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STUDY OF DIFFERENT NANOSTRUCTURED LIPID CARRIER SYSTEM SURFACTANTS FOR THE DEVELOPMENT OF QF-LOADED NLC

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Abstract

Formulation of NLCs requires few ingredients *viz.* solid lipids, liquid lipids, surface active agent and water. The NLC is a smarter drug delivery system with unique advantages such as higher drug loading; higher entrapment of drug, sustained drug release behaviour and eventually enhanced drug absorption as compared with other lipid-based drug delivery systems and the feasibility of large-scale production makes NLCs a versatile delivery system. In the present study, QF-loaded NLCs were prepared using hot homogenization followed by ultrasonication. NLCs batch F3 (0.1% of QF, 0.7% of GMS,0.4% of campus MCM EP, 1.5% poloxamer 188, 0.6% egg lecithin and water up to 100%) showed excellent stability specified by ZP, high % EE value, drug loading capacity with sustained action. Solubility and dissolution of a poorly water-soluble drug are the two major barriers for formulation scientists in the development of drug delivery. Many of the potent drugs do not show therapeutic effects due to solubility issues but may show toxicity issues when used in high doses. Solid dispersion (SD) technology is an excellent tool for enhancing solubility, dissolution, and related bioavailability.

KEYWORDS: *Central composite design; Nanostructured lipid carriers; Poloxamer 188; Quetiapine Fumarate; Response surface methodology.*

INTRODUCTION

The Second-generation lipid carrier is often made up of a system containing both solid and liquid lipids. Because of the mixing, the melting points of the substrates are lowered, and the mixture becomes NLC, a solid at body temperature. In comparison to SLN, NLC has a significant drug-loading feature with less drug ejection. The majority of the solid lipids utilised in the creation of NLC are glyceryl behenate, glyceryl palmitostearate, glyceryl monostearate, and stearic acid. In the creation of NLC, MCT and oleic acid are often used as liquid lipids. The amount of liquid lipid in the lipid blend also affects the nature and properties of NLC. LDC system improves medication loading up by including medicines attached to lipid particles. Up to thirty-three Percent. However, LDC suffered from a few demerits such as particle size growth,

uncertain gelation tendency, sudden polymeric transitions and low drug loading (Olbrich et al., 2004 and Das et al., 2013). To address LDC disadvantages, the SLN system appeared in the year 1991 as an effective alternate drug delivery system (Radtke et al., 2005). SLN can be characterized as small lipid-containing preparations which are biocompatible and biodegradable systems with large surface areas (Cavalli et al., 1993 and Sarangi et al., 2016). Even more, the SLN strategy has been successfully applied for the oral administration of cyclosporine and paclitaxel ineffective therapy of cancer (Radtke et al., 2005).

MATERIALS AND METHODS

Selection of solid lipids

The solid lipid used in the present work contains a mixture of various chemical compounds with high M.P. (higher than 40ºC). After a n exhaustive literature survey, some biodegradable solid lipids and liquid lipids and emulsifiers from different categories were selected viz. hard fats (stearic acid), triglycerides (money- T18, monegyl-D207), partial glycerides (glyceryl monostearate).In the case of solid lipids, 25 mg of QF was transferred to a glass beaker. Weighed quantity (0.05gm) of various solid lipids was taken and added in small increments in the beaker containing QF and the mixture was heated using a temperature-regulated water bath at 10°C above the M.P. of respective solid lipids. The addition of solid lipid was continued until a clear melt was obtained. Obtained melt was spread on a hot glass slide using a hot spatula and observed microscopically to confirm the formation of a clear lipid mixture (Shah et al., 2016; Sansare et al., 2019).

Selection of liquid lipid

Quantity of liquid lipid (oil) plays an important part in governing PS and the release rate of the drug. It reduces viscosity and surface tension and helps in producing small-sized NLC and higher molecular mobility (Tiwari et al., 2011 Chen et al., 2010). The addition of liquid lipid to solid lipids causes a decrease in PS due to a reduction in viscosity (Chen et al., 2010). Liquid lipid causes enhancement of % EE and solubility of API (Tran et al., 2014). Oil was selected depending on the solubility of the QF in oil. Different oils were selected for the present study namely capmul MCM EP, oleic acid, isopropyl myristate, castor oil and olive oil. Excess QF was placed in vials containing 5 g of oil and the resulting mixture was vortexed for 10 min. Further, vials with stopper were placed in an orbital shaking incubator (Dolphin) at 25± 2.0°C for 48 hours to attain equilibrium. After this, samples were centrifuged (R2, REMI) at 10,000 rpm for 10 min. The quantity of QF in oils was determined by removing the supernatant from each vial. The concentration of QF in each sample was analyzed by UV at 244 nm, after diluting samples with methanol (Talele et al., 2018, Shah NV et al., 2016, Shah B et

Optimization of ratios of solid lipid to liquid lipid

The mixture comprising both lipids was prepared homogenous. To optimize the ratio of lipid, a miscibility test between the selected lipids namely GMS and campus MCM EP was performed. The selected solid lipids and oil were weighed in the different % ratios (60:40, 70:30, 63.636: 36.363) in glass vials. This blend was heated to a temperature 10°C above the M.P. of the solid lipid. Thereafter, the liquid blend vortexed and smeared on glass slide. Upon solidification, a dry filter paper was pressed on this lipid blend and observed for a sign of oil drops, if any. The mixture that does not show any oil drop on filter paper was considered as miscible and was selected for the development of QF-loaded NLCs (Sansare et al., 2019).

RESULTS AND DISCUSSION

Selection of solid lipid

Results of solubility analysis revealed that QF exhibits less solubility in monegyl- D207, monegyl T 18 and stearic acid than solubility in glyceryl monostearate (GMS) (Table 13). QF crystals were completely dissolved in GMS and hence GMS was selected as solid lipid. It is noticeable that GMS is having GRAS status and is biodegradable in nature in vivo.

Table 13: Result of selection of solid lipid

S,No.	Solid lipid type	Solid lipid	Observation
1	Hard fats	Stearic acid	No clear melt
2	Triglycerides	Monegyl-T18 (Glycerol Tri Stearate)	No clear melt
3	Triglycerides	Monegyl-D207 (Glycerol Di Stearate)	No clear melt
4	Partial glycerides	Glyceryl monostearate	Clear melt

Selection of liquid lipid

Results of the study indicated that QF possesses maximum solubility (23.42±0.97 mg/ml) in capmul MCM EP has maximum drug solubility when compared to oleic acid, isopropyl myristate, castor oil, labra fac lipophile WL 1349, olive oil (Table 14 and Figure 15). Notably, campus MCM EP has been known to increase the bioavailability of drugs. Therefore, it was selected as liquid lipid with GMS in the preparation of NLC (Lawrence et al., 2000, Shah B et al., 2016).

Table 14: Solubility of QF in different liquid lipid at 25°C

Sr. No.	Liquid lipid	Solubility (mg/ml
1	Capmul MCM EP	23.32±0.97
2	Oleic acid	17.21±0.50
3	Isopropyl myristate	22.30±0.90
4	Castor oil	10.17±0.58
5	Labrafac lipophile WL 1349	12.70±0.47
6	Olive oil	14.22±0.53

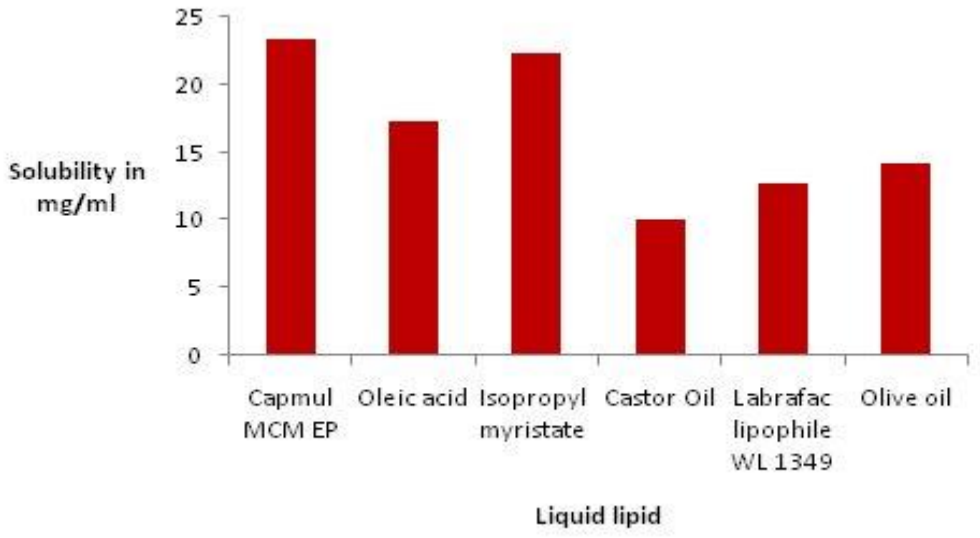

Figure 15: Solubility of QF in different liquid lipid at 25°C

Optimization of ratios of solid lipid to liquid lipid

After solidification of selected solid lipid and liquid lipid in different % ratios (60:40, 70:30, 63.636: 36.363), they were applied to dry piece of filter paper and the sample which did not show any oil droplets on the surface of the filter paper was considered miscible was selected for use in the development of trial batches of QF loaded NLCs.

Conclusion

In present study, QF loaded NLCs was prepared using hot homogenization followed by the ultrasonication method. NLCs batch F3 (0.1% of QF, 0.7% of GMS, 0.4% of campus MCM EP, 1.5% poloxamer 188, 0.6% egg lecithin and water up to 100%) showed excellent stability specified by ZP, high % EE value, drug loading capacity with sustained action. The drug release patterns from the QF-NLCs displayed a biphasic drug release behaviour with burst release at the initial stage followed by sustained release. Thus, NLCs seem to be reasonable delivery systems for the oral administration of QF and may

be used as an alternate strategy to achieve ameliorated release and prolonged action of QF. In future, QF-loaded NLCs may be used in clinical subjects for achieving better outcomes.

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