CHAPTER I

INTRODUCTION

Fat emulsions are commonly used intravenously in critically ill and nutritionally depleted patients of all ages as a regimen in total parenteral nutrition (TPN). They are utilized mainly to prevent the development of essential fatty acid deficiency and as excellent source of calories (Carpentier, 1989). In general, fat emulsions are made up of three basic components: an aqueous phase of isotonic solution, an emulsifying system of lecithins or phospholipids (PL), and a lipid phase of oil or triglycerides (TG) (Dahlan, 1989). Like natural lipoproteins, the particles of fat emulsions suspended in aqueous phase are spherical with TG dissolved as fat doplet in the core and PL or lecithins surrounded in form of monolayer surface. The average diameter of the particles, in the available preparations, varies between 2,200 and 3,200 angstroms, which is within the range for chylomicrons (Dahlan, 1989).

In spite of the various possible choices, fat emulsions available at the present time are generally produced from two major sources: vegetable and/or animal oil and/or synthetic TG as lipid phase and PL from either egg yolk or vegetable as emulsifying system. PL's so-called lecithins have good emulsifying properties because they are amphipathic (Marsh, 1990; New, 1994). Actually, there are a plenty sources of natural lecithins. Each source provides lecithins with different subcomponents (Pardun, 1982). However, there are only two types of lecithins most commonly used for manufacturing fat emulsions, i.e. those derived from egg yolk and soya. Both types of lecithins presenting in fat emulsion still provide some disadvantages due to their contents as well as their nature. More information of lecithins is described in Appendix.

The PL content of fat emulsions is always much higher than that of natural chylomicrons, especially the PL-TG ratios. This is particularly marked in the

10% emulsion which contains the same amount of PL as the 20% emulsion, although its TG content is only one-half of the latter emulsion (Carpentier, 1989). In fact, fat emulsions are made up of not only one but two different particle populations: one consists of TG-rich particles resembling natural chylomicrons and the other containing amounts of PL in excess of those needed to emulsify the TG forms separate PL-rich particles resembling liposomes (Groves et al., 1985; Carpentier, 1989; Dahlan, 1989). Thus higher PL-TG ratio (w/w) in preparation produces a higher PL liposomes appearances in the emulsion. These PL liposomes have been shown to interact with both lipoproteins and blood cells *in vivo* and *in vitro*, particularly by donating PL and fatty acids to the lipoproteins and cells in the mean time acquiring apoproteins, cholesterol and fatty acids in exchange (Dahlan et al., 1992a, 1992b).

William and Scanu (1986) demonstrated that the addition of cholesterol-poor PL liposomes in canine plasma *in vivo* and *in vitro* could substantially alters the distribution of PL, apoproteins and especially cholesterol. Dahlan et al (1992b) reported a depletion of omega-3 polyunsaturated fatty acids (n-3 PUFA) in red blood cell (RBC) membranes after daily intravenous infusion of fat emulsion with egg yolk lecithin as emulsifier in 5 pateints with inflammatory bowel disease for 3 months. The study evidenced that long-term intravenous infusion of fat emulsions caused a redistribution of the PUFA between the n-6 and n-3 families. Huge presentation of n-6 PUFA in TG core as well as in PL surface of fat emulsions in comparison to those of n-3 PUFA could induce an accumulation of n-6 with a disappearance of n-3 PUFA's resulting in a marked depletion of n-3/n-6 ratio in circulating blood cell membranes. Dispappearances of n-3 PUFA from blood cell membranes caused by the excess intravenous infusion of PL lipisome with high n-6 PUFA is a primary concern in the present study.

It is well accepted in the present time that n-3 PUFA are essential for normal growth and development and may play an important role in the prevention and treatment of coronary heart disease (CHD), hypertention, arthritis, other inflammatory and autoimmune disorders and cancer (Simopoulos, 1991). Because humans, like all mammals, cannot make these fatty acids but must

obtain them in their diet, so n-3 PUFA also known as essential fatty acids as same as n-6 PUFA (British Nutrition Foundation, 1994). Omega-3 PUFA's are fatty acids in which the first double bond occurs between the third and fourth carbon atoms from the methyl terminal of fatty acid. The most abundant long-chain n-3 PUFA are EPA (eicosapentaenoic acid, C20:5) and DHA (docosahexaenoic acid, C22:6). These fatty acids are found in high concentrations in marine fish and animals. In mammals and birds the n-3 PUFA are distributed selectively among lipid classes. EPA is found in cholesteryl esters (CE), TG and PL. DHA is found mostly in PL. In mammals, including humans, the cerebral cortex (O'Brien and Sampson, 1965), retina (Anderson, 1970), and testis and sperm (Poulos et al., 1975) are particularly rich in DHA. DHA, like EPA, can be derived only from direct ingestion or by synthesis from dietary EPA or ALA (α-linolenic acid, C18:3n-3).

EPA as a representative of n-3 PUFA and arachidonic acid (AA) of n-6 PUFA presented in membranes are two major precursors of prostanoids in the two series of E_2 and E_3, respectively (Simopoulos, 1991). Recently, British Nutrition Foundation (BNF 1994) has reviewed vast literatures describing deleterious effects of alterations of prostanoid biosynthesis on biochemical changes in the body, e.g. atherogenesis, thrombogenesis, fibrinolysis etc. The alteration of membrane lipids as well as PUFA demonstrated by Dahlan et al (1992b) as earlier mentioned might induce certain effects on membrane function (Dahlan, 1989). Since DHA is a major PUFA of erythrocyte membranes which prone to be impaired in various circumstances, in the present study, we therefore prepared a noval emulsion rich in n-3 PUFA in aiming to utilize such an emulsion for maintaining and if possible improving n-3 PUFA status of the membranes.

Aims of the Present Study

The objectives of the present study are:

1. to find a source of lecithins with high contents of n-3 PUFA by limiting the search in marine origin only,
2. to study its lipid characteristic after the discovery,
3. to establish the extraction procedure employing organic solvent system for obtaining high yield of lecithin from that raw material,
4. to prepare a fat emulsion rich in n-3 PUFA by utilizing lecithin obtained from 3,
5. to study the effect of the prepared fat emulsions on the exchanges of their lipids and fatty acids with erythrocyte by comparing the results with fat emulsions of similar PL-TG ratio but lecithins derived from either egg yolk or soya.