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A CONCISE REVIEW ON TARGETED DRUG DELIVERY SYSTEM OF NAPROXEN

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ABSTRACT

The aim of the work to research to prepare and compare naproxen microspheres. Naproxen and albumin microspheres shall be prepared by using water-in-oil emulsion generation. The *in vitro* release profile will be studied by means of converting numerous processing and method parameters to offer a controlled launch of drug from the microspheres. Targeted drug delivery is a newest approach of delivering drugs patients in such a targeted sequences that increases the concentration of delivered drug to the targeted body part of interest only (organs/tissues/ cells) which in turn improves efficacy of treatment by reducing side effects of drug administration. Basically, Targeted drug delivery drug is to assist the drug molecule to attain ideally to the desired site. The inherent benefit of this method leads to administration of required drug with its reduced dose and decreased its side impact. This inherent benefit of targeted drug delivery system is below high consideration of research and improvement in scientific and pharmaceutical fields as spine of therapeutics and diagnostics too. Various drugs that can be used in this targeted drug delivery are soluble in polymers, biodegradable microsphere polymers (artificial and natural), neutrophils, fibroblasts, artificial cells, lipoproteins, liposomes, micelles and immune micelle. The aim of targeted drug delivery is to prolong, localize, target and have a protected drug interaction with the diseased tissue. Quantum of drug at targeted drug delivery site shall be determined by taking samples at special site via UV spectrophotometer method.

KEYWORDS

Drug delivery, Drug carrier system and Therapeutics.

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INTRODUCTION

Targeted drug delivery is a form of miraculous drug delivery that brings medicine to a patient. This drug delivery system undergoes the absorption of the drug throughout the biological membrane, whereas the intended release mechanism is that the drug is released in the form of doses[1,2].

Targeted drug delivery system is a method that brings a certain amount of long-term therapeutic

agent to a specific disease within the body. This helps maintain the required level of plasma and tissue of the drug; therefore to avoid any damage to healthy tissue with the drug. When using a targeted release program, the design process needs to be considered: drug properties, adverse drug reactions, drug delivery route, target location, and disease[1,3,4].

The products found in such a delivery system are prepared by considering the specific characteristics of the target cells, the nature of the marker or carriers of vehicles or vehicles that transmit the drug to specific receptors and ligands and physically modified components. Targeted drug delivery systems must be biological (non-toxic), require antibodies, must be physically and chemically stable in vivo and in vitro conditions, and must have limited drug distribution to target cells or tissues or organs and demand. With the same distribution of capillary. It should have a manageable and predictable level of drug release and drug release should not affect drug movement. It should have a therapeutic value for drug release and should have minimal drug leakage during transport[5,4].

Used carriers should not rot or have problems removed from the body. Delivery system maintenance should be simple or easy, duplicate and inexpensive. Targeted drug delivery system is preferred over standard drug delivery systems for three important reasons. The first is the reason for making medicines. Ordinary drugs have a lower rate of solubility and drug resistance compared to targeted drug delivery systems. 2nd Medications are usually poorly absorbed, have a short shelf life and require a large amount of circulation. These are its pharmacokinetic properties. Reason 3 includes the pharmacodynamic properties of the drug. Conventional drugs have a lower specificity and lower treatment dosage compared to the targeted drug delivery system. For these reasons the targeted drug delivery system is preferred over the standard drug delivery systems[1,3,4.]

Types of targeted drug delivery

As discussed, targeting a drug in a particular area not only increases the therapeutic potential of the drug but also aims to reduce drug-related toxicity by allowing the dose of the drug to be used medically. To achieve such conditions, two widely used methods are also known as targeted drug categories[6,7,1].

Passive targeting

Refers to the accumulation of a drug or drug delivery system in a particular area such as anti-neoplastic drugs whose meaning may be attributed to the physicochemical or pharmacological properties of the disease. Therefore, in the event of arthritis treatment the size and surface areas of drug delivery of nano-particles need to be controlled mainly to avoid detection using a reticulo-endothelial system (RES) to increase circulation times and targeting ability. The key is called passive targeting. Drug withdrawal or drug actions are limited to selected sites within the body but not in the liver. Other examples include the administration of antimalarial drugs for the treatment of leishmiansis, brucellosis, candiadsis.

Active targeting

Active targeting refers to the interaction of a specific type of ligand-receptor to locate intracellular intake that occurs only after blood circulation and additional release. This effective identification method can be further divided into 3 different targeting levels

Identification refers to the limited distribution of drug administration systems in a capillary bed of a predetermined target area, organ or tissue e.g. partial orientation to lymphatics, peritoneal cavity, plural cavity, ventricles of the brain and eyes, joints.

Directing refers to the selective delivery of drugs to specific cell types such as tumor cells and not to normal cells e.g. Selected drug delivery to Chuffer cells in the liver.

Directing refers to direct delivery of the drug to the intracellular area of target cells e.g. receptor based ligand mediated entry of complex drug into cell by endocytosis[7].

Components of Targeted Drug Delivery

A drug delivery system primarily constitutes a target and drug carriers or markers. Target means specific organ or a cell or group of cells,

which in chronic or acute condition need treatment. Route of administration involves drug carrier as important targeting moiety and after its leakage from its carrier/markers to reach the drug to the specific or targeted site via biological metabolism with its clearance as well as not to reach at non targeted site to make this delivery system more site specific with reduced side effects of drugs and its quantity too. Carrier is one of the special molecule or system essentially required for effective transportation of loaded drug up to the pre-selected sites. These are engineered vectors which retain drug inside or onto them either via encapsulation and/ or via spacer moiety and transport or deliver it into vicinity of target cell[8,6,7].

Drug Delivery Vehicles

Drug delivery vehicles are also referred as drug vectors which are most important entity required for successful transportation of the loaded drug. Drug vectors transports and retains the drug to be delivered it within target. They are made capable of performing such specific functions which can be attributed by slight structural modification[9,7,4].

Characteristics of an ideal drug vehicle

An ideal drug vehicle should be able to cross blood brain barriers and in case of tumour chemotherapy tumour vasculature. It must be recognized by the target cells specifically and selectively and must maintain the specificity of the surface ligands. The drug ligand complex should be stable in plasma, interstitial and other bio-fluids. The drug vehicle used should be non-toxic, non- immunogenic and biodegradable. After recognition, the carrier system should release the drug moiety inside the target organs, tissues or cells. Targeting Moieties includes antibodies, lectins and other proteins, Lipoproteins, Hormones, Charged molecules, Polysaccharides and Low molecular- weight ligands[9-11,4].

Liposomes

Liposomes are small artificially designed vesicles composed of phospholipid bilayers surrounding with the size ranging from 20 to 10,000nm. Many liposome formulations are rapidly taken up through macrophages and this could be exploited either for macrophage-specific transport of medicine or for passive drug focused on which allow sluggish release of the drug over time from those cells into the overall move. Cationic liposomes and lipoplexes have been considerably researched for non-viral vector mediated gene therapy[12].

Monoclonal antibodies and fragments

Most techniques based on antigen detection by antibodies are developed primarily to treat cancer. These strategies are usually aimed at the presence of tumor-related antigens on the body or in the specific term expressed by tumor cells. Antibody-drug conjugates (ADC) is a complex drug containing a monoclonal antibody that provides specialized identification of large numbers of cells or lymphomas. The drug is released by linker enzymatic cleavage under physiological conditions. An example of Antibody-drug conjugates (ADC) is Mylotarg (emtuzamabozogamicin) which was approved by the US Food and Drug Administration (FDA), but was later voluntarily withdrawn from the US market[3]. Conjugates are currently being investigated in clinical trials[13].

Modified protein (plasma)

Modified plasma proteins can be a smart drug transport vehicle due to its melting and small molecular weight. They can be easily altered by attaching different molecules such as peptides, sugars and other ligands to transport the desired drugs making them an ideal route for drug delivery. In the case of liver cell regulation, extensive reversal of protein backbones such as albumin has resulted in the successful delivery of the drug[14].

Soluble synthetic polymers have been extensively studied as flexible drug delivery systems. The polymer chemistry allows for the development of tailor-made conjugates where targeted components and drugs can be trapped in a company molecule. For cancer treatment, N (-2- hydroxypropyl) well-developed methacrylamide (HMPA) polymers have has been extensively studied. It also provides a solution for selected and targeted chemotherapy[5].

Microspheres and nanoparticles

Microspheres and nanoparticles contain compatible polymers and are not soluble or soluble. Carriers of the HPMA polymeric backbone are also prepared

using dextrans, ficoll, sepharose or poly-L-lysine as the main carrier body of the drug. Nanoparticles are smaller (0.2- 0.5μm) than microspheres (30-200μm) and may have a lower drug load than soluble polymers. Drug formation in nanoparticles can occur over particles and in the nucleus, depending on the physicochemical properties of the drug. The drug injection site significantly affects the rate of release from the particles. After systematic management or migration they quickly spread to the target web site and eventually were simply embedded through phagocytic machine cells. externally, microspheres and nanoparticles commonly used in selective drug delivery of cells, have found many of these days studied for their use in oral delivery of peptides and peptidomimetics[15,16,10,17].

Lipoproteins

Lipid particles such as LDL and HDL containing lipid and apoprotein moiety are called natural targeted liposomes and their core can be used to combine lipophilic or lipophilic pro-drugs and does not require a strong bond with the drug. Adjustments to the level of glycolipid insertion can be used to introduce new target components. Most studies on the use of LDL and HDL particles have been performed and improved at the drug-targeting level[18].

Transdermal approach to drug transport

The Transdermal drug delivery system is systematically controlled by drugs in the form of leaflets delivering systemic drugs at a fixed and controlled rate. A transdermal drug delivery device or vehicle may be of functional or non-functional structure and is a device that provides an alternative to controlling an interested drug locally and delivering the drug to the entire skin barrier as well.

Albumin Microspheres modification

Several methods for the production of albumin microspheres have been reported. Many methods include emulsion technology and suspension. The common formulation of these particles uses an aqueous solution of protein, a therapeutic agent in its solubility of fats and vegetable oils suitable to form a w/o emulsion. The emulsion should be solidified after transfer to an oil tank to solidify and subsequently separate the protein particles. They can also be repaired using interfacial polymerization method.

Two methods of stabilizing albumin microspheres will be used:

Temperature fluctuations at a temperature of between 100 and 180C for 2.5 minutes to 24 hours and Chemical reactions using a suitable binding agent, such as formaldehyde, gluteraldehyde, 2, 3-butanedione or tere-epthaloyl dichloride.

Drug Entrapment

Inclusion of a healing agent within albumin microspheres may be attained with the aid of two techniques:

Drug addition inside the aqueous section before emulsification with the oil section and drug addition and equilibration with a suspension of preformed placebo albumin microspheres.

Albumin microspheres launch the entrapped pills constantly, consequently can perform better than different vendors *in-vivo* as they want now not to be phagocytosized or destroyed to release the drug. Focused on the drug to precise organ is to peer that whether or not after focused on the drug, actual preferred quantum of drug recovered from targeted web page. The Estimation of drug shall be accomplished the use of UV spectrophotometer.

Magnetic Microspheres

They are biodegradable microspheres ranging in size from 1-4um containing ultrafine magnetic particles "magnetite (Fe3O4}", the drug and the biodegradable coating materials e.g., albumin. The reaction takes place for Magnetite preparation is as following:

FeSO4 + 2NaOH □ Fe(OH2) + Na2SO4; Fe(OH2) + O□Fe3O4+ 3H2O

Localization of the drug and magnetite bearing microspheres at the desired site can be achieved by the application of an external magnetic field of appropriate strength. Magnetite can be easily introduced into microspheres physically without altering the chemical and physical properties of the polymer. Amount of magnetite which can be

incorporated is 20-50% of the drug weight of drug-carrier complex.

The rationale for selecting magnetite size in albumin microspheres is that it should permit microspheres of size range 1-4um to render capillary level distribution and perfusion of the target. It should be biodegradable, non-toxic and non-immunogenic. It should have magnetic responsiveness to technically achievable external local fields and gradient flow rates found in physiologic system.

Drug Profile of Naproxen

Naproxen is an NSAID used to treat rheumatoid arthritis, osteoarthritis, ankylosing spondylitis, polyarticular juvenile idiopathic arthritis, tendinitis, bursitis, acute gout, primary dysmenorrhea, and mild to moderate pain. It can effectively manage the acute and chronic pain associated with rheumatic diseases and has a negatively studied positive profile. Given its tolerance and efficacy, naproxen can be considered a first-line treatment in a variety of clinical conditions that require analgesia. Naproxen is available in both "fast and delayed release formulations".

Mechanism of action

Like other non-NSAIDs, naproxen exerts its clinical effects by inhibiting the COX-1 and COX-2 enzymes leading to a decrease in prostaglandin synthesis. The enzyme COX-2 mediates the desired antipyretic, analgesic and anti-inflammatory properties provided by Naproxen.

Protein binding

Naproxen is highly binding to protein and> 99% of the drug bound to albumin at therapeutic levels.

Half life

The half-life of naproxen is reported to be 12-17 hours. Naproxen has emerged as one of the first options as it combines efficiency with low incidence of adverse effects, but these side effects can be minimized by making the organ clear.

It was therefore thought to create both 'non-magnetic' and 'non-magnetic' microspheres in naproxen using bovine serum albumin containing anti-inflammatory properties. This will reduce the dose required to achieve the desired therapeutic effect and the hen directing the drug to a particular organ to see that even after identifying the drug, the actual desired amount of drug is returned to the target. The dose will be performed using a UV spectrophotometer.

CONCLUSION

Delivering the drug molecule to its original location is a daunting task in a complex cellular network. Finally, targeted drug delivery is coming as one of the most advanced methods in medical science for the diagnosis and treatment of a few deadly diseases. Childhood has passed and now affects the height of growth in research and development in the medical and pharmaceutical fields. Overall, it can be concluded with a large database of various disciplines, local science or targeted drug delivery wise and intelligent over time and advances in scientific technology. The demonstration of all these techniques and advanced technologies in the medical field leads to a new era of treatment and diagnosis in the future. Many of the problems that arose during the development of clinical identification techniques used in various forms of treatment have been identified. However, such strategies should be evaluated regularly in light of the progress in understanding the many processes that take place in response to the handling of carriers or vehicles with interesting drug-specific information in addition[19,11].

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CONFLICT OF INTEREST

We declare that we have no conflict of interest.

REFERENCES

1. Muller R H, Keck C M. Challenges and solutions for the delivery of biotech drugs-a review of drug nanocrystal technology and lipid nanoparticles, *Journal of Biotechnology,* 113(1-3), 2004, 151-170.
2. Allen T M, Cullis P R. Drug delivery systems: Entering the mainstream, *Science,* 303(5665), 2004, 1818-1822.
3. Mark S W, Torchilin, Vladimir P. Drug delivery systems, *Access Science, McGraw Hill Companies,* 1st Edition, 2011.
4. Vyas S P, Khar R K. Basis of targeted drug delivery, in targeted and controlled drug delivery, *CBS Publishers and Distributors Reprint,* 74, 2008, 42-46.
5. Mastrobattista E, Koning G A, Storm G. Immunoliposomes for the targeted delivery of antitumor drugs, *Advance Drug Delivery Reviews,* 40(1-2), 1999, 103-127.
6. Gref R, Minamitake Y, Peracchia M T, Trubetskoy V, Torchilin V, Langer R. Biodegradable long-circulating polymeric nanospheres, *Science,* 263(5153), 1994, 1600-1603.
7. Gref R, Minamitake Y, Peracchia M T, Trubetskoy V, Torchilin V, Langer R. Biodegradable long-circulating polymeric nanospheres, *Science,* 263(5153), 1994, 1600-1603.
8. Florence A T. Drug delivery: Advances and commercial opportunities, *Connect Pharma, Oxford,* 1994.
9. Grietje Molema and Dirk K F. Meijer. Duncan R. Drug targeting: Organ-specific strategies, *Angewandte Chemie,* International Edition, 41, 2002, 124.
10. Kohler G, Milstein C. Continuous cultures of fused cells secreting antibody of predefined specificity, *Nat,* 256(5517), 1975, 495-497.
11. Gujral S S, Khatri S. A review on basic concept of drug targeting and drug carrier system, *International Journal of Advances in Pharmacy, Biology and Chemistry,* 2(1), 2013, 134-136.
12. Torchilin V P. Multifunctional nanocarriers, *Advance Drug Delivery Reviews,* 58(14), 2006, 1532-1555.
13. Jain S, Jain N K. Engineered erythrocytes as a drug delivery system, *Indian Journal of Pharmaceutical Sciences,* 59(6), 1997, 275-281.
14. Breimer D D. Future challenges for drug delivery research, *Advance Drug Delivery Reviews,* 33(3), 1998, 265-268.
15. Farah R A, Clinchy B, Herrera L, Vitetta E S. The development of monoclonal antibodies for the therapy of cancer, *Critical Reviews in Eukaryotic Gene Expression,* 8(3-4), 1998, 321-356.
16. Kim G J, Nie S. Targeted cancer nanotherapy, *Materials Today,* 8(8), 2005, 28-33.
17. Storm G, Crommelin D J A. Liposomes: Quo vadis? *Pharmaceutical Science Technology Today,* 1(1), 1998, 19-31.
18. Duzgunes N, Nir S. Mechanisms and kinetics of liposome-cell interactions, *Advance Drug Delivery Reviews,* 40(1-2), 1999, 3-18.
19. Agnihotri J, Saraf S, Khale A. Targeting: New potential carriers for targetted drug delivery system, *International Journal of Pharmaceutical Sciences Review and Research,* 8(2), 2011, 120-123.
20. Gupta M, Sharma V. Targeted drug delivery system: A review, *Research Journal of Chemical Sciences,* 1(2), 2011, 134-138.

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