Release rates are important in many topical preparations, in particular in transdermal preparations. Here there are several investigational methods available. In-vitro methods involve placing the ointment on a membrane and measuring the appearance of drug in a receptor compartment on the sink side of the membrane. Hoelgaard and Møllgaard (1983) have, for instance, described the in-vitro release of linoleic acid through an in-vitro membrane. They mounted abdominal human skin in one case and skin from hairless rats in another to open diffusion cells. The dermal side was bathed with a receptor medium stirred at 37°C. The medium was 75 mL of 0.05 N phosphate buffer (pH = 7.4) which contained 0.05% Pluronic F68 and 0.01% butylhdroxytoluene, the latter two ingredients added in order to increase the lipid solubility. Linear, Ficksian diffusion curves were obtained. In a stability program, such tests are obviously useful and should be repeated periodically, but an "internal standard" or "calibrator" should be used, i.e., a stable test substance, the diffusion of which is known (e.g., salicylic acid). Other pseudo-in-vivo methods involve shaved or hairless rabbits, or cadaver skin. The interaction between ointment and container (patch) should also be part of the stability program.

Some of the testing applicable to semisolid emulsion systems is also applicable to ointment systems and will be discussed at a later point.

4. EMULSIONS

An emulsion should be thought of as a metastable system. In most cases the emulsion system (Fig. 7) is thermodynamically more energetic than the ground state system, which would simply be the totality of the two phases, separated. There will, therefore, always be the potential for oil droplets re-merging in an attempt to create the thermodynamically stable system.

Emulsion systems are taken orally (LipoGantracin™, Roche), parentally (as parenteral fat emulsions), and topically (creams).

4.1 The Emulsion Interface

The factors that stabilize the emulsion system are a layer of surfactant and protective colloid on the exterior of the droplet. The amount of these two must be such that they

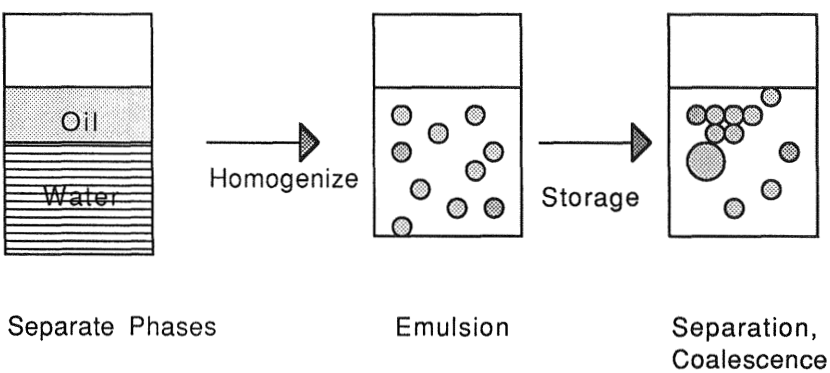

Fig. 7 Emulsion system.