Nanostructured mesoporous silica – carriers for some antihypertensive agents

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INTRODUCTION

For over two decades, the main topic of the both chemical and medical studies has been on to find ways of intervening in disease processes by delivering drugs to the body at a sustained rate, directly to the site of action, with lower toxicity.

Considerable research efforts have been directed toward the development of silica mesoporous carriers as controlled drug delivery matrices whose properties are controlled not only by the chemical composition, also by their properties: stable, uniform porous structure, high surface area, tunable pore size and well-defined surface properties. Moreover, their biocompatibility, high in vivo stability, low toxicity, high carrier capacity, feasibility of incorporation in their structure of both hydrophilic and hydrophobic drugs, and feasibility of variable routes of administration, have improved their applicability. The importance of these materials as drug carriers is based on the ability of the silanol groups in the mesopores walls. In all experiments, the drug loading was carried out by impregnation method.

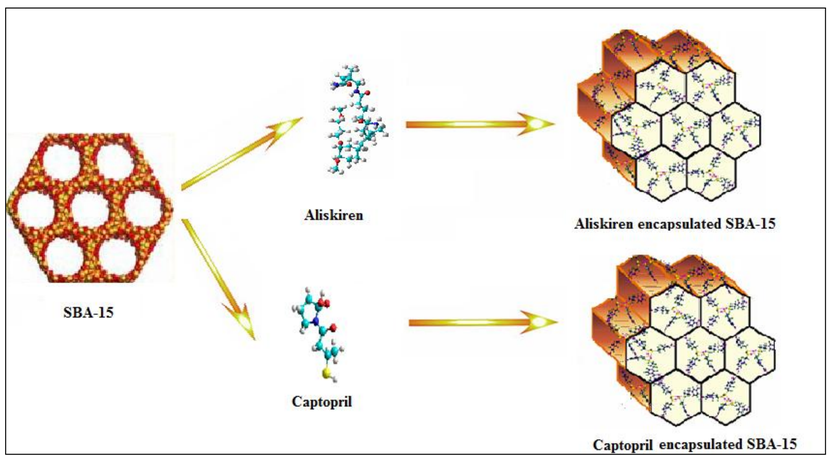


Fig. 1. Schematic illustration of adsorption experiments onto mesoporous silica matrix of the aliskiren and captopril

EXPERIMENTAL

In this paper, SBA-15 mesoporous silica was used as carrier for the following antihypertensive agents: Captopril (the first ACE inhibitor) and Aliskiren (the first in market renin inhibitor) in order to obtain controlled drug delivery formulations (Fig.1).

The release profile of captopril and aliskiren was obtained by soaking drug-loaded powders in a solution of simulated gastric fluid (pH=1.2; aqueous solution containing HCl 0.1 molL–1), as well as in a solution of simulated intestinal fluid (pH=6.8).

The structure of the mesoporous matrices was characterized using powder X-ray diffraction (XRD), nitrogen adsorption and desorption isotherms, Scanning Electron Microscopy (SEM) and FTIR Spectroscopy.

RESULTS AND DISCUSSIONS

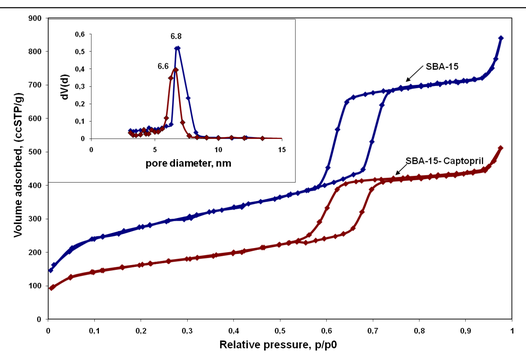
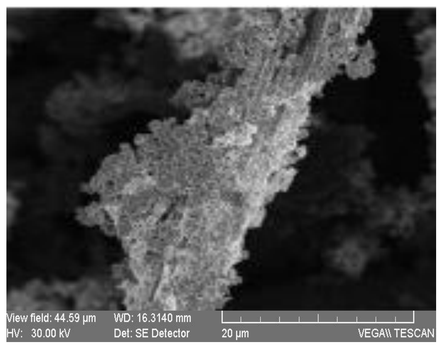


Table 1. Textural properties of the studied samples

SAMPLE	Surface area, m^2/g	Pore volume, cm^3/g	Pore radius, nm
SBA-15	749.5	1.15	6.8
SBA-15- captopril	466.9	0.78	6.6
SBA-15- aliskiren	523.4	0.86	5.3



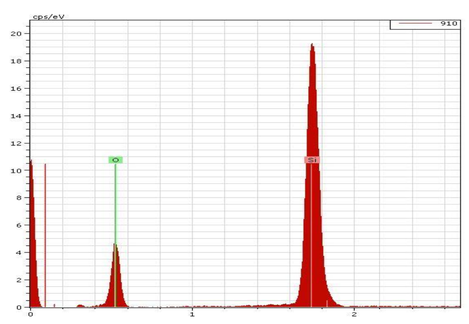


Fig. 4. SEM images and EDAX of the SBA -15

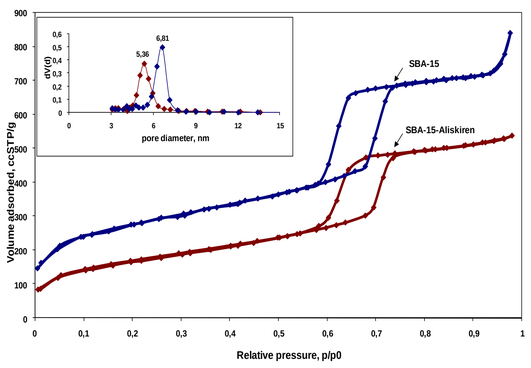


Fig.2. The N_2 adsorption/desorption isotherms of aliskiren -SBA-15 compared with the matrix.

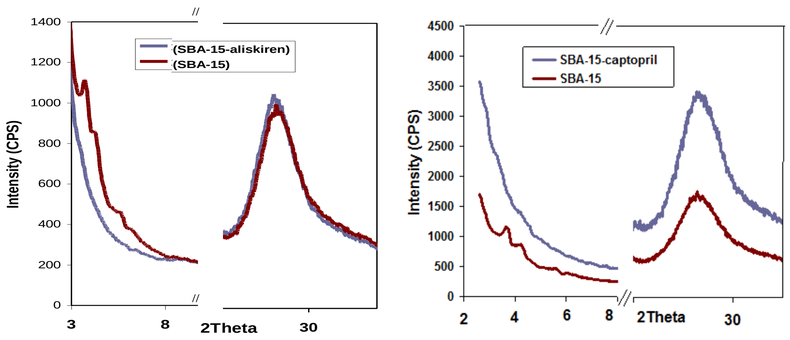


Fig.3. X-ray diffraction patterns of the captopril and aliskiren loaded amino-functionalized SBA-15

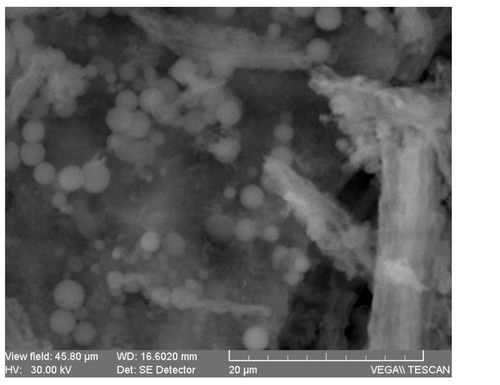


Fig. 5. SEM images of the SBA -15- captopril

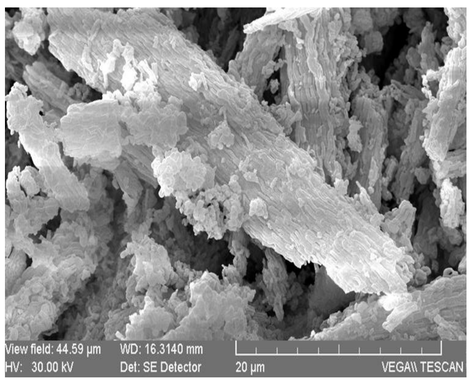


Fig. 6. SEM images of the SBA -15 - aliskiren

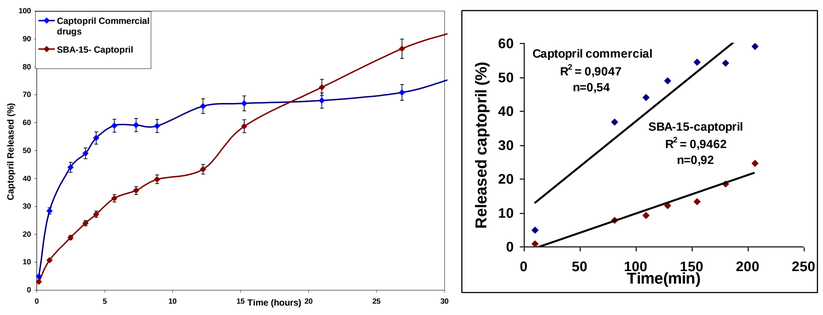


Fig.6. Captopril release in simulated intestinal fluid (PBS) and the representation of "n" pattern calculated from the Korsmeyer–Peppas

In order to analyze the data obtained from the *in vitro* release studies and to evaluate the kinetic release mechanism, we used the Korsmeyer and Peppas equation - a simple, semi-empiric model, when diffusion is the main drug release mechanism, relating exponentially the drug release to the elapsed time (t): $F = ktn$, where K is a kinetic constant characterizing the drug–carrier system, while n is an exponent that characterizes the mechanism of drug release. If the exponent $n \leq 0.45$, then the drug release mechanism is a Fickian diffusion and if $0.45 < n < 0.95$, then it is a non- Fickian or anomalous diffusion.

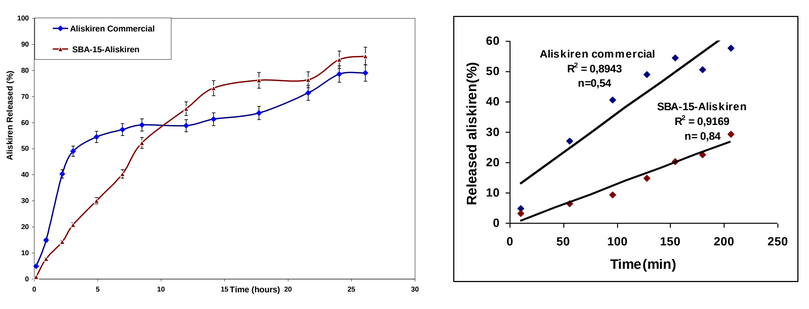


Fig.7. Aliskiren release in simulated intestinal fluid (PBS) and the representation of "n" pattern calculated from the Korsmeyer–Peppas

CONCLUSIONS

Slower release was observed for both aliskiren and captopril products loaded on the SBA-15 matrix when compared to commercial preparations.The function of SBA-15 materials as drug carriers is based on the ability of the silanol groups in the mesopore walls to adsorb molecules of pharmacological interest, followed by a potentially controlled release.

The present results demonstrated that the farmacokinetic parameters of the drugs could potentially be influenced by the matrix loaded. SBA-15 could be an excellent biocompatible inorganic host for drug reservoirs and delivery carriers. The observations through the present method open the opportunity for considering formulations with only once daily administration, which in the context of the polymedication usually associated to hypertension and other related medical conditions, would increase the compliance of the patient and treatment response. The advantages of the prepared delivery systems are the gradual drug release behavior and the lack of toxicity, which open their prospective uses in potential formulations with once per day administration.

Encapsulation of the antihypertensive agents into mesoporous silica might result in new opportunities for cardiovascular therapy.

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