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Tablet water uptake and disintegration force measurements

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Summary

An apparatus that is capable of simultaneously determining the amount of water absorbed and the force developed by the same tablet during its disintegration has been constructed. By measurements performed on model tablets, a mainly linear dependence of the disintegrating force by the amount of water absorbed was found. This correlation allows a deeper understanding of the interactions between water and disintegrant and gives information on the disintegrant efficacy.

Water uptake is a well-described process (Nogami et al., 1969; van Kamp et al., 1986), whereas the mechanism involved in tablet disintegration is a matter of continuous debate between researchers (Shangraw et al., 1984; Caramella et al., 1984a).

In previous research (Colombo et al., 1980), one of us studied tablet disintegration mechanisms by measuring the disintegration force developed by a tablet after immersion in water or other biological fluids. This research showed that, of all the mechanisms suggested by the literature, only the swelling of disintegrant particles could be clearly demonstrated: the tablet disintegrated when a certain amount of disintegration force was developed and this force arose only when the excipients swelled (Caramella et al., 1984b).

Further data (Caramella et al., 1986) indicated that water uptake and disintegration force development are directly connected, but as yet, no methods exist to measure the two processes concomitantly. The availability of an apparatus that was capable of determining water uptake and the consequent force developed would greatly facilitate a description of the tablet disintegration phenomenon at a more molecular level.

The aim of this work was to construct an apparatus that is capable of simultaneously determining the amount of water absorbed and the force developed during tablet disintegration.

Diagram of the apparatus. An extensimetric loading cell (A) (Fig. 1) is bolted to the upper side of a rectangular metallic frame (B); through the lower side of this frame there is a hole which is 3 cm in diameter. A steel punch, passing through the hole without touching the frame wall, is fastened to the lower end of the loading cell. In this way, the cell can measure forces applied to the tip of the punch.

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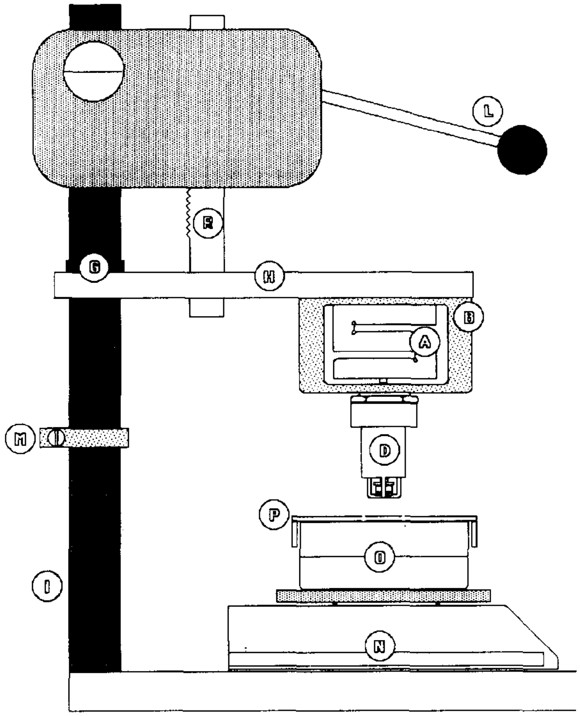

Fig. 1. Disintegration force–water uptake measuring apparatus. A = extensimetric loading cell; B = metallic frame; D = steel cage; G = slide guide; H = steel arm; I = steel bar; L = controlling lever; R = master rack; M = lock, N = precision balance; O = glass container; P = Plexiglas lid.

A cylindrical stainless steel cage (D) has been constructed with threading on the upper section, wide low-position lateral openings, and a syntherized glass disk support at the bottom.

When a tablet is placed on the glass disk and the cage is screwed onto the down-side of the rectangular frame by a threading, the tablet is firmly clamped between the punch tip and the glass disk. The whole system constitutes the measuring head.

The measuring head is bolted to a slide guide (G) by an arm (H) that runs vertically on a steel bar (I), which in turn is tightened to the table. Sliding is controlled by a lever (L), which sets a master rack (R) in motion. A lock (M) makes sure that the steel bar always stops the measuring head at the same level. An electronic precision balance (N) is placed under the measuring head. A glass container (O) filled with water and covered by a Plexiglas lid with a hole in its centre (P), weighs the balance plate.

Theoretical basis of the measurement. The apparatus built for measuring water uptake and disintegration force development is based on the principle that a body immersed in a fluid receives an upward thrust which is equivalent to the weight of the fluid displaced.

The measuring head, after immersion at a fixed depth in the water-filled container on the precision balance, displaces a definite volume of water. The balance displays the weight of the water displaced. If a tablet is inserted in the cage of the measuring head, the balance measures the weight of water displaced by the cage and by the tablet. But when the tablet starts absorbing water, as it is fastened to an external arm, a weight decrease corresponding to the water taken up by the tablet is displayed. The punch linked to the extensimetric loading cell, pressing the tablet against the glass disk of the cage, allows the measurement of the force developed during tablet water absorption. Finally, the apparatus can simultaneously measure the water uptake and the disintegrating force developed by the tablet.

Procedure. Measurements were performed on model tablets (diameter 1.14 cm; thickness 0.44 cm; weight 0.828 g) containing Emcompress, maize starch 6% w/w and magnesium stearate 1%, prepared at the same compression force level.

The tablets measured are covered on the lateral side with impermeable adhesive tape, to ensure that water uptake occurs only at the base. This practice renders tablet water uptake and the disintegration force development more precise (Colombo et al., 1980). The tablet is placed on the sintered glass disk at the bottom of the cage. By screwing down the cage, the tablet receives a load of 5 N. Then the cage is pulled down towards the water container, passing through the hole in the container lid, and is stopped before it contacts the water. The balance is set to zero value and the data acquisition system is started.

The cage is then dipped in the water to the fixed immersion point so that the glass disk is completely immersed, whilst the tablet is only just over the water surface. The balance shows the weight of water displaced by the immersed part of

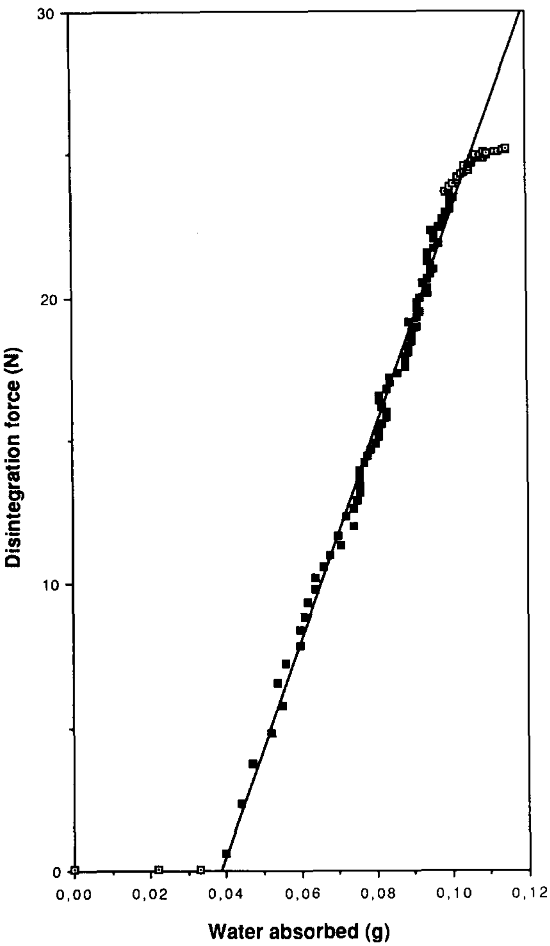

Fig. 2. Relationship between water absorbed and disintegration force developed (the straight line equation was calculated from the values indicated as black squares: $y = -14.440 + 373.471x$).

the cage.

In the beginning, no increase in force is observed, whereas a noticeable weight loss, which is due to porous glass wetting, is displayed. A few seconds after dipping the cage, water reaches the tablet and the transducer measures a force rising to maximum value. The computer (Apple II Europlus with D/A interface) obtains 120 pairs of data for every experiment.

The data collected were elaborated to obtain the amount of water absorbed from zero to the maximum force developed. Plotting force values against amount of water absorbed at the same time, reveals a very interesting relationship (Fig. 2). The relationship starts with a flat part where no force is developed, while a substantial amount of water is absorbed. This is due to the initial absorption of water by the glass disk supporting the tablet. When water reaches the tablet, the plot changes slope. The curvature of this part may be more or less pronounced, but afterwards, the force increases linearly with water absorption.

The final part of the plot may also show more or less evident curvature. Finally, the plot becomes flat, showing water uptake by the tablet or the glass disk without any further force development.

The relationship obtained needs further transformation in order to measure the exact amount of water that interacts with tablet components. The linear part of the plot was analyzed by linear regression analysis and the fitted straight line was determined, as shown in Fig. 2. The intercept of this line expresses the amount of water absorbed by the glass disk or dispersed in the contacts between tablet and system. The subtraction of this amount from the collected water uptake data enables us to determine the exact relationship between the water absorption and disintegration force development, and, in particular, the absolute amount of water that determines the development of disintegration force. According to the results obtained, the prepared tablets absorb an amount of water of 0.075 ± 0.008 ml (95% confidence interval).

A low quantity of water develops a very intense force and this volume concurs significantly with the tablet pore volume calculated from the apparent and true density of the tablet, i.e. 0.0796 ± 0.0008 ml (95% confidence interval).

From the results obtained we can conclude that the measurement of the water absorbed and of the disintegration force developed by pharmaceutical tablets is easily accomplished by the apparatus here described.

Reproducibility of the measurements is satisfactory, and is of a similar degree to that of simple force determination.

The linear relationship found between water absorbed and force developed is an interesting discovery that will be used for a molecular analysis of the phenomenon of disintegrant particles swelling inside a pharmaceutical tablet.

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