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Mechanisms of disintegration and compactibility of disintegrants in a direct compression system

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Fundamental steps involved in the formation of a tablet include filling and rearrangement of particles in the die, elastic and plastic deformation of particles, fragmentation, and fusion of areas of true interparticle contact. The biopharmaceutical and physicochemical performance of a dosage form can be related to the sum of the interactions between the different constituents of formulation and manufacturing methodology. Dissolution rate is directly proportional to disintegration rate of the tablets, and rapid disintegration is especially desirable in the case of slightly soluble drugs. During the past decade, great advances have been made with respect to solubility and disintegration of tablets. With the emergence of new tablet disintegrating agents, the mechanism of disintegration and the influence of disintegrants on physicochemical performance of tablets deserve further investigation, despite substantial coverage in the literature (Shangraw et al., 1980; Lowenthal, 1972; Ingram and Lowenthal, 1966; Nogami et al., 1969; Duchene, 1983; Van Kamp et al., 1986).

Mechanisms of disintegration previously reported include swelling, wicking, deformation, heat of adsorption and particle–particle repulsing forces. Such diversity leads to the conclusion that no simple theory satisfactorily applies to all disintegrating systems. The purpose of the present work has been to investigate mechanisms of disintegration, and the effect of disintegrants on tablet hardness, by adapting a procedure which can predict and make disintegration action more rational. The disintegrants used were: sodium starch glycolate (Primojel) microcrystalline cellulose (Avicel), croscarmellose sodium (AC-DI-Sol) and starch. Emdex powder (received from Edward Mendell Co.) and magnesium stearate B.P. were used as the

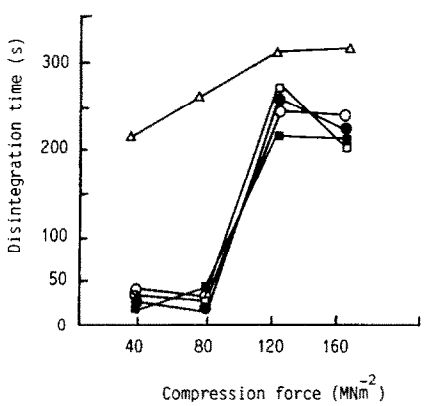

Fig. 1. Plot of the disintegration time vs various compaction pressures. △, control with no disintegrant; □, Avicel; ○, starch; ■, AC-DI-SOL; ●, Primojel.

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tablet base and lubricant, respectively.

Tablets containing 5% m/m disintegrant and 0.5% m/m lubricant were prepared at specified pressures using an instrumented single punch Manesty type F3 tableting machine fitted with 10 mm flat-faced punches. Fig. 1 illustrates a plot of applied pressure versus disintegration times. When the shapes of these plots are compared with the reported mechanisms, it is apparent that compression force dictates the disintegration mechanism more significantly than do the physicochemical properties of the disintegrants. At low compression forces the degree of porosity is high and water uptake accompanied by swelling of the particles, must be the first step in disintegration, although rapid disintegration is associated with the rate and extent of swelling. This mechanism has been extensively studied (Ganderton, 1969; Ganderton and Selkirk, 1970; Ganderton and Fraser, 1970; Lerk et al., 1979; Caramella et al., 1984). At a pressure of 80 $MN \cdot m^{-2}$ the degree of porosity decreases slightly, continuous pathways are formed and water can wick into the tablets as a result of capillary action, with a resulting decrease in disintegration time. A similar decrease in disintegration time with pressure in some direct compression formulas has been described by Khan and Rhodes (1976) and Berry and Ridout (1950). Water penetration and capillary function follows the Washburn equation (1921), indicating that there is a linear relationship between the square of volumetric uptake (V) and the time (t):

$$V^2 = \frac{2m \cdot \gamma \cdot \cos \theta}{K_0 \cdot \eta} \cdot t$$

where m is the hydraulic pore radius, γ the surface tension of the penetrating liquid, θ the contact angle between liquid and solid in the pores, η the liquid viscosity and K_0 a constant dependent on pore shape. Liquid penetration into tablets is proportional to the porosity or mean pore diameter, both of which increase with increasing starch concentration (Couvreur, 1975; Carstensen, 1980). This has been attributed to the compressibility and low cohesiveness of starches (Shangraw et al., 1980). However, at pressures of 120 $MN \cdot m^{-2}$ and 160 $MN \cdot m^{-2}$ particles are deformed and thus energy rich. When exposed to water, relaxation of the stressed particles gives rise to an exothermic process causing expansion and breakage of bonds. This phenomenon is 'mechanical activation' (Huttenrauch et al., 1985) and applied forces, frictions, deformation and fractures contribute to the change in state, transforming mechanical energy into dislocation and distortion energy of the system. This structural disordering implies an increase of both entropy and enthalpy and the development of thermodynamically unstable states associated with an increase in the free enthalpy (ΔG) of the system (Fig. 2). Since the activated state is unstable, the process of activation is reversible, resulting in a deactivation, entropy loss and energy output of the system. Therefore heat of wetting, which causes the entrapped air in the tablet to expand, may be related to the activated state of ingredients. The reversible part of the stored energy that can be transformed into other types of energy is responsible for disruption and disintegration at high compaction pressures. The internal energy of the particles at an applied compression force of 160 $MN \cdot m^{-2}$ (Fig. 1), is higher than the internal energy of particles compressed at 120 $MN \cdot m^{-2}$, and therefore lower disintegration times are attained in the former case. Thus dependence of disintegration time on mechanical activation is greater at the high-pressure end of the plot. Tablets containing 10% m/m of disintegrants were also produced and the same patterns of disintegration mechanisms were observed indicating that greater percentages of disintegrant did not change the above mechanisms. The general mechanisms of disintegration as a function of compaction pressure for tablets may be depicted as in Fig. 3.

The effect of compactibility of various disintegrants on tablet strength was determined by

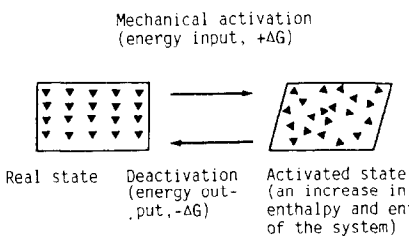

Fig. 2. Principle of mechanical activation of a solid.

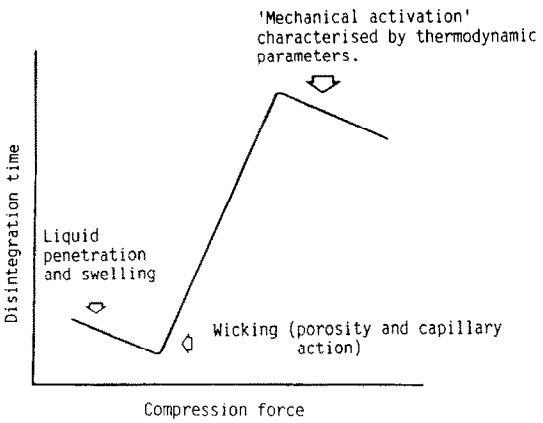

Fig. 3. General mechanisms of disintegration.

measuring the pressure exerted during tableting required to produce tablets having tensile strength of 100 N. Table 1 shows punch pressures required to produce compacts with a hardness of 100 N. The results obtained suggest that the compactibility of Avicel and Primojel is superior to that of AC-DI-Sol and starch. These findings may have implications for powders having a low plasticity index, and in overcoming tablet defects such as capping and lamination.

In conclusion, the mechanisms of tablet disintegration are identified by a plot of compression force vs disintegration time. The observed differences in disintegration actions at low compression forces are due to swelling and wicking, whilst mechanical activation of the particles strongly influences the disintegration rate at higher compression forces. Although there are many parameters (i.e. manufacturing and formulation related factors) influencing tablet strength, compression properties of tablets were improved by Avicel and Primojel.

TABLE 1

THE EFFECT OF COMPACTIBILITY OF DISINTEGRANTS ON TABLET STRENGTH

Disintegrants (5% m/m)	Tablet weight [a] (mg)	Compaction pressure required to produce tablets having tensile strength of 100 N (upper punch pressure $MN \cdot m^{-2}$)
Control (Emdex)	550	116
Avicel	555	108
Primojel	550	98
AC-DI-SOL	545	138
Starch	553	140

[a] Average of 20 determinations.

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