

Article

Mechanochemical Synthesis and Crystal Structure of the Lidocaine-Phloroglucinol Hydrate 1:1:1 Complex †

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† This article is dedicated to Professor Narayan Hosmane on the occasion of his 70th birthday.

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Abstract: Molecular complexation is a strategy used to modify the physicochemical or biopharmaceutical properties of an active pharmaceutical ingredient. Solvent assisted grinding is a common method used to obtain solid complexes in the form of cocrystals. Lidocaine is a drug used as an anesthetic and for the treatment of chronic pain, which bears in its chemical structure an amide functional group able to form hydrogen bonds. Polyphenols are used as cocrystal cofomers due to their ability to form O–H···X (X = O, N) hydrogen bond interactions. The objective of this study was to exploit the ability of phloroglucinol to form molecular complexes with lidocaine by liquid assisted grinding. The formation of the complex was confirmed by the shift of the O–H and C=O stretching bands in the IR spectra of the polycrystalline ground powders, suggesting the formation of O–H···O=C hydrogen bonds. Hydration of the complexes also was confirmed by IR spectroscopy and by powder X-ray diffraction. The molecular structure was determined by single crystal X-ray diffraction.

Keywords: lidocaine; phloroglucinol; crystal structure; hydrogen bond; hydration; molecular complex

1. Introduction

Drug formulation studies are performed with the aim of modifying the physicochemical and biopharmaceutical properties of an active pharmaceutical ingredient (API) to: improve its delivery its release in the target tissue, ensure the stability of the product, offer a comfortable use to patients, and make easier the production of the dosage forms [1]. Active pharmaceutical ingredients can contain solvents in the crystal structure. If the solvent is water, it is called hydrate. The ability of water to act as donor and acceptor of hydrogen bond interactions favors the incorporation of water into the crystalline lattice of APIs, reordering the intermolecular hydrogen bond pattern, obtaining hydrated complexes. Therefore, hydration studies in APIs are important because the presence of water in the crystalline lattice can affect the physicochemical and biopharmaceutical properties of the active pharmaceutical ingredient [2].

Molecular complexation is a strategy used to modify the physicochemical or biopharmaceutical properties of an API [3]. Molecular complexes, or host–guest complexes, are molecular species formed by two or more molecules that are associated by noncovalent interactions. Formation of molecular complexes involves molecular recognition between the functional groups of the molecules [4].