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DIRECT COMPRESSION CHARACTERISTICS OF VITAMIN A-ACETATE

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ABSTRACT

A study of the direct compression characteristics of vitamin A-acetate has been made, using a wide range of compression speeds (24-620 mm/s). Relative powder density, mean yield pressure derived from Heckel analyses and radial tensile strengths were used as the basis of the investigation.

The mean yield pressure appeared to be independent of compression speed in the range 24-60 mm/s, whilst an increase was observed at higher speeds of 150-620 mm/s, attributable to the presence of predominantly fragmentation and plastic deformation mechanisms of consolidation respectively. Changes in tablet radial tensile strength and relative powder bed density (Do) appears to correlate with the hypothesis of a mixed mechanism of consolidation for vitamin A-acetate.

INTRODUCTION

Vitamin A-acetate (for direct compression) is a free-flowing, light yellow powder, consisting of spherical particles composed of vitamin A-acetate oil (USP/BP/Ph.Eur.) distributed in droplets of 1 to 2 microns in a modified food starch coated matrix of gelatin and sucrose with butylated hydroxy toluene as an anti oxidant.

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It has always been a common medical practice to supplement the diet with vitamin-A products, as a result of the likelihood of widespread inadequate dietary intake. However, obtaining stable formulations has been a major problem. Vitamin A is sensitive to oxidation, hence it is desirable to use acetate esters coated with gelatin or gelatin-starch.[4]

The use of various tableting aids in the development of pharmaceutical products, including conventional and chewable vitamin tablets has been reviewed.[2] The stability of vitamin A, thiamine and ascorbic acid compressed in eight commonly used solid matrixes has been reported. Mannitol and lactose were found to yield superior stability and all the three vitamins were quite stable when the moisture content of the tablets was less or equal to 1%.[8]

In a related study of the stability of vitamins in sugar-coated multivitamin tablets, best stability was obtained when vitamin A was in the coatings and the other vitamins in the tablet core.[5]

From the survey of the literature, it appears that no significant work has been reported on the fundamental direct compression characteristics of vitamin A formulations. The principal aim of the present study was to assess the fundamental direct compression properties of vitamin A-acetate using a wide range of compression speeds (24-620 mm/s). Mean yield pressure and relative density of the powder bed (at the point when a measurable force is applied) derived from Heckel analyses and radial tensile strength were used as the basis of the evaluation.

EXPERIMENTAL MATERIALS

Vitamin A-acetate 500 was obtained from Dano Chemo A/S, Ballerup, Denmark, whilst magnesium stearate was obtained from BDH Chemicals, Poole, England.

METHODS

Compression: Compressions were carried out using The Liverpool School of Pharmacy Modified High Speed Compaction Simulator, (ESH Teshing Ltd., Brierley Hill, West Midlands, England), fitted with

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12.5 mm flat faced punches. The simulator consists of a load frame, hydraulic power pack and electronic control unit. A saw tooth time displacement profile was used to control both upper and lower punches. The data points of the profile are output at a pre-determined rate via a digital/analogue converter to the servo-controller in the main control unit and on to the control valves situated on the load frame. The signal supplied to the valves determines the flow of hydraulic fluid from the power pack through the valves to the actuators. It is this flow of fluid which causes movement of the actuators according to the intended profile. The output rate of the profile may be set to produce compaction speeds up to 3000 mm/s and to a maximum compaction force of 50 KN.

500 mg constant weight (250,000 I.U.) of vitamin A-acetate was compressed to a maximum force of 30 KN, four tablets were produced at seven compression speeds from 24 to 620 mm/s. These speeds encompass the speeds of single punch machines (50-150 mm/s) and well above that of rotary tableting machines (100-400 mm/s). The die wall was cleansed with acetone and prelubricated with 4% w/v of magnesium stearate in carbon tetrachloride before each compression.

During compression, upper punch load and punch separation were monitored to an accuracy of ± 0.05 KN and ± 12 µm respectively. The compression data were manipulated using the Heckel equation[3]:

$$\ln \frac{1}{1-D} = KP + A$$

Where D is the relative density of the tablet at pressure P, K is a material constant which is the slope at the straight line region of the plot, the reciprocal of which is the mean yield pressure. A is the value of the intercept of the straight line and is a function of the initial bulk volume. Regression analyses were carried out on the Heckel plots and the mean yield pressure and intercept A from four compressions per speed were determined. The relative density of the powder bed at the point when a measurable force is applied (Do) was evaluated and compression speeds were calculated from the load/time trace using the point at which the first measurable force was detected.

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Radial tensile strength: Tensile strength was determined from the force required to fracture tablets by diametral compression on a motorised tablet hardness tester (Schleuniger, model 2E, Switzerland) and the corresponding tensile strength calculated according to the equation of Fell and Newton.[1]

RESULTS AND DISCUSSION

The compressibility of pharmaceutical powders can be estimated from the mean yield pressures evaluated from the Heckel analysis.[2] The mean yield pressure of vitamin A-acetate appears to be independent of compression speed over the range 24-60 mm/s (Table 1). This observation can be ascribed to an indication that the predominant mechanism of consolidation is by fragmentation within the above speed range. At a higher compression speed range 150 to 620 mm/s, an increase in mean yield pressure was observed, due to a possible change to a predominantly plastic deformation mechanism of consolidation (Table 1). The mechanism responsible for an increase in the mean yield pressure with compression speed is likely to be the time dependent nature of plastic flow with resultant bond formation and/or an increase in brittle behaviour.[6] This observation suggests that vitamin A-acetate manifests some degree of plastic flow and fragmentation, hence suggesting a possibility of a mixed mechanism of consolidation, dependent on compression dwell time.

There was no significant change in radial tensile strength with increasing speed of compression up to 60 mm/s. However a consistent decrease in tablet tensile strength was observed at speeds between 150 to 620 mm/s, which appears to correlate with the hypothesis that consolidation of vitamin A-acetate occurs predominantly by fragmentation at low speeds, with an indication of time-dependent plastic deformation at higher speeds of compression (Table 1).

The tablet tensile strengths were higher at compression speeds of 24 to 60 mm/s, possibly due to extensive fragmentation in this range, which enhanced filling of void spaces, leading to optimum force utilisation, improved consolidation and better

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TABLE 1

Effect of Compression Speed on the Mean Yield Pressure and Radial Tensile Strength of Vitamin A-acetate Tablets.

Compression Speed (mm/s)	Mean Yield Pressure (MPa)	Radial Tensile Strength ($x10^{-4}$, MPa)
24.00	20.65	0.604
43.00	21.68	0.591
60.00	21.05	0.611
150.00	24.21	0.603
330.00	36.36	0.515
500.00	37.45	0.441
620.00	39.45	0.432

TABLE 2

Effect of Compression Speed on the Relative Density of Vitamin A-acetate

Compression Speed (mm/s)	Relative Density (Do)
24.00	0.828
43.00	0.834
60.00	0.809
150.00	0.798
330.00	0.753
500.00	0.721
620.00	0.694

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bonding. The relatively lower tensile strengths at higher speeds of compression is probably due to a progressive reduction in plastic flow as a result of the compression dwell time correspondingly reducing. The relative density (Do) decreases with compression speed (Table 2) due to a decrease in the rearrangement and particle slippage phase of densification of the powder bed. This is as a result of an increase in the frictional and adhesive forces between the particles opposing the rearrangement process.[6]

CONCLUSION

A study of the direct compression characteristics of vitamin A-acetate has been performed. Mean yield pressure and radial tensile strength of the tablets appeared to be independent of compression speed at 24-60 mm/s, however, significant changes were observed at the higher speed range of 150-620 mm/s ascribed to the likely presence of a mixed mechanism of consolidation for vitamin A-acetate.

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