International Journal of Pharmaceutics, 47 (1988) 263–264
Elsevier

IJP 01607

Enhanced dissolution rate of aspirin from aspirin–methacrylic acid, methyl methacrylate coacervates in a simulated intestinal fluid

R.S. Okor

Department of Pharmaceutics, University of Benin, Benin City (Nigeria)

(Received 11 April 1988)
(Accepted 27 April 1988)

Key words: Aspirin–methacrylic acid-methyl methacrylate coacervates: Dissolution rate: Simulated intestinal fluid

Summary

Granular coacervates containing aspirin and methacrylic acid-methyl methacrylate (3 : 2) have been prepared by an evaporation technique and evaluated for dissolution rates in simulated gastric (pH 1.2) and intestinal juice (pH 7.5). In the acid medium (A), the amount of aspirin dissolved from the coacervate was 1% w/w of the initial amount of aspirin (300 mg) after 1 h and from the control (aspirin without polymer) 4.2% w/w after 1 h; a time lag of 45 min preceded the dissolution from the coacervate. In the alkaline medium (B), the amounts of aspirin dissolved were 54% w/w (coacervate) and 38% w/w (control) after 1 h. The polymer therefore reduced the aspirin dissolution rate in A but increased the rate in B. Dissolution ratios, B/A were 9.5 (control) and 54 (coacervate). The results relate to the insolubility of the polymer in A and its high solubility in B.

An implication of enteric coating of drugs is that drug release and absorption is delayed and hence gives a slower onset of drug action. Aspirin is enteric-coated to minimise its side-effects, gastric ulceration and bleeding (Leonards and Levy, 1973); its intestinal absorption rate is low; consequently the enteric-coated form exhibits a slow onset of the analgesic effect. Increase in its intestinal dissolution rate may be expected to lead to a faster absorption rate. Thus the solid dispersion of a drug in a water-soluble polymer has been used to increase its dissolution and absorption rates (Sugimoto et al., 1980). This approach has been applied here to enhance aspirin dissolution rate in a simulated intestinal fluid. The polymer used is soluble in alkaline fluids but acid-resistant so that enteric property can be retained.

Methacrylic acid, methyl methacrylate copolymer (Eudragit, L-100) was obtained from Rhom Pharma (Darmstadt, F.R.G.); it is insoluble in acid and water but soluble in alkaline medium. The ratio of carboxylic acid to the ester is 1 : 1. Aspirin BP was received as fine powder from BDH, Poole, U.K. Ferric chloride solution BP and 0.1 N sodium hydroxide were used for colorimetric analysis.

Aspirin (3 g) and the polymer (2 g) were dissolved in 40 ml of 95% ethanol. The solution was placed in a shallow crucible and was evaporated to dryness (in a fume chamber by heating over a

Correspondence: R.S. Okor, Department of Pharmaceutics, University of Benin, Benin City, Nigeria.

water bath at 90 °C). The dried mass was first crushed (with a pestle and mortar) and then pressed through a sieve of aperture size 710 μm. Particles below 500 μm were sifted out by shaking the granules on a sieve of aperture size 500 μm. Aspirin without polymer was similarly processed and used as an control.

The dissolution test apparatus consisted of a cylindrical basket (height 32 mm, i.d. 10 mm and aperture size 425 μm), and was immersed mid-position in 800 ml leaching fluid (i.e. USP simulated gastric juice (pH 1.2) or intestinal juice (pH 7.5) A sample of granules containing 300 mg aspirin was placed in the basket and the fluid stirred at 100 rpm; the fluid temperature was maintained at 37 ± 0.5 °C. Samples (2 ml) were withdrawn at selected times for analysis.

The samples were heated (2 h, 90 °C) to hydrolyse the aspirin to salicylic acid (Klaus, 1979). Ferric chloride solution BP (1 ml) was added to the sample and the resulting coloured solution was analysed with a Gallenkamp colorimeter (9/CS-ZOO) at λ_{max} 520 nm.

The drug–polymer composition of 3 : 2 in the coarcevate was selected because preliminary experiments had shown that a lower polymer content did not reduce the drug dissolution rate in the acid medium significantly, while a higher polymer content resulted in coacervates that were too hard to reduce in size to granules.

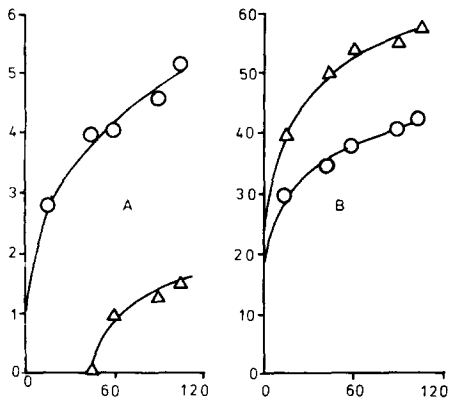

Fig. 1. Percentage of initial amount of aspirin (300 mg) which dissolved (ordinate) at time intervals (abscissa, minutes) from the aspirin–polymer coacervate (3 : 2) △, and pure aspirin (control) ○, in simulated gastric (A) and intestinal (B) juice.

Aspirin dissolution was generally low in the acid medium; for instance, only 4.2% w/w of the initial amount of aspirin (300 mg) dissolved after 1 h from the control and 1% w/w from the coacervate, a time-lag of about 45 min preceded the release from the coacervate at pH 1.2, but this was absent in the control (Fig. 1A). In the alkaline medium (pH 7.5) aspirin dissolved more rapidly, 38% w/w (control) and 54% w/w (coacervate) after 1 h (Fig. 1B). Thus the coacervated system delayed and decreased the dissolution of aspirin in the simulated gastric fluid (A) but increased it in the intestinal fluid (B); the dissolution ratios B/A after 1 h were 9.5 (control) and 54 (coacervate).

In the coacervate, drug–polymer molecular attractions are considerable and possibly greater than the drug–drug molecular attractions (Okor, 1988). This greater cohesiveness together with the insolubility of the polymer in the acid medium resulted in the lower dissolution rate of aspirin from the coacervate, compared with the control. In the alkaline medium the polymer is soluble liberating the aspirin molecules into solution readily.

Two important findings emerged from the study, firstly the system displayed enteric properties and secondly, the dissolution rate in the intestinal fluid was enhanced. Such a system therefore has a potential for increased intestinal absorption.

References

Klaus, F., Aspirin. In *Profile on Drug Substances, Vol. 8*, Academic, London, 1979, pp. 1–46.

Leonards, J.R. and Levy, G., Gastrointestinal blood loss during prolonged aspirin administration. *N. Engl. J. Med.*, 289 (1973) 1020–1022.

Okor, R.S., Modification of solute dissolution rate by coprecipitation with certain acrylate–methacrylate copolymers. *J. Appl. Polymer Sci.*, 33 (1988) 635–640.

Sugimoto, I., Kuchiki, A., Nakagawa, H. and Togigo, K., Dissolution and absorption of nifedipine from nifedipine–PVP coprecipitates. *Drug Dev. Ind. Pharm.*, 6 (1980) 137–160.