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A comprehensive review on Calendula officinalis

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ABSTRACT
Calendula officinalis commonly known as pot marigold, has a long history of use in traditional medicine. This review aims to provide a comprehensive overview of Calendula officinalis, encompassing its botanical characteristics, chemical composition, traditional uses, pharmacological activities supported by scientific evidence, clinical trials, toxicity, and potential future applications. The flowering plant Calendula officinalis belongs to the Asteraceae family. In China, India, and Europe, this plant is utilised as a remedy. It is sometimes referred to as "African marigold" and has been the focus of several pharmacological and chemical studies. A thorough search of relevant databases and review was conducted to gather information. It has a long history as a traditional remedy for inflammation, ulcers, skin and digestive problems, nervousness, insomnia and many other ailments. Calendula contains a wide range of constituents, including terpenoids, carotenoids, flavonoids, volatile oils, polysaccharides and coumarins. Several studies have scientifically confirmed the plant's medicinal properties, including anti-inflammatory, healing, regenerative, antimicrobial, anticancer, antigenotoxic and genotoxic, hepatoprotective, neuroprotective, cardioprotective, gastroprotective, antioxidant, spasmogenic and spasmolytic, antiprotozoal, anthelmintic, acaricidal, antiviral, anti-ageing and immunostimulant effects.

KEYWORDS: Calendula officinalis, pot marigold, phytochemistry, traditional medicine, wound healing, anti-inflammatory, antioxidant.

I. INTRODUCTION

For many, many years, Calendula officinalis, a plant of the Asteraceae family, has been used medicinally. Butterwort, bride of the sun, English marigold, pot marigold, and bull flower are some other names for it.[1] The Latin word "calendas," which means "first of the month," is where the name calendula originates.[2] In addition to being aesthetically pleasing, its vivid orange and yellow flowers have a long history of medical usage that dates back to ancient civilisations. Often utilised in traditional medicinal system such as european herbalism, traditional Chinese medicine, and Ayurveda.

Calendula officinalis's medicinal qualities have been recognised by the Ayurvedic and Unani medical systems. Calendula officinalis is commonly used in homoeopathy to treat a variety of illnesses. Many pharmacological properties have been described, such as antiviral, antibacterial, antifungal, anti-inflammatory, and antioxidant properties. Furthermore, it has both tumor-suppressive and cytotoxic properties. Analgesic, anthelmintic, antifungal, anti inflammatory, antipyretic, antibacterial, disinfectant, spasmolytic, antiviral, emetrol, costringent, bitter, cardiotonic, flatus relieving, diuretic, lymphatic, gall bladder contraction stimulant, uterotonic, and vasodilator are some of its uses that include boosting the immune system. It is commonly used to heal lacerated wounds, open wounds, and inflammations of the outer skin. Mucous membrane inflamations, GI spasms, dysmenorrheal (painful menstruation), peptic and duodenal ulcers, in nervous or anaemic women, duodenal and intestinal mucosa, as well as splenic and hepatic inflammations, are all treated internally. It is often used as a rinse following tooth extraction.[3,4]

The stems, leaves, and flowers contained fifteen amino acids in their free state. Open, lacerated wounds, bleeding wounds, and skin inflammations were all treated with flowers. Additionally, they were turned into externally applied extracts, tinctures, and balms. Ear discomfort in children with acute otitis media has been demonstrated to be alleviated by using herbal ear drops infused with calendula flowers.

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Calendula flower extracts of varying polarity demonstrated antioxidative effects on ferrous ion and ascorbic acid-induced liposomal lipid peroxidation.[5]

The purpose of this study is to review all the available information on Calendula officinalis in a single document. This review summarizes various aspects such as morphological features, geographical distribution, traditional uses, phytochemistry, pharmacological studies, toxicology and future aspects.

This study consolidates dispersed reports on the traditional applications, pharmacological properties, and phytochemistry of Calendula officinalis. However, our focus lies in highlighting the importance of Calendula officinalis as a natural therapeutic remedy, bolstered by positive findings in the literature. The aim of this review is to succinctly outline existing research, bridge any knowledge gaps, and present multiple avenues for researchers already exploring the validation of traditional claims and the safe, efficacious use of Calendula officinalis in treating diverse diseases.

Figure No.1: Calendula officinalis

MORPHOLOGICAL FEATURES

Calendula officinalis has a woody foundation and can grow either monthly or perennially. Usually, it reaches a height of 30 to 60 cm. Its stem is angular, hairy, and solid; its leaves are lower, spatulate, 10–20 cm long and 1- 4 cm wide; upper, oblong and mucronate, 4–7 cm long; bright, unheroic to orange anomocytic stomata within the apical region of the external epidermis, covering and glandular trichomes, stretched sclerenchyma cells, and borderline flower heads; the corolla of the slice flowers is oblong, spatulate, and measures 15–25 mm long and approximately three mm wide; at its stylish, it is tridentate, 1.5–2.5 cm long and 4–7 mm in periphery, with tubular boutonnieres that are 5 mm long. Raw sienna pulverized from C. officinalis has a distinct, sweet scent and a kindly bitter flavor.[6,7] The characteristic feature of Calendula officinalis is its flower heads, which are solitary or borne in loose corymbs. Each flower head comprises an outer row of ray florets (ligulate flowers) and an inner disc of tubular florets, both typically ranging in color from bright yellow to deep orange. The fruit is a curved, boat-shaped achene.

BOTANICAL DESCRIPTION AND CULTIVATION

Calendula officinalis is an annual herbaceous plant belonging to the Asteraceae family. Native to the Mediterranean region, it is now widely cultivated globally. The plant is characterized by its bright orange or yellow daisy-like flowers, which are the primary source of medicinal properties. Calendula officinalis is relatively easy to cultivate, thriving in sunny locations and well-drained soil. Different varieties exist, varying in flower size, color intensity, and resin content, influencing their therapeutic efficacy.

TAXONOMICAL PROFILE

Kingdom: Plantae
Subkindom : Tracheobionta
Division : Magnoliophyta
Class : magnoliopsida
Subclass: Asteridae
Order : Asterales
Family : Asteraceae
Tribe : Calendulea
Genus: Calendula
Species : Officinalis[8]

CHEMICAL CONSTITUENTS

Calendula officinalis's complex chemical composition provides to its wide range of pharmacological actions. The plant includes a wide range of chemical classes, including terpenoids, quinones, coumarins, flavonoids, essential oils, carotenoids, and amino acids, according to several phytochemical studies. The chemical composition of Calendula officinalis includes flavonoids, triterpeneol esters, and saponins. Numerous chemical components that are also used in the food and cosmetic industries include isorhamnetin, rutin, quercetin, and glucoside.[9] Calendula officinalis leaf extract contains fatty acids, triterpenes, sterols, and chloroform extracts. The aqueous extract of Calendula officinalis contained tannin, phenolic compounds, and saponins.[10]

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Calendula officinalis was used to extract other flavonoids, including quercetin, isorhamnetin, and isoquercetin. Calendula officinalis inflorescences accumulated considerable amounts of carotenoids. The primary cause of the yellow-to-orange color of inflorescences is carotenoids.[11]
The major bioactive constituents identified in the plant, particularly in the flowers, include:

- **Triterpenoids:** These are considered the primary active constituents of Calendula, particularly oleanolic acid glycosides and faradiol esters. These include saponins (e.g., calendulosides A-H), which contribute to the plant's anti-inflammatory and wound-healing properties, and triterpene alcohols (e.g., faradiol, arnidiol), known for their anti-inflammatory and antitumor activities.[12]
- **Flavonoids:** These phenolic compounds (e.g., quercetin, rutin, isorhamnetin) contribute to the potent antioxidant and anti-inflammatory effects of Calendula officinalis. They also exhibit antimicrobial and anticancer properties.[13]
- **Carotenoids:** The bright orange and yellow colors of Calendula officinalis flowers are due to the presence of carotenoids (e.g., beta-carotene, lycopene, lutein), which act as antioxidants and contribute to skin protection.[14]
- **Volatile Oils:** The essential oil of Calendula officinalis contains a variety of monoterpenes and sesquiterpenes, including α-cadinol, T-cadinol, and β-caryophyllene, which contribute to the plant's antimicrobial, anti-inflammatory, and wound-healing properties.[15]
- **Polysaccharides:** Calendula contains polysaccharides, which have been shown to stimulate immune responses, These complex carbohydrates contribute to the plant's immune-modulating and wound-healing effects.
- **Coumarins:** Coumarin derivatives such as umbelliferone are present in Calendula and contribute to its anti-inflammatory and anticoagulant properties.

The specific composition of Calendula officinalis can vary depending on factors such as geographical location, cultivation methods, and extraction techniques.

TRADITIONAL USES

Calendula officinalis has a rich history of use in traditional medicine systems worldwide. Some of the most common traditional applications include:[16,17]

- **Wound Healing:** Topical application of Calendula officinalis preparations (e.g., ointments, creams, tinctures) for the treatment of cuts, scrapes, burns, ulcers, and other skin injuries.
- **Skin Conditions:** Treatment of inflammatory skin conditions such as eczema, dermatitis, diaper rash, and psoriasis.
- **Eye Conditions:** Use of Calendula officinalis infusions or eyewashes for the treatment of conjunctivitis and other eye inflammations.
- **Mouth and Throat Infections:** Gargling with Calendula officinalis infusions for the treatment of sore throats, mouth ulcers, and gingivitis.
- **Digestive Complaints:** Oral administration of Calendula officinalis infusions for the treatment of digestive disorders such as stomach ulcers and irritable bowel syndrome (IBS).
- **Menstrual Problems:** Use of Calendula officinalis infusions for the treatment of menstrual cramps and heavy bleeding.
- **Anti-inflammatory:** Internal use for conditions such as arthritis.[18]

PHARMACOLOGICAL ACTIVITIES OF OF CALENDULA OFFICINALIS

Calendula officinalis, commonly known as pot marigold, exhibits a wide range of therapeutic activities, making it a significant plant in traditional and modern medicine. Modern scientific research has investigated the pharmacological properties of Calendula officinalis, providing evidence to support its traditional uses and uncovering new potential applications.
The following sections outline the key activities reported for Calendula officinalis.

Anti-inflammatory

Because of its superior anti-inflammatory properties, Calendula officinalis is presently the subject of research. The plant contains a variety of secondary metabolites that are linked to its anti-inflammatory properties, including alkaloids, tannins, flavonoids, essential oils, sterols, saponins, carotenoids, triterpene alcohols, mucilage, polysaccharides, and resin.[19]

Mostly used as a component of tinctures, ointments, and infusions, Calendula officinalis is used as a wound healing remedy for blisters, scars,

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mucous membranes, skin inflammations, tissue repair, and allergic responses. Calendula extract cream has shown promise in treating burn oedema, according to research. Bacillus subtilis, Escherichia coli, Staphylococcus aureus, Pseudomonas aeruginosa, and Candida albicans are all inhibited in vitro by the essential oil extracted from the flower petals.[20]

Calendula officinalis exhibits potent anti-inflammatory activity, primarily attributed to its triterpenoids, flavonoids, and carotenoids. These compounds inhibit the production of pro-inflammatory cytokines (e.g., TNF-α, IL-1β) and enzymes (e.g., COX-2) involved in the inflammatory response. In vitro studies have shown that Calendula officinalis extracts can effectively reduce inflammation in various cell types, including macrophages and keratinocytes.[21]

Antioxidant activity

Flavonoids and other plant polyphenols are some of the most important natural substances with potent antioxidant qualities. The presence of hydroxyl groups in flavonoids is what causes them to scavenge or chelate radicals. Antioxidants can be found naturally in the leaves and petals of the Calendula officinalis plant. Calendula officinalis extract has been reported to scavenge superoxide and hydroxyl radicals due to the photo reduction of riboflavin.[22,23]

Flavonoids, carotenoids, and phenolic acids are among the several antioxidants found in Calendula officinalis. These substances help the plant's anti-inflammatory, wound-healing, and anti-aging properties by scavenging free radicals and shielding cells from oxidative damage. The antioxidant activity of C. officinalis flower extracts is being studied both in vitro and in vivo. According to reports, the extracts reduce lipid peroxidation in vitro by scavenging nitric oxide, superoxide, hydroxyl, ABTS, and DPPH radicals. An oral extract raised catalase and intracellular glutathione levels and prevented superoxide production in macrophages in vivo in mice, indicating strong antioxidant action.[24]

Cytotoxic and anti-tumor activity

One of Calendula officinalis's isolated active ingredients, saponin, has been demonstrated to have antimutagenic properties. With the growth of complementary and alternative medicine based on herbs as a cancer treatment, interest in the alleged anti-tumor potential of Calendula officinalis extracts and components has increased. found that calenduloside F 6′-O-n-butyl ester and calenduloside G 6′-O-methyl ester, two triterpene glycosides extracted from marigold flowers, had strong cytotoxic action against human colon cancer, leukaemia, and melanoma cancer cells in vitro. It has been demonstrated that the triterpenoids and flavonoids in the plant prevent the growth and multiplication of a number of cancer cell lines, such as leukaemia cells, breast cancer, and colon cancer. Furthermore, Calendula officinalis has been shown to induce apoptosis (programmed cell death) in cancer cells and inhibit angiogenesis, thereby suppressing tumor growth and metastasis.[25,26]

Wound-healing activity

Calendula officinalis flower extract has wound and burn healing properties when applied topically and over time. Increases in collagen hydroxyproline and hexosamine indicate that the patient's or animal's wounds are getting better.[27]

Calendula officinalis may significantly boost collagen metabolism and wound angiogenesis, leading to emollient properties and softer scars. Calendula officinalis flower extract provides therapeutic benefits for burns and wounds when applied topically and taken orally. An increase in hexosamine and collagen-hydroxyproline indicates that the patient or animal is healing their wounds. Calendula officinalis has the ability to prevent macrophage activation and accelerate the migration and growth of fibroblasts and keratinocytes, which are involved in wound healing. This was achieved by lowering oxidative stress at the wound site and inhibiting the release of proinflammatory cytokines.[28]

Hepatoprotective activity

Calendula officinalis extracts were shown to possess hepatoprotective properties against the cytotoxicity and oxidative stress caused by carbon tetrachloride. Overall, it raises haemoglobin levels. Likewise, the hydroalcoholic extract of the flowers exhibits reduced hepato-cytolysis and liver indicators in both in vitro and in vivo settings. Normal levels of hepatic blood markers were restored after the ethanolic extract treatment. Malondialdehyde and total oxidant status were reduced in both the blood and the hepatocytes, while total thiols and antioxidant enzymes (CAT, catalase; SOD, superoxide dismutase; GPx, glutathione peroxidase; and GST, glutathione s-transferases) were also reduced. The extract from Calendula officinalis enhanced the liver's

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histological appearance, biochemical markers, and inflammatory cytokines.[29]

Antimicrobial activity

Over the past few decades, it has been noted that the prevalence of harmful bacteria that are resistant to antibiotics has increased, despite the fact that antibiotics have been effectively used for the past 60 years to treat infectious diseases brought on by bacteria and fungi. Broad-spectrum antibacterial action against a variety of bacteria, fungi, and viruses is exhibited by Calendula officinalis. By rupturing microbial cell membranes and interfering with microbial metabolism, the plant's essential oil and flavonoid contents help to produce its antimicrobial actions. Calendula officinalis is efficient against common infections such Staphylococcus aureus, Escherichia coli, Candida albicans, and herpes simplex virus (HSV), according to in vitro research. Clinical pathogens such as Aspergillus Niger, Bacillus subtulis, Staphylococcus aureus, Escherichia coli, Candida albicans, and Klebsiella pneumonia have all been studied in relation to the antibacterial qualities of methanol and ethanol extracts derived from calendula petals.[30]

When it came to antibacterial activity against the majority of tested microorganisms, Calendula officinalis methanol extract was particularly better than the ethanol extract. Both methanol and ethanol extract showed excellent antifungal efficacy against the test fungus strain. Calendula officinalis plants have demonstrated the anthelmintic effect of saponins, demonstrating their anthelminthic properties.[31]

Cardiovascular effect

Calendula extract has been found to reduce myocardial infarctions. Cardio protection seems to be achieved by transforming the ischaemia-reperfusion-mediated death signal into a survival signal. Extracts from C. officinalis have been shown to be beneficial in the treatment of ischaemic heart disease. By modifying antioxidant and anti-inflammatory pathways, cardio-protective action is achieved by converting the death signal caused by ischaemia reperfusion into a survival signal, as demonstrated by the decrease of TNF-α and the activation of protein kinase B and Bcl2.[32]

CLINICAL APPLICATIONS

The diverse pharmacological properties of Calendula officinalis have led to its use in a variety of clinical applications. While some applications are supported by strong evidence, others require further investigation.[33]

- **Wound Healing:** Clinical trials have investigated the efficacy of Calendula in promoting wound healing. Studies have shown that Calendula ointments can accelerate the healing of surgical wounds, leg ulcers, and pressure sores. However, the quality of evidence varies, and more large-scale, well-designed trials are needed to confirm these findings.
- **Radiation Dermatitis:** Calendula has shown promise in preventing and treating radiation dermatitis, a common side effect of cancer radiation therapy. Several studies have found that Calendula cream is more effective than conventional treatments, such as trolamine, in reducing the severity of radiation dermatitis.
- **Oral Mucositis:** Calendula mouthwashes have been investigated for the treatment of oral mucositis, an inflammation of the oral mucosa that can occur as a result of chemotherapy or radiation therapy. Some studies have found that Calendula mouthwashes can reduce the severity and duration of oral mucositis.
- **Diaper Rash:** Calendula ointments are commonly used to treat diaper rash in infants. Studies have shown that Calendula is effective in reducing inflammation and promoting healing of diaper rash.
- **Vaginal Yeast Infections:** Some studies suggest that Calendula creams may be effective in treating vaginal yeast infections. However, more research is needed to confirm these findings.

Other Applications: Calendula is also being investigated for its potential use in treating other conditions, such as acne, eczema, hemorrhoids, and varicose veins. However, more research is needed to determine its efficacy in these applications.

TOXICOLOGY

Calendula officinalis is generally considered safe for topical use. However, some individuals may experience allergic reactions, particularly those with sensitivities to other plants in the Asteraceae family (e.g., ragweed, chrysanthemums). Oral consumption should be approached with caution, as limited data exists on its safety during pregnancy and breastfeeding. Further research is needed to fully assess the potential risks associated with long-term internal use.

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FUTURE RESEARCH DIRECTIONS

While significant progress has been made in understanding the therapeutic potential of Calendula officinalis, further research is warranted in several areas:

- **Clinical Trials:** Conducting well-designed clinical trials to validate the efficacy of calendula for specific conditions, such as wound healing, dermatitis, and gastrointestinal disorders.
- **Mechanism of Action:** Exploring the precise mechanisms by which calendula exerts its therapeutic effects at the molecular level.
- **Standardization of Extracts:** Developing standardized extracts with consistent levels of bioactive compounds to ensure product quality and efficacy.
- **Combination Therapies:** Investigating the potential benefits of combining calendula with other conventional or herbal therapies.

II. CONCLUSION

C. officinalis is one of the most potent and beneficial flowering plant with multi health benefits and pharmacological actions. It contains different chemical constituents like terpenoids, glycosides, flavonoids, coumarins, polysaccharides, volatile oil, and carbohydrates that results different physiological actions in the body. Calendula officinalis is a valuable medicinal plant with a long history of traditional use and a growing body of scientific evidence supporting its therapeutic properties. Its wound-healing, anti-inflammatory, antimicrobial, and antioxidant activities make it a promising natural remedy for a range of conditions, particularly skin ailments and wound care. While further research is needed to fully elucidate its mechanisms of action and optimize its clinical applications, Calendula officinalis remains a significant and versatile plant with considerable potential for improving human health. Its ease of cultivation, safety profile (for topical use), and affordability further contribute to its appeal as a natural therapeutic agent. Calendula can be effective in treating various conditions, such as radiation dermatitis, diaper rash, and oral mucositis. While generally considered safe, some individuals may experience allergic reactions. Future research should focus on standardizing Calendula products, conducting rigorous clinical trials, and elucidating the mechanisms of action of its bioactive compounds. Calendula officinalis holds significant potential as a safe and effective therapeutic agent for a variety of conditions, and further research is warranted to fully unlock its therapeutic potential. By combining traditional knowledge with modern scientific investigation, Calendula officinalis can continue to play a valuable role in promoting health and well-being.

CONFLICT OF INTEREST

The authors have no conflicts of interest.

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