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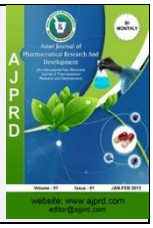

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Review Article

A Review on the Drug Delivery System

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A B S T R A C T

Drug administration is the mechanism or procedure by which a medicinal substance is delivered to produce a beneficial result in humans or animals. Nasal and pulmonary drug delivery pathways are gaining growing significance for the treatment of human illnesses. Such routes provide promising alternatives to the delivery of parenteral drugs particularly for peptide and protein therapies. Many drug delivery devices have been developed for this purpose, and are being tested for nasal and pulmonary delivery. These contain amongst others liposomes, proliposomes, microspheres, gels, prodrugs, cyclodextrins. Nanoparticles made up of biodegradable polymers show confidence that they meet the stringent criteria imposed on such delivery systems, such as the ability to be transferred to an aerosol, stability against forces produced during aerosolisation, biocompatibility, targeting of particular sites or cell populations in the lungs, predetermined release of the drug and degradation within the lungs

Keywords: infected hearts, infectious disorders, liposomal diseases, respiratory diseases, micelles, transdermal diseases

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INTRODUCTION

New drug molecule production is costly, and time consuming. The effort was made to boost the safety effectiveness ratio of "traditional" medications using different approaches, such as individualizing drug delivery, dose titration, and tracking of prescription drugs. Many very appealing approaches are drug distribution at a controlled pace, gradual distribution, guided delivery, and have been followed vigorously. It is important to note that substantial study and several publications from the USA, Europe are published by Indian researchers.[1–3] Several animal and human studies have produced an improved knowledge of the pharmacokinetic and pharmacodynamic rules regulating the function and disposition of potent opioid analgesics, anesthetic agents for inhalation, sedative / hypnotic agents, and muscle relaxation Such findings show that skin and buccal and nasal mucous membranes should be used as potential means of analgesic delivery and anesthetic. Related advances of other substances have created a multitude of new technologies, principles and techniques called Controlled Release Technology (CRT) together. Several examples of CRTs include transdermal and transmucosal controlled release delivery systems, ml6 nasal and buccal aerosol sprays, drug-impregnated lozenges, encapsulated cells, oral soft gels, iontophoretic devices used to administer drugs through the skin, and a variety of programmable, embedded drug delivery devices. There are several reasons that stimulate interest in exploring these new technologies, principles, and techniques. Conventional methods of administering drugs, while widely used, have many problems that these methods may potentially overcome. Equally significant, these developments may appear desirable in comparison to the costs of producing new medicines. Growing research and development prices, alternate funding options for drug companies, fewer pharmaceutical testing companies and the loss of successful patent life have culminated in a reduction in new chemical organizations being developed since the late 1950s. It is currently projected that taking a new drug into research, clinical trials, growth, and regulatory approval would take a decade, and cost well over $120 million. By 2000, new drug delivery technologies could

account for as much as 40 percent of medication products sold in the US[4–6].

BEADED DELIVERY SYSTEM

While not used for oxybutyline, beaded delivery formulations are another approach used to attain long-acting amounts of treatment combined with the ease of once-a-day dosing. This device is known as Detrol LA (Pharmacia, Peapack, NJ) and has been successfully connected to tolterodine tartrate. The beaded network basically consists of many, tiny beads composed of inert substances (such as polystyrene). The active drug is encased in a delivery capsule and overlaid on the beads. This system 's drug distribution is acid-sensitive, because drug levels are dependent on release on gastric acidity. This method generates a pharmacokinetic pattern roughly similar to a zero-order sequence, with C max being collected roughly 4 to 6 hours after intake, and sustained amounts observed 24 hours after initial dose. Comparative benefits for both effectiveness (improved levels of incontinence) and tolerability of Detrol LA over tolterodine that is released instantly are shown. In a double-blind, placebo-controlled, randomized trial of 1529 patients, the LA formulation resulted in 18 percent fewer episodes of incontinence than tolterodine of immediate release, although both formulations were significantly superior to placebo in minimizing urinary frequency and raising the amount of voided urine. The average dry mouth score for tolterodine LA was 23 per cent lower than tolterodine issued immediately. Withdrawal tariffs were identical for all weapons. Van Kerrebroeck concluded that the tolterodine formulation of LA was equivalent to the formulation for immediate release [7–8].

LIPOSOMAL DRUG DELIVERY SYSTEM

In practice, drug delivery systems can provide increased efficacy and/or decreased toxicity for anticancer agents. Long circulating macromolecular carriers such as liposomes can take advantage of the 'enhanced permeability and retention' effect for advantageous extravasation from tumor vessels.[4] Highly effective drug encapsulation has been accomplished by liposomal anthracyclines, resulting in substantial anti-cancer action with decreased cardiotoxicity and includes variants with extremely prolonged circulation, such as liposomal da Pegylated liposomal doxorubucin has shown significant effectiveness both as monotherapy and in conjunction with other chemotherapeutics in the treatment of breast cancer. Additional liposome constructs for supplying other drugs are being developed. Real molecular targeting will be used in the next generation of delivery systems; immunoliposomes and other ligand-directed structures represent an alignment of biological components capable of tumor detection with delivery technologies.

As discussed above, currently licensed liposomal drug delivery systems have reliable structure, have better pharmacokinetics and a degree of 'passive' or 'physiological' targeting of tumor tissue.[6] However, these carriers do not target tumor cells directly. Also avoiding interactions with tumor cells are architecture modifications that shield liposomes from unwanted interactions with plasma proteins and cell membranes, and that contrast them with reactive carriers like cationic liposoms. Rather, liposomes act as a drug-loaded depot within tumor stroma until extravasation into the tumor tissue. Liposomes gradually are susceptible to enzymatic degradation and/or phagocytic attack, resulting in the release of the drug into tumor cells for subsequent diffusion. The next generation under development of drug carriers features direct molecular targeting of cancer cells through antibody-mediated or other ligand-mediated interactions.

Immunoliposomes, in which mAb fragments are conjugated to liposomes, constitute a method for molecularly controlled drug delivery.[9] Anti-HER2 immunoliposomes were formed with either Fab' or scFv fragments linked to long-circulating liposomes. In preclinical experiments, anti-HER2 immunoliposomes are efficiently bound and internalized in HER2-over-expressing cells, resulting in the efficient distribution of encapsulated agents intracellularly. Anti-HER2 immunoliposomes primed with doxorubicin demonstrated effective and selective anti-cancer action against HER2-over-expressing tumors, including dramatically higher effectiveness than all other therapies studied (free doxorubicin, liposomal doxorubicin, free mAb [trastuzumab], and trastuzumab variants of doxorubicin or liposomal doxorubicin[10].

The immunoliposome approach provides a variety of statistical benefits relative to other approaches based on an antibody. The transmission of doxorubicin anti-HER2 immunoliposome that bypass the prohibitive cardiotoxicity associated with combined trastuzumab plus doxorubicin care. Anti-HER2 immunoliposomes can be built using scFv, which lacks antiproliferative action unlike trastuzumab, is incapable of antibody-dependent cell cytototoxicity, and needs threshold amounts of HER2 expression for transmission. Unlike drug immunoconjugates, which consist of a limited number of drugs (typically < 10 drugs per mAb) directly linked to selected residues on the mAb via linkers, immunoliposomes leverage the exponentially greater ability of drug-loaded liposomes (up to 104 drugs per liposome). Immunoliposomes do tend to be non-immunogenic and capable of long dissemination even with repeated administration.[12] In combination with polymer systems, an antibody-based targeting is also being developed. Similarly, ligand-based targeting is pursued in conjunction with both liposomes and polymers using growth factors, hormones, vitamins (e.g., folate), peptides, or other specific ligands. Liposomes are concentratebilayered structures composed of amphipathic phospholipids and are categorized as multilamellar (MLV), small unilamellar (SUVs), or large unilamellar (LUVs), based on the number of bilayers. Which vary in diameter from 0.025-10 µ. The liposomal size and morphology are controlled by the preparation process and composition. Liposomes are used for drug distribution, vaccine production and genomes for a number of disorders[13].

Infectious diseases

Bacchawat and collaborators developed and studied liposomal amphotericin in animal models of fungal infection and leishmaniasis. Kshirsagar and colleagues changed the recipe, developed a sterile pyrogen-free liposomal amphotericin preparation called "Patient

Worthy," and tested it in patients with chronic fungal infections and leishmaniasis. In patients with systemic fungal infection, it was shown to be healthy causing slightly fewer adverse effects compared with simple amphotericin, did not cause nephrotoxicity and could be prescribed to patients with renal injury. It has been used in fluconazole-resistant patients and in simple amphotericin. Like Ambisome (USA), which has to be used at 3 mg / kg / day dosage, this is safe at a dose of 1 mg / kg / day. The same group used the Aspergillus murine style to test various dose regimens of liposomal amphotericin. Liposomal amphotericin was found to be more effective than the comparable dose of free amphotericin B given after a challenge to fungal spore. A large single dose of liposomal amphotericin was more effective than two separated doses, whether administered before or after spore challenge.[14] This was tested in patients with visceral leishmaniasis and shown to be beneficial in patients who had not reacted to antimony, pentamidine and amphotericin. Thanks to its efficacy it can be prescribed at a dosage of 3 mg / kg / day thereby reducing the overall medication time. This was used extensively in an baby with acute leishmaniasis. It is the first liposomal formulation that was developed outside the USA and used in patients. Liposomes with grafted ligand have been developed in an effort to enhance effectiveness and further reduce toxicity. Pentamidine isethionate and its methoxy analog have been encapsulated in liposomes grafted with sugar and tested in vivo against laboratory leishmaniasis. Compared to normal liposome encapsulated drug or free drug, it was shown that sugar grafted liposomes particularly the mannose grafted ones were potent [15].

DRUGS TO FIGHT CANCER

Drugs for anticancer provide existing research on the therapeutic and experimental effects of toxic and non-toxic cancer agents that are primarily aimed at breakthroughs in the treatment of cancer. Mukhopadhya developed antineoplastic drug conjugate daunomycin (DNM) with maleylated serum bovine albumin. The multidrug-resistant version JD100 of the murine-macrophage tumor cell line J774A.1 was picked up with high efficiency via the scavenger receptors resulting in DNA synthesis cessation. Another group of researchers developed and tested a thermosensitive liposomal taxol formulation (heat-mediated, guided drug delivery) in murine melanoma. The harmful side effects of cremophor that is used as an excipient due to poor aqueous solubility of taxol have. Temperature-sensitive liposomes that encapsulate taxol were prepared in conjunction with ethanol using egg phosphatidylcholine and cholesterol. The liposomes have a intermediate step temperature of 43 ° C.[16] In tumor carrying mice infected with a mixture of hyperthermia and theromosensitive liposome encapsulated taxol, a substantial decrease in tumor volume was found compared with animals treated with free taxol with or without hyperthermia in B16F 10 murine melanoma transplanted into C57BI/6 mice. The use of polyvinylpyrrolidone nanoparticles containing taxol prepared by reverse microemulsion process was also explored by Sharma et al. Nanoparticles were observed to have a scale of 50-60 nm. In B16F10 murine melanoma transplanted into C57 B 1/6 mice, the antitumor activity of taxol was measured. The in vivo efficacy of taxol containing nanoparticles as calculated by tumor volume reduction and improved survival time was substantially greater than that of the corresponding free taxol concentration. [17]

OTHER CONTROLLED DRUG DELIVERY SYSTEM

Extended release, slow release and continuous release preparation were developed by pharmaceutical industry and pharmacy departments and investigated for release pattern in vitro and bioequivalence in vivo. [18].

Oral medicine

The oral administration of protein and peptide medications, appropriate instruments for delivering microspheres specifically inserted into the intestine by the therapeutic agent, is a great requirement. Gelatin capsules were filled with specific sodium alginate concentrations and cross-linked with sufficient calcium chloride concentrations, and tested in vitro for exposure to gastric and intestinal media. Gelatin capsules coated with 20 percent w / v of the polymer, which provided the most positive in vitro outcome, have been evaluated for their in vivo gastrointestinal tract actions in human volunteers. Radiographical tests indicate that although the uncoated gelatin capsules disintegrated in the stomach within 15 minutes of ingestion, the alginate-coated gelatin capsules remained intact as long as they were retained in the stomach (up to 3 hours) and then migrated to and disintegrated into the ileocecal region of the intestine. [19-28]. The pellets were coated with ethylcellulose and evaluated for release in vitro, using USP dissolution devices. They observed that PCPM release may be decreased with increasing amounts of ethylcellulose. Rangaiah et al . prepared and analyzed the theophylline's sustained release tablets using Eudragit RL, RS, and Hydroxy propyl methyl cellulose. Studies of bioavailability in volunteers have shown that HPMC and Eudragit formulation provided the drug's continuous plasma concentration. One group 35 developed sustained release capsules of nifedipine providing an initial rapidly usable loading dose in the form of solid dispersion and a sustained release component as microparticles coated with polyvinyl acetate (M.wt 45,000) film using a modified Wurster coating device. The products received initial release of the therapeutic dose of the drug in less than 45 min and sustained r The same group produced a diffusion cell from a topical aerosol formulation for evaluating product release. [29].

Parenteral

Kushwaha used a blend of synthetic polymer polyvinyl alcohol and natural macromolecule gum Arabica and found that the duration and release of the drug depended on the amount of drug loaded into the matrix and the solubility of the drug in the matrix and release medium. The downside of this method is that by changing the plasticizer, homopolymer, and cross linker structure, the release kinetics of the drug from the method can be adjusted to. For the controlled delivery of progesterone, chitosan microspheres of 45-300 μ were used. [30] The in vitro and in vivo release was tested. It was shown that strongly cross-related spheres in 40 days produced just 35 percent of the added steroids, compared to 70 percent of the moderately cross-related spheres. Determination of the in vivo

bioavailability of the steroid through intramuscular injection into rabbits from microsphere formulation showed that a plasma concentration of 1-2 µg / ml was sustained for up to 5 months without a strong burst impact. The data suggest that cross-linked microspheres of chitosan would be an interesting system for long-term steroid delivery. Cross-connected dextran beads have been developed as a carrier for the development of a single contact vaccine delivery system. [31-33] Extensive research has been carried out into the delivery of drugs by biodegradable polymeric devices since bioresorbable surgical sutures entered the market two decades ago. Among the various classes of biodegradable polymers, thermoplastic aliphatic poly (esters) such as poly (lactide) (PLA), poly (glycolide) (PGA), and in particular lactide copolymer and glycolide (PLGA) have generated tremendous interest due to their excellent bio-compatibility, biodegradability and mechanical strength [34]. Most notably, they were Food and Drug licensed by the U.S. [35].

CONCLUSION

In several labs in India the clinical production of the drug delivery system is being followed with zeal. Those are being tested in vitro for sequence of release and, in some cases, in vivo for pharmacokinetics in animals but less commonly for efficacy. Information on clinical trials and the efficacy of the DDS in patients was incomplete. Pharmacologists ought to be interested in the analysis of DDS pharmacokinetics and pharmacodynamics when the drugs have achieved their significant result-clinical usage.

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