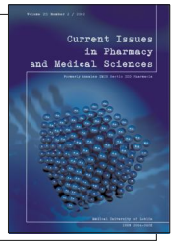
2012 © Curr. Issues Pharm. Med. Sci. Vol. 25, No. 2, Pages 121-125

Current Issues in Pharmacy and Medical Sciences

Formerly ANNALES UNIVERSITATIS MARIAE CURIE-SKLODOWSKA, SECTIO DDD, PHARMACIA
on-line: www.umlub.pl/pharmacy



The influence of starch hydrolysates on properties of suspensions

PIOTR BELNIAK*, KATARZYNA ŚWIĄDER, ŁUKASZ ZIMMER, MICHAŁ SZUMIŁO, REGINA KASPEREK, EWA POLESZAK

Chair and Department of Applied Pharmacy, Faculty of Pharmacy, Medical University of Lublin, Poland

ABSTRACT

Using modified starch in suspensions is commonly practiced in food, pharmaceutical and other industries [3, 6]. The purpose of this study was to investigate the influence of starch hydrolysates, received according to our prescription, on properties of suspensions. Prepared suspensions Z01 – Z05 with PR, as the model drug, were examined for physical tests. The addition of 20 % SH2 or SH4, as suspending agent, increased the stability of preparations (0.04 cm/day and 0.05 cm/day, respectively). Drug release test according to extraction method was conducted during 24 hours. The ethanol used in acceptor medium increased the amounts of released progesterone. The received results confirm an opportunity of using starch hydrolysates as cheap and safe agents modifying physical properties of suspensions.

Keywords: starch hydrolysate, density, dynamic viscosity of suspension, drug release, progesterone.

INTRODUCTION

The typical suspension consists of solid particles, a solvent, and a suspending agent. Uniformity and precision of a single dose are required for pharmaceutical suspensions. Solid sediments formed after standing still must be immediately re-dispersible and distributed homogeneously. In literature, there are many examples of using suspending agents such as modified starch, derivatives of cellulose, xanthan gum or polyvinylopyrrolidone [3, 6, 10, 11, 14]. Suspensions are well known preparations, used in food, medical and other technologies. In medicine, there are many applications of suspensions for external use – transdermal delivery drug [7], ocular delivery drug [8]. There are widely used suspensions for oral [12], respiratory [4], or intravenous treatment [13].

In the literature, there is no data concerning suspensions with starch hydrolysates (SH) received according to our prescription. Therefore, the influence of starch hydrolysates on physical properties of suspensions was tested.

MATERIALS AND METHODS

Materials. Starch (potato starch) used in this study was produced by Nowamyl S.A. Łobez Poland. Progesterone (PR) was purchased from Fluka Chemie, Switzerland, citric acid (CA), glacial acetic acid (GAA), ethanol (760 g/ml) - (ET) were purchased from POCH Poland.

Corresponding author

* Chair and Department of Applied Pharmacy, Faculty of Pharmacy, Medical University of Lublin, 1 Chodzki Str., 20-093 Lublin, Poland
e-mail: piotr.belniak@umlub.pl

Hydrolysis of starch. Starch was treated with CA, GAA solutions and water at 95°C for 2 or 4 hours for obtaining starch hydrolysate SH2 or SH4 respectively. The received sediments were cleaned with ET and evaporated for solvent to be eliminated [1]. Molecular mass of obtained hydrolysates was estimated in cryoscope (Trident 800 CL) on the ground of freezing point determination. Molecular mass of SH2 amounted to 2.356 kDa and 1.105 kDa for SH4.

Preparation of suspensions. Suspensions were prepared as follows: Progesterone (0.4 g) with slight amount of ET was well micronized in mortar. Next, purified water or suitable SH was added according to Table 1. Suspensions were well homogenized by mixing and tested for physical requirements according to Polish Pharmacopoeia VIII edition.

Table 1. Suspension preparation

Suspension	Progesterone (mg/ml)	Aqua (v/v)	Aqueous solution of SH_4(v/v)		Aqueous solution of SH_2(v/v)	
			10%	20%	10%	20%
Z01	4	100	–	–	–	–
Z02	4	–	100	–	–	–
Z03	4	–	–	100	–	–
Z04	4	–	–	–	100	–
Z05	4	–	–	–	–	100

Density and viscosity tests. The relative density of suspension [9] can be estimated by pycnometeric technique and calculated from equation 1:

$$d_m = \left(\frac{m}{w} \cdot 0.997 + 0.0012\right) \text{ [g/cm}^3\text{]}, \qquad \text{Eq. 1}$$

where: d_m – the relative density of tested suspension at 20°C, m – weight of tested substance in pycnometer, w – weight of water in the same volume, 0.997 – density of water at 20°C, 0.0012 – correction of weighing in air atmosphere.

The dynamic viscosity of suspension can be assayed with Höppler viscosimeter, and calculated from equation 2:

$$\eta = K \cdot t \cdot (d_k - d_m) \text{ [mPa x s]}, \qquad \text{Eq. 2}$$

where: η – the dynamic viscosity, K – coefficient of apparatus ball, t – time of falling of ball in sec., d_k – density of ball, d_m – the relative density of tested suspension.

Stability test. Suspensions were tested for stability according to Stokes' law [5], and calculated from equation 3:

$$v = \frac{d^2(\rho_s - \rho_o)g}{18\eta} \text{ [cm/sec]}, \qquad \text{Eq. 3}$$

where: η – the terminal velocity in cm/sec, d – the diameter of the particle in cm, ρ_s and ρ_o – densities of the dispersed phase and dispersion medium respectively, g – the gravitational acceleration and η – the viscosity of the dispersion medium in poise. The results were recalculated to cm/day.

Results of density, viscosity, and stability tests are presented in Table 2.

Table 2. Viscosity, density and stability of suspensions (n=3)

Suspension	Density (g/cm^3)	Viscosity (mPa x s)	Stability (cm/day)
Z01	1.0220	9.02	85.85
Z02	1.0480	29.07	0.15
Z03	1.0872	76.11	0.05
Z04	1.0434	13.04	0.38
Z05	1.0698	88.90	0.04

Drug release test. Dissolution profiles of PR from preparationes – Z01, Z02 and Z04 were determined using extraction method [2]. The suspension (1 ml) was placed into a dissolution medium (99 ml) of phosphate buffer pH 6.8 or solutions of this buffer with 10 %, 20 %, 30 % (v/v) addition of ET. Flasks were gently shaken at intervals, the temperature was maintained at 21°C. Dissolved PR concentration was determined by spectrophotometric method. Dissolution profiles of PR (n = 3) are shown in Figs 1-3.

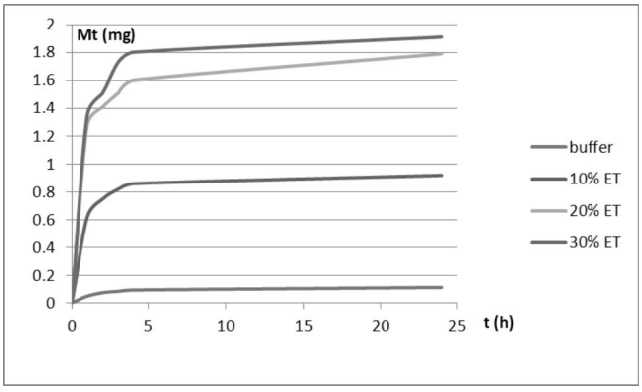


Fig. 1. Release of progesterone from suspension Z01 (n = 3)

RESULTS AND DISCUSSION

Addition of SH changes the physical properties of suspensions. Dynamic viscosity of suspension without SH (Z01) amounts to 9.02 mPa x s. The 10%-addition of SH in suspensions increases the viscosity to values 29.07 mPa x s – Z02, and 13.04 mPa x s – Z04, in case of 20%-addition of SH4, the viscosity increases by 8 times for Z03 – 76.11 mPa x s and nearly 10 times for Z05 with SH2 – 88.9 mPa x s.

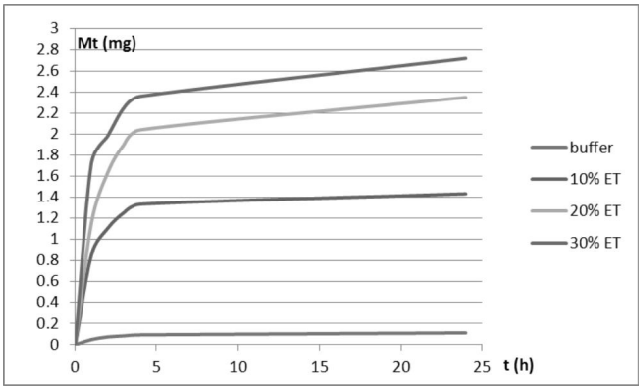


Fig. 2. Release of progesterone from suspension Z02 (n = 3)

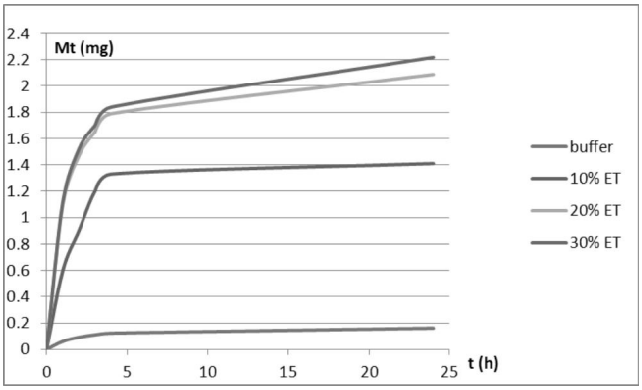


Fig. 3. Release of progesterone from suspension Z04 (n = 3)

Suspensions are more stable with SH. In preparation Z01, sediments were formed quickly – 85.85 cm/day – it may provoke compact mass, difficult to re-distribute. The 10%-addition of SH2 caused increase of stability by 226 times (0.38 cm/day – Z04) and by 572 times for E02 with SH2 – 0.15 cm/day. Better results were obtained by addition of 20% SH2 and SH4 – 0.04 cm/day for Z05, and 0,05 cm/day for Z03 respectively.

During drug release, the test suspensions Z01, Z02, and Z04 released PR according to zero-order process up to 4 hours. Therefore, drug release rate constants (K_0) were calculated, according to the equation 4:

$$K_0 = Mt / t \text{ [mg/h]}, \qquad \text{Eq. 4}$$

where: K_0 – drug release rate constant (mg/h), Mt – quantity of released drug (mg), t – time (h). Suspensions released PR very weakly, from 0.113 mg after 24 h – Z01 to 0.161 mg – Z04.

However, addition of ET to phosphate buffer increases the values of drug release rate constant according to Table 3. The fastest release rate constant of PR appears in case of suspension Z02, which releases drug into phosphate buffer with 30% addition of ET (K_0 = 1.0008 mg/h), the slowest release rate constant has been reported with suspension Z01 releasing PR into pure phosphate buffer (K_0 = 0.0288 mg/h).

Concluding, the presence of starch hydrolysates increases dynamic viscosity and stability of suspensions.

Table 3. Drug release rate constants of preparations (n=3)

Suspension	K_0 (mg/h)			
	Buffer phosphate pH 6.8	Buffer + 10% ET	Buffer +20 % ET	Buffer + 30% ET
Z01	0.0288	0.2933	0.5926	0.6356
Z02	0.0348	0.5110	0.7721	1.0008
Z04	0.0360	0.3333	0.5586	0.5998

The values of released progesterone into pure phosphate buffer pH 6.8 are not significant but addition of ET to acceptor medium increases the release rate constants (K_0). The presence of SH in suspensions also increases the release rate constant of PR.

REFERENCES

1. Czarnecki W. Belniak P.: *Sposób otrzymywania krótkołańcuchowego polisacharydu.* Biuletyn Urz. Patent. 4, 13, 2007.
2. Chorny M. et al.: Study the drug release mechanism from tyrphostin AG-1295-loaded nonospheres by in situ and external sink methods. *J. Cont. Release*, 83, 401, 2002.
3. Freire A.C. et al.: Starch-based coatings for colon-specific drug delivery. Part I: The influence of heat treatment on the physico-chemical properties of high amylose maize starches. *J. Pharm. Biopharm.* 72, 574, 2009.
4. Mc Callion O. et al.: Nebulisation of monodispersible latex sphere suspensions in air-jet and ultrasonic nebulizers. *Int. J. Pharm.* 133, 203, 1996.
5. Martin A. editor (1969): *Physical pharmacy*. Lea & Febiger Phyladelphia, p. 519.
6. Ntawukulilyayo J.D. et al.: Stabilisation of suspensions using sucrose esters and low substituted n-octenylsuccinate starch – xanthan gum associations. *Int. J. Pharm.* 128, 73, 1996.
7. Piao H. et al.: A novel solid-in-oil nanosuspension for transdermal delivery of diclofenac sodium. *Pharm. Research*, 25, 896, 2008.
8. Pignatello R. et al.: Preparation and characterization of eudragit retard nanosuspensions for the ocular delivery of cloricromene. *Pharm. Sci. Tech*. 7, 27, 2006.
9. *Polish Pharmacopeia*, 8th edition, Warsaw 2008.
10. Pongpeerapat A. et al.: Formation mechanism of colloidal nanoparticles obtained from probucol/PVP/SDS ternary ground mixture. *Int. J. Pharm*., 352, 309, 2008.
11. Sethia S., Squillante E.: Solid dispersion of carbamazepine in PVP K30 by conventional solvent evaporation and supercritical methods. *Int. J. Pharm.* 272, 1, 2004.
12. Schiermeier S., Schmidt P.Ch.: Fast dispersible ibuprofen tablets. *J. Pharm. Sci*. 15, 295, 2002.,
13. Unruh T. et al.: Investigations on the melting behaviour of triglyceride nanoparticles. *Colloid Polym. Sci.* 279, 398, 2001,
14. Yasueda S. et al.: Evaluation of ophthalmic suspensions using surface tension. *J. Pharm. Biopharm*. 57, 377, 2004.