Review Article

The Role of Stem Cell Polyphenols in Wound Healing: A Narrative Review

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ABSTRACT

Stem cell polyphenols represent a promising avenue for enhancing wound healing through their multifaceted biological activities. Polyphenols, naturally occurring compounds with potent antioxidant properties, can modulate inflammatory responses, reduce oxidative stress, and promote the proliferation and migration of essential cells involved in tissue repair, such as fibroblasts and keratinocytes. Additionally, they play a critical role in angiogenesis, facilitating improved blood supply to healing tissues. Research indicates that the synergistic use of polyphenols with stem cell therapies could further optimize wound healing outcomes by enhancing stem cell function and survival. As conventional skin disease treatments, primarily corticosteroids, often provide only temporary relief and come with significant side effects, there is increasing interest in stem cell therapies for skin conditions. Stem cells have shown positive outcomes in treating eczema, psoriasis, diabetic wounds, and burns, utilizing both animal and plant stem cell products. However, plant-derived stem cells and natural products, including phytochemicals like resveratrol and curcumin, are preferred due to their reduced side effects and sustainability. These natural compounds aid all stages of wound healing by modulating signaling pathways associated with skin repair and regeneration, thereby minimizing residual wound effects. This review explores the effectiveness of specific natural products and introduces plant derivatives, including plant stem cells and cytokines, highlighting their potential in advancing therapeutic strategies for improved wound healing and skin regeneration. Further clinical investigations are needed to elucidate the optimal types and dosages of polyphenols for clinical applications in regenerative medicine.

KEYWORDS
Plant stem cells; Wound healing; Skin regeneration; Stem cell therapy; Natural compounds

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INTRODUCTION

Stem cells are undifferentiated cells that can divide indefinitely and differentiate into various cell types, playing a crucial role in regenerative processes [1]. In plant and animal organisms, stem cells reside in specific microenvironments called stem cell niches. These niches regulate stem cell behavior through signaling, balancing the production of daughter cells, and the self-renewal of stem cells [2]. Plants possess a remarkable ability to regenerate and dedifferentiate cells, while the regenerative capacity

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of animals varies significantly among species [2]. Invertebrates and amphibians generally exhibit high regenerative abilities, whereas vertebrates, like mice, have relatively limited regeneration capacity [3].

Despite these differences, the fundamental mechanism underlying regeneration in plants and animals involves differentiating stem cells into damaged or missing tissues[4]. Regenerative processes in animals and plants share several similarities. Firstly, they can be categorized into various levels, including cell, tissue, structural, organ, and systemic regeneration. Secondly, injury is the primary stimulus for developing specialized wound tissue that initiates regeneration[5]. Environmental factors like pathogens or predators can also trigger regenerative responses[6]. Following amputation, a regeneration blastema forms in animals, consisting of an outer epithelial layer encasing mesodermal-derived cells, which induces a canonical epithelial/mesenchymal interaction essential for developing complex structures [7, 8]. In plants, regeneration often involves the formation of callus tissue, an unstructured growth of proliferating cells at wound sites, which can give rise to new meristems and regenerate tissues[9-11]. The induction of stem cell regeneration from somatic cells in plants is analogous to the production of induced pluripotent stem cells (iPSCs) in animals. In animals, iPSC production relies on the expression of critical transcription factors [12]. Similarly, the initiation and maintenance of stem cells in plants depend on activating and expressing various crucial transcription factors, such as class B-ARR, WUSCHEL (WUS), and WUSCHEL related Homeobox5 (WOX5)[13, 14]. Therefore, plant stem cells expressing pluripotent genes like WUS or WOX5 can be considered plant iPSCs. Both animal and plant stem cells possess regenerative capabilities, although the extent of these abilities varies significantly among different species and body parts [15, 16].

Higher animals generally have weaker regenerative capacities, which differ considerably among tissues and organs. Skin and specific tissues regenerate quickly, while organs like the heart and stomach have limited regenerative abilities. Conversely, the liver has a relatively high regenerative capacity [17]. Specific nerve tissues, especially those with axonic connections, have almost no regenerative capacity, making certain types of brain damage and conditions like senile dementia largely irreversible without stem cells [6, 18]. In contrast, plants exhibit more robust regenerative abilities, which vary among species [19, 20]. For instance, species like *Taxus chinensis, Metasequoia glyptostroboides*, and *Ginkgo biloba* have weak regenerative capacities, whereas lower plants like *Ficus virens, Laminaria japonica*, and *Undaria pinnatifida* exhibit regenerative solid abilities[21-23].

Stem cells are categorized as pluripotent, totipotent, or unipotent, with significant differences between animal and plant stem cells [24]. Plants harbor pluripotent stem cells in the root apical meristem (RAM) and the shoot apical meristem (SAM), which serve as primary locations for stem cells over long periods [25]. These meristems can differentiate into various plant cell types, forming vegetative and reproductive organs [26]. Plants can also produce calluses, similar to stem cells, formed by somatic cells in response to injury and differentiation [27]. In animals, stem cells are widely distributed in various tissues and organs, though often in small numbers.

Due to evolutionary differences, significant variations exist in the signaling pathways and regulators governing plant and animal regeneration [15]. The feedback regulation between WUS and CLAVATA maintains stem cell homeostasis in the meristems [28]. The SHORT ROOT (SHR) signaling pathway also plays a critical role. In animals, classical signaling pathways like Wnt and Notch regulate the self-renewal of hematopoietic, intestinal epithelial, skin, and neural stem cells [29]. Plant stem cells offer several advantages over animal stem cells. For instance, plant stem cells remain active and capable of producing new organs and tissues throughout the plant's life [1]. They are also readily available in nature and require minimal resources for cultivation. In plants, stem cells are located in the meristems, allowing continuous growth due to unrestricted division[2]. During embryogenesis, the apical meristem of stems and roots contributes significantly to elongation. These meristematic stem cells activate under favorable conditions for organ development but remain inactive before and until germination[30]. The apical meristem contains distinguishable cell layers, including an outer epidermal layer and an inner layer comprising dense vascular tissues. Stem cells in the root meristem around the quiescent center (QC) exhibit low mitotic activity. At the QC, WOX 5 protein controls cap cell differentiation. Generally, auxin promotes root development, while

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cytokinin influences callus formation[1]. Plant stem cells are increasingly used in skincare and cosmetics for their antioxidant and anti-inflammatory properties [31]. These pluripotent stem cells can slow skin aging by providing protective factors[9]. Skincare products often include extracts from apples, tomatoes, argan, and grapes. For example, tomato stem cell extracts protect the skin from damage due to their antioxidant properties and ability to absorb heavy metals[32].

This review examines the potential of natural products derived from plant stem cells in treating skin diseases and promoting wound healing. This review aimed to build on existing knowledge by exploring the benefits of natural products like polyphenols, phenolic acids, and flavonoids, known for their antioxidant, anti-inflammatory, and anti-aging properties. The review also highlights the importance of plant stem cell culture technology in skincare and its potential to drive innovation in the cosmetic market. It offers a comprehensive understanding of the therapeutic potential of plant stem cell-derived products in skin health and regeneration.

RESULTS

The healing process of wounds generally consists of three phases: the first is the reduction of local inflammation around the wound site, the second involves deposition of immunological and inflammatory cells around the wound site, and the third stage is when the actual process of healing begins. Natural products modulate many signaling pathways in the body, an essential aspect of wound healing. In the early phase, the NF-kB signaling pathway is obstructed by the suppression of IL-6, IL-8, and IL-1B (Fig. 1)[33]. This inhibition aids in diminishing inflammation and priming the wound site for subsequent phases of healing. As apoptosis escalates, the residual immunological and inflammatory cells at the wound site are eliminated, hence facilitating the region for repair. Apoptosis normally escalates in the initial phases of wound formation and diminishes during the healing process. This process is regulated through the up regulation of P53, BAX, and BAK while downregulating BCL2 expression [34, 35].

TGFβ is one of the fibroblasts growthfactors and acts as an essential modulator during angiogenesis. TGF-β enhances collagen synthesis along with matrix repair enzyme activity in macrophages and fibroblasts, thus promoting angiogenesis and healing[36]. For instance, the polyphenolic chemical resveratrol, obtained from a variety of plants, has many health advantages. Its attributes encompass antioxidant, anti-inflammatory, anti-aging, and anti-tumor actions. Resveratrol, as an antioxidant, elevates the levels and activity of enzymes including glutathione reductase and glutathione-S-transferase [37].

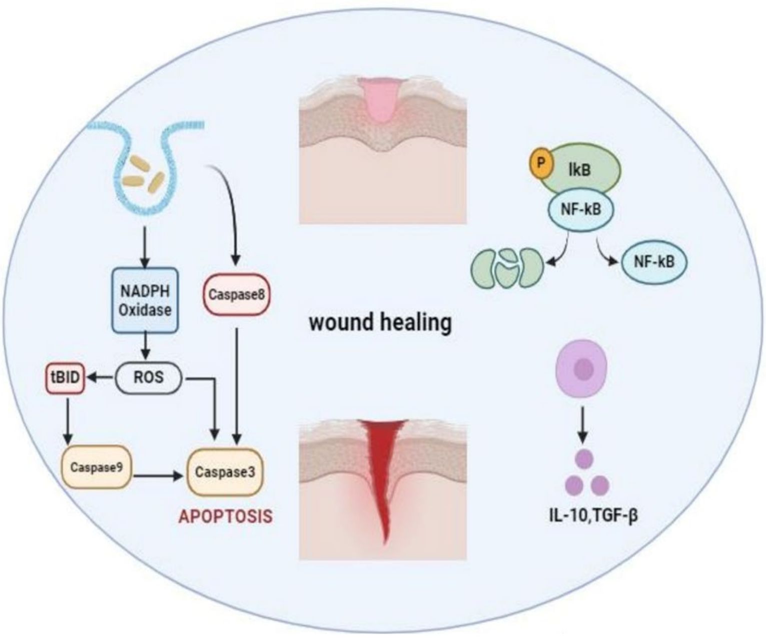

Figure 1: Wound repair and regeneration: Mechanisms, signaling, and translation

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The anti-inflammatory effects are mediated by many signaling mechanisms. Resveratrol inhibits cyclooxygenase, hence reducing the conversion of arachidonic acid to prostaglandins and lowering inflammation. Furthermore, it obstructs the activation of the NF-κB pathway during inflammatory responses, hence regulating the immune system's response to infection and inflammation [2, 3].

Resveratrol additionally demonstrates anti-aging properties by modulating microRNAs (miRNAs) and SIRT1. Resveratrol mitigates miRNA-induced apoptosis and counteracts aging via modulating miRNA expression. It also activates SIRT1, a sirtuin protein implicated in cellular survival and aging mechanisms. The activation of SIRT1 by resveratrol may postpone certain facets of aging and mitigate age-related losses, including diminished melatonin synthesis [37]. Resveratrol exhibits favorable effects on cellular growth and impedes cancer. It inhibits the IGF-1R/AKT/WNT signaling pathway and stimulates the P53 signaling pathway. These effects indicate its potential in oncological treatment and the regulation of processes such as mitosis, metastasis, and angiogenesis[37].

Curcumin is a polyphenol. This substance is found in Asian species, particularly turmeric. Curcumin has antioxidant and anti-inflammatory characteristics and may be used to treat many oxidative stress-related disorders, such as Alzheimer's disease, Parkinson's disease, and rheumatoid arthritis. Over and above that, Curcumin is a tumor suppressor, substance activates transcription factors which effects on gene expression during carcinogenesis, cell proliferation, survival, inflammation, and angiogenesis. Transcriptional activation proteins (Stat), β-catenin, and nuclear factor NF-KB are among them. Other mechanisms by which Curcumin affects cancer and tumorigenesis have been proposed[38]. It prevents angiogenesis and tumor invasion by binding to CD13/amino peptides, inducing apoptosis, and activating P53. For example, Curcumin activates P53 in prostate cancer and down regulates the MDMR oncogene through the PI3K/MTOR/ETS2 signaling pathway, contributing to the therapeutic process[39].

Bergamottin, derived from lemons and grapefruits, is a furanocoumarin compound renowned for its multifaceted properties. It exhibits potent anti-inflammatory and antioxidant effects and notable anti-cancer properties affecting various cancers, including skin and breast cancer.

One of the remarkable attributes of Bergamottin is its ability to inhibit cytochrome P450 and induce apoptosis via tumor necrosis factor activity, leading to the inactivation of NF-κB signaling pathways[40]. Moreover, bergamottin demonstrates significant antioxidant characteristics by reducing oxidative stress by scavenging free radicals. This action contributes to delaying aging processes and preventing chronic illnesses associated with elevated oxidative stress levels[41, 42].

Chronic diseases such as diabetes, neurological disorders, cardiovascular diseases, and cancer are often linked to inflammation. Bergamottin and another furanocoumarin complex inflammatory processes by modulating tumor necrosis factor, interleukin-6, and prostaglandin E2. Bergamottin attenuates these inflammatory factors and reduces nitrite production, highlighting its anti-inflammatory effects[41, 42]. Furthermore, grapefruit-derived furanocoumarins, including bergamottin, exhibit anti-cancer properties by affecting cancer cell signaling pathways such as the NF-κB pathway and mitogen-activated protein kinase. These mechanisms hinder cancer cell proliferation and growth, suggesting the potential of bergamottin in cancer prevention and treatment[42].

Chalcones, classified as phenolic compounds within the flavonoid group, are renowned for their remarkable biological activities, including anti-inflammatory, anticancer, antioxidant, and antibacterial properties. These beneficial effects render chalcones significant constituents found in various vegetables and fruits.

One of the critical attributes of chalcones lies in their antioxidant properties, which play a crucial role in reducing oxidative stress within tissues. By inhibiting the production of free radicals, chalcones maintain cellular homeostasis and defend cells against oxidative damage[43, 44]. Notably, chalcones modulate the expression of antioxidant genes by activating the Nrf2-related transcription factor nuclear factor-erythroid (NF-E2) p45. This activation leads to the upregulation of genes involved in cellular defense processes, such as glutathione S-transferase (GST) and heme oxygenase 1 (HO-1), ultimately reducing inflammation[43].

Furthermore, chalcones exert their anti-inflammatory effects by targeting the NF-κB signaling pathway, which is pivotal in inflammatory

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diseases and cancer progression. By inhibiting vital inflammatory cytokines and factors, chalcones suppress the activation of NF-κB, thereby mitigating inflammatory responses[45]. Additionally, chalcones induce apoptosis in cancer cells by modulating the expression of pro-apoptotic and anti-apoptotic molecules, ultimately leading to cell death. Notably, chalcones such as ionic cocaine demonstrate promising anticancer effects by activating caspase enzymes and increasing the expression of apoptotic markers, including P53 and Bax[45]. Chalcones represent a class of phenolic compounds with potent therapeutic potential. They offer diverse health benefits, ranging from antioxidant and anti-inflammatory effects to anticancer properties. Their multifaceted mechanisms of action make them promising candidates for developing novel therapeutic interventions targeting various diseases, including cancer and inflammatory disorders.

Apigenin, a flavonoid found abundantly in various plants such as thyme, chamomile, parsley, celery, oranges, and tea, stands out for its remarkable therapeutic potential owing to its antioxidant and anti-inflammatory properties. Apigenin exhibits robust antioxidant characteristics, effectively combatting oxidative stress through diverse mechanisms. By inhibiting the function of free radicals and reducing the expression of adhesion molecules associated with inflammation, Apigenin helps maintain cellular homeostasis[46]. Furthermore, it enhances the production of essential antioxidant enzymes like catalase, superoxide dismutase (SOD), and glutathione synthase, thereby neutralizing reactive oxygen species and mitigating oxidative damage[46]. Additionally, suppresses the levels of pro-inflammatory cytokines such as interleukin-6 and tumor necrosis factor-alpha, contributing to its potent anti-inflammatory effects [46]. In cancer cells, Apigenin induces apoptosis by modulating various genes and pathways involved in cell survival and proliferation. By arresting the cell cycle at specific phases and activating intrinsic apoptotic pathways, Apigenin triggers programmed cell death, offering promising therapeutic potential in cancer treatment [47]. Moreover, Apigenin effectively manages inflammatory diseases by activating signaling pathways such as PI3K/AKT and P38/MAPK while inhibiting NF-κB signaling, attenuating inflammatory responses[47]. Apigenin's benefits extend to diabetic conditions. It exhibits anti-diabetic properties by inhibiting alpha-glucosidase activity, enhancing insulin secretion, and neutralizing reactive oxygen species, helping alleviate hyperglycemia dysfunction[47]. In prostate cancer, Apigenin exerts its anti-cancer effects by modulating critical signaling pathways such as PI3K/AKT/FOXO and insulin-like growth factors, ultimately inhibiting cancer cell proliferation and promoting apoptosis[48].

Overall, Apigenin emerges as a potent natural compound (Table 1) with diverse therapeutic applications. It offers significant promise in the management of various chronic diseases, including cancer, diabetes, and inflammatory conditions. Its multifaceted pharmacological effects underscore its potential as a valuable therapeutic agent derived from natural sources.

Quercetin, a polyphenolic compound abundant in fruits and vegetables such as apples, broccoli, and cherries, emerges as a potent natural remedy

Table 1: Natural phenolic compounds, their plant sources, and applications

Natural Compound	Plant / Fruit Source	Application	References
Resveratrol	Grapes	Induction of apoptotic genes	Kazemi et al.[56]
Bergamottin	Grapefruit, Lemon	Inhibition of NF-κB and IL-6 induced inflammation	Shahbazi et al.[58]
Chalcone	Potatoes, Orange	Activation of caspases 8 and 9, and induction of apoptosis	Orouji et al.[59]
Apigenin	Chamomile, Grapefruit, Oats, Yarrow, Avena sativa	Induction of apoptosis, activation of p53, and induction of caspase 9 and 3 release	Mirghaffari et al.[60]
Quercetin	Yarrow, Chamomile, Grapefruit, Oats, Grapes, Strawberries, Parsley	Modulation of apoptosis-related proteins	Shahbazi et al.[61]
Naringin	Lemon, Grapefruit	Inhibition of inflammation (TNF-α, IL-1β, IL-6), increase of anti-inflammatory cytokines (TGF-β, IL-10), regulation of oxidative stress	Smith et al.[57]

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with diverse therapeutic properties, including anti-inflammatory, antioxidant, and anti-cancer effects.

Quercetin showcases remarkable anti-inflammatory effects by inhibiting the production of interleukin-8 (IL-8) and tumor necrosis factor-alpha (TNF-α), crucial inflammatory mediators implicated in various diseases[49]. By suppressing the expression of inflammatory enzymes like cyclooxygenase (COX) and lipoxygenase (LOX), Quercetin effectively mitigates inflammatory processes[50]. Moreover, it inhibits the release of pro-inflammatory cytokines from mast cells and protects endothelial cells from inflammation-induced damage[51].

Quercetin's antioxidant prowess is evident in its ability to regulate enzyme levels involved in scavenging free radicals, thereby reducing oxidative stress and preventing cellular damage[52]. Quercetin demonstrates promising cancer prevention and treatment potential by neutralizing reactive oxygen species (ROS) and suppressing signaling pathways associated with tumor proliferation and migration[53].

Naringin, a flavonoid glycoside abundant in grapefruit, oranges, and other citrus fruits, has a wide range of pharmacological actions, including antioxidant, anti-inflammatory, and wound-healing properties. Naringin exhibits significant wound-healing effects by promoting skin cell proliferation and migration, accelerating healing[52]. Studies have demonstrated its efficacy in enhancing wound closure rates and tissue quality in animal models, highlighting its potential as a therapeutic agent for wound management[54].

Naringin's ability to modulate transforming growth factor-beta (TGF-β) expression further contributes to its wound-healing effects. Naringin facilitates tissue regeneration and repair by boosting TGF-β expression in skin cells, enhancing overall wound healing(Fig. 2) [54, 55].

Quercetin and naringin exemplify nature's bounty of healing compounds, offering promising therapeutic avenues for combating inflammation and oxidative stress and promoting wound healing. Further research into their mechanisms of action and clinical efficacy holds significant potential for developing novel therapeutic interventions derived from natural sources.

DISCUSSION

The regenerative prowess of plants and animals has long captivated researchers, offering insights into novel therapeutic strategies for wound healing and inflammation reduction. Animal regeneration involves activating specialized stem cells and orchestrating tissue repair and rejuvenation. Similarly, plants harness the regenerative

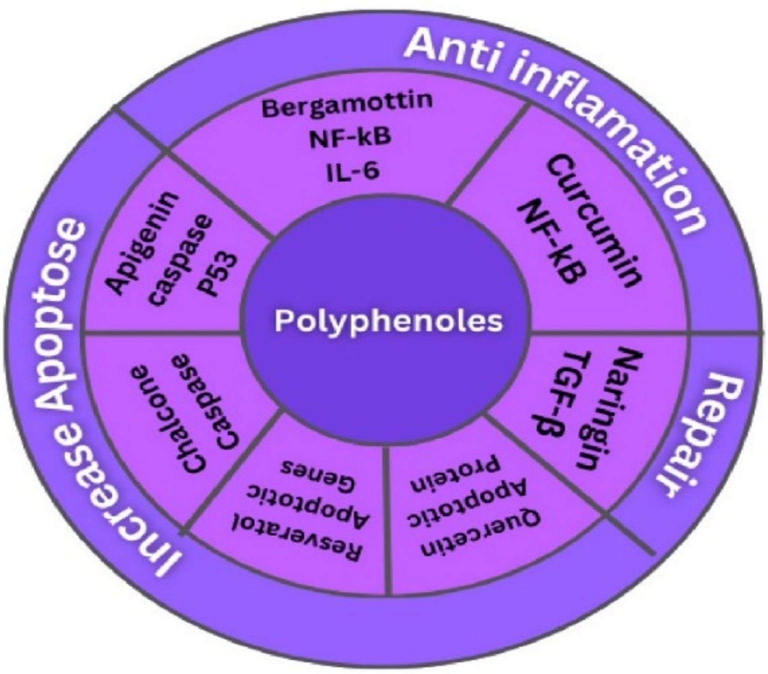

Figure 2: Polyphenols are bioactive compounds found in various plant-based foods that modulate cytokine signaling pathways, which regulate immune response and inflammation

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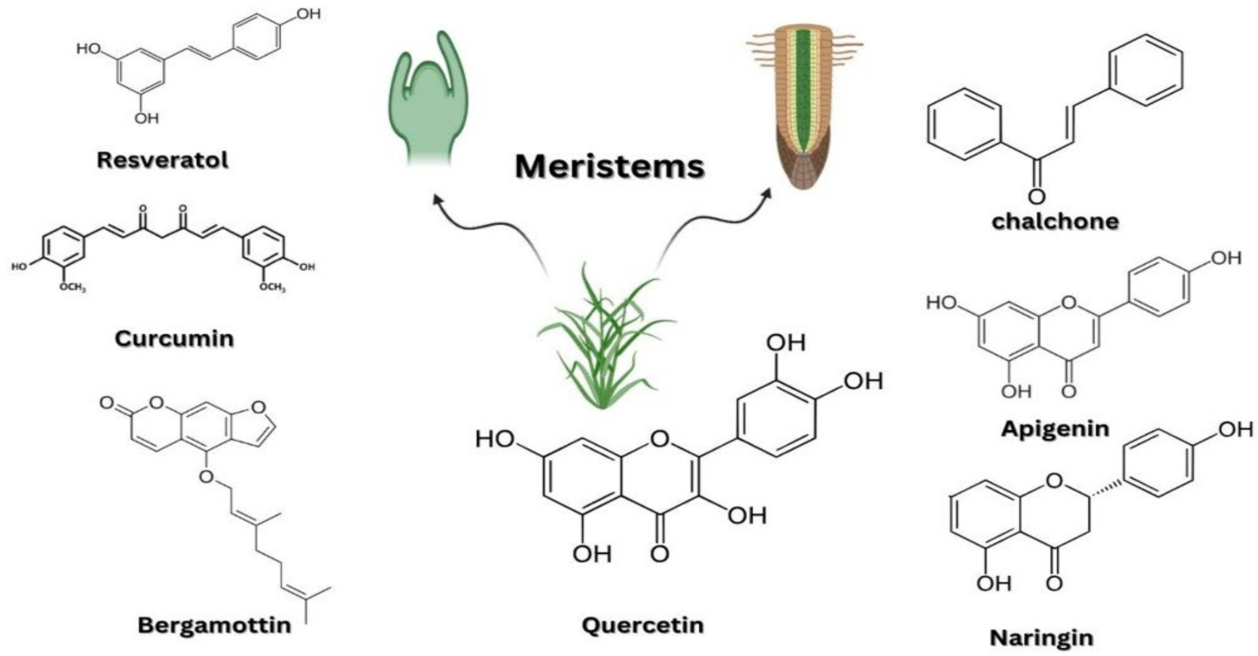

Figure 3: The chemical structure of some polyphenols

capabilities of meristematic cells, enabling the growth of new tissues from various plant parts[4]. The wound-healing process unfolds in a meticulously orchestrated sequence of stages. It commences with inflammation, where immune cells rally to the injury site. Subsequent phases witness the proliferation of new blood vessels and collagen synthesis, culminating in tissue maturation and fortification[5]. Natural products have emerged as promising candidates for enhancing wound healing and alleviating inflammation. Notable examples include Resveratrol, Curcumin, bergamottin, and Apigenin, each endowed with distinct therapeutic properties (Fig. 3) [6].

Resveratrol, abundant in berries and grapes, accelerates wound healing by promoting blood vessel formation and collagen synthesis. Curcumin, derived from turmeric, exerts anti-inflammatory effects, facilitating tissue regeneration[7]. Bergamottin, sourced from citrus fruits, combats infection, and inflammation, fostering wound healing. Apigenin in fruits and vegetables stimulates skin cell proliferation and collagen synthesis, further expediting healing[8]. Despite their promise, evaluating natural products' efficacy poses challenges. Standardized protocols and dosages are imperative for meaningful comparisons across studies. Publication bias and conflicts of interest warrant scrutiny, emphasizing the importance of transparency and adherence to rigorous research methodologies. While preclinical studies provide valuable insights, clinical trials are indispensable for validating findings and determining safety and optimal dosages. Addressing, potential conflicts of interest and ensuring methodological rigor are paramount for fostering trust and credibility in research outcomes.

Over view, natural products' therapeutic potential in wound healing and inflammation reduction holds immense promise. However, navigating challenges related to study design, publication bias, and conflicts of interest is essential for effectively advancing our understanding and harnessing nature's healing bounty. Through concerted efforts and meticulous research, the journey toward innovative therapeutic interventions for various skin conditions remains within reach.

CONCLUSION

In this investigation, we delved into the healing properties of natural substances and were reviewed certain chemicals, including as resveratrol, curcumin, bergamottin, apigenin, quercetin, and naringin, have the ability to improve wound healing. In order to properly validate these treatments, consistent procedures, open reporting, and thorough clinical trials are required. Our researches

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emphasized on the significance of upholding transparency and scientific integrity in the face of possible conflicts of interest. Natural remedies to treat skin diseases and increase our understanding of therapy by encouraging cooperation, upholding moral principles, and placing a high value on scientific rigor.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interests.

REFERENCES

1. Moruś M, Baran M, Rost-Roszkowska M, Skotnicka-Graca U Book. Plant stem cells as innovation in cosmetics. 2014.
2. Heidstra R, Sabatini S. Plant and animal stem cells: similar yet different. *Nat Rev Mol Cell Biol* 2014;**15**(5):301-12.
3. Trehan S, Michniak-Kohn B, Beri K. Plant stem cells in cosmetics: current trends and future directions. *Future Sci OA* 2017;**3**(4):FSO226.
4. Iismaa SE, Kaidonis X, Nicks AM, et al. Comparative regenerative mechanisms across different mammalian tissues. *NPJ Regen Med* 2018;**3**(1):6.
5. Tyler SE. Nature's electric potential: a systematic review of the role of bioelectricity in wound healing and regenerative processes in animals, humans, and plants. *Front Physiol* 2017;**8**:627.
6. Birnbaum KD, Alvarado AS. Slicing across kingdoms: regeneration in plants and animals. *Cell* 2008;**132**(4):697-710.
7. Alvarado AS, Tsonis PA. Bridging the regeneration gap: genetic insights from diverse animal models. *Nat Rev Genet* 2006;**7**(11):873-84.
8. Liang Z, Yang L, Lv Y. Exosome derived from mesenchymal stem cells mediates hypoxia-specific BMP2 gene delivery and enhances bone regeneration. *J Chem Eng* 2021;**422**:130084.
9. Sablowski R. Plant and animal stem cells: conceptually similar, molecularly distinct? *Trends Cell Biol* 2004;**14**(11):605-11.
10. Ozias-Akins P, Vasil IK. Plant regeneration from cultured immature embryos and inflorescences of Triticum aestivum L.(wheat): evidence for somatic embryogenesis. *Protoplasma* 1982;**110**:95-105.
11. Bhaskaran S, Smith RH. Regeneration in cereal tissue culture: a review. *Crop Sci* 1990;**30**(6):1328-37.
12. Wu Q, Yang B, Hu K, Cao C, Man Y, Wang P. Deriving osteogenic cells from induced pluripotent stem cells for bone tissue engineering. *Tissue Eng Part B Rev* 2017;**23**(1):1-8.
13. Jha P, Ochatt SJ, Kumar V. WUSCHEL: a master regulator in plant growth signaling. *Plant Cell Rep* 2020;**39**:431-44.
14. Lee K, Kim JH, Park O-S, Jung YJ, Seo PJ. Ectopic expression of WOX5 promotes cytokinin signaling and de novo shoot regeneration. *Plant Cell Rep* 2022;**41**(12):2415-22.
15. Liu L, Qiu L, Zhu Y, et al. Comparisons between plant and animal stem cells regarding regeneration potential and application. *Int J Mol Sci* 2023;**24**(5):4392.
16. Somorjai IM, Lohmann JU, Holstein TW, Zhao Z. Stem cells: a view from the roots. *Biotechnol J* 2012;**7**(6):704-22.
17. Chen Y, Lüttmann FF, Schoger E, et al. Reversible reprogramming of cardiomyocytes to a fetal state drives heart regeneration in mice. *Science* 2021;**373**(6562):1537-40.
18. Imran SA, M. Hamizul MHA, Khairul Bariah AAN, Wan Kamarul Zaman WS, Nordin F. Regenerative medicine therapy in Malaysia: an update. *Front Bioeng* 2022;**10**:789644.
19. Park KI, Ourednik J, Ourednik V, et al. Global gene and cell replacement strategies via stem cells. *Gene Ther* 2002;**9**(10):613-24.
20. Wei X, Fu S, Li H, et al. Single-cell Stereo-seq reveals induced progenitor cells involved in axolotl brain regeneration. *Science* 2022;**377**(6610):eabp9444.
21. Li Y-Y, Tsang EPK, Cui M-Y, Chen X-Y. Too early to call it success: an evaluation of the natural regeneration of the endangered Metasequoia glyptostroboides. *Biol Conserv* 2012;**150**(1):1-4.
22. Hu Z, Chen J-T, Jiang S-C, Liu Z, Ge S-B, Zhang Z. Chemical components and functions of Taxus chinensis extract. *J King Saud Univ Sci* 2020;**32**(2):1562-8.
23. Hu Y, Šmarda P, Liu G, Wang B, Gao X, Guo Q. High-depth transcriptome reveals differences in natural haploid Ginkgo biloba L. due to the effect of reduced gene dosage. *Int J Mol Sci* 2022;**23**(16):8958.

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24. Kolios G, Moodley Y. Introduction to stem cells and regenerative medicine. *Respir* 2012;**85**(1):3-10.
25. Carles CC, Fletcher JC. Shoot apical meristem maintenance: the art of a dynamic balance. *Trends Plant Sci* 2003;**8**(8):394-401.
26. Smith LG, Greene B, Veit B, Hake S. A dominant mutation in the maize homeobox gene, Knotted-1, causes its ectopic expression in leaf cells with altered fates. *Development* 1992;**116**(1):21-30.
27. Sugimoto K, Gordon SP, Meyerowitz EM. Regeneration in plants and animals: dedifferentiation, transdifferentiation, or just differentiation? *Trends Cell Biol* 2011;**21**(4):212-8.
28. Fletcher JC. The CLV-WUS stem cell signaling pathway: a roadmap to crop yield optimization. *Plants* 2018;**7**(4):87.
29. Yan S, Bin S, Ronghua Y, Lijun Z, Xiaoyin X, Yingbin X. Expression and effect of Wnt and Notch signalings in mammalian cutaneous wound healing. *Chin J Inj Repair Wound Heal* 2014;**2**:151-7.
30. Greb T, Lohmann JU. Plant Stem Cells. *Curr Biol* 2016;**26**(17):816-21.
31. Aggarwal S, Sardana C, Ozturk M, Sarwat M. Plant stem cells and their applications: special emphasis on their marketed products. *3 Biotech* 2020;**10**(7):291.
32. You Y, Jiang C, Huang L-Q. On plant stem cells and animal stem cells. *Chin J Chin Mat Med* 2014;**39**(2):343-5.
33. Park YR, Sultan MT, Park HJ, et al. NF-κB signaling is key in the wound healing processes of silk fibroin. *Acta Biomater* 2018;**67**:183-95.
34. Tang S-C, Ko J-L, Lu C-T, et al. Chloroquine alleviates the heat-induced to injure via autophagy and apoptosis mechanisms in skin cell and mouse models. *Plos one* 2022;**17**(8):e0272797.
35. Tan J-Q, Zhang H-H, Lei Z-J, et al. The roles of autophagy and apoptosis in burn wound progression in rats. *Burns* 2013;**39**(8):1551-6.
36. Bayram P, Aksak Karamese S, Ozdemir B, Salum C, Erol HS, Karamese M. Two flavonoids, baicalein and naringin, are effective as anti-inflammatory and anti-oxidant agents in a rat model of polymicrobial sepsis. *Immunopharmacol Immunotoxicol* 2023;**45**(5):597-606.
37. Zhang L-X, Li C-X, Kakar MU, et al. Resveratrol (RV): A pharmacological review and call for further research. *Biomed Pharmacother* 2021;**143**:112164.
38. Vaiserman A, Koliada A, Zayachkivska A, Lushchak O. Curcumin: A therapeutic potential in ageing-related disorders. *PharmaNutr* 2020;**14**:100226.
39. Fadus MC, Lau C, Bikhchandani J, Lynch HT. Curcumin: An age-old anti-inflammatory and anti-neoplastic agent. *J Tradit Med Complement Ther* 2017;**7**(3):339-46.
40. Kim S-M, Lee E-J, Lee JH, et al. Simvastatin in combination with bergamottin potentiates TNF-induced apoptosis through modulation of NF-κB signalling pathway in human chronic myelogenous leukaemia. *Pharm Biol* 2016;**54**(10):2050-60.
41. Lombardo GE, Cirmi S, Musumeci L, et al. Mechanisms underlying the anti-inflammatory activity of bergamot essential oil and its antinociceptive effects. *Plants* 2020;**9**(6):704.
42. Hung W-L, Suh JH, Wang Y. Chemistry and health effects of furanocoumarins in grapefruit. *J Food Drug Anal* 2017;**25**(1):71-83.
43. Jasim HA, Nahar L, Jasim MA, Moore SA, Ritchie KJ, Sarker SD. Chalcones: Synthetic chemistry follows where nature leads. *Biomol* 2021;**11**(8):1203.
44. Dhaliwal JS, Moshawih S, Goh KW, et al. Pharmacotherapeutics applications and chemistry of chalcone derivatives. *Molecules* 2022;**27**(20):7062.
45. Orlikova B, Tasdemir D, Golais F, Dicato M, Diederich M. Dietary chalcones with chemopreventive and chemotherapeutic potential. *Genes & nutrition* 2011;**6**:125-47.
46. Pisoschi AM, Pop A. The role of antioxidants in the chemistry of oxidative stress: A review. *Eur J Med Chem* 2015;**97**:55-74.
47. Salehi B, Venditti A, Sharifi-Rad M, Kręgiel D, Sharifi-Rad J, Durazzo A. The Therapeutic Potential of Apigenin. *Int J Mol Sci* 2019;**20**.
48. Javed Z, Sadia H, Iqbal MJ, et al. Apigenin role as cell-signaling pathways modulator: implications in cancer prevention and treatment. *Cancer Cell Int* 2021;**21**:1-11.
49. Al-Khayri JM, Sahana GR, Nagella P, Joseph BV, Alessa FM, Al-Mssallem MQ. Flavonoids as potential anti-inflammatory molecules: A review. *Molecules* 2022;**27**(9):2901.
50. García-Lafuente A, Guillamón E, Villares A, Rostagno MA, Martínez JA. Flavonoids as anti-inflammatory agents: implications in cancer and cardiovascular disease. *Inflamm Res* 2009;**58**(9):537-52.
51. Weng Z, Patel AB, Panagiotidou S, Theoharides TC. The novel flavone tetramethoxyluteolin is a potent inhibitor of human mast cells. *J Aller Clin Immunol* 2015;**135**(4):1044-52. e5.
52. Adewole SO, Caxton-Martins EA, Ojewole JA. Protective effect of quercetin on the morphology of pancreatic β-cells of streptozotocin-treated diabetic rats. *Afr J Tradit Complement Altern Med* 2007;**4**(1):64-74.
53. Slika H, Mansour H, Wehbe N, et al. Therapeutic potential of flavonoids in cancer: ROS-mediated mechanisms. *Biomed Pharmacother* 2022;**146**:112442.
54. Kandhare AD, Alam J, Patil MV, Sinha A, Bodhankar

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[DOI: 10.61882/wjps.14.3.27]

SL. Wound healing potential of naringin ointment formulation via regulating the expression of inflammatory, apoptotic and growth mediators in experimental rats. *Pharm Biol* 2016;**54**(3):419-32.
55. Kandhare AD, Ghosh P, Bodhankar SL. Naringin, a flavanone glycoside, promotes angiogenesis and inhibits endothelial apoptosis through modulation of inflammatory and growth factor expression in diabetic foot ulcer in rats. *Chem Biol Interact* 2014;**219**:101-12.
56. Kazemi A, Safa M, Shahbazi A. RITA enhances chemosensivity of pre-B ALL cells to doxorubicin by inducing p53-dependent apoptosis. *Hematology* 2011;**16**(4):225-31.
57. Bajouri A, Orouji Z, Taghiabadi E, Nazari A, Shahbazi A, Fallah N, Mohammadi P, Rezvani M, Jouyandeh Z, Vaezirad F, Khalajasadi Z. Long-term follow-up of autologous fibroblast transplantation for facial contour deformities, a non-randomized phase IIa clinical trial. *Cell Journal (Yakhteh)* 2019;**22**(1):75.
58. Shahbazi A, Zargar SJ, Aghdami N, Habibi M. The story of melanocyte: a long way from bench to bedside. *Cell and tissue banking* 2024;**25**(1):143-57.
59. Orouji Z, Bajouri A, Ghasemi M, Mohammadi P, Fallah N, Shahbazi A, Rezvani M, Vaezirad F, Khalajasadi Z, Alizadeh A, Taghiabadi E. A single-arm open-label clinical trial of autologous epidermal cell transplantation for stable vitiligo: A 30-month follow-up. *J Dermatol Sci* 2018;**89**(1):52-9.
60. Mirghaffari M, Mahmoodiyan A, Mahboubizadeh S, Shahbazi A, Soleimani Y, Mirghaffari S, Shahravi Z. Electro-spun piezoelectric PLLA smart composites as a scaffold on bone fracture: A review. *Regenerative Therapy* 2025;**28**:591-605.
61. Shahbazi A, Zargar SJ, Bajouri A, Mohammadi P, Aghdami N. Differential Gene Expression and Tumorigenicity Analysis of Cultured Melanocyte Comparing Melanoma. *Int J Mol Cellular Med* 2024;**13**(4):387.

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