

Abstract

Acridines are active pharmaceutical ingredients (APIs), having a broad spectrum of activity, such as: antibacterial, antiviral, antiprotozoal, antitumor, antiprionic and others. One of the challenges of modern crystal engineering is to obtain new forms of drugs in the form of multicomponent crystals containing APIs, with improved physicochemical properties in relation to individual active pharmaceutical ingredients. This is possible due to the knowledge and understanding of intermolecular interactions occurring in the crystals. These interactions are the driving force during the formation of such crystals, creating repetitive or unique synthons between different functional groups in the molecules of compounds included in multicomponent crystals and enable the design of new substances with the desired physical and chemical properties.

In my doctoral thesis the syntheses and crystal structures of 23 compounds containing acridine and its derivatives: 9-aminoacridine and 6,9-diamino-2-ethoxyacridine and mono- and di-substituted benzoic acids or non-steroidal anti-inflammatory drugs are presented. Crystals of these compounds were obtained by the method of slow evaporation of the solvent or by grinding with the addition of a solvent. The crystal structures were determined by means of X-ray diffraction methods. An analysis of intermolecular interactions was carried out, which allowed to identify the basic building units occurring in the crystals, such as: heterodimers, heterotetramers, heterohexamers and heterooctamer. This analysis allowed to identify the basic synthons created with the participation of solvent molecules, endocyclic nitrogen atom and amino groups of acridinium cation, as well as carboxylate/carboxyl groups of anion/acid molecule and substituents in an aromatic acid ring, which can form ring, tape, or chain motifs. As a result of numerous syntheses of multicomponent crystals with the participation of non-steroidal anti-inflammatory drugs (NSAIDs) with acridines, it was possible to obtain two multicomponent crystals containing diclofenac (with the 6,9-diamino-2-ethoxyacridine and with the acridine),

two multicomponent crystals containing tolfenamic acid (with the 6,9-diamino-2-ethoxyacridine and with the 9-aminoacridine) and three multicomponent crystals containing naproxen (one with the 9-aminoacridine and two with the acridine). Differences in the crystal structure of these compounds, resulting the occurrence of various intermolecular interactions involving various functional groups have been discussed.

The results of research conducted as part of the doctoral dissertation may be interesting not only from a cognitive point of view but can be used for the rational design of new, crystalline forms of drugs with the use of acridines and/or non-steroidal anti-inflammatory drugs.