CHAPTER IV

POLYMERS INVESTIGATED FOR APPLICATION IN FLOATING TABLETS

POLYMERS IN CONTROLLED RELEASE

Controlled drug delivery is a topic of current interest in pharmaceutical technology. Controlled release drug delivery systems are those formulations designed to release an active ingredient at rates, which differ significantly from their corresponding conventional dosage forms. The controlled release drug delivery systems are aimed at controlling the rate of drug delivery, sustaining the duration of therapeutic activity and/or targeting the delivery of the drug to a tissue. Drug release from these systems should be at a desired rate, predictable and reproducible. Polymers which are used as release retarding and rate controlling materials in the design of controlled release dosage forms play a vital role in controlling the delivery of drug from these dosage forms.

Characteristics of ideal polymer system\(^1,2\):

- It should have good mechanical strength.
- It should be chemically inert and free from leachable impurities.
- It should be non-toxic and compatible with body environment.
- It should be easy and inexpensive to fabricate.
- It should be easily sterilizable.

Types of polymers:

Polymers have been broadly classified as natural and synthetic polymers.

a. Natural polymers: These include nucleic acids, proteins, polysaccharides and complexes of proteins and polysaccharides.
b. **Synthetic polymers:** They include polyesters, polyurethanes, polyamides, polycarbonates, poly siloxanes, polyvinyl compounds and acrylics.

**Classification of Polymers:**

**Non-biodegradable hydrophobic polymers:**

These are inert in the environment of use and are eliminated or extracted intact from the site of administration and serve essentially as rate limiting barriers to the transport and release of drug from the device.

**Eg:** Polyethylene vinyl acetate (EVA), Polydimethyl siloxane (PDS), Polyurethane (PEU), Ethyl cellulose (EC), Cellulose acetate (CA), Polyethylene (PE), Polyvinyl chloride (PVC), etc.

**Hydrogels:**

These swell but do not dissolve when brought in contact with water. They are inert, removed intact from the site of administration and function by forming a rate limiting barrier to the transport and release of drugs.

**Eg:** Polyhydroxyethyl methacrylate (p-HEMA), cross-linked polyvinyl alcohol (PVA), cross-linked polyvinyl pyrrolidone, Polyacrylamide, Dextran, etc.

**Soluble polymers:**

These are moderate polymers without cross links that dissolve in water. These materials can be used alone or in combination with other hydrophobic polymers to provide devices that slowly erode over time.
**Eg:** Polyethylene glycol (PEG), uncross-linked Polyvinyl alcohol, Polyvinyl pyrrolidone (PVP), Hydroxypropyl methylcellulose (HPMC), copolymers of Methacrylic acid and Acrylic acid methyl ester (Eudragit L), etc.

**Biodegradable polymers:**

They slowly disappear from the site of administration; however this disappearance occurs in response to a chemical reaction such as hydrolysis.

**Eg:** Polylactic acid (PLA), Polyglycolic acid (PGA), Polycaprolactone (PCL), several generic classes such as the Polyanhydrides and Polyorthoesters.

**Mucoadhesive polymers:**

Certain polymers become adhesive on hydration and exhibit the property of bioadhesion, i.e. adhesion to a biological tissue or membrane by interfacial forces. In the case of polymer attached to the mucin layer of a mucosal tissue, the term mucoadhesion is used.

**Eg:** Methylcellulose, hydroxyethyl cellulose, hydroxy propyl methyl cellulose, sodium carboxy methyl cellulose, carbomers, chitosan, Poly (acrylic acid, coacrylamide), copolymers, carrageenan, sodium alginate, guar gum polyanhydrides and polylactic acid

Polymers used in oral controlled release systems are summarized in Table 4.1
<table>
<thead>
<tr>
<th>Method of achieving controlled release</th>
<th>Polymer used</th>
<th>Examples of dosage forms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Matrix or Embedding</td>
<td>MethylCellulose, SodiumCMC, CarboxymethylCellulose, Hydroxypropylmethylcellulose, HydroxyethylCellulose, MethacrylateHydrogels, Polyethylene glycols, Galactose mannate, Sodiumalginate, Polyacrylic acid</td>
<td>Multilayer tablets with slow releasing cores, Compression–coated tablets</td>
</tr>
<tr>
<td>(a) Hydrophilic Carriers</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(i) Soluble Carrier (digestible base)</td>
<td>Glycerides, waxes, fatty alcohols, fatty acids</td>
<td>Matrix tablets</td>
</tr>
<tr>
<td>(ii) Insoluble Carrier (non digestible base)</td>
<td>Polyethylene, polyvinyl chloride, polyvinyl acetate, waxes, calcium sulfate</td>
<td></td>
</tr>
<tr>
<td>(b) Hydrophobic Carriers</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reservoir Type</td>
<td>Ethyl Cellulose</td>
<td>Granules, pellets, tablets</td>
</tr>
<tr>
<td>Coating with insoluble membrane</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Osmotic Systems</td>
<td>Vapour permeable walls</td>
<td>Vapour permeable capsules</td>
</tr>
<tr>
<td>----------------------------------------</td>
<td>----------------------------------------------------------------------------------------</td>
<td>----------------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td></td>
<td>Tenite 808A polyethylene</td>
<td>Vapour permeable tablets</td>
</tr>
<tr>
<td></td>
<td>Kynar 460 polyvinylidene</td>
<td>Single and bilayer tablets</td>
</tr>
<tr>
<td></td>
<td>Flouride</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Hydroxypropyl methyl cellulose</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Hydroxypropyl cellulose</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sodium carboxymethyl cellulose</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ethyl cellulose</td>
<td></td>
</tr>
<tr>
<td>Ion – exchange Resins</td>
<td>Dowex 50, 1, 2</td>
<td>Controlled release capsules</td>
</tr>
<tr>
<td></td>
<td>Amberlite IRC 50</td>
<td>Chewable tablets</td>
</tr>
<tr>
<td></td>
<td>With polystyrene – based polymeric backbone</td>
<td>Chewable gums</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Liquid suspension</td>
</tr>
<tr>
<td>Gastric retention Systems</td>
<td>Hydroxypropyl methyl cellulose, Agar, carrageenans, Alginic acid, Oils, porous</td>
<td>Compressed tablets</td>
</tr>
<tr>
<td></td>
<td>calcium silicate, Superporous hydrogels,</td>
<td>Gelatin capsules</td>
</tr>
<tr>
<td></td>
<td>Ion-exchange resin beads coated with bicarbonate, Ethyl cellulose for coatings</td>
<td></td>
</tr>
</tbody>
</table>
In the present investigation two new polymers namely (i) olibanum (a natural gum-resin) and (ii) cross-linked starch urea (a modified starch) were evaluated as matrix formers in the design of controlled release floating tablets in comparison to a widely studied polymer, HPMC K15M. These polymers are described in this chapter.

HPMC K15M and olibanum were procured from commercial sources. Cross-linked starch urea was prepared in the laboratory. The preparation and characterization of cross-linked starch urea were also described in this chapter.
HYDROXY PROPYL METHYL CELLULOSE

O-methylated and O-(2-hydroxypropylated) cellulose

**Structural Formula**

![Structural Formula](image)

Where R is H, CH₃, or CH₃CH (OH) CH₂

**Synonyms:** Hydroxy propyl methylcellulose; HPMC; Methocel; Hypermellose; Methylcellulose propylene glycol ether; Methyl hydroxypropylcellulose; Metolose; Tylopur.

**Grades:** Methocel K100 Premium LVEP, K15M, K4M, K100M, E3, E5, E6, E15, E50 Premium LV, E4M, F50 Premium, E10M Premium CR, Metolose 60SH, 65SH, 90SH

**Physicochemical properties:**

**Melting point:** Browns at 190–200°C; Chars at 225–230°C

**Density:** 0.341 g/cm³

Glass transition temperature: 170–180°C
Acidity/alkalinity: pH 5.5–8.0 for a 1% w/w aqueous solution.

Ash: 1.5–3.0%, depending upon the grade and viscosity.

Moisture content: Hypromellose absorbs moisture from the atmosphere; the amount of water absorbed depends upon the initial moisture content and the temperature and relative humidity of the surrounding air.

Specific gravity: 1.26

Solubility: Soluble in cold water, forming a viscous colloidal solution; practically insoluble in chloroform, ethanol (95%), and ether, but soluble in mixtures of ethanol and dichloromethane, mixtures of methanol and dichloromethane, and mixtures of water and alcohol. Certain grades of hypromellose are soluble in aqueous acetone solutions, mixtures of dichloromethane and propan-2-ol, and other organic solvents.

Viscosity: A wide range of viscosity types are commercially available. Aqueous solutions are most commonly prepared, although hypromellose may also be dissolved in aqueous alcohols such as ethanol and propan-2-ol provided the alcohol content is less than 50% w/w. Dichloromethane and ethanol mixtures may also be used to prepare viscous hypromellose solutions. Solutions prepared using organic solvents tend to be more viscous; increasing concentration also produces more viscous solutions.

Stability and Storage Conditions: Hypromellose powder is a stable material, although it is hygroscopic after drying. Solutions are stable at pH 3–11. Increasing temperature reduces the viscosity of solutions. Hypromellose undergoes a reversible sol–gel transformation upon heating and cooling, respectively. The gel point is 50–90°C, depending upon the grade and concentration of material. Aqueous solutions are
comparatively enzyme-resistant, providing good viscosity stability during long-term storage. However; aqueous solutions are liable to microbial spoilage and should be preserved with an antimicrobial preservative: when hypromellose is used as a viscosity-increasing agent in ophthalmic solutions, benzalkonium chloride is commonly used as the preservative. Aqueous solutions may also be sterilized by autoclaving; the coagulated polymer must be redispersed on cooling by shaking. Hypromellose powder should be stored in a well-closed container, in a cool, dry place.

**Applications in Pharmaceutical Formulation or Technology**

Hypromellose is widely used in oral, ophthalmic and topical pharmaceutical formulations.

In oral products, hypromellose is primarily used as a tablet binder, in film-coating, and as a matrix for use in extended-release tablet formulations. Concentrations between 2% and 5% w/w may be used as a binder in either wet- or dry-granulation processes. High-viscosity grades may be used to retard the release of drugs from a matrix at levels of 10–80% w/w in tablets and capsules.

Depending upon the viscosity grade, concentrations of 2–20% w/w are used for film-forming solutions to film-coat tablets. Lower-viscosity grades are used in aqueous film-coating solutions, while higher-viscosity grades are used with organic solvents. Examples of film-coating materials that are commercially available include AnyCoat C, Spectracel, and Pharmacoat.
Hypromellose is also used as a suspending and thickening agent in topical formulations. Compared with methylcellulose, hypromellose produces aqueous solutions of greater clarity, with fewer undispersed fibers present, and is therefore preferred in formulations for ophthalmic use. Hypromellose at concentrations between 0.45–1.0% w/w may be added as a thickening agent to vehicles for eye drops and artificial tear solutions.

Hypromellose is also used as an emulsifier, suspending agent, and stabilizing agent in topical gels and ointments. As a protective colloid, it can prevent droplets and particles from coalescing or agglomerating, thus inhibiting the formation of sediments.

In addition, hypromellose is used in the manufacture of capsules, as an adhesive in plastic bandages, and as a wetting agent for hard contact lenses. It is also widely used in cosmetics and food products.
OLIBANUM - A NATURAL GUM RESIN FOR CONTROLLED RELEASE

Olibanum is a gum resin obtained from *Boswellia serrata*, Roxburgh and other species of *Boswellia*.

**Classification**¹⁶:

- **Kingdom**: Plantae
- **Division**: Angiospermae
- **Class**: Dicotyledoneae
- **Order**: Geraninales
- **Family**: Burseraceae
- **Genus**: *Boswellia*
- **Species**: *serrata*

**Synonyms:**

Salai guggal, an oleo-gum-resin from *Boswellia serrata* is also known as Frankincense in English and Olibanum in Arabian.

**Biological source:**

*Boswellia serrata* belongs to family Burseraceae.

**Geographical source:**

About 10 species of genus *Boswellia* occurs in tropical parts of Asia and Africa. The plant grows widely on dry hills throughout India, especially in Maharashtra (Vidarbh), Orissa, Rajasthan, Gujarat and south India.

**The plant**¹⁷,¹⁸

It is a medium sized but highly branching tree (Figs. 4.1 & 4.2). It grows upto 12-15 feet in height. The type of leaves distinguishes Indian olibanum into two varieties
called var. serrata, having pubescent and serrate leaves and var. Glabra having glabrous and entire leaves. It is a deciduous medium–sized tree, with ash colored bark, 1–2 meters in diameter, peeling off in thin flakes. The leaves are opposite, variable in shape, resembling to those of nimba leaves, ovate or lanceolate. The flowers are small, fragrant, and white, in axillary racemes. The fruits are trigonous drupes, triangular, 1 cm in diameter and three-valued. The seeds are hard, compressed and pendulous.

The commercially used olibanum is the solidified olio gum-resin exuded from the tree (Fig. 4.3). A good quality is of golden colour and is transparent (Fig. 4.4). The colour varies from golden yellow to dark brown or to dark greenish brown.
Fig. 4.1: *Boswellia serrata* Plant
Fig. 4.2: *Boswellia serrata* Plant leaves and its trunk
Fig. 4.3: *Boswellia serrata* and its trunk with resin exudation
Fig. 4.4: Olibanum gum
Method of preparation:

Oleo-gum-resin is obtained by tapping process between November and June. The average yield per tree per annum is maximum upto 1 kg. The trees with more girth and stunted growth have low yields for exudation, shaving are done, at 2.5 feet height, every after 4-5 days.

Description:

The oleo-gum-resin of Indian olibanum has following characters and compositions:

- Colour : Golden to dark brown
- Odour : Turpentine like, agreeable on burning
- Moisture : 10 -11 %
- Volatile oil : 8 -9 %
- Gum : 20 -23 %
- Resin : 55 %
- Insoluble matter : 4 -5 %
- Melting point : 73 -78°C

Plant part used:

Bark, gum-resin

Chemical constituents:\n
Olibanum contains 8-9 % essential oil, 20-23 % gum, and about 50 % resin.

Properties and Uses:

The bark is sweet, acrid, cooling and tonic. It is good for vitiated conditions of pitta, asthma, dysentery, ulcers, haemorrhoids and skin disease. The gum resin is sweet,
bitter, astringent, antipyretic, antidysenteric, expectorant, diaphoretic, diuretic, stomachic and emmenagogue. It is useful in fevers, diaphoresis, convulsions, dysentery, urethrorrhea, orchipathy, bronchitis, asthma, cough, stomatitis, syphilitic diseases, chronic laryngitis, jaundice and arthritis.

Indian olibanum is mainly used in treatment of rheumatoid arthritis. It is known to regain integrity of vessels in joints from damage or spasm. It is also used in preparation of incense and as a fixative in perfumes.

**Toxicities & Precautions**

Boswellia has been reported safe in humans.

**Pharmaceutical studies on olibanum**

In the present study, olibanum was evaluated as rate controlling matrix former in floating tablets based on gas generating principle.

There are no reports on application of olibanum gum and resin in controlled release. The first reports 19-26 on the application of olibanum gum and resin in controlled release are from our institution. Chowdary et al reported 19-26 first time olibanum and ether soluble resin extracted from olibanum as efficient matrix formers and micro-encapsulating agent for controlled release
CROSS-LINKED STARCH UREA: PREPARATION AND CHARACTERISATION

Modified starches are promising and having good potential as release retardants and rate controlling polymers for controlled release. The controlled release properties of modified starches, generally based on solvent-activation have been intensively investigated. For example, pregelatinized starch\textsuperscript{27}, cross linked amylose\textsuperscript{28}, substituted amylose\textsuperscript{29} and short chained amylase (i.e. amylodextrin)\textsuperscript{30, 31}, all have retarded drug release from matrix tablets. Modified starches are promising and having good potential as release retardants and rate controlling polymers for controlled release. Cross-linked starch urea is a modified starch prepared by gelatinization of starch in the presence of urea and cross linking by treatment with calcium chloride. The cross linked polymers generally swell in water and aqueous fluids to form gelatinized matrices suitable for controlled release. Cross-linked starch urea is reported\textsuperscript{32, 33} as an efficient rate controlling matrix former for controlled release. In the present study cross-linked starch urea was prepared from potato starch, characterized and evaluated as rate controlling matrix former in floating tablets based on gas generation principle.
EXPERIMENTAL

Materials:

Potato starch (Loba Chemie)

Urea (Qualigens)

Calcium Chloride I.P.

All other materials used were of pharmacopoeial grade.

Methods

Preparation of Cross linked Starch urea

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 $85^\circ$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 microscopical 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 DSC and FTIR spectra.

1. Microscopic examination:

   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 cross-linked starch urea are shown in Figs: 4.7 – 4.8.

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-amylose.

3. Melting point:

   Melting point of cross-linked starch urea was determined in a melting point apparatus and also by DSC.

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.
7. **Viscosity:**

Viscosity of a 0.1% w/v homogenized dispersion was determined using Ostwald Viscometer.

8. **Density (g/cc):**

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

9. **Bulk density:**

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

10. **Compressibility index:**

Compressibility index was determined by measuring the initial volume \( (V_o) \) and final volume \( (V) \) after 100 tapings of a sample of cross-linked starch urea in a measuring cylinder.

Compressibility index was calculated using the equation,

\[
\text{Compressibility Index} = \left( \frac{V_o - V}{V_o} \right) \times 100
\]

11. **Angle of repose:**

Angle of repose was determined by fixed funnel method.

The physical and micromeritic properties of cross-linked starch urea prepared are summarized in Table 4.2.

12. **Infrared Spectroscopy:**

FTIR spectra of cross-linked starch urea was recorded on a Perkin Elmer, IR Spectrophotometer Model: Spectrum RXI, using KBr disc as reference.

DSC thermogram of cross-linked starch urea was recorded on Perkin Elmer Thermal Analyser in Sipra Laboratories, Hyderabad. Samples (2-5mg) were sealed into aluminum pans and scanned at heating rate of $10^\circ$ C min$^{-1}$ over a temperature range $35^\circ$ - $350^\circ$ C.
<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 ( \alpha )- amylose</td>
</tr>
<tr>
<td>2</td>
<td>Melting point</td>
<td>Charred at 220(^{\circ})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 740%</td>
</tr>
<tr>
<td>5</td>
<td>pH of 0.1 % aqueous dispersion</td>
<td>8.5</td>
</tr>
<tr>
<td>6</td>
<td>Viscosity of a 0.1 % aqueous dispersion</td>
<td>1.054 cps</td>
</tr>
<tr>
<td>7</td>
<td>Density</td>
<td>0.527 g/cc</td>
</tr>
<tr>
<td>8</td>
<td>Bulk density</td>
<td>0.758 g/cc</td>
</tr>
<tr>
<td>9</td>
<td>Compressibility index</td>
<td>13.25 %</td>
</tr>
<tr>
<td>10</td>
<td>Angle of repose</td>
<td>24(^{\circ}) - 26(^{\circ})</td>
</tr>
</tbody>
</table>
Fig. 4.5. FTIR Spectra of Crosslinked Starch Urea
Fig 4.6  DSC Thermogram of Cross linked Starch urea
Fig 4.7. Photo Micrograph of Potato Starch (Stained with Saffranin)
Fig 4.8. Photo Micrograph of Cross-linked Starch urea (Stained with Saffranin)
Fig 4.9. Swelling of Cross linked Starch Urea Matrix Tablets in Water
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\textsuperscript{34, 35} that starch reacts with urea to form starch carbamate, a starch urea polymer. Khalil, \textit{et al.}\textsuperscript{36} investigated the reactions between starch and urea resulting in the formation of starch urea (starch carbamate). The reactions involved are as follows

\[
\text{heat} \quad \text{St OH} + \text{CO} (\text{NH}_2)_2 \leftrightarrow \text{St OCONH}_2 + \text{NH}_3
\]

\[
\text{heat} \quad 2 \text{St OCONH}_2 \rightarrow \text{St OCONHCOO St} + \text{NH}_3
\]

\[
\text{heat} \quad \text{St OH} + \text{St OCONH}_2 \rightarrow \text{St COO St} + \text{NH}_3
\]

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 as matrix former in controlled release floating tablets.

The cross-linked starch urea was found to be fine, hard and free flowing crystalline powder. It gave a positive iodine test indicating the presence of \( \alpha \)-amylose. The FTIR spectra of cross linked starch urea is shown in Fig.4.5. The presence of IR absorption peaks at 3369.05 cm\textsuperscript{-1} due to \(-\text{NH}_2\) and at 1668.72 cm\textsuperscript{-1} due to \(-\text{C}=\text{O} \) stretch indicated the presence of urea in the polymer. The peaks at 2925.84 cm\textsuperscript{-1} (C-H stretch) and 1271.99 cm\textsuperscript{-1} (C-O-C) indicate the presence of \( \alpha \)-amylose. When tested for melting
point, cross linked starch urea charred at 220°C. DSC of cross-linked starch urea (Fig.4.6) showed a sharp melting peak at 139.9°C which corresponds to the melting of urea present in the polymer.

Microscopic examination indicated that potato starch consists of oval shaped grains (Fig.4.7). Whereas cross-linked starch urea consists of rectangular, transparent crystals (Fig.4.8).

The physical and micromeritic properties of cross-linked starch urea prepared are summarized in Table 4.2. It was insoluble in water, aqueous fluids of acidic pH and alkaline pH. It was insoluble in organic solvents like methanol, petroleum ether, dichloromethane, cyclohexane and chloroform. The pH of a 0.1% aqueous dispersion was 8.5.

Cross-linked starch urea exhibited good swelling in water. The swelling index was 740%. The swelling of cross-linked starch urea matrix tablets in water is shown in Fig. 4.9. All micromeritic properties indicated good flow and compressibility needed for solid dosage form manufacturing.

As cross-linked starch urea is insoluble in aqueous fluids of acidic pH and alkaline pH has good swelling property in water, it is considered suitable as release retarding and rate controlling matrix former for floating tablets. In the present investigation cross-linked starch urea was evaluated as a matrix former for floating tablets of pioglitazone along with olibanum and HPMC K15M.
REFERENCES


