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Original Article

Self emulsifying drug delivery system: Optimization and its prototype for various compositions of oils, surfactants and co-surfactants

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ABSTRACT

Aim: The aim of the present study is to identify and optimize the self emulsifying regions of different compositions of various oils, surfactants and co-surfactants and its prototype.
Methods: The ternary phase diagram was constructed using series concentrations of oils, surfactants and co-surfactants to recognize the self emulsifying region. The selected self emulsifying compositions were evaluated and optimized using self emulsification time, robustness to dilution and globule size analysis.
Results: The percentage of compositions of surfactants and co-surfactants with the oil phase plays a significant role for the formation of nano sized self emulsion.
Conclusion: The prepared self emulsified prototype was ready to incorporate many poorly soluble drugs to improve its solubility and bioavailability as well.

1. Introduction

The oral delivery of many hydrophobic drugs is challenging to the formulators due to its poor solubility and bioavailability. The limitation of its solubility leads to less solubilization in the gastrointestinal tract. To overcome such problems, various formulation strategies are exploited including the use of surfactants, lipids, permeation enhancers, micronization, salt formation, cyclodextrins, nanoparticles and solid dispersions. Among these, self emulsifying drug delivery systems (SEDDS) have received meticulous attention as a means of enhancing oral bioavailability of poorly soluble drugs.[1] SEDDS is mixtures of oils and surfactants, ideally isotropic, and sometimes containing co-solvents, which emulsify under gentle agitation similar to that encountered in gastro-intestinal tract.[2] This system disperse into fine emulsion droplets inside the lumen of the gut where drug remains in solution state, avoiding the dissolution step that frequently limits the rate of absorption of hydrophobic drugs from the crystalline state. The mechanism of self emulsification occurs when the entropy change that favors dispersion is greater than the energy required to increase the surface area of the dispersion. In addition, the free energy of a conventional emulsion formation is a direct function of the energy required to create a new surface between the two phases. The potential advantages of these systems include enhanced oral bioavailability enabling reduction in dose, more

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consistent temporal profiles of drug absorption, selective targeting of drug(s) toward specific absorption window in gastrointestinal tract, and protection of drug(s) from the hostile environment in gut.

In the process of developing SEDDS formulations, different composition of oils, surfactants and co-surfactants have to be evaluated for identifying the best self emulsifying region of the system. However, it is a time consuming process and need to be performed for individual drugs with different compositions. Currently, there is no readily available protocol for this system. To overcome this issue, formulating general protocol for optimized self emulsified regions of various compositions are mandatory field of study in order to provide the readily available self emulsified composition to incorporate many poorly soluble and bioavailable drugs.

2. Materials and methods

2.1. Materials

Cinnamon oil and Lavender oil were obtained from SD Chemicals. Isopropyl myristate was received from Himedia, Mumbai. Brij was obtained from Sigma Aldrich. Labrasol was received as a gift sample from Gattefosse Limited. Capmul MCM and Capmul MCM C8 were obtained as gift samples from Abitec Corporation. All other oils, surfactant and co-surfactants were in pharmaceutical grade.

2.2. Methods

2.2.1. Formulation of SEDDS compositions

The SEDDS compositions were prepared using different natural/semi synthetic oils, hydrophobic and hydrophilic surfactants to water-soluble co surfactants. The selection of different type's excipients was mainly to establish wide range of self emulsifying regions of its compositions. The phase diagram were constructed by right proportion of the above three types of excipients. The self emulsified formulations are in clear dispersion, which should remain stable on dilution in order to make the hydrophobic drugs remain in solubilized from until its absorption.[3] Oils were important ingredient of the system that not only solubilized large amount of lipophilic drugs but also facilitate the transport via intestinal lymphatic system, thereby increasing absorption of lipophilic drugs from the GIT.[4] Natural oils or modified long and medium chain triglyceride oils with varying degree of saturation have been widely used to design SEDDS system.[5] The surfactant is an essential excipient to provide vital emulsifying characteristics to SEDDS and make it possible for large amounts of drug compounds to get dissolved into the system.[6]

2.2.2. Construction of ternary phase diagrams

The series of concentrations of oils (Cinnamon oil, Lavender oil, Peppermint oil, Ethyl oleate, Sesame oil, Olive oil, Castor oil and Hydrogenated sunflower oil), Surfactants (Labrasol, Brij, Cremophore RH40, Cremophore EL, Span 80) and Co-surfactants (Capmul MCM, Capmul MCM C8, Tween 80) were used to construct the system (Table 1). A visual observation was made immediately for spontaneity of emulsification, phase separation and precipitation.[7] Emulsions showing phase separation and coalescence of oil droplets were judged as unstable emulsions. All studies were repeated thrice. The phase diagram was plotted using CHEMIX ternary plot software.

Table 1 – Different composition of various oils, surfactants and co-surfactants.

S. no	Group	Oils	Surfactants	Co-surfactants
1	Group I	Castor oil	Cremophore EL	Capmul MCM C8
2	Group II	Isopropyl myristate	Cremophore RH 40	Tween 80
3	Group III	Peppermint oil	Brij	Capmul MCM
4	Group IV	Sesame oil	Span 80	Tween 80
5	Group V	Lavender oil	Brij	Capmul MCM C8
6	Group VI	Olive oil	Cremophore EL	Capmul MCM
7	Group VII	Sunflower oil	Span 80	Tween 80
8	Group VIII	Cinnamon oil	Labrasol	Capmul MCM C8
9	Group IX	Ethyl oleate	Cremophore EL	Capmul MCM C8

2.2.3. Self emulsification time

The self emulsification time is the time required for a preconcentrate to form a homogenous mixture upon dilution. The efficiency of self emulsification of SEDDS was assessed using USP dissolution apparatus type II. 1 ml of each formulation was added drop wise to 250 ml of purified water at 37 °C; Paddle rotating speed at 60 rpm to provide gentle agitation. The lipid-based formulations were assessed visually according to the rate of emulsification and the final appearance of the emulsion. Grade I – rapidly forming micro emulsion which is clear or slightly bluish in appearance (<1 min); Grade II – rapid forming, slightly less clear emulsion which has a bluish white appearance (<2 min); Grade III – bright white emulsion which is similar to milk in appearance (<3 min); Grade IV – dull, greyish white emulsion with a slightly oily appearance that is slow to emulsify (>3 min).[8]

2.2.4. Robustness to dilution

Robustness of SEDDS to dilution studies was studied by diluting it to 50, 100 and 1000 times with various dissolution media i.e. water, pH 1.2, 3.0 and 6.8. The diluted samples were stored for 24 h and observed for any sign of phase separation or precipitation.

2.2.5. Globule size determination

The effect of various dispersion medium and volume on droplet size was investigated in this study. The selected SEDDS formulations (1 ml) were diluted to 50, 100 and 1000 folds of water, pH 1.2, 3.0 and 6.6. The mean globule size of the formulations was determined using Phase Contrast Microscope (PCM). Three replicate analyses were carried out for each formulation, and data presented as mean ± SD.

3. Result and discussion

3.1. Construction of ternary phase diagram

A series of self emulsifying systems were prepared with varying concentrations of oils (25–70% w/w), surfactants