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γ-CYCLODEXTRIN METAL-ORGANIC FRAMEWORKS AS EFFICIENT MICROCONTAINERS FOR ENCAPSULATION OF SULFASALAZINE

Metal-Organic Frameworks (MOF) are hybrid crystalline materials formed by metal cations that are coordinated through rigid organic ligands. MOF have a porous surface, so they are used in pharmaceuticals as drug carriers.

In this regard, the purpose of this work was to obtain and study the properties of MOF composites with sulfasalazine (SSZ) and pharmacologically significant polymers, which can be used to control the rate of dissolution of the drug compound in biologically significant media.

Sulfasalazine (Fig. 1), used in the treatment of rheumatoid arthritis and other inflammatory diseases, was selected as a model drug compound.

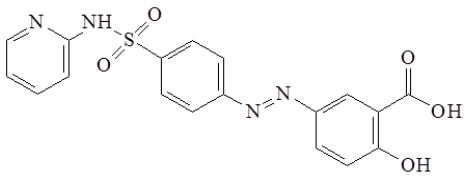

Figure 1. *Structural formula of the SSZ molecule.*

In this paper, we consider an MOF based on γ-cyclodextrin (γ-CD) molecules associated with potassium ions. MOF was obtained by crystallization from an aqueous solution of γ-CD and potassium hydroxide under the action of methanol vapors. Sulfasalazine was loaded into the MOF by adsorption from an alcohol solution. Additionally, various polymers widely used in pharmaceuticals as excipients were added to the resulting MOF/SSZ composite. The obtained samples of MOF/SSZ and MOF/SSZ polymers were characterized by X-ray phase analysis, electron microscopy, DSC and IR spectroscopy. The dissolution processes of MOF/SSZ and MOF/SSZ/polymer were studied in buffer solutions simulating the environment of the stomach and intestines. The results obtained are considered from the point of view of the influence of the structure of polymers and the method of their introduction into the pharmaceutical composition, as well as pH on the rate of

dissolution of SSZ. The dissolution rate of pure SSZ and γCD-MOF + SSZ is shown in figure 2.

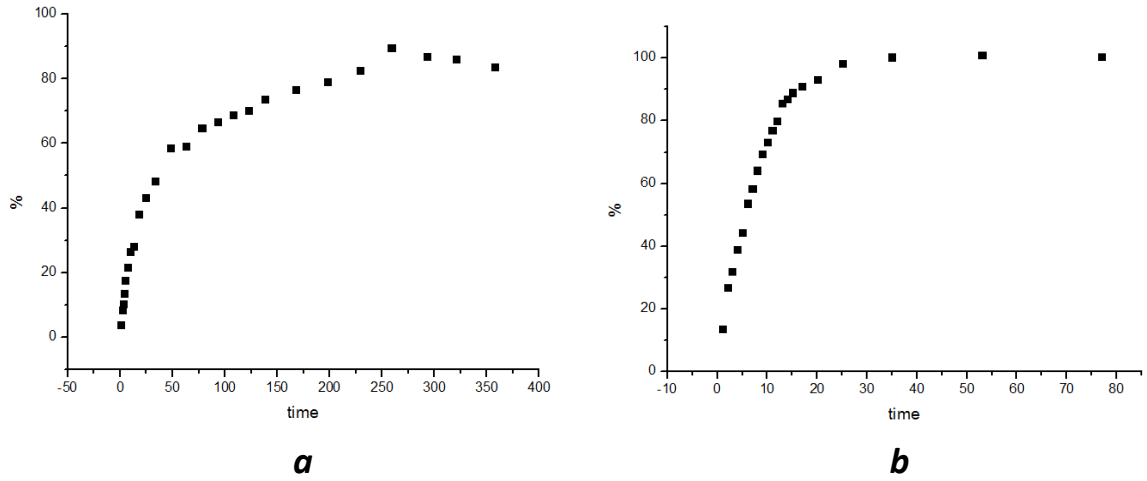

Figure 2. ***a*** *- The dissolution rate SSZ;* ***b*** *- The dissolution rate γCD-MOF+SSZ.*

γCD-MOF shows a significant increase in the rate of dissolution. Only part of the pure SSZ is dissolved in 300 minutes, while the γCD-MOF+SSZ completely dissolves in 35 minutes. The faster dissolution of γCD-MOF+SSZ can be explained by the presence of empty pores in γCD-MOF (Fig. 3). In this case, the solvent fills the pores, which contributes to the destruction of the matrix and faster release of the drug.

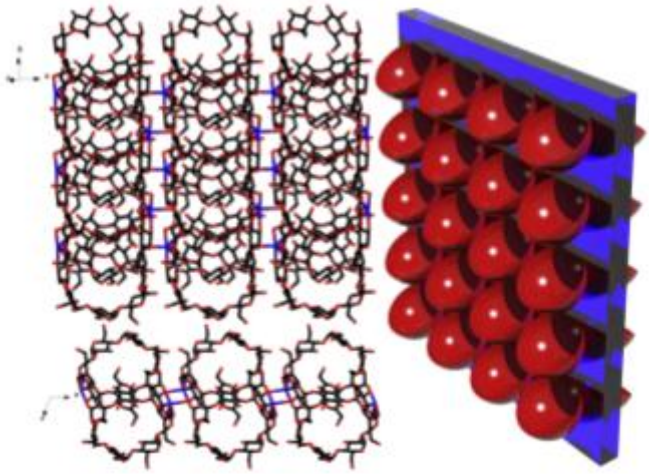

Figure 3. *The porous structure of the γCD-MOF.*

Figure 4 shows that the rate of dissolution of physical mixtures of MOF/SSZ with HPMC, EtCell, CarbMetCell, sodium alginate, pluronic does not differ much from the rate of dissolution of MOF/SSZ, so further studies were conducted with other methods for obtaining compounds. In the results shown in Fig. 5, an increase in the rate of dissolution of composites is observed. Based on this, we consider it appropriate to continue conducting experiments to find the optimal time of dissolution of the drug compound.

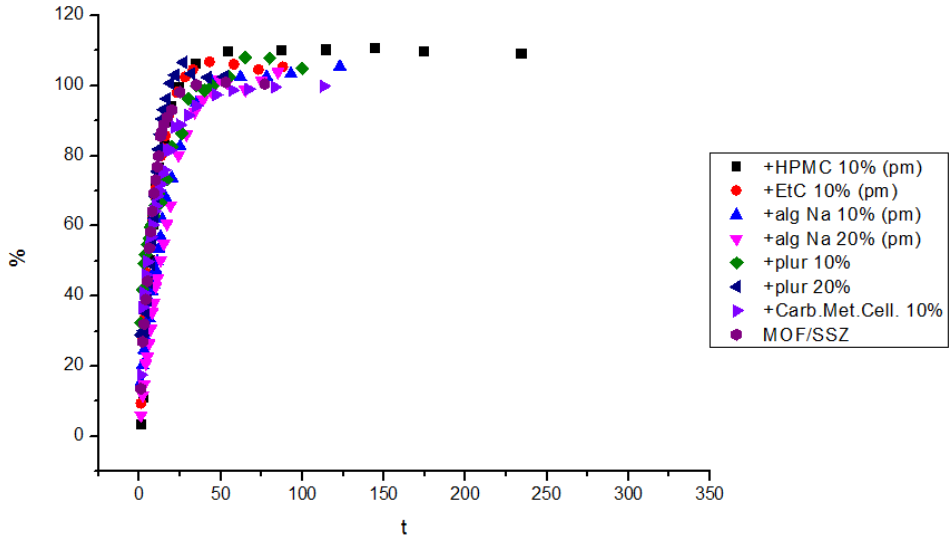

Figure 4. *Comparison of results on the rate of dissolution of physical mixtures.*

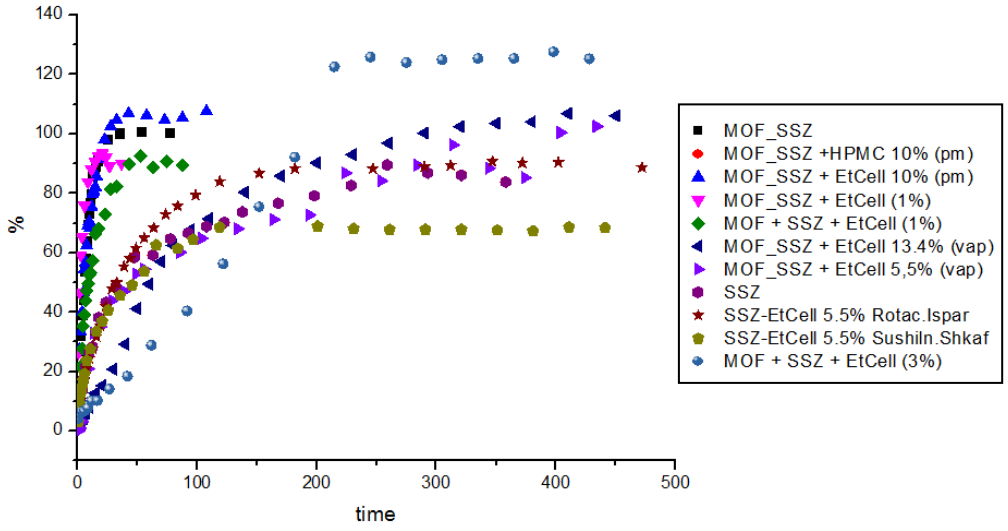

Figure 5. *The Comparison of results on the rate of dissolution of mixtures with cellulose obtained by different methods.*

In this paper, it is shown that the Metal-Organic Frameworks based on the ions γ-cyclodextrin and K+ serves as an effective carrier of sulfasalazine. It has been demonstrated that sulfasalazine can be loaded into γCD-MOF by impregnation. It was observed that sulfsalazine released from γCD-MOF has a higher dissolution rate than in its pure form. The identified features of the dissolution of sulfasalazine encapsulated in γCD-MOF allow us to propose a new strategy for the delivery of this drug.

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