AUTOMATED DRUG DISPENSING SYSTEM AND DEVICES

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Acknowledgement:

Authors are thankful to the Parikrama Diploma in Pharmaceutical Sciences Kashti. Tal: Shrigonda Dist: Ahmednagar Maharashtra, India. For extending requested facilities in Commencement and completion of this work.

ABSTRACT-

The technique of delivering a pharmaceutical ingredient to produce a therapeutic effect in either People or animals is known as drug delivery. The importance of using nasal and pulmonary Medication delivery channels for treating human diseases is growing. These delivery methods Offer viable substitutes for parenteral medication administration, especially in the case of peptide And protein therapies. Numerous drug delivery methods have been developed for this reason, and Pulmonary and nasal delivery are now being researched. These comprise, among other things, Cyclodextrins, liposomes, proliposomes, microspheres, gels, and prodrugs. Biodegradable Polymer-based nanoparticles demonstrate assurance in meeting the demanding specifications Placed on these delivery systems, including the capacity to be converted into an aerosol, stability Against forces produced during aerosolization, biocompatibility, and lung cell population or site Targeting.

Keywords: Brain targeting, infectious diseases, liposomal, lung diseases, micelles, transdermal

AUTOMATED DRUG DISPENSING SYSTEM AND DEVICES

The pharmacodynamics principles governing the action and the technique to develop unique medicinal properties. Molecule is costly and time-consuming. A number of methods, including dose titration, therapeutic drug monitoring, and individualizing drug therapy, have been tried to improve the safety efficacy ratio of "old" medications. Other highly appealing strategies that have received a lot of curiosity include targeted delivery, gradual delivery, and controlled rate delivery of drugs. It is interesting to see Indian researchers write how many articles and a substantial quantity of work from the USA and Europe. [1-2] the pharmacokinetic disposition of powerful opioid analgesics, inhalation anesthetic agents, sedative/hypnotics, and muscle relaxants have been understood more clearly because of numerous animal and human studies. According to these research, skin, as well as the mucous membranes of the mouth, nose, and throat, may be used as an auxiliary analgesic and

BEADED DELIVERY SYSTEMS

Beaded delivery formulations are another approach used to provide long-acting drug levels associated with the ease of once-daily dosing, albeit they are not utilized together with oxybutynin. This system is marketed under the name Detrol LA (Pharmacia, Pea pack, NJ) and has been effectively linked to tolterodine tartrate. The beaded system is made up of several tiny, inert beads made of polystyrene or a number of comparable material. The delivery capsule carrying the active medication is placed on top of the beads. This system's drug delivery is acid sensitive since the drug's release from the drug levels depends on the acidity of the stomach. A pharmacokinetic pattern that is somewhat equivalent to a zero-order pattern has been generated by this procedure; C max becomes apparent 4–6 hours after ingesting, and sustained levels are considered for 24 hours after

LIPOSOMAL AND TARGETED DRUG DELIVERY SYSTEM

In theory, drug delivery systems can give cancer treatments increased efficacy and/or a reduction in toxicity. The "enhanced permeability and retention" effect can be used by long-circulating macromolecular carriers, like liposomes, to achieve preferential extravasation from tumor arteries.[3] Liposomal anthracyclines, which include forms with much extended circulation such liposomal daunorubicin and PEGylated liposomal doxorubicin, have achieved outstanding drug encapsulation, leading to substantial anticancer activity with reduced cardiotoxicity. Treatment for breast cancer with pixelated liposomal doxorubicin has demonstrated substantial efficacy if employed alone or in conjunction with other chemotherapeutics. More liposome structures are being created to deliver different medications. True molecular targeting will be a feature of the next generation of delivery systems; immunoliposomes and other ligand-directed structures are manifestations of an assortment of biological components with tumor recognition powers.

As was previously said, the authorized liposomal drug delivery methods that are currently in use offer stable formulation, enhanced pharmacokinetics, and a certain amount of "passive" or "physiological" targeting to tumor tissue.[4] These carriers do not, however, specifically target tumor cells. In addition to shielding liposomes from unfavorable interactions with cell membranes and plasma proteins, the design changes that set them apart from reactive carriers like cationic

liposomes also stop interactions with tumor cells. Rather, liposomes stay within the tumor stroma as a drug-loaded depot following their extravasation into the tumor tissue. Eventually, phagocytic or enzymatic destruction of liposomes results in the release of medication, which diffuses into tumor cells. Antibody-mediated or other ligand-mediated interactions will enable direct molecular targeting of cancer cells in the upcoming generation of drug carriers that are currently being developed. As mentioned, at this timetable fragments attached to liposomes form immunooliposomes, a tactic for molecularly targeted drug delivery. [5] Fab' or skiff fragments attached to long-circulating liposomes have been used to create anti-HER2 immunoliposomes. Anti-HER2 immunoliposomes bound and internalized in HER2-overexpressing cells with efficiency in preclinical trials, leading to effective intracellular delivery of encapsulated drugs. In addition to demonstrating a markedly superior efficacy over all other treatments tested (free doxorubicin, liposomal doxorubicin, free maybe [trastuzumab], and combinations of trastuzumab plus doxorubicin or liposomal doxorubicin), anti-HER2 immunoliposomes loaded with doxorubicin also demonstrated potent and selective anticancer activity against HER2-overexpressing tumors.[6] Scaling up of anti-HER2 immunoliposomes for clinical trials is presently underway.

Comparing the immunoliposome technique to other antibody-based tactics reveals several potential benefits. Doxorubicin delivered using anti-HER2 immunoliposomes may avoid the exorbitant cardiotoxicity linked to trastuzumab plus doxorubicin therapy. Using skiff, anti-HER2 immunoliposomes can be created. Unlike trastuzumab, these liposomes cannot cause cellular cytotoxicity in response to an antibody, and they require HER2 expression thresholds in order to be delivered. Unlike drug immunoconjugates, which are made up of a few medicines (usually less than ten per maybe) that are directly attached to specific residues on the mob via linkers, immunoliposomes take advantage of the exponentially larger capacity of drug-loaded liposomes, which may hold up to 104 drugs each liposome.

Additionally, immunoliposomes seem to be no immunogenic and have a prolonged half-life, even after repeated doses. [7] Additionally, targeting based on antibodies is being explored in tandem with polymer systems. Similarly, liposomes and polymers are being investigated in conjunction with ligand-based targeting employing growth factors, hormones, vitamins (e.g., folate), peptides, or other particular ligands. Liposomes are amphipathic phospholipid-based concentric layered structures that can be categorized as multilamellar (MLV), small unilamellar (SUVs), or large unilamellar (LUVs) based on the number of bilayers. Their diameters vary from 0.025 to 10 μ. Liposome composition and processing technique control liposome size and shape. Drugs, vaccinations, and genes for a range of illnesses can all be delivered using liposomes. [8]

INFECTIOUS DISEASES

Bacchanal and colleagues, who studied it in animal models of leishmaniosis and fungal infection, created liposomal amphotericin. Kshirsagar et al. altered the formulation; created a sterile liposomal amphotericin preparation dubbed "Patient Worthy," and studied the efficacy of the preparation in patients suffering from leishmaniosis and systemic fungal diseases. It was discovered to be safe, causing noticeably less side effects than ordinary amphotericin in patients with systemic fungal infection. Additionally, it did not cause nephrotoxicity and could be

administered to patients who had renal impairment. In individuals who were intolerant to both ordinary amphotericin and fluconazole, it worked well. This works well at a dose of 1 mg/kg/day, in contrast to Embosomed (USA), which requires 3 mg/kg/day. Using Aspergillus murine mode, the same group investigated several liposomal amphotericin dose regimens.

ANTICANCER DRUGS

Modes:

1

Anticancer drugs provide current information on the clinical and experimental effects of toxic and non-toxic cancer agents and is specifically directed towards breakthroughs in cancer treatment. Mukhopadhya developed conjugate of antineoplastic drug daunomycin (DNM) with alkylated bovine serum albumin. It was taken up with high efficiency by multi drug resistant variant JD100 of the murine-macrophage tumor cell line J774A.1 through the scavenger receptors resulting in cessation of DNA synthesis. A thermosensitive liposomal Taxol formulation (heat mediated targeted drug delivery) in murine melanoma was developed and studied by another group of workers. Chromophore, which is used as excipient due to the low aqueous solubility of Taxol, has toxic side effects.

Anticancer drugs focus primarily on advancements in cancer treatment and offer the most recent data on the clinical and experimental effects of toxic and non-toxic cancer agents. Mukhopadhya created a compound of alkylated bovine serum albumin and the carcinogenic medication daunomycin (DNM). DNA synthesis was stopped when the multidrug resistant variation JD100 of the murine macrophage tumor cell line J774A.1 absorbed it with remarkable efficiency through scavenger receptors. Another team produced and investigated a formulation of thermosensitive liposomal Taxol (heat-mediated targeted drug delivery) in murine melanoma. Chromophore has hazardous side effects and is utilized as an excipient given that Taxol is not soluble in liquids.

Modes:

2

Temperature-sensitive liposomes encapsulating Taxol were prepared using egg phosphatidylcholine and cholesterol in combination with ethanol. The liposomes have a phase transition temperature of 43°C. [9] A significant reduction in tumor volume was noted in tumor bearing mice treated with a combination of hyperthermia and theromosensitive liposome encapsulated Taxol, compared to animals treated with free Taxol with or without hyperthermia in B16F 10 murine melanoma transplanted into C57BI/6 mice. Sharma et al. also investigated the use of polyvinylpyrrolidone nanoparticles containing Taxol prepared by reverse micro-emulsion method. The size of nanoparticle was found to be 50-60 nm. The antitumor effect of Taxol was evaluated in B16F10 murine melanoma transplanted in C57 B 1/6 mice. In vivo efficacy of

Taxol containing nanoparticles as measured by reduction in tumor volume and increased survival time was significantly greater than that of an equivalent concentration of free Taxol.

[10]

Egg phosphatidylcholine, cholesterol, and ethanol were combined to develop temperature-sensitive liposomes that included Taxol. The phase transition temperature of the liposomes is 43°C.[10] When B16F 10 murine melanoma was transplanted into C57BI/6 mice, tumor-bearing mice treated with a combination of hyperthermia and thermoplastic liposome-encapsulated Taxol were compared to animals treated with free Taxol with or without hyperthermia, an important reduction in tumor volume was seen. Sharma et al. also looked into the utilization of reverse micro-emulsion-prepared polyvinylpyrrolidone nanoparticles containing Taxol. It became known that the nanoparticle was 50–60 nm in size. With B16F10 murine melanoma inserted into C57 B 1/6 mice, the anticancer impact of Taxol was investigated. Taxol-containing nanoparticles' in effectiveness in real life as determined through the tumor volume reduction.

LUNG-SPECIFIC DRUG DELIVERY

In comparison with conventional administration techniques, pulmonary medication delivery has number advantageous characteristics for the treatment of respiratory disorders. It is possible to provide medications immediately to the lungs by inhalation therapy. Without requiring high dose exposures from alternate ways of administration, the local pulmonary deposition as well as distribution of the donated drug allows for a tailored therapy of respiratory illnesses, such as pulmonary arterial hypertension (PAH). For the past ten years, the most common form of treatment for individuals with PAH has been the intramuscular administration of short-acting vasodilators. The relative severity of side effects prompted the creation of novel prostacyclin analogs and especially alternate delivery systems. Iloprost (Centavos®), one such equivalent, is a pharmaceutical that has been licensed for use in treating PAH all over the world.

Inhalation of this compound is an attractive concept that minimizes side effects due to its lung selectivity. Unfortunately, the short half-life of iloprost requires frequent inhalation movements, up to 9 times a day. Therefore, a controlled release formulation such as an aerosol would improve the patient & #039; comfort and ease of maintenance. Controlled drug delivery systems have become an increasingly attractive alternative to inhaled therapies. Many delivery systems have been developed and investigated as potential controlled pulmonary drug delivery forms, including drug-loaded lipids and polymer-based particles. The use of colloidal delivery systems for pulmonary delivery of drugs is an area of interest in Nano medicine. The aim of this study was to compare the lung absorption and distribution characteristics of the hydrophilic model drug 5(6)-carboxyfluorescein (CF) after solution or nanoparticle encapsulation in an isolated rabbit lung model (IPL).

CF nanoparticles were prepared from novel biocompatible, rapidly degradable-branched polyesters by a modified solvent displacement method. The physicochemical properties, morphology, encapsulation efficiency, in vitro drug release, nanoparticle stability during nebulization, aerosol properties, and pulmonary absorption and distribution profiles of the dye after nebulization in IPL were investigated. Among the various pulmonary drug delivery systems,

nanoparticles show. Several advantages in the treatment of respiratory diseases, such as prolonged drug release, cell-specific targeted drug delivery, or modified biodistribution of drugs at both cellular and organismal levels. First, it must be understood that the formulation and administration of the compositions as aerosols are difficult. Not only does this involve the preparation of a stable solution or suspension in a medium (propellant) that is not as well characterized as other systems, but the resulting system also has performance limitations. To reach the lungs effectively, it must be atomized into particles with an aerodynamic size of approximately 1-5 µm.

Due to these particle size limitations and respiratory toxicology issues, the range of possible excipients in the formulation phase is greatly reduced. In addition, limiting the concentration of excipients in the formulation is crucial to maintain sufficient aerosol. Thus, the complexity of this relationship makes aerosol composition difficult. Although challenging, successful drug formulation for pulmonary delivery offers a valuable therapeutic approach. The treatment of lung diseases changed significantly with the introduction of the metered dose inhaler (MDI). Since then, inhalers have become the most effective way to manage the symptoms of lung diseases such as asthma and chronic obstructive pulmonary disease (COPD). Later, a reformulation was recommended when chlorofluorocarbon (CFC) propellants were linked to ozone depletion (Molina and Rowland, 1974). With the successful transition to new propulsion systems, inhalable nebulizers continue to be well accepted and very useful among patients worldwide.

Since then, inhalers have become the most effective way to manage the symptoms of lung diseases such as asthma and chronic obstructive pulmonary disease (COPD). Later, a reformulation was recommended when chlorofluorocarbon (CFC) propellants were linked to ozone depletion (Molina and Rowland, 1974). With the successful transition to new propulsion systems, inhalable nebulizers continue to be well accepted and very useful among patients worldwide. In the future, the efficacy, ease of use, and relatively low cost of aerosolized formulations, along with changes in delivery technology and formulation science, are likely to expand disease treatment. Another therapeutically undesirable aspect of pulmonary administration is the rapid absorption of most drugs by the lungs, requiring repeated dosing, for example bronchodilators and corticosteroids. Liposomes are believed to alleviate some of the problems encountered with conventional aerosol delivery due to their ability to: (I) act as a dissolution matrix for poorly soluble substances; ii) acts as a reservoir for sustained release into the lungs; and (iii) facilitates intracellular transport [11]

TARGETING TO BRAIN

Much of the interest in mucosal vaccine administration stems from the fact that mucosal surfaces are the primary entry point for many pathogens. Among other mucosal sites, nasal delivery is particularly attractive for immunization because relatively high permeability, low enzymatic activity, and a significant number of immunocompetent cells characterize the nasal epithelium. In addition to these beneficial properties, the nasal route may offer simplified and more cost-effective vaccination protocols and improve patient compliance. The use of Nano carriers provides a convenient way to deliver antigenic molecules through the nose. In addition to improved protection and facilitated antigen transport, nanoparticle delivery systems can also provide more efficient antigen recognition by immune cells. These are key factors in the optimal processing and presentation of the antigen and thus in the development of an appropriate immune response. In this

sense, the design of optimized vaccine Nano carriers offers a promising way to vaccinate the nasal mucosa. [12]

A common non-invasive approach to brain drug delivery is drugisolipidation. Water-soluble parts of drugs limit the BBB transport of water-soluble drug to lipid-soluble prodrug conversion is a traditional chemical solution to the BBB problem as shown in figure.1

Program overview for the development of blood-brain drug-targeting strategies from either chemistry-based or biology-based disciplines The treatment of diseases of the central nervous system is particularly difficult, because the transport of medicinal molecules to the brain is often prevented by various physiological, metabolic and biochemical barriers, which together form the blood-brain barrier, the blood-brain fluid barrier. , and the blood-tumor barrier. The current outlook for many brain disease patients remains bleak, but recent advances in drug delivery techniques offer reasonable hope that the formidable barriers protecting the brain may be overcome. With the rational design of polymer-based drug delivery systems, the delivery of drugs directly into the brain interstitial has recently been greatly improved.

However, significant progress will only be made if continued vigorous research to develop therapeutic and less toxic drug molecules is combined with an aggressive search for more efficient mechanisms to deliver these drugs to their targets in the brain. [13] Jain et al. developed dopamine hydrochloride containing small positively charged liposomes by sonication of multilamellar vesicles and studied their physical properties and drug efflux and release pattern. In vivo activity was assessed using periodic measurements of chlorpromazine-induced catatonia in Sprague Dawley rats and compared with standard dopamine hydrochloride, dopamine and levodopa carbidopa. Studies have shown that dopamine can be efficiently transported to the brain and its breakdown in the bloodstream can be prevented by encapsulating it in liposomes. [14]

STRATEGIES FOR DRUG DELIVERY TO THE BRAIN

Many drugs do not have sufficient physicochemical properties, such as high lipid solubility, small molecular size, and positive charge, necessary to penetrate the BBB. [15]

DISRUPTION OF THE BBB

The idea behind this approach was to shortly break the blockage by injecting a mannitol solution into the arteries in the neck. The resulting high sugar content in the brain capillaries sucks water from the endothelial cells, limiting them and thus opening the tight junction. The effect lasts 20-30 minutes, during which the drugs freely diffuse, which usually do not cross the BBB. This method made it possible to administer chemotherapy agents to patients with brain lymphoma, malignant glioma and disseminated germ cell tumors of the central nervous system.

Physiological stress, transient increases in intracranial pressure, and unwanted migration of anticancer drugs into normal brain tissue are undesirable side effects of this approach in humans. [08]

INTRAVENTRICULAR/INTRATHECAL DELIVERY

Here a plastic container is used, which is implanted subcutaneously in the scalp and connected to the ventricles of the brain by means of an output catheter. Injection of drugs into the cerebrospinal fluid is an appropriate strategy only near the ventricles. [16]

INTRA NASAL DRUG DELIVERY

After nasal administration, drugs first reach the airway epithelium, where compounds can be absorbed into the systemic circulation by transcellular and par acellular passive absorption, transporter-mediated transport, and absorption by transcytosis. If a nasal drug, preparation is administered deep enough and high enough in the nasal cavity, it is possible to reach the olfactory mucosa and the drug can be transported to the brain and/or cerebrospinal fluid via olfactory receptor neurons. [17]

POSSIBLE SYSTEMS FOR DRUG DELIVERY-COLLOIDAL DRUG CARRIERS

Colloidal drug delivery systems such as micellar solutions, vesicular and liquid crystalline dispersions, and nanoparticle dispersions consisting of small particles are promising as drug delivery systems. The aim is to obtain systems with optimized drug loading and release properties, long shelf life and low toxicity. The added drug participates in the microstructure of the system and can even affect it due to molecular interactions, especially if the drug has amphiphilic and/or melogenic properties.

MICELLES

Micelles formed by the self-assembly of amphiphilic block copolymers (5-50 nm) in aqueous solutions are of great interest in drug delivery applications. Drugs can be physically encased in the core of block copolymer micelles and transported at concentrations that may exceed their natural water solubility. In addition, the hydrophilic blocks can form hydrogen bonds with the aqueous environment and form a dense shell around the micelle core. As a result, the contents of the hydrophobic core are effectively protected against hydrolysis and enzymatic degradation. In addition, Koruna can prevent recognition by the reticuloendothelial system and thus the initial removal of micelles from the bloodstream. The fact that their chemical composition, total molecular weight and block length ratios can be easily changed allows control of the size and morphology of the micelles. Functionalization of block polymers with cross-linkable groups can increase the stability of the corresponding micelles and improve their temporal control. [18]

LIPOSOMES

Alec D. Bingham first produced liposomes in England in 1961. One end of each molecule is water soluble, while the other end is water insoluble. Water-soluble drugs added to water were trapped due to aggregation of hydrophobic ends; fat-soluble drugs were incorporated into the phospholipid layer as figure 2.

In some cases, liposomes attach to cell membranes and appear to fuse with them, releasing them or drugs into the cell. In the case of phagocytic cells, the liposomes are absorbed, the phospholipid walls are affected by organelles called lysosomes, and the drug is released. Liposomal delivery systems are still largely experimental; their exact mechanisms of action in the body are being studied, as well as ways to direct them to specific diseased tissues. [19]

NANO TECHNOLOGY

NANO PARTICULATE SYSTEMS FOR BRAIN DELIVERY OF DRUGS

One way to deliver drugs to the brain is with nanoparticles. Nanoparticles are polymer particles made of natural or artificial polymers with a size between 10 and 1000 nm (1 mm). Drugs can be bound to a solid solution or dispersion, or adsorbed on a surface or chemically attached. Poly (butyl cyanoacrylate) nanoparticles are the only nanoparticles that have been successfully used for in vivo drug delivery to the brain to date. The first drug to be delivered to the brain using nanoparticles was the hex peptide dalargin (Tyr-D-Ala-Glee-Phe-Leu-Arg), a Leu-enkephalin analog with opioid activity.

Nanoparticles and Nano preparations have already been used very successfully as drug delivery systems; and nanoparticle drug delivery systems have even greater potential for many applications, including antitumor therapy, gene therapy and AIDS treatment, delivery of radiotherapy, proteins, antibiotics, biostatic agents and vaccines, and as vesicles to cross the blood-brain barrier [20]

Nanoparticles offer enormous advantages in drug targeting, delivery and release, and their additional potential to link diagnosis and therapy is emerging as one of the most important tools in Nano medicine. The main goal is to improve their stability in the biological environment, mediate the biodistribution of active substances, and improve drug loading, targeting, transport, release and interaction with biological barriers. Cytotoxicity of nanoparticles or their degradation products remains a major concern, and improving biocompatibility is naturally an important concern for future research. [21, 22]

Today, nanotechnology has proven to be more effective in improving the delivery of drugs to the brain. Nanoparticles are a drug delivery system made of various materials such as poly (alkyl cyanoacrylates) (packets), polyacetates, polysaccharides and copolymers. More specifically, the methods of preparation of nanoparticles, their characterization and medical use were reviewed. [23] The exact mechanism by which nanoparticles travel to the brain is unknown, but it likely depends on particle size, material composition and structure. In some cases, it has been reported to mimic molecules that are normally transported to the brain. For example, polylobate-coated nanoparticles are thought to mimic low-density lipoproteins (LDL), allowing them to cross the capillary wall into the brain by binding to the LDL receptor. [24]

THE NANOTECHNOLOGY INCLUDES:

Coated nanoparticles

PEGylated nanoparticles

Solid Lipid nanoparticles (SLN)

Nano gels

TRANSDERMAL DELIVERY

Bio adhesive liposomes with levonorgestrel as a controlled drug delivery system have been investigated. [25] A levonorgestrel mesosphere proliposomal system was prepd. Vesicles were mostly unilamellar and some multilamellar. The release kinetics was zero. Alcohol had a greater effect on skin permeability compared to oils. In vivo studies showed that a significant lag phase was observed before therapeutic levels were reached, suggesting the need for a loading dose. This proliposome system was found to be superior to the PEG-based cream system. A liposomal delivery system containing the local anesthetic benzocaine was developed for locally controlled and localized delivery [26]. The liposome suspension was added to the cream and gel base. The systems delivered the drug at a controlled rate for up to 24 hours, compared to a standard cream whose release rate was rapidly slowed. Penetration of the drug through the skin of the human body was very slow. In vivo studies have shown that the effect of the liposome preparation lasts longer. [27]

MISCELLANEOUS

Near investigated the effect of liposome size and charge on the biodistribution of liposome-encapsulated 99m TC-DTPA after intravenous injection in rats. They found that multilamellar vesicles (MLV) accumulated more than SUVs in the liver, spleen and lungs. More positively charged MLVs than negative or the liver took up neutral MLVs, more positively charged the kidneys took up SUVs, and more MLVs that are neutral were taken up by the lungs than charged. [28] Attempts have been made to improve the stability of the liposome by coupling the drug to the lipid bilayer using a cross-linking agent. [29] Liposomes containing soy phatidylcholine (SPC) were prepared by the calcium-induced fusion method. Positively charged stearylamine was added to the bilayer. Liposomes were coupled to EDAC (1-ethyl-3-(3-dimethylaminopropyl) carbodiimide-HCl) coated with ibuprofen, and coupling was confirmed by UV spectroscopy. It was found that EDAC of SPCs containing stearylamine liposomes significantly delayed the release of ibuprofen. Factors affecting the systemic absorption of nasally administered gentamicin sulfate were investigated in albino rats using an in situ nasal perfusion technique. [27] The surfactant Tween 80 increases permeability by changing membrane structure and permeability. In this study, concentrations of Tween 80 up to 1% (w/v) increased permeability. In the case of 0.25% (w/v) beta-cyclodextrin, the second permeability enhancer was found to increase the permeability significantly initially, but was found to level off later. However, both permeability enhancers were found to decrease the stability and potency of gentamicin. [30]

OTHER CONTROLLED DRUG DELIVERY SYSTEMS

The pharmaceutical industry and pharmaceutical departments have developed a long-acting, slow-release, long-lasting formulation and studied the in vitro release pattern and in vivo bioequivalence. [31]

ORAL

For oral administration of protein and peptide drugs, there is a great need for suitable devices for selective transport of microspheres containing the therapeutic agent in the intestine. Gelatin capsules were coated with different concentrations of sodium alginate, cross-linked with appropriate concentrations of calcium chloride, and tested in vitro for resistance to gastric and intestinal environment. The 20% (w/v) polymer-coated gelatin capsules, which showed the most promising in vitro results, were evaluated in volunteers for their in vivo gastrointestinal behavior. X-ray studies show that while uncoated gelatin capsules disintegrate in the stomach within 15 minutes of ingestion, alginate-coated gelatin capsules remain intact as long as they remain in the stomach (up to 3 hours) and then travel to the ileocecal region of the. Stomach intestine and degraded. [32-32] Varanasi and Nagarsenkar prepared 1 mm: n and 1.65 mm pellets of prochlorperazine maleate using modern granulation technology. The pellets were coated with ethyl cellulose and their in vitro release was assessed using a USP dissolution apparatus. They found that PCPM release could be reduced by adding ethyl cellulose. [33-34] Anaiah et al. prepared and studied theophylline extended-release tablets using Eudragit RL, RS and hydroxypropylmethylcellulose. Bioavailability studies in volunteers showed that HPMC and Eudragit formulations produced sustained drug plasma concentrations. The second group 35 consisted of nifedipine sustained-release capsules containing a loading dose in the form of a rapid solid dispersion and a sustained-release part in the form of micro particles covered with a polyvinyl acetate film (45,000 by weight) using a modified Waster coating. . [36]] the products achieved release of an initial therapeutic dose of medication in less than 45 min and sustained release for 11-12 h. The same group developed a diffusion cell to determine drug release from a topical aerosol formulation. [37]

PARENTERAL

a mixture of the synthetic polymer polyvinyl alcohol and the natural macromolecular gum Arabic and found that the duration and release of the drug depends on the amount of drug loaded in the matrix and the solubility of the drug in the matrix and release environment. The advantage of this system is that the kinetics of drug release from the system can be tailored by adjusting the composition of the plasticizer, photopolymer, and binder. Chitosan microspheres ranging in size from 45 to 300 μ have been used for controlled delivery of progesterone. In vitro and in vivo release was tested. It was found that the strongly cross-linked spheres released only 35% of the added steroids within 40 days, compared to 70% for the lightly cross-linked spheres. In vivo determination of the bioavailability of the steroid obtained from the microsphere preparation in rabbits by intramuscular injection showed that the plasma concentration of 1-2 up/ml was maintained for up to 5 months without a significant release effect. The data suggest that cross-linked chitosan microspheres would be an interesting system for long-term delivery of steroids. Cross-linked dextran beads were developed as a carrier for the development of a one-touch vaccine delivery system.[38-39] Drug delivery using biodegradable polymer devices has been extensively studied since the introduction of bioresorbable surgical sutures two decades ago. Among the different classes of biodegradable polymers are thermoplastic aliphatic polyesters such as poly(lactase) (PLA), poly(glycoside) (PGA), and especially a copolymer of lactase and glycoside

called poly(lactase-co-)glycoside) (PLGA) . Have attracted enormous interest due to their excellent biocompatibility, biodegradability, and mechanical strength.

They can be easily formulated into various devices carrying different classes of drugs such as vaccines, peptides, proteins and macromolecules. Most importantly, the US Food and Drug Administration approve them.

Administration (FDA) for sending drugs. Human and Huller [40 , 41, 42, 43] found that mice immunized with poly(DL-lactase-co-glycoside) (DLPLG) micro particles as carriers for delivery of Mycobacterium tuberculosis H37 Ra 71 coda cell wall-associated protein. Significantly, greater T-cell stimulation and cytokine release compared to Freundand#039 incomplete adjuvant (FIA) and emulsified 71-KDa in the BCG-vaccinated group. In addition, the protective effects of 71 coda-PLG were compared with 71 coda FIA based on survival rates and viable bacilli counts in various organs 30 days after challenge and the median lethal dose (LCD50) of Mycobacterium tuberculosis H37Rv.

71 coda PLG was more effective when challenge was administered 16 weeks after immunization. In addition, the 71KaDa-PLG-immunized group had significantly greater lung and liver bacterial clearance compared with the 71-kDa-FIA-immunized group. Poly (lactase-co-glycoside) (PLG) was used for subcutaneous delivery of diclofenac microspheres and in situ gel-forming systems. Pharmacokinetic and pharmacodynamics studies in rats with adjuvant-induced arthritis showed that the microspheres produced stable therapeutic concentrations in plasma for about 16 days after a single subcutaneous injection. In situ gel formation resulted in significantly higher peak plasma concentrations and inhibition of inflammation lasted for approximately 10 days. [44-45]

DENTAL PRODUCT

Somali et al. used an ethyl cellulose strip as a means for tetracycline and metronidazole to reduce gingival microorganisms in periodontal pockets. Patients received a supragingival scaling and were then divided into five groups based on how long the medication had been in place. Subjects were assigned to the tetracycline, metronidazole, and placebo groups. Subjects were washed and isolated, and microbiological baseline samples were obtained for gram stain and culture methods. [46] After treatment, sub gingival microbiological samples were taken again. Ethyl cellulose strips were removed and analyzed for residual drug. The results showed that tetracycline and metronidazole could be applied topically to periodontal sites using ethyl cellulose strips and significantly suppressed sub gingival bacteria for several days. Tetracycline was more rapidly released; however, metronidazole required a lower concentration to achieve complete reduction of sub gingival flora. A saliva-activated bio adhesive drug delivery system was developed for lidocaine hydrochloride [47] and compared with a topical gel formulation used in dentistry. It was found that DDS attached to the gingiva in one minute and reached maximum effect in 15 minutes and provided stronger anesthesia than the marketed topical gel.

COLON-SPECIFIC DRUG DELIVERY

The increasing number of investigational peptide and protein drugs requires the development of dosage forms with site-specific release. Delivery of drugs into the systemic circulation by colonic

absorption is a novel way to deliver peptide and protein drug molecules and poorly absorbed drugs from the upper gastrointestinal (GI) tract. [48] Oral colon-specific drug delivery systems offer obvious advantages over parenteral administration. Targeting the colon is of course valuable in the local treatment of colon diseases such as Crohn's disease, ulcerative colitis and colon cancer. Sustained release of drugs from the colon may be useful in the treatment of nocturnal asthma, angina pectoris and arthritis. Peptides, proteins, oligonucleotides and vaccines are potential interesting candidates for colon-specific drug delivery. Sulfasalazine, ipsalazide, and olsalazine have been developed as colon-specific delivery systems for the treatment of inflammatory bowel disease (IBD).[47] The extensive microflora of the large intestine and particular enzymes are increasingly used to release drugs in the large intestine. Although the colon is a potential site of drug absorption, effective local delivery of drugs to the colon is associated with difficulties in bypassing the stomach and small intestine. [49] In addition, the different pH conditions and the long transit time of drug preparations from the mouth to the colon cause many technical difficulties in the safe delivery of drugs to the colon. However, recent advances in pharmaceutical technology, including coating drugs with pH-sensitive and bacterially degradable polymers, encapsulating them in bacterially degradable matrices, and designing them as prodrugs, have offered new hope for effective drug delivery to the colon. The use of pH changes is analogous to the more common enteric coating and consists of using a polymer with a suitable pH solubility profile. The use of pH as a trigger for drug release in the colon is based on pH conditions that are constantly changing in the gastrointestinal tract.[50] Polysaccharide and azopolymer coatings, which are persistent in the stomach and small intestine, but are degraded by colonic bacteria, have been used as carriers to specifically target the colon. Finally, the availability of optimal preclinical models and clinical methods has accelerated the rapid development and evaluation of colon-specific drug delivery systems for clinical use. Future research may hopefully lead to improved technology for colon-specific drug delivery systems and better pharmacotherapy of peptide drugs. [51]

The need and benefits of colon-specific drug delivery systems have been recognized and documented. [52] Previously, the main approaches to achieve colon-specific delivery had limited success and included prodrugs, pH- and time-dependent systems, and microflora-activated systems. Accurate conical drug delivery requires that the operating mechanism of the delivery system respond only to the specific physiological conditions of the colon. Therefore, ongoing efforts have focused on the development of colon-specific delivery systems with improved site specificity and versatile drug release kinetics to meet various therapeutic needs. [53]

Among the recently developed colon-specific delivery systems, four were unique in terms of in vivo site specificity, design rationale, and manufacturing process feasibility (pressure-controlled colon-specific delivery capsules (PCDC), CODES, colonic delivery system-based system). Pectin and galactomannan coatings and azohydrogels). This review aims to provide detailed descriptions of the four systems in particular and in vitro/in vivo evaluation of colon-specific drug delivery systems in general. The specific targeting of drugs to the colon is known to have several therapeutic benefits. [54] Drugs destroyed by stomach acid and/or metabolized by pancreatic enzymes have some effect in the colon, and prolonged release of drugs from the colon may be useful in the treatment of nocturnal asthma, angina pectoris, and arthritis. Treatment of colon diseases such as ulcerative colitis, colon cancer and Crohn's disease is more effective when drugs are delivered

directly to the affected area. Similarly, the administration of vermicides and colonic diagnostic agents requires lower colonic doses. Prasad et al. developed a colon-specific oral tablet using guar gum as a carrier. [55]

Colonic drug delivery has grown not only in the delivery of drugs for local colonic disease, but also in the potential for delivery of proteins and therapeutic peptides. [56] To achieve successful colonic delivery, the drug must be protected from absorption and/or the upper gastrointestinal (GIT) environment and then rapidly released into the proximal colon, which is considered the optimal site for colonic drug delivery. . Targeting the colon is of course valuable in the local treatment of colon diseases such as Chronand#039 disease, ulcerative colitis, colon cancer and amebiasis. Peptides, proteins, oligonucleotides, and vaccines are potential candidates for colonic drug delivery. [57]

Drug release studies under conditions that mimic oral to colonic transit have shown that guar gum protects the drug from complete release in the physiological environment of the stomach and small intestine. With guar gum, ph. 6.8 is sensitive to bacterial enzyme activity in the large intestine and the drug is released. Oral pretreatment of rats with an aqueous dispersion of guar gum for 3 days induced an enzyme that acted specifically on guar gum [58], increasing drug release. The result shows the usefulness of guar gum as a possible carrier for the specific transport of drugs in the large intestine. A novel colon-specific drug delivery system based on the polysaccharide guar gum was evaluated in healthy male volunteers using gamma scintillation studies using technetium 99m-DTPA as a tracer. It was found that some of the label on the surface of the tablets was released in the stomach and small intestine, and most of the label in the tablet mass was found in the large intestine. The time for the tablets to reach the large intestine was 2-4 hours. After the tablets entered the large intestine, they were found to disintegrate. In vitro release studies of added 5-fluorouracil were performed in simulated gastric and intestinal fluids. The in vitro release profile in the presence of azoreductase in intestinal flora culture followed a zero-order model. [59]

CONCLUSION

Several laboratories in India are actively engaged in the development of drug delivery system pharmaceutics. They are studied in vitro for release pattern and in some cases in vivo in animals for pharmacokinetics, but less often for efficacy. Little information is available from clinical trials and the benefits of DDS in patients. The involvement of pharmacologists in the study of pharmacokinetics and pharmacodynamics of DDS is essential if the products are to achieve the relevant result of clinical use.

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FIGURE 1.

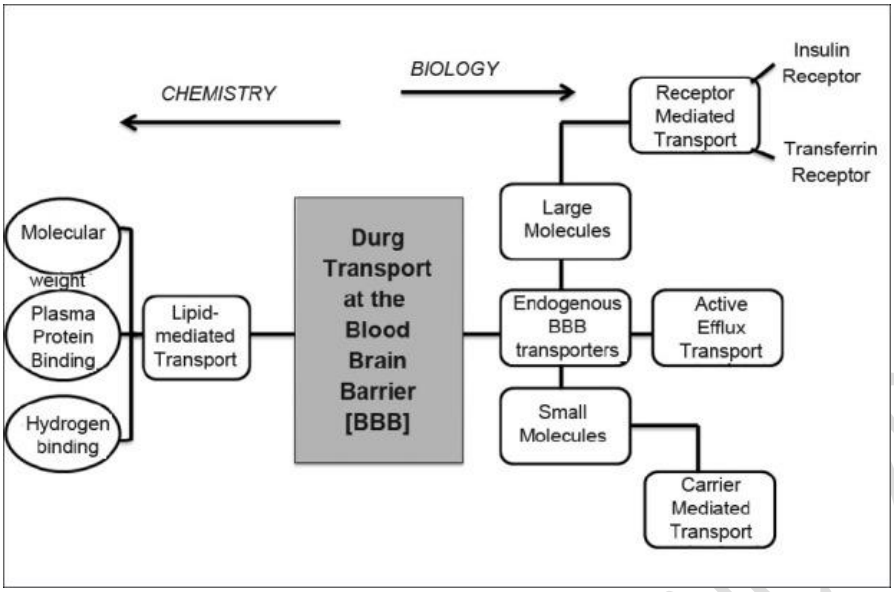
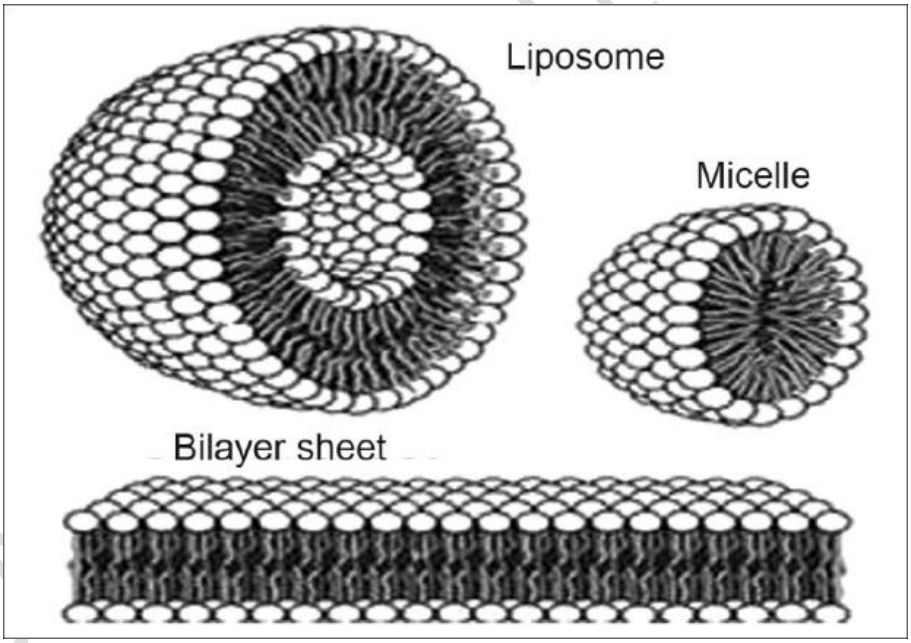

CHEMISTRY
BIOLOGY
Insulin Receptor
Receptor Mediated Transport
Transferrin Receptor
Large Molecules
Molecular weight
Plasma Protein Binding
Hydrogen binding
Lipid-mediated Transport
Durg Transport at the Blood Brain Barrier [BBB]
Endogenous BBB transporters
Active Efflux Transport
Small Molecules
Carrier Mediated Transport

FIGURE 2.


Liposome
Micelle
Bilayer sheet