Evaluation of the Palatability of Three Nonsteroidal Antiinflammatory Top-Dress Formulations in Horses*

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The efficacy of top-dress antiinflammatory drugs ultimately depends on a patient's willingness to consume treated feed. The current study compares the palatability of two phenylbutazone top-dress formulations (Equipalazone Powder, Dechra Pharmaceuticals, and Pro-Dynam, VetXX, Ltd.) and a suxibuzone top-dress formulation (Danilon Equidos, Janssen Animal Health). Results of a three-period, crossover study on 18 healthy horses showed that Pro-Dynam was significantly less palatable, with significantly less consumption of treated feed compared with either Equipalazone Powder or Danilon Equidos. There was no statistically significant difference in terms of consumption of treated feed and palatability scores between Equipalazone Powder and Danilon Equidos.

INTRODUCTION

Lameness from arthritis or musculoskeletal injury accounts for a substantial proportion of the caseload for equine practitioners. Treatment commonly includes NSAIDs, which have a long history of use because of their analgesic and antiinflammatory properties. Phenylbutazone and related compounds (e.g., suxibuzone) are the most commonly prescribed NSAIDs in equine medicine. Oral administration is the most common dosing form and is considered safer and more practical than parenteral administration.

Feed consumption in horses is driven largely by pregastric stimuli related to appearance, taste, odor, and texture (i.e., those features of feed that are sensed before it is swallowed and of which an animal is consciously aware). Palatability can therefore be defined as those characteristics of a feed that trigger sensory re-
sponses by olfactory, gustatory, and tactile stimuli and is the primary influence on the choices made by the animal during foraging and chewing.\(^5\) Palatability in ruminants is best measured by comparison of the intake of more than one feed offered simultaneously, because intake will then be independent of satiety control mechanisms.\(^5\) In horses, however, palatability of medicated feed is not affected by pretreatment fasting.\(^3\) Horses will selectively consume particular elements (e.g., oats\(^8\)) out of a feed mixture and exhibit individual preferences when a variety of foodstuffs is available.\(^9\) In one study, for example, four of five horses showed a preference for sucrose solution instead of water while one horse had zero intake of sucrose solution\(^10\); in another study, four of five ponies preferred diets containing sucrose.\(^11\) Horses offered a choice of forage types have been shown to eat a greater proportion of the forage type that they have been fed previously.\(^12\)

Few studies have evaluated the palatability of top-dress pharmaceutical products in horses. Medicated grain rations have been completely refused by some horses\(^7\) or consumed in varying amounts initially but then eaten in their entirety.\(^13\)

Various NSAIDs are marketed for top-dress application to feed. However, the efficacy of any top-dress formulation ultimately depends on the patient’s willingness to consume treated feed. The current study was designed to determine whether three top-dress NSAID formulations are equally palatable to horses.

**MATERIALS AND METHODS**

Eighteen adult horses (12 mares and 6 geldings) were obtained from commercial sources or from the resident facility herd. The horses were typical light saddle breeds: 11 grade horses (i.e., no specific breed), four Tennessee walking horses, two quarter horses, and one Appaloosa. Ages ranged from 2 to 16 years (median, 6.5 years), and body weights ranged from 303 to 508 kg. Before enrollment, all candidate horses were treated with an approved anthelmintic to remove existing parasitic infections and vaccinated with tetanus toxoid as appropriate. No medications or therapies other than the study treatments were administered during the remainder of the study.

The health status of all animals was determined by physical examination 9 days before trial initiation (day –9); all were in good health. Horses were acclimated to the test facility for 9 days under the food, water, housing, and ambient temperature conditions that would be experienced during the study. Ambient conditions were monitored continually but were not controlled. Animals were housed individually in similar pens, which were assigned before randomization so that treatment group could not be identified by pen location.

Horses were fed a commercial concentrate feed consisting of a mixture of extruded pellets, cracked corn, and hulled oats (Co-Op 11% Sweet Horse Feed Coarse, Tennessee Farmers Cooperative, Lavergne, TN). Each animal was offered a daily quantity of this feed, equal to approximately 0.5% of its body weight, divided into two similar portions offered in the morning and evening. Each horse was also offered a quantity of grass hay equal to 2% of its body weight (similarly divided into morning and
evening portions). Nonmedicated water, supplied by a local utility, was available ad libitum.

**Study Procedures**

This study was a three-period, crossover design comparing the palatability among three top-dress NSAID products: two phenylbutazone formulations (Equipalazone Powder, Dechra Pharmaceuticals [A], and Pro-Dynam, VetXX, Ltd., Thame, Oxfordshire, UK [B]) and one sulibuzone formulation (Danilon Equidos, Janssen Animal Health, High Wycombe, Buckinghamshire, UK [C]). The three study formulations were commercial products obtained from commercial sources packaged in individual sachets containing 1.0 g phenylbutazone or 1.5 g sulibuzone powder for top-dress application. One sachet was sprinkled over the concentrate feed immediately before the morning presentation to the horse. Because the test articles were not identical in appearance or total quantity, the personnel administering the test articles were not involved in the palatability scoring.

One day before initiation of treatment (day –1), horses were ranked by decreasing body weight, with each three consecutively ranked horses comprising a replicate. Six replicates totaling 18 horses were enrolled. Within a replicate, horses were randomized to one of three treatment sequences: sequence 1 (ABC), sequence 2 (BCA), or sequence 3 (CAB) using a random number generator. Animals were dosed with the initial treatment once each morning for 3 consecutive days, followed by a 4-day washout period during which no treatments were given. This process was then repeated for subsequent treatments in the sequence (e.g., B followed by C for sequence 1) until all three products had been administered to each animal.

Each horse was observed immediately after treatment for possible rejection of the test product. Numeric scales were then used for subjective assessment of interest and palatability (see box, left). Any treated concentrate feed that was not consumed within 20 minutes after dosing was collected and weighed to calculate the total amount consumed. The amount of top-dress formulation remaining was estimated using a subjective scoring system (see box).

Animals were monitored twice daily for hay and water consumption. Clinical health observations were conducted once daily by either the clinical investigator (a veterinarian) or by a technician trained to observe equine health. All observations made by technicians were reviewed and approved by the clinical investigator.

The study was performed in the United States by a contract research organization. Animal welfare was considered throughout the study, with adherence to accepted standards of care.

**Data Analysis**

The individual horse was the experimental unit for purposes of statistical analysis. The av-
verage amount of grain consumed by each horse over the 3-day treatment period for each product was analyzed by an analysis of variance appropriate for a three-period, three-treatment crossover study (the MIXED procedure, SAS Institute, Cary NC). The statistical model included sequence, treatment, and period as fixed effects. Animal-within-sequence was included as a random effect. If the main effect of treatment was statistically significant ($P < .05$), then the differences between treatments were assessed in a pairwise fashion.

For the palatability assessment, the most frequent outcome observed during a treatment period was used in the statistical analysis. For example, if the initial interest score was 2 for 2 of 3 days within a treatment period, then the outcome for that treatment period was “eats readily.” Outcomes from each of the daily palatability assessments were then dichotomized as follows:

- **Initial interest score:** Eats readily versus initially interested and then stops eating or no interest or shows aversion behavior (interest score of 2 versus 1 or 0)
- **Subjective palatability:** Palatable versus moderately palatable or not palatable (palatability score of 2 versus 1 or 0)
- **Powder remaining in feeder after 20 minutes:** $<25\%$ of dose remaining (no powder or traces of powder visible) versus $\geq 25\%$ or majority of dose remaining (dose-remaining score of 3 or 2 versus 1 or 0)

Results were recorded as the percent of animals with the higher score on the new dichotomized scale, which was then compared across treatments using the Fisher exact test. In this analysis, sequence and period effects were assumed to be negligible and were ignored. If the Fisher exact test was statistically significant ($P < .05$), then pairwise comparisons were performed among the three treatment groups.

All analyses were repeated using results from the third day of treatment in place of the average (or most frequent) outcome.

### Results

All animals were generally healthy and even gained weight during the acclimation process. Clinical observations during acclimation and treatment revealed several instances of nasal or ocular discharges, but no serious abnormalities of structure, function, attitude, locomotion, or behavior were noted. No animals were disqualified, died, or were euthanized during the study.

A total of 162 portions of medicated feed were offered to the 18 horses over a total of 9 days. In 16 instances (10%), some proportion of the treated feed was not consumed by the recipient within 20 minutes. The quantities of unconsumed treated feed represented 1% to 14% of the amount offered. Of treated feeds that were not completely consumed, an average of 8% was not eaten. All horses consumed 100% of every portion of nonmedicated commercial feed offered in the evening.

The sequence and period effects were not significant for either the amount or percentage of grain consumed. The main treatment effect was statistically significant for both average amount and percentage consumed. Significantly less grain was consumed when top-dressed with treatment B as compared with the other treatments. There was no statistically sig-
TABLE 1. Statistical Results* Comparing the Palatability of Three Top-Dress Antiinflammatory Treatments

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Statistical Coefficient</th>
<th>Treatment</th>
<th>Treatment</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>A</td>
<td>B</td>
<td>C</td>
</tr>
<tr>
<td>Amount consumed (kg)</td>
<td>0.0080</td>
<td>0.98a</td>
<td>0.96b</td>
<td>0.98d</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(0.89, 1.07)</td>
<td>(0.87, 1.05)</td>
<td>(0.89, 1.07)</td>
</tr>
<tr>
<td>Percent consumed</td>
<td>0.0130</td>
<td>99.9a</td>
<td>97.7b</td>
<td>100.0d</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(98.7, 101.1)</td>
<td>(96.5, 98.9)</td>
<td>(98.8, 101.2)</td>
</tr>
<tr>
<td>Initial interest score†</td>
<td>1.0000</td>
<td>100.0</td>
<td>94.4</td>
<td>100.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(81.5, 100.0)</td>
<td>(72.7, 99.9)</td>
<td>(81.5, 100.0)</td>
</tr>
<tr>
<td>Powder remaining†</td>
<td>0.3208</td>
<td>100.0</td>
<td>88.9</td>
<td>100.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(81.5, 100.0)</td>
<td>(65.3, 98.6)</td>
<td>(81.5, 100.0)</td>
</tr>
<tr>
<td>Palatability score†</td>
<td>0.0081</td>
<td>100.0</td>
<td>72.2</td>
<td>100.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(81.5, 100.0)</td>
<td>(46.5, 90.3)</td>
<td>(81.5, 100.0)</td>
</tr>
</tbody>
</table>

*Analyses based on 3-day average consumption or most frequent subjective score. Values in parentheses represent 95% CIs for the mean.
†Treatment results represent the percentage of horses responding favorably on the dichotomized scale.
a, bWithin each row, values with differently lettered superscripts are significantly different ($P < .05$).
A = Equipalazone Powder; B = Pro-Dynam; C = Danilon Equidos.

significant difference in consumption between treatments A and C (Table 1).

Assessments of both initial interest and powder consumption were lower for treatment B compared with the other treatments, but these differences did not achieve statistical significance. However, the palatability score was significantly lower for treatment B compared with the other treatments. Treatments A and C were similarly palatable to the horses in the study (Table 1).

Analyses using third-day results were similar to those using the 3-day average (or most frequent) value. Consumption and palatability scores for treatment B were slightly improved on day 3 (results not shown), but amount consumed was still significantly poorer compared with the other treatments.

**DISCUSSION**

Both treatments A and C were essentially 100% accepted and fully consumed. Treatment B was significantly less palatable, resulting in significantly lower feed consumption. Scores improved slightly on the third day of treatment with B (compared with the 3-day average), suggesting that horses may have accommodated somewhat to the medicated feed. However, third-day consumption was still significantly worse for treatment B compared with the other two formulations.

In general, all study horses ate the majority of their medicated feed, even when they did not eat it all, suggesting some therapeutic benefit of the test formulations despite reduced palatability. However, reduced palatability would tend to provide a smaller effective dose per sachet, leading to underdosing and a less-than-expected therapeutic effect. To increase consumption of a nonpalatable formulation, owners may be tempted to add flavor enhancers to improve palatability, which might alter the stability, purity, or potency of this newly compounded mixture.14

All horses in this study were healthy, without serious musculoskeletal illness. Active pain or discomfort would be expected to reduce appetite and feed consumption, especially for less-palatable formulations. Injured or arthritic animals may therefore consume less of a nonpalatable treatment, which could in turn result in inadequate pain management, prolonged re-
covery, and increased physiologic stress in affected horses.¹

**CONCLUSION**

Both Equipalazone Powder (A) and Danilon Equidos (C) were essentially fully accepted and consumed. By comparison, Pro-Dynam (B) was significantly less palatable, resulting in significantly lower feed consumption and potentially reduced therapeutic effect.

**REFERENCES**