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Review Article

The Science and Tradition of Calendula: A Review of Phytochemistry and Ethnopharmacology

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ABSTRACT

For millennia, people have utilized Calendula officinalis Linn. (CO), a well-known medicinal herb belonging to the Asteraceae family of plants. Flavonoids, triterpenoids, glycosides, saponins, volatile oil, carotenoids, amino acids, steroids, sterols, and quinines are all present in this plant. Numerous biological effects, including hepatoprotective, wound healing, anti-inflammatory, anti-cancer, anthelminthic, and antioxidant properties, are conferred by these chemical compounds. It's also used for gastrointestinal, gynecological, ophthalmic, and skin disorders, as well as some burn situations. We have included contemporary studies on the therapeutic uses of Calendula officinalis over the previous five years in this review, emphasizing the plant's wide range of uses in traditional medicine. We have also clarified the molecular mechanisms and current clinical research of Calendula officinalis. Essentially, the goal of this study is to provide a comprehensive overview, bridge any gaps in the literature, and offer a plethora of opportunities for investigators seeking to support conventional wisdom and promote the responsible and efficient application of calendula officinalis for a range of medical conditions.

INTRODUCTION

Calendula officinalis is a member of the plantae kingdom (family Asteraceae) and has been used medicinally for millennia. Other names for it include butterwort, bride of the sun, English marigold, pot marigold, and bull flower [1]. Many people cultivate calendula officinalis in sunny locations on a range of soil types. Tall, sparsely branched erect stems, rectangular lance leaves with tubular disc florets, and thorns twisting the yellow or orange achene characterize Calendula officinalis. Both in-vitro and in-vivo applications are made of carotenoids, flavonoids, saponins, sterols, phenolic acids, lipids, and other biologically active substances that are present in many plant parts, including leaves and flowers [1].

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It is commonly used as an antiseptic, analgesic, diaphoretic, and anti-inflammatory since it is thought to have therapeutic qualities. Among other things, it is used to treat burns, gastrointestinal problems, gynecological problems, mouth illnesses, eye ailments, and skin injuries [1]. In the free state, fifteen amino acids were found in the stems, leaves, and flowers. Flowers were used medicinally to cure skin inflammations, open, lacerated wounds, and bleeding wounds. They were also made into extracts, tinctures, and balms for external use [2]. The Ayurvedic and Unani medical systems have acknowledged the therapeutic properties of calendula officinalis. Two contemporary use of Calendula officinalis are pot marigold tincture and carophyllenic ointment, which contains carotenoids derived from the flowers. It is one of the components of the homoeopathic medication used to treat acute musculoskeletal injuries and reduce pain and oedema. Calendula flower-infused herbal ear drops have been shown to help children with acute otitis media with their ear pain. Extracts of calendula flowers with different polarity showed antioxidative effects on liposomal lipid peroxidation caused by ferrous ions and ascorbic acid. Isomonatene 3-glycosides from calendula flowers inhibited lipoxygenase. Calendula officinalis promotes blood and lymphatic circulation, which helps the body eliminate toxins because of its high concentration of therapeutic active substances [2]. Although there haven't been any documented pharmacological interactions or contraindications, those who are known to be sensitive to the Compositae family may be more prone to adverse reactions. Calendula mouthwash contains antibacterial and anti-inflammatory qualities that combat periodontopathic bacteria and swollen, inflamed gums. Using cutting-edge analytical techniques, new chemical compounds that are biologically active and used for a variety of functions, like isorhamnetin, rutin, and quercetin glucoside, have been identified [3]. This review paper emphasizes the historic use and clinical value of Calendula species. The goal is to draw global attention to the vast potential and variety of biological activity in treatment aspects among researchers studying natural products. The authors further highlight its crucial role in oral and general treatment.



Figure no.1: Calendula officinalis Linn.

The Genus Calendula:

About 25 herbaceous periodic or imperishable species make up the Genus Calendula (Asteraceae), with common marigold Linn. Being the most common (Calendula arvensis Linn. Calendula suffruticosa Vahl., Calendula stellata Cav, Calendula alata Rech, Calendula tripterocarpa Rupr) [4].

Synonyms: Calendula officinalis is sometimes referred to as common marigold, pot marigold, or ruddles

Morphological Features:

C. officinalis Linn. Grows either monthly or biennially. It grows up to 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; anomocytic stomata within the external epidermis' apical region, covering and glandular trichomes, stretched sclerenchyma cells, and borderline flower heads are bright unheroic to orange in color; the corolla of the slice flowers is oblong, spatulate, and measures 15 – 25 mm long and roughly three mm wide; at its stylish, it's tridentate,

measuring1.5 –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 [5-7].

Table no.1: Taxonomic classification of Calendula officinalis Linn.

Kingdom	Plantae
Subkingdom	Tracheobionta
Division	Magnoliophyta
Class	Magnoliopsida
Subclass	Asteridae
Order	Asterales
Family	Asteraceae
Genus	Calendula
Species	Officinalis

Chemical Constituents:

Numerous phytochemical investigations have shown that the plant contains a variety of chemical classes, including terpenoids, quinones, coumarins, flavonoids, essential oils, carotenoids, and amino acids [8-9]. Extensive analytical and phytochemical methods used to various plant sections verify the existence of several chemical constituents such as isorhamnetin, rutin, quercetin, and glucoside, which are also employed in the food and cosmetic sectors [10].

Calendula officinalis contains flavonoids, triterpeneol esters, and saponins in its chemical composition. Calendula officinalis is a plant whose predominantly orange blossoms are rich in carotenoids. Calendula officinalis leaf extract contains fatty acids, triterpenes, sterols, and chloroform extracts. The aqueous extract of calendula officinalis contained tannin, phenolic compounds, and saponins [1]. In ethanolic extract, alkaloids, flavonoids, and saponins were discovered. In the watery extract, flavonoids and saponins were discovered. In various parts of Calendula officinalis, quinone was separated from phylloquinone, ubiquinone, tocopherol, and protoquinone. Flowers of Calendula officinalis was extracted using petroleum ether, and terpenoids were separated out [11]. Generally speaking, the leaves contained 5% of amino acids, the stems contained 3.5 percent, and the blooms contained 4.5 percent. The fifteen amino acids identified in the flowers were aspartic acid, asparagine, valine, histidine, glutamic acid, leucine, lysine, proline, serine, tyrosine, threonine, methionine, and phenylalanine. 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. Orange cultivars of calendula officinalis contain more hydrocarbons, whilst yellow varieties mostly contain oxygenated derivatives [11].

Table no.2: Phytoconstituents and Biological Activities of Different Parts of Calendula [9, 12]

Extract	Phytoconstituents	Biological activity
Flower extract	Saponin, oleanolic acid, stigmasterol	Antitumor, Anti-inflammatory
Leaves extract	Quinones, plastoquinone phylloquinone	Anti-inflammatory, antioxidant activities
Inflorescence extract	Flavonoids; quercetin, isoquercetin, rutin [9]	Antioxidant activities [9]

Pharmacological effects of Calendula Officinalis:

Calendula officinalis's pharmacological actions are stated as:

- **Antimicrobial and anthelminthic effects:**

Studies have examined the antibacterial properties of methanol and ethanol extracts derived from calendula petals against a variety of clinical

pathogens, including Aspergillus Niger, Bacillus subtulis, Staphylococcus aureus, Escherichia coli, Candida albicans, and Klebsiella pneumonia [1]. Calendula officinalis methanol extract outperformed the ethanol extract in terms of antibacterial activity against the majority of tested microorganisms. Excellent antifungal activity was demonstrated by both methanol and ethanol extract against the test fungus strain [13].

Saponins have been shown to have anthelmintic action by Calendula officinalis plants, proving that saponins have anthelminthic activity [14].

- **Anti-inflammatory effects:**

Calendula officinalis is mostly utilized as an ingredient in tinctures, ointments, and infusions that are used as wound healing remedies for skin inflammations, mucous membranes, tissue repair, blisters, scars, and allergic reactions. Research has demonstrated the potential benefits of calendula extract cream in the management of burn oedema. The essential oil from the blossoms inhibits Bacillus subtilis, Escherichia coli, Staphylococcus aureus, Pseudomonas aeruginosa, and Candida albicans in vitro [2, 15].

- **Antioxidant and photoprotective effects:**

Calendula officinalis leaves and petals may naturally contain antioxidants. Calendula extract has been shown to scavenge superoxide and hydroxyl radicals, which are created when riboflavin is photoreduced [16].

- **Cytotoxic effects:**

All the extracts showed no direct mitogenic effect on human thymocytes or lymphocytes, while C.officinalis totally blocked the proliferation of lymphocytes [1].

- **Genotoxic and antigenotoxic effects:**

In acutely infected lymphocytic MOLT-4 cells, flower extract suppresses HIV-1 proliferation, and all saponins have been demonstrated to be non-toxic and non-mutagenic [17, 18].

- **Cardiovascular effect:**

It has been discovered that calendula extract shrinks myocardial infarctions. It appears that the conversion of the ischaemia-reperfusion-mediated death signal into a survival signal is how cardio protection is accomplished [13].

- **Neuroprotective effect:**

Extracts from calendula officinalis can be used with sedative medications like barbiturates and have mild sedative effects of their own. There was also evidence of the aqueous alcoholic extract of florets' calming effect and inhibition of the Central Nervous System (CNS) [2].

- **Hepatoprotective effect:**

It was discovered that extracts from calendula officinalis may have hepatoprotective qualities against the oxidative stress and cytotoxicity brought on by carbon tetrachloride. It increases hemoglobin levels overall. The extract is similar to insulin in consistency. Thus, it is evident from the study that Calendula officinalis hydroalcoholic extract possesses antihyperlipidemic and antidiabetic effects. [19, 20].

- **Wound and Burn Healing**

Calendula officinalis flower extract has wound and burn healing properties when applied topically and over time. An increase in collagen hydroxyproline and hexosamine shows that the wounds in the treated person or animal are healing [8]. The topical preparations containing marigold extract (ME), also known as common marigold extract, have been demonstrated to have a photo-protective impact on skin damage caused by ultraviolet (UV-B) irradiation. Gel formulation is best for applying marigold extract topically. While this formulation is in a position to need attention for lowered glutathione levels, it has no effect on the activities of myeloperoxidase and gelatinase, which rise in response to UVB irradiation. Furthermore, the histological skin changes brought on by UVB irradiations are lessened by gel composition [10].

Traditional and Commercial Use of Calendula:

Because of its lenient characteristics, calendula has been used since the 18th century. Calendula's flower extract is utilized in soothing cosmetics and supplementary skin care treatments, such as after-sun, sensitive skin, and eye contour products, because of its anti-inflammatory qualities [21, 22].

- **Skin care products:**

Because marigold flowers include bioactive substances including luteolin, vitexin, rutin and quercetin derivatives, apigenin, and kaempferol, their extract cream, which is an antioxidant, protects the skin, especially after sunburn, from oxidative damage and reduces the signs of skin aging. Vitexin 11.40%, Rutin 12.29%, Quercetin-3-3galactosid 12.64%, Luteolin-7-glucose 9.27%, Quercetin-3-glucoside 7.38%, Quercitrin 9.83%, Myricetin 10%, Luteolin 10.72%, Apigenin 7.08%, and kaempferol 9.37% are among the nine active compounds found in marigold flower extract, according to HPLC analysis [23].

- **Sedative drugs:**

High doses of calendula formulations were found to have sedative effects in early animal tests. Therefore, using it with sedatives may have cumulative effects. Calendula prolonged mice's hexobarbital-induced sleep duration. Its long-term effects on human systems are still unknown [23].

- **Antihypertensive drugs:**

Calendula formulations at high doses were found to cause hypertension in early animal tests [24]. Therefore, using calendula along with hypertensive medications may have unintended consequences.

- **Hypoglycemic drugs**:

Calendula may enhance the effects of insulin or hypoglycemic drugs [25].

- **Cholesterol-lowering drugs:**

Calendula extracts may have synergistic benefits with medicines that lower triglycerides and lipids [25].

- **Traditional uses:**

The blooms are used as an emmenagogue, stimulant, and antispasmodic in Europe, while the leaves are used as a diaphoretic and resolvent. The blossoms were used to make a posset drink in England to cure smallpox and measles. As a result, the fresh juice was used as a medication for jaundice, constipation, and the suppression of menstrual flow [26]. The florets are used in ointments in India to cure wounds, skin damage, scars, herpes, ulcers, frostbite, and blood purification. External treatment for varicose veins is done using the leaves.

Toxicology of Calendula Species:

It has been discovered that C. officinalis extract is non-toxic, non-mutagenic, and non-genotoxic [1]. Rarely, skin contact with topicals and supplements containing calendula may result in an allergic reaction. There have been reports of allergic contact responses and sensitization to calendula [2]. Additionally, a case of anaphylactic reaction following infusion of calendula was reported [29].

Future Perspectives:

Mankind has been using calendula officinalis for a variety of medicinal purposes for many ages. The Calendula officinalis herb is mostly composed of α-cadinol, a sesquiterpenoid, but it also contains terpenoids, steroids, phenolic compounds, carotenes, triterpenoids, essential oils, quinones, fatty acids, minerals, saponins, carbohydrates, and tocopherols. Calendula officinalis, which is high in these secondary metabolites, has been shown to possess anti-inflammatory, antidiabetic, antioxidant, anti-cancer, antibacterial, anti-ulcer, antifungal, antiviral, anti-thrombogenic, neuroprotective, antiprotozoal, skin-protective, and antifatigue properties. Taking into account the various uses of Calendula officinalis, it is imperative that further research be done on the plant's nonfloral parts, like the seeds, roots, leaves, and stems. Furthermore, it is imperative to concentrate on genus chemistry. Other Calendula

officinalis species, such as C. arvensis, C. tripterocarpa, C. stellata, and C. suffruticose, should have their biochemical profiles and pharmacological characteristics further investigated due to the paucity of existing research. Likewise, comparative research has to be carried out to comprehend discrepancies concerning the age of the plant, extraction technique, or processing approach. It's expected that when extraction techniques improve, more previously undiscovered phytochemicals and an increase of this plant's pharmacological activity range will probably be discovered, creating exciting research opportunities. Furthermore, research on creating novel drug delivery methods with Calendula officinalis is still in its early stages, and we expect that it will continue. Two contemporary computational drug design methods that show a lot of promise for creating new therapeutic candidates for a range of illnesses are molecular docking and molecular dynamics. Furthermore, bioinformatics technologies have created new pathways for identifying the vital amino acids under almost similar physiological conditions, significantly confirming the results of computational approaches. On the other hand, time and money can be saved by exploring the therapeutic potential of a number of bioactive compounds depending on the chemical composition of the drug and its target receptor [27]. Calendula officinalis-containing micro- and nano-formulations offer great potential for treating a variety of illnesses in the near future, and amazing advancements and applications are guaranteed. Additionally, combining activity enhancement with other drugs on the market presents a viable approach that could eventually improve pharmacological results [28].

CONCLUSION:

Throughout history, Calendula officinalis species have demonstrated enormous health benefits. This paper provides a concise explanation of the current state-of-the-art Calendula officinalis in the field of health sciences, together with an in-depth analysis of their molecular mechanisms. Furthermore, numerous Calendulas officinalis-based drug delivery strategies and patents have been created to enhance solubility, targeting, and stability; the analysis has taken into account their active ingredients. This article discussed Calendula officinalis's botanical description, historical uses, pharmacological effects, and applications. Above all, it shows its potential for the good of humanity in terms of dental and medicinal aspects. Calendula officinalis has the potential to be a very novel drug source for treating a wide range of human conditions due to its safety and efficacy.

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