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Comparison of the effect of *Sporobolus virginicus* and Rhodes (*Chloris gayana*) hay diets on the absorption pattern of phenylbutazone in the camel (*Camelus dromedarius*)

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Abstract

The effect of feeding *Sporobolus* and Rhodes hay on phenylbutazone (4 g) relative absorption was examined in six camels using a two-period, two-sequence, two-treatment crossover design. Serum concentration of the drug was measured by high performance liquid chromatography. The measured values (means ± SD) for Rhodes and *Sporobolus* hay, respectively, were C_{max} 35.59 ± 22.36 and 36.55 ± 18.99 μg/mL, T_{max} 26 ± 2.53 and 26.3 ± 1.97 h and $AUC_{0-72\,h}$ 1552 ± 872.6 and 1621 ± 903.6 μg h/mL. Broad plateau concentrations of phenylbutazone in serum were observed between 12 and 36 h. There was no significant difference in any parameter between the two feeding regimens. Multiple peaks in serum concentration–time curve were observed, regardless of the type of grass available to and the animals prior to drug administration. It was concluded that the phasic absorption of phenylbutazone was a particular feature of hay feeding in camels, and the *Sporobolus* hay can be fed to camels without any effect on the rate and extent of phenylbutazone absorption compared to Rhodes grass hay.

Keywords: Camels; Phenylbutazone; Rhodes; *Sporobolus*; Absorption

1. Introduction

Following oral administration, phenylbutazone absorption in horses is subject to marked inter- and intra-animal variations (Gerring et al., 1981; Sullivan and Snow, 1982; Maitho et al., 1986). This variability has been attributed to various factors, such as administration of phenylbutazone orally on different days but at the same time and the same dose rate, single doses at a different level (mg/kg) and dosing following over-night fasting or following feeding.

Considerable attention has been given to the effect of feeding and drug formulation on the fate of orally administered drugs in large animal species where the stomach and the reticulorumen are continually full (Gerring et al., 1981; Rose et al., 1982; Sullivan and Snow, 1982; Lees et al., 1983, 1988; Lees and Higgins, 1986; Snow and Douglas, 1983; Bogan et al., 1984; Maitho et al., 1986). The diet of large herbivorous animals contains large amounts of cellulose, which may adsorb drug molecules and thereby delay their availability for absorption. Additionally, intestinal microbial activity could markedly affect the availability of drugs subjected to digestion by gut microflora. In monogastric species, food can inhibit drug absorption both by the adsorption of drug onto the ingested fibrous materials and by the chelation of drugs by ingested cations (Welling, 1980; Lees et al., 1988).

Sporobolus grass (*Sporobolus virginicus*) is a halophytic plant that grows under arid and semi-arid conditions and with irrigation systems containing a high salt content (20,000 ppm). Rhodes grass (*Chloris gayana*) is a sub-humid tropical and subtropical perennial grass,

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which may be irrigated with ground water of low salinity (2500 ppm). In the United Arab Emirates (UAE), Alhadrami et al. (2003) compared the yield, chemical composition and feed intake by camels and sheep of *Sporobolus* and Rhodes. The chemical composition of the two grasses was similar, except that the crude protein content was greater in Rhodes compared with *Sporobolus*. Camels exhibited a large daily consumption of Rhodes compared with *Sporobolus*.

Since either grass may be fed to camels prior to phenylbutazone administration, this investigation was undertaken to examine whether or not prior intake of *Sporobolus* hay has a greater impact on the oral absorption of phenylbutazone as compared to that associated with Rhodes hay.

2. Materials and methods

2.1. Animals

Six clinically health adult dromedary camels aged 6–8 years and of body weight in the range of 234–365 kg were divided into two groups (A and B). Clinical observations were made before (baseline), during and after drug administration. During the experimental periods, four blood samples were collected from the jugular vein for routine serum biochemistry and haematology on 0, 5, 35 and 40 days. Routine laboratory procedures were used to determine serum concentrations of sodium, potassium, iron, calcium, copper, urea nitrogen, creatinine, total protein, albumen, alkaline phosphatase, aspartate aminotranferase (AST), lactate dehydrogenase (LDH), and glucose. Packed cell volume (PCV) and haemoglobin (Hb) concentration were also determined.

2.2. Experimental design

In the first part of a two part crossover study, the serum concentration–time relationships were established for phenylbutazone administered orally after 35 days ad libitum feeding of *Sporobolus* to group A, and Rhodes to group B. In part two of the crossover, feedings were reversed and maintained for 35 days prior to the date of drug administration

2.3. Drug administration

Phenylbutazone (Butasone-Jaapharm) was administered to camels orally as a maximum bolus dose recommended by the manufacturer for horses (4 g; 13.3 mg/kg). The camel's mouth was opened and its head kept in an upright position by holding the nose and the lower lip. The boluses were placed on the back of the tongue. Then one litre of water was administered as a drench.

2.4. Blood sampling

Blood samples (10 mL) were collected from the jugular vein by direct puncture just before drug administration (pre dose) and at 0.25, 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 3.5, 4, 5, 6, 7, 8, 12, 24, 26, 28, 30, 32, 36, 48, 50, 52, 54, 56, 60 and 72 h after drug administration. The serum recovered after centrifugation (2000*g* for 10 min) was stored at −20 °C until assayed within seven days.

2.5. Drug analysis

Serum phenylbutazone concentration was determined by use of a previously described high performance liquid chromatography method (Gerken and Sams, 1985). All samples from an animal were analysed in a single run. The interassay coefficients of variation for phenylbutazone at concentrations of 5 and 20 μg/mL were 8.13% and 9.74%, respectively. The LOD and LOQ were 100 and 300 ng/mL, respectively.

2.6. Data analysis

Results are expressed as means (±SD). Values of maximum concentration in serum (C_{max}) and time when maximum concentration was reached (T_{max}) were obtained directly from the concentration versus time graph for individual animals. The area under the curve ($AUC_{0–72\,h}$) was calculated by the linear-trapezoidal rule using non-linear regression (Graph Pad Prism Version 2.00)

2.7. Statistics

Statistical comparison between the feeding of *Sporobolus* and Rhodes was carried out applying the Wilcoxon signed-rank test for paired comparison. The level of significance was $P < 0.05$.

3. Results

3.1. Clinical observations

No adverse signs were observed in the camels throughout the period of the experiment. Clinical chemistry values that were measured during the acclimatisation period of the two phases and five days after phenylbutazone administration were similar and within the normal range previously established for camels (Abdalla et al., 1988).

Phenylbutazone concentrations in serum of the camels fed *Sporobolus* or Rhodes are shown in Fig. 1. The maximum serum concentration, the time to maximum serum concentration and the area under the serum concentration–time curve are presented in Table 1.