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The influence of water content on the binding capacity of β-cyclodextrin

F. Giordano [1], A. Gazzaniga [2], G.P. Bettinetti [3] and A. La Manna [1]

[1] *Dipartimento di Chimica Farmaceutica, Università di Pavia, Pavia (Italy),* [2] *Istituto di Chimica Farmaceutica, Università di Milano, Milano (Italy) and* [3] *Dipartimento di Scienze Farmaceutiche, Università di Firenze, Firenze (Italy)*

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Summary

The binding capacities of β-cyclodextrin samples containing different amounts of water have been investigated. Crushing strength of tablets obtained with a single-punch tableting machine was used as a measure of the cohesive properties of powders. The results clearly indicate a determinant role of adsorbed water on powder compactability. The effect of aging is also stressed and discussed.

Introduction

The possibility of using β-cyclodextrin as filler and binder for direct compression has recently been described (Szabo-Revesz et al., 1989). The relationship between crystallinity and tablet characteristics of β-cyclodextrin has been investigated (Nakai et al., 1985) and it has been demonstrated that a decrease in crystallinity increases tablet strength.

It is well known that water can play a significant role in the consolidation properties of materials (David and Augsburger, 1977; Khan et al., 1981; Ragnarsson and Sjogren, 1985; Patel et al., 1989) through the combination of lubricant and plasticizing effects. A typical feature of cyclodextrins (CDs) is represented by variable water contents which depend on factors such as thermal history and storage humidity conditions. The average water content of β-cyclodextrin is about 14–15% (15.98% in the dodecahydrate, which is the solvate with the highest number of water molecules). The considerable hysteresis of water sorption and desorption isotherms of β-cyclodextrin (Nakai et al., 1986) suggests that significantly differing water contents can be achieved depending on the technological operations performed.

The aim of the present study was to evaluate possible water-mediated effects on compaction of cyclodextrins. In particular, β-cyclodextrin was employed as the test material, since it represents the first choice from several points of view (e.g., inclusion compound formation, economical convenience and commercial availability).

Correspondence: A. La Manna, Dipartimento di Chimica Farmaceutica, Università di Pavia, Viale Taramelli 12, 27100 Pavia, Italy.

We report here the results obtained on tablets of β-cyclodextrin: crushing strength was adopted as the parameter for evaluating the compaction capacity. Additional information was also collected through thermal analysis (thermogravimetry).

Materials and Methods

β-Cyclodextrin (Nihon Shokuhin Kako, Tokyo, Japan; BCD) of commercial purity grade (0.146 g/g as mass fraction of water) was used. Mean volume-surface diameter, determined by sieving, was 146 μm.

Materials were compressed with flat 0.95 cm circular punches in a Kilian single-punch reciprocating tablet machine, instrumented as previously reported (Colombo et al., 1978). The tablet machine was set in order to give a tablet height of about 3.00 mm with 300 mg of BCD, at an upper punch pressure of approx. 140 MPa. Samples were fed into the die by hand. Prelubrication of the die was accomplished by two compression cycles of BCD containing an excess of magnesium stearate (0.2 g/g).

The crushing strength of the tablets was tested immediately after compression in a hardness tester operating at a constant speed of 5 mm min^{-1} (Conte et al., 1972).

Thermogravimetry (Mettler TA-3000 and TG 50 cell) was used to assess water content of samples. A heating rate of 10 K min^{-1} in the temperature range 40–120 °C under a nitrogen atmosphere was found to be suitable for achieving dehydration, as confirmed by Karl Fischer titration.

According to thermogravimetric investigations, anhydrous BCD samples (ABCD) were prepared by heating BCD at 120 °C until attainment of constant weight (approx. 2 h). Samples with increasing moisture content were prepared by allowing spontaneous water sorption from the atmosphere at ambient temperature.

Results and Discussion

The crushing strengths, plotted in Fig. 1 vs H_2O percentage or tablet weight, are relevant to

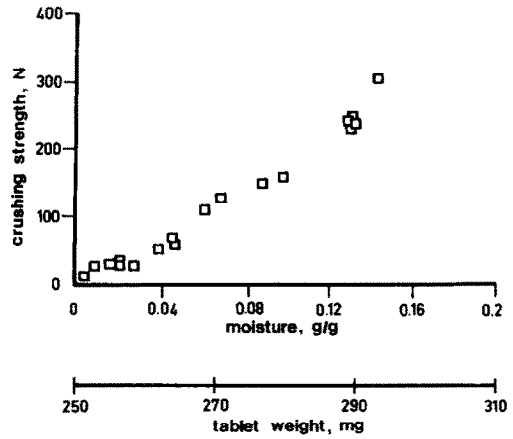

Fig. 1. Relation between crushing strength and moisture contents (as mass fraction of water) or tablet weight of ABCD allowed to adsorb increasing amounts of water.

tablets obtained by compressing 250 mg samples of ABCD, allowed to adsorb increasing amounts of moisture. A linear relationship ($R = 0.985$) can be observed: crushing strength rises from 15 to 300 N, corresponding to a maximum water uptake of about 14.5%. This expected behavior can be attributed to an increase in total mass to compress and water contents, thus resulting in improved consolidation of particles (Patel et al., 1989). In order to elucidate the relative importance of each contribution, crushing strengths on BCD tablets in the same mass range (250–300 mg) were assessed. The results are reported in Fig. 2. In this case also, a linear relationship between crushing strength and powder weight to compress can be seen.

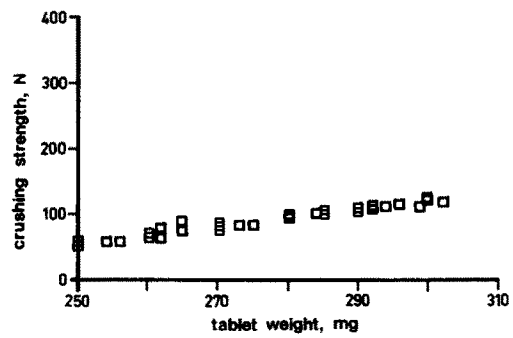

Fig. 2. Relation between crushing strength and tablet weight of BCD powder with constant amount of moisture (0.146 g/g as mass fraction of water).

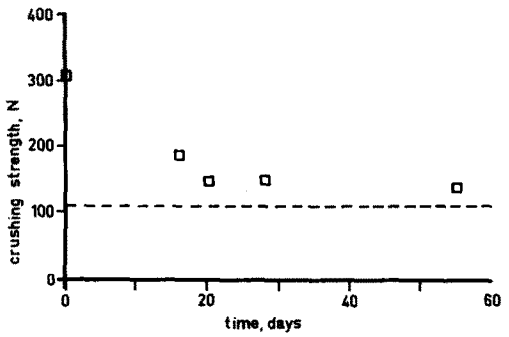

Fig. 3. Relation between crushing strength and aging of tablets prepared from ABCD powder after complete rehydration; the dashed line represents the crushing strength value of commercial BCD. CV for each experimental point below 3%.

It was rather surprising and unexpected anyway that the crushing strength of tablets obtained from ABCD allowed to reach about the same moisture level before drying (14.5%) was more than twice that determined on tablets prepared from BCD (14.6% moisture content).

Moreover, by assessing the variations in compressional behavior with time of ABCD powder after complete rehydration, a decrease in crushing strength was observed from 300 to 150 N (Fig. 3).

It should be pointed out that two different materials (BCD and ABCD allowed to reach the same water content as BCD), from chemical and physical standpoints, are being compared: the same consideration applies when α-lactose monohydrate is compared to the dehydration products regarding the binding capacities (Lerk et al., 1983).

The trend shown in Fig. 3 can be explained if gradual transformation from adsorbed to bonded water is taken into account. The overall process could then be divided into two main steps. Water is first rapidly adsorbed from ambient atmosphere onto the surface of ABCD particles: this water strongly affects the binding properties of the material. Then, a possible migration within the molecular network and formation of hydrates occur slowly. An analogous mechanism has been proposed for dextrose (Armstrong et al., 1986). Besides the major role played by moisture, the compressional behavior could well be influenced by crystallinity as well (Nakai et al., 1985). In fact, in the course of rehydration of ABCD, solid phases with lower crystallinity, i.e. structural disorder, can be obtained (Nakai et al., 1986).

Changes in the binding properties of hydrates by thermal or chemical dehydration have already been reported (Lerk et al., 1983, 1984). For instance, increased binding capacity of α-lactose monohydrate after dehydration was observed and ascribed mainly to an augmented fragmentation during compression leading to a different pore size distribution in tablets. The general behavior here described cannot be explained only on the basis of possible augmented fragility of BCD particles on thermal dehydration, thus resulting in a higher specific surface area produced by compressional forces on ABCD powder; this is proved by the low crushing strength shown by ABCD immediately after its preparation.

Conclusions

The dramatic changes in crushing strength observed on tablets of ABCD, as a function of water contents during the phase of absorption, must be taken into account. An analogous behavior can reasonably be expected when β-cyclodextrin is the main component, in terms of weight, of the formulation, thus affecting other related parameters such as disintegration and dissolution time. As for the utilization of BCD in tableting technology, a number of particular features of this material, such as crystallinity changes, inclusion compound formation, and water sorption and desorption, must be carefully considered. In particular, attention should be paid to the drying process which might become a critical step during operations leading to compression of formulations containing β-cyclodextrin.

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