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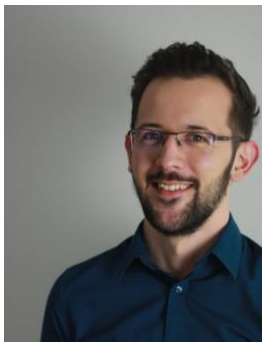

Investigation of the feasibility and efficiency of solvent-free co-grinding with different active substances

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Cyclodextrin (CD) complexation is widely used to improve the solubility of active pharmaceutical ingredients (API). The use of polymers as a third component can further enhance the beneficial effects of CDs. Production of CD complexes via solvent-free methods (e.g., co-grinding (CG)) is an environmentally and economically desirable technology. This work deals with the CG CD complexation of different APIs, the changes in physicochemical properties during the process, the in vitro evaluation of final products, and finally the comparison with different solvent methods.

For these reasons, we used Terbinafine Hydrochloride [1] and Fenofibrate [2] as model APIs and different types of amorphous CD derivatives with and without applying polymers as a third component. CG preparation methods were performed both manually and with laboratory mills. The products were systematically investigated in the solid phase by X-Ray Powder Diffractometry (XRPD), Differential Scanning Calorimetry (DSC), Thermogravimetry (TG), Scanning Electron Microscopy (SEM), Fourier-Transform Infrared spectroscopy (FTIR), Raman microscopy and in vitro dissolution, diffusion, and – for selected products – cytotoxicity studies.

With both APIs, amorphous products have been produced, as confirmed by XRPD, DSC, and TG studies. The intermolecular interactions were presumed by FTIR, and these results were supplemented by Raman spectroscopy if needed. Based on these, selected CDs were able to host the APIs as guest molecules, forming complexes. These presumed complexes were further studied by in vitro studies, showing better dissolution, modified diffusion, and cytotoxicity values. Overall, the results suggest that the preparation of CD complexes without solvent by co-grinding is easy to perform and the products obtained have similar improved properties as those prepared by solvent-based methods.

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References:

1. Kondoros B. Pharmaceutics 14(4), 744 (2022)
2. Kondoros B. Pharmaceutics 14(7), 1329 (2022)