



Original Article

Formulation and Characterization of Self Emulsifying Drug Delivery System of Spironolactone

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Spironolactone is aldosterone antagonist drug belonging to the category of potassium sparing diuretics administered orally that has absolute bioavailability of only 68% due to the poor aqueous solubility. The main aim of the present work was to develop a self emulsifying drug delivery system (SEDDS) to enhance the oral absorption of spironolactone. The solubility of spironolactone in various oils, surfactants, and co surfactants was determined. Pseudo ternary phase diagrams were constructed using castor oil, Tween 80, and polyethylene glycol 400, and distilled water to identify the efficient self-micro emulsion region. Prepared self emulsifying drug delivery system was further evaluated for its emulsification time, drug content, optical clarity, droplet size, zeta potential, in vitro drug release. The results showed that 96.16% drug was released from the SEDDS formulation in 3 hrs. This demonstrated an enhancement in the drug release and thereby, absorption of the drug through the membrane, this was significantly higher than that of the plain drug suspension. Thus, the above findings support that the utility of SEDDS to enhance solubility and dissolution of poorly water soluble compounds which may result in improved Therapeutic performance.

KEY WORDS: Spironolactone, Bioavailability, Solubility, SEDD**ARTICLE INFO:** Received: 23 Dec. 2018; Review Completed: 20 Jan.2019; Accepted: 29 Jan.2019; Available online: 15 Feb. 2019**Cite this article as:**

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INTRODUCTION

Spironolactone is a specific pharmacologic antagonist of aldosterone, acting primarily through competitive binding of receptors at the aldosterone dependent sodium-potassium exchange site in the distal convoluted renal tubule. Spironolactone causes increased amounts of sodium and water be excreted, while potassium is retained⁽¹⁾.

Spironolactone acts both as a diuretic and as an antihypertensive agent. Approximately, 40% of the new drug candidates in development today are water insoluble and associated with poor bioavailability⁽²⁾. There were various formulation approaches reported to overcome these problems; these include the use of drug nanoparticles, solid dispersions, micronization, lipids, surfactants, complexation with cyclodextrin, and permeation enhancers . Majority of these approaches have their limitations because of the need for specialized equipment, complicated manufacturing process, longer processing time, and regulatory complexity^(2,3). Lipid-based formulation approaches, particularly the self-

emulsifying drug delivery system (SEDDS), are well known for their potential as alternative approach for delivery of hydrophobic drugs^(4,5).

The main objective of the study is to increase oral bioavailability of spironolactone using a lipid- based formulation i.e, self emulsifying drug delivery system. In the present work it is proposed to formulate and evaluate self emulsifying drug delivery system of spironolactone in order to achieve a better dissolution rate and preventing the drug from first pass metabolism which would further help in enhancing oral bioavailability

MATERIALS

Spironolactone was generous gift from Piramal Healthcare Pithampur, India, and various oils Soybean oil, Castor oil, Peppermint oil, Oleic acid, Dill oil, Mentha oil, and surfactants Tween 80, Tween 20, Span 20 and co-surfactants PEG 400, Methanol, Ethanol were purchased from local market. Distilled water, was used in all experiments. All other chemicals used were of analytical grade

METHOD

Solubility studies: - The objective of solubility studies is to determine the solubilization capacity for drug in given vehicles. Solubility of spironolactone was estimated in different vehicles by excess solute method and % transmittance.

Screening of surfactants for emulsifying ability - Screening of surfactant for emulsifying ability was done by % transmission studies.

Screening of co surfactants - Screening of co surfactant for emulsifying ability was done by % transmission studies

Selection of ratio of Components by Construction of Pseudo-ternary Phase Diagram - The pseudo-ternary phase diagrams are shown in fig. 1.1 to fig. 1.3. Three sides of the triangle represent the three components and the shaded area in the plot represents the microemulsion region. selection of component by using sigma plot software 11.0 version.

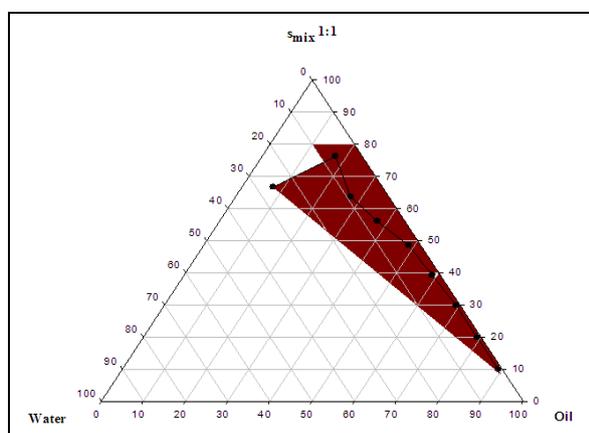


Figure.1: Pseudoternary Phase Diagram for Castor oil as Oil Phase, Tween 80: PEG400 (1:1) as S_{mix} and Water

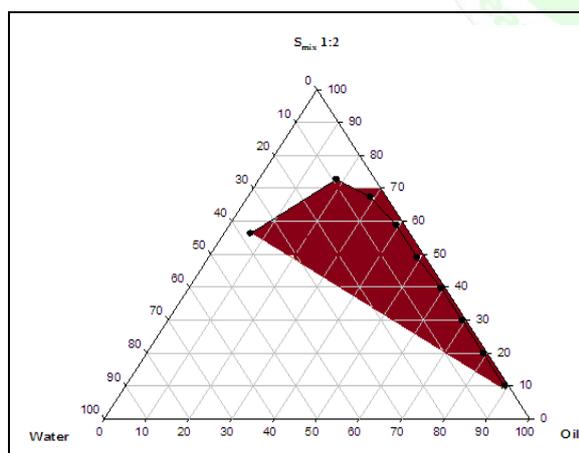


Figure 2: Pseudoternary Phase Diagram for Castor oil as Oil Phase, Tween 80: PEG400 (1:2) as S_{mix} and Water

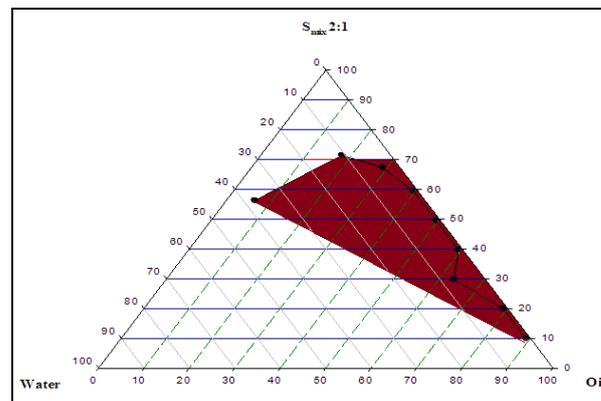


Figure 3: Pseudoternary Phase Diagram for Castor oil as Oil Phase, Tween 80: PEG400 (2:1) as S_{mix} and Water

Construction of Ternary Phase Diagram

Construction of ternary phase diagram was aimed at determining the concentration range of each factor as well as to identify the desired region of self-emulsification possess clear emulsion characteristic.

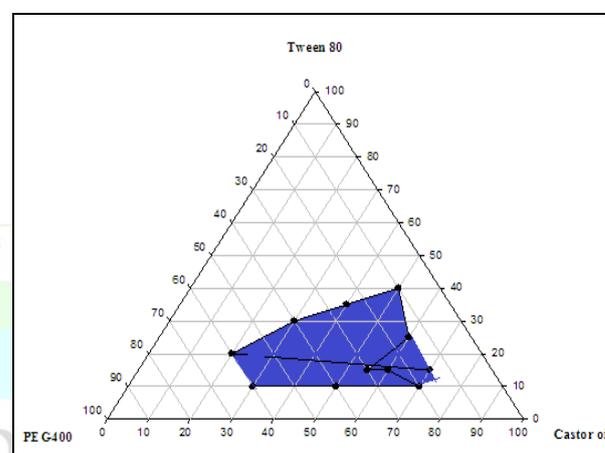


Figure 4: Ternary Phase Diagram for Castor oil, Tween 80 and PEG 400

Table: 1 Concentration Range Obtained From Phase Diagram

| S. No. | Component | Concentration |
|--------|------------|---------------|
| 1 | Castor oil | 50% |
| 2 | Tween 80 | 25% |
| 3 | PEG400 | 25% |

Evaluation of the Optimized SEDDS Formulations of Spironolactone

Table: 2 Optimized Formula For The Formulation of SEDDS.

| S. No. | Evaluation | Result |
|--------|-----------------|-------------|
| 1 | Optical clarity | 99.9 |
| 2 | Droplet size | 128.2 nm |
| 3 | Zeta potential | -11.0 mV |
| 4 | Drug content | 77.0±0.900% |
| 5 | Drug release | 96.16% |

CONCLUSIONS

Spironolactone is aldosterone antagonist drug belonging to the category of potassium sparing diuretics. spironolactone was formulated as a SEDDS in an attempt to increase its solubility. An optimized formulation of SEDDS containing spironolactone was

developed through the construction of In-vitro drug release study and solubility study. SEDDS show increase in solubility compared to pure drug formulation. Thus, the above findings support that the utility of SEDDS. SEDDS can be promising as future, dosage form for drugs which suffer poor aqueous solubility (BCS class II drugs).

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