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Sustained delivery scaffold loaded by cisplatin and curcumin

Cisplatin (CP) is an essential anticancer drug, according to the World Health Organization's List of Essential Medicines. The drug has a number of side-effects, such as nephrotoxicity, neurotoxicity, ototoxicity; and can be the causes of hemolytic anemia, electrolyte disturbance, nausea, and vomiting. Cisplatin resistance is problematic for treatment of many cancers.

Curcumin (CMN) is a diarylheptanoid, the principal curcuminoid of turmeric (Curcuma longa). It exerts potent anti-inflammatory effect, which is protective against some form of cancer progression. In fact, curcumin has additional anti-cancer effect that is independent of its anti-inflammatory activity.

In this research, scaffolds consisting of Zr-dropped hydroxyapatite (Zr-HA), CMN-entrapped β-cyclodextrin (CMN-βCD), and CP-encapsulated polycaprolactone (CP-PCL) were prepared by using the compression molding technique. CMN and βCD were physically mixed. The hydrophilicity of PCL was increased by alkaline hydrolysis. The hydrolyzed PCL was melted into which CP and Zr-HA were added. The mixture of CP/Zr-HA/PCL was set at room temperature. Then, it was ground to fine powder. These two solid phases, e.g., CMN-βCD and CP/Zr-HA/PCL, were mixed and pressed to form scaffolds.

By using FTIR technique, there are specific peaks of hydroxyl groups on the spectra of the hydrolyzed PCL. Upon pressing, there are films of the PCL covering the HA particles, but the films are not completely coated as indicated by XRD pattern. By using DSC technique, CMN is completely entrapped into the βCD structure, and CMN and βCD are compatible with each other. The charge property of the scaffolds was investigated by using toluidine blue (TB) as a drug model. The negative charges of the scaffolds are expected to interact with the positive charges of TB, resulting in its stable binding. The TB binding efficiency varies between 13 and 52%, depending on the degree of PCL hydrolysis. The release of TB is sustained without an initial burst release. The penetration of TB deeply inside the scaffolds was ascertained by using a confocal microscope, indicating that the depth is about 40 μm. The releases of both CP and CMN from the scaffolds were sustained by at least 10 days and the released CP and CMN still exhibit cytotoxicity to cancer cells, according to the MTT assay. The addition of CMN can reduce the CP doses while keeping the constant cytotoxic effect. It seems that side effects of CP can be diminished by using in with CMN.

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