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New Trends: Drug Delivery Systems

S Suhasini1* and CH Ramesh Babu2

¹Department of Biotechnology, Bhopal University, Bhopal, India ²Department of Chemistry, Andhra University, Visakhapatnam, India

Review Article

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*For Correspondence

S. Suhasini, Department of Biotechnology, Bhopal University, Bhopal

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mail:salivendra_suhasini@rediffmail.com

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ABSTRACT

There are many Drug delivery systems are under development. The main aim of Drug delivery system is to reduce drug degradation and loss and to prevent side effects to improve bioavailability. Drug delivery system to target organs or tissues has become one of the challenges of the new century. This type of delivery methods provides major advances in specific delivery.

INTRODUCTION

Drug delivery system is defined as "Formulation of the Drug in to suitable form like oral administration form (Tablet) or Intravenous form (solution).

These new approaches can reduce solvency problems and protects the drugs from the external environment, for example, photo degradation and pH changes, while reducing dumping by controlling the discharge profile [1-8]. Additionally, controlled focusing at the site of activity and lessened time of introduction at non-focusing on tissues in-wrinkles the viability of medications and diminish harmfulness and symptoms in this manner enhancing tolerant consistence and comfort.

TYPES OF 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 [9-15].

Drug delivery systems are classified as follows:-

- Transdermal Delivery Systems
- Carrier Based Delivery System
- Variable Release Delivery Systems
- Implantable Delivery Systems
- Nasal Delivery Systems

Transdermal Delivery Systems It permits the adsorption of skin surface into blood circulation. The advantages of thermal deliver systems are lower dosages are sufficient and side effective are low.

Implantable Delivery Systems Implantable devices are polymeric devises of various shapes and introduced into body tissue [16-22]. The limitations of this type of devices are possibility of infection and irritation of implants. This type of delivery systems is mainly involved in diabetes, cancer, cardiovascular diseases and brain diseases.

Biocompatibility is one of the pharmaceutical methods, and it is designing to fit the physicochemical properties of the drug to new dosage forms. Todays, biodegradability of polymers such as poly (D-L-lac- tide-coglycolide) is using to avoid physiological and path logical problems developing targeting strategies. This Biocompatibility method can improve the pharmacokinetic of drugs through the delivery of a huge dose at the specific site of organs by using ligands, While release and degradation to non-toxic products. Oral administration is one of the most convenient methods for drug delivery system and researchers focussed on the development of carriers that can use as biological barriers such as the gastrointestinal (GI) tract [23-28]. The main advantage of carrier is to protect the drug against host.

Microencapsulation has been important to the development of new therapeutics and has been used to produce microspheres containing both hydrophilic and hydrophobic drugs entrapped within biocompatible polymers [29-38]. The purpose of using these carriers is to obtain a con-trolled release thus maintaining therapeutic drug levels over a specified time period while reducing systemic absorption. These systems have been used in food and cosmetic industry and drug and gene delivery [39-45].

The advantages of Drug Delivery Systems are:-

- Ease administration of drugs
- Quick absorption and onset of action
- Availability of Simple formulations
- favourable environment
- Bio-availability satisfactory
- Reduced hospital outpatient care
- Accurate consistent dosing
- lower manufacturing costs

The disadvantages Drug Delivery Systems are:

- Untoward immunogenic reactions may occur
- Insufficient availability of data for penetration enhancers
- > Pathology may adversely affect

Based on the mechanisms drug delivery systems are divided in to two classes. These are Physical mechanism based drug delivery systems are also known as controlled drug delivery systems, for Eg, osmosis, diffusion, erosion and electro transport (**Figure 1**). Other one is Biochemical mechanism based drug delivery system may include monoclonal antibodies, liposomes, and gene therapy and vector systems. Some of the particles are used as carriers in drug delivery system may include soluble polymers, micro particles, biodegradable polymers, microcapsules and liposomes. These carriers are slowly degradable [46-54].

Phospholipid-based delivery systems

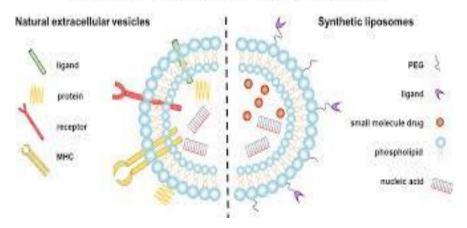


Figure 1: Phospholipid based Drug delivery system

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 [55-62]. A large variety of organic systems like liposomes, micelles, vesicles, nerve fiber polymers, nanoparticles, liquid crystals, microspheres, Implants etc., are used that have vital blessings and few limitations.

They are:-

- Liposome
- Nanoparticles
- Microspheres
- Polymeric micelle formulations
- Implants
- Liposomes

Liposomes

Liposomes are mixture, perishable and spherical vesicles whose size varies from low micrometres vary to tens of micrometers [63-68]. They carry with it a bilayer membrane entrapping associate degree binary compound core. The membranes of liposomes are sometimes derived from phospholipids with mixed lipoid chains and head teams or pure artificial lipids with outlined chemical group chains and head teams. The medicine may be either entrapped at bilayer interface, in binary compound volume or in phospholipids bilayer. Liposomes that are fashioned from phospholipids are largely accustomed modify the pharmacokinetic profile of medication, enzymes etc. This specific drug carrier is extremely advantageous in enhancing the therapeutic result of anti-cancer agents through increasing drug concentration levels in growth cells and decreasing the exposure to traditional cells. Liposomes play a crucial role in solubility sweetening, bioavailability, targeting sites and prolonged unleash of drug.

Liposomes are made up of lipids or fat molecules are surrounded by water core. These types of liposomes are widely used for cancer treatment, infectious diseases and for vaccine preparation [69-73]. The disadvantage of liposomes is leakage with poor controlled release and less encapsulation capacity.

Microspheres

There are varied drug delivery systems to deliver a drug to focus on the site during a sustained controlled release fashion. One amongst the strategies is exploitation microspheres as drug carriers. These are created from solid chemical compound matrices for endovenous and intra-arterial targeted drug delivery systems. Microspheres are spherical in form and size varies from 1-300 µm. There are totally different types of polymers that are used for fabrication of microspheres are albumin, starch, gelatin, dextran, polypropene etc. The administration of drug mediate by these microspheres is controlled by degradation and dissolution of matrix. The drug delivery is affected by the polymer type, size of matrix [74-82]. There are various kinds of strategies to provide these small particulate systems such as evaporation technique, cross linking and high blending technique. The precise benefits of those small particulate systems are they will be injected or ingested and also conjointly they produce sustained release action and site specific delivery.

Polymeric Micelle Formulations

The polymeric micelle consists of fine pharmaceutical properties and is simply manageable. They are the superb drug carrier that contains inner hydrophobic core and outer hydrophilic corona. The inner core is capable of solubilizing lipophilic substances and it's stabilized by hydrophilic chemical compound chains that are towards aqueous surroundings. The outer corona acts as an interface between inner core and binary compound surroundings [83-88].

Implants

Implants measure the compound devices that are used for the sustained drug release or to focus on high drug concentrations to the encompassing space of target tissue. These implants typically applied once when chronic medical aid is indicated in things like chemical castration in prostatic adenocarcinoma treatment, in hormones replacement [89-92]. The Implants are extremely viscous liquids or semisolid formulations that are directly placed within the body fluids, injected or impregnated with biodegradable polymers.

Hydrogels

Hydrogels are capable of binding large amount of water or biological fluids. The compositions of hydrogels are homopolymers or copolymers. These are insoluble in the presence of chemical cross links and physical cross links. Hydrogels as drug delivery systems can be very important materials if is combined with the molecular techniques.

Solid Lipid Nanoparticles

Nanoparticles like nanospheres and nanocapsules are used as carrier for drug delivery systems. Nanoparticles can able to adsorb or encapsulate a drug and protecting it against chemical and enzymatic degradation. These nanoparticles are act as carriers of DNA in gene therapy and genetic engineering studies. Other nanoparticles like nanotubes, nano wires, nanoshells and nanopores are used in drug delivery systems. These types of nanoparticles are used as marker in cancer studies.

Nanoparticles

Nanoparticles are sub-micron sized particles having size of 10 to 200 nm are within the solid state either in amorphous or crystalline type (**Figure 2**). The nanoparticles are wide used as carriers because of their stability and future storage. They will encapsulate or take up the drug and facilitate in protective it from chemical and catalyst degradation [93-88]. Nanoparticles embrace nanocapsules and nanospheres. The nanocapsules are sac systems in which drug is restrained or engulfed in a cavity enclosed by chemical compound membrane; whereas the drug is uniformly unfold within the nanosphere matrix systems. The nanoparticles are terribly economical in delivering each deliquescent and hydrophobic medication. In the recent years the biodegradable polymeric nanoparticles have gained a big attention as potential drug carrier within the applications of targeted drug delivery system, and as an economical carrier of DNA in factor medical aid and conjointly capable to handle proteins, peptides and genes through pre-oral route.

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Drug Loaded Erythrocytes

It is one of the powerful systems for delivery of drugs. Erythrocytes are long circulation can be used with different biologically active substances. Carrier erythrocytes are prepared by using blood sample form organism and separated by different physical and chemical methods.



Figure 2: Types of carriers in Drug delivery system.

CONCLUSION

New technologies have been developed for the treatment of Different diseases. The use of Drug delivery systems in developing drugs for bringing lots of hope in the field of Pharmacology and Medical research. Nanoparticle drug delivery devices have advantages which show higher efficiency than other particle drug delivery systems. But, toxicity of the nanoparticle formulations should be avoided. Full proof procedures should be established to know both the short-term and long-term toxicity analysis of the nanoparticle drug delivery systems.

REFERENCES

- Koushik OS, et al. Nano Drug Delivery Systems to Overcome Cancer Drug Resistance A Review. J Nanomed Nanotechnol. 2016;7:378.
- 2. Gopi S, et al. Effective Drug Delivery System of Biopolymers Based On Nanomaterials and Hydrogels A Review. Drug Des. 2016;5:129
- 3.Nirmala MJ and Nagarajan R. Microemulsions as Potent Drug Delivery Systems. J Nanomed Nanotechnol. 2016;7:e139.
- 4.Mandal B. Personalized Nanotheranotics for Cancer. J Biotechnol Biomater. 2016;6:e127.
- 5.Zaman H. Addressing Solubility through Nano Based Drug Delivery Systems. J Nanomed Nanotechnol. 2016;7:376.
- 6. Dudhipala N, et al. Amoxycillin Trihydrate Floating-Bioadhesive Drug Delivery System for Eradication of Helicobacter pylori:Preparation, In Vitro and Ex Vivo Evaluation. J Bioequiv Availab. 2016;8:118-124.
- 7. Mohsen R, et al. Design, Synthesis, Characterization and Toxicity Studies of Poly (N-lso-Propylacrylamide-co-Lucifer Yellow) Particles for Drug Delivery Applications. J Nanomed Nanotechnol. 2016;7:363.
- 8. AbouAitah KEA, et al. Mesoporous Silica Materials in Drug Delivery System:pH/Glutathione-Responsive Release of Poorly Water-Soluble Pro-drug Quercetin from Two and Three-dimensional Pore-Structure Nanoparticles. J Nanomed Nanotechnol.2016;7:360.
- 9. Van Tilburg CWJ. pinal Analgesic Drug Delivery for Ehlers-Danlos Hypermobility Type Chronic Pain Treatment: A Case Report. J Pain Relief. 2016;5:235.
- Colone M, et al. Redox-active Microcapsules as Drug Delivery System in Breast Cancer Cells and Spheroids. J Mol Genet Med. 2016:10:200.
- 11. Kumar P, et al. Synthesis of Dox Drug Conjugation and Citric Acid Stabilized Superparamagnetic Iron-Oxide Nanoparticles for Drug Delivery. Biochem Physio. 2016;15:194.
- 12. Patil JS. Significance of Particulate Drug Delivery System in Anti-microbial Therapy. Adv Pharmacoepidemiol Drug Safe. 2016;5:139.
- 13. Patil J. Advances in Drug Delivery Strategies for Cancer Therapeutics. J Pharmacovigil. 2016;S3:e002.
- 14. Lopes CM and Soares C. Transdermal Drug Delivery Systems Activated by Physical stimuli:Techniques and Applications. Drug Des. 2016;4:e129.
- 15. Wang X and Lu W. Active Targeting Liposomes:Promising Approach for Tumor-Targeted Therapy. J Bioequiv Availab. 2016;8:013-014.
- 16. Shanmugan P and Bandameedi R. Chronotherapeutic Drug Delivery Systems. J Drug Metab Toxicol. 2015;6:194.
- 17. Patil JS. Hydrogel System: An Approach for Drug Delivery Modulation. Adv Pharmacoepidemiol Drug Saf. 2015:4:e135.
- 18. Naydenov T, et al. Opinion of Bulgarian Pharmacists on Drug Delivery Systems, Orodispersible and Pediatric Dosage Forms. J App Pharm. 2015;8:211.
- 19. Patil J. Hydrodynamically Balanced Gastro-Retentive Site Specific Drug Delivery System: An Innovative Approach J Pharmacovigil. 2015;3:e146.
- 20. Jassim-Jaboori AH and Oyewumi MO. 3D Printing Technology in Pharmaceutical Drug Delivery: Prospects and Challenges. J Biomol Res Ther. 2015;4:e141.
- 21. Saikia C, et al. Chitosan: A Promising Biopolymer in Drug Delivery Applications. J Mol Genet Med. 2015;S4:006.
- 22. Maroof K, et al. Scope of Nanotechnology in Drug Delivery. J Bioequiv Availab. 2015;8:001-005.
- 23, Kamel R. Transdermal Drug Delivery: Benefits and Challenges, J App Pharm, 2015;8:e103
- 24. Awan BN, et al. Bacterial and Liposomal Vector Guided Drug Delivery System via Tumor Markers Carrier Gene to Treat Neoplasm. J App Pharm. 2015;8:206.
- 25. Bhasin S and Patel R. Enhanced Oral Bioavailability of Alitretinoin by Lipid Drug Delivery System. Pharm Anal Acta. 2015;6:433.
- 26. Banala N, et al. Design and Evaluation of Floating Multi Unit Mini Tablets (MUMTS) Muco Adhesive Drug Delivery System of Famotidine to Treat Upper Gastro Intestinal Ulcers. J Pharmacovigil. 2015;3:179.
- 27. Repanas A, et al. Coaxial Electrospinning as a Process to Engineer Biodegradable Polymeric Scaffolds as Drug Delivery Systems for Anti-Inflammatory and Anti-Thrombotic Pharmaceutical Agents. Clin Exp Pharmacol. 2015;5:192.
- 28. Zanchetta B, et al. Self-Emulsifying Drug Delivery Systems (SEDDS) in Pharmaceutical Development. J Adv Chem Eng. 2015;5:130.
- 29. Jethara SI and Patel MR. Optimizing Oral Controlled Release Drug Delivery Systems using Experimental Designs. Intel Prop Rights. 2015;3:135.
- 30. Patil JS. Novel Drug Delivery Strategies: New Concepts. Adv Pharmacoepidemiol Drug Saf. 2015;4:e134.
- 31. Leucuta SE. A New Frontier for Nanoparticulate Drug Delivery Systems to Improve Drug Targeting and Molecular Pharmacotherapy: Subcellular Bioavailability. Clin Pharmacol Biopharm. 2015;4:e118.

- 32. Jethara SI and Patel MR. Optimizing Oral Controlled Release Drug Delivery Systems Using Experimental Designs. Intel Prop Rights. 2015;3:142.
- 33. Aminabhavi TM. Polysaccharide-Based Hydrogels as Biomaterials in Drug Delivery. J Pharma Care Health Sys. 2015;2:e132.
- 34. Nasri M and Mirshekarpour H. Polymeric Nanostructures as Colloidal Drug Delivery Systems: Thermosensitive Hydrogels Containing Self-Assembled Micelles. J Nanomed Nanotechnol. 2015;6:301.
- 35. Farooq U, et al. Design and Development of Multi Particulate System for Targeted Drug Delivery Using Natural Polymer. Pharm Anal Acta. 2015; 6:366.
- 36. Saboktakin MR, et al. pH Sensitive Chitosan-based Supramolecular Gel for Oral Drug Delivery of Insulin. J Mol Genet Med. 2015;9:170.
- 37. Kumar V, et al. Nanostructures for Drug Delivery. J Drug Metab Toxicol. 2015;6:e125.
- 38. Komano Y, et al. Joint-Targeting Drug Delivery System for Rheumatoid Arthritis:siRNA Encapsulated Liposome. Pharm Anal Acta. 2015;6:352.
- 39. Hu D, et al. The Bright Future of Liposome Mediated Drug Delivery. Biochem Physiol. 2015;4:e133.
- 40. Agrawal P. Significance of Polymers in Drug Delivery System. J Pharmacovigil. 2014;3:e127.
- 41. Pawar HA and Bhangale BD. Phytosome as a Novel Biomedicine: A Microencapsulated Drug Delivery System. J Bioanal Biomed. 2015;7:006-012.
- 42. Jafari S and Adibkia K. Application of Hydroxyapatite Nanoparticle in the Drug Delivery Systems. J Mol Pharm Org Process Res. 2014;3:e118.
- 43. Jigar N Shah, et al. Nanoparticulate Transscleral Ocular Drug Delivery. J Biomol Res Ther. 2014;3:114.
- 44. Wen H and Li Y. Redox Sensitive Nanoparticles with Disulfide Bond Linked Sheddable Shell for Intracellular Drug Delivery. Med chem. 2014;4:748-754.
- 45. Malika V, et al. Nano-Carrier for Accentuated Transdermal Drug Delivery. J Develop Drugs. 2014;3:121.
- 46. Gavasane AJ and Pawar HA. Synthetic Biodegradable Polymers Used in Controlled Drug Delivery System: An Overview. Clin Pharmacol Biopharm. 2014;3:121.
- 47. Dutta AK and Ikiki E. Novel Drug Delivery Systems to Improve Bioavailability of Curcumin. J Bioequiv Availab. 2013;6:001-009.
- 48. Tyrrell J and Tarran R. Gaining the Upper Hand on Pulmonary Drug Delivery. J Pharmacovigilance. 2013;2:118.
- 49. Babar MM, et al. Virosomes-Hybrid Drug Delivery Systems. J Antivir Antiretrovir. 2013;5:166-172.
- 50. Phan CM, et al. Insights to Using Contact Lenses for Drug Delivery. Clin Exp Pharmacol. 2013;3:145.
- 51 Madhavi BR, et al. Buccal Film Drug Delivery System-An Innovative and Emerging Technology. J Mol Pharm Org Process Res. 2013:1:107.
- 52. Peddi MG. Novel Drug Delivery System: Liquid Solid Compacts J Mol Pharm Org Process Res. 2013;1:108.
- 53. Al-Achi A and Jonathan Lawrence BS. Micelles:Chemotherapeutic Drug Delivery.Clinic Pharmacol Biopharmaceut. 2013;2:e114.
- 54. Gou M. Promising Application of Nanotechnology in Anticancer Drug Delivery. Drug Des. 2013;2:e117.
- 55. Suresh Kumar R, et al. 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;5:201- 208.
- 56. 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.
- 57. 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;4:288.
- 58. Suedee R. The Use of Molecularly Imprinted Polymers for Dermal Drug Delivery. Pharm Anal Acta. 2013;4:264.
- 59. Mostafavi SH and Jayachandra Babu R. Nano-Sized Drug Delivery. J Mol Pharm Org Process Res. 2013;1:e108.
- 60. Zhu Y. Mesoporous Silica Nanoparticles with a Core-Shell Structure for Drug Delivery. J Bioanal Biomed. 2013;5:e117.
- 61. Weston GS and Yeboah KG. Site-Specific Drug Delivery to the Gastrointestinal Tract. J Mol Pharm Org Process Res. 2013;1:e106.
- 62. Al-Ghananaeem A. Sublingual and Nasal Transmucosal Drug Delivery for Breakthrough Pain: A Frontier in Cancer Therapy. J Bioequiv Availab. 2013;5:e29.
- 63. Gundogdu E, et al. A Microemulsion for the Oral Drug Delivery of Pitavastatin. Pharmaceut Anal Acta.2013;4:209.
- 64. Glavas-Dodov M. Particulate Carriers for Local Colon Drug Delivery. J Bioequiv Availab. 2013;5:e25.
- 65. Rasool Hassan BA. Overview on Drug Delivery System. Pharmaceut Anal Acta. 2012;3:e137.
- 66. Nayak UY. Role of Nano-Particles in Drug Therapy-Drug Delivery Approach. Drug Design. 2013;S5:e001.
- 67. Chen G. Nanotube-Based Controlled Drug Delivery. Pharmaceut Anal Acta. 2012;3:e136.

- 68. Vashist SK and Venkatesh AG. Carbon Nanotubes-Based Electrochemical Sensors and Drug Delivery Systems: Prospects and Challenges. J Nanomed Nanotechol. 2012;3:e121.
- 69. Swain S. Mucoadhesive Micro and Nanoparticles for Oral Controlled Drug Delivery System for Prolongation of Gastric Residence and Its Application. Pharmaceut Reg Affairs. 2012;1:e115.
- 70. Chauhan A. Pulmonary Drug Delivery Systems, A Versatile Technique. Pharmaceut Anal Acta. 2012;3:e117.
- 71. Swaminathan S and Jablonski MM .Non-Biological Membranes as Drug Delivery Systems. J Memb Sci Technol. 2012;2:e108.
- 72. Liu R. Nanostructured Lipid Carriers as the Most Promising Approach in Ocular Drug Delivery System. J Nanomed Biotherapeut Discov. 2012;2:e116.
- 73. Chen Y and YangK. Intra-Articular Drug Delivery Systems for Arthritis Treatment. Rheumatology.2012;2:e106.
- 74. Barakat NS, et al.Target Nanoparticles:An Appealing Drug Delivery Platform. J Nanomedic Nanotechnol. 2012;S4:009.
- 75. Yiv S and Uckun FM. Lipid Spheres as Attractive Nanoscale Drug Delivery Platforms for Cancer Therapy. J Nanomedic Nanotechnol. 2012;3:128.
- 76. Davis ME, et al. Nanoparticle therapeutics:an emerging treatment modality for cancer. Nat Rev Drug Discov. 2008;7:771-782.
- 77. Petros RA and DeSimone JM. Strategies in the design of nanoparticles for therapeutic applications. Nat Rev Drug Disco. 2010;9:615-627.
- 77. Pouton CW, et al. Targeted delivery to the nucleus. Adv Drug Deliv Rev. 2007;59:698-717.
- 78. Ferrari M. Cancer nanotechnology:opportunities and challenges. Nat Rev Cancer. 2005;5:161-171.
- 79. Brewer E, et al. Emerging technologies of polymeric nanoparticles in cancer drug delivery. J Nanomaterials. 2011.
- 80. Guo S and Huang L. Nanoparticles escaping RES and endosome:challenges for siRNA delivery for cancer therapy. J Nanomaterials. 2011.
- 81. Tiwari PM, et al. Functionalized gold nanoparticles and their biomedical applications. Nanomaterials. 2011;1:31-63.
- 82. Zhang L, et al. Nanoparticles in medicine:therapeutic applications and developments. Clin Pharmacol Ther. 2008;83:761-769.
- 83. Park JW. Liposome-based drug delivery in breast cancer treatment. Breast Cancer Research. 2002;4:95-99.
- 84. Dibirdik I, et al. In vivo Anti-Cancer Activity of a Liposomal Nanoparticle Construct of Multifunctional Tyrosine Kinase Inhibitor 4-(4'-Hydroxyphenyl)-Amino-6,7 Dimethoxyquinazoline. J Nanomedic Nanotechnolo.2010:1:101.
- 85. Eshita Y, et al. Mechanism of the Introduction of Exogenous Genes into Cultured Cells Using DEAE-Dextran-MMA Graft Copolymer as a Non-Viral Gene Carrier. II. Its Thixotropy Property. J Nanomedic Nanotechnol. 2011:2:105.
- 86. Ringe K, et al. Nanoparticle Drug Delivery to the Brain. Encyclopedia of Nanoscience and Nanotechnology. 2004;7:91-104
- 87. Shih MF, et al. Bioeffects of Transient and LowIntensity Ultrasound on Nanoparticles for a Safe and Efficient DNA Delivery. J Nanomedic Nanotechnol. 2011;S3:001.
- 88. Tarl Prow, et al. Construction, gene delivery, and expression of DNA tethered Nanoparticles, Molecular Vision. 2006;12:606-615.
- 89. 9. Roldo M, et al. Mucoadhesive thiolated chitosans as platforms for oral controlled drug delivery:synthesis and in vitro evaluation. European Journal of Pharmaceutical Biophamaceutics. 2004;57:115-121.
- 90. Langoth N, et al. Thiolated chitosan:in vitro evaluation of its permeation properties. Journal of Control Release.2004;94:177-186.
- 91. Kast CE, et al. Design and in vitro evaluation of a novel bioadhesive vaginal drug delivery system for clotrimazole. Journal of Control Release. 2002;81:347-354.
- 92. Leitner VM, et al. Mucoadhesive and cohesive properties of poly (acrylic acid)-cysteine conjugates with regard to their molecular mass. European Journal of Pharmaceutical Sciences. 2003;18:89-96.
- 93. Senel S, et al. Enhancing effect of chitosan on peptide drug delivery across buccal mucosa. Journal of Biomaterials. 2000;21:2067-2071.
- 94. Mondal N, et al. Development, physical characterization, micromeritics and in vitro release kinetics of letrozole loaded biodegradable nanoparticles. Pharmazie. 2008;63:361-365.
- 95. Felt O, et al. Chitosan:a unique polysaccharide for drug delivery. Journal of Drug Development and Industrial Pharmacy. 1998;24:979-993.
- 96. Kast CE, et al.Chitosan -thioglycolic acid conjugate:a new scaffold material for tissue engineering. International Journal of Pharmaceutics. 2003;256:183-186.
- 97. Leroux JC, et al. Biodegradable nanoparticles from sustained release formulations to improved site specific drug delivery. Journal of Control Release. 1996;39:339-350.
- 98. Coppi G, et al. Chitisanalginate microparticles as a protein carrier. Journal of Drug Development and Industrial Pharmacy. 2001;27:393-400.

99. Huntera W, et al.Local delivery of chemotherapy:a supplement to existing cancer treatments. A case for surgical pastes and coated stents Adv Drug Deliver. 1997;26:199.

100. Brunnauer S, et al. Adsorption of gases in multimolecular layers. J Am Chem Soc. 1938;60:309-319.