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# DISCUSSING SMEDDS AND DRUG ABSORPTION BY LYMPHATIC DELIVERY

**KAVITA DEVRAJAN**
RESEARCH SCHOLAR SUNRISE UNIVERSITY ALWAR
**DR. ALOK UPADHYAY**
ASSOCIATE PROFESSOR SUNRISE UNIVERSITY ALWAR

## ABSTRACT

*Significant difficulties exist in pharmaceutical formulation when it comes to the oral distribution of active pharmaceutical ingredients (APIs) that are not highly water soluble. Solubility, bioavailability, and therapeutic effectiveness may all be improved by using microemulsion systems as the carrier. Microemulsion systems are being formulated, developed, and optimized for oral administration of poorly water-soluble active pharmaceutical ingredients (APIs) in this research. Selection of appropriate excipients and screening of oil, surfactant, and co-surfactant combinations to generate stable microemulsions are the first steps in the systematic approach used in this study's research technique. Factorial design and response surface methods will be used to optimize the oil-to-surfactant ratio, co-surfactant concentration, and temperature, three of the most important process parameters. The improved microemulsion formulations will be assessed using physicochemical characterization methods as droplet size analysis, zeta potential testing, and transmission electron microscopy.*

**Keywords: -** Medicinal, Compounds, Chemical, NCEs, Biopharmaceutical Classification System (BCS).

## I. INTRODUCTION

More and more newly identified medicinal compounds have low absorption rates after oral administration due to their insolubility in water. About 35% to 40% of all novel chemical compounds have low water solubility, according to a 2002 analysis by Technology Catalysts International. In particular, the problem emerged in the middle of the last century, when drug discovery shifted from wet chemistry to combinatorial chemistry and high throughput screening. Due to an increase in molecular weight and an increase in lipophilicity, aqueous solubility has reduced in NCEs. Despite showing promise in terms of pharmacodynamic efficacy, many drug candidates fail to make it to market due to low water solubility. In addition, in order to obtain adequate plasma levels, presently available medicines with limited water solubility are often given in considerably larger individual doses than are ideal. The establishment of the Biopharmaceutical Classification System (BCS) has established a framework for classifying

medications according to solubility and permeability, the two most important factors influencing absorption. Therefore, methods are used and studied to increase the drug's water solubility and its rate of release.

Several methods, initially focused on altering the drug's physicochemical characteristics, have been developed and documented in literature with the aim of increasing the drug's solubility and dissolution in water. In an effort to increase dissolving, several researchers have turned to strategies including decreasing particle size and increasing salt production. ' I Therefore, formulation strategies that aim to improve medication solubility or dissolution have gained in popularity. One way to increase the effectiveness of a medicine is to modify its dissolving conditions, as indicated by the Noyes-Whitney equation.

## II. LIPID-BASED FORMULATIONS:

Lipid solution, lipid emulsion, microemulsion, and dry emulsion are all examples of lipid drug delivery methods. Due to the complexity of self-emulsifying systems and the wide variety of excipients that can be used to put together lipid-based formulations, a classification scheme known as the lipid formulation classification system (LFCS) was developed. This categorization aids in clarifying the destiny of various lipid formulations in vivo, facilitating the adoption of a systematic and reasonable formulation method that eliminates the need for "trial-and-error" iterations and providing a framework to direct regulatory authorities. Pouton created and recently revised LFCS in the year 2000. |7] Below the Table is a quick explanation of how the LFCS categorizes lipid-based formulations into four distinct classes based on their composition and the potential impact of diluting and digesting the formulation on its capacity to avoid drug precipitation.

In type I systems, the medicine is either dissolved in triglycerides and/or mixed glycerides or is suspended in an oil-in-water emulsion stabilized with modest concentrations of emulsifiers such as polysorbate 60 (1% w/v) and lecithin (1.2%). Drug transport into the colloidal aqueous phase is enhanced when these systems are digested by pancreatic lipase/co-lipase in the GIT, since they often show poor initial aqueous dispersion. As a result, powerful medications or highly lipophilic substances that are sufficiently soluble in oil to enable integration of the appropriate payload (dosage) may be easily formulated using type I lipid formulations.

## III. MICROEMULSION AND SELFMICROEMULSIFYING DRUG DELIVERY SYSTEM (SMEDDS)

Droplet sizes in microemulsions typically vary from 10 to 100 nm, and the systems are isotropic, thermodynamically stable, and transparent (or translucent). All of the fluids in these

homogeneous systems, which may be made with varying amounts of surfactant and oil to water, have a low viscosity.

Thermodynamic stability (long shelf life), ease of formation (zero interfacial tension and almost spontaneous formation), optical isotropy, filtration-based sterilization, high surface area (high solubilization capacity), and very small droplet size are just some of the advantages of microemulsion as a drug delivery tool. The drug molecules may be transported in a more manageable manner and with greater adhesion to membranes thanks to the droplets' size and shape.

**Structure of Microemulsion**

In microemulsions, the interface is constantly and naturally changing states, making the system a dynamic one. Based on their structure, microemulsions may be classified as either oil-in-water (o/w), water-in-oil (w/o), or bicontinuous. Microemulsions may be classified as either w/o (water-in-oil) or o/w (oil-in-water), with the former referring to a mixture of water droplets and the latter to a mixture of oil and water.

**Self Microemulsifying Drug Delivery System (SMEDDS)**

In order to form a fine oil-in-water (o/w) microemulsion upon mild agitation followed by dilution in aqueous media, such as GI fluids, SMEDDS are defined as isotropic mixtures of natural or synthetic oils, solid or liquid surfactants, or alternatively one or more hydrophilic solvents and cosolvents/surfactants. Self-emulsification of SMEDDS occurs in the GI tract due to the agitation provided by the digestive motility of the stomach and intestine.

## IV. ENHANCED DRUG ABSORPTION BY LYMPHATIC DELIVERY:

It is recommended that drugs with a log P >5 and triglyceride solubility >50 mg/ml be considered for lymphatic transport. Lymphatic transport of DDT (log P-6.19) was compared to that of hexachlorobenzene (log P-6.53) to demonstrate the significance of lipid solubility. Despite having equal log P values, the 13-fold differential in triglyceride solubility between DDT and HCB explains why 33.5% of the dosage is transported lymphatically in the former example but only 2.3% in the latter.

High log P and high triglyceride solubility are associated with increased lymphatic transport, however this is not always the case. Intestinal lymph carried just -3% of the dosage of penclomedine, an investigational cytotoxic drug with a log P of 5.48 and a triglyceride solubility of 175mg/ml. Few research have looked at the lymphotropic potential of SMEDDS, even though it has been proposed as a possible route of improved bioavailability.

However, one research looked at the bioavailability and lymphatic transport of ontazolast after oral administration to awake rats and found that different lipid-based formulations had different impacts on both. This medication has a log P of 4, a solubility in soybean oil of 55 mg/ml, and substantial first-pass hepatic metabolism. Ontazolast was tested in a variety of different formulations, including a suspension (lipid-free control), a 20% soybean-o/w emulsion, two SMEDDS comprising Gelucire44/14 and Peceol in ratios of 50:50 and 80:20, and a solution of the medication in Peceol alone. Ontazolast bioavailability was improved across the board with lipid formulations, with SMEDDS resulting in the quickest absorption.

The emulsion combined with the Peceol solution resulted in the greatest lymphatic movement. Emulsions take longer to empty from the stomach, which may be because preabsorptive lipolysis of the triglyceride carrier is required. The ontazolast content in the chylomicron triglyceride was greatest for the SMEDDS formulations. Faster absorption of ontazolast through SMEDDS may result in larger drug concentrations in the enterocytes during absorption, the authors write, which may increase lymphatic drug transport via a concentration-partitioning phenomenon.

## V. CONCLUSION

Microemulsion systems were fonnulated, developed, and optimized for oral administration of weakly water-soluble active medicinal components in the current work. It is hypothesized that microemulsions will be absorbed through the lymphatic pathway, reducing the need for first-pass hepatic metabolism. In addition, the drug's solubilization and finely divided condition would greatly improve its absorbability and bioavailability. Self-microemulsifying drug delivery systems (SMEDDS) are the most widely used alternative and economically viable kind of microemulsion. Under the moderate agitation of GI tract motions, this system is able to quickly self-microemulsify in GI fluids, forming thin O/W microemulsions. If the SMEDDS were formulated as a solid, it would have a more favorable kinetic and thermodynamic stability profile, be more patient-friendly, and be easier to carry and store than its liquid counterpart.

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