprehensive regulation. The European Union's Directive on Traditional Herbal Medicinal Products requires all herbal medicinal products to meet standards of quality, safety, and efficacy before they can be marketed[85]. Similarly, the World Health Organization has issued guidelines to assist national regulatory authorities in assessing the safety and efficacy of herbal medicines. These efforts aim to address the challenges related to the regulatory status, safety monitoring, and quality control of herbal medicines, ultimately ensuring their safe and effective use[86,87]. While the potential for plant-based wound healing remedies holds promise, it's crucial to approach them with caution due to potential risks and side effects. Some plants like *Butea monosperma* lack comprehensive safety data,[88] while others like Eucalyptus oil and Dill oil can cause skin irritation, allergic reactions, and even toxicity if ingested[89,90]. Further research is needed on plants like Noni and *Pistacia atlantica* to fully understand their safety profiles and potential benefits for wound healing[65,91]. Ultimately, responsible utilization involves weighing the potential benefits against the risks, consulting healthcare professionals, and carefully selecting plants based on their proven therapeutic properties and safety profiles. Informed decision-making is key to a safe and effective journey towards natural wound healing.

6. Conclusion

A wide range of medicinal plants and their bioactive phytochemicals present promising alternatives and adjuncts for wound healing. These plants influence various stages of the healing process, including inflammation, reepithelialisation, and angiogenesis, while exhibiting beneficial properties such as anti-inflammatory, antibacterial, and antioxidant effects that help mitigate infection risk and create a conducive environment for tissue repair. However, critical gaps remain in understanding the precise mechanisms of action, efficacy, and potential adverse effects of these plants. A comprehensive scientific investigation is needed to elucidate these factors. Furthermore, the standardization of plant extracts and dosages is essential to ensure reproducibility and consistency of therapeutic outcomes. Although preliminary findings suggest substantial potential, rigorous integration of traditional knowledge with modern scientific methodologies will be crucial for advancing medicinal plants as reliable, accessible, and cost-effective tools in wound care.

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8. Author Contribution

SK, DG and MB conceived the review concept, conducted the literature search, and drafted the initial manuscript. GP and NS. critically reviewed and revised the manuscript, providing expert input on specific topic areas. CA and RM. contributed to the analysis and interpretation of the literature. All authors have read and agreed to the published version of the manuscript.

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