REVIEW ARTICLE

RECORDS OF PHARMACEUTICAL AND BIOMEDICAL SCIENCES

Lipid-Based Nano Systems as Advanced Approach for Drug Delivery

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Abstract

In the past twenty years, the market for drug delivery has finally seen the entry of nanotechnology. The development and application of chemical, physical, and biological systems with structural characteristics ranging from single atoms or molecules to submicron dimensions, as well as the integration of the resulting nanostructures into larger systems, are the domains of nanotechnology. The field of medical nanotechnology has demonstrated a growing tendency towards cost reduction and enhanced efficacy in the use of current medications, diagnostic tools, implants, prosthetics, patient monitors, and personal health care. To maximize activity and minimize side effects, the search for intelligent drug delivery systems was the main objective. This review discusses nano-structured materials as an important category of advanced nanotechnology-based carriers. Polymeric-based, non-polymeric-based, and lipid-based nanosystems can all be classified as nanostructured materials. This review provides an overview of the most recent variations of this classification in particular lipid-based nanosystems, including those that may be considered promising in the fight against cancer disease.

Keywords: Nanotechnology, nano-structured materials, lipid-based nanosystems.

1. Introduction

Drug delivery systems (DDS) have been used in pre-clinical and clinical settings to safely transport therapeutic drugs into various locations in the body as needed to produce the required therapeutic effect and treat diseases. Traditional DDS is administered either orally or intravenously. Conventional DDS has many benefits, such as being simple to administer and well-liked by patients. But it also has some significant drawbacks which include, minimal efficiency when taken orally, many medications have variable rates of absorption. In addition, the low pH environment and digestive enzymes may cause some medications to break down before they reach the bloodstream. Moreover, there is a lack of selectivity due to oral drug delivery's subpar biodistribution, it is not recommended for drugs that need to target specific organs. Drug toxicity may result from high drug uptake in the liver or kidney, which function as detoxification organs (Dang and Guan 2020). Since the introduction of the first Dexedrine sustained-release formulation in the 1950s, modern DDS has been constantly improved (Park 2014).

Nano-based carriers have emerged as one of the most promising DDSs in recent years. Drugs that are enclosed in nano-based carriers have a better therapeutic index and experience fewer negative side effects (Li, Wang et al. 2019). Nano-based carriers range in size from 1 to 100 nm in at least one dimension and have unique biological and physicochemical properties (Azócar, Alarcón et al. 2019). Using nano-based carriers as DDS will increase the efficacy of the drug by increasing it is half-life, increasing the solubility of many hydrophobic drugs, and improving the release of the drug in a sustained or controlled manner (Dang and Guan 2020). The drug components are encapsulated, dissolved, attached to, or trapped within the nano-based carrier matrix (Zahin, Anwar et al. 2020). Because of their small size and large surface area, nano-based carriers are widely used in a variety of industries, including electronics, cosmetics, and both diagnostic and therapeutic medical applications (Missaoui, Arnold et al. 2018). The ability to image nano-based carriers with methods capable of atomic resolution, like scanning tunnelling microscopy, scanning transmission electron microscopy, and tandem electron microscopy, has contributed to the exponential growth and rising interest in nanotechnology (Sharma, Jaiswal et al. 2019; Najahi-Missaoui, Arnold et al. 2020).

2. Types of therapeutic nano-based carrier

Nanomaterials can be categorized into two main types: nanostructured and nanocrystalline, as shown in Figure 1. Nano-structured materials can be classified into polymeric-based, non-polymeric-based, and lipid-based nanoparticles. Polymeric-based nanoparticles include nanoparticles, nanogels, protein nanoparticles, micelles, dendrimers, and drug conjugates. Whilst, non-polymeric-based nanoparticles include metallic nanoparticles, nanodiamonds, carbon nanotubes, quantum dots, and silica-based nanoparticles. Lipid-based nanosystems can be classified into three main types, (I) emulsion-based systems such as, microemulsions, nanoemulsions, self-emulsifying drug delivery systems, and pickering emulsions. (II) vesicle-based systems such as, liposomes, niosomes, pharmacosomes, phytosomes, elastic liposomes, ethosomes, archaeosomes, vesosomes, colloidosomes, aquasomes, cubosomes, sphingosomes, ufasomes, emulsomes, and novasomes. and the third one is (III) the particulate systems which include lipospheres, solid lipid microparticles, solid lipid nanoparticles, Nano-structured lipid carriers, lipid drug conjugates, and smart lipids. The majority of nanoparticles that have been clinically approved for therapeutic use thus far have polymer- or lipid-based constituents. In addition to nano-structured particles, nanocrystalline particles are created when therapeutic agents combine to form crystals (Yetisgin, Cetinel et al. 2020).

2.1. polymeric-based nanoparticles

The most frequently investigated materials for creating modern DDS are polymers. The polymer that is used must be inert, nontoxic, and impurity-free. Both synthetic polymers, such as poly (lactic acid) and poly (lactic-co-glycolic acid), as well as natural polymers, like chitosan and collagen, can be used to create polymeric nanoparticles. The use of polymeric nanoparticles in drug delivery has several benefits, including the ability to easily and cheaply fabricate them in large quantities using a variety of techniques and the ability to increase the stability of any volatile agents (Castro and Kumar 2013).

Polymeric-based nanoparticles, as shown in Figure 2, include:

- Nanoparticles

It is made up of particles with a size range of 1 to 1000 nm and can contain active substances that have been surface-adsorbed onto the polymeric core or are loaded inside them (Zielińska, Carreiró et al. 2020). Polymer-based nanoparticles, whether synthetic or natural, offer an alternative method for therapeutic applications due to certain qualities like biocompatibility, non-immunogenicity, non-toxicity, and biodegradability (Crucho and Barros 2017).

- Nanogels

A nanogel is a gel particle that is composed of polymeric networks that, when in contact with fluid, swell with similar characteristics but a diameter of less than 100 nm (Alemán, Chadwick et al. 2007).

- Protein Nanoparticles

Proteins like fibroins, albumin, gelatin, and ferritin proteins can be used to create protein nanoparticles. The benefits of protein nanoparticles are numerous, including biocompatibility and biodegradability. Furthermore, there were no harmful chemicals or organic solvents used during the creation of protein nanoparticles or the subsequent encapsulation process (Hong, Choi et al. 2020).

- Micelles

Polymeric micelle components are arranged in spheroidal structures with hydrophobic cores

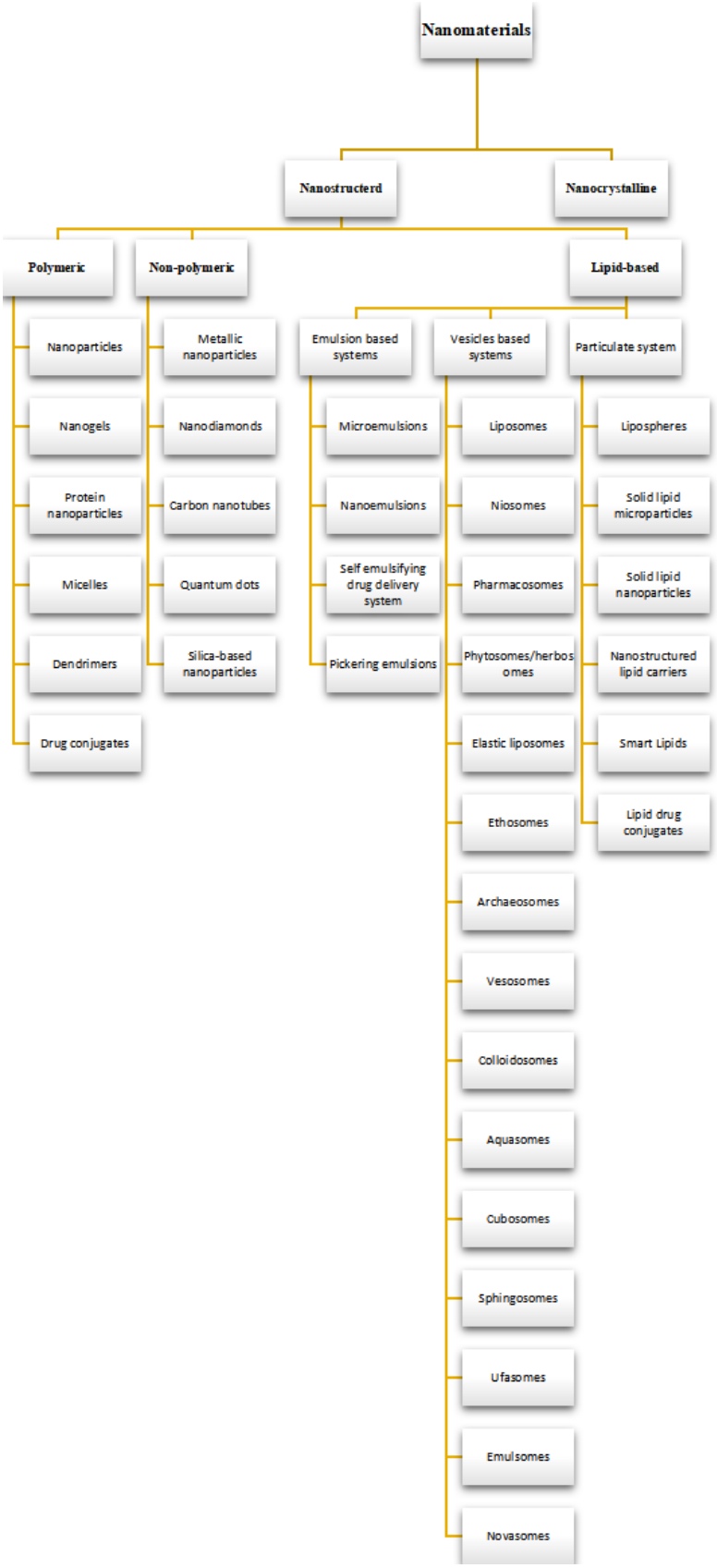

Figure 1. Types of therapeutic nanotechnology-based carrier

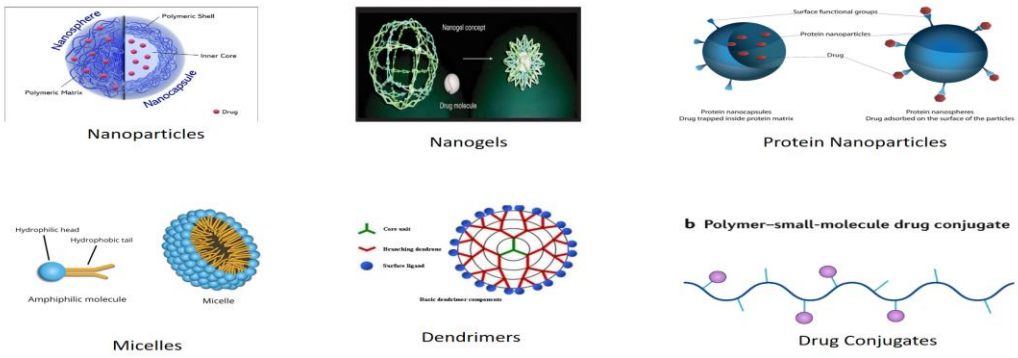

Figure 2. Types of Polymeric-based nanoparticles

encircled by a mantle of hydrophilic groups. Most often, polymeric micelles are used to deliver therapeutic agents that are not water soluble throughout the body (Ahmad, Shah et al. 2014).

- Dendrimers

Dendrimers are radially symmetric, nanoscale molecules with well-defined, homogeneous, and monodisperse structures. They have an outer shell, an inner shell, and a core that is typically symmetric (Abbasi, Aval et al. 2014). Dendrimers made of mono- or copolymers like polyethyleneimine, polyamidoamine, poly(propyleneimine), chitin, etc. are currently used in therapeutic applications. Due to their compartmentalised, hyperbranched structure and high monodispersity, dendrimers are a common polymer used in clinical applications (Hsu, Bugno et al. 2017).

- Drug Conjugates

Low-molecular-weight agents are frequently conjugated with polymers, particularly in the treatment of cancer. The pharmacokinetic disposition in the cells is induced by this conjugation, which raises the molecular weight of the drugs overall (Markovsky, Baabur-Cohen et al. 2014).

2.2. Non-polymeric-based nanoparticles

Non-polymeric nanoparticles may be defined as particles in the nano range of metallic or metal oxide constituents. There are several challenges when preparing non-polymeric nanoparticles, as there is no process that will fit all types of production, and most procedures will differ between institutions and on an industrial scale (Safari and Zarnegar 2014).

Non-polymeric-based nanoparticles, as shown in Figure 3, include:

- Metallic Nanoparticles

Metals such as cobalt, nickel, iron, and gold, as well as their corresponding oxides such as magnetite, maghemite, cobalt ferrite, and chromium dioxide, make up the majority of the 1-100 nm metallic nanoparticles used in medical applications (Yetisgin, Cetinel et al. 2020).

- Nanodiamonds

Nanodiamonds are discrete nanomaterials made of carbon that have a diameter of less than 100 nm and come in a variety of shapes (Torres Sangiao, Holban et al. 2019).

- Carbon Nanotubes

Carbon nanotubes are tubular, carbon-based structures with a diameter of 1 nm and a length of 1–100 nm. These structures can be made by forming a seamless cylinder out of graphene, a single layer of graphite (Yetisgin, Cetinel et al. 2020).

- Quantum Dots

Quantum dots are extremely small particles or nanocrystals of a semiconducting substance with an inorganic core like CdSe and an aqueous organic coated shell-like ZnS, with diameters in the 2–10 nm (Kim, Beack et al. 2018).

- Silica-Based Nanoparticles

Due to their suitability for use in designing intricate systems, silica-based nanoparticles have several advantages in the field of nanotechnology. They are desirable therapeutic delivery tools due to their unique surface properties, porosity, and functionalization ability (Chen, Hableel et al. 2018).

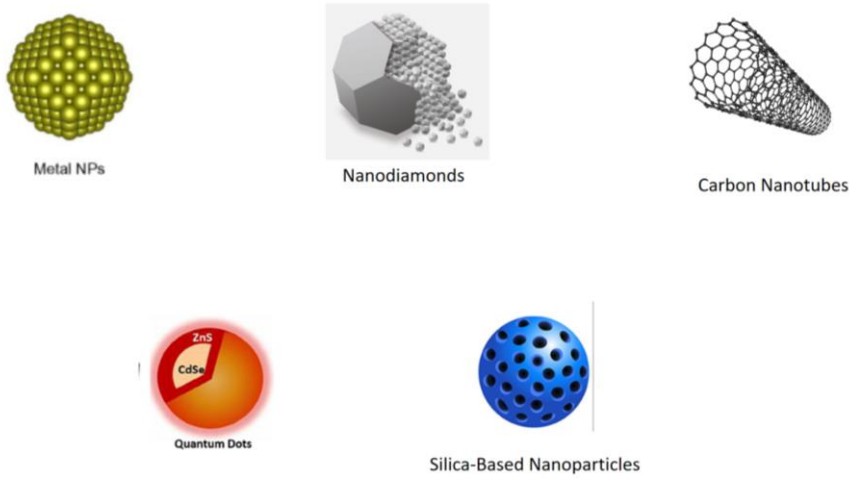

Figure 3. Types of Non-polymeric-based nanoparticles

2.3. Lipid-based nanosystems

Lipids are typically hydrocarbon-containing organic compounds that are obtained from plants and animals using low-polarity solvents. Oils, waxes, cholesterol, triglycerides, monoglycerides, diglycerides, sterols, phospholipids, and fat-soluble vitamins are some examples of used lipids. Lipids are rapidly gaining popularity as potential excipients for both drug delivery and cosmetics (Gonnade, Niranjane et al. 2014). Lipid-based nanoparticles are typically non-spherical in shape, which can either be attributed to the solvent's non-polar lipid hydrocarbon moieties or the electrostatic interaction between the polar/ionogenic phospholipid head and the solvent (Lu, Zhang et al. 2021).

Lipid nanoparticles have risen to the top of the pack among the variety of nanoparticles currently under investigation by scientists due to their obvious preferences for a higher level of biocompatibility and flexibility. Pharmaceuticals that are organised and delivered for topical, oral, pneumonic, or parenteral use can be defined using these frameworks. Lipid-based nanoformulations can be specifically tailored to satisfy a wide range of product requirements that are determined by factors like disease severity, cost, the best administration route, and the viability and stability of the final product. These structures develop as carriers for pharmaceutical formulations due to their efficacy and safety (Attama, Momoh et al. 2012). In addition, Lipid-based nanosystems offer a new method of treating many diseases, including cancer, by delivering drugs to the desired location, thereby enhancing the pharmacokinetics and/or lowering the toxicities of the drugs (Obeid, Tate et al. 2018).

The rationale for investigating lipid-based nanosystems (Pouton and Porter 2008; Čerpnjak, Zvonar et al. 2013):

- Lipidic excipients' flexibility.
- Flexibility in formulation design.
- Low-risk profile.
- Increased oral bioavailability with minimal changes to the plasma profile.
- Superior penetration when applying topically.
- Improved depiction of lipid excipients.
- A high level of market appeal for innovative products.
- Commercialization Possibility.
- Enhanced capacity to handle the crucial issues of technology transfer and manufacturing scale-up.

Features of lipid-based nanosystems (Mishra, Shandilya et al. 2018):

- Targeted and controlled drug release.
- Stability in pharmaceuticals.
- When compared to other carrier systems, the drug content is higher and better.
- The ability to incorporate both hydrophilic and lipophilic drugs.
- Biocompatible and biodegradable.
- Better uniformity of the dose.
- Low therapeutic dose is necessary due to improved drug absorption.
- Low-risk status.
- Simple scalability and sterilization.
- Simple validation.
- More affordable than systems based on polymers or surfactants.
- A decrease in therapeutic dose brought on by better drug absorption.

- Versatility in administration, or the ability to be delivered orally, parenterally, intravenously, intraocularly, intranasally, transdermally, and vaginally. Whereas several routes of administration can be used, the most frequently suggested routes of administration for lipid-based nanosystems (Scioli Montoto, Muraca et al. 2020) are shown in Figure 8

Lipid-based nanosystems were used in different therapeutic fields (Scioli Montoto, Muraca et al. 2020), as shown in Figure 9.

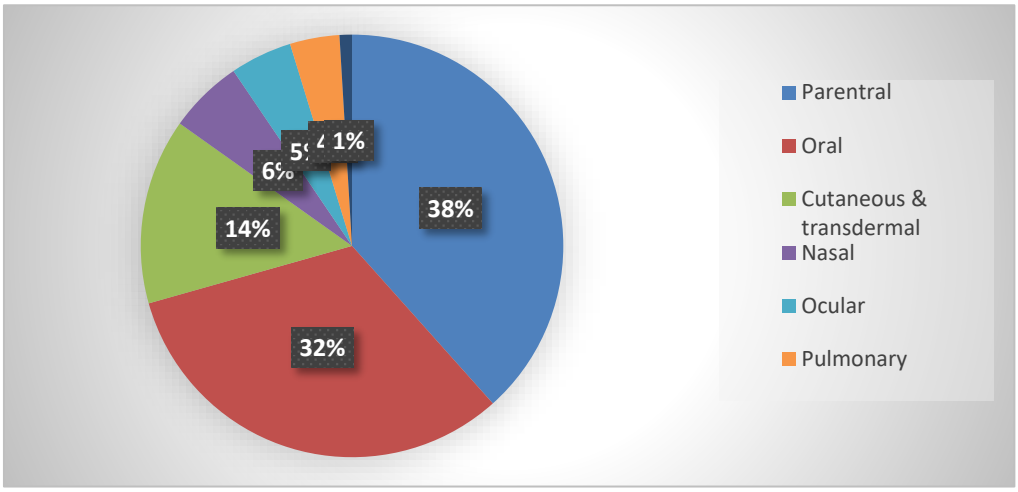

Figure 8. Percentage of publications from 2013 - 2020 by different routes of administration.

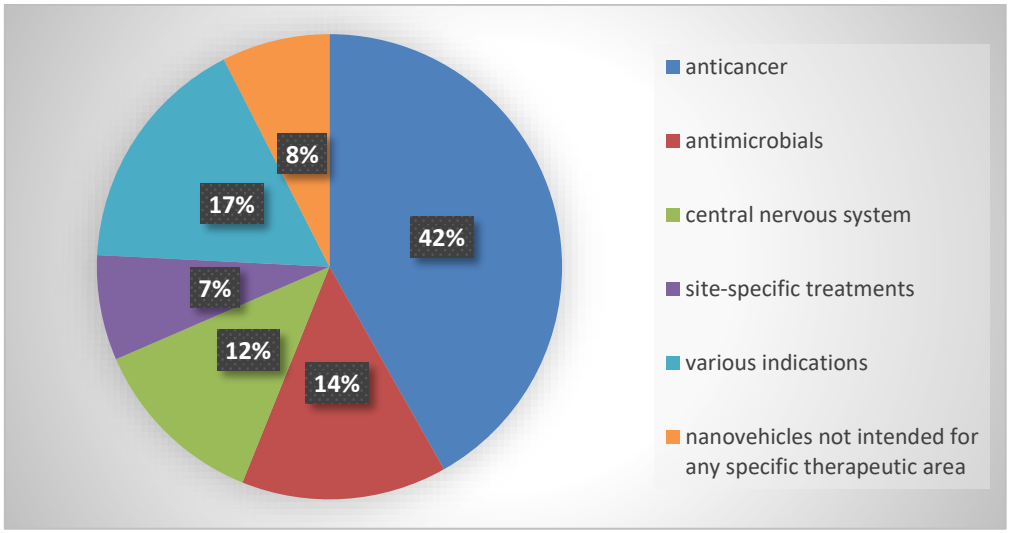

Figure 9. Percentage of publications from 2013 - 2020 by therapeutic field.

2.3.1. Classification of Lipid-based nanosystems

2.3.1.1. Emulsion-based systems:

Oil, surfactant/co-surfactant, and water are valuable ingredients that can be contained, protected, and released using emulsion-based systems. Aqueous droplets are dispersed in the oil phase of a W/O emulsion while oil droplets are dispersed in the continuous water phase of an O/W emulsion. In an emulsion, the liquid that surrounds the droplets is referred to as the "continuous phase," and the liquid that makes up the droplets is referred to as the "dispersed phase." (Nikmaram, Roohinejad et al. 2017). According to the size of their particles, colloidal dispersions can generally be divided into the following categories as shown in Figure 10:

- Microemulsions

An interfacial film of amphiphilic mixtures, such as surfactant and co-surfactant, balances out the optically isotropic arrangement of oil and water in microemulsions. The size and shape of the dispersed particles are the primary distinctions between a microemulsion and an emulsion. Emulsion size ranges from 1 to 20 m, while microemulsion size ranges from 10 to 200 nm (Saroj, Baby et al. 2012).

- Nanoemulsions

Nanoemulsions are emulsions with 100 nm or smaller droplet sizes. Traditional nanoemulsions are made up of an emulsifier, water, and oil. Surfactants are typically used as emulsifiers, but proteins and lipids can also be effective in the creation of nanoemulsions. Nanoemulsions are transporters for hydrolyzable, lipophilic drugs that are biodegradable, biocompatible, and simple to prepare (Lai, Pireddu et al. 2013).

- Self-emulsifying drug delivery systems

They are gentle agitation-induced emulsions of isotropic oil, surfactant, co-surfactant, and therapeutic substance mixtures. They rapidly disperse in the GIT with mild agitation from gastric motility, which results in emulsion formation. The emulsions that are typically created have a cloudy appearance and droplet sizes of between 200 nm and 5 m. One potential method for delivering water-insoluble or poorly soluble compounds orally is self-emulsifying drug delivery systems (Wadhwa, Nair et al. 2012).

- Pickering emulsions

They could be water-in-oil (w/o), oil-in-water (o/w), or even multiple emulsions that are stabilized by solid particles rather than surfactants. High resistance to coalescence is the main stabilization by solid particles main benefit. Pickering emulsions are lipid-based emulsions with internal nanostructures that are stabilised by inert substances like silica, clay, calcium carbonate, and titanium dioxide (Saroj, Baby et al. 2012).

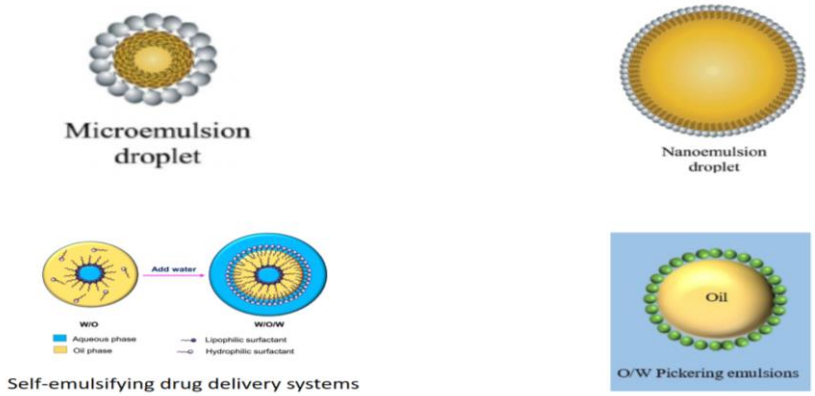

Figure 10. Emulsion-based lipid nanoparticles

2.3.1.2. Vesicle-based systems:

Vesicular drug delivery systems are highly ordered assemblies made up of one or more concentric bilayers that form when the amphiphilic building blocks self-assemble in the presence of water. The ability of vesicular drug delivery systems to localise drug activity at the site or organ of action thereby lowering its concentration at other sites in the body makes them particularly crucial for targeted drug delivery (Jain, Jain et al. 2014). Vesicular drug delivery systems can be divided as shown in Figure 11.

- Liposomes

A bilayer of lipids, which can be made of either natural or synthetic lipids, surrounds an aqueous compartment in a liposome, which is described as a microscopic, colloidal, concentric structure.

Cholesterol serves as a fluidity buffer, and phospholipids like phosphatidylcholine and cholesterol are crucial parts of the liposomal drug delivery system. According to their size and number of bilayers, they can be divided into a variety of types, including multilamellar vesicles (MLVs), small unilamellar vesicles (SUVs), and large unilamellar vesicles (LUVs) (Shamant, Moin et al. 2016).

- Niosomes

Niosomes are tiny unilamellar, oligolamellar, or multi-lamellar nonionic surfactant vesicles created when non-ionic surfactants are added to cholesterol and then hydrated in aqueous media. They share structural similarities with liposomes. Due to the addition of nonionic surfactants, niosomes show increased size and charge on the vesicles, which further increases their entrapment efficiency (Bhardwaj, Tripathi et al. 2020).

- Pharmacosomes

These are lipid-covalently bonded drug colloidal dispersions. Since a drug develops this system to act as a carrier, it is known as a pharmacosome. Depending on the chemical makeup of the drug-lipid complex, they may exist as micelles, hexagonal aggregates, or ultrafine vesicles. They may be a useful tool for achieving desired objectives, such as drug targeting and controlled delivery (Mishra, Shandilya et al. 2018).

- Phytosomes/herbosomes

They have a cell-like design that results from the stoichiometric interaction of phospholipids with constituents of standard extract or polyphenols. These systems have attracted a lot of interest in a variety of industries, including pharmaceuticals, cosmeceuticals, and nutraceuticals (Salome and Ikechukwu 2013).

- Elastic liposomes

A brand-new variety of modified liposomes has been created with the ideal amount of a surfactant or edge activator that provides elasticity. Elastic liposomes, also known as transfersomes, are highly developed, ultra-deformable lipid supramolecular aggregates that can deliver drugs into or through the skin before reaching the systemic circulation (Cevc, Gebauer et al. 1998).

- Ethosomes

Ethosomes, also known as ethanolic liposomes, are a new type of non-invasive, lipid-based carrier system that aids in delivering biologically active agents to deeper layers of the skin and the body's circulatory system. These vesicular systems primarily consist of phospholipids, water, and ethanol at a higher concentration (20–50%) (Dubey, Mishra et al. 2007).

- Archaeosomes

A liposome made of fully saturated bipolar tetra ether lipids is all that an archaeosome is. In a variety of conditions, such as high temperature, acidic or alkaline pH, and oxidative stress, they are discovered to be significantly more stable than conventional lipids. They are nano-sized vesicles made from synthetic or extracted archaeal lipids from archaeobacteria (Asadujjaman and Mishuk 2013).

- Vesosomes

The distinguishing characteristics of vesosomes are multi-compartment array frameworks with distinct inner compartments separated from the external membrane. This framework's multiple compartments provide better protection for the physiological system's encapsulated contents and longer drug release (Salome and Ikechukwu 2013).

- Colloidosomes

These are colloidal microcapsules with densely packed colloidal particles. These systems are appealing for encapsulation and controlled drug release due to the improved control over their physical characteristics (Lee and Weitz 2008).

- Aquasomes

Aquasomes or ceramic nanoparticles are self-assembled nanostructures with three layers that have a solid phase nanocrystalline core and are covered in an oligomeric carbohydrate film that is adhered to with or without modification by biochemically active molecules. Polymers or ceramics make up the nanocrystalline core. Trehalose, cellobiose, sucrose, pyridoxal 5 phosphate, citrate, chitosan, and other coating ingredients are frequently used (Jain, Jain et al. 2014).

- Cubosomes

Cubosomes are described as thermodynamically stable, self-assembled, liquid crystalline nano frameworks that are used as biocompatible drug delivery vehicles because they are composed of specific amphiphilic lipids in specific ratios (Umar, Wahab et al. 2022).

- Sphingosomes

Sphingosomes are classified as bilayered vesicles that completely enclose an aqueous compartment and are primarily made of cholesterol and sphingolipids, either naturally occurring or synthesised, in varying ratios(Jain, Jain et al. 2014).

- Ufasomes

Ufasomes are suspensions of fatty acid and ionic surfactant-based closed lipid bilayers. For effective topical or transdermal delivery of medications, proteins, peptides, or hormones, ufasomes appear to be a promising approach (Jain, Jain et al. 2014).

- Emulsomes

Emulsomes are nanocarriers with integrated emulsion and liposome properties made up of a solid fat core surrounded by one or more phospholipid bilayers (Mishra, Shandilya et al. 2018).

- Novasomes

Formed from a mixture of polyoxyethylene fatty acids (as monoester), free fatty acids, and cholesterol, novasomes are a type of liposomal-based nanocarrier with a diameter that ranges from 0.1 to 1 micron. They have a large amphipathic core that is encased in 2-7 bilayers. Novasomes may have a positive, neutral, or negative surface charge (Alavi, Karimi et al. 2017).

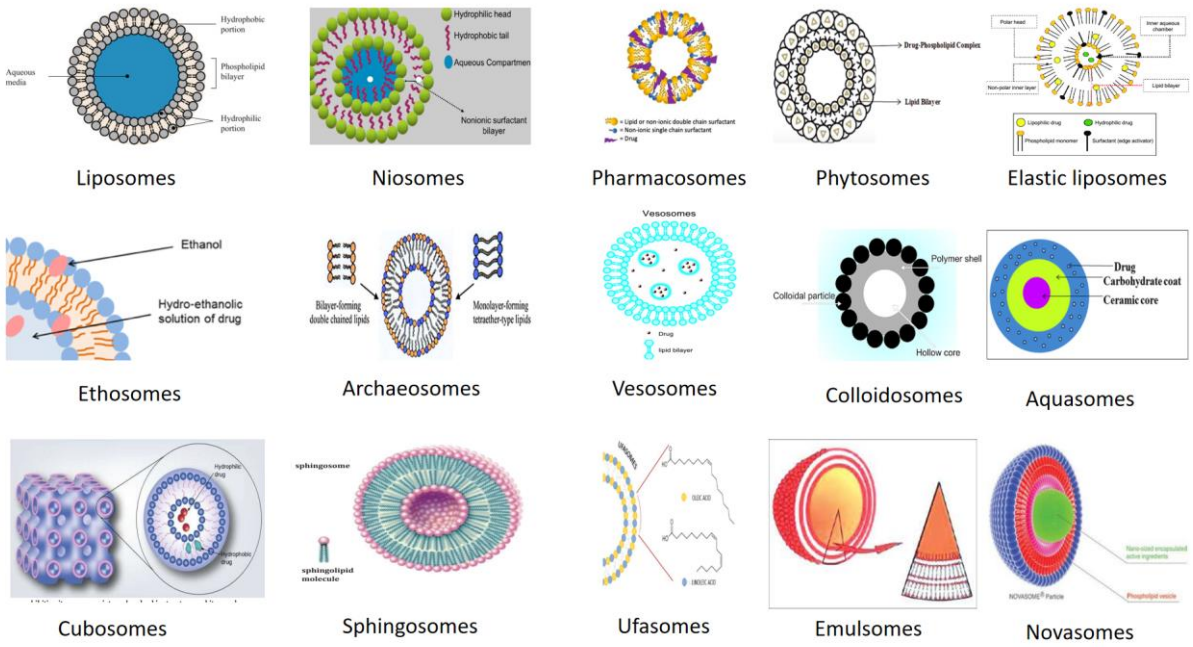

Figure 11. Vesicle-based systems

2.3.1.3. Particulate system:

Particulate drug carriers have a high potential for drug delivery, especially tiny particles like microparticles and colloidal systems in the nanometer range. Improved, and reduced toxicity, enhanced biodistribution, and improved patient compliance are just a few of the benefits that a nanoparticulate drug delivery system may have over conventional dosage forms (Reddy and Shariff 2013). They can be classified as shown in Figure 12.

- Lipid drug conjugates

A new class of lipid-based nanoparticles that are frequently chosen for site-specific delivery. These offer a possible drug delivery site for hydrophilic and lipophilic substances that is appropriate for CNS targeting. The particles' surfaces were altered to direct them toward the CNS, creating a promising delivery system for lipid drug conjugates (Mehanna, Motawaa et al. 2012).

- Lipospheres

Lipid microspheres, also known as lipospheres, are a more recent type of encapsulation based on a lipidic system composed of water-dispersible solid microparticles that range in diameter from 0.1 to 100 m and were created for the delivery of therapeutically active compounds such as anti-inflammatory compounds, local anaesthetics, anticancer, vaccines, and antibiotics agents, particularly lipophilic substances. These are made up of a triglyceride fat core that is solid and hydrophobic, and the phospholipids on its surface stabilize it. The therapeutic compounds are dispersed throughout the lipid matrix in the innermost core (Chime, Attama et al. 2013).

- Solid lipid microparticles

They are solid lipid particles that are spherical and range in size from 1 to 1000 m. These microscopic particles had a stable polymeric core made of lipids found in nature and were stabilized by dispersed surfactant molecules. These can be given by oral, parenteral, pulmonary, topical, ocular, and rectal routes in addition to being given intravenously (Chime, Attama et al. 2013).

- Solid lipid nanoparticles

Solid lipid nanoparticles were introduced in 1991 and consist of a single solid lipid. They attracted the attention of scientists because of their potential as drug-delivery systems for molecules with low solubility and bioavailability. A biocompatible

lipid nucleus and an amphiphilic surfactant in the outer shell, which have sizes ranging from 50 to 1,000 nm, make up a novel colloidal system. Both hydrophilic and hydrophobic drug molecules disperse at these sites. They are used in cancer treatment, vaccine delivery, drug targeting, and gene delivery, and they are an option for targeting the central nervous system. It is also used to deliver a variety of pharmaceuticals, which are easily and conveniently sold for delivery (Miller and Tang 2009).

- Nanostructured lipid carriers

Another type of lipid nanocarrier is nanostructured lipid carriers, which are made up of a combination of biocompatible solid and liquid lipids. As a result, a less-ordered, imperfect structure is formed, which improves physical stability, and drug loading ability, and lowers the possibility of leaking the drug during storage (Beloqui, Solinís et al. 2016). This could help to improve some drawbacks of solid lipid nanoparticles that come from the highly ordered structure of the crystalline solid lipid, which leads to limited drug loading and leakage of drugs during storage (Mura, Maestrelli et al. 2021).

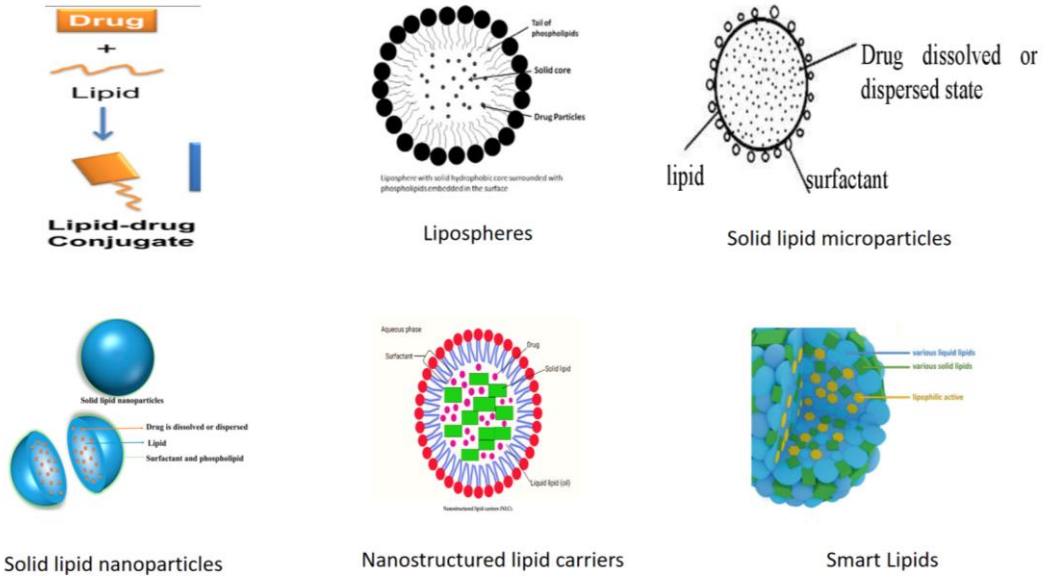

Figure 12. Particulate system

- Smart Lipids

The third generation was then produced by producing highly chaotic lipid mixtures for particle production. The particles were referred to as "Smart Lipids" because they were thought of as a "smart" solution for better "lipid" particle design (Müller, Ruick et al. 2014; Ruick 2015). The lipid mixtures of the Smart Lipids typically contain 5–10 blended solid lipids, or mixtures of solid and liquid lipids as shown in Figure 13. A "wild" lipid mixture with a small number of oils present did not hasten the transition as Nanostructured lipid carrier did. The crystalline structure keeps its original form during storage when a suitable lipid mixture is utilized (Cornier, Keck et al. 2019).

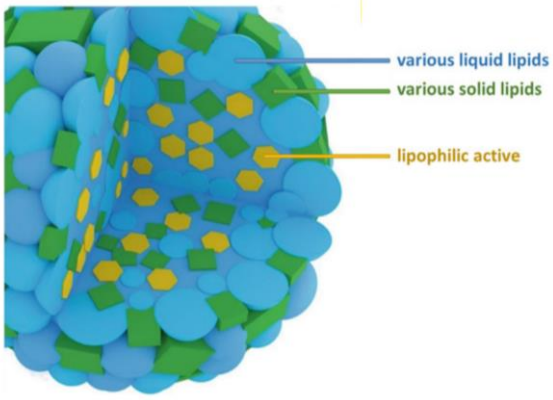

Figure 13. shows a schematic of the Smart Lipids structure. A solid lipid mixture made up of typically 5–10 solid lipids (green squares) and liquid lipids (blue circles) contains lipophilic actives (Cornier, Keck et al. 2019).

The Smart Lipids particles offer also the basic properties of lipid nanoparticles as high adhesiveness to the skin, which results in film formation onto the skin, repair of defects in the natural skin barrier and reinforcement of thin natural lipid film, and re-creation of natural skin barrier, which has an anti-pollution effect, occlusion created by the particle film on the skin, which - increases skin hydration - and normalises skin living condition of the keratinocytes, - increased absorption of molecules generated by the occlusive effect (Ding, Pyo et al. 2017).

The lipid particles in Smart Lipids were chemically designed to have particular properties. Examples include the high cosmetic or pharmaceutical actives' or drugs' firmness inclusion, level of chemical stabilization, and release profile. By describing the three main types of lipid nanoparticle structures—enriched core model, matrix model, and enriched shell model—which broadly apply to all lipid nanoparticles, zur Mühlen and Mehnert (zur Mühlen, Schwarz et al. 1998) demonstrated the impact of particle composition on the release profile.

As was mentioned above, the fact that polymorphic transitions are either limited or nonexistent in Smart Lipids allowed for a noticeable increase in loading capacity, as was seen with retinol (Ding, Pyo et al. 2017). It should be noted, though, that not all complex lipid matrixes exhibit this property by default. The underlying mechanisms for choosing a stable matrix in a foretelling manner are still not fully understood. Therefore, screening experiments are still required. The chemically unstable molecule retinol was found to have improved chemical stability when added to Smart Lipids. It should be noted, though, that a suboptimal Smart Lipids matrix may not be as protective as an optimised NLC particle matrix. In conclusion, manual screening is necessary because a suitable lipid composition cannot yet be predicted by computer simulation (Cornier, Keck et al. 2019).

Since a bulk lipid or lipid mixture must always be shrunk down to the nano dimension, all three generations of lipid nanoparticles can essentially be made using the same techniques. There are several ways to make lipid nanoparticles, including the membrane contractor method (Bagul, Pisal et al. 2018), the ultrasonic-solvent emulsification method (Adel, Khaled et al. 2022), the solvent injection method (Yadav, Shah et al. 2022), the solvent emulsification-diffusion method (Gupta, Sharma et al. 2022), the solvent injection method using multiple emulsions (Jacob, Nair et al. 2022), the microemulsion technique (Khairnar, Pagare et al. 2022), and the high-pressure homogenization method (Khairnar, Pagare et al. 2022).

Conclusion

Interest in nanotechnology, particularly the use of nanostructure-based systems for drug delivery via various routes, has significantly increased over the past few decades. Since they have been the longest-studied carriers, Lipid-based nanosystems have emerged as the most promising candidate for drug delivery. Lipid-based nanosystems provide a wide range of options for the delivery of hydrophobic drugs with low bioavailability. These options are safe, affordable, and encouraging.

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