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Short Communication

Disintegrant Action of *Pleurotus tuber-regium* (Singer: Fr) Powder in Paracetamol Tablets: Effect of Compression Pressure

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The effect of *Pleurotus tuber-regium* (Singer: FR) powder, a potential tablet disintegrant, on some physical properties of paracetamol tablet under different compression pressures has been studied. Granules of paracetamol containing varying concentrations of the powder (0 – 5 % w/w) as disintegrant were made and compressed into flat-faced tablets at varying compression pressures (ranging between 1.5 and 5 kg/cm^2). Tablet hardness was found to increase with both the concentration of the disintegrant and the compression pressure. The tablets exhibited rapid disintegration, a behavior that increased as the tablets became harder. The release of paracetamol from all the tablets compressed at the different compression pressures was unmodified, attaining maximum release at about the same time. These behaviors were ascribed to an enhanced disintegrant activity of the powder when the internal porosity of the tablets decreased under increased compression pressures. The rapid disintegration exposed the entire drug content to the dissolution medium, hence the attainment of 100 % release at short periods. *Pleurotus tuber-regium* powder, therefore, can be classified as a natural product, having very good disintegration characteristics.

Keywords: *Pleurotus tuber-regium* powder; disintegrant; paracetamol tablets; tablet properties.

INTRODUCTION

A wide range of natural materials available in Nigeria have demonstrated potentials for use as pharmaceutical excipients. These include starches, colorants, gums, as well as oils and waxes [1]. Many of these raw materials have been shown to exhibit comparable or superior properties when compared with standard ones [2 – 4]. Recently, the disintegrant activity of *Pleurotus tuber-regium* powder from an edible mushroom that grows widely in the tropical and subtropical regions of the world [5, 6] was reported [7]. The particle size and concentration effects on its disintegrant property in paracetamol tablets have equally been studied [8]. However, the effect of varying the compression pressure on the disintegration and some other physical properties of tablets formulated with pleurotus powder is yet unknown. This study, therefore, seeks to fill this missing link, using paracetamol tablets as the model agent of investigation.

MATERIALS AND METHODS

Materials

These include paracetamol powder, BP, (Mallinckrodt Inc., USA), lactose powder and magnesium stearate powder (BDH Chemicals, UK), sodium hypochlorite solution, 3.5 % w/v (Reckitt and Coleman, Nig. Ltd, Lagos) and maize starch, BP (Merck Darmstadt, Germany). Double distilled water was used, while the *Pleurotus tuber-regium* powder was processed locally. Every other chemical was of analytical grade.

Methods

Processing of *Pleurotus tuber-regium* powder

Details of the procedure of converting the underground growth of the plant into powder have been described earlier [7]. The resulting powder was defatted with acetone and bleached with 3.5 % w/v sodium hypochlorite solution. The powder was dried and then passed through a sieve to produce a fraction having less than 0.18 mm particle size. This fraction was used for both characterization and formulation studies.

Tablet preparation

The active drug was mixed with varying concentrations of pleurotus powder and other excipients to produce six batches of paracetamol granules. The paracetamol granules were prepared by wet granulation method. Fifty per cent of disintegrant in each batch was added intragranularly and the other half, extragranularly. The granules were then compressed into 12.5 mm flat-faced tablets using a

tablet press (Beckman-0025-Glenrothes, Fife, Scotland). For each batch, a total of 200 tablets were compressed at four levels of pressure i.e. 1.5, 2.0, 3.0 and 5.0 kg/cm^2. Half of the tablets were stored in a desiccator containing silica gel for 48 hours at ambient temperature prior to characterization, while the rest were characterized immediately after compression.

Characterization of tablets

Using an electronic balance (B154 Toledo Mettler, Switzerland), the mean tablet weights for each batch were obtained from 20 tablets selected randomly. The average tablet thickness and diameter for each batch were also determined using a micrometer screw-gauge. Their mean and standard deviations were also calculated. Using both the tablet weight and dimensions (i.e. thickness and diameter) to calculate the tablet density, the packing fractions (P_f), at varying compression pressures, were calculated from Equation 1:

$$P_f = \frac{Tablet\ \ density}{Particle\ \ density} \qquad 1$$

Employing Equation 2, i.e.

$$\text{Porosity } (P_o) = 1 - P_f \qquad 2$$

values for the internal porosity of the compressed paracetamol tablets were calculated. A Kramer electronic hardness tester was used to measure the crushing strength for each tablet. The force required to break each tablet diametrically was noted. This was replicated five times for each batch and the mean and standard deviation calculated. The obtained values then fitted into equation 3 to obtain the tensile strength, thus:

$$\text{Tensile strength } (T) = \frac{2P}{\pi Dt} \qquad 3$$

where P is compression pressure, D is the diameter of the tablet, and t is the thickness. Tablet friability was assessed in a Roche friabilator (Erweka Apparatebau GmbH, Germany). Ten tablets were randomly selected from each batch and weighed. They were then allowed to tumble in the drum of the friabilator rotating at 25 rpm for 4 minutes. The loss in weight, expressed as percentage of the original weight was calculated as the friability. These tests were run in duplicate and the mean results were used. The disintegration times of 6 tablets from each batch were individually determined in a BP apparatus (MK IV, Manesty Machines, UK) using purified water at 37° ± 0.5°C. The mean value for each batch was calculated and recorded. The dissolution rates of the active drug, paracetamol, from the tablets were determined in a BP apparatus (Caleva ST 7, G.B. Caleva, UK) using 0.01M HCl at 37° ± 0.5 °C as the dissolution medium. Samples withdrawn at specified times were analyzed spectrophotometrically (Spectronic 21D, Milton Roy, USA) at 245 nm. Replacement of withdrawn volumes was done with fresh dissolution medium, pre-warmed to the operational temperature.

RESULTS

Table 1 shows that increase in the concentration of the pleurotus powder in the paracetamol tablet causes an increase in the tensile strength of the tablets; but storing the tablets for 48 hours causes no significant change in the strength. At 100 % content (pure pleurotus compact), there is no noticeable change in its strength when compared with those of tablets containing between 5 and 10 % of the powder. This suggests that pleurotus powder has an innate compressibility, which contributes to the strength of the tablets. From Figure 1, it is clear that the hardness of the tablet increases as the concentration of the disintegrant in the tablet increases. This becomes more pronounced as the disintegrant concentration approaches 5 % and above. There is also a corresponding increase in tablet hardness with increases in compression pressure. Figure 2, however, shows that increase in the concentration of the disintegrant in the tablets produced no significant change in the friability of the tablets, a situation, which may be attributable to the compressibility of pleurotus powder. But the increase in both the disintegrant concentration and compression pressure reduced the porosity of tablets, both for those assessed instantly and after 48 hours of storage (Fig. 3). In this regard, the effect of pressure was minimal especially after 2.5 % of disintegrant concentration. In Figure 4, it can be seen that the disintegrant concentration of 1.5 % and above reduced the disintegration time significantly. It is noteworthy that increasing the compression pressure from 1.5 kg/cm^2 to 5.0 kg/cm^2 caused the tablets to disintegrate a little faster in conformity with the reduction of the internal porosity at increased pressures. Figure 5 shows that increase in the concentration of the disintegrant or the compression pressure did not alter the dissolution rate of the tablets.

TABLE 1: Effect of storage time on the tensile strength of paracetamol tablets formed with pleurotus powder as disintegrant.

Concentration of disintegrant (%w/w)	Tensile strength (MNm^{-2}) of tablets at 0 h	Tensile strength (MNm^{-2}) of tablets after 48 h
0	1.028 ±0.21	0.989 ± 0.11
1.5	1.137 ±0.31	1.194 ± 0.06
2.5	1.250 ±0.08	1.266 ± 0.11
5.0	1.416 ±0.31	1.399 ± 0.21

7.5	1.433 ± 0.10	1.424 ± 0.11
10.0	1.436 ± 0.09	1.429 ± 0.08

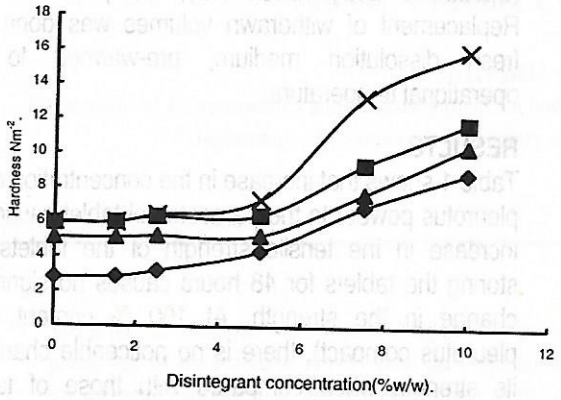


FIGURE 1: Effect of varying the concentration of pleurotus powder and compression pressure on the hardness of paracetamol tablets.

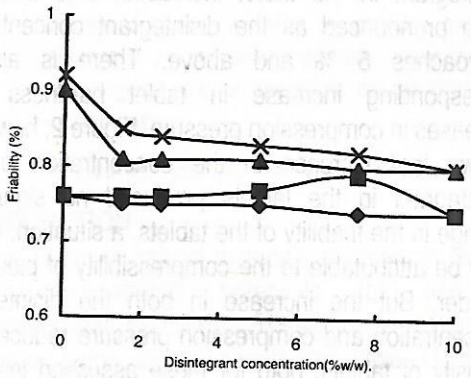


FIGURE 2: Friability versus concentration of pleurotus powder in paracetamol tablets at varying compression pressures.

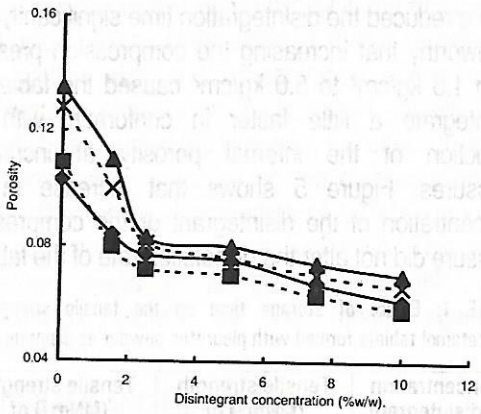
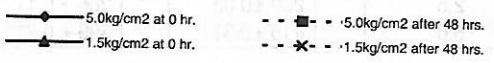


Figure 3: Concentration of pleurotus powder versus internal porosity of paracetamol tablet compressed at 1.5 kg and 5 kg and stored for 48 h.



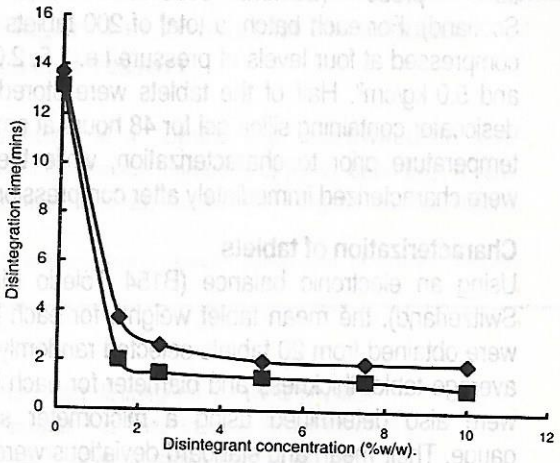


FIGURE 4: Disintegration time versus concentration of pleurotus powder in paracetamol tablets at varying compression pressures.

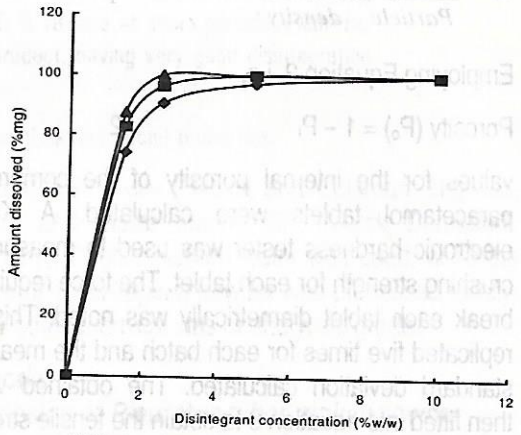
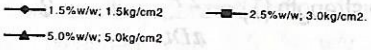


FIGURE 5: Dissolution of paracetamol from tablets containing varying concentrations of pleurotus powder and compressed at different pressures.



DISCUSSION

Pleurotus powder has earlier been shown to possess high disintegrant property [7]. The current result as shown in Fig. 4, where the disintegration time of paracetamol tablets containing this material dropped from about 14 minutes at 0 % concentration to about 4 minutes at 1.5 % concentration is consistent with the earlier observations. But it is interesting to note that increase in the compression pressure (from 1.5 to 5.0 kg/cm^2), which caused an increase in the hardness of the tablets (Fig. 1) produced a faster disintegration in the obviously harder tablet (Fig. 4). This seems to contradict the findings of others [9 – 11] where increase in the compression pressure of the tablets caused corresponding increases in their disintegration times. The faster disintegration

recorded in the present situation can be attributed to a magnified effect of swelling of pleurotus powder when it comes in contact with water [7] especially when the internal porosity of the tablet is decreased under high compression pressures (Fig. 3). The rapid disintegration exposed the entire drug content to the dissolution medium within a relatively short time; hence all the batches showed similar dissolution rates as can be seen in Figure 5. The decrease in the porosity, which corresponds to increase in the packing fraction of the tablets at higher pressures, signifies an increase in inter-particulate bonding within the matrix of the tablet. The resultant harder tablets and the correspondingly higher values of tensile strength confirm this. The low and fairly constant friability values for the various tablets (Fig. 2), apart from confirming the increased particle-particle bonding within the tablet matrix, further suggest that pleurotus powder even when present both intragranularly and extragranularly, does not weaken the interparticulate bonds responsible for tablet strength.

CONCLUSION

In this study, the great potential of pleurotus powder as a tablet disintegrant has been further revealed. Even though harder paracetamol tablets were produced with the inclusion of pleurotus powder in increasing concentrations, the tablets disintegrated faster especially as the compression pressure increased. Nonetheless, dissolution of the tablets proceeded faster than would normally be expected from correspondingly hard tablets that are produced with standard excipients. There seems, therefore, to be increasing evidence, from the past and present investigations, as to the real potential of pleurotus powder as a natural tablet disintegrant. Interestingly, the desirable disintegrant properties of this natural product are exerted at low concentrations. Pleurotus powder is largely of carbohydrate content, and would be expected to yield an inert pharmaceutical excipient. It is reasonably non-toxic since the subterraneous tuber is widely edible in traditional settings. Its yield is generally high following the processing of the tuber into powder. With an acceptable degree of processing and purification, pleurotus powder may well occupy a place as a pharmaceutical-grade tablet raw material. But further investigation on this material is needed; it would be worthwhile to examine other properties that it may possess, such as its effects on the stability of various drugs formulated in the tablet dosage form.

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