STUDIES ON THE EFFECTS OF CYCLODEXTRIN POLYMER AS A TABLETING AID ON SOME SELECTED ANALGESICS

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ABSTRACT
The clinical effectiveness of tablets depends on at least two factors; (i) the medication must be present in labeled amount (ii) it must be available to the body. The drug availability is usually determined by the rate of release of drug from the tablet, which is governed by the processes of disintegration and dissolution.

In present study, the effect of β-Cyclodextrin on disintegration and rate of dissolution of analgesic tablets (paracetamol) have been studied. The results show that the tablets containing β-Cyclodextrin polymer as a disintegrant enhances the rate of dissolution and reduces the disintegration time as compared to the commercially available tablets which lack β-Cyclodextrin.

Keywords: Disintegration, Dissolution rate, β-Cyclodextrin, Analgesic tablets, Paracetamol.

INTRODUCTION
The analgesics and antipyretic drugs include a small, heterogenous group of compounds which are without significant addiction liability, and therefore are not subject to regulation under the controlled substances Act. Most of these agents affects both pain and fever. Consequently, they are widely used for minor aches and pains, headaches, and the general feeling of malaise that accompanies febrile illnesses, and to alleviate symptoms of rheumatic fever, arthritis, gout and other musculoskeletal disturbances.

The number of non-steroidal anti-inflammatory drugs (NSAIDs) has increased to the point where they warrant a separate classification. All of these drugs inhibit the synthesis of prostaglandins.

Paracetamol is included in this category of drugs (Swingard, 1985). It is a popular domestic analgesic and antipyretic for adults and children. Its analgesic therapeutic efficacy is equal to that aspirin aspirin but in therapeutic doses, it has no useful anti-inflammatory effects, i.e., it inhibits prostaglandins synthesis in the brain but hardly at all in the periphery. Paracetamol is effective in mild to moderate pain such as that of headache or dysmenorrhoea and it is also useful in patients who should avoid aspirin because of gut intolerance, a bleeding tendency or allergy, or because they are aged under 12 years.

Paracetamol having half-life 2 h, is well absorbed from alimentary tract and is inactivated in the liver principally by conjugation as glucuronide and sulphate. Minor metabolites of paracetamol are also found of which one oxidation product, N-acetyl-p-benzoquinone-imine, is highly reactive chemically (Laurence and Benette, 1992).

In recent years, absorption enhancer have been actively investigated. In present investigation, β-Cyclodextrin is investigated as a disintegrant which enhances dissolution rate, ultimately resulting in the enhancement of absorption. Faster the drug is absorbed, quicker it produces therapeutic effect. Pain is a
Studies on the Effects of Cyclodextrin Polymer

Problem with which the sufferer wants to be relieved as quick as possible, so analgesic drug was chosen for the present study. But β-Cyclodextrin can be used as a disintegrant in other classes of drug also.

**MATERIAL AND METHODS**

All the materials used in this study were of analytical grade.

The method used to prepare tablets on laboratory scale was wet granulation method. There were in total, three types of formulation.

Three different ratios of Lactose corn starch, gelatin and β-Cyclodextrin were used (Table-1) which are as follows:

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Ingredients</th>
<th>Formulation No. 1 (per tablet)</th>
<th>Formulation No. 2 (per tablet)</th>
<th>Formulation No. 3 (per tablet)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Paracetamol</td>
<td>0.5 g</td>
<td>0.5 g</td>
<td>0.5 g</td>
</tr>
<tr>
<td>2.</td>
<td>Lactose</td>
<td>0.125 g</td>
<td>0.625 g</td>
<td>0.1 g</td>
</tr>
<tr>
<td>3.</td>
<td>Corn starch</td>
<td>0.025 g</td>
<td>0.075 g</td>
<td>0.05 g</td>
</tr>
<tr>
<td>4.</td>
<td>Gelatin</td>
<td>0.75 g</td>
<td>0.075 g</td>
<td>0.05 g</td>
</tr>
<tr>
<td>5.</td>
<td>β-Cyclodextrin</td>
<td>0.25 g</td>
<td>0.0375 g</td>
<td>0.05 g</td>
</tr>
<tr>
<td>6.</td>
<td>Talc</td>
<td>0.005 g</td>
<td>0.005 g</td>
<td>0.005 g</td>
</tr>
<tr>
<td>7.</td>
<td>Mg. stearate</td>
<td>0.0025 g</td>
<td>0.0025 g</td>
<td>0.0025 g</td>
</tr>
</tbody>
</table>

All the formulations were compressed at some pressure with all other ingredients in a similar ratio including 500mg paracetamol as an active ingredient.

Each batch was tested for official and unofficial tests and compared with standard paracetamol 500mg tablets available in local market, as described elsewhere (Fatima et al, 2004).

All the studies were carried out according to the specifications of individual monograph stated in British Pharmacopoeia (2002) Vol. I.
RESULTS AND DISCUSSION

The Pharmacopoeial and non-pharmacopoeial control tests were used to evaluate the paracetamol tablets for the uniformity of weight, thickness, diameter, friability, hardness, % drug content, disintegration time and dissolution rate. The tests were performed on both experimental and standard brand tablets for a comparative study. The analytical data is given in Tables 2, 3 and 4. A comparative study can be made from the graph.

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Formulations</th>
<th>Disintegration Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Exp. Batch # 1</td>
<td>13 minutes</td>
</tr>
<tr>
<td>2.</td>
<td>Exp. Batch # 2</td>
<td>10 minutes</td>
</tr>
<tr>
<td>3.</td>
<td>Exp. Batch # 3</td>
<td>08 minutes</td>
</tr>
<tr>
<td>4.</td>
<td>Exp. Batch # 4</td>
<td>15 minutes</td>
</tr>
</tbody>
</table>

Table-3
Disintegration Times of Different Batches

Graph

From the results it was found that all the tablets were of an average weight 600mg (+5%) which is in agreement with the B.P limits. The deviation in thickness and diameter is within +5%. This is tolerable for the normal manufacturing practices.

In all formulations, values for active ingredient are with ±5% which is in confirmation with the limits given in B.P (2002) Vol. II.

When the tablets were evaluated for the uniformity of hardness, it was found that all tablets lie within x ± 25 limits. Table-1 shows that, the greater the hardness of the tablets, the lesser is the percentage friability. The possible reason for this result may be that, at high compressional force the granules are packed strongly together and there is low degree of crumbling during friability test. Percentage friability of all the batches lie within the limits i.e., < 1 %.

The disintegration time determines whether tablets or capsules disintegrate within prescribed time when placed in a liquid medium under the prescribed experimental conditions (King and Schwitz, 1985).

In our study β-Cyclodextrin is used as disintegrant and the results show that the disintegration time decreases as the quantity of β-Cyclodextrin increases.

Like the disintegration time, the dissolution test does provide a means of control in assuming that a given tablet formulation is the same as regards dissolution as the batch of tablets shown initially to be clinically effective. It also provides on in vitro control procedure to eliminate variations among production batches (Banker and Anderson, 1986).

It is clear from Table-2 that the dissolution rate of our experimental tablets containing β-Cyclodextrin is increased. This result is concordant with the results obtained by other workers, who used β-Cyclodextrin to increase the dissolution rate. Kenya et al

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Formulations</th>
<th>5 Minutes</th>
<th>10 Minutes</th>
<th>15 Minutes</th>
<th>20 Minutes</th>
<th>25 Minutes</th>
<th>30 Minutes</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Exp. Batch # 1</td>
<td>40.5</td>
<td>56.7</td>
<td>72</td>
<td>–</td>
<td>87.3</td>
<td>95.4</td>
</tr>
<tr>
<td>2.</td>
<td>Exp. Batch # 2</td>
<td>45</td>
<td>–</td>
<td>75.6</td>
<td>84.6</td>
<td>–</td>
<td>94.3</td>
</tr>
<tr>
<td>3.</td>
<td>Exp. Batch # 3</td>
<td>59.4</td>
<td>72.4</td>
<td>83.2</td>
<td>–</td>
<td>96.3</td>
<td>99.0</td>
</tr>
<tr>
<td>4.</td>
<td>Exp. Batch # 4</td>
<td>52.2</td>
<td>61.2</td>
<td>67.5</td>
<td>73.4</td>
<td>–</td>
<td>81.3</td>
</tr>
</tbody>
</table>

Table-4
Percent Dissolution at Different Time Intervals
Studies on the Effects of Cyclodextrin Polymer (1989), used β-Cyclodextrin and PVP to enhance the dissolution rate of tolbutamide (Kenya et al., 2000).

Paola et al (2005) used a combination of drug-cyclodextrin-arginine to improve the dissolution rate of naproxen, a poorly water soluble anti-inflammatory drug (Paola et al., 2005).

Yun-Shang et al (2004) investigated the effect of cyclodextrins on the solubility of flavonal veronicafolin in water and found that Hydroxy-propyl- β-cyclodextrin dramatically increased the solubility of flavonol, where as β-Cyclodextrin decreased its solubility. Similarly Katsutoshi (2003) enhanced the solubility of YM 466 in aqueous solution by the addition of cyclodextrin polymer (Katsutoshi 2003). Moreover Ghorab and Christionah (2003) found that in vivo results are far better than in vitro due to the effect of bile salts when ibuprofen cocranulated with β-Cyclodextrin (Ghorab and Christianah, 2003).

CONCLUSION

This study and other investigations show that β-Cyclodextrin is a suitable disintegrant for a variety of drugs. The solubalities, disintegration and dissolution rate of poorly water soluble drugs are found to be increased by utilizing β-Cyclodextrin as a tableting aid.

REFERENCES


