Liposome as Effective Drug Delivery Systems: A Review

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ABSTRACT

Liposomes were the first drug to be considered on the nanoscale for clinical use in 1995. From that point forward, the innovation has developed extensively and continuing work in liposome-based delivery systems has achieved remarkable heights with necessary clinical developments. These contain long- looping liposomes, stimuli-responsive liposomes, nebulized liposomes, versatile liposomes for topical, oral and transdermal delivery and covalent lipid-based complexes for improved drug plasma membrane to bind particular organelles. While the regulatory evaluation of liposomes is very well documented, current guidelines that address new delivery systems are not clear. This article mainly discusses insight into the present class of new liposomal delivery systems and gives a basic review of the current documented guidelines encompassing the commercialization aspect of more significant level complexity systems, the normal requirements and the obstacles looked that by companies try to put up novel liposome-based systems for clinical use for sale to the public. At present "lipid-mediated" delivery is accepted by all pharmaceutical industries. So delivery of drug is an effective potential system in the drug industry.

Keywords - Clinical, Drug delivery, Immunology, Insoluble, Liposome, Nucleic acids

1. INTRODUCTION

This century has witnessed advances within the discipline of drug delivery. "Physician-endorsed, " drugs have basically made out of simple, quick acting substances intensifies that square measures are appropriated orally, as injectables or applied parentally (Gregoriadis,1 9 7 3) There is an urgent need for new drugs from the revelations of bioactive debris and citron treatments; pharmaceutical research holds tight the drop-off of yet one increasingly great headway (Gregoriadis,1976). These techniques of drug delivery show explicit issues, for instance, some medicinal drug potencies and remedial affects degree (Hong *et al.* 2019).The objective of all refined remedy conveyance frameworks in the end, is to ship medicines unblemished to explicitly target additives of the frame via a medium that could the board the treatment's organization by implying that of either a physiological or synthetic trigger to perform this objective moreover , new ideas on fundamental pharmacological drugs, pharmacodynamics, indistinct immunogenicity, bio-recognition and adequacy of drugs were created (Alahari *et al.*, 1998). The clinical software of maximum run of the mill chemotherapeutics is prohibited both with the aid of the weak point to carry restorative medication fixations to the target tissues or with the aid of extreme and dangerous lethal impacts on conventional organs and tissues to weaken sedate

corruption and misfortune, Thwart hazardous symptoms and to increase medicate bioavailability by means of enhancing medicinal drugs specializing in explicitness, various medicine conveyances and medicinal drugs specializing in frameworks square measures by and by below advancement (Poste *et al.*, 1976).

2. LIPSOMES

The name Liposomes is derived from two Greek words: 'Lipos' that signifies 'fat' and 'Soma' that signifies 'body'. Liposomes were initially made in a European country in 1961 by Alec D. Bangham,. (Juliano and Stamp, 1978; Sessa and Weissmann, 1970). The United Nations organization learns phospholipids and turning sour three Alec Bangham introductory depicted anyway layer particles, for example phospholipids, move with water to make unmistakable structures at present perceived as liposomes and found that phospholipids joined with water straightforwardly formed a circle because one completion of each atom is water solvent, while the contrary completion is water -insoluble (Gregoriadis and Florence, 1993). Water solvent prescriptions side to the water bait inside the total of the hydrophobic finishes; fat-dissolvable meds are consolidated into the phospholipid layers (Noble *et al*., 2014). Lipids are amphipatic molecules with water-friendly and water-hating parts.

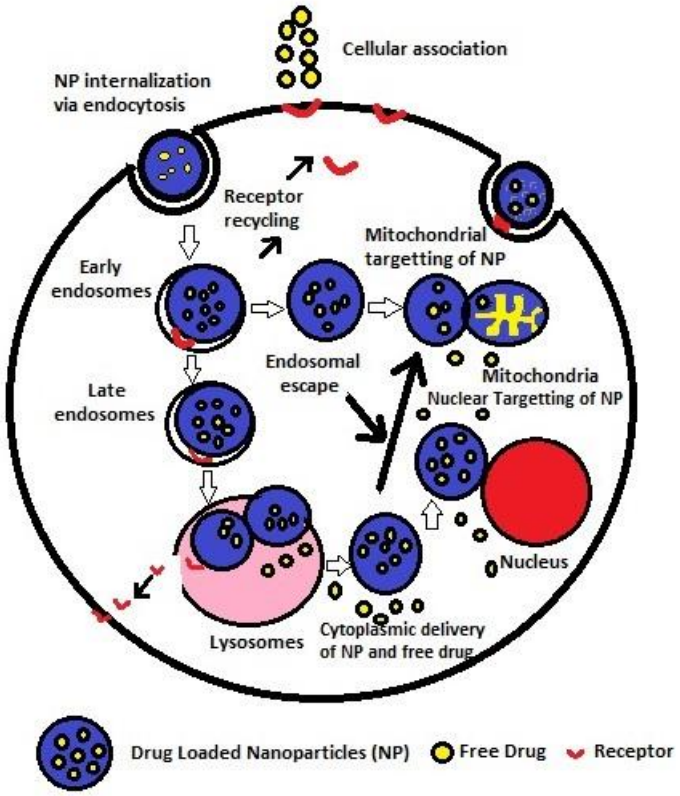

Figure 1: Schematic diagram indicates Liposome incapsulation for drug delivery system .

3. PHARMACOSOME FOR POORLY SOLUBLE DRUG

The term pharmacosome is used to help the bioavailability of much less solvent or inadequately dissolvable drug. Pharmacosome are made by reducing part bonds between medicine and amphiphilic phospholipids. In

sum, there may be likewise valence, power, and H securities amongst the delivery system (Semalty *et al*., 2010). Pharmacosome are found within the type of molecule, comparable to hexangular teams (Shivhare *et al*., 2012). Therefore, in case of dissolution of drugs in pharmacosome is a much higher medicine. *(*Li *et al* 2019). A study showed that the pharmacosome of aceclofenac drug provided a 100% higher disintegration profile than free aceclofenac molecule, corrosive once investigated through diverse strategies (Leserman *et al*., 1980). But not soley about disintegration rate, anyway moreover., solvency turned into resolved to be progressed in the pharmacosome than free corrosive kind. In step with the past report, for the reason that the drug was maintained inside the pimple , it stepped forward the electricity of the prescription *(*Lee H ***et al*** 2017 *)* There is also the adaptability of the exploitation pharmacosome-embodied prescription since is going to manipulate orally, topically, and extra-or intra-vascularly. (Wu .Y . *et al* 2018)

4. RECEPTOR MEDIATED ENDOCYTES WITH LIPOSOMES

Receptor- mediated endocytosis is created through the exact authoritative of antibodies to objective cells and in the cysts (Leserman *et al*., 1980; Straubinger *et al*., 1983). For an explicit official of antibodies and growth, there were numerous procedures were being created. An examination directed by (Heath *et al*., 1983) indicated that a counter- acting agent focused on sore will extensively improve the harmfulness of metastatic tumor drugs to the way of living cells (Heath *et al*., 1983). Antibody-focused pimples limited their dispersion exclusively to the objective site and discharged from the body quickly in this way, and they show the least danger (Balchandran *et al*., 2018). Another examination also prompted that everyone component that compass to the objective site cannot build the convergence of medication to the target (Riviere *et al*., 2011). Before dealing with novel delivery to the objective site, there zone unit a few impediments like sorts of tumor and scope of physiological obstructions should be considered (Bulbake U *et al.,* 2017*)*. Attaching the tumor cells and tumor porosity territory unit shifted wagering on the molecule size of the pimple. Connection to the immune response will direct the circulation of growth inside the mind. The coupling conjugates of growth with cerebrum tranquilize transport vector passes the blood-mind boundaries through receptor-interceded transcytosis and assimilation directed transcytosis (Charrois and Allen, 2003; Bibi *et al*., 2012; Mok and Cullis, 1997; Hirko *et al*., 2003).

5. SYSTEM OF VACCINE DELIVERY THROUGH LIPOSOMES

The safety and efficacy of the liposomal mediated drug response makes it a decent alternative for mesenchymal undifferentiated cell- based treatment to convey the viral quality. This is a favoured medication suitable for the antibody and antigen because it has an absence of immunogenicity, insignificant harmfulness and can capture huge quality for demand. (Wang *et al*., 1995; Filion and Phillips, 1997). At an assortment of infections are treated with liposomal antigen-based delivery of medicine. Antibody and protein encapsulated in liposomes utilize different micelles of parts like lipid surfactants and other dissolvable (Pastorino *et al*., 2006; Madeira *et al*., 2010; Shilpa *et al*., 2011; Wassef *et al*., 1994). Liposomal novel delivery is of great importance for antibody is set up by blending different mixes like organisms to be inoculated, antigen in solvent structure, and cytokines from DNA and liposome. Antigens are typically covalently clung to the liposomal membrane (Allison and Gregoriadis, 1974). Liposome in immunological treatment were first utilized for diphtheria toxicity to improve safe reactions. (Nageeb El-Helaly *et al* , 2017)

6. DELIVERY OF NUCELIC ACID THROUGH LIPOSOMES

The delivery of nucleic acid -based pairs is seen in neighbourhoods than fundamental zone of the protein active site, regardless of the fact that there are numerous cationic lipids that have been mixed as of late, and next to directing them, there were important harmful symptoms that were watched. It is apparent that DNA or other nucleic acids conjugated with ligand-bearing liposome have demonstrated a huge increase in first-rate articulation than non-focused on conveyance of nucleic acids. .(Kim JS *et al* 2016). There are sorts of vectors utilized in liposomal DNA the conveyance, such as LPD-I and LPD-II (liposome ensnared, polycation-consolidated DNA). These two vectors are relatively flexible and secure vectors than other. The latest utilizations of liposome is DNA immunization and great treatment to treat disease approximately by using hereditary inadequacies (Gregoriadis, 1995).

7. LIPOSOME IN CANCER MEDICAL AID

The principal drawback of the antineoplastic prescription is their low remedial report inferable from low restorative document traditional doses of those that are required for implied sway makes lethality normal cells. (Zylberberg C *et al.* 2016). Directed conveyance of medicine to the improvement cells by way of vesicle are altered as example of malignancy treatment. (Burns N *et al*. 2018) . Because of the focused-on conveyance of cytotoxic antineoplastic prescription, its poisonous fine has been diminished fantastically than conveyance of loose antineoplastic medicine. The barrier of adversity to neoplastic prescription drastically swelled its life, weakened its corruption rate, extended affidavit in the development cells, and constrict take-as much as conventional cells. Liposomes with inactively centred on development cells will make bigger tube-molded shape porosity. Doxil, Caelyx and Myocet area unit some generally utilized liposomal detailing utilized in malignant boom treatment. (Hong .C. *et al.* 2019)

8. CONCLUSION

Liposomal drug delivery systems have grown up since their modest beginnings of more than fifty years ago.FDA has approved over dozens of liposome-based drug delivery systems and many more are in different phases of development. The FDA's some conclusions on clinically approved particulate drug delivery systems have helped commercialization endeavors. However, with the rapid speed of development of liposome-based drug delivery systems, regulatory ethics have not kept as, and hence regulatory demands are still obsolete. This increases responsibility of researchers working on the generation of new systems through the development process , thus giving insight into the regulatory body about updates regarding the potency and efficacy of these products .For approval of the drug , an open exchange between industry and scholarly world is deliberately required to encourage the full clinical capability of liposomal drug delivery systems .

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10. REFERENCES

Akbarieh, M, Besner, J.G, Galal, A., and Tawashi, R. 1992. Liposomal delivery system for the targeting and controlled release of praziquantel. *Drug Dev Ind Pharm*, 18: 303–317.

Alahari, S.K, DeLong, R., Fisher, M.H., Dean, N.M., Viliet, P., Juliano, R. L. 1998. Novel chemically modified oligonucleotides provide potent inhibition of P-glycoprotein expression. *Journal of Pharmacology and Experimental Therapeutics*, 286 (1): 419-428.

Allison A.G., Gregoriadis G. 1974. Liposomes as immunological adjuvants. *Nature*, 252:252.

Balachandran B, Yuana Y. 2020.Extracellular vesicles-based drug delivery system for cancer treatment. Cogent Medicine .13. 432-435

Bangham, A.D., Standish, M.M., Watkins, J.C. 1965. Diffusion of univalent ions across the lamellae of swollen phospholipids. *Journal of Molecular Biology*, 13(1):238-52.

Bibi, S., Lattmann, E., Mohammed, A.R., Perrie, Y. 2012. Trigger release liposome systems: Local and remote controlled delivery? *Journal of Microencapsul*, 29:262-76.

Bulbake U, Doppalapudi S, Kommineni N, et al. Liposomal formulations in clinical use: an updated review. Pharmaceutics. 2017;9(2).

Burns N, Shuken SR, Mercer JAM, et al. 2018. The Board of Trustees of the Leland Stanford Junior University. Ladderane lipid compounds and liposomes and methods of preparing and using the same. WO2018045094; 2018.

Charrois, G.J., Allen, T.M. 2003. Rate of biodistribution of stealth liposomes to tumor and skin: Influence of liposome diameter and implications for toxicity and therapeutic activity. *Biochim Biophysics Acta*, 1609:102-8.

Filion, M.C., Phillips, N.C. 1997. Toxicity and immunomodulatory activity of liposomal vectors formulated with cationic lipids toward immune effector cells. *Biochimica et Biophysica Acta(BBA)- Biomembranes*, 1329:345-56.

Gregoriadis, G. 1973. Drug entrapment in liposomes. *FEBS Letters*, 36(3):292-6.

Gregoriadis, G. 1976. The carrier potential of liposomes in biology and medicine (second of two parts). The *New England Journal of Medicine*, 295(14):765-770.

Gregoriadis, G. 1995. Engineering liposomes for drug delivery: Progress and problems. *Trends in Biotechnology*, 13:527-37.

Gregoriadis, G., Florence, A.T. 1993. Liposomes in Drug Delivery. Clinical, Diagnostic and Ophthalmic Potential. Drugs, 45:15-28.

Heath, T.D., Montgomery, J.A., Piper, J.R., Papahadjopoulos, D. 1983. Antibody-targeted liposomes: Increase in specific toxicity of methotrexate-gamma-aspartate. *Proceedings of the National Academy Sciences of the United States of India*, 80:1377-81.

Hirko, A., Tang, F., Hughes, J.A. 2003. Cationic lipid vectors for plasmid DNA delivery. *Current Medicinal Chemistry*, 10:1185-93.

Hong C, Wang D, Liang J, et al. Novel ginsenoside-based multifunctional liposomal delivery system for combination therapy of gastric cancer. Theranostics. 2019;9-4437-49

Juliano, R.L., and Stamp, D. 1978. Pharmacokinetics of liposome-encapsulated anti-tumor drugs: Studies with vinblastine, actinomycin D, cytosine arabinoside, and daunomycin. Biochemical Pharmacology, 27(1):21-27.

Kimelberg, H.K., Tracy, T.F. Jr, Biddlecome, S.M., Bourke, R.S. 1976. The effect of entrapment in liposomes on the *in vivo* distribution of [3H] methotrexate in a primate. *Cancer Res*, 36(8):2949-57.

Lee H, Shields AF, Siegel BA, et al. 2017. (64)Cu-MM-302 positron emission tomography quantifies variability of enhanced permeability and retention of nanoparticles in relation to treatment response in patients with metastatic breast cancer. Clin Cancer Res. 23:4190–202.

Leserman, L.D., Weinstein, J.N., Blumenthal, R., Terry, W.D. 1980. Receptor-mediated endocytosis of antibody-opsonized liposomes by tumor cells. *Proceedings of the National Academy Sciences of the United States of India*, 77:4089-93.

Li M, Du C, Guo N, et al. 2019. Composition design and medical application of liposomes. Eur J Med Chem. 164:640–53.

Madeira, C., Mendes, R.D., Ribeiro, S.C., Boura, J.S., Aires- Barros, M.R., da Silva, C.L. 2010. Nonviral gene delivery to mesenchymal stem cells using cationic liposomes for gene and cell therapy. *Journal of Biomedicine and Biotechnology*, 735349.

Mok, K.W., Cullis, P.R. 1997. Structural and fusogenic properties of cationic liposomes in the presence of plasmid DNA. *Biophysical Journal*, 73:2534-45.

Mozafari, M.R. 2005. Liposomes: An overview of manufacturing techniques. Cellular and Molecular Biolology Letter, 10(4):711-9.

Nageeb El-Helaly S, Abd Elbary A, Kassem MA, et al. 2017. Electrosteric stealth Rivastigmine loaded liposomes for brain targeting: preparation, characterization, ex vivo, bio-distribution and in vivo pharmacokinetic studies. Drug Deliv. 24:692–700

Noble, G.T., Stefanick, J.F., Ashley, J.D., Kiziltepe, T., Bilgicer, B. 2014. Ligand-targeted liposome design: Challenges and fundamental considerations. Trends in Biotechnology, 32(1):32-45.

Pastorino, F., Brignole, C., Di, Paolo, D., Nico, B., Pezzolo, A., Marimpietri, D. 2006. Targeting liposomal chemotherapy via both tumor cell-specific and tumor vasculature- specific ligands potentiates therapeutic efficacy. *Cancer Research*, 66:10073-82.

Piffoux M, Silva AKA, Wilhelm C, et al. 2018. Modification of extracellular vesicles by fusion with liposomes for the design of personalized biogenic drug delivery systems. ACS Nano. 12:6830–42. 96.

Poste, G, Papahadjopoulos, D., 1976. Lipid vesicles as carriers for introducing materials into cultured cells: Influence of vesicle lipid composition on mechanism (s) of vesicle incorporation into cells. Proc. Natl Acad Sci, 73:1603-1607.

Riviere, K., Huang, Z., Jerger, K., Macaraeg, N., Szoka, F.C., Jr. 2011. Antitumor effect of folate-targeted liposomal doxorubicin in KB tumor-bearing mice after intravenous administration. *Journal of Drug Targeting*, 19:14-24.

Semalty, A., Semalty, M., Rawat, B.S., Singh, D., Rawat, M.S. 2010. Development and evaluation of pharmacosomes of aceclofenac. Indian J Pharm Sci, 72(5):576-581.

Sessa, G., Weissmann, G. 1970. Incorporation of lysozyme into liposomes. A model for structure-linked latency. *Journal of Biological Chemistry*, 245:3295-301.

Shilpa, S., Srinivasan, B.P., Chauhan, M. 2010. Niosomes as vesicular carriers for delivery of proteins and biologicals. International Journal of Drug Delivery, 3:14-24.

Shivhare, R, Pathak, A, Shrivastava, N, Singh, C, Tiwari, G, Goyal, R. 2012. An update review on novel advanced ocular drug delivery system. *World journal of pharmacy and pharmaceutical sciences*, 1:545-68.

Straubinger, R.M., Hong, K., Friend, D.S., Papahadjopoulos, D. 1983. Endocytosis of liposomes and intracellular fate of encapsulated molecules: Encounter with a low pH compartment after internalization in coated vesicles. *Cell*, 32:1069-79.

Wang, S., Lee, R.J., Cauchon, G., Gorenstein, D.G., Low, P.S. 1995. Delivery of antisense oligodeoxyribonucleotides against the human epidermal growth factor receptor into cultured KB cells with liposomes conjugated to folate via polyethylene glycol. *Proc Natl Acad Sci U S A*, 2:3318-22.

Wassef, N.M., Alving, C.R., Richards, R.L. 1994. Liposomes as carriers for vaccines. *ImmunoMethods*, 4:217-222.

Wu Y; 2018 Jiangsu Mendel Gene Technology Co., Ltd. Use of liposome for treatment of chronic viral hepatitis B. WO2018177140.

Zylberberg C, Matosevic S. 2016. Pharmaceutical liposomal drug delivery: a review of new delivery systems and a look at the regulatory landscape. Drug Deliv. 23:3319–29.