EFFECTS OF THE INCLUSION OF A MODEL DRUG ON THE PERFORMANCE OF SELF EMULSIFYING FORMULATIONS

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Vegetable oil/non-ionic surfactant mixtures can be formulated such that self-emulsification occurs when the mixtures make contact with aqueous solutions. Self-emulsifying formulations may be useful vehicles for the administration of lipophilic drugs by the oral route but as yet little information is available about the effects of a) inclusion of drug in the formulation or b) the gastric contents on the efficiency of emulsification.
A range of concentrations of benzoic acid were dissolved in a self-emulsifying system (30%w/w Tween 85/ 70%w/w Miglyol 812). The efficiencies of emulsification of these formulations in distilled water and in 0.1M HCl at 25°C were compared using methods previously described (Pouton 1984). Table 1 lists the emulsification times (t_{90}) and the resultant mean particle sizes (Coulter Nanosizer).

Table 1. Efficiency of emulsification as a function of benzoic acid content

%w/w benzoic acid in formulation	in distilled water at 25°C		in 0.1M HCl at 25°C	
	t_{90} (secs)	mean size (nm)	t_{90} (secs)	mean size (nm)
zero	11.3 ± 1.4	278 ± 2	42.3 ± 2.6	343 ± 16
0.05	14.8 ± 1.7	276 ± 4	41.5 ± 1.8	305 ± 4
0.10	15.5 ± 1.4	291 ± 10	25.7 ± 3.8	305 ± 8
0.20	25.7 ± 3.0	276 ± 3	47.6 ± 2.9	299 ± 11
0.50	24.0 ± 1.8	271 ± 5	30.2 ± 3.2	278 ± 10
1.00	24.3 ± 3.0	201 ± 6	27.1 ± 5.4	184 ± 5
1.50	11.7 ± 1.3	168 ± 3	13.6 ± 0.9	166 ± 6
2.00	13.1 ± 0.6	166 ± 1	13.8 ± 0.9	162 ± 4
5.00	8.7 ± 0.2	206 ± 4	8.8 ± 0.3	203 ± 4
7.50	8.0 ± 0.2	204 ± 4	7.7 ± 0.2	214 ± 13

data are presented as mean ± s.d. for 5 replicate emulsifications

The control self-emulsifying system (SES) without benzoic acid emulsified rapidly in distilled water to give fine dispersions with narrow size ranges. Emulsification times were longer and the mean particle sizes larger when the control system was emulsified in 0.1M HCl. Light microscopic inspection of the latter emulsions revealed the presence of particles up to 10μm in diameter whereas no particles could be seen in the corresponding emulsion formed in distilled water. When benzoic acid was dissolved in SES the major effect was to improve the efficiency of emulsification. Formulations containing more than 0.5% benzoic acid emulsified as efficiently in 0.1M HCl as they did in distilled water; overcoming the adverse effects of the electrolyte. Formulations containing between 1.50% and 2.00% benzoic acid were particularly efficient. Equilibrium phase diagrams of formulations were studied in the presence of water and 0.1M HCl. The enhancement of self-emulsification by benzoic acid corresponded with modifications to the phase diagram; the critical solubilization temperature was lowered towards 25°C and liquid crystal formation was more evident. The deleterious effects of 0.1M HCl were reflected in the phase diagram by decreased liquid crystalline involvement.
The data shows that self-emulsifying systems will be sensitive to the inclusion of drugs and also that the efficiency of existing systems can be improved. Phase diagrams can help a formulator to understand and predict the influence of drugs on the efficiency of emulsification.

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