**INTRODUCTION**

**Management of Weight Loss in Cats**

Weight loss and anorexia in cats are common problems secondary to numerous underlying diseases. Prolonged anorexia and weight loss can lead to serious sequelae such as hepatic lipidosis [1], reduced immune function [2], delayed wound healing [2], decreased survival times [3], and indirectly influence an owner’s decision to euthanize cats with chronic disease [4]. Regardless of the underlying disease, appetite modulation via pharmacotherapy can play a valuable role to improve a patient’s nutritional status and ability to recover from the underlying illness or injury [2]. There are no approved veterinary products to manage weight loss in cats.

**Mirtazapine**

Mirtazapine is a noreadnergic and specific serotonin antagonist with antidepressant and appetite-stimulating properties. Its presynaptic α2-adrenergic receptor antagonism results in increased norepinephrine which likely contributes to its appetite-stimulating effects [2]. Mirtazapine blocks three serotonin (5-HT2A, 5-HT2C and 5-HT3) and histamine (H1) receptors. Antagonism of 5-HT2C and/or H1 receptors potentially stimulate appetite regulated by the hypothalamus thus leading to weight gain [5]. Antagonism of 5-HT3 reduces nausea and vomiting in humans [6]. Mirtazapine has been shown to increase food intake and weight gain in both humans [7] and cats [2, 8].

**RESULTS**

**Application**

Cats received 0.5 mg/kg by mouth (oral administration) or to the inner pinna (transdermal application). Following a 5-day washout, each cat received the alternate treatment. All cats wore Elizabethan collars throughout the course of the study.

**Assessments**

Plasma was collected pre-dose and at 1, 2, 4, 6, 8, 12, 24, 48, 72, and 96 h after administration. Mirtazapine concentrations were measured using an LC-MS/MS method. The following PK parameters were calculated (via standard methods WinNonlin Professional 5.3) and statistically compared (via Wilcoxon signed rank test with significance set at p < 0.05).

- Cmax: time to maximum (peak) concentration
- Tmax: maximum (peak) concentration
- T1/2: elimination half-life
- AUC: area under the concentration-time curve

**Table 1: Mirtazapine PK parameters**

<table>
<thead>
<tr>
<th></th>
<th>Transdermal Application (n=8)</th>
<th>Oral Administration (n=8)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tmax (h)</td>
<td>Mean (SD)        Median (range)</td>
<td>Mean (SD)        Median (range)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(15.6)          (9.0) (1.0-48.0)</td>
<td>(11.3)          (1.0) (1.0-2.0)</td>
<td>0.02†</td>
</tr>
<tr>
<td>Cmax (ng/mL)</td>
<td>Mean (SD)          Median (range)</td>
<td>Mean (SD)          Median (range)</td>
<td></td>
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<td></td>
<td>(43.5)          (6.6) (21.1-129)</td>
<td>(83.1)          (31.2) (43.4-128)</td>
<td>0.04†</td>
</tr>
<tr>
<td>AUC_{trans} (ng*h/mL)</td>
<td>Mean (SD)        Median (range)</td>
<td>Mean (SD)        Median (range)</td>
<td></td>
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<tr>
<td></td>
<td>(260)          (247) (204-397)</td>
<td>(434)          (494) (208-590)</td>
<td>0.09</td>
</tr>
<tr>
<td>T1/2 (h)</td>
<td>Mean (SD)          Median (range)</td>
<td>Mean (SD)          Median (range)</td>
<td>0.01†</td>
</tr>
<tr>
<td></td>
<td>(6.0)          (4.2) (1.9-13.4)</td>
<td>(10.1)          (4.7) (1.7-10.0)</td>
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</tr>
</tbody>
</table>

Oral mirtazapine was rapidly absorbed from the gastrointestinal tract. The absorption of transdermal mirtazapine was slower compared to oral administration. The mean ± standard deviation relative bioavailability of transdermal mirtazapine compared to oral mirtazapine was 64.9%.

**DISCUSSION**

Absorption of mirtazapine was faster, more consistent, and about 2-fold higher compared to transdermal application.

**REFERENCES**


