Bulletin of Pure and Applied Sciences
Zoology (Animal Science), Vol.43B, No.2S,
July-December 2024: P. 641-659

Print version ISSN 0970-0765
Online version ISSN 2320-3188

Original Research Article
Content Available online at: www.bpasjournals.com

"A REVIEW ON MICROEMULSION AND MICROSPHERE : A PROMISING OPTIMIZING TECHNIQUE FOR ADVANCED DRUG DELIVERY SYSTEM "

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ABSTRACT

Microspheres and microemulsions have become adaptable carriers in the field of novel drug delivery systems (NDDS), providing distinct benefits for improved therapeutic results. Because of their spherical shape and micron-sized dimensions, microspheres offer a platform for the regulated and prolonged release of a variety of medicinal substances. They are useful for adjusting drug release patterns and enhancing bioavailability because of their capacity to encapsulate a variety of medications, including both hydrophobic and hydrophilic combinations. Furthermore, the pharmacokinetic advantages of microemulsion microspheres are highlighted, emphasizing their potential to overcome challenges associated with poor drug solubility and limited bioavailability. Case studies illustrating successful applications of this innovative drug delivery approach for specific therapeutic agents are presented, underscoring the versatility and efficacy of microemulsion microspheres across various drug classes. In the context of innovative delivery of drugs, this study examines the uses, formulation techniques, and most current developments in microspheres and microemulsions.Their contribution to resolving issues with medication solubility, stability, and controlled release are noted. Furthermore, the complementary possibility of merging microspheres and microemulsions for an all-encompassing and customised drug delivery strategy is explored.

Keywords: drug delivery system, microemulsion, microsphere, patient, disease,target.

INTRODUCTION

The maximum therapeutic efficacy is obtained by delivering the drug to targeted tissue by right amount and right period. The Novel drug delivery system (NDDS) is a significant approach to deliver drug at appropriate rate to the body's need during the drug therapy or

the disease treatment. The NDDS has ability to control or to monitor drug release rate or to deliver the drug to targeted site or tissue or organ.
The drug must deliver for prolonged period of time and have to take simultaneously in case of chronic patients suffering from severe diseases. The Traditional drug delivery system (TDDS) has been used but it comes with some drawback. In case to overcome the drawbacks of TDDS the NDDS is invented. The various types of controlled release dosage forms are altered and formulated using the NDDS. It increases patients' compliance through prolonged effect and by lowering peak plasma concentration the adverse effect of drug decreased. The controlled release dosage form can be maintained by constant drug level in plasma byreleasing the drug at predetermined rate for extended time period.
The MICROSPHERE and MICROEMULSION as carriers of herbal drugs became a NOVEL approach of controlled release dosage form in NDDS. The MICROEMULISON andMICROSPHERE have gained remarkable attention in PHARMACEUTICALS field as well as particularly in the drug development. The main aim is to enhance the solubility, stability, bioavailability and targeted delivery of herbal drug extracts and bioactive compounds using MICROEMULSION and MICROSPHERE.

3**: MICROSPHERE:**

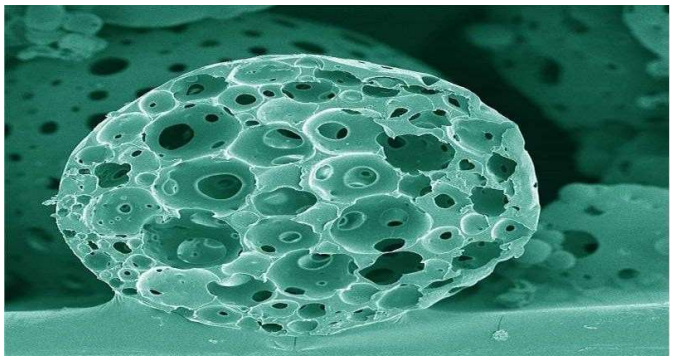

Figure 1: Microsphere

The microspheres are used as the carrier to transport or deliver the drug to the targeted tissue by using controlled release of drug. The targeted and accurate site-specific delivery of drug can be
obtained or achieved by attaching bioactive molecule to the herbal drugs. The bioactive molecule includes – Liposomes, Phytosomes, Nanoparticles,etc. One of these bioactive molecules includes microsphere. Microspheres are used to deliver or to control the release of drugs, vaccines, antibiotics and hormones, etc. One of these bioactive molecules includes MICROSPHERES. Microspheres are used to deliver or to control the release of drugs, vaccines, antibiotics and hormones. (1)
Microspheres are mainly free flowing powder which consists of protein or synthetic polymer. These polymers are biodegradable in nature. The size of these ranges between 1 –1000 um (2). Microsphere are defined as – Monolithic sphere or therapeutic agent which are distributed throughout the matrix or can be defined as: it is a structure made of continues phase of one or morepolymers in which drug particles are dispersed. The particle size ranges between 1 – 1000 nm (3).
Microspheres are multiparticulate drug delivery system which is used in various fields such as OralDrug Delivery, Targeted Drug Delivery, Opthalmic Drug Delivery, Gene Delivery, Cosmetics. There are various approaches are invented for supplying medicinal drug to

targeted tissue for prolonged time and in continues manners. The microsphere as a drug carrier is one of suchstrategies. (2,3)
CLASSIFICATION :

NATURAL POLYMER

SYNTHETIC POLYMER

NATURAL POLYMER:
Natural polymers are also of two types which includes following:a . Carbohydrates
b. Protein- albumin, collagen, gelatin

c. Chemically modified – poly starch (1,4,5)

SYNTHETIC POLYMER:

synthetic polymers are also divided into two types which are as follows-

Biodegradable Polymers:

Lactides, Glycosides & their co polymers
Poly alkyl cyano Acrylates

Poly anhydrides

Non-biodegradable Polymers:

Poly methyl methacrylate (PMMA)

Acrolein

Glycidyl methacrylate

Epoxy polymers (1,6,7)

4: TYPES OF MICROSPHERES:

BIO-ADHESIVE MICROSPHERES

FLOATING MICROSPHERES

RADIOACTIVE MICROSPHERE

MAGNETIC MICROSPHERE

POLYMERIC MICROSPHERE

BIO ADHESIVE MICROSPHERE : The definition of adhesion is the drug's ability to attach to a membrane through the use of the water-soluble polymers' sticky characteristic.

Bioadhesion is the phrase used to describe the adherence of a medication delivery device to a mucosal membrane, such as the nasal, rectal, ophthalmic, or buccal. These microspheres havea longer residence period at the application site, which results in close contact with the absorption site and improves the therapeutic effect. (8,9,10)

FLOATING MICROSPHERE: Because the bulk density of floating kinds is lower than that of gastric fluid, they float in the stomach without slowing down the rate at which the stomach empties. If the system is floating on gastric content, it increases gastric residencyand generates fluctuations in plasma concentration. The medicine is released gradually at the desired rate. Additionally, it lessens the likelihood of dosage dumping and striking. Another way it lowers dose frequencies is by producing a sustained therapeutic effect. Ketoprofen medication used in this manner(1,11,12)

RADIOACTIVE MICROSPHERE : In radiological immobilisation 10–30 nm microspheres are encountered; they tap into the first capillary bed because they are larger
than capillaries. They are injected into the arteries that supply the targeted tumour. Under all these circumstances, radioactive microspheres provide strong radiation doses to the intended regions without endangering the healthy tissues nearby. Different from medicine delivery systems, it functions from inside a radioisotope usual distance instead of releasing radioactivity from microspheres. There are three types of radioactive microspheres: α, ß, andγ emitters.(13,14)

MAGNETIC MICROSPHERE : The ability to deliver the medication precisely to the required spot makes this kind of delivery method crucial. In this situation, a higher amount offreely circulating medicine will be replaced by a smaller amount of magnetically focused drug. In reaction to a magnetic field, chitosan, dextran, and other integrated materials used in magnetic microspheres exhibit magnetic properties. (2,3,15)

POLYMERIC MICROSPHERE :

There are different types of polymeric microsphere and are classified as follows -

Biodegradable Polymeric Microsphere

Synthetic Polymeric Microsphere

Biodegradable Polymeric Microsphere: Natural polymers like starch are biocompatible, biodegradable, and bio adhesive, hence they are used in formulation of dosage form. Biodegradable polymers have a high degree of swelling in aqueous media, which prolongs their residence duration in contact with mucous membranes and causes gels to develop. The rate and extent of medication release are controlled by the polymer concentration and the release pattern throughout time. The primary drawback is the complex drug loading performance of biodegradable microspheres in clinical settings, which makes controlling drug release challenging.Nonetheless, they have a wide range of uses in microsphere-based therapy. (2,3)
Synthetic Polymeric Microsphere: Synthetic polymeric microspheres are a popular choice for clinical applications. Additionally, it has been shown to be safe and biocompatible when utilised as a bulking agent, filler, embolic particles, drug delivery vehicles, etc. However, the primary drawback of these microspheres is their tendency to disperse from the injection

site, which increases the risk of embolism and additional organ damage. (16,18))

CRITERIA FOR MICROSPHERE PREPARATION:

By using the microencapsulation process, solid, liquid, or gaseous materials can be included into one or more polymeric coatings (1,17). The manufacture of distinct microspheres using different procedures is dependent on factors such as particle size, mode of administration, drug release duration, and the previously mentioned factors connected to rpm, drug ofcross-linking, evaporation time, coprecipitation, etc (1,19)

The criteria for microsphere preparation involves - (1,20)

The capability to add the medication at suitably high doses

Regulated particle size and dispersibility in aqueous injection vehicles

The preparation's stability after synthesis and its therapeutically acceptable shelf life

Chemical modification susceptibility

Biocompatibility combined with regulated biodegradability.

5: METHOD OF PREPERATION -

Emulsion Solvent Evaporation Technique 2.Coacervation Method

Spray Drying Technique

Emulsion Cross Linking Method

Single emulsion techniques

Double emulsion technique

Emulsion Solvent Evaporation Technique: This method involves dissolving the medication in a polymer that has already been dissolved in chloroform, and then adding the resultant solution to an aqueous phase that contains 0.2 percent sodium PVP as an emulsifying agent. Sree Giri Prasad et al,1961–1972 described how the above-mentioned combination was agitated at 500 rpm to release the medication and polymer (eudragit), whichthen turned into small droplets that hardened into rigid microspheres b solvent evaporation. The mixture was then collected by filtration and cleaned with water that had been demineralized and dried for 24 hours at room temperature (1)

Coacervation Method: Co-acervation thermal change: A weighed quantity of ethyl cellulose was heated to 800 C while being vigorously stirred and dissolved in cyclohexane.After that, the medication was thoroughly crushed and mixed into the solution above, and phase separation was achieved by lowering the temperature and utilising an ice

bath. The previously mentioned substance was then air dried, rinsed twice with cyclohexane, and sieved (sieve no. 40) to produce individual microcapsules. Coacervation NON solvent addition: developed by dispersing the medication into a closed beaker and swirling it with a magnetic stirrer for six hours at 500 rpm after weighing a quantity of ethyl cellulose was dissolved in toluene containing propylisobutylene. The stirring was then maintained for fifteen minutes. Phase separation is then carried out five times using petroleum benzoin(1,2)

Spray Drying Technique: Prior to being spray dried, the polymer is first dissolved in an appropriate volatile organic solvent, such as acetone or dichloromethane. Next, high-speed homogenization is used for dispersing the chemical in a polymer solution. After that, a

heatedair current vaporises this dispersion. The process of atomization produces minute droplets or fine mist, from which the solvent instantly evaporates to form microspheres with a diameter of one to one hundred micrometres. A cyclone separator is used to separate the microparticlesfrom the heated air, and vacuum drying is used to eliminate the solvent residue. The procedure's feasibility of action in aseptic circumstances is one of its key advantages. Porous microparticles are formed as a result of this quick process (1,2)

Emulsion Cross Linking Method: With this technique, the aldehyde group of crosslinking agents forms a crosslink with the reactive functional group of polymers. This technique involved emulsifying the polymer aqueous solution in the oily phase to create a water-in-oil (w/o) emulsion. Using an appropriate surfactant, such as span 80 or dioctyl sodium sulphosuccinate, aqueous droplets were stabilised. To harden the droplets, the stable emulsion was cross-linked using a suitable cross-linker, such as glutaraldehyde. To get rid of any remaining oil residue, microspheres were filtered and repeatedly cleaned with petroleum ether or hexane. After washing them with water to remove the cross-linkers, they were let to dry for a full day at room temperature. (1,2)

Single emulsion techniques: You may make a range of carbohydrates and proteins with this procedure. The natural polymers are first dissolved in an aqueous phase and then distributed in a non-aqueous phase called the oil phase. That is the process's first stage. Thereare two ways to cross-link the subsequent action as follows :

Cross-linking by heat:The dispersion can be added to heated oil, however this is inappropriate for thermolabile medications

- Chemical cross-linking agent:

with the use of chemicals such as formaldehyde, diacid chloride, glutaraldehyde, etc. When used during preparation and then centrifuged, cleaned, and separated, it is harmful to the unwarranted exposure of active components to chemicals. Apply w/o emulsion of the chitosan solution (in acetic acid) to the liquid paraffin that has a surfactant in it. A 25 percent solution of glutaraldehyde is used as cross-linking agent to create microsphere (2)

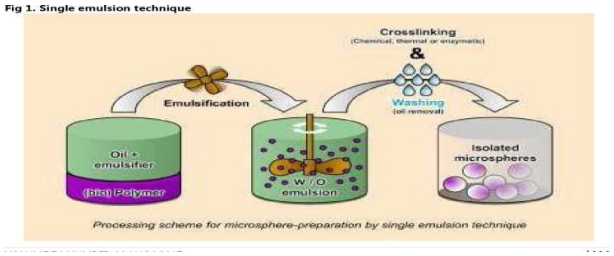

Figure 2: Single Emulsion Technique

Double emulsion technique: It involves creating multiple emulsions; for example, to make W/O/W, the original w/o emulsion is poured into an aqueous polyvinyl alcohol solution. For thirty minutes, this w/o/w emulsion must be constantly stirred. Water should be added to the emulsion gradually over the course of 30 minutes. Filtration-based microcapsule collection, followed by vacuum-drying. Water-soluble medications, peptides, proteins, and vaccinations are all excellent candidates for it. Both synthetic and natural polymers can be employed in this procedure. A continuous organic lipophilic phase distributes the aqueous protein solution. The active components in this protein solution will be present.27 Disperse inoil/organic phase homogenization/vigorous, i.e., after the initial emulsion is prepared, add thePVA (Poly Vinyl Alcohol) aqueous solution, (2)

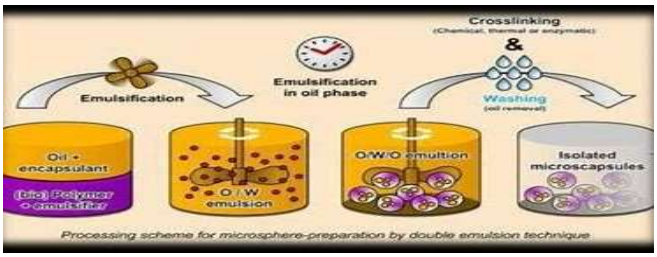

FIGURE 3: Double Emulsion Technique

6: ADVANTAGES OF MICROSPHERE :

Microspheres offer consistent and extended therapeutic benefits.
Increased drug use will increase bioavailability and decrease the frequency or severity of sideeffects. (1)
It decreases dose frequency which leads to better patient compliance
The particles were small and spherical, so they could be injected into the body.

All aspects of microsphere morphology are dependent on controlled variations in drugrelease and breakdown (2)
To make oils and other liquids easier to handle, they are solidified
Modify the drug release and reactive core's separation from other substances.
Dependable way to modify the drug's target site and deliver it specifically, while maintainingthe desired concentration at the place of interest without causing side effects
Restrict the core's responsiveness towards the external environment.

It has been discovered that factors such as microsphere size, surface charge, and surfacehydrophilicity affect how particles behave in vivo.
Reduce the rate at which the volatile core material evaporates.
protects the GI tract from the medication's irritating effects

Compared to larger polymer implants, biodegradable microspheres have the advantage of notrequiring surgery for placement or removal.

Drug release rates are regulated by biodegradable microspheres, which reduces harmful sideeffects and does away with an inconvenience of repeated injection (3)

DISADVANTGES OF MICROSPHERE :

The rate of release through the gastrointestinal tract and food are two examples of variablesthat can affect the controlled release dosage form's release rate.
Variations in the rate of release between doses

Since controlled release formulations often have larger drug loads, any compromise to thedosage form's release properties could potentially be hazardous.
These dosage forms shouldn't be chewed or crushed. (1,21)

Application of microsphere

Using Microspheres to Deliver Vaccines: Protection against the microorganism or its harmful product is a need for any vaccine. The optimal vaccination should meet the followingcriteria: it should be safe, effective, affordable, and easy to administer. Safety and minimisingnegative reactions are complicated topics (1,22). The technique of application

has an immediate effect on both the safety factor and the level of antibody response. One potential
solution to address the shortcomings of conventional vaccines is the use of biodegradable delivery vehicles for parenteral vaccinations. (1,23). Parenteral (subcutaneous, intramuscular,or intradermal) carriers are of interest because they provide certain benefits such as:
Adjuvant activity results in improved antigenicity

Altering the release of antigens

Antigen stabilisation.

Microparticulate Carriers for Targeting: The well-established principles of site-specific medication delivery, or targeting, is receiving a lot of attention. The drug's ability to bind to and specifically interact with its target receptors determines how effective it is as a treatment.The core of a drug's activity is its capacity to exit the pool in a repeatable, effective, and targeted manner through the employment of a carrier system. When particles are placed in discrete anatomical compartments, they become retained due to the physical characteristics ofthe surrounding environment or the biophysical interaction between the particles and the target tissue's cellular composition. (3)
Imaging: The microspheres have been utilised for targeting and have undergone substantial research. Microspheres that have been radiolabelled can be used to imaging a variety of cells,cell lines, tissues, and organs. The variety of microsphere particle sizes plays a crucial role in deciding which locations to image. The intravenous particles will get stuck in the lung's capillary bed if they are injected somewhere other than the portal vein. This phenomenon is used with tagged human serum albumin microspheres for scintiographic imaging of lung tumour masses (3)
Monoclonal Antibodies Mediated Microspheres Targeting : Microspheres targeted by monoclonal antibodies are considered immunological microspheres. Selective targeting to particular areas is accomplished with this targeting technique The molecules known as monoclonal antibodies are very selective. Monoclonal antibodies (Mabs) with their high specificity can be used to direct microspheres containing bioactive compounds to specified locations. Covalent coupling allows Mabs to be bonded to the microspheres directly. The antibodies can be connected to the free aldehyde, amino, or hydroxyl groups on the microspheres' surface. The following techniques can be used to affix the Mabs to the microspheres:
Adsorption that is non-specific
Sorption

Straight connection

Reaction through reagent (3)

Topical Porous Microspheres: Microsponges are a type of porous microsphere that consist of several interconnected voids with particle sizes ranging from 5 to 300 µm. These porous microspheres with active ingredients can be added to formulations like creams,lotions, and powders. Additionally, these microsponges, which have the ability to entrap a wide range of active ingredients like emollients, fragrances, essential oils, etc., are used as thetopical carry system. The non-collapsible structures of microsponges have a porous surface that allows for the regulated release of active substances. (1)

MICROEMULSION

A thermodynamically stable, isotopically transparent dispersion of two immiscible liquids, such as water and oil, stabilized by an interfacial coating of surfactant molecules is referred toas a "micro- emulsion." The phrase was first used by Schulman and Co. Micro-emulsions appear as clear or translucent solutions due to their small particle sizes. They have particles that are between 10 and 300 nm in size. (28)
Structure:

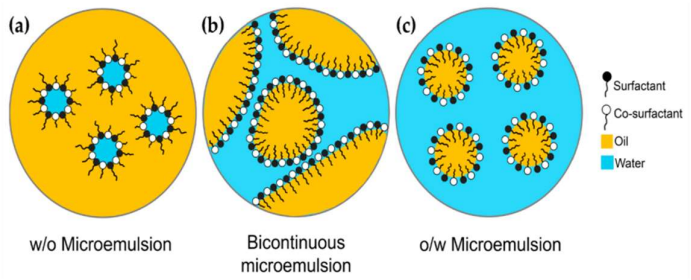

FIGURE : MICROMULSION

The three structural types of micro emulsions are oil in water (O/W), water in oil (W/O), andbi-continuous micro emulsions. Micellar emulsions, another name for micro emulsions, are dynamic systems where the interface varies naturally and continuously. (29)
:TYPES:

While O/W micro emulsions form while oil droplets are dispersed in th continuous aqueous phase, W/O micro emulsions discuss water droplets in the continuous oil phase.Thermodynamically stable micro emulsions are found only in specific, well-defined conditions. Winsor states that there are four different kinds of micro emulsion phases that canbe found in equilibrium; these phases are also known as Winsor phases. They are :
Winsor I, or oil-in-water micro emulsion
Winsor II, or water-in-oil micro emulsion
Winsor III or continuous micro emulsion
Winsor IV, a single-phase homogeneous mixture (30,31)
Winsor or micro emulsion of oil in water :
In micro emulsions of the oil-in-water type, the continuous phase, or internal phase, is formedby a film of surfactants (and sometimes co-surfactants) encircling the oil droplets. This kind of micro emulsion has a bigger interaction volume than w/o micro emulsions.
Winsor or water in oil micro emulsion I :
A film of surfactants, or possibly co-surfactants, surrounds the oil droplets in oil-in-water micro emulsions, forming the continuous internal phase dispersed throughout the water.Compared to w/o micro emulsions, this kind of micro emulsion often has a bigger interaction volume.
Winsor ill or bi-continuous micro emulsion :
The amount of oil and water in a bi-continuous micro emulsion system is equal; in this instance, the two phases are continuous. When water and oil are mixed, an uneven channel forms that resembles a “sponge.”
Winsor IV or single-phase homogeneous mixture :
The oil, water, and surfactants are homogeneously mixed in a single phase homogeneous mixture, also known as Winsor IV. (30,31)

10: Components of microemulsions:

Even though oils and surfactants are freely accessible, their use is restricted due to their toxicity, irritability, and unclear mode of action. It is imperative that the oils and surfactant used in the microemulsion formulation process are safe, nontoxic, and appropriate for use in clinical settings. Selecting the component that is "generally regarded as safe" (GRAS) is the main goal. Despite the abundance of oils and surfactants on the market, their use in the creation of microemulsions is restricted due to their possible toxicity, irritability, and unclear mechanism of action.The oils and surfactant used in the formulation process need to be

biocompatible, nontoxic, and therapeutically acceptable in order to produce a mild and nonaggressive microemulsion. Additionally, emulsifiers must be used within the appropriate concentration ranges.

Oil Phase

Aqueous Phase

Primary Surfactant

Secondary Surfactant (co-surfactant)

.Co-solvent

(32,44) 1.Oil

Phase-

Oil is one of the most important components of a micro emulsion because it has the ability to solubilize the required dosage of the lipophilic drug and increase the amount of lipophilic medication delivered by the intestinal lymphatic system. Oil is defined as any liquid having low polarity and low water miscibility. Mineral oil, vegetable oil, cyclohexane, and toluene are a few examples of this phase. Among the most important excipients in the formulation is the oil, which can solubilize the necessary dosage of the lipophilic medicine and increase the amount of lipophilic drug delivered by the intestinal lymphatic system based on the molecular makeup of the triglyceride. As a result, the gastrointestinal tract absorbs more material. Curvature is affected by the oil component because it has the ability to penetrate and swell the tail group region of the surfactant monolayer. The tail group region swells morebecause of short chain oils penetrating it more deeply than long chain alkanes do, causing negative curvature and decreasing effective HLB.

The various oils listed below are typically used to formulate microemulsion

Lauric, myristic, and cupric acids are examples of saturated fatty acids.

Unsaturated fatty acids: linoleic, oleic, and linolenic acids.

Lauric, myristic, and oleic acid fatty acid esters—ethyl or methyl esters. (30)

Aqueous Phase:

Preservatives and hydrophilic active ingredients are typically found in the aqueous phase.Buffer solutions are occasionally employed as the aqueous phas

Primary Surfactant : The chosen surfactant must be able to significantly lowerinterfacial tension in order to facilitate the dispersion process during the preparation of the microemulsion. It should also possess the appropriate lipophilic character to give the correct curvature at the metafacal region and be sufficiently flexible to easily deform around the

roplets. A micro emulsion system's stabilizing surfactant could include: (1) Not ionic, (I) Zwitterion, 19/8 cationic, or (IV) anticoagulants. (44)

Dispersants- . The principal justifies behind the use of cosurfactants in microcapsule formulation are as follows: They offer the interfacial film sufficient flexibility to absorb different curvatures required to generate microemulston under a wide range of circumstances.Alcohols with short to medium chain lengths (0C8) result in more fluid and less tense surfaces between fibers (30,32)

Co solvents

Relatively high surfactant concentrations are required for optimal micro emulsion production (usually greater than 30% w/w). Organic solvents such as ethanol, propylene glycol (PG), andpolyethylene glycol (PEG) are suitable for oral administration because they provide for the large-scale dissolution of the drug or hydrophilic surfactant in the lipid bas These solventscan even act as co-surfactants in microemulsion systems.(32,44)

11: Methods of microemulsions:

Method of Phase Titration

Microemulsions are made by the phase titration method, also known as the spontaneous emulsification method. A useful technique for studying the complex web of interactions that can occur when different substances are combined is phase diagram construction.Along with microemulsions, other association structures such as emulsion, micelles, lamellar, hexagonal, cubic, and various gels and oily dispersions are formed based on the chemical composition and concentration of each component.)The area can be categorized as either w/o or o/w microemulsion based only on how much water or oil makes up the region (35)

Method of phase inversion

Phase inversion of the micro emulsion technique: An o/w micro emulsion at low temperaturebecomes a w/o micro emulsion by varying the system's temperature. For non-ionic surfactants, physical alterations as well as changes in particle size could have an impact on drug release both in vitro and in vivo. This is also known as the transitional phase inversion method. As the system cools and maintains surface tension while crossing the zero-point spontaneous shape, oil droplet dispersion forms more easily. This phase inversion method may result in a transition in the radius due to changes in the water volume fraction. A w/o micro emulsion can be stabilized by temperature by raising the proportion of water in the mixture and the amount of surfactants.(36)

12: Factor affecting formulation of micro emulsion technique

Property of oil phase:

Surfactants are divided into two groups: lipophilic and hydrophilic groups. One of the hydrophilic single chain surfactants, cetylethyl ammonium bromide, tends to form an o/w micro emulsion and completely dissociates in diluted solution. When surfactant is used in high concentrations or in the presence of salt, the degree of polar group dissociation decreases, potentially leading to a w/o type system. Curvature is also influenced by the oil phase, which penetrates and swells the surfactant monolayer's tail group region. Tail group swelling is the cause of this increased negative curvature to w/o micro emulsion (32)

Packing Ratio

The type of microemulsion is determined by the surfactant's HLB, which affects packing and film curvature. The examination of the film's curvature to look for surfactant associations thatcause microemulsion formation.(32)

Temperature

The effective head group IC surfactants are highly dependent on temperature. Because of their hydrophilicity, they form a normal o/w system at low temperatures. they form w/o systems at higher temperatures because they are lipophilic. Microemulsion forms a bicontinuous structure at an intermediate temperature when it coexists with excess water.(32)

The Chain length, Type and Nature of Co-surfactants

Alcohols are widely used as co-surfactants in micro emulsions. Longer chain co-

surfactant,on the other hand, favors w/o type because alcohol swells the chain region more than the head region. Shorter chain co-surfactant adds a positive curvature effect because alcohol swells the head region more than the tail region, making it more hydrophilic and favoring o/wtype. Curvature is also influenced by the oil phase, which penetrates and swells the surfactant monolayer's tail group region. Tail group swelling is the cause of this increased negative curvature to w/o micro emulsion. (32)

13: Evaluation Of Micro emulsions

Visual Inspection

2.Thermodynamic

Stability

Measurement of P^H

Viscosity Measurements

Zeta Potential Determination

Particle Size Determination

Drug Content Uniformity (28)

Visual Inspection

Following each addition of water to the mixture of oil, surfactant, and co-surfactant, a visual inspection was conducted. By using visual inspection, the samples were classified as micro emulsion, emulsion, or gel formation.(28)

Thermodynamic Stability

To solve the metastable formulation issue. Tests of thermodynamic stability were conducteda)Centrifugation-

To guarantee physical stability, the formulation was centrifuged for 30 minutes at 3500 rpm.b)Stress Test-

The purpose of these tests was to determine the ideal micro emulsion formulation for harsh environments. Stress was applied for 48 hours at 4 °C and 45 °C for six cycles, and then for 48 hours at 25 °C and 21 °C for roughly three cycles. We examined the samples for phase separation, cracking, and coalescence.(28)

Measurement of pH

Using a calibrated pH meter (Digital Potentiometer Model EQ-601 Equip-Tonics), the electrode was submerged directly into the dispersion to determine the pH values of the optimized formulation.(28)

Viscosity measurements

The optimized formulation's viscosity was measured using a Brookfield viscometer (DV-E Brookfield Viscometer Model-LVDVE) without any dilution.(28)

Zeta potential Determination

Zeta sizer was used to measure the zeta potential of the samples. Samples were put into single-use, transparent zeta cells, and the outcomes were noted. Cuvettes were cleaned with methanol and rinsed with the sample that was going to be measured prior to each experiment,before being filled with fresh material.(28)

Particle Size Determination

The drug-loaded micro emulsion’s mean particle size and particle size distribution were ascertained by. Nanoparticle analyzer Horiba SZ-100, operating at 28°C. It gauges the variation in scattered light intensity brought on by particle movement. Every sample was measured three times.(28)

Drug Content Uniformity

A 100 mg medication micro emulsion was dissolved in 100 ml 0.IN HCI in a volumetric flask. After filtering the solvent, 1 milliliter was taken in 50 milliliters of volumetric solution,diluted to the appropriate level with 0.1N HCI, and measured at 295 nm using spectroscopy. The drug's standard calibration curve was used to determine the

concentration in milligrams per milliliter. Three separate drug content analyses were performed for every formulation batch.(28)

: The Micro emulsion System's Advantages:
Because of their improved thermodynamic stability, micro emulsions are simple to prepare andrequire no energy.
Micro emulsion formation is reversible.

They can become unstable at low or high temperatures, but the micro emulsion reforms when thetemperature goes back into the stable range.
Micro emulsions enable the system to self-emulsify and are a thermodynamically stablesystem.(28,30,)
In comparison to emulsions, micro emulsions are less viscous

Drugs that are insoluble in both aqueous and hydrophobic solvents can be dissolved by usingmicro emulsions, which function as super solvents for drugs.
Possessing the capacity to transport hydrophilic and lipophilic medications.

Hydrophilic or lipophilic drugs may be stored in the dispersed phase of lipophilic or hydrophilic(O/W or W/O micro emulsions) micro emulsions, respectively.
The efficacy of a drug can be increased by using micro emulsion delivery systems, whichminimizes side effects by reducing the total dose.(29,44)
The Micro Emulsion Systems Disadvantages :
consuming insufficient solubilizing volume when using components that melt quickly
Large amounts of surface-active agents are required for each evirating droplet.
Temperature and hydrogen ion concentration are two conservational structures that impedemicro-emulsion constancy.(28,48)
The micro-emulsion system's limitations
The use of micro-emulsion systems in pharmaceutical submissions is restricted for the following reasons:
Phase separation is a prevalent issue in the context of micro-emulsions.

The concentrations of the surfactants and co-surfactants need to be kept low due to toxicity concerns.
Due to the toxicity of the formulation, micro-emulsion systems are not very suitable for intravenous use, and there have only been a very small number of studies conducted on them to date.
In order to lessen the toxicity of the micro-emulsion systems, "Generally-Regarded-as-Safe" (GRAS) class surfactants must be used. (30,44)
Applications of Micro emulsion
Micro emulsions in Pharmaceuticals-

Parenteral administration: Due to the extremely low amount of drug that is actually delivered to the intended site, parenteral administration (particularly via the intravenous route) of drugs with limited solubility poses a significant challenge to the pharmaceutical industry. When administered parenterally, micro emulsion formulations offer definite advantages over macro emulsion systems due to the line particle, which causes micro emulsion to be cleared more slowly than coarse partied emulsion and to have a longer residence time in the body. Parenteral administration can be accomplished with either /w

or W/O micro emulsion. (32)
The administration of Oral Compared to conventional coral formulation, oral administration of micro emulsion formulations has a number of advantages, such as better clinical potency, lower drugpricity, and increased absorption. Thus, it has been suggested thatmicro emulsion is the best way to administer medications like antibiotics, diuretics, and steroid hormones.(30)
The physiological functions of pharmaceutical drugs containing proteins and peptides are extremely specific and powerful. But the majority is challenging to take orally, with less than10% oral scalability in traditional non-micro emulsion formulations. When taken orally, they
typically have no therapeutic effect. The majority of protein medications are only offered in parenteral formulations due to their poor oral bioavailability. Nevertheless, parenteral administration of peptide medications results in an exceptionally brief biological half-life, necessitating multiple dosing.(32)
Topical drug administration: This approach can be superior to other approaches for a number of reasons, including the avoidance of the drug's hepatic first pass metabolism and associated toxicity effects. Either is the medication's ability to target the affected area of the skin or eyes and deliver it directly.(48)
Ocular and pulmonary delivery: In order to treat eye conditions, medications areprimarily administered topically. Micro emulsions have been studied for secular administration in order to decrease the absorption of poorly soluble medications and achievea desired release profile. (48)
Micro emulsions in Biotechnology-The use of micro emulsions in biology Pure organic or aqua-organic media are used for a variety of enzymatic and bio catalytic reactions. Such reactions also take place in biphasic media. The biocatalysts become desaturated when pure polar media is used. Utilizing water-resistant media has some benefits. Low-water-content enzyme displays and has:
Greater solubility in reactants that is non-polar.

The potential to change the thermodynamic equilibrium to condensations advantage.

Enzyme thermal stability has improved, allowing reactions to occur at higher temperatures.

Numerous enzymes, such as lipases, esterase's, dehydrogenases, and oxidases, frequently work in hydrophobic microenvironments within cells. Many enzymes in biological systems function at the interface between hydrophobic and hydrophilic domains, and polar lipids and other naturally occurring amphiphilic typically stabilize these interfaces. Numerous reactions,including the synthesis of esters, peptides, and sugar acetyls transesterification; different hydrolysis reactions; and steroid transformation, have been catalyzed by enzymes in micro emulsions. Lipases are the most frequently utilized class of enzymes in micro emulsion-basedreactions. (32)
Solubilization of Drug In Micro emulsion- Drug solubility in micro emulsion Interesting physicochemical characteristics of micro emulsions includes high solubilization power, low
viscosity, transparency, and thermodynamic stability. These unique characteristics of micro emulsion make it a promising candidate for drug delivery systems. Drugs from various categories can be dissolved in micro emulsion systems to improve their therapeutic effectiveness.(32)
Micro emulsions as Coating and Textile Finishing-Because micro emulsified resins solve many of the drawbacks of more conventional water-based systems without posing the same

risks to human health and the environment as solvent-based coatings, the coating application area of micro emulsion technology is a very promising and quickly expanding field. When consistency and uniformity of the final product are required, micro emulsions are the best option because of their stability and small droplet size. Compared to paint formulations made with emulsions, those made with micro emulsions have demonstrated greater stain resistance,better color intensity, and higher scrub resistance.
There are, in theory, three ways to use micro emulsions for coating applications:

For employing micro emulsified monomers to create micro dispersions,

To introduce non-water-soluble polymers into aqueous solutions,

For using polymerization in a w/o system to achieve particular effects.(32)

Micro emulsions in Cosmetics- Emulsions are frequently used in cosmetic applications, such as skin care products, where water serves as the continuous phase. It is anticipated that the micro emulsion formulation will cause the skin to absorb the substance more quickly. Cost and safety (many surfactants cause skin irritation when used in When creating micro emulsions, high concentrations and careful ingredient selection—such as using surfactants and surfactants—are crucial.
Specialized micro emulsions have been created as hair care products. They contain an acid and/or a metal salt along with a nonionic surfactant called amino-functional polyorganosiloxane. In micro emulsions, flavored oils and fragrances can be dissolved. Therehave been reports of transparent and translucent cosmetic micro emulsions made from silicone oils through emulsion polymerization. However, due to silicone oil's poor solubility in the surfactants, these products lack thermodynamic stability.Condensation-method-prepared ultra-fine emulsions have good stability, safety, and controllable droplet size, which make them useful for use in cosmetic and medicinal products. Since ultrafine emulsions are O/W emulsions with droplet sizes comparable to micro emulsions, they can be thought of as thermodynamically unstable
microemulsions.Investigations are conducted into the use of commercial nonionic surfactantsand cosmetic oils in cosmetic formulations for skin care products.(32)
Micro emulsion in Food -There are natural micro emulsions in some foods. Food preparation has thus made use of micro emulsions, a functional form of lipids. In the intestine, micro emulsions are created during the breakdown and absorption of fat. However, one area of food technology that has received little attention is the possibility of intentionally creating micro emulsions and using them as instruments in food production. In the field of food technology, excellent component solubilization, enriched reaction efficiency, and extraction techniques have a lot of promise. Due to the potential for a synergistic interaction between lipophilic and hydrophilic antioxidants, one significant use of micro emulsion is to increase the effectiveness of autoxidation. It is well known that soybean oil can be effectivelyprotected when it is contained in a 12-phase solution created by mixing water with sunflower oil monoglycerides. Enough monoglycerides to triglycerides must be present in the L2-phase at a ratio of roughly 1:5 (about 5 weight percent). Compared to traditional methods of dissolving or dispersing antioxidants in oils, 200 ppm of tocopherol in the oil and 5%ascorbic acid in the reverse micelles give a dramatic antioxidant effect in such a system. The same micro emulsion-based technique has also been applied to fish oils to produce anantioxidant-protective effect. Water has been replaced with glycerol to further increase the productivity
Utilizing Microemulsion These are a few applications for medicine delivery that micro

emulsions have. For the past 20 years, micro emulsions have been utilized as a drug delivery system due to their advantages in thermodynamic stability, optical clarity, and ease ofpenetration.(32)

Parenteral Delivery- Formulating lipophilic and hydrophilic drugs for parenteral delivery has proven to be difficult. The formulation of w/o micro emulsions is useful for the parenteral delivery of sparingly soluble drugs when it is not necessary to administer suspensions.Regular drug administration requires a high concentration. They have greater physical stability in plasma than liposomes or other vehicles, and the internal oil phase is more resistant to drug leaching. For parenteral administration, a variety of medications that areonly weakly soluble have been mixed to form o/w micro emulsions. To create an almost balanced middle phase in micro emulsions by maintaining a flexible surfactant film, von Corse want, and Thorne adopted a different strategy in which parenterally acceptable co surfactants, such as polyethylene glycol (400)/polyethanol glycol (600) 12-hydroxy stearate ethanol, were used in place of C3 and C4 alcohols. . Regular drug administration requires a

high concentration.They have greater physical stability in plasma than liposomes or other vehicles, and the internal oil phase is more resistant to drug leaching. Several poorly soluble medications have been blended to produce o/w micro emulsions for parenteral delivery(30,48)

Oral Delivery - It has been challenging to develop effective oral delivery systems because drug instability or poor solubility in gastrointestinal fluid can limit drug efficiency. Particularly for BCS class II/class IV medications, the micro emulsions enhance the solubilization of poorly soluble pharmaceuticals. Likewise, resolve the bioavailability problems related to dissolution. the presence of polar, non-polar, and interfacial domains. Hydrophilic drugs are encapsulated with different solubility macromolecules. By protecting the combined drugs from agonist oxidation, enzymatic degradation, and increased membrane permeability, these mechanisms have been in place. For oral delivery, there are two commercially available microemulsions: Sand immune Neural (cyclosporine A) and Fort vase (saquinavir). Nervier, Ritonavir, etc. In gastrointestinal fluids, increasing the solubility of medications that are poorly soluble in water may increase their oral bioavailability and be helpful in the creation of micro emulsions.(29,48)

Topical Delivery- One advantage of drugs administered topically is that they do not undergo the hepatic first-pass metabolism and related toxicity effects. These make it possible to administer the medication to the skin and eyes directly, where it is required. the area wherethe most research has been done on the penetration of medications through the skin. To increase drug penetration, these studies include both lipophilic (oestradiol, finasteride, ketoprofen, meloxicam, felodipine, triptolide) and hydrophilic (5-fluroracil, diphenhydramine, Apo morphine hydrochloride, hydrochloride, tetra Caine hydrochloride, methotrexate) drugs. The creation of micro emulsions requires a high surfactant concentration. When applying makeup for extended periods of time, particular consideration should be given to aspects that irritate the skin. (32,29,)

Nasal Delivery -Delivery by Nasal Micro emulsions has recently been researched as a delivery mechanism to improve medication absorption via the nasal mucosa. Mucoadhesive polymers contribute to extended residence duration on the mucosa. Leanly and colleagues examining the impact of diazepam on the status of emergency treatment. (48,29,32)

CONCLUSION :

This review is an attempt to present a concise profile of microsphere and microemulsion as drug delivery system. Because microspheres and microemulsion have better patient enforcement and targeting accuracy than other medication delivery technologies, they are

safer to utilize.The most popular drug delivery method is the use of microspheres due to its benefits in terms of bioavailability, lower dose frequency, improved stability, continuous and controlled-release action, and dissolving rate. Research on drug delivery via microemulsions is a promising field with the goal of obtaining regulated release for medication targeting to different body locations and for increased bioavailability

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