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Review Article

Novel Drug Delivery System: Brief Review

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Abstract

Current developments in our knowledge of the pharmacokinetic and pharmacodynamics behaviour of drugs provide a more logical framework for designing the best possible drug delivery system. It is understandable that multidisciplinary efforts will play a major role in the success of drug delivery research in the future. Any therapeutic agent that has the potential to be safer, more effective, and use an enhanced drug delivery mechanism offers pharmaceutical companies significant marketing prospects as well as advancements in the treatment of illnesses. Since ancient times, humans have utilized plants as food and medicine, viewing them as nature's solutions. The underlying idea is that every sickness has a remedy that is concealed in better ways using ayurvedic, homeopathic and allopathic. However, in order to promote sustained release, improve patient compliance, etc., the way herbal medications are delivered must also be modified. Because of challenges with processing, standardizing, extracting, and identifying them, herbal medications had historically been unable to draw scientists' attention to the development of novel drug delivery methods. However, with today's technological advancements, the development of herbal revolutionary drug delivery systems is made possible by novel drug delivery systems (NDDS). It is possible to achieve protection against toxicity, stability enhancement, enhanced bioavailability, and protection against chemical and physical degradation of herbal formulations through the application of advanced procedures which must give the result in better or faster way. In this review we will get the method of preparations of NDDS and the Application of NDDS.

Keywords: Herbal Drugs, Enhanced drug delivery, Phytosomes, Nanoparticles, liposomes.

INTRODUCTION

A herbal formulation is a dosage form that contains one or more raw or processed herbs in specified quantities to offer particular health, nutritional, or cosmetic benefits. Plant parts, whole plants, or broken or chopped plants are subjected to processes including distillation, extraction, expression, fractionation, purification, concentration, or fermentation to create herbal medicines. These consist of separated or tinctured botanical resources, processed exudates, expressed juices and necessary oils[1]. The efficacy of a medication can be significantly impacted by the way it is administered. Certain medications have an ideal concentration range where the greatest therapeutic benefit can be obtained; dosages above or below this range may be hazardous or have no effect at all. Conversely, the sluggish advancement in the effectiveness of treating severe diseases has indicated an increasing demand for a multidisciplinary strategy in delivering medicines to targets within tissues. This led to the development of novel concepts for managing the pharmacokinetics, pharmacodynamics, non-specific toxicity, immunogenicity, bio recognition, and effectiveness of pharmaceuticals. These innovative tactics, which go by the name "drug delivery systems" (DDS), are founded on multidisciplinary methods that bring together molecular biology, pharmaceutics, polymer science, and bio conjugate chemistry[2]. The process of delivering a medication to a patient in a way that raises the drug's concentrations in the body and boosts its therapeutic efficacy is known as novel drug delivery. Prolonged, localized, targeted, and protected therapeutic interactions with sick tissues are the goals of targeted drug delivery. Compared to the targeted drug release system, which releases the medication in the dose form, traditional drug delivery involves the drug being absorbed across a biological membrane. The benefits of a targeted release system involve reducing a patient's dosage, improving the medication's therapeutic impact gradually, eliminating adverse effects, and minimizing variations in the drug's level in circulation. NDDS is the advance technique and new dosage forms which are far better than conventional dosage form. Researchers have recognized for more than 20 years the potential advantages of nanotechnology in offering significant advancements in medication delivery and targeting. Patients stand to gain greatly through improved delivery methods that reduce toxicity and increase efficacy, and this also creates new opportunities for pharmaceutical and medication delivery businesses. Other methods of drug delivery focus on discovering acceptable and alternate routes for the delivery of protein drugs other than via the gastrointestinal tract, where degradation can happen, or on beating specific barriers to delivery, like the blood-brain barrier (BBB), in order to more effectively target the drug and enhance its effectiveness[3].

Various Drug Delivery Systems:

1.) Carrier based Drug Delivery System:

A) Liposomes

B) Nanoparticles

C) Microspheres

D) Niosomes

F) Resealed erythrocytes as drug carriers

2.) Transdermal Drug Delivery Systems:

A) Sonophoresis

B) Osmotic pump

C) Microencapsulation

1.) Carrier based Drug Delivery System:

A) LIPOSOMES

Liposomes are drug-based, self-assembling phospholipid-based vesicles that surround a core aqueous compartment in the shape of a concentric series of several bilayers (multilamellar) or a bilayer (uni-lamellar)[4]. The phospholipid bilayer of liposomes is 4-5 nm thick, and their sizes range from 30 nm to the micrometre scale[5]. British scientist Alec Bangham and associates at Babraham Cambridge established the science of liposomology in the middle of the 1960s [6], publishing the structure of liposomes for the first time in 1964 [7]. Since then, a great deal of research has been done on liposomes as delivery systems for protein, nucleic acid, small molecules, and imaging agents[8,9,10,11,12]. To increase patient compliance and treatment efficacy, various delivery routes, including parenteral, pulmonary, oral, transdermal, ocular, and nasal routes, have been established [13, 14,15,16,17]. Furthermore, liposomes have been used in field of food [18]and cosmetics [19].

Manufacturing of liposomes

Liposomes can be formulated using different approaches. The process of liposome manufacture and the phospholipids type critically affects the final liposomes characteristics[20]. Liposome's fabrication procedures can be classified into:

The Bangham method of thin-film hydration -Using a round-bottom flask, all lipids and the hydrophobic medication are dissolved in an appropriate organic solvent in this approach [21]. A thin film layer was then produced by the organic solvent gradually evaporating at lower pressure [22]. After that, an aqueous buffer solution is used to hydrate the resulting thin film at a temperature higher than the utilized lipid's transition temperature (Tm). A hydrophilic medication or drugs to be inserted into the liposomes' aqueous core may be present in the hydration solution. The efficiency of drug encapsulation is dependent on the rate of hydration [20, 21]. The slower the rate of hydration, the better the encapsulation efficiency. The regulation of liposome resizing, lamellarity types and particle distributions can be achieved through two methods: using bath or probe sonicators, or extrusion through polycarbonate membranes with precise pore diameters. Compared to sonication, the extrusion approach provides more stable liposomes with higher encapsulation efficiency. In addition to producing SUVs liposomes, sonication can hydrolyse or break down medications and/or lipids that are encapsulated. Probe sonication has the potential to contaminate liposome solutions with metal (Figure 1) [22]

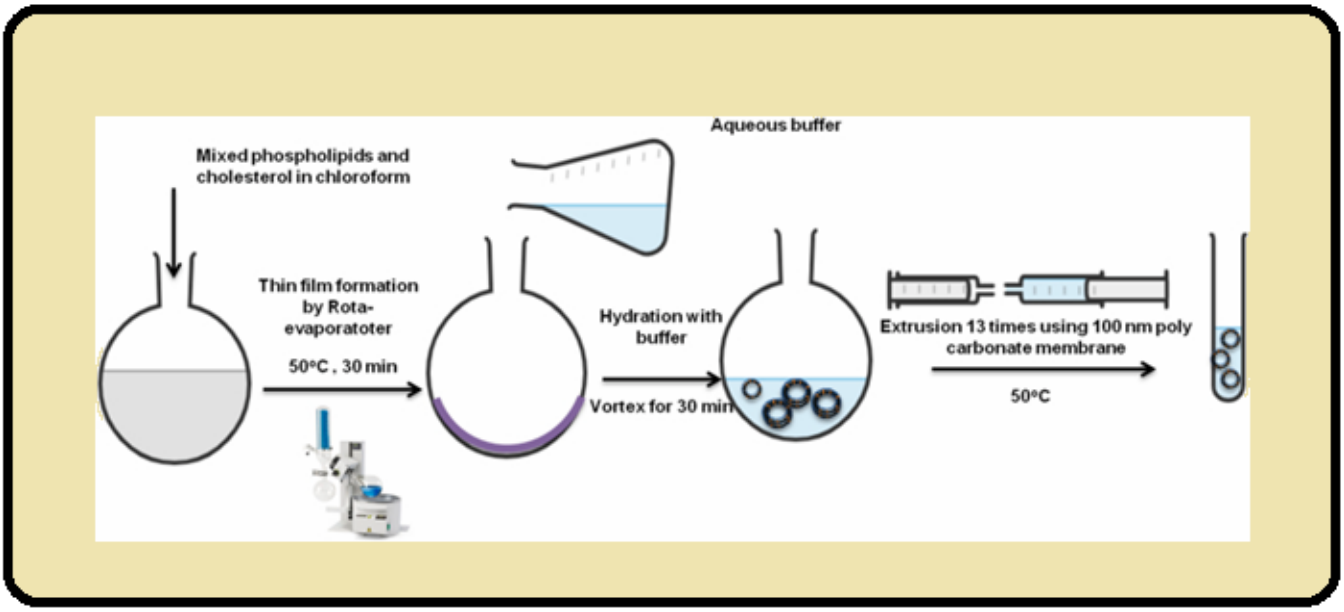

Figure 1: Liposomes preparation *via* thin-film hydration extrusion technique[22]

Reverse phase evaporation technique- Inverted micelles or water-in-oil emulsions, in which the organic phase is made up of lipids to form liposomal bilayers and the aqueous phase contains the pharmaceuticals of interest, are the basis of the reverse phase evaporation technique. (To obtain lipid films, we add this lipid mixture to a flask and evaporate the solvents. The lipid films are then dissolved once more using an organic phase that is primarily made of isopropyl ether and/or diethyl ether. A two-phase system is created by the addition of the water phase, and a homogenous dispersion is the outcome of the next sonication. As the organic solvent gradually evaporated, the mixture changed into a thick gel that created an aqueous suspension containing liposomes. Higher internal aqueous loading is one advantage of the reverse phase evaporation technique over the thin-film hydration method. While some organic solvent may remain and be able to interact further with the lipids or the drugs, techniques like centrifugation and dialysis can be used to remove the remaining solvent.)[23, 24, 25.]

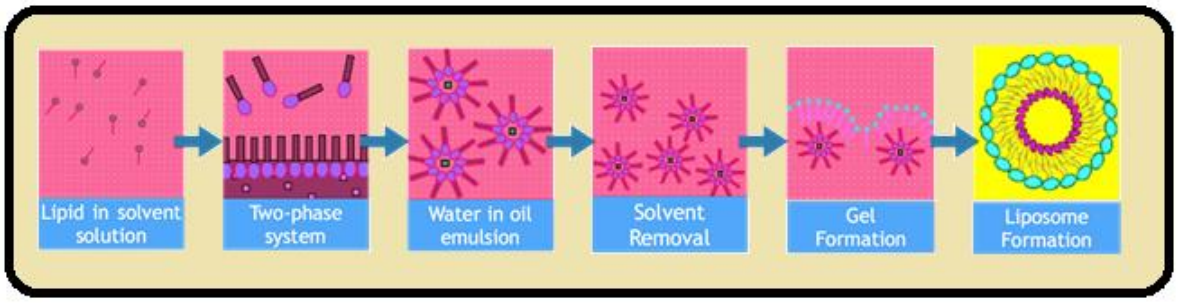

Figure 2: Flow Chart of Reverse Phase Evaporation[23,24,25]

B) NANOPARTICLES

Generally speaking, a particle of matter with a diameter of one to one hundred nanometers (nm) is referred to as a nanoparticle or ultrafine particle [26,27]. The phrase can also refer to fibres and tubes that are less than 100 nm in just two directions, or larger particles up to 500 nm[28]. In the lowest range, metal particles that are smaller than one nanometre are typically referred to as atom clusters. Because of their smaller size, which leads to very different physical or chemical properties, such as colloidal properties and ultrafast optical effects, nanoparticles are typically distinguished from microparticles (1-1000 µm), "fine particles" (sized between 100 and 2500 nm), and "coarse particles" (ranging from 2500 to 10,000 nm)[29] or electrical characteristics[30].

Method of Preparation

The preparation techniques for nanoparticles can be broadly divided into two groups i.e, dispersion of preformed polymers and polymerization of monomers. Among the techniques for dispersing preformed polymers are:

1. Solvent evaporation method

2. Spontaneous emulsification method

3. Salting out/emulsion diffusion method

4. Non aqueous phase separation method

1. Solvent evaporation method

Using an organic solvent like chloroform, acetone, or ethyl acetate, preformed polymers like polylactic acid or poly (d,l-lactic co-glycolic acid) are dissolved. In order to create an oil-in-water emulsion, the payload medication is typically dissolved in the polymer solution and then transferred to an aqueous phase containing a surfactant, such as polyvinyl alcohol [31,32]. If the homogenization process is carried out for a long enough duration, it can help the organic solvent evaporate. Ultracentrifugation is used to gather the nanoparticles at the conclusion of the homogenization process. Figure 3 shows a schematic representation of this procedure. To obtain the required particle size, process variables can be changed, including the ratio of polymer to organic solvent, the kind of organic solvent, and the speed and duration of homogenization[31].

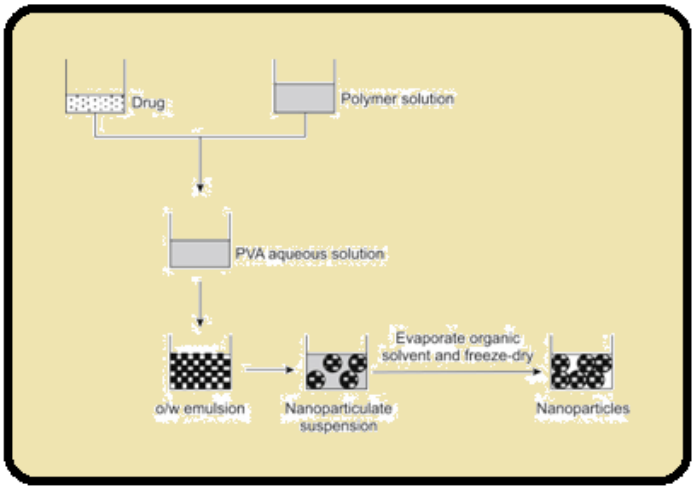

Figure 3: Nanoparticle preparation by emulsion solvent evaporation method. *O/w*, oil in water; *PVA*, polyvinyl alcohol[31]

C) MICROSPHERES

Another name for the microspheres is micro-particles. They are made to improve a drug's therapeutic efficacy and address some of the issues with traditional therapy. To achieve the intended effect, the drug must deliver the maximum therapeutic effect and the least amount of side effects to the target tissue at the right time. The prolonged release of the anticancer drugs and their ability to target the tumour with the microspheres attracted a lot of attention. The spherical microparticles known as microspheres are utilized in applications where a consistent and predictable particle surface area is crucial. The medication is contained in the center of the microspheres, where it is protected by a special polymeric membrane[32].

METHOD OF PREPERATION:

The various methods of preparations are:

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. After 500 rpm of agitation, the drug and polymer (eudragit) were separated into fine droplets, which were then collected by filtration, cleaned with demineralized water, and dried at room temperature for a full day. The solidified microspheres were formed by solvent evaporation[33, 34] .

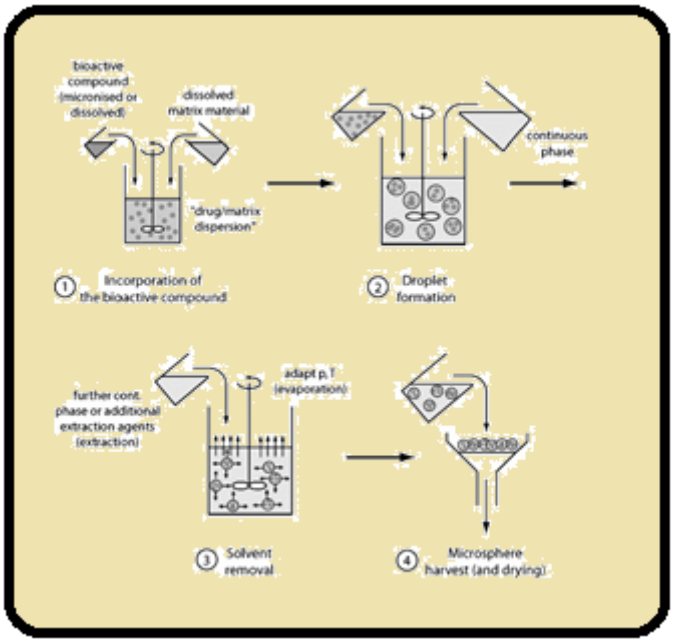

Figure 4: Microspheres by Solvent Evaporation Technique[35]

D) NIOSOMES

Niosomes are a novel vesicular drug delivery system that can be used to deliver drugs in a targeted, controlled, and sustained manner The first vesicular drug delivery system was liposomes, however they have a number of drawbacks, including toxicity, low cost, and stability problems at varying pH. Research interest in niosomes has increased as a result of liposome drawbacks. Unilamellar, oligolamellar, and multilamellar niosomes are possible. Niosomes are non-toxic because they are composed of non-ionic surfactants, which is why they are called Niosomes. They may also contain charged molecules and cholesterol or its derivatives in addition to non-ionic surfactants. The preparation remains stable due to the charged molecule in the cholesterol, which gives the structure rigidity. When non-ionic surface-active agents assemble themselves, niosomes are formed. They can be used to load and deliver both hydrophilic and hydrophobic drugs due to their structure [36].

METHOD OF PREPARATION

To prepare niosomes, a lipid mixture and surfactant are hydrated at high temperatures. Niosome size reduction is then optionally performed to produce a colloidal suspension [39]. Niosome preparation can be done using a number of well-researched conventional techniques. Examples include sonication, hand shaking, ether injection, and micro fluidization technique[37,38,40].Then, by centrifugation, gel filtration, or dialysis, the unentrapped drug is separated from the entrapped drug [39] .

Reverse-phase evaporation method

In addition to ether and chloroform, the reverse-phase evaporation method employs a combination that includes cholesterol and surfactant in a 1:1 ratio. The target drug-containing aqueous phase is added to the mixture, and it is then sonicated at a temperature of 4-5°C. A tiny quantity of phosphate-buffered saline is added to the mixture, and then the sonication process is resumed. Phosphate-buffered saline is used to dilute the residual suspension after the organic solvent is extracted at 40°C while operating at low pressure. The final product, niosomes, is formed by heating the mixture at 60°C for 10 minutes [38,41,42]. Figure 5 shows how the reverse-phase evaporation method is used to manufacture niosomes.

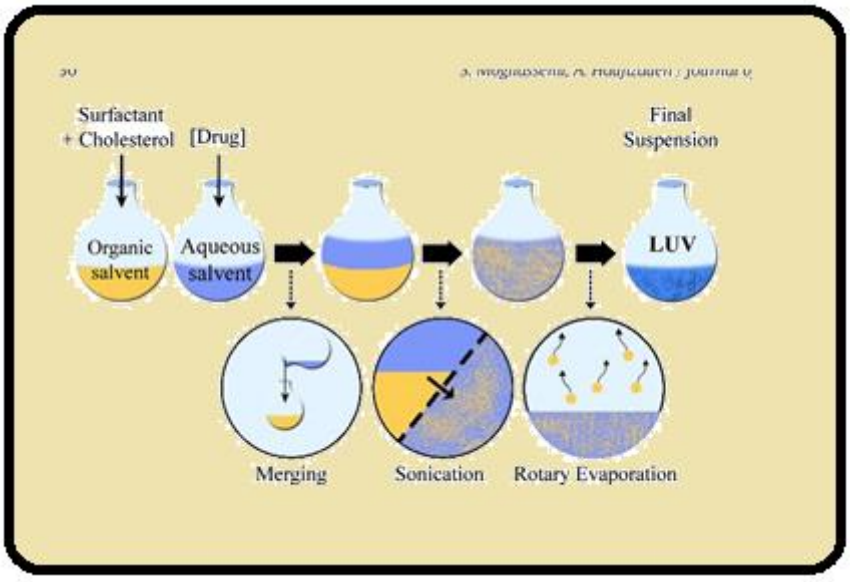

Figure-5 Niosome preparation through reverse phase evaporation method [43].

E) RESEALED ERYTHROCYTE AS DRUG CARRIER

The medicine is introduced into the erythrocytes by a variety of techniques that break the cells. Afterward, the erythrocytes are sealed shut, and the resultant carriers are referred to as "resealed erythrocytes." As a medication administration method, resealed erythrocytes have a great potential to raise patient compliance and the therapeutic index. It offers enormous potential for achieving site-specific medication delivery with minimal drug waste and for extending the drug's release. Many medications with numerous negative effects, such as steroids, aspirin, and cancer medicines, are lessened by resealed red blood cells. The properties, drug loading techniques, and uses of resealed erythrocytes are indicated in this review[44].

Methods of Drug Loading in Resealed Erythrocytes:

There are a number of techniques for loading medications or other bioactive substances .The physical properties of erythrocytes, such as electrical systems based on osmosis, the pulse technique, and chemical techniques (such as the chemical disturbance of the membrane of erythrocytes). Regardless of the technique employed, the ideal qualities for the In order to successfully ensnare the compound, the medication must include a significant amount of water solubility and durability against deterioration within the physical or chemical erythrocyte membrane contact, as well as clearly established pharmacokinetic and pharmacodynamics attributes[45].

Chemical Perturbation of the Membrane: This technique is predicated on the observation that erythrocytes exposed to specific chemicals exhibit an increase in membrane permeability. Erythrocytic membrane permeability rises in response to polyene antibiotics such amphotericin B [46]. This technique was successfully applied in 1980 to entrap daunomycin, an anticancer medication, in mouse and human erythrocytes[47]. These techniques are not particularly well-liked, though, because they cause the cell membrane to undergo irreparable damage.

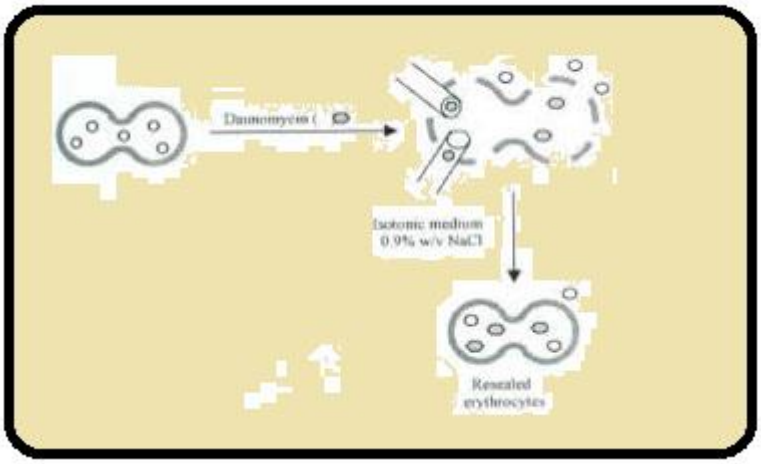

Figure-6 Chemical perturbation of the membrane[48].

2.) Transdermal Drug Delivery Systems

A) SONOPHORESIS

It is a method that uses ultrasonic radiation to dramatically accelerate the absorption of topical chemicals (transdermal administration) into the skin's dermis, epidermis, and appendages[53] . One quick, easy, non-invasive, targeted way to transfer macromolecules and low molecular weight medications to the skin are using sonophoresis[54].Sonophoresis is thought to improve medication delivery mechanistically by altering skin tissue through a mix of chemical, mechanical, and thermal changes[51]. Sonophoresis has been achieved using ultrasound at different frequencies between 20 kHz and 16 MHz, with intensities up to 3W/cm[49,52,55] . Percutaneous absorption is known to be impacted by ultrasound parameters, with frequency, intensity, and length of treatment being the most significant[56]. Sonophoresis happens when ultrasonic waves raise the total kinetic energy of the molecules that make up topical medicines and induce micro-vibrations beneath the skin's epidermis. Drug distribution is likely improved by ultrasound by cavitation, microstreaming, and heating[50,53] .

In hospitals, sonophoresis is frequently used to administer medication through the skin. In order to compound the medications, pharmacists combine them with a coupling agent (gel, cream, or ointment) that allows the ultrasound transducer to transmit ultrasonic energy to the skin[50, 53] .

MECHANISMS OF ACTION

Even while sonophoresis has received a lot of interest in recent years, its mechanics have not been fully understood. recognized, acknowledging the possibility of several occurrences in after being exposed to ultrasonography. These consist of:

*Cavitation (generation and oscillation of gas bubbles).

*Thermal effects (temperature increase).

*Induction of convective transport

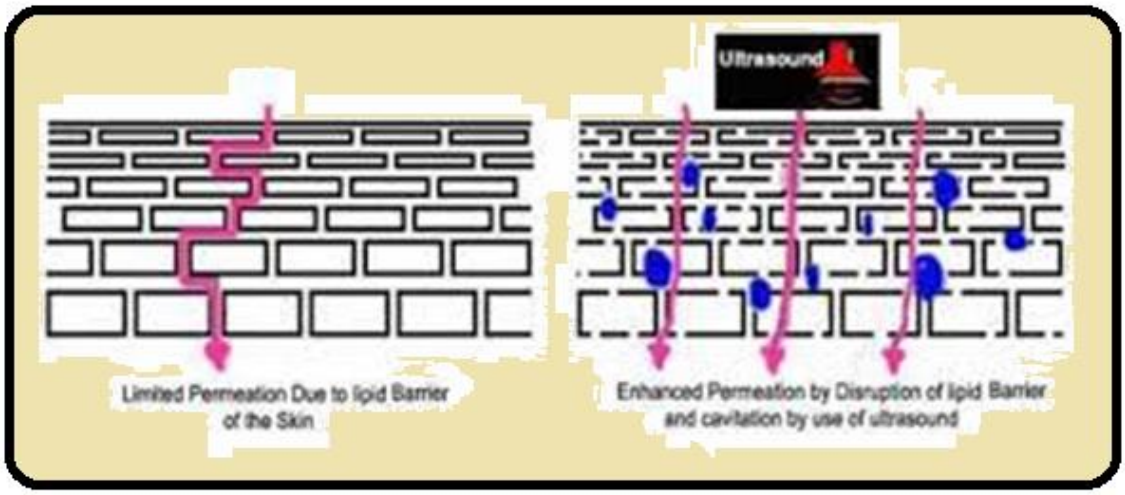

Figure 7: Enhanced transdermal permeation by cavitation upon application of ultrasound[57].

B) Osmotic PUMP

Osmogen and a drug-filled core make up the majority of osmotic delivery devices, also known as osmotic pumps. These are covered with a semi-permeable membrane with one or more drug delivery pores, allowing the medication to be delivered gradually as a suspension or solution[59]. The heart of an oral osmotic system is a compressed tablet covered in a semi-permeable membrane, through which delivery orifices are drilled using a mechanical drill or a laser beam[58]. These regulated systems are not affected by different gastrointestinal variables and are based on osmosis and osmotic pressure. Nonetheless, it is important to remember that a number of crucial elements, such as drug solubility, delivery orifices, osmotic pressure, semi-permeable membrane, and others, affect how osmotically controlled drug delivery systems are designed its membrane thickness, plasticizer type and quantity, and polymer type and nature[60,61]. The next breakthrough was the implanted pump, a gadget that was meant to be inserted beneath the skin in order to avoid using a catheter. Drug release is continuous with these devices[63]. The 1970s saw more developments in implanted pumps, which were then limited to use in animals. This novel strategy was based on osmosis, and the new pumps might be more compact than conventional constant-rate pumps[64]. In the 1970s and 1980s, Alza Corporation and Felix Theseus produced a number of modifications and enhancements to this idea, which led to the development of the elementary osmotic pump (EOP)[62].Different types of osmotic pumps are used now a days such as-

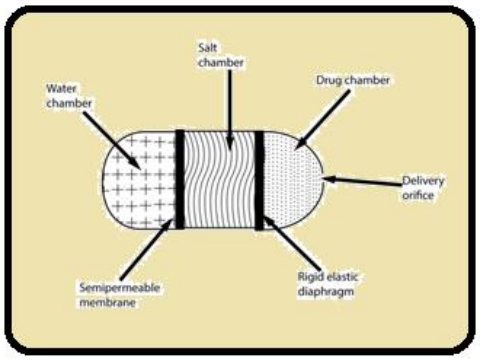

Figure 8: The Rose–Nelson pump[65]

C) MICROENCAPSULATION

Through the process of microencapsulation, thin wall material coatings are formed around solids, liquids, or even gases, enclosing them in microscopic particles. The business

machines sector developed the method in the late 1930s as a cleaner alternative to carbon paper and carbon ribbons. A variety of microencapsulated materials, including medications, were developed as a result of the breakthrough invention of replication paper and ribbons in the 1950s that contained dyes in microscopic gelatine capsules that were released upon hit by a typewriter key or the pressure of a pen or pencil [66,67] .and the technique is also known as "microencapsulation "which involves coating or encircling minuscule liquid or solid droplets with a continuous polymeric layer. Bioencapsulation, which is more limited to enclosing a biologically active material (such as DNA or a complete cell or group of cells) in order to increase its performance and/or prolong its shelf life, is a subset of microencapsulation[68,69]. Through microencapsulation, liquids may be turned into solids, surface and colloidal properties can be changed, the environment can be protected, and the release characteristics or availability of coated materials can be managed. Many of these characteristics can be obtained by macro packaging techniques, but what makes microencapsulation special is the size of the coated particles and how easily they can be used and adapted to a broad range of dosage forms, even if this hasn't been theoretically possible [70] .

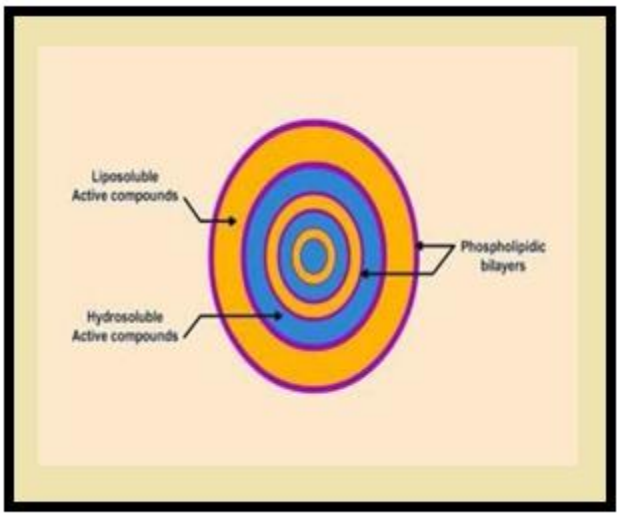

Figure-9 The microencapsulation process [71]

Three processes are typically involved in coacervation-phase separation microencapsulation, which is done under continuous agitation: (a) production of three immiscible chemical phases; (b) coating deposition; and (c) coating rigidization. There are two types of coacervation-phase separation: simple coacervation and complicated coacervation. The former suggests incorporating a very hydrophilic material into a colloid solution. Two phases are created as a result of this additional material. The process of complicated corrosion is primarily pH dependent. Microcapsules are created by manipulating the system's basic or acidic composition. Depending on how basic or acidic the system is, it may form microcapsules over a particular threshold pH value. They won't develop at pH values lower than that. Complex coacervation typically addresses the system containing more than one colloid[72, 73,74] .

APPLICATIONS

With NDDS, medication or encapsulated bioactive might be released under controlled conditions. The desired release pattern will undoubtedly enhance the drug's pharmacokinetics and, consequently, pharmacodynamics. When it comes to treating Helicobacter pylori, the regulated distribution of antibiotics by NDDS is a more efficient method than the traditional one. Likewise, a drug's gradual and steady release from an implant prevents needless dose changes and guarantees patient compliance. There are several uses for NDDS, including regulated and sustained drug delivery. A few of them have already been covered in the parts that came before.

CONCLUSION

Adopting a Novel Drug Delivery System the novel dosage forms in NDDS are a combination of advanced technology and superior to traditional dose forms. The following are benefits of the novel drug delivery system: optimal dosage at the proper time and place; efficient use of costly medications and excipients; lower manufacturing costs; benefits to patients; better therapy; and enhanced comfort and level of living. Targeted drug delivery systems, controlled drug delivery systems, etc. are examples of basic new drug delivery system modalities. Pharmaceutical science uses novel approaches for medication delivery and drug targeting such as focusing on the administration of drugs, vaccines, gene therapy, and the commercial development of new carriers.

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