

*Full Length Research Paper*

## Effects of antimicrobial herbal palatal mucoadhesive tablet on oral malodor in dogs.

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Canine oral malodor is a common complaint among dog owners. The aim of this study was to test the effect of an antimicrobial herbal palatal mucoadhesive tablet on oral malodor in dogs. Twelve dogs suffering from oral malodor participated in the study. Palatal mucoadhesive tablets were prepared with or without the herbal medicinals: Echinacea (*Echinacea angustifolia*), Mastic gum (*Pistacia lentiscus*), Lavender (*Lavandula angustifolia*) and Sage (*Salvia officinalis*). Measurement included odor judge scores (two judges) and volatile sulfide compounds (VSC) readings by a sulfide monitor (Halimeter<sup>®</sup>). Application of the palatal adhesive tablets containing herbal formulation resulted in a 60% reduction in oral malodor scores and 73% in VSC levels. These results suggest that the palatal mucoadhesive tablets containing herbal formulation may serve as an effective means of treatment for oral malodor in dogs.

**Key words:** Herbal medicinals, mucoadhesive, dogs, oral malodor.

### INTRODUCTION

Canine oral malodor is a common complaint among dog owners. This disturbing condition may have a negative effect on owner-companion relationship (Simone et al., 1994). In most cases, canine oral malodor originates from the oral cavity itself (Culham and Rawlings, 1998; Eubanks, 2006; Hennes et al., 1995), and is considered to result from the proteolytic activity of anaerobic Gramnegative oral bacteria (Hennes et al., 1995). These bacteria break down salivary and oral proteins into their amino acid building blocks. Some of these amino acids (for example, methionine and cysteine) are further metabolized yielding malodorous volatile sulfide compounds (VSC) such as methylmercaptan and hydrogen sulfide (Persson et al., 1990). The measurement of these compounds in the oral cavity using a portable sulfide monitor has been

previously shown to correlate with oral malodor levels in dogs (Hennes et al., 1995). Maintaining good oral health is considered the most important factor in preventing this condition. Professional treatment and good oral hygiene were shown to be most effective in reducing oral malodor levels (Gorrel and Bierer, 1999; Gorrel et al., 1999). However, in case that the dog cannot withstand standard treatment or when mechanical treatment is insufficient, the use of antibacterial agents should be incorporated. We have previously demonstrated the antibacterial activity of Echinacea (*Echinacea angustifolia*), Mastic gum (*Pistacia lentiscus*), Lavender (*Lavandula angustifolia*) and Sage (*Salvia officinalis*) against malodor producing bacteria (Sterer and Rubinstein, 2006). The use of oral bioadhesive tablets as a means of administering local chemical antiseptics to dogs has been previously reported (Gruet et al., 1995). The aim of this study was to test the effect of these herbal active ingredients delivered using a sustained release mucoadhesive tablet on oral malodor reduction in dogs.

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## MATERIALS AND METHODS

### Preparation of mucoadhesive tablets

Mucoadhesive tablets were prepared under GMP conditions as previously described by Sterer et al. (2008), whereas the adhesive polymers hydroxypropyl cellulose (Hercules Co., Wilmington, DE) and carbopol (Goodrich Co., Cleveland, OH) were mixed in a ratio of 4:1. The mixture (250 mg) with or without the active herbal ingredients (as placebo) were pressed for 30 s at a pressure of 3 ton/cm<sup>2</sup> into a mold using a laboratory Carver press (Carver Machine Works, Inc, In, USA). This process produced tablets of 12 mm in diameter and 2.5 mm in thickness with one side flat and the other side curved to fit the shape of the palate.

The active ingredients included four herbal medicinals: Echinacea (*Echinacea angustifolia*), Mastic gum (*Pistacia lentiscus*), Lavender (*Lavandula angustifolia*) and Sage (*Salvia officinalis*), supplied as dried powders (SupHerb, Nazerat Iit, IL).

### Study population

This study included twelve dogs of various breeds whose owners complained about their oral malodor. The dogs ranged in age from 1-14 years (mean of 7.1) and ranged in weight from 6-34 kg (mean of 16.5). All the dogs that participated in the study did not receive any kind of home dental care or took antibiotics in the month prior to the study. The experimental protocol was reviewed and approved by the animal research facility of the Hebrew University on 13th of May, 2005.

### Experimental protocol

Dog owners were instructed to avoid feeding or watering the dogs for two hours prior to the experiment. Measurements (described in detail subsequently) included odor judges' scores and volatile sulfide measurements.

The dogs were randomly assigned into one of the two treatment groups: (i) palatal herbal mucoadhesive tablet (HMT) (Treatment group, n=6), (ii) palatal mucoadhesive tablet without any active ingredients (Placebo, n=6). Following baseline measurements of oral malodor-related parameters by two odor judges and a sulfide monitor, the mucoadhesive tablets were applied to the dogs' palates. Measurements were repeated four times more (30, 60, 90 and 120 min) following application.

### Organoleptic measurements

Oral malodor was scored by two trained and calibrated odor judges, who were blinded to one another's scores, as well as to the other data. Malodor was scored using a semi integer scale of 0-5 with description as follows: 0 –

no odor, 1 - barely noticeable odor, 2 - slight but clearly noticeable odor, 3 - moderate odor, 4 - strong odor, 5 - extremely strong odor (Greenman et al., 2004).

### Sulfide monitor

Intra-oral headspace volatile sulfide levels were determined by means of a portable sulfide monitor (Halimeter®, Interscan). The monitor was zeroed on ambient air, and the measurements were performed by the insertion of a disposable ¼-inch plastic straw approximately 5 cm into the partially opened oral cavity. Dogs' mouths were held open by the clinician during measurements. Results were recorded as peak ppb hydrogen sulfide equivalents.

### Statistical analysis

To compare the quantitative variables (sulfide monitor measurements of VSC levels), ANOVA was applied, while for the rank variables (odor judge scores), the Mann-Whitney non-parametric test was applied for pairwise comparisons. The Spearman non-parametric correlation coefficient was calculated to estimate the association between pairs of variables. All the tests applied were two-tailed, and p≤0.05 was considered as statistically significant.

## RESULTS

Results (mean results ± standard deviation) of the odor judges' scores and sulfide monitor readings are presented in Figures 1 and 2. The treatment group (herbal mucoadhesive tablet, HMT) showed moderate significant reduction of 60% in malodor ratings (p=0.02), and 73% in VSC levels (p=0.045), following treatment as compared to baseline. The treatment group maintained malodor ratings of under 2 and VSC levels of under 50 ppb at the end of the experiment. No change was observed in both malodor-related parameters in the placebo group, however malodor and VSC levels remained high (over 3.5 and 250 ppb, respectively). Besides, no difference was observed between the two groups at baseline.

The strength of the association between the different parameters was evaluated using the Spearman correlation (Table 1). The scores of the two odor judges were highly correlated with the VSC levels (p<0.01) as well as with the scores of one another (p=0.028).

## DISCUSSION

The active herbal ingredients (Lavender, Echinacea, Sage and Mastic gum) demonstrated selective antibacterial activities, VSC conversion properties and proteolysis inhibition abilities (Sterer and Rubinstein, 2006). In this study, the efficacy of this mode of treatment

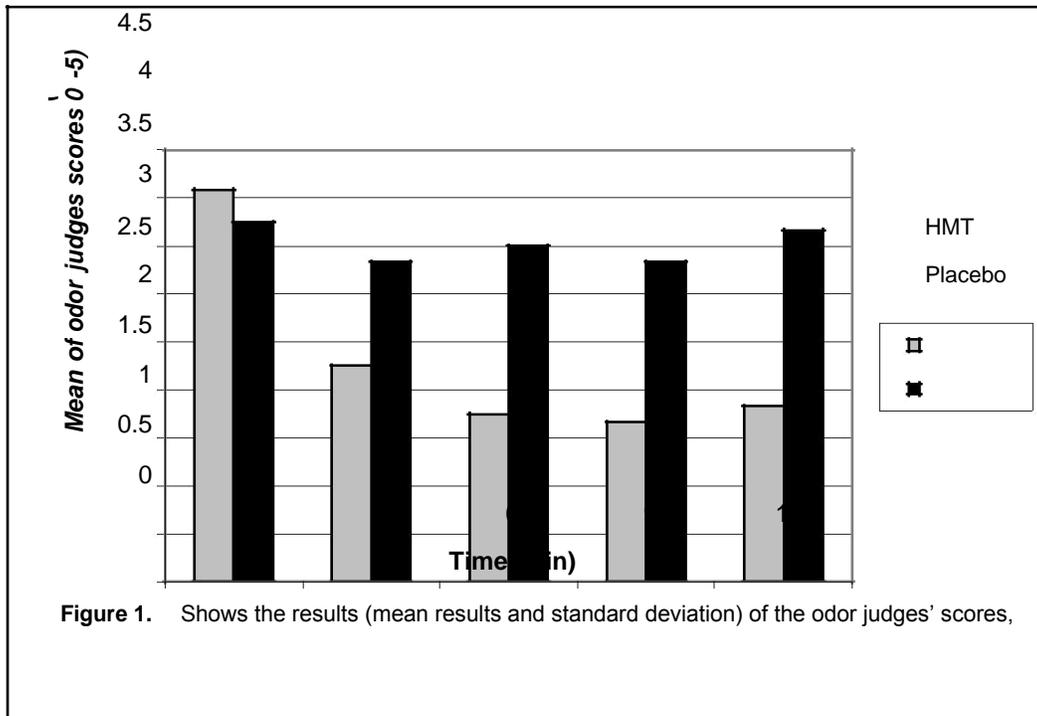


Figure 1. Shows the results (mean results and standard deviation) of the odor judges' scores,

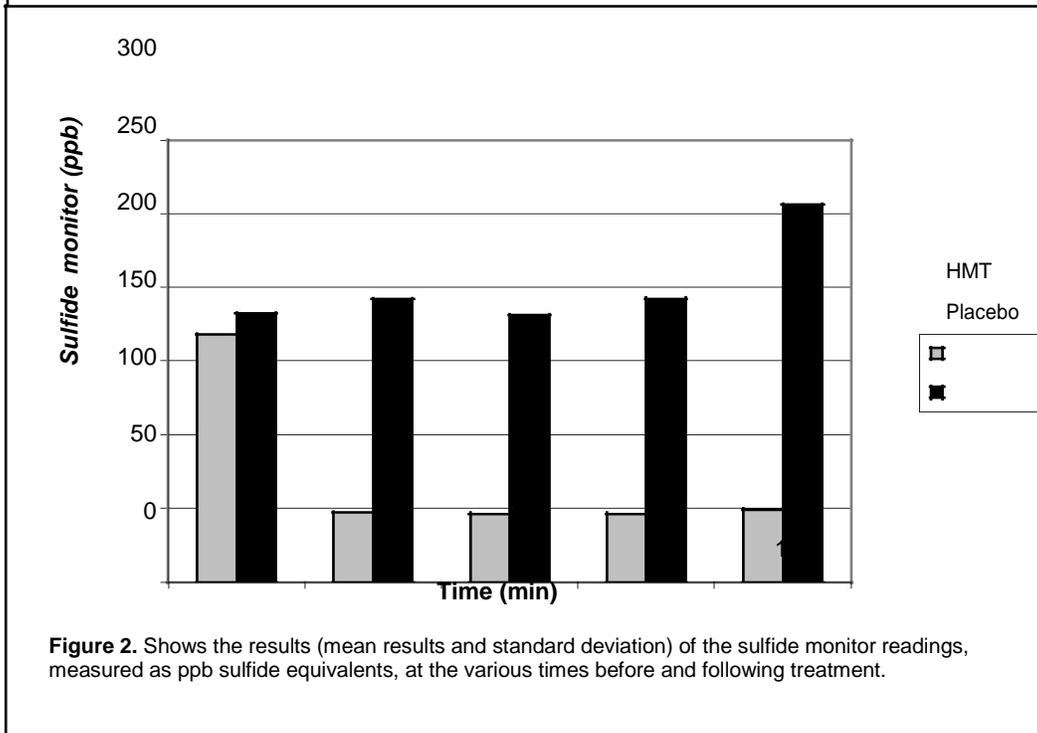


Figure 2. Shows the results (mean results and standard deviation) of the sulfide monitor readings, measured as ppb sulfide equivalents, at the various times before and following treatment.

Table 1. Spearman correlation among malodor parameters (n=12).

|              | Sulfide monitor   | Odor judge 2      |
|--------------|-------------------|-------------------|
| Odor Judge 1 | r=0.66<br>p=0.007 | r=0.54<br>p=0.028 |
| Odor Judge 2 | r=0.61<br>p=0.01  |                   |

was tested on reducing canine oral malodor.

Results indicated that the adhesive tablet containing the herbal formulation is effective in reducing oral malodor and VSC levels in dogs. Malodor scores and VSC levels were reduced below noticeable levels (odor judge scores <2; sulfide monitor readings <50 ppb), following treatment with the active tablets. The fact that malodor scores and VSC levels in the placebo group remained high (odor judge scores >3.5; sulfide monitor readings >250 ppb) confirmed that the herbal formulation is indeed the active cause for this reduction.

Despite its relatively subjective nature, odor judge scores remain the golden standard for oral malodor measurements. However, the measurement of volatile sulfides, a malodor related parameter, using a sulfide monitor was previously shown to be highly associated with oral malodor scores in dogs (Hennet et al., 1995). In this study, both odor judges' score were highly associated with the sulfide monitor readings yielding spearman correlation coefficients of 0.66 and 0.61 (odor judges 1 and 2, respectively) similar to those of other studies (Hennet et al., 1995; Culham and Rawlings, 1998). Furthermore, significant correlation was seen between both judges.

Despite the fact that the tongue dorsum is considered as the most common source for oral malodor in humans (Delanghe et al., 1997), most studies addressing this issue in dogs regard periodontal disease as the prime cause. In this study, regardless of the fact that all the dogs suffered from oral malodor, only one-third of them showed any signs of periodontal disease (data not shown). This combined with the results of the study suggests that the tongue dorsum may play an important role in oral malodor in dogs as well.

Most researchers and clinicians agree that oral hygiene for both professional and home care is essential in treating oral malodor in dogs (Rawlings and Culham, 1998a, b). However, in some cases, the malodor persists even following dental treatment. Furthermore, some dogs cannot withstand the general anesthesia required for these procedures due to poor health or advanced age. In these cases, the use of antibacterial agents may help to alleviate this condition. Results of this study suggest that the herbal mucoadhesive tablet may serve as an effective mean to achieve this goal and offer an effective reduction of oral malodor in dogs.

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