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File: ■ Mangosteen (*Garcinia mangostana*, Clusiaceae)
■ Propolis
■ Gingivitis
■ Periodontitis

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RE: Mangosteen and Propolis Extract May Reduce Gingivitis

Park J-Y, Ko K-A, Lee J-Y, et al. Clinical and immunological efficacy of mangosteen and propolis extracted complex in patients with gingivitis: a multi-centered randomized controlled clinical trial. *Nutrients*. July 2021; 13(8):2604. https://doi.org/10.3390/nu13082604.

Gingivitis is an inflammatory condition, caused by the accumulation of dental biofilm, and associated with gingival swelling and redness. Often gingivitis can progress unnoticed to periodontitis which can cause permanent loss of teeth. Good oral hygiene is key to treating and preventing both inflammatory disorders. Standard care for periodontitis involves mechanical debridement and topical antimicrobials. Research has shown that immunity is linked to the inflammation and destruction of the periodontium. Immune-modulation therapies have been used; however, these therapies have adverse side effects. Mangosteen (*Garcinia mangostana*, Clusiaceae) fruit has been traditionally used to treat diarrhea, infected wounds, suppuration, and chronic ulcers. Propolis from bees is used for its antimicrobial, anti-inflammatory, and antioxidant properties. The authors proposed an eight-week, multi-centered, double-blinded, parallel-armed, placebo-controlled randomized clinical trial to test the clinical, immunological, and patient-reported outcomes of mangosteen and propolis extract (MAEC) on patients with gingivitis and incipient periodontitis.

This study was conducted between September 2019 and March 2020 in South Korea at the Department of Periodontology, Yonsei University Dental Hospital; Department of Periodontology, Kyung Hee University Dental Hospital; and Veterans Health Service Medical Center. The inclusion criteria included patients diagnosed with generalized or localized gingivitis or stage 1 periodontitis who are between 20 and 75 years old, are generally in good health, have a minimum of 18 teeth, have bleeding on probing sites of > 10%, and have at least one tooth with probing depth of > 3 mm and ≤ 5 mm. Exclusion criteria were failure to provide written informed consent, received preventive periodontal therapy within three months, have a serious oral mucosal disease, have > 5 carious teeth, diagnosed with chronic moderate or advanced periodontitis, smoke, have taken antibiotics within the last three months, have uncontrolled diabetes, have elevated aspartate transaminase or alanine aminotransferase levels > 3x the upper limit of

normal, have creatinine level > 2x the upper limit of normal, have a bleeding disorder or history of hemorrhage, take antiplatelet or anticoagulant medication, have a significant cardiovascular, immunological, infectious, or oncological illness, have a mental illness, are allergic to the test substance, pregnant or lactating, are participating in other clinical trials, or are judged to be unsuitable for study inclusion by the clinician.

At baseline, week 4, and week 8 the following clinical parameters were recorded: gingival index (GI), probing depth (PD), clinical attachment loss (CAL), plaque index (PI), bleeding on probing (BOP), and gingival recession (GR). The following salivary and crevicular fluid biomarkers were also recorded: interleukin-1β (IL-1β), interleukin-6 (IL-6), matrix metalloproteinase-8 (MMP-8), matrix metalloproteinase-9 (MMP-9), and oral health impact profile (OHIP-14). Nutritional and immunological analyses were also performed.

Patients were randomly allocated to the test group and control group. The test group received one capsule containing 194 mg of MAEC daily for eight weeks and the control group received a placebo daily for eight weeks. The dosage and extraction ratio of 1:35 by weight mangosteen to propolis for MAEC was used. The extraction included α-mangostin from the pericarp of mangosteen fruit and the total flavonoids from propolis. The MAEC also contained lactose powder, microcrystalline cellulose, sucrose esters of fatty acids, magnesium stearate, and silicon dioxide. The placebo contained lactose powder, microcrystalline cellulose, magnesium stearate, caramel color, and food blue No. 1. It was not stated if the capsules appeared similar, how testing was performed for the MAEC, or the origin of the ingredients.

Patients were not provided with oral prophylaxis at the beginning or during the study. Patients were to continue their daily oral hygiene and avoid consumption of foods containing mangosteen and propolis. After the study, scaling was provided for those who completed the study.

Of the 104 patients that were enrolled, seven were lost due to deviation from inclusion and exclusion criteria (n = 6) and to follow-up (n = 1). This left 48 in the MAEC group and 49 in the control group. After analysis, it was found that 10 patients attended outside the visit window, four failed to sign the consent forms, and three had taken contraindicated medications, leaving 41 in the MAEC group and 39 in the control group for final analysis. The mean age for the placebo group was 33.41 ± 6.89 with seven males and 32 females. The MAEC group had 12 males and 29 females with a mean age of 35.95 ± 10.64. There were no significant differences between groups at baseline.

It was found that the MAEC group had a significant improvement in GI compared to placebo at week 4 ($P = 0.018$) and week 8 ($P = 0.041$). PD, CAL, PI, BOP, and GR showed no significant difference between groups. There was a significant reduction in the MAEC group between baseline and week 8 for IL-6 ($P = 0.006$), an increase in MMP-9 ($P = 0.041$), and a significant decrease in MMP-9 for the placebo group ($P = 0.022$); however, when adjusting for covariates and full analysis, there was no significant difference for salivary markers. There was a significant worsening in OHIP-14 for the control group between baseline and week 4 ($P = 0.034$) and between placebo and MAEC ($P = 0.049$) at four weeks.

There were eight patients who reported nine mild adverse effects in the MAEC group, and eight patients in the placebo group who reported 10 mild adverse effects. There

were no significant differences between groups. The most frequent adverse effects were infection or parasitic infection and acute gastroenteritis.

The authors conclude that there is a significant reduction in GI when using MAEC, and it could potentially have anti-inflammatory effects. More research is needed with a larger trial group to verify these results. It was determined that MAEC was safe and did not have major adverse effects. The authors conclude no conflict of interest.

—Dani Hoots

Referenced article can be accessed at https://www.mdpi.com/2072-6643/13/8/2604.