

A REVIEW ON NOVEL DRUG DELIVERY SYSTEM

Vaibhav A. Borase*, Rahul S.Kapadnis**,Ashok Y. Chaudhari¹,Dr. Rishikesh S. Bachhav^{1*}

*Department of Pharmaceutical Quality Assurance. R.G.Sapkal College of Pharmacy,Anjaneri, Nashik -422213, Maharashtra, India.

**Department of Pharmaceutical Quality Assurance. R.G.Sapkal College of Pharmacy,Anjaneri, Nashik -422213, Maharashtra, India.

¹Department of Pharmaceutics. Loknete DR.J.D.Pawar College of Pharmacy,Manur,Nashik-423501,Maharashtra ,India

^{1*}Department of Pharmacology. R.G.Sapkal College of Pharmacy, Anjaneri, Nashik -422213, Maharashtra, India.

In Recent times, understanding of pharmacokinetic & pharmacodynamic behaviour of the drug have offer a more rational approach to the development of optimal drug delivery system. Now it's appreciable that in the future success in Drug delivery research will largely to be the result of multidisplinary efforts. If any therapeutic agent that can be the more effective and safe using and improved drug delivery system represent both good marketing opportunities for pharmaceutical company and advancement in the treatment of Many diseases of human being. An ideally design of the drug delivery system delivers a specified amount of drug to the target at the particular site at an appropriate time and rate is reached or desired by the physiological needs of the body. Conventional Pharmaceutical Dosage forms are incapable of controlling the rate of drug delivery towards the target site. As a result the distribution of drug in non-target tissue and body fluids necessitate therapeutic doses that could far exceed the amount required in target cells, the higher doses often lead to serious adverse reaction during treatment thus, the novel drug delivery systems (NDDS) are such carriers which maintain the drug concentration in therapeutic range for longer period of time and also, in addition may deliver the required amount to the specific site of action as per requirements.

KEYWORDS: Drug delivery systems, Bioavailabilty, therapeutic agent, diseases, Specific target sites, body fluids, non- targeting tissues, drug etc.

INTRODUCTION

A Novel drug delivery systems is the new system advances in the understanding of Pharmacokinetic & Pharmacodynamic behaviour of the drug which offer a more rational approach to the development of optimal drug delivery system. The novel drug delivery system (NDDS) are carriers which maintain the drug concentration in

therapeutic ranges for longer time There are several advantages of novel drug delivery systems over conventional drug delivery,as follows

1. Optimum therapeutic- drug concentration in the blood system or in a tissue may be maintained over a prolonged period of time.
2. Pre- determined rate of the drug which helps to extend drug action.
3. Short half- life drug may be increased.
4. By targeting the site of action, side effects may be decreased.
5. Frequent dosing and wastage of the drug may be reduced.
6. Better patient compliance.

Novel drug delivery systems

There are Various drug delivery systems have been developed and some of them under development with an aim to minimize drug loss, to prevent from harmful side effects and to increased drug bioavailability and also to favour and facilitate the accumulation of the drug in the required bio- zone (site). There are number Of Novel carries which have been established and documented to be useful for controlled and Sustained drug delivery. It is important to evaluate different terms used under the different broad categories of Novel drug delivery system.

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

Table 1.0 Classification of sustained or controlled release system based on their rate – controlled mechanism.

Type of System	Rate control Mechanism
Diffusion – controlled	
Reservoir systems (Ocusert)	Diffusion through membrane
Monolithic systems (Transdermal drug) Delivery system- Nitro -dur)	Diffusion through membrane
Water penetration controlled	
Osmotic systems (Oros, Alzet osmotic pump)	Osmotic transport of water through semi-permeable membrane
Swelling system(hydrogel)	Water penetration into glassy polymer
Chemically - controlled	
Pendent systems	Combination of hydrolysis of pendent group diffusion from bulk polymer
Ion – exchange resins	Exchange of acidic or basic drug with the ions present on resins

Carrier system for the targeted and sustained drug delivery purpose may be classified on the basis of their nature, mechanism of drug release and nature of the drug (Table 1.0). Diffusion occurs when bioactive agent is hydrophilic(water loving) and passes through the polymer, the key building block and controlled release concept. Many environmentally – responsive system are also designed that retains their content until appropriately placed in biological by an environment and are activated by an external or internal stimulus for the release of drug. Show the mechanism of drug release from various drug – delivery systems.

Reservoir- Type drug delivery system

In the reservoir- type drug delivery systems, drug is encapsulated in the drug reservoir compartment those drug – releasing surface is covered by a rate- controlling an embryonic polymer membrane.

The drug in the reservoir compartments can be drug in liquid or solid type dispersion of drug in a liquid or solid type dispersion medium. The polymeric membrane can be fabricated from a homogeneous or heterogeneous non – porous polymeric material or semi- permeable membrane. The release of drug from this type of delivery system obtained at a nearly constant rate (Q/t).

Ocusert

A truly continuous, controlled- release and zero – order kinetic release was achieved using ocusert. First marketed by Alza Corporation, California, the pilocarpine ocusert improved the non compliance problems, low intra -ocular drug bioavailability and potential systemic side effect of pilocarpine. The systems consist of a pilocarpine-alginate core of (drug) sandwiched between two transparent rate – controlling ethylene- vinyl acetate co- polymerbased thin membrane. When this is placed under the upper eyelid, The pilocarpine molecules after getting dissolved in the lachrymal fluid are released through the rate controlling membranes at a pre determine rate.

A mixture of pilocarpine and alginic acid in the drug reservoir releases the drug for up to one week. A thin membrane of ethylene vinyl acetate (EVA) co polymer encloses the reservoir above and below. A restraining ring of the same material impregnated with titanium dioxide encloses the drug reservoir circumferentially (fig.1.1).

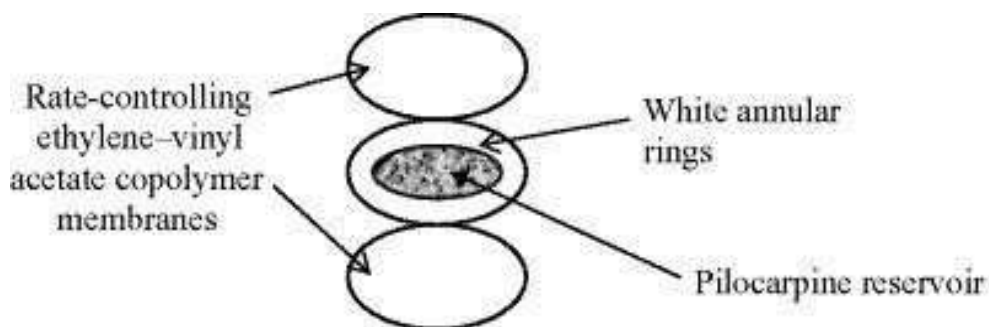


Fig 1.1: Schematic representation of ocusert.

NOVEL CARRIER FOR CONTROLLED & TARGETED DRUG DELIVERY

As per the knowledge of the molecular nature and pathophysiology of diseases has expanded, more therapeutically accurate and purpose specific drug are being developed. These newly prepared drug have high potency (low

therapeutic window) and required their localization of the particular site of their action. Most of the drugs are administered by conventional immediate-release dosage forms. They distributed freely throughout the systemic circulation & accumulate the non-specific organs in an undesirable manner and hence produce adverse side effects. To reduce these slides and enhance their therapeutic benefits, they should be delivered to their respective site of action, and thus suitable carrier systems becomes mandatory requirement. Various novel carriers have been developed for the purpose Among these colloidal carriers such as liposomes, nano-particles & supra molecular system, i.e. micelles have gained more effect in the field of controlled and targeted drug delivery. Recently new carriers such as the inorganic particles, liquids crystal, aquasomes, carbon nano tubes, dendrimers etc. Are also investigated for the specialized purpose. In the following section, these carriers for the same purpose are brief.

Colloidal carrier

Liposomes

Liposomes were discovered in the early 1960s by Bingham and co-workers and subsequently became the most extensive-explored drug-delivery system. Initially, through they used to study in vitro simulated – biomembrane behaviour, subsequently, they engaged as strong therapeutic tools most notably in drug delivery and drug targeting.

Structurally, liposomes are phospholipid-based colloidal vesicular structures in which hydrophilic core is entirely enclosed by membranous lipid bilayer's. They may be classified on the basis of method of preparation, structural parameters or special function.

Nanosomes

Non-ionic surfactants vesicles (niosomes) or NSVS) are now widely studied as an alter native to liposomes. Non-ionic surfactants vesicles results from the self-assembly of hydrated surfactants monomers. Non-ionic surfactants of vast variety of structural types have been found to be useful alternatives to phospholipids. Through the terminology suggests that distinctions exist between niosomes and liposomes of which the former is having chemical differences in the monomers units, niosomes posses physical properties, which are similar to liposomes, which are formed from phospholipids. As the name indicated, generally non-ionic surfactants vesicles are prepared by the incorporation of components containing non-ionic surfactants. However, they may also prepared with various ionic amphiphiles such as dicetylphosphate, stearylamine, etc. In order to acheived stable vasicular suspension. It is important to identify and know the basic structural units of NSVs. while an amphiphilic head groups. The vesicles forming non-ionic compounds are mainly alkyl ether lipids. These can be broadly divided into two major classes based on nature of their hydrophilic head groups, i.e. Alkyl ethers in which the hydrophilic head group consists of repeat glycerol subunits, related isomers or larger sugar molecules, and those in which the hydrophilic head group consists of repeat ethylene oxide subunits. In addition, alkyl esters, amides and fatty acids, and amino acids compounds also from vesicles.

The ultimate identity of any niosomal system and hence its properties are determined by the factors listed in Fig. 1.2. It is thus obvious that all these variables must be carefully controlled in the design of a niosomal drug-delivery system.

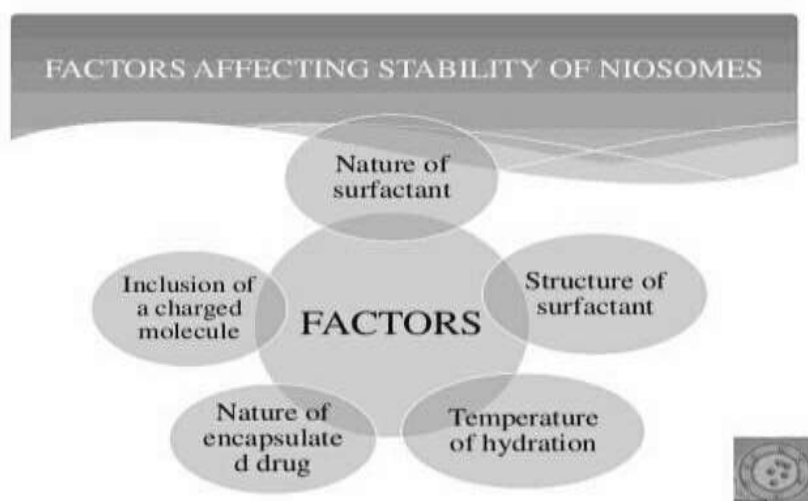


Fig. 1.2: factors Influencing Physical stability of niosomes .

Although pharmaceutical niosomes formulations have yet to be commercially exploited, a number of studies have demonstrated the potential of niosomes in drug delivery. Niosomes have been proved to be useful in the delivery Of anti-infective agents, anti- cancer agents, anti-inflammatory agents, and fairly recently, as a vaccine adjuvants. These systems have been proven to target certain areas of the mammalian anatomy and may be exploited as a diagnostic imaging agents.

Examination of the literature reveals that on IV administration of niosomes, the highest drug level are found in the liver. However, there were exceptions. When DOX 850 nm C16G3 niosomes were administrated, DOX liver levels are initially low (~0.5% of administrated dose 10 nm after dosing) in case solution administration, they are higher for niosome formulation. The cause of this non-liver uptake is not apparent although smaller DOX niosomes are found to accumulate in the liver following IV administration.

Microparticles

The” microcapsules “are as a spherical particles with size varying from 50 nm to 2µm, containing a core substance. Microspheres are, in real sense, spherical empty particles. However, the term microcapsules & microspheres are often used interchangeably. In addition some related terms are used as well for example, “microbeads” & “beads” are used alternatively. Sphere and spherical particles are also used for particles of large size & rigid morphology. The dried microspheres from free flowing powders .they consist of proteins or synthetic polymers, which bio degradable & ideally have a size range less than 200 µm. The solid bio degradable microspheres bearing a drug dispersed or dissolved throughout particles matrix have potential in controlled- release of drugs.

These carriers received much more attention not only prolonged- release formulations but an also for the carrier potential in drug targeting particularly anti- cancer drugs the tumour.

Pre-requisites for ideal micro particulate carriers are follows.

- Longer duration of action
- control in drug release
- Increased of therapeutic effect
- Protection of drug

- Biocompatibility
- Relative stability
- water -solubility or Dispensability
- Bioresorbability
- Targetability
- Polyvalency

Microspheres can be prepared by using appropriately selected method including in situ polymerization, solvent evaporation, coacervation phase separation, spray drying and spray congealing, etc., but the choice of techniques depends on the nature of the polymer used, the drug, the intended use and duration of therapy. The choice of method is depend on the following Determinants.

1. The particles size requirements.
2. The drug or the protein should not be adversely affected by the process.
3. Reproducibility of the release profile and the method.
4. No any stability Problem.
5. There should be non toxic product associated with the final product.

A number of different substances both biodegradable as well as non- biodegradable have been investigated during preparation of microspheres.

These materials include the polymer of natural synthetic origin and also modified natural substances. Synthetic polymers employed as carriers materials are methyl methacrylate, acrolein, lactide, Glycolide and their co-polymers, ethylene vinyl acetate copolymer, polyanhydrides etc.

The natural polymers used for the purpose include albumin gelatin, starch, collagen & carrageenan, etc.

APPLICATIONS OF NOVEL DRUG DELIVERY SYSTEMS

Sustained and controlled- drug delivery

Controlled release of drug or encapsulated bioactives should be achieved using NDDS. Desired release pattern will definitely improve the pharmacokinetics effect and pharmacodynamics of drug. The controlled delivery of antibiotics in the treatment of H. Pylori via NDDS is an effective process compared to conventional one. Similarly, slow and sustained release of drug from implants avoids regular administration of drug hence ensures patients compliance. Numerous applications of NDDS is sustained and controlled delivery of drug are enumerated. Some of them have already been discussed in preceeding sections.

Deport formulations of short -acting peptides have been successfully developed using microparticle technology. Such peptides include leuprorelin acetate and triptoreline, Both lutenizing hormone releasing hormone agonist. Leuprorelin polylactided acid co-glycolide microspheres may be used as a monthly and three monthly dosage forms in the treatment of advancement prostrate cancer, endometriosis and other hormone responsive conditions. These microspheres effectively halt the progression of prostate cancer or endometeriosis in patients and currently marketed as prostap SR.

Other peptides formulated as sustained release microparticles include the angiotensin receptors- antagonist, L - 158809, for the treatment of hypertension, thyrotropin releasing hormone for central nervous system stimulation, salmon calcitonin for the treatment of hypercalcemia or postmenopausal osteoporosis and the immunosuppressant drug cyclosporin A. There are no. Of products available in the market for clinical studies as listed in Table 1.1.

Table 1.1: list of various marketed formulations based on novel drug delivery systems.

DRUG	INDICATION	COMPANY NAME
Dexorubicin	Kaposi's sarcoma	SEQUUs
Daunorubicin	Advanced kaposi's sarcoma	NeXstar
Amphotericin B	Systemic fungal infection	NeXstar
Amphotericin B	Systemic fungal infection	SEQUUS
Leuprolide acetate	Prostate cancer	Takeda-Abott
Triptorelin	LHRH agonist	Novartis

CONCLUSION

Novel Drug delivery System (NDDS) is a combination of advance techniques and newly designed dosage forms which are much more better than conventional dosage forms. Advantages of Novel Drug Delivery System are Optimum dose at the right time and right location, Efficient use of expensive drugs, excipients and reduction in production cost, Beneficial to patients, better therapy, improved comfort and standard of living. Basic modes of novel drug delivery systems are: Targeted Drug Delivery System, Controlled Drug Delivery System etc.

Novel Drug delivery & drug targeting is new techniques which is used in pharmaceutical science. Like targeting drug molecules, vaccine delivery, Gene therapy, commercial development of novel carriers (liposomes).

Future prospects

Targeting drug delivery is the major focus on current research. After the concept of magic bullet, only a few targeted formulations could reach to the market. The discovery of area of molecular biology, biotechnology & pharmacogenomics regularly demand the practical key issues of targeting of biomolecules to the center of attention. Like Tumour targeted drug/ gene delivery is the most demanded therapeutic requirements of the Future prospective.

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