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ORIGINAL ARTICLE

Comparison of physicochemical properties of suppositories containing starch hydrolysates

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Abstract The purpose of this work was to determine the effect of starch hydrolysates (SH) on the physicochemical properties of suppositories. The study was conducted with suppositories with acetaminophen (AAP) a typical antipyretic analgesic, as model drug on lipophilic (cocoa butter) and hydrophilic base (polyethylene glycol 1500 + 400). The suppositories with and without the addition of SH were examined for physicochemical tests according to European Pharmacopoeia 8th edition (Ph. Eur.): the uniformity of mass of single-dose preparation test, the softening time determination of lipophilic suppositories test, the disintegration of suppositories test, and dissolution test with flow-through apparatus. The results confirm the possibility of using starch hydrolysates as a cheap and safe addition to modify physicochemical properties of suppositories.

1. Introduction

The rectal route for drug administration is useful because it can avoid hepatic first-pass effect, decrease gastrointestinal side effects and avoid undesirable effects of meals on drug absorption (de Boer et al., 1979, 1982). Drugs with systemic effect such as, antipyretic, anti-rheumatic, muscle relaxants, hypnotics are used in the rectal suppositories (Lou et al., 2012; Setoguchi et al., 2013). Drugs with local effect are mainly used: anti-inflammatories, and local anesthetics astringent normally used in the treatment of hemorrhoids, and substances with laxative activity (Carbone et al., 2013; Ramadan, 2013). Suppositories are currently a small part of the available dosage forms. However, the administration by the rectal route is important for patients with peptic ulcers, children and geriatric's treatment. Sustained release suppositories are preferable to conventional suppositories because they reduce the frequency of drug administration. Several approaches have been performed to prepare the controlled release suppositories by using various additives such as lecithin (Nishihata et al., 1985), sucrose fatty ester (Nakajima et al., 1990), carboxyvinyl polymer (Azechi et al., 2000; Yahagi et al., 2000) and various hydrogel formulations (Morimoto et al., 1989; Miyazaki et al., 1998).

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 physicochemical properties of suppositories.

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2. Materials and method

2.1. Materials

The following materials were used: potato starch (Nowamyl S. A., Lobez, Poland), acetaminophen (AAP) (Sigma-Aldrich, St. Louis, MO, USA), citric acid (CA), glacial acetic acid (GAA), ethanol (760 g/L) - (ET), and phosphate buffer (pH 7.2) - (PB), (Avantor Performance Materials S.A., Gliwice, Poland).

2.2. Methods

2.2.1. Hydrolysis of starch

Potato starch was treated with solutions of CA, GAA and water at 95 °C for 2 or 4 h to obtain starch hydrolysate SH2 or SH4 respectively. Received sediments were cleaned by ET and evaporated to eliminate the solvent (Czarnecki and Belniak, 2007). Molecular mass of obtained hydrolysates was estimated in cryoscope (Trident 800 CL, Poland) on the ground of freezing point determination. Molecular mass of SH2 amounts 2.356 kDa and 1.105 kDa for SH4. Both hydrolysates are readily soluble in water and in PB. Hydrolysates dissolved in water form solutions of pH 3.74 and pH 3.54 while PB solutions reach pH 7.11 and pH 7.07, respectively for the SH2 and SH4.

2.2.2. Preparation of suppositories

Rectal suppositories were prepared by fusion method at 36 °C on lipophilic base - cocoa butter and 60 °C on a hydrophilic base - PEG 1500 + PEG 400 (95:5, m/m). Each one contains 125 mg of AAP. The molten bases were mixed with SH2, SH4 (Table 1), and poured into polyethylene molds of capacity 1 g. After solidification, formed suppositories were stored at 4 °C until use.

2.2.3. Physical tests of suppositories

The uniformity of mass of single-dose preparation test was carried out as follows: twenty suppositories were individually weighted (Mettler AT201 FACT Switzerland) from each formula. Average mass and standard deviation (SD) were calculated.

The softening time determination of lipophilic suppositories test was conducted using apparatus for measuring the softening time of suppositories ($n = 3$).

The disintegration of suppositories test was performed in water maintained at 37 °C ± 0.5 °C using ST30 apparatus (Erweka, Germany) ($n = 3$).

The resistance to rupture of suppositories test was carried out on 10 suppositories using SBT apparatus (Erweka, Germany) at room temperature (22 °C ± 0.5 °C). Results of above tests are shown in Table 2.

2.2.4. Assay of acetaminophen by spectrophotometry

Spectrophotometric measurements were carried out on spectrometer Helios Omega UV–VIS (Thermo Scientific, USA). Absorbance of AAP in PB was taken at 242 nm and was plotted against its respective concentrations to obtain standard curve. The amount of AAP was calculated from the linear regression equation $A = 0.0625\ C + 0.0188$ ($r = 0.9997$).

2.2.5. Chemical test of suppositories

The uniformity of content of single-dose preparation test. The content of AAP in suppositories was tested on five suppositories randomly selected from each formula. The suppository was individually placed in 1000 ml standard flask containing 100 ml of PB and heated. The flask was shaken until complete dissolution of AAP from suppository. Then 10 ml of solution was taken, filtrated through PVDF membrane filter (Sartorius 0.2 μm) and assayed spectrophotometrically against the blank prepared using respective suppository without AAP. The mean contents of drug ± SD were calculated and are given in Table 2.

The dissolution test for solid dosage forms. The dissolution test of suppositories was carried out according to the flow-through method. Each suppository was located in dual chamber cell (Sotax, Switzerland) through which PB was pumped (4 mL/min) at a temperature of 37 ± 0.5 °C. The eluate was filtered (Whatman GF/D 3 μm) upon leaving the cell and then was collected in fractions with fraction collector (Buchi, Switzerland). Samples were suitably diluted and assayed spectrophotometrically at 242 nm against PB. Results were expressed as the mean of five determinations.

2.2.6. Statistical analysis

Presented data, as mean ± SD ($n = 3$) were analyzed by the one-way analysis of variance ANOVA with post-hoc Dun-

Table 1 Code and constituents of suppositories.

Codes	Substances (g)					
	AAP	SH2	SH4	Cocoa butter	PEG 1500	PEG 400
C0	0.125	–	–	0.875	–	–
C1	0.125	0.1	–	0.775	–	–
C2	0.125	0.2	–	0.675	–	–
C3	0.125	0.3	–	0.575	–	–
C4	0.125	–	0.1	0.775	–	–
C5	0.125	–	0.2	0.675	–	–
C6	0.125	–	0.3	0.575	–	–
P0	0.125	–	–	–	0.831	0.044
P1	0.125	0.1	–	–	0.736	0.039
P2	0.125	0.2	–	–	0.641	0.034
P3	0.125	0.3	–	–	0.546	0.029
P4	0.125	–	0.1	–	0.736	0.039
P5	0.125	–	0.2	–	0.641	0.034
P6	0.125	–	0.3	–	0.546	0.029