Transdermal drug therapy represents a milestone in veterinary pharmacotherapy. The noninvasive nature of transdermal gels facilitates compliance for any owner, alleviates the stress of patients, and bypasses the physiologic barriers to systemic bioavailability, such as hepatic first-pass metabolism and metabolism by gut-wall enzymes and microflora. Many drugs used in veterinary medicine have the potential to be absorbed transdermally and to safely produce desired therapeutic plasma concentrations. Historically, drugs such as nitroglycerin, fentanyl, fipronil, imidacloprid, ivermectin, selamectin, and other parasiticides have been administered to veterinary patients as approved transdermal products. Although scientific studies on compounded transdermal veterinary therapies are lacking, there are many cases in which the benefits of transdermally applied medication outweigh the risks, and veterinarians are prescribing this dosage form more frequently.

By considering the specific pharmacodynamic disposition of a drug in a given species and by determining objective assessment parameters for efficacy and toxicity, the veterinarian can attempt to predict whether the transdermal route will be safe and effective for a particular drug in a given patient. The anecdotal reports of many veterinarians attest to the efficacy of transdermally administered drugs (particularly those used in feline patients). Information about methimazole, the most commonly proposed drug for transdermal administration in cats, and suggestions for ensuring successful therapy are presented in this article.

Methimazole

Transdermal methimazole therapy is without a doubt effective in reducing the T4 level in many hyperthyroid cats. Because methimazole exerts very measurable effects on the circulating T4 level and produces very specific toxic effects in hepatic and hematologic tissues, it is the perfect drug for titrating safe and effective transdermal doses. At least two colleges of veterinary medicine (Purdue University and the University of Wisconsin) are currently conducting scientific studies on the bioavailability and efficacy of transdermal methimazole in cats. Although no data have yet been published, anecdotal reports indicate that transdermal methimazole is safe and effective in the treatment of feline hyperthyroidism (L Anderson, K Bush, T Currin, A Johnson, B Sigmon, and W Simpson, written communications, 2000). Hyperthyroid cats suffering from thyrotoxic cardiomyopathies do not benefit from the stress of forced oral administration, and in those patients, transdermal application is a valuable medication tool. A recent retrospective review (GD, unpublished data, 2000) revealed that 11 of 12 cats treated with 2.5 to 5 mg of methimazole transdermally twice daily in a penetration-enhancing gel exhibited a serum T4 level within the normal range within several weeks of the initiation of therapy. In those 12 cats, the diagnostic T4 value ranged from 3.9 to 24 µg/dL at the initiation of treatment.

The pharmacodynamic parameters of methimazole indicate that it might be more bioavailable after transdermal administration. The bioavailability of methimazole after oral administration can range from 48% to 90% in cats,¹ and the drug is...
apparently hepatically metabolized; only about 10% of the drug is excreted unchanged in the urine. Because transdermal methimazole bypasses the hepatic portal system and rate-limiting oral absorption factors, adverse effects may be more prevalent in cats that receive transdermal methimazole at oral dosage rates. Currently recommended oral doses for methimazole are 10 to 15 mg per cat daily and should be adjusted according to the severity of disease and the corresponding response to therapy. In a retrospective review, (L Anderson, K Bush, T Currin, A Johnson, B Sigmoid, and W Simpson, written communications, 2000), a higher incidence of blood dyscrasias was noted in feline patients when oral dosages of methimazole were administered transdermally. One of the prescribers (TC) in that review uses initial doses of transdermal methimazole of 2.5 mg TD every 12 hours. Cats receiving that dosage should be rechecked 2 weeks after the initiation of therapy to determine the T4 level and to evaluate hematologic and hepatic status. Depending on laboratory results at the recheck, transdermal methimazole can be incrementally increased or decreased in both dose and frequency to achieve desired results. T4 and laboratory parameters should be monitored monthly until the T4 level has stabilized. After a safe and effective transdermal dose of methimazole is established, the veterinarian should recheck the patient every 3 to 6 months. Rapid decompensation of renal function is another possible adverse event of correcting hyperthyroidism in cats. Hyperthyroidism usually causes increased renal perfusion and may mask signs of senile renal failure. After hyperthyroidism has been corrected, renal perfusion decreases and renal function deteriorates rapidly. Although this also occurs as a result of oral methimazole therapy, the increased bioavailability and correspondingly rapid decrease in the T4 level associated with transdermal therapy may be more likely to precipitate this syndrome. Renal function parameters should be carefully monitored when safe and effective transdermal doses of methimazole are determined. In some cats undergoing treatment for hyperthyroidism, treatment with all forms of methimazole induces acquired myasthenia gravis.

Monitoring parameters for the efficacy of transdermal methimazole
- The T4 level returns to a normal value (1 to 4 µg/dL)
- Clinical symptoms of hyperthyroidism dissipate (vocalization, polyphagia, weight loss, polyuria, polydipsia, vomiting, poor hair coat)

Monitoring parameters for the toxicity produced by transdermal methimazole
- Bone marrow suppression and decreased white blood cell count
- Worsening of vomiting
- Dermal reactions and excoriations
- Hepatic dysfunction as indicated by the levels of alanine transaminase (ALT) and aspartate transaminase (AST)
- Decompensation of renal function

Pharmacodynamic consideration
- An oral bioavailability of 48% to 90% in cats necessitates reducing the initial transdermal dose to determine therapeutic and toxic effects.

References