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EFFECT OF GRANULATING METHOD ON DISSOLUTION RATE OF COMPRESSED TABLETS. III

SUDEB DAS* and CHARLES I. JAROWSKI[X]

The Department of Allied Health and Industrial Sciences
College of Pharmacy and Allied Health Professions
St. John's University, Jamaica, N.Y. 11439

ABSTRACT

The dissolution rates of dexamethasone granules prepared by all the methods were slower than the dissolution rates of the corresponding tablets. This was shown to be the result of a reduction of the average particle size on compaction. The dissolution rates of sulfadiazine tablets prepared by microgranulating and slugging were slower than the corresponding granules. This was demonstrated to be the result of enlargement of the granules on compaction. For both drugs the microgranulating procedure gave the most rapid dissolution of tablets and granules. In case of the dexamethasone formulation, direct compression exhibited the slowest dissolution rate. The dissolution rates of sulfadiazine granules and tablets prepared by the wet granulating method were also unsatisfactory.

*Present address: Johnson & Johnson, Research, New Brunswick, N.J. 08903

INTRODUCTION

The effect of formulation and tablet processing factors on the dissolution rate of active ingredients from compressed tablets have been reported by several investigators (1). Various factors such as granule size and distribution, nature and quantity of filler, binder, disintegrant, lubricant and surfactant, compressional force, polymorphism, solubility have been recorded to influence the dissolution rate.

The scope of the present investigation was to study the effect of four different granulating methods and the influence of compaction behavior of dexamethasone and sulfadiazine granules on the dissolution rate of their corresponding compressed tablets.

EXPERIMENTAL

Preparation of Tablets - Dexamethasone 0.25 mg per tablet and sulfadiazine 130 mg per tablet were manufactured using all USP grade materials by four different granulating methods described previously (2).

Dissolution Studies - The dissolution rate measurements were carried out by the method specified in USP XIX with a 100 - rpm rate of rotation. The dissolution medium was 0.1 N HCl. The quantity used was 100 ml with dexamethasone and 500 ml in case of sulfadiazine tablets and granules. At appropriate intervals samples of the dissolution medium were withdrawn, filtered and analyzed by the method as reported previously (3).

RESULTS AND DISCUSSION

The dissolution rates of dexamethasone granules prepared by four different methods were slower than the rate of dissolution from their tablets (Figures 1 and 2). One possible explanation for the increase in dissolution rate may be the compaction behavior of dexamethasone formulation. During compaction the particle size is reduced and the distribution narrowed (2). As a result, the specific surface area of the disintegrated granules was increased and thus increasing the dissolution rate. A second reason may be that the drugs were more rapidly wetted when contained in the tablets, due to the fact that the tablets were submerged into the dissolution medium and disintegrated rapidly, whereas the granules were found to float over the surface of the fluid and settled more slowly.

Figures 3 and 4 reveal that the release rate of sulfadiazine from the granules was faster than that from the tablets. The reason may be as before - compaction behavior of sulfadiazine granules. The slugs and microgranulates had consolidated into larger particles under normal compressional force (2). This reduced the specific surface area of the disintegrated tablets and hence, the dissolution rate of the tablet. So it was not surprising that sulfadiazine tablets prepared from microgranulates disintegrated within 4 minutes and still had a very slow dissolution rate. The 200 micron micro-granulates which had a release rate of 80% in 10 minutes, on compaction increased to 355 microns reducing the specific surface to almost one-half and the release rate to 45% in 15 minutes. It was reported earlier that compaction behavior is dependent on the granulating procedure (2). Dexamethasone tablets prepared from

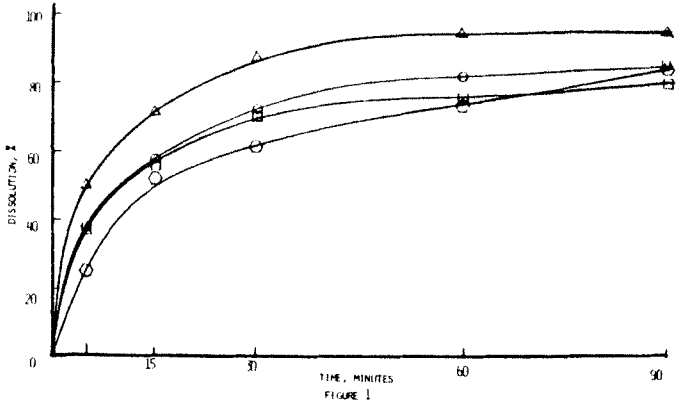

FIGURE 1

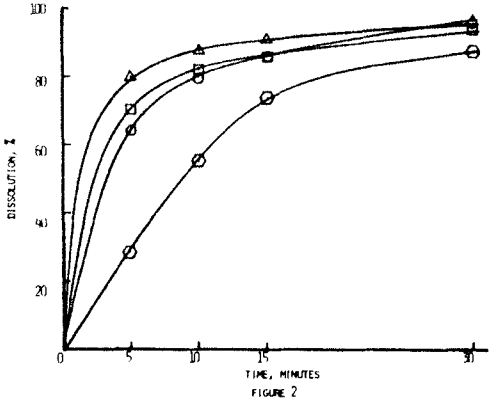

FIGURE 2

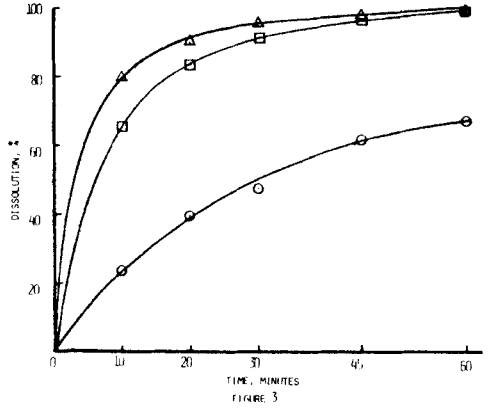

FIGURE 3

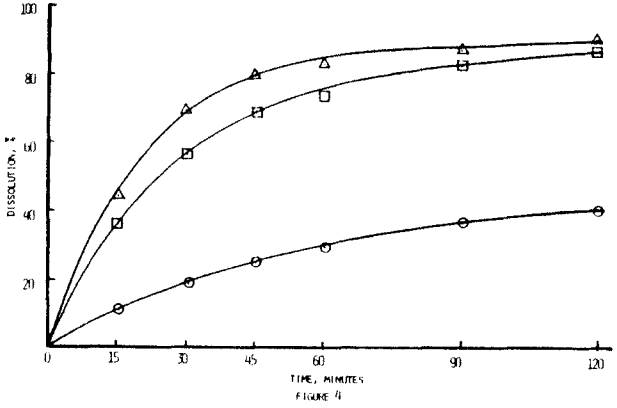

FIGURE 4

Dissolution Rates of Dexamethasone and Sulfadiazine Granules and Tablets Prepared by Different Methods. Figure 1 - Dexamethasone Granules; Figure 2 - Dexamethasone Tablets; Figure 3 - Sulfadiazine Granules; Figure 4 - Sulfadiazine Tablets.
Key: △ , Microgranulation; ◻ , Slugging; ⊙ , Wet Granulation; ⊙ , Direct Compression.

the slugs had faster dissolution rates than the tablets prepared by the wet granulating method, even though the slugs had larger particle sizes and a slower dissolution rate. Thus, neither rapid disintegration nor fine granule size is a guarantee of a fast dissolution rate. Therefore, during formulation it is very important to consider the compaction behavior of a material. It has been further observed that the disintegration test sometimes did not forecast the dissolution characteristics at all. The sulfadiazine tablets prepared by the slugging method failed to comply with the limits of the USP XIX disintegration test (3). However, the dissolution rate for these tablets was comparable to the tablets prepared by the microgranulation procedure (Figure 4). Further, sulfadiazine tablets prepared by the wet granulating method disintegrating within the USP limit of 30 minutes (3), showed a poor dissolution rate, i.e., 20% in 30 minutes (Figure 2).

Both dexamethasone and sulfadiazine microgranulates and their tablets had the fastest dissolution rates. This characteristic of microgranulates was attributed to their small particle size, narrow size distribution and a process which renders the particles more hydrophilic.

The dexamethasone tablets prepared by direct compression showed the slowest dissolution rate (Figure 2). This was partly due to the slower dissolution of directly compressible lactose and partly due to a higher requirement of lubricant in the formulation.

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