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NOVEL DRUG DELIVERY SYSTEM: A NEW APPROACH FOR DRUG DELIVERY

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ABSTRACT

Novel drug delivery system is an advanced technique to deliver the drug efficiently to the targeted site to improve the patient compliance by reducing repeated dosing and to maintain the consistent drug concentration in the blood, to reduce the adverse effects by enhancing the bioavailability of the drug. drug delivery is achieved by the aid of carriers like liposomes, niosomes, nano-emulsions, microspheres, nanospheres, nano-suspension etc.

INTRODUCTION

Compared to type-based drug delivery systems, novel drug delivery systems(NDDS) provide a wider range of carriers. The typical dosage forms are characterized by high dose and limited availability, instability, first pass effect, variable plasma drug levels, and rapid release of pharmaceuticals. NDDS will mitigate these problems by improving patient compliance, product shelf life, performance, and safety. Because of the increasing environmental performance of man-made nano-size particles and the growing awareness of their possibly detrimental effects on human health and environmental sustainability, nanoparticles are currently receiving attention. Numerous technologies are used to produce and utilize nanoparticles in a variety of applications. Interesting theoretical issues arise in their calculation and characterization. A particle having a diameter of 10–100 nm is called a nano-size particle. Both small and large compounds pharmacodynamic and pharmacokinetic characteristics are changed to aid in their dispersion. They are categorized as systems that contain dissolved active chemicals that are encapsulated or adsorbed in the matrix material in order to feed the target tissue. It has been shown that the impact of medication on the target tissue increases the retention stability through the use of enzymes and intravascular

solubilization of nano-size particles. The release pattern, size, and surface features of nano-size particles are critical controls that determine the specific site of action at optimal rates with the appropriate dose scheme. These factors must be taken into consideration during the design process. A non-biodegradable polymeric framework (polyacrylamide, polymethyl-methacrylate, polystyrene) served as the foundation for the first nanoparticles ever reported.[1]

The drug is known as a dissolved, trapped, encapsulated, or nano-size particle-attached to nano-size particle matrix as a particulate dislocation or a solid particulate with sizes between 10 and 1000nm. Nano-size particles are in solid form and are either amorphous or crystalline[2-5] like nanospheres and nanocapsules of the size 10-200nm. For the preparation of nano-size particles, polymeric materials were commonly used.[6] Nanoparticles, nanospheres or nanocapsules may be obtained according to the preparation method. Nanocapsules are systems in which the medicinal product is confined to a cavity with a unique polymeric membrane, while the nanosphere is a matrix system that physically and consistently disperses the pharmaceutical product.

Due to their ability to circulate as a specific organ for an extended period of time and their capacity to supply proteins, PE, and other DNA in gene therapy, hydrophilic polymers like polyethylene glycol(PEGs) have been particularly useful as potential devices to supply proteins and other nanoparticles in the field of gene therapy.[7-10]

The use of nano-size particles as a targeted medicine delivery mechanism has been extensively researched.[11] Targeted drug delivery can be achieved by either passive or active targeting. One way for active medication targeting to happen is when the drug molecule combines with a ligand that is specific to a certain cell or tissue.[12] It is possible to achieve passive drug targeting by encasing a therapeutic molecule within micro or nanoparticles. Natural, synthetic, and semi-synthetic polymers make up the Colloidal Framework for Drug Delivery of Nano-size particles (NP). The diameter of nano-size particles ranges from 10 nm to 1,000 nm.[13] This colloidal drug delivery system's unique internal structure are:

- Matrix-type nanospheres.
- Reservoir-type nanocapsules.

OBJECTIVES[14]

In order to attain therapeutically optimum rate and dosing schedule with site-specific effect, the primary objectives while creating the Nano-size particles as an input device are to monitor particle size, surface qualities, or release of pharmacologically active substances in order to produce site specific action at the therapeutically optimal rate and dosage scheme.

As a result, the drug is specifically designed to have as few side effects as possible and an improved therapeutic index in order to produce the intended pharmacological response in one site while avoiding negative interactions in other sites.

For example: enzymes with cancer treatment as replacement therapy.

Advantages of nano-size particles

1. They are non-toxic, site-specific, biodegradable, and store for a minimum of a year.
2. Targeting a medicine to a specific location within the body can be accomplished through magnetic guiding or the addition of specific ligands to particle surfaces.
3. They provide regulated drug release rates and particle degradation properties that are readily adjustable by matrix constituent selection.
4. Drugs can be administered into the systems with a high loading of medication and no chemical reaction, which is a crucial component to ensure the safety of drug operation.
5. They work better as a therapy and in terms of total response and unit dose.
6. Various routes, including oral, nasal, intraocular, and maternal, can be utilized with this device.
7. Particle size and surface properties of nanoparticles can be readily modified to achieve both passive and active pharmacological targets after parenteral administration.

Disadvantages of nano-size particles

1. Bio-acceptability has its boundaries.
2. Difficult to produce in large quantities.
3. Because of their small size and vast area, the particles can be difficult to agglomerate, which makes handling them physically challenging in both liquid and dry forms of nanoparticles.
4. The huge surface area and fine particle size are caused by restricted loading and explosion. These pragmatic issues need to be resolved before nanoparticles can be made commercially or clinically accessible.

5. The current work is a step toward the creation of drug delivery systems for nanoparticles, surface modification, drug loading techniques, release control, and other potential uses for nanoparticles.[16]

Drug delivery mechanism by nano-size particles

Through enhanced permeability, retention effect, and targeting, nano-size particles deliver the medication at the spot by blocking the reticulo-endothelial system. Drugs that carry nano-size particles use one of two methods:

a. Surface bound: The drug molecules have a surface connection to the nanoparticles.

b. Core bound: Using this method, the drug particles are condensed into the nano pharma matrix and then delivered to the target inside the body. As a solution containing previously prepared Nano-size particles is polymerized, drugs can be loaded onto the particles by adding the reaction mixture. The interaction between nanoparticles and therapeutic products may primarily include chemistry, surface adsorption, or any binding or contact. Depending on the drug and polymer chemical structures, drug loading circumstances, drug binding, and drug-nanoparticle interaction are made.[17]

TYPES OF NOVEL DRUG DELIVERY SYSTEM

1. Phytosome

While other words mean "cell-like," "Phyto" denotes plants. Plants are referred to as "phyto" The method of vesicular delivery of phytoelectric components in herbal extracts and lipid-binding (one molecular phyto-constituent, bound to a phospholipid at least molecular) substances was called phytosomes. Phytosomes prevent key components of herbal extracts from degrading. Gut bacteria that have improved absorption and digestive secretions offers enhanced biological, pharmacokinetic, and pharmacological properties, as well as increased availability. Characteristics of traditional herbal extracts and the differences between liposomes and phytosomes are shown below.

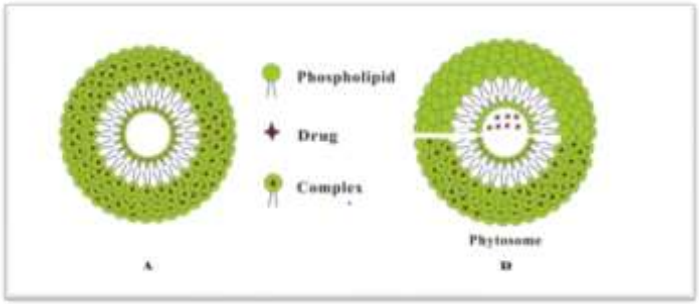


Figure shows: Liposomes and Phytosomes.

Advantages of phytosome

1. Enhanced bioavailability of phospholipid complexes.
2. Better absorption in the GIT.
3. Higher bioavailability is thought to contribute to better treatment outcomes.
4. Low dosage is necessary due to high bioavailability.
5. More steadiness.
6. Great lipophilicity leads to great penetration, which is why liposomes are not utilized in cosmetics.
7. Notable therapeutic benefits.
8. Phosphatidylcholine protects the liver rather than acting as a carrier.[18]

2. Liposomes

Liposomes are bilayered vesicles that are condensed and have an entirely enclosed aqueous volume. A bilayer of lipid membrane made mostly of synthetic or natural phospholipids. The term liposome refers to its constituent phospholipids rather than its physical dimensions. Liposomes can be created in a variety of sizes as single or multi-lamellar structures. Most of the time Liposomes are synthetic vesicles made of a bilayer of lipid. Liposomes are filled with Medicines for cancer and other illnesses. It is possible to prepare biological membranes like sonic disruption. These are colloidal or micro particulate carriers, usually ranging in diameter from 0.05 to 5.0 μm, that arise naturally in aqueous conditions when these lipids hydrate. Liposomes consist of an aqueous, biodegradable, and biocompatible substance. The quantity of lipids, synthetic or natural, entangled in one or more bilayers. A wide range of drugs having different lipophilicity can be contained in liposomes, either in the phospholipid bilayer or otherwise the volume of aqueous materials trapped at the two-layer interface.

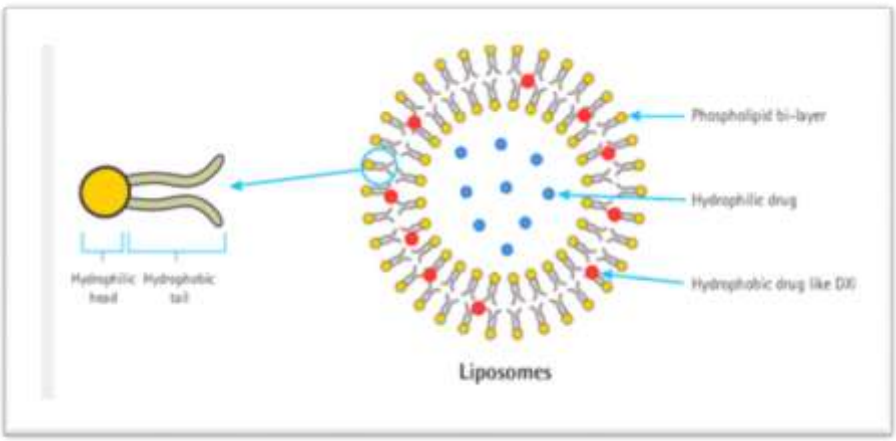


Figure shows: LIPOSOMES.

Liposome classification based on structural features[19]

1. MLV - Multilamellar large vesicles
2. OLV - Oligolamellar vesicles
3. UV - Unilamellar vesicles

a. SUV- Small unilamellar vesicles

b. MUV - Medium unilamellar vesicles

c. LUV - Large unilamellar vesicles

d. GUV - Giant unilamellar vesicles

4. MVV -Multivesicular vesicles

Liposome classification based on method of liposome preparation[19]

1. REV -Single or oligolamellar vesicle made by reverse phase evaporation method.
2. MLV / REV -Multilamellar vesicles made by reverse phase evaporation method.
3. SPLV -Stable plurilamellar vesicles.
4. FAT-MLV Frozen and thawed MLV.
5. VET- Vesicles prepared by extrusion method.
6. FUV-Vesicles prepared by fusion.
7. FPV -Vesicles prepared by French press.
8. DRV- Dehydration-rehydration vesicle.

Advantages of Liposome[20]

1. Liposome doxorubicin allows for selective passive targeting to malignant sites.
2. Enhanced treatment index and efficacy.
3. Stability increased through encapsulation.
4. The encapsulated agents' toxicity has decreased.
5. The effect of site avoidance.
6. Better pharmacokinetic outcomes (lower elimination, longer circulation durations).

3. NIOSOMES

These are microscopic structures and they are created by adding cholesterol, a nonionic surfactant, and a charges-inducer to watery media, followed by hydration. Because of the hydrophobic and hydrophilic moiety of niosomes, a wide variety of pharmacological compounds can be included. A number of medicinal applications have evaluated niosomes. The capacity to minimize clearance from the body by slowing drug release of such agents is

one of the significant benefits in clinical use, along with the potential to lessen systemic toxicity by encapsulation.

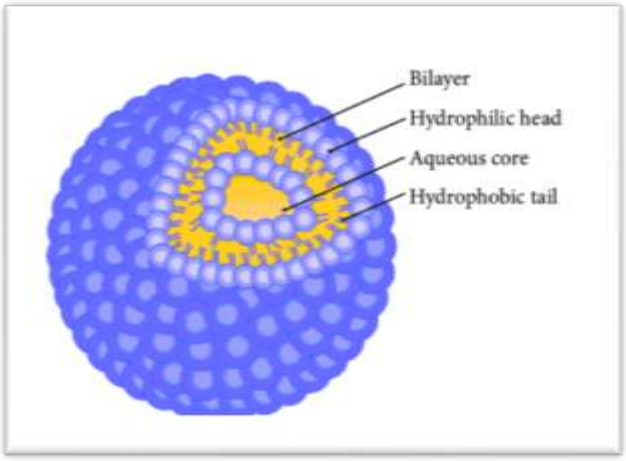


Figure shows: NIOSOME.

TYPES OF NIOSOMES[21]

Niosomes are classified based on number of bilayer, size and method of preparation.

1. Mulitlamellar- 0.5µm to 10µm in diameter.
2. Larger unilamellar- 0.1µm to 1µm in diameter.
3. Small unilamellar – 25-500nm in diameter.

Advantages of Niosomes[22]

1. Niosomes are compatible, biodegradable, non-toxic, and non-immunogenic.

2. Niosomes have the ability to encapsulate a lot of material in a tiny volume of vesicles.

3. A wide variety of chemicals-amphiphilic, lipophilic, and hydrophilic—can be captured by noisome.

4. Niosome characteristics are readily observable, including type, flow, and size alteration to the production techniques and structural makeup.

5. There are other ways to deliver noisome, including oral, parenteral, and administration. Accessible in a range of forms, including topical, semisolids, powders, or solutions.

6. The niosome is easy to store due to the chemical stability of its structure.

4. Transferosome

In 1991, Gregor Cevc presented the concept and definition of transferosome. The Latin word "transferee," which means "to carry," is the source of the title. It is combined with the Greek word "body," "soma" fora, to signify "to transport." A vesicle that resembles the cell's typical

vesicle. As such, it is appropriate for controlled and focused drug delivery. Transfersome is a highly adaptive and stress-responsive dynamic aggregate. It is a pliable vesicle encircled by the intricate fat bilayer and featuring an aqueous core. The bilayer's shape and local composition determine the vesicle's self-control and self-improvement. In addition to acting as a non-intrusive target drug transport agent, this aids the client in successfully navigating various hurdles. The incredibly flexible membrane has repeatable drug delivery capabilities, either via or into the medication. Depending on the application or administration method, the skin has a good quality. These transfersomes are ideal for skin penetration since they are several orders of magnitude more elastic than standard liposomes. In order to cause problems with skin penetration, the transfers happen by forcing them through the stratum corneum's intracellular lipid. By combining the right surfactive components, the transfersome membrane can be made versatile.[23–27]

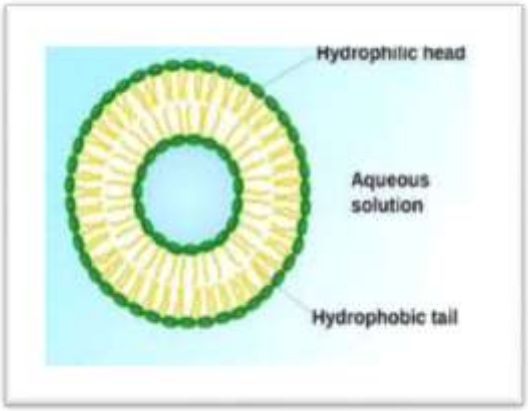


Figure shows: TRANSFEROSOME.[28]

Transferosomes Advantage[29]

1. Small constriction (5–10 times smaller) may result after a transfer. Save for their own diameter, without discernible loss.
2. With regard to lipophilic medications, they have a high 90% capture efficiency.
3. The undamaged vesicles are able to penetrate more deeply.
4. They are able to provide medications with varying molecular weights, such as analgesics, antibiotics, albumin, gender hormone, corticosteroids, bluetongue, and insulin.
5. Hydrophilic and hydrophobic infrastructures characterize transfers. Consequently, pharmacological molecules with diverse solubility range together.
6. By gradually releasing their contents, they operate like a store house.

5. Mouth-dissolving tablets

Asoka Life Science Limited introduced Res-Q, the first mouth dissolving tablet made of polyherbal ingredients and a fast-acting medication. It causes a novel medication delivery mechanism to occur, resulting in higher efficacy. This is an initial attempt to improve the efficacy of medications in treating chronic illnesses in the field of Ayurvedic medicine. Res-Q is a highly effective polyherbal medication for respiratory conditions like asthma and lung issues. With this special mouth dissolving medication delivery technology, the drug is guaranteed to enter the bloodstream immediately and to avoid the first pass metabolism. It becomes dissolved in the mouth through salivary mixing and absorption. Within fifteen minutes, this Res-Q relieves respiratory distress. As a result, the product bears a striking resemblance to the effectiveness of Sorbitrate, a ground-breaking medication used to treat cardiac distress.[30]

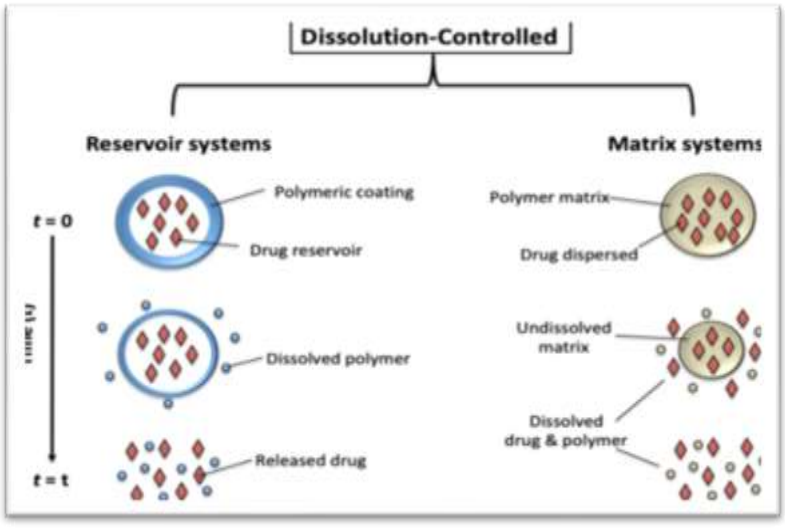
Figure shows: MOUTH DISSOLVING TABLETS.

Advantages of Mouth dissolving tablets

1. No need of water to swallow the tablet.
2. Can be easily administered to pediatric,elderly and mentally disabled patients.
3. Accurate dosing as compared to liquids.
4. Excellent mouths feel property produced by use of flavours and sweetners.
5. Convenient to administer during travelling without need of water.
6. Fast disintegration of tablets leads to quick dissolution and rapid absorption which may produce rapid onset of action.

6. Controlled release formulation

An oral administrable formulation, consisting of a granulated herb and a carrier, is described in a patent as having a controlled release or stable storage of granulated herb. The formulation releases 75% of the active components between 4 and 18 hours after administration. The group that includes echinacosides, hypericin, and hyperforin is chosen to contain the active ingredients. By offering an oral dosage form that is easy to take and provides optimal plasma concentrations of the biologically active chemicals in a form that promotes user compliance, the invention aims to improve herbal preparations. Granulated herb is available in oral controlled and stable release dosage forms in matrix formulations, like matrix tablets, or multiparticulate formulations, like microcapsules placed within two-piece capsules. These formulations are used to hold a drug delivery system, ensuring an ongoing supply of the active ingredients for an extended period of time.[31] A new stable herbal medicinal formulation in the form of G. biloba extract-containing prolonged-release microgranules, together with the method for creating them, is another US patent invention. Plant extracts are not very compressible or have good flow characteristics. Because uniform extract combinations containing pharmacological excipients are needed for every compression strap, it is challenging to express such extracts in the form of sustained release tablets. Various techniques can be used to remove microgranules, such as the fluid-air bed process, cutting pan method, or extrusion-spheronization technique. Pellets with a high amount of active ingredients can be processed by extrusion-spheronization, although additional equipment is needed. Since the cutting pan method just needs basic tools and instructions, it is recommended for the production of the invention's grains.[32]



Figureshows: Controlled Release Formulation.

Advantages of controlled release formulation

1. The frequency of drug administration is reduced.
2. Patient compliance can be improved.
3. The drug administration is more convenient.
4. There is better control of drug absorbtion.
5. Bioavailability of drug is improved.

7. Proniosome

The proniosome gel system is an advancement over niosomes, and it can be used in a number of ways to transport actives to the intended location.[33] Protosomal gels are formulations that become niosomes when they are hydrated in situ using skin-derived water.[34] Proniosomes are surfactant-coated, water-soluble carrier particles that can be hydrated right before usage to create niosomal dispersion after a brief agitation in heated aqueous fluid.[35] below diagram provides a few instances of proniosomal compositions.[36]

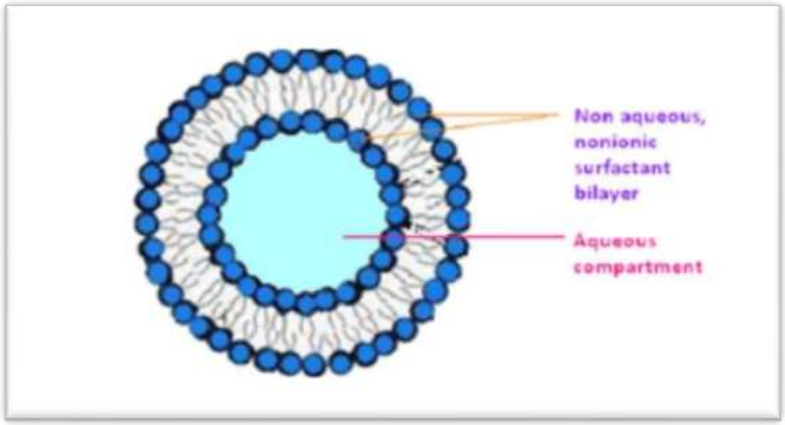


Figure shows: PRONIOSOME.

Advantages of proniosome

1. Proniosome do not require any special conditions of storage as in case of noisome and liposomes.
2. They are physically stable compared to niosomes.
3. Proniosomes are easy to handle, store and transport.
4. They are easy to use as they can be hydrated just before use.
5. Proniosomes are uniform in size.

8. Transdermal drug delivery system

In order to conveniently provide medications systemically as well as locally for the treatment of diseased skin (topical delivery), TDDS has become more involved in skin-based drug administration.[37] With other medications, though, they did not achieve the anticipated level of success. Transdermal drugs, however, have enormous potential as smart drug delivery systems in the future.[38] In Controlled medication distribution, improved bioavailability, fewer side effects, and ease of application are the benefits of transdermal delivery systems. One of the first attempts to use Ayurvedic drugs through transdermal drug delivery system (TDDS), which uses skin as a site for continuous drug administration into the systemic circulation, is the formulation of transdermal films incorporating herbal drug components like boswellic acid (Boswellia serrata) and curcumin (Curcuma longa). In addition to providing a prolonged drug delivery with infrequent doses via zero order kinetics and the ability to easily stop the therapy at any time, this delivery system eliminates the first pass metabolism of the drug without the inconvenience associated with injection. Turmeric in TDDS is also considered a nascent form of the Ayurvedic turmeric poultice or jump, which is used to promote the local action of the medicine at the place of delivery.[39]

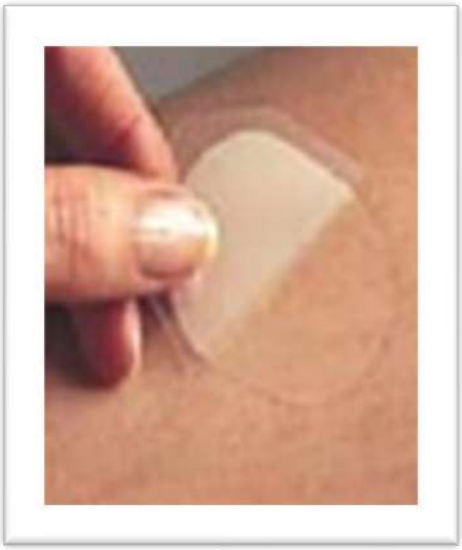


Figure shows: Transdermal Patches.

Advantages of Transdermal drug delivery system

1. Avoids first pass hepatic metabolism.
2. Maintain constant blood level for longer period of time.
3. Decrease the dose of administration.
4. Decrease unwanted side effects.

5. Easy to discontinue in case of toxic effects.

9. Nanosponges

Among the newer types of materials is nanosponge, which is composed of microscopic particles with a few nanometer-wide hollow. Different kinds of materials can be inserted into these small holes. These microscopic particles have the capacity to contain both lipophilic and hydrophilic medicinal substances and can stabilize poorly water-soluble pharmacological substances or compounds.[40]

The three-dimensional polyester network or scaffold known as "nanosponges" is able to break down spontaneously. To create Nanosponges, these polyesters are combined with a crosslinker in a solution. In this case, polyester degrades somewhat in the body because it is often biodegradable. When the nanosponge scaffold disintegrates, the drug molecules that are loaded are released in an unfavorable way.

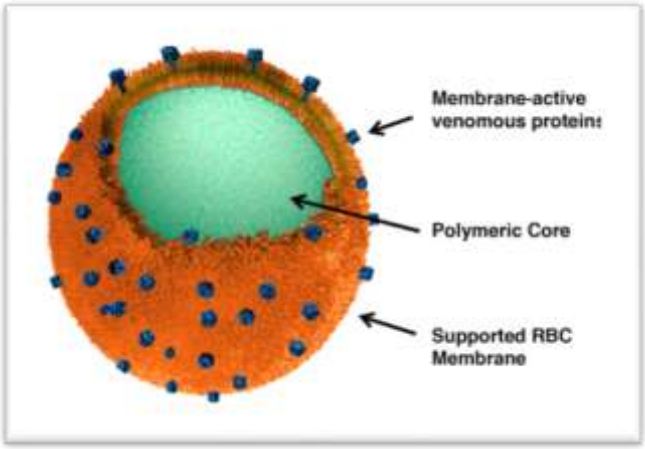


Figure shows: Nanosponges.

Advantages of Nanosponges

1. Enhances aqueous solubility of the poorly water-soluble drug.
2. Drug molecules can be released in a predictable manner using nanosponges.
3. Bacteria cannot pass through the Nanosponges' minuscule 0.25 µm whole size, which causes them to function as self-sterilizers.
4. The drug delivery system using nanosponges is safe, non-toxic, and non-mutagenic.
5. The removal of venomous and harmful substances from the body is assisted by nano sponges.
6. The use of nano sponges in medicine delivery reduces adverse effects.

7. Improve both the flexibility and stability of the formulation.
8. Lessen the frequency of doses.
9. Improved adherence from patients.
10. Complexes of nanosponges are stable at temperatures of 130 degrees Celsius and across a broad pH range (i.e., 1–11).[41-43]

9. Microspheres

Microspheres are distinct, spherical particles with an average size between 1 and 50 µ.[44] As a dependable method of delivering drugs to specific target sites and achieving the intended concentration in relevant situations without causing side effects, microparticulate drug delivery systems are being researched and implemented. One helpful technique that greatly increases patient compliance and lengthens the duration of the drug's action is microencapsulation. In the end, a constant plasma concentration is maintained, thus the whole dosage and a small number of side effects may be reduced.[45] Thus far, several plant active components have been synthesized into microspheres, including rutin, camptothecin, zedoary oil, tetrandrine, quercetine, and extract from Cynara scolymus. Furthermore, findings on magnetic and immunological microspheres have become more common in recent years. The antibody and antigen that were adsorbed or coated on the polymer microsphere gave rise to the immunological competence of the immune microsphere.[46]

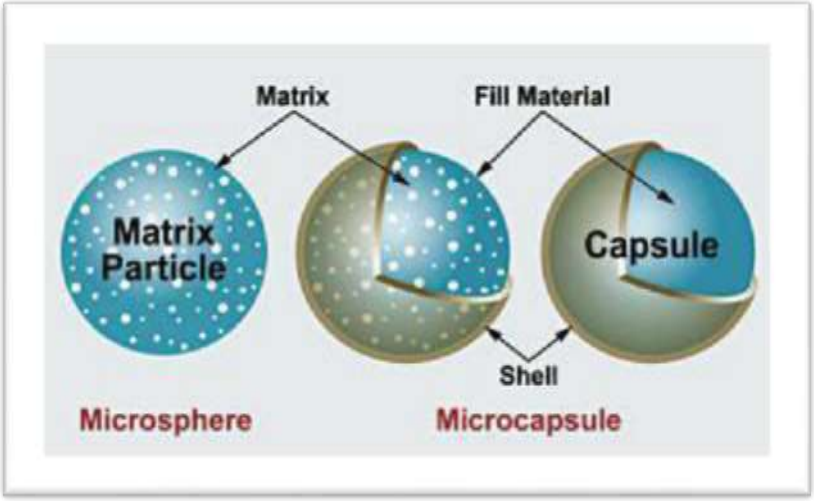


Figure shows: Microsphere And Microcapsules.

Advantages of Microspheres

1. They facilitate accurate delivery of small quantities of potent drug and reduced concentration of drug at site other than the target organ or tissue.

2. They provide protection for unstable drug before and after administration, prior to their availability at the site of action.
3. They provide the ability to manipulate the in vivo action of the drug, pharmacokinetic profile, tissue distribution and cellular interaction of the drug.
4. They enable controlled release of drug. Ex: narcotic, antagonist, steroid hormones.
5. Particle size reduction for enhancing solubility of the poorly soluble drug.
6. Provide constant and prolonged therapeutic effect.
7. Provide constant drug concentration in blood there by increasing patient compliance.

10. Nano-Emulsion

A non-homogeneous dispersion system known as an emulsion is made up of two different types of liquids that cannot dissolve one another but instead scatter as droplets in the other liquid.[47] The oil phase, water phase, surfactant, and sub surfactant make up the emulsion, in general, It looks like a transparent or translucent liquid. Emulsions can be classified as sub-micro emulsions (100–600 NM), micro emulsions (10–100 NM), and regular emulsions (0.1–100 μm). Micro emulsions are also known as nano emulsions, whereas sub micro emulsions are also known as lipid emulsions. Emulsion is a drug delivery technique that distributes itself in vivo in the targeted locations because of its affinity for lymphatic fluids Furthermore, the medication's prolonged sustained release is possible due to its inner phase packaging, which keeps it away from the body's surface and bodily fluids.[48] Following the preparation of oily or lipophilic medications into O/W or O/W/O emulsions, the oil droplets are phagocytozed by macrophages and accumulate in the liver, spleen, and kidney, where the amount of the dissolved drug is extremely heavy. Even when a water-soluble medication is made into a W/O or W/O/W emulsion, it can be injected intramuscularly or subcutaneously to effectively compress the lymphatic system. Its target dispersion is influenced by the emulsion particle's size. In addition to providing the intended prolonged release, the herbal medication will be produced into an emulsion, which will increase the stability of the hydrolyzed materials, enhance drug penetration via the skin and mucous membranes, and lessen the stimulant effect of the drug on the tissues. Thus far, emulsions have been created from a number of herbal medications, including camptothecin, Brucea javanica oil, coixenolide oil, and zedoary oil. For instance, Kun Z et al.[49] looked at how the protein formulation and human lung adenocarcinoma cell line A549 were affected by the aluminum emulsion. The growth and multiplication of A549 cells were significantly inhibited by the aluminum emulsion in vitro, according to the results, which also revealed a time- and dose-

dependent connection. One class of novel anticancer medication with promising application potential is elemenum emulsion. Moreover, it does not cause liver or tenderness harm or marrow inhibition.

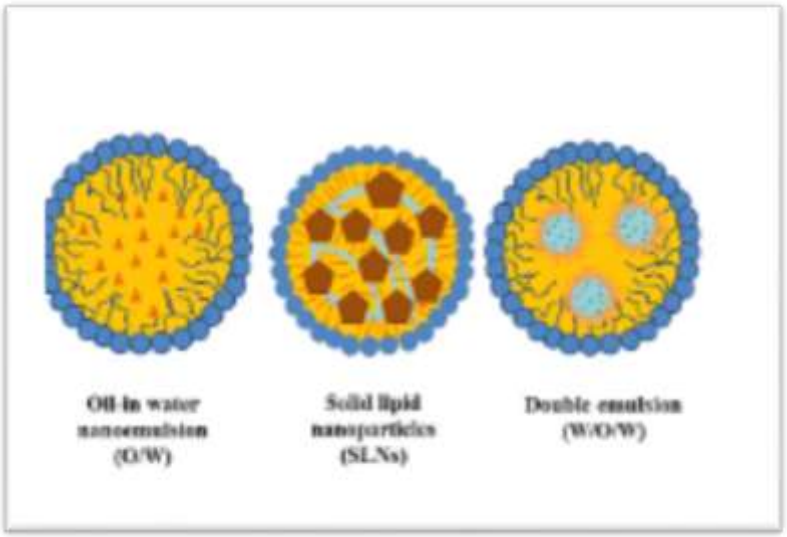


Figure shows: Nanoemulsion.

Advantages of nano emulsion

1. Thermodynamically and kinetically stable therefore flocculation, aggregation, creaming and coalescence do not occur.
2. Non-toxic and non-irritant.
3. Taste masking.
4. Administered by various routes, such as oral, topical, parenteral and transdermal etc...
5. Can deliver both lipophilic and hydrophilic drugs.

Advantages of NDDS over conventional drug delivery system

1. Improve absorption, utilization and thereby enhancing bioavailability.
2. Decreased local and systemic side effects reduced gastro intestinal irritation.
3. Improve safety and efficacy ratio.
4. Reduction dosing frequency.
5. Better patient acceptance and compliance.
6. Reduction in the health care cost.

CONCLUSION

Novel drug delivery system is one of the convenient and novel approach to deliver the drug efficiently to the targeted site, with number of advantages, and limited disadvantages.

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