

## Original Research Article

# Studies on a Hydrophilic Cellulose Matrix derived from *Ipomoea batatas* Tubers III: Application as a Disintegrant in Paracetamol Tablet Formulation

### ABSTRACT

**Aims:** A new hydrophilic cellulose matrix (*I-hydrocel*) was evaluated as a tablet disintegrant in paracetamol tablet formulation in comparison with maize starch (MS).

**Methods:** Applying *I-hydrocel* (IH) as a disintegrant at 5, 10 and 15 % w/w, granules containing paracetamol (80.65 % w/w), gelatin (3.5 % w/w) and lactose was prepared by the wet granulation method. Similar batches of granules were prepared with maize starch (MS). The micromeritic properties of the granules were evaluated. They were lubricated with 0.5 % w/w magnesium stearate and compressed at 4.50 kgF using a single punch tablet press fitted with a 12.50 mm punch. The tablet properties were studied using the British Pharmacopoeia methods.

**Results:** The granules were flowable and compressible. The uniformity of weight of the tablets was within acceptable range. The tablets prepared with either IH or MS disintegrated in less than 15 min with those containing MS disintegrating in lesser time ( $P = 0.000$ ). Though, the friability of the tablets from either IH or MS was generally less than 1%, there was no significant difference for the friability between the tablets containing 5 % w/w IH and 5 % w/w MS, 15 % w/w IH and 10 % w/w MS, 15 % IH and 15 % w/w MS ( $P = 0.000$ ). The tablets prepared with MS presented with higher mechanical strength than those containing IH at all the concentrations studied ( $P = 0.000$ ). All the batches of tablets released over 50 % of paracetamol in less than 10 min and above 80 % in less than 30 min.

**Conclusion:** *I-hydrocel* compared favourably with maize starch as a tablet disintegrant, yielded tablets with good mechanical strength and also aided the maximal release of paracetamol and could be a

veritable substitute for maize starch as a disintegrant in paracetamol tablet preparation.

*Keywords: Hydrophilic Cellulose Matrix, Ipomoea batatas, disintegrant, paracetamol*

## 1. INTRODUCTION

The pharmaceutical industry sector has witnessed the development of several drug delivery systems, especially those targeting specific therapeutic sites. This notwithstanding, tablets, one of the oral solid dosage forms which up till now have been in existence since the 19th century, continue to be the most recurrent dosage form of choice for many. This continued acceptance includes the fact that the oral route of delivery is possibly the minimally disturbing approach of delivering medicinal products. The oral method of drug use being the utmost key means of drug application to achieve physiological impact in the human body, patients can afford to administer the medicine themselves. The tablet provides safe and suitable means of active pharmaceutical ingredients (API) usage with exceptional physiochemical strength in contrast to some other dosage forms, and deliver precise dosing. Tablets and other solid dosage forms are easy to be produced, making use of affordable technology. They are stable forms of medicinal preparations that are compact and easily moved around [1]. Several methods used in the preparation of tablets are direct compression, wet granulation, mass extrusion methods, etc. [2]. The tablet could be formulated in the immediate or sustained release form. Most conventional or immediate release oral drug products, such as tablets and capsules, are formulated to discharge the API instantly when taken orally. There is no modification of drug release rate when an immediate release or conventional medicinal products are designed. The understanding of the instant-release pharmaceutical products is that their use results in moderately swift drug absorption and the onset of action [3]. Immediate release solid oral dosage forms are categorized as either having rapid or slow dissolution rates and include those dosage forms for which  $\geq 85$  % of the considered amount of API dissolves within 30 min. The major hindrance to drug release is simply the disintegration.

The capability of the API in a medicinal product to be absorbed by the body hinge on its bioavailability which, in turn, depends on the solubility of the API in the gastrointestinal fluids as the drug passes through the intestines. All these will be achieved if the tablet disintegrates. Disintegration opposes the binding forces which hold the particles that made up the tablets when it is compressed [4]. To improve dissolution and hence bioavailability of any medicinal product from immediate-release tablets, disintegration is one of the significant process [5, 6]. The excipients known as disintegrants are therefore added to a tablet or capsule blend to help in the break-up of the compacted mass or tablet when it is in contact with a liquid. Disintegrants are employed in immediate release tablets to increase dissolution and hence bioavailability of any drug [7-10].

Tablet disintegration may occur by swelling, porosity/capillary (wicking), deformation, etc. The disintegrants that yield their action through swelling when in contact with water overcome the adhesiveness of other ingredients in the tablet, causing the compacted mass to crumble. However, those that do not swell are thought have the mechanism of working through porosity and capillary action. Tablet porosity delivers channels for the saturation of fluid into tablets. For that to occur, a liquid is drawn up or “wicked” into these paths through capillary action and break the inter-particulate ties causing the tablet to break apart. Considering disintegrant action by deformation, starch grains are largely thought to be “elastic” in nature. This means that grains that are distorted under pressure will regain their initial shape when that pressure is no more there. But, with the compression forces involved in tableting, these grains are believed to be deformed more permanently and are said to be “energy-rich” with this energy being released upon exposure to water. In other words, the ability for the starch to swell is higher in the “energy-rich” starch grains than it is for starch grains that have not been deformed under pressure. It is believed that no single mechanism of disintegration is responsible for the action of most disintegrants. But rather, it is more likely the result of inter-relationships between these major mechanisms.

Starch has been in use as a disintegrant. Maize starch or potato starch was known to cause tablet disintegration and is still in use in the concentration 5-10 % [11]. In addition to starch, other disintegrants include pregelatinised starch (Starch 1500, with effective use concentration between 5-10 % w/w), microcrystalline cellulose (Avicel<sup>(R)</sup>, the concentration of use, 10-20 % w/w), etc. Due to the increase in

the demand for faster dissolution, a set of new disintegrants designated as superdisintegrants are now available. They swell to a great extent when in contact with water. They include the modified starches such as sodium starch glycolate (Explotab, Primogel, effective at 4-6 % w/w, functioning by rapid and extensive swelling with minimal gelling), the cross-linked polyvinylpyrrolidone, a water-insoluble and strongly hydrophilic substance functioning by water wicking, swelling and possibly some deformation recovery with effective concentration of 2-4 % w/w) and the modified cellulose internally cross-linked form of sodium carboxymethylcellulose (Ac-Di-Sol<sup>®</sup>), functions by wicking due to fibrous structure and swelling with minimal gelling. It has effective concentration of 1-3 % w/w (direct compression), 2-4 % w/w (wet granulation) [11].

In this work, a new hydrophilic cellulose matrix (*I-hydrocel*) derived from the tuber of *Ipomoea batatas* is investigated as a tablet disintegrant using maize starch BP for comparison. The processing and physicochemical properties of *I-hydrocel* have been documented [12].

## 2. MATERIAL AND METHODS

### 2.1 Materials

The following materials were used as procured and includes magnesium stearate (BDH, England), lactose (SureChem, UK), ethanol (96%), hydrochloric acid (HCl) (JHD, China), gelatin, maize starch (BDH, England), sodium hypochlorite, 3.5 % w/v (Multipro, Nigeria), n-hexane (JHD, China), paracetamol (Cipla, India). *I-hydrocel* was processed in the Department of Pharmaceutics and Pharmaceutical Technology laboratory, Faculty of Pharmaceutical of Sciences, University of Port Harcourt, Port Harcourt, Nigeria.

### 2.2 Methods

#### 2.2.1 Preparation of a novel hydrophilic cellulose matrix (*I-hydrocel*)

This was prepared using the procedure documented by Ugoeze, *et al* (2017) [12].

#### 2.2.2 Preparation of granules containing paracetamol

Using the wet granulation method, three batches of granules containing *I-hydrocel* (IH) as a disintegrant in concentrations of 5, 10 and 15 % w/w respectively, added intragranularly were prepared. Each batch also contains, paracetamol (80.65 % w/w) and gelatin (3.5 % w/w) (as a binder), magnesium stearate (0.5 % w/w as a lubricant) and lactose as a filler. Similar batches of granules were prepared with maize starch (MS) for comparison. A blend of paracetamol, lactose and *I-hydrocel* was wet massed in an aqueous slurry of gelatin. Wet and dry screening stages were carried out with a stainless steel sieves 10 (1.70 mm) and 16 (1.00 mm) (Retch, Germany). Each drying procedure was carried out in an oven (Memmert, England) at 60 °C. The granules were stored for further studies.

## 2.2.3 Granule properties

### 2.2.3.1 Bulk, tapped and particle densities

A 20.0 g quantity of the granules was employed in the determination of bulk and tapped densities using Stampfvolumeter (STAV 2003JEF, Germany) [13, 14]. The particle density was determined by displacement method using a 25 ml pycnometer and n-hexane as a non-solvent [15]. The bulk, tapped and particle densities of the respective samples were calculated from equations 1, 2 and 3 below respectively after three replicate determinations:

$$\text{Bulk density} = \text{Weight of Powder} / \text{Bulk volume} \dots\dots\dots (1)$$

$$\text{Tapped Density} = \text{Weight of Powder} / \text{Tapped volume} \dots\dots\dots (2)$$

$$\text{Particle Density, } \rho_t = w_2 \times w_3 / (w_3 - w_4 + w_2 + w) \dots\dots\dots (3)$$

Where:  $v$  is the volume of pycnometer, 25 ml,  $W$  = weight of empty pycnometer,

$W_1$  = weight of pycnometer and n- hexane,  $W_2$ = the difference between the  $W$  and  $W_1$

$W_3$ = weight of *granules*,  $W_4$ = weight of *granules* + n- hexane + pycnometer.

### 2.2.3.2 Determination of flow properties

The flow rate of the granules was determined using the funnel method [16]. The angle of repose was determined using the modified method reported Jones and Pilpel [17]. The angle of repose,  $\theta$  was calculated after three replicate determinations from equation 4 below:

$$\theta = \tan^{-1} \frac{2h}{d} \dots\dots\dots (4)$$

Where h = the height of the heap, d = base diameter of the heap.

Hausner's ratio (HR) [18] of the granules was obtained as:

$$HR = \text{Tapped density} / \text{Bulk density} \dots\dots\dots (5)$$

Compressibility Index (CI) [19] of the granules was calculated from equation 6 below:

$$\text{Carr's index} = (\text{Tapped density} - \text{Bulk density}) \div \text{Tapped density} \times 100 \dots\dots (6)$$

Porosity ( $\rho$ ) of the granules was determined from the expression in equation 7:

$$\rho = \left( 1 - \frac{\text{Bulk density}}{\text{True density}} \right) \times 100 \dots\dots\dots (7).$$

## 2.2.4 Compression of tablets

The respective batches of the granules were lubricated with 0.5 % w/w of magnesium stearate and compressed at a pressure of about 4.0 - 4.5 kgF using a single punch tableting machine (Cadmach single punch automatic tablet machine, model SSF3, India) fitted with a punch of diameter, 12.5mm and a rounded lower punch curvature.

## 2.2.5 Evaluation of tablet properties

The evaluation of the tablet properties was carried out using the methods outlined in the British Pharmacopeia (BP, 2012) [20]. Tablets were examined for colour, odour, shape, taste and texture. The uniformity of tablet weight was studied with 20 tablets (Mettler, Germany) while 10 tablets were used to evaluate for tablet hardness and thickness respectively using a diametrical digital tablet hardness tester

(Veego, India). The friability of 10 tablets from each batch was determined in tablet friabilator (Erweka TAR 220, Germany).

The tensile strength [21] of the tablets were calculated from equation 8 below:

$$T = \frac{2P}{\pi dt} \dots\dots\dots (8)$$

Where  $T$  = radial tensile strength,  $t$  = tablet thickness,  $d$  = tablet diameter.

A total of 6 tablets per batch was utilized to study the disintegration time using a tablet disintegration apparatus (Erweka, ZT 122, Germany) in 900 ml of 0.1 N HCl maintained at  $37 \pm 1^\circ \text{C}$ . Dissolution rate studies were carried out in a dissolution apparatus (Erweka DT600, Germany). The rotating paddle method of the United States Pharmacopeia (USP, 2007) [13] was used in 900 ml of 0.1 N HCl at  $37 \pm 1^\circ \text{C}$  at a paddle speed of 50 rpm [13]. A 5 ml of dissolution sample was withdrawn at predetermined intervals of 10, 20, 30, 40, 50, 60 min and replaced with the same volume of 0.1 N hydrochloric acid at the same temperature. The absorbance of the each sample solution was determined in an ultraviolet (UV) spectrophotometer (Jenway, model 6405, England) at a wavelength of 245 nm. The  $T_{50}$  and  $T_{80}$  of each batch of tablets were determined.

## Statistical analysis

All the statistical analysis was performed using IBM SPSS Statistics 20 software.

## 3. RESULTS AND DISCUSSION

### 3.1 Granule properties

The granule properties are shown in Table 1. The results of the densities and flow properties showed that the granules are flowable and compressible.

162 Table 1: Granule properties

| Ingredient             | <i>I-hydrocel</i> (IH) |            |            | Maize starch (MS) |            |                   |
|------------------------|------------------------|------------|------------|-------------------|------------|-------------------|
|                        | Batch                  |            |            | Batch             |            |                   |
|                        | 5%w/w                  | 10%w/w     | 15%w/w     | 5%w/w             | 10%w/w     | 15%w/w            |
| Flow rate (g/s)        | 7.59±0.66              | 9.69±0.45  | 10.88±0.61 | 10.15±0.88        | 9.45±0.66  | <b>9.85±0.72</b>  |
| Angle of repose (deg.) | 35.17±0.18             | 36.87±0.10 | 34.94±0.19 | 33.94±1.54        | 34.43±0.25 | <b>34.66±0.11</b> |
| Bulk density (g/ml)    | 0.36±0.02              | 0.37±0.01  | 0.38±0.03  | 0.36±0.01         | 0.37±0.01  | <b>0.39±0.01</b>  |
| Tapped density(g/ml)   | 0.38±0.01              | 0.42±0.01  | 0.44±0.02  | 0.43±0.01         | 0.44±0.01  | <b>0.45±0.01</b>  |
| True density (g/ml)    | 1.02±0.18              | 1.06±0.22  | 1.19±0.02  | 1.00±0.28         | 1.06±0.10  | <b>1.16±0.13</b>  |
| Porosity (%)           | 64.71±0.01             | 65.09±0.01 | 68.07±0.02 | 64.00±0.02        | 65.09±0.01 | <b>66.64±0.02</b> |
| Hausner's ratio        | 1.06±0.02              | 1.14±0.01  | 1.16±0.01  | 1.18±0.02         | 1.19±0.02  | <b>1.15±0.02</b>  |
| Carr's index (%)       | 5.26±0.68              | 11.91±0.72 | 13.64±2.44 | 16.27±1.39        | 15.91±1.38 | <b>13.33±1.48</b> |

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### 164 3.2 Tablet properties

165 The tablet properties are presented in Table 2. The uniformity of weight of the respective batches of the  
 166 tablets was within acceptable range. The British Pharmacopeia [20] allows a limit of 5 % maximum  
 167 variation in tablet weight for tablets weighing more than 324 mg. In all the tablet batches studied, the  
 168 variation in weight falls within the range, 0.39-2.79%.

169 The respective batches of tablets prepared with either IH or MS disintegrated in less than 15 min. The BP  
 170 (2012) specifies a maximum disintegration time of 15 min for conventional or immediate release tablets.  
 171 However, for each corresponding concentration of disintegrants, the tablets prepared with MS  
 172 disintegrated in lesser time than those containing IH (P = 0.000).

The tablets prepared with either IH or MS showed good values for friability. Tablet friability less than 1 % is acceptable for uncoated tablets for immediate release [22]. Though, tablet friability was generally below unity across the disintegrants, statistically, there was no significant difference for the friability between the tablets containing 5 % w/w IH and 5 % w/w MS, 15 % w/w IH and 10 % w/w MS, 15 % IH and 15 % w/w MS (P= 0.000).

Considering the tablet hardness, tensile strength or hardness friability ratio (HFR), the tablets prepared with MS presented with higher mechanical strength than those containing IH at all the concentrations studied (P = 0.000).

Table 2: Tablet properties

| Ingredient                  | <i>l-hydrocel</i> |          |          | Maize starch |          |               |
|-----------------------------|-------------------|----------|----------|--------------|----------|---------------|
|                             | Batch             |          |          | Batch        |          |               |
|                             | 5 % w/w           | 10 % w/w | 15 % w/w | 5 % w/w      | 10 % w/w | 15 % w/w      |
| <b>Weight (mg)</b>          | 627.95            | 635.25   | 622.42   | 637.32       | 631.54   | <b>633.14</b> |
|                             | ±1.48             | ±2.75    | ±1.53    | ±6.15        | ±1.60    | <b>±1.50</b>  |
| <b>Disintegration (min)</b> | 9.92              | 4.92     | 3.41     | 7.64         | 4.60     | <b>3.22</b>   |
|                             | ±0.07             | ±0.07    | ±0.44    | ±0.59        | ±0.40    | <b>±0.24</b>  |
| <b>Friability (%)</b>       | 0.93              | 0.80     | 0.70     | 0.92         | 0.70     | <b>0.79</b>   |
|                             | ±0.04             | ±0.03    | ±0.02    | ±0.03        | ±0.02    | <b>±0.10</b>  |
| <b>Hardness (kgF)</b>       | 3.31              | 7.17     | 8.45     | 5.27         | 6.61     | <b>10.64</b>  |
|                             | ±0.19             | ±0.08    | ±0.26    | ±0.23        | ±0.09    | <b>±0.28</b>  |
| <b>Thickness (mm)</b>       | 4.61              | 3.83     | 4.11     | 4.99         | 5.01     | <b>4.47</b>   |
|                             | ±0.03             | ±0.06    | ±0.10    | ±0.11        | ±0.39    | <b>±0.12</b>  |
| <b>HFR</b>                  | 3.67              | 9.43     | 12.74    | 5.77         | 9.57     | <b>16.07</b>  |
|                             | ±0.12             | ±0.15    | ±0.14    | ±0.13        | ±0.14    | <b>±0.18</b>  |
| <b>Tensile Strength</b>     | 37.22             | 95.69    | 106.68   | 56.36        | 67.43    | <b>123.48</b> |
|                             | ±0.15             | ±0.21    | ±0.67    | ±1.75        | ±0.14    | <b>±0.17</b>  |

(N/m<sup>2</sup>)

Figure 1 represents the dissolution profile for the different batches of tablets containing either IH or MS. Though the USP (2007) [13] specifies that not less than 80% of the labelled amount of paracetamol is expected to dissolve in 30 min *in vitro*, each of the batch of tablets prepared with either IH or MS at every concentration released above 80 % of its paracetamol content before 30 min ( $T_{80} < 30$  min) and  $T_{50}$  was generally less than 10 min.

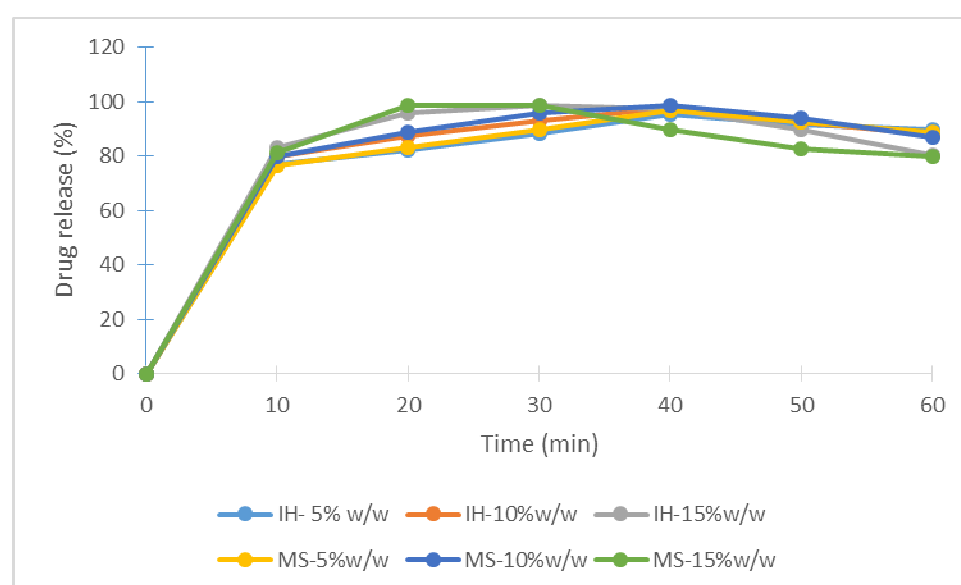


Figure 1: Dissolution profile for tablets prepared with various concentrations of I-hydrocel or maize starch BP

#### 4. CONCLUSION

The study evaluated the suitability of *I-hydrocel*, a new hydrophilic cellulose matrix derived from the tubers of *Ipomoea batatas* as a tablet disintegrant in comparison with the long existing tablet disintegrant, maize starch. The general results of the tablet properties indicated that *I-hydrocel* compared favourably with maize starch and could serve as a veritable substitute to maize starch.

## CONSENT

It is not applicable

## ETHICAL APPROVAL

It is not applicable

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