ABSTRACT

DOCTORAL THESIS:

"Mechanisms responsible for improving the physical stability of amorphous pharmaceuticals after using silica nanoporous materials."

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The doctoral dissertation presents a series of three thematically related scientific papers, which mainly focus on (i) the evaluation of the stabilization efficiency of various amorphous pharmaceuticals after the use of nanoporous silica materials (NSM) and (ii) determining the mechanisms responsible for the observed changes in the physical stability of amorphous substances under the influence of the used NSM.

For this purpose, a series of studies were conducted on three active substances: simvastatin, celecoxib, and aripiprazole, which are diversified in chemical structure and medical application. Methods such as differential scanning calorimetry (DSC) or broadband dielectric spectroscopy (BDS) allowed the characterization of pure substances, mainly in terms of their thermal properties, molecular dynamics, and tendency to crystallize.

The effect of using the NMK additive was assessed based on studies using DSC and BDS methods, which were carried out for binary drug-silica compositions, prepared in several different concentrations. As a result of these experiments, it was proven that the silica additive does not significantly affect the value of the glass transition temperature and the temperature dependence of the times of the primary and secondary relaxation processes. However, it was shown that NSM has a significant effect on the physical stability of the investigated materials. In the case of amorphous simvastatin, it was proven that the size of the particles of the used silica additive plays a key role in inhibiting the recrystallization process. The observed effect was also confirmed in the case of the investigated celecoxib. However, the second mechanism was also responsible for the observed improvement in the physical stability of amorphous celecoxib, namely the interaction of the investigated substance molecules with the surface of the used NSM. The presence of both mechanisms was also confirmed in the case of the investigated aripiprazole. It is concluded that the effectiveness of silica materials in inhibiting the recrystallization process also depends on the stabilized amorphous material. The case of aripiprazole showed that by using NSM it is possible not only to stabilize the amorphous form of the drug but also to control its recrystallization process in such a way as to obtain crystalline medicinal material in a specific polymorphic form.