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DISSOLUTION TEST FOR TABLETS: DESIGN AND STUDY OF A ROTATING DISC METHOD

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A nondisintegrating type rotating disc apparatus for the determination of dissolution rate of tablets is deisgned and reported, studies on dissolution behaviour of pericyazine tablets (10 mg) are conducted and equation for determining experimental dissolution constant (K_e) is derived.

INTRODUCTION

With growing importance of *in vitro* assessment of tablet dissolution characteristics, official compendia [1–3] have prescribed dissolution test for tablets and capsules. The apparatus described in official compendia have been modified by several workers, and a number of devices for the determination of dissolution rate are reported in literature, these devices have been tested and evaluated for their accuracies.

Slight moficiations in pharmacopoeial methods are reported, e.g. the USP XVII apparatus is redesigned and sieve of 10 mesh is replaced with that of 100 mesh [4] making the apparatus suitable for testing of sustained release tablets. Bates *et al.* [5] have described a simple method where they have employed a1–1three-neck-flask and wherein the agitation is provided by a controlled speed stirrer at the rate of 150 rev/min. Similar apparatuses have been used by other workers for stuides of solid dosage forms [6]. A rotating flask at very low speed, i.e. 0.9–2.4 rev/min has also been used as a dissolution vessel [7], this apparatus is also suitable for timed release tablets. Heyd *et al.* [8] have designed a dissolution cell, and a sample holder of stainless-steel, which is fixed in the dissolution vessel and wherein the agitation is provided by a magnetic stirrer, the cell is so designed that it is suitable for holding and studying dissolution of macromolecules such as ethylene malic acid copolymers.

Lin *et al.* [9] have dealt with the methodology in detail, and have disscussed various techniques for determining dissolution rate of capsules. They have used hydrophobic adhesives for sticking the capsules to a rotating device, to a basket or to a stirrer paddle. They have concluded that the size of stirrer is critical factor in the dissolution rate studies.

Khalel *et al.* [10] have converted the B.P. disintegration apparatus to a dissolution apparatus by slowing its speed from 30 strokes/min to 20 strokes/min. Horinger *et al.* [11] have compared two modified devices with USP and NF apparatus, they have employed a L-shaped teflon holder/stirrer, which provides greater flow of dissolution medium over the tablets, the device has been claimed to be more suitable than USP XVIII apparatus. Tablets embedded in paraffin and mounted in a holder so that only a flat surface is exposed to the dissolution medium have been used and reported [12].

Present work reports a nondisintegrating type rotating disc apparatus in which the tablets were wrapped in a 60 mesh nylon sieve and in which the agitation was provided by the disc itself.

EXPERIMENTAL

A 2-1 beaker was kept on a thermostatic magnetic stirrer hot plate (Gallenkamp cat. No. SWT 500-010), approximately 250 ml of ordinary water was added and warmed till its temperature reached about 38°. Another 1-l beaker was then put inside this 2-l beaker carrying in it exactly 500 ml of dissolution medium (simulated gastric juice USP XVIII omitting pepsin). This dissolution vessel carries a thermometer, the liquid was stirred manually till its temperature reaches 37° ± 0.5°.

Rotating Disc. A high density polythene round disc dia 41 mm and height 12 mm was employed, a magnetic follower (Gallenkamp cat. No. SWX 310) was fixed in its hollowed lower side, this magnet aids in its rotation over magnetic stirrer, the disc was marked on one side to aid in counting the revolutions per minute. The disc has 2 small holes in centre, two pericyazine tablets (10 mg) held side by side to each other were wrapped in a 60-mesh nylon sieve and were tied on the upper flat surface of the disc with the aid of stainless-steel wire. This disc rotates uniformly in the bottom of dissolution medium.

The experiments were conducted at 120±5 and 210±7 rev/min, the temperature of dissolution medium was kept

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at 37°±0.5, sampling volume each time, was 5 ml and solution being replaced by 5 ml of fresh dissolution medium after each withdrawl.

Colorimetric Determination of Pericyazine. Pericyazine was estimated colorimetrically at 472 nm on a model SP 500 Pye Unicam spectrophotometer.

Well known reaction of phenothiozines with palladous chloride was used to estimate pericyazine colorimetrically. References for other phenothiazines are available [13]. The method was of choice as regards accuracy and reproducibility, and was thus preferred over a UV method. 5 ml samples were drawn after suitable intervals, and transferred to a 10-ml volumetric flask, 2 ml of palladous chloride reagent (0.02% w/v palladium chloride in hydrochloric acid and sodium acetate buffer) and 1 ml 0.1*N* methanolic sulphuric acid was added and volume was made up to 10 ml with dissolution medium, optical density of this solution was recorded at 472 nm, taking as blank 2 ml palladous chloride reagent, 1 ml methanolic sulphuric acid and made up to 10 ml with dissolution medium.

RESULTS AND DISCUSSION

Dissolution proceeds either via disintegration or diffusion. A via diffusion process occurs either in a nondisintegrating tablet or in a tablet which is physically handicapped from deformation or loosing its shape, here we have prevented deformation by wrapping the tablet in a 60-mesh nylon sieve. In most of the experiments the volume of dissolution medium, temperature and speed of rotation are constant, and the dissolution, therefore, remains a function of changing surface area, time and the amount of drug present at that time.

Wagner [14] has interpret per cent dissolved time plots from *in vitro* testing of conventional tablets and observed that under the conditions of constant surface area the Hixon and Crowell equation* can be derived to equation.

$$\log (VC_s - W) = \log VC_s - kt/2.303 \qquad (1)$$

Here V is the volume of dissolution medium, C_s is the equilibrium solubility of the solute, W is amount of drug in solution at time t, and k is the first order rate constant.

From equation (1), equation for rate constant (k) can be simplified and written as

$$k = 2.303 \log W/t \qquad (2)$$

*Hixon and Crowell equation is $dW/dt = k_s^{\wedge} (C_s - C)$, where W is the amount present at time t, s is the surface area, and C_s is the equilibrium solubility of the solute.

Since the dissolution process is diffusion-dependent and as the time proceed more and more surface area is generated resulting in change of rate of diffusion and this change can be related to time (t). Relationship of diffusion to the square root of time has been discussed [15], where the amount released have been related to the square root of time, by the equation:

$$Q = 2\, C_0\, (Dt/\pi)^{1/2} \qquad (3)$$

where Q is the amount released/100 ml, C_0 is the initial concentration of drug in mg/g and D is the diffusion coefficient. The above equation is for a process where the drug is released from an ointment base which is mostly hydrophobic and where partitioning between two phases occurs. The diffusion in this case is across the phases, from this equation it can, however, be deduced that

$$t^{1/2} \propto Q$$

Where t is time and Q is the release rate. In our case the plot of $t^{1/2}$ against rate constant (k) was a straight-line, and no linearity was observed of a first order plot, i.e. log W against time, Wagner [14] has reported deviations from first order law of the dissolution process and concluded that dissolution processes are in fact *pseudo* first order type, and are not merely dependent on concentration at time (t).

The equation of the plot from Fig. 1 is.

$$k = X + Y$$

putting the values of X and Y the quation becomes:

$$k_e = 10^{-1} t^{1/2} + 10\,(2.303 \log W/t)$$

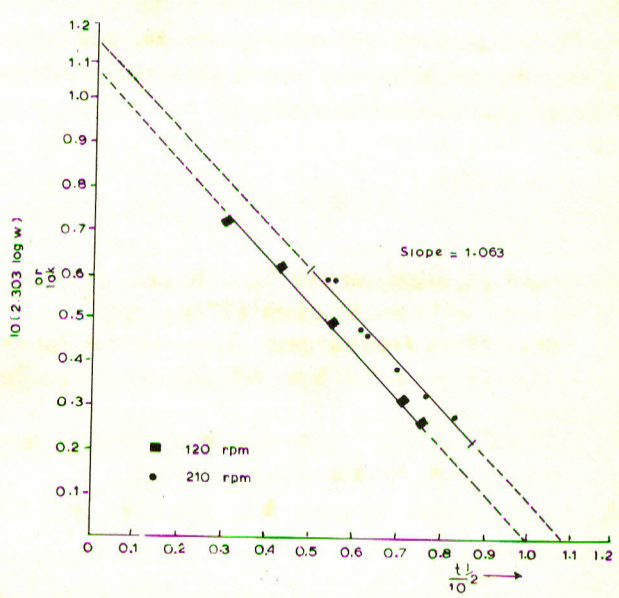

Fig. 1. Regression line of $t^{1/2}/10$ (min) against 10 (2.303 log w)/t or 10 k

Table 1. Determination of standard deviation of experimental dissolution constant at different speed of rotations.

Speed (rev/min)	X	Y	Ke X + Y	$\bar{Ke}$	Ke−$\bar{Ke}$	(Ke−$\bar{Ke}$)^2	S^2	S
120	0.316	0.747	1.063		−1.5	2.25		
	0.447	0.628	1.075		−0.3	0.09		
	0.548	0.526	1.074	1.078	−0.4	0.16	1.734	1.316
	0.632	0.442	1.074		−0.4	0.16		
	0.707	0.376	1.083		+0.5	0.25		
	0.774	0.328	1.102		+2.4	5.76		
210	0.548	0.595	1.143		+1.1	1.21		
	0.362	0.482	1.114	1.132	−0.8	0.64	0.833	0.912
	0.707	0.424	1.131		−0.1	0.01		
	0.774	0.366	1.140		+0.8	0.64		
210	0.548	0.601	1.149		+2.4	5.76		
	0.632	0.471	1.103	1.125	−2.2	4.84		
	0.707	0.399	1.106		−1.9	3.61	4.677	2.162
	0.774	0.348	1.122		−0.3	0.09		
	0.837	0.309	1.146		+2.1	4.41		
210	0.548	0.594	1.142		+1.1	1.21		
	0.632	0.499	1.131	1.131	0	0	1.125	1.060
	0.707	0.415	1.122		−0.9	0.81		
210	0.548	0.617	1.165		+2.4	5.76		
	0.632	0.496	1.128	1.141	−1.3	1.69	2.633	1.622
	0.707	0.428	1.135		−0.6	0.36		
	0.774	0.364	1.138		−0.3	0.09		

Ke is introduced here as an experimental dissolution constant. This equation is hypothetical and generates a law that under given experimental conditions such as these the rate constant or K is proportional to the square root of time. The law, however, needs further experimental verifications.

Table 1 indicates that under normal and well-defined experimental conditions very little variation occurs between values of Ke at different intervals.

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