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Phytochemistry and Pleiotropic Pharmacological Properties of *Calendula officinalis* - A Review.

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Review Article

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ABSTRACT

Calendula officinalis Linn. (Asteraceae) is an aromatic, erect, annual herb that is native to Europe, cultivated commonly in North America, Balkans, Eastern Europe, Germany and India. It is also known as "African marigold" and has been a subject of several chemical and pharmacological studies. Phytochemical studies have underlined the presence of various classes of compounds, the main being triterpenoids, flavonoids, coumarines, quinones, volatile oil, carotenoids and amino acids. Plenty of studies have reported about the anti-inflammatory, antioxidant, antitumour, antigenotoxic, chemo protective and hepatoprotective, anti-HIV, cytotoxic, spasmolytic and spasmogenic properties of this plant. In this review, we have explored the phytochemistry and pharmacological activities of C. officinalis in order to collate existing information on this plant as well as highlight its multi-activity properties as a medicinal agent. This is as a result of the worldwide cultivation of the plant and increasing published reports on it.

INTRODUCTION

The herbal drugs have made their importance felt in the last few decades whose prevalence is continuously increasing in both developing and developed countries due to their naturalorigin and lesser side effects. [1] *Calendula officinalis* , commonly known as marigold related to family Compositae, is an aromatic, erect, annual herb that grows up to 60 cm in height with angular and glandular stems; leaves 2.5-7.5 cm long; lower spathulate, entire, upper lanceolate with cordateamplexicaul base; flower-heads terminal, heterogamous, light yellow to deep orange; ray florets fertile; achenes 1.0-1.5 cm long, boat-shaped, faintly ribbed; Indigenous to central, eastern and southern Europe, cultivated commonly in North America, Balkans, Eastern Europe, Germany and India. [2-4] *Calendula officinalis* has a long history of usage by the folk systems because of its rich medicinal values that have been reported to possess potent anti-inflammatory, antitumour, antioxidant, antibacterial, anti-HIV, anti-ulcer, antigenotoxic, chemoprotective and antiseptic properties. [5-7] Moreover, a large number of phytochemicals have been found in various parts of the plants that include calenduline and oleanolic acid glycosides, sterol glycosides, alpha-and beta-amyrin, taraxasterol, lupeol,brein, faradiol, arnidiol, erythrodiol, calenduladiol, coflodiol and manilladiol. [8-10]

The present review article discusses about the various phytochemicals present in the plant. Moreover, various pharmacological properties exhibited by the plant have been demarcated.

Taxonomic description

The plant is classified as shown in Table 1.

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Phytochemistry

A number of phytochemical studies have well reported about the presence of several classes of chemical compounds, the main ones being terpenoids, flavonoids, coumarines, quinones, volatile oil, carotenoids and amino acids in the plant.

Terpenoids

Various terpenoids (Table 2) have been reported from the petroleum ether extract of *C.officinalis* flowers. They include sitosterols, stigmasterols[12], diesters of diols[13], 3- monoesters of taraxasterol, ψ-taraxasterol, lupeol[14,15], erythrodiol, brein[16,17], ursadiol[18], faradiol-3-O-palmitate, faradiol- 3-O-myristate, faradiol-3-O-laurate[19], arnidiol-3-O-palmitate, arnidiol-3-O-myristate, arnidiol-3-O-laurate, calenduladiol-3-Opalmitate, calenduladiol-3-O-myristate[20,21] oleanolic acid saponins: calenduloside A-H[22-23], oleanane triterpene glycoside: calendulaglycoside A, calendulaglycoside A6-O-n-methyl ester, calendulaglycoside A6'-O-n-butyl ester, calendulaglycoside B, calendulaglycoside B 6-O-n-butyl ester, calendulaglycoside C, calendulaglycoside C 6-O-n-methyl ester, calendulaglycoside C 6- O-n-butyl ester, calenduloside F6_-O-n-butyl ester, calnduloside G6-O-n-methyl ester, glucosides of oleanolic acid (mainly found in roots of grown and senescing plants) I, II, III, VI, VII [24,25], and glucuronides (mainly found in flowers and green parts) F, D, D2, C, B and A[26]. One new triterpenic ester of olanane series has been isolated from flowers was cornulacic acid acetate from flowers [27].

Table 1: Taxonomic classification of *Calendula officinalis* [11]

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

Figure 1: The leaf, stem and flower of *C. officinalis*

Leaves with stem

Flower

Flavonoids

Various flavonoids (Table 3) have been isolated from the ethanol extract of the inflorescence of C. officinalis. They include quercetin, isorhamnetin[29], isoquercetin, isorhamnetin-3-O–D-glycoside, narcissin, calendoflaside [30], calendoflavoside, calendoflavobioside, rutin, isoquercitrin neohesperidoside, isorhamnetin-3-Oneohesperidoside, isorhamnetin-3-O-2G- rhamnosyl rutinoside, isorhamnetin-3-Orutinoside, quercetin-3-O-glucoside and quercetin-3-O-rutinoside[21].

Coumarins

The ethanol extract of the inflorescence of the *C. officinalis* reported to contain coumarins - scopoletin, umbelliferone and esculetin [31].

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Quinones

Quinones reported from *C. officinalis* were plastoquinone, phylloquinone, _-tocopherol in the chloroplast, ubiquinone, phylloquinone, _ tocopherol in mitochondria, and phylloquinone in the leaves [32].

Volatile oil

C. officinalis flowers contain maximum volatile oil at full flowering stage (0.97 %) and minimum during the preflowering stage (0.13 %) [33]. The composition also showed different patterns at different phases of vegetative cycles. Various monoterpenes and sesquiterpenes have been reported in the volatile oil : α-thujene, α -pienene, sabinene, β-pienene, limonene, 1,8-cineol, p-cymene, trans- β -ocimene, ϒ-terpenene, δ-3-carene, nonanal, terpene-4-ol, 3-cylohexene-1-ol, α- phellandrene, α -terpeneol, geraniol, carvacrol, bornyl acetate, sabinyl acetate, α - cubebene, α -copaene, α-bourbonene, cubebene, α-gurjunene, aromadendrene, β -caryophyllene, α-ylangene, α-humulene, epibicyclo-sequiphellandrene, germacrene D, alloaromadendrene, β -saliene, calarene, muurolene, δ -cadinene, cadina 1,4-diene, α-cadinene, nerolidol, palustron, endobourbonene, oplopenone, α-cadinol, Tmuurolol. The essential oil was found to be rich in α -cadinene, α -cadinol, t-muurolol, limonene, and 1,8-cineol with p-cymene at lower levels at the post-flowering periods[33].

Table 2 and 3 : Shows the structure and activity of some terpenoids andflavonoids present in this plant[28].

Table 2: Structures and activities of some terpenoids

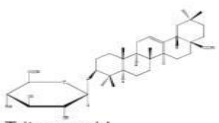
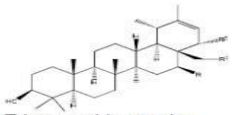
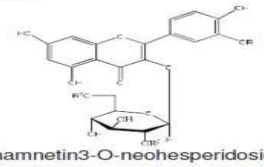
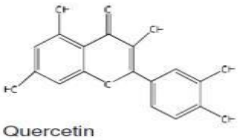
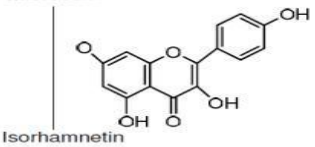
Structure		Activity
 Triterpenoid	Calendulaglycoside A: R^1=Glc, R^2=Gal, R^3=H, R^4=Glc; Calendulaglycoside A6'-O-methyl ester: R^1=Glc, R^2=Gal, R^3=Me, R^4=Glc; Calendulaglycoside A6'-O-n-butyl ester: R^1=Glc, R^2= Gal, R^3=n-Bu, R^4=Glc; Calendulaglycoside B: R^1=Glc, R^2=Gal, R^3= H, R^4= H; Calendulaglycoside B6'-O-n-butyl ester: R^1=Glc, R^2=Gal, R^3=n-Bu, R^4=H; Calendulaglycoside C: R^1=H, R^2=Gal, R^3=H, R^4=Glc; Calendulaglycoside C6'-O-methyl ester: R^1= H, R^2=Gal, R^3=Me, R^4=Glc; Calendulaglycoside C6'-O-n-butyl ester: R^1=H, R^2=Gal, R^3=n-Bu, R^4=Glc; Calendulaglycoside F6'-O-n-butyl ester: R^1=H, R^2=Gal, R^3=Me, R^4=H	Responsible for antitumor, anti-inflammatory and antioedematous activities.
 Triterpenoid saponin	Faradiol: R^1=OH, R^2=R^3=H ψ-Taraxasterol: R^1=R^2=R^3=H	Responsible for anti-inflammatory and antioedematous activities.

Table 3: Structures and activities of some flavonoids

Structure		Activity
 Isorhamnetin3-O-neohesperidoside	R^1=Me, R^2=Rha, R^3=H; Isorhamnetin3-O-2^G-rhamnosylrutinoside: R^1=Me, R^2=Rha, R^3=Rha; Isorhamnetin3-O-rutinoside: R^1=Me, R^2=H, R^3=Rha; Quercetin-3-O-glucoside: R^1= H, R^2=H, R^3=H; Quercetin-3-O-rutinoside: R^1=H, R^2=H, R^3=Rha	Responsible for antioxidant and wound healing activities
 Quercetin		Responsible for antioxidant activities
 Isorhamnetin		Responsible for antioxidant activities

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Carotenoids

The methanol extract of leaves, petals and pollens of *C. officinalis* flowers showed a number of carotenoids. The carotenoids found in the pollens and petals were neoxanthin, 9Z-neoxanthin, violaxanthin, luteoxanthin, auroxanthin, 9Z-violaxanthin, flavoxanthin, mutatoxanthin, 9Zanthroxanthin, lutein, 9/9'A-lutein, 13/13'Zlutein, α -cryptoxanthin,β-cryptoxanthin, z-cryptoxanthin, lycopene, α -carotene, and β- carotene. Total carotenoids (mg/g dry weight) was 7.71 % for petals and1.61 % for pollens.

Reported carotenoid compositions of the leaves and stems reported were neoxanthin, 9Z-neoxanthin, violaxanthin, luteoxanthin, 9Zviolaxanthin, 13Z-violaxanthin, antheraxanthin, mutatoxanthin epimer 1, mutatoxanthin epimer 2, lutein, 9/9' 2-lutein,α-cryptoxanthin, β-cryptoxanthin, β-carotene. Total carotenoids (mg/g dry weight) for the leaves is 0.85 % and for stems 0.18 % [34,35]. Glycosides of quercetin and isorhamnetin were the predominant components of the flavonoids, while betacarotene and lutein were the most abundant carotenoids. [36]

In another study the authors evaluated the analysis of carotenoid composition in petals of *Calendula officinalis* . Nineteen carotenoids were identified in extracts of petals of orangeand yellow-flowered cultivars of calendula. In addition, ten carotenoids were unique to orange-flowered cultivars. The ultraviolet (UV) visible absorption maxima of these ten carotenoids were at longer wavelengths than that of flavoxanthin, the main carotenoid of calendula petals providing the evidevce that these carotenoids are responsible for the orange color of the petals. Six carotenoids had a cis structure at C-5 (C-5') and it is conceivable that these (5Z)- carotenoids are enzymatically isomerised at C-5 in a pathway that diverges from the main carotenoid biosynthesis pathway.

Among them, (5Z, 9Z)-lycopene, (5Z, 9Z, 5'Z, 9'Z)- lycopene, (5'Z)-gamma-carotene, (5'Z, 9'Z)-rubixanthin and (5Z, 9Z, 5'Z)-lycopene have been identified. [37].

According to the Reseach work on specificity of the tonoplast transport of oleanolic acid monoglycosides in the vacuoles from *Calendula officinalis* leaves, the proper structure of both parts of oleanolic acid monoglycoside, i.e. aglycon and the sugar moiety, are required for binding to a specific tonoplast carrier. [38] These two glycosides were isolated from leaf protoplasts of the plant with the use of chemically synthesized analogues.

In another study the authors investigated the structures of new ionone and sesquiterpene glycosides from Egyptian *Calendula officinalis* . Two new ionone glucosides (officinosides A and B) and two sesquiterpene oligoglycosides (officinosides C and D) were isolated from the flowers of Egyptian *Calendula officinalis* , the structures of which were elucidated on the basis of chemical and physicochemical evidences. [39]

Amino acids

The ethanol extract of the flowers of the plant is reported to show the presence of 15 amino acids in free form: alanine, arginine, aspartic acid, aspargine, valine, histidine, glutamic acid, leucine, lysine, proline, serine, tyrosine, threonine, methionine and phenylalanine.

Amino acid content of the leaves is about 5 %, stems 3.5 % and flowers 4.5 % [40].

Carbohydrates

The ethanol extract of the inflorescence of plant showed the presence of polysaccharides, PS-I,-II, and -III having a (1_3)-_-D-galactam backbone with short side chains at C-6 comprising _-araban-(1_3)-araban and alpha-L-rhamnan-(1_3)- araban along with monosaccharides [41,42].

Lipids

The lipids in the petroleum ether extract of the seeds, leaves and flowers of *C. officinalis* have been analyzed. The amount of neutral lipids in the seeds was 15.7 %, phospholipids 0.6 % and glycolipids 0.9 %. Fatty acids of monols, sterol esters, 3-monoesters, 3-monoester diols reported in flowers were lauric, myristic, palmitic, stearic, oleic, linoleic and linolenic acid. The fatty acids of marigold seeds contain about 59% of an 18:3 conjugated trienic (trans-8,trans-10, cis-12) acid and

about 5% of 9-hydroxy-18:2 (trans-9,cis-11) acid - dimorphecolic acid [43,44] one oxygenated fatty acid also reported from the seed oil of *C. officinalis* was D-(+)-9-hydroxy-10,12-octadecadienoic acid [45].

Other constituents

Other phtytochemicals include the bitter constituent, loliolide (calendin) [46], calendulin [47] and n-paraffins [48].

Pharmacological properties

C.officinalis has a broad range of biological effects, some of which are very useful for possible future development.

Anti-inflammatory and antioedematous activities

Ethyl acetate soluble fraction of the methanol extract of *C. officinalis* flowers exhibited themost potent inhibition (84 %) of 12-otetradecanoyl phorbol-13-acetate (TPA)- induced inflammation (1 µg/ear) in mice with an ID50 value of 0.05 - 0.20 mg/ear compared with indomethacin as reference drug. Furthermore, activity-guided isolation showed that its activity was mainly due to oleananetype triterpene glycoside[18]. A dose of 1200 µg/ear of an aqueous-ethanol extract showed 20 % inhibition in croton oil-induced mouse edema. The activity was attributed to the presence of triterpenoids, the three most active compounds of which were the esters of faradiol-3-myristic acid, faradiol-3-palmitic acid and 4-taraxasterol [49,50].

Dichloromethane extract of the plant's flower heads inhibited croton oil-induced oedema, and further isolation showed that the esters of faradiol-myristic acid, faradiol-palmitic acid and _-taraxasterol had antioedematous activity with an oedema inhibition of nearly 50 % at a dose of 240 µg/cm2. Furthermore, when the doses of these two faradiol esters were doubled, oedema inhibition increased to 65 and 66 %, respectively, without any synergism between them [51]. A cream containing calendula extract has been reported to be effective in dextran and burn oedemas as well as in acute lymphoedema in rats. Activity against lymphoedema was primarily attributed to enhancement of macrophage proteolytic activity [52].

Anti-HIV activity

In another study the authors evaluated Anti-HIV activity of extracts from *Calendula officinalis* flowers which were examined for their ability to inhibit the human immunodeficiency virus type 1 (HIV-1) replication. Both organic and aqueous extracts were relatively nontoxic to human lymphocytic Molt-4 cells, but only the organic one exhibited potent anti-HIV activity in an in vitro MTT/tetrazolium-based assay.

Calendula officinalis flowers caused a significant dose-and time-dependent reduction of HIV-1 reverse transcription (RT) activity. An 85% RT inhibition was achieved after a 30 min treatment of partially purified enzyme in a cell-free system. These results suggested that organic extract of flowers from *Calendula officinalis* possesses anti-HIV properties of therapeutic interest. [53]

Antibacterial and antifungal activities

The methanol extract and 10 % decoction of the plant's flowers were assessed for their activity against anaerobic and facultative aerobic periodontal bacteria, namely, *Porphyromonos gingivalis*, *Prevotella* spp., *Furobacterium nucleatum, Caphocytophaga gingivalis, Veilonella parvula, Eikenella corrodens, Peptostreptococcus micros* and *Actinomyces odontolyticus*. The results showed marked inhibition against all tested microorganisms with MIC _2048 mg/L [54].

When the essential oil of the flowers was tested (using disc diffusion technique) against various fungal strains, namely, *Candida albicans(ATCC64548), Candida dubliniensis (ATCC777), Candida parapsilosis (ATCC22019), Candida glabrata(ATCC90030), Candida krusei (ATCC6258),* and yeast isolated from humans, viz, *Candida albicans, Candida dubliniensis, Candida parapsilosis, Candida glabrata, Candida tropicalis, Candida guilliermondii, Candida krusei* and *Rhodotorella* spp., it showed good potential antifungal activity (at 15 µl/disc) [55].

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Anticancer and lymphocyte activation dual activities

The ethyal acetate soluble fraction of the methanol extract of *C. officinalis* flowers has shown cytotoxic activity in *vitro* [21]. Further activity-guided isolation of that fraction showed that the active compounds were: calenduloside F6'-O-n-butyl ester, which is active against leukaemia (MOLT-4 and RPMI 8226), colon cancer (HCC-2998) and melanoma (LOXIMVI, SK-MEL-5 and UACC- 62)] cell lines with GI50 values of 0.77-0.99 µmole, except for leukaemia (CCRF-CEM, GI50 = 23.1 µmole), renal cancer (AK-1, 17.2 µmole; UO-31, 12.7 µmole) and breast cancer (NCI/ADR-RES, >50 µmole)] cell lines; and calenduloside G6'-O-methyl ester, which is active against all the cancer cell lines mentioned above with GI50 20 µmole except for ovarian cancer (IGROVI, GI50 = 20.1 µmole) and renal cancer (VO-31, 33.3 µmole) cell lines[18]. Aqueous laser-activated calendula flower extract (LACE) showed potent in vitro inhibition of tumour cell proliferation when assayed against a wide variety of human and murine tumour cell lines. The inhibition ranged from 70 – 100 % with an IC50 concentration of 60 µg/mL. The mechanisms of the inhibition were identified as cell cycle arrest in G0/G1 phase and caspase-3 induced apoptosis. On the other hand, when LACE was assayed against human peripheral blood lymphocyte (PBLs) and human natural killer cell lines (NKL) it showed in vitro induction of proliferation and activation of these cells, mainly Blymphocytes, CD4+, T lymphocytes and NKT lymphocyte[56]. Various extracts of the leaf, flower and whole plant have also been found to be cytotoxic to MRC5, HeP2, ascetic cells from Ehrlich carcinoma. The saponin rich fraction of these extracts displayed antitumoural activity in vivo in the Ehrlich mouse carcinoma model [57].

In another study the authors evaluated the cytotoxic anti-tumor activity and lymphocyte activation of the whole plant extract of *Calendula officinalis* . The in vitro cytotoxic anti-tumor and immunomodulatory activities and in vivo anti-tumor effect of Laser Activated Calendula Extract (LACE) were evaluated.

Effect of LACE on human peripheral blood lymphocyte (PBL) proliferation in vitro was also analyzed. Studies of cell cycle and apoptosis were performed in LACE-treated cells.

In vivo anti-tumor activity was evaluated in nude mice bearing subcutaneously human Ando-2 melanoma cells. The results indicated that LACE aqueous extract showed cytotoxic tumor cell activity and lymphocyte activation activities of the extract. Moreover, the LACE extract presented in vivo anti-tumoral activity in nude mice against tumor growth of Ando-2 melanoma cells that further confirmed its dual effect. [58]

Hepatoprotective activity

The hydroalcohol extract of the flowers, when given to CCl4-intoxicated liver in albino male Wistar rats at a dose of 10 mL/kg, resulted in a reduction of hepatocytolysis by 28.5 % due to reduction in glutamo-oxalate-transaminase (GOT) and glutamo-pyruvate-transaminase (GPT). However, histoenzymology showed reduction of steatosis of lactate dehydrogenase (LDH), succinate dehydrogenase (SDH), cytochromoxidase (Cyox) and Mg2+-dependant adenosine triphosphatase (ATPase) [52]. The hot water extract of C. officinalis flowers exhibited antihepatoma activity against five human liver cancer cells - HepG2/C3A, SK-HEP-1, HA22T/VGH, Hep3B and PLC/PRF/5 - with an inhibitory effect of 25 – 26 % at a dose of 2000 µg/mL [59].

Immunostimulant activity

The polysaccharide fraction of C. officinalis extract showed immunostimulant activity, based on in vitro granulocyte test.

Polysaccharide III showed the highest phagocytosis (54 – 100 %) at a concentration of 10-5 - 10-6 mg/mL, while PS-I and PS-II exhibited 40 – 57 and 20 – 30 % phagocytosis, respectively [41,42].

Antioxidant activity

A 70 % methanol extract of the plant was successively extracted with ether, chloroform,ethyl acetate and n-butanol leaving a residual aqueous extract which was assayed for antioxidant activity by liposomal lipid peroxidation-induced Fe2+ and ascorbic acid.

The ether, butanol and water extracts, containing flavonoids, showed antioxidant activity [60]. Propylene glycol extracts of the petals and flower heads, assayed for antioxidant activity by lipid peroxidation, indicate that the extract of the petals was more potent than the flower head extract, based on analysis of plasma and urine malondialdehyde (MDA) and urine isoprostane invent rations (ipf2α-VI) [61].

The author investigated antioxidative responses of *Calendula officinalis* under salinity conditions. A decrease in total glutathione and an increase in total ascorbate (AsA+DHA), accompanied with enhanced glutathione reductase (GR, EC 1.6.4.2) and ascorbate peroxidase (APX, EC 1.11.1.11) activities, were observed in leaves extract. In addition, salinity induced a decrease in superoxide dismutase (SOD, EC 1.15.1.1) and peroxidase (POX, EC 1.11.1.7) activities. The decrease in dehydroascorbate reductase (DHAR, EC 1.8.5.1) and monodehydroascorbate reductase (MDHAR, EC 1.6.5.4) activities further suggested the antioxidant potential of the plant. [62]

Wound healing activity

The ethanol extract of the plant's flowers was investigated against experimentally induced thermal burns in rats. Among the various extract doses (20, 100, and 200 mg/kg of body weight), the 200 mg/kg dose showed significant improvement in healing of wounds as indicated by increase in collagenhydroxyproline and hexosamine contents.

The level of acute phase proteins (heptaglobin, orosomycid and tissue damage marker enzymes - alkaline phosphatase), alanine and aspartate transaminase decreased significantly. The decrease in lipid peroxidation might be due to its antioxidant property [63].

Authors carried out genotoxicity studies of an extract of *Calendula officinalis* that displayed genotoxic properties when assayed for mitotic segregation in the heterozygous diploid D-30 of *Aspergillus nidulans*. The extract of Calendula exhibited dose-dependent toxicity ndgenotoxicity (both mitotic crossing-over and chromosome malsegregation being observed) to Aspergillus in the range of five plate concentrations from 0.1 to mg of solids/ml assayed providing the evidence of genotoxicity. [64] Authors evaluated the activity of cytoplasmic proteinases from rat liver in Heren's carcinoma during tumor growth and treatment with medicinal herbs. It was determined that during tumor development, the enzymatic activity level of both the acid and neutral proteinases increased by two to six folds. The natural preparation of the herbs *Calendula officinalis* investigated enzymes and coefficients of the liver weights of the sick animals. The chemical medicinal preparation 5, 6-benzcumarine-5-uracil normalized the activity of the neutral cytoplasmatic proteinases and reduced the level of the proteolytic activity of the acid enzymes in comparison with the control group of the animals as well as increased the liver weight coefficients.[65]

Another study carried out the treatment of chronic catarrhal gingivitis with polysorb immobilized calendula. The use of traditional and modern methods of periodontal diseases treatment in clinics showed that the highest effect of calendula immobilized on the polysorb in the nearest period after its treatment. [66]

The extract of *Calendula officinalis* against lipid peroxidation of rat liver microsomes by acting as a potent free radical scavenger and an antioxidant property were evaluated. The results obtained from the study suggested that the butanolic fraction of *Calendula officinalis* possessed a significant free radical scavenging and antioxidant activity and that the proposed therapeutic efficacy of this plant could be due, in part, to these properties. [67]

Toxicological Study

The hydroalcohol extract of *C. officinalis* flowers,, based on assessment in rats and mice, did not show acute toxicity following administration of an oral dose of up to 5.0 g/kg. It didn't show haematological alterations at doses of 0.025, 0.25, 0.5 and 1.0 g/kg.

However, the biochemical parameters, blood urea nitrogen (BUN) and alanine transaminase (ALT), were elevated due to renal and liver overload [68].

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Contraindication

The extract was found to cause allergy in 9 patients out of 443 (2.03 %) when assessed by patch testing method[69]. Therefore, it is advisable that the persons who have an established allergy to the Asteraceae (daisy) family should use it with caution [70,71].

CONCLUSION

In this review, we have explored the phytochemistry and pharmacological activities of *Calendula officinalis* Linn in order to collate existing information on this plant and also its various pharmacological properties as a medicinal plant.In the future the scientific research on *Calendula officinalis* Linnwill be increased to produce more active principles to cure harmful diseases.

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