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Title

Formation Mechanisms of Bridging Bonds via Oxygen due to Soft Mechanochemical Synthesis Containing SiO_2 as the base and the Application to Material and Drug Product

Abstract

Rapid solid state mechanochemical reaction containing hydroxyl groups leads to formation of bridging bonds via oxygen. The process is called a soft mechanochemical reaction. The bridging bonds are applied to prepare complex oxide precursors or solid drug products. In this study, mechanisms of an incipient reaction in $Ca(OH)_2$-SiO_2 or dug-SiO_2 under mechanical stresses were studied on the basis of changes in the hydroxyl groups, role of radical species, formation of bridging bonds and short range ordering precursor for further reactions. Indomethacin (IM), being sparingly soluble drug, was employed as a drug substance and the effect of the drug-carrier interaction by a soft mechanochemical reaction was estimated in conjunction with the physical stability of amorphous IM.

The first half in this study, emphasis was laid on the mechanochemical dehydration due to acid-base interaction between silanol groups and surface OH groups on $Ca(OH)_2$. This leads to the Ca-O-Si bridging bonding, by grinding a mixture of fine $Ca(OH)_2$ and SiO_2 particles. A radical species of O^- on $Ca(OH)_2$ surface and E'-center on SiO_2 surface were consumed by recombination, leading to Ca-O-Si bonding. Subsequent charge transfer enables to form a precursor of complex oxide with a short range ordering structure of Ca_3SiO_5.

Enhanced dissolution characteristics of drugs are often achieved by amorphization. However, inhibition of crystallization is importance for the practical use. The second half in this study is dedicated to the stability of the amorphous IM with SiO_2, which is higher for those prepared by co-grinding than by melt-quenching. In co-grinding mixtures, a specific chemical interaction of IM with SiO_2 was observed. The chemical interaction immobilizes the indomethacin molecules to suppress the recrystallization. By using the combination of two kinds of carrier, which shows rapid soft mechanochemical reaction, the stability of the amorphous IM is higher than by SiO_2 alone.

By accounting for the change in the coordination number during mechanical stressing, the bridging bond formation by mechanochemical reaction was explained by the principle of electronegativity equalization based on a discrete variational (DV) –Xα method.