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COMMUNICATIONS

EVALUATION OF MICROWAVE DRYING FOR PHARMACEUTICAL GRANULATIONS

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ABSTRACT

The experiments were designed to compare the granule characteristics following the microwave drying and conventional tray drying. The formulations were designed to study the effect of microwave radiation under different conditions. This later criterion was studied by using granules prepared with different granulating fluids. The granules were prepared by using sulfathiazole as a model drug, lactose as a diluent, and starch as a disintegrating agent. The granulating fluids were 5% solution of PVP in 100% water, 50% water 50% ethanol, and 100% ethanol, respectively. The granules were dried in a microwave oven and in a conventional tray oven at 40 ± 2^{0} C. The loose and bulk densities were measured in a 100 ml glass cylinder. The granule morphology was examined using a scanning electron microscope. Dissolution rates of the granules were monitored using a rotating paddle dissolution apparatus. The loose and tapped bulk densities, the percentage compressibility, hardness, and the time required for 100% dissolution of the granules dried in the microwave oven and in the conventional tray oven were not significantly different ($p>0.05$). The scanning electron micrographs of the granules also showed no evidence of morphological changes or thermal damage to the granule surface or interior. In conclusion, the microwave radiation has no significant effect on the granules' characteristics.

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INTRODUCTION

Drying is most commonly used in some formulating operations as a unit process in the preparation of granules, which can be dispensed in bulk or converted into tablets or capsules (1). Various drying conditions are used in the pharmaceutical granulations utilizing conduction, convection, and radiation heat transfer (2). Recently, microwave drying is gaining importance in pharmaceutical industry because of its faster drying rate (3-6). It also reduces the occurrences of shrinkage, overheating, and structural damage of granules, which are not uncommon in conventional drying (7). Although, microwaves have been used for food processing and biomedical research for several decades, their use for the preparation of granules is relatively new. Several equipment manufacturers have recently developed and introduced microwave drying units for granulation (8,9). However, an extensive evaluation of the effect of microwave radiation on the granules characteristics is yet to be done (10). The objective of this project was to evaluate the granule characteristics following microwave drying.

MATERIALS AND METHODS

MATERIALS

Polyvinylpyrrolidone (PVP) (Arthur H. Thomas, Co. U.S.A.), Starch (A.E.Staley Mfg. Co., U.S.A.), lactose (Mallinckrodt Chemical Works, U.S.A.), and sulfathiazole (Sigma Chemical Co., U.S.A.) were used as received. Varying proportions of ethanol (Sigma Chemical Co., U.S.A.) were used as binding solvent.

METHODS

Experimental design

The experiments were designed to compare the granules' characteristics following the microwave drying and conventional tray drying. The formulations were designed to study the effect of microwave radiation under different conditions. This later criterion was studied by using granules prepared with different granulating fluids.

Preparation of granules

The granules were prepared by using sulfathiazole as a model drug, lactose as a diluent, and starch as a disintegrating agent. The granulating fluids were 5% solution of PVP in 100% water, in 50% water 50% ethanol, and in 100% ethanol, respectively. The drug, lactose, and starch were thoroughly mixed in a V-blender (The Petterson-Kelley Co., U.S.A.) for 15 minutes. The powder mixture was moistened thoroughly using a 5% PVP solution either in water or in ethanol, or in a mixture of both the solvents. Table 1 listed the composition of each formulation. The moist mass was then passed through a 12 mesh sieve. The granules were divided into two equal portions.

TABLE 1

Composition of the Granules

Formula	Sulfathiazole (gm)	Lactose (gm)	Starch (gm)	Binding Fluid: 5% PVP in
A	10	45	45	100% water
B	10	45	45	50% water 50% ethanol
C	10	45	45	100% ethanol

Drying of granules

The drying time was determined based on the moisture content determination. The moisture content of the granules was immediately determined using a moisture balance (Ohaus Scale Co., U.S.A.) and the drying time was determined based on the time required to plateau the drying time versus percent moisture curve. The microwave oven (Model MDS 2000, CEM Corporation, U.S.A.) was standardized to maintain the desired internal chamber's temperature throughout the drying process. The standardization was performed by measuring the temperature of 200 ml distilled water in a 10 inch diameter and 1 inch deep pyrex glass tray at different time intervals. The standardization was performed to ascertain the drying temperature. Table 2 listed the temperatures at different times. The conventional tray (Lab-Line Instruments, Inc., U.S.A.) oven was used at 40 ± 2^0 C. The granules were dried in both ovens at similar temperatures to eliminate the effect of temperature on the granules characteristics during the physical comparison. The only difference in the two batches of the same formula is the presence or absence of microwave radiation. The first portion was dried in the microwave oven at the previously standardized setting and the second portion was dried in the conventional tray oven at the 40 ± 2^0 C.

Bulk density determination

The loose and tap bulk densities were measured in a 100 ml glass cylinder and the sample weights were maintained at 20 gm. For loose bulk density measurement, the sample was placed into the graduated cylinder and the sides were tapped slightly to achieve a uniform horizontal level. The same sample was tapped 1000 times prior to the tap bulk density measurement.

Morphology study

The granule morphology was examined using a scanning electron microscope (Amray, U.S.A.).

Dissolution study

The dissolution rates of the granules were monitored using a Vankel dissolution apparatus (Vankel, U.S.A.). 1000 ml of distilled water was used as

TABLE 2

Standardization of the microwave oven

Time (min)	Inlet air temperature (^{0} C)	Outlet air temperature (^{0} C)	Water temperature (^{0}C)
0	29	29	29
5	29	30	31
10	29	31	36
15	29	33	40
20	29	32	41
25	29	32	42
30	29	32	42

dissolution media and the temperature was maintained at 37 ± 1^0 C. The USP II, rotating paddle dissolution method was used at a rotation speed of 50 rpm. One gram granules (8/12 mesh fraction) were poured into the dissolution vessel and one milliliter samples were collected at various times by means of a filter pipet.

Analysis

The amount of sulfathiazole dissolved at any time was determined Spectrophotometrically (Beckman, U.S.A.) at 257 nm.

Statistical analysis

Physical characteristics of the granules: loose bulk density, tapped bulk density, percentage compressibility, hardness, and dissolution, were compared using one-way analysis of variance (ANOVA). The means were compared for a statistical significance difference. A p value of <0.05 was considered as a significant result.

RESULTS AND DISCUSSION

Table 3 listed the average loose and tapped bulk densities, percentage compressibility, hardness, and dissolution time (100% dissolution) of the granules. The dissolution time for the granules are similar because the first samples were collected at five minutes and complete dissolution had occurred by that time. The other physical characteristics differed from one formulation to the other ($p<0.05$) but granules from the same formula dried in two different conditions, conventional tray oven and the microwave oven were not significantly different ($p>0.05$). These observations lead to the conclusion that the microwave radiation had no significant effect on the granules' physical characteristics. The

TABLE 3

Physical Characteristics of the Granules

Formula	Drying Method	Drying Time (min)	Loose bulk density (gm/cc)	Tapped bulk density (gm/cc)	Percentage compressibility[a]	Hardness (kg)	Dissolution[e] time (min)
A	Tray drier	120	0.355[b] (0.003)[c]	0.448 (0.006)	20.68 (1.69)	1.25 (0.264)	5[d]
	Microwave	45	0.353 (0.003)	0.448 (0.006)	21.14 (1.06)	1.26 (0.255)	5
B	Tray drier	100	0.395 (0.004)	0.480 (0.006)	17.77 (1.18)	0.70 (0.258)	5
	Microwave	20	0.396 (0.004)	0.484 (0.006)	18.17 (1.39)	0.60 (0.211)	5
C	Tray drier	70	0.335 (0.003)	0.467 (0.010)	28.26 (1.56)	0.30 (0.105)	5
	Microwave	15	0.337 (0.003)	0.460 (0.009)	26.74 (1.77)	0.28 (0.079)	5

[a] Percentage compressibility = [(Tap - Loose)/Tap] 100%
[b, d] Mean of six determinations
[c] Standard deviation
[e] 100% dissolution

morphological study of the granules also showed no evidence of morphological changes or thermal damage to the granule surface or interior.

In summary, the loose and tap bulk densities and the dissolution rate of the granules dried in the microwave oven are not significantly different than the granules dried in the conventional tray oven. Moreover, the microwave radiation does not cause any morphological change and thermal damage to the granules surface. Therefore, this study provides support for the use of microwave radiation as a drying source for pharmaceutical granulations.

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