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COMPATIBILITY STUDIES BETWEEN IBUPROFEN AND PHARMACEUTICAL EXCIPIENTS

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Abstract

An important issue during preformulation studies is the identification of possible incompatibilities between the active pharmaceutical ingredient (API) and various excipients. This study aims to investigate the interactions and compatibilities between ibuprofen and some commonly used excipients by two different experimental techniques Differential Scanning Calorimetry (DSC) and High Performance Liquid Chromatography (HPLC). The techniques employed were able to provide different but complementary information, enabling a complete understanding of the possible interactions that occurred in the binary mixtures drug-excipient.

Introduction

Formulation of a drug substance often requires blending of the active pharmaceutical ingredient (API) with different excipients, to improve manufacturability and to boost product's capacity of administering the dose effectively. Excipients are commonly used to facilitate administration, modulate drug release and also stabilize the product against degradation from the environment [1]. However, potential physico-chemical interactions between drugs and excipients can affect the chemical nature, the stability and bioavailability of the products, and consequently, their therapeutic efficacy and safety [2].

Several methods have been used for drug-excipient compatibility screening. Most of them consist in evaluating physical mixtures of the drug and excipients by Differential Scanning Calorimetry (DSC) or accelerated stability tests followed by analytical determination of the drug with High Performance Liquid Chromatography (HPLC) [3,4]. DSC has been proposed as a valuable method of assessing possible incompatibilities between the formulation compounds derived from appearance, shift or disappearance of peaks and/or variations in the corresponding ΔH [5-9]. Although DSC is a valuable technique, conclusions based on DSC results alone can be misleading and inconclusive. Therefore, results obtained with DSC should always be confirmed with other techniques [10]. This study examined the compatibility of ibuprofen, a non steroidal anti-inflammatory drug (NSAID), which exhibits good anti-inflammatory, analgesic and antipyretic properties, with various excipients like magnesium stearate, *lactose monohydrate and* polyvinylpyrrolidone (PVP). Binary mixtures of ibuprofen in a 1:1 ratio with each different excipient were analyzed by DSC and HPLC. The influence of manufacturing processes like simple blending, co-grinding, kneading or tabletting on drug stability was also evaluated.

Materials and methods

Materials

The following materials were used: ibuprofene (Angelini A.C.R.A.F. Ancona, Italy), Magnesium stearate (A.C.E.F., Piacenza, Italy), Lactose monohydrate (Eigenmann & Veronelli; Rho (Milan), Italy), Polyvinylpirrolidone K30 (BASF Aktiengesellschaft, Germany), Ethanol (96% v/v pure Panreach Quimica, Barcelona, Spain), Ethanol HPLC grade (Lichrosolv®, Merck KgaA, Darmstadt, Germany), Water for HPLC (Lichrosolv®, Merck KgaA, Darmstadt, Germany), Acetic acid 99 – 100% (Baker Analyzed® Reagent, J.T. Baker B.V. Netherland), Acetonitrile HPLC grade (Lichrosolv®, Merck KgaA, Darmstadt, Germany).

Methods

Mixture preparation (1:1 w/w)

a) Physical mixtures: 2 g of ibuprofen were gently mixed with 2 g of each excipient in separate mortars.

b) Co-grinded mixtures: The same amounts of ibuprofen and excipients were transferred in a mortar and grinded vigorously with a pestle for five minutes.

c) Kneaded mixtures: The mixed powders were kneaded with ethanol 96% in a mortar until a uniform mass was obtained. Then, the mass was dried in a crystallizer