Acta Poloniae Pharmaceutica – Drug Research, Vol. 72 No. 4 pp. 785–789, 2015 ISSN 0001-6837
Polish Pharmaceutical Society

PHARMACEUTICAL TECHNOLOGY

EFFECT OF STARCH HYDROLYSATES IN THE PROCESS OF DISSOLUTION OF SOLIDS

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Abstract: The purpose of this work was to investigate the influence of starch hydrolysates in the dissolution process of the substance practically insoluble in water. Progesterone and ibuprofen were chosen as model substances. The study was conducted with a constant amount of the drug (25 mg/mL) or constant amount of starch hydrolysate (50 mg/mL). Next, the influence of ethanolic solutions (10-30% v/v) on solubility of drug was tested. The results confirm the possibility of using starch hydrolysate as a cheap and safe addition to increase the solubility of practically insoluble drugs.

Keywords: starch hydrolysate, dissolution of solids, progesterone, ibuprofen

Nowadays in medicine, a large number of active substances, occurring in many forms and formulations, is being used. There are solid, semi-solid and liquid forms. Depending on the route of administration, the drug is liberated from formulation and dissolved in water or body liquids. So, drug's solubility and permeability are very important for the bioavailability. In accordance with the above physical properties, the Biopharmaceutics Classification System (BCS) categorizes drug into four classes (1). Solubility and dissolution rate are the most essential factors controlling the rate and extent of drug absorption. Inadequate aqueous solubility of therapeutically active entities is a great concern in pharmaceutical formulation, hence solubilization of insoluble or practically insoluble drugs in the formulation of various dosage forms, especially in parenteral medications has recently been in the centre of attention (2).

A large group of substances used in medicine are compounds which are difficult to dissolve in water, so their bioavailability is not sufficient to obtain the optimal therapeutic effect. Hence, using a variety of techniques and methods, the aim is to ensure that the drug substance dissolves in water or body fluids. There are many techniques of increasing solubility of solids, for example by change of pH (1, 3, 4), using cosolvents (2, 5), hydrophilic additions (6, 7) or complex formation with cyclodextrins (8, 9), hydrotropic solubilization (10, 11) and formation of prodrugs (12, 13).

Unfortunately, the amount of data on formulations containing starch hydrolysates is limited. Therefore, the purpose of this study was to demonstrate the effect of starch hydrolysis products on the solubility of the substance practically insoluble in water, such as ibuprofen and progesterone.

EXPERIMENTAL

Materials

Starch (potato starch) used in this study was made by Nowamyl S.A. Lobez Poland. Progesterone (PR) was purchased from Fluka Chemie, Switzerland, ibuprofen (IB) IOL Chemicals and Pharmaceuticals Ltd., Ludhiana, India. Citric acid (CA), glacial acetic acid (GAA), ethanol (760 g/mL, ET) and sodium hydroxide (4 g/L, SO) were purchased from POCh Poland.

Hydrolysis of starch

Starch was treated with solutions of CA, GAA and water at 95^{o}C for 2 or 4 h to obtain starch hydrolysate SH2 or SH4 respectively. Received sed-

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iments were cleaned by ET and evaporated to eliminate the solvent (14). Molecular mass of obtained hydrolysates were estimated in cryoscope (Trident 800 CL) by freezing point determination. Molecular mass of SH2 amounts 2.356 kDa and 1.105 kDa for SH4.

Analytical methods

Analytical dilution of pure IB and PR were prepared in SO and ET (10% w/w), respectively. Their absorbances were taken at 263 nm for IB and 249 nm for PR on spectrometer Helios Omega UV-VIS (Thermo Scientific) and were plotted against their respective concentrations to obtain standard curve. The amount of IB and PR was calculated from standard curve.

Solubility determination

The solubility extent of IB and PR in water was measured in three steps.

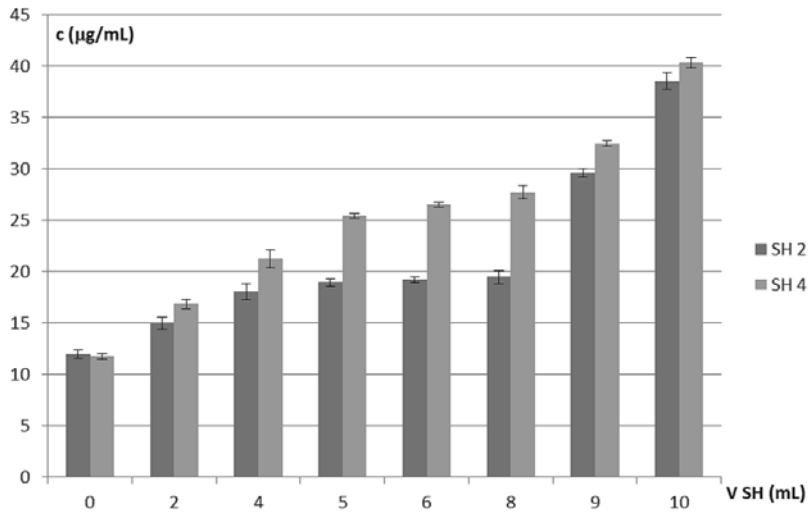


Figure 1. The effect of increasing amount of SH on dissolution of ibuprofen, (n = 5)

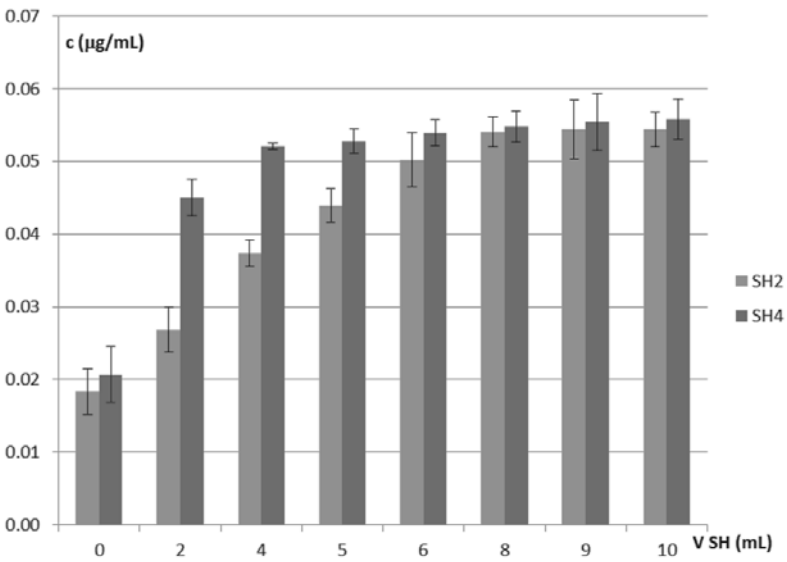
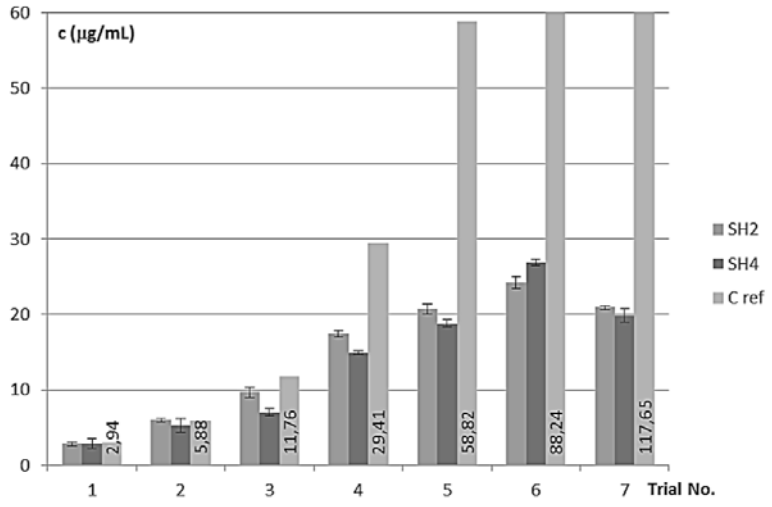


Figure 2. The effect of increasing amount of SH on dissolution of progesterone, (n = 5)



Figre 3. The effect of constant amount of SH (50 mg/mL) on dissolution of ibuprofen, (n = 5)

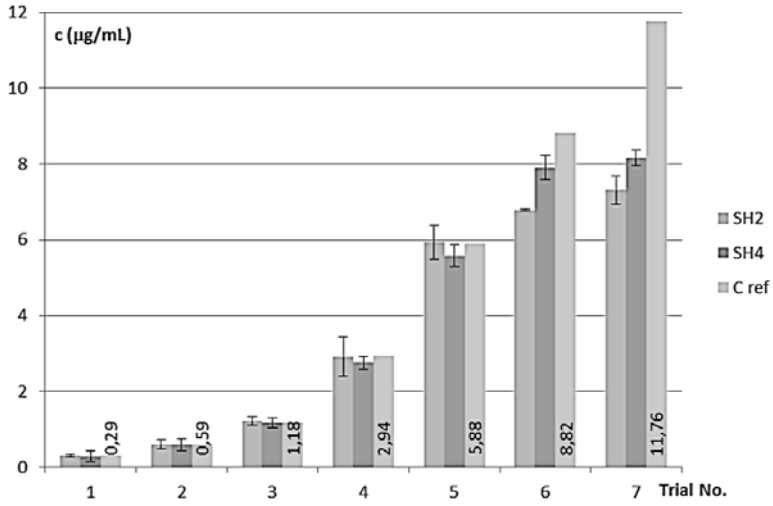


Figure 4. The effect of constant amount of SH (50 mg/mL) on dissolution of progesterone, (n = 5)

In the first, solutions 10% w/v of SH2 and SH4 were made. Next, with constant quantity of IB or PR (25 mg/mL), amount of SH solutions (v) were increased from 0 mL up to 10 mL and water was added to obtain the same volume. Test tubes were closed for 24 h and shaken temporary, then, suspensions were centrifuged with 5000 rpm (centrifuge machine, MPW-223e Med. Instruments, Poland) and 3 mL of the supernatant liquid was diluted up to 25 mL with suitable solvent - SO or ET (10% w/w). The absorbance was determined spectrophotometrically at appropriate wavelength. Determined concentrations of IB and PR (n = 5) are shown in Figures 1 and 2.

In the second step, with constant quantity of SH2 or SH4 (50 mg/mL), the amount of IB and PR were increased according to Table 1. Trials were prepared and examined as above. Determined concentrations of IB and PR (n = 5) are shown in Figures 3 and 4.

In the third step, influence of addition of ET was examined. Solutions of SH2 or SH4 (50 mg/mL) were prepared in ET 10%, 20% and 30% (v/v). The amount of IB or PR were added accord-

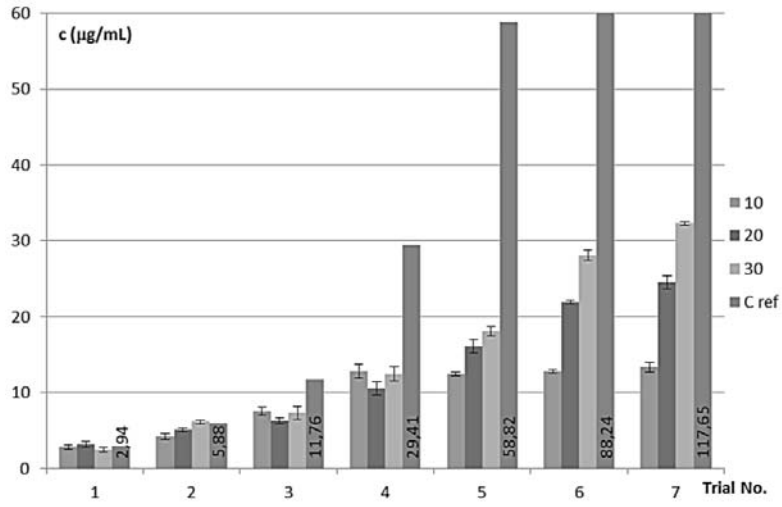


Figure 5. The effect of constant amount of SH (50 mg/mL) on dissolution of ibuprofen in ethanolic solution (10, 20, 30% v/v), (n = 5)

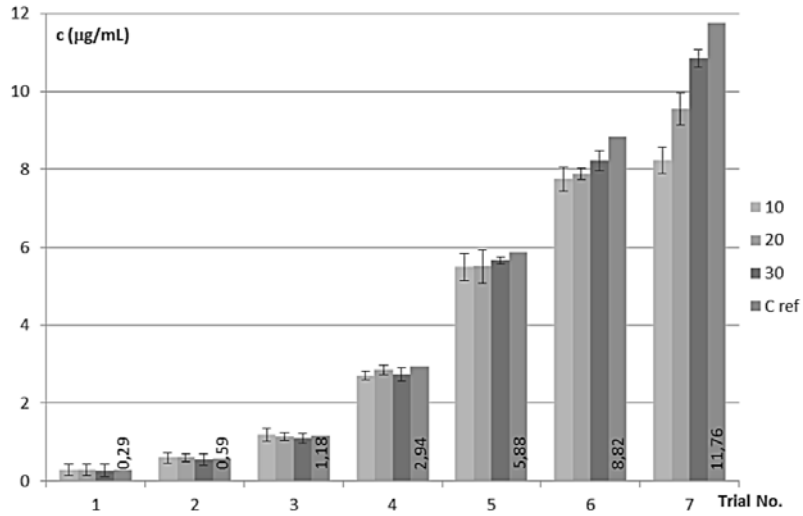


Figure 6. The effect of constant amount of SH (50 mg/mL) on dissolution of progesterone in ethanolic solution (10, 20, 30% v/v), (n = 5)

Table 1. Concentrations of ibuprofen and progesterone in trials

Trial No.	Concentration of ibuprofen C ref. (µg/mL)	Concentration of progesterone C ref. (µg/mL)
1	2.94	0.29
2	5.88	0.59
3	11.76	1.18
4	29.41	2.94
5	58.82	5.88
6	88.24	8.82
7	117.65	11.76

ing to Table 1. Trials were prepared and examined as above. Determined concentrations of IB and PR (n = 5) are shown in Figures 5 and 6.

RESULTS AND DISCUSSION

The effect of starch hydrolysates in the process of dissolution of drugs practically insoluble in water was assessed. The best composition of the addition of SH was tried to find, so it was decided to divide tests in three steps. The first – with constant quantity of drug, the second – with constant quantity of SH, and the third – with addition of solutions of ethanol – 10%, 20% and 30% (v/v).

In the first phase, solubility of IB and PR increased with increasing addition of SH2 or SH4 solution. It was noticed, that addition of 10 mL of SH2 or SH4 solution caused the increase of solubility of IB – 3.22 or 3.54 times, respectively, and for PR the increase was on level 2.97 or 2.71 times, respectively, for SH2 or SH4. None of increases was linear, so it was chosen the average amount of solution of SH – 5 mL which corresponding to 50 mg/mL of SH.

In the next phase, the presence of SH helped to dissolve added IB in 100% up to 5.88 mg/mL, greater amounts of IB were not completely dissolved, at the highest concentration of tested IB (117.65 mg/mL), dissolution was on level of 17%. The presence of SH2 also helped to dissolve 100% added PR up to 5.88 mg/mL, while the presence of SH4 caused complete dissolution of PR up to 1.18 mg/mL. At the highest concentration of PR (11.76 mg/mL), SH2 and SH4 helped to dissolve 62.2% and 69.4% of drug, respectively.

In the third phase, solutions of ET additionally increased dissolution of tested drugs. Solution of ET 10% (v/v) did not affect on dissolution of IB and at the highest concentration of IB only 11.3% was dissolved, for solutions of ET 20%, 30% it was 20.9% and 27.3%, respectively. Better situation was observed during dissolution of PR, with increasing concentration of drug, in the presence of solution of ET 10, 20 and 30%, increased concentration of dissolved PR. At the highest concentration of PR, it was 69.9, 81.2 and 96.3% of dissolved PR, respectively.

CONCLUSION

The presence of starch hydrolysates increases three times dissolution of drug practically insoluble in water. Differences between SH2 and SH4, in the process of dissolution aren't significant. Solutions of ET 10–30% additionally enhance dissolution of drug.

The use of starch hydrolysates in the process of dissolution of drug practically insoluble in water seems promising.

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Received: 24. 06. 2014