CHAPTER VI
PREPARATION AND CHARACTERIZATION OF CROSS LINKED STARCH UREA Polymers, which are used as release-retarding materials in the design of controlled release drug delivery systems, play a vital role in controlling the delivery of drug from the systems. The success of controlled drug delivery systems depends on how well the polymer regulates the release of drug from the systems. Though a wide range of polymers and other release retarding polymers are available there is a continued need to develop new and more efficient release retarding polymers for controlled release. In the present investigation a new modified starch namely cross-linked starch urea was prepared and evaluated for its application in the formulation of floating tablets. Studies carried out on the preparation and characterizations of cross-linked starch urea are described in this Chapter.

EXPERIMENTAL
Materials:
- Potato starch (LobaChemie)
- Urea (Qualigens)
- Calcium Chloride I.P.
- All other materials used were of pharmacopoeial grade.
Methods
Preparation of Crosslinked Starch-Urea Polymer

Potato starch (9 parts) was dispersed in purified water (10 parts) to form starch slurry. Urea (1 part), calcium chloride (1 part) were dissolved in purified water (40 parts) and the solution was heated to boiling. While boiling, the starch slurry was added and mixed. Mixing while heating was continued for 20 minutes to form cross-linked starch-urea polymer. The mass formed was spread on to a stainless steel plate and dried at 85°C for 6-8 h. The dried polymer was powdered and passed through mesh No. 120.

Characterization of cross-linked starch urea

The cross-linked starch urea prepared was characterized by microscopic examination, chemical and physical tests to determine its melting point, solubility, swelling index, pH, viscosity and various micromeritic properties namely bulk density, tap density, compressibility index and angle of repose and also by FTIR spectr a.

1. Microscopic examination

(i) Slurry (1%) of each of (i) potato starch and (ii) cross-linked starch urea in a mixture of equal volumes of glycerin and water were prepared. A smear of the slurry was made and examined under microscope. Photomicrographs of potato starch and crosslinked starch urea are shown in Figs: 6.3–6.4.
1. Introduction

2. Chemical test:
Iodine test: A slurry of cross-linked starch urea in water was treated with iodine test solution. A reddish violet colour was observed indicating the presence of α-amylase.

3. Melting point:
Melting point of cross-linked starch urea was determined in a melting point apparatus.

4. Solubility:
Solubility was tested in water, aqueous buffers of pH 1.2 and 7.4, methanol, petroleum ether, dichloromethane, cyclohexane and chloroform.

5. Swelling index:
Cross-linked starch urea (1g) was taken into two graduated 25ml measuring cylinders, one containing petroleum ether and other containing water and stored for 24 h. Swelling index of cross-linked starch urea was determined using the formula:

\[
\text{Swelling index (\%)} = \left( \frac{V_w - V_0}{V_0} \right) \times 100
\]

Where, \(V_0\) is the volume of the sediment in petroleum ether and \(V_w\) is the volume of the sediment in water.

6. pH:
The pH of a 0.1% w/v aqueous dispersion was measured.
Viscosity of a 0.1%w/v homogenized dispersion was determined using Ostwald Viscometer.

Density was determined by liquid displacement method using petroleum ether as liquid.

Bulk and tap density was determined by 3 tap method in a graduated cylinder.

Compressibility index was determined by measuring the initial volume (Vo) and final volume (V) after 100 tappings of a sample of crosslinked starch urea in a measuring cylinder. Compressibility index was calculated using the equation.

Angle of repose was determined by fixed funnel method. The physical and micromeritic properties of crosslinked starch urea prepared are summarized in Table 6.1.

Infrared Spectroscopy: FTIR spectra of crosslinked starch urea was recorded on a Perkin Elmer, IR Spectrophotometer Model: Spectrum RXI, using KBr disc as reference.
<table>
<thead>
<tr>
<th>S.No</th>
<th>Property</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Iodine test</td>
<td>Positive indicates the presence of α-amylose</td>
</tr>
<tr>
<td>2</td>
<td>Melting point</td>
<td>Charred at 210°C</td>
</tr>
<tr>
<td>3</td>
<td>Solubility</td>
<td>Insoluble in water, aqueous fluids of acidic and alkaline pHs and in organic solvents</td>
</tr>
<tr>
<td>4</td>
<td>Swelling index</td>
<td>Swells in water with a swelling index of 630.2%</td>
</tr>
<tr>
<td>5</td>
<td>pH of 0.1% aqueous dispersion</td>
<td>9.10</td>
</tr>
<tr>
<td>6</td>
<td>Viscosity of a 0.1% aqueous dispersion</td>
<td>1.013 cps</td>
</tr>
<tr>
<td>7</td>
<td>Density</td>
<td>0.516 g/cc</td>
</tr>
<tr>
<td>8</td>
<td>Bulk density</td>
<td>0.735 g/cc</td>
</tr>
<tr>
<td>9</td>
<td>Compressibility index</td>
<td>13.89%</td>
</tr>
<tr>
<td>10</td>
<td>Angle of repose</td>
<td>26.0°-27.0°</td>
</tr>
</tbody>
</table>

Note: The table above summarizes physical and micromeritic properties of cross-linked starch-urea.
Fig 6.2: Photo Micrograph of Potato Starch (Stained with Saffranin)
Fig. 6.3: Photomicrograph of the crosslinked starch urea blend.
RESULTS AND DISCUSSION
Starch urea cross-linked with calcium was prepared by gelatinizing potato starch in the presence of urea and calcium chloride. It is known that starch reacts with urea to form starch carbamate, a starch urea polymer. Khalil et al. investigated the reactions between starch and urea resulting in the formation of starch urea (starch carbamate). The reactions involved are as follows:

$$\text{heat} \quad 2 \text{NH}_2 \text{OCONH}_2 \text{St} \leftrightarrow 2 \text{NH}_2 \text{COOH} \text{St}$$

$$\text{heat} \quad 2 \text{NH}_2 \text{StOCONH}_2 \text{StOCONH}_2 \text{St} \leftrightarrow 2 \text{NH}_2 \text{StOCONH}_2 \text{StOH} \text{St}$$

Where St OH is starch.

Starch urea was cross-linked by treatment with calcium chloride. The formation of cross-linked starches with calcium salts is known in polymer chemistry. As the cross-linked polymers generally swell in water and aqueous fluids and form gelatinous matrices suitable for controlled release, it is thought worthwhile to investigate starch urea cross-linked with calcium chloride for its application in controlled release floating tablets. In the present study it was evaluated as matrix forming polymer in the preparation of floating tablets. The crosslinked starch urea prepared was found to be fine, hard and free flowing crystalline powder. It gave a positive iodine test indicating the presence of α-amylose. The FTIR spectra of cross linked starch urea is shown in Fig. 6.1. The presence of IR absorption peaks at 3369.05 cm$^{-1}$ due to –NH$_2$ and at 1668.72 cm$^{-1}$ due to –C=O stretch indicated the presence of urea in the polymer. The peaks at...
The C-H and C-O-C stretching vibrations
of α-amylose starch are indicated by the peaks at 2925.84
and 1271.99 cm$^{-1}$, respectively. These bands are
characteristic of the starch structure and indicate the
presence of α-amylose. When tested for melting point,
cross-linked starch urea charred at 210°C.

Microscopic examination indicated that potato starch
consists of oval shaped grains (Fig. 6.2). Whereas
crosslinked starch urea consists of rectangular,
transparent crystals (Fig. 6.3).

The physical and micromeritic properties of
crosslinked starch urea prepared are summarized
in Table 6.1. It was insoluble in water, aqueous fluids
of acidic and alkaline pHs. It was insoluble in
organic solvents like methanol, petroleum ether,
dichloromethane, cyclohexane and chloroform. The
pH of a 0.1% aqueous dispersion was 9.10.

Crosslinked starch urea exhibited good swelling
in water. The swelling in dextrose was 630.2%. All
micromeritic properties indicated good flow and
compressibility needed for solid dosage form
manufacturing.

As crosslinked starch urea is insoluble and has
good swelling in water, it is considered suitable
as release retarding and rate controlling matrix
polymer for floating tablets.

REFERENCES
1. Abdel-Thalouth, I., El-Kashouti, M.A. and Hebeish, A., Starch,
2. Hebeish, A., Refai, R., Ragab, A. and Abdel Thlouth, I., Starch,
3. Khalil, M.I., Farag, S., Mostafa, Kh. M. and Hebeish, A., Starch,
1994, 46, 312-316.