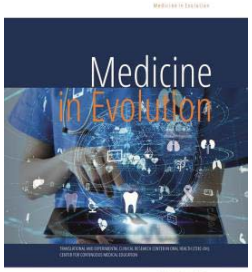
The benefits of Calendula officinalis extract as therapeutic agent in oral healthcare



Potra-Cicalău G.I.[1], Ciavoi G.[1], Todor L.[1], Iurcov R.C.[1], Iova G.[1], Ganea M.[2], Scrobotă I.[1]

[1]*Department of Dental Medicine, Faculty of Medicine and Pharmacy, University of Oradea, Romania*
[2]*Department of Pharmacy, Faculty of Medicine and Pharmacy, University of Oradea, Romania*

Correspondence to:
Name: Liana Todor
Address: Department of Dental Medicine, Faculty of Medicine and Pharmacy, University of Oradea, Romania, December 1st Square no.10, 410068 Oradea, Bihor County, Romania
Phone: +40723 517 100
E-mail address: liana.todor@gmail.com

Abstract

People's health is favorable impacted by medicinal plants. In addition to their conventional purpose, many isolated chemicals from herbs have beneficial therapeutic characteristics for treating various disorders. In this review, the usage of *Calendula officinalis* will be discussed in relation to pathologies that affect the oral cavity, such as dental caries, gingivitis or periodontitis. *Calendula officinalis* extract is able to decrease inflammation through pro-inflammatory cytokines down modulation and promotes antioxidant and immunomodulatory effects—as a result of the presence of polysaccharides and flavonoids in the plant—the main biological actions that make it effective in oral healthcare.

Keywords: natural extracts, *Calendula officinalis*, oral health

INTRODUCTION

Different plant extracts have been proven to have medicinal properties, benefic to oral healthcare. Tulsi (*Ocimum sanctum*), oregano (*Origanum vulgaris)*, green tea (*Camellia sinensis)*, red gum (*Eucalyptus camaldulensis)*, magnolia (*Magnolia officinalis)*, hibiscus (*Hibiscus sabdariffa)*, aloe vera (*Aloe barbadensis)*, mint (*Mentha Piperita)* and rosemary (*Rosmarinus officinalis*) have been established to inhibit a series of bacterial agents responsible for the occurrence of dental caries and periodontal disease [1, 2, 3, 4, 5]. Along with these, marigold (*Calendula officinalis*) is also counted, due to its phytotherapeutic properties [6, 7, 8, 9, 10].

Calendula officinalis, also known as marigold, pot marigold, bride of the sun or butterworth, grows in shrubs and it is native to the Mediterranean area, but it is widely spread around the world, being met especially in the sunny soils areas [11, 12]. About twenty five herbaceous annual or perennial species make up the genus Calendula (Asteraceae), with *Calendula officinalis Linn.*, *Calendula arvensis Linn.*, *Calendula suffruticosa Vahl.*, *Calendula stellata Cav.* and *Calendula alata Rech.* being the most popular [13].

This yellow-orange iridescence flower is considered to be a therapeutic plant due to its multiple medicinal qualities, including those that are antibacterial, anti-inflammatory, antioxidant, antifungal, re-epithelializing and immunomodulatory. *Calendula officinalis* is widely utilized in traditional medicine [12]. The extract of *Calendula officinalis* can be presented as tinctures, lotions, ointments or infusions [11].

Flavonoids, sterols, polysaccharides, saponins, triterpene alcohols, phenolic acids, tannins, glycosides and carotenoids are all present in the marigold flowers and leaves natural extract [11, 12]. Utilizing cutting-edge analytical technology, fresh chemical compounds with biological activity such as isorhamnetin, rutin and quercetin glucoside have been identified in *Calendula officinalis* extract [6]. These numerous biological active elements have been identified both in-vitro and in-vivo [14].

Aim and objectives

This review objective is to discuss the use of *Calendula officinalis* in conditions affecting the oral cavity, including dental caries, gingivitis and periodontitis. We also intend to emphasize the applicability of this extract in endodontics, dento-alveolar surgery and diabetology.

CALENDULA OFFICINALIS PHARMACOLOGICAL EFFECTS

Numerous studies have looked into the medical benefits of calendula extract, which can be used in both dental and general medicine.

The three primary biological actions of calendula that make it effective in dental care are its ability to reduce pro-inflammatory cytokines, decrease inflammation and promote antioxidant and immunomodulatory effects due to the presence of polysaccharides and flavonoids in the plant [8, 9, 15, 16].

Several researchers reported the antibacterial properties of marigold extract [17]. *Calendula officinalis* extract can modulate the formation of the oral microbiome induced by *Streptococcus Mutans*, chronic gingivitis, while also having fungistatic activity against *Candida albicans* [6, 7, 10, 18].

In terms of anti-inflammatory activity, it has been demonstrated that the oral administration of 250-500 mg/kg of body weight significantly inhibits plantar edema induced by carrageenan and dextran in experimental animals [8]. Since the presence of dextran and

carrageenan, *Calendula officinalis* extract exhibits anti-inflammatory effects on plantar edema, the anti-inflammatory impact being comparable to indomethacin dosages [19].

Also, the increased levels of pro-inflammatory cytokines (TNF-α, IL-1β, 1L-6), respectively acute phase proteins (C-reactive protein (CRP) and cyclooxygenase-2 (COX-2)) are significantly inhibited in mice by marigold extract treatment [8].

The amount of cytokines can be controlled by *Calendula officinalis* extract, which can also lessen oxidative stress and increase polymorphonuclear cell activity. *Calendula officinalis* containing mouthwashes can be used as an adjuvant in oral prophylaxis because they have been found to lower bacterial plaque load and prevent gingival irritation [6].

It has been stated that the antioxidant properties of *Calendula officinalis* extract are due to the content of quercetin, lutein, ruby, xanthophylls, ubiquinone and carotenoids [6, 7, 10, 18]. At the same time it was highlighted that the extract of *Calendula officinalis* of different polarity shown antioxidative activity on liposomal lipid peroxidation caused by ferrous ion and ascorbic acid [20]. In-vitro and in-vivo assessments showed that the antioxidant potential of marigold extract is due to the removal of superoxide radicals and OH groups [19].

DISCUSSIONS

Even though there is little information in the literature about the antibacterial activities of plant extracts against periodontal diseases, many mouthwashes containing medicinal plant extracts are routinely utilized for maintaining oral hygiene. From this point of view, *Calendula officinalis* extract has been intensively investigated.

In an vitro study, Priyanka et al. demonstrated the significant antibacterial effect of *Calendula officinalis* on dental plaque pathogens, but still inferior to chlorhexidine (CHX) and tetracycline gels [21]. Khairnar et al. in an experimental study on human subjects demonstrated that mouthwashes containing marigold extract can be effective in reducing the oral microbiome involved in the formation of bacterial dental plaque and in the occurrence of gingivitis. In case of using mouthwash with marigold tincture, periodontal indices (PI, GI, SBI) are significantly reduced, even in the absence of scaling [6]. Another clinical study, carried out by Amoian et al. investigated the anti-inflammatory effect of a mouthwash with marigold extract in case of patients diagnosed with gingivitis and demonstrated that the incorporation of this extract into oral toothpastes reduces PI, GI and BOP index, recommending its introduction as an adjunctive treatment in improving the gingival status [22]. The results of these authors show that this extract has phytotherapeutic properties, beneficial in the prevention and control of dental plaque, gingivitis and periodontitis [6, 21, 22].

Mouthwashes containing *Calendula officinalis* have been identified as alternatives to the use of CHX 0.12%, which did not exert the expected results in postoperative healing after free gingival grafts. The use of marigold extract mouthwash promotes fast healing of the affected oral mucosa in a few days and has antimicrobial effect [23]. As opposed to that, other researchers stated after a clinical research that phytotherapeutic mouthwashes containing *Calendula officinalis* delivers similar effects to CHX 0.12% mouthwashes in patients with chronic periodontitis, regarding clinical parameters (PI, BOP, CAL). In case of GI index, CHX showed superior effects [24].

Besides the antibacterial activity, another important aspect is mouthwashes is the taste. A clinical study by Arief et al. demonstrated that a commercial preparation with marigold extract - Plandula® - resulted in obtaining a slightly higher average plaque index compared to the use of CHX, but statistically insignificant [25].

The outcomes of a mouthwash based on hydrophilic extracts of *Zingiber officinale*, *Rosmarinus officinalis* and *Calendula officinalis* were compared to those attained after using

mouthwashes containing CHX by Mahyari et al. in patients with gingivitis and the results were similar [26]. These plant extracts have the potential to reduce bacterial plaque and gingivitis [27]. Other authors have shown that the association of *Calendula officinalis* extract with propolis in mouthwashes with different pharmaceutical formulas can be useful in maintaining oral hygiene and preventing periodontal disease [28].

Gram-positive and gram-negative flora is greatly reduced by *Calendula officinalis* leaves extract, as demonstrated by Chakraborty et al. [7]. Shankar et al. investigated the antimicrobial activity of *Calendula officinalis* against five gram-positive and gram-negative germs involved in tooth decay pathology (*Streptococcus Mutans*), respectively in periodontal pathology (*Aggregatibacter actinomycetemcomitans*, *Porphyromonas gingivalis, Prevotella intermedia*, *Fusobacterium nucleatum*) and demonstrated that *Calendula officinalis* is very effective against *Streptococcus Mutans* (3.12 µg/ml), having a MIC close to CHX 0.2% (6.25 µg/ml). Also, *Porphyromonas gingivalis* and *Prevotella intermedia* showed sensitivity to *Calendula officinalis*, while *Aggregatibacter actinomycetemcomitans* and *Fusobacterium nucleatum* showed reduced sensitivity. Accordingly, *Calendula officinalis* represents a potential treatment in the case of periodontal disease, but especially in the prevention of dental caries [29].

When calendula oil was used, Yadav et al. have shown in vitro that it has antimicrobial activity against numerous periodontal pathogens. *Porphyromonas gingivalis* showed sensitivity at the concentration of 0.8 µg/ml, *Aggregatibacter actinomycetemcomitans* showed sensitivity at the concentration of 25 µg/ml, *Fusobacterium nucleatum* showed sensitivity at the concentration of 100 µg/ml and *Tanerella forsythia* showed resistance through out [30]. Rodriguez-Garcia et al. sought to develop bioadhesive films based on polymers and natural extracts with antimicrobial activity against periodontal pathogens, including calendula extract. They identified the MIC for *Calendula officinalis* as being 62.5 mg/ml for *Porphyromonas gingivalis* and 250 mg/ml for *Aggregatibacter actinomycetemcomitans* and the MBC of *Calendula officinalis* was 250 mg/ml for *Aggregatibacter actinomycetemcomitans* and 111 mg/ml for *Porphyromonas gingivalis* [31].

Thus, mouth rinsing with calendula will allow its anti-inflammatory properties to work against the swollen, irritated gums and its antibacterial properties deal with the periodontopathic microorganisms [32].

Tanideh et al. demonstrated in an experimental study on rats that the association of the hydrophilic extract of *Calendula officinalis* with *Hypericum perforatum* can be an adjuvant in periodontal therapy by decreasing the inflammatory marker IL-1β, while increasing the antioxidant capacity (2,2-diphenyl-1-picrylhydrazyl (DPPH) and ferric reducing antioxidant power (FRAP)) [33].

In a clinical study on human subjects, Jamwal et al. investigated the effect of different concentrations of calendula extract on the pathogens involved in periodontal disease, demonstrating that mouthwash with a 100% concentration of *Calendula officinalis* is the most effective in reducing the periodontal microbiome, compared to mouthwash with 5% or 20% content of *Calendula officinalis*, so it can be used as a treatment for patients with gingivitis and periodontitis [34].

Recent in vivo research illustrated that *Calendula officinalis* favors postextractional bone preservation, due to its collagenogenic effect and through its antiseptic and analgesic properties [35], while experiments on rats demonstrated that *Calendula officinalis* modulates bone resorption and reduces inflammation in periodontal disease induced in experimental animals, emphasizing the anti-inflammatory effects of this plant extract and the involvement in bone metabolism [36]. In addition, Lima et al. highlighted that *Calendula officinalis* extract exhibit antiresorptive effect, preserves collagen fibers and present antioxidant activity [37]. Calendula mouthwash has anti-inflammatory and antibacterial effects that fight periodontopathic bacteria as well as swollen, inflamed gums [6]. These clinical and

experimental results show that *Calendula officinalis* is a potential therapeutic adjuvant in the treatment of periodontal disease and bone resorption.

In stopping desquamative gingivitis and reducing the progression of periodontal disease, *Calendula officinalis* actively participates by reducing the growth factor of hepatocytes, mediated by the breakdown of collagen and the activity of matrix metalloproteinases (MMP) [38]. Machado et al. proposed a gel based on clobetasol and *Calendula officinalis* as a treatment for desquamative gingivitis [39].

Parente et al. showed in an experimental investigation that *Callendula officinalis* extract has anti-inflammatory and antibacterial activities, improving the healing process by reducing inflammation and promoting the growth of fibroblasts in the experimental model [40]. Another research investigated the effects of chamomile and calendula mouthwash on human fibroblasts, demonstrating that they do not have anti-proliferative effects on fibroblastic cells, calendula extract also favoring wound healing [41]. Following an in vitro experiment, Saini et al. concluded that *Calendula officinalis* extract inhibits human gingival figroblast-mediated collagen degradation and MMP-2 in a superior way compared to quercetin at similar concentration [42].

This extract has also found applicability in endodontics. In an in vitro study, Vinola et al. made a comparison between the antimicrobial effect of the extract of *Calendula officinalis* with CHX 2% and identified that the extract of *Calendula officinalis* has antimicrobial and antifungal activity against *Enterococcus faecalis* and *Candida albicans*, thus being an alternative in endodontic infections treatment [43]. In a clinical experiment on human subjects, Yalgi et al. have demonstrated that *Calendula officinalis* can be used as a promising endodontic treatment, in order to suppress microorganisms from the root canal, especially *Streptococcus Mutans*, the results obtained by endocanalicular lavages being similar to those of sodium hypochlorite, used by choice in endodontic treatment [44].

El-Sayed et al. proposed topical formulas based on *Calendula officinalis* with the aim of being used post-surgically after free gingival graft surgeries, the topical gel with marigold extract exerting the best healing during the second postoperative week [45]. *Calendula officinalis* mouthwashes promote wound healing by enhancing local vascularization and increasing the rate of hyaluronic acid deposition, which actively contributes to the differentiation of mesenchymal cells. They also reduce the microbial load and the adhesion of microorganisms to the suture threads used postextractional [38]. Furthermore, Faria et al. found that *Calendula officinalis* and *Camellia sinensis* incorporated in mouthwash and used for a week, until the suture threads are removed, show antimicrobial activity, but the antimicrobial effect is not as efficient as that of CHX 0.12% [46].

Calendula officinalis has also been studied as an alternative treatment in exfoliative cheilitis [38]. Because of its anticancer properties, *Calendula officinalis* could be effective in treating oral mucositis in radiation therapy patients. It has cytotoxic effect on tumor cell lines [47].

Not least, Ebrahimi et al. have investigated the effects of this aromatic hydroalcoholic flower extract on the biological and histological parameters in diabetic rats and demonstrated trat the oral administration of this extract reduce body wight and decreed blood glucose. Also the diabetes mellitus complications upon pancreas, liver and kidneys were improved after treatment with marigold extract [48]. The therapeutic impact on diabetes raises the possibility that it may also be helpful in avoiding or controlling periodontal disease given that it is one of the complications of diabetes mellitus [49, 50].

Rare cases of anaphylactic shock following gargling with *Callendula officinalis* infusion and allergic reactions to skin contact with marigold plants have both been documented [20]. Other scientists, however, contend that the marigold extract is not toxic, genotoxic or mutagenic [12]. To further understand this issue, more research is required.

CONCLUSIONS

Plant extract-based mouthwashes, such as *Calendula officinalis*, stand out as a preventive treatment in dentistry since they offer a straightforward way to avoid tooth decays and periodontal diseases.

Given its antibacterial, anti-inflammatory and antioxidant excipients qualities, natural extract of *Calendula officinalis* can successfully be included in the oral cavity pathologies treatment, particularly in gingivitis and periodontitis.

It is essential to develop innovative dental therapies that are safe for the body, non-toxic and without negative consequences.

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