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Marigold – an ornamental plant with medicinal application

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ABSTRACT

Marigold (*Calendula officinalis* L.) is a widespread ornamental and medicinal plant with a long history of use in traditional medicine. *Calendula officinalis* contains many secondary metabolites that benefit human health and relieve skin ulcers and wound pain. Its essential oil is rich in monoterpenes and sesquiterpenes. Specific amounts of geraniol, limonene, thujene, and pinene in essential oil made it desirable in the cosmetics and perfume industries. Ethanolic extracts *of Calendula officinalis* contain flavonoids – substances with potent antioxidant properties. Due to carotenoids in flowers, Calendula officinalis extracts can be used as natural food colourants. The newest studies pointed out the potential of *Calendula officinalis* extracts as anti-inflammatory, anti-cancer, antibacterial and antifungal agents.

Keywords: *Calendula officinalis, essential oil, terpenes, carotenoids, cytotoxicity*

Introduction

Marigold (lat. *Calendula officinalis* L., belonging to the *Asteraceae* family) originates from India and can be found in the Mediterranean, Central Europe, and North America. *Calendula officinalis* is an annual, self-seeded or cultivated ornamental plant with no demanding growth and bloom conditions. Stem and leaves are densely covered in glandular hairs. Flower heads are slightly aromatic, sweet-scented, and single or double-flowered and appear from bright yellow to intensive orange (Figure 1).

Calendula officinalis has been used in traditional medicine for centuries. People have combined flower petals with vegetable oils to prepare balms, salves and skin lotions. Numerous plant secondary metabolites in *Calendula officinalis* (steroids, terpenoids, glycosides, volatile oil, amino acids, flavonoids) provide anti-inflammatory, antioxidant, antibacterial, antifungal, and wound-healing activities (Efstratiou et al., 2012; Rigane et al., 2013; Yalgi and Bhat, 2020; Vinola et al., 2021; Shahane et al., 2023).

Figure 1. *Calendula officinalis* (photo taken from https://unsplash.com/)

The chemistry of marigold – diversity in action

Aerial parts of the plant – flowers and leaves- have similar chemical composition regarding individual phenolic compounds. Gallic acid, rutin, scopoletin-7-*O*-glucoside, quercetin-3-*O*-glucoside and isorhamnetin-3-*O*-glucoside were identified in different quantities in leaves and flowers by using HPLC and LC/MS analysis (Rigane et al., 2013). In another research, flavonoids such as quercetin-rutinoside and quercetin-neohesperidoside, as well as calendoflavosides - isorhamnetin-neohesperidoside and isorhamnetin-rutinoside, were also identified (Ukiya et al., 2006). The presence of the mentioned compounds contributes to the antioxidant activity of *Calendula* e *officinalis* extracts.

The extracts obtained from the flowers *Calendula officinalis* contained a high quantity of polyphenolic compounds and exhibited good antioxidant activity. Antioxidant activity correlated significantly with the content of polyphenols and flavonoids (Veličković et al., 2014).

Flowers contained nearly twice as much total phenols and flavonoids than leaves (Rigane et al., 2013). Based on the results of the spectrophotometric determination of flavonoids in their study, Raal et al. (2016) stated that there is no clear relation between the colour of the flowers of *Calendula officinalis* and the total flavonoid content. The authors concluded that the content of flavonoids depended on either the place of cultivation or the cultivar of *Calendula officinalis* (Raal et al., 2016).

However, the plant pigments are responsible for the attractive colour of flowers. Flower petals of *Calendula officinalis* are exceptionally rich in carotenoids and contain flavoxantin, rubixantin, α-carotene, β-carotene, lycopene, and lutein and its derivatives (Kishimoto et al., 2005). The cultivars with higher carotenoid content usually have orange, dark-orange or even brownish flower petals (Raal et al., 2009). According to the results of HPLC analysis, there were 19 identified peaks in chromatograms of orange-coloured and only 10 identified peaks in yellow-coloured flowers, clearly indicating a more significant number of different carotenoids in the orange-coloured cultivars of *Calendula officinalis* (Kishimoto et al., 2005).

Calendula officinalis was recognised as an essential oil-bearing plant. The oil is dominantly accumulated in the flowers and is rich in terpenoids. However, the amount of oil is vegetation-dependent, with the maximum at the full-flowering period and the minimum at the pre-flowering period (Okoh et al., 2007).

Steam distillation is the standard procedure for determination of the content of essential oils in plant material. However, this way, only the "free" essential oil accessible to steam is extracted. A highly efficient alternative to steam distillation is high-pressure solvent extraction (Kajeh et al., 2004; Petrović et al., 2007; Yousefi et al., 2019). For instance, the amount of essential oil obtained from the subcritical and supercritical CO_2 extracts was more than two times higher than that obtained from the steam distillation (Petrović et al., 2007). One of the reasons may be the presence of waxes, fatty oil, and resins in *Calendula officinalis*, where some of the essential oil is dissolved. Subcritical and supercritical CO_2 extraction provides not only the extraction of free essential oil but also the extraction of fatty oil, waxes and resins containing dissolved essential oil (Petrović et al., 2007).

The major component of essential oil is sesquiterpene α-cadinole (Figure 2), followed by τ-cadinole, γ-cadinene and viridiflorol (Petrović et al., 2007; Raal et al., 2016).

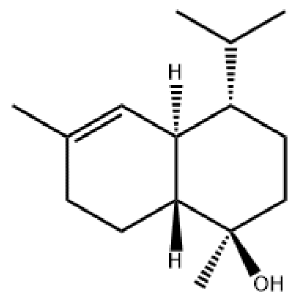

Figure 2. The structural formula of α-cadinole

According to the results of GC/MS analysis, an essential oil also contained several dozen compounds contributing to characteristic aroma: τ-muurolol, hexadecanoic acid, carvacrol, carvenone, *trans*-β-ocimene, α-terpeneol, α-thujene, α-pinene, β-pinene, limonene, geraniol, and many other volatiles (Okoh et al., 2007; Petrović et al., 2007; Sahingil, 2019). τ-cadinol and α-cadinol were reported to suppress the nitric oxide production induced by lipopolisaccharides and possess significant anti-inflammatory activity (Tung et al., 2011). α-pinene and β-pinene are fungicidal agents but are also intensively used as flavours, fragrances, and antiviral and antimicrobial agents (Salehi et al., 2019).

Promising alternative to antibiotics against pathogens

Since the extensive use of antibiotics and chemical agents has caused increasing bacteria resistance to these substances, there is an urgent necessity for efficient substitutes, and the solution could be found in the plant kingdom. In a recent study conducted by Vinola et al. (2021), the antibacterial and antifungal efficiency of the methanolic extract of Calendula officinalis has been compared to the widely used disinfectant chlorhexidine (a common constituent of mouthwash solutions). Even though chlorhexidine was found to be more potent due to its inability to dissolve pulp tissue or remove debris, its use as a routine irrigant has certain limitations. On the other hand, the extract of

Calendula officinalis exhibited lower antibacterial and antifungal activity but can be used as an effective alternative irrigant, safely applied daily (Vinola et al., 2021).

According to the newest *in vivo* study (Yalgi & Bhat, 2020) conducted on *Streptococcus mutans* as a teeth root canal irrigant, treatment with Calendula officinalis caused inhibition of growth or decrease in a number of colonies forming units (CFU). Therefore, *Calendula officinalis* was recognised as a promising medicament for bacterial elimination in teeth root canals (Yalgi & Bhat, 2020). Efstratiou et al. (2012) concluded that methanolic and ethanolic extracts of *Calendula officinalis* petals exhibited antifungal activity against several *Candida* and *Aspergillus* strains. In the same study, the antibacterial activity of both types of extracts was observed. However, methanolic extracts showed slightly higher antibacterial activity against various *Klebsiella, Pseudomonas, Staphylococcus* and even ampicillin-resistant *Escherichia coli* strains (Efstratiou et al., 2012).

Antibacterial activity is a consequence of the very complex composition of essential oil. Due to lipophilic properties, essential oils can pass through the cellular wall of the bacteria. The latter interaction with phospholipids and polysaccharides causes the permeabilisation of the bacteria membranes, further associated with loss of ions and membrane potential reduction (Bakkali et al., 2008). Furthermore, according to the results of molecular docking, α-cadinol showed binding affinity for three antibacterial target proteins, namely topisomerase IV subunit B, DNA gyrase subunit B, and penicillin-binding protein 2X, which are common in most of the bacterial species (Singh et al., 2018).

Exploring cytotoxic potential: Is it present here?

Depending on the part of the plant, extraction solvent, and the cancer cell line used for the study, the results of the cytotoxic efficiency of *Calendula officinalis* extracts varied significantly.

According to Matysik et al. (2005), the cytotoxic activity of the nonpolar heptane extract was due to the presence of different terpenes, while flavonoid glycosides were assigned for the cytotoxic activity of the polar, methanolic extract. Triterpene glycosides (methyl and butyl esters of calenduloside) in the methanolic extract of *Calendula officinalis* showed cytotoxic activity *in vitro* towards melanoma cell line, lung cancer, breast cancer, ovarian cancer and renal cancer (Ukiya et al., 2006). α-Cadinol was reported to be cytotoxic against human hepatocellular cancer cells, lung adenocarcinoma, melanoma, and leukaemia cells (Su & Ho, 2013).

One of the previously mentioned carotenoids found in aerial parts of *Calendula officinalis* – lutein exhibited selective cytotoxic activity towards breast cancer cell lines *in vitro* (Behbahani, 2014). A significant anticancer effect of geraniol was noticed by inducing apoptosis and DNA damage in colon cancer cells (Qi et al., 2018) and prostate cancer cells (Kim et al., 2011). Encapsulation of geraniol increased its cytotoxic activity towards lung cancer cells (Rodenak-Kladniew et al., 2023),

Based on those mentioned above, it is evident that the scientific community's interest in studying *Calendula officinalis* remains the same. This precious plant represents an actual reservoir of natural compounds with diverse biological activities, and many of them are yet to be investigated.

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