ClearH2O®

TECHNICAL BULLETIN

The Use of **MediGel® Sucralose** as an Oral Delivery System for Carprofen

A STUDY TO DETERMINE DRUG HOMOGENEITY, STABILITY AND GEL STERILITY

Introduction

MediGel®Sucralose is a thermoreversible, sweetened soft gel designed for oral medication delivery for rodents. It contains 98% water and is often used as the rodent's sole water source. **MediGel®** can be used for delivering a variety of oral medications such as meloxicam, carprofen, and buprenorphine. Ensuring that medications can be mixed into the gel matrix homogenously is critical for proper dosing of rodents. Further, it is also critical to understand the stability of the medication in the gel and the sterility of the gel after mixing. Therefore, what is needed is a standard mixing protocol for medications which confirms medication homogeneity, stability and sterility. This study confirms that liquid carprofen, when mixed into heated and liquefied **MediGel®Sucralose**, is indeed homogeneous, stable and does not impact the sterility of the gel.

Materials

Injectable carprofen (Rymadyl, Zoetis), 50mg/ml, was used for stability testing. From this solution, 0.6ml was added to 1 ml of the autoclaved blue-dyed saline (1.6 ml total volume). Then, 0.06 ml of this solution was injected into each 2 oz. cup of **MediGel®Sucralose** that was heated to 60C and liquefied. Since there is an average of 60 ml of gel per cup, the resulting carprofen concentration on average, was estimated to be 25 mg/kg (+/- 3mg/kg).

Protocol

MediGel®Sucralose cups were heated in a 60° C water bath for 10 minutes in order to liquefy the gel. The cups were removed and the lids were sanitized with alcohol. The carprofen/blue dye solution was then injected through the sanitized foil lid. A sticker was placed over the injection site.

To achieve cooling and re-solidification of the gel, the samples were then either left out at room temperature or refrigerated in accordance with the group treatment protocol.

The following groups were prepared:

1) **MediGel®Sucralose**, unrefrigerated, mixed by hand only for 10 seconds; 2) **MediGel®Sucralose**, refrigerated, mixed by hand only for 10 seconds; 3) **MediGel®Sucralose**, unrefrigerated, mixed 15 seconds by hand and 15 seconds by vortex; 4) **MediGel®Sucralose**, refrigerated, mixed 15 seconds by hand and 15 seconds by vortex.

Sterility testing was done by Charles River Laboratory for both anaerobic and aerobic bacteria.

Samples were shipped overnight to MMS Analytical laboratories for stability testing. One sample from each group was used for analysis. To confirm the homogeneity of the drug within the groups 3 samples were taken from each cup at different locations and subjected to HPLC analysis. Once homogeneity was confirmed, additional testing was conducted at days 7, 14, 21 and 28 by HPLC analysis to confirm stability.

Results

The groups that were only hand-shaken did not display complete drug homogeneity, with the non-refrigerated cups having an average concentration of 16.93 mg/kg and the refrigerated cups having an average concentration of 18.90 mg/kg. In contrast, the 15 second hand-shaken/vortexed samples did display homogeneity, with the non-refrigerated cups having an average concentration of 23.66 mg/kg and the refrigerated samples having an average concentration of 23.80 mg/kg. Stability testing was then conducted on only the 15 second hand-shaken/vortexed samples.

Stability testing on the 15 second hand-shaken/vortexed samples, both refrigerated and non-refrigerated, demonstrated drug stability at day 14, with concentrations of 27.08 mg/kg for the refrigerated sample and 26.01 mg/kg for the non-refrigerated sample (Fig.1). At day 28 the refrigerated sample had a concentration of 22.03 mg/kg whereas the non-refrigerated sample had a concentration of 23.48 mg/kg. These results were within the range of +/- 3 mg/kg from the original calculated concentration of 25 mg/kg (Fig.1).

For sterility testing, refrigerated and non-refrigerated gel samples of **MediGel® Sucralose** with carprofen/blue dye solution tested negative for bacterial growth out to 28 days with the exception of one positive result for non-refrigerated on day 7 (Table 1). Given that day 14, 21 and 28 tested negative, the positive sample at day 7 was considered an anomaly and likely due to contamination during sampling. The results indicate that the refrigerated and non-refrigerated gel remains sterile out to day 28.

Fig.1: Carprofen stability

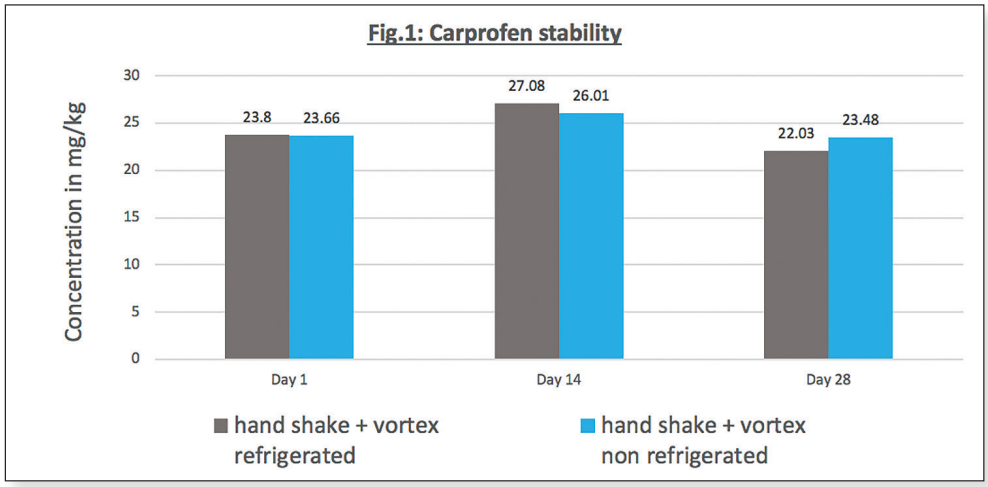

Table 1:
Sterility Testing Out to 28 Days

SAMPLE	REFRIGERATED	NON-REFRIGERATED
Day 7	Negative	Negative
Day 14	Negative	One Positive
Day 21	Negative	Negative
Day 28	Negative	Negative

Discussion

MediGel® Sucralose is an effective water gel delivery system for rodents. Previous studies have demonstrated that **MediGel® Sucralose** can be used as a delivery system for a variety of medications including carprofen. When liquefied at 60C, injected with carprofen and hand-shaken/vortexed for 15 seconds, **MediGel® Sucralose** displayed homogeneous mixing, drug stability and sterility out to 28 days for both refrigerated and non-refrigerated samples. These results indicate that **MediGel® Sucralose**, when used under the care and supervision of a veterinarian, can potentially be a very effective oral delivery method for carprofen.

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

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