THEOPHYLLINE-GLYCINATE SUPPOSITORIES: A POTENTIALLY MORE STABLE SOURCE OF THEOPHYLLINE THAN AMINOPHYLLINE SUPPOSITORIES B.P.

R.H. Pryce-Jones, D. Watt, Miss K. Kraisintu, Department of Pharmaceutical Chemistry, University of Strathclyde, 204 George Street, Glasgow, G1 1XW.

Mathews (1977) reported that the rate of release of theophylline from Aminophylline Suppositories B.P. formulated in triglyceride suppository bases decreases with ageing. The time and point of melting (m.pt.) of such suppositories, stored at ambient or elevated temperatures also rise with age (De Blaey and Rutten-Kingma, 1977).

Traditional pharmaceutical technique was used to prepare 1g suppositories containing either 360 mg aminophylline or equimolar amounts of theophylline, ethylenediamine, theophylline-sodium acetate, theophylline-sodium glycinate or theophylline-piperazine. The possibility of changes in the suppositories being partly initiated in the moulten state was minimised by making preparation time as short as possible. The rate of dissolution of theophylline at 37° in 0.05M phosphate buffer pH7.4 using a modified B.P. apparatus was based on absorbance at 272 nm. Ethylenediamine and m.pts. were determined by the B.P. methods(1973).

Table 1. Effect of temperature on percentage release of theophylline in 20 minutes from suppositories stored for 14 weeks

Temperature	amino-phylline	theo-phylline	theophylline ion pairs with: sodium acetate	sodium glycinate	piperazine
4°C	87%	60%	90%	96%	134%
32°C	11%	10%	103%	98%	92%

Suppositories of aminophylline released more theophylline than those of theophylline after storage of both at 4°C. Stored at 32°C however each type only released a small proportion of its total theophylline content. Suppositories of aminophylline and ethylenediamine contained slightly less than the incorporated amount of ethylenediamine after storage at 4°C whilst this amount fell markedly after storage at 32°C for both types. Theophylline suppositories stored at 32°C for 18 weeks had a melting point of 33.9° whilst those of aminophylline did not melt below 80°C. Both types stored at 4°C retained the low melting point,33.8°C of the original base. Thus the data suggest that theophylline reacts with the triglyceride bases both alone and in the presence of ethylenediamine and that in aminophylline suppositories this interaction may be independent of that of ethylenediamine with the same base. It may also be inferred that the observed rise in melting point is due to the reaction of ethylenediamine with the base and that the interaction of theophylline with base may be an independant phenomenon.

All the other theophylline ion pairs gave better than 90% release of theophylline after 14 weeks at both 4° and 32°C. The results from theophylline-piperazine may be spurious because of the high release after storage at 4°C. Piperazine like ethylenediamine is slightly irritant (Martindale) and is thus the least suitable. Sodium acetate reduced the release of theophylline in the first ten weeks and resulted in increased viscosity of the moulten base and difficulty in pouring.

It is concluded that the high release of theophylline, apparent lack of undesireable interaction and low toxicity of glycine (a natural amino acid) make theophylline-sodium glycinate a suitable subject for study as a possible replacement for aminophylline in suppositories.

Mathews, T., (1977) B.P. Commission personal communication.
De Blaey, C.J., Rutten-Kingma, J.J. (1977) Pharm. Acta. Helv. 52: 11-14.
British Pharmacopoeia (1973) Her Majesty's Stationery Office.
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