dx.doi.org/10.14227/DT240117P40

Technical Note: Analysis of Compounded Animal Drug Samples

Kent Alleman
Zoetis, Analytical Sciences, Kalamazoo, MI
e-mail: kent.s.alleman@zoetis.com

ABSTRACT

Samples of an animal health solid oral dosage form were obtained from four compounding pharmacies in the United States. Standard quality and performance tests were conducted on the samples including dissolution testing. Results are presented, and the value of dissolution testing as part of a quality assessment is discussed.

KEYWORDS: Animal health; dissolution; quality test; compounding pharmacy.

INTRODUCTION

Compounding is an integral part of pharmacy practice and is important for addressing individual patient needs. The pharmacist is responsible for compounding preparations of acceptable strength, quality, and purity with appropriate packaging and labeling in accordance with good pharmacy practices, official standards, and current scientific principles (*1*). The *USP* General Chapter <1163> Quality Assurance in Pharmaceutical Compounding includes testing as one of the nine components of a quality assurance program for compounded drugs. *USP* General Chapter <795> Pharmaceutical Compounding–Nonsterile Preparations specifically mentions that providing high-quality compounded preparations extends to animal patients. The focus of the quality systems and testing is on ensuring the identity, potency/strength, absence of contamination, and microbial quality. However, product performance tests such as dissolution testing are not typically emphasized. Because many physical (particle size, crystal form) and chemical (salt form, solvates) quality parameters can affect dissolution rate, it can be a powerful technique for evaluating product quality along with identification and potency tests.

EXPERIMENTAL

Samples of "product X" were obtained from four different compounding pharmacies in the United States. The approved dosage form of "product X" is an immediate-release film-coated tablet. The active ingredient in "product X" is a salt of a freebase. The freebase is practically insoluble in water, while the salt is soluble at about 40 mg/mL in water. Compounded samples came in the form of 8-mg capsules, 16-mg capsules, 16-mg tablets, and 12-mg tablets. Limited samples were available for testing, so complete characterization with many replicates was not possible. Samples were subjected to identification, counterion, potency, and dissolution testing. A high-level summary of the results is shown in Table 1.

Table 1. Summary of Test Results for "product X" Obtained from Compounding Pharmacies

Sample	Sample Type	Identification	Correct Counterion	Potency (% of label)	Dissolution[a] (% of label)
Pharmacy A	8-mg capsule	Positive	No	95 (*n* = 5)	88
Pharmacy B	16-mg capsule	Positive	No	86 (*n* = 3)	63
Pharmacy C	16-mg tablet	Positive	Yes	98 (*n* = 3)	97
Pharmacy D	12 mg tablet	Positive	No	112 (*n* = 5)	89

[a]*Dissolution results are the average of six dosage units calculated as % of label claim dissolved at 30 min. The dissolution specification is Q = 75% at 30 min.*

RESULTS AND DISCUSSION

All of the samples contained the correct active ingredient, but only one sample contained the approved counterion. The counterion (and polymorph) are critical quality parameters that can affect many physiochemical and biopharmaceutical properties such as solubility, stability, hygroscopicity, intrinsic dissolution rate, and toxicity.

Assay (or potency) was conducted on individual dosage units or composite samples. A variety of potency results were obtained ranging from 86% to 112% of label claim. Pharmacy A and C samples were within the range of 90–110% of label, while those from Pharmacies B and D were outside of that range. Further testing was not possible due to sample amount limitations.

Dissolution conditions for "product X" are typical for an immediate-release tablet, USP Apparatus 2 (paddle) at 50 rpm in 900 mL of pH 4.5 acetate buffer. The dissolution specification for "product X" is Q = 75% at 30 min. Sinkers were employed for capsule samples. Individual unit dissolution results are shown in Table 2 and Figure 1.

Table 2. Individual Unit Dissolution Results from Pharmacies A–D

Sample	% of Label Dissolved
Pharmacy A	102, 92, 76, 85, 86, 85 (RSD 10%)
Pharmacy B	71, 65, 34, 72, 57, 80 (RSD 26%)
Pharmacy C	97, 101, 92, 96, 96, 99 (RSD 3%)
Pharmacy D	88, 88, 88, 89, 91, 90 (RSD 1%)

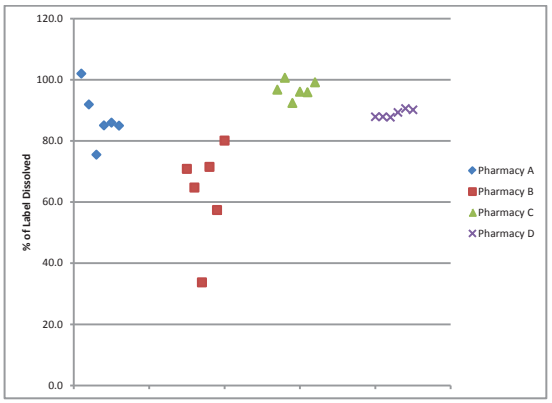

Figure 1. Plot of individual unit dissolution results from Pharmacies A–D.

Three of the four samples had acceptable dissolution results. Samples from Pharmacies C and D passed *USP* General Chapter <711> Dissolution Stage 1 requirements (all units ≥Q+5). Pharmacy A samples showed slightly higher variability and did not pass Stage 1 criteria. Samples from Pharmacy B showed high variability (26% RSD) and would fail all stages due to a very low result of 34% released in one sample. Recall that Pharmacy B samples were subpotent at 86% of label, which will affect the dissolution results. From the results available, the source of variability is not clear; it could be a sign of content uniformity problems, poor or inconsistent dissolution characteristics, or incorrect salt form.

Dissolution testing is an important part of quality testing for compounded drugs whether they are for animal or human use. Dissolution testing alone can indicate a multitude of quality issues. Identity, high and low potency, incorrect salt form, incorrect polymorph form, and content uniformity can all affect dissolution performance. If sample availability allows, dissolution results should be interpreted in light of additional testing such as identity, potency, and salt form.

CONFLICT OF INTEREST

No conflict of interest has been declared by the author.

REFERENCE

Allen, L. V., Jr. Guidelines for Compounding Practices. In *The Art, Science, and Technology of Pharmaceutical Compounding*, 4th ed.; American Pharmacists Association: Washington, DC, 2012; pp 1–18.