Dr Yuriy Abramov, Pfizer, gave this presentation at the "Guiding Optimal Compound Design and Development Symposium" held in Cambridge, MA, USA on 19 March 2015.

Abstract

One of the major concerns in modern drug discovery and development is chemical and physical stability of small molecule pharmaceuticals. Chemical stability is crucial for compounds at all stages of pharmaceutical R&D, from early drug discovery to formulation of liquid or solid dosage forms. Physical stability is typically related to stability of the pharmaceutical solid form.

QSPR models of oxidative chemical stability were built based on a large data set of electrochemical measurements. In addition a quantum chemical approach was proposed for oxidative chemical stability ranking of small organic molecules. Examples of the models application to pharmaceutical compounds will be discussed.

A typical physical instability issue of solid pharmaceuticals is related to a hydrate formation during formulation or product shell life. Transformation from anhydrate to hydrate solid form can have a significant impact on product performance and may also lead to a chemical instability. A model describing propensity of an API solid form to hydrate formation will be presented. In addition a rational coformer selection to enhance hydration stability of a co-crystalline form of API at a high relative humidity will be discussed.

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