

STUDY OF THE EFFECT OF HYDROTROPES ON THE HEAT COAGULATION OF BSA BY PHOTON CORRELATION SPECTROSCOPY

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Cross linking of bovine serum albumin (BSA) by heat coagulation or chemical means is an essential step in the preparation of albumin microspheres as drug carriers. In the former process, coagulation of ESA (25% aqueous solution emulsified in cottonseed oil) is effected by heating at 125°C (Gallo et al, 1984). The possible effect of drugs and additives on the heat coagulation of BSA has not been investigated. Hence, the objective of the present communication was to assess the effect of two hydrotropic solubilizers, namely sodium benzoate and sodium salicylate on the heat coagulation of BSA.

Photon correlation spectroscopy was used to determine the extent of physical swelling of ESA molecules in aqueous solutions, 20mg/ml, as a function of concentration of the two hydrotropic salts (0-20%). The change in the hydrodynamic diameter, D_i , was further determined following denaturation by heating for 1hr at various temperatures ranging from 40 to 90°C. The effects of the two hydrotropes under study on the initial hydrodynamic diameter, D_i , and the transition temperature, T_m , are shown in table 1.

Table 1. Effect of sodium benzoate and sodium salicylate on D_i and T_m .

	Concentration, gm%						
	0.0	0.1	0.5	2.0	5.0	10.0	20.0
Sod. benz.							
D_i , nm	5.4	6.0	7.1	7.8	7.5	7.3	7.3
T_m , °C	65	70	75	75	75	70	55
Sod. sal.							
D_i , nm	5.4	5.8	6.6	7.5	7.6	7.6	7.8
T_m , °C	65	70	75	75	75	70	60

The observed increase in D_i in the presence of sodium benzoate and sodium salicylate may be explained by the possible unfolding of BSA molecules as a result of binding of these salts to some specific binding sites on the albumin molecules. Results in table 1 also show that T_m increases as a function of hydrotrope concentration up to 5%, which may indicate that the unfolded BSA-hydrotropic salt complex resists further denaturation by heat. However, the decrease in T_m at higher hydrotrope concentrations, which would affect the nature of the solvent medium (Saleh et al., 1983), might imply a reduction in the resistance to denaturation. Moreover, it was observed that aqueous solutions of BSA, 20mg/ml, containing up to 10% of either salt, coagulate upon heating at 90°C.

In conclusion, hydrotropic salts affect the heat coagulation of BSA. From a practical standpoint, inclusion of such salts in the preparation of albumin microspheres would allow the use of much lower concentrations of BSA and a relatively lower coagulation temperature in addition to the possible incorporation of water insoluble drugs in a solubilized form.

Gallo, J.M. et al., (1984) Int. J. Pharm., 22, 63-74.

Saleh, A.M. et al., (1983) *ibid.*, 17, 115-117.