DRUG DEVELOPMENT AND INDUSTRIAL PHARMACY, 17(17), 2401-2407 (1991)

QUANTITATION OF SCOPOLAMINE HYDROBROMIDE WHEN ADSORBED ONTO MICROCRYSTALLINE CELLULOSE AND SODIUM CARBOXYMETHYLCELLULOSE IN TABLETS

Yashoda Pramar and V. Das Gupta
Department of Pharmaceutics, University of Houston
1441 Moursund St., Houston, TX 77030

ABSTRACT

Both scopolamine and lidocaine (the internal standard) got adsorbed onto sodium carboxymethylcellulose and microcrystalline cellulose, which are commonly added to the tablets/capsules as excipients. In one tablet formula which contained both adsorbents, about 42% of scopolamine and 45% of lidocaine got adsorbed. Sodium carboxymethylcellulose by itself, adsorbed both drugs about 26.2 times more than microcrystalline cellulose, when compared on the basis of same weights. If hydrochloric acid was used in the extraction procedure, both scopolamine and lidocaine got desorbed and recovery was quantitative.

BACKGROUND

Sodium carboxymethylcellulose and microcrystalline cellulose are very commonly used excipients for tablets and capsules. The adsorption/complexation properties of sodium carboxymethylcellulose in solutions have been reported (1-2). The purpose of these investigations was to quantify scopolamine hydrobromide which was

adsorbed onto microcrystalline cellulose and sodium carboxymethylcellulose in tablets.

MATERIALS AND METHODS

Chemicals and Reagents: All the chemicals and reagents were USP-NF or ACS quality and were used without further purification. Scopolamine hydrobromide was purchased from City Chemical Company, New York, NY, and lidocaine hydrochloride injection (4%) was of a commercial lot by LyphoMed, Rosemont, IL.

Apparatus: A high-pressure liquid chromatograph (Waters ALC 202) equipped with a universal injector (Rheodyne Model 7125), a multiple wavelength detector (Schoeffel's SF 770, Kratos, Inc.) and a recorder (Omniscribe 5213-12, Houston Instruments, Austin) was used. A micro C_{18} column (Waters Associates, 30 cm x 3.9 mm i.d.) was the stationary phase.

Chromatographic Conditions: The mobile phase contained acetonitrile (34 % v/v) and 0.0066 M octanesulfonic acid in water. The pH was 3.5 ($\pm$ 0.05). This mobile phase and the assay method have been reported (3) by Walters, but it does not apply to the quantitation of scopolamine when adsorbed onto the excipients. The flow rate was 1.0 ml/min., the wavelength was 220 nm (sensitivity 0.1 AUFS), the chart speed was 30.5 cm/hr and the temperature was ambient.

Preparation of Stock and Standard Solutions: A stock solution of scopolamine hydrobromide was prepared fresh every day by dissolving 20.0 mg of the powder in enough water to make 100.0 ml of the solution. A stock solution of lidocaine hydrochloride (the internal standard) was prepared by diluting a commercial injection of the drug (stepwise) with water to contain 40.0 µg/ml of the drug. The standard solutions were

TABLE 1

THE FORMULA OF TABLETS

	Name of the Ingredient	Brand Name, (if applicable)	Manufacturer	Quantity per 100 tablets
1.	Scopolamine HBr		City Chemical Co.	40 mg
2.	Crystallized dextrose-maltose	Emdex	Edward Mendell Co.	14.71 g
3.	Microcrystalline cellulose	Emcocel	Edward Mendell Co.	4.13 g
4.	Polyvinyl pyrrolidone K-15	PVP K-15	GAF Corp.	198 mg
5.	As above, XL	PVP XL	GAF Corp.	107 mg
6.	Fumed Silica	HDK-N20	Wacker Chemical Co.	10 mg
7.	Sodium carboxy-methylcellulose (or croscarmellose sodium)	Ac-Di-Sol	FMC Corp.	346 mg
8.	Magnesium stearate		Ruger Chemical	98 mg
9.	F D & C Blue #1 (11% Lake)		Warner Jenkinson	3.5 mg

prepared (i) either by mixing 2.0 ml of the stock solution of scopolamine with 6.0 ml of the stock solution of the internal standard, or (ii) same as above, except a 0.2 ml quantity of ∿1N HCl was also added.

Extraction From Tablets: The tablet formula is presented in Table 1. Five tablets (each tablet containing 0.4 mg of scopolamine hydrobromide) were weighed and ground to a fine powder. The powder was mixed with 10 ml of water, 1.0 ml of ∿1N HCl (in some extractions HCl

was not added, to prove the adsorption problem) and 30.0 ml of the stock solution of the internal standard. The mixture was stirred for 3-4 minutes, filtered (Fisher's 9-803-5E filter paper), the first 5 ml of filtrate were rejected, and then the clear filtrate was collected for analysis. Additional extraction experiments and assays were conducted using mixtures of scopolamine hydrobromide with a single inactive ingredient (Table 1) at a time, in order to determine which one(s) is/are adsorbing scopolamine.

Assay Procedure: A 50 µl quantity of the assay solution was injected into the chromatograph using the conditions described. For comparison, an identical volume of the standard solution (with HCl if the assay solution also contained it, otherwise without HCl) was injected after the sample eluted. The standard solution contained identical concentrations of the drug (based on the label claim) and the internal standard.

Calculations: Since the ratio of peak heights are related to concentrations of scopolamine (3), the results were calculated using a simple equation:

$$\frac{(R_{ph})_a}{(R_{ph})_s} \times 100 = \text{percent of the label claim found,}$$

where $(R_{ph})_a$ is the ratio of the peak heights of drug to internal standard in the assay solution and $(R_{ph})_s$ that of the standard solution.

RESULTS AND DISCUSSION

The results indicate (Table 2, without HCl) that scopolamine is adsorbed onto sodium carboxymethylcellulose up to about 75% (Figure 1A), and onto microcrystalline cellulose (∿32%). In tablets which

TABLE 2

ASSAY RESULTS

Composition of the tablet, or mixture	Percent of the label claim found With HCl[a] (see text)	Without HCl (see text)
Tablets (Table 1)	57.8	99.9
Scopolamine with Microcrystalline cellulose only (Table 1)	68.3	100.2
Scopolamine with Sodium carboxymethylcellulose only (Table 1)	24.8	99.7
Scopolamine with the other ingredients (Table 1)	Results with and without adding HCl during the extraction procedure were similar. The heights of the peaks were similar to the heights from the standard solutions. There was no adsorption of scopolamine or lidocaine.	

[a] When scopolamine was adsorbed, the peaks from the assay solutions were too short. Even lidocaine (the internal standard) was adsorbed. Therefore, the results were calculated by comparing the peak heights of scopolamine of the assay solution with that of the standard solution.

contained both of the inactive ingredients, the adsorption was ∿42%. Even lidocaine was adsorbed onto these ingredients, ∿77% onto sodium carboxymethylcellulose, ∿34% onto microcrystalline cellulose and ∿45% in tablets. However, when hydrochloric acid was used in the extraction procedure, both scopolamine and lidocaine got completely desorbed and the peak heights were similar (Figure 1B) to the peak heights from the

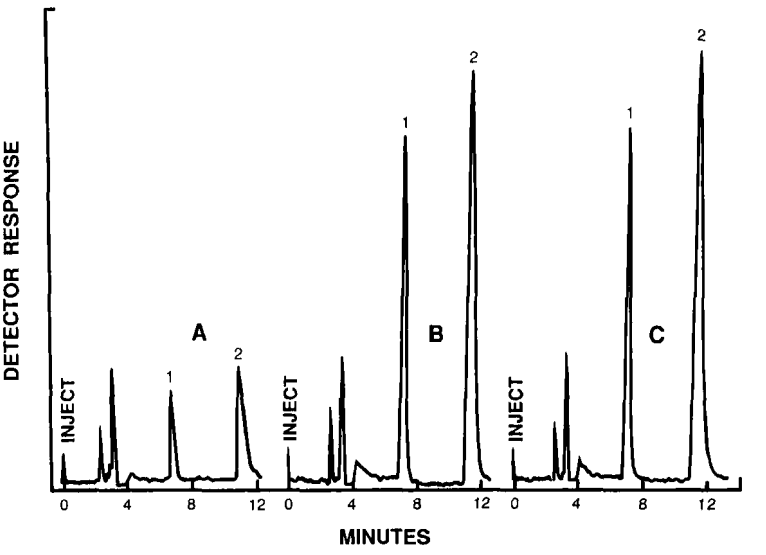

Figure 1 Sample chromatograms. Peaks 1-2 are from scopolamine hydrobromide and lidocaine hydrochloride (the internal standard), respectively. Chromatogram A is from a mixture containing sodium carboxymethylcellulose (mixture 3, Table 2) when hydrochloric acid was not used; chromatogram B is the same as A, except that hydrochloric acid was used; and chromatogram C is from a standard solution (hydrochloric acid was added). For chromatographic conditions, see text.

standard solution with hydrochloric acid (Figure 1C). The peak heights from the standard solution without hydrochloric acid were also approximately of the same size as those from the standard solution containing hydrochloric acid. This was expected since the standard solutions were prepared from the pure drugs, i.e. no adsorbents (sodium carboxymethylcellulose and microcrystalline cellulose) were added. In order to keep the extraction conditions the same (for a uniform assay

procedure), hydrochloric acid should be added to both, the assay and the standard solutions.

Apparently, hydrochloric acid caused the ionization of both drugs (scopolamine and lidocaine), which resulted in the desorption process, since ionized drugs have much less affinity for non-polar adsorbents. The implications of adsorption of scopolamine in tablets when taken orally, is unknown. However, it is reasonable to assume that drug will get desorbed in the stomach because of the presence of hydrochloric acid in the gastric secretions.

ACKNOWLEDGEMENT

This project was partially financed by A. C. Engle & Co., Houston, Texas.

REFERENCES

1. L. Kennon and T. Higuchi, J. Am. Pharm. Assoc., Sci. ed., 45, 157-60, (1956).
2. R. G. Hollenbeck, Int. J. Pharm., 47, 89-93, (1988).
3. M. J. Walters, J. Assoc. Off. Anal. Chem., 61, 1428-1430, (1978).