



"*Calendula officinalis*: A Comprehensive Review of its Medicinal Properties, Traditional Uses, and Modern Applications"

Review Articles by : Durgesh Sanjay Pardeshi*, Nikhil Nandkishor Pandit

B. Pharm, Final year 2023-2024.

ABSTRACT

Calendula officinalis (*Calendula*), a member of the Asteraceae family, is often known as English Marigold or Pot Marigold. Marigold is a fragrant herb that has been used in traditional medicine for centuries. *Calendula* species have been highlighted in order to better understand their diverse biological activities and modes of action. Carotenoids, flavonoids, glycosides, steroids and sterols, quinines, volatile oil, and amino acids are all found in abundance in this plant. *Calendula* oil is still used as an anti-tumour agent in medicine, which is also a wound healing agent. Among herbal medicines, *Calendula* suspension or tincture is used to treat acne locally, reduce inflammation, control bleeding and soothe irritated tissues. This *Calendula* plant's extract, a pure chemical extracted from it, have been shown to have a variety of pharmacological properties including anti-inflammatory, antioedematous, antioxidant activity, antibacterial and antifungal activity, anti-Human Immunodeficiency Virus (HIV) and antiviral activity, wound healing and immunostimulant activity. Anticytotoxic, hepatoprotective, spasmolytic properties and also impacts on exhibiting increased levels of proinflammatory cytokines Interleukin (IL)-1 beta, IL-6, Tumor Necrosis Factor (TNF)-alpha and Interferons (IFN)-gamma and acute phase protein, C-reactive protein. *C.officinalis* may have an important future impact on the development of new cancer treatment strategies, and until now it has been specifically used to reduce the side-effects of radiotherapy. This review looked at the traditional uses pharmacological activities, as well as the description, and active chemical constituents of *Calendula officinalis* in order to fill in the gaps in current knowledge about this plant and to highlight its potential applications as a medicinal agent.

INTRODUCTION

Calendula officinalis is a well-known therapeutic herb that was used for millennia and belongs to the kingdom plantae, family Asteraceae. It is also known as English marigold, pot marigold, Bride of the Sun, bull flower, and butterwort are some of its other names. *Calendula officinalis* is widely grown in sunny areas and in a variety of soils. *Calendula officinalis* is a tall plant with sparsely branching erect stems, rectangular lance leaflets with tubular disc florets, and thorns curving achene that is yellow or orange in colour. Carotenoids, flavonoids, saponins, sterols, phenolic acids, lipids, and other biological active elements found in numerous components of the plant such as leaves and flowers, are employed both in-vitro and in-vivo. It is believed to have medicinal properties and

is widely used as an anti-inflammatory, diaphoretic, analgesic, and antiseptic. It is used to treat gastrointestinal issues, gynaecological issues, oral disorders, eye diseases, skin injuries, and certain burns, among other things. Fifteen amino acids were discovered in the free state in the leaves, stems, and flowers. Flowers were turned into extracts, tinctures, and balms for external application, and were therapeutically used to treat skin inflammations, open, lacerated wounds, and bleeding wounds.

Calendula officinalis has medicinal capabilities that have been stated in the Ayurvedic and Unani systems of medicine. Carophyllenic ointment (containing carotenoids obtained from the flowers) and pot marigold tincture are two recent *Calendula officinalis* treatments. It is one of the ingredients in the homoeopathic drug, which is used to relieve the pain and oedema associated with acute musculoskeletal injuries. Herbal ear drop formulations containing *Calendula* flowers have been beneficial for ear pain in children with acute otitis media. On liposomal lipid peroxidation generated by ferrous ion and ascorbic acid, extracts of *Calendula* flowers of various polarity displayed antioxidative properties. Lipoxygenase was inhibited by isorhamnetin 3-glycosides from *Calendula* flowers. As *Calendula officinalis* is high in medicinal active ingredients, it increases blood and lymphatic circulation, which aids in the removal of toxins from the body. There have been no reported contraindications or drug interactions, although people who have a known sensitivity to the compositae family may be more susceptible to allergic responses. *Calendula* mouthwash has anti-inflammatory characteristics that fight swollen, irritated gums, as well as antibacterial properties that fight periodontopathic germs. Fresh chemical compounds such as isorhamnetin, rutin, and quercetin glucoside which are biologically engaged and employed for various purposes, have been isolated using advanced analytical technique.

The traditional usage and clinical significance of *Calendula* species are highlighted in this review paper. It is aimed to attract attention of natural product researchers from around the world to the enormous potential and diverse biological activities in treatment aspects. Furthermore, the authors emphasise its key function in both general and oral treatment.

CHEMICAL CONSTITUENTS

Saponins, triterpeneol esters, and flavonoids were found in the chemical make-up of the *Calendula officinalis* plant. *Calendula officinalis* has high carotenoids in its blossom, which is mostly orange in colour. Fatty acids, chloroform extracts, triterpens, and sterols are all present in *Calendula officinalis* leaf extract. *Calendula officinalis* water extract contained saponins, phenolic compounds, and tannin. Alkaloids, flavonoids, and saponins were found in ethanolic extract. Flavonoids and saponins were found in aqueous extract. Plastoquinone, phyloquinone, tocopherol, and ubiquinone were isolated from quinone in different sections of *Calendula officinalis*. Terpenoids were isolated from the petroleum ether extract of *Calendula officinalis* flowers.

In general, roughly 5% of amino acids were found in the leaves, 3.5 percent in the stems, and 4.5 percent in the flowers. Alanine arginine, aspartic acid, asparagine, valine, histidine, glutamic acid, leucine, lysine, proline, serine, tyrosine, threonine, methionine, and phenylalanine were among the fifteen amino acids found in the flowers. Quercetin, isorhamnetin, isoquercetin, and other flavonoids were also extracted from *Calendula officinalis*. Inflorescences of *Calendula officinalis* acquired significant levels of carotenoids. Carotenoids are primarily responsible for the yellow-to-orange hue of inflorescences. *Calendula officinalis* orange types have more hydrocarbons, while yellow varieties have mostly oxygenated derivatives.

The main pigments identified were flavoxanthin, lutein, rubixanthin, β -carotene, γ -carotene and lycopene. The total oils extracted from the dried flowers of *Calendula officinalis* compounds isolated from *Calendula officinalis* flower were also be added in part of its chemical constituents.

PHARMACOLOGICAL EFFECTS OF CALENDULA OFFICINALIS

The pharmacological effects of *Calendula officinalis* are listed as:

- a. Antimicrobial and antihelminthic effects
- b. Anti-inflammatory effects
- c. Antioxidant and photoprotective effects
- d. Cytotoxic effects
- e. Genotoxic and antigenotoxic effects
- f. Cardiovascular effect
- g. Neuroprotective effect
- h. Hepatoprotective effect

Antimicrobial effects: Methanol and ethanol extracts from *Calendula* petals has been tested for antibacterial activity against clinical pathogens, including bacteria and fungi such as *Bacillus subtilis*, *Staphylococcus aureus*, *Escherichia coli*, *Klebsiella pneumonia*, *Candida albicans* and *Aspergillus niger*. The methanol extract of *Calendula officinalis* showed better antibacterial activity than against most of the bacteria tested and was better than the ethanol extract. Both methanol and ethanol extract showed excellent antifungal activity against the fungal test strain.

Antioxidant and photoprotective effects: *Calendula officinalis* leaves and petals may be a natural source of antioxidants. It was reported that *Calendula* extract scavenges hydroxyl radicals and superoxide radicals which is produced by photo reduction of riboflavin.

Cytotoxic effects: Although none of the extracts demonstrated a direct mitogenic impact on human lymphocytes or thymocytes, *C.officinalis* inhibited lymphocyte proliferation completely.

Antihelminthic effects: The *Calendula officinalis* plants contain saponins and have also demonstrated anthelmintic action, indicating that saponins have anthelmintic activity.

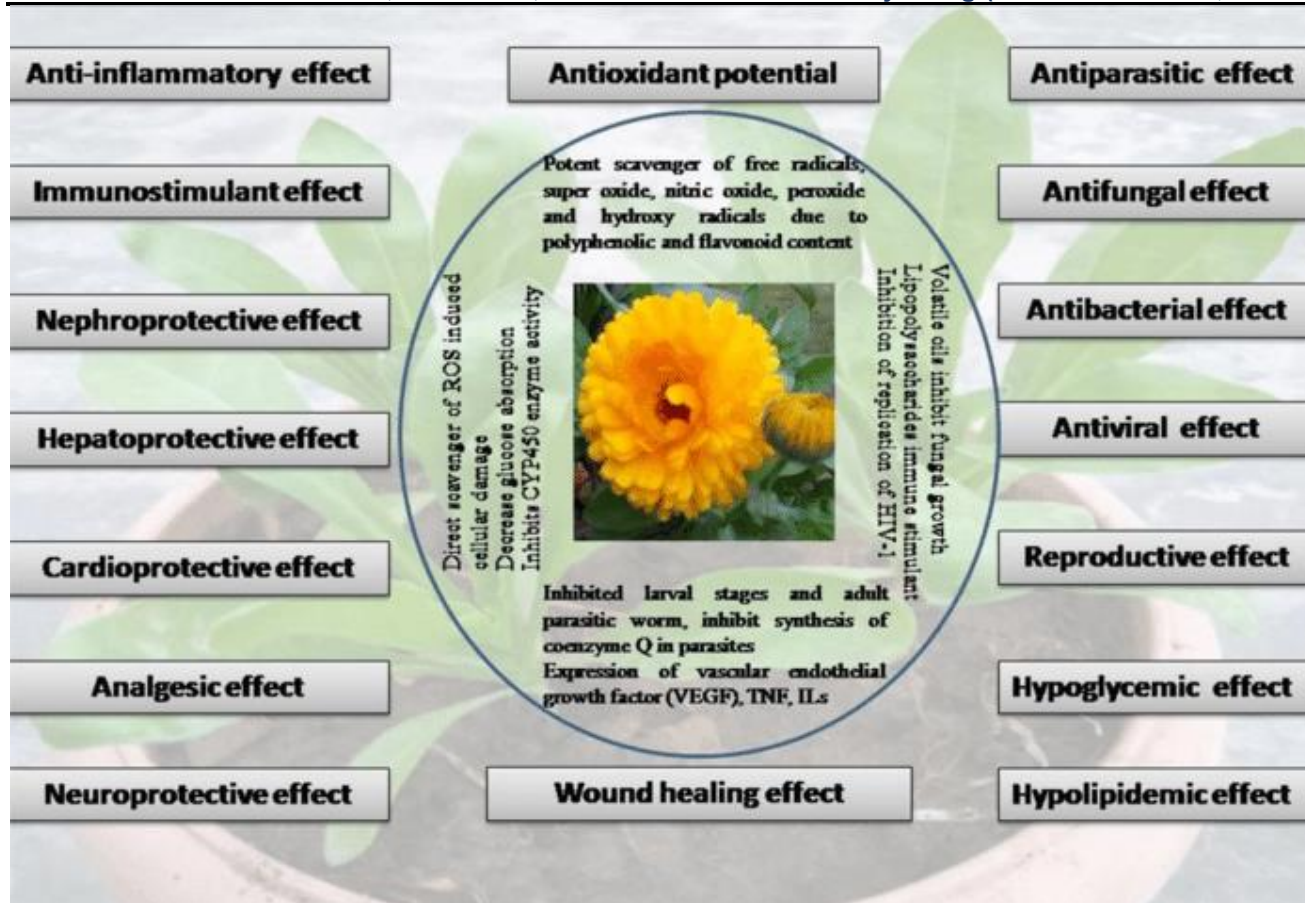
Genotoxic and antigenotoxic effects: All saponins were shown to be non toxic and non mutagenic and floral extract inhibits HIV-1 multiplication in acutely infected lymphocytic MOLT-4 cells.

Neuroprotective effect: *Calendula officinalis* extracts also have modest sedative effects and can work in conjunction with sedative drugs like barbiturates. The Central Nervous System (CNS) inhibitory impact of aqueous alcoholic extract of florets was also observed, as well as sedative action.

Cardiovascular effect: *Calendula* extract has been found to reduce the size of myocardial infarction. It seems that cardio protection is achieved by changing the ischaemia-reperfusion-mediated death signal into a survival signal.

Anti-inflammatory effects: *Calendula officinalis* preparations are mostly used as a wound healing medicine for inflammations of the skin, mucous membranes, tissue repair, scars, blisters, and allergic rashes in the form of infusions, tinctures, and ointments. *Calendula* extract cream has been shown to be beneficial in the treatment of burn oedemas. *Bacillus subtilis*, *Escherichia coli*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *Candida albicans* were all inhibited in-vitro by the essential oil from the flowers

Hepatoprotective effect: *Calendula officinalis* extracts were found to have potential hepatoprotective properties against cytotoxicity and oxidative stress caused by carbon tetrachloride. It raises total haemoglobin levels. The extract has a comparable consistency to insulin. As a result, the research clearly reveals that *Calendula officinalis* hydro alcoholic extract has both antidiabetic and antihyperlipidemic properties.



TOXICOLOGY OF CALENDULA SPECIES

C. officinalis extract has been found to be non toxic, non mutagenic, and non genotoxic. In rare cases, contact with *Calendula* supplements and topicals on skin can cause an allergic reaction. Sensitisation and allergic contact reactions to *Calendula* were reported. There was also a case of anaphylactic shock after gargling with *Calendula* infusion.

Classification of *Calendula officinalis*

Kingdom—*Plantae*
 Subkingdom—*Tracheobionta*
 Division—*Magnoliophyta*
 Class—*Magnoliopsida*
 Subclass—*Asteridae*
 Order—*Asterales*
 Family—*Asteraceae*
 Tribe—*Calenduleae*
 Genus—*Calendula*
 Species—*officinalis*



EFFECT OF CALENDULA OFFICINALIS IN DENTISTRY

Calendula officinalis is a medicinal herb with antiseptic, antibacterial, and anti-inflammatory effects. Triterpene saponins, triterpene alcohols and their fatty acid esters, carotenoids, flavonoids, coumarins, essential oil, hydrocarbons, and fatty acids are all found in the plant components and are utilised in pharmaceutical and cosmetic products.

Effect in Oral Health

Calendula officinalis was investigated as a possible treatment for exfoliative cheilitis [20]. After extraction of unerupted third molars, mouthwashes containing *Calendula officinalis* minimises the amount of micro-organisms adherent to the sutures. *Calendula* aqueous extract promotes wound healing by boosting neovascularisation and the rate of hyaluronic acid deposition. In bone wounds, hyaluronic acid can accelerate new bone creation by promoting mesenchymal cell differentiation.

Effect in Gingivitis and Periodontitis

In the treatment of desquamative gingivitis, *Calendula officinalis* is used which may assist to reduce periodontal disease progression by reducing Hepatocyte Growth Factor (HGF) -mediated collagen breakdown and Matrix Metalloproteinases (MMP) activity.

Effect in Oral Mucositis

Calendula officinalis has a cytotoxic effect on tumour cell lines, and its anticancer activity demonstrates its efficacy in the treatment of oral mucositis in radiation therapy patients. It has its own efficacy by reducing the intensity of radiation with high radical scavenging activity, and it plays a crucial role in maximum safeguarding against oxidative stress caused by high levels of reactive oxygen species in the body.

Effect in Dental Plaque

Calendula's anti-inflammatory, antioxidant, and immunomodulatory properties treat severe periodontal disease by regulating cytokine levels, reducing oxidative stress, and stimulating phagocytic activity of Polymorphonuclear (PMNs) leukocytes. This study showed that *Calendula* mouthwash is effective in reducing plaque and gingivitis as an adjunct to oral prophylaxis.

THE GENUS CALENDULA

The genus *Calendula* (*Asteraceae*) includes approximately 25 *herbaceous* annual or perennial species, most common being *Calendula officinalis* Linn., *Calendula arvensis* Linn., *Calendula suffruticosa* Vahl., *Calendula stellata* Cav., *Calendula alata* Rech., *Calendula tripterocarpa* Rupr. The genus is native to the Mediterranean countries.

Ethnopharmacology

Traditional uses

C. officinalis Linn. (Pot marigold) has been traditionally used in the treatment of inflammations of internal organs, gastrointestinal ulcers and dysmenorrhea and as a diuretic and diaphoretic in convulsions. It is also used for inflammations of the oral and pharyngeal mucosa, wounds and burns. *Calendula* is a cleansing and detoxifying herb and the infusion treat chronic infections. The dried flower heads have been used for their antipyretic, anti-tumor and cicatrizing effects. Topical application of infusion of flowers is used as antifungal and antiseptic in wounds, marks, freckles, sprain and conjunctivitis. *Calendula* tea is used as eyewashes, gargles, diaper rashes and other inflammatory conditions of the skin and mucous membranes. Mother tincture of *C. officinalis* is used in homoeopathy for the treatment of mental tension and insomnia.

Medicinal properties of *C. officinalis* have been mentioned in Ayurvedic and Unani system of medicine indicating that leaves and flowers are antipyretic, anti-inflammatory, antiepileptic and antimicrobial. In traditional and homoeopathic medicine, *C. officinalis* has been used for poor eyesight, menstrual irregularities, varicose veins, hemorrhoids and duodenal ulcers. In the middle ages, *Calendula* flowers were used for liver obstructions, snake bites and to strengthen the heart. It was used in the 18th century as a remedy for headache, jaundice and red eyes. The plant was employed in the civil war to treat wounds and as a remedy for measles, smallpox and jaundice. Decoction and infusion of *Calendula persica* C.A. Mey aerial parts are employed for the treatment of kidney stones.

In Europe, the leaves are used as resolvent and diaphoretic whereas the flowers are used as a stimulant, antispasmodic and emmenagogue. In England, the decoction of the flowers was used as a posset drink for the treatment of measles and smallpox, and therefore the fresh juice as a medicine for jaundice, costiveness (constipation) and suppression of menstrual flow [28]. In India, the florets are utilized in ointments for treating wounds, herpes, ulcers, frostbite, skin damage, scars and blood purification. The leaves are used for treating varicose veins externally

Modern Applications

COMMERCIAL USES

The use of calendula for its 'lenitive properties' dates to the XII century. Due to anti-inflammatory properties of Calendula, its flower extract is used in adjunctive skin care treatments and cosmetics with soothing properties such as after-sun, sensitive skin and eye contour products

Skin care products

The results of a clinical study showed that using a cream made from marigold flowers extract can protect the skin from damage caused by the sun and reduce signs of aging. This is because the extract contains certain bioactive compounds like rutin and quercetin derivatives, vitexin, luteolin, apigenin, and kaempferol. Through HPLC analysis, it was found that the extract contains nine different active compounds, including vitexin at 11.40%, rutin

at 12.29%, quercetin-3-galactosid at 12.64%, luteolin-7-glucose at 9.27%, quercetin-3-glucoside at 7.38%, quercitrin at 9.83%, myricetin at 10%, luteolin at 10.72%, apigenin at 7.08%, and kaempferol at 9.37%.

Sedative drugs

In early animal studies, researchers found that consuming large amounts of calendula preparations had a sedative-like effect. Therefore, if combined with other sedative agents, it may result in even stronger sedation. In experiments with mice, it was observed that calendula prolonged the duration of sleep induced by hexobarbital. However, the overall impact of calendula on humans is still not well understood.

Antihypertensive drugs

In previous studies on animals, it was found that using high doses of calendula preparations could lead to increased blood pressure. Therefore, if calendula is used alongside medications for hypertension, it may cause additional effects.

Hypoglycemic drugs

Calendula might increase the effects of hypoglycemic medications or insulin.

Cholesterol-lowering drugs

Extracts of calendula may cause additive effects with agents that reduce lipids and triglycerides.

Alternative and complementary medicinal uses

Among the various species of the genus *Calendula*, *C. officinalis* is the only one, which is extensively used clinically throughout the world. The plant is listed in German Commission E, European Scientific Co-operative on Phytotherapy, British Herbal Pharmacopoeia, World Health Organization monographs for wound healing and anti-inflammatory actions. *C. officinalis* preparations are used in various complementary and alternative medicine systems mainly for burns, cuts, rashes, dermatitis and varicosis. It is also included as part of treatment for dry skin, bee stings and foot ulcers. The essential oil of the plant is used for soothing central nervous system and as a wound healer.

C. officinalis preparations currently in use include carophyllenic ointment (containing carotenoids extracted from the flowers) and pot marigold tincture. It is one of the constituents of proprietary homeopathic medicine Traumeel®, used for treating the symptoms associated with acute musculoskeletal injuries including pain and swelling. Otikon otic solution and naturopathic herbal extract ear drops solution, ear drop formulations of naturopathic origin containing *Calendula* flowers, have been reported to be effective for the management of otalgia associated with acute otitis media in children.

Morphology and microscopy

C. arvensis Linn. is an annual herb, not generally exceeding 15 cm in height. Leaves lance-shaped; stem slender, hairy; inflorescence single flower head up to 4 cm wide with bright yellow to yellow-orange ray florets around a center of yellow disc florets.

C. officinalis Linn. is an annual or biennial plant attaining height of 30-60 cm. Leaves lower spatulate, 10-20 cm long and 1-4 cm wide; higher oblong and mucronate, 4-7 cm long; stem angular, hairy and solid; flower heads bright yellow to orange; marginal flowers in cultivated plants multi-seriate, corolla oblong spatulate, 15-25 mm long and 3 mm wide; corolla of disc flowers rounded, at the top tridentate, 1.5-2.5 cm long and 4-7 mm in diameter with 5 mm long tubular florets.

The powdered *C. officinalis* is yellowish brown with a characteristic, aromatic odor and a slightly bitter taste; comprises fragments of the corolla, anomocytic stomata in the apical region of outer epidermis, covering and glandular trichomes, elongated sclerenchymatous cells, pollen grains, fragments of the walls of the ovaries containing brown pigment, fragments of stigma, fragments of the fibrous layer of the others.

C. stellata Cav., is a small, attractive annual growing to a height of 30 cm or more. Leaves oval or oblong, somewhat pointed, wavy-toothed; stems scabrous; achenes outer five with membranous toothed margins, the five inner ones "boat-shaped" and smooth on the back, the rest angular and muricated on the back.

C. suffruticosa Vahl., is a perennial plant reaching a height between 20 cm and 40 cm. Leaves lance-shaped, slightly toothed, covered with short sticky hairs; stem young one first erected, later begin to hang and spread to the soil; flowers bright yellow, each measuring about 2.5 cm in diameter.

Phytoconstituents

Four species of *Calendula* have been investigated phytochemically. Below table summarizes the phytoconstituents of different species of *Calendula*.

Species	Phytoconstituents
<i>C. officinalis</i>	Triterpene glycosides: Calendulaglycoside A, calendulaglycoside A 6'-O-methyl ester, calendulaglycoside A 6'-O-n-butyl ester, calendulaglycoside B, calendulaglycoside B 6'-O-n-butyl ester, calendulaglycoside C, calendula glycoside C 6'-O-methyl ester, calendulaglycoside C 6'-O-n-butyl ester, calendulaglycoside D, calendulaglycoside D ₂ , calendulaglycoside F, calendulaglycoside F 6'-O-butyl ester, calendulaglycoside G 6'-O-methyl ester, calendasaponins A-D; ^[9,11] triterpene alcohols: Free and esterified (with fatty acids) monols, diols and triols of ψ -taraxastane-type including ψ -taraxasterol, faradiol, heliantriol B ₀ , heliantriol C, taraxastane-type including taraxasterol, arnidiol, heliantriol B ₁ , lupine-type including lupeol, calenduladiol, heliantriol B ₂ , ursane-type including α -amyrin, brein, ursadiol, ursatriol, oleanane-type including β -amyrin, maniladiol, erythrodiol, longispinogenin, heliantriol A ₁ , ^[34,35] flavonoids: Quercetin, isorhamnetin, kaempferol, rutin, hyperoside, isoquercitrin, astragalol, quercetin 3-O-glucoside, quercetin 3-O-rutinoside, quercetin 3-O-neohesperidose, quercetin 3-O-2 ^G -rhamno-sylrutinoside, isorhamnetin 3-O-glucoside, isorhamnetin 3-O-rutinoside, isorhamnetin 3-O-neohesperidoside, iso-rhamnetin 3-O-2 ^G -rhamnosylrutinoside; ^[11] ionone glucosides: Officinoides A and B; sesquiterpene glycosides: Officinoides C and D; ^[36] carotenoids: Lutein, zeaxanthine, flavoxanthin, auroxanthin, β -carotene, luteoxanthin, violaxanthin, β -cryptoxanthin, mutaxanthin; ^[37] hydroxycoumarins: Scopoletin, umbelliferone, esculetin; phenolic acids: Chlorogenic acid, caffeic acid, coumaric acid, vanillic acid; ^[38] volatile oils: α -cadinol, T-cadinol; ^[39] α -cadinene, limonene, 1,8-cineol; ^[40] quinones: α -tocopherol, phylloquinone; ^[41] fatty acids: Calendic acid, dimorphecolic acid; ^[42] others: Sterols, mucilage, carbohydrates, resin, tannins, amino acids, bitter principle calendin ^[43]
<i>C. arvensis</i>	Triterpenoid saponins: Arvensoside A and B, ^[44] arvensoside C, ^[45] calenduloside C and D, ^[46] calendulaoside G and H; ^[43] sesquiterpene glycosides: Arvoside A and B; ^[47,48] flavonoids: Isoquercitroside, rutoside, narcissoside; ^[49] volatile oils: δ cadinene, α -cadinol; ^[26] fatty acids: Calendic acid, ^[50] dimorphecolic acid; others: Amino acids, ^[51] alkaloids, ^[43] lutein, ^[52] phenolic acids, tannins, malic acid, salicylic acid, mucilages ^[53]
<i>C. persica</i>	Fatty acids: Palmitic acid, linoleic acid ^[54]
<i>C. stellata</i>	Fatty acid: Calendic acid; ^[55] volatile oils: Linalool, linalyl acetate, limonene ^[2]

Pharmacological reports

The available literature reveals that amongst 12-20 species of *Calendula*, only three species, i.e., *C. officinalis*, *C. arvensis* and *C. suffruticosa* have been evaluated for their pharmacological activities.

Tincture of *C. arvensis* was active against *Staphylococcus aureus* at concentrations of 10 mg/ml or 25 mg/ml. Sesquiterpene glycosides from *C. arvensis* were able to inhibit vesicular stomatitis virus infection. A saponin containing fraction from the aerial parts of *C. arvensis* had hemolytic activity *in vitro* and anti-inflammatory activity against carrageenan induced paw edema in rats. Saponins showed antimutagenic activity against benzo (a) pyrene 1 µg and mutagenic urine concentrate from a smoker (SU) 5 µL with a dose-response relationship.

Preparations of *C. officinalis* are mainly applied in the form of infusions, tinctures and ointments as a wound healing remedy for inflammations of the skin, mucous membranes, for poorly healing wounds, bruises, boils and rashes, e.g., pharyngitis and leg ulcers. In the mixed lymphocyte reaction, 70% ethanol extract showed stimulatory effects at 0.1-10 µg/ml, followed by inhibition at higher concentrations. Phagocytosis of human granulocytes was stimulated by polysaccharides isolated from aqueous extract of *Calendula* flowers. Extracts of *Calendula* flowers of differing polarities exhibited anti-oxidative effects on liposomal lipid peroxidation induced by Fe²⁺ and ascorbic acid. Isorhamnetin 3-glycosides from *Calendula* flowers inhibited lipoxygenase from rat lung cytosol at a concentration of 1.5×10^{-5} M. In a test system based on porcine buccal membranes, strong concentration dependent adhesive processes were observed with a low viscosity polysaccharide enriched extract (98% carbohydrates) of *Calendula* flowers. These findings suggested that the polysaccharides may contribute to therapeutic effects in the treatment of irritated mucosa. A triterpene enriched fraction given orally to mice inoculated with Ehrlich mouse carcinoma prevented the development of ascites and increased survival time compared to control. Triterpenes such as faradiol and taraxasterol inhibit experimental tumor promotion and are therefore considered as inhibitors of tumor growth.

A saponin rich fraction administered orally at 50 mg/kg body weight to hyperlipemic rats reduced the serum lipid level. The aqueous alcohol extract of *C. officinalis* showed central nervous system inhibitory effect with marked overall sedative activity as well as hypotensive effect. The alcohol extract of flowers of *C. officinalis* possesses anti-HIV properties. A cream containing *calendula* extract has been reported to be effective in dextran and burn edemas as well as in acute lymphedema in rats. Activity against lymphedema was primarily attributed to enhancement of macrophage proteolytic activity. The essential oil of the flowers inhibited the growth *in vitro* of *Bacillus subtilis*, *Escherichia coli*, *S. aureus*, *Pseudomonas aeruginosa* and *Candida albicans*. Acetone, ethanol or water extracts inhibited the growth *in vitro* of the fungus *Neurospora crassa*. A flavonoid fraction isolated from the flowers inhibited the *in vitro* growth of *S. aureus*, *Sarcina lutea*, *E. coli*, *Klebsiella pneumonia* and *Candida monosa*. The 50% ethanol extract of the plant showed spermicidal activity in rats at 2% concentration.

C. suffruticosa inhibited pathogenic micro-organisms, especially *Pseudomonas syringae*, *Pseudomonas fluorescens*, *Xanthomonas campestris*, *Agrobacterium tumefaciens*.

Overview of toxicological/safety data from clinical trials in humans

Type	Study	Test Product(s)	Number of subjects	Type of subjects	Adverse reactions	Comments
					adverse events were reported	
Duran V <i>et al.</i> , 2005	Observational study	Verum: ethanolic extract; Placebo: saline solution dressing Topically, twice daily 1 g ointment/ cm ² of ulcer Duration: 3 weeks	34 patients Verum (n=21) Placebo (n=13)	Patients with venous ulcers	No adverse events were reported	Good tolerability of study medication
Buzzi <i>et al.</i> , 2016a	Observational study	Verum: hydroglycolic extract of <i>Calendula officinalis</i> , with a total flavonoid content of 120 mg/ml Topically Duration: 30 weeks	41 patients Group J (n=51) Group K (n=51)	Patients with pressure ulcer	No adverse events were reported	Good tolerability of study medication
Buzzi <i>et al.</i> , 2016b	Non-randomised controlled study	Verum: hydroglycolic extract of <i>Calendula officinalis</i> , with a total flavonoid content of 120 mg/ml+ collagenase (0.6 U/g), chloramphenicol (10 mg/g), and 1 % silver sulfadiazine; Control: saline solution + collagenase (0.6 U/g), chloramphenicol (10 mg/g), and 1 % silver sulfadiazine. Topically, twice daily Duration: 30 weeks	57 patients Verum (n=38) Control (n=19)	Patients with pressure ulcer	No adverse events were reported	Good tolerability of study medication

Conclusion

Calendula officinalis L. (Compositae) is a Mediterranean-derived annual plant. It is said to have been brought to England in the 13th century and then spread across Europe as a cultivated plant. Its therapeutic usage seems to be most widespread from the 13th century onwards, particularly in wound healing. During the North American Civil War and the First World War, it was utilized as a balm and cream and an antiseptic and anti-inflammatory agent. Most studies on *C. officinalis* therapeutic effectiveness were conducted in European or Asian nations using plants grown in those areas. Different culturing conditions may change specific patterns of vegetal metabolism, allowing some metabolic pathways to be activated or inactivated. The quantitative examination of bibliographic content is known as bibliometric analysis. It gives a broad view of a study subject that may be divided into categories based on articles, authors, and journals.

The current study is the first to use bibliometric tools to understand the literature related to *C. officinalis*. 1,252 research documents were retrieved from the Scopus database. It is noted that the annual output of the number of research documents on this plant is increasingly occurring. The top-producing author is Janiszowska, W. (Poland). 98 countries accommodated the scientific production related to *C. officinalis*. In terms of citations to researchers, organizations, and countries, the essential parts of research show a wide range of intellectual dynamics. Mapping the science of this plant confirmed the diversity of research to include several fields and an excellent geographical spread. Based on the data gathered, the worldwide research network for *C. officinalis* was formed of 124 nations, indicating international solid collaborative research linkages.

Calendula officinalis is found in plenty of herbal compositions which might be utilized in medical settings to treat a whole lot of diseases. The phytoconstituents of *Calendula* species had been studied in component. In mild of ethnopharmacology, phytochemical, and pharmacological findings as well as low toxicity and frequent use. *Calendula officinalis* seems to have a variety of capacity for research into diverse biological approaches. It may be observed in a variety of bureaucracy such as gel, cream, ointment, mouth washes, and systemic infusions. It is a completely promising plant that wishes indepth studies and that can be used to extract active substances, to synthesise extraordinary tablets, to prevent various diseases, and extensively utilized to manage distinct pathologies.

This article addressed the botanical description, historic usage, pharmacological results, outcome of research with exceptional combos and packages of *Calendula officinalis*. Most importantly, it exhibits its capability in phrases of clinical. Because of its effectiveness and protection, *Calendula officinalis* has great ability for the improvement of modern medications to treat plenty of human ailments.

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