

PREFORMULATION STUDIES ON INGREDIENTS OF SUPPOSITORY BASES

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Fatty suppository bases are complex mixtures of triglycerides. In order to study the physico-chemical interactions within suppositories, especially interactions between the drug and the excipient, it is desirable initially to simplify the system. This may be achieved by examining binary mixtures of pure monoacid triglycerides to obtain a composition whose characteristics resemble those of commercial bases. An explanation for increases in melting point observed on storage of suppositories is proposed here.

Differential thermal analysis and thermal microscopy of binary mixtures of tricaprin (C), trilaurin (L), trimyristin (M), tripalmitin (P), tristearin (S) (Dynasan Grade) gave either monotectic phase diagrams (Type A) or eutectic phase diagrams (Type B) one arm of which corresponded to simultaneous melting of both components at the eutectic temperature. Mixtures of triglycerides of similar molecular weight tended towards Type B behaviour, whereas those of dissimilar molecular weight tended towards Type A behaviour; the phase diagrams often showed polymorphic transitions below the eutectic or monotectic temperature. On storage, the phase diagrams changed due to the transition of unstable to stable polymorphic forms, causing an increase in the melting point of the mixtures. This explains the same problem of elevated melting point frequently encountered with commercial bases (Möes & Jaminet 1976; Jones and others, 1977). Addition of dosage quantities of ketoprofen (3.47% w/w) or metronidazole (23.4% w/w) to binary triglyceride mixtures narrowed the composition range corresponding to simultaneous melting (see Table below). The ketoprofen addition also lowered the eutectic temperature.

Components of mixture (ketoprofen 3.47% w/w metronidazole 23.4% w/w)	Simultaneous melting composition range % w/w of tricaprin with respect to total triglyceride.	Eutectic Temperature °C.
tricaprin trilaurin alone	60 - 100	33
tricaprin trilaurin ketoprofen	70 - 100	32
tricaprin trilaurin metronidazole	70 - 100	33
tricaprin trimyristin alone	80 - 100	36
tricaprin trimyristin ketoprofen	90 - 100	35
tricaprin trimyristin metronidazole	90 - 100	36

The thermal methods of analysis indicated that the properties of the commercial bases are reproduced by the following simple mixtures; C 50-60% w/w in L, C 82-94% w/w in M, C 84-100% w/w in P, C 94-100% w/w in S. Their exact compositions are being derived by further comparisons of the properties of these mixtures with those of the commercial bases Witepsol E75, Witepsol W35 and Suppocire A using the following techniques; capillary U-tube melting point, open tube melting point, solidification point (Shukoff method) and viscosity using a Deer Rheometer.

Jones, T.M., Jordan, D. and others. (1977) Proc. 1st Inter. Conf. Pharmaceut. Technol. Paris. 31st May - 2nd June 1977

Möes, A. & Jaminet, F. (1976) Pharm. Acta Helv. 51, 119-125

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