Comparative Evaluation of Detarium Microcarpium Seed Gum as a Potential Polymer for Film Coating of Normal Release Tablets

Momoh MA1, Onunkwo GC2, Chime SA2 and Akpabio EI2

1Department of Pharmaceutics and Pharmaceutical Technology, University of Uyo, Nigeria
2Department of Pharmaceutical Technology and Industrial Pharmacy, University of Nigeria, Nsukka 410001, Nigeria

The aim of the study was to formulate a normal release sodium salicylate coated tablet using a natural hydrophilic polymer and to evaluate the in vitro properties of the tablets. Gum from the seed of Detarium microcarpium was evaluated as coating film for the formulation of sodium salicylate coated tablet and was compared with sodium carboxymethylcellulose (SCMC) and gelatin as standards. The tablet core of sodium salicylate was formulated using acacia as the binder. The granules prepared were characterised in terms of flow rate, angle of repose, bulk and tapped densities, Carr’s index and Hausner’s ratio. Tablets were coated with 1, 2 and 4 % w/v of polymer film of both the test and the standard polymers. The coated tablets were evaluated using the necessary official and unofficial tests for coated tablets. Results showed that both Detarium microcarpium seed gum (DMSG), SCMC and gelatin had good film coating properties. However, batches H1 – H3 coated with different concentrations of SCMC (F1 – F3) exhibited significantly higher hardness values (p < 0.05), while DMSG showed hardness values comparable to tablets coated with gelatin (G1 – G3). Therefore, DMSG showed better in vitro release properties as a coating film for sodium salicylate tablet than the gelatin. Tablets coated with 4 % of polymer film exhibited better in vitro properties significantly different (p < 0.05) from other batches containing 1 % and 2 % of the polymer film. The performance of the tablets coated with 4 % polymer film could be ranked thus: H3 > F3 > G3.

Key words: Film Coating, Detarium microcarpium, Polymer, Gelatin

INTRODUCTION

The use of natural gums for coating of both normal and sustained release tablet preparation has been studied (Spear et al., 2001; Chukwu et al., 1997; Cunningham et al., 2001). This is because of their cost effectiveness and availability. Natural gums have been used in producing tablets with different mechanical strength and drug release properties for different pharmaceutical purposes (Emeje et al., 2008). These gums are generally non-toxic and widely available, hence the continued interest (Odeku, 2003). Selection of the required polymer matrix materials often goes along with detrimental effects on incorporated drug during manufacturing of formulations or during the erosion of the polymers after application (Reithmeir et al., 2001). The widening availability of natural gums with specific characteristics offers flexibility of application with respect to improving the bioavailability of drugs and manipulating their release profile. Detarium microcarpium (Guill and Sperr) seed gum has been evaluated as basis for drug delivery (Chukwu et al., 1997; Okorie, 2011; Adikwu and Alozie, 2007; Onunkwo, 2003). Gums from plants are mainly long chain, straight or branched chain polysaccharides that contain hydroxyl groups which bond to water molecules (Ibezin et al., 2008). Investigations show that D. microcarpium (Family Caesalpinaceae) is the most common member of its three known species and grows best in the Savannah forest of the drier type (Okorie et al., 2011; Dalziel, 1955). Nutritionally, the seed which is used as a traditional soup thickener contain lipids, carbohydrates, proteins, crude fibre and the essential elements: Na, K, Mg, Ca, S, P and Fe (Abreu and Relva, 2002; Abreu et al., 1998). Saponins, phytates and cyanides are reportedly present as anti-nutrients (Ebi and Afieroho, 2011; Anhwange et al., 2004).

Preparation of tablets containing non-steroidal anti-inflammatory drugs (NSAIDs) present challenges because of their potentials to cause severe gastric irritation. NSAIDs induce injury/bleeding via three key pathways: inhibition of cyclooxygenase (COX)-1 activity, inhibition of COX-2 activity, and direct cytotoxic effects on the epithelium. Effects produced via only one of these pathways (e.g., selective inhibition of COX-1 or of COX-2) are unlikely to produce significant damage (Wallace, 2008). NSAIDs can also diminish the ability of epithelial growth factors (EGF) to promote epithelial repair. The mechanisms through which NSAIDs produce damage in the stomach can be subdivided into local (topical) actions and systemic actions (Wallace, 2008). The topical actions of NSAIDs on the gastric epithelium may involve several mechanisms. Some NSAIDs, particularly those of acidic nature, can directly kill epithelial cells. Various mechanisms have been proposed for this cytotoxic action, including the induction of osmotic lysis subsequent to trapping of charged NSAIDs with the epithelial cells, and death of the epithelial cell subsequent to uncoupling of oxidative phosphorylation. NSAIDs can also reduce mucus and bicarbonate secretion, thereby decreasing the effectiveness of the juxtamucosal pH gradient in protecting the epithelium. NSAIDs can disrupt the layer of surface-active phospholipids on the mucosal surface, independent of effects on prostaglandin synthesis.

Such an action would render the mucosa less able to resist damage induced by luminal acid (Wallace, 2008). There are several techniques for coating of tablets. Sugar coating was one of the earliest methods, and the process is still widely used in the confectionery industry. Wurster coating is another means. It employs a cylindrical chamber in which tablets are suspended by air and a coating solution is introduced into the air stream. Fluid-bed coating is a similar process. Dry coating is the technique of making a tablet within a tablet. But the principle means of applying a coating to pharmaceutical and nutraceutical tablets is called film coating (Tousey, 2011).
This study was carried out to evaluate the in vitro properties of sodium salicylate tablets coated with *Detarium microcarpium* seed gum.

**MATERIALS AND METHODS**

Sodium salicylate (Sigma–Aldrich, Germany), hydrochloric acid, lactose (Merck, Germany), maize starch, acetone, gelatin, acacia (BDH, England), SCMC and Magnesium stearate (May & Baker, England), distilled water (Lion water, Nsukka, Nigeria). *Detarium microcarpium* seed gum was obtained from a batch processed in our laboratory. All other reagents and solvents were analytical grade and were used as supplied.

**Extraction of gum:**

Ripe *Detarium microcarpium* seeds sourced locally were properly identified and authenticated at the University of Nigeria, Nsukka herbarium. The seeds were sorted, cured by oven drying at 50°C for 24 hours, soaked for 12 h, peeled and milled into small particles. The milled particles were soaked in 0.1 % sodium metabisulphite solution for 12 h and sieved with muslin cloth. The gum was precipitated with acetone and left under room temperature for 3 h. The precipitate was collected on a Buchner funnel by means of pressure from a vacuum pump. It was placed in a vacuum desiccator for 4 days until dried. The dried material was then milled into smaller particles and was sieved with 250 µm sieve and the fine particles were collected into a clean, amber-coloured bottle and stored in a cool condition until used. This procedure is in accordance with an earlier reported one (Adikwu and Alozie, 2007; Okorie et al., 2011; Chukwu, 1992; Ozumba and Bandgudu, 1992).

**Table 1: Formulation composition of sodium salicylate tablets core**

<table>
<thead>
<tr>
<th>Ingredients</th>
<th>Quantity/tablet (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium salicylate</td>
<td>25.0</td>
</tr>
<tr>
<td>Acacia (2 %w/w)</td>
<td>6.0</td>
</tr>
<tr>
<td>Maize starch</td>
<td>15.0</td>
</tr>
<tr>
<td>Magnesium stearate</td>
<td>3.0</td>
</tr>
<tr>
<td>Lactose qs</td>
<td>300.0</td>
</tr>
</tbody>
</table>

**Preparation of granules:**

Granules were prepared by using wet granulation method by using different binder systems. Details of granulation are discussed elsewhere (Lachman et al., 1990; Shendge et al., 2010).

**Preparation of tablets:**

Initially granules were treated with lubricant i.e. magnesium stearate. Tablets were prepared by compressing the lubricated granules at 46-48 kgf using a 9.0mm punch and die set fitted into an automated F3 Manesty Single Punch tabletting machine (Okorie et al., 2011).

**Bulk and Tapped Densities:**

A 30g of sample was weighed out and placed in a 100 ml measuring cylinder. The cylinder was tilted before the sample was poured inside; the volume occupied by the sample was noted as the bulk volume. The bulk density was obtained by dividing the mass of the sample weighed out by the bulk volume,as shown in Equation 1(Aulton, 1999).

Bulk density = \frac{\text{Mass of Powder (M)}}{\text{Bulk volume of powder (V_b)}} \quad (1)

The cylinder was tapped on a wooden platform by dropping the cylinder from a height of one inch at 2 seconds interval until there was no change in volume reduction. The volume occupied by the sample was then recorded as the tapped volume. The tapped density was calculated using the formula:

Tapped density = \frac{\text{Mass of sample(M)}}{\text{Tapped volume(V_t)}} \quad (2)

**Flow rate and angle of repose:**

A funnel was properly clamped on to retort stand. The funnel orifice diameter, base diameter and efflux tube length were appropriately measured. A 30 g quantity of the sample was weighed out and gradually placed into the funnel with the funnel orifice closed with a shutter. The time taken for the entire sample in the funnel to flow through the orifice was noted. The flow rate was gotten by dividing the mass of the sample by the time of flow in seconds.

The static angle of repose was determined using the fixed base cone method (Aulton, 1999). A 30 g of the sample was transferred into an open-ended cylinder placed on a static base cone on a horizontal surface. The cylinder was gradually withdrawn vertically and the sample formed a cone-shaped heap. The height of the sample was determined using a cathetometer; the radius was gotten by dividing the fixed diameter by two. Angle of repose (θ) for each sample was gotten using the equation;

θ = \tan^{-1} \frac{h}{r} \quad (3)

**Compressibility index and Hausner’s quotient**

Carr’s compressibility indices (%) of the lyophilized SLMs were obtained using the formula (Aulton, 1999).

\[
\text{Carr’s Index} = \frac{\text{Tapped density} - \text{Bulk density}}{\text{Bulk density}} \times 100 \quad (4)
\]

While Hausner ratio was obtained using Equation 5

\[
\text{Hausner’s ratio} = \frac{Tapped \, density}{Bulk \, density} \quad (5)
\]

**Coating of compressed tablets:**

*Detarium microcarpium* seed gum (DMSG) were used as the test film coating material, while gelatin and sodium carboxy methyl cellulose (SCMC) respectively were used as the standards at concentrations of 1 %, 2 % and 4 %w/v. In each case, appropriate quantities of the material was dissolved in water and stirred until homogeneous dispersion was formed. The tablets were coated by dip method, drying was done after each coating using hot air. The coated tablets were allowed to dry at room temperature and thereafter, stored properly.

**Statistical analysis:**

Statistical analysis was carried out using SPSS version 14.0 (SPSS Inc. Chicago, IL, USA). All values are expressed as mean ± SD. Data were analysed by one-way ANOVA. Differences between means were assessed by a two-tailed student’s T-test. P < 0.05 was considered statistically significant.
RESULTS AND DISCUSSIONS

EVALUATION OF TABLETS

Disintegration time test:
Disintegration time test was conducted using an Erweka ZT 120 basket and rack assembly. A sodium hydrochloric acid maintained at 37.0 ± 1.0 °C as the disintegration medium. A minimum of ten tablets from each batch was used for the test and the procedure being as stipulated in the BP, 2001 for coated tablets.

Uniformity of Weight:
Twenty tablets were randomly selected from each batch. The tablets were weighed individually using an electronic balance (Ohaus Adventurer, China) and the individual weights recorded. The mean weight, standard deviation and percentage deviation were calculated (BP, 2001).

Tablet friability test:
Twenty tablets were randomly selected from each batch of the tablet. The tablets were dedusted and weighed. The tablets were placed into the drum of the friabulator (Erweka GmbH, Germany) and rotated at 25 rpm for 4 min. The tablets were removed from the friabulator, dedusted and reweighed. The friability result was expressed as loss of mass expressed as a percentage of the initial mass (BP, 2001). The abrasion resistance B was calculated from the equation below:

\[
B = 100 \left[ 1 - \frac{W}{W_0} \right] \quad \text{(6)}
\]

Where \(W_0\) and \(W\) are the initial weight and final weight of the tablets respectively. (Ofoefule, 2002).

Hardness/Crushing Strength Test:
This test was carried out using a Monsanto-stokes hardness tester. Ten tablets from each batch were randomly selected. Each tablet was placed between the jaws of the hardness tester and force was applied by adjusting the knob of tester until the tablet integrity failed. The results were recorded in KgF.

In vitro release studies:
Beer’s calibration curve was obtained at a concentration range of 0.8 – 12.8 mg % for sodium salicylate in 0.1 N HCl at a predetermined wavelength of 540 nm. The in-vitro dissolution profile for each batch of tablet was determined using the paddle method (BP, 2001) with an Erweka DT 600 Dissolution apparatus. The dissolution medium consisted of 900 ml of freshly prepared 0.1 N HCl. The temperature of the medium was maintained at 37 ± 1 °C. A tablet from each batch was placed inside a tightly secured basket and the basket was placed in the bottom of the beaker. The paddle was rotated at 100 rpm. At various intervals, 5 ml-sample was withdrawn from the dissolution medium, filtered with a non adsorbent filter paper. Two drops of ferric chloride was added to an aliquot of the filtrate and assayed using spectrophotometer (Unico-UV 2102 PC) at 540 nm. An equal volume of the withdrawn sample was replaced with a fresh medium to maintain sink condition. The amount of drug released at each time interval was determined with reference to the Beer’s plot for the drug.

RESULTS AND DISCUSSIONS

The flow properties of the granules were determined using both the direct and the indirect methods of assessing flow ability of particles. Powder fluidity is important in tabletting because variation in particle flow will automatically cause variation in tablet weight and active ingredient variation. The results of micromeristic studies are presented in Table 2.

<table>
<thead>
<tr>
<th>Batch</th>
<th>(f_0) (g/ml)*</th>
<th>(f_1) (g/ml)*</th>
<th>AR *°</th>
<th>HR *°</th>
<th>CI *°</th>
<th>Flower rate (g/Sec)</th>
</tr>
</thead>
<tbody>
<tr>
<td>E</td>
<td>0.57 ± 0.001</td>
<td>0.07 ± 0.005</td>
<td>0.32 ± 0.4</td>
<td>1.20</td>
<td>15.0</td>
<td>7.79 ± 0.21</td>
</tr>
</tbody>
</table>

Values shown are mean ± SD (*n = 3); E: sodium salicylate granule prepared with acacia as binder; \(f_0\) and \(f_1\): Bulk and tapped densities, AR = Angle of repose, HR = Hausner’s ratio, CI = Carr’s compressibility index.

From the result presented in Table 2, the samples had bulk density of 0.57 g/ml, showing good flowability of the granules. Angle of repose was used as indirect methods of assessing flowability of powder because of their relationship with inter particle cohesion. The result of angle of repose showed that the samples had good flowability (Aulton, 1999; Onyechi, 2008). Hausner’s ratio less than or equal to 1.25 indicates good flow, while Hausner’s ratio greater than 1.25 indicate poor flow. Therefore, the granules were within the specified limits for good flow. Also, Carr’s indexes between 5-16 indicate good flow (Aulton, 1999). Therefore, sodium salicylate granules exhibited good flowability.

Table 3 shows the results obtained from the evaluation of the tablets coated with Detarium microcarpium seed gum in comparison with the tablets coated with gelatin and SCMC respectively. All the batches of the coated tablets passed the uniformity of weight test and deviations obtained complied with BP standards of not more than 5% for tablets weighing 250 mg or more (BP, 2001; Ofoefule, 2002).

From the result presented in Table 3, all the tablet batches complied with the BP specifications for crushing strength test of ≥ 5 KgF. However, batches H1 – H3 coated with different concentrations of SCMC exhibited significantly higher hardness values (p < 0.05), while the Detarium microcarpium seed gum (DMSG) showed hardness values comparable to the tablets coated with gelatin. Therefore, tablets coated with DMSG exhibited good mechanical properties. The result showed that the mechanical properties of the tablet will not be compromised during long term storage. DMSG coated tablets will effectively withstand the processes of handling, packaging and transportation without breaking.

The tablets coated with DMSG exhibited good friability results comparable to the tablets coated with the two standard coating polymers used in the study. Values of friability (B) up to 0.8 – 1% are quoted as upper level of acceptance (Ofoefule, 2002). From Table 3, all the batches of the coated sodium salicylate tablets formulated complied with BP standards for friability test. The DMSG coated tablets can withstand handling, packaging and transportation without cracking the coat.

The disintegration time of all the tablets increased with increase in the concentration of the film coating polymer. Optimum disintegration time was achieved at 4 % polymer concentration. However, batch F3 tablet coated with 4 % DMSG showed the highest disintegration time of 62.8 min, unlike other batches whose disintegration time was less than

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60 min. This was significantly different from other batches and complied with BP specifications for coated tablets.

**Table 3.** Properties of sodium salicylate coated and uncoated tablets

<table>
<thead>
<tr>
<th>Batch/Tablet code</th>
<th>Weight (mg ± CV)*</th>
<th>Hardness (Kgf)</th>
<th>Friability (%)</th>
<th>Disintegration Time (min)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1 (1% gum)</td>
<td>293.3 ± 1.80</td>
<td>4.90 ± 0.20</td>
<td>0.00</td>
<td>37.0 ± 0.30</td>
</tr>
<tr>
<td>F2 (2% gum)</td>
<td>296.6 ± 1.66</td>
<td>5.11 ± 0.20</td>
<td>0.00</td>
<td>34.4 ± 0.27</td>
</tr>
<tr>
<td>F3 (4% gum)</td>
<td>298.9 ± 0.48</td>
<td>4.96 ± 0.08</td>
<td>0.00</td>
<td>62.8 ± 0.32</td>
</tr>
<tr>
<td>G1 (1% gelatin)</td>
<td>293.5 ± 2.39</td>
<td>4.96 ± 0.08</td>
<td>0.00</td>
<td>36.1 ± 0.36</td>
</tr>
<tr>
<td>G2 (2% gelatin)</td>
<td>296.2 ± 1.15</td>
<td>4.89 ± 0.20</td>
<td>0.00</td>
<td>40.8 ± 0.50</td>
</tr>
<tr>
<td>G3 (4% gelatin)</td>
<td>296.4 ± 1.33</td>
<td>4.86 ± 0.23</td>
<td>0.00</td>
<td>36.8 ± 0.72</td>
</tr>
<tr>
<td>H1 (1% SCMC)</td>
<td>294.8 ± 1.98</td>
<td>5.36 ± 0.31</td>
<td>0.00</td>
<td>27.9 ± 0.80</td>
</tr>
<tr>
<td>H2 (2% SCMC)</td>
<td>297.6 ± 1.03</td>
<td>5.00 ± 0.00</td>
<td>0.00</td>
<td>37.8 ± 1.19</td>
</tr>
<tr>
<td>H3 (4% SCMC)</td>
<td>298.4 ± 0.75</td>
<td>5.26 ± 0.33</td>
<td>0.00</td>
<td>54.2 ± 1.10</td>
</tr>
<tr>
<td>I (Uncoated tablets)</td>
<td>299.4 ± 1.88</td>
<td>5.70 ± 0.07</td>
<td>0.07</td>
<td>18.8 ± 0.68</td>
</tr>
</tbody>
</table>

*Mean for 20 tablets, *a*Mean for 10 tablets ± SD, CV: coefficient of variation SD. standard deviation, F1 - F3: coated with D. microcarpium seed gum, G1 - G3: coated with gelatin and H1 - H3: coated with sodium carboxy methyl cellulose. P < 0.05 was considered significant.

The release profiles of sodium salicylate from different batches of coated tablets are presented in Figs. 1-3. Drug release in 0.1 N HCl showed that batches F1-F3 tablets coated with DMSG exhibited good release of drug and had more prolonged release than batch G1-G3 coated with different concentrations of gelatin. Therefore, DMSG showed better in vitro release properties as a coating film for sodium salicylate tablet than the gelatin. However, SCMC coated sodium salicylate tablets (H1-H3) exhibited more prolonged release of the drug in vitro significantly different from the tablets coated with DMSG.

Tablets coated with 4% of polymer film exhibited better in vitro properties significantly different from other batches containing 1% and 2% of the polymer film. The performance of the tablets coated with 4% polymer film could be ranked thus: H3 > F3 > G3.

**CONCLUSION**

DMSG showed significant better film coating properties than gelatin. However, DMSG coated tablets showed in vitro mechanical properties comparable to SCMC coated tablets. The tablets coated with DMSG exhibited properties that complied with BP specifications for coated tablets. Therefore, DMSG can be recommended for use as an alternative to SCMC, gelatin or other film coating polymers in the formulation of normal release coated tablets.
REFERENCES


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