

SUMMARY

TRIACETIN BASED SELF EMULSIFYING FORMULATION OF A POORLY WATER SOLUBLE DRUG

Introduction:

Furosemide is a high loop diuretic used as an adjuvant in treatment of hypertension¹. However, the low aqueous solubility and poor dissolution of this molecule in gastric fluid affects its rate of absorption, resulting in a low and variable oral bioavailability².

Objective:

Self emulsifying formulations (SEF) consists of a mixture of oil, surfactants and cosurfactants. SEF results in a fine transparent microemulsion on dilution under condition of mild agitation³. Triacetin is a co-solvent, having affinity for both lipophilic and hydrophilic phases. This property of triacetin makes it an interesting excipient to work with especially in case of self emulsifying formulations as it can serve a dual purpose of co-solvency as well as an emulsification aid. Thus the objective of the present study was to develop a triacetin based SEF of furosemide.

Experimental Methods:

1. SOLUBILITY STUDIES:

Solubility of drug in various oils, co-solvent and surfactants were carried out in order to screen for the components to be used for formulation development. Analysis of the drug was carried out on UV Spectrophotometer (JASCO) at 275nm.

2. PSEUDO-TERNARY PHASE DIAGRAM:

The boundaries of micro-emulsion domain in the triangular diagrams were determined by progressive titration of the component mixtures⁴. At each value ratio a mixture of oil, surfactant and co-surfactant was progressively enriched in aliquots of purified water. Same procedure was repeated with inclusion of triacetin in oil phase.

3. PREPARATION OF SELF EMULSIFYING FORMULATION:

Formulation was prepared using ratios of components determined from phase diagrams. Gentle heating aided with sonication and vortex mixing was applied to hasten the process.

4. EVALUATION OF SELF EMULSIFYING FORMULATION:

A] In-vitro dissolution studies: Dissolution studies of samples were performed according to USP XXIII type II apparatus in distilled water. The temperature was maintained at $37\pm 0.5^{\circ}\text{C}$ and the rotation speed was 100 rpm. The samples were withdrawn at various time intervals and analyzed spectrophotometrically.

B] Micro-emulsifying efficiency: Dilution study was carried out to evaluate the micro-emulsifying efficiency of the formed system.

C] Particle size analysis: A Malvern Photon Correlation Spectrometer model 4700 equipped with an argon laser was utilized for evaluating the particle size and particle size distribution. Light scattering was monitored at 90° angle and 25°C.

D] System stability: Optimized formulation was subjected to Freeze Thaw cycling and centrifugation studies to confirm the stability of the system

Results and Discussion:

Formulation components were selected based on their apparent solubilizing capacity towards drug. Triacetin was found to show an increase in the micro-emulsion existence field as evident from the results of phase diagram studies. Such observation could be attributed to the amphiphilic nature of triacetin which gives it an emulsifier like properties. It was evident from the *in vitro* dissolution data of samples, that the SEF exhibited a faster dissolution rate as compared to the drug alone with complete drug release in 15 minutes. This could be attributed to formation of in-situ micro emulsion in the release medium which keeps the drug dispersed in nano sized oil droplets. Results from particle size analysis (<100 nm) was also in accordance with the above assumption. Developed system was also found to be stable in terms of system integrity.

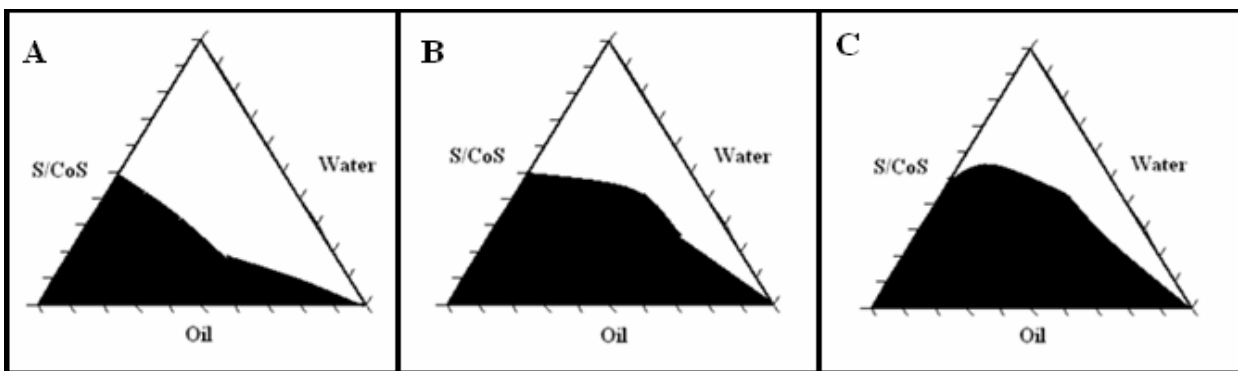


Figure: Pseudo ternary diagram A] without triacetin B] with 20% triacetin and C] with 40% triacetin

Conclusion:

The rate of dissolution of Furosemide from Self emulsifying formulation was found to be significantly higher than drug alone. Thus, a Self Emulsifying Formulation of furosemide with increased dissolution efficiency was successfully developed using triacetin as a cosolvent.

Bibliography:

1. Physician's Desk Reference 2000; 54th Edn, Medical Economics Company, Inc., pg.1325.
2. Althal, K.S., et.al., DDIP, Vol 26, pg 595, 2000.