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COMPRESSIONAL PROPERTIES OF SOME DIRECTLY COMPRESSED GRISEOFULVIN TABLET FORMULATIONS

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ABSTRACT

As an extension of previously reported work on the formulation of direct compression griseofulvin tablets studies were conducted on an instrumented tablet press to determine the relationship between applied compression force, ejection force and tablet weight, thickness, apparent density, hardness (Erweka), and disintegration time. Quantitative data is included on the use of Emcompress(R) in direct compression griseofulvin tablets.

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INTRODUCTION

In a previous publication (1) the present authors described studies designed to explore the utility of preparing direct compression tablets of griseofulvin.

In this report we provide some quantitative evidence on the compressional properties of some selected formulations. We have also included Emcompress(R), which is basically similar to one of the formulations previously studied. (Both contain dicalcium phosphate dihydrate as the main diluent).

EXPERIMENTAL

Materials - As previously described with the addition of Emcompress(R) supplied by Edward Mendell Inc.

Methods - The methods used, including that used to obtain compaction and ejection forces, have been previously described (1, 2).

The following formulations were investigated.

Formula A	Griseofulvin, fine	125
	Dicalcium phosphate dihydrate	570
	Calcium-phosphato-carbonate complex	30
	Cation exchange resin	14.5
	Colloidal silica	3.6
	Magnesium stearate	10.8

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Formula B	Griseofulvin (pretreated 16 mesh granules, using 4% P. V. P. equivalent to griseofulvin	125
	Calcium-phosphato-carbonate complex	19
	Dicalcium phosphate dihydrate	356
	Cation exchange resin	10
	Magnesium stearate	7.5
	Colloidal silica	2.5
Formula C	Griseofulvin, fine	125
	Microcrystalline cellulose	438
	Spray dried lactose	187
	Magnesium stearate	3 8
Formula D	Griseofulvin, fine	125
	Microcrystalline cellulose	156
	Sta-R_x 1500 Starch$^{(R)}$	462
	Stearic acid	7
Formula E	Griseofulvin, fine	125
	Emcompress$^{(R)}$	625

Results are shown in Tables I through V.

RESULTS AND DISCUSSION

Table I and II show the compressional properties of griseofulvin tablets. Although both griseofulvin formulations exhibit

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Table I

The properties of griseofulvin tablets prepared from formula A :

Applied Compression force kg	Weight mg	Thick-ness mm	Apparent tablet density g cm^{-3}	Hardness (Erweka)	Ejection force kg	Disintegra-tion time min
696.6	664.3	4.09	1.66	4.6	59.8	9.0
1150.9	648.5	3.79	1.75	5.6	62.4	1.5
2080.8	665.6	3.75	1.81	>15	85.5	2.36
3013.7	648.3	3.12	2.12	>15	121.1	4.5

Table II

The properties of griseofulvin tablets prepared from formula B:

Applied Compression force kg	Weight mg	Thick-ness mm	Apparent tablet density g cm^{-3}	Hardness (Erweka)	Ejection force kg	Disintegra-tion time min
548.2	699.6	4.67	1.53	4.6	49.5	6.0
1211.5	696.0	4.32	1.64	14.0	76.3	1.36
2780.5	694.5	4.06	1.79	>15	111.9	2.5
3240.9	696.6	4.01	17.9	>15	122.9	3.0

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satisfactory hardnesses and applied force profiles those containing the drug pretreated with polyvinylpyrrolidone produce harder tablets (when compared at an applied force of about 1200 kg). This increase in hardness is probably due to the action of polyvinylpyrrolidone as a binding agent. Also, for both formulations an increase in compressional force produces a minimum in the disintegration time. The reason that softer tablets (those compressed at about 600 kg) take a great deal longer to disintegrate than those compressed at higher force may be mainly due to action of swelling type disintegrants (cation exchange resin). Disintegration properties of dicalcium phosphate dihydrate tablets containing a variety of disintegrants have been described. The relationship between applied force and disintegration time in terms of the mechanism of action of disintegrants used in these formulations was discussed.

Table III shows the properties of griseofulvin tablets prepared from formulation C. These tablets were prepared by aiding the flow of mixture into the die (flow properties were very poor)(The reasons were described in the previous paper (1). Ejection forces are considerably lower than those produced with dicalcium phosphate dihydrate formulations. The reason that microcrystalline cellulose formulation generate lower ejection forces have been described previously (3).

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Table III

The properties of griseofulvin tablets prepared from formula C:

Applied Compression force kg	Weight mg	Thickness mm	Apparent tablet density g cm^{-3}	Hardness (Erweka)	Ejection force kg	Disintegration time min
357.4	401.2	3.48	1.18	7.4	33.0	4.0
1017.5	416.6	3.17	1.35	10.0	30.5	40
1436.0	427.6	3.13	1.41	> 15	45.9	60

Note - The flow properties of this formulation were very poor, the tablets were prepared by aiding the flow of mixture into the die.

It is also evident that in spite of the fact that the formulation contains about 58% microcrystalline cellulose the disintegration time of tablets compressed at a moderate force of 10/7 kg is 40 minutes. This may appear surprising, since it is claimed that microcrystalline cellulose produces self disintegrating tablets. If self disintegration means disintegration within a reasonable time then the results presented in Table III and those shown previously (3) suggest that microcrystalline cellulose formulations may present disintegration problems when compressed at a moderate or high compressional force. Also the disintegration properties

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of microcrystalline cellulose formulation appear to be very pressure dependent. It is suggested that it may be useful to include an additional tablet disintegrant in a microcrystalline cellulose formulation (to reduce the effect of pressure on disintegration).

The flow properties of the Formulation D were also extremely poor (Table IV). The results presented in Tables III and IV show that formulations containing microcrystalline cellulose Sta-Rx 1500 are unsuitable for the direct compression of griseofulvin. It may be assumed that the use of these direct compression bases for drugs with fine particle size and low bulk densities may also present similar difficulties.

Table IV

The properties of griseofulvin tablets prepared from formula D:

Applied Compression force kg	Weight mg	Thickness mm	Apparent tablet density g cm^{-3}	Hardness (Erweka)	Ejection force kg	Disintegration time min
199.9	361.7	3.48	-	0.1	29.3	very variable
345.3	348.9	very variable	-	very variable	31.2	(5.0 approx)

Note - The flow rate of this formulation was very poor, tablets prepared even after aiding the flow showed variable results.

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Table V

The properties of griseofulvin tablets prepared from formula E:

Applied Compression force kg	Weight mg	Thickness mm	Apparent tablet density g cm^{-3}	Hardness (Erweka)	Ejection force kg	Disintegration time min
908.7	666.5	4.08	1.67	6.2	62.4	0.64
3150.0	670.3	3.72	1.84	>15	148.6	0.96
3452.9	627.4	3.46	1.85	>15	224.9	1.22

As expected the properties of griseofulvin tablets using Emcompress (Table V) are basically similar to those prepared from formulations A and B. The ejection forces, however, are significantly higher. This may be caused by the fact that Emcompress formulation contains less magnesium stearate.

The data presented in this paper together with that reported previously (1) indicates the potential of the direct compression technique for griseofulvin.

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