

Therapeutic effects of a topic gel, with hyaluronic acid and other natural extracts, on the healing of gums and oral mucosa

There has been an increase in the use of natural and herbal medicines over the last 15–20 years. There is widespread belief amongst the public that these medicines are safe because they are made from natural sources. Numerous reports have demonstrated the use of traditional plants and natural products in the treatment of oral diseases. The aim of this study was to evaluate the most important research on the natural ingredients found in Oraflogo gel in terms of their ability to heal the soft tissues of the mouth, particularly tissues affected by periodontal disease, ulcers of a traumatic or aphthous nature, and in post-extraction treatment. Oraflogo gel contains natural ingredients like hyaluronic acid, Aloe barbadensis, Macadamia alternifolia, Centella asiatica, Cupressus sempervirens, Horse chestnut, Coenzyme Q10.

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/// THE EFFECT OF VARIOUS NATURAL INGREDIENTS ON WOUNDS IN ORAL PATHOLOGY

• Hyaluronic acid (hyaluronate)

Due to the potential role of hyaluronate in modulating the healing of wounds, applying it to periodontal wounds could achieve comparable beneficial effects in periodontal tissue regeneration and periodontal disease treatment. In the field of dentistry, hyaluronate is proven to have an anti-inflammatory, antiedematous and anti-bacterial effect in the treatment of gingivitis and periodontitis. (1)



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However, it is also possible that the application of hyaluronic acid to periodontal wounds could contribute to periodontal tissue regeneration and periodontal disease treatment.[2]

For the purposes of this study, the Pubmed/Medline database was searched for the keywords "Hyaluronic acid and periodontal disease" and "Hyaluronic acid and gingivitis", which resulted in 89 and 22 articles respectively. Only highly relevant articles from an electronic and manual search within English literature were selected for this review.

In the field of dentistry, hyaluronic acid has shown anti-inflammatory and anti-bacterial effects in the treatment of periodontal diseases. Due to its tissue-healing properties, it could be used as an adjunct to mechanical therapy in the treatment of periodontitis. Further studies are required to determine the clinical efficacy of hyaluronic acid in healing periodontal lesions (3).

• Aloe Barbadensis (Aloe vera)

Aloe vera is a cactus-like, succulent plant which grows in tropical climates. Aloe vera is widely used in a variety of cosmetics including creams and toiletries. Some studies conducted in animals have suggested that Aloe vera may help wound healing (4).

The action of the gel extract as a whole or in single glycoprotein fractions was analysed, either as aloe gel extract complete or in the single components that have been identified in it, namely aloesin, mannose-6-phosphate, G1G1M1DI2 glycoprotein and aloe-emodin. There have been reports of its effects on stimulating the migration and proliferation of keratinocytes and fibroblasts in tissue repair processes (5-8) and also its angiogenetic properties (9). Biologically it also promotes wound healing, and has antifungal, anti-inflammatory, anticancer and immunomodulatory properties. Gingival fibroblasts play an important role in oral wound healing. Double blind-con-

trolled trials are needed to determine its real efficacy in oral health. (10)
Aloe vera has also proved useful in plaque-induced gingivitis (11).

• Coenzyime Q10 (Ubiquinone)

The specific activities of the succinate dehydrogenase-coenzyme Q10 reductase in gingival tissue from patients with periodontal disease were compared with the corresponding specific activities of normal human periodontal tissue. The gingival biopsies from patients with diseased periodontal tissue showed a deficiency of coenzyme Q10, in contrast to those with normal periodontal tissue, which showed no deficiency. The presence or absence of a deficiency of coenzyme Q10 in the succinate-coenzyme Q10 enzyme system is assessed by determining the specific activity in the absence and again in the presence of exogenous coenzyme Q3. An increase in specific activity of this mitochondrial enzyme system in the presence of exogenous coenzyme Q3 reflects the mitochondrial deficiency of coenzyme Q10. Such increases ranged from 38-120% and averaged 81% for the individuals with periodontal disease, and were highly significant statistically (12).
Topical application of Coenzyme Q10 (CoQ10) to the periodontal pocket was evaluated with and without subgingival mechanical debridement. These results suggest that topical application of CoQ10 improves adult periodontitis not only as a sole treatment but also in combination with traditional nonsurgical periodontal therapy (13).
Some other trials have also been carried out on the use of CoQ10 in periodontal disease, and have shown how its topical application has resulted in improvement in the gingival index and bleeding index, both as single treatment and when combined with non-surgical therapy (14,15).

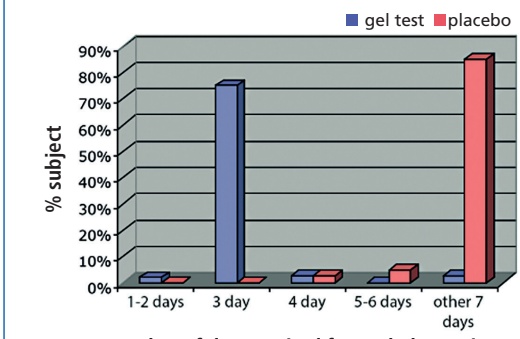
/// MACADAMIA ALTERNIFOLIA (TEA-TREE OIL)

Tea-tree-oil is an essential oil made up of a mixture of at least eight different oils. The antioxidant property is linked with the polyphenols it contains, especially flavonoids, also called catechins; some catechins have demonstrated that they modulate biochemical processes connected with cell proliferation and inflammatory response (16, 17). Although studies are required, the anti-inflammatory properties of oil containing tea-tree oil, when applied topically to inflamed gingival tissues may prove to be a useful non-toxic adjunct to chemotherapeutic periodontal therapy (18).

• Centella asiatica

This is made up of triterpenes (the most effective of which are asiaticoside and asiatic acid), which are able to modulate the development of connective tissue, stimulating cell proliferation, glycosaminoglycan and collagen synthesis. They also promote faster and more effective re-epithelialization, with the formation of a thicker, tighter tissue but without cheloid scar formation. These are responsible for healing wounds and inhibiting scar formation due to their vascular effects. Centella asiatica also promotes angiogenesis and improves capillary circulation (19-22).

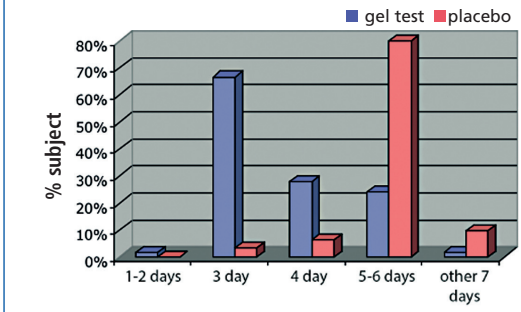
Disappearance of pain



Number of day required for oral ulcer pain to disappear with trial gel and with placebo

Fig.1

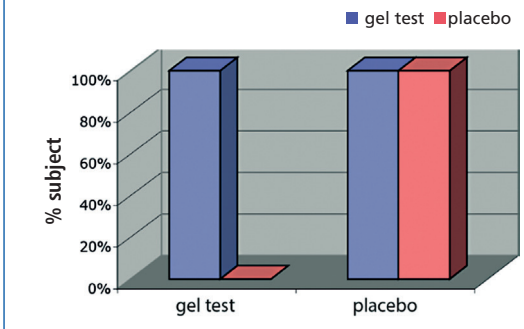
Disappearance of post-extraction bleeding



Number of day required for post-extraction bleeding to stop with trial gel and placebo

Fig.1

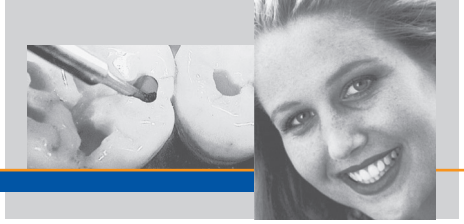
Givingal bleeding



Givingal bleeding index

Fig.3

Centella asiatica is commonly used for wound healing and microangiopathy (23 -25). It has been found to increase collagen production and stimulate cellular hyperplasia in granulation tissue due to higher levels of DNA, protein, and hexosamine (26). In studies, the tensile strength of the healing wound was enhanced through greater cross-linking of collagen, as well as a more rapid re-epithelialization process (27- 28). Centella asiatica has also been found to reduce activity levels of ß-glu, an enzyme that is often elevated at sites of gingival inflamma-



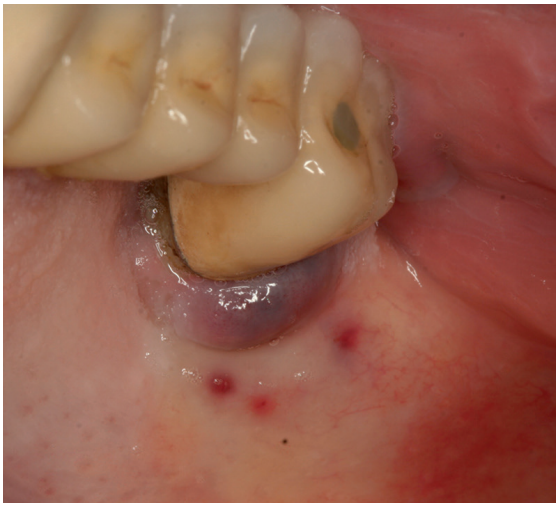


Figure 1a - Periodontitis with a deep pocket (6mm), bleeding, wobbly tooth, pain on pressure

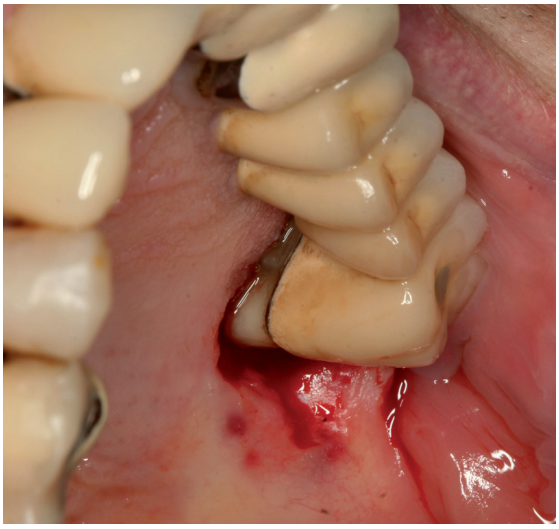


Figure 1b - Surgical gingiva wound following gingivoplasty and cleaning of root surfaces

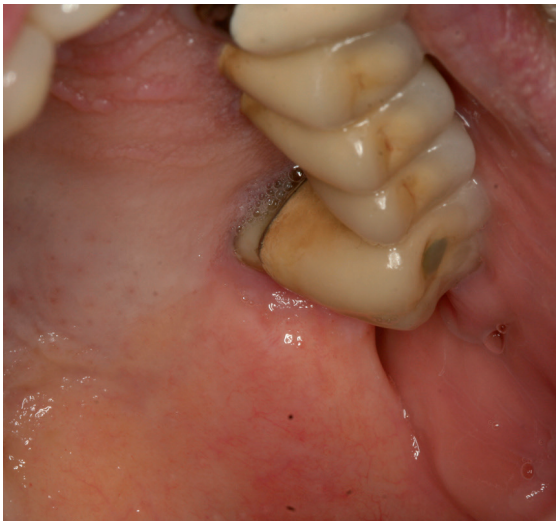


Figure 1c - Completely healed wound, day 7 after surgery, with the use of trial gel containing hyaluronic acid and herbal extracts

tion (28). Sastravaha et al. studied the effects of Centella asiatica, implanted together with the herb Punica granatum as a biodegradable chip in the subgingiva. There was a significant improvement of the GI score with respect to subgingival implants when compared to controls at 3 and 6 months, while PI scores between the groups did not differ (29). Centella asiatica has demonstrated antibacterial activity in an in vitro model (30).

• Aesculus hippocastanum (horse chestnut)

Horse chestnut extracts have been traditionally employed both in the West and East for the treatment of peripheral vascular disorders including hemorrhoids, varicose veins, leg ulcers and bruises (31). It is used in the treatment of chronic venous insufficiency and peripheral edema (32).
The principal extract and medicinal constituent of horse chestnut seed is aescin, a mixture of triterpenoid saponin glycosides (33, 34).
Aescin decreases the transcapillary filtration of water and proteins. It has been used to treat a wide variety of inflammatory and edematous conditions, to reduce swelling associated with bruises, fractures, brain trauma, post-operative and post-traumatic soft tissue swelling, and acute thrombophlebitis (35, 34). Aescin reduces lysosomal enzyme activity by stabilizing lysosomal membranes and limiting enzyme release (34, 36). Aescin also improves venous tone by enhancing the constricting effect of noradrenaline.
Aesculus hippocastanum (horse chestnut) has an antibacterial effect against the oral microorganisms which play a major role in dental problems such as dental caries and periodontal disease. Horse chest nut seed extract is found to be active against oral microbes like streptococcus mutans, streptococcus salivarius, streptococcus mitis, streptococcus sanguis and Lactobacillus acidophilus (37).

• Cupressus sempervirens

Its dried fruit is used to treat inflammation, toothache, and laryngitis and as a contraceptive and astringent (38). In addition, its dried seeds have been used to treat wounds, ulcers, bruises, sores, pimples, pustules, skin eruptions and erysipelas. The essential oil from the leaves and cones is used externally for headaches, colds, cough, and bronchitis. Given these medicinal and pharmacological advantages, Cupressus sempervirens is widely used as a cosmetic ingredient in perfumery and soap-making, including its essential oil distilled from shoots (39).

Few studies have investigated their antimicrobial activities (40-42).
Cupressus sempervirens essential oil may also be taken into consideration when developing products for controlling microbial infections. Results indicate the possibility of using the extract originating from Cupressus sempervirens as effective inhibitors of biofilm in K. pneumoniae. This is the first report in the literature on the antibiofilm activities of Cupressus sempervirens essential oil. The isolated compounds are expected to be useful for the study of antibiofilm agents in the future (43).

It has also been reported that the extracts obtained from

Cupressus semipervirens has an antiviral effect against Herpes Simplex Virus Type 1. Different parts of this medicinal plant were tested and the fruit's extract appeared to possess the strongest anti- HSV activity. In conclusion, all of the extracts tested in this survey showed significant antiviral potency (44).

• Trigonella foenum graecum

Some research focused on plant medicines used in traditional medicine as they could be good sources for natural analgesic agents. There are several reports on the antinociceptive and anti-inflammatory effects of Trigonella foenum graecum seeds in Moroccan traditional medicine (Bellakhdar, 1997). This plant is known to contain alkaloids, saponins, flavonoides, Sali-cylate, and nicotinic acid (Saxena and Shalem, 2004; Yingmei et al., 2001). The present study was designed to investigate if the Tfg seeds extract has antinociceptive effect.

Trigonella foenum-graecum L. (Leguminosae), known in Morocco as "Helba", is used in folk medicine for its anti-ulcer, anti-inflammatory, cicatrizing activities and to treat various pain-related physiological conditions. The cited study attempted to verify the possible antinociceptive action of different extracts obtained from the seeds of this plant. Three experimental models were used (acetic acid, formalin, and hot-plate tests) in order to characterize the analgesic effect. The extracts significantly, and in a dose-dependent manner, reduced the pain. The results suggest that the compounds present in the extracts activated both central and peripheral mechanisms to elicit the analgesic effect (45).

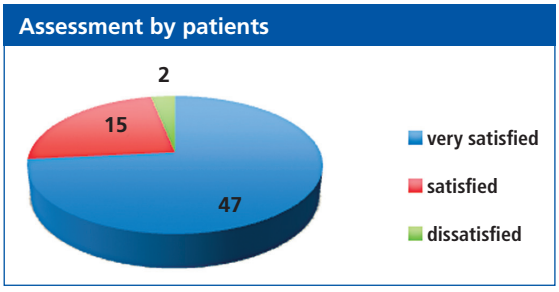


Chart 1: Assessment of satisfaction with Oraflogo gel by all patients participating in the study (figures in the chart represent the number of patients).

/// COMBINATION OF HYALURONIC ACID WITH ALOE BARBADENSIS, MACADAMIA ALTERNIFOLIA, CENTELLA ASIATICA, CUPRESSUS SEMPERVIRENS AND COENZYME Q10) ON THE HEALING OF GUMS AND ORAL MUCOSA

Given its different components, this combination demonstrated cicatrizing, anti-hemorrhagic, analgesic and anti-inflammatory capacities on soft tissue, contributing in particular to reducing the pain connected with ulcerative lesions of the mouth and following operations to extract dental elements, as well as bleeding linked with gingival inflammation and surgical operations on the mouth (46). Results of a second study show significantly greater patient satisfaction with the gel (hyaluronic acid, Q10 and herbal extracts) when applied to heal wounds in the oral cavity, alleviate pain, reduce bleeding and oedema, compared with previous products the patients had been using to alleviate their problems (Chart 1, Figures 1)(47).

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An attempt has been made to outline the natural ingredients in Oraflogo gel in order to evaluate their effect in oral pathology. Separately, these ingredients have been recognized as beneficial to oral medicine. Results are particularly good when a combination of these natural ingredients are found in the form of a topical gel as they serve to reduce postsurgical bleeding, gingival bleeding and periodontal diseases. Using appropriate concentrations of these natural extracts in a pharmaceutical gel form may yield promising results in the healing of soft oral soft tissue.

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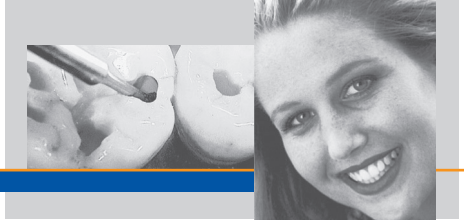
16_)_ _K_a_t_i_y_a_r_ _S_K_,_ _A_h_m_a_d_ _N_,_ _M_u_k_t_h_t_a_r_ _H_S_._ _G_r_e_e_n_ _t_e_a_ _a_n_d_ _s_k_i_n_._ _A_r_c_h_ _D_e_r_m_a_t_o_l_ _2_0_0_0_;_1_3_6_:_9_8_9_-_9_9_4_._ _

17)_K_a_t_i_y_a_r_ _S_K_,_ _M_a_t_s_u_i_ _M_S_,_ _E_l_m_e_t_s_ _C_A_,_ _M_u_k_t_h_t_a_r_ _H_S_._ _P_o_l_y_p_h_e_n_o_l_i_c_ _a_n_t_i_o_x_i_d_a_n_t_ _–)_-_e_p_i_g_a_l_l_o_c_a_t_e_c_h_i_n_-_3_-_g_a_l_l_a_t_e_ _f_r_o_m_ _g_r_e_e_n_ _t_e_a_ _r_e_d_u_c_e_s_ _U_V_B_-_i_n_d_i_c_e_d_ _i_n_f_l_a_m_m_a_t_o_r_y_ _r_e_s_p_o_n_s_e_s_ _a_n_d_ _i_n_f_i_l_t_r_a_t_i_o_n_ _o_f_ _l_e_u_k_o_c_y_t_e_s_ _i_n_ _h_u_m_a_n_ _s_k_i_n_._ _P_h_o_t_o_c_h_e_m_ _P_h_o_t_o_b_i_o_l_ _1_9_9_;_6_9_:_1_4_8_-_5_3_._ _

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