**ABSTRACT**

**Aim:** This research was aimed at evaluating the use of *Grewia mollis* Juss. (Tiliaceae) stem bark gum as a compression coating-agent in a formulation intended to deliver ibuprofen to the colon.

**Place and Duration of Study:** Department of Pharmaceutics and Pharmaceutical Microbiology, Department of Pharmacology and Therapeutics (both in Ahmadu Bello University Zaria) and National Agency for Food and Drug Administration and Control (NAFDAC), Kaduna Laboratory between October 2012 and March 2014.

**Methods:** Ibuprofen core tablets were prepared by the direct compression method and four different compression-coated formulations were produced using powdered and granulated *Grewia* gum (GG) or hydroxypropyl methyl cellulose (HPMC). The compression-coated tablets were also evaluated for tablet parameters; the in vitro drug release studies were carried out in different simulated gastro-intestinal fluids. An in vivo study was conducted in New Zealand rabbits using the optimized compression-coated tablet and compared with a conventional ibuprofen tablets. The pharmacokinetic parameters were estimated from concentration of ibuprofen in the rabbit plasma using the high performance liquid chromatograph (HPLC).
1. INTRODUCTION

The colon drug delivery system (CDDS) is an example of the targeted delivery system; researches into the development of this system have increased over the past two decades. This is because the colon is a site for both local and systemic delivery of drugs [1]. The colon delivery system prevents the premature release of drug in the upper part of the gastrointestinal tract (GIT) but rapidly releases the drug in the colon following oral administration [2]. This delivery system is designed to improve the efficacy of the drug by concentrating the drug molecules where they are needed most and also minimize the potential side effects and drug instability which might be associated with premature release of drug in the upper parts of the GIT (the stomach and small intestine) [3].

The transit time and pH of the GIT are important factors that affect drug release from the CDDS. The normal transit time in the stomach is about 2 h (although this may vary with different individuals), the small intestinal transit time is 2-4 h while that of the large intestine where the colon belongs is about 20-30 h [4,5]. The pH of the stomach is as low as pH 1.5-2.0, that of the small intestine is about 7.7 and the colon has a pH of 6.6-6.8 [6]. An efficient colon delivery system is therefore, expected to be able to withstand the various transit times and pH of the upper GIT until it arrives in the colon. Various approaches have been postulated in the development of the colon delivery system [7,8] and the polysaccharide based approach is documented as the most site specific approach. This is because the factor that brings about drug release via this approach is specific to the colon; that is, the presence of micro-organisms [9]. Grewia gum is a polysaccharide that has been exploited for its use as a binder [10], suspending agent [11] and abio-adhesive agent [12]. The muco-adhesive properties of compacts made from Grewia gum has also been reported by [13] to compare favorably with guar gum and hydroxypropyl methylcellulose.

This investigation explores the use of powdered and granulated grewia gum as compression-coats over core tablets containing ibuprofen. The ability of GG to be effectively used as a compression-coating agent, its effect in retarding the release of ibuprofen in the upper GIT and its ability to deliver ibuprofen to the colon was compared with that of HPMC.

2. MATERIALS AND METHODS

2.1 Materials

Conventional 100mg Ibuprofen tablets (NGC, Nigeria), hydroxypropyl methylcellulose (HPMC) low grade; 80 -120 cp (H9262 Sigma-Aldrich, USA), ibuprofen powder BP (IBU/1211/0742, IOL Chemicals, India). Grewia mollis gum (prepared in the laboratory, Department of Pharmaceutics and Pharmaceutical Microbiology, Ahmadu Bello University, Zaria, Nigeria). All other chemicals used were of analytical grade.

2.2 Methods

Grewia mollis gum was extracted according to an already described method [14]. The percentage yield, organoleptic properties, moisture content, angle of repose, bulk density, tapped density, Carr’s compressibility index and Hausner ratio were determined according to standard methods.

2.2.1 Compression of ibuprofen core tablets

The core tablets were prepared by the direct compression method according to the formula in Table 1; the target weight for each tablet was 200 mg. Ibuprofen was geometrically mixed with...
the lactose (diluent) and maize starch (disintegrant) in a porcelain mortar. Grewia gum (GG) was incorporated into the mix as dry binder, talc and magnesium stearate (lubricant and glidant) were also incorporated in the mix. The powder mix was manually filled into the die and compressed into tablets in the Erweka single punch laboratory tableting machine (Erweka AR 400 Germany) at compression pressure of 9 metric tons using the 8mm punch and die.

2.2.2 Evaluation of physical parameters of core tablets

Weight variation of the core tablets was evaluated by weighing 20 tablets on an electronic balance (Digital Balance top loading HF 2000 (USA) and taking the average. The thickness and diameter of the core tablets were measured using the Digital Vernier Calliper (USA) TOH-700K (USA). The average crushing strength of 5 tablets were determined by the Mosanto hardness tester (Phillips Harris Ltd, England) while the friability was determined in the Erweka friabilator Type A3R, (Germany). The disintegration time of 6 tablets was estimated in the Erweka Disintegration apparatus (Type ZT3, Germany) and the dissolution studies were performed using the Multipurpose DGN Dissolution Apparatus (Shanghai China).

2.2.3 Compression-coating of core tablets

The target weight of the compression-coated tablets was 550 mg therefore; each coat weight was maintained at 350 mg. Coating with the powdered polymers was achieved by geometrically mixing the appropriate quantities of GG (Table 2) with microcrystalline cellulose (diluent), talc (lubricant) and magnesium stearate (glidant). Fifty percent (50% w/w) of the calculated coat quantities was then placed into the die cavity; the core tablet was carefully positioned at the centre and filled with the remaining quantity (50% w/w) of coat. This was compressed into tablets in the Erweka single punch laboratory tableting machine (Erweka AR 400 Germany) using the 12 mm punch and die assembly at compression pressure of 10 metric tons. The same procedure was repeated for compression-coating with HPMC at compression pressure of 12 metric tons.

The granulated coats were prepared by mixing the polymer with the diluent as done above and then wetting with water (3 ml) to make a damp mass. The mass was screened through 1.7 mm mesh-size, dried in the Gallenkamp oven at 40°C for 20 min screened again through 0.8 mm mesh-size sieve and re-dried in the oven at 40°C for 20 min. The granules were then mixed with the appropriate quantities of talc and magnesium stearate for 5 min and compression was carried out as already stated. Compression using the granulated GG was done at 8.5 metric tons while the compression pressure for the granulated HPMC was 9 metric tons.

2.2.4 Evaluation of compression-coated tablets

The compression-coated tablets were evaluated for the following; average weight, thickness, diameter, crushing strength, friability and swelling capacity. The following parameters also evaluated;

2.2.4.1 In-vitro drug release studies

This was carried out using the basket method in the DGN multipurpose, dissolution apparatus (Shanghai China) at 37±1°C and 100 rpm. The dissolution commenced in 500 ml of simulated gastric fluid; SGF (acidic buffer pH 1.2) for the first 2 h, continued in simulated intestinal fluid; SIF (phosphate buffer pH 7.4) for the next 3 h and then continued again in simulated colonic fluid; SCF (phosphate buffer pH 6.8) until the end of the study. One (1) ml sample was withdrawn at specified time (every hour until the end of the experiment) and replaced with same volume of the specified medium after each withdrawal. The withdrawn samples were then diluted to 10 times its volume and the absorbance of each sample was read using a UV Spectrophotometer (MNF, thermo scientific, Type Helious Zeta, UVZ-164617, England) at 221nm. The amount of ibuprofen released was determined from the calibration curve.

2.2.4.2 Calibration curve

The Beer Lambert’s calibration curve was obtained by dissolving 10 mg of ibuprofen powder in 1000 ml of phosphate buffer pH 6.8. Serial dilution was carried out until concentrations of 25, 20, 15, 10 and 5 µg were obtained. The absorbance of each dilution was measured by the UV spectrophotometer (MNF, thermo scientific, Type Helious Zeta, UVZ-164617, England) at 221nm as specified by the USP, (2006).
Table 1. Formula for preparing ibuprofen core tablets

<table>
<thead>
<tr>
<th>Ingredients (g)</th>
<th>Per tab (mg)</th>
<th>Per batch of 80 tablets (g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ibuprofen</td>
<td>100</td>
<td>8</td>
</tr>
<tr>
<td>Lactose</td>
<td>75</td>
<td>6</td>
</tr>
<tr>
<td>Maize starch (10% w/w)</td>
<td>20</td>
<td>1.6</td>
</tr>
<tr>
<td>Grewia gum (GG) (1% w/w)</td>
<td>2</td>
<td>0.16</td>
</tr>
<tr>
<td>Talc (1% w/w)</td>
<td>2</td>
<td>0.16</td>
</tr>
<tr>
<td>Magnesium stearate (0.5% w/w)</td>
<td>1</td>
<td>0.08</td>
</tr>
<tr>
<td>Total</td>
<td>200</td>
<td>16</td>
</tr>
</tbody>
</table>

Table 2. Formula for preparing ibuprofen compression-coated tablets

<table>
<thead>
<tr>
<th>Ingredients (g)</th>
<th>F1</th>
<th>F2</th>
<th>FH1</th>
<th>FH2</th>
</tr>
</thead>
<tbody>
<tr>
<td>GG</td>
<td>9.13</td>
<td>9.13</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>HPMC</td>
<td>-</td>
<td>-</td>
<td>9.13</td>
<td>9.13</td>
</tr>
<tr>
<td>MCC (10% w/w)</td>
<td>1.05</td>
<td>1.05</td>
<td>1.05</td>
<td>1.05</td>
</tr>
<tr>
<td>Talc (2% w/w)</td>
<td>0.21</td>
<td>0.21</td>
<td>0.21</td>
<td>0.21</td>
</tr>
<tr>
<td>Mag. St. (1% w/w)</td>
<td>0.11</td>
<td>0.11</td>
<td>0.11</td>
<td>0.11</td>
</tr>
<tr>
<td>Total weight</td>
<td>10.5</td>
<td>10.5</td>
<td>10.5</td>
<td>10.5</td>
</tr>
</tbody>
</table>

Key: GG = grewia gum, HPMC = hydroxylpropyl methylcellulose, MCC = microcrystalline cellulose, Mag. St = magnesium stearate, F1 = ibuprofen tablets compression coated with GG powder, F2 = ibuprofen tablets compression coated with GG granules, FH1 = ibuprofen tablets compression coated with HPMC powder, FH2 = ibuprofen tablets compression coated with HPMC granules

2.2.4.3 Similarity factor
This was calculated according the described method [15].

\[ f^2 = \frac{50 \times \log \left(1 + \frac{1}{n} \sum (Rt - Tt)^2\right)^{0.5} \times 100}{1} \]

Where Rt = cumulative percentage of reference product dissolved at time t, Tt = cumulative percentage of test product dissolved at time t, n = number of time points.

2.2.4.4 Kinetics modeling
The data from the dissolution studies were fitted into various kinetics models such as zero order, first order, Higuchi, Hixson-Crowell and Korsmeyer-Peppas; the equations used were adapted.

2.2.4.5 Kitazawa analysis
The dissolution data were also subjected to the Kitazawa equation [16].

\[ \ln \left( \frac{C_s}{(C_s - C)} \right) = kt \]

Cs = total amount of drug released at infinite time, C = amount of drug released at various time intervals, t.

2.2.4.6 In-vivo studies
Six male New Zealand rabbits of 2.5-3.0 kg weight were used for the in-vivo pharmacokinetic study according to the described method [17]. The optimized compression-coated formulation from the in-vitro release study; (F2) containing 100 mg ibuprofen was compared with a conventional marketed tablet formulation (MKT) containing 100 mg of ibuprofen.

The experiments were conducted according to the Institutional and International Ethical Standards regarding the handling and use of laboratory animals (UNDP/World Bank/WHO, 2001).

The plasma concentration data of ibuprofen was analyzed using the Moment Analysis Software. The pharmacokinetics parameters measured included the maximum concentration (C_max), time to achieve maximum concentration (T_max), absorption half-life (t_1/2), elimination rate constant (k_e), area under the curve (AUC) and mean residence time (MRT). The plasma concentration of ibuprofen per time was computed by dividing the area under the curve (AUC) from the chromatograms by the slope of ibuprofen calibration curve [18,19].
3. RESULTS AND DISCUSSION

3.1 Physicochemical Characterization of GrewiaGum

The yield of grewia gum from Grewia mollis stem bark was calculated to be 32% w/w (Table 3) which is similar to 32.4% w/w [14]. The moisture content was lower than the maximum limit (11-15% w/w) stated for gums used in both pharmaceutical and food industries [20] and it was also lower than 10.6% w/w already reported [14]; this could be due to differences in climate conditions of the location of research.

The angle of repose indicates the flow ability of a powdered material or a granular substance; materials with angles of repose between 23º and 35º are considered to possess good flow properties while cohesive materials have high values of between 40º and 60º and do not flow properly [21]. An angle of repose below 27º therefore, indicates that GG has good flow properties.

The compressibility index (18.75%) and Hausner ratio (1.23) of GG powder show that it has a moderate flow profile. This implies that on application of pressure, GG might not produce good compacts; but the addition of other tableting excipients and processing of the GG powder into granules could improve its compressibility. Such compression behavior has also been reported with some other plant gums [25,26].

Plant polymers swell when hydrated and the swelling capacity indicates the extent of its hydration and water retention. The swelling on hydration is responsible for the glass to rubber transition exhibited by these polymers and is a major factor in influencing drug release from a formulation [27]. The high swelling capacity of GG indicates that when it is incorporated in a formulation, it will give longer disintegration and dissolution time hence controlling drug release.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percentage yield (% w/w)</td>
<td>32</td>
</tr>
<tr>
<td>Moisture content (% w/w)</td>
<td>7.33</td>
</tr>
<tr>
<td>Color</td>
<td>Light brown</td>
</tr>
<tr>
<td>Odor</td>
<td>Odorless</td>
</tr>
<tr>
<td>Taste</td>
<td>Characteristic</td>
</tr>
<tr>
<td>Texture</td>
<td>Fluffy</td>
</tr>
<tr>
<td>Angle of repose (º)</td>
<td>26.92</td>
</tr>
<tr>
<td>Bulk density (g/ml)</td>
<td>0.26</td>
</tr>
<tr>
<td>Tapped density (g/ml)</td>
<td>0.32</td>
</tr>
<tr>
<td>Carr's index (%)</td>
<td>18.75</td>
</tr>
<tr>
<td>Hausner ratio</td>
<td>1.23</td>
</tr>
<tr>
<td>Viscosity (1%w/v) (cp) 50 rpm</td>
<td>103.8</td>
</tr>
<tr>
<td>Swelling capacity (%)</td>
<td>237.5</td>
</tr>
</tbody>
</table>

3.2 Evaluation of Core and Compression-coated Tablets

The average weight of the core tablets (Table 4) was within the official specification for tablets with 200 mg weight [20]. The crushing strength and corresponding high friability values attributed to the formation of weak bonds between the particles which could not prevent abrasion of the tablets. The disintegration time was fast (25.67 sec) and can be attributed to high concentration of disintegrant (10% w/w) incorporated into the formulation. The calibration curve (Fig. 1) was used in calculating the concentration of drug released from the core and compression coated tablets. Drug release from the core tablet was fast and complete drug release was attained by 20 min (Fig. 2). The core tablets were formulated with the intention for fast disintegration and dissolution so that there would be prompt and complete drug release immediately the tablet formulation arrives in the colon.

3.3 Evaluation of Compression-coated Ibuprofen Tablets

All the batches of the coated tablets had average weights within the official range for tablets with weights ≥324 mg [20]. The thickness of the coated tablets was much higher than the core due to the coat applied unto the core. The thickness and diameter of the tablets (F1-FH2)
were also different across the different coating materials used (Table 4) and this was significant at p=0.05; this could be due to differences in the densities of GG and HPMC used to coat the tablets.

The crushing strength of all coated tablets was higher than that of the core tablet due to the formation of strong inter-particulate bridges around the core in the presence of the polymers used as coating agents [28]. It could also be attributed to formation of particle to particle contact between the polymer coat creating stronger bonds and resulting in stronger tablets [29]. The crushing strengths of the coated formulations were similar irrespective of the processing carried out on the polymer used for coating. The friability values of all the coated tablets were low (≤1%) due to high mechanical strength of the tablets making them strong and resistant to abrasion and shocks. The drug content of all the compression-coated tablets was within the official limit of 90-110% [30].

![Graph of absorbance versus conc. (µg/ml) for the calibration curve of ibuprofen in PBS 6.8](image1)

![Graph of drug release (%) versus time (min) of ibuprofen core tablets in phosphate buffer 6.8](image2)
3.4 Effect of Compression-coating on Swelling of Ibuprofen Tablets

Hydration of the tablets caused swelling of the polymers used to coat the tablets and this led to increase in tablet weight; it also produced varying degrees of gelatinous layer around the tablets depending on the amount and type of polymer used as coating agents (Fig. 3). The difference in swelling capacities of the coated tablet formulations was significant at p=0.05.

Formulation F1, coated with 350 mg powdered GG, gave the highest swelling which could be attributable to formation of strong, stable gelatinous layer around the tablets due to the high swelling ability of GG thus preventing the influx of fluid into the tablets and enabling the tablets retain their integrity for a longer time [27]. The formulations coated with HPMC granules (FH2) had the lowest swelling capacity due to formation of weak gelatinous layer around the compressed tablets. The minimal increase in weights exhibited by the formulations coated with HPMC (FH1 and FH2) confirms the report [31] that HPMC formulations do not hydrate rapidly although they are capable of forming gels around tablet formulations.

A significant difference at p=0.05 was observed in the swelling capacities of the coated tablets with the powdered coats (GG or HPMC) exhibiting higher swelling than the granulated coats (GG or HPMC). Powder particles aggregate on granulation making them more porous and more permeable to the dissolution fluids, this would lead to minimal tablet swelling, erosion and disintegration of the tablets [32]. The tablets coated with powdered polymers are less porous and have the ability to imbibe more fluid thus retarding drug release better than the granulated coats. Slower formation of gelatinous layer around tablets formulated with granulated carbopol® 71G NF have been documented to lead to rapid penetration of fluid, disintegration and dissolution of the tablets more than when the powdered polymers were used to coat [33].

3.5 Effect of Compression Coating on Drug Release

On exposure of the tablets to the dissolution medium, hydration of the coating polymers (GG or HPMC) occurred with subsequent formation of viscous gelatinous (gel) layer around the tablets. This slowed down the entry of dissolution fluid into the tablet core; increasing the path length of drug transportation and reducing the rate of drug release from the formulation.

Drug release from formulation F1 in the SGF (4.05%), 13.88% in SIF and complete drug release at 12 h (Fig. 4) while that of F2 was 14.37% (SGF), 24.32% (SIF) and complete drug release at 10 h showing faster release from F3. This can be attributed to the formation of thicker gelatinous layer around the F1 as observed from swelling studies thereby reducing the rate at which the drug was being released from the formulation. It was observed from Figs. 4 and 5 that the powdered polymers (F1, FH1) had better ability at retarding drug release than granulated polymers (F2, FH2) which could be attributed to the swelling capacities of these formulations. It could be because granules have more interparticulate spaces and higher porosity than
powders, therefore, penetration of fluid into granule pores would be easier leading to rapid disintegration, increase in granule dissolution and rate of drug release [33].

Powders, on the other hand, are cohesive therefore packing of the polymer powder into the die cavity could have resulted in better consolidation and higher bond strength making the annihilation of the forces holding the particles together more difficult [34]. Similar behavior in drug release rate between powdered and granulated materials has been reported [32,35].

Fig. 3. Graph of weight gain (%) versus time (h) of ibuprofen tablets coated with GG and HPMC in phosphate buffer 7.4

Fig. 4. Graph of cumulative drug release (%) versus time (h) of ibuprofen tablets coated with powdered GG (F1) and granulated GG (F2) in the simulated GI fluids
The drug release from tablets coated with the powdered polymers shows F1 has better ability to protect drug release in the upper part of the GIT with 13.88% release against 16.01% release from FH1 although both formulations achieved 100% release at 12 h (Fig. 6). This could be attributed to the ability of F1 to absorb more fluid than FH1 and also the formation of more viscous gelatinous layer greater around F1 than FH1 (Fig. 3) leading to retardation of drug release. All the coated formulations however were capable of retaining their integrity until entry into the colon (SCF) with complete drug release achieved at 10 or 12 h.

Sudden “drug-burst” was observed for all the coated formulations at different times in the SCF indicating the onset of erosion of the coat or erosion of most of the coat. The “drug-burst” from F1 between 8 and 10 h was 26% to 87% which was more rapid than the burst observed from the other coated formulations. Erosion of the coat from formulations F2, FH1 and FH2 was gradual and not required for formulations intended for colonic delivery. Formulation F1 exhibited the ability to travel farther into the colon than the other coated formulations before erosion of the coat occurred at 8 h (Fig. 7). This shows the ability of the powdered GG coat to retain the integrity of the formulation for a longer time than the other polymer coats.

The similarity factor (f2) in Table 5 shows only formulations F1 and FH1 have similar drug release profiles. This suggests that either of these two formulations could be used to successfully deliver ibuprofen to the colon.

### Table 5. Comparison of dissolution profile of compression-coated tablets

<table>
<thead>
<tr>
<th>Batches</th>
<th>Similarity factor (f2)</th>
<th>Inference</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1 and FH1</td>
<td>59</td>
<td>S</td>
</tr>
<tr>
<td>F1 and F1</td>
<td>40</td>
<td>NS</td>
</tr>
<tr>
<td>F2 and FH2</td>
<td>46</td>
<td>NS</td>
</tr>
</tbody>
</table>

The most predominant release kinetic for the compression-coated formulations is the zero order indicating that drug release was independent of time or initial concentration (Table 6).

The Korsemeyer-Peppas values were all between 0.50 and 0.60 signifying that the mechanism of release from all the coated formulations was by anomalous or non-fickian diffusion. Therefore, the rate of drug release from the coated formulations, irrespective of the type of processing carried out on the coating material, occurred due to the combined effect of erosion of the polymer coat and drug diffusion through the polymer coat. This phenomenon has also been reported [36] in the formulation of ibuprofen colon delivery system that was compression-coated with chitosan.
The *in-vitro* drug release showed that the optimized coated formulation (F1) was able to provide a form of barrier to drug release in the upper GIT where only 4% of the drug was released. The *in-vivo* studies also show concentration of ibuprofen detected in the plasma of New Zealand rabbits after the oral administration of F1 was minimal in the first 2 h; indicating that there was a form of barrier to drug release in the upper GIT of the rabbits (Fig. 8).

![Graph of cumulative drug release (%) versus time (h) of ibuprofen tablets coated with powdered GG (F1) and powdered HPMC (FH1) in simulated GI fluids](image1)

**Fig. 6.** Graph of cumulative drug release (%) versus time (h) of ibuprofen tablets coated with powdered GG (F1) and powdered HPMC (FH1) in simulated GI fluids

![Graph of Ln(Cs/Cs - C) versus time (h) of ibuprofen core tablets compression-coated with GG or HPMC](image2)

**Fig. 7.** Graph of Ln(Cs/Cs - C) versus time (h) of ibuprofen core tablets compression-coated with GG or HPMC

| Table 6. Kinetics and mechanism of ibuprofen release from compression-coated tablets |
|-------------------------------------|-----|-----|-----|-----|-----|-----|
| Batches           | Zero order | First order | Higuchi model | Hixson-Crowell model | Korsmeyer-Peppa's model | n  |
| F1                | 0.83 | 0.08 | 0.63 | 0.72 | 0.97 | 0.58 |
| F2                | 0.89 | 0.04 | 0.68 | 0.68 | 0.80 | 0.59 |
| FH1               | 0.81 | 0.09 | 0.60 | 0.78 | 0.89 | 0.51 |
| FH2               | 0.87 | 0.10 | 0.66 | 0.81 | 0.89 | 0.59 |
The pharmacokinetic parameters in Table 7 show $C_{\text{max}}$ for F1 as 1038.70 µg/ml and the AUC$_{0-12}$; 4715.05 µg.h/ml which were achieved at 1 h and 8 h respectively and they were lower than those of MKT (1413.60 µg/ml and 5456.55 µg.h/ml respectively). This indicates minimal absorption of ibuprofen on administration of F1 compared to rapid absorption from the upper GIT and increased bioavailability of the drug after administration of MKT; this is expected since MKT is an immediate release formulation. The lower $C_{\text{max}}$ (1038 µg/ml) and delayed $T_{\text{max}}$ of 8 h for F1 indicates that the maximum plasma concentration occurred at a much latter time than $T_{\text{max}}$ (1 h) from MKT showing that ibuprofen was delivered to the colon. This can be attributed to the presence of GG employed as coat which offered barrier to drug release consequential to the swelling effect of GG around the tablet by the production of viscous gelatinous layer. Similar results have been reported [37, 38] with the use of okro mucilage as matrix-former and film-coating agent in colon drug delivery. The long half-life ($t_{1/2}$) of 8.66 h and short elimination rate constant; $k_e$ (0.08 h$^{-1}$) of F1 shows that the drug remained in the system for a long period of time compared to $t_{1/2}$ of 2.16 h and elimination rate constant; $k_e$ of 0.32 h$^{-1}$ from MKT. The MRT for F1 was longer (7.43 h) than 3.07 h for MKT indicating a longer residence time of F1; it also shows the ability of F1 to provide sustained release. The calculated oral relative bioavailability (F%) of F1 was 87.65% indicating good bioavailability and possible reduction in the associated side effects of ibuprofen when formulated as a colon delivery system.

The in-vitro / in-vivo plot (IVIVC) of F1 shows a good correlation (0.926) from the coefficient of the graph indicating that a good relationship exists between the cumulative drug release obtained in-vitro and the in-vivo drug absorbed; thus validating the results of the in-vitro studies (Fig. 9).

![Fig. 8. Graph of plasma concentration (µg) versus time (h) of ibuprofen in rabbits after oral administration of optimized coated formulation (F1) and marketed formulation (MKT)](image)

### Table 7. Pharmacokinetic parameters of ibuprofen in rabbits after oral administration of MKT and F1

<table>
<thead>
<tr>
<th>Parameters</th>
<th>MKT</th>
<th>F1</th>
</tr>
</thead>
<tbody>
<tr>
<td>$C_{\text{max}}$ (µg/ml)</td>
<td>1413.60</td>
<td>1038.70</td>
</tr>
<tr>
<td>$T_{\text{max}}$ (h)</td>
<td>1.00</td>
<td>8.00</td>
</tr>
<tr>
<td>MRT (h)</td>
<td>3.07</td>
<td>7.43</td>
</tr>
<tr>
<td>AUC$_{0-12}$ (µg.h/ml)</td>
<td>5456.55</td>
<td>4715.05</td>
</tr>
<tr>
<td>AUMC$_{0-12}$ (µg.h/ml)</td>
<td>16745.25</td>
<td>35019.01</td>
</tr>
<tr>
<td>$k_e$ (h$^{-1}$)</td>
<td>0.32</td>
<td>0.08</td>
</tr>
<tr>
<td>$t_{1/2}$ (h)</td>
<td>2.16</td>
<td>8.60</td>
</tr>
<tr>
<td>F%</td>
<td>-</td>
<td>87.65</td>
</tr>
</tbody>
</table>

Key: $C_{\text{max}}$ = peak plasma concentration, $T_{\text{max}}$ = time to reach peak plasma concentration, $K_e$= elimination rate constant, $t_{1/2}$ = elimination half-life, AUC$_{0-12}$ = area under curve from onset to 12 h, AUMC$_{0-12}$ = area under moment curve from onset to 12 h, MRT = mean residence time, F% = bioavailability, MKT = conventional marketed ibuprofen formulation
Fig. 9. Graph of cumulative AUMC (µg-h/ml) versus in-vitro drug release (%) of optimized coated formulation (F1)

4. CONCLUSION

_Grewia mollis_ stem bark gum (GG) has been investigated and found to be an effective compression-coating agent. The powdered polymers (GG or HPMC) achieved better compression-coating than the granulated polymers (GG or HPMC). Compression-coating with powdered GG offered better protection to drug release in the upper GIT and also delivered ibuprofen effectively to the colon than all the other coated formulations. The pharmacokinetic parameters extrapolated from the _in-vivo_ studies showed that the optimized formulation (F1) was successful in delivering ibuprofen to the colon with very minimal release in the upper GIT.

CONSENT

It is not applicable

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES


31. Latha K, Uhumwangho MU, Sunil SA, Srikanth MV, Ramana MK. Preparation and in-vitro evaluation of compression coated


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