



Evaluation of Medicated Gel as a Supplement to Providing Acetaminophen in the Drinking Water of Sprague Dawley Rats After Surgery

Laura E. Riddle, DVM, MPH¹ and Nicole K. Rowley, DVM, MPH²

¹US Army Institute of Surgical Research, JBSA Fort Sam Houston, TX

²Department of Laboratory Animal Resources, Uniformed Services University of the Health Sciences, Bethesda, MD



The opinions or assertions contained herein are the private views of the author and are not to be construed as official or as reflecting the views of the Department of the Army or the Department of Defense.

Introduction

- Regulations and performance-based standards pertaining to animal research stipulate that pain and distress must be alleviated or reduced to improve the welfare of animals used in scientific studies.
- Analgesics that are orally self-administered by an animal can reduce distress by eliminating handling and the potential disruption of the animal's diurnal rhythm⁴⁻⁶.
- One method of providing oral analgesics to laboratory rodents is in the drinking water^{1,5}.
- Acetaminophen is a commonly used rodent analgesic that is easily obtained and is not a controlled substance, though neophobia has sometimes been reported^{1,3}.
- Many new gel products are available for rodents that can deliver various drugs and nutrients; studies have been performed in mice to evaluate the preference of self-administered acetaminophen consumption in water and/or a gel delivery system^{2,3}, but no research has been done to evaluate the ingestion of oral medication in gel products by rats.

Objectives

- **Objective:** Establish whether the rats displayed a preference for medicated water, gel, or a combination following a surgical procedure.
- **Hypothesis:** Each delivery system would be consumed equally as well and that providing both delivery methods (water and gel) would increase the likelihood that the animals received a targeted therapeutic dose.

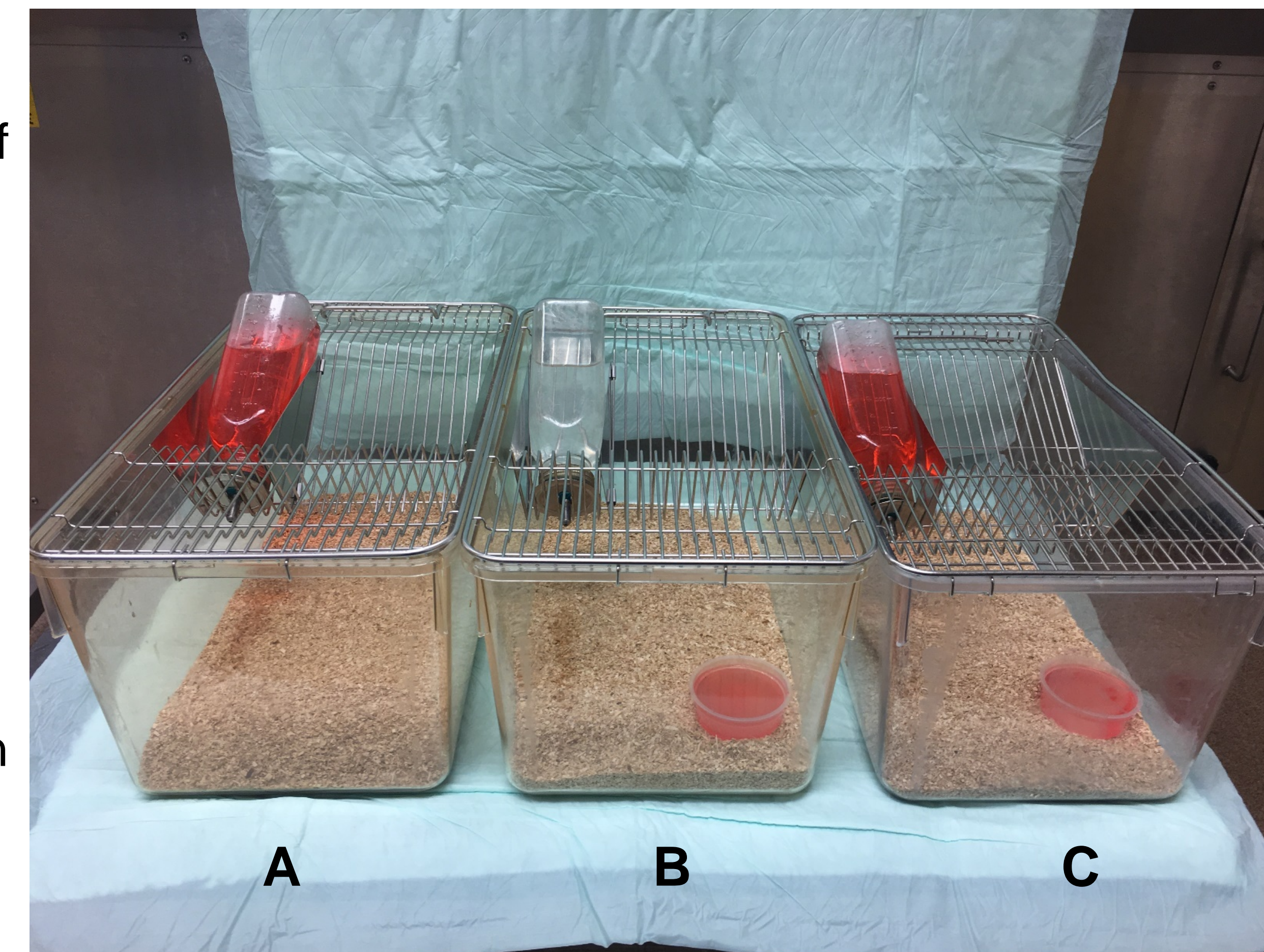
Methods

- Anesthetized male Sprague Dawley rats (n=30) underwent a laparotomy using a modified version of an established surgical model of postoperative pain in rats.
- Rats were randomly assigned to one of 3 treatment groups post-surgery with n=10/group: acetaminophen in water (AW), acetaminophen in gel (AG), and acetaminophen in water and gel group (AWG) (Figure 1).
- Measurements were taken from the day prior to surgery (day -1) to three days post-surgery (days 1-3). Rats were weighed daily for the duration of the study. Water bottles were weighed on days 0 and 3. Gel cups were weighed daily, and a new gel cup was weighed and placed into the cage daily for rats assigned to the AG and AWG groups; the old gel cup was also weighed and then discarded daily.

Methods

- The acetaminophen dose provided was calculated to fall within the recommended oral dosage range of 110 to 305 mg/kg for rats⁵, and the desired concentration of the water and gel was 2 mg/mL to achieve a targeted dose of 200 mg/kg, which falls within the therapeutic range.
- The amount of water and/or gel ingested in mL per rat was then multiplied by the acetaminophen concentration in the water or gel to obtain a total amount of acetaminophen ingested per animal.

Figure 1. Cage Set Up for Treatment Groups. Acetaminophen in water group - AW (A). Acetaminophen in gel group - AG (B). Acetaminophen in water and gel group - AWG (C).



Results

Delivery system for acetaminophen was consumed equally as well among the three treatment groups, and all groups exceeded the targeted therapeutic dose of 200 mg/kg.

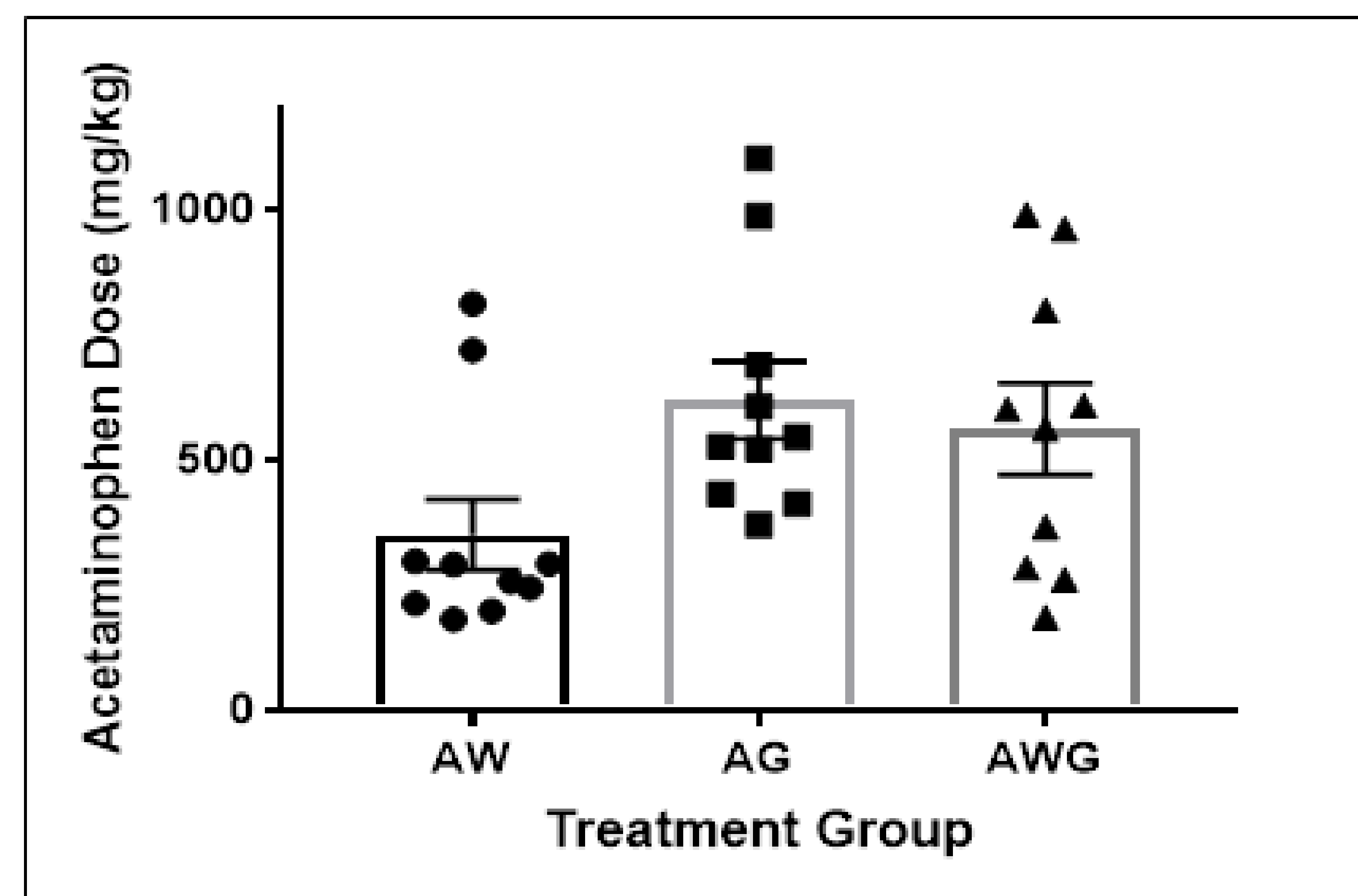


Figure 2. Daily average acetaminophen dose per rat in each treatment group by gel and/or water consumption (mg/kg; mean ± SEM). AW group is depicted by circles, AG group is depicted by squares, and AWG group is depicted by triangles. There was no significant difference in average daily acetaminophen dose between the treatment groups.

Conclusions

- A preference of delivery system was not observed, as there was no significant difference among the three treatment groups.
- Based on average daily water consumption, it was assumed that the rats would consume 38-52 mL of water and/or gel per day; each of the three treatment groups fell within or exceeded this expected range.
- Neophobia did not appear to be a factor in the amount of acetaminophen consumed.
- The weights of the rats in each group decreased significantly the day following surgery, though all three groups showed varying rates of weight gain in the 3 days post-surgery, with the AG group gaining the least.

Future Studies

- In long term studies, it may be beneficial to provide both acetaminophen-treated water and gel, as a preference was not observed and this may allow for an increased rate of weight gain beyond what was observed when the rats were provided gel alone.
- The gel cups may need to be replaced more frequently, i.e. very 12 hours, to prevent the possible ingestion of foreign material, as this could have deleterious effects on the health and well-being of the animals and confound data.

Acknowledgements

- The authors would like to thank the technicians and veterinarians at Uniformed Services University for their help in completing this project.
- We would also like to thank Sorana Raiciulescu and Cara Olsen for their help with study design and statistics.

References

1. Bauer, DJ et al. (2003) Acetaminophen as a postsurgical analgesic in rats: a practical solution to neophobia. *Contemporary Topics* 42(2):20-24
2. Brunell, MK et al. (2017) Evaluation of consumption of self-administered acetaminophen in drinking water and two gel delivery systems in C57BL/6 mice. *Internet Journal of Veterinary Medicine* 14(1). doi: 10.5580/IJVM.52393
3. Christy, AC et al. (2014) Evaluation of medicated gel as a supplement to providing acetaminophen in the drinking water of C57BL/6 mice after surgery. *Journal of the American Association for Laboratory Animal Science*.
4. Cooper DM, et al. (1997) Analgesic efficacy of acetaminophen and buprenorphine administration in the drinking water of rats. *Contemporary Topics* 36(3):58-62.
5. Flecknell, PA. (1984) *Laboratory Animal Anesthesia*. Academic Press.
6. Fox, JG et al. (2015) *Laboratory Animal Medicine*. Academic Press.

Statements

Research was conducted in compliance with the Animal Welfare Act, the implementing Animal Welfare Regulations, and the principles of the Guide for Care and Use of Laboratory Animals, National Research Council. The facility's Institutional Animal Care and Use Committee approved all research conducted in this study. The facility where this research was conducted is fully accredited by AAALAC..