Journal of Pain & Relief
ISSN: 2167-0846
Robert, J Pain Relief 2022, 11:10
Mini Review Open Access

Treatment Routes of Drug Delivery Gaining Increasing Importance

Robert L*
Department of Medicine and Health Sciences, Universiti Sultan Zainal Abidin, Malaysia

Abstract

Drug delivery systems can in principle provide enhanced efficacy and reduced toxicity for anticancer agents. Long circulating macromolecular carriers such as liposomes can exploit the enhanced permeability and retention' effect for preferential extravasation from tumor vessels.

Keywords: Liposomes; Circulation; Dopamine; Solubility; Brain; Chemotherapeutic agents

Introduction

Liposomal anthrax-cyclines have achieved highly efficient drug encapsulation, resulting in significant anticancer activity with reduced cardio-toxicity, and include versions with greatly prolonged circulation such as liposomal daunorubicin and pegylated liposomal doxorubicin Pegylated liposomal doxorubucin has shown substantial efficacy in breast cancer treatment both as mono-therapy and in combination with other chemotherapeutics. Additional liposome constructs are being developed for the delivery of other drugs. The next generation of delivery systems will include true molecular targeting; immune-liposomes and other ligand-directed constructs represent an integration of biological components capable of tumour recognition with delivery technologies [1]. As discussed, currently approved liposomal drug delivery systems provide stable formulation, provide improved pharmacokinetics, and a degree of passive or physiological targeting to tumour tissue. However, these carriers do not directly target tumour cells. The design modifications that protect liposomes from undesirable interactions with plasma proteins and cell membranes, and which contrast them with reactive carriers such as cationic liposomes, also prevent interactions with tumour cells. Instead, after extravasation into tumour tissue, liposomes remain within tumour stroma as a drug-loaded depot. Liposomes eventually become subject to enzymatic degradation and/or phagocytic attack, leading to release of drug for subsequent diffusion to tumour cells. The next generation of drug carriers under development features direct molecular targeting of cancer cells via antibody-mediated or other ligand-mediated interactions [2]. Immuno-liposomes, in which fragments are conjugated to liposomes, represent a strategy for molecularly targeted drug delivery [3]. Anti- immuno-liposomes have been developed with either Fab or fragments linked to long-circulating liposomes. In preclinical studies, anti-immuno-liposomes bound efficiently to and internalized in overexpressing cells, resulting in efficient intracellular delivery of encapsulated agents. Anti-immuno-liposomes loaded with doxorubicin displayed potent and selective anticancer activity against overexpressing tumours, including significantly superior efficacy versus all other treatments tested Anti-immuno-liposomes are currently undergoing scale up for clinical studies . The immune-liposome approach offers a number of theoretical advantages as compared with other antibody-based strategies. Anti-immuno-liposome delivery of doxorubicin may circumvent the prohibitive cardio-toxicity associated with combined trastuzumab plus doxorubicin treatment. Anti-immuno-liposomes can be constructed using that, unlike trastuzumab, lack anti-proliferative activity, are incapable of antibody-dependent cellular cytotoxicity, and require threshold levels of expression for delivery. In contrast to drug immune-conjugates, which consist of a small number of drugs directly coupled via linkers to selected residues, immune-liposomes exploit the exponentially greater capacity of drug loaded liposomes [4]. Immuno-liposomes also appear to be non-immunogenic and capable of long circulation even with repeated administration. Antibody-based targeting is also being developed in conjunction with polymer systems. Similarly, ligand-based targeting using growth factors, hormones, vitamins, peptides or other specific ligands is being pursued in conjunction with both liposomes and polymers. Liposomes are concentric bi-layered structures made of amphipathic phospholipids and depending on the number of bilayer, liposomes are classified as multi-lamellar, small uni-lamellar, or large uni-lamellar. The size and morphology of liposomes are regulated by the method of preparation and composition. Liposomes are used for delivery of drugs, vaccines, and genes for a variety of disorders. Bacchawat and co-workers developed liposomal amphotericin and investigated it in animal models of fungal infection and leishmaniasis. Kshirsagar and co-workers modified the formulation, developed a Patient Worthy sterile pyrogen free liposomal amphotericin preparation and investigated it in patients with systemic fungal infections and leishmaniasis [5]. It was found to be safe producing significantly less adverse effects compared to plain amphotericin in patients with systemic fungal infection, did not produce nephrotoxicity and could be given to patients with renal damage. It was effective in patients resistant to fluconazole and plain amphotericin [6]. The same group studied different dosage regimens of liposomal amphotericin using Aspergillus murine mode. It was found that liposomal amphotericin was more effective than equal dose of free amphotericin B given after fungal spore challenge. A large single dose of liposomal amphotericin was more effective, whether given before or after spore challenge, than given as two divided doses. It was investigated in patients with visceral leishmaniasis and found to be effective in patients who had not responded to antimony, pentamidine, and amphotericin. Because of its safety, it can be given at 3 mg/kg/day dose thus reducing total duration of treatment. It was successfully used in a child suffering from visceral leishmaniasis. This is the first liposomal preparation developed outside of USA, which has been used in patients.

***Corresponding author:** Robert L, Department of Medicine and Health Sciences, Universiti Sultan Zainal Abidin, Malaysia, Tel: 08572222264, E-mail: smeet762@gmail.com

Received: 23-Sep-2022, Manuscript No. JPAR-22-78242; **Editor assigned:** 26-Sep-2022, PreQC No. JPAR-22-78242 (PQ); **Reviewed:** 08-Oct-2022, QC No. JPAR-22-78242; **Revised:** 14-Oct-2022, Manuscript No. JPAR-22-78242 (R); **Published:** 21-Oct-2022, DOI: 10.4172/2167-0846.1000467

Citation: Robert L (2022) Treatment Routes of Drug Delivery Gaining Increasing Importance. J Pain Relief 11: 467.

In an attempt to improve efficacy and reduce toxicity further, liposomes with grafted ligand have been developed [7]. Pentamidine isethionate and its methoxy derivative were encapsulated in sugar grafted liposomes and tested against experimental leishmaniasis in vivo. It was seen that sugar grafted liposomes specially the mannose grafted ones were potent in comparison to normal liposome encapsulated drug or free drug. Anticancer drugs Anti-cancer drugs provide current information on the clinical and experimental effects of toxic and non-toxic cancer agents and are specifically directed towards breakthroughs in cancer treatment. Mukhopadhya developed conjugate of antineoplastic drug daunomycin with maleylated bovine serum albumin. It was taken up with high efficiency by multi drug resistant variant of the murine-macrophage tumour cell line through the scavenger receptors resulting in cessation of DNA synthesis [8]. A thermosensitive liposomal taxol formulation in murine melanoma was developed and studied by another group of workers. Cremophor which is used as excipient due to the low aqueous solubility of taxol has toxic side effects. Temperature-sensitive liposomes encapsulating taxol were prepared using egg phosphatidyl-choline and cholesterol in combination with ethanol. The liposomes have a phase transition temperature. A significant reduction in tumor volume was noted in tumor bearing mice treated with a combination of hyperthermia and thermo-sensitive liposome encapsulated taxol, compared to animals treated with free taxol with or without hyperthermia in murine melanoma transplanted into mice. Sharma also investigated the use of polyvinyl-pyrrolidone nanoparticles containing taxol prepared by reverse micro-emulsion method [9]. Pulmonary drug delivery offers several advantages in the treatment of respiratory diseases over other routes of administration. Inhalation therapy enables the direct application of a drug within the lungs. The local pulmonary deposition and delivery of the administered drug facilitates a targeted treatment of respiratory diseases, such as pulmonary arterial hypertension, without the need for high dose exposures by other routes of administration. The intravenous application of short acting vasodilators has been the therapy of choice for patients over the past decade. The relative severity of side effects led to the development of new prostacyclin analogues and alternative routes of administration. One such analogue, is a worldwide approved therapeutic agent for treatment. Inhalation of this compound is an attractive concept minimizing the side effects by its pulmonary selectivity. Unfortunately, the short half-life of iloprost requires frequent inhalation manoeuvres, ranging up to 9 times a day. Therefore, an aerosolizable controlled release formulation would improve a patient's convenience and compliance. Controlled drug delivery systems have become increasingly attractive options for inhalation therapies. A large number of carrier systems have been developed and investigated as potential controlled drug delivery formulations to the lung, including drug loaded lipid and polymer based particles. The use of colloidal carrier systems for pulmonary drug delivery is an emerging field of interest in medicine [10]. Physicochemical properties, morphology, encapsulation efficiency, in vitro drug release, stability of nanoparticles to nebulization, aerosol characteristics as well as pulmonary dye absorption and distribution profiles after nebulization in an IPL were investigated Among the various drug delivery systems considered for pulmonary application, nanoparticles demonstrate several advantages for the treatment of respiratory diseases, such as prolonged drug release, cell-specific targeted drug delivery or modified biological distribution of drugs, both at the cellular and organ level. It must first be recognized that formulating compounds and delivering them as aerosols is complex. Not only does it involve the formulation of a stable solution or suspension in a medium that is not as well characterized as other systems, but the resultant system is also subject to performance limitations. Due to these particle size constraints, as well as inhalation toxicology concerns, the range of possible excipients to choose from during the formulation phase is substantially reduced. Additionally, limiting the concentration of excipients in a formulation is crucial for maintaining adequate aerosol performance. Thus, given the complexity of this relationship, formulating aerosols is a challenging endeavour. Although, the successful formulation of drugs for pulmonary delivery provides a valuable therapeutic route. Upon introduction of the metered dose inhaler, medical treatment of lung diseases changed significantly. Since that time, they have become the most effective means of controlling symptoms of lung diseases such as asthma and chronic obstructive pulmonary disorder. More recently, formulation modifications were merited then chlorofluorocarbon propellants were linked to the depletion of the ozone layer. With the successful transition to new propellant systems, MDIs are still well accepted and highly utilized by patients across the globe today. Looking forward, the effectiveness, ease of use, and relatively low cost of aerosol preparations in combination with modifications in delivery technology and formulation sciences, will likely expand the treatment of diseases. Another, therapeutically undesirable aspect of pulmonary drug delivery is rapid absorption of most drugs from the lung, necessitating frequent dosing, e.g., of bronchodilators and corticosteroids. Liposomes are believed to alleviate some of the problems encountered with conventional aerosol delivery due to their ability to serve as a solubilisation matrix for poorly soluble agents, act as a pulmonary sustained release reservoir, and facilitate intracellular delivery of Targeting to brain. The great interest in mucosal vaccine delivery arises from the fact that mucosal surfaces represent the major site of entry for many pathogens. Among other mucosal sites, nasal delivery is especially attractive for immunization, as the nasal epithelium is characterized by relatively high permeability, low enzymatic activity and by the presence of an important number of immune-competent cells. In addition to these advantageous characteristics, the nasal route could offer simplified and more cost-effective protocols for vaccination with improved patient compliance. The use of nano-carriers provides a suitable way for the nasal delivery of antigenic molecules. Besides improved protection and facilitated transport of the antigen, nano-particulate delivery systems could also provide more effective antigen recognition by immune cells. These represent key factors in the optimal processing and presentation of the antigen, and therefore in the subsequent development of a suitable immune response. In this sense, the design of optimized vaccine nano-carriers offers a promising way for nasal mucosal vaccination. The usual non-invasive approach to solving the brain drug delivery problem, The water -soluble parts of the drugs restricts transport conversion of water-soluble drug into lipid-soluble pro-drug is the traditional chemistry driven solution to problem. The treatment of CNS diseases is particularly challenging because the delivery of drug molecules to the brain is often precluded by a variety of physiological, metabolic and biochemical obstacles that collectively comprise the Blood Brain barrier, blood cerebrospinal fluid barrier, Blood tumour barrier. The present outlook for patients suffering from many types of brain diseases remains poor, but recent developments in drug delivery techniques provide reasonable hope that the formidable barriers shielding the brain may ultimately be overcome. Drug delivery directly to the brain inter-stitium has recently been markedly enhanced through the rational design of polymer-based drug delivery systems. Substantial progress will only come about, however, if continued vigorous research efforts to develop more therapeutic and less toxic drug molecules are paralleled by the aggressive pursuit of more effective mechanisms for delivering those drugs to brain targets. Jain developed

dopamine hydrochloride bearing positively charged small liposomes by sonicating multi-lamellar vesicles and studied their physical attributes and drug leakage and release pattern. In vivo performance was assessed by periodic measurement of chlorpromazine induced catatonia in Sprague Dawley rats and was compared with plain dopamine hydrochloride, dopamine and levodopa carbidopa. The studies showed that dopamine can be effectively delivered into the brain and its degradation in circulation can be prevented by incorporating it into liposomes. Several drugs do not have adequate physiochemical characteristics such as high lipid solubility, low molecular size and positive charge which are essential to succeed in traverse. The thought behind this approach was to break down the barrier momentarily by injecting solution into arteries in the neck. The resulting high sugar concentration in brain capillaries takes up water out of the endothelial cells, shrinking them, thus opening tight junction. The effect lasts for minutes, during which time drugs diffuse freely, that would not normally cross. This method permitted the delivery of chemotherapeutic agents in patients with cerebral lymphoma, malignant glioma and disseminated CNS germ cell tumors. Physiological stress, transient increase in intracranial pressure, and unwanted delivery of anticancer agents to normal brain tissues are the undesired side-effects of this approach in humans.

Conclusion

The presence of wires and cables on the floor often made it impracticable for mechanical aids to be used. There is appreciable evidence of a causal association for kneeling/squatting, climbing stairs or ladders, heavy lifting, walking/standing, and slips and trips hazards as risk factors. The evidence of a causal association is plausible but less clear for jumps from height, driving and sitting.

Acknowledgement

None

Conflict of Interest

None

References

1. Świeboda P, Filip R, Prystupa A, Drozd M (2013) Assessment of pain: types, mechanism and treatment. Ann Agric Environ Med EU 1: 2-7.
2. Nadler SF, Weingand K, Kruse RJ (2004) The physiologic basis and clinical applications of cryotherapy and thermotherapy for the pain practitioner. Pain Physician US 7: 395-399.
3. Trout KK (2004)The neuromatrix theory of pain: implications for selected non-pharmacologic methods of pain relief for labor. J Midwifery Wom Heal US 49: 482-488.
4. Cohen SP, Mao J (2014) Neuropathic pain: mechanisms and their clinical implications. BMJ UK 348: 1-6.
5. Ozgoli G, Goli M, Moattar F (2009)Comparison of effects of ginger, mefenamic acid, and ibuprofen on pain in women with primary dysmenorrhea. J Altern Complement Med US 15: 129-132.
6. Raeder J, Dahl V (2009) Clinical application of glucocorticoids, antineuropathics, and other analgesic adjuvants for acute pain management. CUP UK: 398-731.
7. Mello RD, Dickenson AH (2008) Spinal cord mechanisms of pain. BJA US 101: 8-16.
8. Bliddal H, Rosetzsky A, Schlichting P, Weidner MS, Andersen LA, et al. (2000) A randomized, placebo-controlled, cross-over study of ginger extracts and ibuprofen in osteoarthritis. Osteoarthr Cartil EU 8: 9-12.
9. Maroon JC, Bost JW, Borden MK, Lorenz KM, Ross NA, et al. (2006) Natural anti-inflammatory agents for pain relief in athletes. Neurosurg Focus US 21: 1-13.
10. Birnesser H, Oberbaum M, Klein P, Weiser M (2004) The Homeopathic Preparation Traumeel® S Compared With NSAIDs For Symptomatic Treatment Of Epicondylitis. J Musculoskelet Res EU 8: 119-128.