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Herbaceuticals : A modern approach for drug delivery

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ABSTRACT:
Nanotechnology is defined as the study and use of structures between 1 nanometer and 100 nanometers in size. To give you an idea of how small that is, it would take eight hundred 100 nanometer particles side by side to match the width of a human hair. Scientists have been studying and working with nanoparticles for centuries, but the effectiveness of their work has been hampered by their inability to see the structure of nanoparticles. In recent decades the development of microscopes capable of displaying particles as small as atoms has allowed scientists to see what they are working with. Ayurveda is considered to be a form of complementary and alternative medicine (CAM) within the United States of America, where several of its methods—such as herbs, massage, and Yoga as exercise or alternative medicine—are applied on their own as a form of CAM treatment.

Keywords: Introduction, Nanoparticle, Techniques, Herbal drug delivery

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INTRODUCTION

Nanotechnology is defined as the study and use of structures between 1 nanometer and 100 nanometers in size. To give you an idea of how small that is, it would take eight hundred 100 nanometer particles side by side to match the width of a human hair. Scientists have been studying and working with nanoparticles for centuries, but the effectiveness of their work has been hampered by their inability to see the structure of nanoparticles. In recent decades the development of microscopes capable of displaying particles as small as atoms has allowed scientists to see what they are working with.

Definition:-

Nanoparticles are sub-nanosized colloidal structures composed of synthetic or semi synthetic polymers. The continual quest and manoeuvering towards physical stability improvisation of liposomes resulted into development of solid core nanoparticles in eighties as an alternative drug carrier. The first reported nanoparticles were based on nano biodegradable polymeric systems (polycrylamide, polymethyl- -methacrylate, polystyrene etc.). The possibilities of chronic toxicity due to tissue and immunological response towards polymeric burden, their use for systemic administration however, could not be considered. Soon the biodegradable polymers were taken up and nanoparticles based on poly (cyanoacrylate) were extensively studied. The polymeric nanoparticles can carry drug(s) or proteinaceous substances, i.e. antigen(s). These bioactives are entrapped in the polymer matrix as particulates enmesh or solid solution or may be bound to the particle surface by physical adsorption or chemically. The drug(s) may be added during preparation of nanoparticles or to the previously prepared nanoparticles. The term paniculate is suggestively general and doesn't account for morphological and structural organization of the system. Thus they could be nanospheres, nanocapsules, nanocrystals or nanoparticulates.

Nanospheres may be defined as solid core spherical particulates, which are nanometric in size. They contain drug embedded within the matrix or adsorbed on to surface nanocapsules are vesicular system in which drug is essentially encapsulated within the central volume surrounded by an embryonic continuous polymeric sheath. In the later, drug(s) is mainly encapsulated in the solution system.

The physical chemistry of these systems remains to be the same as of typical colloidal dispersions. The surface charges, dispersibility, density, hydrophobicity and hydrophilicity are some critical factors which determine the absolute stability characteristics of a system.

Ayurveda:

Ayurveda (Devanāgarī:, the 'science of life') is a system of traditional medicine native to India,[9] and practiced in other parts of the world as a form of alternative medicine.[10] In Sanskrit, the word Ayurveda comprises the words āyus, meaning 'life' and veda, meaning 'science'.[9] Evolving throughout its history, Ayurveda remains an influential system of medicine in South Asia.[11] The earliest literature of Ayurveda appeared during the Vedic period in India.[10] The Sushruta Samhita and the Charaka Samhita were influential works on traditional

medicine during this era.[10] Ayurvedic practitioners also identified a number of medicinal preparations and surgical procedures for curing various ailments and diseases.[12]

Ayurveda has become an alternative form of medicine in the western world, where patents for its medicine have been passed, and the intellectual property rights contested by Western and Indian institutions.[13] Ayurveda is considered to be a form of complementary and alternative medicine (CAM) within the United States of America, where several of its methods—such as herbs, massage, and Yoga as exercise or alternative medicine—are applied on their own as a form of CAM treatment.[14]

Ayurveda believes in 'five great elements' (Devanāgarī: ; earth, water, fire, air and space) forming the universe, including the human body.[9] Blood, flesh, fat, bone, marrow, chyle, and semen are believed to be the seven primary constituent elements (Devanāgarī:) of the body.[15] Ayurveda stresses a balance of three substances: wind/spirit/air, phlegm, and bile, each representing divine forces.[15] Acording to Ayurvedic beliefs, the doctrine of these three Doshas (Devanāgarī:)—vata (wind/spirit/air), pitta (bile) and kapha (phlegm)—is important.[16] Traditional beliefs hold that humans possess a unique constellation of Doshas.[16] In Ayurveda, the human body has 20 Guna (Devanāgarī:, meaning quality).[17] Surgery and surgical instruments are employed.[17] It is believed that building a healthy metabolic system, attaining good digestion, and proper excretion leads to vitality.[17] Ayurveda also focuses on exercise, yoga, meditation, and massage.[18]

The concept of Panchakarma (Devanāgarī:) is believed to eliminate toxic elements from the body.[19] Eight disciplines of Ayurveda treatment, called Ashtanga (Devanāgarī:), are given below:[20]

- Surgery (Shalya-chkitsa).
- Treatment of diseases above the clavicle (Salakyam).
- Internal medicine (Kaya-chikitsa).
- Demonic possession (Bhuta vidya): Ayurveda believes in demonic intervention and—as a form of traditional medicine—identifies a number of ways to counter the supposed effect of these interferences.[21] Bhuta vidya has been called psychiatry.[10]
- Paediatrics (Kaumarabhrtyam).
- Toxicology (Agadatantram).
- Prevention and building immunity (rasayanam).
- Aphrodisiacs (Vajikaranam).

Herbal drugs

Herbs

Herbs include crude plant material such as leaves, flowers, fruit, seed, stems, wood, bark, roots, rhizomes or other plant parts, which may be entire, fragmented or powdered.

Herbal materials

Herbal materials include, in addition to herbs, fresh juices, gums, fixed oils, essential oils, resins and dry powders of herbs. In some countries, these materials may be processed by various local procedures, such as steaming, roasting, or stirbaking with honey, alcoholic beverages or other materials.[2]

Herbal preparations

Herbal preparations are the basis for finished herbal products and may include comminuted or powdered herbal materials, or extracts, tinctures and fatty oils of herbal materials. They are produced by extraction, fractionation, purification, concentration, or other physical or biological processes. They also include preparations made by steeping or heating herbal materials in alcoholic beverages and/or honey, or in other materials.

Use of medicinal plants can be as informal as, for example, culinary use or consumption of an herbal tea or supplement, although the sale of some herbs considered dangerous is often restricted to the public. Sometimes such herbs are provided to professional herbalists by specialist companies. Many herbalists, both professional and amateur, often grow or "wildcraft" their own herbs.

Some researchers trained in both western and traditional Chinese medicine have attempted to deconstruct ancient medical texts in the light of modern science. One idea is that the yin-yang balance, at least with regard to herbs, corresponds to the pro-oxidant and anti-oxidant balance. This interpretation is supported by several investigations of the ORAC ratings of various yin and yang herbs.

Eclectic medicine came out of the vitalist tradition, similar to physiomedicalism and bridged the European and Native American traditions. Cherokee medicine tends to divide herbs into foods, medicines and toxins and to use seven plants in the treatment of disease, which is defined with both spiritual and physiological aspects, according to Cherokee herbalist David Winston.

In India, Ayurvedic medicine has quite complex formulas with 30 or more ingredients, including a sizable number of ingredients that have undergone "alchemical processing", chosen to balance "Vata", "Pitta" or "Kapha."

In addition there are more modern theories of herbal combination like William LeSassier's triune formula which combined Pythagorean imagery with Chinese medicine ideas and resulted in 9 herb formulas which supplemented, drained or neutrally nourished the main organ systems affected and three associated systems. His system has been taught to thousands of influential American herbalists through his own apprenticeship programs during his lifetime, the William LeSassier Archive[64] and the David Winston Center for Herbal Studies

Many traditional African remedies have performed well in initial laboratory tests to ensure they are not toxic and in tests on animals. Gawo, a herb used in traditional treatments, has been tested in rats by researchers from Nigeria's University of Jos and the National Institute for Pharmaceutical Research and Development. According to research in the African Journal of

Biotechnology, Gawo passed tests for toxicity and reduced induced fevers, diarrhoea and inflammation

Drug delivery

Drug delivery is the method or process of administering a pharmaceutical compound to achieve a therapeutic effect in humans or animals[1] [2]. Drug Delivery technologies are patent protected formulation technologies that modifies drug release profile, absorption, distribution and elimination for the benefit of improving product efficacy & safety and patient convenience & compliance[3]. Most common methods of delivery include the preferred non-invasive peroral (through the mouth), topical (skin), transmucosal (nasal, buccal/sublingual, vaginal, ocular and rectal) and inhalation routes [4][5]. Many medications such as peptide and protein, antibody, vaccine and gene based drugs, in general may not be delivered using these routes because they might be susceptible to enzymatic degradation or can not be absorbed into the systemic circulation efficiently due to molecular size and charge issues to be therapeutically effective. For this reason many protein and peptide drugs have to be delivered by injection. For example, many immunizations are based on the delivery of protein drugs and are often done by injection.

Current efforts in the area of drug delivery include the development of targeted delivery in which the drug is only active in the target area of the body (for example, in cancerous tissues) and sustained release formulations in which the drug is released over a period of time in a controlled manner from a formulation.

Recent Advances in Novel Drug Delivery Systems

The method by which a drug is delivered can have a significant effect on its efficacy. Some drugs have an optimum concentration range within which maximum benefit is derived, and concentrations above or below this range can be toxic or produce no therapeutic benefit at all. On the other hand, the very slow progress in the efficacy of the treatment of severe diseases, has suggested a growing need for a multidisciplinary approach to the delivery of therapeutics to targets in tissues. From this, new ideas on controlling the pharmacokinetics, pharmacodynamics, non-specific toxicity, immunogenicity, biorecognition, and efficacy of drugs were generated. These new strategies, often called drug delivery systems (DDS), are based on interdisciplinary approaches that combine polymer science, pharmaceutics, bioconjugate chemistry, and molecular biology.

To minimize drug degradation and loss, to prevent harmful side-effects and to increase drug bioavailability and the fraction of the drug accumulated in the required zone, various drug delivery and drug targeting systems are currently under development. Among drug carriers one can name soluble polymers, microparticles made of insoluble or biodegradable natural and synthetic polymers, microcapsules, cells, cell ghosts, lipoproteins, liposomes, and micelles. The carriers can be made slowly degradable, stimuli-reactive (e.g., pH- or temperature-sensitive), and even targeted (e.g., by conjugating them with specific antibodies against certain characteristic components of the area of interest). Targeting is the ability to direct the drug-loaded system to the site of interest. Two major mechanisms can be distinguished for addressing the desired sites for drug release: (i) passive and (ii) active targeting. An example of passive targeting is the preferential accumulation of chemotherapeutic agents in solid tumors as a result of the enhanced vascular permeability of tumor tissues compared with healthy tissue. A strategy that could allow active targeting involves the surface functionalization of drug carriers with ligands that are selectively recognized by receptors on the surface of the cells of interest. Since ligand–receptor interactions can be highly selective, this could allow a more precise targeting of the site of interest.

Controlled drug release and subsequent biodegradation are important for developing successful formulations. Potential release mechanisms involve: (i) desorption of surface-bound /adsorbed drugs; (ii) diffusion through the carrier matrix; (iii) diffusion (in the case of nanocapsules) through the carrier wall; (iv) carrier matrix erosion; and (v) a combined erosion /diffusion process. The mode of delivery can be the difference between a drug's success and failure, as the choice of a drug is often influenced by the way the medicine is administered. Sustained (or continuous) release of a drug involves polymers that release the drug at a controlled rate due to diffusion out of the polymer or by degradation of the polymer over time. Pulsatile release is often the preferred method of drug delivery, as it closely mimics the way by which the body naturally produces hormones such as insulin. It is achieved by using drug-carrying polymers that respond to specific stimuli (e.g., exposure to light, changes in pH or temperature).

For over 20 years, researchers have appreciated the potential benefits of nanotechnology in providing vast improvements in drug delivery and drug targeting. Improving delivery techniques that minimize toxicity and improve efficacy offers great potential benefits to patients, and opens

up new markets for pharmaceutical and drug delivery companies. Other approaches to drug delivery are focused on crossing particular physical barriers, such as the blood brain barrier, in order to better target the drug and improve its effectiveness; or on finding alternative and acceptable routes for the delivery of protein drugs other than via the gastro-intestinal tract, where degradation can occur.

Drug Delivery Systems

The global market for advanced drug delivery systems was more than €37.9 billion in 2000 and is estimated to grow and reach €75B by 2005 (i.e., controlled release €19.8B, needle-less injection €0.8B, injectable/impantable polymer systems €5.4B, transdermal €9.6B, transnasal €12.0B, pulmonary €17.0B, transmucosal €4.9B, rectal €0.9B, liposomal drug delivery €2.5B, cell/gene therapy €3.8B, miscellaneous €1.9B). Developments within this market are continuing at a rapid pace, especially in the area of alternatives to injected macromolecules, as drug formulations seek to cash in on the €6.2B worldwide market for genetically engineered protein and peptide drugs and other biological therapeutics.

Drug Delivery Carriers

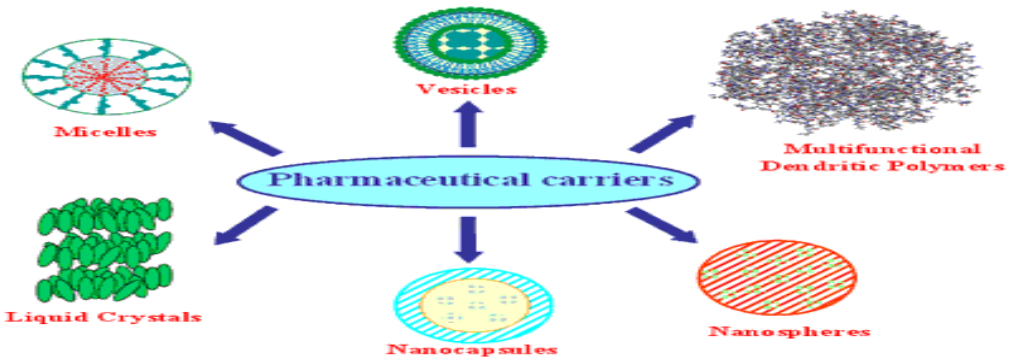

Figure1. Pharmaceutical carriers

Colloidal drug carrier systems such as micellar solutions, vesicle and liquid crystal dispersions, as well as nanoparticle dispersions consisting of small particles of 10–400 nm diameter show great promise as drug delivery systems. When developing these formulations, the goal is to obtain systems with optimized drug loading and release properties, long shelf-life and low toxicity. The incorporated drug participates in the microstructure of the system, and may even influence it due to molecular interactions, especially if the drug possesses amphiphilic and/or mesogenic properties.

Micelles formed by self-assembly of amphiphilic block copolymers (5-50 nm) in aqueous solutions are of great interest for drug delivery applications. The drugs can be physically entrapped in the core of block copolymer micelles and transported at concentrations that can exceed their intrinsic water- solubility. Moreover, the hydrophilic blocks can form hydrogen bonds with the aqueous surroundings and form a tight shell around the micellar core. As a result, the contents of the hydrophobic core are effectively protected against hydrolysis and enzymatic degradation. In addition, the corona may prevent recognition by the reticuloendothelial system and therefore preliminary elimination of the micelles from the bloodstream. A final feature that makes amphiphilic block copolymers attractive for drug delivery applications is the fact that their chemical composition, total molecular weight and block length ratios can be easily changed, which allows control of the size and morphology of the micelles. Functionalization of block copolymers with crosslinkable groups can increase the stability of the corresponding micelles and improve their temporal control. Substitution of block copolymer micelles with specific ligands is a very promising strategy to a broader range of sites of activity with a much higher selectivity.

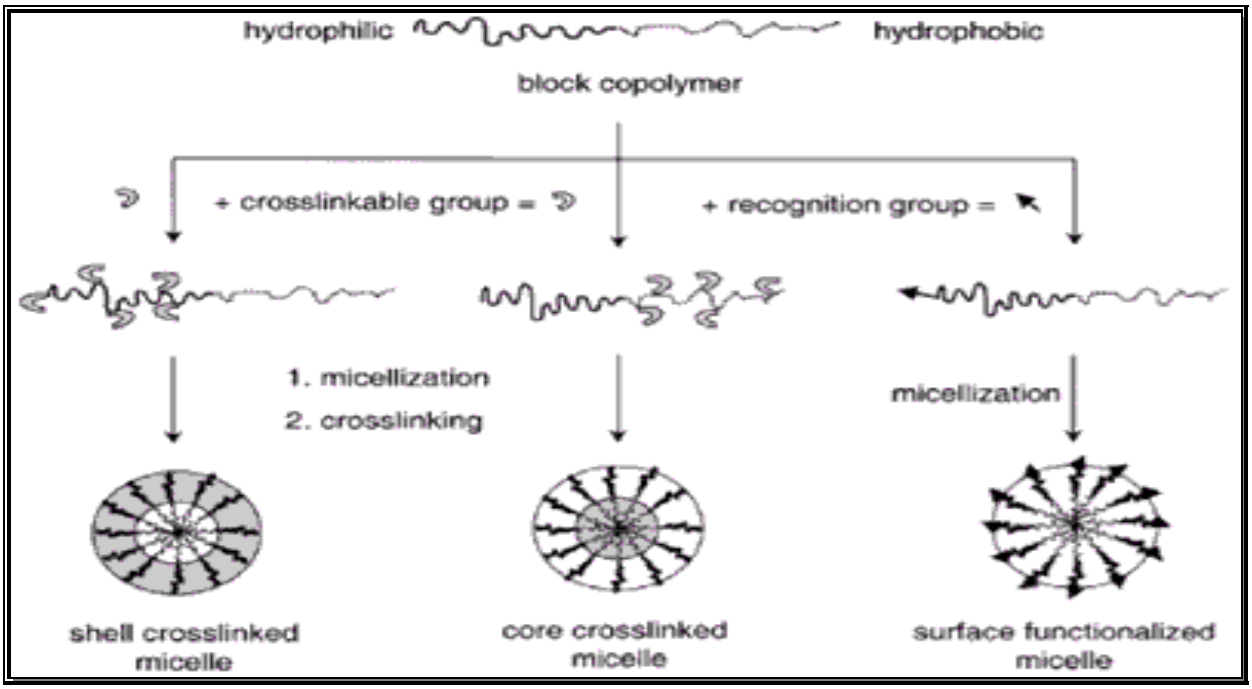

Figure 2. Block copolymer micelles

Liposomes are a form of vesicles that consist either of many, few or just one phospholipid bilayers. The polar character of the liposomal core enables polar drug molecules to be encapsulated. Amphiphilic and lipophilic molecules are solubilized within the phospholipid bilayer according to their affinity towards the phospholipids. Participation of nonionic surfactants instead of phospholipids in the bilayer formation results in niosomes. Channel proteins can be incorporated without loss of their activity within the hydrophobic domain of vesicle membranes, acting as a size-selective filter, only allowing passive diffusion of small solutes such as ions, nutrients and antibiotics. Thus, drugs that are encapsulated in a nanocage-

functionalized with channel proteins are effectively protected from premature degradation by proteolytic enzymes. The drug molecule, however, is able to diffuse through the channel, driven by the concentration difference between the interior and the exterior of the nanocage.

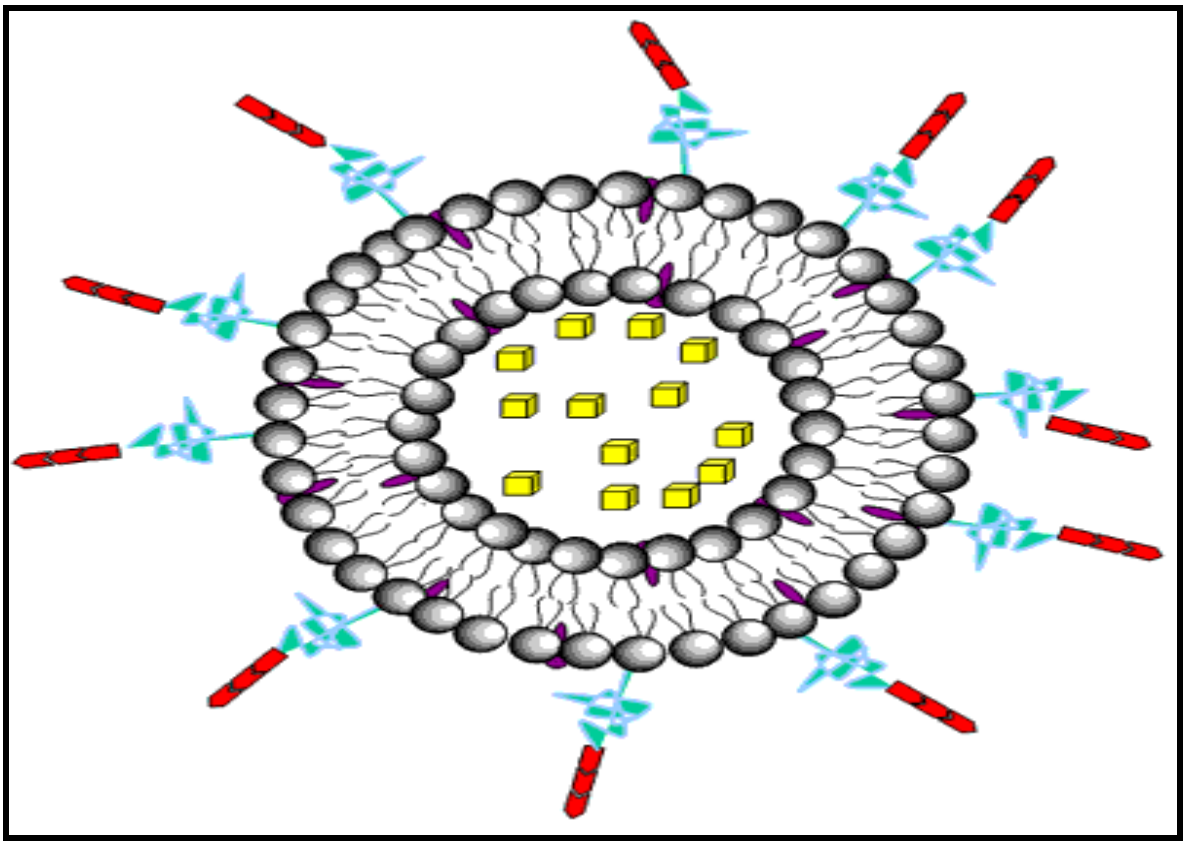

Figure 3. Drug encapsulation in liposomes.

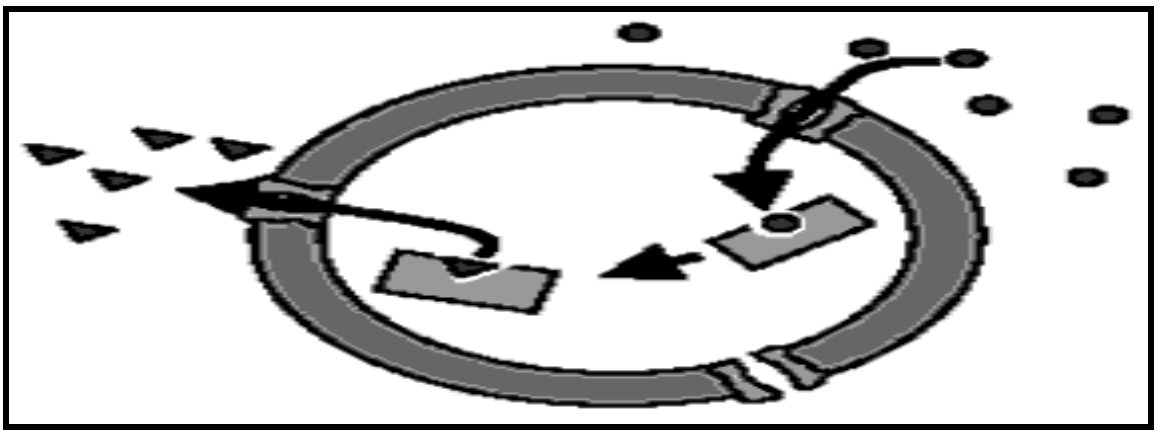

Figure 4. A polymer-stabilized nanoreactor with the encapsulated enzyme

Dendrimers are nanometer-sized, highly branched and monodisperse macromolecules with symmetrical architecture. They consist of a central core, branching units and terminal functional groups. The core together with the internal units, determine the environment of the nanocavities and consequently their solubilizing properties, whereas the external groups the solubility and chemical behaviour of these polymers. Targeting effectiveness is affected by attaching targeting ligands at the external surface of dendrimers, while their stability and protection from the Mononuclear Phagocyte System (MPS) is being achieved by functionalization of the dendrimers with polyethylene glycol chains (PEG).

Liquid Crystals combine the properties of both liquid and solid states. They can be made to form different geometries, with alternative polar and non-polar layers (i.e., a lamellar phase) where aqueous drug solutions can be included.

Nanoparticles (including nanospheres and nanocapsules of size 10-200 nm) are in the solid state and are either amorphous or crystalline. They are able to adsorb and/or encapsulate a drug, thus protecting it against chemical and enzymatic degradation. Nanocapsules are vesicular systems in which the drug is confined to a cavity surrounded by a unique polymer membrane, while nanospheres are matrix systems in which the drug is physically and uniformly dispersed. Nanoparticles as drug carriers can be formed from both biodegradable polymers and non-biodegradable polymers. In recent years, biodegradable polymeric nanoparticles have attracted considerable attention as potential drug delivery devices in view of their applications in the controlled release of drugs, in targeting particular organs / tissues, as carriers of DNA in gene therapy, and in their ability to deliver proteins, peptides and genes through the peroral route.

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