COMPARATIVE IN VITRO EVALUATION OF IBUPROFEN 200MG TABLETS SOLD IN PHARMACIES KHARTOUM SUDAN

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ABSTRACT

Objective: The study was carried out to evaluate the quality of ibuprofen tablets sold in retail and wholesale pharmacies in Khartoum, Sudan. Methods: The study was done for four different brands of ibuprofen (AB1, AB2, AB3 and AB4) obtained from different pharmacies in Khartoum, Sudan from local and international factories. The standard ibuprofen obtained from Shangahi-Sudan pharmaceutical. The properties of the tablets were evaluated by some tests in quality control laboratories, namely: uniformity of weight, thickness and diameter, friability, dissolution test and disintegration test. chromatographic method (HPLC) was used to determine the percentage of ibuprofen and to assay the tablets. These tests done according to united state pharmacopeia (BP). Results: We found that all the four different manufacturing brands are comply with BP requirements. Conclusion: All the Four brands of the ibuprofen tablets evaluated in this study could be regarded as being pharmaceutically and chemically equivalent.

KEYWORDS: Brands, Ibuprofen Tablets Disintegration, Dissolution, Friability.

INTRODUCTION

IBUPROFEN TABLETS

Properties: (Isobutyl phenyl propionic acid) Ibuprofen is a white powder with a melting point of 74-77° C and is very slightly soluble in water (<1 mg/mL) and readily soluble in organic solvents such as ethanol and acetone.
The structural formula is represented below

![Structural formula](image)

**IUPAC name:** (RS)-2-(4-(2-methylpropyl) phenyl) propanoic acid

**Molecular Formula:** C13H18O2

**Melting point:** 76°C

**Molar weight:** 206.29 g/mol

**Inactive ingredients:** colloidal silicon dioxide, croscarmellose sodium, magnesium stearate, microcrystalline cellulose, polyethylene glycol, polyvinyl alcohol, pregelatinized starch, talc, stearic acid, and titanium dioxide.

**Ibuprofen as enteric coated tablets:** Ibuprofen is a propionic acid derivative that belongs to the class non steroidal anti-inflammatory drugs (NSAIDs). Major adverse reactions associated with Ibuprofen are related to GIT and include peptic and mucosal ulcers and irritations, dyspepsia, severe gastric pain and bleeding, that results in excessive treatment failure. As a solution of this problem enteric coated ibuprofen tablets was developed in order to avoid gastric mucosal irritation, diffusion of drug across mucosal lining and to let active ingredient be absorbed easily in small intestine. The formulation was developed and manufactured through the direct compression process, the simplest, easiest and most economical method of manufacturing.

Drug is coated with polymer that does not dissolve under acidic condition (i.e. the stomach) but does dissolve under more alkaline conditions of small intestine (i.e. the pH>4). Hydroxypropyl methylcellulose (HPMC) was selected as a base polymer to develop novel enteric coating agents for acid protection, in contrast to ethyl cellulose it is water soluble and might leach out of the film coating, creating water filled pores through which drug diffuses more rapidly than (HPMC); another polymers which may use are Methacrylate copolymers, hydroxypropyl methylcellulose acetate, succinates and cellulose acetate phthalate.
An ideal enteric coating material should have the following properties
1- Resistance to gastric fluids.
2- Permiability to intestinal fluids.
3- Compatibility with most coating components and drug substrate.
4- Stability alone and in coating solution.
5- Formation of continuous film.
6- Non toxicity.
7- Low cost.

CLINICAL PHARMACOLOGY
The 2-arylpropionic acid derivative, Ibuprofen [RS-2-(4-isobutyl-phenyl)propionic acid], is one of the most potent orally active antipyretic, analgesic and nonsteroidal anti-inflammatory drug (NSAID) used extensively in the treatment of acute and chronic pain, osteoarthritis, rheumatoid arthritis and related conditions. This compound is characterized by a better tolerability compared with other NSAIDs.

Mechanism of Action: Ibuprofen appears to exert its pharmacologic actions by inhibiting cyclooxygenase enzyme and thus blocking the first step in the synthesis of Prostaglandins.

Clinical pharmacokinetics: It is rapidly absorbed after oral administration from the gastrointestinal tract and peak plasma concentration occur about 1 to 2 hours after ingestion.

It is extensively bound to plasmaproteins (99%), and has a half life of about 2 hours. It has relatively short elimination half-life.

Ibuprofen is metabolized by oxidation in the liver to produce two major metabolites: 2-hydroxy- and 2-carboxy-ibuprofen.

The conjugated and the unconjugated forms of these metabolites, as well as up to 10% unchanged ibuprofen, are excreted in urine.

INDICATIONS
- Ibuprofen tablets are indicated for relief of mild to moderate pain and the signs and symptoms of rheumatoid arthritis and osteoarthritis.
- For the treatment of primary dysmenorrhoea.
- Post-operative pain.
- Migraine.
- Musculoskeletal and joint disorders.

METHODS AND MATERIALS

Materials

Samples

Ten strips each of 4 brands of ibuprofen tablets manufactured by various pharmaceutical companies were collected from different pharmacies located in khartoum, sudan. The quality control tests were carried out. The tablet brands include:

**Company A – B –C - D**

Coated tablets ibuprofen 200mg.

**Instruments:** Disintegration tester, Electronic balance(DHONE), ErwekaFriabilator (Erweka TA20, England), High performance liquid chromatography (HPLC), porcelain mortar and pestle, vernier caliper, pipette, measuring cylinder, volumetric flasks, filter paper, sonicator and water bath

**Chemical**

Water, methanol, orthophosphoric acid.

METHODS

**Weight variation test**

The variation of the weight of individual tablets is a valid indication of the corresponding variation in the drug content. The average tablet weight was determined by weighing 20 units or tablets individually using an analytical balance. Weight variation should be within limit prescribed:

±10% for tabs weigh 120mg or less,
±7.5% for tabs weigh 120-300mg,
±5% for tabs weigh more than 300mg.

**The test consider correct if**

Not more than 2 tabs fall outside range (for 20 tabs sample), & not more than 1 tab fall outside range (for 10 tabs sample). The mean ± S.D. of each formulation is measured. Film-coated tablets fail this test it may be because of variability in the thickness (mass) of the coatings.
**Thickness and width measurement**

The thickness of a tablet was determined by the amount of fill permitted to enter the die and the amount of pressure applied during compression. 20 tablets were taken and their thickness and width were determined individually by vernier caliper. Mean was calculated. The values should not be deviated from mean by more than 1.

**Friability test**

Friability test can be performed to evaluate the ability of the tablets to withstand abrasion in packing, handling and transporting. The Friabilator consists of a plastic chamber divided into two parts and revolves at 25 rpm. A fixed number of tablets (10 tabs.) were weighed, placed in the tumbling chamber and rotated for four minutes of 100 revolutions. During each revolution the tablets fell from a distance of six inches to undergo shock. After 100 revolutions the tablets were again weighed. The loss in weight indicates the friability. The acceptable limits of weight loss should not be more than 0.8%.

The percent friability was determined by using following formula:

\[
\text{% friability} = \left(\frac{\text{initial weight} - \text{final weight}}{\text{initial weight}}\right) \times 100
\]

**Disintegration test:** Disintegration is evaluated to ensure that the drug substance is fully available for dissolution and absorption from the gastrointestinal tract. Disintegration time was measured for 6 tablets by inserting disks using 900ml purified water at 37±2°C in Disintegration Apparatus. Test was finished when the 6 tablets were completely disintegrated and no palpable parts of the tablets present in the screen of the disk. Disintegration time should not exceed 30 minutes as recommended in B.P.

**Identification**

Content uniformity test and Identification of ibuprofen were carried out by using HPLC; retention time was used to determine the presence of ibuprofen.

**Assay (content uniformity)**

- Preparation of methanol/water mobile phase: as recommended in B.P.: 3 volumes of orthophosphoric acid, 247 volumes of water and 750 volumes of methanol.
The following steps were done to prepare 0.2% w/v of ibuprofen in mobile phase

-10 tablets of each brand were weighed using sensitive electronic balance and crushed using porcelain mortar and pestle until fine powder was achieved. The following samples’ powder weights equivalent to (0.2 g of ibuprofen) were weighed using the electronic balance and were dissolved in a known volume of mobile phase in volumetric flasks of 50ml as following:

- Standard sample: 27 mg in 25 ml of mobile phase.
- Sample A: 83 mg in 25 ml of mobile phase.
- Sample B: 82 mg in 25 ml of mobile phase.
- Sample C: 82 mg in 25 ml of mobile phase.
- Sample D: 82 mg in 25 ml of mobile phase.

Sonicator was used for 15 minutes to enhance solubility of samples in the mobile phase. After cooling, mobile phase in each flask were continued to 50ml and about 10ml of each sample was filtered using syringe with a special filter paper. HPLC took place 4 times for standard sample and each other sample. Area under curve (AUC) for standard sample and other samples were determined to find out content percent as following:

\[
\text{content percent} = \frac{\text{AUC of sample} \times \text{concentration of standard} \times \text{average w.t of sample} \times 100}{\text{AUC of standard} \times \text{concentration of sample} \times 0.2}
\]

According to B.P., content percent of ibuprofen should be between 95.0 to 105.0% of the stated amount.

Retention time for each sample was determined to identify ibuprofen.

**Weight Uniformity results**

- deviation (D) = | tablet weight – average weight |
- D % = D/individual tablet weight*100
* Table No.2 (weight uniformity results)

<table>
<thead>
<tr>
<th>Sample No.</th>
<th>A</th>
<th>D%</th>
<th>B</th>
<th>D%</th>
<th>C</th>
<th>D%</th>
<th>D</th>
<th>D%</th>
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<td>0.3</td>
<td>0.009</td>
<td>1.9</td>
<td>0.002</td>
<td>5.6</td>
<td>0.005</td>
<td>9.6</td>
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<td>2</td>
<td>0.004</td>
<td>1.2</td>
<td>0.016</td>
<td>3.4</td>
<td>0.001</td>
<td>2.8</td>
<td>0.015</td>
<td>3.0</td>
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<td>0.008</td>
<td>2.5</td>
<td>0.004</td>
<td>8.2</td>
<td>0.001</td>
<td>2.8</td>
<td>0.016</td>
<td>2.9</td>
</tr>
<tr>
<td>4</td>
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<td>4.3</td>
<td>0.014</td>
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<td>0.026</td>
<td>5.0</td>
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<td>5.05</td>
<td>0.013</td>
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<td>0.001</td>
<td>2.8</td>
<td>0.004</td>
<td>0.7</td>
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<tr>
<td>6</td>
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<td>1.2</td>
<td>0.018</td>
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<td>0.1</td>
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<td>0</td>
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<td>0.002</td>
<td>5.6</td>
<td>0.007</td>
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<td>0.008</td>
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<td>0.004</td>
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<td>0.061</td>
<td>11.9</td>
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<td>2.8</td>
<td>0.000</td>
<td>0</td>
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<tr>
<td>11</td>
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<td>0.027</td>
<td>5.7</td>
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<td>0.046</td>
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<td>0.011</td>
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<td>0.001</td>
<td>2.8</td>
<td>0.031</td>
<td>6.1</td>
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<td>1.9</td>
<td>0.012</td>
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<td>0.000</td>
<td>0</td>
<td>0.011</td>
<td>2.1</td>
</tr>
<tr>
<td>16</td>
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<td>0.002</td>
<td>4.2</td>
<td>0.003</td>
<td>8.6</td>
<td>0.001</td>
<td>0.1</td>
</tr>
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<td>17</td>
<td>0.008</td>
<td>2.5</td>
<td>0.027</td>
<td>5.9</td>
<td>0.004</td>
<td>1.1</td>
<td>0.011</td>
<td>2.1</td>
</tr>
<tr>
<td>18</td>
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<td>1.5</td>
<td>0.002</td>
<td>4.1</td>
<td>0.004</td>
<td>1.1</td>
<td>0.005</td>
<td>0.9</td>
</tr>
<tr>
<td>19</td>
<td>0.028</td>
<td>8.2</td>
<td>0.002</td>
<td>4.1</td>
<td>0.004</td>
<td>1.1</td>
<td>0.010</td>
<td>3.6</td>
</tr>
<tr>
<td>20</td>
<td>0.009</td>
<td>2.9</td>
<td>0.003</td>
<td>6.3</td>
<td>0.004</td>
<td>1.1</td>
<td>0.019</td>
<td>3.8</td>
</tr>
</tbody>
</table>

Comment
The Four brands are out of the accepted values as recommended in the B.P (more than two tablet had deviation % more than 5%). This is may be because of variability in the thickness (mass) of the coatings or a problem in tablet content. In this case, content uniformity (assay) test should take place.

Friability Test results
Friability%= (Weight before – weight after/ weight before)* 100

*Table No.3 (Friability test)

<table>
<thead>
<tr>
<th>Sample</th>
<th>Weight before</th>
<th>Weight after</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>3.053</td>
<td>3.050</td>
<td>0.098%</td>
</tr>
<tr>
<td>B</td>
<td>3.497</td>
<td>3.497</td>
<td>0%</td>
</tr>
<tr>
<td>C</td>
<td>5.118</td>
<td>5.1175</td>
<td>0.009%</td>
</tr>
<tr>
<td>D</td>
<td>4.970</td>
<td>4.966</td>
<td>0.080%</td>
</tr>
</tbody>
</table>

Comment
All Samples were within the accepted recommended values
Disintegration Test results

*Table No.4 (disintegration test)

<table>
<thead>
<tr>
<th>Sample</th>
<th>Disintegration time (min.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>3</td>
</tr>
<tr>
<td>B</td>
<td>1</td>
</tr>
<tr>
<td>C</td>
<td>6</td>
</tr>
<tr>
<td>D</td>
<td>7</td>
</tr>
</tbody>
</table>

Comment
The four brands (A, B, C, and D) had accepted disintegration values as recommended in B.P.

*3-4: Assay (content uniformity) results

*Table No.5 (content uniformity)

<table>
<thead>
<tr>
<th>Sample</th>
<th>Content percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>standard</td>
<td>100%</td>
</tr>
<tr>
<td>A</td>
<td>103.2%</td>
</tr>
<tr>
<td>B</td>
<td>99.9%</td>
</tr>
<tr>
<td>C</td>
<td>98.3%</td>
</tr>
<tr>
<td>D</td>
<td>104.0%</td>
</tr>
</tbody>
</table>

Comment
The all four brand (A, B, C, and D) had accepted content percentages of active ingredient as recommended in B.P.

Identification using HPLC retention time

<table>
<thead>
<tr>
<th>Sample</th>
<th>Retention Time (min.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>standard</td>
<td>3.5</td>
</tr>
<tr>
<td>A</td>
<td>3.4</td>
</tr>
<tr>
<td>B</td>
<td>3.4</td>
</tr>
<tr>
<td>C</td>
<td>3.3</td>
</tr>
<tr>
<td>D</td>
<td>3.4</td>
</tr>
</tbody>
</table>

show that the four brands have relatively the same retention times as the standard sample that means that they all are ibuprofen.

CONCLUSION
Our results indicated that all generic ibuprofen tablets included in this study comply with BP specifications. They can be considered bioequivalent.
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