

REVIEW ON NDDS AS NOVEL TRENDS

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Abstract : Drug delivery is that the methodology or method of administering a pharmaceutical compound to attain a therapeutic result in humans or animals. For the treatment of human diseases, nasal and pulmonic routes of drug delivery are gaining increasing importance. These routes give promising alternatives to epithelial duct drug delivery significantly for amide and macromolecule medicine. For this purpose, many drug delivery systems are developed and are being investigated for nasal and pulmonic delivery. These embrace liposomes, proliposomes, microspheres, gels, prodrugs, cyclodextrins, among others.

IndexTerms -.DRUG DELIVERY , NDDS , NANO PARTICLE ETC.

INTRODUCTION

Novel drug delivery systems square measure designed to attain benefits of this idea embrace diminution of drug connected facet effects thanks to controlled therapeutic blood levels rather than oscillatory blood levels, improved patient compliance thanks to reduced frequency of dosing and the reduction of the total dose of drug administered[1,2]

NDDS is one in all the necessary tool increasing drug markets in pharmaceutical business. NDDS will minimize issues by enhancing effectiveness, safety, patient compliance and product shelf life[3]

In the novel drug delivery systems (NDDS), there are various novel carriers which have advantage over conventional dosage forms. Conventional dosage forms show high dose and low availability, in-stability, first pass effect, plasma drug level fluctuations and rapid release of the drug.[4]

Novel drug delivery systems

Various drug delivery systems have been developed and some of them under development with an aim to minimize drug degradation or loss, to prevent harmful side effects and to improve drug bioavailability and also to favour and facilitate the accumulation of the drug in the required bio- zone (site). There are no. Of novel carries which have been established and documented to be useful for controlled and targeted drug delivery. It is important to critically evaluate different terms used under the different broad categories of novel drug delivery system.

- Sustained- or controlled- drug delivery systems provide drug action at a pre determined rate by providing a prolonged or constant (Zero-order) release respectively, at the therapeutically effective levels in the circulation.
- Localized drug delivery devices provide drug action through spatial or temporal control of drug release (usually rate-limiting) in the vicinity of the target.
- Rate- pre-programmed drug delivery systems provide drug action by manipulating the release of drug molecules by system design which control the molecular diffusion of drug molecules.
- Targeted drug delivery provides drug action by using carries either for passive or active targeting or one base or self programmed approach, usually anchored with suitable sensory devices, which recognize their receptor at the target. [5]

Advantages of novel drug delivery system

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

Phytosome

Phytosomes are lipid compatible molecular complex which are composed of “phyto” which means plant and “some” meaning cell-like [7]. Complexing the polyphenolic phytoconstituents in the molar ratio with phosphatidyl choline results in a new herbal drug delivery system, known as “Phytosome”. Phytosomes square measure advanced kinds of flavourer product that square measure higher absorbed, utilized to produce better results than those produced by conventional herbal extracts. Phytosomes show better pharmacokinetic and therapeutic profiles than conventional herbal extracts [8].

Advantages of phytosome

1. Phytosome will increase the absorption of active constituents, so its dose size required is small.

2. there's considerable drug denial and improvement within the solubility of digestive juice to flavourer constituents, and it can target the liver.

3. In Phytosome, chemical bonds are formed between phosphatidylcholine molecules, so it shows good stability [9].

4. Phytosome improves the percutaneous absorption of herbal phyto-constituents [10]

Liposome

Liposomes are concentric bi-layered vesicles in which aqueous volume is entirely enclosed by a membranous lipid bi-layer mainly composed of natural or synthetic phospholipids. The liposomes are spherical particles that encapsulate the solvents which are freely floating in the interior [11].

Advantages of liposomes

1. The high biocompatibility.
2. The easiness of preparation.
3. The chemical versatility that allows the loading of hydrophilic, amphiphilic, and lipophilic compounds.

The simple modulation of their pharmacokinetic properties by changing the chemical composition of the bilayer components [12].

Emulsions

. Among them, the microemulsion is also called nanoemulsion, and the sub-micro-emulsion is called liquid emulsion [13]. Microemulsion is a clear, thermodynamically stable, frequently in combination with a co-surfactant [14].

Advantages of emulsion-based formulations

1. It will unharness the drug for an extended time as a result of it's packed within the inner section and makes direct.
2. contact with the body and other tissues.
4. as a result of the emulsion contains flavorer formulation, it will increase the stability of hydrolyzed formulated material and improve the penetrability of drug into skin and mucous.
5. The new type, viz., Elemenum emulsion, is used as an anti-cancer drug and causes no harm to the heart and liver [15].

Microsphere

Microsphere comprises of small spherical particles, with diameters in the micrometer range, typically 1 μm to 1000 μm (1 mm). Microspheres are sometimes referred to as micro-particles. Microspheres will be factory-made from numerous natural and artificial materials. Solid and hollow microspheres vary widely in density and therefore are used for different applications [16].

Advantage of microsphere formulation

1. Administration of medication via micro-particulate system is advantageous because microspheres can be ingested or injected, and they can be tailored for desired release profiles and used for site-specific delivery of drugs and in some cases will even offer organ-targeted unharness.
2. Drug may be simply discharged from the formulation.
3. It will shield the particular operate of medicine, and might unharness the medication into associate degree outer part for an extended amount.

Ethosomes

are developed by mixture of phospholipids and high concentration of ethanol. This carrier will penetrate through the skin deeply result in improve drug delivery into deeper layer of skin and in blood circulation. These formulations are helpful for topical delivery of alkaloids in variety of gel and cream for patients comfort. Unstable nature and poor skin penetration are limits for Ethosomes topical delivery. The Ethosomes were developed and examined for their ability the topical absorption of Tetrandrine through dermal delivery, and the relation of formulations to the pharmacological activity of Tetrandrine loaded in the formulation was also accessed. Result of the drug levels in rat plasma showed that when Tetrandrine-loaded Ethosomes were topically administered in rats the drug level was low to be detected in rat plasma. By providing fewer delivery of Tetrandrine into blood, topical administration might offer favorable efficacy with reduced side effects, thus leading to improve patient's compliances. In conclusion, Ethosomes were demonstrated to be promising carrier for improving topical delivery of Tetrandrine via skin [17].

Advantages of ethosomal drug delivery

- Ethosomes enhance percutaneous permeation of drug through skin.
- Ethosomes are a platform for the delivery of enormous amounts of various teams of medicine.
- Ethosomal drug is administered in semisolid form resulting in improvement in patients compliance [18].

Niosomes

Niosomes are multilamellar vesicles shaped from non-ionic surfactants of the alkyl radical or dialkyl polyglycerol ether category and sterol. Niosomes are different from liposomes in that they offer certain advantages over liposomes [19].

Proniosomes

Proniosomes gel system is discovery to niosome, which can be utilized for various applications in delivery of actives at desired site. Proniosomal gels are the formulations, which on in situ hydration with water from the skin are converted into niosomes [20].

Advantages of Proniosomes

1. More stable during storage and sterilization.
2. Easy to transfer and distribution

Transdermal Drug Delivery System

Transdermal drug delivery system has been associate degree enlarged interest within the drug administration via the skin for each native therapeutic effects on pathological skin (topical delivery) still as for systemic delivery of drugs. But immense potential lies in transdermal drug as future smart drug delivery devices [21]. These are the devices in which drug present in the formulation permeates into the systemic circulation by diffusion to stratum corneum and further to the effected organ. These devices use compound matrix, adhesive bandage and permeation enhancers.

Advantages of Transdermal Drug Delivery System

1. Controlled drug delivery, enhanced bioavailability, reduction in side effects and easy application.
2. percutaneous delivery of flavoring medication ar to extend the penetration and sustained action.e.g.transdermal films containing boswellic acid (Boswellia serrate) and curcumin (Curcuma longa) were formulated for the treatment of inflammation (synergistic effect).
3. Limitations are hepatic first pass metabolism, increased herapeutic effect, and maintenance of steady state concentration in the serum [22].

Dendrimers

Dendrimers are nanometer-sized, highly branched and monodisperse macromolecules with symmetrical architecture while their stability and protection from the Mononuclear Phagocyte System is being achieved by functionalization of the dendrimers with polyethylene glycol chains (PEG) [23].

Liquid Crystals

Liquid Crystals mix the properties of each liquid and solid states. They can be made to from different geometries, with alternative polar and non-polar layers (i.e., a lamellar phase) where aqueous drug solutions can be included [24].

Hydrogels

Hydrogels ar three-dimensional, hydrophilic, polymeric networks capable of imbibing large amounts of water or biological fluids. They are used to regulate drug release in reservoir-based, controlled release systems or as carriers in swellable and swelling-controlled release devices [25].

Nanoparticles

Nanotechnology is science of matter and material that modify the particle size in nanometers. The word “Nano” is derived from Latinword, which means dwarf (1nm=10⁻⁹m). Nanoparticles ar outlined as particulate dispersions or solid particles with a size within the vary of 10-1000nm. The drug is dissolved, entrapped, encapsulated or attached to a nanoparticle matrix [26]. Nanoparticles supply some specific blessings like they assist to extend the steadiness of drugs/proteins and possess helpful controlled unharness properties. It can be modified to achieve both active and passive targeting; drug loading is very high and can be administered by various routes such as parenteral, nasal, intra ocular and oral routes [26].

IDEAL CHARACTERISTICS

- Targeted drug delivery system should be biochemically inert (non-toxic),
 - Non-immunogenic both physically & chemically stable in vivo & in vitro.
 - Controllable & predicate rate of drug release.
 - Drug release does not affect drug action.
 - Therapeutic amount of drug release.
 - Minimal drug leakage during transit.
 - Carriers used must be biodegradable (or) readily eliminated from the body without any problem & no carrier induced modulation of diseased state.
- The preparation of the delivery system should be easy (or) reasonably simple reproductive & cost effective. [28].

Advantages of nanoparticles:

1. They are biodegradable,
2. non- toxic, site specific and capable of being stored for at least one year.
3. They are capable of targeting a drug to a specific site in the body by attaching targeted ligands to surface of particles or use of magnetic guidance.
4. They offer controlled rate of drug release and particle degradation characteristics that can be readily modulated by the choice of matrix constituents.

Disadvantages

1. Presents bio-acceptability restrictions.
2. Difficult to manufacture in large scale.
- 3 These practical problems have to be overcome before nanoparticles can be used clinically or commercially made available. [29]

Advantages of herbal nanoparticle delivery system

1. Nanoparticulate system delivers the herbal formulation directly to the site of action.
2. Increased efficacy and therapeutic index.
3. Increased stability via encapsulation.
4. Improved pharmacokinetic effect.
5. Producibile with various sizes, compound surface properties [27].

MECHANISM OF DRUG DELIVERY VIA NANOPARTICLE

Nanoparticles exerts its site-specific drug delivery by avoiding the system, utilizing enhanced permeability and retention effect and target-specific targeting. Two styles of approaches area unit applied with drug victimization nanoparticle as carrier.

Nature of interaction of nanoparticle to the drug could also be chemical, surface adsorption, and no binding or interaction at all. The amount of certain drug and therefore the variety of interaction of drug and Nanoparticles depend upon the chemical structure of the drug and therefore the compound and therefore the conditions of drug loading. [30]

TYPES OF NANOPARTICLES

The classes of nanoparticles listed below are all very general and multi-functional; however, some of their basic properties and current known uses in nanomedicine are described here.

- 1) Solid lipid nanoparticles (SLNs)
- 3) Nanostructured lipid carriers (NLC)
- 7) Super paramagnetic nanoparticles. [31]

Solid lipid nanoparticles (SLNs)

SLNs primarily comprise lipids that are unit in solid part at the space temperature and surfactants for emulsification, the mean diameters of which range from 50 nm to 1000 nm for colloid drug delivery applications. [32] 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, nutraceuticals and other materials.[33]

Solid lipids utilised in SLN formulations embrace fatty acids (e.g. palmitic acid, decanoic acid, and behenic acid), triglycerides (e.g. trilaurin, trimyristin, and tripalmitin), steroids (e.g. cholesterol), partial glycerides (e.g. glyceryl monostearate and glyceryl behenate) and waxes (e.g. cetyl palmitate). Several types of surfactants are commonly used as emulsifiers to stabilize lipid dispersion, including soybean lecithin, phosphatidylcholine, poloxamer 188, sodium cholate, and sodium glycocholate. [34]

Nano structured lipid carriers (NLC)

Nanostructured Lipid Carriers are produced from blend of solid and liquid lipids, but particles are in solid state at body temperature. Lipids are unit versatile molecules which will type otherwise 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.[35] The NLC production is based on solidified emulsion (dispersed phase) technologies. NLC can present an insufficient loading capacity due to drug expulsion after polymorphic transition during storage, particularly if the lipid matrix consists of similar molecules. Drug release from lipid particles happens by diffusion and at the same time by lipid particle degradation within the body. In some cases it'd be fascinating to own a controlled quick release going on the far side diffusion and degradation. Ideally this release should be triggered by an impulse when the particles are administered. NLCs accommodate the drug as a result of their extremely unordered lipid structures. A desired burst drug release can be initiated by applying the trigger impulse to the matrix to convert in a more ordered structure. NLCs of certain structures can be triggered this way. [36]

NLCs will usually be applied wherever solid nanoparticles possess benefits for the delivery of medicine. Major application areas in pharmaceuticals are topical drug delivery, oral and parenteral (subcutaneous or intramuscular and intravenous route). LDC nanoparticles have proved particularly useful for targeting water-soluble drug administration. They also have applications in cosmetics, food and agricultural products. These have been utilized in the delivery of anti-inflammatory compounds, cosmetic preparation, topical cortico therapy and also increases bioavailability and drug loading capacity. [37]

Nanoshells

Nanoshells are ill-famed 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[38,39,40]

Nanoshell particles are highly functional materials show modified and improved properties than their single component counterparts or nanoparticles of the same size. Their properties can be modified by changing either the constituting materials or core-to-shell ratio. [41]

Nanoshell materials can be synthesized from semiconductors (dielectric materials such as silica and polystyrene), metals and insulators. Usually dielectric materials such as silica and polystyrene are commonly used as core because they are highly stable [42,43]

Metal nanoshells are unit a completely unique variety of composite spherical nanoparticles consisting of a material core lined by a skinny gold shell that is often gold. Nanoshells possess extremely favorable optical and chemical properties for medicine imaging and therapeutic applications. Nanoshells supply alternative benefits over typical organic dyes together with improved optical properties and reduced status to chemical/thermal denaturation. Furthermore, the same conjugation protocols used to bind biomolecules to gold colloid are easily modified for nanoshells [44]

When a nanoshell and polymer matrix is illuminated with resonant wavelength, nanoshells absorb heat and transfer to the local environment. This causes collapse of the network and release of the drug. In core shell particles-based drug delivery systems either the drug can be encapsulated or adsorbed onto the shell surface.[45]

The shell interacts with the drug via a particular purposeful cluster or by static stabilization technique. When it comes involved with the biological system, it directs the drug. Nanoshell materials have received considerable attention in recent years because of potential applications associated with them.[37]

Quantum dots (QD)

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

[46,47] Semiconductor nanocrystals have unique and fascinating optical properties, become an indispensable tool in biomedical research, especially for multiplexed, quantitative and long-term fluorescence imaging and detection [48,49,50,51]. Hydrophilic therapeutic agents including small interfering RNA (siRNA) and antisense oligodeoxynucleotide (ODN) and targeting biomolecules such as antibodies, peptides and aptamers can be immobilized onto the hydrophilic side of the amphiphilic chemical compound via either valence or non-covalent bonds. This absolutely integrated nanostructure could behave like magic bullets that may not solely establish, however bind to pathologic cells and treat it. It will also emit detectable signals for real-time monitoring of its trajectory [52]

Super paramagnetic nanoparticles

Superparamagnetic molecules are those who are interested in a field of force however don't retain residual magnetism once the sphere is removed. Nanoparticles of iron oxide with diameters

in the 5–100 nm vary are used for selective magnetic bioseparations. The main benefits of superparamagnetic nanoparticles are that they will be useful in resonance imaging (MRI) because of their magnetic properties; they will be guided to a location by the use of magnetic field and heated by magnetic field to trigger the drug release.[53]

Superparamagnetic nanoparticles belong to the class of inorganic based particles having an iron oxide core coated by either inorganic materials (silica, gold) and organic (phospholipids, fatty acids, polysaccharides, peptides or other surfactants and polymers)[54,55,56]

In distinction to alternative nanoparticles, superparamagnetic nanoparticles supported their inducible magnetization, their magnetic properties allow them to be directed to a defined location or heated in the presence of an externally applied AC magnetic field. These characteristics

make them enticing for several applications, starting from numerous separation techniques and distinction enhancing agents for magnetic resonance imaging to drug delivery systems, magnetic hyperthermia (local heat source in the case of tumor therapy), and magnetically assisted transfection of cells[57,58,59,60]

Already marketable products, so-called beads, are micron sized polymer particles loaded with SPIONs. Such beads are functionalized with molecules that permit a particular sorption

of proteins or alternative biomolecules and ulterior separation in a very field of force gradient for diagnostic functions. The trans disciplinaryity of basic and translational research carried out in superparamagnetic nanoparticles during the last decades lead to a broad field of novel applications for superparamagnetic nanoparticles. There are several potential applications of superparamagnetic nanoparticles.

The following issues are not yet fully understood such as

- The mechanisms utilized by cells to take up multifunctional SPIONs in human cells in culture,
- Are there membrane molecules involved?,
- Specific adsorption of SPIONs to targeted subcellular components after uptake, transport of drugs, plasmids or other substances to specific cells followed by controlled release,
- Separation of SPIONs from the cells after cell-uptake and specific adsorption to sub cellular components or to biomolecules like proteins without interfering with cell function,
- Prevention of uncontrolled agglomeration of modified SPIONs in physiological liquids,
- Short and long-term impact on cell functions by loading cells of different phenotypes with such nanoparticles.[61]

Dendrimers

The structure of dendrimers consists of 3 distinct subject field regions as a focal moiety or a core, layers of branched repeat units emerging from the core, and functional end groups on the outer layer of repeat units. They are celebrated to be robust, covalently mounted, 3 dimensional structures possessing each a solvent-filled interior core (nanoscale container) similarly as a regular, mathematically outlined, exterior surface practicality. [62,63] Dendrimers are generally prepared using either a divergent method or a convergent one [64] with an architecture like a tree branching out from a central point.

Dendrimeric vectors are most ordinarily used as canal injections, either directly into the tumor tissue or intravenously for systemic delivery[65] Dendrimers used in drug delivery studies typically incorporate one or more of the following polymers: polyamidoamine (PAMAM), melamine, poly L-glutamic acid (PG), polyethyleneimine (PEI), polypropyleneimine (PPI), and polyethylene glycol (PEG), Chitin. Dendrimers may be used in two major modalities for targeting vectors for diagnostic imaging, drug delivery, gene transfection also detection and therapeutic treatment of cancer and other diseases, namely by (1) passive targeting-nanodimension mediate via EPR (enhanced porousness retention) result involving primary neoplasm vascularization or organ-specific targeting [66,67] (2) active targeting-receptor-mediated cell-specific targeting involving receptor-specific targeting groups[68] There are several potential applications of dendrimers in the field of imaging drug delivery, gene transfection and non-viral gene transfer.

FULLERENES

A C is any molecule composed entirely of carbon, within the style of a hollow sphere, ellipsoid, or tube. Spherical fullerenes also are referred to as buckyballs, and cylindrical ones square measure referred to as carbon nanotubes or buckytubes.[69] Buckyball clusters or buckyballs composed of less than 300 carbon atoms

are unremarkably called endohedral Cs and embody the foremost common fullerene, buckminsterfullerene, C₆₀. Megatubes square measure larger in diameter than nanotubes and ready with walls of various thickness that is probably used for the transport of a range of molecules of various sizes [70]

Nano “onions” are spherical particles based on multiple carbon layers surrounding a buckyball core which are proposed for lubricants [71]

Liposomes

Liposomes square measure sac structures with Associate in Nursing liquid core encircled by a hydrophobic macromolecule bilayer, created by the extrusion of phospholipids. Phospholipids are GRAS (generally recognised as safe) ingredients, therefore minimizing the potential for adverse effects. The lipid bilayer of liposomes can fuse with other bilayers such as the cell membrane, which promotes release of its contents, making them useful for drug delivery and cosmetic delivery applications. Liposomes that have vesicles in the range of nanometers are also called nanoliposomes.[72,73]

Liposomes will vary in size, from 15 nm up to several lm and can have either a single layer (unilamellar) or multiple phospholipid bilayer membranes (multilamellar) structure. Unilamellar vesicles (ULVs) can be further classified into small unilamellar vesicles (SUVs) and large unilamellar vesicles (LUVs) depending on their size range [74] The unique structure of liposomes, a lipid membrane close Associate in Nursing liquid cavity, enables them to carry both hydrophobic and hydrophilic compounds without chemical modification. These versatile properties of liposomes created them to be used as potent carrier for numerous medication like antibacterials, antivirals, insulin, antineoplastics and cellular inclusion DNA

Conclusion :

In this review descriptive manner various types of drug delivery system are included such as Phytosome ,Liposome ,Emulsions ,Dendrimers , transdermal drug delivery system , nanoparticle and its types etc. This gives an idea about drug delivery system and its novelty and recent advancement in drug delivery system.

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