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A REVIEW ON ARGEMONE MEXICANA NANOEMULSION

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ABSTRACT

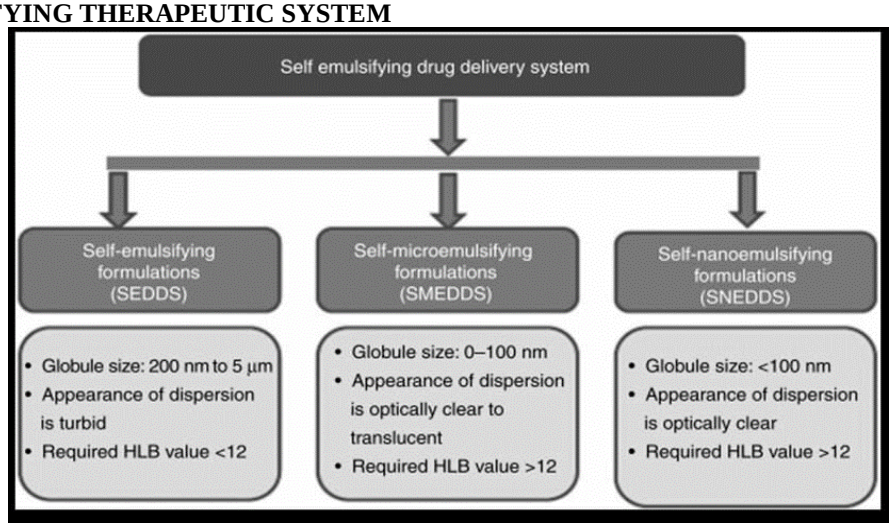
Argemone mexicana is a wildly growing weed adapted well to harsh condition. The entire plant is used to treat asthma. The sap (cut ends) of the stem is used in the treatment of toothache. In African nations the leaves are used for cosmetic purposes. In India, minute quantity of the seeds is mixed with mustard oil to increase the pungency, but above the minimal quantity of the seed is considered as adulteration. But every organism created by mother nature has it's value. Nothing is useless. Argemone- argemos means white spot or cataract, which the plant was believed to cure. Hence the entire plant was collected dried and extract of the same was tested for the treatment of eye infections by using self- nano emulsifying drug delivery system. It's a novel drug delivery system that is applicable for the parenteral, ophthalmic, intranasal, and cosmetic drug delivery system. The current review demonstrates the preparation, mechanism of self -nano emulsification, biopharmaceutical aspects, characterization, methods and application of self- nano emulsifying drug delivery system.

KEYWORDS: Argemone mexicana, Nano-Emulsion, Self-Nano emulsifying drug delivery system.

INTRODUCTION

Argemone species have been used in traditional medicine from ancient culture. According to the ethnobotanical interpretation of archaeobotanical and iconographic records, Argemone ochroleuca subsp. stenopetala was identified as a medicinal plant potentially used by Teotihuacan culture. In Mexico infusions of aerial parts of their plant are still used in the treatment of eye such as conjunctivitis, respiratory, dermatological and oral infections as well as for wounds. Some communities such as Tepotzotlan, Ahuacatlan, among others also use these infusions because of their stimulant hallucinogenic effects. Other medicinal properties of Argemone species have been reported in different Latin American countries, such as analgesic use of A. subfusiformis in Argentina, or Bolivia, against cough and cold. Moreover, Argemone species are also part of the traditional medicine of Saudi Arabia, and India where they have been used against diseases such as dropsy, jaundice, as well as eye and skin infections such as scabies and leprosy. Nano-emulsions are considered as the most promising solution to improve the delivery of ophthalmic drugs. The extract of the same was tested for the treatment of eye infections by using self- nano emulsifying drug delivery system. It's a novel drug delivery system that is applicable for the parenteral, ophthalmic, intranasal, and cosmetic drug delivery system. Self- nano emulsifying drug delivery system (SNEDDS) are regarded as nanoemulsion proconcentrates or as anhydrous form of the nanoemulsion. Self-nano emulsifying Drug delivery system is an isotropic mixture of the natural or synthetic oil surfactants and co-surfactants and alternatively, aqueous media were followed by one or more hydrophilic solvents and the co solvents /surfactants ability to generate fine oil in water (O/W) Nano emulsion under mild agitation conditions. The size range of globules in the Self nano emulsifying Drug Delivery system is less than 100 nm when dispersed in water.

SELF EMULSIFYING THERAPEUTIC SYSTEM



COMPOSITION OF SNEDDS

- Drug
- Oil
- Surfactant
- Co-surfactant
- Co-solvents

Drugs

SNEDDS are often prepared for drugs that have a poor water solubility. For most circumstances, BCS class II and class IV medicines are often used in manufacture of SNEDDs. Physicochemical parameters of the drug, such as log P, pka, molecular structure and weight, presence of ionizable groups, and quantity, all have a significant impact on SNEDDS performance. High melting point drugs with log p values of about 2 are poorly suitable for SNEDDS. While, lipophilic drugs having log p values greater than 5, are good drug candidates for SNEDDS.

Oil

The oil phase has great importance in the formulation of SNEDDS as physicochemical properties of oil such as molecular volume polarity and viscosity significantly govern the spontaneity of the nano emulsification process, droplet size of the nano emulsion, drug solubility and biological fate of nano emulsion it's mainly related to O/W nano emulsion. The oil is crucial for maximum solubilizing ability for selected drug candidate is important selection of oily phase for Nano-emulsion Formulation. This is often most important approach having the high drug stability. The naturally also as synthetically occurring the mixture of oils and fats are triglycerides contain in long fatty acids in order to decrease the degree of unsaturation and is important to prevent oxidative. The nano emulsion size is directly proportional to the lipophilicity of the oil and concentration of oily phase in SNEDDS. For instance, a mixture of fixed and medium-chain triglyceride is used in certain cases have good balance between drug loading and. Due to their inability to solubilize higher concentrations, edible oils are not included in the SNEDDS formulation. Due to the creation of improved emulsification systems with more surfactants acceptable for oral administration, hydrolysed vegetable oils are used. They propose formulation and physiological remuneration. Medium-chain semi-synthetic chemicals, referred to as amphiphilic compounds that possess surfactant characteristics, are substituting the oils in SNEDDS.

Surfactant

Surfactant are defined as molecules and ions are adsorbed at interface. It's having ability to prevent the interfacial tension and provide interfacial area. The selection of surfactant is additionally critical for the formulation of SNEDDS. Surfactant properties such as hydrophilic-lipophilic balance (in oil), cloud point, viscosity, and affinity for the oily phase have a significant impact on the Nano emulsification process, self-nano emulsification region, and hence nano emulsion droplet size. The concentration of the surfactant with in the SNEDDS has considerable influence on the droplet size of nano emulsions. The acceptability of the elected surfactant for the desired route of administration and its regulatory status must also be considered during surfactant selection.

Water soluble surfactants like Tween 20, Tween 80, Cremophor EL, and poloxamer 108, and so forth entrapped in an increased ocular bioavailability because surfactants act as penetration enhancers which can remove the mucus layer and break junctional complexes.

Co-surfactant

Co surfactants are typically employed in the SNEDDS for pharmaceutical use. They can be incorporated in SNEDDS for different purpose including:

- To increase the drug loading to SNEDDS.
- To modulate self- nano emulsification time of SNEDDS.
- To modulate droplets size of Nano-emulsion.

The addition of co-surfactants into SNEDDS isn't obligatory for many non-ionic surfactants33. In

SNEDDS Co-surfactants with HLB values ranging from 10 to 14 are employed in SNEDDS. Alcohols with medium chain lengths, such as hexanol, pentanol, and octanol, are hydrophilic co-surfactants that minimize the interface between oil and water, facilitating for impulsive microemulsion formation

Co surfactant	Chemical name	HLB
PEG 400	Polyethylene glycol 400	11.6
HCO 60	Peg 60 Hydrogenated castor oil	14

Co solvent

Usually, an effective self-emulsifying formulation requires a high concentration of surfactant. Accordingly, co-solvents like ethanol, propylene glycol and polyethylene glycol are essential to facilitate the dissolution of large quantities of hydrophilic surfactant. These co-solvents play the role of the co-surfactant with in the microemulsion system. On contrary, alcohol and other volatile co solvents have the limitation of evaporating into the shell of soft or hard gelatin capsules, resulting in the precipitation of the drug.

Polymers

We use an inert polymer matrix that represents 5 to 40% composition relative to the weight, is non-ionizable at physiological pH, and can form a matrix. hydroxyl propyl methyl cellulose, ethyl cellulose are two examples of surfactant.

Mechanism of Self nano emulsification

According to Reiss, Self-emulsification occurs when the entropy change that favours dispersion is greater than the energy required to increase the surface area of the dispersion. The free energy of the conventional emulsion is a direct function of the energy required to create a new surface between oil and water phases can be described by the equation.

$$DG = SN\ p\ r\ 2s$$

Where DG = free energy associated with the process,
N = number of droplet
r = radius of droplets
s = interfacial energy

The two phases of emulsion tend to separate with time to reduce the interfacial area and subsequently, the emulsion is stabilized by emulsifying agents, which forms a monolayer of emulsion droplets and hence reduce the interfacial energy as well as providing a barrier to prevent coalescence. The specificity of surfactant combination required to allow spontaneous emulsification may be associated with a minimization of the phase inversion technique, thereby increasing the ease of emulsion.

Preparation of SNEDDS

The nano emulsifying drug delivery system (SNEDDS) is prepared by using two ways

Preparation of Liquid SNEDDS

It's important method for preparation of self-Nano emulsifying drug delivery system having the surfactant/co-surfactant ratio and oil/ surfactant/co surfactant ratio was selected From the Pseudo ternary phase diagram. Different concentrations of oil, surfactant, and Cosurfactant were used to process a number of series of the formulation. The oil and surfactant were weighed in appropriate proportions, and the drug was dissolved in this mixture, which was then stored at room temperature.

Preparation of Solid SNEDDS

It is the second most vital method for preparation of Self Nanoemulsifying drug delivery system (SNEDDS). Drug was added into accurately weighed amount of oil in a screw capped vials and melted in water bath if necessary. Then by using a positive displacement pipette the surfactant and cosurfactant were added to the oily mixture and stirred with a vortex to obtain homogeneous solution. Solid Self nanoemulsifying drug delivery system (SSNEDDS) was prepared by adding selected liquid SNEDDS dropwise onto suitable novel adsorbents like Neusillin and are mixed well with glass rod. The damp substance that resulted was sieved no. 120 and dried at room temperature.

METHODS OF PREPARATION

Pseudo ternary Phase Diagram

Pseudo ternary phase diagram is important for determination of SNEDDS. It's diagrammatic representation of oil, surfactant and co-surfactant (S mix), water is known as Pseudo ternary phase diagram. It was constructed using the Phase titration and Phase inversion methods. Preparing solutions was step in the process. These solutions, which contained oil and hence had variable surfactant-to-co-surfactant weight ratios, such as 1:1, 2: 1, 3:1, and so on, were vortexed for five minutes, producing in an isotropic mixture. They're being examined to see if they're turbid or clear. The appearance of turbidity in the samples indicates the formation of a coarse emulsion, whereas the appearance of a clear or transparent isotropic solution indicates the formation of a Nano emulsion (SNEDDS) Percentage of oil, S mix and water. Pseudo ternary phase diagram was created using the values. This diagram corner can illustrate a 100% concentration of each phase's material. The diagram is helpful for presenting information on binary mixtures of two components, such as surfactant/cosurfactant, water/drug, or oil/drug.

Components ratio of SNEDDS

S.NO	Formula	Carrier oil	Surfactant	Co-surfactant
1	I	1	1	1
2	II	1	2	1
3	III	1	3	1
4	IV	1	4	1
5	V	1	5	1

CHARACTERISATION OF NANO EMULSION

Morphological Study

Morphological study is important since it provides information about the formulation's external appearance, such as colour, odour, consistency, density, and look. The transmission electron microscope (TEM) has been used to examine globules in the self-Nano emulsifying drug delivery system (SNEDDS).

Centrifugation

Centrifuged thaw cycles between 21°C and +25°C with storage at each temperature for not less than 48 hours are performed at 3500rpm for 30 minutes. The freeze thaw stress test is performed on formulations that do not exhibit any phase separation.

Freeze thaw cycle

The stability of SNEDDS was assessed via freeze thawing. Three freeze-thaw cycles were performed on the formulations, with freezing at 4°C for 24 hours and thawing at 40°C for 24 hours. For 5 minutes, centrifugation was performed out at 3000 RPM. After that, the preparations were examined for phase separation. The formulations that passed this test demonstrated excellent stability, with no phase separation, creaming, or cracking.

Dispersibility Test

A standard USP XXII dissolution apparatus 2 is used to evaluate the efficiency of self-emulsification of oral nano or microemulsions. At 37 0.5 0C, one millilitre of each formulation was added to 500 mL of water. Gentle agitation was provided by a conventional stainless steel dissolution paddle rotating at 50 rpm. The following grading system has been used to visually assess the formulation's in vitro performance.

Table 2: Visual Grading System.

Grade A	Within 30 secs	Rapidly forming nano emulsion which is clear and transparent, high spreadability	Bluish tinge
Grade B	Within 1 min	Rapid nano emulsion formation which is slightly less transparent, less clear	Bluish white tinge
Grade C	Within 2 mins	Rapid nano emulsion formation, which is turbid in nature formed.	Milky white tinge
Grade D	Within or longer than 3 mins	Nano emulsion devoid of or slow to minimal emulsification, with non-uniform distribution of oil droplets	Dull, greyish white tinge having slightly oily appearance
Grade E	Longer than 3 mins	Formulation exhibiting either less, poor or minimal emulsification	Large oil globules

When dispersed in GIT, Grade A and Grade B formulations will remain as nano emulsions. For the SNEDDS formulation, a formulation in Grade C may be recommended.

Droplet Size Analysis Particle Size Measurements

Photon correlation spectroscopy (which analyses fluctuations in light scattering due to Brownian motion of the particles) and a Zeta sizer capable of measuring sizes between 10 and 5000 nm are used to quantify the droplet size of the emulsions. Light scattering is monitored at the 25°C at an 90° angle, after external standardization with spherical polystyrene beads. Even after the 100 times dilution with water, the nanometric size range of the particle is retained then that proves the system's compatibility with excess water.

Viscosity Determination

The SEDDS system is usually administered in soft gelatin or hard gelatin capsules. As a result, it's frequently easy to pour into capsules, and such a system shouldn't be too thick to cause a problem. Brookfield viscometer is used to test the micro emulsion's rheological properties. This viscosities determination conforms whether the system is water/oil or oil/water. If the system has low viscosity, then it's o/w type of the system and if high viscosities then it's w/o type of the system.

Stability Study

The stability study is crucial for determining the Nano emulsion system's quality and purity. The tolerance of a formulation is determined by its stability. The stability of several nano emulsion formulations was evaluated by subjecting them to mechanical stress conditions (centrifugation at 2000-4000 rpm) and storing them at

various temperatures ranging from 4 1 °C to 40 1 °C for various time intervals. The influence of mechanical stress conditions on the Physiochemical stability of the nano emulsion was measured by measuring % phase separation, breaking of the nano emulsion, or any physical change. After 60 minutes of centrifugation at 2000 rpm, there was no discernible change in the formulations.

In Vitro Diffusion Study

Using the dialysis technique, in vitro diffusion tests are carried out to determine the release behaviour of formulation from the liquid crystalline phase around the droplet.

Drug Content

The drug is extracted from pre-weighed SEDDS by dissolving it in a suitable solvent. The drug content in the solvent extract was compared to a standard drug solvent solution using a suitable analytical method.

Bioavailability Study

Based on the self-emulsification properties, particle size data and stability of micro emulsion the formulation is selected for bioavailability studies. The in vivo study is performed to compute the drug after the administration of the formulation. Pharmacokinetic parameters of the utmost plasma concentration (C max) and therefore the drug's corresponding time (t max) following administration is calculated. The following equation to determine the relative bioavailability of the SEDDS formulation.

Relative Bioavailability (%) = (AUC test/AUC reference) X (Dose reference/Dose test).

APPLICATION

Improving Water Solubility of Poorly Water-Soluble Drug

The Self-Nanoemulsifying Drug Delivery System (SNEDDS) is vital to improved water solubility of poorly water-soluble drug and increases oral bioavailability of poorly water soluble drug.

Applications of Nano emulsion in Drug Delivery

Nano emulsions (SNEDDS) have been used in a wide range of drug delivery systems, including cosmetics and transdermal drug delivery, cancer therapy, vaccine delivery, cell culture technology, formulations are important for increasing oral delivery of poorly soluble drugs, ocular and otic drug delivery systems, intranasal drug delivery, parenteral drug delivery and pulmonary delivery of drugs as well as intranasal drug delivery system.

Protection Against Biodegradation

SNEDDS, SMEDDS, and SEDDS are essential for delivering macromolecules such as peptides, hormones, and enzyme substrates, which are inhibitors that must be protected against enzymatic degradation.

CONCLUSION

Plants are our natural healers, and not a single plant on this earth is futile. Nature has something in everything either explored or unexplored till date. On the basis of a number of studies, regarding this weed it is apparent that this habitually ignored, but remarkably shown plant of the arid regions remarkably has a range of benefits related to health issues beside its illegal utilization as a contaminant in mustard oil. In recent years, developments in SNEDDS research have been extensively investigated for improving the solubility and oral bioavailability of class II medicines. The transition of liquid SNEDDS to solid SNEDDS reduced the rate of drug degradation but did not totally eradicate it. Self-Nano emulsifying drug delivery system (SNEDDS) is an Isotropic mixture of oils, surfactants, Co-surfactant (S mix) and co-solvent. Under mild agitation, it emulsifies spontaneously in the aqueous phase to yield fine o/w Nano emulsion. For the formulation of poorly water-soluble medicines, SNEDDS is a good alternative. SNEDDS enhances the dissolution of the drugs due to increased surface area on dispersion and Absorption rate of Drug molecule. To improve bioavailability with future development of this technology SNEDDS will continue to enable novel applications in drug delivery and solve problems associated with the delivery of poorly water-soluble drugs.

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