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CALENDULA OFFICINALIS – OVERVIEW ON APPLICATIONS AND PHARMACEUTICAL USES

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Abstract
Calendula officinalis, commonly named marigold, is a vibrant, adaptable, and versatile herbaceous plant esteemed across centuries for its decorative, culinary, and medicinal effects. It has long been known for its content of bioactive compounds, including flavonoids, carotenoids, and triterpenoids, which provide numerous health advantages, such as antibacterial, antioxidant, skincare, wound healing, and anti-inflammatory properties, and even on cancer treatment. We developed this study to describe Calendula officinalis history, botanical characteristics, pharmacological properties, toxicity, and modern-day applications. Calendula officinalis emerges as a remarkable representative among botanical species, that not only embellishes our gardens, but also contributes profoundly to our well-being and health in diverse ways. Calendula's edible flowers add a burst of color and flavor in culinary dishes and infusing. Through its multifaceted potential for various purposes and pharmacological properties, this plant has demonstrated a promising capacity in various fields including pharmaceuticals, food, textiles, cosmetics, and agrochemicals.

Keywords: marigold, medicinal plant, bioactive compounds, pharmacological properties.

1. INTRODUCTION

Pot marigold (*Calendula officinalis* Linn.) is an annual or short-lived perennial herbaceous plant of Mediterranean origin. It is spreading quickly throughout the temperate zone of the continents due to its well-known ability to accumulate soil pollutants in roots and high tolerance to stress factors (Abdelwahab *et al.*, 2022; Hristozkova *et al.*, 2016). Based on its wide distribution, it is used as a medicinal plant in Europe, United States and Asia (Figure 1) (Avci and İNan, 2021; Muley *et al.*, 2009). It served as ingredient in balms, ointment, creams, and lotions, functioning as antiseptic, antimicrobial and anti-inflammatory agent during both the North American Civil War and the First World War (Parente *et al.*, 2012).

Following the significant decrease in the late 1990s, the cultivation and selection of medicinal plants have seen a surge in recent times. Industrial applications of plants with therapeutic value include the production of drugs, pharmaceuticals, and cosmetics, with an anticipated faster growth in their utilization compared to therapeutic chemicals (Suetin *et al.*, 2021).

Pot marigold is a member of the sunflower family identified *via* way of means, in numerous dialects, which incorporate: Gălbenele (Romanian), Fleur de souci (French) Ringelblume (German), Ringblomma (Swedish), Chin Chan Ts'ao (Chinese), Zergul (Hindi), Pot Marigold and Common Marigold (English) (Muley *et al.*, 2009; Wichtl, 2004). It was noted that marigold holds

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significance due to its bioactive compounds, making it a valuable medicinal crop. The chemical composition includes essential volatile oils, terpenoids, carotenoids, coumarins, quinines, flavonoids, amino acids, carbohydrates, lipids, and other different minimal components (Hristozkova *et al.*, 2016).

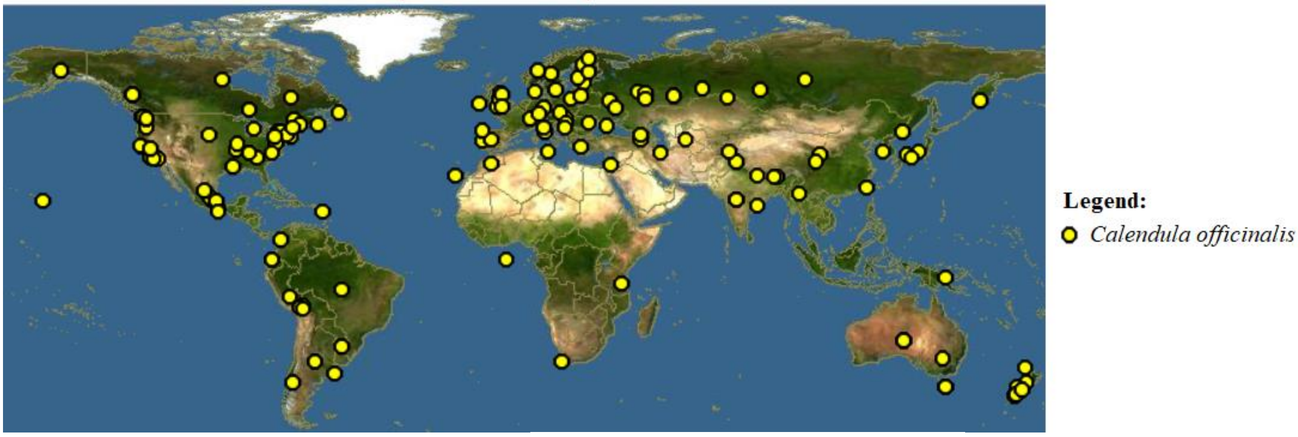

Figure 1. Calendula officinalis world distribution
(https://www.discoverlife.org/mp/20m?kind=Calendula+officinalis)

The main objective of the current study was to conduct a comprehensive review of national and international literature focusing on the significance, utilization, and economic potential of marigold. The literature review was based on scientific data derived from books, journal papers and electronic sources provided by scientific entities-databases: SCOPUS, Web of Science, ScienceDirect, Wiley, SpringerLink.

2. GROWTH AND COMPOSITION OF *C. OFFICINALIS*

Taxonomic and botanical description

C. officinalis is an erect herb (Figure 2), attaining a height ranging from 30 to 60 cm, occasionally reaching 80 cm, characterized by a stem that is angular and glandular in its structure, branching either from the bottom or at a higher point.

Tracheobionta **Subkingdom**
Magnoliophyta **Division**
Magnoliopsida **Class**
Asteridae **Subclass**
Asterales **Order**
Asteraceae **(Compositae) Family**
Calenduleae **Tribe**
Calendula **Genus**
C. officinalis **Species**

Figure 2. Calendula officinalis botanical classification

The leaves situated in a spiral arrangement are oblong-lanceolate, from 2.5 to 7.5 cm long and the terminal flowerheads are upon a receptacle shaped like a green crown measuring 4-7 cm in width.

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The flowerheads had numerous orange - yellow ligulate florets alongside a few tubular florets (commonly known as petals) and its disc florets exhibit pseudohermaphroditic characteristics, with the female counterpart being sterile. The fruit takes the form of a curved achene and measures between 1.0 and 1.5 cm long (Dhingra *et al.*, 2022; Mullaicharam *et al.*, 2014; Muley *et al.*, 2009; Wichtl, 2004; Khalid and Teixeira da Silva, 2012; Mohammad and Kashani, 2012).

Ecological requirements for cultivation

C. officinalis is extensively cultivated and can flourish across diverse soil types and sunlit environments. It can be one of the easiest and most versatile flowers to be cultivated in a garden. Seeds are typically sown in temperate climates during the spring, resulting in blooms that persist throughout the summer and often into autumn.

Although known as perennial, it is generally grown as an annual, especially in colder regions with insufficient winter sustenance and warm summer climates where it struggles to persist. Plants thrive in well-lit areas with nutrient-rich, well-drained soil, while seeds proliferate in sunny or partially shaded locations (Mohammad and Kashani, 2012).

Pot marigold prefers full sunlight, yet it may show signs of wilting on hot days unless it receives some midday shade. This plant is adaptable to a broad spectrum of soil pH levels but prefers weakly acidic to neutral soils (pH: 6-7). It should be regularly watered until the plants are established. Once they are mature, can thrive with occasional watering, to avoid overwatering (Dhingra *et al.*, 2022).

Composition of *C. officinalis* flowers

The constituents of *C. officinalis* flowers include a rich array of compounds, from essential oils to flavonoids (Table 1), each contributing to its distinctive color, fragrance, and potential therapeutic properties. The primary source for active compounds is the inflorescence, comprising both ligulate (ray) and tubular (disc) flowers. The study of lipids in *C. officinalis* inflorescences has been limited in comparison to phenolic compounds and triterpenoids, with carotenoids being the primary focus of studies (Marzouk *et al.*, 2024).

Table 1. Main chemical constituents present in C. officinalis flowers

Compound group	Content (%)	Reference
Carotenoids	0.7 – 2.7	Balázs *et al.*, 2023, Sausserde and Kampuss 2014, Raal *et al.*, 2016
Volatile oils	0.13 – 0.97	Ak *et al.*, 2021, Muley *et al.*, 2009
Terpenoids	0.028 – 1.340	Shahane *et al.*, 2023, Neukirch *et al.*, 2004
Flavonoids	0.53 –0.70	Al-Huqail *et al.*, 2023, Honório *et al.*, 2016

3. CURRENT APLICATIONS OF *C. OFFICINALIS*

Ornamental flower *C. officinalis*

The results of the study of Nejad and Shakib, (2013) showed how varying levels of nitrogen impact the morphological aspects and duration of blooming of *C. officinalis*, a bedding ornamental plant, within the temperate climate. Nitrogen fertilizer is recognized to play a crucial role in maximizing the yield of food and ornamental plants, however, its impact on the environment is a growing concern.

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Studies confirm that the blue shade nets inhibit the growth of ornamental foliage and flowers, while red and yellow nets, promote vegetative growth. Furthermore, the influence of photoselective shade nets on light spectrum variation and its subsequent effect on plant antioxidant capacity, pigments, and normal growth was analyzed on ornamental plant *C. officinalis*. The experiments were conducted in a greenhouse at the Ornamental Plant and Flower Research Station of Lahijan, Iran. Given the significance of flower quantity in ornamental plants, the study revealed an increase in flower numbers under the yellow net. Therefore, it is imperative to employ this shade net within the flower industry (Abbasnia Zare *et al.*, 2019).

Food coloring

C. officinalis is on the FAO list (Food and Agriculture Organization of the United Nations) of „Herb and spices", and it is mentioned that its flowers and leaves are edible. Freshly chopped *C. officinalis* flowers can be incorporated into salads, while dried petals are utilized in teas, as well as for flavoring cakes, cookies, puddings, and soups. Additionally, similar to saffron, *C. officinalis* is employed to add color to butter and cheese, enhancing the flavor of stews, chowders, soups, seafood, roast meats, and chickens (Duke, 2008; Facciola, 1998).

Dying fibers and textiles

According to Mijas *et al.*, (2022), *C. officinalis* proves to be a favorable option for dyeing hemp and cotton fabrics, due to its superior performance in terms of washing and rubbing resistance. A higher percentage yield of dye extract was observed in *C. officinalis* using ethanol as solvent, while the lowest yield was obtained with ethyl acetate solvent, on dyed paper-made of *Datura stramonium* (Ganie *et al.*, 2017).

The utilization of *C. officinalis* flower dye offers a versatile way to enrich natural fibers with an array of hues, valuing strategic mordant application. Despite persistent challenges like color fading and washability, inherent in natural dyeing processes, Mariselvam *et al.*, (2023) highlighted the promising potential of *C. officinalis* dye not only as a colorant, but also as an antibacterial agent.

Antiparasitic and insecticidal agents

A current investigation highlights the effectiveness of powdered aerial parts of pot marigold in combating digestive parasites in pigs. When administered at 140 mg/kg once per day for 10 days, *C. officinalis* demonstrated potent antiprotozoal activity and moderate anthelmintic effects. Notably, this study represents the first documented evidence in Romania of *C. officinalis* antiparasitic effects against digestive parasites, in swine (Băieş *et al.*, 2023). However, their discovery confirms that marigold represents an accessible antiparasitic remedies, suggesting their potential as an alternative therapy to chemical treatments for combating digestive parasitic infections in pigs.

In another study, conducted by Bhardwaj *et al.*, (2021) the anthelmintic activity was evaluated by employing the adult Indian earthworms, *Pheretima posthuma*. The observations were recorded regarding the duration required to disrupt the motility and survival of individual worms over a period of two hours. The ethanolic extracts of *C. officinalis* exhibited notable effectiveness against worms in relation to the administered dose.

Furthermore, the *C. officinalis* extract had a promising antiparasitic activity, subjected to *in vitro* testing on promastigote and amastigote forms of *Leishmania major*. Also, the *in vivo* antimalarial activities of the extract and his compounds were tested, against *Plasmodium berghei* ANKA strain-

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infected mice, uncovering their promising antimalarial benefits in tropical diseases (Al-Huqail *et al.*, 2023).
Plant derivatives can be toxic to insect species, but without phytotoxic properties and can be analyzed for using as natural pesticides. Utilization of insecticides for controlling pests is ascending, but even so, they are developing resistance to many actual insecticides.
The study developed by Medhini *et al.*, (2014) mentioned that *C. officinalis* has been widely used due to its antioxidant, antiviral, antimicrobial and anti-inflammatory effects, but without a deep knowledge on their role as pesticides. Thus, the above investigation was carried to find out how insect physiology is affected by the plant extracts. They observed that *C. officinalis* exhibited notable effects on the nutritional physiology and decreased digestive efficiency across all tested pest tissues, making it a promising botanical pesticide.

4. PHARMACOLOGICAL PROPERTIES OF *C. OFFICINALIS*

C. officinalis is a staple in many traditional healing practices, addressing a variety of health issues. It contains various phytochemicals such as flavonoids, terpenoids, carotenoids, and quinones, which have demonstrated antioxidant, anti-inflammatory, antibacterial, antifungal, antiviral, antidiabetic, antitumor, cytotoxic, and immunostimulating activities (Baskaran, 2015; Jan *et al.*, 2017; Muley *et al.*, 2009). Marigold is also commonly used topically for several skin-related conditions, including skin inflammation, open wounds, as well as lacerated wounds that lead to bleeding. Furthermore, this botanical remedy is used in the relief of minor ailments such as razor burn and windburn (Shahane *et al.*, 2023).

Antioxidant Activity

C. officinalis contains antioxidant compounds, such as carotenoids (flavoxanthin, chrysanthemaxanthin, and luteoxanthin epimers) and flavonoids (quercetin, isoquercitrin, lupeol, narcisin, protocatechuic acid, rutin and isorhamnetin) as well as triterpenoids (Ak *et al.*, 2021; Balázs *et al.*, 2023). These chemical compounds not only perform a strong antioxidant role by capturing unpaired electrons and stimulating wound recovery by facilitating artificial cross-linking, but also prevent the formation of reactive oxygen species (ROS) due to cellular processes and free radicals that participate in chronic inflammatory and autoimmune disorders.
Moreover, they interact with antioxidant enzymes, form coordinated bonds with metal catalysts and reduce the presence of alpha-tocopherol radicals, thus reducing oxidative stress and increasing general well-being (Hassanpour and Doroudi, 2023). In addition, by influencing the behavior of distinct proteins in intracellular signaling cascades such as protein kinase C (PKC) and phosphoinositide 3-kinase (PI3K)/AKT signaling pathways, these compounds make a valuable contribution to the promising pharmacological potential of *C. officinalis*, demonstrating its botanical diversity and health advantages (Hou and Kumamoto, 2010).
Previous studies postulated that hydroxyl and superoxide radicals are eliminated by *C. officinalis* extract due to the photoreduction of riboflavin. Thus, Preethi *et al.*, (2006) demonstrated that the extract derived from *C. officinalis* possessed strong antioxidant attributes, efficiently scavenging free radicals, and preventing lipid peroxidation under laboratory conditions. The extract was effective at various concentrations (500, 480, and 2000 µg/ml) in inhibiting different processes. Furthermore, the authors showed that the extract efficiently neutralized free radicals (ABTS and DPPH) at low concentrations (6.5 and 100 µg/ml).

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The antioxidant attributes of *C. officinalis* leaves and flowers were examined using techniques including TBA (thiobarbituric acid) and FTC (ferric thiocyanate) (Pandey and Despande, 2022). The aqueous extract prepared from the leaves and petals demonstrated a high degree of antioxidant activity comparable to vitamins C and E. In particular, it was observed that petals exhibited higher level of antioxidant activity compared to that of leaves.

Mubashar Sabir *et al.*, (2015) indicate that hot-water extracts of *C. officinalis* flowers and leaves have remarkable antioxidant activities, preventing lipid peroxidation induced by various prooxidants in rat liver and brain homogenates. The extracts demonstrated strong free radical scavenging capabilities with IC_{50} values of 184.16 µg/mL for DPPH quenching assay and 28.1 µg/mL for deoxyribose assay.

Likewise, the antioxidant properties of *C. officinalis* were previously reported by Garrido-Suárez *et al.*, (2023), who showed that creams with different concentrations of marigold demonstrated the ability to improve pain and edema (swelling) in rats through mechanisms involving antioxidants, reducing inflammation, and possibly affecting opioid receptors outside the central nervous system (peripheral) in various experimental models of inflammation. Braga *et al.*, (2009) showed that *C. officinalis* extract has concentration-dependent antioxidant and anti-nitrosative activities, exhibiting significant effects even at very low concentrations.

Additionally, Tanideh *et al.*, (2020) showed that *C. officinalis* extract together with *Hypericum perforatum* exhibits beneficial antioxidant effects and on inflammatory markers and microscopic tissue changes in a rat model of periodontitis induced in male Sprague-Dawley rats. Moreover, (Hussein *et al.*, 2010) showed that pre-treatment of hepatocytes with extracts derived from *C. officinalis* or *Morus alba* resulted in the reduction of CCl_4-induced hepatotoxic effects and oxidative stress. This intervention resulted in a statistically significant increase in cell survival and attenuated release of intracellular enzymes (especially ALT, AST and LDH).

Antibacterial and antifungal agents

Multiple studies have highlighted the antibacterial effects of *C. officinalis*. Thus, Safdar *et al.*, (2010) demonstrated the antimicrobial properties of extracts obtained from *C. officinalis* using ethanol, methanol, acetone, and chloroform against a range of bacterial strains including *Escherichia coli*, *Salmonella typhi*, *Staphylococcus aureus* and *Vibrio cholerae*. The study revealed that an ethanol extract showed antimicrobial activity against harmful bacteria like *E. coli, V. cholerae* and fungi like *Candida albicans* on the other hand, a chloroform extract showed antimicrobial activity against all tested microorganisms, while an acetone extract showed antimicrobial effects exclusively against *E. coli*.

The *Calendula spp.* oil was examined for its antibacterial properties on *S. aureus* (ATCC 29213), *B. cereus* (ATCC 14579), *P. aeruginosa* (ATCC 27853) and *E. coli* (ATCC 25922), using a series of diluted solutions added to liquid cultures of bacteria. The essential oil of *Calendula spp.* had minimal inhibitory activity against *E. coli* and *B. cereus* at the 8 mg/mL, no activity against *S. aureus* and *P. aeruginosa* (Servi *et al.*, 2020).

Moreover, Karnwal, (2022), investigated the efficacy of extracts derived from three distinct flower varieties, namely *Chrysanthemum indicum, Hibiscus rosa* and *C. officinalis*, against a range of bacterial strains associated with food contamination. The study employed a panel of ten bacterial strains from the MTCC collection, including four gram-positive (*S. aureus*, *B. cereus*, *C. perfringens*, *L. monocytogenes*) and three gram-negative (*E. coli*, *S. typhi* and *P. aeruginosa*) strains. All three aqueous extracts of flower exhibited antimicrobial activity against the evaluated

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bacterial panel. Moreover, extract from *C. officinalis* made with alcohol (ethanol and methanol) showed exceptionally strong efficacy against all pathogenic examined bacteria.
In the study of Vinola *et al.*, (2021), the antifungal effects of *C. officinalis* and a 2% chlorhexidine solution have been investigated on *Candida albicans*. Compared to *C. officinalis*, chlorhexidine was observed to exhibit significantly stronger antifungal activity against *C. albicans*. However, *C. officinalis* showed some degree of efficacy against *C. albicans*, which is concentration-dependent.
Dey *et al.*, (2024) highlighted the antifungal and cytotoxic effects of two alcoholic (ethanol and methanol) extracts of *C. officinalis*, comparing them with standard samples such as fluconazole and 5-fluorouracil. The author's results reveal remarkable antifungal activity at low concentrations of *C. officinalis* extract, while the MTT assay reveals an IC_{50} of 125 µg/ml for *C. officinalis* extract and 15.6 µg/ml for 5-fluorouracil.

Antidiabetic agent

The antidiabetic properties of *C. officinalis* have been highlighted in several published studies. In the study of Ebrahimi *et al.*, (2019), oral gavage of the hydroalcoholic extract of *C. officinalis* flower to the streptozotocin (STZ)-induced diabetic rat model resulted in body weight normalization and a marked reduction in fasting plasma glucose (FBS) concentrations, as well as serum alanine aminotransferase (ALT) concentrations. The liver function markers, albumin and bilirubin, showed significant improvements upon treatment completion. The extract also stimulated insulin secretion and ameliorated STZ-induced pancreatic, renal, and hepatic complications in animal models. Also, Abudunia *et al.*, (2020) indicated that aqueous and methanolic extracts of *Calendula spp.* showed a significantly higher inhibitory effect of this extract on α-amylase, α-glucosidase, and ß-galactosidase activities compared to the hexane extract, suggesting a hypoglycemic effect of the plant through enzyme inhibition activities.

Anti-Tumoral agent

A *C. officinalis* flower extract was investigated to determine its anti-proliferative potential on breast cancer cell lines compared to epithelial cell lines. Extracts from *C. officinalis* flowers strongly inhibited the proliferation rate of MDA-MB-231 TNBC cell lines (about 20% cell survival), supporting that *C. officinalis* extract can be a promising candidate for treating breast cancer (Mandrich *et al.*, 2023). In another study, investigating the specific cytotoxicity, biochemical characteristics, and molecular impacts of two extracts derived from *C. officinalis* (flowers and leaves) on various *in vitro* breast cancer cell lines were examined. The cytotoxic activities of both extracts were found to be selective towards cancerous cells in comparison to non-cancerous endothelial cells, with the flower extract displaying superior efficacy in both cytotoxicity and selectivity. Gene expression pattern evaluation showed that treatment with these extracts influenced the expression level of multiple genes implicated in apoptosis like BAX, BBC3, and anti-apoptotic gene like BCL2, as well as cell cycle regulatory gene like CCND1 respectively, highlighting their anticancer properties (Cruceriu *et al.*, 2020).
Furthermore, in an investigation that measured the *in vitro* antitumor and immunomodulatory potential of a *C. officinalis* extract, the authors showed that the extract exhibited a strong inhibition of tumor cell proliferation, ranging from 70 to 100%, using a variety of human and rodent cancer cell lines. The identified inhibition mechanisms included G0/G1 cell cycle phase and arrest and caspase-3-dependent apoptosis of cancer cells. The extract demonstrated divergent effects on human peripheral blood lymphocytes and the NKL cell line, stimulating proliferation and activation

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of these cells. Administering LACE extract intraperitoneally or orally to mice resulted in inhibiting *in vivo* tumor growth of Ando-2 melanoma cells and extending the survival time of the mice. These findings suggest that the LACE extract displays dual *in vitro* activities that synergistically contribute to its potential antitumor therapeutic efficacy: cytotoxicity towards tumor cells and activation of lymphocytes (Jiménez-Medina *et al.*, 2006).
Preethi *et al.*, (2010) investigated the impact of *C. officinalis* flower extract on lung metastasis of B16F-10 melanoma cells in C57BL/6 mice. Taken orally for 10 consecutive days of 250 mg per kilogram of body weight, the extract increased the lifespan of treated animals by 43.3% and effectively suppressed the activity of salicylic acid and γ-glutamyl transpeptidase, which are markers of proliferation, in the serum of treated laboratory animals. Following B16F-10 cell injection, administration of the extract for 21 days resulted in a significant reduction in lung tumor nodules and inhibited lung metastases, influencing metastasis markers and investigated the impact on the transcriptome, focusing on genes associated with the regulation of extracellular matrix synthesis and degradation. These results suggest that *C. officinalis* flower extract not only prolongs lifespan but also demonstrated significant anti-metastatic properties, reducing lung tumor formation in mice with established tumors.

Anti-Inflammatory agent

Alexandre *et al.,* (2018) evaluated the anti-inflammatory and anti-resorptive impact of *C. officinalis* on alveolar bone loss (ABL) in rats. The results of the study showed that ligation-induced bone loss for 11 days induced leukopenia, leukocyte infiltration, increased myeloperoxidase (MPO) activity, increased levels of pro-inflammatory cytokines TNF-α and IL-1β in the gingival tissue, accompanied by a decrease in RANKL, a key mediator of osteoclastogenesis (bone resorption), while osteoprotegerin (OPG) immunopositive in periodontal tissue and leukocytosis increased.
C. officinalis at 90 mg/kg reduced bone loss, neutrophilia, levels of pro-inflammatory mediators and RANKL expression, while increased the OPG immunopositive cells and their corresponding serum protein levels of bone-specific alkaline phosphatase (BALP). Serum AST/ALT levels remained unchanged, indicating no alterations in kidney or liver function following treatment.
Preethi *et al.*, (2006) examined the impact of *C. officinalis* flower extract on burns that were experimentally induced in rats. Findings provided evidence that administration of the extract accelerated the wound healing process, leading to improved healing markers while simultaneously reducing tissue damage and lipid peroxidation. Histopathological analysis provided further validation of *C. officinalis* extract's ability to facilitate skin healing following burns. Silva *et al.*, (2021) investigated the impact of pot marigold flower extract on the generation of NO, a proinflammatory radical that is generated by nitric oxide synthase (iNOS) and abundantly secreted by innate immune cells in inflammation-related conditions. The induction of NO production was triggered by the Toll-like receptor 4 agonist lipopolysaccharide (LPS) in macrophages at concentrations that did not compromise the viability of the cells. The compound exhibited a dose-dependent inhibition of NO, achieving a 50% reduction at 147 µL/mL without causing any cytotoxic effects.
Simultaneously, another study evaluated the antinociceptive effects of *C. officinalis* cream in bradykinin (BK)-induced pain models of acute inflammation in mice. The results demonstrated that the cream formulated with the active ingredient at either 10% or 30% *w/w* concentration, reduced pain behavior, edema and inflammatory markers, suggesting its potential as a topical treatment for painful inflammatory conditions (Garrido-Suárez *et al.*, 2023).

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5. TOXICOLOGICAL EFFECTS OF *C. OFFICINALIS*

Lagarto *et al.*, (2011) investigated the toxicity of *C. officinalis* extract at various doses, in rats. A single high dose (2000 mg/kg) caused no immediate harm, while lower daily doses administered for 90 days (50, 250, and 1000 mg/kg) affected certain blood chemistry values, though not severely.

Also, in another study of Silva *et al.*, (2007), the hydroalcoholic extract of *C. officinalis* underwent assessment for its acute oral toxicity in both rats and mice, along with its subacute impact on hematological, biochemical, and morphological aspects in rats. During the acute toxicity evaluation, administration of the extract at doses up to 5.0 g/kg did not result in mortality among the animal subjects. Oral administration of *C. officinalis* extract at varying doses of 0.025, 0.25, 0.5, and 1.0 g/kg did not elicit any hematological alterations when compared to the control cohort. An elevation was observed in the levels of blood urea nitrogen and alanine transaminase (ALT) with respect to the biochemical parameters. Examination of the morphology of the brain, kidneys, and heart did not uncover any deviations. Nevertheless, regions of inflammation were observed in the pulmonary and hepatic tissues, linked to the administration through the oral route and a potential hepatotoxic impact. The extract of *C. officinalis* exhibited no toxicity in the rat subjects; however, indications of renal and hepatic burden were noted.

6. CONCLUSIONS

Calendula officinalis represents a versatile and valuable botanical species with a rich history of traditional use gaining a growing scientific interest. Through its multifaceted potential for various purposes and pharmacological properties, *C. officinalis* became a promising tool in various fields including pharmaceuticals, food, textiles, cosmetics, and agrochemicals. The widespread traditional use of *C. officinalis* throughout history is supported by contemporary scientific research. It serves as a safety alternative, with minimal reported adverse effects and a large biocompatibility.

However, more rigorous clinical trials and standardized dosage forms are needed to fully establish guidelines for optimal utilization of a *C. officinalis* natural-based remedy for various health conditions.

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