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Review Article

DESCRIPTION, IDENTIFICATION & PHARMACOLOGICAL ACTION OF *CALENDULA OFFICINALIS*: A REVIEW

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ABSTRACT

Ayurveda is the ancient thought and treatise that deals with the knowledge of living a healthy life. There are several types of medicaments that are being used in the Ayurvedic mode of treatment. The source of these drugs is diverse and belongs to different category. The category ranges from plants and animals to minerals and encircles around different types of species of plants and animals with vivid habitats. Ayurvedic plants have shown their effects on various kind of diseases. Those properties of the plants are sublimed in some molecules in the plants, which can be extracted out by performing various kind of processes (eg. Soxhlation, Percolation). Many plants which are used by the human being in daily life, also have some effects in curing some disease conditions. *Calendula officinalis* is a plant that possess many pharmacological actions due to it contains numerous polyphenols & antioxidants, so this plant is studied both in the laboratory as well as in clinical setting for different therapeutic aspects. This review makes a humble effort to summaries & gather knowledge about the Description, Identification & Pharmacological Properties of the said plant. The study shows that this plant not only possessed wound healing properties, but also it has a wide range of pharmacological uses. Furthermore experiments & clinical trials needed to confirm those founded results.

Keywords: Pharmacological Action, Soxhlation, Percolation, Poly-phenol, Anti-Oxidant, Wound Healing, Clinical Trial.

INTRODUCTION

Calendula officinalis is a plant in the genus Calendula of the family Asteraceae. It is probably native to southern Europe, though its long history of cultivation makes its precise origin unknown, and it may possibly be of garden origin. It is also widely naturalized further north in Europe (north to southern England) and elsewhere in warm temperate regions of the world. *Calendula officinalis* is a short-lived aromatic herbaceous perennial, growing to 80 cm (31 in) tall, with sparsely branched lax or erect stems. The leaves are oblong, lanceolate, 5–17 cm (2–7 in) long, hairy on both sides, and with margins entire or occasionally waved or weakly toothed. The inflorescences are yellow, comprising a thick capitulum or flower head 4–7 cm diameter surrounded by two rows of hairy bracts; in the wild plant they have a single ring of ray florets surrounding the central disc florets. The disc florets are tubular and hermaphrodite, and generally of a more intense orange yellow colour than the female, tridentate, peripheral ray florets. The flowers may appear all year long where conditions are suitable. The fruit is a thorny curved achene[1-4]. The anti-inflammatory and anti-oedematous properties of *Calendula officinalis* have been linked to the pentacyclic mono-, di- and trihydroxy triterpenoid fatty acid esters, especially the faradiol esters, faradiol 3-O-laurate, faradiol 3-O-palmitate and faradiol 3- O-myristate[5-10]. The unesterified faradiol produced by hydrolysis, has been found to have the same effect as an equimolar dose of indomethacin which is a Non-Steroidal Anti-Inflammatory Drug (NSAID)[11]. It is also reported that the effect of this leaf in enhancing the blood clotting time is due to present of Lutein & Zeaxanthin present in this leaf. Thus, it has been suggested that the concentrations of the triterpenoid fatty acid esters in *Calendula officinalis* formulations may be an effective method to assess and monitor the quality of products on the market[9].

HISTORY

The plant has been grown in European gardens since the 12th century, and its folkloric uses are almost as old. Tinctures and extracts of the florets were used topically to promote wound healing and to reduce inflammation; systemically, they have been used to reduce fever, control dysmenorrhea, and treat cancer. The plant is listed in the German Commission E Monographs for wound healing and anti-inflammatory actions[12].

The dried petals have been used like saffron as a seasoning and have been used to adulterate saffron[13]. The pungent odor of the marigold has been used as an effective pesticide. Marigolds are often interspersed among vegetable plants to repel insects[14].

IDENTIFICATION

DNA-Based Identification of *Calendula officinalis*

Five markers (ITS, rbcL, 5' trnK-matK, psbA-trnH, trnL-trnF) of 10 Calendula species were sequenced and analyzed for species-specific mutations. With the application of two developed primer pairs located in the trnK 5' intron and trnL-trnF, *C. officinalis* could be distinguished from other species of the genus and all out-group samples tested. With the developed assay, *C. officinalis* can

be reliably identified and admixtures of this species as adulterant of saffron can be revealed at low levels[15].

PHARMACOLOGICAL ACTION

Action on Tobacco-Induced Homogeneous Leukoplakia

The study comprised of sixty patients of clinically diagnosed and histo-pathologically confirmed cases of homogeneous leukoplakia which were divided into Group I and Group II with thirty patients each. Group I patients were dispensed *C. officinalis* extract gel (Image 1) whereas Group II patients were given lycopene gel. [16]

The therapy was instituted for 1 month to assess the change in the size of the lesion at the baseline and post treatment.

The mean difference in the reduction in size before (Image 2) and after (Image 3) treatment for Group I was 2.0% ±1.0 cm while for the Group II, it was 1.57% ±0.87 cm (Image 4).

So it can be concluded by this study that *C. officinalis* extract gel can be effectively used as an alternative to conventional treatment modality.

Anti-Acetyl cholinesterase Activity

The study was carried out on 23 varieties of *C. officinalis* flowers, one of them was Greenheart Orange variety due to the superior content of flavonoids (46.87 mg/g) and the highest inhibitory activity against acetyl cholinesterase (IC_{50}63.52 µg/mL). Flavonoids, isorhamnetin and quercetin derivatives were revealed as potential inhibitors with the application of high-performance liquid chromatography (HPLC) activity-based profiling. [17]

The results of their experiments show the inhibitory activity of isorhamnetin glycosides demonstrated the maximal potency for isorhamnetin-3-*O*-(2",6"-di-acetyl)-glucoside (IC_{50} 51.26 µM) and minimal potency for typhaneoside (isorhamnetin-3-*O*-(2",6"-di-rhamnosyl)-glucoside; IC_{50} 94.92 µM). Among quercetin derivatives, the most active compound was quercetin-3-*O*-(2",6"-di-acetyl)-glucoside (IC_{50} 36.47 µM), and the least active component was manghaslin (quercetin-3-*O*-(2",6"-di-rhamnosyl)-glucoside; IC_{50} 94.92 µM).

So the results clarified that isorhamnetin and quercetin and its glycosides can be considered as potential anti-acetyl cholinesterase agents.

The supportive HPLC Chromatograms for those experiments of 60% ethanol extract from *C. officinalis* of the Greenheart Orange variety at 350 nm (A) and HPLC-based anti-acetylcholinesterase activity (AChE) profiling (B). The bar graphs on B show the inhibitory activity of the individual HPLC fractions collected from a single separation. Compounds: 1, 3-*O*-caffeoylquinic acid; 2, caffeic acid; 3, manghaslin; 4, calendoflavobioside; 5, typhaneoside; 6, rutin; 7, isoquercitrin; 8, quercetin-3-*O*-(2″-ramnosyl)-rhamnoside; 9, calendoflavoside; 10, 3,5-di-*O*-caffeoylquinic acid; 11, quercetin-3-*O*-(6″-acetyl)-glucoside; 12, 1,5-di-*O*-caffeoylquinic acid; 13, narcissin; 14, isorhamnetin-3-*O*-glucoside; 15, calendoflaside; 16, 4,5-di-*O*-caffeoylquinic acid; 17, isorhamnetin-3-*O*-(6″-acetyl)-glucoside, as shown in Image 5, Image 6, Image 7.

Action on Oxidative Stress and Bone Loss

Evaluation the effect of *Calendula officinalis* on oxidative stress and bone loss in rats subjected to experimental periodontitis (EP). For this, 72 male Wistar rats were divided into groups: Negetive, Saline (SAL) and *Calendula officinalis*. Rats received SAL or *Calendula officinalis* (90 mg/kg) (Image-8) 30 min before ligature and daily until the 11th day. Negetive group experienced no manipulation. After 11 days, the animals were euthanized, and left maxillae collected for macroscopic analysis of alveolar bone loss (ABL) (Image-9, 10). Periodontium was analyzed by macroscopy, scanning electron microscopy, confocal and light polarized microscopy. Immunohistochemical examination of DKK1, WNT (Image-11) 10b and β-catenin (Image-12) was performed. The gingival tissue was collected to reduced glutathione (GSH), superoxide dismutase (SOD), catalase (CAT) and malondialdehyde (MDA) analyses (Image-13). The 11 days of ligature induced bone loss, breakdown of collagen fibers, increased the immunostaining DKK-1 while reduced WNT 10b and β-catenin expressions. Periodontitis reduced GSH, SOD, CAT and increase MDA. All findings were reversed by 90 mg/kg of *Calendula officinalis*. In summary our findings demonstrated that *Calendula officinalis* reduced oxidative stress and bone loss and preserved collagen fibers in rats with EP. [18]

Action on Chronic Prostatitis / Chronic Pelvic Pain Syndrome Type III

The study enrolled 60 consecutive patients affected by CP/CPPS III. Patients between 20 and 50 years of age with symptoms of pelvic pain for 3 months or more before study. Patients were then allocated to receive placebo (Group A) or treatment (Group B). Treatment consisted of rectal suppositories of Curcumin extract 350 mg (95%) and Calendula extract 80 mg (1 suppository/die for 1 month). Patients of Group B received 1 suppository/die for 1 month of placebo. The primary end point of the study was the reduction of NIH-CPSI. The secondary outcomes were the change of peak flow, IIEF-5, VAS score and of premature ejaculation diagnostic tool (PEDT). A total of 48 patients concluded the study protocol. The median age of the all cohort was 32.0 years, the median NIH-CPSI was 20.5, the median IIEF-5 was 18.5, the median PEDT was 11.0, the median VAS score was 7.5 and the median peak flow was 14.0. After 3 months of therapy in group A they observed a significant improvement of NIH-CPSI (-5.5; p < 0.01), IIEF-5 (+ 3.5; p < 0.01), PEDT (-6.5; p < 0.01), peak flow (+2.8; p < 0.01) and VAS (-6.5; p < 0.01) with significant differences over placebo group (all p-value significant). In this phase II clinical trial, they showed the clinical efficacy of the treatment with Curcumin and Calendula in patients with CP/CPPS III. The benefits of this treatment could be related to the reduction of inflammatory cytokines and of inflammatory cells. [19]

Chemical Variability, Antioxidant and Antifungal Activities of Essential Oils and Hydrosol Extract of Calendula

18 Algerian sample locations were investigated using statistical analysis. Chemical analysis allowed the identification of 53 compounds amounting to 92.3 - 98.5% with yields varied of 0.09 - 0.36% and the main compounds were zingiberenol 1 (8.7 - 29.8%), eremoligenol (4.2 -12.5%), β-curcumene (2.1 - 12.5%), zingiberenol 2 (4.6 - 19.8%) and (E,Z)-farnesol (3.5 -23.4%). Different concentrations of essential oil and hydrosol extract were prepared, and their antioxidant activity were assessed using three methods (2,2-diphenyl-1-picrylhydrazyl, Ferric-Reducing Antioxidant Power Assay and β-carotene). The results showed that hydrosol extract presented an

interesting antioxidant activity. The *in vitro* antifungal activity of hydrosol extract produced the best antifungal inhibition against *Penicillium expansum* and *Aspergillus niger*, while essential oil was inhibitory at relatively higher concentrations. Results showed that the treatments of pear fruits with essential oil and hydrosol extract presented a very interesting protective activity on disease severity of pears caused by *P. expansum*. [20]

Action on Venous Leg Ulcer Healing

Patients treated with *Calendula officinalis* extract (n=38) and control patients (n=19) were evaluated every two weeks for 30 weeks or until their ulcers healed. Assessments included determination of the wound area by planimetry, infection control, and evaluation of the clinical aspects of the wounds. The percentage of healing velocity per week (%HVw), taking the initial area at baseline into account, was also determined. The proportion of the treatment patients achieving complete epithelialisation was 72 % and 32 % in the treatment and control groups, respectively. The average healing time was approximately 12 weeks in the treatment group and 25 % in control patients. Patients with ulcers treated with *Calendula officinalis* extract had a significant 4-fold increase in percentage healing velocity per week, 7.4 %, compared with 1.7 % in the control group. No adverse events were observed during the *Calendula officinalis* extract treatment. The findings indicate that *Calendula officinalis* extract is an effective treatment for venous leg ulcers. [21]

Wound Healing Properties of *Calendula officinalis* Extracts

The effect of three different extracts from Calendula flowers (n-hexanic, ethanolic, aqueous) on the inflammatory phase of wound healing was studied in human immortalized keratinocytes and human dermal fibroblasts. An electrophoretic mobility shift assay on NF-κB-DNA binding, qRT-PCR and ELISA experiments were performed. The effect of Calendula extracts on the new tissue formation phase of wound healing was evaluated by studying the migratory properties of these extracts, triterpene mixtures and single compounds in human immortalized keratinocytes using the scratch assay. Finally, the effect of the extracts was studied using bacterial collagenase isolated from Clostridium histolyticum and the determination of soluble collagen in the supernatant of human dermal fibroblasts. The n-hexanic and the ethanolic extracts from Calendula flowers influence the inflammatory phase by activating the transcription factor NF-κB and by increasing the amount of the chemokine IL-8, both at the transcriptional and protein level, in human immortalized keratinocytes. The migration of the keratinocytes during the new tissue formation phase was only marginally influenced in the scratch assay. The results contribute to a better understanding of the wound healing properties of the traditional medicinal plant *Calendula officinalis*. [22]

Effect on Vaginal Candidiasis

Married women aged 18-45 years with vaginal Candidiasis (n = 150) were recruited from April to October 2014 and randomized into Calendula and clotrimazole groups, using 5-g vaginal cream every night for seven nights. Clinical and laboratory assessments were conducted at 10-15 and 30-35 days after intervention and the female sexual function index was assessed at 30-35 days. Six women were lost to follow-up. The frequency of testing negative for Candidiasis in the Calendula group was significantly lower at the first (49% vs. 74%; odds ratio (OR) 0.32; 95% confidence interval (CI) 0.16-0.67) but higher at the second (77% vs. 34%; OR 3.1; 95% CI 1.5-6.2) follow-up compared to the clotrimazole group. The frequency of most signs and symptoms were almost equal in the two groups at the first follow-up but were significantly lower in the Calendula group at the second follow-up. Calendula vaginal cream appears to have been effective in the treatment of vaginal Candidiasis and to have a delayed but greater long-term effect compared to clotrimazole. [23]

Bioaccessibility and Antioxidant Activity of *Calendula officinalis*

Marigold Extracts produced without co-solvent was richer in taraxasterol, lupeol, α-amyrin, and β-amyrin than extracts with co-solvent by Supercritical Extraction. All terpenes showed high bioaccessibility without OO (>75%). Significant correlations were found between the molecular properties of compounds (logP and number of rotatable bonds) and their bioaccessibility. Codigestion with OO enhanced the bioaccessibility (around 100% for PT), which could be related to a higher abundance of low-size particles of the digestion medium. The antioxidant activity of the digested Marigold Extracts increased around 50%, regardless of OO. PT-rich extracts from marigold display high bioaccessibility and improved antioxidant activity after *in vitro* digestion, although complete bioaccessibility of PT can be reached by co-digestion with oil, without affecting antioxidant activity. [24]

On Repairing Diabetic Foot Ulcers

The sample consisted of 32 diabetic patients of both genders. Participants were randomly divided into four groups. Doppler Ultrasound evaluation of the Ankle-Brachial Index, brief pain inventory and analog pain scale were performed at baseline and after 30 days. Regarding the Ankle-Brachial Index and Doppler Ultrasound, all groups remained stable. By analyzing lesion area reduction, Low-level laser therapy associated with Essential fatty acids group showed a significance of p=0.0032, and the Low-level laser therapy group showed p=0.0428. Low-level laser therapy performed alone or associated with the *Calendula officinalis* oil was effective in relieving pain and accelerating the tissue repair process of diabetic foot. [25]

Wound Healing

Calendule officinalis hydroethanol extract (CEE) and its active fraction (water fraction of hydroethanol extract, WCEE) on primary human dermal fibroblasts (HDF) was studied. *In vivo*, CEE or WCEE were topically applied on excisional wounds of BALB/c mice and the rate of wound contraction and immune histological studies were carried out. We found that CEE and only its WCEE significantly stimulated the proliferation as well as the migration of HDF cells. Also they up-regulate the expression of connective tissue growth factor (CTGF) and α-smooth muscle action (α-SMA) *in vitro*. *In vivo*, CEE or WCEE treated mice groups showed faster wound healing and increased expression of CTGF and α-SMA compared to placebo control group. In addition, HPLC-ESI MS analysis of the active water fraction revealed the presence of two major compounds, rutin and quercetin-3-O-glucoside. Thus, our results showed that *C. officinalis* potentiated wound healing by stimulating the expression of CTGF and α-SMA and further we identified active compounds[26].

An ointment containing 5% flower extract in combination with allantoin markedly stimulated epithelialization in surgically induced wounds. On the basis of histological examination of the wound tissue, it was concluded that the ointment increased

glycoprotein, nucleoprotein, and collagen metabolism at the site[33].

Effects on Acute Necrotizing Pancreatitis

The effect of ethanol extract (95%) of *Calendula officinalis* flowers in l-arginine induced acute necrotizing pancreatitis in rats. Rats were divided into four groups: normal control, l-arginine control, *Calendula officinalis* extract (COE) treated, and melatonin treated (positive control), which were further divided into subgroups (24 h, day 3 and 14) according to time points. Two injections of l-arginine 2 g/kg i.p. at 1 h intervals were administered in l-arginine control, COE and melatonin-treated groups to produce acute necrotizing pancreatitis. Biochemical parameters [serum amylase, lipase, pancreatic amylase, nucleic acid content, total proteins, transforming growth factor-β1 (TGF-β1), collagen content, lipid peroxidation, reduced glutathione and nitrite/nitrate] and histopathological studies were carried out. COE treatment (400 mg/kg p.o.) was found to be beneficial. Nucleic acid content (DNA 21.1 and RNA 5.44 mg/g pancreas), total proteins (0.66 mg/mL pancreas) and pancreatic amylase (1031.3 100 SU/g pancreas) were significantly improved. Marked reduction in pancreatic oxidative and nitrosative stress; collagen (122 μmoles/100 mg pancreas) and TGF-β1 (118.56 pg/mL) levels were noted. Results obtained were comparable to those of positive control. Hence, the study concludes that COE promotes spontaneous repair and regeneration of the pancreas. [27]

Cytotoxic Activity

The CH_2Cl_2 extract from the flowers of *C. officinalis* by MTT and LDH assays in human epithelial gastric cells AGS. This bioassay-oriented approach led to the isolation of several sesquiterpene glycosides which were structurally characterized by spectroscopic measurements, chemical reactions and MM calculations. The conformational preferences of viridiflorol fucoside were established and a previously assigned stereochemistry was revised. The compounds 1a, 2a and 3f showed comparably high cytotoxicity in the MTT assays, whereas the effect on LDH release was lower. This study provides new insights on the *C. officinalis* extracts that could be responsible for cytotoxic effects at gastric level. [28]

Action on Radiodermatitis

A double-blind controlled clinical trial with 51 patients with head and neck cancer in radiotherapy treatment divided into two groups: control and experimental. There is statistically significant evidence (p-value = 0.0120) that the proportion of radiodermatitis grade 2 in Essential Fatty Acids group is higher than Calendula group. Through the Kaplan-Meier survival curve it was observed that Essential Fatty Acids group has always remained below the Calendula group survival curve, due to the lower risk of developing radiodermatitis grade 1, which makes the usage of Calendula more effective, with statistical significance (p-value = 0.00402)[29].

A decrease in grade 2 or higher dermatitis was found with the calendula preparation containing 4 g fresh plant in 20 g petroleum jelly; however, application of the preparation proved difficult in 30% of the participants. A reduction in pain was also reported for calendula[34,35,36].

Anti- Inflammatory Activity

Triterpenoid-containing extracts of calendula have been investigated in chemical-induced inflammation in mice[30,31]. Calendula extracts alleviated signs of chronic conjunctivitis and other chronic ocular inflammatory conditions in rats[32], the extracts also had a systemic anti-inflammatory effect.

Prothrombin Time (PT) Test of *Calendula officinalis*

Butanol & Water extract of Calendula leaf was prepared & citrated plasma & brain tissue thromboplastin was used as standard. The found results are as follows-

Leaf Extract	Standard	Coagulation Time
Butanol Extract	Citrated Plasma	4.10 min
Butanol Extract	Citrated Plasma + Brain Tissue Thromboplastin	2 min
Water Extract	Citrated Plasma	1 min.
Water Extract	Citrated Plasma+ Brain Tissue Thromboplastin	20 sec.

So the study clearly demonstrate that the water extract of *Calendula officinalis* leaf has better coagulating activity. [37]

Image 1: Application of gel at the site of lesion

Image 2: Pretreatment homogeneous leukoplakia

Image 3: Post treatment after application of gel

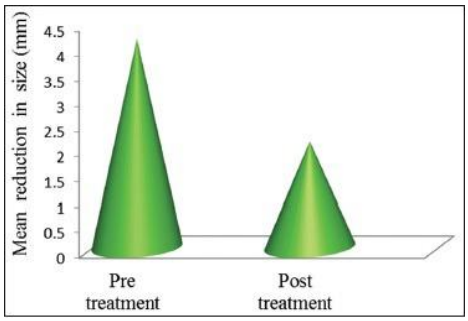

Image 4: Comparison of change in size after gel application

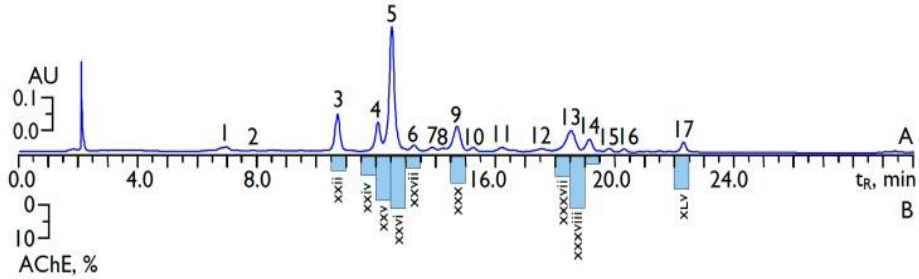

Image 5: Chromatograms

1, 3-*O*-caffeoylquinic acid; 2, caffeic acid; 3, manghaslin; 4, calendoflavobioside; 5, typhaneoside; 6, rutin; 7, isoquercitrin; 8, quercetin-3-*O*-(2″-ramnosyl)-rhamnoside; 9, calendoflavoside; 10, 3,5-di-*O*-caffeoylquinic acid; 11, quercetin-3-*O*-(6″-acetyl)-glucoside; 12, 1,5-di-*O*-caffeoylquinic acid; 13, narcissin; 14, isorhamnetin-3-*O*-glucoside; 15, calendoflaside; 16, 4,5-di-*O*-caffeoylquinic acid; 17, isorhamnetin-3-*O*-(6″-acetyl)-glucoside

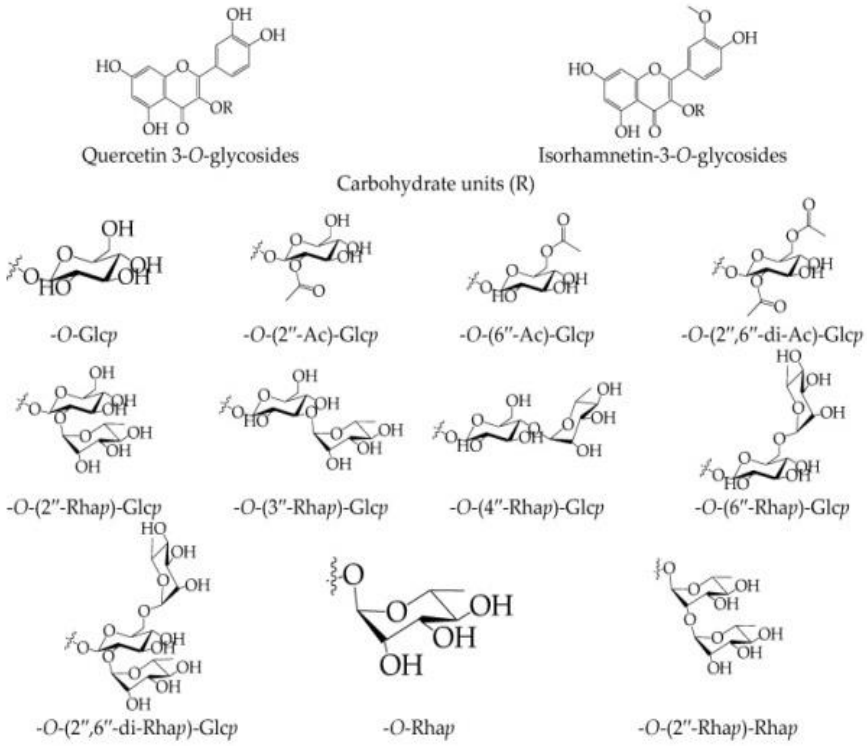

Image 6: Structures of quercetin and isorhamnetin glycosides from *C. officinalis*. abbreviations used: glc*p*, glucopyranose; ac, acetyl; rha*p*, rhamnopyranose.

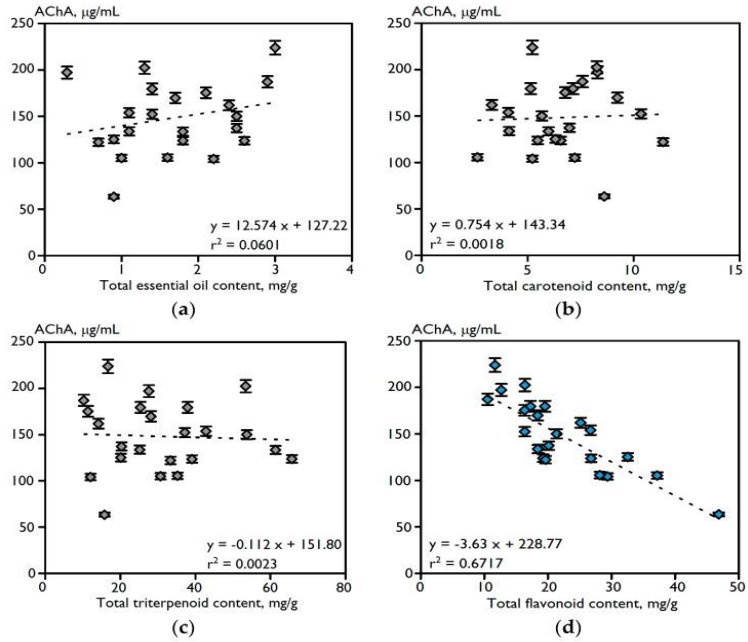

Image 7: Correlation graphs (dashed lines) between total content of essential oil (a**) total essential oil content mg/g, (**b**) total carotenoid content mg/g, (**c**) total triterpenoid content mg/g, (**d**) total flavonoid content mg/g in total extracts of flowers of 23 varieties of *C. officinalis* and their anti-acetylcholinesterase activity value (acha; ic_{50}, µg/ml).**

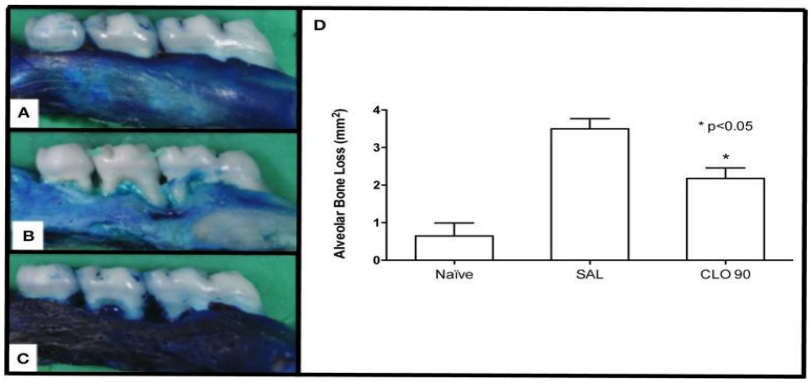

Image 8: Effect of *Calendula officinalis* on rats with experimental periodontitis negetive hemimaxilla (a), hemimaxilla from saline group (b), hemimaxilla tretated with *Calendula officinalis* 90 mg/kg (c), macroscopic analysis (d). bars represent the mean ± sem of 6 animals per group. $^{*}p < 0.05$ was considered to be significantly different compared with saline (anova followed by the bonferroni test). (a–c, 4x magnification).

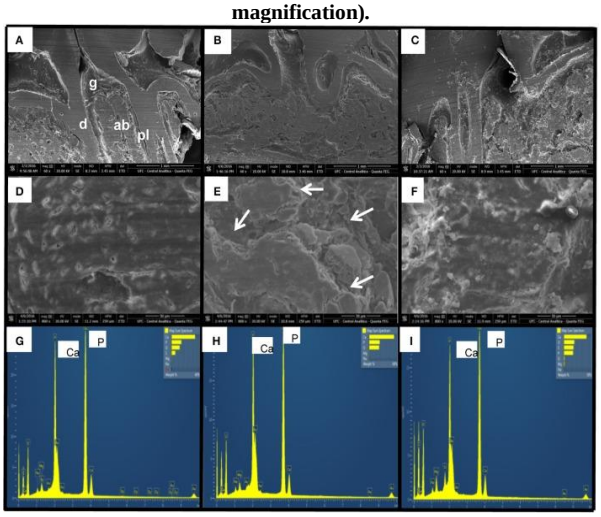

Image 9: Effect of *Calendula officinalis* on topography and mineral distribution of alveolar bone of rats with experimental periodontitis negetive (a,d,g), saline (b,e,h), *Calendula officinalis* (c,f,i). dentin (d); alveolar bone (ab); periodontal ligament (pl); gingiva (g). arrows indicate irregularity on bone tissue. (magnification 60x a–c**; magnification 800x** d–f**).**

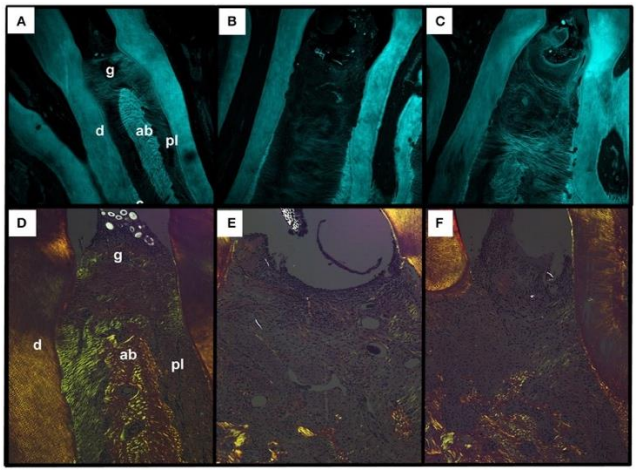

Image 10: Effect of *Calendula officinalis* on collagen fibers of alveolar bone of rats with experimental periodontitis negetive (a,d), saline (b,e), *Calendula officinalis* (c,f). dentin (d); alveolar bone (ab); periodontal ligament (pl); gingiva (g). (magnification 40x).

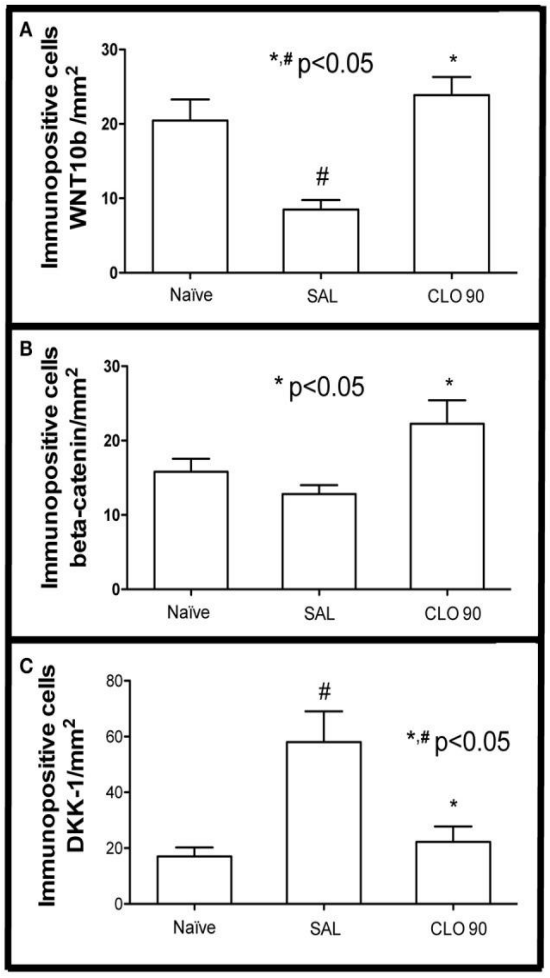

Image 11: Effect of *Calendula officinalis* on quantification of immunopositive cells for markers of wnt pathway. wnt 10b (a)**, beta-catenin** (b)**, dkk-1** (c)**. bars represent the mean ± sem of 6 animals per group. $^{\#}p < 0.05$ was considered to be significantly different compared with negative. $^{*}P < 0.05$ was considered to be significantly different compared with saline (ANOVA followed by the Bonferroni test).**

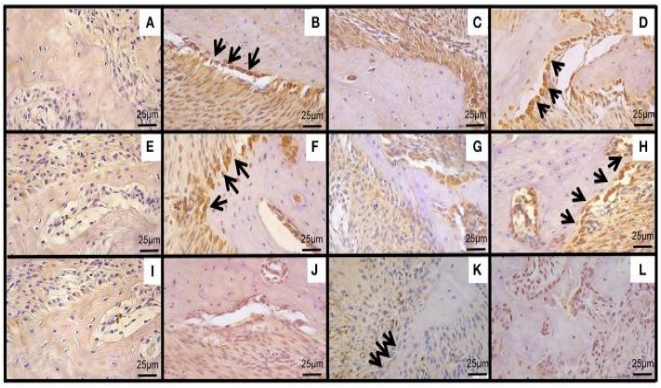

Image 12: Effect of *Calendula officinalis* on immunoexpression of wnt pathway in periodontium of rats with. Wnt 10b (b–d)**, β-catenin** (f–h) **and dkk-1** (j–l)**, between first and second molar of a periodontium from naïve group** (b,f,j)**, periodontium from sal group** (c,g,k)**, periodontium of animals treated with *Calendula officinalis* 90 mg/kg** (d,h,l)**. negative controls of wnt 10b** (a)**, β-catenin** (e)**, dkk-1** (i)**. (magnification 400x). (→) indicate immunopositive osteoblasts. bar = 25 µm.**

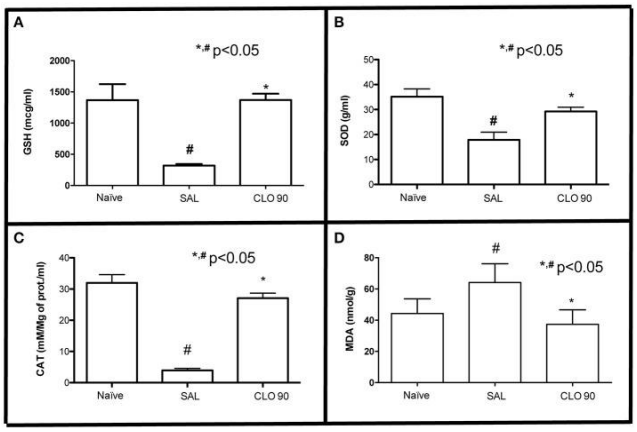

Image 13: Effect of *Calendula officinalis* on oxidative stress markers in gingival tissue of rats with experimental periodontitis glutathione (a), **superoxide dismutase (b)**, **catalase (c)**, **malondialdehyde (d)**. **bars represent the mean ± sem. $^{\#}p < 0.05$ was considered to be significantly different compared with negative. $^{*}p < 0.05$ was considered to be significantly different compared with saline (ANOVA followed by the bonferroni test).**

CONCLUSION

Now a days when the world keeps a turn to the Harbal or Ayurvedic medicine, & Billions of people using those medicine, because of its more effectiveness, at that era *Calendula officinalis* can perform a major role. It shows a variety of actions, which increase the probability & interest of researchers & pharmaceutical industries to research & develop various kind of products using this plant or extracted bio active molecule of this plant.

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