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COMMUNICATION

Influence of Surfactants over the Dissolution of Mequitazine

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ABSTRACT

Influence of surfactants over the dissolution of mequitazine was investigated by studying the dissolution of mequitazine (a poorly water-soluble drug) in different binary media prepared by adding different amounts of surfactants (Brij 35, Tween 20 or sodium lauryl sulfate (SLS)) into 1 liter of water. An improvement in drug dissolution rate was observed from all of the binary dissolution media, except those containing lower amounts of sodium lauryl sulfate. At lower concentrations, SLS acts as a true salt, and a competition is produced between drug and SLS for water molecules. Due to this saline effect, a decline in drug dissolution was observed from binary media with lower concentration of SLS.

INTRODUCTION

In pharmaceutical formulations, use of surfactants to improve the drug dissolution is a classical method. In commercial oral solid dosage forms, some surfactants are used extensively to optimize the dissolution of very poorly water-soluble drugs. So, it is noted that polysorbate 80 is used in the formulation of nifedipine tablets, and the use of sodium lauryl sulfate is also very common in different tablet formulations such as lidoflazine, griseofulvin, and albendazol (1). Official compendia sometimes recommend carrying out dissolution tests of certain drugs such as griseofulvin, estradiol, megestrol acetate, and norethindrone acetate, introducing a small amount of sodium lauryl sulfate in the dissolution medium (2).

Mequitazine is a poorly water-soluble drug, but it has been proven that its dissolution can be enhanced by binary solid dispersions with PEG 6000 (3) and ternary solid dispersions with PEG 6000 and Tween 20 (4).

The aim of this paper is to study the dissolution behavior of mequitazine using different binary media with

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different surfactants at different proportions with a focus on the possible interactions between molecules of every surfactant and drug.

MATERIALS

Mequitazine (M) was a gift from Rhône Poulenc Rorer (Madrid, Spain). Sodium lauryl sulfate (SLS) was supplied by Panreac (Barcelona, Spain), and Tween 20 (T-20) and Brij 35 (B-35) were purchased from Sigma (St. Louis, MO, USA).

METHODS

A Sotax AT-7 dissolution apparatus with paddles was employed to carry out all of the tests. The volume of dissolution medium, experimental temperature, and paddle speed were 1000 ml, 37 ± 0,1°C, and 100 rpm, respectively. A sample of 10 mg of pure mequitazine with a particle size lower than 100 μm was studied in every test. The duration of assay was 3 hr and samples were withdrawn at measured time interval and filtered with a Whatman filter paper (Type 42). Dissolved drug was assayed at a wavelength of 253 nm in a Beckman DU-6 Spectrophotometer and 3 replicates of each dissolution assay were carried out. The dissolution media used was distilled water and different binary media having different amounts of surfactant. Amounts of surfactants were 50, 100, 150, 200, 250, 300, 350, 400, 450, and 500 mg in all media.

RESULTS AND DISCUSSION

It is well established that the addition of a surface-active agent to the dissolution medium augments the dissolution rate of poorly water-soluble drugs by decreasing the surface tension of the solvent and subsequently increasing the wettability of solute, even when the concentration of surfactants is below its critical micelle concentration (CMC). This fact was observed over the mequitazine dissolution study, when amphiphiles were B-35 and T-20. But a different dissolution behavior was observed when SLS was in dissolution media. Figure 1 shows the dissolution profiles of mequitazine in different binary media containing different amounts of B-35. A proportional increment in drug dissolution is observed as the quantity of surfactant increases. There were no marked differences in the dissolution efficiencies obtained from binary dissolution

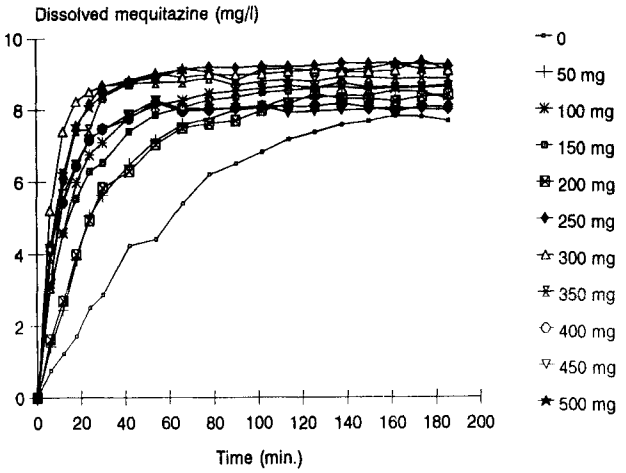

Figure 1. Dissolution profiles of M obtained from distilled water and binary dissolution media with B-35 containing different amounts of the same.

media with B-35 (Fig. 4) although the concentration of surfactant was above its CMC (130 mg liter^{-1}) (5).

Figure 2 shows the results of mequitazine dissolution from binary dissolution media with T-20. Dissolution patterns suggest that with the increasing concentration of T-20, there is an increase in dissolution rate and dissolution efficiency (Fig. 4). From the data, it is also evident that formation of micelles of T-20 (CMC of T-20 = 60 mg liter^{-1}) (6) does not markedly affect the process of dissolution.

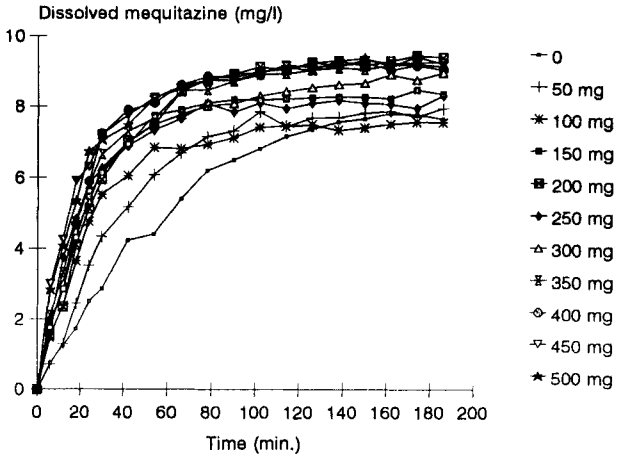

Figure 2. Dissolution profiles of M obtained from distilled water and binary dissolution media with T-20 containing different amounts of the same.

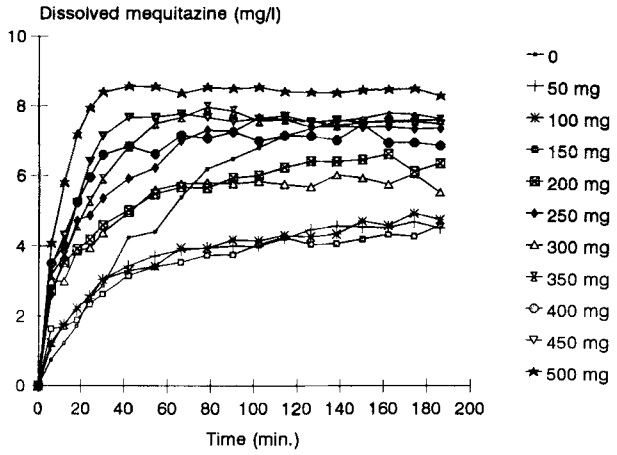

Figure 3. Dissolution profiles of M obtained from distilled water and binary dissolution media with SLS containing different amounts of the same.

An anomalous behavior was obtained when SLS was used in binary dissolution media (Fig. 3). In every dissolution medium, the concentration of SLS was below its CMC (2.34 g liter^{-1}) (7); when SLS was at lower concentrations (50–150 mg liter^{-1}), a decrease in drug dissolution was exhibited. But at higher concentrations (350–500 mg liter^{-1}), enhanced drug dissolution was observed with respect to the data obtained from distilled water. At intermediate concentrations of SLS (250–350 mg liter^{-1}), the dissolution profile was similar to that obtained from distilled water. These results correspond with the dissolution efficiency values shown in Fig. 4. The explanation of this behavior is obscure. It seems that this may be due to the marked hydrophilicity of SLS, which has an HLB value of approximately 40 (5). The dissolution of sodium lauryl sulfate in water is due to the process of solvation. So, in water, at lower concentrations, it exists practically in ionized form. The water molecules then remain oriented around two ionic radicals of the surfactant, sodium and lauryl sulfate. In this stage, water molecules remain engaged with SLS and in consequence, at lower concentration, SLS impedes the drug dissolution by saline effect. At higher concentrations, SLS manifests its surface-active property and increases the wettability of drug, which facilitates the drug dissolution.

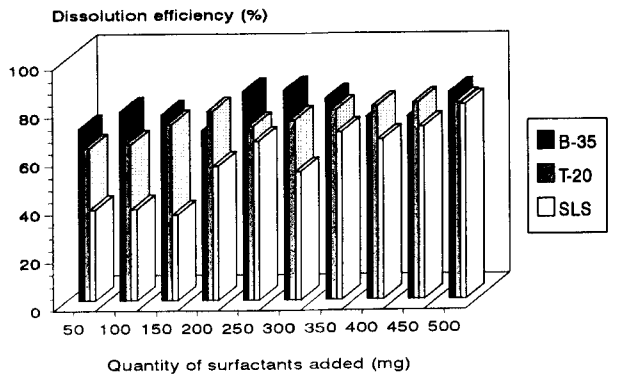

Figure 4. Dissolution efficiency (% of M dissolved at 186 min) obtained from distilled water and dissolution media with different amount of B-35, T-20, and SLS. The star (*) corresponds to the dissolution efficiency in distilled water.

CONCLUSIONS

The dissolution rate of mequitazine increases in accordance with the amount of surfactants added. This increment is independent of the nature and CMC of surface agent, except SLS. In the case of SLS, in lower concentration, a decrement is observed because of the saline effect produced during the dissolution of the amphiphile in water.

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