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A COMBINATION DISINTEGRATION-DISSOLUTION APPARATUS FOR FAST-DISINTEGRATING TABLETS

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ABSTRACT

A combination disintegration-dissolution apparatus for fast disintegrating tablets is described. Preliminary investigation using sodium carboxymethyl starch as the disintegrant indicated that the apparatus was capable of detecting differences in the disintegration time both due to disintegrant concentration as well as due to the intensity of agitation used in the apparatus. No difference in the disintegration times could be observed when similar tablets were evaluated using the existing disintegration apparatus.

The combination apparatus described is simple in construction and design and can be fabricated quite easily and economically in the laboratory. Due to the anticipated increase in the availability of fast-disintegrating tablets, this apparatus will be useful to the pharmaceutical formulator as a valuable quality control tool. In addition, the

apparatus is adaptable to various other agitational systems in common usage and can be used by laboratories carrying out combined disintegration and dissolution tests using automated equipment.

INTRODUCTION

In the formulation of solid dosage forms in general and tablets in particular, the pharmaceutical formulator has always strived to incorporate a disintegrating agent which will assure the disintegration of the dosage form within the time stipulated in the official compendia.

With the increasing importance of bioavailability the present trend appears to be the formulation of fast-disintegrating tablets, except in the case of tablets which are intended to be chewed or those which exhibit sustained action without undergoing disintegration. Thus, in recent years the formulators have shown a tendency to replace the conventional tablet disintegrant, e.g., starch, with agents such as starch derivatives which swell 200 to 300 times in water and disintegrate the tablets within a few minutes.

In its January 17, 1976 meeting, the USP Executive Committee of Revision adopted a policy statement declaring that:

> "The dissolution behavior of oral solid dosage forms has been shown to be a useful criterion for controlling formulation and process variables that can influence the bioavailability of

the active ingredient(s) of the dosage forms. While in vitro testing may or may not correlate with in vitro bioavailability results, dissolution testing is a desirable aid in controlling the variables in the manufacturing process.

Therefore, the USP Executive Committee of Revisions favors the inclusion, during the 1975-1980 revision period, of a Dissolution test in monographs for all official oral solid dosage forms except where such inclusion is judged inappropriate."

Since the dissolution measurement is a reliable indicator of uniformity in manufacturing, it is conceivable that it may very well replace the disintegration test required in some current monographs. Nevertheless, the disintegration test has been and perhaps will remain an important quality control tool for the formulator in order to ensure lot-to-lot uniformity of the solid dosage forms in general and tablet formulations in particular (1).

The determination of disintegration time of relatively fast-disintegrating tablets with the existing official disintegration test apparatus (2, 3) does not help the formulator in quality control because the apparatus fails to discriminate inter - tablet variability due to the high turbulance introduced in the apparatus (4-7). This communication re-

ports a combination disintegration dissolution apparatus for the fast disintegrating tablets.

DESCRIPTION OF THE APPARATUS

Since the tablets disintegrate rapidly, it was theorized that the disintegration apparatus should use a milder degree of agitation such as is used in the official dissolution apparatus (8). Hence the dissolution apparatus may be modified to serve the dual purpose.

Fig. 1 shows the schematic of the modification. A 10-mesh screen was placed in the dissolution basket which was then clamped to the shaft through a plexiglass tube. The tablet was placed on the 10-mesh screen and the disintegration of the tablet was observed through the plexiglass tube while the dissolution of the tablet was being examined.

RESULTS AND DISCUSSION

Fast-disintegrating tablets were prepared with varying concentrations of sodium carboxymethyl starch. The tablets containing 1-4% of the disintegrant exhibited similar disintegration times (less than two minutes) when determined with the existing disintegration apparatus (2, 3). When compared with the modification described above, the tablets exhibited disintegration times which were related both to the concentration of the disintegrant as well as to the speed of agitation.

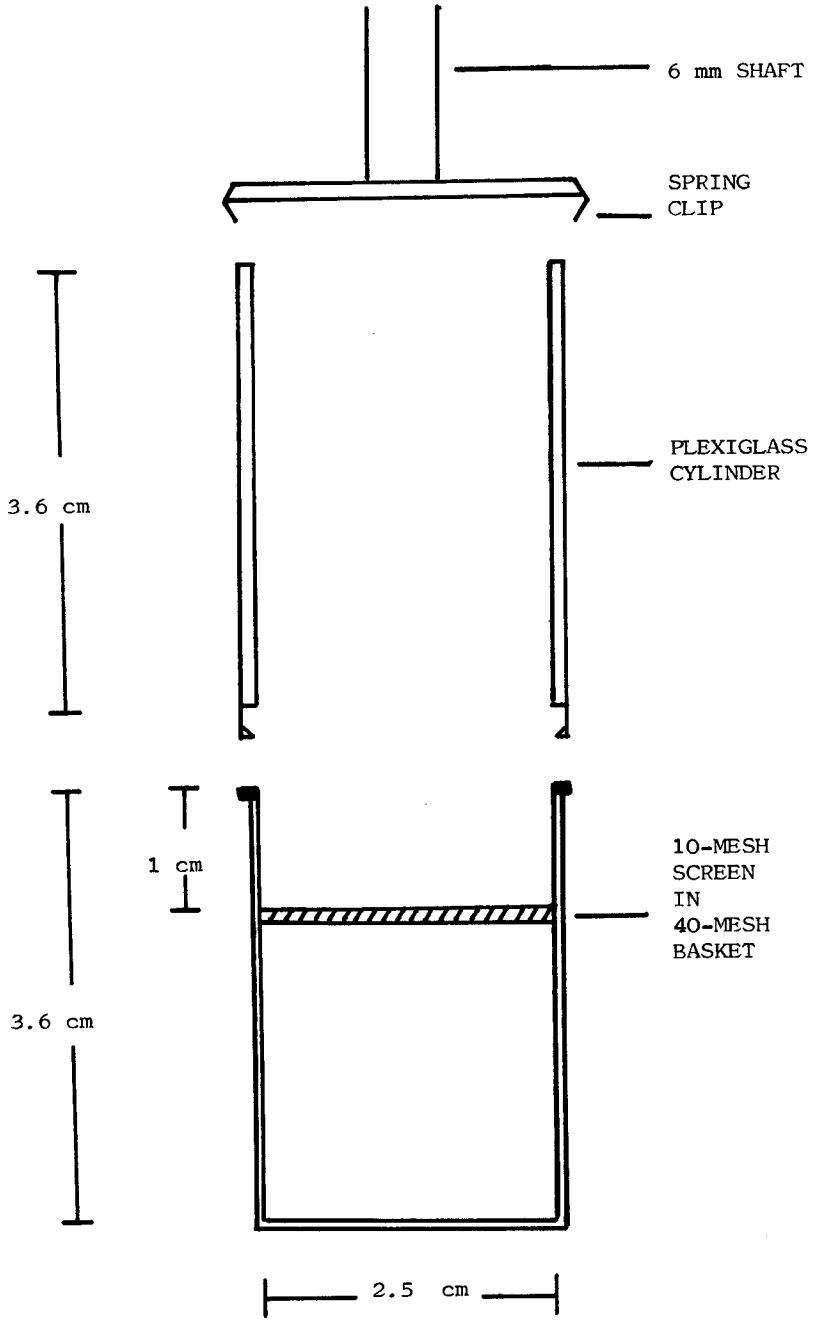

FIGURE 1

SCHEMATIC DIAGRAM OF THE COMBINATION DISINTEGRATION-DISSOLUTION ROTATING BASKET ASSEMBLY

Fig. 2 shows a plot of the disintegration time of the tablets as a function of the concentration of disintegrant when the apparatus was operated at 30 revolutions per minute. From these results it is clear that the modified apparatus is capable of detecting differences due to the concentration of the disintegrant in the fast-disintegrating tablets.

In order to evaluate the apparatus for the effect of speed of agitation, the disintegration times of the tablets were determined at 30, 40, 50, and 60 revolutions per minute. Fig. 3 shows a plot of disintegration times of a batch of tablets containing two percent disintegrant. These results also demonstrate the usefulness of the apparatus in distinguishing differences.

Since the apparatus is designed to serve a dual purpose, the dissolution rates of the drug contained in the tablets were determined in the experiments cited above. It was found that in each case the dissolution rates were almost identical. Thus, the determination of the dissolution rate alone would not have served any useful purpose as far as quality control is concerned.

From the results of this preliminary investigation it is clear that the combination disintegration-dissolution apparatus is capable of discriminating differences which the existing apparatus may not be able to detect. The effect of other formulation factors including the nature of various other types of disintegrants used in the formulation of fast-disin-

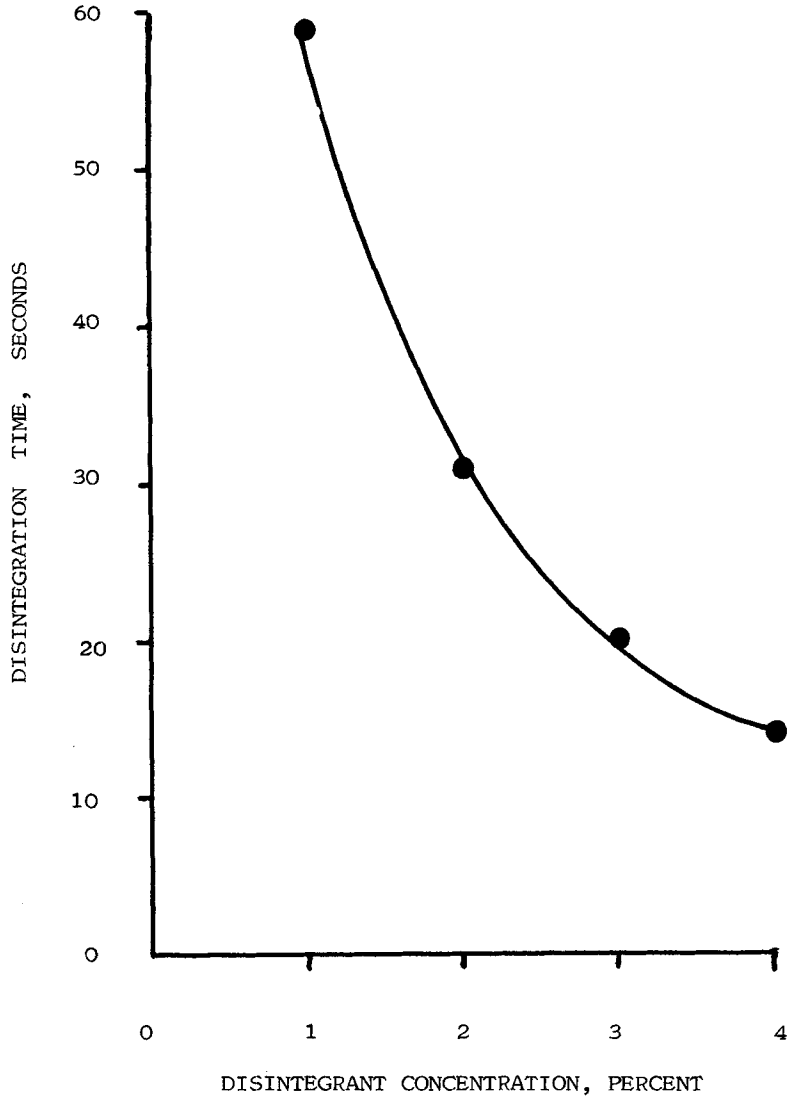

FIGURE 2

DISINTEGRATION TIME AS A FUNCTION OF DISINTEGRANT CONCENTRATION

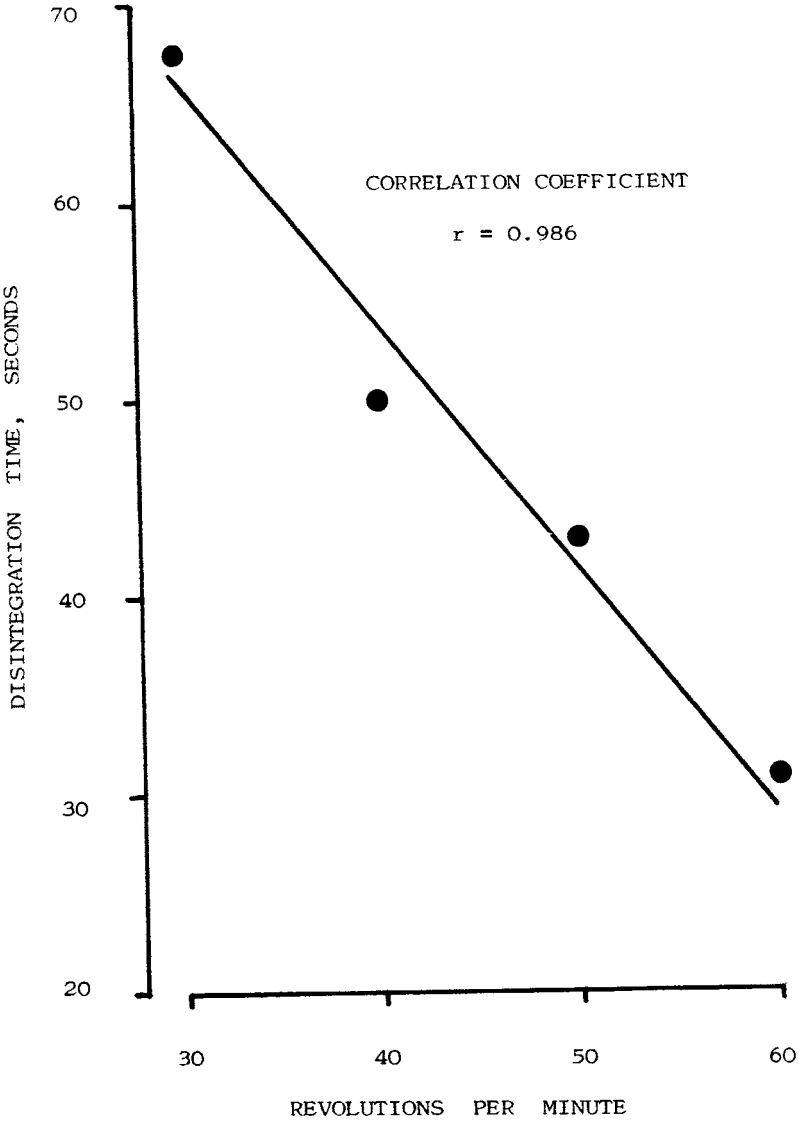

FIGURE 3

DISINTEGRATION TIME AS A FUNCTION OF INTENSITY OF AGITATION

tegrating tablets is currently being studied and will be the subject of a future communication.

The modification described above is simple in design and can be conveniently and economically fabricated in the laboratory. Since more and more tablet formulations may be formulated as fast-disintegrating tablets and at present no quality control tool for the disintegration of such tablets is available, it is hoped that the modification described will be useful to the pharmaceutical formulator. In addition, the modification is adaptable to various other agitational systems in common usage (9, 10) and can be used by laboratories carrying out combined disintegration and dissolution tests using automated equipment (9-11).

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