FORMULATION OF ASPIRIN TABLETS USING FEWER EXCIPIENTS BY DIRECT COMPRESSION

SAIMA ERUM, FOUZIA HASSAN, SYED MUHAMMAD FARID HASAN*
AND SABAHAT JABEEN
Department of Pharmaceutics, Faculty of Pharmacy,
University of Karachi, Karachi, Pakistan

ABSTRACT:
The objective of the present study was to formulate aspirin tablets by direct compression method using fewer excipients and to compare this formulation with the other brands. Design formulation besides aspirin contained excipients that comprises of lactose, corn starch and aerosil. The blend was compressed on a single punch machine, tablets were subjected to various tests (uniformity of weights, diameter and thickness, hardness, disintegration, dissolution and assay of the drug) and the results were compared with some of the available brands. The studied formulation showed close resemblance with the available marketed brands and were also in compliance with the official specifications. Using the present approach, further studies should be designed using other actives and excipients to get a cost effective product.

Keywords: Aspirin, tablet formulation, direct compression.

INTRODUCTION

Though, pharmaceutical research have been focused on development of new and more compliant dosage forms, tablets still remain popular due to their stability, ease of handling and convenience of dosing and account for more than 80% of all dosage forms administered (Jivraj et al., 2000). These are manufactured by wet granulation, dry granulation and direct compression (DC) methods (Jones, 2008). DC is advantageous over other methods of tablet manufacturing as it requires fewer unit operations, consequently low cost and less time consumption, generates optimum possible bioavailability (Yasmeen et al., 2005), low microbial level due to absence of moisture (Ibrahim and Olurinola, 1991) and produces faster dissolution rates for certain compounds (Jivraj et al., 2000). This method is preferred for tablet manufacturing especially in case of thermolabile and moisture-sensitive drugs (Jivraj et al., 2000). Aspirin is a commercial example of a DC tablet granulation prepared by the dry granulation technique. It is most widely used drug in the world (Michael Gossop, 2007) as an analgesic, anti-inflammatory and antipyretic agent (Sweetman, 2009), however, many workers have investigated its clinical profiles in a number of other medical conditions such as cardiovascular (Buring, 2006, Moyad, 2001, Berger et al., 2009), cancer (Moyad, 2001, Chan et al., 2009, Cook et al., 2005) and diabetes (Yang et al., 2009, Ong et al., 2010) and have found promising results.

The objective of the present study was to make a new formulation of aspirin tablets by DC using a fewer excipients in three trail batches and to compare this formulation with the available brands in the local market containing aspirin in the same strength.

MATERIALS AND METHODS

Reagents
Sodium hydroxide, hydrochloric acid, acetonitrile, formic acid, glacial acetic acid, sodium 1-heptane sulphonate, acetate buffer

Correspondence to: e-mail: faridsm2002@yahoo.com
and phenol red, all reagents were purchased from Merck Germany.

**Formulation Composition**

A new formulation was designed consisting of: Aspirin (donated by Reckitt Benckiser, Pakistan Ltd.), lactose, starch and aerosil (FMC Corporation, USA). Composition of the formulation is given in Table 1.

**Commercial Brands**

Different brands of aspirin 300mg were purchased from the local market and were assigned randomly as B1, B2, B3, B4 and B5.

**Trial Batches**

Active pharmaceutical ingredient (API) and all the other excipients, as mentioned in Table 1, were accurately weighed and were passed through 20 mesh sieve in order to remove foreign material and to get uniform particle size. The powder was blended in a poly bag by tumbling for five minutes. The blend was transferred directly into the hopper of single punch machine (Erweka, GmbH, Germany) having caplet shaped concave punch and was compressed manually. Three trial batches (T1, T2 and T3) were prepared using the same procedure on alternate days as described above and each batch was tested on day of compression in order to avoid any change in hardness, moisture content and any other physical parameter. All the batches were compressed at room temperature.

**Evaluation of Tablet Properties**

All the trial batches of aspirin and the commercial brands were evaluated using USP 28/NF 23 (USP 28/NF 23, 2005) and by non-pharmacopoeial tests.

**Weight variation test**

Weight variation test of each trial formulation and commercial brands was carried out by taking average weight of 20 individually weighed tablets on an analytical balance (Sartorius GmbH type A 6801) and compared with permissible limits.

**Diameter and Thickness**

Random samples of 10 tablets were selected from each of the trial batches and commercial brands and their diameter and thickness was calculated in centimeters with the help of micrometer screw gauge.

**Hardness**

Hardness of randomly selected 10 tablets of each brand and trial formulation batch was measured using Hardness Tester (Fujiiwara, Seisukusho Corporation, Japan). Load was given to tablets in a diametric direction to determine an actual load when the tablet was broken.

**Friability Testing**

Friability test was performed on twenty randomly selected tablets of each brand and trial formulation batches which were cleared from any loose dust with help of soft brush and weighed accurately for their initial weight. Each set of tablets were placed separately in Friability Tester (H. Jurgens and Co- GmbH, D2800, Germany) and run for 4 minutes (25rpm). After removing from tester, tablets were cleared from any loose dust and their final weight was determined to calculate loss.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Composition of Aspirin 300mg tablets prepared by DC</th>
</tr>
</thead>
<tbody>
<tr>
<td>S. No.</td>
<td>Ingredients</td>
</tr>
<tr>
<td>1.</td>
<td>Aspirin</td>
</tr>
<tr>
<td>2.</td>
<td>Lactose</td>
</tr>
<tr>
<td>3.</td>
<td>Corn starch</td>
</tr>
<tr>
<td>4.</td>
<td>Aerosil</td>
</tr>
<tr>
<td></td>
<td>Total</td>
</tr>
</tbody>
</table>
of weight which is indicative of mechanical strength to withstand this type of wear.

**Disintegration Test**

Disintegration time was measured by putting 6 tablets of each of the studied formulation separately in basket rack assembly (Erweka ZT-2, Germany) using disks to avoid floating of tablets in 900 ml distill water maintained at 37±2°C.

**Dissolution Test**

Dissolution of commercially available brands and formulated aspirin tablets was measured by paddle method in dissolution apparatus (Erweka GmbH, Germany) using 0.05M acetate buffer solution 500 mL (pH 4.5) at 50 rpm, maintained at 37±0.5°C. After 30 minutes the absorbance of suitably diluted portions in same medium was determined against absorbance of standard preparation at 265nm using UV-VIS Spectrophotometer (Shimadzu UV-150-02 Double beam spectrophotometer).

**Assay**

Twenty tablets were accurately weighed and than triturated in a mortar with pestle, amount equivalent to 100 mg of aspirin was transferred to a 50 mL volumetric flask, diluted by 20 mL of diluting solution (acetonitrile and formic acid 99:1). The volumetric flask was shaken manually, centrifuged at 3000 rpm for 5 minutes and than the stock prepared was diluted. An aliquot of the diluted solution was injected into a liquid chromatograph with a detector set at 280 nm. The responses were compared with the standard to determine the quantity in mg of aspirin present in the sample.

**RESULTS AND DISCUSSION**

Although aspirin formulation is manufactured by dry method which involves few steps as compare to wet granulation, yet there is a wide variation among the cost of various brands available in the local market. Thus, the purpose of the present work was to formulate aspirin formulation by DC using a simplified formula that contains only few ingredients and from the finding further work will be planned by varying the composition using optimization until a perfect formulation of this drug is obtained. Various excipients are available for DC method, we selected those excipients that are used commonly. Since the major part of the formulation is active ingredient (75%), the remaining bulk is adjusted by the excipients (25%). These include lactose, corn starch and aerosol. Microcrystalline cellulose/lactose in formulations gives improved average potency compared to microcrystalline cellulose/dicalcium phosphate anhydrous (Morris et al., 2009). Tablets containing lactose showed rapid disintegration (Kamp et al., 1986). Starch, commonly used as binder, offers various advantages such as its abundance, inexpensiveness, relative inertness and no reaction with majority of active drug substances that promote its use for pharmaceuticals as directly compressible material as indicated by many workers (Haware et al., 2009, Elvira et al., 2002, Korhonen et al., 2000, Sanghvi et al., 1993). Incorporation of glidants in direct compression formulations is aimed to improve powder flow and control tablet weight. Due to their small particle size and extremely low-density silica-type glidants are most efficient among several other groups (Sheth et al., 1980, Varthalis and Pilpel 1977). Gazikolović et al., presented results of lithium carbonate tablets made by DC concluding that lactose and corn starch give best properties to tablets (Gazikolović et al., 1999). In another evaluation best characteristics were observed in calcium acetate tablets prepared by DC and wet granulation method using maize starch (Obrenovic et al., 2000).

All the trial batches (T1, T2 and T3) were easily compressed on single punch machine and the resulting tablets were evaluated using pharmacopoeial and nonpharmacopoeial tests. The weight variation test is simplified and alternative to content uniformity test to assure therapeutic utility (Katori et al., 2001) and is an indicator of variations in the drug content
Since various factors effect uniformity of weight of single-unit dose, pharmacopoeias have established standards and specifications that provide permissible limits for weight variation. All the trial batches complies weight variation test according to specification given in the USP pharmacopeia 2005 (USP 28/NF 23, 2005). The weight of twenty tablets (X±S.D) of the trial batches and the commercial brands are given in Table 3. A close resemblance in tablet weight is evident from the Table 3. Following Figure represents weight of tablets versus number of tablets of one trial batch (T1) for illustration. It appears that the compression weight of B3 is lower as compare to other commercial brands studied in the present work but all of these likewise our batches found to fulfill the requirements of weight variation test as stated by the US pharmacopoeia.

The diameter, thickness and hardness (X ±SD) ranged from: 1.14±0.0425cm to 1.61±0.0348cm (B1 and B5), 0.44±0.0690cm to 0.71±0.0922cm (B4 and B2), 2.17±0.4514Kg to 6.94±1.4276Kg (B1 and B5) while friability ranged from 0.23% to 0.58% (B2 and B1), for commercial brands, 1.33±0.0638cm to 1.34±0.0639cm (T1 and T2), 0.38±0.2541cm to 0.39±0.2499cm (T3 and T2), 4.74±1.2541Kg to 4.90±1.7986Kg (T2 and T3) while friability ranged from 0.24% to 0.31% (T1 and T3) for trial batches, respectively. Comparison of these values for trial batches shows no difference in diameter, hardness and friability as all these are within

### Table 2
**Unofficial Tests**

<table>
<thead>
<tr>
<th>Formulation Code</th>
<th>Diameter (cm) X ±SD, n = 10</th>
<th>Thickness (cm) X ±SD, n =10</th>
<th>Hardness (Kg) X ± SD, n = 10</th>
<th>Friability (%) n=20</th>
</tr>
</thead>
<tbody>
<tr>
<td>B1</td>
<td>1.14±0.0425</td>
<td>0.56±0.0438</td>
<td>2.17±0.4514</td>
<td>0.58</td>
</tr>
<tr>
<td>B2</td>
<td>1.59±0.0205</td>
<td>0.71±0.0922</td>
<td>4.84±1.0368</td>
<td>0.23</td>
</tr>
<tr>
<td>B3</td>
<td>1.56±0.0394</td>
<td>0.58±0.0410</td>
<td>6.26±1.8616</td>
<td>0.24</td>
</tr>
<tr>
<td>B4</td>
<td>1.16±0.0940</td>
<td>0.44±0.0690</td>
<td>4.41±0.7790</td>
<td>0.52</td>
</tr>
<tr>
<td>B5</td>
<td>1.61±0.0348</td>
<td>0.70±0.0343</td>
<td>6.94±1.4276</td>
<td>0.26</td>
</tr>
<tr>
<td>T1</td>
<td>1.33±0.0638</td>
<td>0.38±0.2541</td>
<td>4.74±1.2541</td>
<td>0.24</td>
</tr>
<tr>
<td>T2</td>
<td>1.34±0.0639</td>
<td>0.39±0.2499</td>
<td>4.67±1.1918</td>
<td>0.28</td>
</tr>
<tr>
<td>T3</td>
<td>1.34±0.0328</td>
<td>0.38±0.0850</td>
<td>4.90±1.7986</td>
<td>0.31</td>
</tr>
</tbody>
</table>

### Table 3
**Official Tests with permissible limits (USP 28/NF 23, 2005)**

<table>
<thead>
<tr>
<th>Formulation Code</th>
<th>Weight (g) X ± SD, n = 20</th>
<th>Average Disintegration time (Sec.), n=6</th>
<th>Average Dissolution (%), n=6</th>
<th>Assay n=20</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>±5 %</td>
<td>Within 30 minutes</td>
<td>Not less than 80%</td>
<td>95-105%</td>
</tr>
<tr>
<td>B1</td>
<td>0.37±0.0056</td>
<td>13</td>
<td>85.09</td>
<td>97.28</td>
</tr>
<tr>
<td>B2</td>
<td>0.38±0.0103</td>
<td>15</td>
<td>78.07</td>
<td>96.74</td>
</tr>
<tr>
<td>B3</td>
<td>0.33±0.0061</td>
<td>10</td>
<td>89.08</td>
<td>98.88</td>
</tr>
<tr>
<td>B4</td>
<td>0.36±0.0082</td>
<td>10</td>
<td>99.08</td>
<td>100.11</td>
</tr>
<tr>
<td>B5</td>
<td>0.36±0.0057</td>
<td>15</td>
<td>81.01</td>
<td>97.21</td>
</tr>
<tr>
<td>T1</td>
<td>0.40±0.0215</td>
<td>20</td>
<td>100.65</td>
<td>99.07</td>
</tr>
<tr>
<td>T2</td>
<td>0.39±0.0261</td>
<td>15</td>
<td>95.00</td>
<td>97.01</td>
</tr>
<tr>
<td>T3</td>
<td>0.40±0.0125</td>
<td>20</td>
<td>91.00</td>
<td>96.05</td>
</tr>
</tbody>
</table>
the range of the commercial brands. Only thickness of the trial batches differs yet not far from commercial brands (Table 2).

After physical test the tablets were subjected to chemical tests that include assay, disintegration and dissolution. Assay of the tablet indicates amount of active in the composite sample, our results of assay shows that both the formulations under study meets the official requirement of the assay (95% to 105%) as shown in the Table 3. Disintegration evaluates availability of a drug for dissolution and absorption from the gastrointestinal tract (Block, 2007). When disintegration data was evaluated, the results revealed rapid disintegration of some brands. In case of Commercial brands, B3 and B4 took short time to disintegrate i.e; 10 seconds, B1 took 13 seconds while B2 and B5 both took 15 seconds (Table 3). The trial batches T1 and T3 took similar (20 Sec.) but slightly higher time to disintegrate as compare to T2 (15 Sec.). All meets disintegration limits as set by USP (USP 28/NF 23, 2005). Fast disintegration is required for analgesics in order to get a prompt effect. Finally, when the dissolution test was carried out for commercial brands, B2 showed least dissolution rate i.e. 78%, thus failing pharmacopoeial requirements while highest percentage release was obtained by B4 which is 99%. The remaining brands give more than 80% release of the active within 30 minutes. Dissolution of trial batches was found to be better than most of commercial brands tested (range: 91% to 101% for T3 and T1.

![Fig. Weight of tablets v/s No. of Aspirin Tablets (T1)](image)

$\bar{x} = 0.400 \quad \sigma = 0.012

\bar{x} + 1\sigma = 0.412 \quad \bar{x} + 2\sigma = 0.424

\bar{x} - 1\sigma = 0.388 \quad \bar{x} - 2\sigma = 0.376 \quad \bar{x} - 3\sigma = 0.364

\text{Upper Limit (+5%)} = 0.42 \quad \text{Lower Limit (-5%)} = 0.38$
respectively), this might be due to the use of few excipients. Rapid disintegration of tablets favors high dissolution rates.

**CONCLUSION**

In the present work, aspirin tablets using fewer excipients were manufactured successfully that fulfills all the pharmacopoeial limits. This type of study may also be done on other drugs to get a cost effective product. Further work using optimization technique is recommended for future studies using present data as a reference guide.

**ACKNOWLEDGEMENTS**

We are grateful to Yasir Faraz Abbasi, Department of Pharmacy, Ziauddin Medical University, Karachi, Pakistan for his co-operation and useful suggestions.

**REFERENCES**


