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CALENDULA OFFICINALIS: UNVEILING ITS THERAPEUTIC POTENTIAL AND DERMATOLOGICAL BENEFITS

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ABSTRACT

Calendula officinalis, commonly known as pot marigold, has been valued in traditional medicine for its versatile therapeutic properties, particularly in treating skin ailments. Rich in bioactive compounds such as carotenoids, flavonoids, and terpenoids, C. officinal is demonstrates anti-inflammatory, antimicrobial, antioxidant, and wound-healing activities. This review consolidates current findings on its phytochemistry and pharmacological applications, highlighting its benefits in dermatology, anti-HIV activity, diabetes management, cardiovascular health, and wound care. The molecular mechanisms underlying these effects, including cytokine modulation and growth factor promotion, support its efficacy in inflammation reduction, skin regeneration, and chronic disease management. Additionally, its role in commercial skincare, cosmetics, and adjunctive therapies for dermatitis, eczema, and acne showcases its potential in modern healthcare. However, caution is advised for individuals allergic to the Asteraceae family. This review underscores Calendula's therapeutic versatility and potential for safe and effective plant-based treatments.

I. INTRODUCTION

Calendula officinalis, commonly known as pot marigold or English marigold, belongs to the Asteraceae family and has a rich history in traditional medicine. This plant, native to the Mediterranean region, contains a wide range of bioactive compounds, including carotenoids, flavonoids, saponins, sterols, phenolic acids, and essential fatty acids. Various parts of the plant, especially the flowers, have been utilized in herbal medicine for their therapeutic properties, which include anti-inflammatory, analgesic, antimicrobial, and wound-healing effects [1].

Calendula flowers are traditionally prepared as tinctures, extracts, and salves, applied to the skin to help soothe and heal wounds, burns, and other skin inflammations. Modern research has identified significant compounds, such as isorhamnetin and rutin, which contribute to its therapeutic efficacy. In addition to its medicinal uses, C. officinal is popular in the cosmetic and food industries for it yellow-orange flowers, used as a natural colorant and ingredient in skin-care products. The plant's anti-inflammatory and antioxidative effects have been validated in recent studies, highlighting its potential in addressing chronic inflammation and oxidative stress [2].

Given its extensive medicinal properties, Calendula officinal is continues to attract interest for developing new natural remedies. Its applications span across dermatology, gynaecology, and oral care, making it a valuable herb in traditional and modern therapeutic practices. This review aims to consolidate current knowledge on the Pharmacological activities and applications of C. officinalis, contributing to the development of safe and effective plant-based treatments [4].

II. CALENDULA OFFICINALIS

Kingdom–Plantae

Subkingdom-Tracheobionta

Division-Magnoliophyta

Class-Magnoliopsida

Subclass- Asteridae

Order-Asterales [6]

Synonyms [7]

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Pot marigold, Bride of the Sun, Bullflower, butterwort English marigold, [6]

Figure 1: Pictorial representation of flower of Calendula officinalis Linn.

III. PHYTOCHEMISTRY OF CALENDULA OFFICINALIS

The medicinal plant Calendula officinalis, commonly known as calendula, is well-studied for its rich phytochemistry. Extensive phytochemical analyses have revealed various classes of bioactive compounds within the plant, including terpenoids, flavonoids, coumarins, quinones, volatile oils, carotenoids, and amino acids. Each of these classes contributes to the unique therapeutic potential of calendula [8**]**

3.1. Morphological Features:

Officinalis Linn. Is an annual or biennial plant, reaching 30-60 cm in height. The stem is angular, hairy, and solid. Leaves vary from lower spatulate leaves (10-20 cm long, 1-4 cm wide) to higher oblong and mucronate leaves (47cmlong). Anomocytic stomata represent on the apical region of the outer epidermis, with covering and glandular trichomes, elongated sclerenchyma cells. Marginal flower heads are bright yellow to orange; the corolla is oblong spatulate, measuring 15 cm**. [9-10]**

3.2. Phytochemical Components:

Terpenoids:

Terpenoids, primarily found in the flowers and roots of Calendula officinalis, are well-known for their antioxidant and anti-inflammatory properties. These sesquiterpenoids, such as τ-cadinol, α-cadinol, and τ-muurolol, exhibit antioxidant activity by scavenging free radicals, contributing to the management of conditions involving oxidative stress, including Alzheimer's disease, skin hyperpigmentation, and complications related to diabetes. Their anti-inflammatory action is mediated by inhibiting the COX-2 enzyme (Cyclo-oxygenase-2), reducing pro-inflammatory cytokines like Interleukins 1 and 6, tissue necrosis factor, and the synthesis of prostaglandins.

Terpenoids, also referred to as isoprenoids, are a diverse group of natural products responsible for the characteristic fragrance in flowers and plants. They are prevalent in the leaves and fruits of plants like citrus and eucalyptus. Terpenoids are categorized into simple (found in steam-volatile essential oils from plant sap and tissues) and complex forms (from non-volatile sources like plant gums and resins).

Various terpenoids have been extracted from the petroleum ether of C. officinalis flowers, including sitosterols, stigmasterols, diesters of diols, monoesters of taraxasterol, lupeol, erythrodiol, brein, ursadiol, faradiol-3-O-palmitate, faradiol-3-O-myristate, and faradiol-3-O-laurate. Other compounds include arnidiol-3-O-palmitate, arnidiol-3-O-myristate, arnidiol-3-O-laurate, and calenduladiol-3-O-palmitate. Additionally, oleanolic acid saponins (suchascalendulasideA-H), oleanane triterpene glycosides (e.g., calendula glycoside A, B, and C, along with their methyl and butyl esters), and glucosides of oleanolic acid found in roots and glucuronides in flowers and green parts have been identified. A novel triterpenic ester of the oleanane series, cornulacic acid acetate, was also isolated from the flowers of C. officinalis**.[11]**

Flavonoids:

Flavonoids, especially quercetin are known for their wound-healing effects. This activity primarily works through antioxidant action by scavenging radicals and enhancing fibroblast adhesion, which supports cellular

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activity in affected areas. Flavonoids also exhibit anti-plaque and anti-gingivitis effects by mechanisms such as inhibiting lysosomal hydrolase, reducing collagen breakdown through inhibition of matrix metal proteinases (MMPs), and increasing collagen concentration.

Additionally, C. officinalis contains other skin-protective flavonoids, including rutin, a pigen in, kaempferol, vitexin, and luteolin, which protect skin through antioxidant mechanisms. Quercetin and rutin are noted for their anti-depressant properties, acting through the inhibition of monoamine oxidases (MAOs)and reducing GABA levels. Isorhamnetin, along with quercetin derivatives like 3-O-(rhamnosyl)-glucosides and 3-O-acetyl-glucosides, displays anti-acetylcholinesterase activity, attributed to the acetyl and rhamnosyl groups in their structure. Another flavonoid, hyperoside, plays a role in osteosarcoma management by inhibiting cell proliferation and promoting osteogenic differentiation.

Flavonoids, as a group of phytonutrients, are widely found in fruits and vegetables, with compounds like quercetin, is quercetin, narcissin, and rutin isolated from C. officinalis's ethanolic extract**. [8-11]**

Coumarins:

Coumarins, abundantly present in the flowers of Calendula officinalis, help prevent oxidative cell damage. coumarins include umbelliferone, scopoletin, and esculetin. Umbelliferone serves as a skin- protective agent in sunscreen products due to its antioxidant properties. Scopoletin exhibits spasmolytic action by relaxing muscle contractions in the urogenital and gastrointestinal systems. Esculetin, another coumarin, acts as a phlebotonic and anti-inflammatory agent, reducing capillary permeability and improving venous tone. **[11]**

Additionally, esculetin has anti-thrombotic properties, enhancing the occlusion time of thrombotic platelet plug formation.Ethanolic extractsofC. Officinalis in florescences have been reported to contain coumarins such as scopoletin, umbelliferone, and esculetin**.[8][11][12]**

Quinones:

The quinones reported in C. officinal is include plastoquinone, phylloquinone, and to copherol, primarily located in the chloroplasts and mitochondria. These compounds play a significant role in photosynthesis and cellular respiration, enhancing the plant's bioactivity in photoprotective skincare products**.[13]**

Volatile Oils:

Volatile oils in C. officinalis are most abundant during the full flowering stage, reaching0.97%composition. These oils contain monoterpenes and sesquiterpenes such as α-thujene, α-pinene, sabinene, β-pinene, limonene, and p-cymene. Volatile oils contribute to calendula's aroma and potential therapeutic properties, especially in aromatherapy**.[11][13]**

Carotenoids

Carotenoids, mainly lycopene, β-carotene, lutein, and flavoxanthin, are responsible for calendula's bright orange petals. Studies indicate that carotenoids act as antioxidants, reducing free radicals and offering photoprotective effects on the skin**.[13]**

The leaves, petals, and pollen of Calendula officinalis flowers have been shown to contain carotenoids when extracted with methanol. Among the carotenoids identified in the pollen and petals are violaxanthin, neoxanthin, auroxanthin, lutein, flavoxanthin, mutatoxanthin, lycopene, and alpha-carotenes. **[24]**

Amino Acids

Amino acids, often referred to as the building blocks of proteins, play a vital role in various metabolic processes. In flowers, research has identified the presence of 15 free-form amino acids, including Alanine, Arginine, Asparagine, Valine, Histidine, Glutamic acid, Leucine, and Lysine, among others, when extracted using ethanol.

Free amino acids like alanine, arginine, valine, and lysine have been detected in calendula flowers. Amino acids aid in skin hydration and repair, making them valuable in skincare products containing calendula**.[14][8]**

Carbohydrates and Lipids

Calendula also contains polysaccharides and various lipid classes; including neutral lipids and phospholipids **[14]** Carbohydrates provide moisturizing properties, while the lipids support the skin barrier, enhancing calendula's topical benefits.

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IV. PHARMACOLOGY OF CALENDULA OFFCINALIS

Anti-HIVactivity:

Dichloromethane-methanol (1:1) extract of C. Officinalis flowers exhibited potent anti-HIV Activity in in vitro MTT/tetrazolium-based Assay. This activity was attributed to inhibition Of HIV1-RT (Reverse Transcription) at a concentration of 1,000 µg /mL as well as suppression of the HIV-Mediated fusion at 500 µg/mL **[12].**

Antioxidant activity:

Calendula officinalis (CO) contains flavonoids and phenolic compounds with strong antioxidant properties. The plant's leaves and petals scavenge free radicals, with the petals showing higher antioxidant activity than the leaves. Studies have shown CO extracts are effective in reducing peroxide production and exhibit strong radical-scavenging abilities, comparable to vitamins C and E. These antioxidant properties make CO extracts potentially Beneficial for treating ailments like heart disease, cancer, diabetes, and more**.[11]**

A70% methanol extract of Calendula officinalis was sequentially extracted with ether,chloroform,ethyl acetate, n-butanol, and water. The ether, butanol, and water extracts, rich in flavonoids, showed antioxidant activity. Additionally, propylene glycol extracts of the petals demonstrated strong antioxidant effects than flowerhead extracts, based on malondialdehyde (MDA) and isoprostane levels in plasma and urine **[6]**

Antidiabetic and anti hyperlipidemic activities:

The hydroalcoholic extract of Calendula officinalis showed significant antidiabetic and antihyperlipidemic effects in alloxan-induced diabetic rats. At doses of 25, 50, and 100 mg/kg, it reduced blood glucose, urine sugar, and serum lipids, with the 100mg/kg dose restoring the parameters to normal levels. The extract also increased total hemoglobin levels and showed effects similar to insulin. Additionally, the principal saponins from CO flowers inhibited serum glucose increase and gastric mucosal lesions in rats**.[17]**

Cardiovascular effect:

Calendula extract has been found to reduce the size of (MI) myocardial infarction. It seems that cardioprotectionis Achieved by changing the ischaemia-reperfusion-mediated death signal into a survival signal **[18]**

4.1 Commercial Uses of Calendula officinalis:

The beneficial use of calendula for its soothing, healing effects dates back to the 12th century. Known for its anti-Inflammatory and antioxidant properties, calendula flower extract is a popular in gradient in various skin care and medicinal products.

4.2 Skin care Products:

Calendula extract is widely used in skincare due to its ability to calm and protect the skin. Clinical studies highlight its effectiveness in soothing skin after sun exposure, reducing inflammation, and minimizing signs of aging. Thisis attributed to bioactive compounds such as rutin, quercetin, luteolin, and kaempferol, which have strong antioxidant properties. High-performance liquid chromatography (HPLC) analysis shows that calendula flowers contain significant percentages of active compounds ,including vitexin, rutin, quercetin,and myricetin. These compounds help neutralize free radicals and protect the skin from oxidative damage,making calendula valuable addition to products for sensitive skin, after-sun care, and eye contour treatments.

4.3. Sedative Uses:

Research involving animal models suggests that high doses of calendula preparations may have sedative effects. Studies in mice have shown that calendula can extend the sleep duration induced by sedative drugs, such as hexobarbital. While these preliminary results hint at potential calming effects, the exact impact of calendula on human sleep and relaxation is still under study. Its use with other sedative medications may amplify these effects.

4.4. Antihypertensive Applications:

Early animal studies also indicate that calendula might influence blood pressure. High doses of calendula preparations in some animal studies appeared to have blood pressure-lowering effects. This suggests that calendula could interact with other antihypertensive drugs, potentially enhancing their effectiveness. However, more research is needed to understand its precise role in human blood pressure regulation**.**

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V. DERMATOLOGICAL APPLICATIONS

5.1. Wound Healing:

Wound healing is classified into acute and chronic types, based on factors like injury depth, healing time, and underlying conditions. Acute wounds (e.g., surgical, burns) heal quickly, while chronic wounds(e.g.,diabetic ulcers) have prolonged healing times. **[20]**

Process of wound healing by four phases:

1. Hemostasis (Phase 1): Immediately after injury, blood vessels constrict, platelets migrate, and a fibrin clot forms to control bleeding and create a matrix for cell migration.**[15]**
2. Inflammation (Phase 2): Begins hours after injury, marked by the presence of leukocytes and macrophages. Macrophages release growth factors the at promote tissue regeneration and transition to the next phase.
3. Proliferation (Phase 3): Occurs 3-21 days post- injury, characterized by granulation tissue formation, re-epithelialization, and wound contraction. Fibroblasts produces collagen, and new blood vessels are grow near wound.
4. Remodeling (Phase 4):This final phase can last years, involving there organization of collagen fibers to form new skin, which rarely regains its original strength.**[20]**

5.2.Treatment of Dermatitis and Eczema:

Calendula officinalis has demonstrated significant therapeutic potential, particularly in dermatology, for conditions like dermatitis, eczema, and other skin issues. Its anti-inflammatory properties help reduce redness, itching, and irritation, which are key symptoms of eczema and dermatitis. Clinical studies show that Calendula extract effectively all both acute and chronic inflammation by inhibiting pro-inflammatory cytokines such as IL-1β, IL-6, TNF-α, and IFN-γ **[11]**

5.3. Skin Moisturizing and Anti-aging Effects:

The plant's antioxidant compounds help protect against UV-induced skin damage and support skin hydration, reducing the appearance of fine lines and wrinkles.

Other Skin Conditions: Beyond wound care,C. officinalis has shown effectiveness in managing conditions uch as acne and rosacea due to its antimicrobial and anti-inflammatory properties.**[21]**

5.4 Antinflamatory:

Calendula officinalis (CO)show strong anti-inflammatory effects, largely due to its triterpenoid fatty acid esters, like faradiol esters. These compounds inhibit pro inflammatory cytokines and COX-2, reducing both acute and chronic inflammation. CO's dried flower heads and ligulate flowers are rich in bioactive compounds, including flavonoids and essential oils, enhancing its medicinal and cosmetic applications.**[11]**

Thee than olic extract's Calendula officinalis(250and500mg/kg) significantly reduced inflammation in animal models, with notable inhibition of pawedema induced by carrageenan (50.6–65.9%) and dextran (42.4–42.9%). The extract also inhibited inflammatory cytokines (IL-1β, IL-6, TNF-α, IFN-γ) and COX-2 in mice, reducing prostaglandin synthesis. Topically, it reduced croton oil-induced ear edema in mice by 20% at 1.2 mg/ear.**[17]**

5.5 Antimicrobial and Anthelmintic Effects:

Methyl alcohol (CH3OH) and ethyl alcohol (C2H6O) Extracts of common marigold petals show antimicrobial activity in case clinical pathogens including bacteria (Bacillus subtilis and Staphylococcus aureus, E.coli) and fungi (Candida glabrata, and Candida albicans). Mouthwashes Containing common marigold reduce the number of Microbes adhered to the molars and premolars. Organic Extracts of Calendula officinalis found sensitive against HIV-1 reverse transcriptase **[8]**

VI. MECHANISM OF ACTIONS

6.1. Anti-inflammatory Activity of Calendula officinalis (CO)

Calendula officinalis (CO) is renowned for its potent anti-inflammatory properties, attributed to its rich profile of secondary metabolites, including alkaloids, tannins, flavonoids, essential oils, sterols, saponins, carotenoids, triterpene alcohols, polysaccharides, and resins. These metabolites contribute to its therapeutic efficacy in both medicinal and cosmetic applications. **[21]**

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Key Mechanisms and Bioactive Compounds:

1. Bioactive Compounds in CO Flowers:

Ligulate flowers are particularly rich in triterpene alcohols, saponins. flavonoids, carotenoids, coumarins, and essential oils.

Triterpenoid fatty acid esters (e.g., lauryl, myristoyl, and palmitoyl esters of faradiol) have been identified as the primary agents responsible for CO's anti-inflammatory effects.

2. Pharmacological Activities:

In acute and chronic inflammation models in mice, CO flower extract demonstrated significant effectiveness.

The mechanism is linked to the inhibition of pro-inflammatory cytokines, including:

IL-6 (Interleukin-6)

IL-1β (Interleukin-1 beta)

TNF-α (Tumor Necrosis Factor-alpha)

IFN-γ (Interferon-gamma)

CO extract also inhibits cyclooxygenase-2 (COX-2), which plays a key role in the inflammatory response.

3. Dose-Dependent Effects:

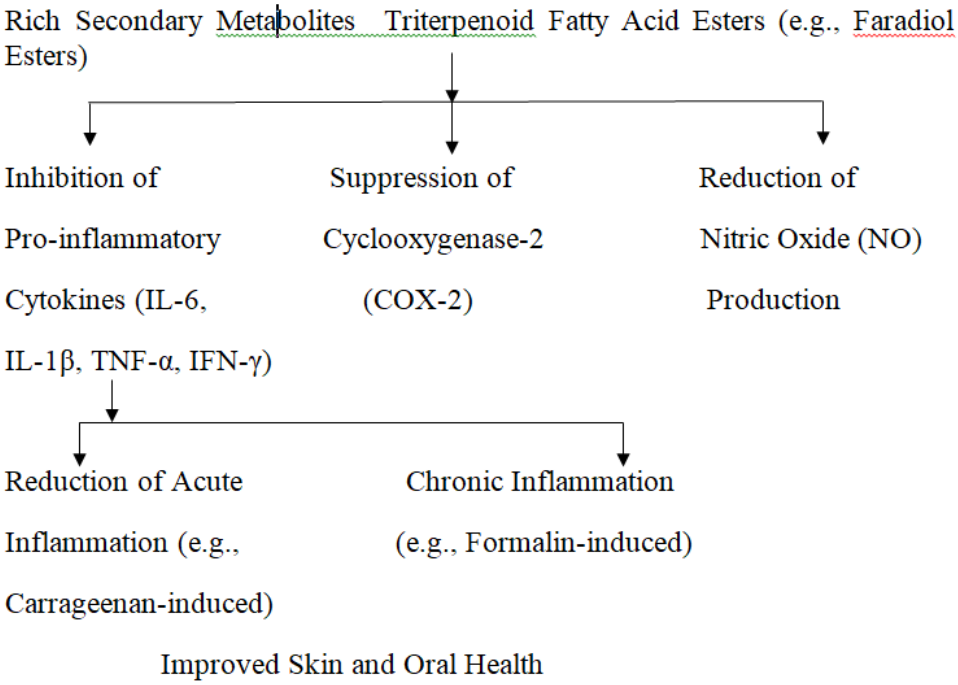
The extract reduced nitric oxide (NO) production in a dose-dependent manner, with cytotoxicity only observed at high concentrations (147 µL/mLand above). **[21]**

4. Topical Formulations and Applications:

CO cream (20–30% w/w) significantly decreased TNF-α levels and suppressed COX-2 activity in inflammatory hyper-nociception tests on rats. Nanoemulsion formulations enhanced the anti-inflammatory effects of CO on skin cells, supporting wound healing and soothing properties.

5. Clinical Observations:

In newborns, CO minimized dermatitis caused by diaper friction more effectively than Aloe vera. Mouth rinses with CO tincture reduced gingival inflammation. **[25]**



Flow chart of anti inflammatory mechanism **[25]**

6.2. Wound healing Activity of Calendula officinalis (CO)

Chronic wounds and delayed healing pose significant medical and socioeconomic challenges. Since ancient times, herbal remedies, including preparations from Calendula officinalis (CO), have been widely used to

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enhance wound healing. CO-based preparations, such as alcoholic and lipophilic extracts from its flowers, have been shown to effectively treat mild skin inflammations and slow-healing wounds by promoting blood and oxygen flow to the wound site, encouraging new tissue formation. **[26]**

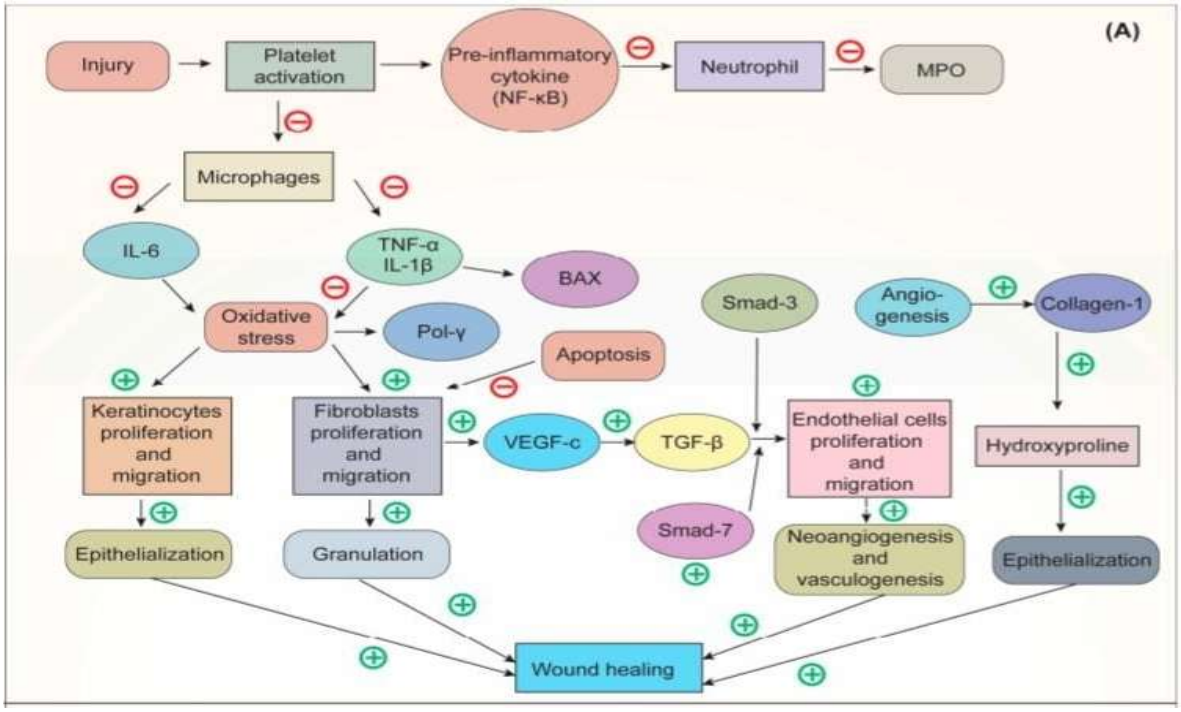

Figure 2: Mechanism of action of CO on Interleukin 6. [11]

Mechanism steps:

1. Injury:Triggers a series of cellular responses to repair tissue damage.
2. Platelet Activation: Platelets release signals that activate the immune system and promote wound healing. They regulate the production of NF-κB (Nuclear Factor Kappa B), a pro-inflammatory cytokine.
3. Pre-Inflammatory Cytokine (NF-κB) Activates neutrophils, a type of white blood cell involved in early inflammation. Neutrophils release MPO (Myeloperoxidase), which can exacerbate oxidative stress.
4. Macrophages Activated macrophages release IL-6 (Interleukin-6), TNF-α (Tumor Necrosis Factor-alpha), and IL-1β (Interleukin-1 beta). These are pro- inflammatory cytokines.
5. Oxidative Stress and Poly-γ (Poly-Gamma)Oxidative stress is caused by a imbalance of free radicals and antioxidants, which can damage cells. Poly-γ proteins regulate mitochondrial function, helping manage oxidative stress. Excess oxidative stress triggers BAX (Bcl-2-associated X protein), which promotes apoptosis (programmed cell death).
6. VEGF-C (Vascular Endothelial Growth Factor-C) Promotes the proliferation and migration of fibroblasts and keratinocytes. These cells are essential for granulation tissue formation and epithelialization (repair of the skin barrier).
7. TGF-β (Transforming Growth Factor-Beta) A growth factor that regulates tissue repair by promoting angiogenesis (formation of new blood vessels) and collagen synthesis. Interacts with Smad-3 to enhance wound healing but is counterbalanced by Smad-7, which inhibits excessive repair.
8. Endothelial Cell Proliferation and Migration Facilitates neovascularization (new blood vessel formation) and vasculogenesis, improving oxygen and nutrient supply to the wound.
9. Collagen-1 and Hydroxyproline Collagen-1 is the primary structural protein in skin repair. Hydroxyproline is a marker of collagen synthesis and contributes to skin strength.
10. Outcome: Wound Healing The processes collectively lead to wound closure, including granulation, re-epithelialization, and restoration of vascular integrity **[11]**

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6.3. Molecular mechanism of platelets on wound Healing:

In the initial stage of injury platelets were activated and it has an important role in clot formation during Hemostasis after aggregation and attachment to the Exposed collagen surfaces. The cytokines and other Growth factors regulate the process. Cytokines acts on target cells by various routes like endocrine, Paracrine, autocrine or intracriner outstand activate Target cells thereby activating other cell signaling pathway. Cytokines can play various roles by acting on different targets.**[20]**

VII. CONCLUSION

Calendula officinalis, commonly known as pot marigold, is a versatile medicinal plant with an extensive profile of bioactive compounds, including terpenoids, flavonoids, carotenoids, coumarins, quinones, amino acids, and volatile oils. These components contribute to its pharmacological activities, including anti-inflammatory, antimicrobial, wound-healing, antioxidant, antidiabetic, and cardioprotective effects. The plant's therapeutic potential has been validated through various studies, highlighting its significant applications in dermatology, gynecology, and general healthcare.

Key findings include:

1. Phytochemical Richness: Calendula exhibits a wide array of bioactive compounds, such as flavonoids (quercetin and rutin) and terpenoids, which impart antioxidant and anti-inflammatory properties.
2. Wound-Healing and Skin Care: The plant promotes wound healing by enhancing fibroblast activity and reducing inflammation, making it a valuable ingredient in skincare products for conditions like dermatitis, eczema, and aging skin.
3. Anti-inflammatory and Antimicrobial Effects: Its triterpenoid esters and flavonoids effectively inhibit pro-inflammatory cytokines and pathogens, supporting its use in topical and oral formulations.
4. Antioxidant Potential: Calendula is rich in carotenoids and phenolic compounds, offering protection against oxidative stress and associated chronic diseases.
5. Broader Pharmacological Uses: Beyond skin applications, calendula demonstrates antihypertensive, antidiabetic, and sedative properties, showing promise in systemic therapeutic applications.

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