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# A Modern Era Prospective of Novel Drug Delivery System

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**ABSTRACT**
Novel Drug delivery system is an approach to formulate technologies and system for transporting a pharmaceutical compound into the body to achieve its desired therapeutic effect. In the recent times conventional dosage form were used frequently. But novel drug delivery is an advance technique that has replaced conventional dosage form increasingly. It has proved itself in showing better patient compliance, safety and efficacy. The main aim for developing such delivery system is to minimize drug degradation and loss to prevent harmful side effects and to increase bioavailability. Based on the physical and biochemical mechanism, novel drug delivery is designed. The present review gives information regarding various novel techniques to target therapeutic efficacy. Targeting can be achieved by delivering drug to the site of interest via drug carriers. Drug carriers are formed of soluble polymers and the micro particles are made of insoluble or biodegradable natural or synthetic polymers, nanoparticles, liposomes. Hence, Novel Drug Delivery will help to overcome various issues.

KEYWORDS: Novel Drug Delivery System, Drug targeting delivery system, liposome, Nanoparticles, Noisome, Hydrogels.

## 1. INTRODUCTION: -

### 1.1 Novel drug delivery system:

Novel drug delivery system has opened a new gate for the researchers in the field of science where materials in Nano scale range are employed to serve as a diagnostic tool to deliver drug or agents to specific target sites in a controlled manner. Novel drug delivery has not only helped to suppress conventional dosage form but also rebuilt new strategies to overcome its toxicity and side effects caused by it. Novel Drug Delivery Systems has captured interest in both national and international pharmaceutical research organization. It is an expression associated to enhance the performance of bio therapeutic agents when compared to conventional dosage form.

The ever-improving deliverysystem is not only beneficial to the patient but also reduce complication association with the induction of drug in the body. Recurrently, the pharmaceutical drug delivery system consists of: -

1. A suitable dosage forms.
2. The release mechanism of drug from the dosage form to the organ /cells of targeting after administration.
3. An optimum pharmaceutical technique used for manufacturing the dosageform.

The substitution of this system could be replaced and obtained by NDDS via: -

1. Formulation of smart Nano carrier based drug delivery systems to improve the cell selectivity for enhanced targeting.
2. Extended release of drug delivery systems.
3. Utilization of novel techniques of manufacturing.

Added large size materials used in conventional dosage drug possess major challenges including instability, in vivo instability, poor bioavailability, and poor solubility, poor absorption in the body, issues with target-specific delivery, and tonic effectiveness. Therefore, using new delivery system might solve the problems for critical issues. Hence nano-materials play an important role for drug formulation, targeting arena and controlled drug release[1,2].

Nano-materials can be defined as the particles ranging between 1 to 100nm which means it employs curative agents at Nano scale level to develop Nano medicine. Nano-materials are designed at molecular or atomic level i.e.,Nano sphere. Hence, they can freely move in the body as compared to large particles[3]. These nanostructures stay in blood for longer period of time in the body and enable release of Amal gated drug as per the specific dose and thus they cause few plasmas fluctuation and reduce side effects [4].

The use of the nano-materials is based on the physiochemical properties of the drug. There is an essential relation between the nanoscience and bioactive natural compounds. It presents several advantages for delivery of natural products for the treatment of cancer, inducing cancer suppressant or acting as antimicrobial agent [5].These properties have been shown in curcumin and caffeine whereas for antimicrobial agents are shown in cinnamaldehyde, carvacrol, curcumin and eugenol [6][7].

Thus, nanotechnology offers numerous benefits in treating chronic human disease by site specific and target-oriented delivery system. Considering the above facts, the review aims to report different Nano-based delivery system.

### 1.2 SmartNano-carrier based drug delivery systems: -

A carrier-based drug delivery system is defined as the drug molecules that are loaded into vesicles or polymeric systems. Some of the same are nanoparticles, liposomes, dendrimers, and polymeric micelles[8]. The main goal for designing a successful pharmaceutical product is to design a Nano system with optimum characteristic such as higher drug loading capacity, smaller particle size and controllable release profile[9].

The term ‘SMART’ means that the Nano carrier drug delivery system can release the drug in response to physiological stimuli thereby targeting it to the diseased cell/tissue with an extended or controllable manner[10]. After the administration of the Nano system, there are three possible ways delivery mechanism that might occur:

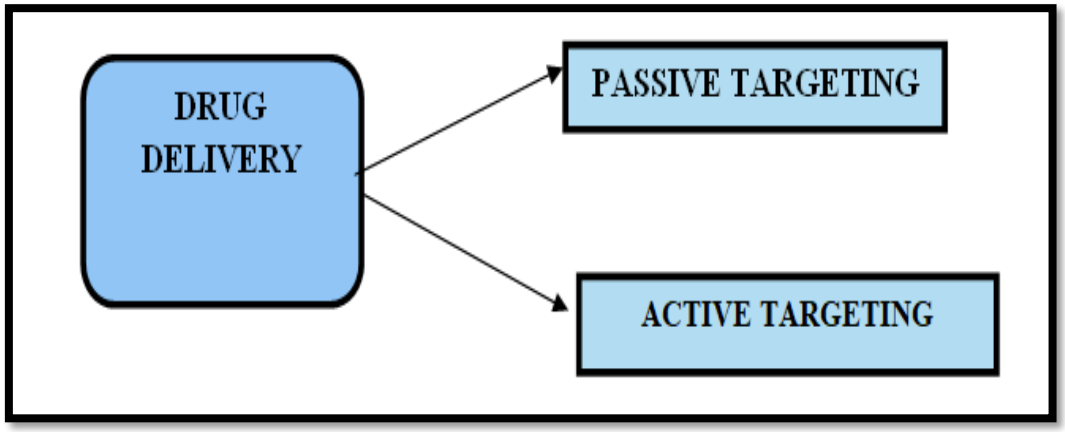


FIG 1.1: TYPES OF DRUG TARGETING

**1.2.1 Mechanism of Nano carrier transport throughout the systemic circulation reaching the specific target**

**1.2.1.1 Passive Targeting: -**

Passive targeting is the primary pathway for a colloidal Nano system through enhanced permeability and retention (EPR) effect. It has beenthoroughly studied and these studies show that EPR effect highly depends on the degree of vascularity and efficiency of lymphatic damage at the site of targeting. Thus, increase in leakage of blood vessels and inefficient lymphatic drainage might enhance the EPR effect and achieve accumulation of Nano carrier in targeted tissues[11] .These marks to maximize the delivery of the non-colloidal system to cancer or tumour tissues due to enhanced vascular permeability when compared to healthy tissues [12].

These outcomes into a limitation of drug transport via passive diffusion or convection in the lack of site selectivity which may lead to several side effects and drug resistance [13].This can be overcome by formulating a colloidal Nano system that can be actively and selectively bind with targeted cell after extravasation[14].

**1.2.1.2 Active Targeting: -**

Active targeting isa fore most strategy to ensure selective and specificity of SMART Nano system to the target site. The main strategy of this system is to treat the cancer tissue and to reduce the effect of drugs on healthy tissues. The basic principle behind this technique is that during preparation of SMART non colloidal system via the functionalization of the surface of the carrier with ligands which bins to its receptor on the surface of the target cell. Ligand-receptor bond can ensure that the Nano systemwill deliver the rug to the disease cells rather than the surrounding healthy tissues [15].

SMART Nano system has been broadly used as a nano carrier drug delivery system for cancer therapy. It binds to its specific ligand to its active target site. The cancer highly expresses its specific receptor that can be targeted with their ligand. The limitation of this clinical trial is that it leads to immunogenicity of the targeted ligands and impaired dose delivery because of lysosomal digestion followed by endocytosis which remains as challenge that needs to be resolved[16].

**1.2.1.3Responsive to stimuli targeting**

The concept behind this that the Nano systems start to release their encapsulated drug content after exposure to an external trigger[17].These triggers might ph., temperature, light, ultrasound, magnetic

field[19, 20, 21]. This technique includesto enhance of Nano system internalization and binding to the targeted cell and also efficient drug distribution throughout the tumour mass[22].

### 1.2.2 TYPES OF NANO-BASED DRUG DELIVERY SYSTEM: -

#### 1.2.2.1 LIPOSOMES-

Liposomes have gained immense interest in the field of research to develop novel and innovative drug delivery technique in the medical and pharmaceutical fields. It has been considered as the most known assemblies in the drug delivery systems. liposomes were first described by British haematologist Dr Alec D Bangham FRS in 1961 (published 1964), at the Babraham Institute, in Cambridge and discovered by Bangham and R.W. Horne where he was testing for the new microscope by adding new strain and found that it was similar to plasma lemma which consists of cell membrane of bilayer lipid structure.

The name liposome has been derived by 2 Greek words lipos means fat and soma means body. A liposome is composed of layered/bilayer of phospholipids organized in vesicular form separating an aqueous medium from one another. The phospholipid group consists of polar head groups and two hydrophobic hydrocarbon chain. Liposomes are classified into noisome, phytosomes, ethosomes and transferors[23]. The vesicular shape of the liposomal vesicular is used to encapsulate different categories of bio therapeutic agents which have different physicochemical properties and three-dimensional structures

Liposomes are composed of phospholipids. These contain two major categories including glycerophospholipids and sphingomyelins. Glycerol is considered as the backbone of glycerophospholipids. Glycerophospholipids consists of hydrophilic head group and hydrophobic side chain. These are selected as a head group variation.

For egphosphatidylcholine, phosphatidylethanolamine, phosphatidylserine, phosphatidylinositol.Sphingosine (SM) are present in the animal cell. Sphingosine is the backbone of SM. It has cis-double bond in amide-linked acyl chains. These are capable to form intermolecular and intramolecular hydrogen bonds. They provide good entrapment efficiency, greater serum stability.

Liposomes are prepared through 4 basic steps: -

1. Drying lipids through the evaporation of the organic solvent.
2. The lipid dispersion in an aqueous media.
3. Liposome purification
4. Analysis of the final product

Delivery across blood brain barrier-

Since brain is very sensitive and delicate organ, it is separated from the blood stream by a dynamic physical and biological barrier that plays a key role in regulating its internal environment. The blood brain barrier protects the brain from various virus, bacteria, and toxins and also preventxenobiotic from the blood to the brain including anticancer drugs, antibiotics. Due to its specific properties the barrier prevents 98% small particles and 100% large particles from reaching the brain [23] .the barrier contains of a membrane which consists of receptors, enzymes and specific proteins to transport of glucose as well as amino acid from blood to the brain. However the pores helps for the selective passage of many compounds is enabled.

Liposomes have following advantages :-

1. Liposomes are non-toxic, biocompatible, biodegradable, and no immunogenic for systemic and non-systemic administrations.
2. The efficacy and therapeutic index of drug Actinomycin can be increased, by formulating it as liposomes.

3. Liposomes has flexibility to bind with site-specific ligands, in order to achieve active targeting.
4. Site-specific targeting of Anti-cancer, Anti-inflammatory drugs.
5. has high penetration into tissues (Corticosteroids, anaesthetics, and insulin)

### 1.2.2.2 NIOSOMES

Noisome are vesicular shaped and are considered for the use of sustained, controlled as well as targeted delivery of the drugs[24].It has the same vesicular structure like liposomes due to its some disadvantages like toxicity, low cost, stability issues at different ph, liposomes are overcome by noisome[25].Noisome can be unilamellar,oligolamellar or multilamellar[26]. Significant application of niosomes is that it helps to reduce systemic toxicity by encapsulating agents which include to decrease clearance from the body by slowing the drug release of such agents [27].

Advantages of Niosomes: -

1. As compared to liposomes niosomes offer more chemical stability, osmotic acivity and longer shelf life.
2. It can be mdified due to presence of a functional group on the hydrophilic head.
3. Due to the charge niosomes are less toxic and more compatible.
4. Niosomes can enhance the bioavailabilty of the active pharmaceutical ingredient by increasing the stability.
5. Patient compliance is better since given as aqueous suspension.
6. Niosomes can be used for targeted, controlled as well as sustained delivery of a drug [28].

Disadvantage of Niosomes: -

1. Major disadvantage could be the stability of the aqueous suspension.
2. Drug leakage from the entrapment site and aggregate formation of noisome may also occur[29].

Structure of Niosome: -

Niosomes are bi-layered structure of non-ionic surface- active agents and are thermodynamically stable formed when surfactants and cholesterol are mixed in proper proportion[30].Because of the special geometry it can encapsulate hydrophilic as well as hydrophobic drug in the structure. Entrapment can occur in the central aqueous domain and can absorb on the bilayer surface.

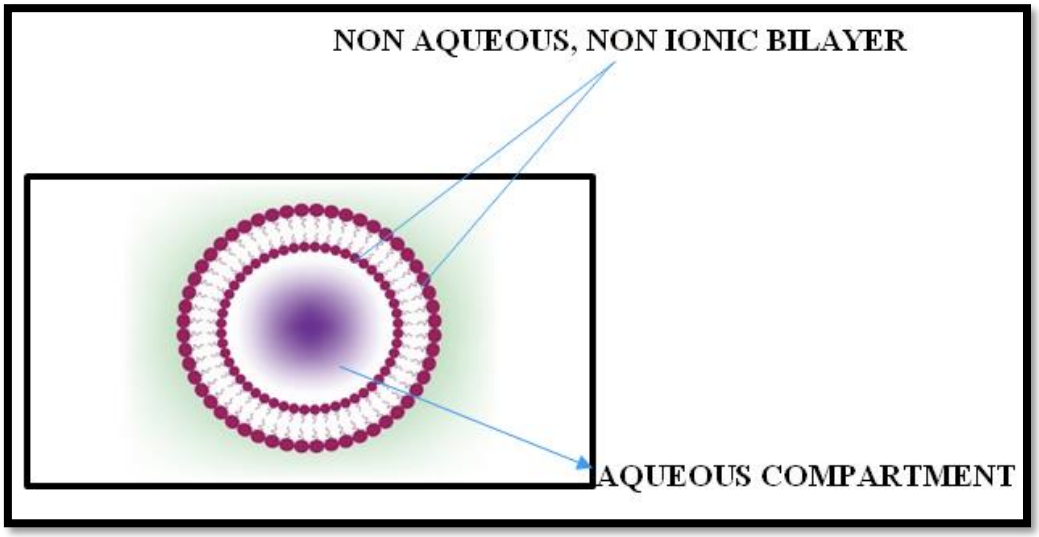


FIGURE 1.2- STRUCTURE OF NIOSOME

Application of niosomes: -

1. Enhancement of bioavailability-

Niosome can help to improve the bioavailability of drugs. Some of the niosomes that help to improve the bioavailability of oral drug are paclitaxel [31], cefdinir [32], benzyl penicillin [33] and tenofovirdisoproxilfumarate [34]. Niosomes of diltizem were also prepared for the enhancement of bioavailability through nasal administration.


FIG 1.3: APPLICATION OF NIOSOMES

2. Targeted drug delivery-

Niosomes for target delivery of drugs to tumour cells were prepared by Tavano et al. [35] and A. Massoti. [36]Tavano et al. prepared to transfer conjugated plutonicniosomes of doxorubicin for delivery to tumour cells. A. Massotti prepared pH-sensitive niosomes for delivery of a drugtohepatoblastoma. Targeting was done using surface modification and no pH sensitive molecule was used. These niosomes undergo protonation of amino groups present on their surface after penetration into the cell and release their cargo by 'sponge effect'.

3. Delivery of vaccines and antigen-

Niosomes were prepared for oral delivery of vaccines. It was prepared by the incorporation of bile salt in the bilayer of the vesicles. These Niosomesprotects the antigens from degradation b enzymes present in the GIT.

**1.2.2.3 NANOPARTICLES: -**

Nanotechnology devices or systems manufacture at the molecular level and is a multidisciplinary scientific field which is undergoing explosive development. Nanotechnology can be traced to be revolutionary advances across medicine, communication, genomics and robot due to its nanosized and unique behaviour. Hence new approaches are evolved that enhance the quality of the human life.

Nanoparticles are classified into different several categories of nanoparticles with different configuration such as Nano capsules, Nano sphere, Nano shells, with particle size ranging from 20 to 250nm. These nanoparticles have polymeric shell that encapsulate the drug into their

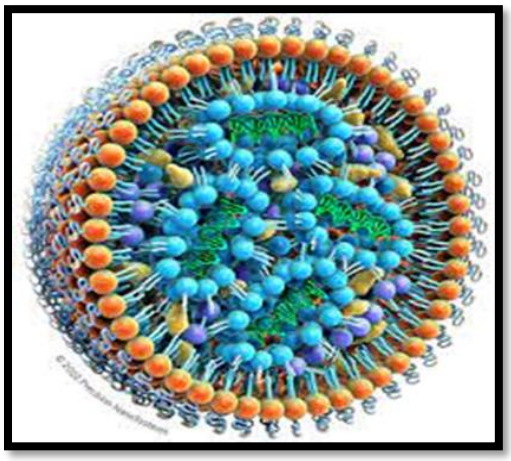

FIG 1.4: STRUCTURE OF LIPID BASED NANOPARTICLE

internal phase or in some cases free drug molecules that might be adsorbed on the surface for initial burst release for short period of administration [36].Polymeric materials such as polylactic-co-glycolic acid and its co block (PLGA-PEG-PLGA or PEG-PLGA-PEG) have been widely used in preparation due to their biocompatibility and biodegradability [37].

For cellular targeting, the first step is to activate the surface of NP with functionalized groups for cell targeting. Then there is a linkage formed between the target ligand and receptors on the cell surface. A second mechanism that uses ph responsive polymers and receptor on the cell surface. A second mechanism that uses ph responsive polymers for encapsulating anticancer drugs can also be employed. The polymeric matrix starts to lose its architecture in the acidic medium of cancerous tissues, enabling the drug molecules to move freely after localization in the cancerous cell. The third targeting mechanism is to use densely positively charged polymers that will be attracted to infected cells [38]. PEG chains can also be added on the surface of NP to extend its presence in the systemic circulation via the stealth effect [39].

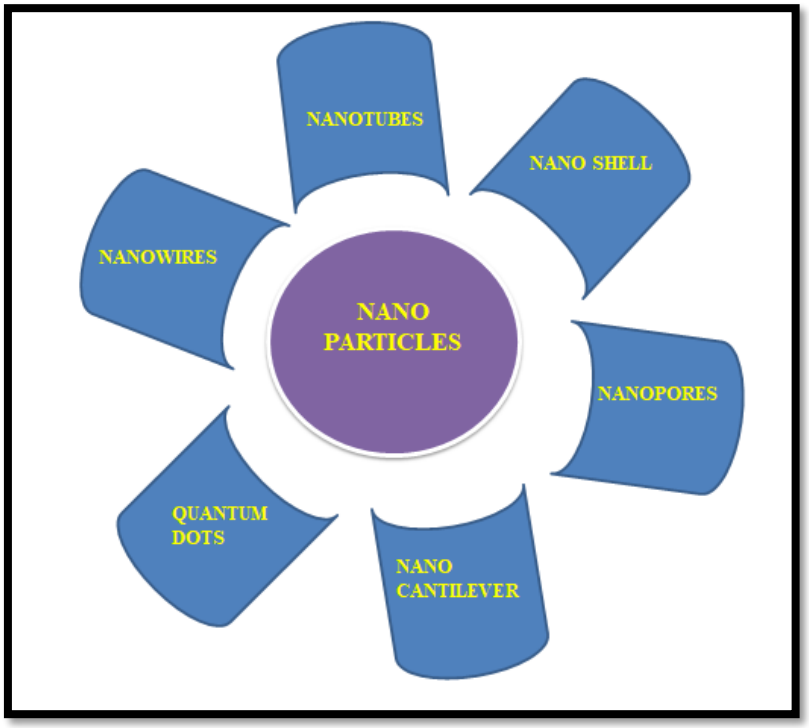


FIG 1.5: TYPES OF NANOPARTICLES

ADVANTAGES OF NANOPARTICLES:-

1. Offers uniform delivery of drug with great bioavailability.
2. It can be administered through different routes.
3. Smaller in size with high surface area.
4. Low drug dose is required[40][41].

**1.2.2.4HYDROGELS**

It is three dimensional, hydrophilic, polymeric networks capable of incorporating large amount of water or biological fluids. The networks are composed of homopolymers or co polymers and are insoluble to the chemical crosslinks or physical crosslinks. It exhibits a thermodynamic compatibility with water which allows swelling in aqueous media.

CLASSIFICATION:-

1) Based on the methods of preparation – homopolymeric, copolymerise hydrogel
2) Stimuli sensitive hydrogels- temperature sensitive hydrogels, ph. sensitive hydrogels.
3) Based on the mechanism of release diffusion controlled, swelling controlled.

ADVANTAGES:-

1) Biocompatible, biodegradable can be injected.
2) Hydrogels possess wide degree of flexibility similar to natural tissue.
3) Have good transport properties and easy to modify[40][41][42][43].

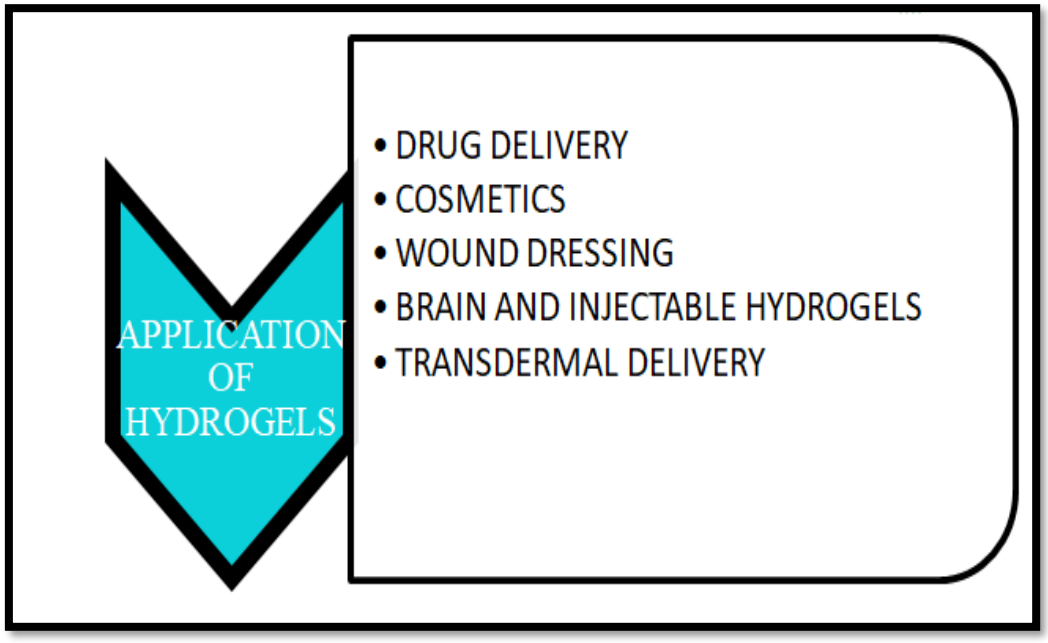


FIG 1.6: APPLICATION OF HYDROGELS

**1.2.2.4 NEW DRUG DELIVERY SYSTEM CAN PROVIDE IMPROVED OR UNIQUE CLINICAL BENEFITS SUCH AS:-**

i. Improved patient compliance.
ii. Improved out comes.
iii. Reduction of adverse effects.
iv. Improvement of patient acceptance of treatment.
v. Reduction in overall use of medicinal resources.
vi. For intracellular delivery.
vii. Cell and gene targeting.
viii. User friendly.
ix. Tissue engineering.
x. Better disease markers in terms of sensitivity and specify.[45][46][47][48]

**Table 1.1: Various NDDS formulations already available [49][50][51]**

| S.NO. | NDDS FORMULATION | AVAILABLE NDDS FORMULATION | COMPANY |
|---|---|---|---|
| 1. | Liposomes | a. ANTHRASAFE Doxorubicin Hydrochloride liposome injection | Miracallus |
| | | b. Amphotec (acute promyelocyticleukemia) | Sequus pharmaceutical inc. |
| | | c. Depodur (post surgical pain relief) | Pacira pharmaceutical inc. |

| | | | |
|---|---|---|---|
| | | d. Dauoxome (Kaposi sarcoma in AIDS)<br>e. Evacet (metastatic breast cancer) | Glen ltd<br>The liposome company,USA |
| 2. | Niosomes | a. LANCOME Anti-aging cream | Loreal Group |
| 3. | Nanoparticles | a. Avinza (psycho stimulant)<br>b. Pacliall (breast cancer)<br>c. Tricor (primary lipidemia)<br>d. Emend(anti-emetic)<br>e. LEP-ETU(advanced cancer) | King Pharma<br>Panacea<br>Abbott lab(USA)<br>Merck,Elan<br>Neopharm |
| 4. | Hydrogels | a. SQZ gel oral release systemChitosen and polyethylene glycol(hypertension)<br>b. Hycore-V and Hycore-R(vaginal and rectal infection)<br>c. Cervidil vaginal(PEG2)(cervical ripening)<br>d. Smart Hydrogel( development of buccal,nasal,vaginal and transdermal)<br>e. Aquamere (skincare) | Macromed<br>CeNes drug delivery<br>Insert forest pharmaceuticals USA<br>Plymouth UK<br>Hydromer USA |

## 2. CONCLUSION:-

For the treatment of diseases new technologies have been developed. The method of delivery of drug is a significant effect of delivery on its efficacy. Some drugs have an optimum concentration range within which benefit is achieved and concentration above or below can be toxic or produce no therapeutic benefit at all. The use of drug delivery systems brings a lot of hope in developing drugs for bringing lots of hope in the field of medical research. Novel drug delivery is a new technique which is used in pharmaceutical science. Like targeting drug delivery, vaccine delivery, gene therapy and other commercial development.

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