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COMPATIBILITY STUDY BETWEEN PROPRANOLOL HYDROCHLORIDE AND TABLET EXCIPIENTS USING DIFFERENTIAL SCANNING CALORIMETRY

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ABSTRACT

Propranolol HCℓ was found to interact with a number of commonly used tablet excipients. These included magnesium stearate, Emcompress®, calcium phosphate monohydrate, Primojel®, stearic acid, Avicel® and lactose.

INTRODUCTION

The use of thermal analysis or combinations thereof with stress methods is well described [1,3,5,7].

In this work, the compatibility of propranolol HCℓ with a number of excipients commonly used in tablet and capsule manufacture was investigated as a preformulation study. This was achieved by comparing the DSC thermograms of propranolol HCℓ and each of the investigated excipients with 1:5 mixtures of propranolol HCℓ and excipients. Although it cannot be conclusively stated that an interaction will occur during storage

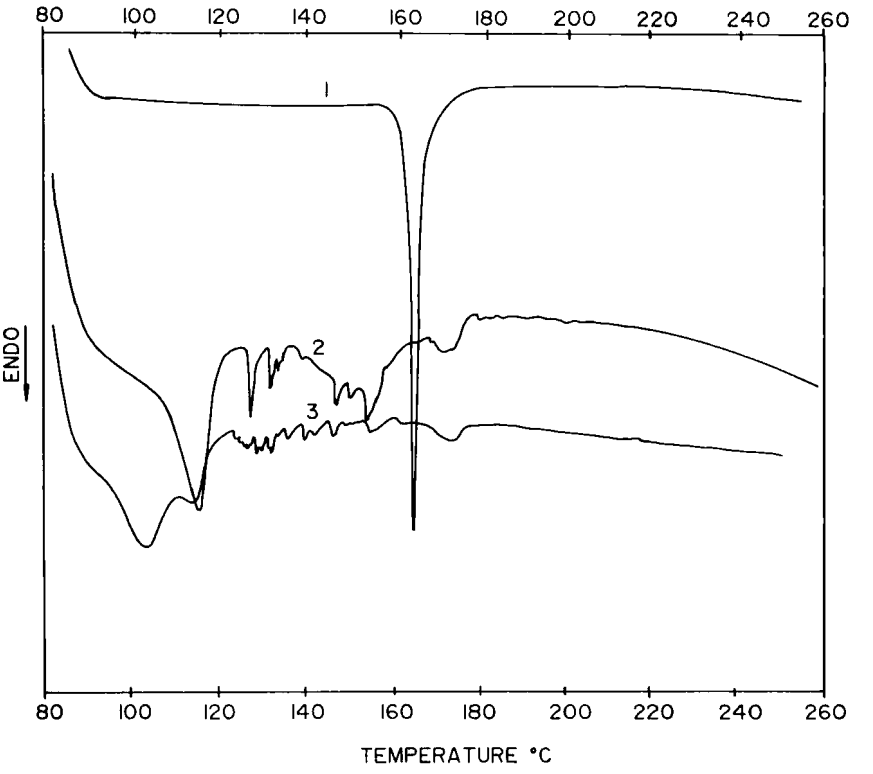

FIGURE 1

DSC thermograms of propranolol (1), magnesium stearate (2) and 1:5 physical mixture of propranolol : magnesium stearate (3).

at room temperature, there are often sufficient excipients available to chose only those unlikely to cause problems [6].

METHOD

DSC runs (Du Pont 910 DSC system) of 1:5 mixtures (1 - 6 mg) of propranolol HCℓ with excipients were performed. Commercially available tablets were crushed and DSC runs were performed on the tablet powder.

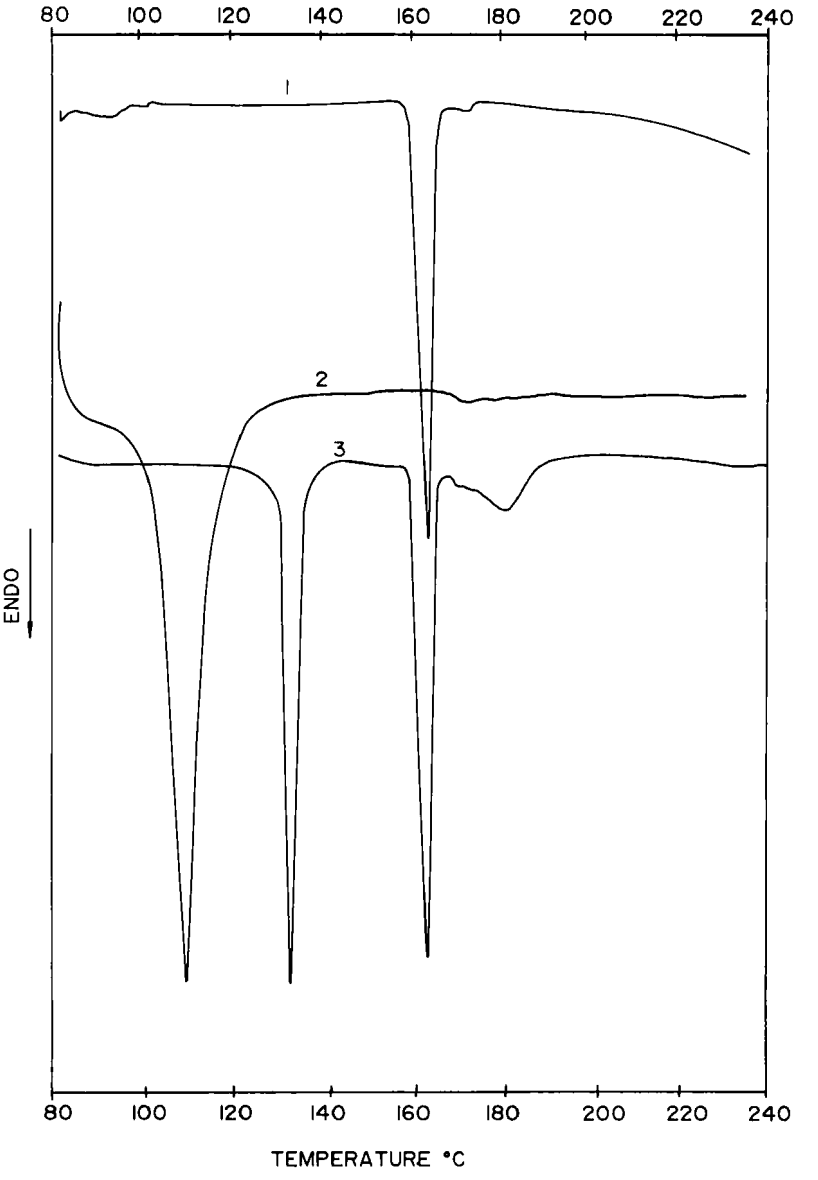

FIGURE 2

DSC thermograms of propranolol (1), Emcompress® (2) and 1:5 physical mixture of propranolol : Emcompress® (3).

The thermal behaviour of samples were studied under nitrogen purge at a heating rate of 10°C per minute. The temperature range was between 80°C and 260°C depending on the melting points of the excipients.

RESULTS

Propranolol HCℓ was found to be compatible with starch, Sta-Rx 1500®, Primojel®, Avicel PH 101®, Elcema G250® and Ac-Di-Sol®. Interactions between propranol HCℓ and magnesium stearate, Emcompress®, calcium phosphate monohydrate, Primojel®, stearic acid, avicel and lactose were evident. Similar interactions could be detected in the tablet powder samples of most generic formulations on the local market. No interactions could be detected in the ICI product which was the first propranolol HCℓ formulation to be marketed.

DISCUSSION

The 1:5 physical mixture of propranolol HCℓ and magnesium stearate (figure 1) showed the melting endoterm of magnesium stearate shifted to about 105°C, while the endoterms between 120 and 140°C and the endoterm of propranolol HCℓ disappeared.

When a 1:5 physical mixture of propranolol HCℓ and Emcompress® (figure 2) was heated the melting endoterm of Emcompress® shifted to a higher melting range on the thermogram (130°C) and an additional melting endoterm appeared at a higher melting range than propranolol HCℓ.

In the thermogram of a physical mixture of propranolol HCℓ and lactose (figure 3) an amine reaction with lactose as described by Duvall [2] was detected.

The melting endoterm of calcium phosphate broadened (figure 4) with two melting points at 155°C and 170°C after being mixed physically with propranolol HCℓ.

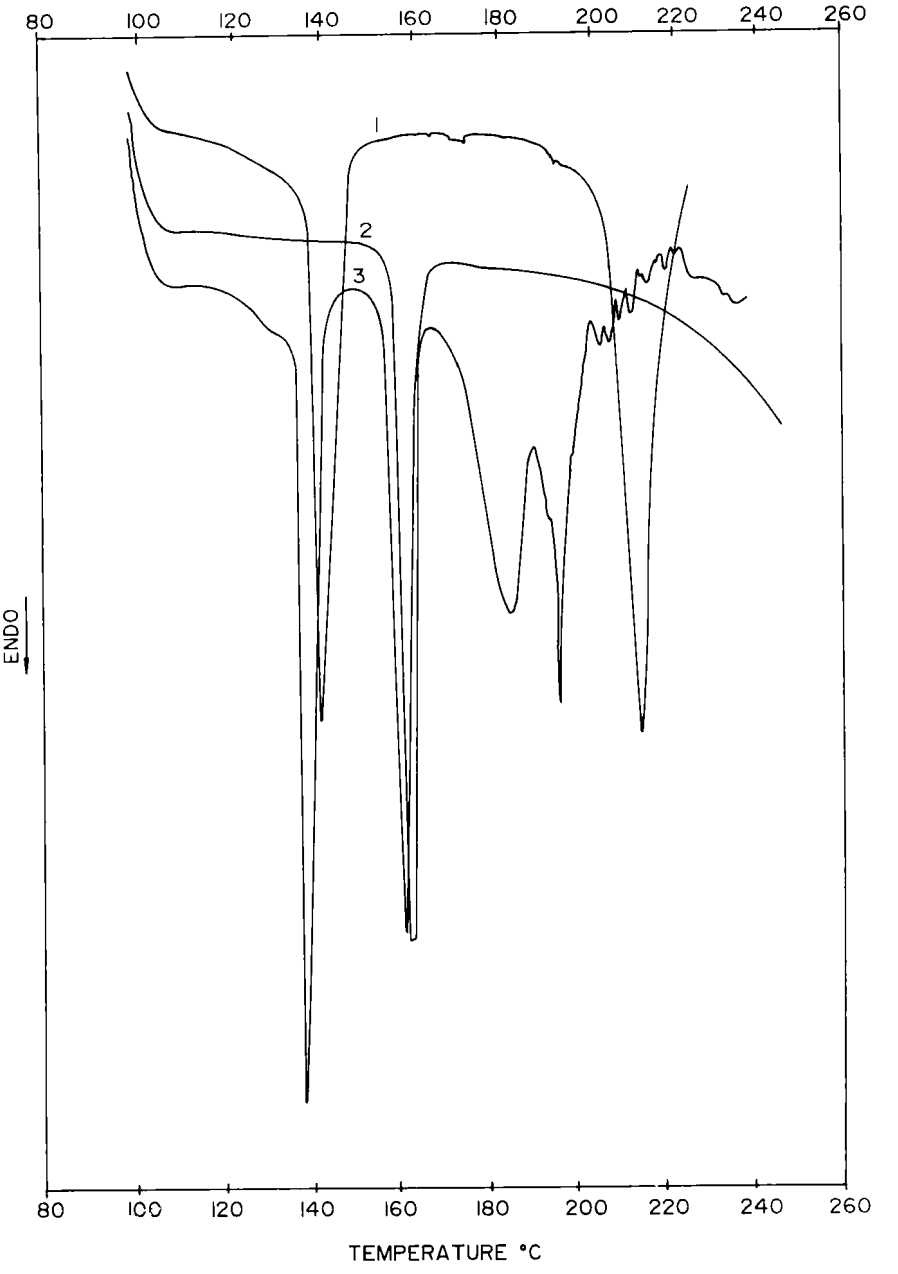

FIGURE 3

DSC thermograms of propranolol (2), lactose (1) and 1:5 physical mixture of propranolol : lactose (3).

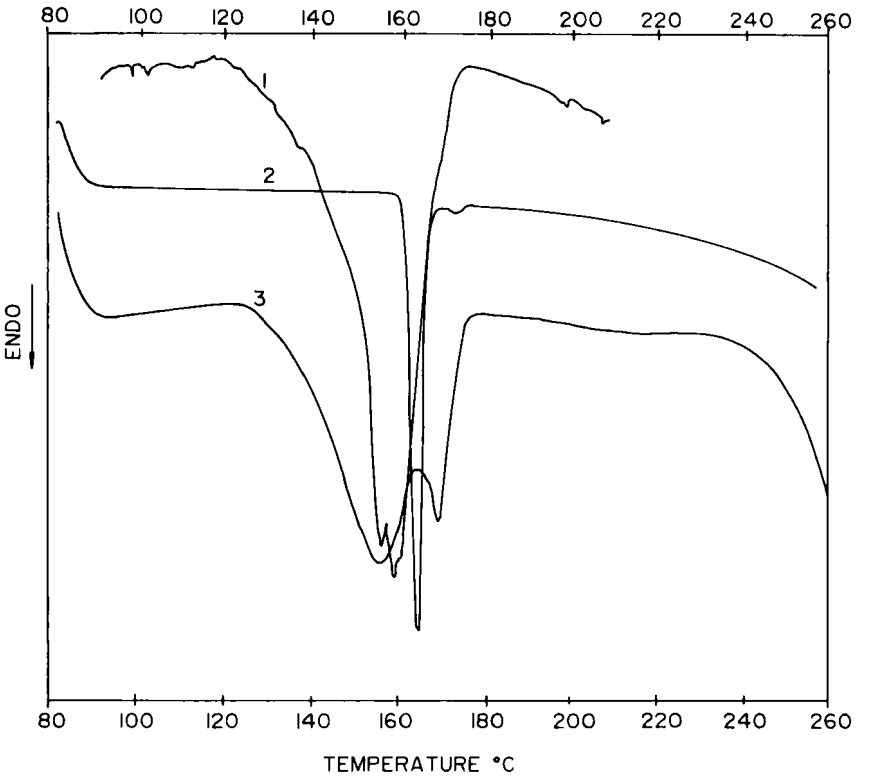

FIGURE 4

DSC thermograms of propranolol (2), calcium phosphate monohydrate (1) and 1:5 physical mixture of propranolol : calcium phosphate monohydrate (3).

In the 1:5 physical mixture of propranolol HCℓ and Primojel® the propranolol HCℓ melting endoterm broadened with a shift to about 10°C lower than the melting point of propranolol HCℓ.

In the 1:5 physical mixture of propranolol HCℓ and stearic acid the propranolol HCℓ melting endoterm shifted down 20°C, almost disappearing.

A 1:5 physical mixture of propranolol HCℓ and Avicel® caused the melting endoterm of propranolol HCℓ to shift to a temperature about 5°C lower than propranolol HCℓ alone.

It can be concluded that when proprnaolol is formulated into tablets care should be taken and the use of these commonly used excipients be avoided.

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