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A COMPARISON OF DISSOLUTION FROM COMMERCIAL TABLETS AND FROM CAPSULES CONTAINING A POWDERED TABLET

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ABSTRACT

In clinical trials it may be necessary to convert a commercial tablet to a capsule so that the identity of each drug being tested remains unknown until the trial is completed. This study shows that for six commercial tablets, after pulverization and encapsulation of the powder, the in vitro dissolution was faster for one product, slower for two products and essentially unchanged for three products.

INTRODUCTION

Recently in manufacturing several capsule formulations for a comparative clinical study, it was necessary to use a commerical tablet as the source of one of the medicinal compounds because the pure compound was unavailable. As the size of the capsule had been determined by previous developmental and clinical studies of the new compound being evaluated, it was necessary to mill the commercial tablet so that it could be encapsulated into the same size and color capsule, which could be used in a blind study to conceal from the patient and the physician the identity of the various formulations.

Under these conditions in which a fixed diluent can not be used with each medicinal compound, the question arises as to whether milling alters the release pattern of the active ingredient. This report compares the dissolution profiles of several medicinal compounds from hard gelatin capsules containing pulverized

tablets as only the effect of grinding and encapsulation was being investigated.

EXPERIMENTAL

Preparation of Capsules. Tablets were triturated with a mortar and pestle, and the powder was passed through a 100-mesh sieve. A quantity of the powder equal to the weight of a tablet was filled without packing into a No. 1 hard gelatin capsule.

Procedure. The U.S.P. dissolution apparatus was used at 100 and 150 rpm to determine the dissolution profiles of the tablet and the capsule in 900 ml of dissolution medium maintained at 37 ± 0.5°C. If there was an official dissolution specification for a tablet, the dissolution medium specified by the U.S.P. was used. Aliquots were withdrawn at various intervals of time by means of pipet fitted with a filter. After each withdrawal of a sample, an equal volume of dissolution medium was added to the dissolution vessel. Modified Sorensen phosphate buffer was used to prepare a pH 7.6 buffer; the pH was verified by measurement with a pH-meter. The samples were appropriately diluted, and the absorbances were measured by a spectrophotometer at the wavelengths specified in the official monographs. The concentration was determined by use of a standard curve. The dosage form was allowed to dissolved, and this solution was assayed for the amount of active ingredient in the dosage form. The percent dissolved was then calculated. Dissolution profiles were drawn, and the time required for 50% and for 60% of the medicinal compound to dissolve was determined.

RESULTS AND DISCUSSION

Six commercial tablets (see Table 1) containing different chemical types of medicinal compounds were converted to capsules. The dissolution profiles were constructed from data obtained by using the N.F. Method II dissolution apparatus and the U.S.P. dissolution apparatus operating at 100 and 150 rpm. It was found that the N.F. Method II dissolution apparatus did not provide a

TABLE 1

Commerical Tablets Used

Tablet of	Content, mg	Company and Lot Number	Expiration Date
Acetaminophen	325	McKesson 6K047	November 1979
Aminophylline	200	Searle 976-001	July 1981
Dicumarol	50	Abbott 47-11-AA-22	February 1980
Hydrochlorothiazide	50	Esdrix®, Ciba 11021	January 1982
Pentazocine hydrochloride	50	Talwin®, Winthrop B005NE	May 1978
Sulfisoxazole	500	Gantrisin®, Roche 8632-1-136	October 1981

TABLE 2

Comparison of $t_{50\%}$ from Commerical Tablet and from Capsule Containing Powdered Tablet

Dissolution Medium	Compound	$t_{50\%}$, min, 100 rpm[a]		$t_{50\%}$, min, 150 rpm[a]	
		Tablet[b]	Capsule[b]	Tablet[b]	Capsule[b]
Distilled water	Acetaminophen	2.0	6.5	1.6	3.2
Distilled water	Aminophylline	5.7	12.2	4.3	9.8
Phosphate buffer pH 7.6	Dicumarol	21.7	16.6	14.3	13.7
HCl (1 in 12:15)[c]	Hydrochlorothiazide	3.8	5.0	3.8	4.8
HCl (1 in 100)[c]	Pentazocine hydrochloride	1.8	5.0	1.3	3.8
HCl (1 in 100)[c]	Sulfisoxazole	6.0	19.6	4.0	13.4

[a] U.S.P. dissolution apparatus

[b] average of two determinations

[c] U.S.P. dissolution medium

low intensity of agitation which would allow detection of differences in dissolution profiles.

The times ($t_{50\%}$) required for 50% of the medicinal compounds to dissolve in the U.S.P. apparatus are shown in Table 2. The dissolution of the gelatin shell and the exposure of the contents of the capsule to the dissolution medium occurs in approximately three minutes. The dissolution of dicumarol was faster from the capsule than from the tablet.

If one discounts the lag time due to dissolution of the gelatin shell, the dissolution of acetaminophen, hydrochlorothiazide and pentazocine hydrochloride was essentially unchanged by pulverization and encapsulation of commercial tablets.

The dissolution of aminophylline and sulfisoxazole was slowed by pulverization and encapsulation of commerical tablets.

The data demonstrate that conversion of a tablet to a capsule may not change dissolution, may slow dissolution or may increase dissolution. Since the formulations of the tablets are unknown, no comment can be made on the reasons for these effects. It is purpose of this report to shown that dissolution may be altered by conversion of a tablet to a capsule and that the effect on dissolution can not be predicted but must be experimentally determined.