Enhancing Drug Solubility with Mesoporous Silica: Formulation of Lipophilic Drugs for 3D Printed Pharmaceutical Forms

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3D printing has arrived as a disruptive technology, revolutionizing manufacturing processes, including in pharmaceuticals. In 2015, precision medicine gave a step forward with the first FDA-approved 3D printed medicine; however, plain implementation of this technology in current health services still faces challenges. 3D printed dosage forms containing lipophilic drugs, for example, face the intrinsic problem of their low aqueous solubility, which later reflects in low bioavailability and efficacy. Mesoporous silica are known drug nanocarriers providing tailored drug release, but has been risingly explored also due to its ability to stabilize drug amorphous form due to pore confinement effects. Drug amorphization leads to an increase in apparent aqueous solubility, hence, bioavailability. The goal has been to study the mesoporous silica as ally in the development of printable formulations containing hydrophobic drugs, in which triamcinolone acetonide (TA) and clobetasol propionate (CP) were used as drug models. The drugs were encapsulated in mesoporous silica, SBA-15 and MCM-41, respectively, and later incorporated in hydrated polymer printable inks. Carboxymethyl cellulose and pectin were used as main polymers for the production of hydrogels. TA@SBA-15 and CP@MCM-41 were characterized firstly by N_2 sorption analysis, in which a decrease in pore volume and surface area prove the encapsulation of the drugs into silica mesopores. Differential scanning calorimetry and X-ray analysis demonstrate the amorphization of the drugs when encapsulated, consistent with pore confinement effects. *In vitro* drug dissolution was evaluated by the dialysis bag method and demonstrated the significant increase in the drugs dissolution rate, in which release of the drugs was attained with a similar release profile to that of the drug solubilized in ethanol, unlike crystalline TA and CP, which aqueous suspension poorly dissolved. After incorporation of TA or CP-loaded mesoporous silica into polymer hydrogels, they presented improved printability by semisolid extrusion printing technique when compared to the unmodified hydrogels, observed by an increase in viscosity without increasing yield stress values. This indicates that a better flow during 3D printing might be achieved with the incorporation of mesoporous silica in the hydrogels. 3D printed films were obtained with homogeneity and reproducibility in drug content, as well as improved mechanical properties and bioadhesion after silica incorporation, which indicates easier handling of the films and longer retention time of the dosage form when administered for mucosal or topical delivery. Therefore, these results are a proof of concept of the multifunctionality of mesoporous silica for the development of 3D printed drug dosage forms, enabling the formulation of lipophilic drugs in aqueous environment, as well as improving printability, handling and bioadhesion of the 3D printed forms. Finally, these convey higher bioavailability, efficacy, and better patient outcomes for 3D printed personalized nanomedicines.

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