Research Article

Preliminary investigation into the use of *Pleurotus tuber-regium* powder as a tablet disintegrant

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**Abstract**

**Purpose:** This investigation aims at developing a pharmaceutical excipient from local sources. *Pleurotus tuber-regium* powder is used locally as a soup thickener because of its ability to swell in water and add bulk to the soup. Since swelling is one of the mechanisms of action of some tablet disintegrants it was thought that the powder of *P. tuber-regium* would be able to act as a tablet disintegrant.

**Method:** The powder obtained from the mycelia of the edible giant mushroom, *Pleurotus tuber-regium* was characterised. Its disintegrant ability in comparison with maize starch BP was investigated in paracetamol tablets prepared via the wet granulation method.

**Results:** *P. tuber-regium* and maize starch BP have similar true, bulk and tapped density values. The *Pleurotus* powder, however, showed superior flow, swelling capacity as well as water retention capacity to maize starch BP. The swelling capacity was three times that of maize starch BP. Tablets prepared with *P. tuber-regium* powder disintegrated faster than those prepared with maize starch BP at concentrations below 10% w/w. At the disintegrant concentration of 10% w/w paracetamol tablets made from both *Pleurotus* powder and maize starch BP had similar disintegration times and dissolution profiles. It is believed that the ability of *Pleurotus* powder to swell by over three times its volume in the presence of water may explain its ability to function as a tablet disintegrant.

**Conclusion:** *Pleurotus tuber-regium* powder may therefore be used as an alternative to maize starch BP as a tablet disintegrant.

**Key words:** *Pleurotus tuber-regium*, physical characteristics, paracetamol tablets

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Introduction

Although *Pleurotus tuber-regium* (FR) singer has been successfully grown in the laboratory\textsuperscript{1,2} it is a basidiomycete which grows wildly in the tropical and subtropical regions of the world\textsuperscript{3,4}. The sclerotium is often dark brown on the surface and white inside. The sizes and weights of the sclerotium could vary, and may be as large as 30 cm and weigh over 5 kg. It enjoys popular use in Nigeria as food and medicine. The sclerotia are usually harvested from decaying logs; the dark brown exterior is peeled off and the white compact mycelial tissue is used for food or medicine. The sclerotia can also be cut up and buried in the soil, and then watered regularly to produce the sporophore (mushroom) which is consumed. One of the most common dietary applications of *P. tuber-regium* in Nigeria is as a soup thickner. The white tissue is blended into fine powder and when added to soup, it swells and adds bulk to the soup. It is this swelling characteristic of *P. tuber-regium* which has advised the investigation into the possible use of this non-poisonous basidiomycete as a tablet disintegrant.

Since a tablet is not useful until its active component is made available for absorption, the disintegrant is arguably the most important excipient in a tablet. A compressed tablet disintegrant is that excipient which facilitates the break up of the tablet in a liquid environment into fine particles prior to dissolution of the active drug and its absorption from the gastro-intestinal tract. Several mechanisms have been proposed to rationalize the action of disintegrants. These include porosity and capillary action, rate of water uptake into the tablet, swelling of disintegrant particles, gas release, melting and enzymatic action, heat of wetting and lysis of physico-chemical bonds\textsuperscript{5-8}.

The aim of this study was to investigate the disintegrant activity of *P. tuber-regium* powder, to evaluate its mechanism of disintegrant action, and also to evaluate the powder as a dissolution aid in compressed tablets.

Materials and Method

Materials

All materials were used as received and included paracetamol powder BP (Mallinikrodt Inc., USA), hydroxypropylmethyl cellulose HPMC NFXII (Shin-Etsu, Japan), 3.5% sodium hypochlorite (Reckitt and Colman Nig. Ltd., Lagos), 95% ethanol, magnesium stearate (both from BDH Chemicals, UK), talc, lactose monohydrate and maize starch BP (all from Merck Darmstadt, Germany), and light liquid paraffin (Halewood Chemicals, UK). Water was double distilled and every other chemical was of analytical reagent grade.

Method

Preparation of *Pleurotus tuber-regium* powder from the sclerotia

The dark brown skin of the sclerotia purchased from a local market was removed with a knife, and the white tissue cut into small pieces. The pieces were ground into powder in a dry manual mill and further reduced in a dry electric mill. Further micronization was done in a ball mill. The fine white powder was bleached whiter with the sodium hypochlorite solution as earlier described\textsuperscript{9}. The wet material was slurried with ethanol in a stainless steel vessel and left to stand in a water bath at a temperature of 60 °C with continuous stirring (Silverson, UK) for a period of 60 min. The slurry was then squeezed using a fine muslin cloth. This process was meant to enhance drying. After drying in an oven at 50 °C for 23 h the resulting powder was classified and the <0.180 mm fraction was used for the tests.
Characterisation of the \textit{P. tuber-regium} powder

The flow property of the powder was investigated by measuring its angle of repose. 10 g of powder was poured into a cylindrical paper roll fixed on to a flat base whose diameter is known and the same as the internal diameter of the cylinder. The cylinder was slowly pulled out vertically so as to form a cone of powder on the base. The height of the cone was measured. This is a modification of the method of Jones and Pilpel\textsuperscript{10}. The angle of repose, $q$, is given by the following equation:

$$q = \tan^{-1} \left( \frac{h}{r} \right) \quad (I)$$

where $h$ is height of conical powder heap, and $r$ is radius of circular base.

Triplicate determinations were made and the mean angle of repose calculated.

The swelling capacity of the powder was estimated by a modification of the methods of Bowen and Vadino\textsuperscript{11} and Iwuagwu and Okoli\textsuperscript{12}. The tapped volume occupied by 5 g of the powder $V_x$, was noted. The powder was then dispersed in 85.0 ml of water and the volume made up to 100 ml with more water. After 24 h of standing, the volume of the sediment, $V_s$, was estimated. The swelling capacity was computed as follows:

$$\text{Swelling capacity} = \frac{V_y}{V_x} \quad (II)$$

The mean of two determinations was calculated.

The hydration capacity (water retention capacity) was determined by the method of Ring\textsuperscript{13}. 1 g of powder was placed in a centrifuge tube and covered with 10 ml of water. The tube was shaken intermittently over a 2 h period and left to stand for 30 min. This was then centrifuged for 10 min at 3000 rpm. The supernatant was decanted and the weight of the powder after water uptake and centrifugation, $x$ was determined.

$$\text{Hydration capacity} = \frac{x}{y} \quad (III)$$

where $x$ is weight of moist powder after centrifugation and $y$ is weight of dry powder. The values of hydration capacity listed were the means of two determinations.

The specific gravity of the powder was determined using the specific gravity bottle method as earlier detailed\textsuperscript{12}. Light liquid paraffin was the liquid of known density used in the determination. Bulk and tapped densities were determined by a modification of the method of Kumer and Kothari\textsuperscript{14}. The powder (25 g) was placed inside the measuring cylinder of a tapped density apparatus and the bulk volume, $V_1$, was recorded and subjected to 100 taps and the tapped volume, $V_2$, was recorded. The bulk and tapped densities were computed as:

$$\text{Bulk density} = \frac{\text{weight of powder}}{V_1} \quad (IV)$$

$$\text{Tapped density} = \frac{\text{weight of powder}}{V_2} \quad (V)$$

The powder porosity was computed from the bulk density and true density (specific gravity) values using the equation below:

$$E = 1 - \frac{D_b}{D_t} \quad (VI)$$

where $E$ is powder porosity, $D_b$ and $D_t$ are bulk and true densities, respectively. The powder (5 g) was slurred in 10 ml ethanol and diluted with water to 50 ml. The pH was determined in an electronic pH meter (3020 pH meter, Jenway, UK) after 15 min. Particle size was microscopically estimated by placing a small quantity of the powder suspended in light liquid paraffin on a slide and covered with a cover slip. The eyepiece graticule was used to
view the powder sample at the highest magnification of the microscope. Each division of the eye-piece graticle was calculated to 0.3 μm using the stage micrometer. The number of divisions for each fragment of the mycelia was noted and after multiplication by 0.3 μm the mean was taken. A camera lucida was used to measure the sizes.

Preparation of paracetamol granules

Table 1 shows the formulations used to determine the disintegrant properties of *P. tuber-regium* powder in tablets. The granules were prepared by the wet granulation method.

Table 1: Formula for paracetamol granules

| Ingredients                 | Quantity          |
|-----------------------------|-------------------|
| Paracetamol                 | 100g              |
| Lactose                     | 8g                |
| Disintegrant*               | 0, 2.5, 5.0, 7.5, 10.0% w/w |
| Binder solution (5% w/v HPMC)| q.s.             |
| Magnesium stearate**        | 1% w/w            |

*The disintegrant, *P. tuber-regium* powder or maize starch BP, was added 1:1 (intra- and extra-granularly).

**The quantity of magnesium stearate added was calculated as a percentage w/w of the granules.

For each batch, paracetamol, lactose and 50% of the required amount of disintegrant (extragranular) were mixed with the granules in the tumbling/rotating mixer for 3 min. The blend was compressed in a single punch tablet press (Köln Niehl, Germany) fitted with 12.5 mm flat faced punches at a constant pressure of 7.0 units. Target weight was 580 mg. Tablets were stored in well labeled glass jars in a humidity chamber containing dry silica gel and characterized after at least 72 h of storage at ambient temperature.

Characterisation of tablets

The weights of 20 tablets were individually determined using an electronic balance (B154 Toledo, Mettler, Switzerland) and the mean weight was calculated. Friability was determined using a Roche friabilator (Erweka Apparatebau GmbH, Germany). Ten tablets per batch were weighed and caused to cascade in the drum of the friabilator which rotated at 25 rpm for 4 min. The tablets were dusted and reweighed. The loss in weight expressed as a percentage of the original weight of the ten tablets was calculated as the friability of the tablets. The crushing strength of each of 10 tablets was determined using a motorized hardness tester (Model 2E/205, Schleuniger, Switzerland). The mean crushing strength was calculated. Disintegration times of six tablets per batch were individually determined in a BP specification apparatus (Mk IV, Manesty Machines, UK) containing purified water at 37 ± 0.5°C. The mean disintegration times were calculated. The dissolution rates of the active drug from the tablets were determined using a BP specification equipment (Caleva ST 7, G.B. Caleva, UK). The dissolution medium was 0.01M HCl at 37 °C. The paddles were caused to rotate at 100 rpm. Samples were withdrawn at specified times and spectrophotometrically analysed for paracetamol at 245 nm. Samples removed for
Table 2: Some physical characteristics of *P. Tuber-regium* powder and maize starch BP

| Characteristics               | Maize starch BP | Pleurotus powder |
|------------------------------|-----------------|------------------|
| Angle of repose (°)          | 56.31           | 30.96            |
| True density (g/cm³)         | 1.30            | 1.20             |
| Bulk density (g/cm³)         | 0.56            | 0.50             |
| Tapped density (g/cm³)       | 0.67            | 0.67             |
| Hausner ratio                | 1.20            | 1.27             |
| pH                           | 5.73            | 6.46             |
| Swelling capacity            | 1.33            | 3.42             |
| Water retention capacity     | 1.49            | 3.32             |
| Porosity                     | 0.57            | 0.56             |

Results and Discussion

The physico-chemical characteristics of *P. Tuber-regium* powder and maize starch BP are listed in Table 2. The angle of repose of a powder provides an insight into the magnitude of the cohesiveness of the powder, and hence its flowability. Mildly cohesive powders have angles of repose between 40 and 60° when measured by any of the standard methods as was done in this study. This has been discussed extensively by Neumann. While maize starch BP has an angle of repose of 56.3°, *Pleurotus* powder has an angle of repose of 31°. It could be inferred that *P. Tuber-regium* powder being less cohesive has superior flow property.

The Hausner ratio (i.e., the ratio of tapped density to bulk density) previews the degree of densification which could occur during tabletting. The higher the ratio, the greater the propensity of the powder to densify. This phenomenon may cause tablets which lack uniformity of weight and content to be produced. *Pleurotus* powder densified more than maize starch BP; this could also be an indication of its superior flowability. Both powders shared similar values for bulk, tapped and true densities.

The pH of the maize starch BP (5.73) is slightly acid while that of *P. tuber-regium* powder (6.46) is in the neutral range. This implies that if *P. tuber-regium* powder is dispersed in a liquid medium, an alkaline or acidic medium will not result, since this may encourage product instability via effects on the gastro-intestinal tract absorption of the active drug.

The common feature of all theories of disintegration is that penetration of water (or liquid medium) into the tablet must precede disintegration. The swelling capacity and water retention capacity of the *Pleurotus* powder were over two times those of maize starch BP, respectively. These results may suggest that *Pleurotus* powder may be a superior disintegrant to maize starch BP. The particles of *Pleurotus* powder are larger (mean 3.8 μm, range 1.6 to 5.7 μm) than those of maize starch BP (mean 1.4 μm, range 0.6 to 3.5 μm). This implies that a powder bed of *P. Tuber-regium* may have a higher porosity than a bed of maize starch BP.

All the tablets passed the BP uniformity of weight test. The weights of the tablets ranged from 563 – 581 mg. The highest value of standard deviation recorded was 28.3 mg, giving a relative standard deviation of 5.02%.

Figures 1 and 2 show how the disintegrants and their concentrations affect the friability and crushing strength of the paracetamol tablets. For tablets containing maize starch BP disintegrant, both values of friability and crushing strength did not vary significantly.

The internally added starch may have
Figure 1: The effect of disintegrant type and concentration on the friability of paracetamol tablets prepared with maize starch BP (●) and Pleurotus powder ( ).

Figure 2: The effect of disintegrant type and concentration on the hardness of paracetamol tablets prepared with maize starch BP (●) and Pleurotus powder ( ).

Figure 3: The effect of disintegrant type and concentration on the disintegration time of paracetamol tablets prepared with maize starch BP (●) and Pleurotus powder ( ).

Figure 4 illustrates the profiles of paracetamol dissolution from tablets containing Pleurotus powder and maize starch BP (at similar concentrations of 5 and 10%). All the batches of tablets passed the BP dissolution test for increased.

The effect of disintegrant type and concentration on the disintegration time of the tablets is illustrated in Figure 3. At every disintegrant concentration below 10% w/w, tablets containing Pleurotus powder disintegrated faster than tablets containing maize starch BP. This result confirms the results of swelling capacity and water retention capacity (Table 2) which showed that Pleurotus powder absorbed more water and swelled to a greater extent than maize starch BP. Considering the mechanisms of disintegrant action and the results of this investigation, it is proposed that the mechanism of action of Pleurotus powder as a disintegrant may be by wicking, swelling and development of disruptive hydrostatic forces in the compact.

Contributed to the increasing the crushing strength of the tablets since wetting the starch may have turned a fraction of it into mucilage which acted as a binder. For those tablets containing Pleurotus powder their crushing strength decreased as the concentration of disintegrant increased; and the friability marginally decreased as the crushing strength...
Figure 4: Dissolution rate of paracetamol from tablets as a function of disintegrant type and concentration prepared with maize starch BP (●) and Pleurotus powder (○). Solid line represents 5% concentration while broken line represents 10% concentration.

tables which specifies that at least 70% of the drug should be in solution after 30 min. There was no significant difference between the dissolution rates of paracetamol from the tablets containing 10% of the disintegrants. However, some difference became obvious when the tablets containing 5% disintegrants were subjected to dissolution testing. At this concentration Pleurotus powder was a superior dissolution aid to maize starch BP. This result perhaps derives from the faster disintegration of paracetamol tablets containing 5% Pleurotus powder as disintegrant than the tablets containing the same concentration of maize starch BP. Although disintegration precedes dissolution of drug from a tablet, rapid disintegration may not necessarily imply rapid dissolution. Rubinstein and Wells \(^\text{24}\) demonstrated that the particle size, and therefore the surface area into which a tablet disintegrates determines the dissolution rate of the active drug from the compact. The size of the particles which the tablets of this investigation deaggregated into was not estimated.

Conclusion

This study has established some physical characteristics of Pleurotus tuber-regium powder. Its disintegrant ability relative to that of maize starch BP has also been demonstrated in paracetamol tablets. Although the flow characteristics of Pleurotus powder were superior to those of maize starch BP, all the other physical characteristics determined were similar. The physical characteristics of the paracetamol tablets produced via wet granulation with Pleurotus powder and maize starch BP as disintegrants were pharmaceutically acceptable and similar. Pleurotus powder was superior to maize starch BP as a disintegrant, particularly at low concentrations (below 10% w/w). The dissolution rates of paracetamol from tablets containing 10% of both disintegrants were similar. However, at a lower disintegrant concentration of 5%, dissolution was faster from tablets containing Pleurotus powder. In order to comprehensively distinguish between disintegrants and dissolution aids, it may be necessary to study the physical characteristics of the tablets at both high and low concentrations of the materials in the tablets.

Pleurotus powder may be a good substitute for maize starch BP as a compressed tablet disintegrant. The authors propose wicking, swelling and development of disruptive hydrostatic forces in a compact as the mechanism of action of P. tuber-regium powder as a compressed tablet disintegrant.
Acknowledgement

The authors acknowledge Ufelle, U.A. and Ibeagwa, N.M, for technical assistance. M.A.I. is grateful to the University of Benin for research grant (No. URPC 1/99/68)

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