Selected antifungals in small animal dermatology: Part 1

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It's been a hard old year for those of us that graduated in the previous millennium. Thanks to Section 29 (of the Medicines Act, 1981) and changes in human treatments, a number of medical therapies that we have used for many years are no longer available. In dermatology, two drugs used on a weekly, if not daily, basis were griseofulvin and ketaconazole; the first our go-to drug to treat dermatophyte infections in both dogs and cats, the second used to treat canine Malassezia dermatitis. Neither drug is used in human medicine now because of health risks, especially hepatoxicity. The risks in animals would appear to be much less (Mayer et al., 2008) but nevertheless they are no longer available. The good news is that both these drugs have been replaced by either better, safer drugs or less expensive drugs or both.

As the 7th Edition of *Muller & Kirk's Small Animal Dermatology* points out (Miller *et al.*, 2013), fungi are omnipresent in our environment. Consequently mycoses, diseases caused by fungi, are common. Dermatophytosis, a superficial infection of keratinized structures (hair, claw, and stratum corneum), caused by (usually) *Microsporum* or *Trichophyton*, is a common disease in small animal medicine. *Microsporum canis* is the most common cause of dermatophytosis in cats and dogs (Miller *et al.*, 2013). The treatment of dermatophytosis in rescued cats housed in colonies, so-called shelter cats, provides a very good model for picking efficient, cost effective medications as well as providing a model for treatment regimes.

Karen Moriello of the University of Wisconsin-Madison has been working with shelter cats for many years designing treatment protocols and testing medications for dermatophytosis. In 1995 she and Doug DeBoer compared the efficacy of griseofulvin and itraconazole in experimental feline dermatophytosis. Griseofulvin at 50 mg/kg, once daily achieved mycological cures in 63-70 days while itraconazole at 10 mg/kg, once daily achieved culturenegative status in all cats in 56 days. Subsequently, in 2004 in her review of dermatophytosis treatment in dogs and cats (Moriello, 2004), she made the following recommendations: the optimum treatment for dogs or cats with dermatophytosis involves a combination of clipping of the hair coat, twice-weekly topical antifungal therapy, concurrent systemic antifungal therapy and environmental decontamination.

Following this, Dr Moriello co-authored two articles (Newbury *et al.*, 2007 and 2011) on the use of oral itraconazole in combination with different twice weekly rinses to treat naturally infected shelter cats. Itraconazole was well tolerated by cats, and in the 2011 study there were no adverse effects. All cats received oral itraconazole, 10 mg/kg, once daily for 21 days. In the 2007 study Itraconazole and twiceweekly lime sulphur rinsing gave a 100% cure rate by day 49. The same itraconazole regime in the 2011

It would appear that Itraconazole at 10 mg/kg, once daily for three weeks, in combination with topical treatment, or Itraconazole at 5 mg/kg, once daily, alternating weeks for 4 cycles (56 days) in combination with topical treatment will result in cures, in 49 and 56 days respectively in shelter situations. The average household dermatophyte infection would be much less demanding than this.

Itraconazole

Itraconazole is a synthetic cytochrome P450 inhibitor. Capsule absorption is variable and is improved when given with food. Oral formulations require 14 to 21 days to reach a steady state in dogs and cats. Miller et al. (2013) says that compared to ketaconazole, itraconazole has increased potency, decreased toxicity, and a wider spectrum of activity. Why haven't we been using it previously? When it was only available as Sporanox, itraconazole was very expensive. Now there is a generic formulation available at approximately \$5.00 for 15 100 mg capsules. Compare this with the 10 mg/ml oral Sporanox suspension which is \$163.80 plus GST for 150 mls. The suspension is 50 times more expensive. The fact that itraconazole is only available as capsules (if we consider the suspension too expensive for routine use) means that the average cat would get ½ capsule, which is less than convenient. However since it should be given with food, dividing capsules is a possibility. In this way, a standard 3-4 week treatment would cost less than \$5 (excluding dispensing fee or mark-up).

In a recent study described in Veterinary Dermatology (2013), Dr Moriello compares two treatment trials using oral terbinafine for either 14 or 21 days, combined with twice-weekly lime sulphur rinses (diluted 6 mls of lime sulphur to 100 mls of water).

Terbinafine

Terbinafine is now available as a generic, while previously it was only available as Lamisil, another expensive brand. It is an allylamine antifungal with a high margin of safety for use in mammals (Morris, 2009). The current recommended oral dose rate is 30 mg/kg once daily given with food to improve absorption and this is approximately the dose used in Dr Moriello's study. Terbinafine comes in a 250 mg tablet; in her study, cats less than 2.8 kg received ½ tablet (22 mg/kg), cats between 2.8 and 5.5 kg received ½ tablet (44 mg/kg to 22.7 mg/kg), and cats more than 5.5 kg received one tablet (45 mg/kg).

study gave an 87% cure rate at day 42 (27 out of 31) with the remaining 4 cats curing after 45 days (n=2), 62 days (n=1) and 69 days (n=1). A French study by Didier Carlotti *et al.* (2010) used itraconazole at 5 mg/kg, once daily, every other week combined with twiceweekly rinsing in enilconazole. All cats were cured within 56 days.

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Study results

Mycological cure was defined as two consecutive negative weekly fungal cultures. Twenty-one cats were treated with the 14-day protocol and although all improved, they relapsed and had to be treated with the itraconazole rescue treatment with 100% resolution (the rescue treatment was 21 days of itraconazole at 10 mg/kg, once daily plus lime sulphur rinses). Sixtyfour cats were treated with a 21-day protocol of oncedaily terbinafine as described above. The mean and median number of days to cure was 22.7 days with the range being 13 to 39 days. This shows that 21 days of oral terbinafine at approximately 30 mg/kg oncedaily with concurrent lime sulphur dipping is a highly effective way of treating feline dermatophytosis. At current prices, this treatment would be under \$5.00 (excluding mark up and GST).

We are fortunate in New Zealand to have two relatively safe, inexpensive treatments for a common disease. Although the studies describe the use of terbinafine and itraconazole in feline dermatophytosis, there is no evidence that they wouldn't be just as effective in canine dermatophytosis.

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