Silicon Oxycarbide Nanoparticles as New Drug Delivery Materials for Infectious Disease Treatments

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Infectious diseases are responsible for considerable mortality globally. Human immunodeficiency virus/acquired syndrome (HIV/AIDS), Tuberculosis (TB) and malaria rank among the most deadly of infectious diseases. The World Health Organization reported over 1.7 million deaths from HIV in 2011, 1.4 million deaths from TB in 2012 and 660.000 deaths from malaria in 2010. In the absence of effective vaccines against these diseases, drug therapy remains the only treatment option. The increasing prevalence of drug resistant pathogenic strains including growing HIV has become a global concern. The development of new therapies based on nanomedicines, to reduce drug doses and dose frequencies and to shorten treatment duration, with the goal of increasing patient compliance, improving treatment outcomes and reducing occurrence of drug resistance, is a major priority for these diseases. In this aspect the new generation of nanomedicines can be designed to delivering drugs by means of selecting pharmacologically active ligands chemically of physically adsorbed on porous nanoparticles. Thus, these pharmacologically nanoparticles can deliver therapeutic drug concentrations inside the cell to prevent specific diseases. In this work we have prepared a new class of materials named as silicon oxycarbide ceramics with different kinds of porosities where acyclovir has been adsorbed in different concentrations. Acyclovir has been selected for its potent and selective antiviral activity against viruses of the herpes group. Silicon oxycarbide nanoparticles present on their surfaces a wide dispersion of active sites where acyclovir can be adsorbed with different intensities and, then when in use it can be delivery with doses according to any specific disease or in a wide range of days. Silicon oxycarbide nanoparticles present hydroxyl and carbonyl or phenol groups on silicon oxide, carbon and oxycarbide phases and these groups have been modified with amino groups or have been increased by means of strong oxidation. In all cases the absorption and delivery of acyclovir have been characterized by means of UV-vis spectroscopy and the results have been compared with those of typical mesoporous silica materials generally studied for this subject. It has been observed that the new silicon oxycarbide nanomaterials present high absorption capacities than mesoporous silicas and that the acyclovir release is effective over a prolonged period while for mesoporous silicas occurred in few minutes. These results indicate the interesting properties of these new nanomaterials for drug delivery in infectious diseases.

Figure 1 shows the nitrogen adsorption-desorption isotherms of different SiOC nanoparticles surface modified with 3-amine propil trimethoxy silane (3APS) and Figure 2 shows the corresponding pore size distributions (PSD). In this case the SiOC nanoparticles present a clear bimodal pore distribution with pores sizes close to 6 and 60 nm. Surface modification of these nanoparticles with 3APS modifies the amount of pores and mainly the pore sizes higher than 80 nm. Thus 3APM molecules tend to adsorb on the high sized pores rather than on low sized ones.

Figure 3 shows the nitrogen isotherms of SiOC nanoparticles surface oxidized to create different active sites. Figure 4 shows their corresponding PSD. In this case the nanoparticles present a monomodal pore distribution with pores close to 3 nm and a minor part of 20 nm. Surface

oxidation only modify the amount of low sized pores but the distribution shape can be assigned to a typical ink-bottle distribution where small pores are located on the nanoparticle surface while wide pores are located in the bulk.

All of these nanoparticles have been analyzed by means of Attenuated Transmission Infrared Spectroscopy (ATR) and the interaction of APS molecules on the surface of the SiOC nanoparticles have been described in accordance with the physical adsorption on Si-OH and C-OH grous where the APS molecules can be found in normal or parallel configurations over the SiOC nanoparticle surface. On the other hand, the surface oxidation mainly removes Si-OH groups of the silica phase and creates new C-OH groups on both carbon and silicon oxycarbide phases. These new surfaces of the SiOC nanoparticles give different interaction with acyclovir molecules and then different release kinetics in a given medium.

The absorption and release of acyclovir on these SiOC nanoparticles have been analyzed and compared with two conventional silicas normally used as controlled release materials. Table 1 shows absorbed amounts of acyclovir by the SiOC nanoparticles and two silicas and the corresponding released amounts after 30 minutes. It is clear the high capacity of acyclovir absorption of the SiOC nanoparticles compared to the mesoporous silicas and the possibility of release in different concentration depending on the surface modification of the SiOC material.

Table 1.- Properties of nanomaterials respect to controlled release of acyclovir

Nanomaterial	**Modification**	**Surface Properties**		**Acyclovir**	
		Surface Area ($m^2.g^{-1}$)	**Pore size (nm)**	**Absorbed (%)**	**Released (%)**
SiOC bimodal	-	440	9.6	99	5
	0.25 APS	400	9.7	96	6
	5 APS	310	11.0	79	16
	10 APS	115	16.0	80	33
SiOC monomodal	-	200	3.5	95	4
	1 hour	390	3.5	83	15
	32 hours	320	3.3	46	17
Porous Silica	-	524	6.3	2	98
Mesoporous Silica	-	905	2.5	3	97

Figures

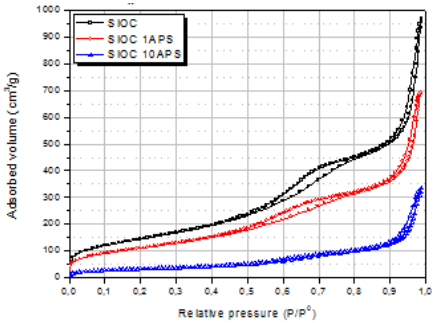

Figure 1

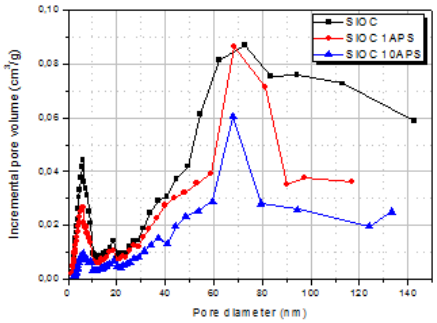

Figure 2

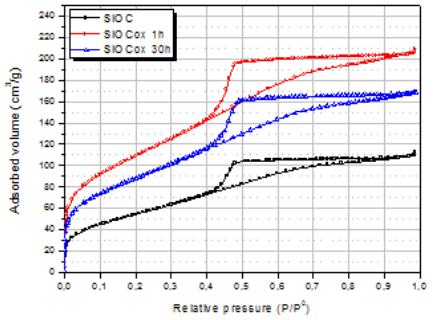

Figure 3

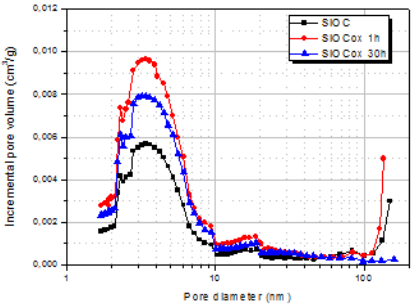

Figure 4