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Physicochemical considerations of ibuprofen and its sodium salt in different solvents

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1. Introduction

From a pharmaceutical point of view, one of the most significant actions is the physicochemical information through characterization of the pharmacologically active molecules. This paper deals about characterization of some aspects of racemic compound (R,S)-(±)-ibuprofen or (R,S)-(±)-2-(4-isobutylphenyl) propionic acid (IBP) and (R,S)-(±)-ibuprofen salt, ibuprofen (IBPNa) [1-3], using solvent precipitation method with different types of instrumental analysis, to describe the possible differences detected respect crystallization, polymorphic conversion, desolvation or dehydration [1-3].

2. Methods and materials

IBP and IBPNa were purchased from Sigma-Aldrich and 13 pure solvents were selected, double distilled water, 1,4-dioxane, benzene, 1-pentanol, acetone, chloroform, cyclohexane, absolute ethanol, ethyl acetate, formamide, N,N-dimethyl formamide, N-hexane, N-heptane (spectrophotometric grade. Panreac, Monplet & Esteban), belongs to five different classes, in the ascending order of Hildebrand parameters. Suspensions were prepared adding a small excess of drugs into the solvent selected into a thermostatized bath at 25 ºC, provided with constant agitation. The solid-state phases were filtered and allowed to recrystallize by spontaneous cooling and evaporation at room temperature. Crystals were stored in the absence of light and in desiccator prior to analysis, so as not to affect the crystal structure or the solvent retained in the interstices of the network. Differential scanning calorimetry (DSC, Mettler DSC3) and Fourier Transform Infrared Spectroscopy (FTIR, Perkin Elmer® System 20000FT-IR) determined the polymorphism, crystallinity and drying control of the solid samples. Furthermore, scanning electron microscopy (SEM, Zeiss DSM 950) was used to understand the formation of crystal habit.

3. Results and discussion

Comparing IBP and IBPNa spectrums obtained using FTIR (Fig. 1) there were regions that were identical, such 2, because the presence of a C-O bond, others with slight differences as bond stretching, as in 3 for C=O, overtones in benzene zone 4, and C-H bonds in zone 5. Finally, it was a huge difference in intensity in 6, the O-H bond zone, since its absence in the IBPNa spectrogram [4].

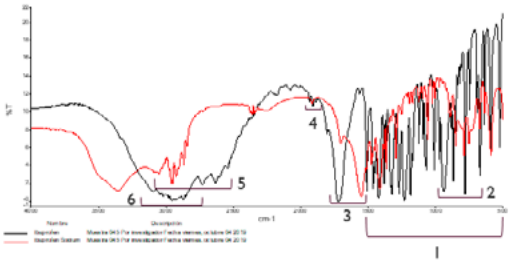

Fig 1. Comparison IBP and IBPNa IR spectrums.

In Table 1 appears the onset (TF, °C) and the molar enthalpy of fusion (ΔHF, J/mol) of the original powders obtained at different heating rates using DSC, in both cases these peaks

are followed by decomposition caused by the oxidation of organic residue accompanied by a loss of weight, and for IBP the melting point trend slightly increase as the heating rate rise. Purity of 98.5 % and 97.05 % were calculated according Van't Hoff equation with ΔHF = 375 and 545 kJ/mol for both drugs (Table 1).

Table 1. Onset and molar fusion enthalpy for each drug at different heating rates

Heating rate (ºC/min)	IBP		IBPNa		IBPNa	
	Onset, °C	ΔHF, J/mol	Onset, °C	ΔHF, J/mol	Onset, °C	ΔHF, J/mol
5	73.81	333	97.31	549	-	120
10	74.37	371	97.29	510	-	135
20	74.59	375	98.05	-518	172	545

An only sharp event for all samples of IBP, which indicates that, the modified samples are isomorphic with the starting material. These results are in agreement with previous reports indicating that IBP in equilibrium with their saturated solutions in a wide range of solvents exists as a stable crystalline solid exhibiting a typical melting range (75 – 77 °C). In general, salts are characterized by the presence of several peaks, for IBPNa a first endotherm was located at temperatures about 100 ºC, are attributed to dehydration of the hydrate, followed by fusion nearby 170 ºC (Figs. 2 and 3).

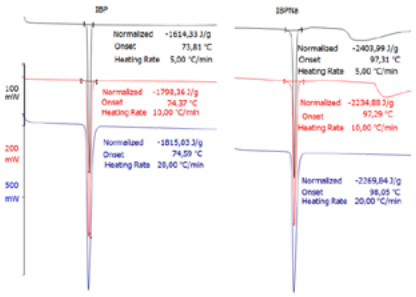

Fig 2. Comparison IBP and IBPNa DSC thermograms (first endothermal event).

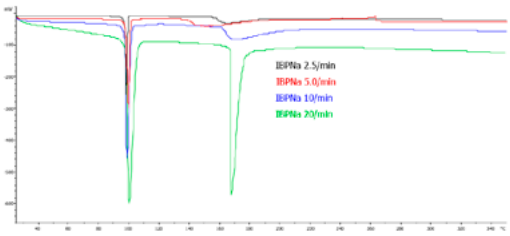

Fig.3. IBPNa thermograms at different heating rates

The formation of a hydrate (pseudo polymorphism) was observed in the aqueous solid phase for IBPNa in water (Fig. 4).

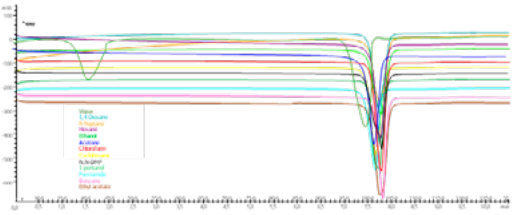

Fig.4. Comparison IBPNa thermograms solid phases in different solvents.

The endothermic event associated with the hydrate disappears when it has been previously heated to 120 ºC, but slowly reappears when the anhydrous forms are stored in a humid environment. Salt has a slightly complex decomposition compared to other salts such as diclofenac [5]. When desolvation or dehydration occurs, solvates/hydrates can undergo a phase transition and thus, form non-solvated/ anhydrous polymorph or can lose crystallinity and thus, form amorphous. Most strikingly, the melting peak is best evidenced at higher heating rates (Fig. 3).

Finally, these results should be contrasted with the use of new techniques and consider new identifications of polymorphic forms of drug, such as SEM. This technique also provides a qualitative assessment of size, shape, morphology, porosity, size distribution, crystal form. The results are presented using 500 µm resolution, in all cases any significant change was appreciate, as example is included Fig. 5.

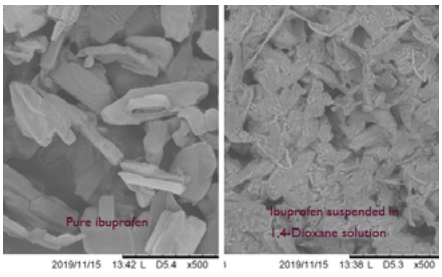

Fig. 5. SEM of IBP and IBP-dioxane.

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