A comparative in vitro drug release prospective with two different polymers for the development of floating single unit dosage form of imatinib mesylate for chronic myelogenous leukemia
Vinod KR, Santosh V, Sandhya S, Otilia BJ, David B, Padmasri A

Conocimiento sobre tabaco y sus métodos de deshabituación entre los estudiantes de 1º, 3º y 5º curso de Farmacia en España. Estudio PRECOTABAC. Parte II.

Formulation and evaluation of controlled release matrix tablet of diltiazem HCl by using HPMC and guar gum as polymeric matrix material.
Shah UH, Patel BK, Patel MR

Binding of desloratadine and atenolol with bovine serum albumin and their in-vitro interactions
Shihab-us-Sakib K, Islam MA, Moniruzzaman M, Hussein A, Hossain M, Mazid MA

Analysis and evaluation of prescriptions in Al-Ahsa (Saudi Arabia)
Sangi S, Turki M, Otaibi G, Hazoom MAK, Harsha S

Artículo Especial

Vaginistis: Etiología, diagnóstico y profilaxis
Martin Villena MJ, Morales Hernández ME, Clares Naveros B, Ruiz Martínez MA
Formulation and evaluation of controlled release matrix tablet of diltiazem HCl by using HPMC and guar gum as polymeric matrix material.

Shah UH¹, Patel BK¹, Patel MR².
1. Ramanbhai Patel College of Pharmacy, Charotar University of Science and Technology, CHARUSAT Campus, (Anand, Gujarat, India)
2 B.M.Shah College of Pharmaceutical Science and Research, (Modasa, SK, Gujarat, India)

RESUMEN

Objetivos: En el presente trabajo se describe el desarrollo de comprimidos matriciales de clorhidrato de diltiazem.

Métodos: Se obtienen comprimidos matriciales mediante el uso de goma guar y HPMC. Se estudian distintas formulaciones en las que se cambia la composición de estos materiales matriciales como controladores de la cesión. Los comprimidos se prepararon por el método de granulación húmeda y se evaluaron uniformidad de contenido, índice de hinchamiento, estabilidad y velocidad de liberación.

Resultados: La capacidad de hinchamiento aumenta con el porcentaje utilizado de HPMC. Las formulaciones F7, F8 y F9 son las que muestran mejores características de liberación. Los estudios de estabilidad de la formulación seleccionada demuestran una buena resistencia a la rotura, capacidad de hinchamiento y control de la velocidad de disolución durante el estudio de estabilidad.

Conclusiones: Las formulaciones F7, F8 y F9 tienen unas buenas propiedades de control de liberación del fármaco durante al menos 8 horas. La cinética de liberación se pueden ajustar a un orden cero.

PALABRAS CLAVE: HPMC, goma guar, Diltiazem HCl, comprimidos matriciales, liberación controlada.

ABSTRACT

Aim: The present investigation concerns the development of controlled release matrix tablet of Diltiazem HCl.

Methods: Matrix tablet of Diltiazem HCl was formulated by using HPMC and Guar gum as a polymeric matrix forming materials in various concentrations (%w/w) to study their ability to retard the release. The tablets were prepared by wet granulation method and evaluated for physical properties, content uniformity, swelling index, stability and in-vitro drug release.

Results: Swelling was increased as the concentration and viscosity of HPMC increases. Tablets formulated using guar gum and HPMC alone were gave initial burst effect followed by controlled release for 8 hr. It was evident from the study that the formulations F7, F8 & F9 have optimum swelling index and in vitro drug release up to 44% in 8hrs. The stability studies of optimized batch showed that there was no change in hardness, swelling index and in-vitro release up to 12 weeks.

Conclusions: The batches F7, F8 and F9 possessed the high potential to release the drug gradually for more than 8 hours. The zero-order release kinetic indicates concentration independent drug release ensuring that the formulated tablet showed promising result to be a sustained release formulation.

KEY WORDS: HPMC, Guar gum, Diltiazem HCl, controlled release, matrix tablets.
INTRODUCTION

Diltiazem HCl, an orally active calcium channel-blocking agent, is used in treatment of angina pectoris (variant & classical angina), hypertension and arrhythmias.\(^1,2\) It is highly water soluble drug and is rapidly and almost completely (60-70%) absorbed from GIT, followed by oral administration, but undergoes extensive hepatic metabolism. The biological half-life of drug is 3.5 ± 1.2 h\(^3\). It is typically administered three or four times daily, in the form of conventional tablet. Thus frequently administration leads to constant change in blood concentration. To overcome the frequently administration and to minimize the peak to through oscillation of the blood concentration, control release formulation are developed. So, it has desired duration of action and localize the dosage form in a specific region and control the release rate of drug.\(^3\)

Guar gum is natural gum and chemically; it is galactomannan polysaccharide. The gum consists of the pulverized endosperm of the seed of C. tetragonolobus. Guar Gum forms viscous colloidal dispersions when hydrated in cold water. It is used as a thickening agent for lotions and creams in concentration up to 2.5%, tablet binder (10%), emulsion stabilizer (1%). Chemically; HPMC is mixed alkyl-hydroxyalkyl cellulose ether containing methoxyl and hydroxypropyl groups. HPMC also forms viscous colloidal solution in cold water. It is used as a film former (2-10%), binder (2-5%). High viscosity grades are used to retard the release of water-soluble drugs. The present study aim to formulating controlled release matrix tablet of Diltiazem HCl, with the controlled release soluble matrix material (HPMC and Guar gum).\(^4\)

MATERIAL AND METHODS

Materials

Diltiazem HCl was obtained as a gift sample from Sun pharmaceuticals Ltd, Baroda, India. HPMC K4M (Methocel®K4M) was obtained from Colorcon Asia Pvt. Ltd, Goa. Guar gum was obtained from the laser chemicals, Baroda. All other chemicals used were analytical grade and double distilled water used throughout the experiments.

Preparation of controlled release tablets of diltiazem

Controlled release tablets were prepared by wet granulation method. Hydroxypropyl methylcellulose, Guar gum was used as retardant material for preparation of tablets. Other excipients were dicalcium phosphate, magnesium stearate as a lubricant and talc as a glident. Distilled water was employed as a granulating fluid.

For preparation of controlled release tablets of Diltiazem, drug and polymer were weighed accurately, mixed thoroughly then other excipients were added and mixed by triturating. The resultant mixture was granulated by using distilled water and wetted mass pass through the 20 mesh sieve and retained on 40 mesh sieve. Then it was dried at 60°C for half an hour in an oven and processed to get 20:40 mesh granules. The dried 20:40 granules were mixed with glident(talc) and lubricant (Magnesium stearate). After mixing compressed into tablets using a Rotary tablet machine (Rimek Rotary tablet machine RSB-4 mini press) 12 mm die, and punches were used 400 mg is adjusted as a weight of each tablet and hardness between 3-5 kg/cm\(^2\).\(^5,6\) The composition of formulation is shown in (Table-1). These matrix tablets were evaluated for their physical properties (Table-2).

Evaluation of formulation:

Physical parameters:

Tablets were tested for hardness, friability, weight variation and drug content. Hardness of the tablets was tested using a Monsanto hardness tester and Friability of the tablets was determined in a Roche friabilator (Model EF2, Electrolab, Mumbai, India).\(^7\)

Drug content:

The prepared tablets were analyzed for Diltiazem HCl contents. Tablets were crushed into fine powders and

<table>
<thead>
<tr>
<th>Ingredients</th>
<th>F1</th>
<th>F2</th>
<th>F3</th>
<th>F4</th>
<th>F5</th>
<th>F6</th>
<th>F7</th>
<th>F8</th>
<th>F9</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diltiazem HCl</td>
<td>120</td>
<td>120</td>
<td>120</td>
<td>120</td>
<td>120</td>
<td>120</td>
<td>120</td>
<td>120</td>
<td>120</td>
</tr>
<tr>
<td>Hydroxy propyl m unl cellulose</td>
<td>30</td>
<td>30</td>
<td>30</td>
<td>40</td>
<td>40</td>
<td>40</td>
<td>50</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>Guar gum</td>
<td>30</td>
<td>40</td>
<td>50</td>
<td>30</td>
<td>40</td>
<td>50</td>
<td>30</td>
<td>40</td>
<td>50</td>
</tr>
<tr>
<td>Di-Calcium Phosphate</td>
<td>211</td>
<td>201</td>
<td>191</td>
<td>201</td>
<td>191</td>
<td>181</td>
<td>191</td>
<td>181</td>
<td>171</td>
</tr>
<tr>
<td>Talc</td>
<td>6</td>
<td>6</td>
<td>6</td>
<td>6</td>
<td>6</td>
<td>6</td>
<td>6</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>Magnesium stearate</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>% of polymer to the total tablet weight</td>
<td>15%</td>
<td>17.5%</td>
<td>20%</td>
<td>17.5%</td>
<td>20%</td>
<td>22.5%</td>
<td>20%</td>
<td>22.5%</td>
<td>25%</td>
</tr>
</tbody>
</table>

F1 to F9 = Designed different batches according to different polymeric HPMC: Guar gum ratio
Diltiazem HCl was extracted into water by shaking the crushed powder with water in a volumetric flask. The solution was filtered out and diluted with water and estimated in UV-Spectrophotometer (UV-1601, Shimadzu, Japan) at 235 nm after suitable dilution.\(^8\)

**Swelling index:**
The extent of swelling was measured in terms of % weight gain by the tablet. The swelling behavior of formulation F1 to F9 was studied. One tablet from each formulation was kept in a Petri dish containing pH 7.2 phosphate buffers. At the end of 1 hr, the tablet was withdrawn, kept on tissue paper and weighed. Then for 2 hr and every 2 hr, weights of the tablet were noted and the process was continued for 8 hr. The % weight gain by the tablet was calculated by formula.\(^9\)

\[
S.I = \frac{(M_t - M_0)}{M_0} \times 100 \quad (1)
\]

Where, \(S.I\) = Swelling index; \(M_t\) = weight of tablet at time \(t'\); \(M_0\) = weight of tablet at time \(t = 0\)

Swelling behavior of controlled release matrix tablets were represented in Figure 2.

**In-vitro drug release studies:**
A tablet was placed in USP XXIII paddle-type dissolution test apparatus (Model TDL-08, Electro lab, Mumbai, India) and immersed in 900 ml of dissolution media phosphate buffer (pH 7.2), maintained at 37°C ± 0.5°C. Aliquot samples were withdrawn every hour up to a period of 8 hours. After each withdrawal, the withdrawn amount of dissolution media was replaced with buffer. The absorbance of the withdrawn samples, after appropriate dilution was measured at 237 nm against appropriate buffer blanks.\(^10,11\)

**Stability study**
Optimized batch of Diltiazem HCl tablets (Formulation F7 to F9) were kept for a short term stability study in high density polyethylene sealed cover at 40 ± 2 °C / 75 ± 5% RH as per ICH Guidelines. Samples were withdrawn for six and twelve weeks of storage and evaluated for appearance, drug content and in vitro dissolution.

**RESULT AND DISCUSSION:**
Controlled release matrix tablets were evaluated for its
Table 3. Comparison of r² value of zero order Vs Higuchi’s diffusion equation

<table>
<thead>
<tr>
<th>Batch No</th>
<th>Zero order r²</th>
<th>Higuchi’s diffusion r²</th>
</tr>
</thead>
<tbody>
<tr>
<td>F7</td>
<td>0.9944</td>
<td>0.9728</td>
</tr>
<tr>
<td>F8</td>
<td>0.970</td>
<td>0.935</td>
</tr>
<tr>
<td>F9</td>
<td>0.992</td>
<td>0.977</td>
</tr>
</tbody>
</table>

Table 4. Stability study of batch F7 to F9

<table>
<thead>
<tr>
<th>Formulation</th>
<th>Parameter</th>
<th>F7</th>
<th>F8</th>
<th>F9</th>
<th>F7</th>
<th>F8</th>
<th>F9</th>
<th>F7</th>
<th>F8</th>
<th>F9</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hardness( kg/cm²)</td>
<td>3.95 ± 0.62</td>
<td>3.80 ± 0.38</td>
<td>3.80 ± 0.68</td>
<td>4.20 ± 0.28</td>
<td>4.20 ± 0.80</td>
<td>69.63 ± 0.085</td>
<td>74.2 ± 0.023</td>
<td>80.5 ± 0.012</td>
<td>80.75 ± 0.019</td>
</tr>
<tr>
<td>After 6 week</td>
<td>Swelling index</td>
<td>40.91</td>
<td>44.85</td>
<td>43.13</td>
<td>40.25</td>
<td>44.69</td>
<td>42.80</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
use as pharmaceutical excipients in the formulation and manufacturing of controlled release matrix tablets of Diltiazem HCl. The batches F7, F8 and F9 possessed the high potential to release the drug gradually for more than 8 hours. It confirmed the fact that the formulated tablet showed promising result to be a sustained release formulation. It is evident from overall studies that hydroxy propyl methyl cellulose (HPMC) and guar gum possess potential for sustained release of Diltiazem HCl from the matrix tablet.

REFERENCES: