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COMPARISON OF THE DISSOLUTION CHARACTERISTICS OF LONG-ACTING QUINACRINE HYDROCHLORIDE PELLETS USING BASKET, PADDLE AND CONTINUOUS FLOW METHODS III

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ABSTRACT

In this study the dissolution rate profiles of formulated long acting quinacrine hydrochloride pellets were investigated by using basket, paddle and continuous flow methods.

There was no significant difference observed between these dissolution profiles.

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INTRODUCTION

Dissolution rate tests may vary, depending upon the drug delivery system. The mechanism of dissolution, the technical realization and physical conditions under which the test is conducted.

The official test is usually the rotating basket method (Method I, USP XX) (1), but stirrer (paddle) and beaker methods are also very common (Method II, USP XX) (1). These rotating methods are relatively easy to handle but the precision of the results, especially with diffusion-governed dissolution process, is not always satisfactory. This is the reason why, for research, flow columns with a uniform or pulsating stream of preheated solvents are usually taken (2, 3) . But also, with flow columns, the technical conditions must be precisely controlled because the dissolution pattern depends significantly on flow conditions. For routine work automatic flow columns with constant input of solvent, constant flow through the flow cell, automatic reading device registration and the calculation of dissolution are used today (4) . Such automatic dissolution rate testers give typical dissolution patterns.

The make-up of a drug preparation or more precisely, the properties of a solid drug delivery system like dissolution and release of the active principle from the dosage form are important factors which finally decide upon the bioavailability of a drug, bioequivalency of dosage forms and biological activity of a medicament generally.

Therefore, drug release testing is one of the most important controls for the evaluation of a medicament and, therefore, the technical methods to check drug release must be discussed.

The main aim of each release test is to ensure that the active drug component incorporated in a preparation will first be liberated quantitatively from the dosage form under fixed conditions, for instance: time, temperature, environment, etc. (5).

Several methods are employed for measuring the dissolution of the common solid dosage forms, capsules and tablets. This report presents the methodology for determining the dissolution rate profiles of long-acting quinacrine hydrochloride pellets (6) using the USP rotating basket, USP paddle and continuous flow methods.

EXPERIMENTAL

Materials

Quinacrine Hydrochloride Dihydrate[1], Cholesterol[2], Carnauba wax[3], Magnesium Stearate[4] were used as received.

Methods

Long-acting Quinacrine HCl pellets - Quinacrine HCl, Cholesterol, Carnauba wax, and Magnesium stearate were used to prepare long-acting quinacrine HCl pellets. Each pellet has a 25 mg quinacrine HCl. The pellets were compressed using Stokes model[5] single-punch tablet machine.

Dissolution Tests: Rotating-basket method. Dissolution profiles of five long-acting quinacrine HCl pellets which have 25 mg quinacrine HCl were determined at 37°C in 1000 ml of water using the USP rotating-basket method at 100 r.p.m.

The USP rotating-basket method was employed for investigating drug release from the pellets. One pellet was placed in the basket, which was immersed in 1000 ml of distilled water previously warmed to 37°C. The basket was rotated at 100 r.p.m. and the water bath was maintained at 37°C ± 0.05°C for 25 hours. The samples were assayed hourly using a flow cell and spectrophotometer[6].

Paddle method - Dissolution profiles of five long-acting quinacrine HCl pellets were determined at 37°C in 1000 ml of water using the USP paddle method at 100 r.p.m. The apparatus consists of cylindrical 1000 ml roundbottom flask secured in a multiple-spindle dissolution drive apparatus and immersed in a controlled temperature bath maintained at 37°C ± 0.5°C. The paddle was positioned to extend to exactly 2.5 cm above the flask bottom. Paddle rotation was engaged and controlled at a constant 100 r.p.m. using a dissolution stirrer drive. The samples were assayed hourly using a flow cell and spectrophotometer.

Continuous flow method - Dissolution profiles of five long-acting quinacrine HCl pellets were determined at 37°C in water using the continuous flow method. The two Buchner

funnels are used as a dissolution cell. These two Pyrex coarse type Buchner funnels (each one has 2 ml volume) is connected with plastic tubbing. One pellet was placed in the cell, which was immersed in a controlled temparature bath maintained at 37°C ± 0.5°C. The constant inlet and outlet of water has been used in this system. The constant flow through the dissolution cell is maintained by the pump[7], which has the flow rate was 4.8 ml/min. The samples were assayed hourly using a flow cell and spectrophotometer.

Assay of Quinacrine HCl - The samples were assayed from the dissolution medium by measuring its absorbance at 425 nm against a water blank.

Data analysis - The dissolution data for the three methods were treated by converting observed drug concentrations at each sampling time to amounts dissolved and, in turn to percents dissolved. Values at sampling time were compared statistically using student t test.

RESULTS

The dissolution limits for the long-acting quinacrine HCl pellets is 80 - 90% release in 800 minutes (13 hours and 20 minutes) (6). Table I shows the avarage percent cumulative release of three different methods. And Table II shows the average percentage cumulative release in 800 minutes.

Figure 1 shows the average percentage cumulative released as a function of time for quinacrine HCl pellets.

TABLE I: In Vitro Dissolution Profiles of Quinacrine HCl Pellets Using Different Methods

Dissolution Method	Rotating-Basket	Paddle	Continuous Flow
Time (hours)		% Cumulative Release[+]	
0-1			25.099
1	29.83	31.225	38.529
2	42.16	44.830	47.191
3	51.14	54.413	53.880
4	58.51	61.913	59.416
5	64.56	68.112	64.108
6	69.82	73.678	68.173
7	74.35	77.789	71.767
8	78.08	82.112	74.978
9	81.49	85.258	77.927
10	84.23	88.099	80.677
11	86.84	90.333	83.197
12	88.77	92.604	85.552
13	90.44	94.407	87.754
14	91.69	95.671	89.758
15	92.73	96.597	91.61
16	93.81	96.993	93.298
17	94.64	97.431	94.799
18	95.21	97.515	96.157
19	95.66	97.558	97.274
20	95.78	97.558	98.15
21	95.99	97.558	98.882
22	96.16	97.558	99.308
23	96.44	97.558	99.394
24	96.5	97.558	

[+]% Cumulative release is the average of 5 pellets.

TABLE II

MEAN PERCENT DISSOLVED OF QUINACRINE HCl, USING THE ROTATING BASKET, PADDLE AND CONTINUOUS FLOW METHODS

Dissolution Time	Dissolution Method	% Cumulative Release
800 minutes	Rotating-basket	% 90.5
	paddle	% 95
	continuous flow	% 88

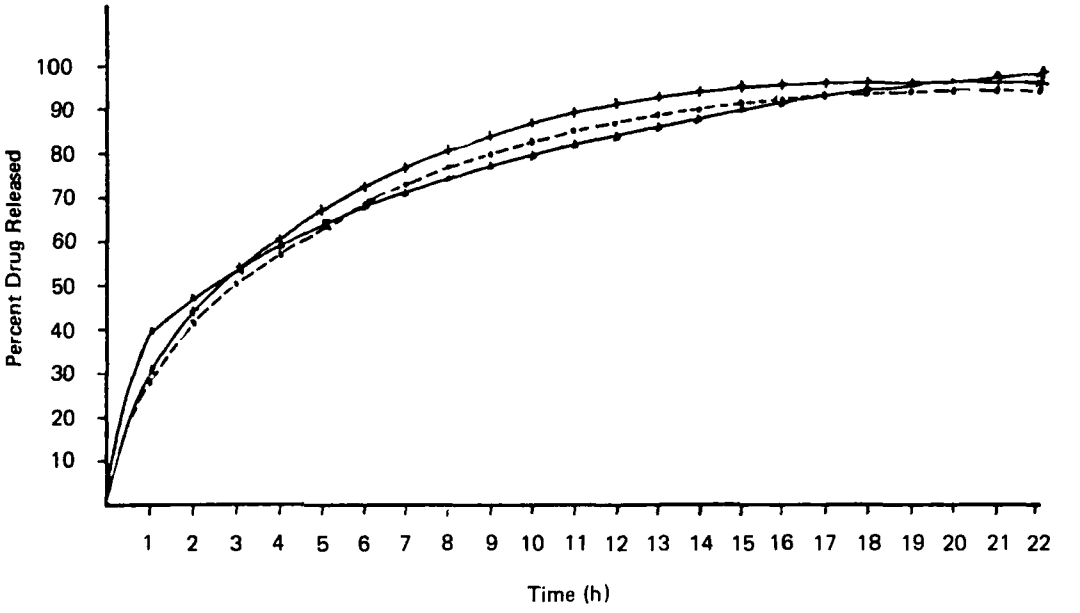

FIGURE 1

Release Profiles of Quinacrine Hydrochloride Pellets.
Key: ●——● Basket, ▲——▲ Continuous Flow, ✦——✦ Paddle.

DISCUSSION

Analysis of the dissolution data obtained using the USP rotating-basket, USP paddle method and continuous flow method demonstrated a substantial difference in the dissolution characteristic of Quinacrine HCl pellets statistically.

The entire dissolution profiles of quinacrine HCl are shown in Figure 1 for the three methods. According to the results presented in Figure 1, the amount of Quinacrine HCl dissolved using paddle method is greater than the official rotating-basket method. This greater amount of drug dissolved (or this greater percent cumulative released) may be directly related to the agitating rate of the paddle. On the other hand, the amount of quinacrine HCl dissolved using continuous flow method is greater in the first 3 hours than the rotating basket method. This effect may be directly related to the quinacrine amount on the tablet surface has been released fast and flow of the fresh dissolution fluid. After the 3 hours, the amount of drug dissolved is lower than the rotating-basket method because the release rate reaches a constant value and related to (the absence of stirring speed) the constant flow through the flow cell.

At the end of dissolution studies after 24 hours quinacrine HCl had been released, 96.5% in rotating-basket, 97.5% in paddle and 99.39% in continuous flow method. Also, this higher released might be assumed that quinacrine dif-

TABLE III

STATISTICALLY SIGNIFICANT DIFFERENCES BETWEEN DISSOLUTION DATA USING T-TEST

Sampling Time (hours)	Dissolution Method	Statistical Evaluation
1,2,5,7,10,15	Rotating-basket Paddle	$P > 0.05$
1,2	Rotating-basket Continuous Flow	$P < 0.05$
5,7,10,15	Rotating-basket Continuous Flow	$P > 0.05$

fusion through the matrix or leaching out the drug must be continuously by the dissolution fluid in continuous flow method.

Table III shows analysis of the dissolution data obtained using three methods. The dissolution characteristics of quinacrine HCl statistically significant difference ($P < 0.05$) existed between the rotating-basket and continuous flow methods for the percent of drug dissolved at the first and second hours sampling times using both methods. There were no significant differences in percent drug concentration at 5, 7, 10, 15 hours sampling times. Also, there were

no significant difference ($P > 0.05$) (statistical differences) at the 1, 2, 5, 7, 10, 15 hours sampling times for rotating-basket and paddle methods.

Quinacrine HCl which is formulated into a long-acting dosage form is used to compare these three methods. We believe that there is no significant difference between these dissolution methods according to our results. This could be due to the high solubility characteristics of quinacrine hydrochloride.

ACKNOWLEDGEMENT

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FOOTNOTES

[1]Sigma Chemical Co.,St.Louis, MO.

[2]Amend Drug and Chemical Company.

[3]Z.D. Gilman Inc.

[4]Mallinckrodt

[5]Stokes Model E Single-Punch Tablet Machine

[6]Hitachi model spectrophotometer.

[7]Crouzet type 82-344 pump 10 r.p.m.

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