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## Customized Medications for Small Animals

### Transdermal Methimazole in the Treatment of Cats with Hyperthyroidism

The application of methimazole on the inner pinna offers an attractive alternative for drug administration. Hoffman et al. of School of Veterinary Medicine, Louisiana State University, retrospectively evaluated clinical and laboratory data from 13 cats with hyperthyroidism who were treated with methimazole formulated in a pluronic lecithin organogel (PLO)-based vehicle which was applied to the inner pinna of the ear at a dosage ranging from 2.5 mg/cat every 24 hours to 10.0 mg/cat every 12 hours. During the treatment period, cats were re-evaluated at a mean of 4.3 weeks and 5.4 months. At both rechecks, clinical improvement was observed, and significant decreases in thyroxine concentrations were measured compared to pretreatment concentrations. No adverse effects were reported.<sup>1</sup>

Lecuyer et al. of the University of Montreal treated thirteen cats newly diagnosed with hyperthyroidism with a transdermal formulation of methimazole at a dose of 5 mg (0.1 mL) (concentration of 50 mg/mL) applied to the internal ear pinna every 12 hours for 28 days. Baseline hematologic and biochemical values, along with serum thyroxine (T4) levels, were obtained on presentation. Cats were evaluated on day 14 and day 28 following transdermal therapy. At each visit, a physical examination, a complete blood cell count, a serum biochemical analysis, and a serum T4 evaluation were performed. Ten cats completed the study. Clinical improvement, as well as a significant decrease in T4, was noted in all cats. Serum T4 measured on days 14 and 28 was significantly lower at 27.44 nmol/L and 14.63 nmol/L, respectively, as compared with values at presentation (97.31 nmol/L). Only one cat showed a cutaneous adverse reaction along with a marked thrombocytopenia. The results of this prospective clinical study suggest that transdermal methimazole is an effective and safe alternative to conventional oral formulations.<sup>2</sup>

A study by Sartor et al. at University of Wisconsin-Madison School of Veterinary Medicine found that cats treated with oral methimazole had a higher incidence of gastrointestinal (GI) adverse effects (4 of 17 cats) compared to the cats treated with transdermal methimazole (1 of 27), but no differences were found between groups in the incidence of neutropenia, hepatotoxicity, or facial excoriations.<sup>3</sup>

**Note:** The vehicle (base) in which the drug is incorporated greatly affects the rate and extent of transdermal drug absorption. "Transdermal drug dosing will undoubtedly grow in importance in the coming years, with other classes of drugs, for example, antibiotics, pain medications, and cancer chemotherapy drugs, being formulated for such usage. Even the most stubborn and disagreeable cat is no match for a quick smear of a measured dose of gel inside the ear."<sup>4</sup>

<sup>1</sup> Journal of Feline Medicine & Surgery 5, 2 , April 2003, pp 77-82

<sup>2</sup> Can Vet J. 2006 Feb;47(2):131-5

<sup>3</sup> J Vet Intern Med. 2004 Sep-Oct;18(5):651-5

<sup>4</sup> Arnold Plotnick MS, DVM, ACVIM, ABVP

[http://www.manhattancats.com/Articles/transdermal\\_drugs\\_and\\_their\\_use\\_.html](http://www.manhattancats.com/Articles/transdermal_drugs_and_their_use_.html)

#### Sample Prescription

##### Compounded Medication

Methimazole Transdermal Cream

Strength:  2.5mg/0.1mL  5 mg/0.1mL  other

Sig: Apply 0.1mL to inner ear twice per day or as directed.

Disp Qty:  mL

#### Sample Prescription

##### Compounded Medication

Methimazole Liquid Solution

Strength:

Sig:

Qty:

## Feline Constipation, Obstipation, and Megacolon

Feline chronic constipation is a complicated and frustrating condition for both pet owners and veterinarians. Untreated, chronic constipation results in accumulation of hard, dry feces in the colon leading to megacolon, obstipation, or life-threatening sepsis from translocation of bacteria across the gut wall. Not only is the disease difficult and frustrating to manage, but multimodal therapy can be a compliance nightmare for both owner and cat.

### Principles of Therapy

Medical therapy for chronic constipation involves the 5 following principles: (1) rehydration, (2) removal of feces, (3) addition of dietary fiber, (4) use of laxatives, and (5) administration of prokinetic agents to stimulate colonic motility. Rehydration may be accomplished by the administration of subcutaneous fluids, by feeding moist canned food, and by encouraging drinking by utilizing cat water fountains. Removal of feces should only be attempted at the veterinary clinic to avoid perforation of the colon and to avoid vomiting from vagal stimulation. Dietary fiber may be added by feeding high-fiber cat food or by adding poorly digestible fiber such as oat or wheat bran and canned pumpkin (1-2 tbsps of each) added to food once daily. Psyllium has also been added to the food at a rate of 1-2 teaspoonsfuls once or twice daily. Various laxatives may be utilized including emollients (DSS), lubricants (petrolatum), hyperosmotics (lactulose, kristalose, and polyethylene glycol), and stimulants (bisacodyl). Finally, prokinetic agents are often added to stimulate colonic contractions to facilitate passage of feces.

### Prokinetic Agents-Present and Future

An understanding of feline gut neuroanatomy is required to determine which prokinetics will be effective and which ones will not. Agents typically used in stimulating colonic motility in other species are not necessarily effective in stimulating feline colonic motility. While there are many pharmacological agents marketed as prokinetics for humans, very few of them are useful for treating feline constipation. Of the known prokinetic agents, cisapride stands alone in providing therapeutic benefit in cats with chronic constipation. Since cats suffering from megacolon do not respond to stimulation by acetylcholine, therapeutic benefit must arise from the serotonergic (5HT) mechanisms. Cisapride stimulates the release of acetylcholine, is a muscarinic and 5HT4a receptor agonist and is also a 5HT3 receptor antagonist. Metoclopramide is also a 5HT4 agonist but is of little value in stimulating feline colonic motility. Ranitidine and nizatidine have been shown to stimulate feline colonic motility in vitro, but famotidine and cimetidine do not. Dr. Robert Washabau, at the University of Pennsylvania, recently completed a study (Morris Animal Foundation-February 2005) in which he demonstrated that some of the newer 5HT4a agonists, tegaserod (Zelnorm®-Novartis) and prucalopride (RO93877-Janssen) stimulated feline colonic motility in vitro. Also, prostaglandin E1 analogs such as misoprostol stimulate feline colonic smooth muscle in vitro. Further studies of these agents in cats are warranted to determine safe and effective doses. Until that time, cisapride remains the only safe and effective prokinetic agent in treating feline constipation. Ironically, cisapride was removed from the human market in 2000 for safety reasons, and it is currently only available through compounding pharmacists.

### Compounding For Compliance

Drug therapy for chronic constipation is multimodal. A typical therapeutic regimen for a chronically constipated cat might include the following: lactulose 1cc PO TID, cisapride 10mg PO BID, Miralax® (PEG 3350) 1/8–1/4 tsp PO BID, and ranitidine 10mg PO BID. If the therapeutic regimen is employed using individual dosage forms, the resulting number of daily administrations is 9 daily for the rest of the cat's life. Lactulose is sticky, and ranitidine syrup causes profuse salivation in cats; neither of these products is suitable for facilitating compliance in a lifelong condition. Compounding must therefore be employed and plays a valuable role in providing effective therapy for feline constipation. As previously mentioned, cisapride, the only known effective prokinetic agent in cats, is available only through compounding pharmacies. The possibilities in providing cisapride in compounded dosage forms are limitless. Cisapride can be compounded into oral suspensions, or patient-specific chewable treats or capsules. Polyethylene glycol 3350 (PEG 3350) can be worked into liquid suspending vehicles for cisapride suspensions, and PEG 3350, kristalose (crystallized lactulose) or psyllium can be utilized as fillers for cisapride capsules. Various forms of poorly absorbed dietary fiber can also be utilized in formulating cisapride treats. Combining various therapies into one capsule (e.g. cisapride, ranitidine, PEG 3350, kristalose) can also decrease the number of daily medication administrations, reducing stress to both owner and cat. Through collaboration with veterinarian and owner, the compounding pharmacist can create dosage forms that greatly facilitate management of this disease.

#### Sample Prescription

##### Compounded Medication

Cisapride Capsules

Strength:  2.5 mg  5 mg  other  
Sig: Take one capsule by mouth 2 - 3 times/day, 30 min.  
prior to meal.

Disp Qty: #  capsules

#### Sample Prescription

##### Compounded Medication

Cisapride Liquid Suspension

Strength: \_\_\_\_\_  
Sig: \_\_\_\_\_  
Qty: \_\_\_\_\_

#### Sample Prescription

##### Compounded Medication

Cisapride Transdermal Cream

Strength: \_\_\_\_\_  
Sig: \_\_\_\_\_  
Qty: \_\_\_\_\_

## Ursodiol in a Dog with Chronic Hepatitis

A dog with severe cholestasis secondary to chronic hepatitis was treated with ursodeoxycholic acid (ursodiol) orally. After 2 weeks of daily treatment, the dog was more active and had an improved appetite. Monthly serum biochemical determinations and analysis of individual bile acid profiles documented improvement in hepatobiliary tests and a marked reduction in the concentrations of potentially hepatotoxic endogenous bile acids. These effects were maintained for approximately 6 months. J Vet Intern Med 1997 May-Jun;11(3):195-7

Studies have found an extemporaneously compounded ursodiol suspension to be stable for up to 35 days refrigerated. This drug is well absorbed orally and enters the liver directly from the portal system, and is then secreted into bile. Ursodiol should be administered orally as the first-pass effect is vital for effectiveness.

#### Sample Prescription

##### Compounded Medication

Ursodiol Capsules

Strength:  50 mg  100 mg  other  
Sig: Take one capsule by mouth every 24 hours or as directed.  
Disp Qty: #  capsules

#### Sample Prescription

##### Compounded Medication

Ursodiol Liquid Suspension

Strength: \_\_\_\_\_  
Sig: \_\_\_\_\_  
Qty: \_\_\_\_\_