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File: ■ Pineapple (*Ananas comosus*, Bromeliaceae)
■ Bromelain
■ Inflammation

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RE: Bromelain Improves Facial Swelling following Oral Surgery

Bormann KH, Weber K, Kloppenburg H, Koch A, Meiser P, Gellrich NC. Perioperative bromelain therapy after wisdom teeth extraction – a randomized, placebo-controlled, double-blinded, three-armed, cross-over dose-finding study. *Phytother Res*. December 2016;30(12):2012-2019.

Bromelain is an extract comprised of protease enzymes from pineapple (*Ananas comosus*, Bromeliaceae) fruit. Bromelain is studied for its anti-inflammatory and digestive health properties, including the reduction of pain and inflammation resulting from surgery. The determination of adequate dosing for bromelain based on empirical evidence is lacking, according to the authors of this study. As a result, a randomized, 3-armed, placebo-controlled, crossover study was performed with bromelain to determine dose dependence in a population of healthy subjects after surgical removal of wisdom teeth.

A total of 75 healthy subjects, aged 15-40 years, with intact wisdom teeth were recruited for a study conducted at the Department of Oral and Maxillofacial Surgery, Hannover Medical School; Hannover, Germany. Subjects were randomly assigned to 1 of the 3 dosage arms consisting of a combination of bromelain tablets (Bromelain-POS®; URSAPHARM Arzneimittel GmbH; Saarbrücken, Germany) and an identical placebo tablet. Treatment groups included bromelain dosages of 1000, 3000, and 4500 FIP (Fédération Internationale Pharmaceutique) standardized units vs placebo. All subjects consumed either one of the active doses of bromelain or placebo tablets, 3 times per day, for 9 days after surgery.

Subjects acted as their own control, undergoing 1 surgery with an active dose, and the other surgery with placebo. Each surgery removed either molars 18 and 48 (right side of face) or molars 28 and 38 (left side). All subjects had a 4-week washout and recovery period between the first and second surgery. Subjects were given rescue medication of 20 acetaminophen tablets (500 mg) to be taken as needed.

Endpoints included 3D face scanning (FaceScan3D; 3D-Shape GmbH; Erlangen, Germany) to detect swelling of the face based on a phase-measuring triangulation

method. The output of the measurement is a "wire-mesh representation" of the face that can be used to measure differences in facial volume in milliliters (mL). Area under the curve (AUC) of facial volume was the primary endpoint, and secondary endpoints included maximum facial volume, visual analog scales for pain and difficulty in swallowing, and postoperative use of analgesics. All endpoints were measured before surgery and days 2, 4, and 7 post-surgery.

Sixty-eight subjects completed the study and were analyzed in a modified intent-to-treat analysis. No differences in baseline group characteristics were observed. The number of adverse events among study groups was the same. No significant effects were observed in any study group, although a trend for reduced swelling of approximately 20% was observed for all pooled bromelain dosage groups compared to placebo (P=0.089). No dose dependency was observed, and the most benefits appear to have been in the lowest dosage (1000 FIP) group. Analysis of pooled treatments trended towards increased effectiveness of bromelain versus placebo for all assessments.

The authors list some study limitations, such as the potential lack of validation for the 3D face scanning measurement, and the lack of controls for the use of rescue analgesics and local use of cooling and topical medications. The authors suggest that future studies should consider combining the parameters used in this study to better understand the overall clinical benefit of the treatment.

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—*Blake Ebersole*