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NOVEL DRUG DELIVERY SYSTEM: A REVIEW

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ABSTRACT
Novel Drug delivery System (NDDS) refers to the approaches, formulations, technologies, and systems for transporting a pharmaceutical compound in the body as needed to safely achieve its desired therapeutic effects. Other than conventional drug delivery system Novel Drug Delivery System (NDDS) is a system for delivery of drug and a combination of advance techniques. NDDS are far better new dosage forms than conventional dosage forms. In terms of patient compliance, safety and efficacy, evolution of an existing drug molecule from a conventional form to a novel delivery system can significantly improve its performance. Various approaches involves in Novel Drug Delivery System like medical devices or drug-device combination products. The main aim for developing such delivery systems is to minimize drug degradation and loss, to prevent harmful side effects and to increase bioavailability. Based on physical and biochemical mechanisms, Novel drug delivery systems are designed. Physical mechanism or controlled drug delivery system includes dissolution, osmosis, erosion and diffusion. Biochemical mechanism includes gene therapy, liposomes, nanoparticles, monoclonal antibodies. Currently, various drug delivery and drug targeting systems are under development. One of the growing and potential systems for delivery of drugs and enzymes is drug loaded erythrocytes.

KEYWORDS: NDDS, Polymer, Dosage forms, Conventional, Drug release.

INTRODUCTION

Drug delivery is the process of administering the drug or pharmaceutical product, in order to achieve desired therapeutic effect. 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.[1][2][3][4] 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), which 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.[1]

Novel drug delivery systems can include those based on physical mechanisms and those based on biochemical mechanisms. Physical mechanisms also referred as controlled drug delivery systems include osmosis, diffusion, erosion, dissolution and electro transport. Biochemical mechanisms include monoclonal antibodies, gene therapy, and vector systems, polymer drug adducts and liposomes. Therapeutic benefits of some new drug delivery systems include optimization of duration of action of drug, decreasing dosage frequency, controlling the site of release and maintaining constant drug levels.[5][6][7][8][9] 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.

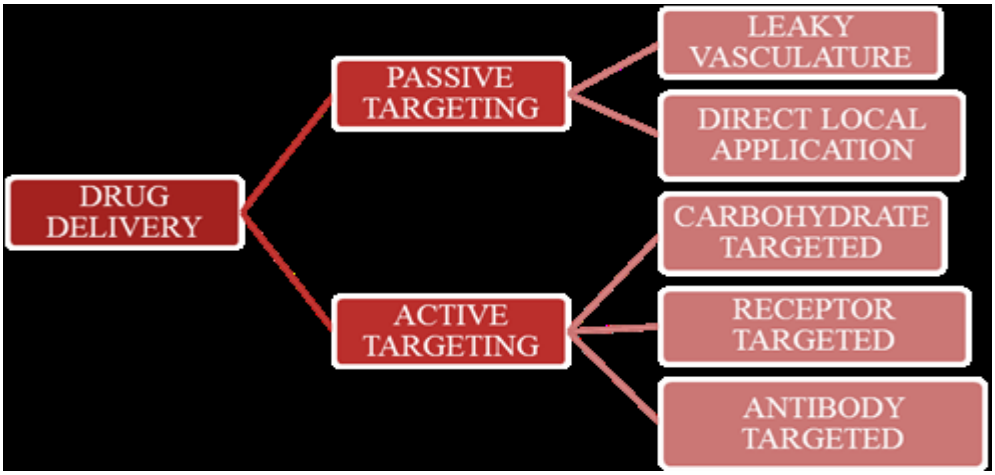

Fig. 1: Types of Drug Delivery.

VARIOUS DRUG DELIVERY SYSTEMS

New drug delivery systems are under investigation to improve the potential of the respective drug. On the other hand, scientists mainly focus on the microenvironment of the cells and their interaction with these new drug dosage forms.[10][11][12][13] [14][15][16]

Liposomes

Tiny pouches made of lipids, or fat molecules surrounding a water core widely used for clinical cancer treatment. Several different 0kinds of liposomes are widely employed against infectious diseases and can deliver certain vaccines. During cancer treatment they encapsule drugs, shielding healthy cells from their toxicity, and prevent their concentration in vulnerable tissues such as those of patient kidneys and liver. Liposomes can also reduce or eliminate certain common side effects of cancer treatment such as nausea and hair loss. They are form of vesicles that consist either of many, few or just one phospholipid bilayers. The polar character of liposomal core enables polar drug molecules to be encapsulated. Amphiphilic and lipophilic molecules are solubilised within phospholipid bilayer according to their affinity towards phospholipids.[17]

Mechanism: Liposomes are small lipodial vesicles enclosing aqueous solution inside a hydrophobic membrane, in order to deliver the molecules to targeted site, the lipid bilayer can fuse with other bilayers such as the cell membrane, thus liposomes act as drug carrier for drug delivery.[18][19][20][21]

They are various clinical approved liposomal drugs like: liposomal daunorubicin, doxorubicin, Liposomal amphotericin B, Liposomal cytarabine.

Liposomes have following advantages

1. Liposomes are non-toxic, biocompatible, biodegradable, and nonimmunogenic for systemic and non-systemic administrations.
2. The efficacy and therapeutic index of drug Actinomycin can be increased, by formulating it as liposomes.
3. Liposomes has flexibility to bind with site-specific ligands, in order to achieve active targeting.
4. Site-specific targeting of Anti-cancer, Anti-inflammatory drugs.
5. Has high penetration into tissues (Corticosteroids, anesthetics, and insulin).

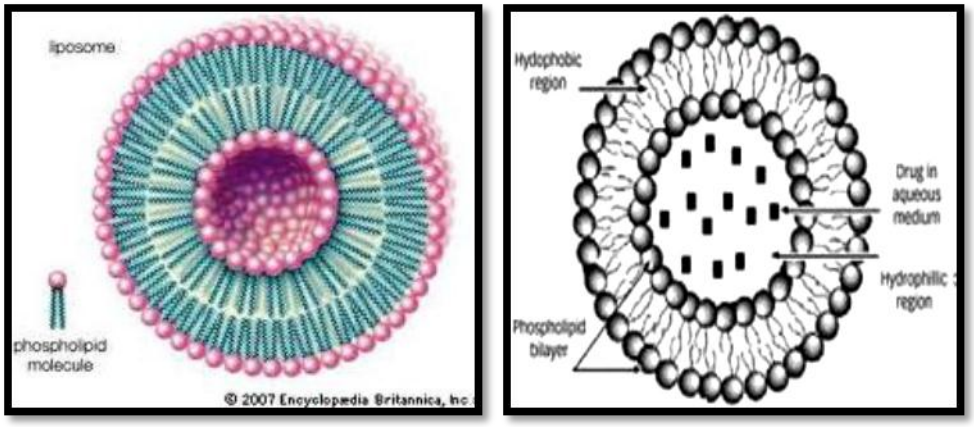

Fig. 2: Structure of Liposomes.

Table 2: Marketed Liposomal Based Products.[22]

Trade Name	Trade Name	Manufacturer	Indication
AmBisome	Amphotericin B	NeXstar Pharmaceuticals	Systemic fungal infections
Abelcet	Amphotericin B	The Liposome Company	Systemic fungal infections
Amphotec	Amphotericin B	Sequus Pharmaceuticals	Systemic fungal infections
Doxil	Doxorubicin	Sequus Pharmaceuticals	Kaposi's sarcoma
DaunoXome	Daunorubicin	NeXstar Pharmaceuticals	Kaposi's sarcoma

Hydrogels

Hydrogels are three-dimensional, hydrophilic, polymeric networks capable of imbibing large amounts of water or biological fluids. The networks are composed of homopolymers or copolymers, and are insoluble due to the presence of chemical crosslinks (tie-points, junctions), or physical crosslinks, such as entanglements or crystallites. Hydrogels exhibit a thermodynamic compatibility with water, which allows them to swell in aqueous media. They are used to regulate drug release in reservoir-based, controlled release systems or as carriers in swellable and swelling-controlled release devices. On the forefront of controlled drug delivery, hydrogels as enviro-intelligent and stimuli-sensitive gel systems modulate release in response to pH, temperature, ionic strength, electric field, or specific analyte concentration differences. In these systems, release can be designed to occur within specific areas of the body (e.g., within a certain pH of the digestive tract) or also via specific sites (adhesive or cell-receptor specific gels via tethered chains from the hydrogel surface). Hydrogels as drug delivery systems can be very promising materials if combined with the technique of molecular imprinting.[ix]

Classification of hydrogels

- Based on the methods of preparation- Homo-polymeric Hydrogel, Co-polymeric hydrogel, Inter Penetrating Network,
- Stimuli-sensitive hydrogels- Temperature-sensitive hydrogels, pH-sensitive hydrogels, Dual pH-thermal sensitive systems
- Based on mechanism of release-Diffusion controlled, swelling controlled.

Advantages of Hydrogels

1) Biocompatible, biodegradable and can be injected
2) Hydrogels possess wide degree of flexibility similar to natural tissue.
3) Have good transport properties and easy to modify.[23][24][25][26]

Nanoparticles

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.[27][28][29][30][31][32] 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.[33][34]

Classification of nanomaterials

a) Nanotubes

They are hollow cylinders made of carbon atoms. They can also be filled and sealed, forming test tubes or potential drug delivery devices.

b) Nano wires

Glowing silica nano wire is wrapped around a single strand of human hair. It looks delicate. It is about five times smaller than virus applications for nano wires include the early sensing of breast and ovarian malignancies.

c) Nanocantilever

The honey comb mesh behind this tiny carbon cantilever is surface of fly's eye. Cantilevers are beams anchored at only one end. In nano world, they function as sensors

ideal for detecting the presence of extremely small molecules in biological fluids.

d) Nanoshells

Nanoshells are hollow silica spheres covered with gold. Scientists can attach antibodies to their surfaces, enabling the shells to target certain shells such as cancer cells. Nano shells one day also are filled with drug containing polymers.

e) Quantum dots

Quantum dots are miniscule semiconductor particles that can serve as sign posts of certain types of cells or molecules in the body. They can do this because they emit different wavelengths of radiations depending upon the type of cadmium used in their cores. Cadmium sulfide for ultra violet to blue, cadmium selinide for most of the visible spectrum and cadmium telluride for far - infra red and near infra red.

f) Nano pores

Nano pores have cancer research and treatment applications. Engineered into particles, they are holes that are so tiny that DNA molecules can pass through them one strand at a time, allowing for highly precise and efficient DNA sequencing. By engineering nanopores into surface of drug capsule that are only slightly larger than medicines molecular structure, drug manufacturers can also use nanopores to control rate of drug's diffusion in body.

g) Gold Nanoparticles

These nanoparticles, seen in transmission electron micrograph image, they have solid core. Researchers at north western university are using gold particles to develop ultra sensitive detection systems for DNA and protein markers associated with many forms of cancer, including breast prostrate cancer.

h) Bucky balls

Bucky ball is common name for a molecule called buckminsterfullerene, which is made of 60 carbon atoms formed in shape of hollow ball, discovered in 1985. Bucky balls and other fullerenes because of their chemistry and their unusual hollow, cage like shape extremely stable and can withstand high temperatures.[35][36][37]

Applications

1) Bucky balls may see widespread use in future products and applications, from drug delivery vehicles for cancer therapy to ultra hard coating and military harmor.
2) Bucky ball – antibody combination delivers antitumor drugs.
3) Bucky balls to fight allergy.
4) Bucky balls as powerful antioxidant and also inhibitor of HIV.

Demerits

1) Bucky balls hurt cells.
2) Bucky balls have high potential to accumulate in living tissue.
3) Difficulty of targeting drug delivery location.[38][39][40][41][42][43]

Mechanism: The release of the dug from the formulation is by controlled diffusion or erosion mechanism. Thus the release of the drug occurs from the core, across the polymer matrix or membrane. Thus the membrane acts as a barrier for drug release. Therefore solubility and diffusivity of drug in polymer membrane becomes the determining factor for drug release.

Advantages

1) Nanosomes offer uniform delivery of drug, with greater bioavailability.
2) It can be administered through different routes.
3) Smaller in size with high surface area.
4) Low drug dose is required.[44][45]

Drug loaded erythrocytes

Drug loaded erythrocytes is one of the growing and potential systems for delivery of drugs and enzymes. Erythrocytes are biocompatible, biodegradable, posse's long circulation half–life and can be loaded with variety of biologically active substances. Carrier erythrocytes are prepared by collecting blood sample from the organism of interest and separating erythrocytes from the plasma. By using various physical and chemical methods cells are broken and drug is entrapped into erythrocytes, finally they are resealed and resultant carriers are then called as "resealed erythrocytes". Upon re injection the drug loaded erythrocytes serve as slow circulation depots, targets the drug to reticulo-endothelial system.[46][47]

Advantages

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.
6) Isolation of erythrocyte is easy and larger amount of drug can be encapsulated in small volume of cells
7) They can target the drug within reticuloendothelial system.
8) They facilitate incorporation of protein and nucleic acid in eukaryotic cells by cell infusion with RBC.

Disadvantages

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.[48]

Fig. 3: Erythrocytes.

Drug Delivery Carriers

In recent years the wide advances in drug delivery systems have enabled simpler routes of administration. To deliver the medicine to their specific target tissues, drug carriers (the substances that play crucial role in vital delivery and effectiveness of drugs) are used.[49][50][51][52][53][54][55][56] 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.[57][58]

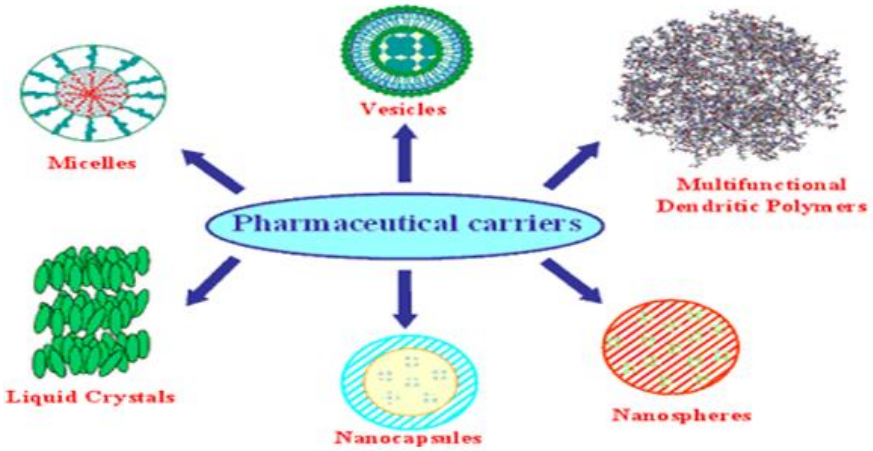

Fig. 4: Different Pharmaceutical Carriers.

Dendrimers

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.[59][60]

Fast dissolving tablet

A novel tablet concept which offers ease of oral administration and benefits of increased patient compliance is fast dissolving tablet (FDT). This tablet format is designed to allow administration of oral solid dosage form in absence of water or fluid intake. Such tablets readily dissolve or disintegrate in saliva generally within less than 60 seconds. When put on tongue, this tablet disintegrate instantaneously, release in the drug. Good in chemical stability. Suitable during traveling where water is may not be available.[61][62][63][64][65]

Iontophoresis (IP)

Novel topical systems include iontophoresis and phonophoresis. It is an electro chemical method that enhances the transport of some solute molecule by creating a potential gradient through the skin with an applied electrical current or voltage. It induces increased migration of ionic drugs into skin by electrostatic repulsion at active electrode. Negative ions are delivered by cathode and positive ion by anode. Typical

iontophoresis devices consist of battery, microprocessor controller, drug reservoir and electrodes.[66]

Advantages of IP

1) Control of delivery rates by variations of current density, pulse voltage, drug concentration and ionic strength.
2) Eliminating gastro intestinal incompatibility, erratic absorption and first pass metabolism.
3) Reducing side effects and variation among patients.
4) Avoiding risks of infections, inflammation, and fibrosis associated with continuous injection and infusion

Phonophoresis

Phonophoresis (ultra sound, sonophoresis, ultra sonophoresis, ultra phonophoresis) is the transport of drugs through the skin using ultra sound. It is the combination of ultra sound therapy with topical drug therapy to achieve therapeutic drug concentrations at selected sites in the skin. It is widely used by physiotherapists. Today that product is applied to the skin and some time is allowed for drug to begin absorption into the skin. Then ultra sound unit is applied. The ultra sound emitted from the unit is actually a sound wave outside the normal human hearing range.[67]

Carbon nanotubes

Carbon nanotubes can be modified to circulate well within the body. Such modifications can be accomplished with covalent or non covalent bonding. Modifications can increase or decrease circulation time within the body. Carbon nanotubes no significant toxicity when they have modified so as to be soluble in aqueous body type fluids. They enter readily into the cells.

Cancer cells in tumor are larger than normal cells and also exhibit leakage. Large molecules which circulate slowly can leak into and accumulate in cancer cell. Carbon nanotubes carrying active agents have been demonstrated in animal studies to do this. Researches have also used carbon tubes to deliver the precursors of active drug which they call a prodrug. eg: Cisplatin.[68]

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.[68] Delivery via the transdermal route is an interesting option because transdermal route is convenient and safe.

The positive features of delivery drugs across the skin to achieve systemic effects are:

- Avoidance of first pass metabolism
- Avoidance of gastro intestinal incompatibility
- Predictable and extended duration of activity
- Improving physiological and pharmacological response
- Termination of therapy is easy at any point of time
- Greater patient compliance due to elimination of multiple dosing profile
- Provide suitability for self administration
- Enhance therapeutic efficacy.[70]

Microspheres

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

1. Synthetic polymers are divided into two types.

a. Non-biodegradable polymers

- Poly methyl methacrylate (PMMA)
- Glycidyl methacrylate
- Epoxy polymers

b. Biodegradable polymers

- Lactides, Glycolides & their co polymers
- Poly alkyl cyano acrylates
- Poly anhydrides

1. 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 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.

2. Natural polymers obtained from different sources like proteins, carbohydrates and chemically modified carbohydrates.

Proteins: Albumin, Gelatin, and Collagen.

Carbohydrates: Agarose, Carrageenan, Chitosan, Starch.

Chemically modified carbohydrates: Polydextran, Polystarch.

Natural polymers: Albumin is a widely distributed natural protein. It is considered as a potential carrier of drug or protiens (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.[71]

Mucoadhesive Drug Delivery Systems: Bioadhesion may be defined as the state in which two materials, at least one of which is biological in nature, are held together for extended period of time by interfacial forces. In pharmaceutical sciences, when the adhesive attachment is to mucus or a mucous membrane, the phenomenon is referred to as mucoadhesion.

The potential of mucoadhesive polymers was shown in ocular, nasal, vagina and buccal drug delivery systems leading to a significantly prolonged residence time of sustained release delivery systems on this mucosal membranes. In addition, the development of oral mucoadhesive delivery systems was always of great interest as delivery systems capable of adhering to certain gastrointestinal (GI) segments would offer various advantages.[72]

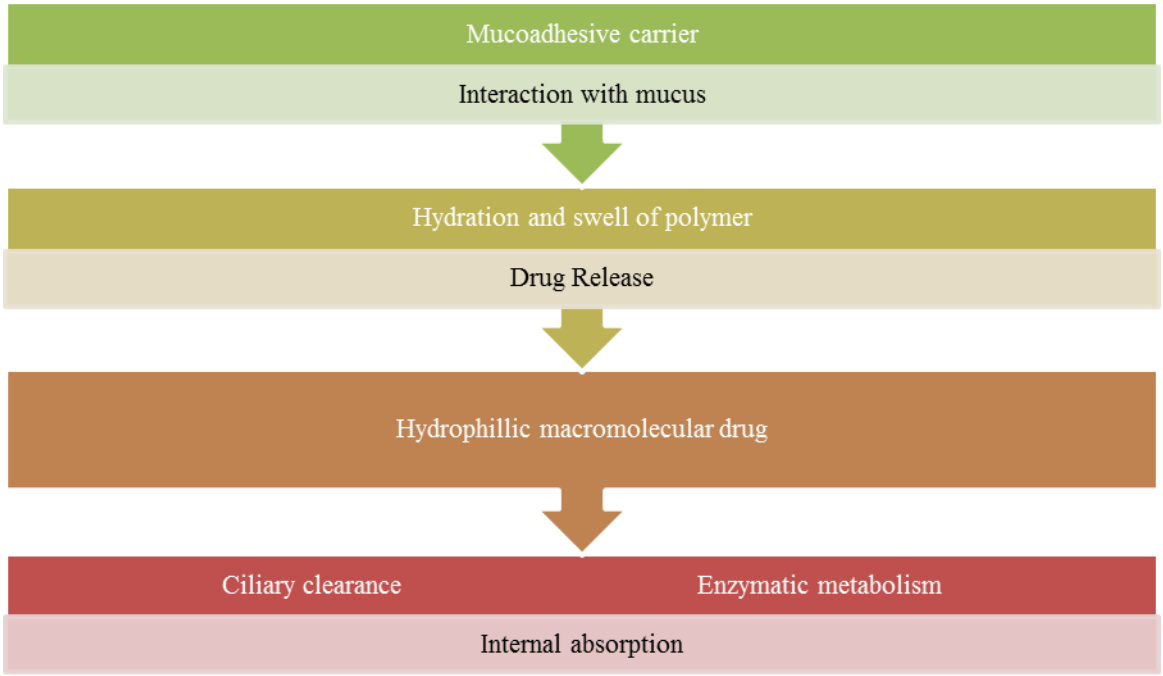

Fig. 5: Mechanism of Mucoadhesion.

New drug delivery systems can provide improved or unique clinical benefits such as

- ✓ Improvement in patient's compliance.
- ✓ Improved out comes.
- ✓ Reduction of adverse effect.
- ✓ Improvement of patient's acceptance of treatment.
- ✓ Avoidance of costly interventions such as laboratory services.
- ✓ Allowing patients to receive medications as out patients and possibly.
- ✓ Reduction in overall use of medicinal resources.
- ✓ Nano-drug delivery systems that deliver large but highly localized quantities of drugs to specific areas to be released in controlled ways
- ✓ Controllable release profiles, especially for sensitive drugs.
- ✓ Materials for nanoparticles those are biocompatible and biodegradable.
- ✓ Architectures / structures, such as biomimetic polymers, nanotubes.
- ✓ Technologies for self-assembly.
- ✓ Functions (active drug targeting, on-command delivery, intelligent drug release devices/

bioresponsive triggered systems, self-regulated delivery systems, systems interacting with the body, smart delivery).

- ✓ Virus-like systems for intracellular delivery.
- ✓ Nanoparticles to improve devices such as implantable devices / nanochips for nanoparticle release, or multi reservoir drug delivery-chips.
- ✓ Nanoparticles for tissue engineering; e.g. for the delivery of cytokines to control cellular growth and differentiation, and stimulate regeneration; or for coating implants with nanoparticles in biodegradable polymer layers for sustained release.
- ✓ Advanced polymeric carriers for the delivery of therapeutic peptide/proteins (biopharmaceutics) and also in the development of: Combined therapy and medical imaging, for example, nanoparticles for diagnosis and manipulation during surgery (e.g. thermotherapy with magnetic particles);
- ✓ Universal formulation schemes that can be used as intravenous, intramuscular or peroral drugs
- ✓ Cell and gene targeting systems.
- ✓ User-friendly lab-on-a-chip devices for point-of-care and disease prevention and control at home.
- ✓ Devices for detecting changes in magnetic or physical properties after specific binding of ligands on paramagnetic nanoparticles that can correlate with the amount of ligand.
- ✓ Better disease markers in terms of sensitivity and specificity[73][74][75][76]

CONCLUSION

For the treatment of Different diseases new technologies have been developed. 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. The use of Drug delivery systems in developing drugs for bringing lots of hope in the field of Pharmacology and Medical research. Novel Drug delivery & drug targeting is new techniques which is used in pharmaceutical science. Like targeting drug delivery, vaccine delivery, Gene therapy, commercial development of novel carries (liposomes).

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REFERENCES

1. Kotturi N. Novel Drug Delivery System. RRJPNT, 2015; 3(2): 2347-7849.
2. Vijaya SB, Tiruckovela M, Varanasi PK. An Imperative Note on Novel Drug Delivery Systems. J Nanomedic Nanotechnol, 2011; 2(7): 125.
3. Agrawal P. 2015. Significance of Polymers in Drug Delivery System. J Pharmacovigil, 2015; 3(1): e127.
4. Nikalje AP. 2015. Nanotechnology and its Applications in Medicine. Med chem, 2015; 5(2): 081-089.
5. Bhagwat RR and Vaidhya IS. Novel Drug Delivery Systems: An Overview. Int J Pharm Sci Res, 2013; 4(3): 970-982.
6. Manivannan R, Kugalur GP. Recent Advances in Novel Drug Delivery System. IJRAP, 2010; 1(2): 316-326.
7. Niculescu-Duvaz I, Springer CJ. Antibody-directed enzyme prodrug therapy (ADEPT): a review. Advanced Drug Delivery Reviews, 1997; 26(2-3): 151-72.
8. Manabe T, Okino H, Maeyama R, Mizumoto K, Nagai E, Tanaka M, Matsuda T. Novel strategic therapeutic approaches for prevention of local recurrence of pancreatic cancer after resection: transtissue, sustained local drug-delivery systems. Journal of Controlled Release, 2004; 100(3): 317-330.
9. Ziaie B, Baldi A, Lei M, Gu Y, Siegel RA. Hard and Soft Micro machining for Biomems. Review of Techniques and Examples of Applications in Microfluidics and Drug Delivery. Advanced Drug Delivery Reviews, 2004; 56(2): 145-72.
10. Van Tilburg CWJ. pinal Analgesic Drug Delivery for Ehlers-Danlos Hypermobility Type Chronic Pain Treatment: A Case Report. J Pain Relief., 2016; 5(2): 235. 10.
11. Patil JS. Significance of Particulate Drug Delivery System in Anti-microbial Therapy. Adv Pharmacoepidemiol Drug Safe, 2016; 5(2): 139.
12. Colone M, Kaliappan S, Calcabrini A, Tortora M, Cavalieri F, et al. Redox-active Microcapsules as Drug Delivery System in Breast Cancer Cells and Spheroids. J Mol Genet Med, 2016; 10(1): 200.
13. Wang X, Lu W. Active Targeting Liposomes: Promising Approach for Tumor-Targeted Therapy. J Bioequiv Availab., 2016; 8(1): 013-014.
14. Kumar P, Agnihotri S, Roy I. Synthesis of Dox Drug Conjugation and Citric Acid Stabilized Superparamagnetic Iron-Oxide Nanoparticles for Drug Delivery. Biochem Physiol, 2016; 5(1): 194.
15. Patil J. Advances in Drug Delivery Strategies for Cancer Therapeutics. J Pharmacovigil, 2016; S3(002).
16. Lopes CM and Soares C. Transdermal Drug Delivery Systems Activated by Physical stimuli: Techniques and Applications. Drug Des., 2016; 4(2): e129.
17. Byrne ME, Park K, Peppas N. Molecular imprinting within Hydrogels. Advanced Drug Delivery Reviews, 2002; 54(1): 149-61.
18. Lee JH, Ivkov R, Blumenthal R. Magnetically Triggered Drug Release from Liposome Embedded Gel. J Nanomedine Biotherapeutic Discov, 2014; 4(3): 130.
19. Hu D, Tang S, Peng H, Wang Q. The Bright Future of Liposome Mediated Drug Delivery. Biochem Physiol, 2015; 4(1): e133.

20. Fathalla D, Soliman GM, Fouad EA (2015) Latanoprost Liposomes for Glaucoma Treatment Development and in vitro/in vivo Evaluation of Liposomal Gels for the Sustained Ocular Delivery of Latanoprost. J Clin Exp Ophthalmol, 2015; 6(1): 390.
21. Pawar HA, Bhangale BD. Phytosome as a Novel Biomedicine: A Microencapsulated Drug Delivery System. J Bioanal Biomed, 2015; 7(1): 006-012.
22. Verma RK, Garg S, Current Status of Drug Delivery Technologies and Future Directions, Pharmaceutical Technology On-Line, 2001; 25(2): 1–14.
23. Agostino AD, Gatta AL, Busico T, Rosa MD, Schiraldi C. (2012) Semi-interpenetrated Hydrogels Composed of PVA and Hyaluronan or Chondroitin Sulphate: Chemico-Physical and Biological Characterization. J Biotechnol Biomater, 2012; 2(4): 140.
24. Chen Q, Zhu L, Zhao C, Zheng J. Hydrogels for Removal of Heavy Metals from Aqueous Solution. J Environ Anal Toxicol, 2012; 2(7): 001.
25. Zhu J. Biomimetic Hydrogels as Scaffolds for Tissue Engineering. J Biochips Tiss Chips, 2012; 2(4): e119.
26. Venturini M, Mazzitelli S, Mičetić I, Benini C, Fabbri J, Mucelli SP, Benetti F, Nastruzzi C. Analysis of Operating Conditions Influencing the Morphology and In vitro Behaviour of Chitosan Coated Liposomes. J Nanomed Nanotechnol, 2014; 5(4): 211.
27. Kakran M, Sahoo GN, Lin Li. Fabrication of Nanoparticles of Silymarin, Hesperetin and Glibenclamide by Evaporative Precipitation of Nanosuspension for Fast Dissolution. Pharm Anal Acta., 2015; 6(1): 326.
28. Esposito E, De Vries HE, Van der Pol SMA, Boschi F, Calderan L, Mannucci S, Drechsler M, Contado C, Cortesi R, Nastruzzi C. Physico-Chemical Characterization and Biodistribution Studies of Lipid Nanoparticles. J Nanomed Nanotechnol, 2015; 6(1): 256.
29. El-Feky GS, El-Rafie MH, MA El-Sheikh, Mehrez E El-Naggar, Hebeish A. Utilization of Crosslinked Starch Nanoparticles as a Carrier for Indomethacin and Acyclovir Drugs. J Nanomed Nanotechnol, 2015; 6(1): 254.
30. Manikandan A, Sathiyabama M. Green Synthesis of Copper-Chitosan Nanoparticles and Study of its Antibacterial Activity. J Nanomed Nanotechnol, 2015; 6(1): 251.
31. Morris B, Behzad F. The Effects of Gold and Silver Nanoparticles on an Enzymatic Reaction Between Horseradish Peroxidase and 3,3',5,5'-Tetramethylbenzidine. Biochem Pharmacol, 2014; 3(6): 146.
32. Hussein FH, Shaheed MA. Preparation and Applications of Titanium Dioxide and Zinc Oxide Nanoparticles. J Environ Anal Chem., 2015; 2(1): e109.
33. Soppimath KS, Aminabhavi TM, Kulkarni AR, Rudzinski WE. Biodegradable polymeric nanoparticles as drug delivery devices. Journal of Controlled Release, 2001; 70(1-2): 1-20.
34. Agnihotri SA, Mallikarjuna NN, Aminabhavi TM. Recent advances on chitosan-based micro and nanoparticles in drug delivery. Journal of Controlled Release, 2004; 100(1): 5-28.
35. Jiang W, Kim BY, Rutka JT, Chan WC. Nanoparticle-mediated cellular response is size-dependent. Nat Nanotechnol, 2008; 3(3): 145-50.
36. Chan WCW. In: Bio-Applications of Nanoparticles. Landes Bioscience, Austin, TX, USA, 2007.
37. Kamal Singh Rathore, Rohit lowalekar, Nema RK, Jain CP. The Pharma Review, 2006; 30-32.
38. Sitharaman B, Tran LA, Pham QP et al. Contrast Media Mol. Imaging 2007; 2: 139-146.
39. Bolskar RD, Benedetto AF, Husebo LO, Price RE, Jackson EF, Wallace S, Wilson LJ, Alford JM. First soluble M@C60 derivatives provide enhanced access to metallofullerenes and per-mit in vivo evaluation of Gd@C60[C(COOH)2]10 as a MRI contrast agent. J. Am. Chem. Soc., 2003; 125: 5471-5478.
40. Tóth E1, Bolskar RD, Borel A, González G, Helm L, Merbach AE, Sitharaman B, Wilson LJ. Water-soluble gadofullerenes: toward high-relaxivity, pH-responsive MRI contrast agents. J. Am. Chem. Soc., 2005; 127(2): 799-805.
41. Szoka F. Annu. Rev. Biophys. Bioeng, 1980; 9: 467-508.
42. Hirsch LR1, Gobin AM, Lowery AR, Tam F, Drezek RA, Halas NJ, West JL. Metal nanoshells. Ann. Biomed. Eng., 2006; 34(1): 15-22.
43. Tomalia DA, Reyna LA, Svenson S. Dendrimers as multi-purpose nanodevices for oncology drug delivery and diagnostic imaging. Biochem Soc Trans, 2007; 35(Pt 1): 61-7.
44. Agostino AD, Gatta AL, Busico T, Rosa MD, Schiraldi C. Semiinterpenetrated Hydrogels Composed of PVA and Hyaluronan or Chondroitin Sulphate: Chemico-Physical and Biological Characterization. J Biotechnol Biomater, 2012; 2(4): 140.
45. Zhu J. Biomimetic Hydrogels as Scaffolds for Tissue Engineering. J Biochips Tiss Chips., 2012; 2(4): e119.
46. Kuchekar BS, Mahajan S, Bandhan AC. Mouth dissolve tablets of sumatriptan. Indian Drugs, 2004; 41(10): 592-598.
47. Lalla JK, Mamania HM, Fast dissolving Rofecoxib tablets. Ind J Pharm Sci, 2004; 59: 23-26.
48. Sahoo CK. An overview on resealed erythrocytes: Anovel approach to drug delivery. IJPPS, 2012; 4(2).
49. Kumar RS, Syamala US, Revathi P, Devaki S, Raghuveer P and Kuppuswamy Gowthamarajan K Self Nanoemulsifying Drug Delivery System of Olanzapine for Enhanced Oral Bioavailability: In vitro, In vivo Characterisation and In vitro -In vivo

Correlation. J Bioequiv Availab, 2013; 5(4): 201- 208.
50. Kondrashina OV. A Targeted Drug Delivery System of Gd3+ for Neutron Capture Therapy against Cancer is Metalorganic Magnetic Nanoparticles. J Nanomedine Biotherapeutic Discov, 2013; 3: 116.
51. Gallud A and Silva AD. Functionalized Nanoparticles for Drug Delivery, One- and Two-pho ton Photodynamic Therapy as a Promising Treatment of Retinoblastoma. J Clin Exp Ophthalmol, 2013; 4(4): 288.
52. Suedee R. The Use of Molecularly Imprinted Polymers for Dermal Drug Delivery. Pharm Anal Acta., 2013; 4(8): 264.
53. Mostafavi SH, Jayachandra Babu R. Nano-Sized Drug Delivery. J Mol Pharm Org Process Res., 2013; 1(4): e108.
54. Zhu Y. Mesoporous Silica Nanoparticles with a Core-Shell Structure for Drug Delivery. J Bioanal Biomed, 2013; 5: e117.
55. Weston GS and Yeboah KG. Site-Specific Drug Delivery to the Gastrointestinal Tract. J Mol Pharm Org Process Res., 2013; 1(3): e106.
56. Al-Ghananaeem A. Sublingual and Nasal Transmucosal Drug Delivery for Breakthrough Pain: A Frontier in Cancer Therapy. J Bioequiv Availab, 2013; 5(3): e29.
57. Vasir J, Tambwekar K, Garg S. Bioadhesive microspheres as a controlled drug delivery system. International Journal of Pharmaceutics, 2003; 255(1): 13-32.
58. Winterhalter M, Hilty C, Bezrukov S M, Nardin C, Meier W, Fournier D. Controlling membrane permeability with bacterial porins. Applications to encapsulated enzymes. Talanta, 2001; 55: 965-71.
59. Abdelbary G, Eouani C, Prinderre P, Joachim J, Reynier J, and Piccerelle, P. Determination of the in vitro disintegration profile of rapidly disintegrating tablets and correlation with oral disintegration. Int. J. Pharm, 2005; 292(1-2): 29-41.
60. Yoshio K, Masazumi K, Shuichi A, and Hiroaki N, 2005; J. Control. Release, 105(1-2): 16-22.
61. Corveleyn S, Remon, JP. Formulation and production of rapidly disintegrating tablets by lyophilisation using hydrochlorothiazide as a model drug. Int. J. Pharm, 1997; 152(2): 215-225.
62. Ringard J, Guyot-Hermann AM, Calculation of disintegrant critical concentration in order to optimize tablets disintegration. Drug Dev. Ind. Pharm, 1997; 14(15-17): 2321-2339.
63. Akagi, H, Kajiyama A, Yanagisawa M, 2005, Rapidly disintegrable Pharmaceutical composition, U.S. Patent 6,899,899.
64. Francesco Cilurzo. Eur. J. Pharm. Sci., 2001; 24: 355-361.
65. Rasetti-Escargueil C, Grange, V. Pharmacokinetic profiles of two tablet formulations of piroxicam. Int. J. Pharm, 2005; 295(1-2): 129-34.
66. Manabe T, Okino H, Maeyama R, Mizumoto K, Nagai E, Tanaka M, Matsuda T. Novel strategic therapeutic approaches for prevention of local recurrence of pancreatic cancer after resection: transtissue, sustained local drug-delivery systems. Journal of Controlled Release, 2004; 100(3): 317-30.
67. Sood A, Panchagnula R. Peroral Route: An Opportunity for Protein and Peptide Drug Delivery. Chemical Reviews, 2000; 101: 3275-303.
68. Manivannan R. Recent Advances In Novel Drug Delivery System. IJRAP., 2010; 1(2): 316-326
69. Arunachalam A., karthikeyan M., Vinay Kumar D. et al. Transdermal Drug Delivery System:A Review. Current Pharma Research, 2010; 1(1): 70-81.
70. Sharma B, Saroha K, Yadav B. Sonophoresis: An advanced tool in transdermal drug delivery system. IJCPR., 2011; 3(3): 89-97.
71. O'Neil, Jacklyn, "Controlling drug delivery for the application of extended or sustained-release drug products for parenteral administration". Chemistry Master's Theses, 2010; Paper 14.
72. Vinod KR., Reddy R., Banji D., Reddy V., Sandhya S. Critical review on mucoadhesive drug delivery systems. Hygeia journal for drugs and medicines, 2012; 6(1): 7-28.
73. P. Dario, MC Carrozza, A Benvenuto, A Menciassi, J Micromech. Microeng, 2000; 10: 235-244.
74. Iddan G, Meron G, Glukhovsky A and Swain P. Wireless capsule endoscopy. Nature, 2000; 405: 417-418.
75. Wagner B, Quenzer HJ, Hoerschelmann S, Lisec T, Juerss M, Int. Conf. IEEE Eng. in and Biology Soc., 1996; 254: 1998.
76. Santini JT, Richards AC, Scheidt R, Cima MJ, Langer R. A Controlled release microchip. Nature, 1999; 397: 335-338.