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Microemulsion-based organogels: a novel matrix for transdermal drug delivery

G. D. REES, S. KANTARIA AND M. J. LAWRENCE

Department of Pharmacy, King's College London, Manresa Road, London SW3 6LX

Addition of gelatin to a water-in-oil (w/o) microemulsion can result in the formation of a rigid microemulsion-based organogel (MBG). MBGs stabilised by Aerosol-OT (AOT) in a hydrocarbon oil comprise an extensive, interconnected network of hydrated gelatin stabilised by a monolayer of surfactant, which coexists with a population of conventional w/o microemulsion droplets (Fig.1).

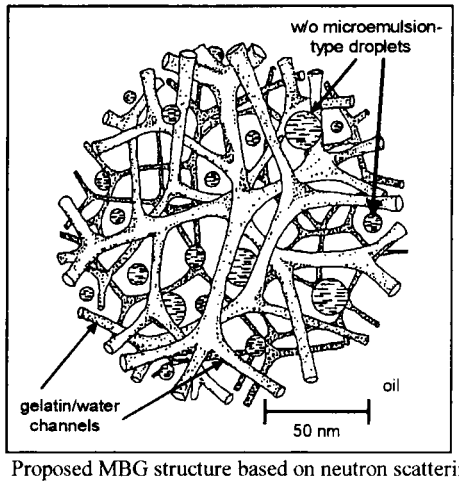

Fig.1. Proposed MBG structure based on neutron scattering.

The MBG is an effective immobilisation matrix for proteins such as lipase. Dispersal occurs at the molecular level with full retention of catalytic activity, and enhanced stability. The MBG is thermodynamically stable, and is structurally stable in contact with apolar solvents, including the parent hydrocarbon. This feature facilitates the granulation of protein-containing MBGs and their exploitation in kilogram-scale biotransformations in organic media (Jenta et al, 1997; 1997).

The attraction of MBGs for use in transdermal delivery stems from their general stability and high solubilisation capacity in comparison to the parent w/o microemulsions. Gel formulations are practically and aesthetically superior for topical application, and the unique properties of MBGs allow the solubilisation of both hydrophilic, amphiphilic and hydrophobic drugs. The presence of surfactant in the MBG formulation may improve drug delivery, however, pharmaceutical acceptability demands the elimination of the n-alkanes currently employed, and ideally the replacement of synthetic surfactants such as AOT.

Recent formulation studies conducted in this laboratory show that MBGs can be formed using mixed non-ionic:ionic surfactant systems stabilised predominantly by either Tween 85, Tween 81 or Tween 21 in isopropyl myristate (IPM). The IPM has a well recognised application as a penetration enhancer. Successful formation of MBGs appears to require a degree of percolation in the parent w/o microemulsion prior to addition of gelatin, or that percolation be induced by its addition. The continuous hydrated network present in the MBG is manifested by a large increase in conductivity suggesting application in iontophoresis. The newly formulated MBGs containing salicylate as a model hydrophilic drug were successfully integrated as part of a transdermal iontophoretic drug delivery system as illustrated in Fig.2.

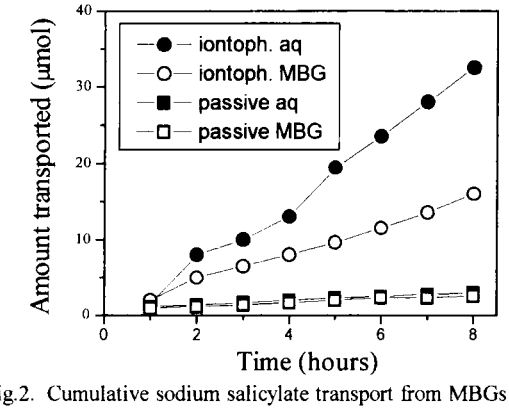

Fig.2. Cumulative sodium salicylate transport from MBGs and aqueous solution under equivalent passive and iontophoretic conditions. MBG contained 2:1 Tween 85:AOT in IPM. Current density: 0.385mA cm^{-2}.

Jenta, T.R-J., Batts, B., Rees, G.D. and Robinson, B.H. (1997) Biotechnol. Bioeng. 53, 121-131.

Jenta, T.R-J., Batts, B., Rees, G.D. and Robinson, B.H. (1997) Biotechnol. Bioeng. 54, 416-427.