〔S. T. P. Pharm. Sci., 2, 270-278 (1992)〕 [Lab. of Pharm. Engineering]

Lyophilization and Size Contorol of Liposomes Entrapping Alkaline Phosphatase Prepared by Freeze/Thawing Method ; The Efffect of Additives : Sugar, Amino Acid, Protein and Water-Soluble Polymer.

YOSHIAKI KAWASHIMA*, TOMOAKI HINO, HIROFUMI TAKEUCHI, TOSHIYUKI NIWA, KENJI MATSUI

Alkaline phosphatase was entrapped in liposomes by the freeze/thaw method. Prepared liposomes were lyophilized, rehydrated, and size-contorolled. The deactivation of the enzyme during liposome preparation was very slight, but deactivation and leakage of the enzyme and increase in the liposomal vesicle sizes by lyophilization were remarkable. The most suitable phospholipid and additives to co-formulate in the liposomal system to prevent these undesirable phenomena that occurred during lyophilization were sought from candidate materials such as sugar, water-soluble polymer, amino acid and protein. Trehalose and polyvinyl alcohol were found to be the most recommendable additives to overcome these problems. It was important to add them in the foumulation prior to freeze/thawing for preparing the large multilamellar vesicles to exert successfully the cryoprotective action. The aggregation of the vesicles after size control of the rehydrated lyophilized liposomes was avoided by co-formulating dicetylphoshate, although co-formulation made size control difficult.

〔Chem. Pharm. Bull., 40, 1240-1246 (1992)〕 [Lab. of Pharm. Engineering]

Stabilization of Water/Oil/Water Multiple Emulsion with Hypertonic Inner Aqueous Phase.

YOSHIAKI KAWASHIMA*, TOMOAKI HINO, HIROFUMI TAKEUCHI, TOSHIYUKI NIWA

Water/oil/water emulsion (w/o/w emulsion) was prepared with liquid paraffin, a hydrophobic surfactant (Span 80) and a hydrophilic surfactant (Tween 20) by a two-step emulsion procedure. The percentage of solute entrapped in the inner aqueous phase and the viscosity of the emulsion system increased with an increase in the concentration of solute (glucose or sodium chloride) initially added to the inner phase of the emulsion. The oil membrane of the w/o/w emulsion, which entrapped the hypertonic inner aqueous phase, was thick, and the release of the solute from the emulsion was slow. The viscosity of w/o/w emulsion entrapping a hypertonic inner aqueous phase was lager, and consequently, separation of the aqueous phase was delayed. A decrease in the encapsulation efficiency of w/o/w emulsion during storage was considered to be the result of a rupture of the oil membrane. Destruction of the w/o/w emulsion followed first-order kinetics. The rate constant of destruction of w/o/w emulsion at room temperature could be predicted by measuring the destruction rate at a higher storage temperature.

〔Int. J. Pharm., 85, 19-28 (1992)〕 [Lab. of Pharm. Engineering]

Improvement of the Formation Percentage of Water-in-Oil-in-Water Multiple Emulsion by the Addition of Surfactants in the Internal Aqueous Phase of the Emulsion.

TAKAYUKI OHWAKI, KATSUMI NITTA, HIROSHI OZAWA, YOSHIAKI KAWASHIMA*, TOMOAKI HINO, HIROFUMI TAKEUCHI, TOSHIYUKI NIWA

In order to improve the formation percentage of w/o/w emulsions, experiments were conducted in order to elucidate the influence of the addition of various kinds of surfactants in the internal aqueous phase of the emulsion, the formation percentage of w/o/w emulsion as compared with that without additives, and with sodium chloride or sorbitol. Several physico-chemical properties of intact w/o/w emulsion or each phase, such as the osmolarity, interfacial tension and viscosity, were investigated in order to determine the governing factor in improving the formation percentage of w/o/w emulsion. W/o/w emulsion was prepared via a two-step emulsification procedure. New coccine was employed as a marker to evaluate the formation percentage of w/o/w emulsion. Sodium alkylsulfonate, sodium alkylcarbonate and polyoxyethylene (20) sorbitan monooleate were used as additives in the internal aqueous phase of w/o/w emulsion as well as sodium chloride and sorbitol.