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A Review on Novel Drug Delivery System

Mandira Marwadi, Priyanka Borade, Snehal Kandalkar
Snd college of pharmacy babhulgaon, Yeola, dist-nashik423401 Maharashtra India

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ABSTRACT:
Evolution of an existing drug molecule from a conventional form to a novel delivery system can significantly improve its performance in terms of patient compliance, safety and efficacy. Drug deliveryis the method or process of ad transferosomes ministering a pharmaceutical compound to achieve a therapeutic effect in humans or animals.over the past several years great advance have been made on development of novel drug delivery system.from synthetic and natural bioactive such as polymeric nanoparticles, nanocapsuls, liposomes, Phytosomes, Nano emulsion, microsphere, and ethosomes have been reported. The need for delivering drug to patient efficiently and with fewer side effects has prompted pharmaceuticalcompanies to enage in the development of new drug delivery system. This article covers the basic information regarding novel drug delivery system and also different type of the same.

Keywords: Novel drug delivery system , Nanoparticles, Target site, drugs, Microsphere

INTRODUCTION

The methodby 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. [1]Development of new drug molecule is expensive and time consuming. Improving safety efficacy ratio of "old" drugs has been attempted using different methods such as individualizing drug therapy, dose titration, and therapeutic drug monitoring. Delivering drug at controlled rate, slow delivery, targeted delivery are other very attractive methods and have been pursued vigorously. It is interesting to note that considerable work and many publications from USA, Europe are authored by Indian researchers.[2]

The method by which drug delivered is important, as it has significant effect on its efficacy. Novel drug delivery system involves various approaches like medical devices or drug-device combination products. Novel drug delivery system (NDDS) involves combining polymer science, pharmaceutics and molecular biology [3]

Classification:

- Microsphere

Microspheres are characteristically free flowing powders consisting of proteins or synthetic polymers which are biodegradable in nature and ideally having a particle size less than 200 µm. Materials used for preparing Microspheres are polymers. They are classified into two types:
1. Synthetic Polymers
2.Natural polymers

Synthetic polymers are divided into two types.

- Non-biodegradable polymers
- Poly methyl methacrylate (PMMA)
- Glycerylmethacrylate
- Epoxy polymers
- Biodegradable polymers
- Lactides, Glycoside's& their co polymers
- Poly alkyl cyano acrylates
- Poly anhydrides

Synthetic polymers:Poly alkyl cyano acrylates is a potential drug carrier for parenteral as well as other ophthalmic, oral preparations. Poly lactic acid is a suitable carrier for sustained release of narcotic antagonist, anti cancer agents such as cisplatin, cyclo phosphamide, and doxorubicin.

Sustained release preparations for anti malarial drug as well as for many other drugs have been formulated by using of co-polymer of poly lactic acid and poly glycolic acid. Poly anhydride

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microspheres (40µm) have been investigated to extend the precorneal residence time for ocular delivery.

Poly adipic anhydride is used to encapsulate timolol maleate for ocular delivery. Poly acrolein microspheres are functional type of microspheres. They do not require any activation step since the surfacial free CHO groups over the poly acrolein can react with NH_2 group of protein to form Schiff's base.

In case of non-biodegradable drug carriers, when administered parenterally, the carrier remaining in the body after the drug is completely released poses possibility of carrier toxicity over a long period of time. Biodegradable carriers which degrade in the body to non-toxic degradation products do not pose the problem of carrier toxicity and are more suited for parenteral applications

Natural polymers: Albumin is a widely distributed natural protein. It is considered as a potential carrier of drug or proteins (for either their site specific localization or their local application into anatomical discrete sites). It is being widely used for the targeted drug for the targeted drug delivery to the tumour cells.

Gelatin microspheres can be used as efficient carrier system capable of delivering the drug or biological response modifiers such as interferon to phagocytes. Starch belongs to carbohydrate class. It consists of principle glucopyranose unit, which on hydrolysis yields D-glucose. It being a poly saccharide consists of a large number of free OH groups. By means of these free OH groups a large number of active ingredients can be incorporated within as well as active on surface of microspheres. Chitosan is a deacylated product of chitin. The effect of chitosan has been considered because of its charge. It is insoluble at neutral and alkaline pH values, but forms salts with inorganic and organic salts. Upon dissolution, the amino groups of chitosan get protonated, and the resultant polymer becomes positively charged .[4]

US20110151004[5]	Wu; Daging; et al.	January 27, 2011	Injectable Microspheres
US20090318569[6]	S K Chemicals Co. LTD. Gyeonggi-di, KR	August 31, 2007	Method For Producing Microspheres Loaded With Drugs & Microspheres Loaded With Drugs Produced Thereby

TABLE 1 : EXAMPLES OF PATENTS FOR MICROSPHERES

Advantage:

1) They are natural part of body, so they are biodegradable in nature.
2) The entrapment of drug does not require the chemical modification of drugs
3) The entrapment of drug also does not require the chemical modification of the substance to be entrapped.
4) They are non immunogenic in action and can be targeted to disease tissue/organ..
5) They prolong the systemic activity of drug.

Disadvantage:-

1) They have a limited potential as carrier to non-phagocyte target tissue.
2) Possibility of clumping of cells and dose dumping may be there [7]

- **Nanoparticles**

Nanoparticles are amorphous or crystalline compounds ranging from 10-200 nm, which are used for novel drug delivery system.[8]Various Nano devices for drug delivery includes: Nano tubes, quantum dots, Nano robots, den dimers, Nano wires, Nano shells and Nano pores.[9]

Mechanism of drug delivery via nanoparticle-

Nanoparticles exerts its site-specific drug delivery by avoiding the reticuloendothelial system, utilizing enhanced permeability and retention effect and target-specific targeting. Two types of approaches are applied with drug usingnanoparticle as carrier.

a. Surface bound: The drug molecules are adhered to the surface of nanoparticles

b. Core bound: In such methodology the drug particles are concentrated to the matrix of the

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nanoparticle and carried to the target in the body. Drugs can be loaded onto Nanoparticles by adding them to a solution that contains previously prepared Nanoparticles or by adding them to the reaction mixture during the polymerization process. Nature of interaction of nanoparticle to the drug may be chemical, surface adsorption, and no binding or interaction at all. [10]

Types of Nanoparticles:

1.Solid lipid nanoparticles (SLNs)
2.Nanostructured lipid carriers (NLC
3.Fullerenes
4.Nanoshells
5. Quantum dots (QD)
6. Super paramagnetic nanoparticles

1)Solid lipid nanoparticles (SLNs)

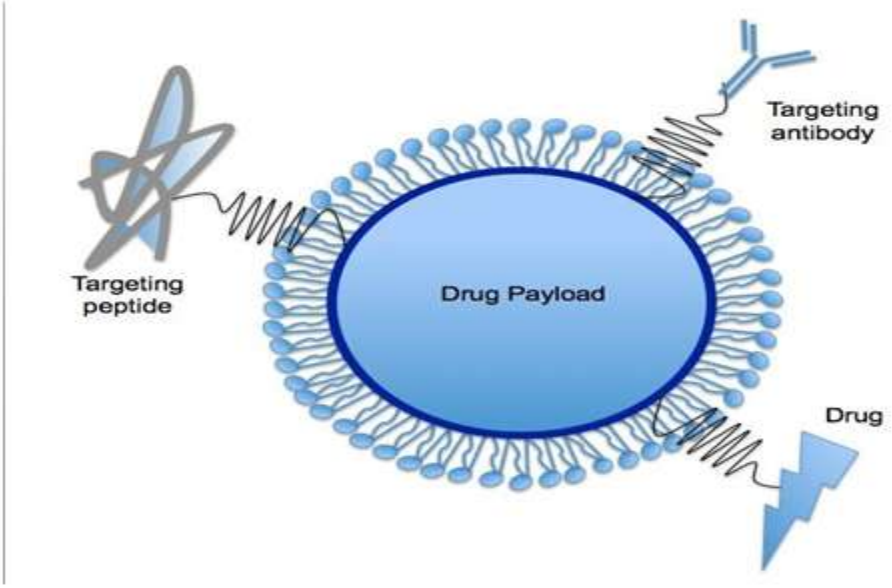

Figure No. 1 : Solid Lipid Nanoparticles

SLNs mainly comprise lipids that are in solid phase at the room temperature and surfactants for emulsification, the mean diameters of range from 50 nm to 1000 nm for colloid drug delivery applications SLNs offer unique properties such as small size, large surface area, high drug loading, the interaction of phases at the interfaces, and are attractive for their potential to improve performance of pharmaceuticals, neutraceuticals and other materials The typical methods of preparing SLNs include spray drying , high shear mixing ,ultra-sonication and high pressure homogenization (HPH) Solid lipids utilized in SLN formulations include fatty acids (e.g. palmitic acid, decanoic acid, and behenic acid).

2)Nanostructured lipid carriers (NLC)14:

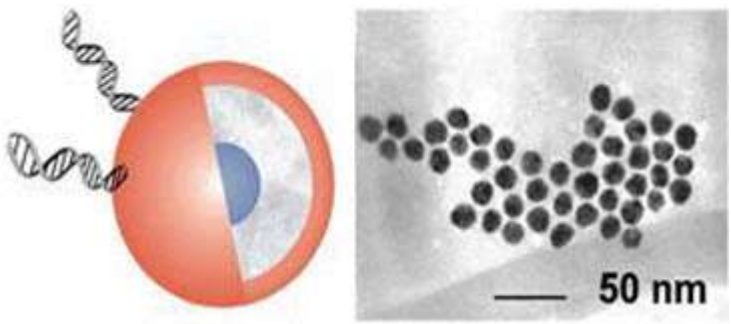

Figure. no.2: Nanostructured lipid carriers

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Nanostructured Lipid Carriers are produced from blend of solid and liquid lipids, but particles are in solid state at body temperature. Lipids are versatile molecules that may form differently structured solid matrices, such as the nanostructured lipid carriers (NLC) and the lipid drug conjugate nanoparticles (LDC) that have been created to improve drug loading capacity. The NLC production is based on solidified emulsion (dispersed phase) technologies.

3)Fullerene

Figure No. 3 : Endohedral Aza[60]fullerenes

A fullerene is any molecule composed entirely of carbon, in the form of a hollow sphere, ellipsoid, or tube. Spherical fullerenes are also called buck balls, and cylindrical ones are called carbon nanotubes or buck tubes. Fullerenes are similar in structure to the graphite, which is composed of stacked grapheme sheets of linked hexagonal rings, additionally they may also contain pentagonal (or sometimes heptagonal) rings to give potentially porous molecules.

4)Nanoshells

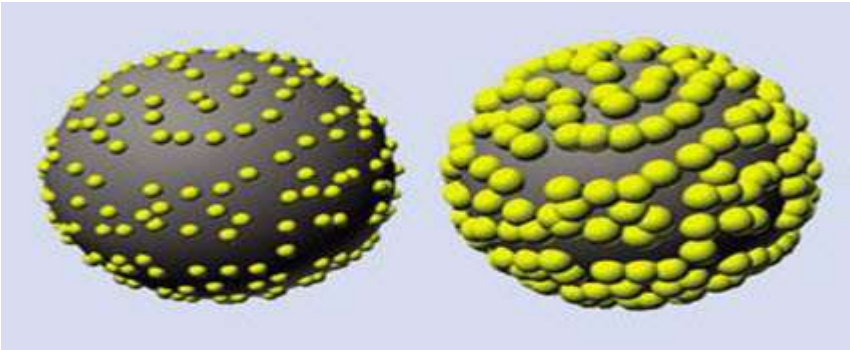

Figure No. 4 : Nanoshells

Nanoshells are also notorious as core-shells, nanoshells are spherical cores of a particular compound (concentric particles) surrounded by a shell or outer coating of thin layer of another material, which is a few 1–20 nm nanometers thick Nano shell particles are highly functional materials show modified and improved properties than their single component counterparts or nanoparticles of the same size.

5)Quantum Dots (QD)

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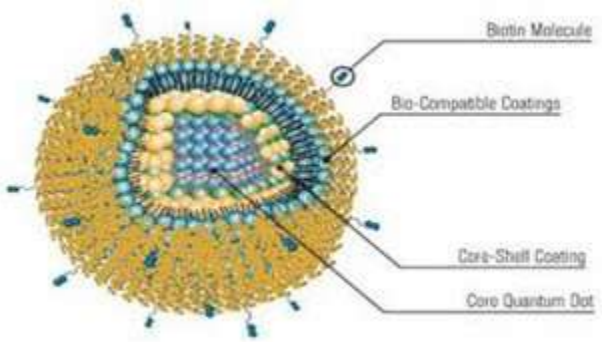

Figure No. 5 : Quantum Dots with Coatings

The quantum dots are semiconductor nanocrystals and core shell nanocrystals containing interface between different semiconductor materials. The size of quantum dots can be continuously tuned from 2 to 10 nm, which, after polymer encapsulation, generally increases to 5–20 nm in diameter. Particles smaller than 5 nm are quickly cleared by renal filtration.

6) Super paramagnetic nanoparticles

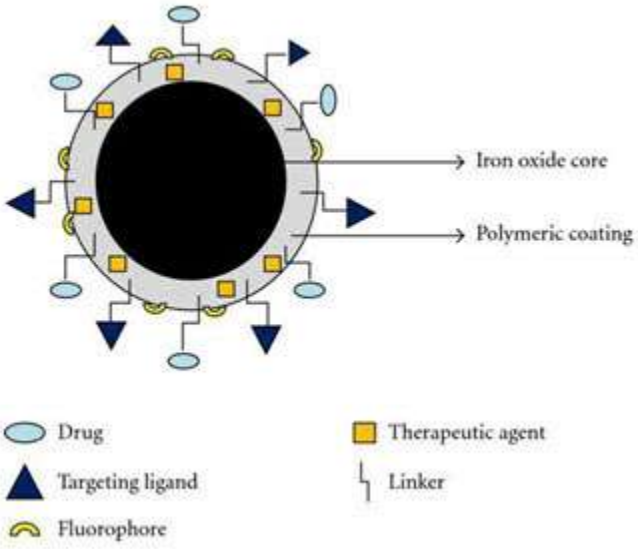

Figure No. 6.: Super Paramagnetic Nanoparticle

Super paramagnetic molecules are those that are attracted to a magnetic field but do not retain residual magnetism after the field is removed. Nanoparticles of iron oxide with diameters in the 5–100 nm range have been used for selective magnetic bio separations. Typical techniques involve coating the particles with antibodies to cell-specific antigens, for separation from the surrounding matrix.[11]

- **Niosomes**

Niosomes are bilayered, non-ionic surfactant vesicles that can entrap both hydrophilic and lipophilic drugs. Niosomes are stable chemically, and their non-ionic nature causes it to have a low toxicity. They offer several advantages, due to which they are preferred for ocular use over other vesicular formulations.[12]

Khalil et al. studied novel proniosomal gel as carriers for delivery of Lomefloxacin HCl (LXN) into the eye. Their most optimum formulation showed very high entrapment efficiency (EE %) of 83.95% ± 0.3% and an optimum particle size. It showed a controlled in vitro release of LXN for over 12 h, acceptable stability, and optimum pH. Transmission electron microscopy (TEM) images showed distinct spheres with smooth surface morphology. The formulation

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was non-irritant when applied topically and showed better bacterial inhibition than the commercial LXN eye drops Orchacin.[13]

- **Microencapsulation**

Microencapsulation is a technique by which thin coatings of wall material are formed around the substances which may be solids, liquids or even gases, enclosed in microscopic particles. The origin of this technique is in the l1930s as cleaner substitute for carbon paper and carbon ribbons as sought by the business machines industry. In the 1950s, the paper and ribbons were developed that contained dyes in small gelatin capsules which were released on impact by a typewriter key or the pressure of a pen or pencil.[14]

Microspheres are considered as free flowing powders having biodegradable polymers. Microencapsulation technique helps for controlling the release characteristics of different coated materials, converting the liquids to solids, changing the colloidal and surface properties and providing environmental protection. advantage of microencapsulation is smallness of the coated particles and their subsequent use and adaptation to a wide variety of dosage forms and product application. Drug moieties can be widely distributed throughout the gastrointestinal tract, because of smallness of particles, thus potentially improving drug sorption.15

Microencapsulation Techniques: [16,17]

In general microencapsulation techniques are divided into two basic groups, namely chemical and physical, with the latter being further subdivided into physicochemical and physico-mechanical techniques. The techniques are shown in table 2:

Table2: Different techniques used for microencapsulation:

Chemical processes	Physical processes	
	Physico-chemical	Physico-mechanical
· Suspension, dispersion and emulsion polymerization · Polycondensation · Solvent evaporation method	· Coacervation · Layer-by-layer (L-B-L) assembly · Sol-gel encapsulation · Supercritical CO_2-assisted microencapsulation	· Spray-drying · Multiple nozzle spraying · Fluid-bed coating · Centrifugal techniques · Vacuum encapsulation

Application of Microencapsulation:[18,19]

1. General Application
2. Controlled Release and Sustained Release Dosage Forms
3. Radioactive microsphere application
4. Cosmetics
5. Photography

- **Phytosomes**

Phytosomes, complex of natural active ingredients and phospholipid(s), increase absorption of herbal extracts or isolated active ingredients when applied topically or orally. Phytosomes are cell like structures which result from the stoichiometric reaction of the phospholipids (phosphatidylcholine, phosphatidylserine, etc.) with the standardized extract or polyphenolic constituents (like flavonoids, terpenoids, tannins, xanthones) in a non-polar solvent, which are better absorbed, utilized and as a result produce better results than conventional herbal extracts.Phospholipids are the main building blocks of life and are one of the major components of cellular membranes. In general, they are considered as natural digestive aid and carriers for both polar and non-polar active substances. Most of phospholipids possess nutritional properties, like phosphatidylserine which acts as a brain cell nutrient, phosphatidylcholine which is important in liver cell regeneration. Soya phospholipids have lipid reducing effect and hydrogenated phospholipids serve as basis for preparation of stable liposomes because of their amphiphilic charater.[20]

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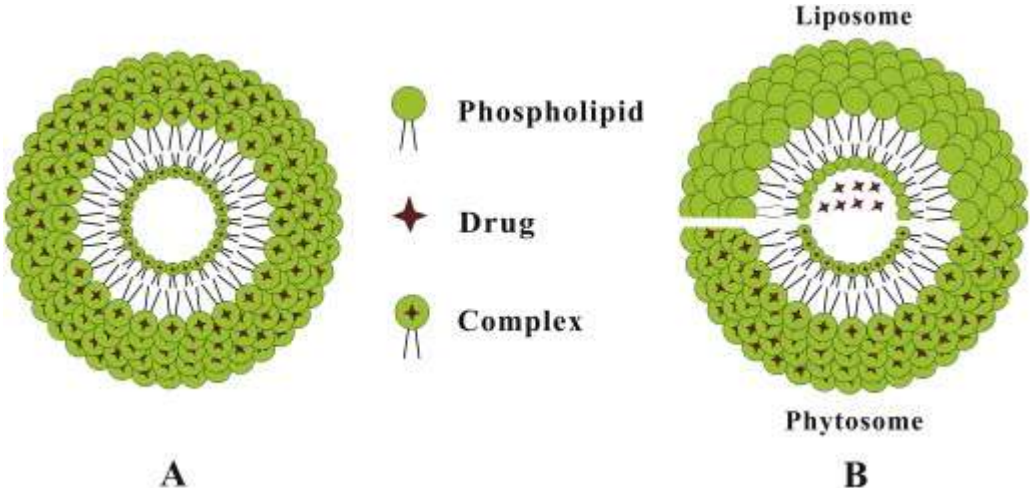

- Advantages of Phytosomes
- Phytosomes increase the absorption of active constitutents, so its dose size required is small.
- There is appreciable drug entrapment and improvement in the solubility of bile to herbal constituents, and it can target the liver.
- In phytosome, chemical bonds are formed between phosphatidylcholine molecules, so it shows good stability.
- Phytosome improves the percutaneous absorption of herbal phytoconstituents.[21]

- **Liposome**

- Liposomes — Nano-sized phospholipid bubbles — have attracted much attention as potential drug carriers. Liposomes are easy to prepare, highly biocompatible and can be loaded with a broad variety of drugs, DNA and diagnostic agents. Their in vivo properties are easy to control. Many liposomal drugs are currently under development and some of them are already approved for clinical use.
- Liposomes have been targeted to specific tissues by attaching specific ligands to their surface. Long-circulating liposomes have also been prepared by grafting the liposome surface with certain chemically and biologically inert synthetic polymers. Current liposomal preparation can combine longevity and targetability.
- Various strategies have been developed to load liposomes with various biologically active substances including proteins (enzymes), peptides and DNA. Their in vivo properties, as well as their pharmacokinetics, have been investigated in many models. Drugs incorporated into liposomes do not provoke undesirable toxic or immune responses and are not inactivated by biological surroundings.
- Currently used ligands for liposome targeting include antibodies and their fragments, folate, transferrin and certain peptides. Liposomes can be made stimuli-sensitive — that is, capable of releasing their contents at abnormal pH values and temperatures characteristic of pathological sites, such as cancers, in the body.
- Liposomal drugs can be administered via different routes, including parenteral and oral administration, used in topical applications and can be delivered to the lungs using liposomal aerosols. Liposomes are also effective immunological adjuvants for protein and peptide antigens and are widely used in experimental immunology and for vaccine preparation.
- New-generation liposomes have been proposed for the treatment of various diseases, including cancer. They are used as carriers of the agents used in photo-dynamic therapy, and the delivery of haemoglobin and bio-energic substrates. Liposomes are prepared possessing magnetic properties and ability to penetrate cell membranes and deliver their loads into cell cytoplasm.[22]

- **Transdermal drug delivery system:**

Transdermal drug delivery is defined as self contained, discrete dosage forms which, when applied to the intact skin, deliver the drug, through the skin at controlled rate to the systemic circulation. Transdermal drug delivery system (TDDS) established itself as an integral part of novel drug delivery systems. Delivery via the

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transdermal route is an interesting option because transdermal route is convenient and safe.

Product name	Chemical	Developer/Marketer	Indication
Alora	Estradiol	TheraTech/Proctor and Gamble	Postmenopausal syndrome
Catapres-TTS	Clonidine	Alza/Boehinger Ingelheim	Hypertension
Deponit	Nitroglycerin	Schwarz-Pharma	Angina pectoris
Minitran	Nitroglycerin	3M Pharmaceuticals	Angina pectoris
Transderm-Scop	Scopolamine	Alza/Novartis	Motion sickness
Motion sickness	Estradiol	Noven Pharmaceuticals, Inc./ Novartis	Postmenopausal syndrome

TABLE 3: SOME COMMERCIALLY AVAILABLE MARKETED TRANSDERMAL SYSTEMS.

- **Advantages of novel drug delivery system**

1.Protection from physical and chemical degradation.
2.Sustained delivery.
3.Improved tissue macrophagesdistribution.
4.Enhancement of stability.
5.Enhancement of pharmacological activity.
6.Protection from toxicity.
7.Increased bioavailability.
8. Enhancement of solubility.

- **Disadvantages of novel drug delivery system**

1.Unconscious patients cannot take dose.
2.Low solubility and permeability.
3.Degradation by gastro intestinal flora.
4.first pass metabolism.
5.food interaction.
6.poor bioavailability.[23]

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