OBJECTIVE

The purpose of this study was to evaluate multiple dose pharmacokinetics (PK) of mirtazapine in a novel ointment formulation following 14 days of transdermal application in cats.

METHODS

This study was a masked, randomized, three-arm parallel study to determine the plasma PK of two doses (0.5 and 2.0 mg/kg) of mirtazapine ointment applied transdermally once daily for 14 days.

Twenty healthy purpose-bred cats were acclimated for 7 days. Baseline physical examination, hematology and serum biochemistry were evaluated.

RESULTS (CONT’D)

Table 2. Mirtazapine PK parameters

<table>
<thead>
<tr>
<th>Treatment Group (n=8)</th>
<th>Time (h)</th>
<th>Median (range)</th>
<th>Mean (SD)</th>
<th>Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control 0.5 mg/kg</td>
<td>T_{1/2} (h)</td>
<td>2.1 (1.3)</td>
<td>2.0 (1.0-4.0)</td>
<td>3.0 (1.1)</td>
</tr>
<tr>
<td>mirtazapine 0.5 mg/kg</td>
<td>C_{max} (ng/mL)</td>
<td>39.6 (9.7)</td>
<td>40.9 (27.2-35.0)</td>
<td>98.2 (55.0)</td>
</tr>
<tr>
<td>mirtazapine 2.0 mg/kg</td>
<td>AUC_{0-∞} (ng*h/mL)</td>
<td>647 (225)</td>
<td>590 (453-1167)</td>
<td>2045 (525)</td>
</tr>
</tbody>
</table>

Mean ± SD body weight for cats that received 0.5 mg/kg mirtazapine was 5.4 ± 1.1 kg prior to treatment and 5.7 ± 1.2 kg after 14 days of treatment.

Mean ± SD body weight for cats that received 2.0 mg/kg mirtazapine was 5.3 ± 1.1 kg prior to treatment and 5.7 ± 1.2 kg after 14 days of treatment.

Mean ± SD body weight for control cats was 5.8 ± 1.2 kg at baseline and 6.1 ± 1.2 kg after 14 days.

Mild redness of the pinna (application site) was noted in all control treated cats, but no pinnal excoriation or ulceration was observed in any cat.

DISCUSSION

The absorption of both 0.5 and 2.0 mg/kg transdermal mirtazapine after 14 days was relatively consistent and rapid with a mean T_{1/2} between 2.1 to 3.0 h and mean C_{max} of 39.6 to 98.2 ng/mL, respectively.

Mean terminal half-lives were similar between the 0.5 and 2.0 mg/kg groups (20.7 and 28.4 hours, respectively).

In the 0.5 mg/kg group, average concentration over the dosing interval was 16.4 ng/mL and the mean fluctuation in plasma concentrations over the dosing interval was 210%.

In the 2.0 mg/kg group, average concentration over the dosing interval was 47.4 ng/mL and the mean fluctuation in plasma concentrations over the dosing interval was 142%.

Weight gain was seen in both groups receiving mirtazapine but statistical comparison was not performed in this pilot study.

As age and kidney function pharmacokinetics of oral mirtazapine, a possible limitation of the study is the variable age of the cats and unknown urine specific gravity. However it is not known if age and early kidney disease affect the pharmacokinetics of transdermal mirtazapine in the same manner.

REFERENCES