Powder Technology 230 (2012) 106–111

Contents lists available at SciVerse ScienceDirect

Powder Technology

journal homepage: www.elsevier.com/locate/powtec

Application of SBA-15 mesoporous material as the carrier for drug formulation systems. Papaverine hydrochloride adsorption and release study

Michał Moritz, Marek Łaniecki *

Faculty of Chemistry, A. Mickiewicz University, Grunwaldzka 6, 60-780 Poznań, Poland

ARTICLE INFO

Article history:
Received 7 December 2011
Received in revised form 28 June 2012
Accepted 30 June 2012
Available online 9 July 2012

Keywords:
Mesoporous materials
Phosphodiesterase inhibitor
Drug delivery
Drug reservoir
Drug release kinetics

ABSTRACT

SBA-15 mesoporous material was used as a matrix in three different drug formulations (powders, granules and tablets). Hydroxypropyl cellulose (HPC) and stearic acid (SA) were applied as modifiers of papaverine hydrochloride release from mesoporous carriers. The samples were characterized by thermogravimetry, differential scanning calorimetry (DSC), X-ray diffraction (XRD) and nitrogen sorptometry at −196 °C. High pressure applied during the drug formulation (granules, tablets) decreases both specific surface area and porosity of SBA-15. The changes in BET surface area were also observed after drug deposition. The Korsmeyer–Peppas model was applied to evaluate the kinetics of papaverine hydrochloride release from hydroxypropyl cellulose- and stearic acid-containing drug formulations. The extended drug release resulted from slow diffusion of the active substance from micro- and mesoporous channels blocked by hydrophobic stearic acid and organic polymer.

1. Introduction

The recently observed enormous growth of chronic diseases such as asthma, hypertension and diabetes inspired scientific groups to develop new drug formulations with extended active substance release. The treatment of these diseases requires continuous doses of a drug during the daytime. Repeated drug administration of traditional drug formulation is very frequently troublesome, especially for the elder. Therefore the Drug Delivery System (DDS) providing the constant therapeutic drug concentration in blood serum might markedly improve therapy [1].

Mesoporous siliceous materials of e.g. MCM-41 or SBA type are a new class of matrices applied in DDSs. Initially, these materials served as supports in heterogeneous catalysis [2,3]. Later on, mesoporous materials demonstrated the potential of an excellent drug carrier [4]. Both MCM-41 and SBA-15 have been already tested in drug adsorption and drug delivery [5]. Mesoporous materials are characterized by large surface area (>1000 m^2/g), uniform pore size distribution and large pore volume (~1.0 cm^3/g). Moreover, high biocompatibility [6,7], low toxicity [8] and the presence of micropores (in SBA-15) [9] promote their application as carriers in drug formulations of prolonged release. The application of MCM-41 loaded with ibuprofen was described in 2001 for the first time [10]. Since then, numerous studies with other mesoporous siliceous materials (SBA, MSU type) as drug carriers were undertaken. Siliceous mesoporous systems were loaded with a wide range of active substances such as antibiotics [11,12], vitamins [13], antiinflammatory drugs [14–16], hypertension drugs [17,18], natural antimicrobial agents [19] and other biomolecules [20,21].

In order to improve the adsorption properties of mesoporous matrices and to obtain better kinetics of the drug release from the drug–carrier complex these materials should be appropriately functionalized. The presence of free silanol groups inside the SBA-15 mesoporous channels can significantly improve its adsorption properties during modification with alkoxysilanes [22–24]. Moreover, modification of mesoporous materials with suitable organic polymers influences the kinetics of the drug release [25,26]. Photo-sensible [27] and magnetic [28] drug delivery systems based on mesoporous materials have been described. It should be mentioned that the industrial production techniques based on spray-drying process have been also considered [29].

This paper describes the application of SBA-15 mesoporous material as the carrier for papaverine hydrochloride. Papaverine hydrochloride is known as a non-selective smooth muscle relaxant [30]. The activity of this drug is based on the inhibition of cyclic adenosine monophosphate (cAMP) and cyclic guanosine monophosphate (cGMP) phosphodiesterases [31]. Moreover, this alcaloid can be also applied in vasospasmic diseases such as spasm associated with subarachnoid hemorrhage [30], erectile dysfunction [32] and spasms of alimentary channel [33]. The aim of this study was to formulate a drug (tablets, granules and coated powders) based on SBA-15, papaverine and excipients and to achieve the extended-release profiles of the active substance.

* Corresponding author. Tel.: +48 61 8291339; fax: +48 61 8291505.
E-mail address: laniecki@amu.edu.pl (M. Łaniecki).

0032-5910/$ – see front matter © 2012 Elsevier B.V. All rights reserved.
doi:10.1016/j.powtec.2012.06.061

2. Experimental

2.1. Synthesis of SBA-15

SBA-15 was synthesized according to the procedure described by Zhao et al. [34] applying triblock copolymer Pluronic P123 as a template and tetraethoxyorthosilicate (TEOS) as a source of silica. During the synthesis 48 g of block copolymer of Pluronic P-123 was dissolved in 360 cm^3 of water and 1440 cm^3 of 2 M HCl at 35 °C. After complete dissolution of co-polymer, 102 g of TEOS was added and the obtained mixture was stirred 20 h at 35 °C. Next, the suspension was transferred into tightly closed vessel and kept for 24 h at 110 °C without stirring. The obtained white solid was filtered and washed repeatedly with deionized water. The air-dry white powder was next calcinated at 500 °C for 6 h (heating rate 1 °C/min).

2.2. Adsorption of papaverine hydrochloride on SBA-15

10.0 g of pure, dehydrated powder of SBA-15 was introduced into 500 cm^3 of water solution of papaverine hydrochloride (15 mg/cm^3). The adsorption process was performed at 25 °C for 24 h. After adsorption the sample was filtered and dried at room temperature for 24 h and another 24 h at 100 °C. The amount of papaverine hydrochloride in dry carrier was estimated from elemental analysis. This sample was marked as SBA-15-Pap.

2.3. Drug formulation

2.3.1. Granulation of SBA-15 materials

The granules of pure SBA-15 and SBA-15-Pap samples were obtained in dry granulation process. The discs of 25 mm in diameter were formed from 10.0 g of appropriate powder using a hydraulic press. The compression pressure was 10–20 MPa. Next, the sample was crushed (Erweka apparatus) and fractionated by sieve analyzer (Fritsch). The fraction between 0.5 and 1.0 mm was collected. Samples were designated as SBA-15-GX and SBA-15-Pap-GX for granules of pure SBA-15 and granules of SBA-15 loaded with papaverine hydrochloride, respectively. The X value corresponds to the applied pressure (in MPa).

2.3.2. Coating process

2.5 g of SBA-15 loaded with papaverine hydrochloride was introduced into 100 cm^3 of 0.5 wt.% n-hexane solution of stearic acid (SA). The suspension was stirred at room temperature for 2 h. Next, the sample was filtered and the remaining n-hexane solvent was removed at 40 °C for 24 h in a vacuum. The obtained sample was designated as SBA-15-Pap-SA.

2.3.3. Tablet preparation

The tablets were prepared from an appropriate amount of mechanically mixed SBA-15-Pap and hydroxypropyl cellulose (HPC). The tablet weight was 0.7 g. The amount of HPC in tableting bulk was from 10 to 50 wt.%. Next, the mixture was compressed into 15 mm discs under pressure of 6 MPa. These samples were designated as SBA-15-Pap-TX%, where X represents the amount of the applied HPC (wt.%).

2.4. Release of papaverine hydrochloride from the drug formulation

The release of papaverine hydrochloride from powdered samples, granules and tablets was performed in Erweka DT 60 apparatus, according to US Pharmacopeia (paddle method) in 0.1 M HCl (500 cm^3) at 37 °C with stirring rate of 50 rotations per minute. After the indicated period of time (0.25–24 h) the solution of the drug (alternatively suspension) was centrifuged. The amount of released drug was calculated from the absorbance value measured spectrophotometrically at 250 nm (0.1 M HCl).

2.5. Characterization of the sample

Both thermogravimetric analysis and differential scanning calorimetry were performed in the air with Setsys-TG-DSC apparatus from Setaram. The XRD measurements of powdered samples were performed using an AXS D8 Advance diffractometer from Bruker ($CuK\alpha = 1.5406$ Å — Bruker). The amount of drug in the carrier and the amount of stearic acid in the formulated samples were based on calculation of C and N contents established in elemental analysis (Vario EL III Elemental Analyser). The amount of released drug was determined from absorbance values at 250 nm using Cary 100 UV–vis spectrophotometer. Adsorption and desorption isotherms of nitrogen at −196 °C were measured using an ASAP 2010 sorptometer (Micromeritics). Before nitrogen adsorption–desorption measurements all samples were degassed at 120 °C for more than 12 h.

3. Results and discussion

3.1. Characteristics of SBA-15 and SBA-15-Pap samples

Thermogravimetric analysis of SBA-15 loaded with papaverine hydrochloride (SBA-15-Pap) shows that adsorption of the drug within the hexagonal channels of mesoporous material does not influence its thermal stability (Fig. 1). Comparison of the DSC curves (see insert in Fig. 1) of pure papaverine hydrochloride and that of SBA-15 loaded with the drug, indicates the absence of an endothermic peak at ~230 °C in the case of the drug–carrier complex. Differential scanning calorimetry confirms an amorphous character of adsorbed papaverine hydrochloride. Endothermic peak on DSC curve (a) corresponds to the melting point of papaverine hydrochloride (220 °C). An amorphous character of the adsorbate is due to its molecular dispersion at the surface of mesoporous SBA-15 structure. Similar results were obtained by Mellaerts et al. [35] while adsorption of itraconazole on SBA-15. Amorphous character of adsorbed papaverine hydrochloride was also confirmed in wide angle X-ray diffraction measurements [17].

Synthesized SBA-15 material had BET surface area of 776 m^2/g, pore volume of 0.89 cm^3/g and microporosity of 0.0863 cm^3/g. These parameters are in agreement with those presented in the literature [36]. Large BET surface area of hexagonal channels in SBA-15, the presence of micropores and free silanol groups [5] at the surface of mesoporous matrix promote the drug adsorption. The results of elemental analysis of the SBA-15-Pap sample indicated that the amount

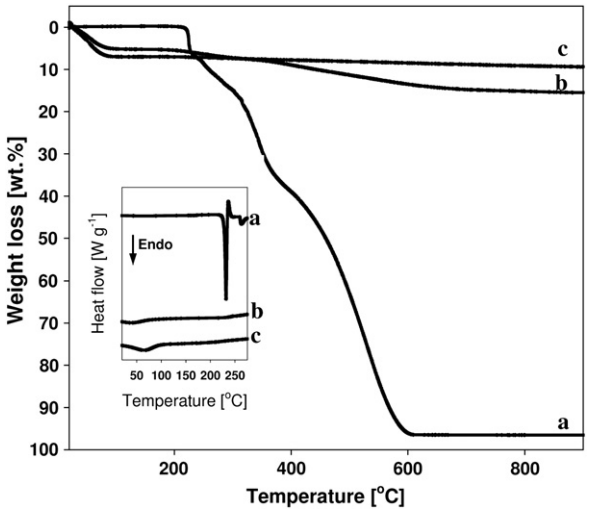


Fig. 1. Thermogravimetric analysis of the sample: (a) papaverine hydrochloride, (b) SBA-15 loaded with papaverine hydrochloride, (c) SBA-15. Insert: curves of differential scanning calorimetry analysis of these samples.

Table 1
Characteristics of SBA-15 and SBA-15-Pap samples.

Sample	Form	Pressure of compression (MPa)	BET surface area (m^2/g)	BJH pore volume (cm^3/g)	t-plot micropore volume (cm^3/g)	BJH average pore diameter (nm)
SBA-15	Powder	–	776	0.89	0.0863	5.7
SBA-15-G10	Granules	10	768	0.89	0.0799	5.6
SBA-15-G15	Granules	15	741	0.85	0.0766	5.5
SBA-15-G20	Granules	20	735	0.83	0.0752	5.4
SBA-15-Pap	Powder	–	478	0.78	0.0104	5.6
SBA-15-Pap-G20	Granules	20	390	0.60	0.0000	5.3
SBA-15-Pap-SA	Powder	–	300	0.54	0.0000	5.2

of adsorbed papaverine hydrochloride was 9.4 wt.%. After the drug adsorption BET surface area and pore volume (both meso- and micropores) were reduced nearly 38% and 12%, respectively (see Table 1). The adsorption of papaverine hydrochloride on SBA-15 results in a decrease of adsorbed nitrogen volume (Fig. 2). This indicates that mainly micropores are blocked after the drug deposition. The same shape and position of hysteresis loop after the drug adsorption confirm that hexagonal array of SBA-15 has been preserved.

3.2. Drug formulation

Granulation of pure SBA-15 and SBA-15 loaded with papaverine hydrochloride resulted in partial destruction of well-defined structure of mesoporous siliceous matrix. The low-angle XRD diffraction patterns [mainly (100) Miller index] of the compressed samples, shown in Fig. 3, clearly demonstrate the reduction of the initial structure. An increase of the compression pressure from 10 to 20 MPa resulted in a decrease of reflection intensity values from 31 to 42%, respectively. This fact demonstrated the collapse of the structure. Compression of SBA-15 matrix (20 MPa) loaded with papaverine hydrochloride resulted in a 53% decrease of reflex intensity (100) in comparison with powdered sample. This is in agreement with the results of Ghedini et al. [37] obtained during compression of SBA-15 and MCM-41 loaded with metoprolol tartrate.

It is well known that an increase of the compression pressure results in lowering the symmetry of mesoporous siliceous materials [37]. The results of sorptometric analysis (Table 1) confirm earlier XRD data indicating no marked changes of mesoporous SBA-15 structure related to compression pressure increase. Under the pressure of 10, 15 and 20 MPa the specific surface area of obtained granules decreased by 1.0, 4.5 and 5.3%, respectively in comparison with powdered SBA-15. Compression of drug loaded SBA-15 sample (SBA-15-Pap) at 20 MPa decreased its BET surface area and pore volume by 18.4 and 23.1%, respectively. Complete collapse of granulated SBA-15-Pap sample (SBA-15-Pap-G20) micropores was observed. Inferior mechanical properties of papaverine hydrochloride-loaded SBA-15 sample possibly come from the negative influence of water environment (acidic drug solution) on the stability of the mesoporous structures as suggested by Izqierdo-Barba et al. [38].

Nitrogen adsorption and desorption isotherms of the compressed samples (Fig. 2) showed characteristic fold of desorptive branch (at value p/p_0 0.4–0.6) of the hysteresis loop (see insert in Fig. 2). This bend is connected with the plugging of mesoporous channels due to the partial degradation of SBA-15 hexagonal channels as suggested

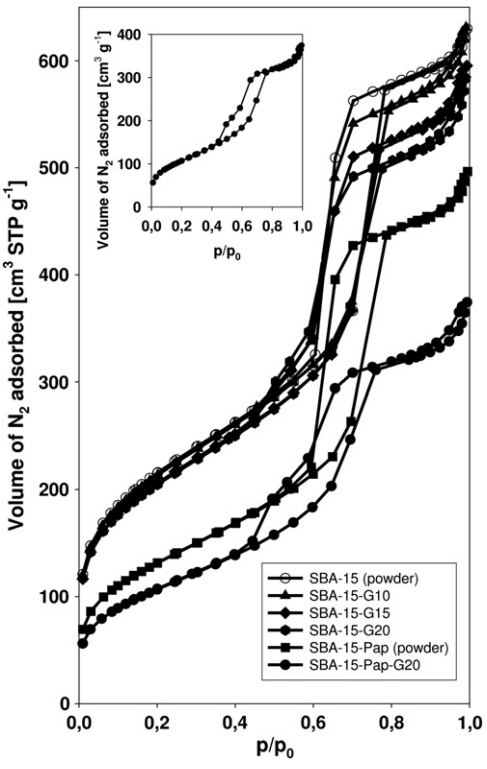


Fig. 2. Nitrogen adsorption–desorption isotherms (−196 °C) of SBA-15 and sample of SBA-15 loaded with papaverine hydrochloride in powder and granulate. Insert: nitrogen adsorption–desorption isotherms of SBA-15-Pap-G20 sample.

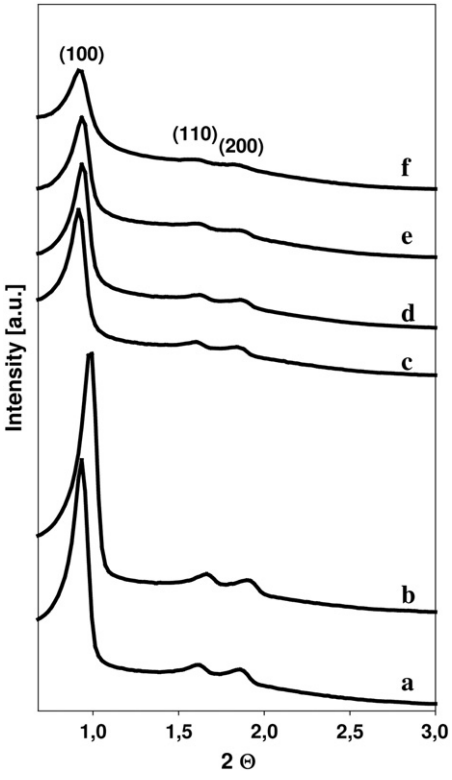


Fig. 3. XRD diffraction patterns (wide angle) of SBA-15 and SBA-15 loaded with papaverine hydrochloride in the powder and granulate. (a) SBA-15, (b) SBA-15-Pap, (c) SBA-15-G10, (d) SBA-15-G15, (e) SBA-15-G20, (f) SBA-15-Pap-G20.

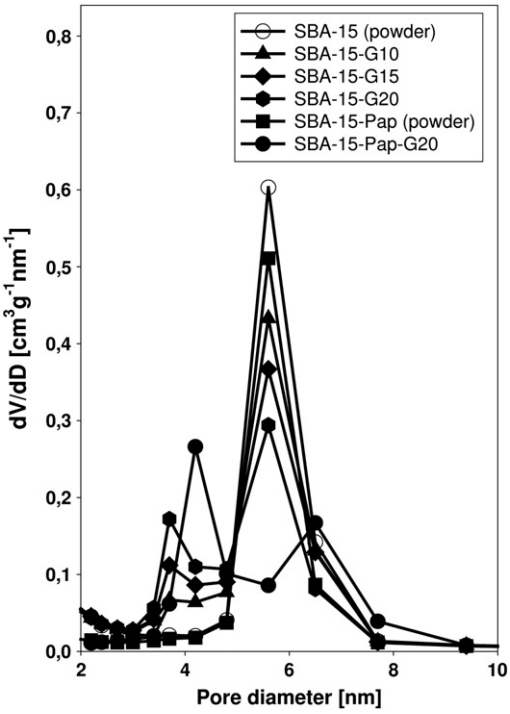


Fig. 4. Pore size distribution of SBA-15 and SBA-15-Pap samples in the powder and granulate.

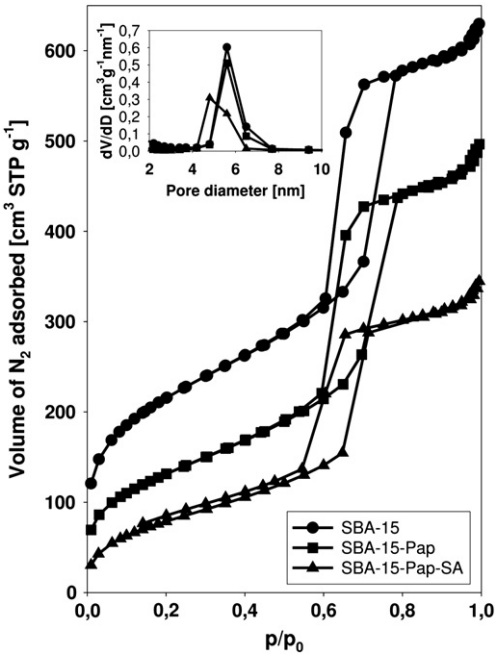


Fig. 5. Nitrogen adsorption–desorption isotherms of SBA-15, SBA-15-Pap samples and SBA-15-Pap sample coated with stearic acid. Insert: pore size distribution of these formulations.

by Chytil et al. [39]. In this case the shape of nitrogen adsorption and desorption isotherms is similar to those obtained for PHTS (plugged hexagonal templated silica) materials with partially blocked channels by silica amorphous nanoparticles [40]. Pore size distribution of SBA-15 after papaverine hydrochloride adsorption (BJH method) presented in Fig. 4 indicates only the decrease of pore volume, whereas compression of this sample under 20 MPa resulted in bimodal pore size distribution. This is in agreement with the measurements of Ghedini et al. [37]. The increase of compression pressure resulted in an increase of pore fraction with smaller diameter (SBA-15-G15, SBA-15-G20 and SBA-15-Pap-G20 samples).

The SBA-15-Pap-SA sample contained 8.8 wt.% of papaverine hydrochloride and 5.7 wt.% of stearic acid. The comparison of nitrogen adsorption–desorption isotherms of uncoated SBA-15-Pap sample with those containing stearic acid shows the decrease of BET surface area and pore volume by 37% and 30%, respectively (see Table 1 and Fig. 5). After adsorption of stearic acid the complete clogging of micropores (t-plot calculations) was observed. Simultaneously, the pore size distribution of SBA-15-Pap-SA sample showed the shift towards smaller pores (see insert in Fig. 5).

3.3. Drug release profiles of papaverine hydrochloride from the drug formulation

Appropriate kinetics of active substance release from the therapeutic systems is a crucial point for every patient. Suitable drug release may limit the number of taken daily doses and provide therapeutic concentration of the drug in the blood serum. The kinetics of papaverine hydrochloride released from powdered SBA-15, granulated SBA-15 and coated SBA-15 systems was studied as a function of time (Fig. 6). The release of papaverine hydrochloride adsorbed on pure powdered SBA-15 occurred very rapidly. After 15 min, 2 h and 6 h the amount of released drug was 85%, 91% and 94%, respectively (Fig. 6, curve a). Slightly slower dissolution (71, 84 and 90%) after the same time intervals was found for granulated SBA-15-Pap-G20 sample (Fig. 6, curve b). This effect is caused by the active substance diffusion limitation from the partially destroyed mesoporous channels during compression. In both cases, nearly total release of papaverine hydrochloride from SBA-15-Pap and SBA-15-Pap-G20 samples was observed after 24 h. The release of active substance from the compressed materials was discussed also by A.L. Doadrio et al. [41] in the work concerning adsorption and release of gentamicin from SBA-15. The authors established that the decrease of the surface area pore volume of the carrier renders difficulties in drug diffusion. Similar conclusion is given also by Ghedini et al. [37] in the work describing the compression of SBA-15 and MCM-41 with adsorbed metoprolol tartrate.

The treatment of SBA-15-Pap with stearic acid (SA) resulted even in much slower (Fig. 6, curve c) release of papaverine hydrochloride (61, 72 and 78% after 15 min, 2 h and 6 h, respectively). Moreover, after 24 h only 80% of papaverine hydrochloride was released from the SA-coated sample. The observed slow release of the drug from this sample is connected with hydrophobic character of stearic acid and difficulties in water molecule diffusion inside the meso- and microporous channels internally covered by stearic acid.

The release profiles of papaverine hydrochloride from tablets containing various amounts of hydroxypropyl cellulose are shown in Fig. 7. The release profile of papaverine hydrochloride from non-modified powdered SBA-15 carrier is shown as a reference (Fig. 7, curve a). The obtained results indicate that the process of

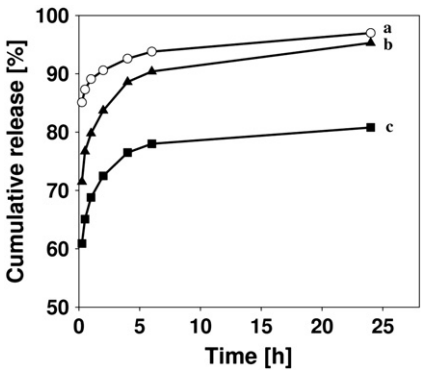


Fig. 6. Cumulative release profiles of papaverine hydrochloride from: (a) SBA-15-Pap, (b) SBA-15-Pap-G20, and (c) SBA-15-Pap-SA.

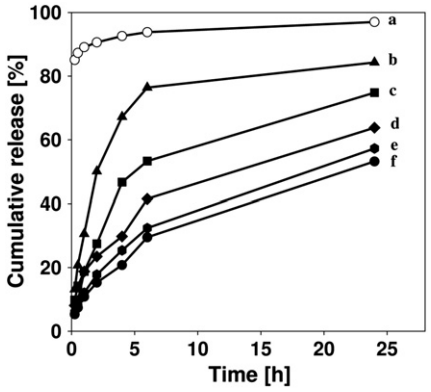


Fig. 7. Cumulative release profiles of papaverine hydrochloride from tablets containing HPC, (a) SBA-15-Pap (powder), (b) SBA-15-Pap-T10%. (c) SBA-15-Pap-T-20%, (d) SBA-15-Pap-T-30%, (e) SBA-15-Pap-T40%, (f) SBA-15-Pap-T50%.

drug release was the fastest for tablets with low content of HPC and the slowest for formulation containing 50 wt.% of HPC. The equation based on Korsmeyer–Peppas [42] model was applied to examine the kinetics of papaverine hydrochloride release from tablets prepared from SBA-15-Pap and HPC.

$$M_t/M_\infty = kt^n$$

where M_t and M_∞ describe the amount of the drug released after time t and the initial amount of the drug in the carrier, respectively, M_t/M_∞ is a fractional release of drug, k is a constant incorporating structural and geometric characteristics of drug formulation, n is the release exponent, and t represents duration time of release. This model was used for controlled drug release from polymeric system [42]. The values of n and k parameters of Korsmeyer–Peppas equation were calculated by linear regression method for the ratio $M_t/M_\infty < 0.6$. The results presented in Table 2 show that in all cases the process of release proceeds according to Fickian diffusion mechanism (n-value: 0.47–0.51). Kinetic constant k was the highest for the formulation of the lowest content of polymer. Prolongation of the drug release process from the formulation containing high-molecular hydrophilic polymer is due to difficult diffusion of the drug molecules through the layer of formed hydrogel. Retardation of release process may result from slower penetration of water inside meso- and microporous channels due to the polymer layer formation. The effect of slow release is discussed by Fagundes et al. [43] in the work presenting atenolol release from SBA-15 matrix containing collagen. This effect is explained by the presence of hydrogen interactions between the drug and biopolymer. Such explanation is also given by Xu et al. [26] in the work describing drug release process from SBA-15 tablets coated with hydroxypropyl methylcellulose phthalate.

Siliceous mesoporous materials can be an alternative for traditionally applicable polymers in drug formulation such as poly(lactic acid), poly(lactic-co-glycolic acid) [44] and hydroxypropyl methyl cellulose [45]. However, modification of mesoporous surface with hydrophilic polymers allows to combine unique property of polymers (diffusion through hydrogel layer) and textural property of mesoporous matrices (diffusion with long channels). The results demonstrated by Tatavarti et al. [46] in the work describing the drug formulation with papaverine hydrochloride based on hydroxypropyl methyl cellulose (25 wt.%) and other excipients indicated very slow drug release ca. 40% after 15 h. The release profiles of papaverine hydrochloride from SBA-15 tablets containing 20 wt.% and 30 wt.% of HPC are presented in Fig. 7 and Table 2. These formulations demonstrated good pharmaceutical availability after 24 h (75% and 64%, respectively).

Table 2
Kinetics of papaverine hydrochloride release from tablets with SBA-15-Pap and HPC.

Sample	Amount of HPC in tablet (wt.%)	Exponent (n)	Release constant (k)	R^2
SBA-15-Pap-T10%	10	0.50	0.28	0.9865
SBA-15-Pap-T20%	20	0.47	0.20	0.9709
SBA-15-Pap-T30%	30	0.47	0.16	0.9721
SBA-15-Pap-T40%	40	0.51	0.12	0.9951
SBA-15-Pap-T50%	50	0.51	0.11	0.9968

4. Conclusions

SBA-15 siliceous mesoporous material can be used as a carrier for papaverine hydrochloride in DDS. The use of simple physical processes (compression, granulation, and coating) can slow down the drug release. An addition of stearic acid and hydroxypropyl cellulose as modifiers allows to extend the drug release. Extended-release of granules was the result of partial degradation of hexagonal mesoporous channels during the compression. Prolonged drug release from coated powder resulted from the locking of meso- and microporous channels and hydrophobic character of stearic acid. The most convenient and very promising results were obtained during the formulation of tablets containing 10 wt.% and 20 wt.% of hydroxypropyl cellulose as high-molecular polymer. In this case the best kinetics of drug release and the highest pharmaceutical availability were achieved.

List of abbreviation and symbols

BET	Brunauer–Emmett–Teller isotherm
BJH	Barrett–Joyner–Halenda isotherm
cAMP	Cyclic adenosine monophosphate
cGMP	Cyclic guanosine monophosphate
DDS	Drug delivery system
DSC	Differential scanning calorimetry
GX	Granules (X described pressure of compression)
HPC	Hydroxypropyl cellulose
k	Structural and geometrical drug formulation constant
M_t	Drug release amount
M_∞	Initial drug amount in the carrier
MCM-41	Mobil Composition of Matter (silica)
MSU	Michigan State University (silica)
n	Release exponent
p/p_0	Relative pressure
Pap	Papaverine hydrochloride
PHTS	Plugged hexagonal templated silica
SA	Stearic acid
SBA-15	Santa Barbara Amorphous (silica)
STP	Standard temperature and pressure
t	Time
T%X	Tablet (X described the amount of HPC in drug formulation)
TEOS	Tetraethyl orthosilicate
TG	Thermogravimetry
XRD	X-ray diffraction

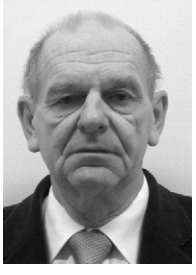
Acknowledgement

This work was financially supported by "Scholarship support for Ph.D. students specializing in majors strategic for Wielkopolska's development", Sub-measure 8.2.2 Human Capital Operational Programme, co-financed by European Union under the European Social Fund and by the Ministry of Science and Higher Education-Poland (grant no. NN204 028038).

References

[1] A.K. Dash, G.C. Cudwarth II, Therapeutic applications of implantable drug delivery systems, Journal of Pharmacological and Toxicological Methods 40 (1998) 1–12.
[2] N.K.K. Raj, S.S. Deshpandale, R.H. Ingle, T. Raja, P. Manikandan, Heterogenized molybdovanadophosphoric acid on amine-functionalized SBA-15 for selective oxidation of alkenes, Catalysis Letters 98 (2004) 217–224.
[3] X. Zhang, Y. Yue, Z. Gao, Chromium oxide supported on mesoporous SBA-15 as propane dehydrogenation and oxidative dehydrogenation catalysts, Catalysis Letters 83 (2002) 19–25.
[4] S. Wang, Ordered mesoporous materials for drug delivery, Microporous and Mesoporous Materials 117 (2009) 1–9.
[5] M. Vallet-Regí, F. Balas, D. Arcos, Mesoporous materials for drug delivery, Angewandte Chemie International Edition 46 (2007) 7548–7558.
[6] T. López, E.I. Basaldella, M.L. Ojeda, J. Manjarrez, R. Alexander-Katz, Encapsulation of valproic acid and sodic phenytoin in ordered mesoporous SiO_2 solids for the treatment of temporal lobe epilepsy, Optical Materials 29 (2006) 75–81.
[7] A. Díaz, T. López, J. Manjarrez, E. Basaldella, J.M. Martinez-Blanes, J.A. Odriozola, Growth of hydroxyapatite in a biocompatible mesoporous ordered silica, Acta Biomaterialia 2 (2006) 173–179.
[8] S.P. Hudson, R.F. Padera, R. Langer, D.S. Kohane, The biocompatibility of mesoporous silicates, Biomaterials 29 (2009) 4045–4055.
[9] C.G. Sonwane, P.J. Ludovice, A note on micro- and mesoporous in the walls of SBA-15 and hysteresis of adsorption isotherms, Journal of Molecular Catalysis A: Chemical 238 (2005) 135–137.
[10] M. Vallet-Regí, A. Ramila, R.P. del Real, J. Pérez-Pariente, A new property of MCM-41: drug delivery system, Chemistry of Materials 13 (2001) 308–311.
[11] A.L. Doadrio, J.C. Doadrio, J.M. Sánchez-Montero, A.J. Salinas, M. Vallet-Regí, A rational explanation of the vancomycin release from SBA-15 and its derivative by molecular modeling, Microporous and Mesoporous Materials 132 (2010) 559–566.
[12] M. Vallet-Regí, J.C. Doadrio, A.L. Doadrio, I. Izquierdo-Barba, J. Pérez-Pariente, Hexagonal ordered mesoporous material as a matrix for the controlled release of amoxicillin, Solid State Ionics 172 (2004) 435–439.
[13] Z. Wu, Y. Jiang, T. Kim, K. Lee, Effects of surface coating on the controlled release of vitamin B_1 from mesoporous silica tablets, Journal of Controlled Release 119 (2007) 215–221.
[14] D. Halamová, M. Badaničová, V. Zeleňák, T. Gondová, U. Vainio, Naproxen drug delivery using periodic mesoporous silica SBA-15, Applied Surface Science 256 (2010) 6489–6494.
[15] C. Charnay, S. Begu, C. Tourne-Peteilh, L. Nicole, D.A. Lerner, J.M. Devoisselle, Inclusion of ibuprofen in mesoporous templated silica drug loading and release property, European Journal of Pharmaceutics and Biopharmaceutics 57 (2004) 533–540.
[16] W. Xu, Q. Gao, Y. Xu, D. Wu, Y. Sun, W. Shen, F. Deng, Controllable release of ibuprofen from size-adjustable and surface hydrophobic mesoporous silica spheres, Powder Technology 191 (2009) 13–20.
[17] M. Moritz, M. Łaniecki, Modified SBA-15 as the carrier for metoprolol and papaverine: adsorption and release study, Journal of Solid State Chemistry 184 (2011) 1761–1767.
[18] F. Qu, G. Zhu, S. Huang, S. Li, J. Sun, D. Zhang, S. Qiu, Controlled release of captopril by regulating the pore size and morphology of ordered mesoporous silica, Microporous and Mesoporous Materials 92 (2006) 1–9.
[19] S.-Y. Park, P. Pendleton, Mesoporous silica SBA-15 for natural antimicrobial delivery, Powder Technology 223 (2012) 77–82.
[20] Y. Lu, Y. Go, Y. Wang, X. Liu, Y. Wang, Y. Guo, Z. Zhang, G. Lu, Immobilized penicillin G acylase on mesoporous silica: the influence of pore size, pore volume and mesophases, Microporous and Mesoporous Materials 114 (2008) 507–510.
[21] F. Balas, M. Manzano, M. Colilla, M. Vallet-Regí, L-Trp adsorption into silica mesoporous materials to promote bone formation, Acta Biomaterialia 4 (2008) 514–522.
[22] W. Xu, Q. Gao, Y. Xu, D. Wu, Y. Sun, W. Shen, F. Deng, Controlled drug release from bifunctionalized mesoporous silica, Journal of Solid State Chemistry 181 (2008) 2837–2844.
[23] M. Vallet-Regi, F. Balas, M. Collila, M. Manzano, Bioceramics and pharmaceuticals: a remarkable synergy, Solid State Sciences 9 (2007) 768–776.
[24] J.C. Doadrio, E.M.B. Sousa, I. Izquierdo-Barba, A.L. Doadrio, J. Perez-Pariente, M. Vallet-Regí, Functionalization of mesoporous materials with long alkyl chains as a strategy for controlling drug delivery pattern, Journal of Materials Chemistry 16 (2006) 462–466.
[25] Y. Zhu, J. Shi, A mesoporous core-shell structure for pH-controlled storage and release of water-soluble drug, Microporous and Mesoporous Materials 103 (2007) 243–249.
[26] W. Xu, Q. Gao, Y. Xu, D. Wu, Y. Sun, pH-controlled drug release from mesoporous silica tablets coated with hydroxypropyl methylcellulose phthalate, Materials Research Bulletin 44 (2009) 606–612.
[27] N.K. Mal, M. Fujiwara, Y. Tanaka, T. Taguchi, M. Matsukata, Photo-switched storage and release of guest molecules in the pore void of coumarin-modified MCM-41, Chemistry of Materials 15 (2003) 3385–3394.
[28] Y. Zhu, S. Kaskel, T. Ikoma, N. Hanagata, Magnetic SBA-15/poly(N-isopropylacrylamide) composite: preparation, characterisation and temperature-responsive drug release property, Microporous and Mesoporous Materials 123 (2009) 107–112.
[29] P.B. Sarawade, J.-K. Kim, A. Hilonga, H.T. Kim, Preparation of hydrophobic mesoporous silica powder with a high specific surface area by surface modification of a wet-gel slurry and spray-drying, Powder Technology 197 (2010) 288–294.
[30] Y.J. Gao, S. Stead, R.K.M.W. Lee, Papaverine induces apoptosis in vascular endothelial and smooth muscle cells, Life Sciences 70 (2002) 2675–2685.
[31] J.R. Carhuapoma, A.I. Qureshi, R.J. Tamargo, J.M. Mathis, D.F. Hanley, Intra-arterial papaverine-induced seizures: case report and review of the literature, Surgical Neurology 55 (2001) 159–163.
[32] E.D. Kim, R. El-Rashidy, K.T. McVary, Papaverine topical gel for treatment of erectile dysfunction, The Journal of Urology 153 (1995) 361–365.
[33] P. Lebeau, M.M. Janot, Traité de Pharmacie Chimique, VI^{em} edition Masson et C^{ie} Editeurs, Paris, 1956. Tome IV.
[34] D. Zhao, Q. Huo, J. Feng, B.F. Chmelka, G.D. Stucky, Nonionic triblock and star diblock copolymer and oligomeric surfactant syntheses of highly ordered, hydrothermally stable, mesoporous silica structures, Journal of the American Chemical Society 120 (1998) 6024–6036.
[35] R. Mellaerts, K. Houthoofd, K. Elen, H. Chen, M. Van Speybroeck, J. Van Humbeeck, P. Augustijns, J. Mullens, G. Van den Mooter, J.A. Martens, Aging behavior of pharmaceutical formulation of itraconazole on SBA-15 ordered mesoporous silica carrier material, Microporous and Mesoporous Materials 130 (2010) 154–161.
[36] V. Meynen, P. Cool, E.F. Vansant, Verified syntheses of mesoporous materials, Microporous and Mesoporous Materials 125 (2009) 170–223.
[37] E. Ghedini, M. Signoretto, F. Pinna, V. Crocella, L. Bertinetti, G. Cerrato, Controlled release of metoprolol tartrate from nanoporous silica matrices, Microporous and Mesoporous Materials 132 (2010) 258–267.
[38] I. Izquierdo-Barba, M. Collila, M. Manzano, M. Vallet-Regí, In vitro stability of SBA-15 under physiological conditions, Microporous and Mesoporous Materials 132 (2010) 442–452.
[39] S. Chytil, L. Haugland, E.A. Blekkan, On the mechanical stability of mesoporous silica SBA-15, Microporous and Mesoporous Materials 111 (2008) 134–142.
[40] P. Van Der Voort, P.I. Ravikovitch, K.P. De Jong, M. Benjelloun, E. Van Bavel, A.H. Janssen, A.V. Neimark, B.M. Weckhuysen, E.F. Vansant, A new templated ordered structure with combined micro- and mesopores and internal silica nanocapsules, The Journal of Physical Chemistry. B 106 (2002) 5873–5877.
[41] A.L. Doadrio, E.M.B. Sousa, J.C. Doadrio, J. Pérez-Pariente, I. Izquierdo-Barba, M. Vallet-Regí, Mesoporous SBA-15 HPLC evaluation for controlled gentamicin drug delivery, Journal of Controlled Release 97 (2004) 125–132.
[42] P. Costa, J.M.S. Lobo, Modeling and comparison of dissolution profiles, European Journal of Pharmaceutical Sciences 13 (2001) 123–133.
[43] L.B. Fagundes, T.G.F. Sousa, A. Sousa, V.V. Silva, E.M.B. Sousa, SBA-15-collagen hybrid material for drug delivery application, Journal of Non-Crystalline Solids 352 (2006) 3496–3501.
[44] M. Miyajima, A. Koshika, J. Okada, M. Ikeda, K. Nishimura, Effect of polymer crystallinity on papaverine release from poly (L-lactic acid) matrix, Journal of Controlled Release 49 (1997) 207–215.
[45] R. Espinoza, E. Hong, L. Villafuerte, Influence of admixed citric acid on the release profile of pelanserin hydrochloride from HPMC matrix tablets, International Journal of Pharmaceutics 201 (2000) 165–173.
[46] A.S. Tatavarti, K.A. Mehta, L.L. Augsburger, S.W. Hoag, Influence of methacrylic and acrylic acid polymers on the release performance of weakly basic drugs from sustained release hydrophilic matrices, Journal of Pharmaceutical Sciences 93 (2004) 2319–2331.

Michał Moritz received his M.Sc. (Faculty of Biology) from Adam Mickiewicz University (Poznań, Poland) in 2007. In 2008, he received his M.Sc. (Faculty of Pharmacy) from Poznan University of Medical Science (Poland). He received his Ph.D. (Faculty of Chemistry) from Adam Mickiewicz University in 2011. His research interests include application of mesoporous materials and nanomaterials in pharmacy and medicine, drug formulation, drug stability, and photogeneration of hydrogen with purple bacteria.



Marek Łaniecki received his M.Sc. (1971) and his Ph.D. (1977) from Adam Mickiewicz University (Poznań, Poland). After a post-doctoral stay at Northwestern University (USA) from 1978 to 1979, he was a member of a research group at Fritz-Haber-Institut der Max-Planc-Gesselshaft (West Berlin) from 1985 to 1987. He received his D.Sc. from Adam Mickiewicz University (Poznań, Poland) in 1997. Since 2007, he is a Professor at Adam Mickiewicz University. He was President of Polish Zeolite Association from 2003 to 2006. He was a Visiting Professor at Platforma Solar de Almeria (2002) and University of Utah (2007). His research interests include catalysis, photocatalysis, zeolites, HDS reaction, and mesoporous materials as supports for drugs, photocatalytic and photofermentative generation of hydrogen.