Preparation & evaluation of paracetamol solid lipid nanoparticles by hot homogenization method

Abstract

The aim of this study was to prepare Paracetamol solid lipid nanoparticles by hot homogenization technique. Glycerol Monostearate (GMS) was used as a lipid. Tween 80 was used as a hydrophilic surfactant and soya lecithin as the lipophilic surfactant. Three formulations of paracetamol solid lipid nanoparticles prepared by varying the concentration of the lipid (1gm, 1.5gm, 2gm). Among the three formulations second formulation 1:1.5 gm drug lipid ratio showing better drug content (97.8%) and in vitro release rate (79.8%) compared to 1st and 3rd formulation.

Keywords: glycerol monostearate, lipid nanoparticles, hot homogenization

Abbreviations: GMS, glycerol monostearate; SLNs, solid lipid nanoparticles; HHM, hot homogenization method

Introduction

The solid lipid nanoparticles (SLNs) are sub-micron colloidal carriers (50-100nm) which are composed of physiological lipid dispersed in water or in an aqueous surfactant solution. SLNs are colloidal drug carrier combines the advantages of polymeric nanoparticles, fat emulsion and liposomes simultaneously and avoiding some of their disadvantages. To overcome the disadvantages associated with the liquid state of the oil droplets, the liquid lipid was replaced by a solid lipid which eventually transformed into solid lipid nanoparticles.

Speiser, 1990 conducted the basic work in the area of solid lipid particles a decade back. The lipid nanopellets were prepared by first melting the lipid and it was then dispersed in a hot aqueous surfactant solution by stirring or ultrasonic treatment.

SLN is a better alternative carrier system than conventional oil in water emulsion if a prolonged drug release is desired. The drug incorporated into the solid lipid matrix is naturally better protected than in the oily internal phase of emulsion and liposomes. Also, SLNs facilitate prolonged drug release but this is not feasible with conventional emulsions. In comparison to polymeric nanoparticles, the SLNs possess lower cytotoxicity. As compared to liposomes the SLNs protect the drug more effectively against chemical degradation since water has little or negligible access to the inner core of lipid particles.

Advantages of SLNs

a. Small size and relatively narrow size distribution which provide biological opportunities for site specific drug delivery by SLNs.
b. Controlled release of active drug over a long period can be achieved.
c. Protection of incorporated drug against chemical degradation.
d. SLNs can be lyophilized as well as spray dried.
e. No toxic metabolites are produced.
f. Avoidance of organic solvents.
g. Relatively cheaper and stable.
h. Application versatility.

Disadvantages of SLNs

a. Particle growth occurs.
b. Unpredictable gelation tendency.
c. Drug loading capacity is poor.
d. Drug expulsion after polymeric transition during storage occurs.
e. Water content of the dispersions is high (70-99.9%).

Materials and methodology

Materials

I. Drug: Paracetamol
II. Lipid: Glycerol Monostearate
III. Surfactant: Tween 80 and soya lecithin

Experimental methodology

Paracetamol solid lipid nanoparticles were prepared by hot homogenization method.

Hot homogenization method

Preparation of solid lipid nanoparticles via hot homogenization method was performed at a temperature above the melting point of lipid. Formulations were prepared using the solid lipid, Tween 80 as the hydrophilic surfactant, soya lecithin as the lipophilic surfactant. Appropriate quantities of lipid, active ingredient (drug), and lipophilic surfactants were weighed and mixed at a temperature 10°C above the melting point of the lipid in a water bath. In another beaker, water was heated to the same temperature along with the hydrophilic surfactant and was placed under continuous stirring. The aforementioned lipid phase was then added drop wise to the aqueous surfactant solution and kept under stirring for a few hours at 2700 Rpm. The dispersion was then sonicated for 30-40 min and stored. A thermodynamically stable system was formed (Table 1).

Keywords: glycerol monostearate, lipid nanoparticles, hot homogenization
Table 1 Composition of the prepared solid lipid nanoparticle formulations

<table>
<thead>
<tr>
<th>Formulations</th>
<th>Paracetamol (mg)</th>
<th>Lipid glycerol monostearate (gms)</th>
<th>Lipophilic surfactant (Soya lecithin) (mg)</th>
<th>Hydrophilic surfactant (Tween 80) (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>50</td>
<td>1</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>2</td>
<td>50</td>
<td>1.5</td>
<td>100</td>
<td>100</td>
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<tr>
<td>3</td>
<td>50</td>
<td>2</td>
<td>100</td>
<td>100</td>
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</tbody>
</table>

**Evaluation studies:** The obtained formulations of paracetamol loaded solid lipid nanoparticles by hot homogenization method are evaluated for the following parameters.

**Determination of drug content**

Solid lipid nanoparticles suspension equivalent to 5mg was separately taken in a 10 ml volumetric flask and the volume was made with N, N Dimethylformamide to disperse the nanoparticles by thoroughly shaking up to 10 minutes and from this 0.1 ml of solution was taken and suitable dilutions were made and the concentration of the drug was analyzed using UV spectrophotometer at 257nm.

**In vitro drug release kinetics**

*In vitro* release profiles of paracetamol from the SLNs were obtained by a dissolution test in phosphate buffer solution (USP Phosphate buffer pH 6.8. Regenerated cellulose membrane (Dialysis membrane50, Hi-Media) was used. Paracetamol loaded SLNs dispersion was placed into a dialysis bag and was immersed into 900 ml phosphate buffer solution and the system was maintained at 37°C under mild agitation of 100 RPM/min.18,19 The release medium (5ml) were withdrawn and assayed for drug release and replaced by 5ml of fresh buffer (pH .6.8 phosphate buffer). Paracetamol in the release medium was quantified by UV spectrophotometer at 257nm against the blank and cumulative drug release of paracetamol was calculated based on a pre-generated calibration curve.

**Results**

The obtained formulations were evaluated for the above mentioned parameters and the results are discussed as follows:

**Evaluation of paracetamol SLNs by hot homogenization method (HHM)**

Paracetamol SLNs were formulated at various drug-lipid ratios (1:1, 1:1.5, and 1:2 gm).

**Evaluation studies of paracetamol SLNs**

i. **Drug content:** The drug content of all three formulations was evaluated. From the Figure 1, 2nd formulation showed maximum drug content 97.8% compared to 1st and 3rd formulations.

ii. **In vitro drug release studies:** The drug release studies of all formulations of Paracetamol SLNs were conducted by means of dissolution apparatus for a time period of 12 hrs. From the drug release studies as depicted in Figure 2, the results showed that 2nd formulation showed maximum drug release rate of 79.8% within 12 hrs. Whereas 1st and 3rd formulation showed only 69.4% & 61.8% drug release rate.

iii. **Microscopic images of the investigated SLNs:** Photographic samples from the prepared paracetamol SLNs are exhibited in Figure 3.

**Discussion**

In this present study paracetamol SLNs was prepared by HHM by using GMS as a lipid, Soya lecithin as lipophilic surfactant and Tween 80 as a hydrophilic surfactant. Each of three formulations was prepared by varying the concentrations of drug and lipid ratios (1:1, 1:1.5, and 1:2gm). Among the three formulations 2nd formulation show better drug content and *in vitro* drug release rate. The effect of lipid concentration upon the formulation was studied. When the lipid concentration was higher than drug concentration the percentage of drug content and drug release was enhanced in formulation 2.
When the lipid concentration was further enhanced the drug content and drug release was decreased. So 1:1.5 ratio of drug to lipid was yielding better results.20–22

Conclusion

In the present study paracetamol SLNs were prepared by hot homogenization method. Among the three formulation 2nd formulation (1.5 gm. lipid) show better drug content and in vitro drug release rate.

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Conflict of interest

The authors declare no conflict of interest.

References

