<table>
<thead>
<tr>
<th>Serial No</th>
<th>ISSN:0006-6648</th>
</tr>
</thead>
<tbody>
<tr>
<td>Author 1</td>
<td>OFOEFULE, S. I</td>
</tr>
<tr>
<td>Author 2</td>
<td>OKAFOR, I. S</td>
</tr>
<tr>
<td>Author 3</td>
<td>UDEALA, O. K</td>
</tr>
<tr>
<td>Title</td>
<td>A Comparative Study of Modified Starches in Direct Compression of a Water Soluble Drug- Chloroquine Phosphate</td>
</tr>
<tr>
<td>Keywords</td>
<td>Modified Starches; Chloroquine Phosphate; Direct Compression; Tablets Dissolution</td>
</tr>
<tr>
<td>Description</td>
<td>A Comparative Study of Modified Starches in Direct Compression of a water Soluble Drug- Chloroquine Phosphate</td>
</tr>
<tr>
<td>Category</td>
<td>Biological Science</td>
</tr>
<tr>
<td>Publisher</td>
<td>Bollettino Chimico Farmaceutico</td>
</tr>
<tr>
<td>Publication Date</td>
<td>2000</td>
</tr>
</tbody>
</table>
BOLLETTINO CHIMICO FARMACEUTICO
Fondato da E. Vescardi nel 1861
Rivista di Scienze Farmaceutiche e Biologiche

ESTRATTO

6
Novembre/Dicembre 2000
VOLUME
139

Società Editoriale Farmaceutica
Via Ausonio, 12 - 20123 Milano
A comparative study of modified starches in direct compression of a water soluble drug-chloroquine phosphate

I.S. Okafor1, S.I. Ofoefule2, O.K. Udeala2

1 Dept. of Pharmaceutics and Pharmaceutical Technology, University of Jos, Nigeria
2 Dept. of Pharmaceutics Technology and Industrial Pharmacy, University of Nigeria, Nsukka, Nigeria

*Correspondence
Preveasie in Rezalzione il 3 settembre

ABSTRACT

Some in vivo properties of chloroquine phosphate tablets formulated with four modified starches were investigated. The drug was formulated into tablets containing 250 mg of chloroquine phosphate and produced by the direct compression technique. The starches were isolated from maize, rice, rye, Oryza sativa, Triticum turgidum, and Xanthosoma sagittifolium. They were modified through physicochemical means. Sta-Rx 1500, a finely compressible starch was used as basis for comparison. The hardness of the chloroquine tablets generally decreased to a minimum with the modified starches at concentration level of 40% and with maximum hardness obtained when their concentration was increased to 60%. The least hardness values were obtained with modified xylana starch while the highest hardness values were obtained with modified rice starch. Modifying rice and cassava starches produced chloroquine tablets that exhibited higher mechanical properties than those of modified maize starch, curdlan starch and Sta-Rx 1500. On the basis of dissolution profile of chloroquine phosphate tablets, the modified starch samples were ranked in order of increasing dissolution in modified xylanase and Sta-Rx 1500 causes a rise in starch samples. The release rate of chloroquine was found to be dependent on the physicochemical properties of the individual modified starch granules in a particle size and degree of gelatinization.

KEY WORDS: Modified starches; Chloroquine phosphate; Direct compression; Tablets; Dissolution.

INTRODUCTION

The introduction of direct compression as a method of tablet manufacture has stimulated interest in the area of excipients. These excipients are in most cases modified natural products. The currently marketed direct compression excipients may be classified as follows:

A) Lactose modifications (Fast-Fl o lactose, Lactose for direct compression)
B) Sucrose modifications (Di-Pac, NaT Tab)
C) Cellulose products (Avicel, Emodex)
D) Starch products (Acasta, Emodex, Sta-Rx 1500, anylose)
E) Inorganic salts (Emcompress, compacted)

Excipients used in direct compression are generally evaluated on the basis of flowability, compressibility, dissolution characteristics, particle size and size distribution and other characteristics. Soludex, anylose microcrystalline cellulose and compressible starch have been evaluated as directly compressible excipients in this way. The physicochemical properties, and the flow and compression characteristics of the starches used in this work as well as their application to the direct tabletting of saccharic acid tablets have been reported previously.

Chloroquine phosphate is a relatively high dose, water soluble and a poorly compressible soluble drug. It is generally administered as tablets containing 250 mg of active drug with appropriate quantities of excipients. It is usually formulated by the wet granulation technique. In this study, attempt was made to tablet the drug by the direct compression technique using the modified starch as the only filler-binder-disintegrant.

MATERIALS AND METHODS

Preparation of tablets.

Materials

Sta-Rx 1500, a brand of compressible starch (A.E. Staley Manufacturing Co., Decatur, Illinois); Chloroquine phosphate B.P. (Bayer, Germany); Searic acid (Baker Co., U.S.A.); Magnesium stearate B.P. (Amed Drug and Chemical Co., U.S.A.); and Aerosil (De Gussa Inc., New Jersey, U.S.A.) and modified starches obtained according to the procedure described below.
Methods: extraction and modification of the starchy

The individual starch samples were extracted using standard techniques, and defatted according to the method of Schaal. A 40% w/w slurry of each starch sample in dihydroxyacetone solution was heated to 60 °C with constant stirring for 4 hr, or a water bath. The reaction mixture was cooled and neutralized to a pH of 7.0 with dilute sodium hydroxide solution. The recovered starch was washed and dried at 60 °C for 6 hr.

Preparation of chloroquine phosphate tablets

All batches of chloroquine phosphate tablets were produced by the direct compression technique. The following formula was used for the production of the tablets:

<table>
<thead>
<tr>
<th>Component</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chloroquine</td>
<td>250.00 mg</td>
</tr>
<tr>
<td>Modified starch</td>
<td>154.00 mg</td>
</tr>
<tr>
<td>Stearic acid</td>
<td>1.36 mg</td>
</tr>
<tr>
<td>Magnesium stearate</td>
<td>1.04 mg</td>
</tr>
<tr>
<td>Acetate</td>
<td>2.08 mg</td>
</tr>
</tbody>
</table>

In this formulation, the mixture of excipients and drug without the lubricants (stearic acid and magnesium stearate) was preheated for 5 min in a mortar mixer (Polaris Equipment Co., Leicester, England). The predetermined quantities of the lubricants were then added after being baked through at 75-85 mm aperture sieve at increased surface area. Blending was continued for 5 min. A combination of 0.25% magnesium stearate, 2.0% stearic acid and 0.5% Acetate when employed as lubricants, as employed in this study is reported to be ideal for tablets, as employed in this study is reported to be ideal for tablets containing high proportion of starch (2, 8). An F-3 single punch tabletting machine (Manesty Machines, England) fitted with 9.5 mm normal concave-faced punches were used to compress the tablets at a fixed compressional load.

The target tablet weight was ±16.48 mg. The disintegration time and dissolution rate of the tablets were evaluated 24 hr after the tablets have been made.

Hardness and friability measurements

Ten tablets randomly selected from each batch were assessed for hardness using an Erweka electronic hardness tester, while friability of ten tablets randomly selected from each batch and subjected to abrasive shock in an Erweka Friabilator operated at 25 r.p.m. for 4 min.

Disintegration time studies

The disintegration time of the tablets was determined by the O. P. method using the Erweka disintegration apparatus (Erweka apparatus GTV Model) and 0.1N HCl as the disintegration medium.

The apparatus has the facility for testing six tablets simultaneously.

The test was performed three times and the average of the longest disintegration time within each group of six tablets was recorded.

Dissolution profile studies

The dissolution rate of the tablets was monitored using a USP XX dissolution apparatus (Erweka DTD Model). The dissolution medium was 1000 ml of 0.1N HCl maintained at 37 °C. The revolution of the basket containing the test tablet was ±21 r.p.m. Aliquots of the dissolution medium were withdrawn at predetermined time intervals. Each volume of each sample withdrawn was replaced with an equivalent volume of dissolution medium maintained at the same temperature. The absorbance of the samples were read at 343 nm using a UV spectrophotometer (SP 6200, Pye Unicam, England). Six dissolution studies were performed on the tablets for each batch and the average percent drug dissolved plotted against time to generate a dissolution curve.

RESULTS AND DISCUSSIONS

Initially, the effect of varying the proportion of chloroquine phosphate-modified starch content in each tablet on the hardness of tablets was investigated. Fig. 1 shows the result obtained for the four modified starches including Sta-Rx 1500 which was used as basis for comparison. The hardness of the chloroquine phosphate-modified starch tablets decreased initially as the concentration of modified starch increased up to 40% w/w modified starch content. Above this level of starch content, the hardness of the tablets increased. The strongest tablets were obtained from

---

Fig. 1: Effect of Starch Content on the hardness of direct compression chloroquine phosphate tablets containing modified □ Maize, △ Cassava, □ Cocoyam, X Rice, • Sta-Rx 1500 starch samples
compression mixtures containing 80% w/w modified starch for all starch samples. Chloroquine phosphate tablets containing 250 mg of the drug and 37% w/w modified starch had high thickness/diameter ratio. Equally, tablets containing 50% w/w of the starch had similar high
thicknes to diameter ratio which maximum compression force of
the machine was used. When the starch content was less than 37% w/w lubrication was a problem as the tablets were
adhesive to the punchies and dies. Chloroquine phosphate
tablets containing 250 mg of the drug and 37% w/w modified
starch were found to possess reasonable size and lubrication.

Unfortunately, the friability of these tablets did not follow
any particular trend and their values were omitted for clarity.
Chloroquine phosphate tablets formulated with the modified starch samples disintegrated within 4 min (Table 1).

The official disintegration time allowed for this type of
tablets is 15 min. Thus all batches of tablets passed the
Disintegration Test. The high rate of disintegration of the tablets may be attributed to the high level of modified starch in the tablets. The state of starch as a disintegrate is usually
2-8% w/w. In the formulation used for the disintegration test, the modified starch was present in a 37% w/w composition in each case. The modification process
employed for the starches did not destroy their disintegrant properties.

The disintegration times for tablets formulated with modified
rice, cassava and rice-starch-starch samples were 3.2, 3.1 and 3.3 min respectively. The corresponding disintegration
times for tablets made with modified maize and
coconut-maize grains were 2.8 and 3.0 min respectively.

The order of efficiency of disintegration of chloroquine
phosphate tablets was therefore modified maize-cassava rice
Sta-Rx 1500.

The dissolution profiles of chloroquine phosphate tablets
containing 37% w/w modified starch samples are shown in
Fig. 2. Three dissolution parameters, namely, dissolution
efficiency (D.E.) after 15 min, T50 and T90 values were
considered for evaluating the dissolution characteristics of the tablets. Table 1 shows the D.E., T50 and
T90 values obtained for the tablets. A 99 percent drug re-
solution was obtained for formulations containing modified
cassava starch after 15 min. Formulations containing modified
rice and Sta-Rx 1500 released 98 and 99 percent of the drug respectively after the same period of time.

The corresponding percent release for formulations con-
taining modified cassava and rice starch samples were 94
and 93 respectively at the end of the same time period.

These results show fast release of chloroquine phosphate
used to estimate when half of the drug contained in a dosage form has dissolved. The T90, on the other hand, is the time taken for 90 percent of the drug in the dosage form to dis-

Table 1: Disintegration and disintegration characteristics of directly compressed 250 mg chloroquine phosphate tablets

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Sta-Rx 1500</th>
<th>Maize</th>
<th>Cassava</th>
<th>Rice</th>
<th>Coconut</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disintegration time (min)</td>
<td>3.3</td>
<td>2.8</td>
<td>3.1</td>
<td>3.2</td>
<td>3.0</td>
</tr>
<tr>
<td>Dissolution Efficiency (D.E.) % at 15 min</td>
<td>96.0</td>
<td>98.0</td>
<td>94.0</td>
<td>93.0</td>
<td>99.0</td>
</tr>
<tr>
<td>T50 (min)</td>
<td>5.5</td>
<td>5.0</td>
<td>5.0</td>
<td>6.5</td>
<td>5.0</td>
</tr>
<tr>
<td>T90 (min)</td>
<td>11.5</td>
<td>9.0</td>
<td>12.5</td>
<td>13.5</td>
<td>9.0</td>
</tr>
</tbody>
</table>

254
from the tablets. No binding of the drug onto the modified starches is indicated.

The T90 values obtained were 5.0 min each for formulations containing modified maize, cassava and cocoyam starch samples; and 5.5 and 6.5 min for those formulations which Sta-Rx 1500 and modified rice starch respectively were used. Dissolution results presented in Table I also indicate that the T90 values range from 9.0 min for formulations containing modified cocoyam starch to 13.5 min for those in which modified rice starch was used. On the basis of these, the modified starches are ranked in order of increased release of chloroquine phosphate from tablets as cocoyam maize Sta-Rx 1500 cassava rice starch samples.

The granule size of starch is known to influence the disintegration of tablets containing starch. The smaller the granule size, the faster is the disintegration process because more pores would be made available for the penetration of water into the tablet. Rice starch granules are the smallest in size of the four starches investigated. This is followed by those of cocoyam starch. The granule size of the other starch samples are essentially similar. A previously published work on these modified starches showed that the proportion of gelatinized rice starch granules at the temperature employed in the modification process was high compared with those of the other starches. This may have retarded the dissolution of chloroquine phosphate from tablets containing this starch. A low rate of hydration is often the case with gelatinized starch. The proportion of cocoyam starch granules of this starch may have brought about the high release rate of chloroquine phosphate observed with this starch. The many pores created by the granules of this starch should facilitate the penetration of water into the tablet with consequent disintegration of tablet and dissolution of the drug. Similar results were obtained for the release of ascorbic acid from tablets containing modified starches. It may be concluded that these modified starches are very efficient in releasing chloroquine phosphate from tablet dosage forms. This release rate is dependent on the physicochemical properties of the individual modified starch granules.

Acknowledgment

The authors are grateful to the technical staff of the Department of Pharmaceutical Technology and Industrial Pharmacy, University of Nigeria, Nsukka and to Mr. G.E. Nwanadi who typed the manuscript.

References


Bell. Chem. Pharm. - Ann 139 - n. 6 November/December 2000 255