International Journal of Biomedical and Advance Research
ISSN: 2229-3809 (Online); 2455-0558 (Print)
Journal DOI: https://doi.org/10.7439/ijbar
CODEN: IJBABN **Review Article**

Phytochemicals and biological potentials of *Calendula officinalis* Linn: a review

Khaled Rashed*

Department of Pharmacognosy, National Research Centre, 33 El-Bohouth st.-Dokki, Giza, P.O.12622, Egypt

Abstract

Calendula officinalis is from the family of Asteraceae, commonly known as English Marigold or Pot Marigold is an aromatic herb which is used in Traditional system of medicine for treating wounds, ulcers, herpes, scars, skin damage, frost-bite and blood purification. It is mainly used because of its various biological activities to treat diseases as analgesic, anti–diabetic, anti-ulcer and anti-inflammatory. It is also used for gastro-intestinal diseases, gynecological problems, eye diseases, skin injuries and some cases of burn. Calendula oil is still medicinally used as, an anti-tumor agent, and a remedy for healing wounds. Plant pharmacological studies have suggested that Calendula extracts have antiviral and anti-genotoxic properties. Chemical studies have underlined the presence of various classes of compounds, the main being triterpenoids, flavonoids, coumarines, quinones, volatile oil, carotenoids and amino acids. The extract of this plant as well as pure compounds isolated from it, have been demonstrated to possess multiple pharmacological activities such as anti-HIV, cytotoxic, anti-inflammatory, hepatoprotective, spasmolytic and spasmogenic, amongst others.

Keywords: *Calendula officinalis,* chemical compounds, bioactivities.

***Correspondence Info:**
Dr. Khaled Rashed
Department of Pharmacognosy,
National Research Centre,
33 El-Bohouth st.-Dokki, Giza, P.O.12622, Egypt

***Article History:**
Received: 03/06/2022
Revised: 28/07/2022
Accepted: 12/08/2022
DOI: https://doi.org/10.7439/ijbar.v13i8.5703

QR Code

How to cite: Rashed K. Phytochemicals and biological potentials of *Calendula officinalis* Linn: a review. *International Journal of Biomedical and Advance Research* 2022; 13(08): e5703. Doi: 10.7439/ijbar.v13i8.5703 Available from: https://ssjournals.com/index.php/ijbar/article/view/5703

1. Introduction

Plants are a valuable source of a wide range of secondary metabolites, which are used as pharmaceuticals, agrochemicals, flavors, fragrances, colors, pesticides and food additives [1]. *Calendula officinalis* Linn. is used medicinally in Europe, China, US and India. It belongs to the family, Asteraceae, and is commonly known as Zergul (Hindi), African marigold, Calendula, Common Marigold, Garden Marigold, Marigold, Pot Marigold (English), Butterblume (German), Chin Chan Ts'ao (Chinese), Galbinele (Romanian) and Ringblomma (Swedish) [2,3]. *Calendula officinalis* contained a wide range of chemical constituents including saponins, tritrpenes, triterpendiol esters, flavonoids, steroids, tannin, quinines, coumarins, carotenoids, amino acids, polysaccharides, essential and volatile oils and many other chemical groups. *Calendula officinalis* has many therapeutic effects including antibacterial, antifungal, anthelmintic, antiviral, cytotoxic, antioxidant, anti-inflammatory, analgesic, hepatoprotective, cardioprotective, gastroprotective, wound healing and many other effects. The flowers and the leaves are the chief parts which used medicinally. The essential oil from flowers was also used medicinally [4]. The present review was designed to highlight the chemical constituents and the pharmacological effects of *Calendula officinalis* plant.

2. Chemical compounds

The plant had saponins, triterpendiol esters and flavonoids. The orange flower contained high caroteniodes [5-8]. The phytochemical screening of petroleum ether, chloroform, methanol and water extracts of *Calendula officinalis* leaf showed that petroleum ether extracts contained fatty acids, chloroform extracts contained triterpens and sterols. Flavonoids, carbohydrates, amino acids and saponins were present in methanol extract, while, saponins, phenolic substances and tannins were present in the water extract of *Calendula officinalis* [9,10]. However,

in another study, petroleum ether extract showed the presence of carotenoids, steroids, saponins and tannin. Chloroform extract showed the presence of steroids, triterpens and tannin. Ethanolic extract showed the presence of alkaloids, flavonoids, and saponins. Aqueous extract showed the presence of flavonoids and saponins. Quinones were isolated from different parts of *C. officinalis*. They were included plastoquinone, phylloquinone, α-tocopherol and ubiquinone [11].

Coumarins included scopoletin, umbelliferone and esculetin were isolated from the ethanol extract of the inflorescence of the *C. officinalis*. Many terpenoids were isolated from the petroleum ether extract of *C. officinalis* flowers, including calenduladiol-3-O-palmitate, calenduladiol-3-O-myristate, oleanolic acid saponins: calenduloside AH, 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, 3- monoesters of taraxasterol, Ψ-taraxasterol, lupeol, erythrodiol, brein, ursadiol, faradiol-3-O-palmitate, faradiol- 3-O-myristate, faradiol-3-O-laurate,arnidiol-3-O-palmitate, arnidiol-3-O-myristate, arnidiol-3-O-laurate, glucosides of oleanolic acid I, II, III, VI, VII , glucuronides F, D, D2, C, B and A. and ester of olanane [12, 13].

The amino acids in the leaves were about 5 %, in the stems 3.5 % and in the flowers 4.5 %. Fifteen amino acids were isolated from the ethanol extract of the flowers included alanine, arginine, aspartic acid, aspargine, valine, histidine, glutamic acid, leucine, lysine, proline, serine, tyrosine, threonine, methionine and phenylalanine [14].

Babaee *et al* found that the total antioxidant, polyphenol and flavonoid and quercetin concentration of the 2% flowers extract were 2353.4±56.5 µM, 313.40±6.52 mg/g, 76.66±23.24 mg/g, and 19.41±4.34 mg/g, respectively. However, Fonseca *et al* found that the total polyphenols, total flavonoids, rutin and narcissin contents of *Calendula officinalis* were 28.6 mg/g, 18.8 mg/g, 1.6 mg/g and 12.2mg/g, respectively. On the other hand, more flavonoids were isolated from *Calendula officinalis* included quercetin, isorhamnetin, isoquercetin, isorhamnetin-3-O-β-D-glycoside, rutin, isoquercitrin, neohesperidoside, isorhamnetin-3-O-neohesperidoside, isorhamnetin-3-O-2-rhamnosyl rutinoside, isorhamnetin-3-O-rutinoside, quercetin-3-O-glucoside, quercetin-3-O-rutinoside, narcissin, calendoflaside, calendoflavoside and calendoflavobioside. Water-soluble polysaccharides reached (15%) included rhamnoarabinogalactans and arabinogalactans [15, 16].

Calendula officinalis L. accumulated large amounts of carotenoids in its inflorescences. The yellow-to-orange color of inflorescences is mostly due to carotenoids. The carotenoid content and profile was investigated in four selected varieties of Calendula: Double Esterel Orange, Radio Extra Selected, Bonbon Abricot and Double Esterel Jaune. The carotenoid content was higher in orange varieties: 276 mg/100 g fresh flowers for Double Esterel Orange and 111 mg/100 g fresh flowers for Radio variety. All varieties contain the same pigments but there were significant differences for the ratio between individual pigments. Orange varieties contain higher amounts of hydrocarbons: 44.5% of total carotenoid as in Double Esterel Orange; while yellow varieties contain mostly oxygenated derivatives: 97% of total carotenoids as in Double Esterel Jaune. The main pigments identified were: flavoxanthin, lutein, rubixanthin, β-carotene, γ-carotene and lycopene [17,18]. The total oils extracted from the dried flowers of *Calendula officinalis* ranged from 0.1 to 0.3% [19,20].

The essential oil compounds isolated from *Calendula officinalis* flower were included: α-copaene, α -ionone, α-humulene, geranylacetone, α-muurolene, β-ionone, ledene, α -muurolene, α -cadinene, α-cadinene, α -cadinene, α -calacorene, caryophyllene oxide, copaen-4-α-ol, β-oplopenone, viridiflorol, ledol, 1,10-di-epi-cubenol, 1-epi-cubenol, epi-α-muurolol, α -cadinol and cadalene. The volatile fraction obtained from *Calendula officinalis* flowers were included α-cubebene, α-copaene, β-cubebene, α-gurjunene, β-cariophyllene, α-ionone, α-humulene, γ-muurolene, β-ionone, α-muuronele, γ-cadinene, δ-cadinene and α-cadinene [21].

However, the lipid content of seeds varied between 13.6 and 21.7 g oil/100 g seeds. The calendic and linoleic acids were the two dominant fatty acids in the total lipids (51.4 to 57.6% and 28.5 to 31.9% respectively). Polar lipids were also characterized by higher unsaturation ratios (with the PUFAs content between 60.4 and 66.4%), while saturates (consisted mainly of palmitic and very long-chain saturated fatty acids) [22].

3. Bioactivities

3.1 Anti-inflammatory and antioedematous potentials

Ethyl acetate soluble fraction of the methanol extract of *C. officinalis* flowers exhibited the most potent inhibition (84 %) of 12-o-tetradecanoyl phorbol-13-acetate (TPA)-induced inflammation (1 µg/ear) in mice with an ID_{50} 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 oleanane-type triterpene glycoside. A dose of 1200 µg/ear of an aqueous-ethanol extract showed 20 % inhibition in croton oil-induced mouse oedema. 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 [23, 24].

3.2 Antibacterial and antifungal potentials

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 [25]. 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) [26].

3.3 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*. 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, GI_{50} = 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 $GI_{50}\leq$ 20 µmole except for ovarian cancer (IGROVI, GI_{50} = 20.1 µmole) and renal cancer (VO-31, 33.3 µmole) cell lines. 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 IC_{50} 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 B-lymphocytes, CD^{4+}, T lymphocytes and NKT lymphocyte [27]. 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 [28].

3.4 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 Fe^{2+} and ascorbic acid. The ether, butanol and water extracts, containing flavonoids, showed antioxidant activity [29]. 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 inventrations [30].

3.5 Insecticidal activity

The acetone: methanol (2:1 v/v) extract of the flowers showed insecticidal activity when it was tested on milk weed bug [31].

3.6 Inhibition of heart rate

The aqueous extract was tested on the heart of male Wistar rats and found to inhibit heart rate contractility by up to 100 % at a dose of 0.3mg/L [32].

3.7 Antiviral activity

A tincture of the flowers suppressed the replication of herpes simplex, influenza A2 and influenza APR-8 viruses *in vitro* [33].

4. Conclusion

This review had phytochemistry and pharmacology of *C. officinalis* Linn. (Asteraceae), a medicinal plant found in central and southern Europe, western Asia and the United States, amongst others. A variety of phytochemicals such as terpenoids, flavonoids, coumarins, quinones, volatile oil, carotenoids and others have been reported to be present in this plant. It exhibits several pharmacological activities such anti-HIV, anti-cancer (dual activity), anti-inflammatory, hepatoprotective, spasmolytic and spasmogenic.

References

[1]. Al-Snafi AE. Central nervous and endocrine effects of *Myristica fragrans*. 4th Arabic Conf. of Medicinal plants, Thamar Univ. Yemen, 1999, 111-121.

[2]. Lt. Colonel Kirtikar KR, Major Basu BD. Indian Medicinal Plants. Vol II, Deharadun, India, International Book Distributor, 1993, pp 1413-1414.

[3]. The Wealth of India, Raw Materials, A Dictionary of Indian Raw Material & Industrial Products. Vol 3, New Delhi, Publications & Information Directorate CSIR, 1992, pp 55-58.

[4]. Priyanka M, Patidar A, Gupta D, Agrawal S. Treatment of acne with herbal remedie- *Calendula officinalis*: An overview. *International Journal of Pharmaceutical & Biological Archives*, 2011; 2(4): 1020-1023.

[5]. Kumar N, Sharma J, Sharma S. Pharmacognostical and phytochemical investigation of *Calendula officinalis*. *Journal of Advanced Scientific Research*, 1(1); 2010: 61-66.

[6]. Roopashree TS, Raman D, Shobha RRH, Narendra R. Antibacterial activity of antipsoriatic herbs: Cassia tora, *Momordica charantia* and *Calendula officinalis*. *International J of App lied Research in Natural Products*, 2008; 1(3): 20-28.

[7]. Neukirch HD, Ambrosio M, Dalla Via J, Guerriero A. Simultaneous quantitative determination of eight triterpenoid monoesters from flowers of 10 varieties of *Calendula officinalis* and characterization of new triterpenoid monoesters. *Phytochem Anal*, 2004; 15(1): 30-35.

[8]. WHO Monographs of selected medicinal plants. 2, 2004, 35.

[9]. Sindhu CG. Phytochemical screening of *Calendula officinalis* Linn leaf extract by TLC. *IJRAP*, 2010; 1 (1): 131-134.

[10]. Khare CP. Indian medicinal plants – An illustrated dictionary. Springer Science and Business Media, 2007: 111-112.

[11]. Janiszowska W, Michalski W, Kasprzyk Z. Polyprenyl quinones and α -tocopherol in *Calendula officinalis*. *Phytochemistry*, 1976; 15: 125-127.

[12]. Wilkomirski B, Kasprzyk Z. Free and ester-bound triterpene alcohols and sterols in cellular subfractions of *Calendula officinalis*. *Phytochemistry*, 1979; 18: 253-255.

[13]. Naved T, Ansari SH, Mukhtar HM, Ali M. New triterpenic esters of oleanene-series from the flowers of *Calendula officinalis* Linn. *Org Chem Incl Med Chem*, 44, 2005, 1088-1091.

[14]. Abajova RL, Aslanov SM, Mamedova ME. Amino acids of *Calendula officinalis*. Chemistry of Natural Compounds, 1994; 30(15): 641-641.

[15]. Varlijen J. Structural analysis of rhamnoarabinogalactans and arabinogalactans with immunostimulating activity from *Calendula officinalis*. *Phytochemistry*, 1989: 28: 2379-2383.

[16]. Matysik G, Wojciak KM, Paduch R. The influence of *Calendula officinalis* flos extracts on cell cultures, and the chromatographic analysis of extracts. *J Pharm Biomed Anal*, 2005; 38: 285-292.

[17]. Wagner H, Proksch A, Riess MI, Vollmar AS. Odenthal, Stuppner H, Jurcic K, Le Turdu M and Fang Jn.. Immunstimulierend wirkende Polysaccharide (Heteroglykane) aus höheren Pflanzen. *Arzneimittel-Forschung*, 1985;7:1069-1075.

[18]. Pintea A, Bele C, Andrei S, Socaciu C. HPLC analysis of carotenoids in four varieties of *Calendula officinalis* L. flowers. *Acta Biologica Szegediensis*, 2003; 47(1-4): 37-40.

[19]. Bunghez IR, Ion RM. Complex spectral characterization of active principles from marigold (*Calendula officinalis*). *Journal of Science and Arts*, 2011; 1(14): 59-64.

[20]. Chalchat JC, Garry RPH, Michet A. Chemical composition of essential oil of *Calendula officinalis* L. (Pot Marigold). *Flavour Fragr J*, 1991; 6: 189-192.

[21]. Gazim ZC, Rezende CM, Fraga SR, Filho PB, Nakamura CV, Cortez DA. Analysis of the essential oils from *Calendula officinalis* growing in Brazil using three different extraction procedures. Brazilian Journal of Pharmaceutical Sciences, 2008; 44(3): 391-395.

[22]. Dulf FV, Pamfil D, Baciu AD, Pintea A. Fatty acid composition of lipids in pot marigold (*Calendula officinalis* L.) seed genotypes. *Chem Cent J* 2013; 7(1):7-8.

[23]. Della LR. Topical anti-inflammatory activity of *Calendula officinalis* extracts. *Planta Med*, 1990; 56: 658-658.

[24]. Della LR, Della LR, Tubaro A, Sosa S, Becker H, Saar S, Isaac O. The role of triterpenoids in topical anti-inflammatory activity of *Calendula officinalis* flowers. *Planta Med*, 1994; 60: 516-520.

[25]. Iauk L, Lo-Bue AM, Milazzo I, Rapisarda A, Blandino G. Antibacterial Activity of Medicinal Plant Extracts Against Periodontopathic Bacteria. *Phytother Res*, 2003; 17: 599-604.

[26]. Gazim ZC, Rezende CM, Fraga SR, Svidzinski TE, Cortez DG. Antifungal activity of the essential oil from *calendula officinalis* l. (asteraceae) growing in brazil. *Braz. J. Microbiol* 2008; 39:23-29.

[27]. Medina EJ, Lora AG, Paco L, Algarra I, Collado A, Garrido F. A new extract of the plant *Calendula officinalis* produces a dual *in vitro* effect: cytotoxic antitumor activity and lymphocyte activation. *BMC Cancer*, 2006; 6: 119-132.

[28]. Boucard-Maitre Y, Boucard-Maitre Y, Algernon O, Raynaurd, J. Genotoxic and antitumoral activity of *Calendula officinalis* extracts. *Pharmazie* 1988; 43: 220-221.

[29]. Popovic M, Kaurinovic B, Mimica-Dukic N, Vojinovic-Miloradov M, Cupic V. Combined effects of plant extracts and xenobiotics on liposomal lipid peroxidation. Part 1. Marigold extract-ciprofloxacin/pyralene. *Oxidation Commum*, 1999; 22: 487-494.

[30]. Frankic T, Salobir K, Salobir J. The comparison of *in vivo* antigenotoxic antioxidative capacity of two propylene glycol extracts of *Calendula officinalis* (Marigold) and vitamin E in young growing pigs. *J Anim Physiol Anim Nutr*, 2008; 41: 1-7.

[31]. Alexenizor M, Dorn A. Screening of medicinal and ornamental plants for insecticidal and growth regulating activity. *J Pestic. Sci*, 2007; 80: 205-215.

[32]. Perez-Guitierrez S, Vargas-Solis R, Miguel ZS, Perez-G C, Perez-G RM. Inhibitory effect of five plant extracts on heart rates of rats. *Phytother Res*, 1998; 12: S49-50.

[33]. Bogdanova NS, Nikolaeva IS, Shcherbakova LI,. Study of antiviral properties of *Calendula officinalis*. *Farmakol Toksikol (Moscow)*, 1970; 33: 349.