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PREPARATION AND CHARACTERIZATION OF SOLID LIPID MICRO/NANOPARTICLES
I. EFFECT OF LIPID CONCENTRATION, SURFACTANT TYPE AND CONCENTRATION ON PHYSICAL CHARACTERISTICS OF SOLID LIPID MICRO/NANOPARTICLES

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ABSTRACT

The objective of this study was to determine the best conditions to formulate solid lipid Nanoparticles using Glyceryl monostearate as lipid matrix which has advantage to be biocompatible and easily degraded in vivo. Different formulation factors were studied including lipid concentration and surfactant concentration and type. Different concentrations of Glyceryl monostearate were tested for feasibility of formulation of solid lipid nanoparticles. As the concentration of lipid increased from 1 t- 10 % w/w, particle size of produced particles was reduced to be in nanometer range. It was found that Tween 80 surfactant had produced smaller particle size than Tween 20 did. According to concentration of surfactant ,it was found that increasing concentration from 0.5 % w/w to 5% w/w have pronounced effect on physicochemical properties of formulated solid lipid Micro/nanoparticles especially particle size. Reduction of particle size to be in micro/nanorange will enhance dissolution of drug and penetration of drug loaded particles through different body tissues. Besides that, lesser dose will be required that will reduce adverse effects and overall cost.

INTRODUCTION

Solid Lipid Nanoparticles (SLN) combines the properties of polymer Nanoparticles (solid matrix for controlled release) and o/w type Emulsions. They can consist of lipids and surfactants which are traditionally used in pharmaceutical preparations, e.g., in tablets or pellets also can be produced from food lipids[1].

Depending on the intended type of application, different pharmaceutical and cosmetic surfactants and surfactant blends, e.g. poloxamers, bile salts and polysorbates, can be used as stabilizers[2].

Recently solid lipid nanoparticles have gained increasing attention as a colloidal drug carrier, particularly for lipophilic drugs[3].

Due to their physiological composition SLN are well tolerated by the human body and this low associated toxicity facilitates the regulatory issues. Lipid particles, more specifically, seem to have advantages over other colloidal carriers, such as liposomes and emulsions, in terms of stability and protection of the incorporated active compounds .They have been proven by several authors to be suitable for use in inhalable delivery systems, dermatological applications, parenteral and oral administration[4]. SLN are typically manufactured using the hot homogenization process. A liquid lipid phase (carrier lipid melt and/or lipophilic functional ingredient) and an aqueous surfactant solution are homogenized at a temperature above the melting temperature of the lipids to produce a fine-disperse oil-in water emulsion. The emulsion is then cooled to a temperature below the crystallization temperature of the carrier lipid leading to the formation of solid particles[5].

A number of studies have recently been published about production, physico-chemical characterization of particles and drug incorporation and release. Some years ago the first results have been published about the chemical stability of pharmaceutical drugs and cosmetic actives incorporated into SLN formulations. In addition, intensive analyses regarding lipid crystallization including polymorphic transitions have been performed. However, in contrast to stability data of active agents incorporated into SLN, nobody looked at the stability of the lipids matrices themselves[1].

The aim of this study was to describe the effect of lipid concentration, surfactant type, and ratio, concentrations on the physical characteristics of SLN (especially particle size and polydispersity index)

EXPERIMENTAL

Materials

Glyceryl monostearate-technical self-emulsifying (BDH Chemicals Ltd Poole-England). Tween 80 (polysorbate 80), Tween 20 (polysorbate 20), ICI Americas (Wilmington, DE, USA), lecithin, (Spectrum

Chemicals & Laboratory Products New Brunswick, NJ). Other chemicals are of analytical grade.

Methods

1- Preparation of solid lipid micro/ nanoparticles:

Solid lipid nanoparticles were prepared by several techniques using various ratios of Glyceryl monostearate as lipid phase, Tween 80 or Tween 20 as surfactant and lecithin as co-surfactant. Firstly, the lipid was melted (60-70°C) and dispersed in hot aqueous solution with different surfactant concentrations (0.5, 1, 5 % w/w) and 1% w/w lecithin at the same temperature, by high –speed stirring, using an Ultra-Turrax homogenizer (Ultra- Turrax T – 25, IKA, Germany) at 6,000 rpm for 10 minutes, with 30 seconds intervals every two minutes[6]. The obtained pre-emulsion were cooled to room temperature (25°C) and their particle size was measured.

The resulting dispersion was then cooled and each sample was diluted with water before measurement and particle size was measured using dynamic laser light scattering apparatus at 25°C. (Mastersizer 2000 vers. 5.54, hydro 2000 S, Malvern instruments Ltd., Malvern, Worcs, UK). Each measurement was performed in triplicate and the particle average diameter and polydispersity index (PI) were determined.

RESULTS AND DISCUSSION

1.Effect of surfactant type and concentration: Figures (1, 2) showed that increasing surfactant concentration from 0.5 % to 5.0 % will cause particle size reduction of formed SLNs. Lower concentrations of surfactant produce batches containing larger amount of microparticles with PI more than 1 indicating heterogeneity. However, high concentrations of the emulsifier reduce the surface tension and facilitate the particle partition during homogenization[6], which is confirmed by various literatures, that decrease in particles size at high surfactant concentrations is due to effective reduction in interfacial tension between the aqueous and lipid phases, leading to the formation of emulsion droplets of smaller size, which on cooling results in smaller nanoparticles. Furthermore, high surfactant concentrations effectively stabilize the particles created by forming a steric barrier on the particle surface, thereby protecting the particles from coagulation [6-8].

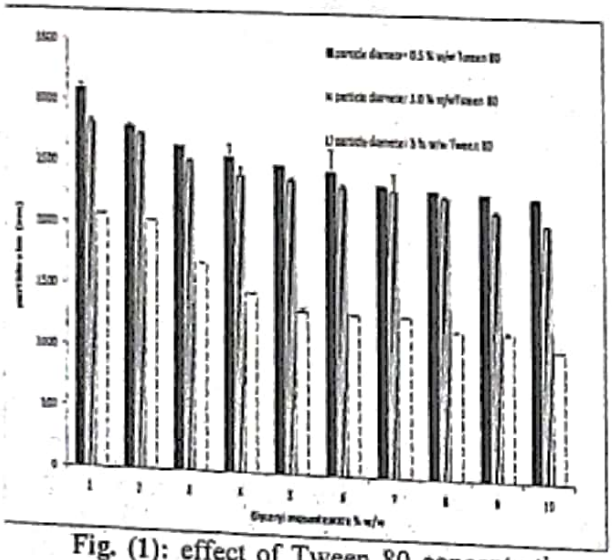

Fig. (1): effect of Tween 80 concentration on particle diameter of SLNs prepared by hot homogenization technique at6, 000 rpm

By comparing particle diameter of formed SLNs using Tween 80 or Tween 20 as surfactants, it was found that Tween 20 produced larger particles with solubilizing capacity of lipophilic drugs. This decrease in solubilizing capacity, may be reason for the formation of fine emulsion droplets in case of Tween 80 (HLB= 15) and larger droplets in case of Tween 20 (HLB= 16.7) [3].

2. Effect of lipid concentration :

Figures (3,4) showed that increase concentration of lipid will reduce particle diameter of formed particles due to increase of viscosity, while increasing lipid content above 10 % w/w results in larger particles and broader particle size distribution with decrease of homogenization efficiency and increase in particle agglomeration.

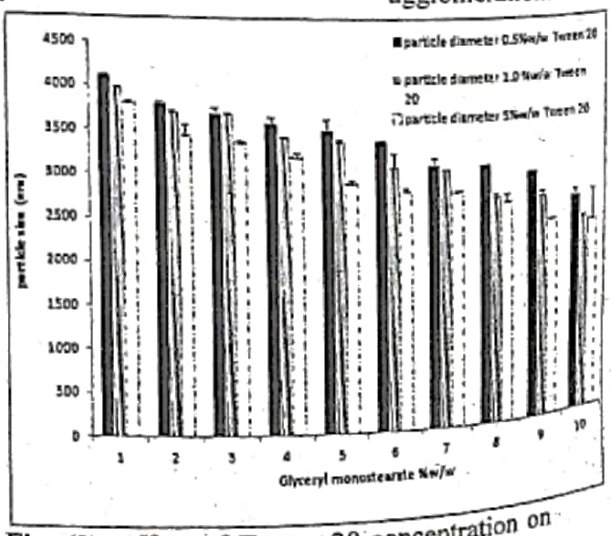

Fig. (2): effect of Tween 20 concentration on particle diameter of SLNs prepared by hot homogenization technique at 6,000 rpm.

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These results agreed with [9] but not in agreement with Freitas and Muller [10], who stated that the amount of larger particles decreased with decreasing lipid content but was still higher than in the original dispersion. Trotta et al.[11] prepared Glyceryl monostearate nanodispersions and found that increasing lipid concentration from 2.5 to 10 % increased the mean diameter from 250 nm to 695nm. According to Abdelbary and Fahmy [12], it could be noted that, for formulations composed of a mixture of surfactants, Compritol® ATO 888 as a lipid material produced SLNs which were larger in size than those produced using Imwitor® 900K. It was suggested that glycerol monostearate is not only used as a lipid matrix but also as a surfactant that facilitates emulsification and formation of SLNs of smaller particle sizes. These results were augmented by Hou et al and Rowe et al. [13, 14]

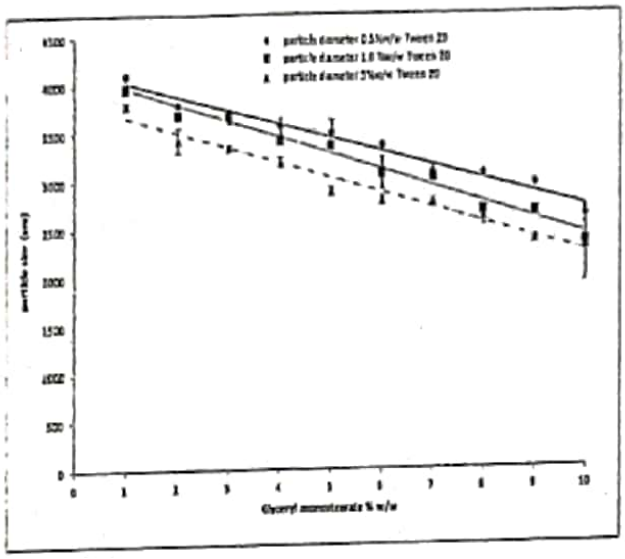

Fig. (3) Effect of GMS concentration on particle diameter of SLNs with Tween 20 as surfactant using hot homogenization technique

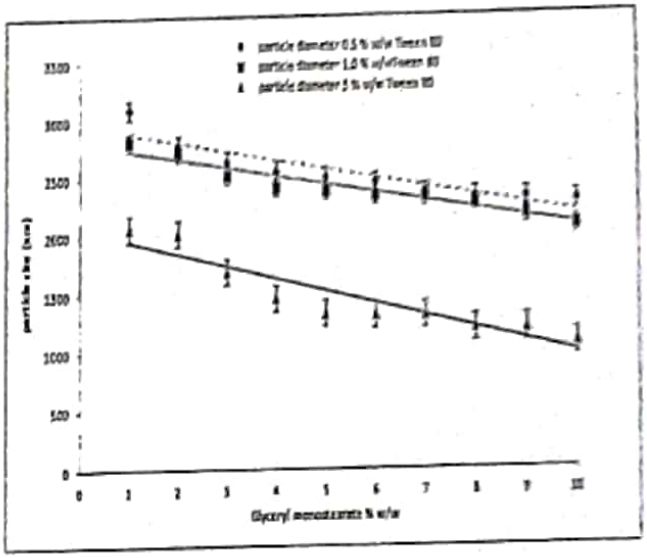

Fig (4): effect of GMS concentration on particle diameter of SLNs with Tween 80 as surfactant using hot homogenization technique at 6,000 rpm.

CONCLUSION

Particle diameter of solid lipid Micro/nanoparticles prepared with Glyceryl monostearate and Tween 20 or Tween 80 as surfactants and lecithin as co-surfactants affected by variation of process parameters such as surfactant type and concentration. Changing surfactant from polysorbate 20 to polysorbate 80 produced particles of smaller diameter. Increasing concentration of surfactants, reduced particle diameter of formed solid lipid Micro/nanoparticles. Glyceryl monostearate concentration affect particle diameter of formed solid lipid Micro/nanoparticles.

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تحضير و توصيف الجزيئات الدقيقة ذات الأوساط الدهنية الصلبة

1. تأثير تركيز الدهن، نوع و تركيز معامل الاستحلاب على الخواص الفيزيائية للجزيئات الدهنية ذات الأوساط الصلبة.

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تهدف هذه الدراسة لقياس أفضل العوامل الخاصة بتحضير الجزيئات الدقيقة ذات الأوساط الصلبة من مادة جلسريل احادى الستيرات و الذي تتميز بكونها متوافقة حيويا و سهلة الايض داخل الجسم .تم تحضير الجسيمات الدهنية الدقيقة ذات الأوساط الصلبة باستخدام طريقة التقليب الساخن. تمت دراسة عدة عوامل و مدى تأثيرها على الخواص الفيزيائية للجزيئات الدهنية ذات الأوساط الصلبة و أبرزها مقياس الجزيئات ومن أهم هذه العوامل دراسة تأثير تركيز الدهن و كذلك نوع و تركيز معامل الاستحلاب . و قد وجد انه كلما زاد تركيز الدهن المستخدم ، يقل مقياس قطر الجزيئات.أما بالنسبة لنوع معامل الاستحلاب، فقد وجد أن عديد السوربات 80 يعطى جزيئات أصغر من تلك المحضرة باستخدام عديد السوربات 20. بالإضافة إلى ذلك ، فإنه كلما زاد تركيز معامل الاستحلاب ، فإن ذلك يؤدى إلى تقليل مقياس حجم الجزيئات المحضرة.