Mirtazapine is a noradrenergic and specific serotonergic antidepressant with antiemetic 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**

The following PK parameters were calculated (via non-compartmental methods WinNonlin Professional 5.3) and statistically compared (via Wilcoxon Signed Rank test with significance set at p < 0.05):

- $T_{max}$: time to maximum (peak) concentration
- $C_{max}$: maximum (peak) concentration
- $T_{1/2}$: elimination half-life
- AUC: area under the concentration-time curve

**Analyses**

- 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 and treated cats, but no pinna 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 $T_{max}$ between 2.1 to 4.0 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 affect 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.