Preparation and evaluation of microparticles containing Oxybutynin Chloride for controlled release

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ABSTRACT:
In the present research, an attempt has been made to prepare microparticles of Oxybutynin chloride. Particulate technologies have often proven popular among the oral controlled drug delivery technologies because of their simplicity, easy in manufacturing, high level of reproducibility and easy of scale up and process validation. Oxybutynin chloride is antimuscarinic and antispasmodic drug used for the treatment of urine incontinence in women. Different formulations were prepared by solvent evaporation method by using different ratios of drug and polymer (HPMC K45M, Ethyl Cellulose). The prepared microparticles were evaluated for drug polymer compatibility, the results shown that there were no significant interactions. The encapsulation efficacy was ranging from 56-96%. The in-vitro drug release studies indicate the release of drug in a controlled manner over a period of 12 hrs. It was found that the Oxybutynin release rate increased with a decreased amount of polymer. This can be adjusted by maintaining the concentration of the polymers.

Keywords: Oxybutynin chloride, HPMC K45M, Ethyl Cellulose, Particulate matrix, Controlled release.

INTRODUCTION:
In the recent years, considerable attention has been focused on the development of Novel Drug Delivery Systems (NDDS). The reason for this paradigm shift is due to the low development cost and time required for developing a NDDS for the existing drugs, rather than developing a new drug molecule. In the form of NDDS, existing drug molecule can get a new life, thereby increasing the market value and product patent.

Controlled drug delivery systems containing polymeric carriers has gained increased interest in last two decades, because they can be fabricated into films, rods capsules and microparticles, they mask the unacceptable taste or odor of drugs, they stabilize drugs sensitive to oxygen, moisture or light, they eliminate incompatibilities among drugs. Oxybutynin reduces muscle spasms of the bladder and urinary tract. Oxybutynin is used to treat symptoms of overactive bladder, such as frequent or urgent urination, incontinence and increased night-time urination. It competitively antagonizes the M1, M2, and M3 subtypes of the muscarinic receptor. It also has direct spasmolytic effects on bladder smooth muscle as a calcium antagonist and local anesthetic. Here an attempt was made to reduce the dosing frequency and to maintain the drug level at therapeutic concentration range, by formulating a Controlled drug delivery system in the form of microparticles using blend of HPMC and ethyl cellulose. The mixture of polymeric materials HPMC and ethyl cellulose used in the current study have good pharmaceutical and biological properties.

METHODS
Determination of λ max of Oxybutynin chloride in pH 7.4 buffer
Stock solution of Oxybutynin chloride in pH 7.4 buffer (100 mg in 100 ml) was prepared. From the stock solution 30 µg/ml solution of was prepared in pH 7.4 buffer and scanned between the wavelength of 200-400 nm.

Preparation of microparticles:
Oxybutynin chloride microparticles were used by solvent evaporation technique. Different ratios of HPMC and Ethyl cellulose combination were dissolved in 8.5 ml acetone separately and dispersed by using a magnetic stirrer. The core material, Oxybutynin chloride was added to the polymer solution and mixed for 15 minutes, followed by mag.

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nesium stearate (100mg) and then mixed thoroughly. The resulting dispersion was added in a thin stream to a mixture of 90 ml liquid light paraffin and 10 ml n-hexane contained in a 250 ml beaker, while stirring at 700 rpm using a mechanical stirrer. Stirring was continued for 3 hrs until the acetone evaporated completely. The microspheres formed were filtered using Whatman no.1 filter paper. The residue was washed 4-5 times with 50 ml portions of n-hexane. The product was then dried at room temperature for 24 hours.

<table>
<thead>
<tr>
<th>Formulation No.</th>
<th>Ingredients in (mg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Oxybutynin chloride</td>
</tr>
<tr>
<td>F1</td>
<td>2.5</td>
</tr>
<tr>
<td>F2</td>
<td>2.5</td>
</tr>
<tr>
<td>F3</td>
<td>2.5</td>
</tr>
<tr>
<td>F4</td>
<td>2.5</td>
</tr>
<tr>
<td>F5</td>
<td>2.5</td>
</tr>
<tr>
<td>F6</td>
<td>2.5</td>
</tr>
</tbody>
</table>

Table 1: Formulation chart of Oxybutynin chloride loaded microspheres

**In vitro drug release studies**

Release of Oxybutynin chloride was determined using dissolution test apparatus USP type II at 100 rpm. The dissolution was studied using 900 ml of 0.1 N HCl, phosphate buffer 5.5, phosphate buffer pH 7.2. The temperature was maintained at 27±0.5°C. Aliquots (10 ml) of dissolution media were sampled at specified time intervals and replaced with fresh media immediately after sampling. Samples were analyzed for drug content by UV Visible spectroscopy.

**RESULTS AND DISCUSSION**

**Ultraviolet spectroscopy:**

Accurately weighed 10 mg of Oxybutynin chloride was transferred to a 100 ml volumetric flask and 1% tween80 was added to increase the solubility of Oxybutynin chloride (stock solution). 3ml of stock solution was added to the 50ml volumetric flask and volume adjusted up to the mark with phosphate buffer. The scanning was done from 200-400 nm. The sharp peak was observed at 220.0 nm, which was taken as λ max.

**Drug-excipient Compatibility Studies:**

The compatibility of drug and polymers under experimental conditions is important prerequisite before formulation. It is therefore necessary to confirm that the drug does not react with the polymers and excipients under experimental conditions and affect the shelf life of product or any other unwanted effects on the formulation. The DSC thermograms of the pure drug and formulation were taken, the obtained results indicates that there were no significant interactions between drug and polymer.

**Drug loading and encapsulation efficiency**

100 mg of microparticles were weighed and transferred to 100 ml volumetric flask containing pH 7.4 phosphate buffer. From this, 1 ml of solution was transferred to 10 ml volumetric flask and diluted up to the mark. Further 1 ml of this solution was diluted to 10 ml and absorbance was measured. The drug content was calculated by using the formula:

\[
\text{Amount of drug = Conc. from standard graph} \times \text{X dilution factor} / 1000
\]

Percentage encapsulation efficiency is found out by calculating the amount of drug present in 100 mg of microparticles. It is further calculated by using formula

\[
\% \text{Encapsulation Efficiency} = \frac{b}{a} \times 100
\]

Where, ‘a’ is the theoretical drug content and ‘b’ is the drug entrapped.

increase in the polymer concentration. From the results it can be inferred that there is a proper distribution of Oxybutynin chloride in the microparticles and the deviation is within the acceptable limits. The decrease in the drug content in the product probably can be due to the loss of drug with the evaporation of the solvent.

<table>
<thead>
<tr>
<th>Formulation</th>
<th>Drug loading (%) mean ± SD*</th>
<th>Encapsulation efficiency (%) mean ± SD*</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1</td>
<td>57.74±0.23</td>
<td>95.23±0.36</td>
</tr>
<tr>
<td>F2</td>
<td>42.26±0.18</td>
<td>70.43±0.25</td>
</tr>
<tr>
<td>F3</td>
<td>40.68±0.24</td>
<td>67.80±0.24</td>
</tr>
<tr>
<td>F4</td>
<td>33.85±0.21</td>
<td>56.41±0.17</td>
</tr>
<tr>
<td>F5</td>
<td>57.38±0.29</td>
<td>97.96±0.21</td>
</tr>
<tr>
<td>F6</td>
<td>50.82 ±0.27</td>
<td>86.36 ±0.19</td>
</tr>
</tbody>
</table>

Table 2: Drug loading and encapsulation efficiency of prepared microparticles

In-vitro drug dissolution:
Release of Oxybutynin chloride was determined using dissolution test apparatus USP type II at 100 rpm. The dissolution was studied using 900 ml of 0.1 N HCl, phosphate buffer 5.5, phosphate buffer pH 7.2. The temperature was maintained at 27±0.5°C. The sample were withdrawn at different time intervals 1, 2, 3, 4, 6, 8, 10 and 12 hrs filtered through whatman filter paper and replaced equal volume of dissolution medium. Sample was suitably diluted and analyzed for Oxybutynin chloride using UV-visible spectrophotometer. The percentage of Oxybutynin chloride release was calculated.

<table>
<thead>
<tr>
<th>Dissolution Medium</th>
<th>Time (hrs)</th>
<th>% Cumulative Drug Release</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.1N HCl</td>
<td>1</td>
<td>3.94</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>8.25</td>
</tr>
<tr>
<td>5.5 pH buffer</td>
<td>3</td>
<td>13.34</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>23.52</td>
</tr>
<tr>
<td>7.2 pH buffer</td>
<td>6</td>
<td>49.14</td>
</tr>
<tr>
<td></td>
<td>8</td>
<td>67.63</td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>82.41</td>
</tr>
<tr>
<td></td>
<td>12</td>
<td>95.05</td>
</tr>
</tbody>
</table>

Table 3: In-vitro drug release profile of the formulations

CONCLUSION:
The objective of this study was to prepare and evaluate microparticles loaded with Oxybutynin chloride for controlled release using HPMC and Ethyl cellulose by solvent evaporation method using different ratios of drug to polymer and prepared microparticles were characterized. The method is simple, rapid, and economical and does not imply the use of toxic organic solvents. The method used was suitable for both water-soluble and insoluble drugs.

The Drug to polymer blend ratio of 2.5:10:5(F5) produced discrete spherical microparticles. The DSC thermogram obtained for the pure drug and formulation shows no significant shift in the endothermic peaks confirming the stability of the drug in the formulation. From the results of drug content determination, it can be inferred that there was a proper and uniform distribution of drug in the micro particles. The in vitro drug release data showed the release of a drug in a controlled manner.

REFERENCES: