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REVIEW ARTICLE

From Botanical Extracts to Pharmacological Pathways: Exploring the Anti-keloid Effects of Plant-derived Compounds

Vasanth Kumar Mohan[1], Mukesh Kumar Dharmalingam Jothinathan[2], Kayal Louis[3], P. Dharani Prasad[4] and Malarkodi Velraj[5,*]

[1]*Department of Pharmacognosy, Faculty of Pharmacy, Bharath Institute of Higher Education and Research, Selaiyur, Chennai, Tamil Nadu, India;* [2]*Centre for Global Health Research, Saveetha Medical College and Hospitals, Saveetha Institute of Medical and Technical Sciences (SIMATS), Saveetha University, Chennai, Tamil Nadu, India;* [3]*Deparment of Dental Surgery, Govt. Stanley Medical College, The TN Dr MGR Medical University, Chennai, 600001, Tamil Nadu, India;* [4]*Department of Pharmacology, MB School of Pharmaceutical Sciences, Mohan Babu University, Tirupati, Andhra Pradesh, India;* [5]*Department of Pharmacognosy, School of Pharmaceutical Sciences, Vels Institute of Science Technology and Advanced Studies, Old Pallavaram, Chennai, 117, Tamil Nadu, India*

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Abstract: Keloids are a challenging dermatological condition, characterized by abnormal wound healing and excessive fibrosis, resulting in raised, disfiguring scars that can significantly impact patients' quality of life. Despite the availability of various treatments, including corticosteroid injections, laser therapy, and surgical excision, effective and consistent therapeutic options remain elusive due to high recurrence rates and limited efficacy. This study investigates the potential of botanical extracts to influence keloid formation and modulate underlying cellular and molecular processes. Using a combination of *in vitro* and *in vivo* models, we screened a diverse range of plant-derived compounds for their effects on fibroblast proliferation, collagen synthesis, and extracellular matrix remodeling. Detailed molecular analyses have revealed that several compounds exhibit strong anti-keloid activity by targeting key pro-fibrotic signaling pathways, such as TGF-β/Smad and MAPK/ERK. These compounds also demonstrated the ability to induce fibroblast apoptosis, reduce excessive collagen deposition, and normalize extracellular matrix organization. Furthermore, our findings suggest that these plant-based compounds may act synergistically with current treatments to enhance their efficacy while minimizing side effects. The study highlights the therapeutic promise of botanical extracts in managing keloids and underscores the importance of natural products as a source of innovative treatments. Future research should focus on optimizing the pharmacological properties of these compounds for clinical applications, investigating their long-term safety and efficacy, and exploring their potential integration into multimodal therapeutic strategies. These efforts could pave the way for the development of novel, targeted approaches to improve keloid management and patient outcomes.

Keywords: Keloid, botanical extracts, anti-fibrotic, wound healing, cellular pathways, plant-derived compounds.

1. INTRODUCTION

Keloids are abnormal scars that result from dysregulated wound healing, often causing physical discomfort, psychological distress, and aesthetic concerns. Their raised, hyperpigmented appearance and tendency to recur make them particularly challenging to treat [1]. The exact mechanisms behind keloid formation involve excessive fibroblast activity, collagen deposition, and prolonged inflammation, but they remain only partially understood. Current treatments, including surgical removal, steroid injections, and laser therapy, are often ineffective and carry high rates of recurrence [2]. This unmet need for effective therapies has driven research into alternative treatments, including botanical extracts. Plant-derived compounds offer a promising avenue due to their diverse pharmacological properties and anti-inflammatory, anti-fibrotic, and wound-healing effects. Investigating these compounds may lead to more targeted, natural therapeutic options for mitigating keloid formation and improving patient outcomes. This introduction sets the stage for exploring the anti-keloid effects of plant-derived compounds by providing insights into the complex molecular and cellular mechanisms underlying keloid formation and progression [3]. Understanding keloid pathogenesis is essential for developing targeted strategies to mitigate their deleterious effects and improve patient outcomes.

*Address correspondence to this author at the Department of Pharmacognosy, School of Pharmaceutical Sciences, Vels Institute of Science Technology and Advanced Studies, Old Pallavaram, Chennai, 117, Tamil Nadu, India; E-mail: malarkodiv.sps@velsuniv.ac.in

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While previous studies have explored the role of botanical extracts in scar management, the molecular mechanisms underlying their anti-keloid effects remain underexplored. This study uniquely investigates specific plant-derived compounds, curcumin, epigallocatechin gallate (EGCG), asiaticoside, and glycyrrhizin, by elucidating their effects on the TGF-β/Smad and MAPK/ERK pathways. By focusing on fibroblast proliferation, collagen synthesis, and apoptosis, this study provides a deeper mechanistic understanding of how these compounds modulate keloid progression. These insights set the foundation for targeted, plant-based anti-keloid therapies.

2. STUDY SELECTION AND METHODOLOGY

A literature search was conducted using PubMed, Scopus, Web of Science, and Google Scholar. The following keywords and Boolean operators were applied: 'keloid treatment' AND 'botanical extracts' OR 'phytochemicals' AND 'fibroblast inhibition' OR 'collagen synthesis' AND 'TGF-β/Smad' OR 'MAPK/ERK pathway'. The search covered studies published from 2000 to 2024 and additional references were manually retrieved from selected papers.

Studies were included if they investigated plant-derived compounds in keloid models (*in vitro*, *in vivo*, or clinical trials) and provided mechanistic insights into fibrosis-related pathways. Exclusion criteria included review articles lacking primary data, non-keloid fibrosis studies, and retracted or outdated papers published before 2000.

Two independent reviewers screened all titles and abstracts, with full-text articles assessed for eligibility based on predefined criteria. Discrepancies were resolved through discussion or a third-reviewer consultation to ensure selection accuracy.

3. BOTANICAL EXTRACTS: A PROMISING THERAPEUTIC AVENUE

Botanical extracts have emerged as promising therapeutic agents for a range of dermatological conditions, including keloids [4]. These extracts contain a wealth of bioactive compounds that exhibit pharmacological properties such as anti-inflammatory, antioxidant, anti-fibrotic, and wound-healing effects. For instance, *Aloe vera* is widely recognized for its ability to reduce inflammation and promote healing, while *Centella asiatica* has been shown to modulate collagen production and improve scar formation. *Curcumin*, the active component in turmeric, also demonstrates the potential to inhibit excessive collagen deposition, making it a compelling option for keloid management. Botanical extracts are accessible, affordable, and culturally accepted in many regions, making them attractive candidates for both topical and systemic use. However, despite their potential, there are notable challenges. One major limitation is the bioavailability of certain plant compounds, as many active ingredients may degrade during processing or have low absorption rates when applied topically. Additionally, the variability in composition between different plant batches due to factors such as soil quality and harvesting conditions can lead to inconsistent therapeutic effects. Ensuring standardization in extraction and formulation methods will be essential to overcoming these limitations [5].

Overall, while botanical extracts offer a natural and multi-target approach to keloid management, addressing these challenges is critical to optimizing their therapeutic potential and ensuring consistent outcomes in clinical applications. This section explores the potential of botanical extracts as a novel therapeutic avenue for mitigating keloid formation and progression, highlighting their natural origins, multi-target effects, and potential synergies with conventional therapies. Understanding the pharmacological properties and mechanisms of action of botanical extracts is crucial for harnessing their therapeutic potential and advancing personalized approaches to keloid treatment [6].

4. EXTRACTION OF BOTANICAL COMPOUNDS

Plant materials were dried at 40°C and ground into fine powder. For curcumin extraction, 10 g of *Curcuma longa* powder was subjected to Soxhlet extraction using 95% ethanol at 60°C for 6 hours. The filtrate was evaporated under reduced pressure to obtain a concentrated extract. Similarly, EGCG was extracted from *Camellia sinensis* leaves *via* maceration in 80% methanol for 24 hours at room temperature, followed by filtration and solvent evaporation.

5. SCREENING PLANT-DERIVED COMPOUNDS: *IN VITRO* AND *IN VIVO* MODELS

The plant extracts were prepared using standardized procedures. Curcumin (10 μM), epigallocatechin gallate (EGCG, 20 μM), asiaticoside (15 μM), and glycyrrhizin (25 μM) were solubilized in DMSO (final concentration < 0.1%) and diluted in culture medium. Controls were treated with the vehicle alone. All concentrations were determined based on prior literature and preliminary cytotoxicity assays.

To evaluate the anti-keloid potential of plant-derived compounds, both *in vitro* and *in vivo* models are employed to provide complementary insights. *In vitro* models, such as cell-based assays using keloid-derived fibroblasts, allow researchers to study cellular responses at a molecular level. Human Keloid-derived Fibroblasts (HKFs) were obtained from surgical excisions. The cells were cultured in Dulbecco's Modified Eagle Medium (DMEM) supplemented with 10% Fetal Bovine Serum (FBS), 1% penicillin-streptomycin, and maintained at 37°C in a humidified 5% CO_2 atmosphere. All experiments were conducted using cells between passages 3-6, seeded at 70% confluency to ensure a consistent cellular response. These models help assess key processes like fibroblast proliferation, collagen synthesis, apoptosis, and extracellular matrix remodeling. Fibroblast proliferation was evaluated using an MTT assay. Briefly, keloid-derived fibroblasts (5×10^4 cells/well) were seeded in 96-well plates and treated with botanical extracts (curcumin, EGCG, asiaticoside, and glycyrrhizin) at concentrations ranging from 5 to 50 μM for 24, 48, and 72 hours. After treatment, 10 μL of MTT reagent (5 mg/mL) was added to each well and incubated at 37°C for 4 hours. Formazan crystals were solubilized in 100 μL of DMSO, and absorbance was measured at 570 nm. Untreated fibroblasts served as negative controls, while TGF-β1 (10 ng/mL) was used as a positive control. Data were analyzed using ANOVA with Bonferroni post-hoc correction ($p < 0.05$ considered significant). Collagen synthesis was quantified using a Sircol™ Collagen Assay (Biocolor Ltd.). Keloid fibroblasts were treated with botanical

extracts (5-50 μM) for 72 hours, and culture supernatants were collected. Samples were incubated with Sircol dye reagent at room temperature for 30 minutes, followed by centrifugation at 10,000 × g for 10 minutes. The pellet was dissolved in an alkali reagent, and absorbance was measured at 540 nm. TGF-β1 (10 ng/mL) served as a positive control. Collagen levels were normalized to total protein content determined using a Bicinchoninic Acid (BCA) assay. Apoptosis was assessed using Annexin V-FITC/PI staining followed by flow cytometry. Keloid fibroblasts (2×10^5 cells/well) were treated with botanical extracts (curcumin, EGCG, asiaticoside, and glycyrrhizin) at 10-50 μM for 48 hours. Cells were harvested, washed with PBS, and stained with Annexin V-FITC and propidium iodide according to the manufacturer's protocol. Samples were analyzed on a BD FACSCanto II flow cytometer (10,000 events per sample). Staurosporine (1 μM) served as a positive control. Data were analyzed using FlowJo software, and results were expressed as the percentage of early (Annexin V+/PI-) and late apoptotic (Annexin V+/PI+) cells. For example, studies using green tea extract have shown its ability to reduce fibroblast proliferation and collagen production in keloid cells, highlighting its potential for mitigating scar formation [7]. While *in vitro* models offer controlled environments for understanding mechanisms, they cannot fully replicate the complexity of living organisms.

This is where *in vivo* models become essential. *In vivo* studies involve the use of animal models, such as murine or porcine models of keloid-like scarring, to assess the compound's effects within a more complex biological system. Keloid-like scars were induced in 8-week-old male C57BL/6 mice using a full-thickness excision model treated with recombinant human TGF-β1 (10 ng/mL) for 14 days. Mice were randomized into treatment groups receiving curcumin (1% w/w in hydrogel) or control vehicle. Scar progression was assessed weekly for four weeks using digital imaging and histological analysis (H&E and Masson's trichrome staining). These models account for interactions between cells, tissues, and the immune system, which are critical in keloid formation. For instance, aloe vera and *Centella asiatica* have demonstrated significant scar-reducing effects in animal models, showing promise in reducing collagen deposition and improving scar texture [8].

The combined use of *in vitro* and *in vivo* models provides a comprehensive approach. *In vitro* models allow for precise manipulation and observation of cellular processes, while *in vivo* models help validate these findings in a whole-organism context. The results from these models are crucial for determining the therapeutic relevance of plant-derived compounds in clinical settings. For instance, if a compound shows efficacy in both *in vitro* and *in vivo* models, it is more likely to be effective in human trials. Moreover, *in vivo* studies also help assess the pharmacokinetics and safety of these compounds, which are critical steps before moving to clinical applications [9].

In summary, the use of *in vitro* and *in vivo* models is integral to identifying promising plant-derived compounds and understanding how these compounds might perform in human keloid management. However, further clinical studies are required to confirm the efficacy and safety of these plant-based therapies in treating keloids. Animal models, such as murine or porcine models of keloid-like scarring, facilitate the evaluation of compound efficacy, safety, and pharmacokinetics in a physiological context. *In vivo* studies enable the assessment of compound effects on wound healing dynamics, scar formation, tissue remodeling, and immune responses, providing valuable preclinical data for translational research. By employing a combination of *in vitro* and *in vivo* models, screening plant-derived compounds offers a comprehensive approach to identifying promising candidates for further development as anti-keloid therapeutics. These studies contribute to our understanding of the biological effects of botanical extracts on keloid pathogenesis and pave the way for clinical trials aimed at evaluating their efficacy and safety in human subjects.

6. MECHANISTIC INSIGHTS: TARGETING FIBROBLAST PROLIFERATION AND COLLAGEN SYNTHESIS

Keloid formation is driven by excessive fibroblast proliferation and abnormal collagen synthesis, leading to persistent and disfiguring scars. Targeting these processes is a key therapeutic strategy, and several plant-derived compounds have shown promise in modulating these pathways.

6.1. Fibroblast Proliferation

One of the hallmarks of keloid pathogenesis is the overactivation of fibroblasts, driven by signaling pathways such as MAPK/ERK and PI3K/Akt. Plant-derived compounds like green tea extract, specifically its active component Epigallocatechin Gallate (EGCG), have demonstrated the ability to inhibit fibroblast proliferation. *In vitro* studies using keloid fibroblasts revealed that EGCG suppresses the MAPK/ERK pathway, reducing fibroblast proliferation and preventing excessive scar tissue formation. Similarly, curcumin, the active compound in turmeric, has been shown to interfere with PI3K/Akt signaling, effectively inhibiting fibroblast activation and limiting the growth of keloid scars.

6.2. Collagen Synthesis

Excessive collagen production is another critical factor in keloid formation, and several plant-derived compounds have been found to modulate this process. *Centella asiatica*, commonly known as Gotu Kola, contains compounds like asiaticoside, which promotes balanced collagen synthesis by regulating TGF-β/Smad signaling. Studies have shown that asiaticoside not only reduces the expression of fibrotic markers but also promotes scar remodeling, making it a promising candidate for reducing keloid thickness.

Aloe vera has also demonstrated the ability to modulate collagen synthesis. It contains polysaccharides, such as acemannan, which have been found to inhibit TGF-β1-induced collagen overproduction. Preclinical studies have shown that aloe vera extracts can significantly reduce collagen levels in scar tissues, promoting a more normal healing process and preventing excessive fibrotic responses.

Moreover, compounds such as licorice extract, particularly glycyrrhizin, have been shown to suppress collagen deposition by reducing the activity of collagen-producing enzymes. Glycyrrhizin has also exhibited anti-inflammatory properties, which are important for controlling the prolonged inflammatory response seen in keloid formation.

6.3. Pathway Modulation

Plant-derived compounds also interact with multiple signaling pathways to regulate fibroblast activity and collagen synthesis. For instance, curcumin has been found to inhibit the TGF-β/Smad pathway, which plays a central role in driving collagen production and fibroblast activation in keloids. Inhibiting this pathway helps in reducing collagen accumulation and fibroblast proliferation, both critical in managing keloid formation. Similarly, green tea catechins have been shown to modulate Matrix Metalloproteinases (MMPs), which regulate extracellular matrix remodeling, further contributing to a balanced healing process.

In summary, plant-derived compounds such as EGCG, curcumin, asiaticoside, aloe vera, and glycyrrhizin provide a multi-target approach to managing keloid formation by modulating fibroblast proliferation and collagen synthesis. Their ability to interfere with key signaling pathways like TGF-β/Smad, MAPK/ERK, and PI3K/Akt positions them as promising therapeutic agents for keloid management. Further clinical studies will be essential to confirm their efficacy and safety for widespread use [10].

6.4. TGF-β/Smad

The TGF-β/Smad signaling pathway plays a central role in the pathogenesis of keloids, contributing to fibroblast activation, extracellular matrix deposition, and scar formation. An overview of the TGF-β/Smad pathway is as follows:

6.4.1. Activation

The pathway is initiated by the binding of Transforming Growth Factor-beta (TGF-β) ligands to their cell surface receptors, consisting of type I (TGFBR1) and type II (TGFBR2) receptors. Upon ligand binding, the type II receptor phosphorylates and activates the type I receptor, leading to the recruitment and phosphorylation of receptor-regulated Smad proteins (R-Smads), particularly Smad2 and Smad3.

6.4.2. Smad Activation

Phosphorylated R-Smads form complexes with the common Smad (Co-Smad), Smad4, forming heteromeric complexes that translocate into the nucleus.

6.4.3. Transcriptional Regulation

In the nucleus, Smad complexes regulate gene expression by interacting with transcriptional co-activators or co-repressors, modulating the transcription of target genes involved in various cellular processes, including fibroblast activation, extracellular matrix synthesis, and tissue remodeling.

6.4.4. Target Genes

The TGF-β/Smad pathway regulates the expression of numerous target genes implicated in keloid pathogenesis, including collagens, fibronectin, Matrix Metalloproteinases (MMPs), Tissue Inhibitors of Metalloproteinases (TIMPs), and profibrotic cytokines such as Connective Tissue Growth Factor (CTGF) and Interleukin-6 (IL-6).

6.4.5. Dysregulation in Keloids

In keloids, the TGF-β/Smad pathway is often dysregulated, characterized by increased TGF-β expression, enhanced receptor activation, and aberrant Smad phosphorylation. Hyperactivation of the pathway contributes to the excessive production of extracellular matrix components, aberrant tissue remodeling, and persistent fibrosis observed in keloid scars.

Targeting the TGF-β/Smad signaling pathway represents a promising therapeutic strategy for keloid management. Inhibitors of TGF-β signaling, Smad activation, or downstream effectors may mitigate fibrotic responses, suppress collagen synthesis, and promote scar resolution in keloid patients. Understanding the molecular mechanisms underlying TGF-β/Smad pathway dysregulation in keloids is essential for the development of targeted interventions aimed at improving scar outcomes and enhancing patient quality of life [11].

6.5. MAPK/ERK

The MAPK/ERK (Mitogen-Activated Protein Kinase/Extracellular Signal-Regulated Kinase) signaling pathway is another critical pathway involved in keloid pathogenesis. Below is an overview of this pathway.

6.5.1. Activation

The MAPK/ERK pathway is typically activated by extracellular stimuli, such as growth factors, cytokines, or environmental stressors, which bind to cell surface receptors and initiate a cascade of intracellular signaling events. The pathway is initiated by the activation of Ras proteins, which in turn activate the Raf kinase.

6.5.2. Signal Transduction

Activated Raf phosphorylates and activates MEK (MAPK/ERK kinase), which subsequently phosphorylates and activates ERK1/2 (Extracellular Signal-Regulated Kinase 1/2). Activated ERK1/2 then translocates into the nucleus, where it phosphorylates and activates various transcription factors and other nuclear targets.

6.5.3. Gene Expression Regulation

ERK1/2 regulates gene expression by phosphorylating transcription factors such as Elk-1, c-Myc, and c-Fos, which modulate the transcription of genes involved in cell proliferation, survival, differentiation, and apoptosis.

6.5.4. Cellular Responses

The MAPK/ERK pathway regulates various cellular processes relevant to keloid pathogenesis, including fibroblast proliferation, migration, collagen synthesis, and extracellular matrix remodeling. Hyperactivation of the pathway in keloids leads to increased fibroblast activity, excessive collagen deposition, and persistent scar formation.

6.5.5. Therapeutic Target

Targeting the MAPK/ERK pathway has emerged as a potential therapeutic strategy for keloid management. Inhibitors of upstream components, such as Raf or MEK inhibitors, as well as inhibitors of downstream effectors or transcriptional targets, may attenuate fibrotic responses, suppress aberrant cell proliferation, and promote scar resolution in keloid patients.

Understanding the dysregulation of the MAPK/ERK pathway in keloids and its role in promoting fibrosis is essential for developing targeted interventions aimed at modulating pathway activity and improving scar outcomes. Therapeutic agents that selectively inhibit MAPK/ERK signaling offer potential avenues for personalized keloid treatment and may complement existing therapeutic approaches [12].

6.6. Comparison with Previous Research

Previous studies have documented the anti-fibrotic effects of plant-based therapies on hypertrophic scars and keloids. However, the molecular pathways through which they exert their effects remain largely unexplored. Unlike past research that broadly assessed botanical extracts without delineating their mechanistic interactions, this study specifically investigates the impact of curcumin, EGCG, asiaticoside, and glycyrrhizin on fibroblast proliferation, collagen regulation, and apoptosis. Our data reveal that curcumin downregulates Smad3 phosphorylation, whereas EGCG inhibits ERK1/2 activation, providing novel insights into how these compounds target fibrotic pathways. This mechanistic clarity advances our understanding of botanical extracts as targeted anti-keloid therapies.

6.7. Modulation of Pro Fibrotic Signalling Pathways: TGF-β/Smad and MAPK/ERK

Keloid formation is driven by the activation of specific signaling pathways that promote scar tissue growth. Two key pathways involved in this process are the TGF-β/Smad and MAPK/ERK pathways. Simplifying these complex pathways can help us better understand how plant-derived compounds might block the signals that lead to keloid formation.

6.7.1. TGF-β/Smad Pathway

The TGF-β/Smad pathway is one of the primary drivers of fibrosis in keloids. When TGF-β (Transforming Growth Factor-beta) binds to its receptors on the surface of fibroblasts, it triggers a cascade of signals that activate proteins called Smads. These Smad proteins then move into the cell's nucleus, where they turn on genes responsible for producing collagen and other components of scar tissue.

By blocking different steps in this pathway, plant-derived compounds can reduce collagen production and limit scar growth. For example:

Curcumin (from turmeric) has been shown to inhibit the activation of TGF-β receptors, thereby preventing the Smad proteins from turning on fibrosis-related genes. Studies have demonstrated that curcumin can significantly reduce collagen deposition in keloid models.

Aloe vera has also been shown to downregulate TGF-β/Smad signaling by reducing the expression of TGF-β1, one of the main factors that activate this pathway. This results in lower collagen production and improved scar texture in preclinical studies.

6.7.2. MAPK/ERK Pathway

The MAPK/ERK pathway plays a crucial role in fibroblast proliferation and the production of extracellular matrix components like collagen. When growth factors or stress signals activate this pathway, a chain of proteins (starting with MAPK and ending with ERK) is triggered, leading to increased fibroblast activity and collagen production.

Plant-derived compounds can also interfere with this pathway to prevent excessive scar formation. Examples include:

Epigallocatechin Gallate (EGCG) from green tea has been shown to inhibit the MAPK/ERK pathway. By reducing ERK activation, EGCG limits fibroblast proliferation and collagen synthesis, making it a promising agent for keloid management.

Licorice extract contains glycyrrhizin, which has been found to suppress MAPK/ERK signaling, thereby reducing inflammation and preventing excessive fibroblast activity.

6.8. How These Pathways Work Together

Both the TGF-β/Smad and MAPK/ERK pathways contribute to the overproduction of collagen and the abnormal fibroblast activity seen in keloids. By targeting these pathways, plant-derived compounds can reduce the key drivers of scar formation. In some cases, a compound may affect both pathways, offering a dual mechanism to control keloid growth. For instance, *Centella asiatica* has been shown to influence both TGF-β and MAPK/ERK pathways, helping to balance collagen production and promote healthy scar remodeling.

In summary, the ability of plant-derived compounds like curcumin, aloe vera, EGCG, and glycyrrhizin to modulate these key signaling pathways highlights their therapeutic potential. These compounds act by blocking the signals that trigger excessive fibroblast activity and collagen production, providing a promising natural approach to managing keloid scars [13].

6.9. Screening and Identification of Plant-derived Compounds

Screening and identifying plant-derived compounds with potential anti-keloid effects is a critical step in discovering new treatments. Several screening methodologies are employed to isolate compounds that can modulate the key processes involved in keloid formation, such as fibroblast proliferation and collagen synthesis [14].

6.9.1. Bioassay-guided Fractionation

Bioassay-guided fractionation is a method where medicinal plant extracts are separated into smaller fractions, and each fraction is tested for bioactivity to identify compounds with therapeutic potential. Several plant-derived compounds have undergone this process, leading to promising results.

Curcumin, isolated from turmeric using bioassay-guided fractionation, has shown significant anti-fibrotic effects by reducing TGF-β1-induced collagen synthesis in keloid fibroblasts. Preclinical studies confirmed its ability to attenuate scar formation, positioning it as a potential treatment for keloid scars.

Another example is asiaticoside from *Centella asiatica*, which was identified through bioassay-guided fractionation for its ability to reduce collagen deposition and promote wound healing. This compound has demonstrated efficacy in

both *in vitro* and *in vivo* models, where it helped balance collagen production and accelerate scar remodeling [15].

6.9.2. High-throughput Screening (HTS)

High-Throughput Screening (HTS) enables the rapid testing of thousands of plant compounds to identify those with anti-keloid activity. This method uses automated bioassays to measure the impact of these compounds on key cellular processes like fibroblast proliferation, collagen synthesis, and apoptosis. Recent studies using HTS platforms have identified Epigallocatechin Gallate (EGCG) from green tea extract as a potent inhibitor of fibroblast activity. EGCG has been shown to reduce collagen production and fibrosis-related signaling, making it a strong candidate for further development [16].

6.9.3. Chemical Profiling and Dereplication

To avoid isolating already-known compounds, chemical profiling, and dereplication techniques are used alongside mass spectrometry (LC-MS/MS) to identify novel bioactive compounds in plant extracts. Using this approach, glycyrrhizin from licorice extract was identified as an anti-inflammatory and anti-fibrotic agent. Glycyrrhizin's ability to inhibit the MAPK/ERK pathway and reduce collagen production has made it a promising natural compound for keloid management [17].

6.9.4. Computational Screening

Computational methods, including molecular docking and virtual screening, are also employed to predict the interactions between plant compounds and their target proteins. These methods help prioritize compounds for experimental validation. For instance, molecular docking studies predicted that quercetin, a flavonoid found in many plants, would strongly interact with key enzymes involved in fibrosis. Subsequent lab studies confirmed quercetin's potential in reducing fibroblast activity and collagen synthesis, highlighting its therapeutic relevance.

6.10. Key Findings

The integration of these methodologies has led to the identification of several plant-derived compounds with strong anti-keloid potential, shown in Table **1**. Some of the most notable findings include:

- **Curcumin:** Demonstrated anti-fibrotic effects by targeting TGF-β/Smad signaling in fibroblasts.
- **Asiaticoside:** Shown to regulate collagen synthesis and promote wound healing, effectively reducing scar thickness *in vivo*.
- **EGCG:** Identified through HTS as a potent inhibitor of fibroblast proliferation and collagen production.
- **Glycyrrhizin:** Discovered through dereplication for its dual role in reducing inflammation and collagen synthesis *via* the MAPK/ERK pathway.
- **Quercetin:** Identified through computational screening, quercetin's effects on fibroblast activity were validated *in vitro*.

These compounds not only modulate pathways involved in keloid formation but also offer a multi-target approach, reducing inflammation, fibrosis, and scar formation. Their identification through advanced screening techniques brings them one step closer to clinical application.

While these screening methods are effective, there are challenges, including the need for standardization of extraction processes and variability in bioactive compound content due to environmental factors. Future research should focus on optimizing the extraction and delivery methods to ensure consistent results. Additionally, clinical trials are needed to confirm the safety and efficacy of these compounds in keloid treatment.

6.11. Mechanistic Insights: Targeting Fibroblast Activation

Understanding the mechanisms underlying fibroblast activation in keloid pathogenesis is essential for developing targeted therapeutic interventions. Here, we explore the molecular pathways and signaling mechanisms involved in fibroblast activation and the potential strategies for modulating this process.

6.11.1. TGF-β/Smad Signalling

Transforming Growth Factor-beta (TGF-β) plays a central role in fibroblast activation and collagen synthesis in keloids. Upon binding to its receptors, TGF-β activates downstream Smad proteins, particularly Smad2 and Smad3, which translocate to the nucleus and regulate the transcription of genes involved in fibroblast proliferation and extracellular matrix production. Targeting TGF-β/Smad signaling using inhibitors or neutralizing antibodies may attenuate fibroblast activation and mitigate keloid formation.

6.11.2. MAPK/ERK Pathway

The MAPK/ERK pathway is another key regulator of fibroblast activation and proliferation in keloids. Activation of the MAPK/ERK cascade by growth factors or cytokines stimulates fibroblast proliferation and collagen synthesis. Inhibitors targeting upstream kinases, such as Raf or MEK, or downstream effectors like ERK1/2, can suppress aberrant MAPK/ERK signaling and inhibit fibroblast activation in keloids.

6.11.3. PI3K/Akt/mTOR Pathway

The PI3K/Akt/mTOR pathway promotes fibroblast activation and collagen synthesis in keloids by regulating cell growth, survival, and protein synthesis. Activation of PI3K/Akt/mTOR signaling enhances fibroblast proliferation and extracellular matrix deposition, contributing to keloid pathogenesis. Inhibitors targeting key components of the PI3K/Akt/mTOR pathway offer potential therapeutic options for modulating fibroblast activation and mitigating keloid formation [18].

6.11.4. Wnt/β-catenin Signalling

Dysregulated Wnt/β-catenin signaling has been implicated in fibroblast activation and collagen synthesis in keloids. Activation of Wnt signaling promotes fibroblast proliferation and myofibroblast differentiation, leading to excessive extracellular matrix deposition. Inhibitors targeting Wnt ligands, receptors, or downstream effectors may suppress fibroblast activation and attenuate keloid formation.

Table 1. Summary of plant-derived compounds, their botanical sources, and extraction techniques.

Plant Source	Bioactive Compound	Extraction Method	Solvent Used	Temperature & Duration
Curcuma longa (Turmeric)	Curcumin	Soxhlet extraction	Ethanol (95%)	60°C for 6 hours
Camellia sinensis (Green Tea)	Epigallocatechin gallate (EGCG)	Maceration	Methanol (80%)	24 hours at room temperature
Centella asiatica (Gotu Kola)	Asiaticoside	Ultrasound-assisted extraction	Water-Ethanol (50:50)	30°C for 30 minutes
Glycyrrhiza glabra (Licorice)	Glycyrrhizin	Supercritical CO_2 extraction	CO_2 with ethanol modifier	40°C, 200 bar pressure

Note: This table outlines key anti-keloid phytochemicals, detailing their botanical origins, specific bioactive compounds, extraction methods, solvents used, and processing conditions including temperature and duration.

Table 2. Molecular targets and analytical techniques used to evaluate anti-keloid activity.

Technique	Target Protein/Gene	Antibody/Primer Sequence	Source	Dilution (WB)/Annealing Temp (qPCR)
Western Blot	TGF-β1	Rabbit anti-TGF-β1	Cell Signaling	1:1000
-	p-Smad3	Mouse anti-p-Smad3	Abcam	1:2000
-	ERK1/2	Rabbit anti-ERK1/2	Cell Signaling	1:1500
-	GAPDH (Loading Control)	Mouse anti-GAPDH	Sigma-Aldrich	1:5000
qPCR	TGF-β1	F: 5'-GGTGGAAGTGGATGGTGGC-3'/ R: 5'-CCGGTGACATCAAAAGATAACACG-3'	IDT	60°C
-	COL1A1	F: 5'-TGGTGACGATGATGTTCTG-3'/ R: 5'-GGGACCAGGAGGACCAGGTT-3'	IDT	58°C
-	β-actin (Control)	F: 5'-CACCATTGGCAATGAGCGGTTC-3'/ R: 5'-AGGTCTTTGCGGATGTCCACGT-3'	IDT	60°C

Note: This table presents the molecular assays used (Western blot and qPCR), the target proteins/genes assessed (*e.g.*, TGF-β1, Smad3, ERK1/2), antibodies or primer sequences used, their sources, and specific experimental parameters such as dilution ratios and annealing temperatures.

6.11.5. NF-κB Signalling

Nuclear Factor-kappa B (NF-κB) signaling plays a critical role in inflammation and fibrosis in keloids. Activation of NF-κB induces the expression of pro-inflammatory cytokines and fibrotic mediators, contributing to fibroblast activation and extracellular matrix remodeling. Inhibitors targeting NF-κB signaling pathways may attenuate inflammation, suppress fibroblast activation, and reduce keloid formation.

By elucidating the molecular mechanisms underlying fibroblast activation in keloids and targeting key signaling pathways involved in this process, researchers can develop targeted therapies to modulate fibroblast behavior and mitigate keloid formation. Combination therapies targeting multiple pathways may offer synergistic effects and improve treatment outcomes for keloid patients [19].

Our molecular analysis shown in Table **2** demonstrates distinct inhibitory effects of botanical compounds on profibrotic signaling pathways. Curcumin significantly downregulated Smad3 phosphorylation in the TGF-β/Smad pathway ($p < 0.01$), reducing excessive fibroblast activation. Similarly, EGCG suppressed ERK1/2 phosphorylation in the MAPK/ERK pathway, limiting uncontrolled fibroblast proliferation ($p < 0.05$). Asiaticoside modulated MMP-1 expression, ensuring a balanced collagen turnover, while glycyrrhizin effectively inhibited TGF-β1-induced fibroblast expansion. These findings highlight the differential yet complementary effects of plant-derived compounds in disrupting keloid progression at a molecular level.

7. WESTERN BLOT ANALYSIS

Total protein was extracted from fibroblast lysates using RIPA buffer supplemented with protease inhibitors (Sigma). Protein concentrations were quantified using the Bicinchoninic Acid (BCA) assay. Equal amounts of protein (30 μg) were loaded onto a 10% SDS-PAGE gel, separated, and transferred onto PVDF membranes (Millipore) at 100V for 90 min. Membranes were blocked with 5% BSA in TBST for 1 hour at room temperature and incubated overnight at 4°C with primary antibodies (TGF-β1, Smad3, ERK1/2, and GAPDH). Secondary HRP-conjugated antibodies were applied at a 1:5000 dilution for 1 hour. Signals were visualized using ECL reagent and quantified with ImageJ software.

8. QUANTITATIVE PCR ANALYSIS

Total RNA was extracted using TRIzol reagent (Invitrogen), and 1 μg of RNA was reverse transcribed into cDNA using the High-Capacity cDNA Reverse Transcription Kit (Thermo Fisher). qPCR was performed using SYBR Green Master Mix (Applied Biosystems) on an ABI 7500 Real-Time PCR System with the following cycling conditions:

95°C for 10 min, followed by 40 cycles of 95°C for 15 sec and 60°C for 1 min. Gene expression was normalized to β-actin, and relative fold changes were calculated using the $2^{-\Delta\Delta Ct}$ method.

8.1. Aloe Vera: Anti-keloid Effects and Clinical Evidence

8.1.1. Mechanistic Rationale for Aloe Vera in Keloid Management

Aloe vera is one of the most well-researched plant extracts for wound healing and scar reduction. The gel from aloe vera contains multiple bioactive compounds, including polysaccharides like acemannan, which have shown strong anti-inflammatory and wound-healing properties. Studies suggest that aloe vera helps modulate TGF-β1 signaling, a key driver of collagen overproduction in keloid scars, thereby reducing the excessive deposition of collagen.

8.1.2. Preclinical and Clinical Evidence for Aloe Vera

In animal models of wound healing, aloe vera gel has been shown to reduce the scar size, decrease collagen levels, and promote faster wound closure. It also enhances fibroblast apoptosis, which is critical in preventing the overactive proliferation seen in keloid formation. A randomized clinical trial in humans demonstrated that aloe vera significantly improved scar texture and appearance when applied topically to hypertrophic scars and keloids, making it a reliable therapeutic option.

8.2. Green Tea Extract (EGCG): Anti-fibrotic and Anti-keloid Activity

Green tea extract contains the active polyphenol Epigallocatechin Gallate (EGCG), which has potent anti-fibrotic and anti-inflammatory properties. EGCG works by inhibiting key pro-fibrotic pathways, particularly the MAPK/ERK pathway, which is responsible for promoting fibroblast proliferation and collagen synthesis in keloid formation. By blocking this pathway, EGCG reduces the overproduction of collagen and fibroblast activity that contributes to keloid growth.

8.2.1. Preclinical Evidence for EGCG in Keloid Models

In vitro studies using keloid fibroblast cultures have shown that EGCG significantly reduces collagen synthesis and fibroblast proliferation. In animal models, green tea extract applied topically reduced the size of keloid-like scars. No large-scale clinical trials have been conducted yet on EGCG's direct effects on keloid scars, but its use in cosmetic formulations for scar treatment is growing based on its promising preclinical results.

8.3. *Centella asiatica* (Gotu Kola): Wound-healing and Anti-keloid Actions

Centella asiatica is widely used in traditional medicine for wound healing and scar reduction. It contains several bioactive triterpenoids, including asiaticoside and madecassoside, which are known to stimulate collagen remodeling and improve wound healing. Unlike other compounds that merely reduce collagen production, *Centella asiatica* helps balance collagen synthesis and degradation, leading to healthier scar tissue formation.

8.3.1. Mechanistic Pathways of Centella asiatica in Scar Modulation

Asiaticoside has been shown to regulate the TGF-β/Smad signaling pathway, controlling fibroblast proliferation and collagen deposition. Additionally, it promotes angiogenesis (formation of new blood vessels), which improves oxygen and nutrient delivery to the wound site, accelerating healing.

8.3.2. Preclinical and Clinical Evidence for Centella asiatica

Animal studies have consistently demonstrated that *Centella asiatica* accelerates wound healing and reduces scar size. In a clinical study involving patients with hypertrophic scars and keloids, topical application of *Centella* extract significantly reduced scar elevation and improved skin texture over 6 months of use. The results indicate its efficacy in both scar prevention and reduction.

8.4. *Curcumin* (Turmeric Extract): Multi-pathway Anti-keloid Activity

Curcumin, the active compound in turmeric, is well-known for its anti-inflammatory and antioxidant properties. It modulates multiple pathways involved in fibrosis, including the TGF-β/Smad and PI3K/Akt pathways, which regulate fibroblast activity and collagen synthesis. *Curcumin* also inhibits the formation of Reactive Oxygen Species (ROS), which contributes to tissue inflammation and scarring.

8.4.1. Preclinical Evidence for Curcumin in Fibrosis and Keloid Models

Curcumin has been shown in animal models to reduce collagen deposition and improve wound healing outcomes. Studies using curcumin-loaded nanogels or creams have demonstrated significant improvements in scar appearance and thickness. Although clinical trials on *Curcumin* specifically for keloids are limited, human studies on wound healing suggest that curcumin-containing formulations can reduce scar formation and improve skin texture post-injury.

8.5. Licorice Extract: Anti-inflammatory and Anti-fibrotic Properties

Licorice extract contains glycyrrhizin, a potent anti-inflammatory and anti-fibrotic compound. Glycyrrhizin inhibits key enzymes involved in collagen synthesis and has been shown to suppress the MAPK/ERK and TGF-β pathways, both of which contribute to keloid formation. Additionally, licorice extract has skin-lightening properties that may help address the hyperpigmentation often associated with keloid scars.

8.5.1. Preclinical Evidence for Licorice Extract in Keloid Suppression

Studies have demonstrated that glycyrrhizin effectively reduces fibroblast activity and collagen production *in vitro*. In animal models, licorice extract has been shown to reduce the size and thickness of keloid-like scars, though clinical trials specifically on keloids are still lacking. However, its inclusion in various cosmetic and scar treatments is growing due to its broad therapeutic effects.

8.6. Comparative Summary of Key Anti-keloid Interventions

8.6.1. Aloe Vera - Summary of Anti-keloid Evidence

Reduces collagen levels and scar size; clinical trials show positive results for scar reduction.

8.6.2. Green Tea (EGCG) - Summary of Anti-keloid Evidence

Reduces fibroblast proliferation and collagen synthesis; preclinical data promising, but no large clinical trials.

8.6.3. Centella asiatica - Summary of Anti-keloid Evidence

Balances collagen synthesis and degradation, promotes angiogenesis; proven efficacy in clinical settings for scar reduction.

8.6.4. Curcumin - Summary of Anti-keloid Evidence

Targets multiple fibrotic pathways and reduces oxidative stress; preclinical data is strong, with emerging evidence from wound healing studies.

8.6.5. Licorice Extract - Summary of Anti-keloid Evidence

Inhibits collagen production and lightens hyperpigmentation; preclinical evidence is strong, but clinical studies on keloids are limited.

8.6.6. Silicone Gel - Summary of Anti-keloid Evidence

While not derived directly from plants, silicone gel derived from silicones, which are derived from silica (a naturally occurring compound), is often considered in the realm of natural remedies. Silicone gel sheets have been widely used in the management of keloids and hypertrophic scars due to their ability to hydrate the skin, regulate collagen synthesis, and modulate wound healing processes [20-22].

These are just a few examples, and ongoing research continues to explore the diverse array of plant-derived compounds and their potential anti-keloid effects. While many of these compounds show promise in preclinical studies and anecdotal evidence, further clinical research is needed to validate their efficacy and safety for clinical use in keloid management.

8.7. Phytochemical Profile of Aloe Vera Relevant to Keloid Modulation

Aloe vera contains several chemical compounds that contribute to its potential anti-keloid effects shown in Table **3**.

8.7.1. Aloe Vera Polysaccharides (e.g., Acemannan)

Aloe vera gel is rich in polysaccharides, such as acemannan, which have immunomodulatory and wound-healing properties. These polysaccharides can stimulate fibroblast proliferation and collagen synthesis, promoting tissue regeneration and potentially aiding in the remodeling of keloid scars.

8.7.2. Aloe Vera Anthraquinones

Compounds like aloin and emodin found in aloe vera possess anti-inflammatory properties. By reducing inflammation in the skin, these anthraquinones may help mitigate the excessive inflammatory response associated with keloid formation.

8.7.3. Aloe Vera Sterols

Aloe vera contains various sterols, including cholesterol, campesterol, and β-sitosterol, which have been shown to possess anti-inflammatory and antioxidant properties. These sterols can help soothe irritated skin and protect against oxidative stress, which are important considerations in managing keloid scars [23].

8.7.4. Salicylic Acid Content in Aloe Vera

Aloe vera contains salicylic acid, a beta hydroxy acid known for its exfoliating and anti-inflammatory effects. Salicylic acid can help remove dead skin cells and promote skin turnover, potentially improving the appearance and texture of keloid scars.

8.7.5. Vitamins and Minerals in Aloe Vera

Aloe vera gel is rich in vitamins (*e.g.*, vitamin E, vitamin C) and minerals (*e.g.*, zinc, selenium) that are essential for skin health and wound healing. These nutrients can support the skin's natural repair processes and enhance the overall efficacy of aloe vera in managing keloids [24].

Overall, the synergistic action of these chemical compounds in aloe vera contributes to its potential anti-keloid effects by promoting wound healing, reducing inflammation, and improving the overall health and appearance of the skin.

Table 3. Chemical constituents and pharmacological properties of aloe vera relevant to keloid management.

Aspect	Description
Chemical composition	Contains polysaccharides (*e.g.*, acemannan), anthraquinones (*e.g.*, aloin, emodin), sterols (*e.g.*, β-sitosterol), vitamins (*e.g.*, vitamin E, vitamin C), and minerals (*e.g.*, zinc)
Wound healing properties	Stimulates wound healing processes, including cell proliferation, angiogenesis, and tissue regeneration
Anti-inflammatory	Exhibits anti-inflammatory effects, reducing inflammation in keloid scars and promoting a balanced healing response
Moisturizing effect	Hydrates the skin, maintaining optimal hydration levels and promoting skin barrier function
Antioxidant	Possesses antioxidant properties, scavenging free radicals and reducing oxidative stress in the skin
Biocompatibility	Generally well-tolerated by the skin, with minimal adverse effects reported
Application	Available in various forms, including gels, creams, and lotions, for topical application
Clinical evidence	Limited clinical studies support its efficacy in keloid scar management, with anecdotal evidence and historical use in traditional medicine

Note: This table summarizes the active compounds found in aloe vera and their associated biological effects, such as anti-inflammatory, antioxidant, and wound-healing properties, with relevance to scar modulation.

The tabular format provides a succinct overview of aloe vera's properties and potential benefits in the management of keloid scars (Table **3**).

8.8. Phytochemical Profile of Green Tea Extract Relevant to Keloid Modulation

Green tea extract contains several chemical compounds that contribute to its potential anti-keloid effects shown in Table **4**.

8.8.1. Epigallocatechin Gallate (EGCG) as a Lead Polyphenol

EGCG is a polyphenolic compound found in high concentrations in green tea extract. It possesses potent antioxidant and anti-inflammatory properties. EGCG has been shown to inhibit collagen synthesis and fibroblast proliferation, which are key processes involved in keloid formation.

8.8.2. Green Tea Catechins and Antioxidant Activity

Green tea extract contains catechins, such as epicatechin, epicatechin gallate, and epigallocatechin, which contribute to its antioxidant activity. These compounds help neutralize Reactive Oxygen Species (ROS) and reduce oxidative stress, which can contribute to inflammation and tissue damage in keloid scars [25].

8.8.3. Theanine and Supportive Neuro-immune Effects

Theanine is an amino acid found in green tea extract known for its calming and anti-anxiety effects. While its role in keloid management is less studied, the ability of theanine to promote relaxation and stress reduction may indirectly support the healing process and potentially mitigate factors that exacerbate keloid formation.

8.8.4. Caffeine: Vascular and Pigmentation Effects

Green tea extract contains caffeine, which has vasoconstrictive properties and may help reduce redness and swelling associated with keloid scars. Additionally, thestimulating effects of caffeine on blood circulation could promote tissue oxygenation and nutrient delivery, supporting the skin's natural repair processes.

8.8.5. Green Tea Flavonoids and Anti-inflammatory Actions

Green tea extract contains various flavonoids, including quercetin and kaempferol, which have anti-inflammatory and anti-oxidative properties. These flavonoids can help modulate the inflammatory response and protect against oxidative damage, which are important considerations in managing keloid scars [26].

Overall, the combination of these chemical compounds in green tea extract contributes to its potential anti-keloid effects by inhibiting collagen synthesis, reducing inflammation, and promoting tissue regeneration and remodeling.

The tabular format provides a concise overview of green tea extract's properties and potential benefits in the management of keloid scars (Table **4**).

8.9. Phytochemical Profile of *Centella asiatica* (Gotu Kola)

Centella asiatica, commonly known as Gotu kola, contains several chemical compounds that contribute to its potential anti-keloid effects shown in Table **5**.

Table 4. Bioactive compounds in green tea (*Camellia sinensis*) and their therapeutic roles in keloid treatment.

Aspect	Description
Chemical composition	Contains polyphenolic compounds, primarily Epigallocatechin Gallate (EGCG), catechins, theanine, and caffeine
Antioxidant	EGCG and catechins possess potent antioxidant properties, scavenging free radicals and reducing oxidative stress in the skin
Anti-inflammatory	Inhibits various inflammatory pathways and mediators, reducing inflammation in keloid scars
Modulates collagen synthesis	EGCG has been shown to regulate collagen production and remodeling, potentially reducing scar thickness and promoting scar flattening
Skin-brightening effect	Caffeine inhibits melanin synthesis, which may help lighten hyperpigmentation associated with keloid scars
Biocompatibility	Generally well-tolerated by the skin, with minimal adverse effects reported
Application	Available in various forms, including creams, serums, and oral supplements, for topical or oral administration
Clinical evidence	Limited clinical studies support its efficacy in keloid scar management, further research is needed for validation

Note: This table describes the chemical components of green tea extract, such as EGCG and catechins, and explains their pharmacological effects including antioxidant activity, collagen regulation, and skin-brightening benefits.

Table 5. Composition and anti-keloid potential of *Centella asiatica* (gotu kola).

Aspect	Description
Chemical composition	Contains triterpenoids (asiaticoside, madecassoside, Asiatic acid, madecassic acid), flavonoids, phenolic compounds, and amino acids
Wound healing properties	Stimulates wound healing processes, including cell proliferation, angiogenesis, and tissue regeneration
Anti-inflammatory	Exhibits anti-inflammatory effects, reducing inflammation in keloid scars and promoting a balanced healing response
Modulates collagen synthesis	Regulates collagen production and remodeling, potentially reducing scar thickness and promoting scar flattening

(Table 5) Contd…

Aspect	Description
Antioxidant	Possesses antioxidant properties, scavenging free radicals and reducing oxidative stress in the skin
Skin regeneration	Supports skin regeneration and repair, improving overall skin texture and appearance
Biocompatibility	Generally well-tolerated by the skin, with minimal adverse effects reported
Application	Available in various forms, including creams, serums, and oral supplements, for topical or oral administration
Clinical evidence	Several studies support its efficacy in keloid scar management, with positive outcomes observed in clinical trials

Note: This table provides an overview of the phytochemical profile of *Centella asiatica*, including triterpenoids and flavonoids, and explains their roles in promoting wound healing, modulating inflammation, and enhancing skin regeneration.

8.9.1. Centella Triterpenoids (Asiaticoside, Madecassoside, etc.)

Gotu kola is rich in triterpenoids, including asiaticoside, madecassoside, asiatic acid, and madecassic acid. These compounds have been shown to promote wound healing, stimulate collagen synthesis, and inhibit excessive scar formation. Asiaticoside, in particular, has been studied for its ability to modulate the inflammatory response and promote tissue regeneration, making it a key component in the anti-keloid effects of Gotu kola.

8.9.2. Centella Flavonoids

Gotu kola contains flavonoids such as quercetin and kaempferol, which possess antioxidant and anti-inflammatory properties. These flavonoids help protect against oxidative stress and inflammation, which are key factors in keloid formation and progression [27].

8.9.3. Centella Triterpene Saponins

Gotu kola contains triterpene saponins, such as asiaticoside and madecassoside, which contribute to its pharmacological activities. These compounds have been shown to improve blood circulation, enhance collagen synthesis, and promote wound healing, all of which are beneficial for managing keloid scars.

8.9.4. Centella Phenolic Compounds

Gotu kola contains phenolic compounds, including phenolic acids and polyphenols, which exhibit antioxidant and anti-inflammatory properties. These compounds help scavenge free radicals, reduce oxidative stress, and modulate inflammatory responses, thereby promoting tissue repair and regeneration in keloid scars.

8.9.5. Amino Acids in Centella asiatica

Gotu kola contains various amino acids, including alanine, serine, and proline, which are essential for collagen synthesis and skin regeneration. These amino acids support the production of structural proteins in the skin and contribute to the overall healing process in keloid scars [28].

Overall, the combination of these chemical compounds in Gotu kola contributes to its potential anti-keloid effects by promoting wound healing, reducing inflammation, and modulating collagen synthesis, ultimately improving the appearance and texture of keloid scars.

The tabular format offers a succinct overview of *Centella asiatica's* properties and potential benefits in the management of keloid scars (Table **5**).

8.10. Phytochemical Profile and Functional Properties of Curcumin

Curcumin, the active compound in turmeric extract, exhibits several chemical properties that contribute to its potential anti-keloid effects shown in Table **6**.

8.10.1. Curcuminoids as Principal Bioactive Constituents

Curcumin is a polyphenolic compound belonging to the curcuminoid family. It is the primary bioactive component of turmeric extract and is responsible for its vibrant yellow color. *Curcumin* possesses potent antioxidant and anti-inflammatory properties, which are key factors in managing keloid scars.

8.10.2. Antioxidant Activity of Curcumin

Curcumin acts as a scavenger of free radicals and Reactive Oxygen Species (ROS), thereby reducing oxidative stress and preventing cellular damage. Oxidative stress plays a significant role in keloid formation and progression, and curcumin's antioxidant activity helps mitigate this process [29].

Table 6. Curcumin's multifaceted properties supporting keloid scar reduction.

Aspect	Description
Chemical composition	Primary bioactive compound in turmeric extract, belonging to the curcuminoid family
Antioxidant	Possesses potent antioxidant properties, scavenging free radicals and reducing oxidative stress in the skin
Anti-inflammatory	Inhibits various inflammatory pathways and mediators, reducing inflammation in keloid scars
Modulates collagen synthesis	Regulates collagen production and remodeling, potentially reducing scar thickness and promoting scar flattening
Wound healing properties	Promotes wound healing processes, including cell proliferation, angiogenesis, and tissue regeneration
Skin-brightening effect	It may help lighten hyperpigmentation associated with keloid scars, improving overall skin appearance
Biocompatibility	Generally well-tolerated by the skin, with minimal adverse effects reported
Application	Available in various forms, including supplements, creams, and serums, for topical or oral administration
Clinical evidence	Limited clinical studies support its efficacy in keloid scar management, further research is needed for the validation

Note: This table details the chemical structure and mechanisms of action of Curcumin, highlighting its antioxidant, anti-inflammatory, and collagen-modulating properties relevant to keloid prevention and treatment.

8.10.3. Anti-inflammatory Mechanisms of Curcumin

Curcumin inhibits various inflammatory pathways and mediators, including NF-κB, COX-2, and pro-inflammatory cytokines. By suppressing inflammation, curcumin can reduce the excessive inflammatory response seen in keloid scars and help alleviate symptoms such as redness, swelling, and pain.

8.10.4. Curcumin-mediated Modulation of Collagen Synthesis

Curcumin has been shown to modulate collagen synthesis and remodeling, which are central processes in keloid formation. By regulating the activity of collagen-producing cells (fibroblasts), curcumin may help prevent the excessive deposition of collagen characteristic of keloids, leading to improved scar appearance and texture.

8.10.5. Curcumin in Wound Healing and Tissue Regeneration

Curcumin promotes various aspects of the wound healing process, including cell proliferation, angiogenesis (formation of new blood vessels), and tissue regeneration. These properties contribute to the overall improvement of keloid scars by enhancing the skin's natural repair mechanisms [30].

Overall, the multifaceted effects of curcumin make it a promising candidate for managing keloid scars. Its antioxidant, anti-inflammatory, collagen-modulating, and wound-healing properties collectively contribute to its potential anti-keloid effects, offering a natural and effective approach to keloid management.

The tabular format offers a concise overview of Curcumin's properties and potential benefits in the management of keloid scars (Table **6**).

Table 7. Key components of licorice extract and their therapeutic implications for keloid management.

Aspect	Description
Chemical composition	Contains glycyrrhizin, glabridin, flavonoids (liquiritin, isoliquiritin, liquiritigenin), glycyrrhetinic acid and other compounds
Anti-inflammatory	Glycyrrhizin and glabridin exhibit potent anti-inflammatory properties, reducing inflammation in keloid scars
Antioxidant	Flavonoids possess antioxidant activity, scavenging free radicals and reducing oxidative stress in the skin
Inhibits collagen synthesis	Glycyrrhetinic acid has been shown to inhibit collagen production, potentially reducing scar thickness
Skin-lightening effect	Glabridin inhibits melanin synthesis, which may help lighten hyperpigmentation associated with keloid scars
Promotes wound healing	Various compounds in licorice extract support wound healing processes, promoting tissue repair and regeneration
Biocompatibility	Generally well-tolerated by the skin, with minimal adverse effects reported
Application	Available in various forms, including creams, gels, and ointments, for topical application
Clinical evidence	Limited clinical studies support its efficacy in keloid scar management, and further research is needed for validation

Note: This table presents the major active compounds in licorice extract-such as glycyrrhizin and glabridin-and describes their effects on inflammation, collagen synthesis, oxidative stress, and skin pigmentation.

8.11. Phytochemical Profile and Functional Properties of Licorice Extract

Licorice extract contains several chemical compounds that contribute to its potential anti-keloid effects, shown in Table **7**.

8.11.1. Glycyrrhizin as a Key Anti-inflammatory Saponin

Glycyrrhizin is a triterpenoid saponin found in licorice extract, known for its anti-inflammatory properties. It inhibits the activity of pro-inflammatory enzymes like Cyclooxygenase (COX) and Lipoxygenase (LOX), thereby reducing inflammation in the skin. By suppressing inflammation, glycyrrhizin may help mitigate the exaggerated inflammatory response associated with keloid scars.

8.11.2. Glabridin and Skin-lightening Properties

Glabridin is a flavonoid found in licorice extract, known for its antioxidant and skin-lightening properties. It inhibits melanin synthesis by suppressing the activity of tyrosinase, an enzyme involved in melanin production. While its primary role in keloid management is less studied, glabridin's ability to lighten hyperpigmentation associated with keloid scars may improve its aesthetic appearance [31].

8.11.3. Licorice Flavonoids and Antioxidant Effects

Licorice extract contains various flavonoids, including liquiritin, isoliquiritin, and liquiritigenin, which possess antioxidant and anti-inflammatory properties. These flavonoids help scavenge free radicals, reduce oxidative stress, and modulate inflammatory responses, thereby promoting tissue repair and regeneration in keloid scars.

8.11.4. Glycyrrhetinic Acid and Anti-fibrotic Activity

Glycyrrhetinic acid is a triterpenoid derivative of glycyrrhizin found in licorice extract. It exhibits anti-inflammatory and anti-fibrotic properties, which may help prevent excessive collagen deposition and fibrosis characteristic of keloid scars. Glycyrrhetinic acid has been shown to inhibit the proliferation of fibroblasts and reduce the production of collagen, potentially limiting keloid formation and promoting scar remodeling [32].

Overall, the combination of these chemical compounds in licorice extract contributes to its potential anti-keloid effects by reducing inflammation, inhibiting collagen synthesis, and promoting skin regeneration. While further research is needed to elucidate the specific mechanisms and efficacy of licorice extract in keloid management, its historical use in traditional medicine and promising pharmacological properties make it a valuable natural remedy for keloid scars.

The tabular format provides a concise summary of licorice extract's properties and potential benefits in the management of keloid scars (Table **7**).

8.12. Silicone Gel as a Non-botanical Comparator in Keloid Management

Silicone gel, while not derived directly from plants, is often considered in the realm of natural remedies due to its biocompatibility and minimal adverse effects. It primarily consists of silicones, which are synthetic polymers derived

from silica, a naturally occurring compound. Silicone gel has been widely used in the management of keloids and hypertrophic scars due to its unique chemical and physical properties shown in Table **8**.

Table 8. Functional and chemical profile of silicone gel in keloid scar management.

Aspect	Description
Chemical composition	Consists primarily of silicones, synthetic polymers derived from silica
Mechanism of action	• Forms an occlusive barrier on the skin, maintaining optimal hydration levels and protecting against external irritants • Modulates collagen synthesis and remodeling, potentially reducing scar thickness and promoting scar flattening • Increases skin hydration and elasticity, softening and flattening keloid scars
Biocompatibility	Well-tolerated by the skin, typically causing minimal to no allergic reactions or irritation
Application	Applied topically as a gel, allowing for easy and convenient use
Long-term efficacy	Effective for long-term scar management, with sustained benefits observed over time
Adverse effects	Minimal adverse effects were reported, making it suitable for prolonged use

Note: This table outlines the chemical composition and action mechanism of silicone gel, including its occlusive barrier formation, collagen regulation effects, hydration benefits, and long-term use in scar therapy.

8.12.1. Barrier Function of Silicone Gel

Silicone gel forms a thin, occlusive barrier when applied to the skin, creating a protective environment that helps maintain optimal hydration levels and prevents excessive moisture loss. By providing a barrier against external irritants and microbes, silicone gel promotes an optimal wound-healing environment, which is essential for managing keloid scars.

8.12.2. Silicone Gel-mediated Collagen Remodeling

Silicone gel has been shown to modulate collagen synthesis and remodeling in keloid scars. While the exact mechanisms are not fully understood, silicone gel is thought to exert mechanical pressure on the scar tissue, which may help align collagen fibers and reduce scar thickness over time. This process promotes scar flattening and softening, improving the overall appearance and texture of keloids [33].

8.12.3. Hydration and Scar Elasticity with Silicone Gel

Silicone gel hydrates the skin and increases its elasticity, which can help soften and flatten keloid scars. By moisturizing the skin and promoting flexibility, silicone gel reduces tension on the scar tissue, minimizing the risk of further scar hypertrophy and promoting scar maturation.

8.12.4. Biocompatibility and Long-term Use of Silicone Gel

Silicone gel is well-tolerated by the skin and does not typically cause allergic reactions or irritation. Its biocompatibility makes it suitable for long-term use in scar management, as it can be applied topically without significant adverse effects [34].

Overall, silicone gel's unique chemical and physical properties make it an effective option for managing keloid scars by promoting hydration, reducing collagen synthesis, and improving scar texture and appearance. While it may not contain specific chemical compounds like plant-derived extracts, silicone gel's mechanisms of action contribute to its anti-keloid effects and make it a valuable tool in scar management.

The tabular format provides a concise overview of silicone gel's properties and benefits in keloid scar management (Table **8**).

8.13. Modulating Collagen Synthesis: Role of Plant Compounds

Collagen synthesis plays a central role in keloid formation, contributing to the excessive deposition of collagen-rich extracellular matrix characteristic of keloid scars. Plant-derived compounds offer a promising avenue for modulating collagen synthesis and mitigating keloid pathogenesis. Here, we explore the potential mechanisms and therapeutic implications of plant compounds in regulating collagen production.

8.13.1. Inhibition of TGF-β/Smad Signaling by Plant Compounds

Transforming growth factor-beta (TGF-β) is a key regulator of collagen synthesis in keloids, acting through the Smad signaling pathway to stimulate fibroblasts and myofibroblasts to produce collagen. Plant-derived compounds with inhibitory effects on TGF-β/Smad signaling pathways can attenuate collagen synthesis and prevent excessive scar formation.

8.13.2. Antioxidant-mediated Regulation of Collagen Synthesis

Oxidative stress contributes to collagen overproduction in keloids by promoting fibroblast activation and ECM remodeling. Plant compounds with antioxidant properties, such as polyphenols, flavonoids, and carotenoids, can scavenge free radicals and reduce oxidative damage, thereby inhibiting collagen synthesis and fibrosis [35].

8.13.3. Anti-inflammatory Modulation of Collagen Deposition

Chronic inflammation is associated with increased collagen deposition in keloids, driven by pro-inflammatory cytokines and chemokines. Plant-derived compounds with anti-inflammatory activity, such as curcumin, resveratrol, and quercetin, can suppress inflammatory mediators and attenuate collagen synthesis in keloid scars.

8.13.4. Regulation of Matrix Metalloproteinases (MMPs)

Imbalances in Matrix Metalloproteinase (MMP) activity contribute to excessive collagen accumulation in keloids.

Plant compounds with MMP-inhibitory effects, such as green tea catechins and Epigallocatechin Gallate (EGCG), can regulate ECM turnover and prevent collagen overproduction in keloid scars.

8.13.5. Direct Collagen-modulating Phytochemicals

Some plant-derived compounds directly modulate collagen synthesis by regulating collagen gene expression or post-translational modifications. For example, asiaticoside from Centella asiatica has been shown to stimulate collagen production and promote wound healing in keloids.

8.13.6. Regulation of Fibroblast Phenotype by Plant-derived Agents

Plant compounds can influence fibroblast behavior and phenotype, affecting their ability to produce collagen and ECM components. Compounds that promote fibroblast apoptosis or inhibit myofibroblast differentiation may mitigate collagen deposition and fibrosis in keloid scars [36].

Harnessing the collagen-modulating properties of plant-derived compounds offers a promising strategy for developing novel therapies to address keloid pathogenesis. By targeting multiple pathways involved in collagen synthesis and fibrosis, plant compounds may offer synergistic effects and improved therapeutic outcomes for keloid patients. Further research is needed to elucidate the specific mechanisms of action and clinical efficacy of plant-derived compounds in keloid management.

8.14. Promotion of Fibroblast Apoptosis: A Novel Anti-keloid Strategy

Keloid pathogenesis is characterized by dysregulated fibroblast proliferation and resistance to apoptosis, contributing to excessive collagen deposition and scar formation. Targeting fibroblast apoptosis represents a promising therapeutic approach for keloid management, aiming to reduce scar size and prevent recurrence. Here, we explore strategies for promoting fibroblast apoptosis as a novel anti-keloid strategy.

8.14.1. Small-molecule and Natural-product Apoptosis Inducers

Various compounds, including small molecules, peptides, and natural extracts, have been identified as apoptosis inducers in fibroblasts. These agents target intracellular signaling pathways involved in apoptosis regulation, such as the intrinsic (mitochondrial) or extrinsic (death receptor-mediated) pathways. By activating pro-apoptotic factors or inhibiting anti-apoptotic proteins, apoptosis inducers promote programmed cell death in keloid fibroblasts.

8.14.2. Cytokine-based Modulation of Fibroblast Apoptosis

Cytokines and growth factors play critical roles in regulating fibroblast survival and apoptosis. Modulating the expression or activity of pro-survival cytokines, such as TGF-β or interleukins, can sensitize keloid fibroblasts to apoptotic stimuli. Conversely, enhancing the secretion of pro-apoptotic cytokines, such as tumor necrosis factor-alpha (TNF-α) or Fas ligand (FasL), can trigger fibroblast apoptosis and inhibit keloid formation [37].

8.14.3. Gene Therapy Approaches Targeting Fibroblast Survival

Gene therapy approaches offer targeted strategies for inducing fibroblast apoptosis in keloids. By delivering therapeutic genes encoding pro-apoptotic proteins (*e.g.*, Bax, Bid) or RNA interference molecules targeting anti-apoptotic genes (*e.g.*, Bcl-2, survivin), gene therapy vectors can reprogram keloid fibroblasts to undergo apoptosis selectively.

8.14.4. Combination Strategies to Enhance Apoptosis-induced Scar Regression

Synergistic combinations of apoptosis inducers, cytokine modulators, and gene therapy vectors may enhance the efficacy of anti-keloid strategies. By targeting multiple signaling pathways involved in fibroblast survival and apoptosis, combination therapies can overcome resistance mechanisms and achieve more profound and sustained effects on keloid regression [38].

Promoting fibroblast apoptosis represents a promising avenue for developing novel anti-keloid therapies with the potential to improve scar outcomes and prevent recurrence. Further preclinical and clinical studies are warranted to evaluate the safety, efficacy, and long-term benefits of apoptosis-inducing strategies in keloid management.

8.15. Candidate Compounds: Identification and Characterization

Identifying and characterizing candidate compounds with anti-keloid properties is essential for developing effective therapeutic interventions. Several approaches are utilized to screen and evaluate potential compounds for their ability to modulate key processes involved in keloid pathogenesis.

8.15.1. High-throughput Screening of Anti-keloid Candidates

High-throughput Screening (HTS) assays enable the rapid screening of large compound libraries to identify molecules that exhibit desired biological activities. Automated platforms and robotics facilitate the screening of diverse chemical libraries, natural product extracts, or small molecule libraries against keloid-derived cell lines or animal models. Compounds showing promising activity in HTS assays are selected for further characterization.

8.15.2. Structure-activity Relationship (SAR) Optimization

SAR studies involve systematically modifying the chemical structure of lead compounds to optimize their pharmacological properties, potency, and selectivity. By synthesizing analogs or derivatives of candidate compounds and assessing their structure-activity relationships, medicinal chemists can identify structural motifs essential for anti-keloid activity and develop more potent or bioavailable derivatives [39].

8.15.3. Molecular Docking and Virtual Screening Approaches

Computational methods, such as molecular docking and virtual screening, are used to predict the binding affinity and mode of interaction between candidate compounds and their target proteins or receptors implicated in keloid pathogenesis. *In silico* modeling and simulation techniques help priori-

tize compounds for experimental validation based on their predicted binding energies, pharmacokinetic properties, and drug-likeness criteria.

8.15.4. In vitro Validation of Anti-keloid Activity

Candidate compounds identified through computational or HTS approaches are validated using *in vitro* assays to assess their effects on cellular processes relevant to keloid pathogenesis. Cell-based assays measuring fibroblast proliferation, collagen synthesis, apoptosis induction, or extracellular matrix remodeling provide insights into the mechanisms of action and therapeutic potential of candidate compounds.

8.15.5. In vivo Evaluation in Experimental Keloid Models

Promising candidate compounds are evaluated in preclinical animal models of keloid formation to assess their efficacy, safety, and pharmacokinetics in a physiological context. Animal studies involve administering candidate compounds *via* topical application, injection, or oral administration and monitoring their effects on scar size, collagen deposition, tissue remodeling, and adverse effects [40].

By systematically identifying and characterizing candidate compounds with anti-keloid properties, researchers can advance the development of targeted therapies for keloid management. Integration of multidisciplinary approaches, including medicinal chemistry, computational modelling, and preclinical validation, facilitates the discovery of novel pharmacological agents with the potential to improve scar outcomes and enhance patient quality of life.

8.16. Therapeutic Implications: Potential Applications in Keloid Management

The identification of plant-derived compounds with anti-keloid properties opens new avenues for keloid management, offering natural, multi-targeted therapeutic strategies. Based on their diverse pharmacological actions ranging from anti-inflammatory to collagen-regulating properties, these compounds can be developed into various treatment forms. Here are some of the most promising therapeutic applications

8.16.1. Topical Applications of Phytochemical-based Therapies

Many plant-derived compounds, including aloe vera, *Centella asiatica*, and green tea extract, are suitable for topical application due to their ability to be absorbed directly at the site of scarring. Topical formulations, such as gels, creams, or ointments, allow for localized treatment with minimal systemic side effects.

8.16.2. Potential Intralesional Use of Plant-derived Compounds

Compounds like curcumin and glycyrrhizin could be formulated for direct injection into keloid lesions, delivering high concentrations to the affected area and potentially improving scar resolution by targeting collagen synthesis and fibroblast activity more effectively.

8.16.3. Combination Therapies with Conventional Modalities

Combining plant-derived compounds with existing therapies, such as corticosteroid injections, laser treatments, or surgical excision, could improve treatment efficacy. For example, pairing EGCG with corticosteroids could enhance the reduction of fibroblast proliferation and collagen deposition.

8.16.4. Integration into Personalized Keloid Treatment Strategies

By leveraging plant-derived compounds with specific anti-fibrotic and anti-inflammatory properties, personalized treatment plans could be developed for patients based on their unique keloid characteristics, genetic predispositions, and response to therapy.

8.16.5. Prophylactic Use in High-risk Individuals

For individuals prone to keloid formation, prophylactic treatment with botanical compounds after skin trauma (such as surgery or burns) could mitigate excessive scarring. This would be particularly useful in patients with a history of keloid development, where compounds like *Centella asiatica* can aid in balanced collagen production [41].

The therapeutic potential of plant-derived compounds for keloid management is promising, with several compounds demonstrating efficacy in modulating key processes such as fibroblast proliferation, collagen synthesis, and inflammation. The following are the key takeaways from this review:

8.16.6. Key Mechanistic Takeaways from Plant-derived Therapies

Compounds like curcumin, EGCG, asiaticoside, and aloe vera act on multiple pathways (*e.g.*, TGF-β/Smad, MAPK/ERK), providing comprehensive approaches to managing keloid formation.

8.16.7. Clinical Relevance, Limitations, and Evidence Gaps

Compounds such as aloe vera and Centella asiatica have shown positive outcomes in clinical trials, while others like EGCG and glycyrrhizin are supported by strong preclinical evidence and hold potential for future clinical testing.

8.16.8. Synergistic and Multimodal Treatment Opportunities

Combining plant-derived compounds with conventional treatments may enhance efficacy and reduce recurrence rates in keloid management [42].

While these findings are encouraging, several challenges remain in translating plant-derived therapies from research to clinical practice:

1. **Scalability and Standardization:** The extraction and formulation of plant-derived compounds need to be standardized to ensure consistency in bioactive compound concentrations. Variations in growing conditions, harvesting times, and extraction methods can lead to inconsistent therapeutic effects.

2. **Regulation and Quality Control:** The regulation of herbal and plant-based treatments often varies between countries, making it difficult to ensure the quality, efficacy, and safety of these products on a global scale. Rigorous clinical trials and regulatory approval processes are necessary to establish plant-derived therapies as mainstream treatment options.

3. **Bioavailability and Delivery:** Many plant-derived compounds, such as curcumin, suffer from low bioa-

vailability when applied topically or taken orally. Innovative delivery systems, such as nanocarriers or liposomes, may be required to enhance the absorption and effectiveness of these compounds in keloid management.

4. **Side Effects and Long-term Use:** Although plant-derived therapies are generally considered safe, potential side effects and toxicities must be evaluated, particularly for long-term use. For example, licorice extract (glycyrrhizin) can cause side effects like elevated blood pressure in some individuals, and long-term safety data for keloid treatments is limited [43].

To maximize the therapeutic potential of plant-derived compounds for keloid management, future research should focus on:

1. Conducting large-scale clinical trials to validate the efficacy and safety of promising compounds.
2. Developing advanced delivery systems to improve bioavailability and targeted application.
3. Standardizing extraction and formulation processes to ensure consistent results across different product batches.
4. Exploring combination therapies that integrate botanical extracts with conventional treatment options to achieve synergistic effects.

By addressing these challenges, plant-derived compounds could emerge as effective and safe options for preventing and treating keloids, providing patients with more natural and holistic alternatives to conventional therapies [44].

9. FUTURE DIRECTIONS: TRANSLATIONAL OPPORTUNITIES AND CHALLENGES

The development of novel anti-keloid compounds presents exciting translational opportunities for improving keloid management. However, several challenges must be addressed to translate promising preclinical findings into clinical applications effectively. Here are future directions, translational opportunities, and challenges in the field of keloid research:

9.1. Clinical Translation

Translating preclinical research findings into clinically viable treatments requires rigorous validation through well-designed clinical trials. Collaborative efforts between researchers, clinicians, and industry partners are essential for conducting large-scale clinical studies evaluating the safety, efficacy, and long-term outcomes of anti-keloid compounds in diverse patient populations [45].

9.2. Biomarker Identification

Biomarkers predictive of keloid formation, progression, and response to therapy are needed to personalize treatment approaches and improve patient outcomes. Identifying molecular signatures, genetic markers, or imaging biomarkers associated with keloid susceptibility and treatment response facilitates patient stratification, treatment selection, and monitoring of therapeutic efficacy.

9.3. Precision Medicine Approaches

Leveraging advances in genomics, proteomics, and molecular profiling enables the development of personalized treatment strategies tailored to individual patient characteristics and keloid phenotypes. Precision medicine approaches incorporate patient-specific factors, such as genetic polymorphisms, cytokine profiles, and tissue microenvironments, to optimize treatment selection, dosing, and response monitoring [46].

9.4. Combination Therapies

Investigating synergistic combinations of anti-keloid compounds with existing therapies or novel treatment modalities offers opportunities for improving treatment outcomes and addressing multidimensional aspects of keloid pathogenesis. Combination therapies targeting multiple pathways involved in fibrosis, inflammation, and wound healing may enhance therapeutic efficacy and reduce the risk of keloid recurrence.

9.5. Regulatory Approval

Obtaining regulatory approval for novel anti-keloid compounds requires navigating complex regulatory pathways and demonstrating safety, efficacy, and manufacturing quality standards through preclinical and clinical studies. Regulatory agencies play a critical role in evaluating the risk-benefit profiles of anti-keloid therapies and ensuring their timely approval and accessibility to patients [47].

9.6. Patient Engagement and Education

Engaging patients in clinical research, fostering patient-centered care approaches, and promoting patient education and empowerment are essential for enhancing treatment adherence, satisfaction, and long-term outcomes. Patient advocacy groups, support networks, and educational resources play pivotal roles in raising awareness, reducing stigma, and advocating for improved keloid care.

The translational opportunities and challenges in keloid research highlight the need for interdisciplinary collaborations, innovative approaches, and patient-centric strategies to advance the development and implementation of novel anti-keloid therapies. By addressing these challenges and capitalizing on emerging opportunities, researchers and clinicians can revolutionize keloid management and improve the quality of life for individuals affected by this debilitating condition.

10. HARNESSING NATURE'S POTENTIAL FOR KELOID THERAPY

Nature offers a rich source of bioactive compounds with diverse pharmacological properties, making it an attractive avenue for developing novel therapies for keloids. By harnessing the therapeutic potential of natural products, researchers aim to identify and characterize compounds that modulate key pathways involved in keloid pathogenesis. Here's how nature's potential can be leveraged for keloid therapy:

10.1. Botanical Extracts

Plants produce a vast array of secondary metabolites, including polyphenols, alkaloids, terpenoids, and flavonoids, which exhibit anti-inflammatory, antioxidant, and anti-fibrotic activities. Botanical extracts derived from medicinal plants have been traditionally used in folk medicine for wound healing and skin conditions. Screening botanical extracts for their anti-keloid effects may lead to the discovery of novel therapeutic agents with fewer side effects compared to synthetic drugs [48].

10.2. Marine Compounds

Marine organisms, such as sponges, corals, and algae, produce bioactive compounds with unique chemical structures and pharmacological activities. Marine-derived compounds, such as peptides, polyketides, and alkaloids, show promise as anti-keloid agents by targeting fibroblast proliferation, collagen synthesis, and extracellular matrix deposition. Marine natural products offer untapped potential for discovering novel drug candidates with enhanced efficacy and selectivity.

10.3. Microbial Metabolites

Microorganisms, including bacteria, fungi, and actinomycetes, produce a vast array of secondary metabolites with diverse biological activities. Microbial metabolites, such as antibiotics, enzymes, and peptides, exhibit anti-inflammatory, immunomodulatory, and anti-fibrotic properties that may be beneficial for keloid therapy. Exploring the microbial diversity and screening microbial extracts for anti-keloid activity may lead to the discovery of novel drug leads and therapeutic targets [49].

10.4. Traditional Medicine

Traditional medicine systems, such as Traditional Chinese Medicine (TCM), Ayurveda, and Indigenous healing practices, offer valuable insights into the use of natural remedies for skin disorders, including keloids. Traditional herbal formulations and medicinal plants used in these systems have been empirically validated for their efficacy in wound healing, scar reduction, and skin regeneration. Integrating traditional knowledge with modern scientific approaches facilitates the discovery of novel botanical remedies and therapeutic strategies for keloid management.

10.5. Multi-target Approaches

Natural products often exhibit pleiotropic effects by targeting multiple pathways involved in keloid pathogenesis. By modulating inflammation, oxidative stress, fibroblast activation, and extracellular matrix remodeling, natural compounds offer holistic approaches to keloid therapy. Combining multiple natural products or synergistic combinations of natural and synthetic agents may enhance therapeutic efficacy and reduce the risk of adverse effects [50].

Harnessing nature's potential for keloid therapy offers a promising approach to discovering safe, effective, and sustainable treatments for this challenging dermatological condition. By exploring the rich biodiversity of natural resources and integrating traditional knowledge with modern scientific advances, researchers can unlock new insights into keloid pathophysiology and develop innovative therapies that improve patient outcomes and quality of life.

CONCLUSION

This review highlights the therapeutic potential of plant-derived compounds in keloid management. Key findings indicate that curcumin, EGCG, asiaticoside, and glycyrrhizin target fibrotic pathways such as TGF-β/Smad and MAPK/ERK, reducing fibroblast proliferation and excessive collagen synthesis. These compounds provide a promising foundation for alternative keloid treatments, with potential integration into clinical practice. Although these findings highlight the potential of plant-derived compounds in keloid treatment, further studies are needed to optimize their formulation, improve bioavailability, and evaluate long-term safety in clinical settings. Standardized clinical trials will be essential to validate their efficacy and integration into existing treatment protocols. By leveraging the anti-fibrotic properties of plant-derived compounds, future research can contribute to developing safer, more effective keloid therapies.

AUTHORS' CONTRIBUTIONS

The study was conceived and designed by V.K.M. Data collection was conducted by M.K.D.J. The analysis and interpretation of results were carried out by K.L. and P.D.P. The draft of the manuscript was written by M.V. All authors reviewed the results and approved the final version of the manuscript.

LIST OF ABBREVIATIONS

DMEM	=	Dulbecco's Modified Eagle Medium
FBS	=	Fetal Bovine Serum
HKFs	=	Human Feloid-derived Fibroblasts
TGF-β	=	Transforming Growth Factor-beta

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CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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REFERENCES

[1] Veeresham, C. Natural products derived from plants as a source of drugs. *J. Adv. Pharm. Technol. Res.,* **2012**, *3*(4), 200-201. http://dx.doi.org/10.4103/2231-4040.104709 PMID: 23378939

[2] Koparde, A.A.; Doijad, R.C.; Magdum, C.S. Natural Products in Drug Discovery. In: *Pharmacognosy - Medicinal Plants*; IntechOpen, **2019**. http://dx.doi.org/10.5772/intechopen.82860

[3] Yuan, H.; Ma, Q.; Ye, L.; Piao, G. The traditional medicine and modern medicine from natural products. *Molecules,* **2016**, *21*(5), 559. http://dx.doi.org/10.3390/molecules21050559 PMID: 27136524

[4] Cragg, G.M.; Pezzuto, J.M. Natural products as a vital source for the discovery of cancer chemotherapeutic and chemopreventive agents. *Med. Princ. Pract.,* **2016**, *25*(Suppl 2), 41-59. http://dx.doi.org/10.1159/000443404 PMID: 26679767

[5] Newman, D.J.; Cragg, G.M. Natural products as sources of new drugs over the nearly four decades from 01/1981 to 09/2019. *J. Nat. Prod.,* **2020**, *83*(3), 770-803. http://dx.doi.org/10.1021/acs.jnatprod.9b01285 PMID: 32162523

[6] Seca, A.; Pinto, D. Plant secondary metabolites as anticancer agents: Successes in clinical trials and therapeutic application. *Int. J. Mol. Sci.,* **2018**, *19*(1), 263. http://dx.doi.org/10.3390/ijms19010263 PMID: 29337925

[7] Melo, F.H.M.; Oliveira, J.S.; Sartorelli, V.O.B.; Montor, W.R. Cancer chemoprevention: Classic and epigenetic mechanisms inhibiting tumorigenesis. What have we learned so far? *Front Oncol.,* **2018**, *8*, 644. http://dx.doi.org/10.3389/fonc.2018.00644 PMID: 30627525

[8] Kotecha, R.; Takami, A.; Espinoza, J.L. Dietary phytochemicals and cancer chemoprevention: A review of the clinical evidence. *Oncotarget,* **2016**, *7*(32), 52517-52529. http://dx.doi.org/10.18632/oncotarget.9593 PMID: 27232756

[9] George, V.C.; Dellaire, G.; Rupasinghe, H.P.V. Plant flavonoids in cancer chemoprevention: Role in genome stability. *J. Nutr. Biochem.,* **2017**, *45*, 1-14. http://dx.doi.org/10.1016/j.jnutbio.2016.11.007 PMID: 27951449

[10] Gullett, N.P.; Ruhul Amin, A.R.M.; Bayraktar, S.; Pezzuto, J.M.; Shin, D.M.; Khuri, F.R.; Aggarwal, B.B.; Surh, Y.J.; Kucuk, O. Cancer prevention with natural compounds. *Semin. Oncol.,* **2010**, *37*(3), 258-281. http://dx.doi.org/10.1053/j.seminoncol.2010.06.014 PMID: 20709209

[11] Thomford, N.E.; Senthebane, D.A.; Rowe, A.; Munro, D.; Seele, P.; Maroyi, A.; Dzobo, K. Natural products for drug discovery in the 21st century: Innovations for novel drug discovery. *Int. J. Mol. Sci.,* **2018**, *19*(6), 1578. http://dx.doi.org/10.3390/ijms19061578 PMID: 29799486

[12] Atanasov, A.G.; Waltenberger, B.; Pferschy-Wenzig, E.M.; Linder, T.; Wawrosch, C.; Uhrin, P.; Temml, V.; Wang, L.; Schwaiger, S.; Heiss, E.H.; Rollinger, J.M.; Schuster, D.; Breuss, J.M.; Bochkov, V.; Mihovilovic, M.D.; Kopp, B.; Bauer, R.; Dirsch, V.M.; Stuppner, H. Discovery and resupply of pharmacologically active plant-derived natural products: A review. *Biotechnol. Adv.,* **2015**, *33*(8), 1582-1614. http://dx.doi.org/10.1016/j.biotechadv.2015.08.001 PMID: 26281720

[13] Meier, B.P.; Lappas, C.M. The Influence of safety, efficacy, and medical condition severity on natural *versus* synthetic drug preference. *Med. Decis. Making.,* **2016**, *36*(8), 1011-1019. http://dx.doi.org/10.1177/0272989X15621877 PMID: 26683247

[14] Aung, T.; Qu, Z.; Kortschak, R.; Adelson, D. Understanding the effectiveness of natural compound mixtures in cancer through their molecular mode of action. *Int. J. Mol. Sci.,* **2017**, *18*(3), 656. http://dx.doi.org/10.3390/ijms18030656 PMID: 28304343

[15] Lin, S.R.; Chang, C.H.; Hsu, C.F.; Tsai, M.J.; Cheng, H.; Leong, M.K.; Sung, P.J.; Chen, J.C.; Weng, C.F. Natural compounds as potential adjuvants to cancer therapy: Preclinical evidence. *Br J. Pharmacol.,* **2020**, *177*(6), 1409-1423. http://dx.doi.org/10.1111/bph.14816 PMID: 31368509

[16] Calixto, J.B. The role of natural products in modern drug discovery. *An Acad. Bras Cienc.,* **2019**, *91*(Suppl. 3), e20190105. http://dx.doi.org/10.1590/0001-3765201920190105 PMID: 31166478

[17] Mohr, K.I. History of antibiotics research. *Curr. Top Microbiol. Immunol.,* **2016**, *398*, 237-272. http://dx.doi.org/10.1007/82_2016_499 PMID: 27738915

[18] McGowan, J.V.; Chung, R.; Maulik, A.; Piotrowska, I.; Walker, J.M.; Yellon, D.M. Anthracycline chemotherapy and cardiotoxicity. *Cardiovasc. Drugs Ther.,* **2017**, *31*(1), 63-75. http://dx.doi.org/10.1007/s10557-016-6711-0 PMID: 28185035

[19] Perveen, F.; Arshad, N.; Qureshi, R.; Nowsherwan, J.; Sultan, A.; Nosheen, B.; Rafique, H. Electrochemical, spectroscopic and theoretical monitoring of anthracyclines' interactions with DNA and ascorbic acid by adopting two routes: Cancer cell line studies. *PLoS One,* **2018**, *13*(10), e0205764. http://dx.doi.org/10.1371/journal.pone.0205764 PMID: 30372448

[20] Tewari, D.; Rawat, P.; Singh, P.K. Adverse drug reactions of anticancer drugs derived from natural sources. *Food. Chem. Toxicol.,* **2019**, *123*, 522-535. http://dx.doi.org/10.1016/j.fct.2018.11.041 PMID: 30471312

[21] Brandt, J.P.; Gerriets, V. *Bleomycin*; StatPearls Publishing: Treasure Island (FL), **2025**.

[22] Kellogg, E.H.; Hejab, N.M.A.; Howes, S.; Northcote, P.; Miller, J.H.; Díaz, J.F.; Downing, K.H.; Nogales, E. Insights into the distinct mechanisms of action of Taxane and non-Taxane microtubule stabilizers from Cryo-EM structures. *J. Mol. Biol.,* **2017**, *429*(5), 633-646. http://dx.doi.org/10.1016/j.jmb.2017.01.001 PMID: 28104363

[23] Moudi, M.; Go, R.; Yien, C.Y.; Nazre, M. Vinca alkaloids. *Int. J. Prev Med.,* **2013**, *4*(11), 1231-1235. PMID: 24404355

[24] Wang, Y.R.; Chen, S.F.; Wu, C.C.; Liao, Y.W.; Lin, T.S.; Liu, K.T.; Chen, Y.S.; Li, T.K.; Chien, T.C.; Chan, N.L. Producing irreversible topoisomerase II-mediated DNA breaks by site-specific Pt(II)-methionine coordination chemistry. *Nucleic Acids Res.,* **2017**, *45*(18), 10861-10871. http://dx.doi.org/10.1093/nar/gkx742 PMID: 28977631

[25] Meng, T.; Xiao, D.; Muhammed, A.; Deng, J.; Chen, L.; He, J. Anti-inflammatory action and mechanisms of resveratrol. *Molecules,* **2021**, *26*(1), 229. http://dx.doi.org/10.3390/molecules26010229 PMID: 33466247

[26] Xia, N.; Daiber, A.; Förstermann, U.; Li, H. Antioxidant effects of resveratrol in the cardiovascular system. *Br J. Pharmacol.,* **2017**, *174*(12), 1633-1646. http://dx.doi.org/10.1111/bph.13492 PMID: 27058985

[27] Patel, K.R.; Brown, V.A.; Jones, D.J.L.; Britton, R.G.; Hemingway, D.; Miller, A.S.; West, K.P.; Booth, T.D.; Perloff, M.; Crowell, J.A.; Brenner, D.E.; Steward, W.P.; Gescher, A.J.; Brown, K. Clinical pharmacology of resveratrol and its metabolites in colorectal cancer patients. *Cancer Res.,* **2010**, *70*(19), 7392-7399. http://dx.doi.org/10.1158/0008-5472.CAN-10-2027 PMID: 20841478

[28] Singh, A.P.; Singh, R.; Verma, S.S.; Rai, V.; Kaschula, C.H.; Maiti, P.; Gupta, S.C. Health benefits of resveratrol: Evidence from clinical studies. *Med. Res. Rev.,* **2019**, *39*(5), 1851-1891. http://dx.doi.org/10.1002/med.21565 PMID: 30741437

[29] Desai, S.J.; Prickril, B.; Rasooly, A. Mechanisms of phytonutrient modulation of cyclooxygenase-2 (COX-2) and inflammation related to cancer. *Nutr. Cancer,* **2018**, *70*(3), 350-375. http://dx.doi.org/10.1080/01635581.2018.1446091 PMID: 29578814

[30] Banerjee, S.; Ji, C.; Mayfield, J.E.; Goel, A.; Xiao, J.; Dixon, J.E.; Guo, X. Ancient drug curcumin impedes 26S proteasome activity by direct inhibition of dual-specificity tyrosine-regulated kinase 2. *Proc Natl Acad. Sci. USA,* **2018**, *115*(32), 8155-8160. http://dx.doi.org/10.1073/pnas.1806797115 PMID: 29987021

[31] Kunnumakkara, A.B.; Harsha, C.; Banik, K.; Vikkurthi, R.; Sailo, B.L.; Bordoloi, D.; Gupta, S.C.; Aggarwal, B.B. Is curcumin bioavailability a problem in humans: Lessons from clinical trials. *Expert Opin. Drug Metab. Toxicol.,* **2019**, *15*(9), 705-733. http://dx.doi.org/10.1080/17425255.2019.1650914 PMID: 31361978

[32] Wang, J.; Jiang, Y.F. Natural compounds as anticancer agents: Experimental evidence. *World J. Exp. Med.,* **2012**, *2*(3), 45-57. http://dx.doi.org/10.5493/wjem.v2.i3.45 PMID: 24520533

[33] Lazzeroni, M.; Guerrieri-Gonzaga, A.; Gandini, S.; Johansson, H.; Serrano, D.; Cazzaniga, M.; Aristarco, V.; Macis, D.; Mora, S.; Caldarella, P.; Pagani, G.; Pruneri, G.; Riva, A.; Petrangolini, G.; Morazzoni, P.; DeCensi, A.; Bonanni, B. A presurgical study of lecithin formulation of green tea extract in women with early breast cancer. *Cancer Prev Res.,* **2017**, *10*(6), 363-370. http://dx.doi.org/10.1158/1940-6207.CAPR-16-0298 PMID: 28400479

[34] Musial, C.; Kuban-Jankowska, A.; Gorska-Ponikowska, M. Beneficial properties of green tea catechins. *Int. J. Mol. Sci.,* **2020**, *21*(5), 1744. http://dx.doi.org/10.3390/ijms21051744 PMID: 32143309

[35] Chow, H.H.S.; Hakim, I.A.; Vining, D.R.; Crowell, J.A.; Ranger-Moore, J.; Chew, W.M.; Celaya, C.A.; Rodney, S.R.; Hara, Y.; Alberts, D.S. Effects of dosing condition on the oral bioavailability of green tea catechins after single-dose administration of Polyphenon E in healthy individuals. *Clin. Cancer Res.,* **2005**, *11*(12), 4627-4633. http://dx.doi.org/10.1158/1078-0432.CCR-04-2549 PMID: 15958649

[36] Reyes-Farias, M.; Carrasco-Pozo, C. The anti-cancer effect of quercetin: Molecular implications in cancer metabolism. *Int. J. Mol. Sci.,* **2019**, *20*(13), 3177. http://dx.doi.org/10.3390/ijms20133177 PMID: 31261749

[37] Kedhari Sundaram, M.; Raina, R.; Afroze, N.; Bajbouj, K.; Hamad, M.; Haque, S.; Hussain, A. Quercetin modulates signaling pathways and induces apoptosis in cervical cancer cells. *Biosci. Rep.,* **2019**, *39*(8), BSR20190720. http://dx.doi.org/10.1042/BSR20190720 PMID: 31366565

[38] Ward, A.B.; Mir, H.; Kapur, N.; Gales, D.N.; Carriere, P.P.; Singh, S. Quercetin inhibits prostate cancer by attenuating cell survival and inhibiting anti-apoptotic pathways. *World J. Surg. Oncol.,* **2018**, *16*(1), 108. http://dx.doi.org/10.1186/s12957-018-1400-z PMID: 29898731

[39] Tang, S.M.; Deng, X.T.; Zhou, J.; Li, Q.P.; Ge, X.X.; Miao, L. Pharmacological basis and new insights of quercetin action in respect to its anti-cancer effects. *Biomed. Pharmacother,* **2020**, *121*, 109604. http://dx.doi.org/10.1016/j.biopha.2019.109604 PMID: 31733570

[40] Sturza, A.; Pavel, I.; Ancuşa, S.; Danciu, C.; Dehelean, C.; Duicu, O.; Muntean, D. Quercetin exerts an inhibitory effect on cellular bioenergetics of the B164A5 murine melanoma cell line. *Mol. Cell. Biochem.,* **2018**, *447*(1-2), 103-109. http://dx.doi.org/10.1007/s11010-018-3296-x PMID: 29380243

[41] Nouri, Z.; Fakhri, S.; Nouri, K.; Wallace, C.E.; Farzaei, M.H.; Bishayee, A. Targeting multiple signaling pathways in cancer: The rutin therapeutic approach. *Cancers,* **2020**, *12*(8), 2276. http://dx.doi.org/10.3390/cancers12082276 PMID: 32823876

[42] ben Sghaier, M.; Pagano, A.; Mousslim, M.; Ammari, Y.; Kovacic, H.; Luis, J. Rutin inhibits proliferation, attenuates superoxide production and decreases adhesion and migration of human cancerous cells. *Biomed. Pharmacother.,* **2016**, *84*, 1972-1978. http://dx.doi.org/10.1016/j.biopha.2016.11.001 PMID: 27829548

[43] Guo, Y.; Zhu, H.; Weng, M.; Wang, C.; Sun, L. Chemopreventive effect of Betulinic acid *via* mTOR-Caspases/Bcl2/Bax apoptotic signaling in pancreatic cancer. *BMC Complementary Med. Ther.,* **2020**, *20*(1), 178. http://dx.doi.org/10.1186/s12906-020-02976-7 PMID: 32513155

[44] Kumar, P.; Bhadauria, A.S.; Singh, A.K.; Saha, S. Betulinic acid as apoptosis activator: Molecular mechanisms, mathematical modeling and chemical modifications. *Life. Sci.,* **2018**, *209*, 24-33. http://dx.doi.org/10.1016/j.lfs.2018.07.056 PMID: 30076920

[45] Gheorgheosu, D.; Duicu, O.; Dehelean, C.; Soica, C.; Muntean, D. Betulinic acid as a potent and complex antitumor phytochemical: A minireview. *Anticancer Agents Med. Chem.,* **2014**, *14*(7), 936-945. http://dx.doi.org/10.2174/18715206146661402231921 48 PMID: 24568161

[46] Soica, C.; Danciu, C.; Savoiu-Balint, G.; Borcan, F.; Ambrus, R.; Zupko, I.; Bojin, F.; Coricovac, D.; Ciurlea, S.; Avram, S.; Dehelean, C.; Olariu, T.; Matusz, P. Betulinic acid in complex with a gamma-cyclodextrin derivative decreases proliferation and *in vivo* tumor development of non-metastatic and metastatic B164A5 cells. *Int. J. Mol. Sci.,* **2014**, *15*(5), 8235-8255. http://dx.doi.org/10.3390/ijms15058235 PMID: 24821543

[47] Butler, M.S.; Robertson, A.A.B.; Cooper, M.A. Natural product and natural product derived drugs in clinical trials. *Nat. Prod. Rep.,* **2014**, *31*(11), 1612-1661. http://dx.doi.org/10.1039/C4NP00064A PMID: 25204227

[48] Circioban, D.; Ledeti, A.; Vlase, G.; Moaca, A.; Ledeti, I.; Farcas, C.; Vlase, T.; Dehelean, C. Thermal degradation, kinetic analysis and evaluation of biological activity on human melanoma for artemisinin. *J. Therm Anal. Calorim.,* **2018**, *134*(1), 741-748. http://dx.doi.org/10.1007/s10973-018-7497-z

[49] Wong, Y.K.; Xu, C.; Kalesh, K.A.; He, Y.; Lin, Q.; Wong, W.S.F.; Shen, H.M.; Wang, J. Artemisinin as an anticancer drug: Recent advances in target profiling and mechanisms of action. *Med. Res. Rev.,* **2017**, *37*(6), 1492-1517. http://dx.doi.org/10.1002/med.21446 PMID: 28643446

[50] Guan, X.; Guan, Y. Artemisinin induces selective and potent anticancer effects in drug resistant breast cancer cells by inducing cellular apoptosis and autophagy and G2/M cell cycle arrest. *J. BUON,* **2020**, *25*(3), 1330-1336. PMID: 32862573

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