Asian Journal of Chemistry Vol. 21, No. 9 (2009), 6715-6718

Differential Scanning Calorimetry Studies of Solid Dispersion of Indometeocin Using Mixed Carriers

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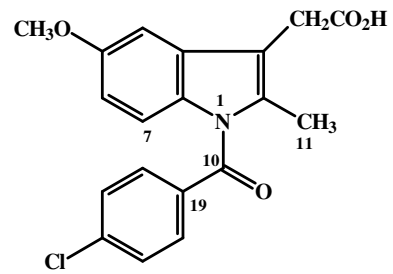
Differential scanning calorimetry study was carried out to investigate the effect of temperature on physical mixture and solid dispersion of indomethacin. Various samples of indomethacin were analyzed at a heating rate of 40 per min using air as medium. Sharp thaw points of pure indomethacin and that of mixtures were determined for comparative study of drug-carrier interactions.

Key Words: Indomethacin, Urea, Mannitol, Sucrose, Dextrose.

INTRODUCTION

Indomethacin is a drug which has been commonly used a NSAIDS. It is a potent drug with a potential of dose related adverse reactions.



1-(*p*-Chlorobenzoyl)-5-methoxy-2-methyl indole-3-acetic acid

Normally the drug is absorbed after oral administration, the peak plasma level reaches in 2 h and 90 % of the drug is protein bound. It has biological half life of 2.6 to 11.2 h, 10 to 20 % of drug is excreted unchanged in urine. The drug is practically insoluble in water, more soluble in buffer having pH 7.2, The usual dose of indomethacin is 50-100 mg/day. Chio *et al.*[1] explained solid dispersion which encompasses all physical methods like eutectic mixtures[2], solid solution, glass solution[3] and dispersions[4]. Increased rates of dissolution[5] are observed in solid dispersion. To study the drug-carrier interaction[5,6] all the solid dispersions of indomethacin were evaluated using DSC. In this sample of solidified mixture is gradually heated and thaw points are calculated.

EXPERIMENTAL

Preparation of solid dispersion using carrier and drug: Weighed quantities of drug and carrier (single/mixed) in ratio of (20:80) were mixed thoroughly by trituration in a glass pestle mortar and passed through sieve no. 100. The mixture was taken in large stainless steel flat type containers and melting was carried out in hot liquid paraffin bath. The mass was mixed thoroughly, melted carefully and allowed to be cooled immediately in the ice bath. The hardened mass was scrapped out with stainless steel spatula, powdered and passed through sieve no. 100 and stored in an air closed container in a desiccators for DSC studies.

DSC study: 2.5 mg of various samples of indomethacin or solid dispersions were analyzed by DSC using Du point differential scanning calorimeter. A heating rate of 4o per minute was selected using air as medium[7]. A sharp exact thaw point of pure drug and that of mixtures were determined in ºC.

Fig. No.	Sample	Thaw point (ºC)
1	Indomethacin	157.0
2	Urea-indomethacin solid dispersion	132.0
3	Urea-indomethacin physical mixture	132.0
4	Mannitol-indomethacin solid dispersion	164.5
5	Mannitol-indomethacin physical mixture	165.0
6	Urea-Mannitol-Indomethacin solid dispersion	100 .0
7	Urea-Mannitol-Indomethacin physical mixture	105.0
8	Mannitol-sucrose-indomethacin solid dispersion	143.0, 154.0
9	Mannitol-sucrose-indomethacin physical mixture	158.0
10	Mannitol dextrose-indomethacin solid dispersion	123.0, 142.5, 144.5
11	Mannitol-dextrose, indomethacin physical mixture	139.0, 158.0

RESULTS AND DISCUSSION

The result showed only one thaw point in case of pure drug, urea-indomethacin solid dispersion and physical mixture, mannitol-indomethacin solid dispersion and physical mixture, mannitol-urea-indomethacin solid dispersion and physical mixture. But in case of mannitol-sucrose-indomethacin solid dispersion showed two thaw points whereas physical mixture of the same showed only one point. Similarly solid dispersion and physical mixture of mannitol-dextrose indomethacin showed more than one thaw point.

In one situation, a eutectic mixture is formed and only one minimum thaw point is obtained. This product has a very fine grained structure which can impart to it different properties like dissolution etc. as compared to physical mixture of the two. This former structure is fine grained because the crystallization was very intimate since crystals of both phases are formed simultaneously and the DU point would

show only single thaw point. This is quite a different situation than the one shown earlier in which the molten mass on cooling starts separating to form plateaus when most of solid phase separates out first and finally the whole of mass solidify including the last part of mixture. The means that solidification occurs in phases in spite of quenching the molten mass on a ice bath. In binary solid dispersion, there is an excess of carrier to the drug *i.e.* 80:20 ratio. In binary solutions where solid dispersions formats were of drug and single carrier minimum melting point could sharply defined as shown in Fig. 1. In ternary solutions there are three substances drug and mixture of two carriers as shown in Fig. 2 and there is a tendency of separation of one or two components in formation of crystals during solidification showing more than one minimum thaw points as shown in Fig. 2, using DU point scanning.

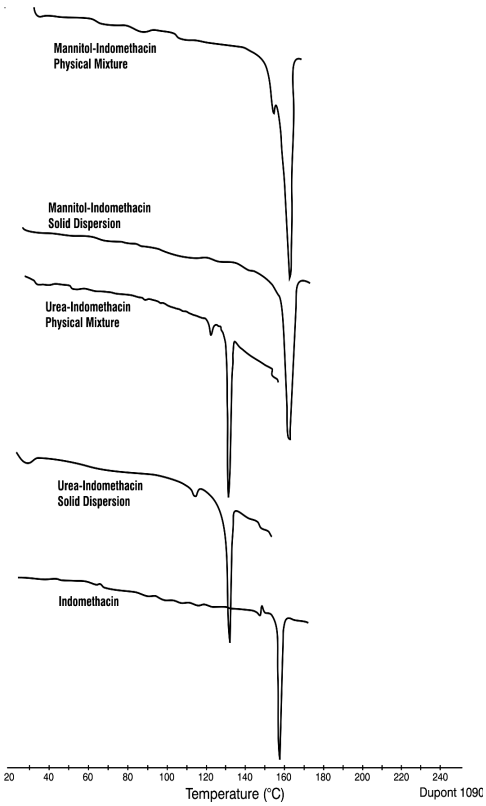


Fig. 1

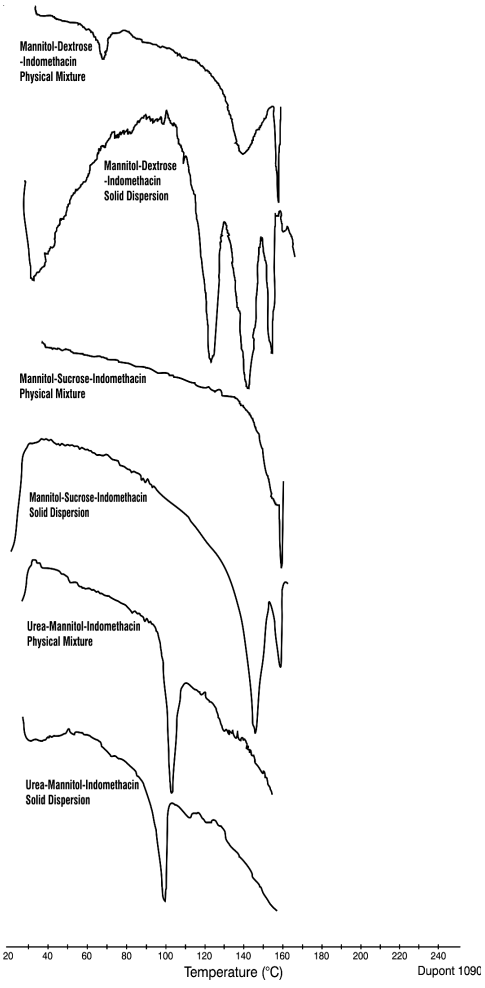


Fig. 2

Conclusion

Hence it was noted that in pure indomethacin as well as in binary mixtures only single minimum thaw points were obtained, but in ternary mixtures indomethacin was mixed with mixtures of two carriers, more than one minimum thaw points were obtained showing some interactions between the drug and carriers.

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(*Received*: 1 August 2008; *Accepted*: 16 July 2009) AJC-7683

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