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Review on Novel Approachof Curcumin loaded SNEDDS and its application

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ABSTRACT:SNEDDS is a novel formulation was developed to enhance the solubility and bioavailability of all the poorly soluble drugs.SNEDDS are the combination of oil, surfactants, solvents as well as cosolvents /surfactants. Curcumin is a naturally occurring active constituent and exhibits several magical activities in treating life threatening diseases, but it belongs to BCS category of class IV which signifies poor solubility along with poor permeability although by the advancement with novel formulation SNEDDS we can improve the solubility and bioavailability of drug. The nano carrier system of SNEDDS improve the loading capacity of curcumin that beneficial its transportation and absorption to various organs by crossing the membrane. The SNEDDS can be prepared by various techniques.SNEDDS is consider as an effectual method for oral delivery of all poorly water-soluble drugs, in order to enrich its bioavailability. The current aim of this article is to resolve and also focuses on investigating the application of SNEDDS in enriching the bioavailability of antihypertensive drugs.

KEY WORDS: Curcumin, SNEDDS, Surfactant, Novel Approach, Solubility

INTRODUCTION:

Curcumin is a naturally occurring compound whose chemical formula is 1, 7-bis (4-hydroxy- 3-methoxyphenyl) -1, 6- heptadiene-3, 5-dione), it's a small molecular weight, hydrophobic polyphenolic compound, that extracted out from rhizomes of *Curcuma longa*, and belongs to Zingiberaceae family [1]. Many kinds of curcuminoids are found in curcumin. The curcuminoids which observed in curcumin are nearly about 5% bisdemethoxycurcumin,15% demethoxycurcumin, along 80% of Curcumin. When curcumin is taken orally, 75% of it excreted in the feces while only traces of curcumin appear in Urine. In BCS curcumin belongs to class IV category, which indicates poor solubility and poor permeabilityof drug. The Curcumin having long list of harness includes antioxidant, anti-inflammatory, anticancer, antimalarial, antiseptic, rheumatism arthritis, asthma, diabetes, analgesic and wound healing activities[2]. The Oral route of regimen of drug is consider to be the most acceptable route in the pharmaceutical area, because of its versatility in the strategy of dosage form than the other routes.In today's worldthe novel delivery of drug by more convenient route has become more prominent research area in the field of pharmaceuticals delivery along with glance of exploration of new chemical entities[3]. Self-emulsifying systems is a novel gift for the bioavailability strengtheningof

poorly aqueous soluble drugs such as curcumin. SNEDDSdraft by the mixture of compoundoil, drug, surfactant, and co-surfactant[4]. The size ranges of SMEDDS dropletfrom 100–250 nm which form clear to translucent dispersions system[5].These formulations are considered that they will show the more prominent effect on increase the absorption of the drug from the GIT on oral intake of dosages form that prolongs the residential time of in systemic circulation due to the controlled release (slow release) of the coated drug (curcumin) [6].

Advantages:

- These formulation enhances the bioavailability of poorly soluble drug, also improvesthe rate and extent of absorption.
- SNEDDS enable targeting delivery.
- SNEDDS possess ability of higher drug loading.
- This dosages form shows controlled drug release profile.
- The unique idea of SNEDDS formulation preserve the active compound from the aggressive environment of the GI tract.

Disadvantages:

- There is wide range of Possibility in leakage and precipitation of drug.
- SNEDDS has the problem of Lower stability.
- SNEDDS are not economic dosages form.
- SNEDDS needs higher concentration of surfactant approximate (30–60%)[7].

Biopharmaceutical Classification System: The BCS isa system which is known for determination of drugs solubility and permeability towards biological membrane. This system is a great tool for development and design of new drug formulation. This system classified basically into four major classes on the basis of high or low solubility and permeability of the drug but now the system is guided by WHOand USFDA [8].

Solubility: According to theguidance of WHO and USFDA, drug is considered to be highly resolvable when the maximum dose (if the API appears on the WHO Model List of Essential Medicines) or maximum dose strength of the marketed formulation as same as an oral solid dosage form (if the API does not appear on the WHO Model List of Essential Medicines) if it is solvable in aqueous medium of about 250ml or less than that medium and the pH ranges from 1.2-6.8[9].

Permeability: Under the guidance of WHO and according to the BCS permeability is defined as the absorption extent of a drug compound in systemic circulation and the rate of mass transfer across the intestinal mucosa. When the drug compound extremely permeable, then absorption rate is considered to be 90% or more of it[10].

Types ofBiopharmaceutical classification system: Thesystem is classified majorly in four categoriesthat is of solubility and permeability, as shown below.

- Class I: High Solubility - High Permeability
- Class II: Low Solubility - High Permeability
- Class III: High Solubility - Low Permeability
- Class IV: Low Solubility - Low Permeability

High solubility
Low solubility

High Solubility

Low permeability

Class 1 High solubility High permeability	Class 2 Low solubility High permeability
Class 3 High solubility Low permeability	Class 4 Low solubility Low permeability

Fig: 1Biopharmaceutical classification system

SNEDDS Mechanism of Action:SNEDDS on oral administration, gets agitated by natural gastric stirring, which form nano-emulsion instantly with size range of Nanometric region i.e. < 200 nm. The nano-particles containactive compound which must be chiefly soluble in oil phase that form interfacial layer to hasten the dispersal in the fluid of gastro intestinal tract[11]. By altering transport mechanism, the interfacial area amplified that finally enhance drug solubility and permeability which is beneficial for better drug response. [12]. Nanosize globules experience speedyuptakewith rapid consumption of drugs like curcumin, which belongs to BCS class IV into the GI tract [13]

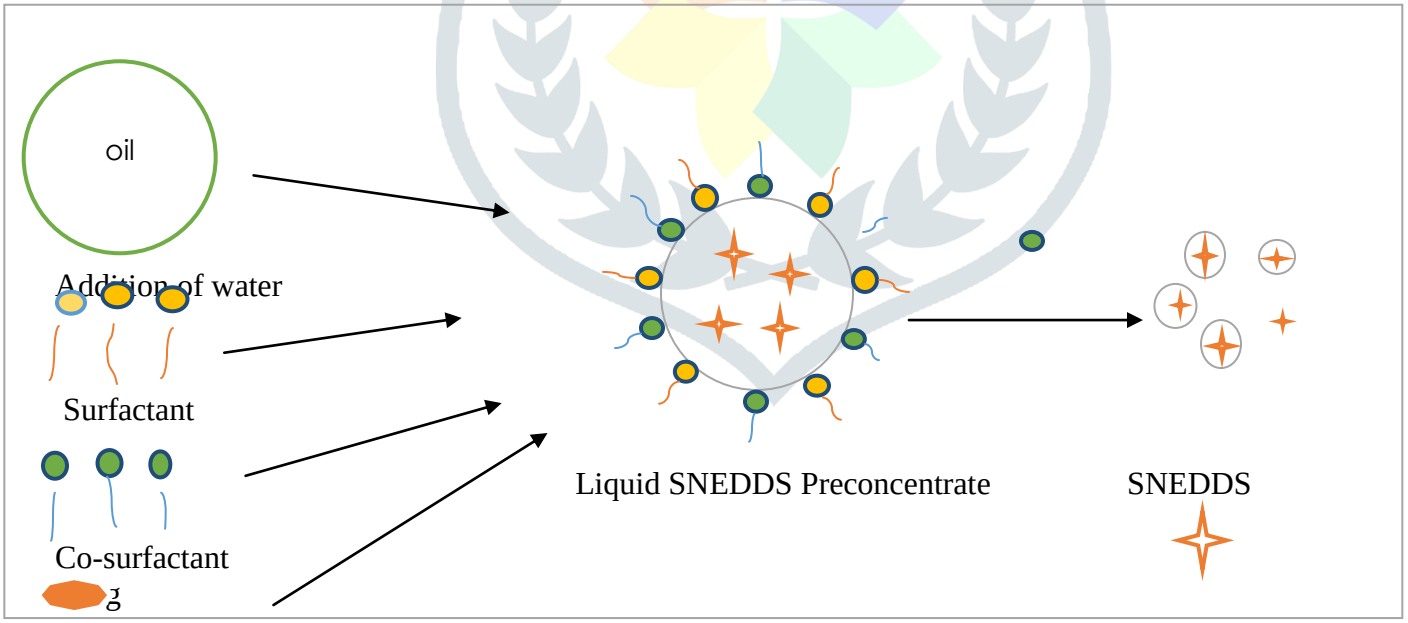

Figure 2: Formulation of SNEEDS

EXCIPIENTS USED IN SNEDDS FORMULATION:

Oils: SNEDDS formulation are prepared by using oil, which acts as solubilizing agent for the lipophilic active compound and that will assist the process of self-emulsification, it also enhances absorption of active compound i.e. drug by accelerating the passage through intestinal lymphatic system. The cooking oils are not consideredfor SNEDDS formulation because they are unable to emulsify higher amount of drug in

formulation. But hydrogenated vegetable oils are prominently used with higher amount of surfactants because it is good in emulsification process so that ease in oral uptake. In response of that amphiphilic compounds can be used because they having lipophilic and hydrophilic property because of that it used in novel formulation [14-15].

Surfactants: The edible surfactants are of non-ionic type that having maximum degree of hydrophilic-lipophilic balance (HLB). The more prominently employed emulsifiers in this formulation are ethoxylated polyglycolyzed glycerides and polyoxyethylene oleate. The Natural emulsifiers system are considered to be safer than the synthetic one but these surfactants are not aware with the property of self-emulsification. Lesser toxicity observed in non-ionic surfactants while the ionic surfactants are more stable and more of this they having higher permeability property through intestinal lumen[16-17].

Co-surfactant: During the process of SNEDDS formulation higher concentration of surfactants is required i.e. (>30%w/w), and on further addition of co-surfactants it gets condensed.The interfacial tension was observed lower to negative value but after mixing all the compounds the interfacial property turns positive this is because the fine droplets adsorbed maximum concentration of surfactant and co-surfactant. The phenomenon is known as "spontaneous emulsification"[18]. The co-surfactant of medium chain length like alcohol, pentanol are used because it reduces the interfacial tension between two phases i.e. oil and water, which finally grease the micro-emulsion formation [19].

Oil phases	Surfactant	Co-surfactant
Oleic oil	Tween 80	Propylene glycol
Olive oil	Tween 40	Ethylene glycol
Mineral oil	Span 80	Ethanol
Soyabean oil	Span 20	PEG 400
Castor oil	Caprol 90	Peg 600
Sesame oil	Polysorbate	

Fig:3List of compounds used in formulation of SNEDDS oils, surfactants and co-surfactants.

Formulation of SNEDDS:

The SNEDDS formulation can be done by different ways.

1. **formulation of liquid SNEDDS:** The novel blueprint is used for formulation of SNEEDS which holding particular ratio ofoil / surfactant /co-surfactant, which is picked from pseudo-ternary phase diagram.liquid SNEDDS was prepared by taking different proportion of oil and surfactant which further blend with drug,finally the blend was resolve and liquid SNEEDS are completely prepared which further proceed for storage at room temperature.

2.formulationof solid SNEDDS:there are many more options for formulation of SNEDDS which was prepared through mingling liquid SNEDDS in mortar and pestle. Now the resulting dough strainer through the sieve number 120 and remove the moisture by providing the temperature [20].

Evaluation of SNEDDS

Drug content: This method is used for determining the content percentage of drug in product as well as its percentage of purity. The parameter guided for considering twenty tablets were weighed separately and the mean weightmust be calculated. further crush all the twenty tablets,the average weight of the specimen was taken and dilute it to analyze by HPLC technique. Dissolution test performed measuring percent of drug content in SNEDDS [21].

Droplet Size: Droplets size of SNEDDS was measured by diluting the preparation into distilled water. For receiving the exact size of formulation the 2ml of the specimen was placed in a cubid and analyzed by using high resolution light scattering technique i.e. diffraction light scattering due to Brownian motion, and with zeta sizer Nano-ZS the light scattering was monitored at 25°C and an angle of 90° [22].

Viscosity measurement: Viscosity measurement of SNEDDS formulation was done by using Brookfield Viscometer which is highly used to know the Consistency of the Formulation.[23]

Morphological study: The morphology of the SNEDDS droplets was measured by using transmission electron microscopy (TEM) and scanning electron microscopy (SEM) because both having magnification value. The sample firstly diluted to a suitable and then little amount is applied over the slide and finally observe its structure.

***In Vitro* Dissolution Studies:** To perform this test USP type 2 apparatus was used that contains 900 ml of phosphate buffer of (pH 7.4),0.1N HCl of (pH 1.2) dissolution medium which mixed together by continuous motion at 100rpm and at 37±5°C of temperature, throughout the process sink condition is maintain. 5ml aliquots was drop backregularly which get replaced with the same quantity of fresh dissolution medium and further filtered through 0.45 μm membrane filter.The sample analyzed spectrophotometrically at the λmax of drug. [24]

Centrifugation study: This test was done to recall the stability study of SNEDDS here the test was performed by using centrifuge that rotate at 5000rpm for 30min. the resulting formulation than observe to find out any kind of instability or not. [25]

Applications of Curcumin:

ANTI-CANCER: Curcumin is the naturally obtained compound which has many magical chemical constituents that shows more effective response against various life threatening diseases.cancer is a result of successive and uncontrolled cell proliferation. In an investigation Curcumin shows anti-cancerous activity by interfering two process i.e. angiogenesis and tumor growth.[26]

ANTI-DIABETIC: In the researchstudy curcumin shows their positive nature in treating diabetes, all this happen by decreasing the production or inhibition of superoxide and also vascular protein kinase C.Major cause was considering oxidative stress that may lead cell death but curcumin consider as promising agent in managing diabetes by way of initiation of cytoprotective enzymes, equally heme oxygenase-1 (HO-1). [27]

ANTI-ARTHRITIS activity: This is a long standing joint provocative disorder, which represented through hyperplasia. A study was carried out on rheumatoid arthritis patient to know the effectiveness of curcumin in comparison to diclofenac sodium. Curcumin shows interesting result because it does not show any kind of side

effect due to of natural origin and observe more effective that diclofenac sodium in treating the inflammation.[28]

Anti-inflammatory activity: Many of the steroids and anti-inflammatory drugs shows their activity in treating and curing the inflammation.while curcumin have many activities along with anti-inflammatory property. This work on basically by overpoweringthe turning on of NF-kBfactor,anddivergent inflammatory cytokines, involving TNF, IL-1, IL-6, IL-8 and chemokines. The best thing of curcumin is it natural origin which make the formulation safe and free of side effects [29].

Wound Healing: Curcumin was significantly recovered as a main aspectfor injury repairing along with re-epithelization, collagen synthesis, granulation tissue formation. curcumin here stimulates the growth factors to promote cell regeneration and stop the proliferation of damaged tissues or cells. The growth factor beta 1, which enhances the injury repairing process, so we can say that curcumin having the maximum manipulating property in TGF β1 activity[30].

Anticoagulant Activity:Curcumin having many chemical constituent and one of by product is bisdemethoxycurcumin which retain antithrombotic activities or on dietary intake of curcumin helps in maintaining the anticoagulant activity. The basic mechanism behind Curcumin anticoagulant activity was achieved by obstructing platelet flocculationwhich activated by arachidonate, adrenaline, and collagenin thoracic aorta ofratthat proceed in-vitro additionally in-vivo[31].

Anti-HIV property: The curcumin derivative is (E)-2-(3,4-dimethoxybenzylidene)-6-{(E)-3-(3,4-dimethoxyphenyl)-acryloyl}cyclohexanone considering more promising human HIV-1 and HIV-2 prostate inhibitor in vitro [32].

CONCLUSION:SNEDDS are the promising drug delivery system for the sustained or controlled release doses forms. SNEDDS used to target various sites like colon, pulmonary, vaginal, ocular, nasal and also found effective in management of Alzheimer's, parkinsonism and cancer like life threatening diseases. SNEDDS shows high drug load with maximum therapeutic effect for drugs of low solubility and permeability. SNEDDS can prepare by using various method at the reasonable cost.

Discussion:this review is completely grounded on promotion of curcumin SNEEDS in current scenario of developing cost effective formulation with lowest toxic effect i.e. why we consider curcumin in our paper. This paper comprehends with numerous techniques which contrast with other techniques, for betterment of formulation activity in management of deadly diseases and other parameter is for maximizing the loading capacity of drugs in novel formulation.

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