DERMATOLOGY PEARLS

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Issues with Compounded Medications in Veterinary Medicine

Doxycycline concentration over time after storage in a compounded veterinary preparation.

Papich MG, Davidson GS, Fortier LA. J Am Vet Med Assoc. 2013 Jun 15;242(12):1674-8.

PROCEDURES: Doxycycline hyclate tablets were crushed and mixed with a 50:50 mixture of syrup and suspension vehicles for oral administration. Doxycycline concentration was measured on days 0 (date of preparation), 1, 4, 7, 14, 21, and 28.

RESULTS: On days 0, 1, 4, and 7, the concentration of each formulation was within 90% to 110% of the reference, which was deemed acceptable. However, doxycycline concentrations had decreased dramatically by day 14 and remained low for the duration of the study period. Doxycycline concentrations on days 14, 21, and 28 were all < 20% of the reference standard, and the quality of the formulations decreased as well. No effect of storage temperatures on doxycycline concentration was identified.

CONCLUSIONS AND CLINICAL RELEVANCE: The concentration of doxycycline, compounded from commercial tablets cannot be assured beyond 7 days.

Bioequivalence of orally administered generic, compounded, and innovator-formulated itraconazole in healthy dogs.

Mawby DI, Whittemore JC, Genger S, Papich MG. J Vet Intern Med. 2014 Jan-Feb;28(1):72-7.

METHODS: Nine healthy, adult research Beagle dogs were used. After a 12-hour fast, each dog received 100 mg (average: 10.5 mg/kg) of either innovator itraconazole, an approved human generic capsule, or compounded. Plasma was collected at predetermined intervals for high pressure liquid chromatography analysis.

RESULTS: Average ratios of compounded and generic formulations to the reference formulation of itraconazole for AUC were 5.52% and 104.2%, respectively, and for C(MAX) were 4.14% and 86.34%, respectively.

CONCLUSION AND CLINICAL IMPORTANCE: Neither generic nor compounded itraconazole is bioequivalent to the reference formulation in dogs. However, pharmacokinetic data for generic formulation were similar enough that therapeutic concentrations could be achieved. Compounded itraconazole produced such low plasma concentrations, it is unlikely to be effective; therefore, compounded itraconazole should not be used in dogs.

Accuracy and precision of compounded ciclosporin capsules and solution.

Umstead ME, Boothe DM, Cruz-Espindola C, et al. Vet Dermatol. 2012 Oct;23(5):431-e82

METHODS: Each compounded cyclosporine sample was acquired by prescription from five pharmacies at three different times, 14-45 days apart. Atopica and three human generic modified cyclosporin formulations were positive controls. Accuracy (percentage predicted) was based on CsA strength measured by high-performance liquid chromatography and precision was based on replications (n = 3) from each pharmacy.

RESULTS: Accuracy of positive controls ranged from 92 to 103%. For compounded solutions, physical characteristics differed markedly between but not within pharmacies. Capsule accuracy was 10 ± 0.98 mg (101%) for 10 mg and 290 ± 9.6 mg (97%) for 300 mg; and solution accuracy was 45 ± 9.9 mg/mL (90%) for 50 mg/mL and 127 ± 18 mg/mL (85%) for 150 mg/mL. The precision for 50 mg/mL oral solution was 0.67-11%, and for 150 mg/mL, 3.7-14%. Accuracy for all preparations varied, with the least accurate deviating by 34% from labelled strength. Precision for all capsules ranged from 0.6 to 8.7%.

CONCLUSIONS AND CLINICAL IMPORTANCE: Compounded CsA solutions may deviate by more than 10% from the labelled strength. Bioavailability and clinical efficacy of compounded CsA remain unknown, and such products should be prescribed only in appropriate circumstances.

Comparison of serum dexamethasone concentrations in cats after oral or transdermal administration using pluronic lecithin organogel (PLO): a pilot study.

Willis-Goulet HS, Schmidt BA, Nicklin CF, et al. Vet Dermatol 2003 Apr;14(2):83-9.

Abstract

The objective of this study was to measure and compare the serum concentrations of dexamethasone after oral and transdermal administration using pluronic lecithin organogel in six healthy cats. The cats received a single dose (0.05 mg kg(-1)) of dexamethasone either orally or transdermally on the inner pinna. Blood samples were taken at 0, 5, 15, 30, 60, 90 and 120 min, and 3, 4, 6, 8, 12 and 24, 48 and 72 h post dexamethasone administration. A mean peak serum concentration of 30.1 ng mL(-1) was detected 15 min after oral administration. Serum concentrations were below detection limits by 24 h. In contrast, there was no significant increase in serum concentrations of dexamethasone after transdermal administration. In cats, transdermal administration of a single dose of dexamethasone did not result in significant serum concentrations compared to oral administration.

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Absorption of transdermal and oral cyclosporine in six healthy cats.

Miller R, Schick AE, Boothe DM, Lewis TP. J Am Anim Hosp Assoc. 2014 Jan-Feb;50(1):36-41

Abstract

Cyclosporine is commonly used orally to treat feline dermatoses. Due to difficulties administering oral medications, veterinarians sometimes prescribe compounded transdermal cyclosporine, despite studies showing limited absorption. The study objective was to compare cyclosporine blood concentrations after oral administration to concentrations after transdermal application of cyclosporine (prepared in pluronic lecithin organogel [PLO]) in six cats. Cats were dosed at 5.1-7.4 mg/kg of cyclosporine q 24 hr either per os for 7 days or transdermally for 21 days. Cyclosporine blood concentrations were measured q 7 days. Median concentrations on the seventh day were 2,208 ng/mL (range, 1,357-3,419 ng/mL) 2 hr after orally administered cyclosporine, and 37 ng/mL (range, 25-290 ng/mL) 2 hr after transdermally applied cyclosporine. Median concentration on day 21 was 58 ng/mL (range, 51-878 ng/mL) 2 hr after transdermally applied cyclosporine. Concentrations were quantifiable for transdermally applied cyclosporine, but considered therapeutic in only one of six cats. Based on those results, transdermally applied cyclosporine is not recommended in cats because of inconsistent absorption.