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COMPATIBILITY STUDY BETWEEN FAMOTIDINE AND SOME EXCIPIENTS USING DIFFERENTIAL SCANNING CALORIMETRY

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ABSTRACT

Based on DSC thermograms, famotidine interacted with kollidon, primojel, crospovidone, emcompress or lactose. There were no interaction between famotidine and talc, Mg stearate or avicel PH 101. HPLC analysis confirmed these interactions between famotidine with emcompress and crospovidone.

INTRODUCTION

Famotidin,[1-amino-3-[[[2-[(diaminomethylene)amino]-4-thiazolyl]methyl] thio] propylidene] -sulfamide[1] is a long acting histamine H_2 -antagonist for the treatment of gastro intestinal ulcers and related disorders. It was reported , that famotidine has a long duration of action and is more potent than ranitidine and cimetidine[2] .

In drug formulation, drugs are in intimate contact with one or more excipients, the latter could affect the stability of the drugs. Knowledge of drug - excipients interaction is therefore very useful in selecting appropriate excipients [3].

Recently various publications used DSC techniques for detection of incompatibilities in drug - drug and drug - excipients interactions [4-8]. The incompatibilities were detected by the appearance, shift or disappearance of peaks in the DSC thermograms.

In this communication , the compatibilities or incompatibilities of famotidine with some commonly used tablet excipients were reported. To confirm some interactions, HPLC analysis was also done for some drug - excipient formulations.

EXPERIMENTAL

Materials

Famotidine,polymorph 1 (Luwitrade),Crospovidone (GAF), Lactose (Meggle), Kollidon 25 (BASF), Mg Stearate (Breyer Chemie), Primojel (Mendell), Avicel PH 101 (Asahi Chemical), Emcompress (Mendell),Talc (Heichen). The purity of famotidine was checked by IR Spectro - photemeter (Hitachi I-2001) using KBr pellets.

Differential scanning calorimeter analysis

Samples (5-6 mg) were measured (Sartorius 4503 micro balance) and hermeticaly sealed in flat bottomed aluminium pans. These samples were heated over the temperature 26 - 200 ^{o}C in atmosphere of nitrogen and thermograms were obtained with a Shimadzu DT-30 Thermal Analyser. The instrument was calibrated with indium standard. Thermograms were obtained by heating at a constant rate 10 ^{o}C per minute. The pure subtances and as well as 1 : 1 physical mixtures of famotidine and excipients prepared by mortar and pestle agate.

HPLC analysis of drug formulations

HPLC analysis of some drug excipient formulations was done according the USP XXII[9] by using a Shimadzu LC 6A and CR 3A - data processor with a column Si 60 (E.Merck) and 20 Ul Rheodyne 7125 injector. Linearity was achieved from 1,0 to 241,0 Ug/ml;LOD = 0.07 Ug/ml; LOQ = 0.23 Ug/ml (according to Carr & Wahlich[10]).

RESULTS AND DISCUSSION

All the DSC thermograms of pure famotidine (Fig. 1-6) showed a sharp endotherm maximum melting point at 164^{o}C. The excipient kollidon, primojel, crospovidone, Mg stearate, Talc and Avicel PH 101 all exhibited shallow broad endotherm peaks. This might correspond to the volatilization of adsorbed water as reported by Botha et al[7].

Fig.1-3 show that the sharp endothermic peaks of famotidine disappeared. This indicates strong interaction of kollidon, primojel,crospovidone with famotidine. It is suggested to avoid using these excipients with famotidine. It is very interesting to know why the peaks of famotidine disappeared.

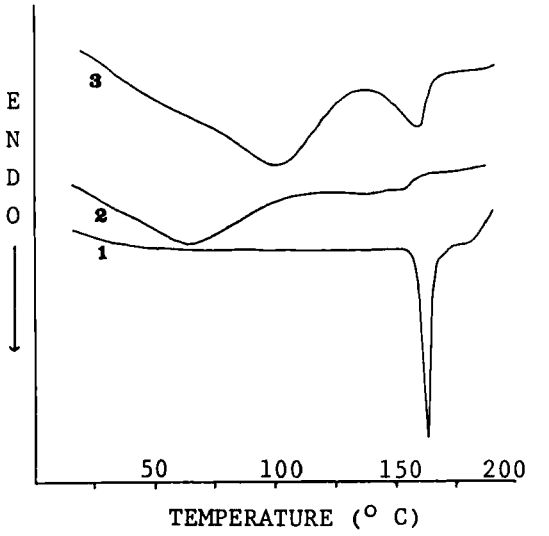

FIGURE 1
DSC thermograms of famotidine (1), kollidon 25(2) and 1:1 physical mixture of famotidine:kollidon 25(3)

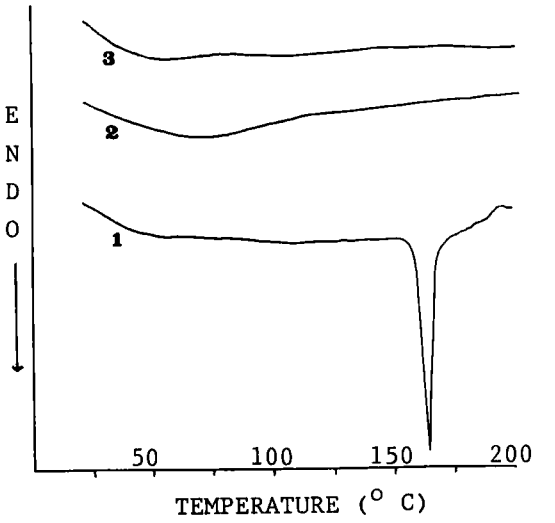

FIGURE 2
DSC thermograms of famotidine (1), primojel (2) and 1:1 physical mixture of famotidine:primojel (3)

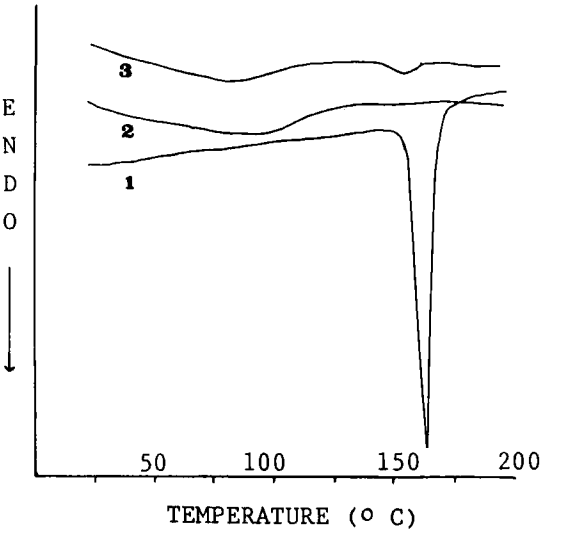

FIGURE 3
DSC thermograms of famotidine (1), crospovidone (2) and 1:1 physical mixture of famotidine:crospovidone(3)

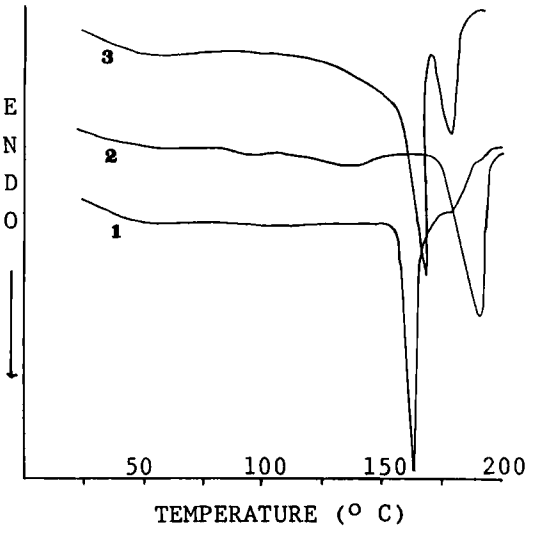

FIGURE 4
DSC thermograms of famotidine (1), emcompress (2) and 1:1 physical mixture of famotidine:emcompress(3)

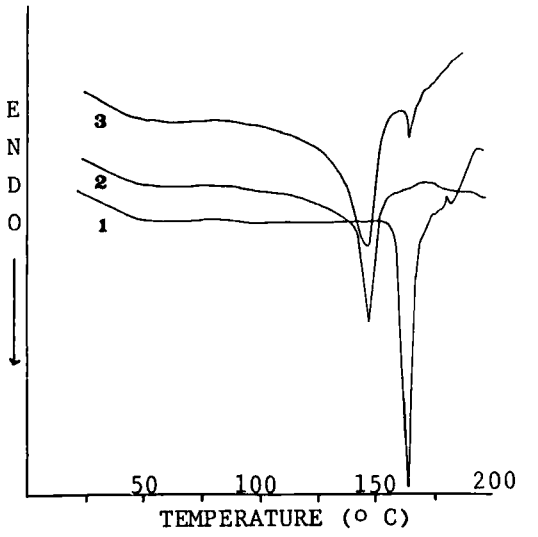

FIGURE 5

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

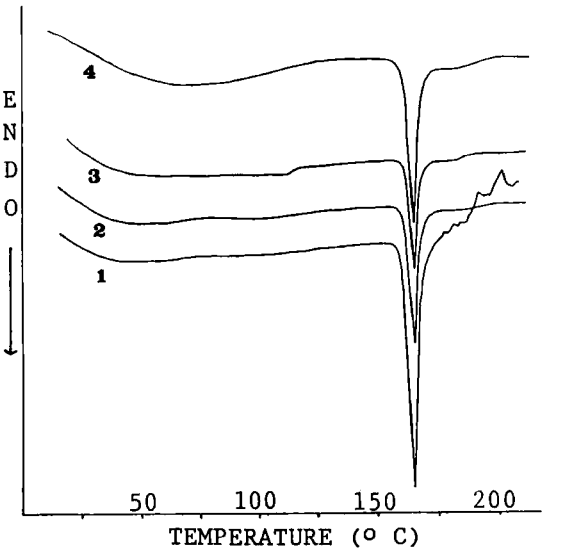

FIGURE 6

DSC thermograms of famotidine (1) and 1:1 physical mixture of famotidine with talc (2), Mg stearate (3) and avicel PH 101 (4).

TABLE 1
Recovery of some famotidine formulations

Formula	Composition	%	Recovery of famotidine (mean ± SE, n=5)
A	Famotidine	11.76	86.49 ± 0.34
	Emcompress	88.24	
B	Famotidine	11.76	91.81 ± 0.76
	Crospovidone	3.53	
	Mg stearate	1.18	
	Emcompress	83.53	
C	Famotidine	11.76	95.70 ± 0.51
	Avicel	88.24	
D	Famotidine	11.76	94.15 ± 0.05
	Crospovidone	3.53	
	Mg stearate	1.18	
	Avicel	83.53	

An interaction between famotidine and emcompress (Fig.4) may be also occured as the peaks of famotidine and emcompress were shifted compared with the pure samples.The smaller peak of famotidine in famotidine-lactose mixture (fig 5) could indicate an interaction. Fig.6 show that the DSC thermograms of famotidine in the mixtures were not affected, these show that no interaction occured between famotidine and Mgstearate, talc, or avicel PH.101.

HPLC analysis (see Table 1) confirmed that interaction were occured between famotidine and emcompress(formula A,B).Only with avicel as excipient (formula C) the recovery is relatively good, because it was no inter - action of famotidine and avicel as observed by DSC. Small concentration of crospovidone can also affect the HPLC determination of famotidine (formula C, D ; t calc.= 3.89, t table = 2.306 at $p < 0.05$).

CONCLUSIONS

Interaction between famotidine and kollidon, primojel, crospovidone, emcompress or lactose were observed by DSC. Famotidine was found to be compatible with talc, avicel PH 101 or Mg stearate. Interaction between famotidine and emcompress or crospovidone affects the HPLC determination of famotidine.

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