



A Review on Targeted Drug Delivery System

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ABSTRACT

New form of drug delivery system is drug targeting. The goal of the drug targeting is to deliver the drug to that targeted site of action without releasing the drug at non targeted site or without damaging other tissues/organs/cells. It has more advantages over conventional drug delivery system like low side effects, improvement of pharmaceutical activity and reduction of administered dose. The main reason of the targeted drug delivery system is to provide good pharmacological therapeutic agents for diseased organs without harming healthy tissues. Cancer treatment with chemotherapeutic agents have more side , targeted drug delivery system serve a purpose to reduce those side effects. various drug carrier which can be used in this advance delivery system are soluble polymers, biodegradable, microsphere polymers (synthetic and natural), neutrophils, nanoparticles, lipoproteins, liposomes, micells, niosomes, these carriers maintain and transport the loaded drug to the pre-selected organ. Drug targeting have a different mechanisms such as passive targeting, inverse targeting, active targeting, physical targeting, ligand-mediated targeting, dual targeting and double targeting. Targeted drug delivery system is useful for delivering the therapeutic agent to a particular site of action without causing any virulent effect to other organs. Goal of tdds To prolong, localize target and have a protected drug interaction with a diseased tissue.

Keywords: Therapeutically active drug, drug delivery, drug targeting, chemotherapeutic agents, therapeutic action

Introduction

Targeted drug delivery is a type of smart drug delivery system which is miraculous in delivering the drug to a patient. This conventional drug delivery system is done by the absorption of the drug across a biological membrane, whereas the targeted release system is that drug is released in a dosage form. Targeted drug delivery is a special form of drug delivery system where the medicament is selectively targeted or delivered only to the site of action and not to the non-targeted organs or tissues or cells. The system has principal of that delivers a certain amount of a therapeutic agent for a prolonged period of time to a targeted diseased area within the body and improves the efficacy and reduces the side effect. This helps maintain the required plasma and tissue drug levels in the body, thereby preventing any damage to the healthy tissue via the drug.

Conventional drug delivery system is the classical methods for the delivery of the drug into the body example tablets, capsules, syrups, ointments etc. These poses few limitations such as poor water solubility, limited targeting, Suffer from poor bioavailability, fluctuations in plasma drug delivery, unable to achieve sustained release. The technology of the targeted drug delivery system has become advanced and controls the drug absorption bioavailability and pharmacokinetic parameters and other limitations of conventional ones. The main principles of targeted drug delivery system requires:

1. Reach the targeted site.
2. Release the drug at specific site at a pre determined time.
3. Avoid the degradation by body fluid.
4. The ability to load the drug to the target site.

Targeted drug delivery mostly used for selective and effective localization of pharmacologically active moiety at predetermined target in therapeutic concentration, while restricting it's access to non target normal cellular linings, thus minimizing therapeutic index.

Targeted drug delivery are often are used to treat several diseases, i .e vascular diseases , polygenic disease etc .but the foremost necessary application of targeted drug delivery is to treat cancerous tumors

Definition

Drug delivery system is a system of specifying the drug moiety directly into its targeted body area (organ, cellular and subcellular level of specific tissue) to overcome the a specific toxic effect of conventional drug delivery, thereby reducing the amount of drug required for therapeutic efficacy.

1. Liposomes, niosomes, nanosphere, microsphere, et
2. Examples for drug carrier

The ideal features of a targeted drug delivery system

The targeted drug delivery system must have certain properties which include:

1. It should be stable, safe (non-toxic), compatible with body fluid and biodegradable.
2. Deliver the drug only to the target site.
3. Control the drug release at a predetermined rate.
4. The rate of drug release not affecting the pharmacological effect.
5. Minimum leakage of the drug during transportation to the target site.
6. Using an inert, biodegradable, or easily eliminated carrier.
7. The preparation process of the drug delivery system should be simple, easy and costless.

Advantages

1. Drugs deliver / releases over extended period of time
2. Toxicity is reduced by delivering drug at the targeted site.
3. Self administration is possible.
4. Enhance absorption of drug.
5. Deliver the drug only to the target site.
6. It should be stable, safe (non-toxic), compatible with body fluid and biodegradable
7. Intermittent dosing can be avoided. . Improve patient compliance.
8. Reduce inter and intra-patient variability.
9. Drug can be administered in a smaller dose to produce the desired side effect.
10. No peak and valley plasma concentration.
11. Control the drug release at a predetermined rate
12. Deliver the drug only to the target site.

Disadvantages

1. Yields comparatively very less
2. Rapid drug elimination from the body results in high dose frequency.
3. The carrier of the targeted drug delivery system may result in the immune response.
4. The drug delivery system is not localized at the tumor tissue for sufficient time.
5. The diffusion and redistribution of released drugs
6. Requires a skill in manufacturing storage, administration.
7. Diffusion and redistribution of drug release.
8. Rapid clearance of targeted systems.
9. Maintaining stability of dosage form is difficult.
10. Highly sophisticated technology requires for formulation

Applications.

1. Enzyme immune assays
2. To cross BBB.

3. In intracellular targeting.
4. Used as a vaccine adjuvant.
5. Widely used in case of cancer therapy.
6. Used in the treatment of ocular drug delivery system.
7. Used in a DNA delivery.
8. Used in case of Oligo nucleotide delivery

Reasons

1. Used in various treatment to prevent diseases.
2. Reduction of drugs side effects and fluctuations in circulating drug levels.

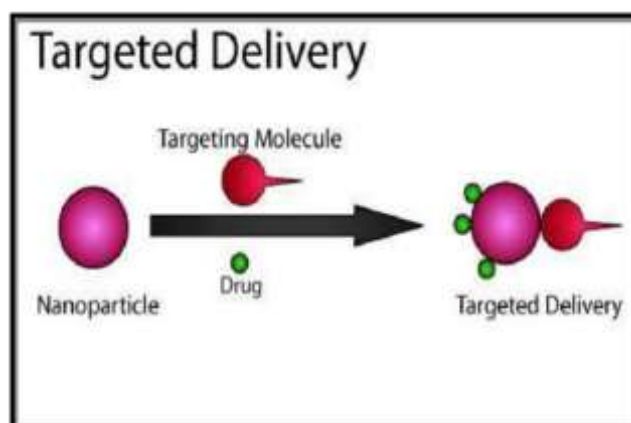


Fig no 1

Methods

As discussed, targeting drug to a specific area is not only increases the therapeutic efficacy of drugs also it aims to decrease the toxicity associated with drug to allow lower doses of the drug to be used in therapy. For the fulfillment of such conditions, few approaches are used extensively, which also know an classification of drug targeting

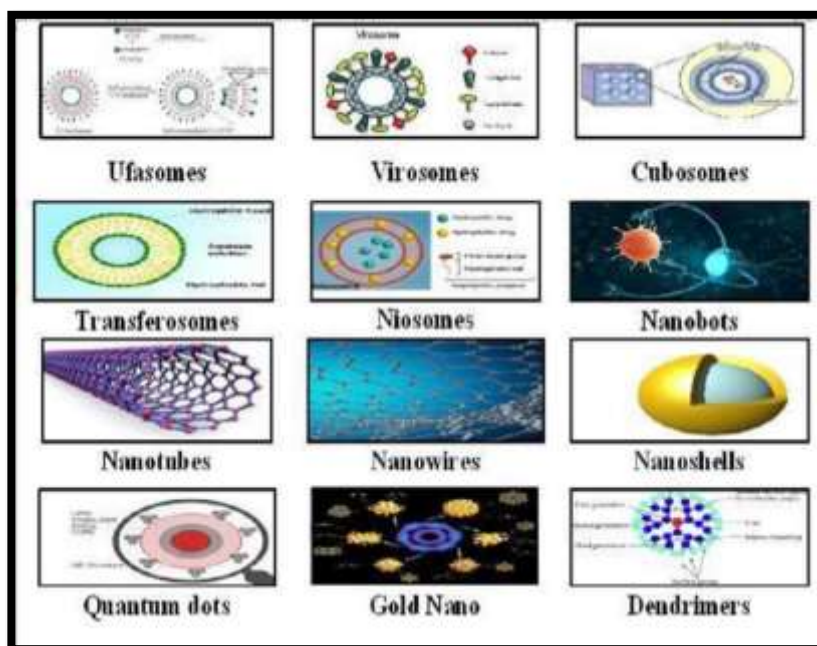


Fig no 2

1. Active targeting
2. Passive targeting
3. Inverse targeting
4. Dual targeting
5. Double targeting
6. Combination targeting

1. Active targeting

Active targeting means a specific ligand- receptor type interaction for intracellular localization which occurs only after blood circulation and extravasation. This active targeting approach can be further classified into three different levels of targeting which are: First order targeting refers to restricted distribution of the drug carrier system to the capillary bed of predetermined target site, organ or tissue e.g.: compartmental targeting in lymphatic, peritoneal cavity, plural cavity, cerebral ventricles. Second order targeting refers to selective delivery of drugs to specific cell types such as tumor cells and not to the normal cells e.g.: selective drug delivery to kupffer cells in the liver. Third order targeting refers to drug delivery specifically to the intracellular site of targeted cell

2. Passive targeting

It refers to the accumulation of drug/ drug carrier system at a specific site. The drugs are Targeted to systemic circulation e.g. receptor based ligand mediated entry of the drug Targeting is occurring because of body's natural complex into a cell by endocytosis. response to physicochemical character of drug.

3. Inverse targeting

This approach leads to a saturation of RES and suppression of defense mechanism by pre- injecting large amount of blank colloidal carriers . This is an effective approach for non- RES organs.

4. Dual targeting

The carrier molecules itself has their own therapeutic activity and therefore increases effect of drug.

5. Double targeting

In this type the temporal and spatial methodologies are combined to target a carrier system.

6. Combination targeting

Similar to double targeting, the combination targeting system for the site specific delivery of proteins and peptides are equipped with molecular specificity. The latter provides a direct access to target site.

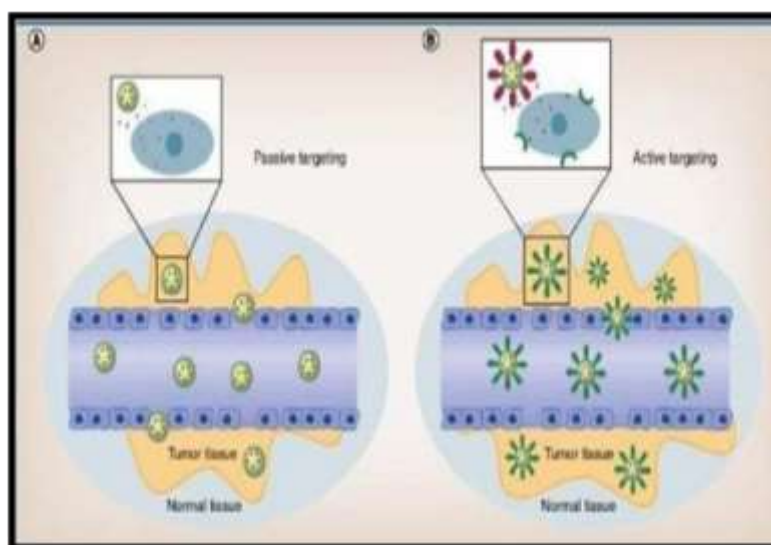


Fig no 3

Carriers Applied For Drug Targeting

Drug targeting can be attained by using carrier system. Carriers are very much important and which required for the transportation of entrapped drug to target sites without releasing its in non targeting site.

Types of carriers which are applied for drug targeting:

1. Nanoparticles

The gold nanoparticles are used by scientists to develop a sensitive ultra-sensitive detection system for DNA and protein markers associated with the presence of different type of cancer.

2. Nanowires

It is wire with a very small diameters made of metal/ other organic compounds. It can be used for detecting the causes and treatment of brain disease like seizures, Parkinson's and similar diseases.

3. Nanotubes

Nanotubes are a type of drug carrier which is hollow cylindrical tube made of carbon that can be easily filled with required drug.

4. Liposomes

These are microscopic bilayer structure vesicles prepared using natural phospholipid.

5. Nanopores

They have very tiny holes that allow the passage of DNA molecules, allow highly exact and effective DNA sequencing. This potential in genetic engineering and biotechnology.

6. Nanoshells

Nanoshells are new strategies of nanoparticles, consisting of a hollow dielectric core of silica covered by a shell of gold^{29,30} It may be used for diagnostic or therapeutic purposes. Nanoshells can be attached with antibodies on their surfaces, allowing them to conjugate certain areas such as cancer cells.³¹ This technique is very effective in targeting the antineoplastic drug.³² Loo et al. studied the ability of nanoshells in imaging and treatment of cancer.³³

7. Virosomes

Virosomes are drug delivery systems described as unilamellar vesicles prepared from phospholipids.^{71,72} The surface of virosomes contains sites to which the virus-derived glycoproteins are attached to facilitate the recognition and targeting of the virosomes to the target site inside the body.⁷³ Lucarini et al. design an innovative platform for the treatment of cerebral tumors using erythro-magneto-HA-virosome.

8. Niosomes

These are the non-ionic surfactant vesicles niosomes can entrap both hydrophilic and lipophilic drug. As like liposomes but the stability of niosomes is higher than the liposomes due to the phospholipid properties. The niosomes are effective for targeting anti-neoplastic drugs, anti-inflammatory, anti-bacterial, anti-fungal and antiviral.

9. Transferosomes

Transferosomes are such a novel vesicular drug delivery system. Transformers are specially self-optimizing, selfregulating, ultra deformable "ultra-flexible". possessing an inner aqueous core surrounded by a complex lipid bilayer with unique properties, due to the presence of "edge activators" into a vesicular membrane, the surfactant has been used as edge activators. So it can penetrate the skin efficiently by squeezing themselves through pores from 5 to 10 times less than their diameter.^{83,84} This will avoid complete rupture of the vesicle and remaining the drug intact after

Conclusion

The objectives of drug targeting are to achieve a desired pharmacological response at a selected site without undesirable interactions at other sites. This is especially important in cancer chemotherapy and enzyme replacement therapy. Drug targeting is achieved by two approaches.

Acknowledgement

We are thankful to management, principal and all the staff members of the college for their guidance and support

Reference

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1. Agnihotri J, Saraf S, Khale A. Targeting: New potential carriers for targeted drug delivery system. Int J Pharm Sci Rev Res. 2011;8(2):117-23.

2. Malik R, Garg T, Goyal AK, Rath G. Polymeric nanofibers: Targeted gastro-retentive drug delivery systems. *J Drug Target.* 2015;23(2):109-24.
3. Mishra B, Patel BB, Tiwari S. Colloidal nanocarriers: A review on formulation technology, types and applications toward targeted drug delivery. *Nanomedicine Nanotechnol Biol Med.* 2010;6(1):9-24.
4. Azarmi S, Roa W, Löbenberg R. Current perspectives in dissolution testing of conventional and novel dosage forms. *Int J Pharm.* 2007;328(1):12-21.
5. Tice TR, Tabibi SE. Parenteral drug delivery: Injectables. In: *Treatise on controlled drug delivery.* Routledge. 2017;31539.
6. Sastry SV, Nyshadham JR, Fix JA. Recent technological advances in oral drug delivery: A review. *Pharm Sci Technol Today.* 2000;3(4):138-45.
7. Singh MD, Mital N, Kaur G. Topical drug delivery systems: A patent review. *Expert Opin Ther Pat.* 2016;26(2):213-28.
8. Mills JK, Needham D. Targeted drug delivery. *Expert Opin Ther Pat.* 1999;9(11):1499-513.
9. Yokoyama M. Drug targeting with nano-sized carrier systems. *J Artif Organs.* 2005;8(2):77-84 .
10. Agnihotri J, Saraf S, Khale A. Targeting: New potential carriers for targeted drug delivery system. *Int J Pharm Sci Rev Res.* 2011;8(2):117-23.
11. Ellis-Behnke R. Nano neurology and the four P's of central nervous system regeneration: preserve, permit, promote, plasticity. *Med Clin North Am.* 2007;91(5):937-62.
12. Akhter MH, Rizwanullah M, Ahmad J, Ahsan MJ, Mujtaba MA, Amin S. Nanocarriers in advanced drug targeting: setting novel paradigm in cancer therapeutics. *Artif Cells Nanomedicine Biotechnol.* 2018;46(5):873-84.
13. Hong H, Shi J, Yang Y, Zhang Y, Engle JW, Nickles RJ, et al. Cancer-targeted optical imaging with fluorescent zinc oxide nanowires. *Nano Lett.* 2011;11(9):3744-50.
14. Wu C, Yu C, Chu M. A gold nanoshell with a silica inner shell synthesized using liposome templates for doxorubicin loading and near-infrared photothermal therapy. *Int J Nanomedicine.* 2011;6:807.
15. Abdollahi SN, Naderi M, Amoabediny G. Synthesis and characterization of hollow gold nanoparticles using silica spheres as templates. *Colloids Surf Physicochem Eng Asp.* 2013;436:1069-75.
16. Sironmani A, Daniel K. Silver nanoparticles–universal multifunctional nanoparticles for bio sensing, imaging for diagnostics and targeted drug delivery for therapeutic applications. *Drug Discov Dev Future.* 2011;463-84.
17. Kolhe S, Parikh K. Application of nanotechnology in cancer: A review. *Int J Bioinforma Res Appl.* 2012;8(1-2):112-25.
18. Loo C, Lin A, Hirsch L, Lee MH, Barton J, Halas N, et al. Nanoshell-enabled photonics-based imaging and therapy of cancer. *Technol Cancer Res Treat.* 2004;3(1):33-40.
19. Reddy AK, Rathinaraj BS, Prathyusha P, BHargav TA, Rajani T, Rajamanickam V, et al. Emerging trends of nanotechnology in cancer therapy. *Int J Pharamc Biolo Arch.* 2011;2(1).
20. Mishra N, Pant P, Porwal A, Jaiswal J, Aquib M. Targeted drug delivery: A review. *Am J Pharm Tech Res.* 2016;6:2249- 3387.
21. Rani K, Paliwal S. A review on targeted drug delivery: Its entire focus on advanced therapeutics and diagnostics. *Sch J App Med Sci.* 2014;2(1C):328-31.
22. Manish G, Vimukta S. Targeted drug delivery system: A review. *Res J Chem Sci.* 2011;1(2):135-8.
23. Agnihotri J, Saraf S, Khale A. Targeting: New potential carriers for targeted drug delivery system. *Int J Pharm Sci Rev Res.* 2011;8(2):117-23.
24. Malik R, Garg T, Goyal AK, Rath G. Polymeric nanofibers: Targeted gastro-retentive drug delivery systems. *J Drug Target.* 2015;23(2):109-24.