Insulin-loaded W/O/W multiple emulsions: comparison of the performances of systems prepared with medium-chain-triglycerides and fish oil

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Abstract

Insulin-loaded W/O/W multiple emulsions (ME) composed of medium-chain triglycerides have been shown to decrease the blood glucose level after oral administration to diabetic rats. Fish oil (very long-chain triglycerides) could be an alternative to medium-chain triglycerides because its chronic consumption has beneficial therapeutic effects. The aim of this work was twofold: to obtain stable fish oil containing ME, based on a formulation optimized in a previous work with low medium-chain triglycerides content, and to compare their characteristics to those of ME composed of medium-chain triglycerides. Due to the higher viscosity and surface tension of fish oil compared to medium-chain triglycerides, preparation of ME appeared difficult to achieve. However, a stable unloaded-ME with low fish oil content was formed, by adapting the emulsification process. The characteristics of unloaded fish oil ME were almost similar to those of medium-chain triglycerides ME. In contrast to medium-chain triglycerides ME, the introduction of insulin did not improve the elasticity and consequently the characteristics and stability of fish oil ME. Nevertheless, the insulin-loaded fish oil containing ME was shown to be stable for 6 weeks at 4 °C.

Keywords: Insulin; Multiple emulsion; Medium-chain triglycerides; Very long-chain triglycerides; Fish oil; Elasticity

1. Introduction

W/O/W multiple emulsions (ME) are systems of increasing interest for the oral delivery of hydrophilic drugs which are unstable in the gastrointestinal tract. Medium-chain triglycerides containing multiple emulsion (MCT-ME) and loaded with insulin, have been shown to decrease glycemia in diabetic rats after oral administration [1,2]. However, side effects such as diarrhea, weight loss and steatosis have been observed after repeated administration of those ME containing 35% of oil. To optimize the oral administration of insulin, ME with a lower content of MCT (20%) have been developed, stabilized by a cetyl dimethicone copolyol, as the low HLB surfactant, and by a copolymer of ethylene oxide and propylene oxide, as the high HLB surfactant [3].

Due to the beneficial therapeutic effects of its chronic consumption, fish oil represents a valuable alternative to MCT. Indeed, its high concentration in omega-3 fatty acids is accounted for enhanced insulin action [4], reduction of inflammatory phenomena [5] and incidence of cardiovascular diseases [6]. This would be of importance for diabetics who tend to show cardiovascular disorders [7,8]. Moreover, ME incorporating 2% of omega-3 fatty acids and administered in the rectum produce a rapid absorption of insulin and a strong reduction of glycemia [9].

The aim of this work was twofold: to obtain a stable fish oil containing multiple emulsion (FO-ME) according to the formula previously optimized using MCT [3] and to compare...