ClearH2O®

TECHNICAL BULLETIN

Stability of antibiotic **trimethoprim-sulfamethoxazole** in three different rodent water formulations

Introduction

The administration of antibiotics, and in general medications, in drinking water is desirable as it results in decreased handling and less stress to the animal while also saving time for research and animal care staff. However, specific guidelines regarding dosages and appropriate formulation preparations are scarce. Previous studies evaluated the efficacy of various antibiotic in water bottle formulations with variable results: mean plasma concentrations measured for the antibiotics were below the lower range of the minimal inhibitory concentration for many pathogens.

The goal of this preliminary study was to determine the stability of pharmaceutical grade trimethopri-sulfamethoxazole (TMP/SMX or TMS) in three different rodent water bottle formulations: reverse osmosis (RO) water, acidified water (AW), and **MediDrop® Sucralose** (MD), a sweetened water gel.

Protocol

Hi Tech Pharmacal SMX/TMP 200mg/40mg per 5ml solution was diluted at 0.8 mg SMX & 0.16 mg TMP per mL in both waters (10ml in 490ml water for both RO and AW) and at 0.4 mg SMX & 0.08 mg TMP per mL in **MediDrop® Sucralose** (MD, 5ml in 495ml), to reach a dosage of 30mg/kg, based on mice drinking 4-6ml of water per day. Please note that the volume used in the SWG suspension was halved due to the product's indicated ability to maintain an additive in homogeneous suspension.

Water bottles were suspended from wire racks in empty standard conventional mouse cages for 7 days and left undisturbed. Sample aliquots of 5 ml were collected from each water bottle lixit to mimic the water the mice would be drinking from the end of the sipper tube. Samples were analyzed by High-performance liquid chromatography (HPLC) at 0h, 4h, 8h, 24h, 4 h, 72h and 168h time points.

For the in vivo studies, blood samples were collected from mice (n=4) at day 3 and day 7 after consumption of the antibiotic formulations, and analyzed by HPLC.

	TMP concentration in mcg/mL						
Time (h)	0	4	8	24	48	72	168
RO	19.8	19.8	19.84	21.62	20.2	19.9	21.92
AC	50.9	45.65	45.73	-	43.87	44.29	44.6
MD	93.01	91.32	91.95	93.02	93.31	94.56	93.36
	SMX concentration in mcg/mL						
Time (h)	0	4	8	24	48	72	168
RO	59.5	31.08	28.62	31.22	33.06	30.77	37.47
AC	116.43	103.07	101.08	-	79.22	83.51	84.66
MD	336.39	333.85	343.73	340.96	348.83	346.92	344.69

Table 1

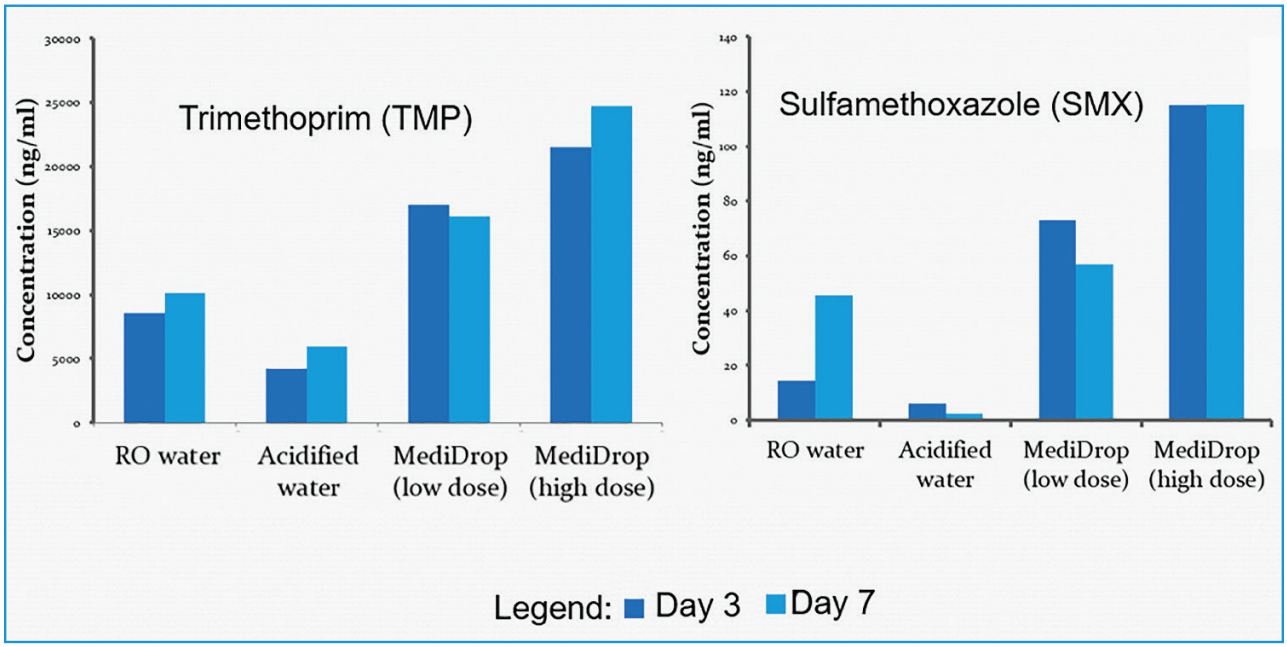

Figure 1

Results & Discussion

In vitro analysis results showed that SMX precipitated out in RO & AW groups, whereas concentration levels of both SMX and TMP remained steady throughout the experimental period in **MediDrop® Sucralose** (Table 1). *In vivo*, levels of both constituents were up to 10 times higher in the plasma of mice when delivered through **MediDrop® Sucralose** compared to water (Figure 1).

The results indicate that the antibiotic TMS concentration available to the animal is influenced by compounding and can vary in different rodent water bottle formulations depending on the characteristics of the solvent. **MediDrop® Sucralose** provides effective dosage of TMS, maintaining medication in suspension and facilitating consistent delivery without the need to shake the bottles daily, saving time and labor.

Acknowledgement: We would like to thank the City of Hope for conducting this study.

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