Open Access   Research Article

Preparation and characterization of Starch–Urea–Borate: A new floating polymer

R. Santosh Kumar [1]*, K.P.R. Chowdary [2]

1. GITAM Institute of Pharmacy, GITAM (Deemed to be University), Rushikonda, Visakhapatnam, A.P 530045, INDIA

2. Ex-Principal, AU College of Pharmaceutical Sciences, Visakhapatnam

ABSTRACT

In recent years considerable attention has been focused on the development of new drug delivery systems known as controlled release drug delivery systems. Such interest is based largely on the fact that the controlled release products have established and retained place in the market based on their uniqueness and their clinical advantages in the practices of medicine. The major types of controlled release systems include matrix tablets, floating tablets, swellable tablets, coated beads, microcapsules and microspheres, mucoadhesive systems, ion exchange resin complexes, osmotic pressure controlled release systems, transdermal systems etc. The principle of floating tablets offers a simple and practical approach to achieve increased gastric residence time to enhance the bioavailability and to obtain controlled release. Floating tablets are designed based on gas generating principle. Design of floating tablets needs a strong matrix forming polymer. Several polymers such as various viscosity grades of hydroxypropylmethyl cellulose (HPMC), Carbopol 934P, Eudragit RL, calcium alginate, chitosan, xanthan gum, guar gum, ethyl cellulose etc., have been used in the design of floating tablets of various active pharmaceutical ingredients (APIs). Though these polymers are available for floating tablets, there is a continued need to develop new, effective and efficient polymers for controlled release floating tablets.The overall objective of the investigation is to develop new, efficient and safe polymer as floating matrix former for floating systems.

Keywords: Floating, Matrix, Polymers, Starch-urea-borate.

INTRODUCTION

Floating drug delivery systems are aimed to remain in the stomach for several hours, increase gastric residence time, release the drug over prolonged period of time and enhance bioavailability by retaining the dosage form at the site of absorption for several hours. Drug release from these systems should be at a desired rate, predictable and reproducible. Polymers which are used as release retarding materials in the design of floating dosage forms play a vital role in retaining the dosage form in a buoyant state in stomach for several hours and delivering the drug in a controlled manner over a prolonged period of time. Though a wide range of buoyant polymers and other effervescent agents are available, there is a continued need to develop new, safe, less dense and effective release retarding polymers for floating drug delivery systems. In the present investigation, starch – urea – borate, a new starch based polymer was prepared and evaluated for its application in the design of floating drug delivery systems. The preparation and characterization of starch – urea – borate will be discussed.

MATERIALS & METHODS

Materials:

Potato starch (Loba Chemie)

Urea (Qualigens)

Borax (Qualigens)

All other materials used were of Pharmacopoeial grade

Preparation of starch – urea – borate:

Starch–urea–borate was synthesized by gelatinizing potato starch in the presence of borax and urea.

Potato starch (50 g) was dispersed in 100 ml of purified water to form starch slurry. Borax (10.0 g) and urea (15.0 g) were dissolved separately in 400 ml of purified water and the solution was heated to boiling. While boiling, the starch slurry was added and mixed. Mixing while heating was continued for 10 minutes to gelatinize starch to form starch–urea–borate polymer. The mass formed was spread on to a stainless steel plate and dried at 80^0C for 6 – 8 h. The dried polymer was powdered and passed through mesh no. 120.

Characterization of starch – urea – borate:

The starch – urea – borate 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 potato starch and starch – urea – borate 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 starch – urea – borate are shown in Figs. 1A, 1B, 2A and 2B. The size of 100 particles was measured using a calibrated eye – piece micrometer. The particle size distribution of potato starch and starch – urea – borate (prepared) are given in Table 1.

2. Chemical test:

Iodine test:

Slurry of starch – urea – borate 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 starch – urea – borate 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:

Starch – urea – borate (1 gm) was taken into two graduated 50 ml measuring cylinders, one containing petroleum ether and other containing water and stored for 24 h. Swelling index of starch – urea – borate was determined using the formula

$$\text{Swelling index (\%)} = \frac{Vw - Vo}{Vo} \times 100$$

Where, Vo is the volume of the sediment in petroleum ether and

Vw is the volume of sediment in water after 24 h

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 and tap densities:

Bulk and tap densities were determined by 3 tap method in a graduated cylinder.

10. Compressibility index:

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

Compressibility index was calculated using the equation,

$$\text{Compressibility index} = \frac{Vo - V}{Vo} \times 100$$

11. Angle of repose:

Angle of repose was determined by fixed funnel method.

The physical and micromeritic properties of starch – urea – borate prepared are summarized in Table 2.

12. Infrared Spectroscopy:

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

13. Differential Scanning Calorimetry (DSC):

DSC thermogram of starch – urea – borate was recorded on Perkin Elmer Thermal Analyser in Sipra Laboratories, Hyderabad. Samples (2-5 mg) were sealed into aluminum pans and scanned at a heating rate of 10 º C min^{-1} over a temperature range 35º – 350.0º C.

Table 1: Particle Size Distribution of Prepared Potato Starch and Starch – urea – borate

Size Range (µm)	Number of Particles	
	Potato Starch	Starch – urea – borate
0 – 50	27	--
50 – 100	60	20
100 – 150	13	53
150 – 200	--	27
$\bar{x}$ ± s.d (µm)	67.5 ± 29.54	128.0 ± 33.21

Table 2: Physical and Micromeritic Properties of Starch – urea – borate Prepared

| S. N.	Property	Result
1.	Iodine test	Positive indicates the presence of α - amylose
2.	Melting Point	Charred at 210^{0}C
3.	Solubility	Insoluble in water, aqueous fluids of acidic and alkaline pHs and in organic solvents
4.	Swelling index	Swells in water with a swelling index of 614.28 %
5.	pH of 0.1 % aqueous dispersion	9.01
6.	Viscosity of a 0.1 % aqueous dispersion	1.011 cps
7.	Density	0.511 g/cc
8.	Tap density	0.721 g/cc
9.	Compressibility index	12.91 %
10.	Angle of repose	22^0 76^1
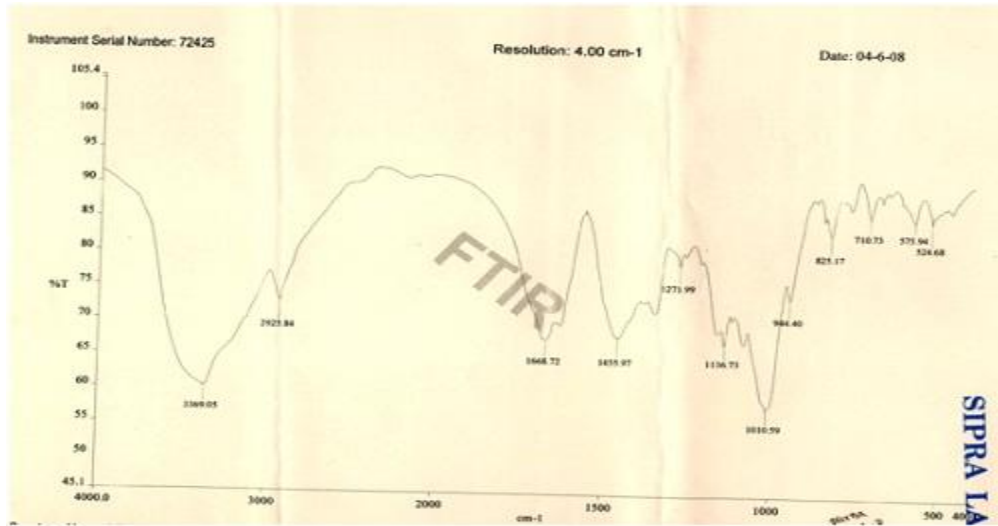
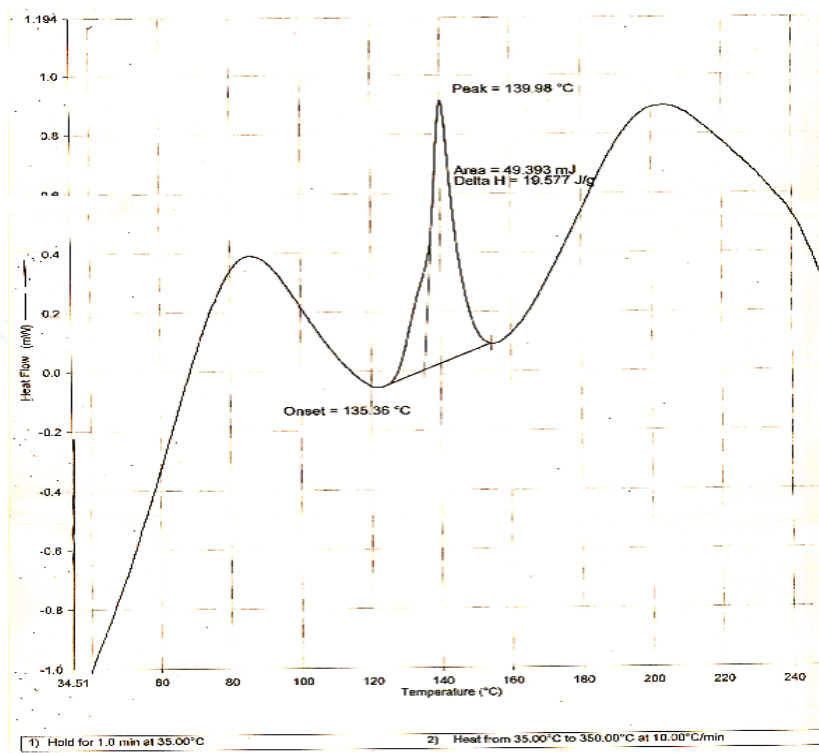**Figure 1: FTIR Spectra of Starch – Urea – Borate**

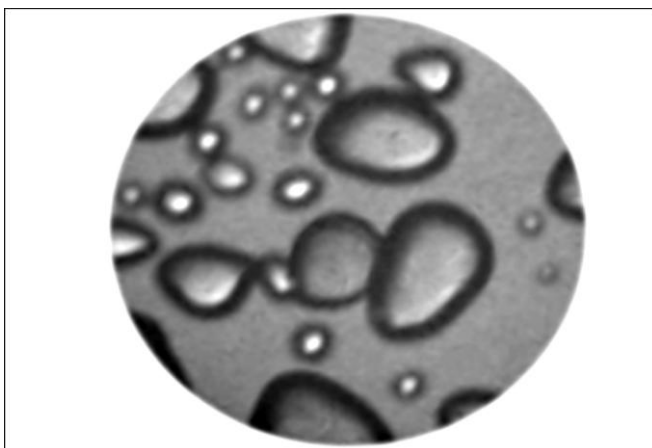**Figure 2: DSC Thermogram of Starch – Urea – Borate**

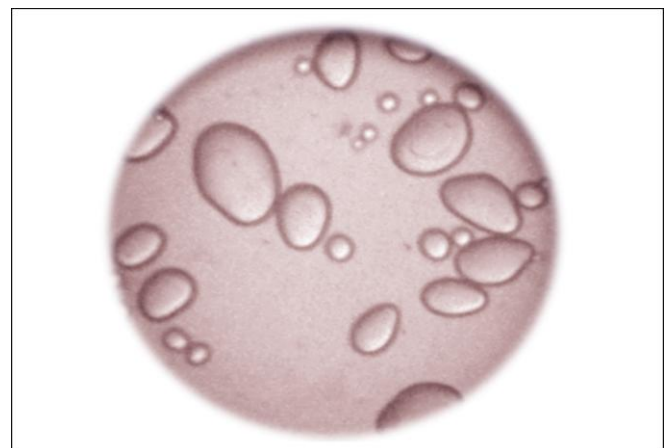**Figure 3A: Photomicrographs of Potato Starch (unstained)**

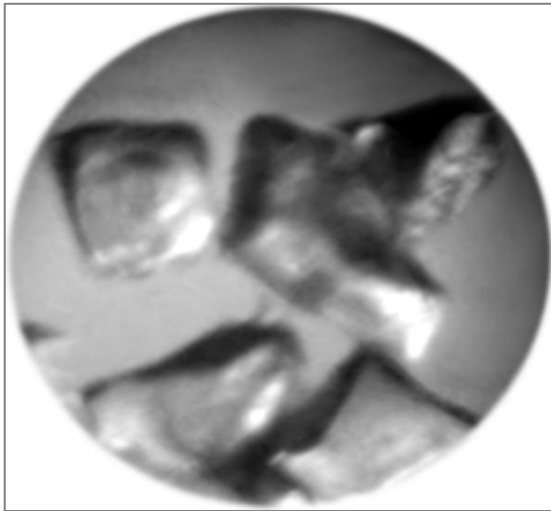**Figue 3B: Photomicrographs of Potato Starch (stained with Saffranin)**

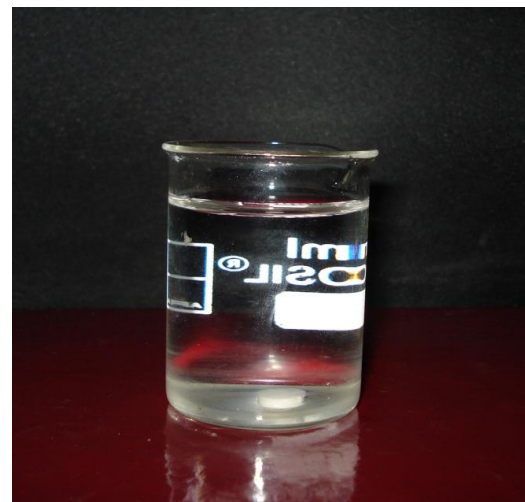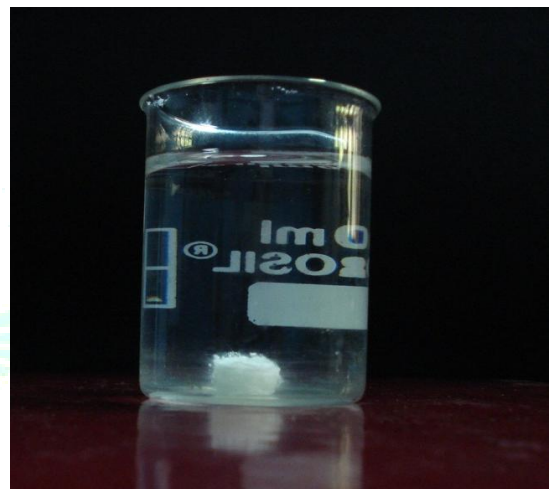**Figure 4A: Photomicrographs of Starch-urea-borate (unstained)**

(A)

Figure 4B: Photomicrographs of Starch-urea-borate
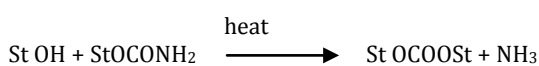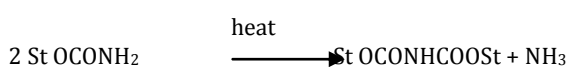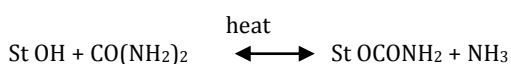
(B)

Figure 5: Swelling of Starch-urea-borate Matrix Tablets in Water

(A) At Zero Time; (B) After One Hour

RESULTS AND DISCUSSION

Starch – urea – borate was prepared by gelatinizing potato starch in the presence of borax and urea. It is known[1, 2] that starch reacts with urea to form starch carbamate, a starch – urea cross linked polymer. Khalil *et al.*[3] investigated the reactions between starch and urea resulting in the formation of starch cross linked with urea. The reactions involved are as follows

$$St\ OH + CO(NH_2)_2 \xrightleftharpoons{\text{heat}} St\ OCONH_2 + NH_3$$

$$2\ St\ OCONH_2 \xrightarrow{\text{heat}} St\ OCONHCOOSt + NH_3$$

$$St\ OH + StOCONH_2 \xrightarrow{\text{heat}} St\ OCOOSt + NH_3$$

Where St OH is starch

Sodium borate serves as a catalyst in the cross linking reaction between starch and urea. Literature on pharmaceutical applications of starch-urea-borate polymer is scanty. In one study[4] it has been used in the controlled release formulation of insecticide acetamiprid. In another patent[5] a controlled release pesticide formulation was developed encapsulating the pesticide (deltamethrin) in a polymer matrix of starch-borax-urea. In the present investigation starch-urea-borate was evaluated for its application as buoyant release retardant and rate controlling polymer in the design of floating controlled release formulations of selected drugs. The starch-urea-borate prepared was found to be fine, hard and free flowing crystalline powder. The density of Starch-urea-borate was found to be 0.511 g/cc (less than the density of water), so it can be used in the formulation of floating drug delivery systems. The compressibility index of Starch-urea-borate was found to be 12.91% and the angle of repose was found to be $22^0 76^1$. Both compressibility index and angle of repose of Starch-urea-borate indicates that the polymer has excellent flow properties, so the polymer can be used in the formulation of tablets. It gave a positive iodine test indicating the presence of α- amylose. The FTIR spectra of starch – urea – borate is shown in Fig. 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 2925.84 cm^{-1} (C-H stretch) and 1271.99 cm^{-1} (C-O-C) indicate the presence of α- amylose. When tested for melting point, starch – urea – borate charred at 210^{0}C. DSC of starch – urea – borate (Fig. 2) showed a sharp melting peak at 139.9^{0}C which corresponds to the melting of urea present in the polymer.

Microscopic examination indicated that potato starch consists oval shaped grains (Fig. 3A and 3B). Whereas starch-urea-borate consists of rectangular, transparent crystals (Fig. 4A and 4B). The particle size in each case was determined by microscopy. The results are given in Table 1. The average size of the potato starch grains was 66.5 ± 30.87 µm. The average size of starch-urea-borate crystals was 127.0 ± 34.58 µm.

The physical and micromeritic properties of starch-urea-borate prepared are summarized in Table 2. It was insoluble in water, aqueous fluids of acidic and alkaline pHs. It was also insoluble in organic solvents like methanol, petroleum ether, dichloromethane, cyclohexane and chloroform. The pH of a 0.1 % aqueous dispersion was 9.01.

Starch-urea-borate exhibited good swelling in water. The swelling index was 614.28 %. The swelling of starch-urea-borate matrix tablets in water is shown in Fig. 5. All micromeritic properties indicated good flow and compressibility needed for solid dosage form manufacturing.

As starch-urea-borate has density of 0.511 g/cc (less than the density of water), excellent flow properties, good swelling property in water, it is considered as suitable buoyant release retarding and rate controlling polymer in floating tablets for obtaining the formulations that remain in the gastric region for prolonged period with controlled release of drug.

REFERENCES

1. Abdel – Thalouth, I, El-Kashouti. M.A. and Hebeish. A, Modification of Rice Starch through Thermal Treatment with Urea, Starch., 1981; 33:306-310.

2. Hebeish. A, Refai. R, Rageb. A. and Abdel Thlouth. I, Factors Affecting the Technological Properties of Starch Carbamate, Starch., 1991; 43:273-280.

3. Khalil. M. I, Farag. S., Mostafa. Kh. M. and Hebeish. A, Some Studies on Starch Carbamate, Starch, 1994; 46:312-316.

4. Yongsong Cao, Lu Haung, Jiuxin Chen, Ji Liang, Shengyou Long and Yitong Lu, Development of a controlled release formulation based on a starch matrix system, Int. J. Pharm., 2005; 298:108-116.

5. Yang, Chien-chun, Kao, Suey-sheng, Tzeng, Ching-chou and Chen, Mei-hueih, United States Patent 5516520, 1996.