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Do the Characteristics of Xanthan Single Molecule Reflect the Behavior of Matrix Tablets?

**S. BAUMGARTNER¹, J. KRISTL¹, B. GOVEDARICA¹, S. SRČIČ¹,
A. ZUPANČIČ VALANT², U. MIKAC³, A. SEPE³**

¹ University of Ljubljana, Faculty of Pharmacy, Ljubljana, Slovenia

² University of Ljubljana, Faculty of Chemistry and Chemical Technology, Ljubljana, Slovenia

³ Jožef Stefan Institute, Ljubljana, Slovenia

E-mail: sasa.baumgartner@ffa.uni-lj.si (S. Baumgartner)

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Introduction: Xanthan (XAN) is a well known negatively charged biopolymer that adopts different conformations in media, which are still poorly understood. XAN tablets in contact with water hydrate, forming a gel layer that regulates the drug release rate [1]. The hypothesis was that XAN molecular structure influences the drug release from matrix tablets. Thus, detailed studies on molecular as well as on macro-scale level were performed.

Experimental: To determine XAN molecular conformations, its solution in water at pH 7.0 or 1.2 was deposited on freshly cleaved mica, dried and images were taken in air using tapping mode *AFM*. In order to determine Young's modulus and investigate properties of single XAN molecule, nanoindentation as well as nanofishing were performed. Ingress of media into XAN tablet, gel structures and drug release were studied by *NMR* and *MRI*, oscillatory rheometer and dissolution USP Apparatus II.

Results and discussion: Our results reveal that XAN adopts single chain conformation in water at pH 7.0, whereas at 1.2 double stranded structures are formed. This was confirmed by *AFM* images as well as by calculated parameters: persistence length of XAN in water was 210.37 compared to 116.83 in pH 1.2. Young modulus of XAN film in water was lower (1.52 GPa) compared to pH 1.2 (1.94 GPa). Higher rigidity of XAN films at pH 1.2 was further confirmed by formation of XAN gels, where elastic G' and loss G'' moduli were higher in the whole deformation range. Double stranded molecules form more cohesive gels, while single stranded are more flexible, due to the higher hydration of negatively charged polymer. *MRI* results proved much higher hydration and consequently the swelling of XAN tablets at pH 7.0 than at 1.2 and the thicker gel layer as well. Surprisingly, drug release in pH 1.2 media was faster regardless to firmer gel structure.

Conclusion: High rigidity and low hydration of XAN matrix in pH 1.2 are the consequence of XAN molecular structure regulating drug diffusion in tablets.

- [1] Mikac U, Sepe A, Kristl J, Baumgartner S. A new approach combining different *MRI* methods to provide detailed view on swelling dynamics of xanthan tablets influencing drug release at different pH and ionic strength. *J Control Release*. 2010; 145: 247–256. doi:10.1016/j.jconrel.2010.04.018