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EFFECTS OF GLUCOSE AND OF PH ON TPN MIXTURE STABILITY

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The instability of fat emulsions in total parenteral nutrition mixtures is due to adsorption of electrolytes onto the emulsion droplet, causing a reduction in the surface potential. The effects of other TPN components have not been systematically explored. We have examined the effect of glucose, a major component, which is suspected to destabilize the mixtures by virtue of the pH reduction which it may induce. We have measured by turbidimetry the flocculation of Intralipid 20% by calcium ions in the presence of glucose solutions up to 15% w/v. Intralipid was diluted into glucose solutions to an absorbance of 1.0 and was then mixed with calcium chloride solution and the increase in turbidity measured over a 2-minute period.

Increasing glucose concentrations reduced the flocculation rate of Intralipid 20% without measurably altering the position of the point of zero charge at a calcium concentration of 2-3 mM (Fig. 1). The maximum flocculation rate at 15% glucose is reduced by 93%. The effect is not solely due to the increasing viscosity of the medium, since 15% glucose has a relative viscosity of 1.56, which would by Smoluchowski's equation only cause a reduction in the flocculation rate to 64% of its previous value. Reduction of flocculation by glucose is surprising and has not been previously predicted.

Figure 1

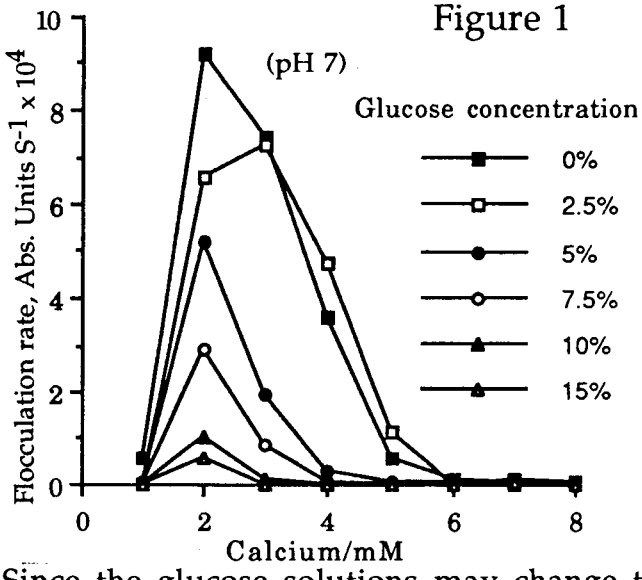
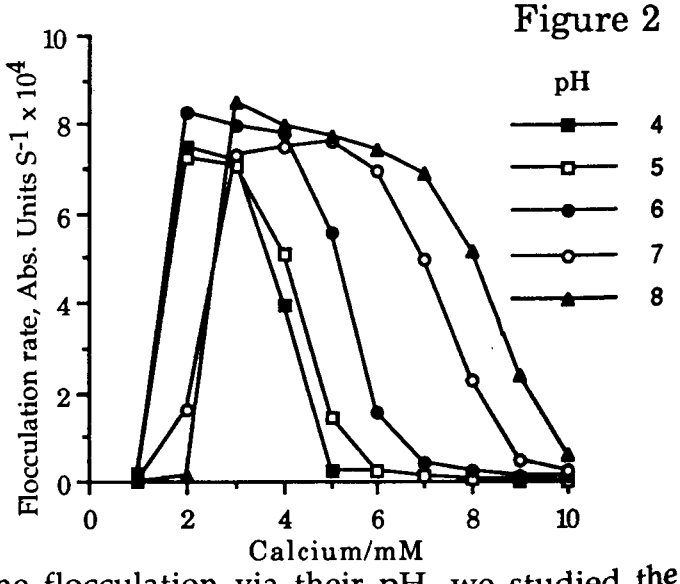


Figure 2



Since the glucose solutions may change the flocculation via their pH, we studied the flocculation of Intralipid by calcium in buffers of pH 4-8. Intralipid was diluted into 1 mM phosphate buffer containing calcium chloride and the flocculation measured as before. Decreasing pH caused a shift in the flocculation curves to lower calcium concentrations (Fig. 2). The maximum flocculation rate was not changed. The effect is understandable since H^+ is specifically adsorbed on these surfaces and would be expected to shift the point of zero charge to lower calcium concentrations. From these data it is unlikely that glucose is exerting an effect via pH alterations, as was previously thought. We have proposed that TPN mixtures owe much of their stability to potentiation of the short-range surface hydration forces by amino-acids (Washington 1990) and it is possible that glucose may have a similar effect. The data suggests that glucose is a major contributor to the stability of the mixtures, which was previously unsuspected.

Washington C. et al. Int. J. Pharm. (1990) in press.