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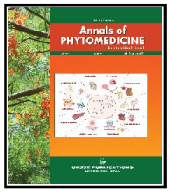

Review Article : Open Access

Pharmaceutical and pharmacognosy studies on Pot marigold (*Calendula officinalis* L.)

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Abstract

Calendula officinalis L. is a herb of the Asteraceae family, is a fragrant plant which is used in traditional medicinal practices in Europe, China and India. It has been referred to as English marigold or pot marigold. Considering pot marigold contains a wide range of phytochemicals, includes quinones, terpenoids, lipids, fatty acids, carotenoids, flavonoids and coumarins. It has received widespread recognition for its medicinal benefits. It is widely utilized in traditional medicinal treatment to address a wide range of illnesses, including ulcers, scars, frostbite, cuts, herps, blood purification and skin damage. Further more, the review covers the variety of pharmacological and pharmacognosy abilities, such as antibacterial, anti-inflammatory, antifungal, antioxidant, anti-HIV, anticancerous, nephronprotective, neuroprotective, hepatoprotective, spasmogenic, spasmolytic, genotoxic and antigenotoxic, hypoglycemic and gastroprotective activities, it had gained attention for its potential applications in topical formulations, cosmetics and herbal supplements. The role of *C. officinalis* in global pharmaceutical research emphasizes sustainable sourcing, need for clinical trials to validate efficacy and regulatory standardization to enhance its broader impact in modern healthcare.

1. Introduction

In the perpetual search for new pharmaceuticals, natural products particularly those derived from plants continue to contribute substantial and distinctive possibilities (Balunas and Kinghorn, 2005). The primary stage of pharmaceutical study is to collect traditionally involved compounds that alleviate ailment. Owing to the tradition of oral transmission of advancing over expertise concerning significant flora and practices for therapeutic purposes, there is a concern that indigenous knowledge of traditional remedies could be progressively losing (Bhatia *et al*., 2014). Many therapeutic plants contain active ingredients that are not fully identified and various factors such as genetics and environmental conditions can influence the concentration of secondary plant compounds. Often, a marker compound is selected to evaluate the potency of the herbal remedy and to guide the formulation's development (Sapna *et al*., 2022).

C. officinalis is an herbaceous plant species that can flower either annually or perennially, which can grow up to a height of 30 to 60 cm with angular, solid stems that have a hairy texture as shown in Figure 1. The lower leaves are spatulate in shape, ranging from 10 to 20 cm in length. The inflorescences consist of a dense capitulum or flower head, with 4 to 7 cm in diameter, encircled by two layers of hairy bracts. The flower heads are typically bright yellow to orange, with the corolla around 15 to 25 mm in length and about 3 mm in width (Arora *et al.,* 2013; Ashwlayan *et al.,* 2018). It is used as a medicine in India, United States, China and Europe. The yellow or orange flowers from the plant serve a purpose for food, colour, spice, tea, ointment and cream in cosmetics. It possesses both cytotoxic as well as tumour-reducing properties from ancient days to novel chemical substances which include isorhamnetin, rutin and quercetin glucoside which have been shown to be physiologically active and employed in both the food and cosmetic industries, have been successfully isolated using improved methods of analysis (Albulescu *et al*., 2004). Numerous pharmacological actions which include antiviral, antibacterial, antifungal, antioxidant and anti-inflammatory properties have been reported. It also exhibits tumour suppressive and cytotoxic characteristics, *viz*., cardiotonic, carminative, cholagogue, derma genic, diaphoretic, diuretic, hemostatic, immunostimulant, lymphatic, uterotonic, vasodilator, antibacterial, antiemetic, antifungal, antiviral, anti-inflammatory, antispasmodic, antiseptic, antipyretic, astringent and candidicide. In addition to that it is widely employed for treating external laceration wounds which have bleeding, open wounds and skin inflammations and many more (Balunas and Kinghorn, 2005). The medicinal properties of plants are often linked to the presence of secondary metabolites or bioactive compounds like glycosides, alkaloids, tannins, steroids, flavonoids, phenols, and volatile oils, which naturally accumulate in the plants and produce specific physiological effects on the human body when consumed (Sandip *et al*., 2021).

Figure 1: Flower image of *C. officinalis*.

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2. Extraction methods

2.1 Steam distillation

C. officinalis flowers weighing 150 g underwent hydrodistillation in a Clevenger type apparatus for 3 h. An anhydrous Na_2SO_4 was used to dehydrate the ensuing oil layers. Depending on the material's dry weight, three studies resulted in yields at an average of 0.1% w/w. In the chromatography (CG) analyses, 1.5 ml of dichloromethane was employed to dissolve 47 mg of oil and 1 ml of the resulting solution was introduced into the GC-MS and GC-FID (Gazim *et al*., 2008).

2.2 Supercritical CO_2 extraction

Supercritical fluid extraction (SFE) experiments were conducted in *C. officinalis* to extract the essential oil using a Hewlett-Packard 7680T automated supercritical fluid extractor. For each extraction, 0.50 ± 0.01 g of dry, ground raw material was used. Carbon dioxide (CO_2) with low water content (<20 ppm) and a purity of 99.9%, were served as extraction fluid. The experiments were carried out at pressures of 9.1 MPa and 15.1 MPa, corresponding to CO_2 densities of 0.30 g/ml and 0.70 g/ml, respectively. The extraction chamber was maintained at 50°C, with 10 ml stainless steel extraction vessel. Each extraction consisted of 2 min static phase, followed by 15 min dynamic phase, with a CO_2 flow rate of 1 ml/min. Analytes were collected on octadecylsilica (ODS) sorbent trap 1 ml held at 5°C. The elution of analytes was performed using 0.7 ml of heptane, with a flow rate of 0.7 ml/min at 45°C (Kaskoniene *et al.,*2011).

2.3 Hydrodistillation extraction

A total of 65 g of fresh *C. officinalis* plant material was ground into small pieces and subjected to hydrodistillation (HD) using a Clevenger-type apparatus for 4 h, yielding 0.16% (w/w) essential oil. The extracted oil was dissolved in 0.5 ml of HPLC grade n-hexane, dried over anhydrous sodium sulphate, and stored at -5ºC in a sealed brown vial (Tosun *et al.,* 2012).

2.4 Microwave distillation

Microwave distillation (MD) was conducted at atmospheric pressure using a Milestone DryDIST microwave apparatus with a fixed power of 750 W for 40 min. The temperature was monitored by an external infrared (IR) sensor. The fresh plant material 65 g of *C. officinalis* were ground into small pieces, placed in 2 l round-bottom flask with 50 ml of water and subjected to microwave distillation using a Clevenger-type apparatus for 30 min, resulting in a yield of 0.86% (w/w). The extracted oil was dissolved in 0.5 ml of HPLC grade n-hexane, dried over anhydrous sodium sulphate and stored at -5ºC in a sealed brown vial (Tosun *et al.,* 2012).

2.5 Headspace solid phase microextraction (HS-SPME)

The fragrance of *C. officinalis* flowers was captured using a 100 mm polydimethylsiloxane HS-SPME (PDMS) fibre. This process involved obtaining flower powder (Jirovetz *et al*., 2002; Kim and Lee, 2002) placing 22 g of finely powdered *C. officinalis* flowers in a 250 ml Erlenmeyer flask at 20°C, allowing it to equilibrate for 30 min. Subsequently being subjected to this condition for 30 min**,** the SPME fibre was taken out and put into the GC injecting device, in which it had been heated to 250°C for 5 min.

2.6 Isolation technique through GC-MS

The essential constituents of *C. officinalis* were identified by using GC-MS. The chloroform extract of *C. officinalis* was used to conduct in a gas chromatograph associated with a mass spectrometer which was filled with a Rtx-5ms column. An electron ionization procedure was carried with a radiation of 70 eV was employed in electrostatic manner for GC-MS analysis. As a gas carrier, 99.999% helium gas was applied at a constant flow rate of 1.25 ml/min, with a total volume of 1 µl. The temperature of the source of ionization was 200°C, the injector had been kept at 250°C, as well as the oven had been set to start at 200°C and rise through 4°C/min until it attains 280°C over a 10 min isothermal phase (Jalill *et al*., 2014). This process takes about 36 min in total to complete. Mass spectral data comprising a wavelength spectrum of 35 to 600 m/z have been measured at 70 eV. The technique for identifying the constituents was to compare their mass spectrum to those reported in the Wilson and NIST libraries. Various essential substances, including gamma sitosterol, stigmasterol, lupeol and caryophyllene were isolated through GC-MS technique and reported that this method is most suitable for the various pharmaceutical properties like antibacterial, antimicrobial and antioxidant activity by flower powder of pot marigold (Sahingil, 2019).

3. Phytochemistry

Every part of the *C. officinalis* plant contains an incredible source for various phytochemical components as well as exhibiting different amount of each component with regard to both quality and quantity found in different plant regions (Liu *et al*., 2010). The various phytochemical ingredients of *C. officinalis* were esterified and free triterpene alcohols, carotene and polyunsaturated fatty acids like calendic acid (Neukirch *et al*., 2004). Further, it contains carotenes, resin, mucilage, saponins, steroidal compounds, flavonoids (Verma *et al*., 2014) and various phytochemicals were enlisted in Table 1.

Table 1: Different bioactive compounds of *C. officinalis* (Nelofer *et al*., 2017)

Active components	Essential constituents	Plant part
Flavonoids	Isoquercitrin, isorhamnetin, quercetin rutin calendoflavoside narcissin isorhamnetin-3-*O*-β-D glycoside	Flower
Coumarin	Esculetin, scopoletin, umbelliferone	Flower
Terpenoid	Calendulaglyco side A, calendulaglycoside B erythrodiol lupeol ø-taraxasterol cornulacic acid acetate	Root, flower
Quinones	Phylloquinone α-tocopherol, ubiquinone, plastoquinone	Leaves
Volatile oil	Oplopanonec methyllinoleate α-cadinol, cubenol	Flower

4. Pharmaceutical properties of *C. officinalis*

Experimental and clinical trials on *C. officinalis* extracts have demonstrated a broad spectrum of pharmacological properties. These findings could potentially lead to the development of new therapeutic strategies for managing various disorders in both humans and animals. The plant exhibits notable anti-inflammatory, antioxidant, antimicrobial and wound-healing effects which was described in Figure 2. Largely attributed to its rich content of flavonoids, triterpenes, carotenoids, lupeol, rutin, narcissin, umbelliferone, α-cadinol, *etc.*, were enlister in Table 2. These compounds contribute to its efficacy in treating skin conditions, promoting wound healing and alleviating symptoms of various inflammatory disorders. Additionally, its use in traditional medicine as a remedy for digestive issues, menstrual discomfort and various issues which underscores its broad therapeutic potential. The use of plants in disease treatment dates back to the earliest human civilizations. Numerous pharmacological and pharmaceutical studies have highlighted that *C. officinalis* possesses a wide array of biological activities, with several of these offering potential for future development (Nelofer *et al*., 2017).

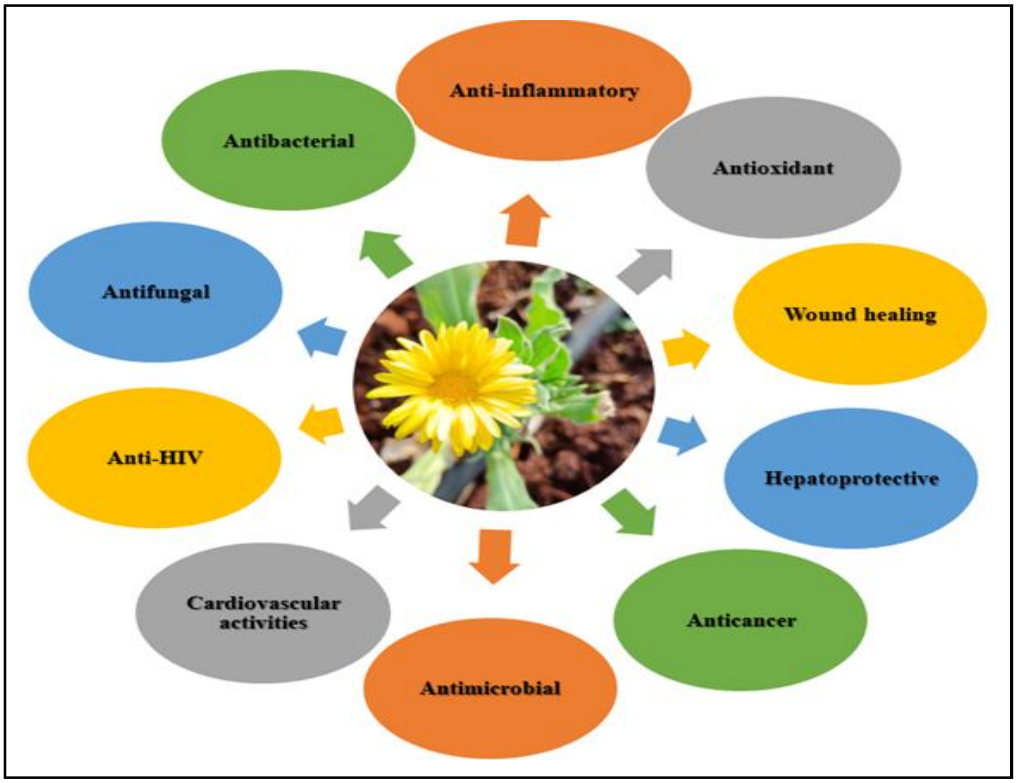
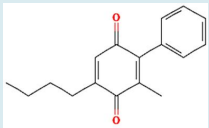
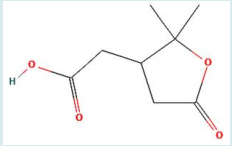
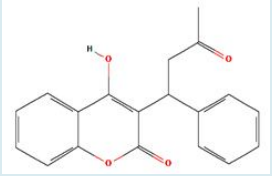
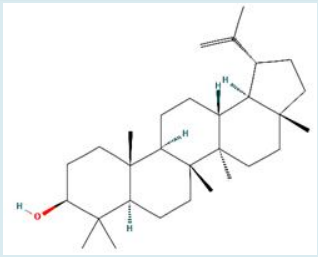
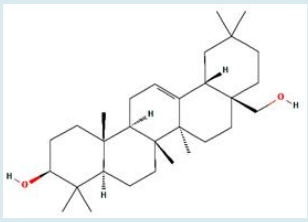
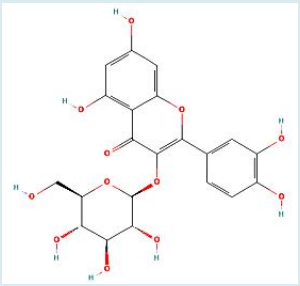
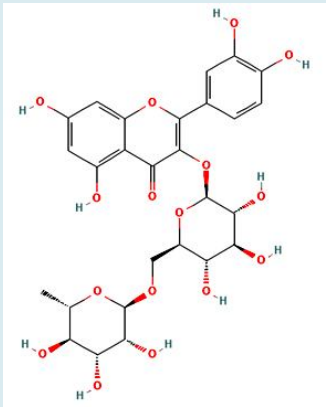
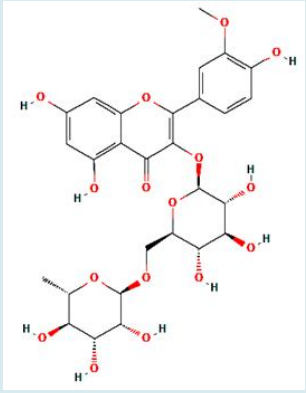
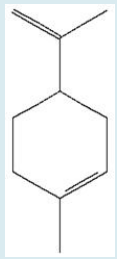
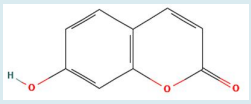
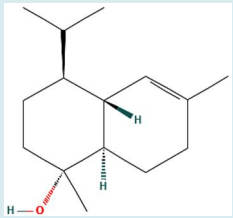
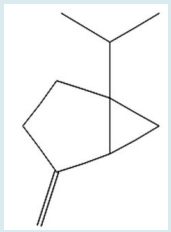
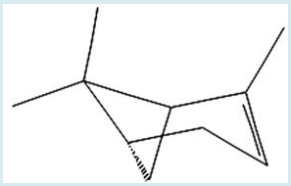


Figure 2: Different pharmaceutical properties of *C. officinalis*.

Table 2: Various phytochemicals and pharmacological properties of *C. officinalis* (Nelofer *et al.*, 2017)

Active components	Pharmacological properties	Structures
Quinones	Anticancer	
Terpenoids	Anti-inflammatory, cardioprotective, antitumor, antidiabetic	
Coumarins	Anti-inflammatory, antioxidant	

Lupeol	Anti-inflammatory activity	
Erythrodiol	Antiviral anti-inflammatory activity	
Isoquercitrin	Hepatoprotective activity, antiviral activity	
Rutin	Antioxidant anti-inflammatory activity	
Narcissin	Cytotoxic activity	

Limonene	Antioxidant activity	
Umbelliferone	Antimicrobial activity	
α-cadinol	Antiviral activity against (Severe acute respiratory syndrome) coronavirus	
Sabinene	Anticancerous activity	
α-pinene	Anti-inflammatory, anticancerous	

4.1 Antioxidant activity

C. officinalis flowers contain numerous biologically relevant chemicals such as polyphenols and carotenoids which influences to its antioxidant capacity (Kishimoto *et al*., 2005; Matysik *et al*., 2005). The flower petals contain an enormous concentration of active antioxidant molecules. Therefore, we compared extracts from petals to extracts from entire flower tops. Among the other multiple factors, the extraction solvent alone to determine the antioxidant property of *C. officinalis* (Cetkovic *et al*., 2003). A mixture of propylene glycol and water which was used in extraction of phenolic compounds and a few amounts of essential oil to obtain reliable extracts that are meant for internal consumption. The free radical scavenging action of these phytochemicals were in significant proportion and also enhance wound healing by deliberate linking (Kuwahara and Kimura, 2015). This free radical scavenging activity were measured by using 1,1-diphenyl-2-picryl-hydrazil (DPPH) with some changes (Huang *et al*., 2011). One of the most reliable methods to assess the scavenging effect of medicinal plants, organically derived medicines, or their formulations is by employing DPPH. It is a frequently used, cost-effective technique for determining antioxidant activity (Salar *et al.,* 2022). The floral extract of *C. officinalis* shows the higher amount of activity in antioxidant than the leaf extract (Mubashar Sabir *et al*., 2015). This antioxidant activity of flower extracts which protects the human skin cells from oxidative damage otherwise it will lead to ageing and skin cancer (Alnuqaydan *et al*., 2015). In addition, the *C. officinalis* extract was analysed for its antioxidant property through alcoholic extract, it has been found to detoxify superoxide radicals which are produced through riboflavin photoreduction and hydroxyl radicals induced by the Fenton reaction,

further more to minimize *in vitro* lipid peroxidation based on the concentration of the doses (Singh *et al*., 2011).

4.2 Antibacterial and antifungal activity

The *in vitro* growth of both Gram-positive bacteria such as *Staphylococcus aureus* and *Bacillus subtilis* and Gram-negative bacteria such as *Pseudomonas aeruginosa* and *Escherichia coli* is inhibited by the volatile oil found in *C. officinalis* flowers, these, *P. aeruginosa* exhibits the greatest inhibition (Roopashree *et al*., 2008). In addition, compared to the petals, the reproductive parts of *C. officinalis* flowers often have lesser antibacterial properties. The essential oil of *C. officinalis* was found to exhibit antifungal properties against the *Candida dubliniensis, C. glabrata, C. parapsilosis, C. albicans, C. krusei* and against yeast that were isolated from humans among them *Streptococcus aureus* was more prone to aqueous extracts than ethanolic, methanolic and petroleum ether extracts of *C. officinalis* flower, implying that aqueous extracts have better antibacterial activity. The stem, leaf, root and flower extracts of *C. officinalis* which show antimicrobial activity against *E. coli*, *P. aeruginosa, C. albicans*, *C. parapsilosis,* Cogulase (+) *Staphylococcus* species, *Enterococcus* species and Cogulase (-) *Staphylococcus* species (Hamad *et al*., 2017).

Table 3: **Essential oil of *C. officinalis* in antifungal activity (Gazim *et al*., 2008)**

Microorganisms	Mean zone of inhibition (mm)	
	Nystatin 20 µg/disc	*C. officinalis* oil 5 µl/disc
C. parapsilosis (ATCC 22019)	12	20
C. dubliniensis (ATCC 777)	11	24
C. albicans (ATCC 64548)	12	16
C. krusei (ATCC 6258)	12	15
C. glabrata (ATCC 90030)	12	15
Rhodotorulla species (Hands colonization)	11	30
C. tropicalis (Urine)	13	11
C. guilliermondii (Hands colonization)	11	25

4.3 Anti-HIV activity

It has been observed that extracts from *C. officinalis* flowers can protect HIV-1-infected lymphocytic MOLT-4 cells from damage. This extract results in a substantial decrease *in vitro* HIV-1 RT activity in a cell free system, subsequently 30 min of treatment with partly purified enzyme in a cell free condition. Reverse transcriptase was adopted to carry out the HIV-1 inhibitory test. The partly purified enzyme was recorded from HIV-1 viruses were generated within the culture medium by HIV-1 highly infected cells, specific enzyme activity was inhibited (67-85%) at doses of 50, 100 and 200 µg/ml. The incubation flower extract with varied concentrations confirmed that a time and concentration were influenced by decrease in HIV-1 RT activity. Furthermore, *in vitro* chronically infected lymphocytic MOLT-4 cells express HIV-1 reverse transcriptase activity in response to a dose dependent manner in the chloroform extract of *C. officinalis* extracts (Kalvatchev *et al*., 1997).

4.4 Anti-inflammatory activity

C. officinalis inflorescence extract shows anti-inflammatory effects on mice's acute paw edema caused by dextran and carrageenan (Preethi *et al*., 2009). In addition, a substantial increase in the level of cytokines associated with inflammation such as IL-1β, IL-6 and TNF-α in the bloodstreams of lipopolysaccharide (LPS) caused animals had been readily observed. The cytokines IL-1, IL-6 and as well as tumour necrosis factor serve as a stimulant medicines in the liver, producing C-reactive protein (CRP) level to rise considerably through acute inflammation. According to the study, increased levels of the pro-inflammatory cytokines IL-6 and TNF-α play an essential role in the development of ovarian epithelial carcinoma as well as kidney diseases (Stenvinkel *et al*., 2005). The activities of cyclooxygenase-2 (COX-2) and 5-lipoxygenase (5-LO) which are essential for the production of pro-inflammatory eicosanoids from arachidonic acid, can be inhibited by the hydroalcoholic extract of *C. officinalis*. When the *C. officinalis* extract was used in place of trolamine, the risk of acute eczema of stage 2 or above were substantially reduced (Herold *et al*., 2003). It has great effectiveness in minimizing acute eczema of stage 2 or above which could be suggested to patients undergoing surgical radiotherapy for breast cancer (Pommier *et al*., 2004).

4.5 Wound healing activity

Aqueous extracts of *C. officinalis* were used in the process of reducing the surface of the wound due to it is utilized in the form of infusions, tinctures, liquid extracts, creams and ointments medicinally and it depends on the healing functions of the tissue, the nature and extent of the injury and the overall status of the tissue's health. The practice of promoting healthy skin over a wound to cover the devoid region, which requires complex and well-orchestrated relations between cells, extracellular matrix and cytokines. This centripetal movement of the edge of the wound appears to be related to myofibroblast activity. The higher degree in healing of wound in herbal ointment treatment could be related to a substantial rise in fibroblast cell proliferation and metamorphosis into myofibroblasts. Furthermore, the existence of flavonoids and saponins, which cause angiogenesis, increased collagen synthesis and cytokine production could explain the influence of the herbal ointment on the healing process (Agnel *et al*., 2018; Muley *et al*., 2009). Furthermore, treatment with the herbal ointment significantly lowers IL-6 and TNF-alpha levels while increasing PDGF and EGF levels in a dose-dependent manner. This results in enhanced wound healing activity through improved collagen synthesis, increased wound contraction and modulation of interleukin 6, epidermal growth factor (EGF), platelet-derived growth factor

(PDGF) and tumour necrosis factor-alpha (TNF-α). The extracted components from *C. officinalis* can therefore be applied in various types of wound treatments (Gunasekaran *et al*., 2020).

4.6 Hepatoprotective activity

Aqueous and ethanolic floral extract of pot marigold were capable of minimizing CCl_4 induced hepatotoxicity which is regulated by a free radical pathway. Likewise, hydroalcoholic extract of the flowers inhibits hepatocytolysis and liver biomarkers in *in vivo* as well as *in vitro* conditions. The cytochrome P_{450} enzyme metabolizes CCl_4 and its products of metabolism, trichloromethyl forms free radicals which are highly reactive and encourage lipid peroxidation of macromolecules, which leads to tissue damage (Taniguchi *et al*., 2004; Noguchi *et al*., 1982). The preliminary treatment of *C. officinalis* flower extract significantly reduced the tissue damage caused by CCl_4. Further the extract contains an ability in order to protect vital organs from the toxins caused by chemical substances. This effect could be attributed in part to extracting the activity that scavenges free radicals in the effective enhancing of the antioxidant system, since many of the active substances that comprises, the extract are effective free radical scavengers. Other mechanisms, such as its influence on Cytochrome P_{450} enzymes, could also be assessed (Preethi and Kuttan, 2009).

4.7 Anticancer activity

The extract of *C. officinalis* was obtained using a specific extraction method to evaluate its immune-modulating and antitumor activities *in vitro*. The key phytochemicals present in the aqueous extracts of *C. officinalis* include triterpenoids, carotenoids, flavonoids, saponins, proteins, fatty acids and polysaccharides. Intense radiation possesses the ability to stimulate the carotenoids components. This biological process required to be identified by using laser therapy of the *C. officinalis* extract. A comparable study using *C. officinalis* extract used without laser therapy resulted in only a slight decrease in the multiplication of cancer cells. The subsequent rise in cellular activity is linked to the use of lasers, which may cause structural changes in oxidation of different components in the extract (Jimenez-Medina *et al*., 2006).

4.8 Cardiovascular activity

C. officinalis has antioxidant properties in addition to anti-inflammatory properties, it greatly lowered the 2,2-Diphenyl-1-picrylhydrazyl radical (Muley *et al*., 2009). The fusion of different flavonoid components, such as lycopene and β-carotene contribute to *C. officinalis* antioxidant activity with its anti-inflammatory and antioxidant properties (Muley *et al*., 2009). *C. officinalis* may help reduce ischemia-related myocardial damage and improve post-ischemic left ventricular function. It has been shown to increase Bcl-2 and HO-1 levels, enhance Akt phosphorylation and decrease infarct size, apoptotic cell death and levels of TNF-α, caspase-3 and cytochrome-c. These effects suggest that *C. officinalis* generates a survival signal through Akt by reducing inflammation (Song *et al*., 2005). An aqueous extract was applied to the hearts of male Wistar rats and it was found that the substance lowered heart rate contractions completely at a dose of 0.3 mg/l could be associated with over stimulating myocardial activity (Perez-Carreon *et al*., 2002). This could be in relation with the plant extract's spasmogenic action, based on the dosage (Bashir *et al*., 2006).

4.9 Neuroprotective activity

The flowers of *C. officinalis* had been reported to have anti-inflammatory properties which could contribute to its neuroprotective activity (Preethi and Kuttan, 2009). *C. officinalis* flowers received recognition for their estrogenic action (Naguib *et al*., 2005). According to accumulating confirmation oestrogen protects neurons towards degeneration in several experimental kinds of neurotoxicity. There are numerous observations confirming that 3-NP-induced neurotoxicity is associated with an allergic reaction of inflammation (Ahuja *et al*., 2008; La Fontaine *et al*., 2000). In addition to its anti-inflammatory and antioxidant properties, the hydroalcoholic extract of *C. officinalis* contains estrogenic activity could have a vital part in thereby protecting animal contrary to 3-NP-induced neurotoxicity. The neuroprotective properties of estrogen depend on its concentration in the bloodstream (Brann *et al*., 2007). Estrogen protects the brain by enhancing cerebral blood flow, reducing the expression of apoptotic hepatic coagulation proteins and boosting antiapoptotic gene expression. It also mitigates cytochrome-c release from mitochondria and reduces inflammation by lowering tumour necrosis factor-alpha levels particularly during stroke conditions (Strom *et al*., 2009).

4.10 Nephroprotective activity

C. officinalis extract has been reported to have more nephroprotective activity, in addition the ethanolic floral extract is more potential for nephroprotective than the aqueous floral extract. The ethanolic extract of *C. officinalis* prevents against the nephrotoxicity caused by cisplatin through rejuvenating the renal tissue antioxidant response. Regeneration of plasma renal biomarkers and histological results in renal tissues (Verma *et al*., 2016). The biological process of nephroprotective activity is undefined; however, it has been suggested due to the antioxidant and free radical scavenging activity of the carotenoids are lutein, zeaxathin and lycopene presented in the extract.

4.11 Hypoglycemia and gastric protective activity

The methanolic extract and its 1-butanol-soluble fraction from dried *C. officinalis* flowers demonstrated the ability to inhibit increases in serum glucose levels, delay gastric emptying and reduce ethanol-induced gastric lesions, making it effective for treating gastrointestinal ulcers. In accordance with its gastroprotective and anti-secretory qualities, ethanolic extract was shown to possess an antiacid and anti-ulcer effect. It also promotes the synthesis of mucus and glutathione levels (GSH) by simultaneously lowering the pepsin levels thereby ensuring gastroprotection (Chandra *et al*., 2015). It was additionally confirmed that various saponins exhibited strong gastro-protective effects. The isolation of four new triterpene oligo glycosides called calenda saponins such as A (1), B (2), C (3) and D (4) two ionone glucosides named officinosides A, B and two new sesquiterpene glycosides termed officinosides C and D from 1-butanol-soluble fraction. While the *C. officinalis* extract had minimal effect on chronic hyperglycemia and kidney tissue issues, it provides protection against oxidative stress, which could be beneficial in lowering blood urea nitrogen (BUN) and creatinine (Cr) levels in diabetics. Furthermore, an important hypoglycemic effects of flower extracts and each of their constituents imply that they could eventually serve as a promising medication for the treatment of diabetes (Yoshikawa *et al*., 2001). Antidiabetic drugs are those that help people with diabetes by treating, managing, preventing or stabilizing their

condition. They also contain ingredients which assist with blood glucose regulation (Kaur *et al*., 2023). A single intraperitoneal dose of alloxan (150 mg/kg body weight) was used to develop diabetes in rats. Rats with diabetes had noticeably higher blood glucose and urine sugar levels than normal rats. When a hydroalcoholic extract was given orally to diabetic rats at doses of 25 and 50 mg/kg body weight, the rat's blood glucose and urine sugar levels were significantly lower than those of the cohort of rats with diabetes. The extract resembles insulin in certain ways. Therefore, it is apparent from the research that *C. officinalis* hydroalcoholic extract has antihyperlipidemic and antidiabetic properties (Ashwlayan *et al*., 2018).

4.12 Spasmogenic and spasmolytic activity

An extract of *C. officinalis* was having spasmogenic action (Bashir *et al*., 2006). The ethanolic or aqueous extract have reduced the instinctive reduction while potassium supported contractions in the muscles. The aqueous ethanol crude extract of *C. officinalis* inhibited spasmolytic activity. With a median effective concentration (EC_{50}) of 0.78 mg/ml the spasmolytic efficacy was depend upon the dosage. Smooth muscle contraction is based on an increase in cytoplasmic free [Ca^{++}], which activates the contractile components (Karaki and Weiss, 1988). These extracts could hinder impulsive contraction when isolated with dichloromethane. Spasmolytic activity was triggered through the process of calcium channel blocking (CCB) (Bashir *et al*., 2006). The blocking of N-type calcium channels prevents unexpected fatal cardiac events (Nattel, 2014). In individuals with hypertension, cardiovascular disease and other metabolic illnesses, N-type calcium channel blocking (NCC) alone or in combination with L-type calcium channel blockade (LCC) can be advantageous (Kuwahara and Kimura, 2015).

4.13 Genotoxic and antigenotoxic activity

The aqueous or ethanolic extract of *C. officinalis* flowers has a genotoxic effect at high doses, while at lower concentrations, it exhibits an antigenotoxic effect (Perez-Carreon *et al*., 2002). The propylene glycol extract has demonstrated an antigenotoxic effect, as assessed by analysing 24 h, urine 8-hydroxy-2'-deoxyguanosine (8-OHdG) levels and lymphocyte DNA fragmentation (Frankic *et al*., 2009). Urinary 8-OHdG serves as a biomarker for carcinogenesis and other progressive disorders. It is crucial for evaluating the endogenous oxidative damage to DNA and is also used to assess the onset and progression of carcinogenesis (Valavanidis *et al*., 2009).

4.14 Anthelminitic activity

Extracts from the flowers and leaves of *C. officinalis* have also been demonstrated to possess anthelmintic properties. The ethanolic extract of the air-dried flower powder was obtained using a Soxhlet apparatus, then concentrated and vacuum dried, resulting in an orange-yellow mass. The extract was analysed for the presence of various phytoconstituents, including carbohydrates, flavonoids, vitamins, coumarins, tannins, alkaloids, proteins and glycosides among others (Bhardwaj *et al*., 2021). Anthelmintics are drugs that either kill or immobilize parasitic worms, allowing them to be expelled from the body. They are also referred to as vermifuges or vermicides (Kommu *et al*., 2023) The experiment was conducted using the adult Indian earthworm, *Pheretima posthuma*, due to its morphological and physiological similarities to the human intestinal roundworm parasite. The worms exposed to the crude extracts of flowers and leaves were paralyzed at 57.6 min and perished at 112.3 min. The plants contain saponins and have also demonstrated its anthelmintic potential (Pandey and Despande, 2021).

5. Personal care and cosmetic products of *C. officinalis*

C. officinalis is widely used in personal care and health products due to its anti-inflammatory, antioxidant and soothing properties. It is commonly found in skincare products like creams and balms for treating irritated skin, promoting wound healing and hydrating dry skin. In hair care, it helps soothe the scalp and improve hair texture. Additionally, it is used in oral care products for its antimicrobial effects and in baby care for its gentle action on sensitive skin. These versatile benefits make *C. officinalis* a popular ingredient in natural and holistic health formulations which was represented in Figure 3.

5.1 Pot marigold ointment

The phytochemicals found in the aqueous extract of *C. officinalis* which include carotenoids, terpenoids, steroids, phenolic compounds, lipids, carbohydrates, tocopherols and quinones provide considerable psychological advantages for individuals (Kishimoto *et al*., 2005; Re *et al*., 2009). The plant's active substances like saponins, esters, flavonoids and triterpeneol which include hyperoside and rutin (Miliauskas *et al*., 2004; Muley *et al*., 2009). An extended interruption in wound healing could result with illnesses such ischaemia, immune compromised states, malnourishment, aging, local infection and local tissue damage. The outer layer of skin recovers spontaneously after impairment through a complicated process termed as wound regeneration. The three stages of wound healing are classified as anti-inflammatory, proliferative and remodelling. Improved leucocyte mobility, greater capillary permeability and higher blood flow in the affected area are characteristics of the inflammatory phase. During the proliferative phase, granulation, contraction and epithelization occur. The remodelling phase influence the healing region's vitality and appearance. The ointment for healing wounds was made by combining an aqueous extract of *C. officinalis* with 10 and 20% (w/w) concentrations with white wax. The process of wound diminishing is influenced depending on the tissue's healing capacity, the severity and type of the injury and the overall wellness of the tissue (Priya *et al*., 2004). Herbal ointment treatment has been found to shrink wounds significantly faster. Herbal ointment (HO) has been shown to accelerate wound healing. This may be due to accelerated fibroblast cell proliferation and myofibroblast transformation. In addition, the herbal ointment's potential impact on wound contraction could be determined by the presence of flavonoids and saponins, which are related to cytokine release, enhanced collagen production and angiogenesis (Agnel *et al*., 2018; Muley *et al*., 2009).

5.2 Pot marigold tincture

C. officinalis extracts enhance the migration and proliferation of NIH-3T3 fibroblasts *in vitro* (Muley *et al*., 2009) and it promotes fibroblast proliferation and migration in both murine and human system. Additionally, homeopathic preparations of *C. officinalis* have been shown to enhance the migration and proliferation of NIH-3T3 fibroblast cells (Hostanska *et al*., 2012). Furthermore, extract has been observed to exhibit angiogenic activity in the chorioallantoic membrane (Parente *et al*., 2012). A distinct signalling process comprising FAK phosphorylation and consequent PI3K-mediated Akt activation is being found to influence the ability of *C. officinalis* tincture to heal wounds. PI3K is a key intracellular signaling pathway that plays a significant role in regulating cell proliferation and

migration. In addition, to determine the primary components present in the *C. officinalis* tincture which are in responsible for wound healing (Dinda *et al*., 2015).

5.3 Pot marigold cream

C. officinalis have been found to encourage physiological regeneration and epithelialization of injured skin (Marti-Mestres and Nielloud, 2002). Thus, it can produce some valuable effects on the skin. Cosmetics ought to be effective as well as having a little chance of skin irritation or sensitization. This is influenced by their composition, the application of their use, quantity and quality of components (Ray *et al*., 2010). The non-invasive topical application of *C. officinalis* cream has a revitalizing effect on human skin. A regular surface application of a cream could result in a reduction of the skin's melanin level, implying that the formulation possesses skin whitening activities. The key benefit of using topical cream is that they could enhance the solubility and bioavailability of therapeutic medications while also favouring the topical absorption of hydrophilic solutes. Additionally, topical emulsions prevent the gastrointestinal environment and the first pass impact (Marti-Mestres and Nielloud, 2002). The ability to considerably diminish external erythema implies that this formulation has anti-inflammatory properties. The cream offers skin nourishing qualities through increased skin moisture content.

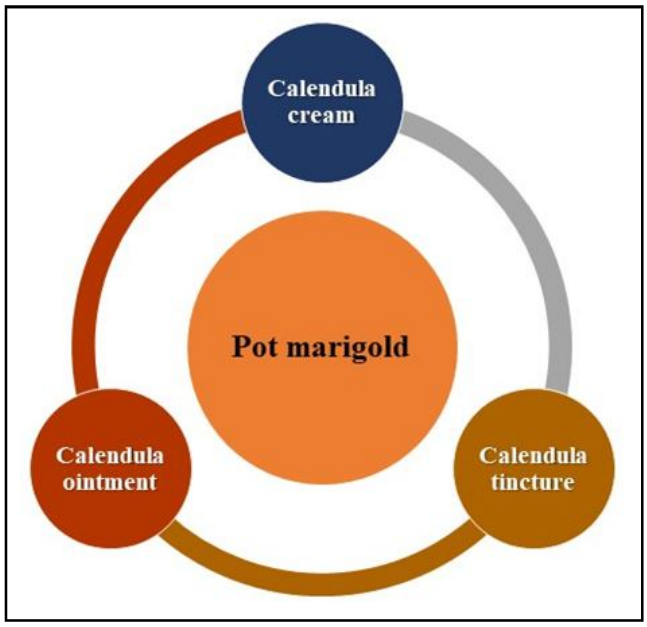


Figure 3: Products of Pot marigold.

6. Future thrust

Future research on *C. officinalis* should focus on exploring its full pharmacological potential, including in-depth studies on its bioactive compounds, mechanisms of action expanding its pharmaceutical applications from a global perspective. Investigating its efficacy in treating chronic diseases such as diabetes and cancer through advanced pharmacological models would be valuable. Additionally, studies on the optimization of extraction methods, standardization of formulations, mechanistic studies, clinical trials and global standards to validate its therapeutic applications could significantly contribute to its integration into modern medicine. Lastly, sustainability and large-scale cultivation strategies should be explored to ensure consistent and high-quality supply for pharmaceutical use.

7. Conclusion

The broad spectrum of phytochemicals and pharmacological effects found in *C. officinalis* makes can be viewed as a promising reservoir for the development of new drugs. It possesses effective anti-inflammatory, antifungal, antibacterial and antioxidant effect with minimal toxicity. In addition, it contains various active compounds, *viz.,* flavonoids, triterpenoids and carotenoids which contribute to its therapeutic effects. This plant holds considerable potential for the extraction of active ingredients that could be utilized in the development of various drugs. Thorough investigation is needed to explore its effectiveness in managing and protecting against various illnesses. Although, *C. officinalis* exhibits potential in a range of areas, further study, clinical trials and thorough scientific investigations are required to assess its safety, effectiveness and ideal application in many medicinal contexts. To enhance its broader applicability globally, standardized cultivation practices, rigorous clinical validation and improved quality control of extracts must be prioritized. Expanding its integration into modern pharmaceutical formulations and natural health products, along with promoting sustainable sourcing and regulatory alignment, can ensure its efficacy and safety while contributing to the global demand for natural therapeutics.

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Conflict of interest

The authors declare no conflicts of interest relevant to this article.

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