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Bioavailability of Ascorbic Acid in Camels (*Camelus dromedarius*) Following Administration by Different Routes.

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ABSTRACT

This study reports the bioavailability of ascorbic acid in four adult female camels following administration at a dose of 50 mg/kg intravenously (i.v.), subcutaneously (s.c.) or orally (p.o.). The half-life of elimination following i.v. Injection (178.3 min.) was longer than after s.c. (145.2 min) or p.o. administration (110.0 min) (P < 0.05). Following s.c. injection, the maximum concentration (C_{max}) obtained (28.4 mcg/ml) was higher than that for p.o. (14.29 mcg/ml) (P < 0.01). However, the time to reach C_{max} (T_{max}) was shorter after p.o. (75.5 min) compared to the s.c. route (181.5 min) (P < 0.01). The bioavailability following s.c. injection was found to be much greater than after giving the drug orally. It can be concluded that, if ascorbic acid administration is justified in camels, the s.c. route is more suitable than the i.v. or the oral route.

Key words: Ascorbic acid, Bioavailability, Dromedary Camel.

INTRODUCTION

Ascorbic acid plays an important role as an antioxidant and important in the formation of connective tissue (Kanter, 1998). It has also been suggested to be of value in alleviating both physiological and pathological stress (Jaeschke, 1984; Hemingway, 1991). Camels are mostly raised under pastoral husbandry conditions in hot dry environments and are therefore exposed to various degrees of stress.

Accordingly, administration of ascorbic acid may be of value in camels to alleviate stress. Knowledge of ascorbic acid pharmacokinetics in camels is necessary in the determination of the dose, the interval of dosing and the appropriate route of administration. As part of our investigation of ascorbic acid in camels it was thought to be of interest to investigate the bioavailability of this vitamin following its administration intravenously (i.v.), subcutaneously (s.c.) or orally (p.o.).

MATERIALS AND METHODS

Animals

Four clinically healthy adult female camels (*Camelus dormedarius*), four to six years of age and weighing 380-425 kg were used. They were bought From Omdurman Animal Market (Sudan) and kept for three weeks for acclimatization before starting the experiment. The animals were fed sorghum stalks and grain, dry grass and drinking water *ad libitum*.

Drug administration and sample collection

One week before the administration of ascorbic acid, samples of blood were collected from each animal to establish baseline given intravenously (i.v.), concentration. The drug was subcutaneously (s.c.) or orally (p.o.) at a dose rate of 50 mg/kg. A washout period of 14 days was allowed between drug administrations. Blood samples (5 ml) were collected in heparinized syringes before treatment and at 5, 10, 20, 40, 60 and 90 min and at 2, 3, 4, 6, 8, 10, 12, 18 and 24 h after i.v. administration and at 0, 15, 30, 45, 60 and 90 min and 2, 3, 4, 6, 8, 10, 12, 16, 20 and 24 h after p.o. or s.c. injection. Immediately after separation of plasma, metaphosphoric acid solution was added and the treated plasma samples were then stored at -20 °C prior to analysis within one week.

Drug analysis

Ascorbic acid concentration in the plasma was determined spectrophotometrically according to the method described by McGown et al., 1982. The limit of quantification of the method was 1.2 mcg/ml. The intra-assay coefficient of variation was less than 6%.

Pharmacokinetic and statistical analysis

For the purpose of Pharmacokinetic analysis, the baseline concentration of ascorbic acid $(4.52 \pm 0.96 \text{ mcg/ml})$ was subtracted from all values obtained. Pharmacokinetic analysis of the plasma concentration versus time data was performed using non-linear regression analysis. The i.v. data were best fitted to biexponential equations. Following p.o. or s.c. administration, plasma concentrations of ascorbic acid versus time were analyzed by adopting a one compartment open model. Pharmacokinetic parameters were calculated according to the equations described by Baggot (1977).

All values of parameters are presented as mean \pm SD. Harmonic means were calculated for half-lives of elimination. Wilcoxon's rank sum test was used to test for significant differences in the half-lives. The other parameters were analyzed using one way analysis of variance or student's *t*-test.

RESULTS AND DISCUSSION

The data of mean plasma concentration versus time in camels given ascorbic acid i.v., s.c. or p.o. at a dose of 50 mg/kg is shown in Fig. 1. Following i.v. injection ascorbic acid plasma level declined in a biexponential manner. Thus, a two compartment open model fit the individual plasma levels data. The absorption of the drug was rapid following p.o. or s.c. administration. Higher maximum concentration was reached after s.c. injection, but the decline in concentration was slower than after the p.o. route which is indicative of the higher bioavailability after s.c. administration.

Table 1, represents some selected pharmacokinetic parameters. The half-life of elimination after i.v. injection (178.4 min) was longer than after s.c. (145.2 min) or p.o. administration (110.0 min) (P < 0.05). The elimination half-life in this work in camels, following i.v. Injection was longer than in sheep (100.8 min) by 76.9% (Black and Hidiroglou, 1996), and considerably shorter than that reported for horses after injection by the same route (297 – 774 min) (Loscher *et*

al., 1984; Snow and Frigg, 1990), which indicates species variations in the elimination of the drug.



Fig. 1: Means plasma concentration versus time after administration of ascorbic acid in four female camels at a dose rate of 50 mg/kg intravenously (◆), subcutaneously (●) or orally (◊). Each point represents the mean of four observations. Standard deviation was less than 10%.

Following s.c. injection, the maximum concentration (C_{max}) obtained (28.4 mcg/ml) was higher than that obtained after p.o. administration (14.29 mcg/ml) (P < 0.01). However, the time to reach C_{max} (T_{max}) was shorter for p.o. (75.5 min) compared to the s.c. route (181.6 min) (P < 0.01). The bioavailability following s.c. injection (340.8%) was found to be much higher than after giving the drug orally (85.5%).

Table 1: Pharmacokinetic parameters of ascorbic acid (mean \pm SD) following intravenous (i.v.), subcutaneous (s.c.) and oral (p.o.) administration in four female camels (dose 50 mg/kg).

Pharmacokinetic Parameter	I.V.	S.C.	Р.О.
$t_{1/2\beta}$ (min)	178.4±15.4	145.20±8.44*	110.04±11.39*
C _{max} (mcg/ml)	-	28.38±2.55	14.29±4.78**
T _{max} (min)	-	181.60±10.44	75.48±6.36**
AUC (mcg.h/ml) ¹	63.20±12.2	215.46±23.35	54.04±9.02
$F(\%)^2$	-	340.8	85.5

*Significantly different P < 0.05 compared to the value obtained after i.v. injection. **Significantly different P < 0.01 compared to the value obtained after s.c. injection. ^{1}AUC = area under the concentration versus time curve. ^{2}F = bioavailability obtained using the relationship AUC_{s.c.} or AUC_{p.o.}/AUC_{i.v.} x 100.

This may be due to the much slower absorption following s.c. injection ($t_{1/2a}$ was 89.2 min compared to 27.8 min for oral route), to a conservation mechanism, or to an impact of endogenous ascorbic acid synthesis since the drug takes more time to be eliminated after s.c. injection. Black and Hidiroglou (1996) reported bioavailability values ranging between 295.8 and 608.6%. after intramuscular administration of ascorbic acid in sheep.

The present study showed considerably higher bioavailability following p.o. administration, than in horses in which very poor absorption of ascorbic acid was reported (Loscher *et al.*, 1984). However, only repeated oral administration was effective in increasing ascorbic acid plasma levels in this animal species (Snow *et al.*, 1987). Loscher and his colleagues (1984) suggested that, the reason for the low systemic availability of ascorbic acid after oral administration in the horse may be related to: 1) Chemical or enzymatic destruction in the gastrointestinal fluid and/or mucosa; 2)

Absorption into the hepatic portal blood but subsequent metabolism in the liver before reaching the general circulation (a first pass effect); 3) Slow entry into the general circulation but relatively rapid excretion through the kidney as soon as it exceeds the endogenous concentration range.

No local reactions were observed following s.c. injection of ascorbic acid in camels of this study, whereas in horses serious swellings at the site of injection i.m. and s.c. were reported (Loscher *et al.*, 1984). Further studies are needed to determine the appropriate ascorbic acid concentrations needed in camels to alleviate stress. So that suitable doses of ascorbic acid in camels can be determined, and to investigate daily oral supplementation in feed to raise systemic ascorbic acid concentrations.

CONCLUSION

In conclusion the present study showed considerably high bioavailability of ascorbic acid in camels following subcutaneous administration compared to the intravenous and oral routes. Moreover, local irritation was not observed. Therefore, it can be suggested that, if ascorbic acid administration is justified in camels, the s.c. route is more suitable than the i.v. or the oral route.

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