**STABILITY OF EXTEMPORANEously COMPOUNDED Piroxicam 10MG/ML SUSPENSION WITH ACETATE BUFFER**

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INTRODUCTION

Piroxicam is a cyclooxygenase-1 and -2 (COX-1, COX-2) inhibiting, non-steroidal anti-inflammatory (NSAID) that is primarily used in the treatment of rheumatoid arthritis, osteoarthritis and rheumatic fever.1-6 NSAI&D’s specifically COX-2 inhibitors are recommended for primary or adjunctive therapy in the treatment and prevention of cancer.6 In veterinary medicine, piroxicam is commonly used as an adjunctive therapy for bladder transitional cell carcinoma in canines and felines. It may also be beneficial in equine sarcoid cell carcinoma, mammary, adenocarcinomas and carpal osteosarcoma in cats.7

Drugs have a limited and transient form, both of which influence its absorption in the body. To compete in its control form, the formulated form of drugs are usually absorbed due to its lipid solubility and lack of charge.8 Piroxicam is an amphiphatic drug; thus, it has the ability to form micelles and solubilize in the formulation.9 Piroxicam is water-soluble and highly acidic (pK=3.91 and 5.60 assigned to the weakly acidic 4-acetic acid and the strong basic 11-aminomethylpyridinium salt).3,10 According to USP <795>, in the absence of stability information the storage period for suspensions not less than (NLT) 90% and not more than (NMT) 110% of the original piroxicam concentration with no visible caking, turbidity or phase separation. Following USP <795> standards, suspensions not less than (NLT) 90% and not more than (NMT) 110% of the original piroxicam concentration in suspension may be stable for up to 90 days at room temperature (20° to 25°C).11

METHOD

**COMPONDING**

Piroxicam is a COX-2 specific inhibitor, specifically COX-2 nonsteroidal anti-inflammatory (NSAID) that is primarily used in the treatment of rheumatoid arthritis, osteoarthritis and rheumatic fever.1-6 NSAI&D’s specifically COX-2 inhibitors are recommended for primary or adjunctive therapy in the treatment and prevention of cancer.6 In veterinary medicine, piroxicam is commonly used as an adjunctive therapy for bladder transitional cell carcinoma in canines and felines. It may also be beneficial in equine sarcoid cell carcinoma, mammary, adenocarcinomas and carpal osteosarcoma in cats.7

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All study groups retained NLT 90 and NMT 101% of the original concentration with no degradation products of piroxicam, particularly 2-aminopyridine, were performed with HPLC.2,3,6

**RESULTS & DISCUSSION**

The accelerated testing conditions of 40°C ± 2°C/75% RH ± 5% is based on the Food and Drug Administration (FDA) accelerated testing guidelines for drug substance and drug products. According to Arthritis’ equation and the accelerated spring time (AES) equation, 28 days under the following test conditions of 40°C ± 2°C/75% RH ± 5% with an aging factor (Qa), is equivalent to 3 months real time at ambient temperature (Ta=23°C).12,13

Following USP <795> standards, suspensions not less than (NLT) 90% and not more than (NMT) 110% of the original piroxicam concentration in suspension may be stable for up to 90 days at room temperature. Due to a lack of established stability studies, this study examines the stability of compounded water soluble acetic acid 10 mg/mL piroxicam suspension with or without acetate buffer in glass amber bottles and plastic amber syringes under room temperature (20° to 25°C) and accelerated conditions (40°C ± 2°C/75% RH ± 5%) is equivalent to 3 months real time.

**OBJECTIVE**

According to USP <795>, in the absence of stability information the storage period for compounded water soluble piroxicam 10 mg/mL suspension with or without acetate buffer in glass amber bottles and plastic amber syringes under room temperature (20° to 25°C) and accelerated conditions (40°C ± 2°C/75% RH ± 5%) is equivalent to 3 months real time.

**MATERIALS**

**PIROXICAM SUSPENSION**

Piroxicam USP-powder (Medisca Pharmacueutical Inc, Montreal, Quebec; lot 612583D) and Piroxicam USP in Oral Suspens (Medisca Pharmacueutical Inc, Montreal, Quebec; lot 100515M-A, expiry February 2018)

**ACETATE BUFFER**

Acetic acid (PCCA, Houston, Texas; lot C176571; expiry September 2018)

**PACKAGING**

Glass Bottle Bottles 60ml (E.D. Luce Packaging, Cornsalls, California; item no. BA02)

Medisca Adapter Caps - Blue II, 20mm (Medisca Pharmacueutical Inc, Montreal, Quebec; lot 12852CD)

Polypropylene Amber Syringes 60ml (Medisca Pharmacueutical Inc, Montreal, Quebec; lot 1271979)

The pH of the both control and buffer groups remained consistent throughout the study with no statistical significant difference comparing Day 1 to Day 28. At the end of the study on Day 28, the control group mean pH and standard deviation was 4.29±0.04, and the buffer group mean pH and standard deviation was 5.13±0.02.

There were several limitations to the study. Due to limited time for the project, only 28 days of real-time stability was explored. Since HPLC was performed offline at KB Analytical, LLC in Oakland, CA, researchers were not able to properly observe the HPLC stability plate during the working days. Due to the advancement of analytical chemistry, drug stability is more commonly associated with formation of low levels of degradation rather than loss of drug potency over time.11 No degradation products of piroxicam, particularly 2-aminopyridine (APA), were noted on any of the TLC plates, but was mentioned in the article referenced as the basis of the stability-indicating HPLC determination of piroxicam.12

Future recommendations for this study is to explore a prolonged stability study with duplicate or triplicate samples. Also, a method development for the stability-indicating HPLC method of piroxicam utilizing other methods such as High Performance Liquid Chromatography (HPLC). Potentially continue this study to a randomized control trial for efficacy and compare the compounded piroxicam 10mg/mL suspension with acetate buffer in canines and felines.

**CONCLUSION**

Piroxicam 10mg/mL suspensions in Oral Suspens with or without acetate buffer stored in glass amber bottle were stable for up 90 days at room temperature (20° to 25°C) and refrigerated temperature (2° to 8°C). When stored in plastic amber syringes, piroxicam suspension with or without buffer can be stable for up to 90 days at room temperature (20° to 25°C) and up to 28 days at refrigerated temperature (2° to 8°C).

**ACKNOWLEDGMENT**

I would like to thank my preceptor Dr. Vishal Purohit and Thibaa Flam, R&D Associate from Medisca, for guidance throughout the study period. I would also like to thank Dr. Srinivasan, Director from KB Analytical LLC, for performing all the HPLC analyses.

**FUNDING**

This study was funded by an unrestricted educational grant from Medisca Pharmaceutical Inc.

**COMPETING INTEREST:** Other than grant support, no competing interests were declared.

**REFERENCES**


10. Ref. 4 above.

11. Ref. 5 above.

12. Ref. 6 above.

13. Ref. 7 above.