ABSTRACT

Now day’s Recent advances in the understanding of pharmacokinetic & pharmacodynamic behaviour of drug have offer a more rational approach to the development of optimal drug delivery system. Now it's appreciable that future success in Drug delivery research will largely be result of multidisiplinary efforts. If any therapeutic agent that can be the more efficacious and safe using and improved drug delivery system represent both lucrative marketing opportunities for pharmaceutical company and advancement in the treatment of diseases of mindkind. An ideally design drug delivery system delivers a specified amount of drug to target particular site at an appropriate time and rate as dictated or desired by the etiological and physiological needs of the body. Conventional Pharmaceutical Dosage forms are incapable of controlling the rate of drug delivery to 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 during treatment thus, the novel drug delivery systems (NDDS) are carriers which maintain the drug concentration in therapeutic range for longer period of time and also, in addition, may deliver the content to the site of action if so desired as per requirements.

KEYWORDS: drug delivery systems, therapeutic agent, diseases, target site, body fluids, non- targeting tissues, drug etc.

INTRODUCTION

Novel drug delivery systems is the new system Recent advances in the understanding of pharmacokinetic & pharmacodynamic behaviour of drug have offer a more rational approach.
to the development of optimal drug delivery system, the novel drug delivery systems (NDDS) are carriers which maintain the drug concentration in therapeutic range for longer period of time. There are several advantages of novel drug delivery systems over conventional drug delivery.

1. Optimum therapeutic-drug concentration in the blood or in tissue may be maintained over a prolonged period of time.
2. Pre-determined release rates of extended period of time may be achieved.
3. Duration for short half-life drug may be increased.
4. By targeting the site of action, side effects may be eliminated.
5. Frequent dosing and wastage of the drug may be reduced or excluded.
6. Better patient compliance may be ensured.

**Novel drug delivery systems**

Various drug delivery systems have been developed and some of them under development with an aim to minimize drug degradation or loss, to prevent harmful side effects and to improve drug bioavailability and also to favour and facilitate the accumulation of the drug in the required bio-zone (site). There are no. Of novel carries which have been established and documented to be useful for controlled and targeted drug delivery. It is important to critically evaluate different terms used under the different broad categories of novel drug delivery system.

- Sustained- or controlled- drug delivery systems provide 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 spatial or temporal control of drug release (usually rate-limiting) in the vicinity of the target.
- Rate- pre-programmed drug delivery systems provide drug action by manipulating the release of drug molecules by system design which control the molecular diffusion of drug molecules.
- Targeted drug delivery provides drug action by using carries either for passive or active targeting or one base or self programmed approach, usually anchored with suitable sensory devices, which recognize their receptor at the target.
Table 1.0 Classification of sustained or controlled release system based on their rate – controlled mechanism.

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

**Fig 1.0:** Schematic depiction of various classes of controlled release system.

Carrier system for the targeted and controlled drug delivery purpose may be classified on the basis of their nature, mechanism of drug release and nature drug incorporation. (Table 1.0 and Fig. 1.0) Diffusion occur when bioactive agent is hydrophilic 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 whose 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 occurs at a nearly constant rate (Q/ t).

**Ocusert**

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

A mixture of pilocarpine and alginic acid in the drug reservoir releases the drug for almost one week. A thin membrane of ethylene venyl acetate (EVA) co polymer encloses the reservoir above and below. A retraining ring of the same material impregnated with titanium dioxide encloses the drug reservoir circumferentially (fig.1.1).
NOVEL CARRIER FOR CONTROLLED & TARGETED DRUG DELIVERY

As the knowledge of the molecular biology and pathophysiology of diseases has expanded, more therapeutically precised and purpose specific drug are being developed. These newly developed drug have high potency (low therapeutic window) and required their localization of the particular site of their action. Most drugs are administrated by conventional immediate-release dosage forms. They distribute freely throughout the body & accumulate the non – specific organs in an undesirable manner and thus produce adverse side effects. To reduce these slides and increased their therapeutic benefits, they should be delivered to their respective site of action, and hence 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 attention in the field of controlled and targeted drug delivery. Recently new carriers such as 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 were used to study in vitro simulated – biomembrane behaviour, subsequently, they enraged 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 alternative to liposomes. Non-ionic surfactants vesicles results from the self-assembly of hydrated surfactants monomers. Non-ionic surfactants of wide 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 achieve a stable vesicular 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 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 form 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 niosomes physical stability.
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 proven 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 although low (~0.5% of administrated dose 10 nm after dosing) in case solution administration, they are higher for noisome 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 defined as a spherical particles with size varying from 50 nm to 2nm, 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 dispensed or dissolved throughout particles matrix have potential in controlled- release of drugs.

These carriers received much attention not only prolonged- release formulations but 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 of drug release
- Increase of therapeutic efficiency
- Protection of drug
- Biocompatibility
- Relative stability
- Water-solubility or Dispensability
Microspheres can be prepared by using any of 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 stability Problem.
5. There should be no toxic product associated with the final product.

A number of different substances both biodegradable as well as non- biodegradable have been investigated for the 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 could be achieved using NDDS. Desired release pattern will definitely improve the pharmacokinetics and hence pharmacodynamics of drug. The controlled delivery of antibiotics in the treatmment 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 leuprolelin acetate and triptoreline. Both lutening hormone releasing hormone agonist. Leuprolelin 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 endometriosis in patients and are currently marketed as prostat 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 immunsuppressant 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.

<table>
<thead>
<tr>
<th>DRUG</th>
<th>INDICATION</th>
<th>COMPANY NAME</th>
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<tbody>
<tr>
<td>Dxorubicin</td>
<td>Kaposi’s sarcoma</td>
<td>SEQUUs</td>
</tr>
<tr>
<td>Daunorubicin</td>
<td>Advanced kaposi sarcoma</td>
<td>NeXstar</td>
</tr>
<tr>
<td>Amphotericin B</td>
<td>Systemic fungal infection</td>
<td>NeXstar</td>
</tr>
<tr>
<td>Amphotericin B</td>
<td>Systemic fungal infection</td>
<td>SEQUUS</td>
</tr>
<tr>
<td>Leuprolide acetate</td>
<td>Prostate cancer</td>
<td>Takeda-Abott</td>
</tr>
<tr>
<td>Triprolin</td>
<td>LHRH agonist</td>
<td>Novartis</td>
</tr>
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</table>

CONCLUSION

Novel Drug delivery System (NDDS) NDDS is a combination of advance technique and new dosage forms which are far 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 delivery, vaccine delivery, Gene therapy, commercial development of novel carries (liposomes).
Future prospects

Targeting drug delivery is the major focus of current research. After the concept of magic bullet, only a few targeted formulations could reach to 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 coming Future.

REFERENCE


30. Chan WCW: In: Bio-Applications of Nanoparticles. 2007, Landes Bioscience, Austin, TX, USA.