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Polymorphism in the Long-acting Sulfonamide Antibiotic Sulfalene

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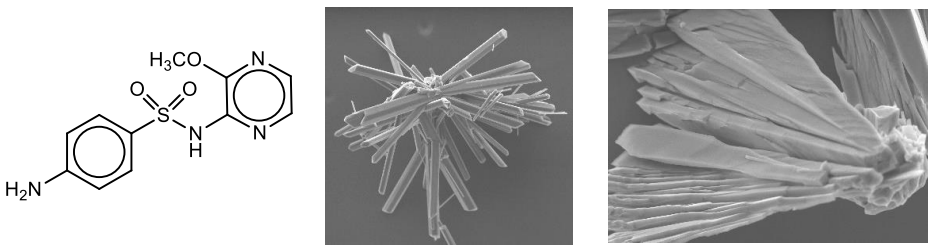
Molecular organic solids used as active pharmaceutical ingredients (APIs) can present more than one crystal structure (polymorphism). Despite being composed by the same molecular unit, different polymorphs should be regarded as unique materials, since they can present dissimilar physical properties (e.g. solubility, fusion point, colour). The preferred method to isolate and purify APIs is crystallization from solution, a process that, from a fundamental point of view, it is still poorly understood. This fact often results in the appearance of new polymorphs during production stages, which can change the properties of a life-saving drug (e.g. the Ritonovir case)[1]. Therefore, polymorphism control is regarded as a major problem in the pharmaceutical industry. Albeit, the sequence of events leading to the formation of a solid form is still largely unknown, it is believed that the nucleation process is a key step in the formation of crystals. Understanding this, can lead to the control over the selective formation of a specific polymorphic form.

This work describes a systematic study of sulfalene (SL, Figure 1) crystallization. Sulfalene belongs to the sulfonamide family, the first group of compounds where antibacterial activity was identified[2]. A literature search showed that only one crystal structure has been reported for sufalene, albeit other members of the family were shown to be prone to polymorphism (e.g. six polymorphs in the case of sulfapyridine)[3]. This work describes a series of crystallization studies suggesting that at least two different SL polymorphs exist.



(a) (b) (c)

Figure 3. (a) Molecular structure of sulfalene and scanning electron microscopy (SEM) images showing the differences in morphology between SL crystals obtained by recrystallization from methanol (b) and acetonitrile (c).

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