

# Compounded Phenylbutazone Powder: Content and Dosing Concerns

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VIEWPOINT

## INTRODUCTION

Phenylbutazone (PBZ) is almost certainly one of the more commonly prescribed pharmaceutical products given to the equine species. PBZ is a weakly acidic nonsteroidal antiinflammatory drug approved by the United States Food and Drug Association (FDA) for use in horses and dogs.<sup>1</sup> Its pain-relieving and anti-inflammatory effects likely relate to inhibition of prostaglandin synthesis.<sup>2</sup>

PBZ is provided from pharmaceutical manufacturers as an oral tablet, an intravenous (IV) preparation, a paste, a powder, or a gel. Unfortunately, all of these methods of administration have some disadvantages, such as per-dose cost (paste or gel), need for intravenous administration (IV preparation), or difficulty in administration due to avoidance by the horse because of taste or method (paste, powder, gel, or pill).

Pharmacy compounding involves formulating a pharmaceutical product to produce a product for medical management. Licensed pharmacists legally compound products when no other FDA-approved product is available, or when a certain formulation is unavailable.<sup>3</sup> Although a powdered PBZ product was recently approved by the United States Food and Drug Administration (FDA; <http://www.fda.gov/cvm/FOI/200-334111805.pdf>, accessed July 15, 2006), compounding pharmacists continue to

respond to the demand for a PBZ product that may avoid some of the administration difficulties posed by other formulations, including the powdered one, by attempting to produce a product that is palatable to the horse and is easily measured by the person administering the product. As such, PBZ is available from numerous compounding pharmacies in a variety of flavors that are distinct from the FDA-approved product, including an apple-flavored powder.

However, some investigations have shown that pharmacy-compounded human drugs may differ in numerous quality parameters from FDA-approved prescription products manufactured in regulated facilities, in areas including, but not necessarily limited to, product appearance, content uniformity, and weight uniformity.<sup>4,5</sup> This study was performed to see whether differences exist in compounded PBZ powder intended for use in horses.

## MATERIALS AND METHODS

Three plastic containers of apple-flavored phenylbutazone (PBZ) powder were ordered from each of five veterinary compounding pharmacies distributed across the United States. Each jar contained a small scoop, which, when filled according to the product label, was purportedly equivalent to 1 g PBZ.

Scoops from each container were taken according to one of two methods. In method 1, a scoop was filled to overflowing, then shaken until level. In method 2, a scoop was filled to overflowing and leveled by scraping against the edge of the container. Each measure was repeated three

times, and the total number of measures was averaged (Table 1).

One scoop of each sample, measured using method 1, was placed in a plastic Ziplock™ bag and labeled from 1 to 15. The investigators were blinded as to the compounding pharmacy that supplied the product.

The contents of each bag were weighed and recorded (see column "Original wt," Table 2). A subsample of each sample was weighed for analysis (see column "Subsampled wt," Table 2). Approximately 50 mg PBZ powder was weighed and placed in a 10-ml volumetric flask. Ten (10) ml high-performance liquid chromatography (HPLC) grade acetonitrile was added to each flask, and each flask was sonicated to ensure complete dissolution of the sample. One (1) microliter of each sample solution was added to 1 ml acetonitrile, vortexed, and capped for analysis by HPLC. Each sample was analyzed in duplicate.

A set of calibrators was prepared using a 1-mg/ml reference standard solution of PBZ. The calibrators consisted of 1, 3, 7, and 10  $\mu$ l, added to 1 ml acetonitrile, respectively.

All samples were analyzed. Concentrations were obtained for each of the sample duplicates and averaged. The average concentration obtained for each sample was multiplied by 10, to obtain the amount of PBZ in the 10-ml flask. To adjust for the fact that a 1- $\mu$ l volume was used (0.001 ml), the concentration was multiplied by a factor of 1,000, to change to concentration units from micrograms to milligrams. The total weight of each sample submitted was divided by each subsample weight. The resulting number was used as the multiplication

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**Table 1.** Phenylbutazone powder—scoops per container

<b>Product Number</b>	<b>Scoops/Container Method 1</b>	<b>Scoops/Container Method 2</b>
1	96	78
2	100	80
3	99	79
4	97	77
5	97	77
6	94	76
7	100	80
8	100	80
9	97	79
10	99	78
11	97	77
12	96	76
13	120	112
14	125	113
15	114	108
Median	97	78

factor to determine the amount of PBZ in the original sample. A variance from intended label content was calculated (Table 2).

## RESULTS

The number of scoops obtained from a container of compounded PBZ

powder product varies by the method of scooping. On average, scooping by method 1 provided approximately 22% more scoops than by method 2. Variance from label content in samples measured by method 1 ranged from -12.0% to +43.5%. The price of the compounded products varied from

\$20.00 to \$13.80 per container, not including shipping charges. Expiration dates on the product packages varied from 6 months to 30 months from the date of purchase.

## DISCUSSION

Compounded apple-flavored PBZ powder appears to be a popular product, according to discussions with the compounding pharmacists contacted for this study. However, this study would indicate considerable variation in that product regarding price, product content, and expiration date.

The price of the various compounded PBZ powders varied by as much as \$6.20 per container. None of the products were purchased at occasionally advertised “specials.” Accordingly, it may be worthwhile for veterinarians purchasing compounded apple-flavored PBZ products to compare prices before purchasing. In addition, if large quantities of PBZ powder are purchased at one time, it may be advisable to ask about the expiration date on the package before purchase so as to avoid the product

**Table 2.** Phenylbutazone powder—product content

Sample #	Conc/ HPLC ( $\mu\text{g}/\text{ml}$ )	$\times 10$	Subsampled Wt (mg)	Original Wt (mg)	Multiplication Factor Orig/ Subsample	PBZ per Total (mg)	PBZ g	% of Claim	Variance
1	3.44	34.4	50.1	1,282.3	25.59	880	0.880	88.0	-12.0
2	3.51	35.1	50.08	1,346.01	26.88	943	0.943	94.3	-5.7
3	3.76	37.6	50.07	1,273.72	25.44	956	0.956	95.6	-4.4
4	4.18	41.8	50.05	1,406.74	28.11	1,175	1.175	117.5	+17.5
5	4.71	47.1	50.09	1,159.95	23.16	1,091	1.091	109.1	+9.1
6	3.67	36.7	50.03	1,545.85	30.90	1,134	1.134	113.4	+13.4
7	4.84	48.4	50.08	1,230.31	24.57	1,189	1.189	118.9	+18.9
8	5.20	52.0	50.0	1,379.92	27.60	1,435	1.435	143.5	+43.5
9	5.19	51.9	50.05	1,107.82	22.13	1,149	1.149	114.9	+14.9
10	5.22	52.2	50.05	1,203.08	24.04	1,255	1.255	125.5	+25.5
11	5.02	50.2	50.08	1,133.66	22.64	1,136	1.136	113.6	+13.6
12	5.26	52.6	50.09	1,255.98	25.07	1,319	1.319	131.9	+31.9
13	2.76	27.6	50.07	2,268.69	45.31	1,251	1.251	125.1	+25.1
14	2.78	27.8	50.06	2,283.56	45.62	1,268	1.268	126.8	+26.8
15	2.56	25.6	50.07	2,675.48	53.43	1,368	1.368	136.8	+36.8

expiring before it can be sold or used.

The method of scooping appears to considerably affect the amount of product obtained from a single container. If the product is scooped, then leveled by scraping on the edge of the container, the number of individual servings may be reduced by an average of 22%. Whether this is due to packing of the PBZ itself or packing of any excipients that may be included in the formulation was not determined by this study. Method 1, shaking of a full scoop until it is level, gives more doses per container.

However, the dose of PBZ delivered in an individual scoop measured by method 1 varied from -12.0% to +43.5% of label content. If, by measuring using method 2, the amount of PBZ delivered is increased 22%, this would mean that an individual scoop could contain as much as 1.5 times more PBZ than was intended

(e.g., 1.5 g instead of 1 g). Because PBZ is characterized by a relatively narrow therapeutic index, accurate dosing is an important consideration.

Unfortunately, this study cannot determine whether a particular sample of PBZ powder will reflect the content of other samples taken at another time. The results obtained from study of one compounded product cannot predict the content of that same product at a future date. Nevertheless, this study indicates that if compounded PBZ products are used, they may contain PBZ; however, differences in dose from that which may have been intended can be expected based on method of scooping and individual product content.

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