Electronic Supplementary Information (ESI)

Effect of silica precursors transformation on diclofenac sodium release

A. Kierys*[a], R. Kasperek[b], P. Krasucka[a], Ł. Zimmer[b], E. Poleszak[b], J. Goworek[a]

[a]Maria Curie-Sklodowska University, Faculty of Chemistry, Department of Adsorption, M. Curie-Sklodowska Sq. 3, 20-031 Lublin, Poland
[b]Medical University of Lublin, Faculty of Pharmacy, Department of Applied Pharmacy, 1 Chodzki Str, 20-093 Lublin, Poland

Corresponding Author
* Correspondence and requests for materials should be addressed to Agnieszka Kierys (agnieszka.kierys@umcs.lublin.pl)

Analysis of actual diclofenac sodium content A portion of the P-DS, P-DS-T and P-DS-ET beads was crushed and powdered in a mortar. An accurately weighed 200 mg sample was transferred into a 100 ml volumetric flask containing 50 ml of phosphate buffer at pH 6.8. The flask was shaken for 2 hours in a mixer (Vortex Genius 3). Next, the flask was diluted with phosphate buffer at pH 6.8 to volume and mixed. The mixture was filtered with the Whatman filter at 0.45 µm sized pore, and 2 ml of the solution was transferred into a 50 ml volumetric flask and diluted with phosphate buffer at pH 6.8. The absorbance of this solution was determined by UV spectrophotometrically at 276 nm (Omega UV – VIS, Thermo Scientific, England) against the blank (phosphate buffer at pH 6.8). The experiment was repeated six times. The actual content of diclofenac sodium salt ranges from 203 mg/g for P-DS to 63 mg/g for P-DS-T and 38 mg/g for P-DS-ET, taking into account the mass of the total carrier system.

Drug release kinetics There are many factors involved in the release of a soluble drug from an insoluble matrix tablet; these include: solubility, drug concentration in the tablet, the drug diffusivity as well as the porosity and tortuosity of the tablet.[1] To study the release kinetics, data obtained from in vitro drug release studies were plotted in various kinetic models: zero order (Eq. 1), as the cumulative percentage of drug release vs. time; first order (Eq. 2), as the log of percent drug remaining to be released vs. time; Higuchi's model (Eq. 3), as cumulative percentage drug release Vs the square root of time; and the Hixson-Crowell model, as cube root of cumulative percentage of drug remaining vs. time (Eq. 4). The obtained drug release data were analyzed taking into account first 60 % drug release data.

The zero order rate describes the systems where the drug release is independent of its concentration.

$$Q = K_0 \times t \qquad \text{(Eq. 1)}$$

where Q is the amount of drug released in time t, K_0 is the zero order rate constant expressed in units of concentration.[2]

The first order describes the release where the release rate is concentration dependent.

$$\text{Log } Q = \text{Log } Q_0 - K_t / 2.303 \qquad \text{(Eq. 2)}$$

where Q is the amount of the drug released in time t, Q_0 is the initial amount of the drug and K is the first order rate constant.[3]

Higuchi's model describes the release of drugs from insoluble matrices as a square root of time dependent process based on Fickian diffusion.

$$Q = K_H t^{1/2} \qquad \text{(Eq. 3)}$$

where Q is the amount of the drug released in time t, K_H is the constant reflecting the design variables of the system.[4] The Higuchi model describes drug release through the diffusion mechanism and it is used to describe drug dissolution from systems such as matrix tablets containing water-soluble drugs.

To evaluate the drug release with changes in the surface area and the diameter of the particles, the data were also plotted using the Hixson-Crowell cube root law,

$$Q_0^{1/3} - Q_t^{1/3} = K_s t \qquad \text{(Eq. 4)}$$

where Q_t is the amount of drug remaining in time t, Q_0 is the initial amount of the drug in the tablet, and K_s is the rate constant incorporating the surface–volume relation. This model assumes that drug release is limited by the dissolution rate of the particles rather than by diffusion through the polymer matrix.[5]

Also, to evaluate the mechanism of the drug release from tablets, the first 60 % of drug release data were plotted in Korsmeyer-Peppas equation (Eq. 5) as the log of cumulative % of the drug released vs. log time, and the exponent n value was calculated through the slope of the straight line.[6, 7]

$$M_t / M\infty = K_t^n \qquad \text{(Eq. 5)}$$

where $M_t/M\infty$ is the fraction of the drug released at time t, k is a constant incorporating the properties of the macromolecular polymeric system and the drug and n is an exponent used to characterize the transport mechanism. For spherical shaped particles, if the exponent n= 0.43, then the drug release mechanism is Fickian diffusion, 0.43 < n < 0.85 for anomalous behaviour or non-Fickian transport, n = 0.85 for Case II transport (relaxational), and n > 0.85 for Super Case II transport[5, 7]. Kinetic analyzes were made using Statistica 8.0 software.

Table S1 Parameters estimated from the fitting diclofenac sodium salt release data to zero order, first order, Higuchi, Hixson-Crowell and Korsmeyer – Peppas equations.

Sample	Zero order		First order		Higuchi		Hixson-Crowell		Korsmeyer's	
	K_0	R^2	K	R^2	K_H	R^2	K_S	R^2	n	R^2
P-DS	5.208	0.741	0.1290	0.721	9.711	0.64	0.114	0.737	0.178	0.972
P-DS-T	8.034	0.836	0.210	0.940	18.519	0.856	0.217	0.722	0.407	0.936
P-DS-ET	6.329	0.476	0.156	0.599	16.432	0.666	0.192	0.353	0.482	0.654

Scanning Electron Microscope

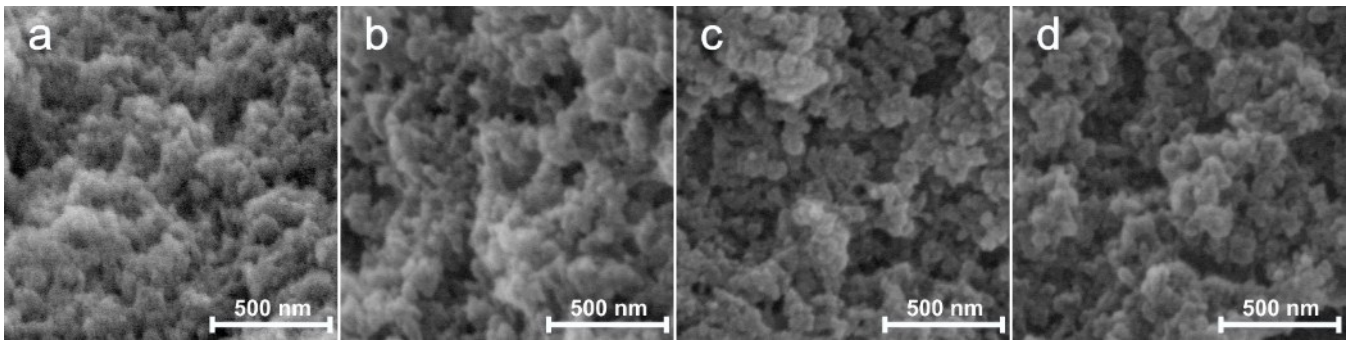

Fig. SI1. SEM micrographs of the interior of the Amberlite XAD7HP before modification (a), the polymer-diclofenac sodium conjugate (P-DS) (b), the polymer-drug-silica (P-DS-T) (c) and polymer-drug-polyethylsilsesquioxane composites (P-DS-ET) (d).

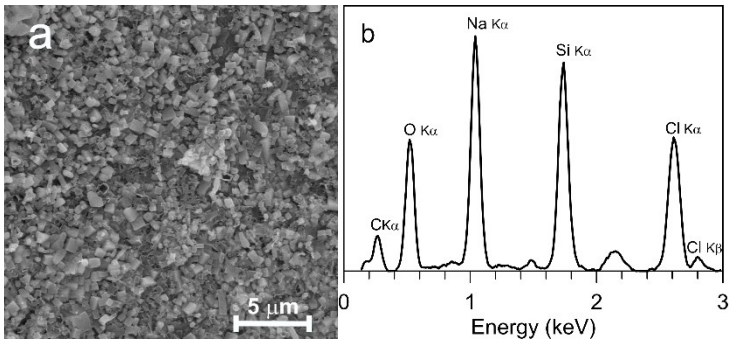

Fig. SI2. SEM micrographs of the bead surface of selected P-DS-T (a) and characteristic EDX spectrum acquired from the marked region in b. The main X-ray lines excited at 10 kV are indicated. The SEM-EDX analysis for the P-DS-ET composite is not shown since it is almost identical with this presented here.

Acknowledgements

The research was carried out with the equipment purchased thanks to the financial support of the European Regional Development Fund in the framework of the Polish Innovation Economy Operational Program (Contract No. POIG.02.01.00-06-024/09 Center of Functional Nanomaterials).

References

1. W.-C. Lin, A. Marcellan, D. Hourdet and C. Creton, *Soft Matter*, 2011, **7**, 6578-6582.
2. T. P. Hadjiioannou, G. D. Christian, M. A. Koupparis and P. E. Macheras, in *Quantitative Calculations in Pharmaceutical Practice and Research*, VCH Publishers Inc, New York, 1993, p. 345.
3. D. W. A. Bourne, in *Modern pharmaceutics, 4th edition*, eds. G. S. Banker and C. T. Rhodes, Marcel Dekker Inc, New York, 2002, ch. 3, p. 67.
4. T. Higuchi, *J Pharm Sci*, 1963, **52**, 1145-1149.
5. P. Costa and J. M. Sousa Lobo, *Eur J Pharm Sci*, 2001, **13**, 123-133.
6. R. W. Korsmeyer, R. Gurny, E. Doelker, P. Buri and N. A. Peppas, *J Pharm Sci*, 1983, **72**, 1189-1191.
7. J. Siepmann and N. A. Peppas, *Adv Drug Deliver Rev*, 2001, **48**, 139-157.