Non Thermally Driven Transformations of Molecular Compounds

M. Descamps, J-F. Willart, A. De Gusseme, S. Desprez,

Laboratoire de Dynamique et Structure des Matériaux Moléculaires,
U.P.R.E.S.A. CNRS 8024, Bât. P5, UST Lille, F-59655 Villeneuve d'Ascq Cedex

Solid compounds can either be obtained as crystals or amorphous glasses. The rapid cooling of their liquid phase traditionally produces this latter state. However, the amorphous state can also be reached without the preliminary melting requirement, via the application of an external driving force. Forcing can be either physical (mechanical grinding, irradiation…) or chemical (reactions, dehydration of hydrate crystals…). Moreover, these perturbations may also yield phase transformations into polymorphic crystalline states.

We present here examples of phase transformations in driven molecular materials, which have not been thoroughly investigated yet despite their considerable implications in pharmaceutical science. Focus is made on transitions induced by mechanical milling and desolvatation, both processes being regularly used in pharmaceutical formulations.

We describe experimental evidence of phase transformations and stabilization of non equilibrium phases in pharmaceutical substances (*indomethacin*, *trehalose*, *fananserine*), subjected to mechanical milling [1]. It is shown that a proper control of the temperature and intensity of the grinding process may give rise either to a glass or to a polymorphic crystalline variety. The same diversity of behaviors could be observed for the dehydration of *trehalose* dihydrate [2].The possibility that these non thermally driven transformations are in fact dynamical phase transition processes is thus discussed. Also discussed are the physically relevant parameters driving these nonequilibrium phase transitions, i.e., transitions between steady states of a dynamical system, rather than between equilibrium states of thermodynamical system. The eventuality of dynamical modes of phase transformation may provide an explanation to the observation of the sub-Tg production of nuclei sometimes observed in pharmaceuticals.

[1] J.F. Willart, A. De Gusseme, S. Hemon, G. Odou, F. Danede, M. Descamps, *Solid State Comm.*, (2001), 119, 501

[2] J. F. Willart, A. De Gusseme, S. Hemon, M. Descamps, F. Leveiller, and A. Rameau ; Vitrification and Polymorphism of Trehalose Induced by Dehydration of Trehalose Dihydrate**,** *The Journal of Physical Chemistry B*; 2002; *106*(13); 3365-3370