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MUCOADHESIVE LIPOSOME AS A PROMISING DRUG DELIVERY SYSTEM"

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ABSTRACT

Development of liposomal mucoadhesive drug delivery system, which is able to improve the bioavailability of poorly absorbed oral drugs by prolonging their gastric and intestinal residence time, through facilitating the intimate contact of the delivery system with the absorption membrane. A liposome is a tiny bubble (vesicle), made out of the same material as a cell membrane. Liposomes can be filled with drugs, and used to deliver drugs for cancer and other diseases. It has been derived on the basis of name of sub cellular particles, ribosomes. Liposomes were first made by A.D Bangham in early 1960s.Their size ranges from 25 to 500nm. Gastro retentive dosage forms are having high potential for the usage as controlled drug delivery systems. A controlled release system designed to improve its residence time in stomach by making contact with the mucosa is achieved through formulating mucoadhesive liposomes.

KEYWORD: Liposomes, oral mucoadhesive drug delivery system.

INTRODUCTION

Novel drug delivery are designed to achieve a continuous delivery of drug at predictable and concept include minimization of drug related side effect due to controlled therapeutics blood level, improved patience compliance due to reduced frequency of dosing and the reduction of the total dose of drug administration.[1]

Liposomes have been receiving a lot of interest as a carrier for advanced drug delivery. Liposomes were first produced in England in1961 by Alec D. Bangham, who was studying

phospholipids and blood clotting. It was found that phospholipids combined with water immediately formed a sphere because one end of each molecule is water soluble, while the opposite end is water insoluble.[2]

Mucoadhesion can be defined as a state in which two components, of which one is of biological origin are held together for extended periods of time by the help of interfacial forces. Generally speaking, bioadhesion is a term which broadly includes adhesive interactions with any biological or biologically derived substance, and mucoadhesion is used when the bond is formed with a mucosal surface.[3]

LIPOSOMES

Liposomes are concentric bilayered vesicle in which an aqueous volume is entirely enclosed by a membranous lipid bilayer mainly composed of natural or synthetic phospholipids. The name liposome is derived from two Greek words: 'Lipos' meaning fat and 'Soma' meaning body. A liposome can be formed at a variety of sizes as uni-lamellar or multi-lamellar construction, and its name relates to its structural building blocks, phospholipids, and not to its size. A liposome does not necessarily have lipophobic contents, such as water, although it usually does. Liposomes are artificially prepared vesicles made of lipid bilayer. Liposomes can be filled with drugs, and used to deliver drugs for cancer and other diseases. Liposomes can be prepared by disrupting biological membranes, for example by sonication. Liposomes are micro particulate or colloidal carriers, usuallay 0.05- 5.0 μm in diameter which form spontaneously when certain lipid are hydrated in aqueous media. Liposomes are composed of relatively biocompatible and biodegradable material, and they consist of an aqueous volume entrapped by one or more bilayer of natural and/or synthetic lipids. Drug with widely varying lipophilicities can be encapsulated in liposomes, either in the phospholipids bilayer, in the entrapped aqueous volume or at the bilayer interface.[4]

ADVANTAGES OF LIPOSOMES

Some of the advantages of liposome are as follows:

- Provides selective passive targeting to tumor tissues (Liposomal doxorubicin).
- Increased efficacy and therapeutic index.
- Increased stability via encapsulation.
- Reduction in toxicity of the encapsulated agents.
- Site avoidance effect.
- Improved pharmacokinetic effects

- Flexibility to couple with site specific ligands to achieve active targeting.[5]

DISADVANTAGE OF LIPOSOME

- Production cost is high.
- Leakage and fusion
- encapsulated drug/molecules.
- Short half-life.
- Stability problem.[6]

APPLICATIONS OF LIPOSOMES IN THE SCIENCES

Mathematics: Topology of two-dimensional surfaces in three-dimensional space governed only by bilayer elasticity.

Physics: Aggregation behavior, fractals, soft and high-strength materials.

Chemistry: Photochemistry, artificial photosynthesis, catalysis, micro compartmentalization.

Biochemistry: Reconstitution of membrane proteins into artificial membranes.

Biology: Model biological membranes, cell function, fusion, recognition.

Pharmaceutics: Model biological membranes, cell function, fusion, recognition.

Medicine: Drug-delivery and medical diagnostics, gene therapy.

LIPOSOMES IN PHARMACEUTICAL INDUSTRY

For solubilization amphotericin B, minoxidil are used in treatment of fungal infections.

For site-avoidance, Amphotericin B is used to reduced nephro toxicity, and doxorubicin is used to decrease cardio toxicity in fungal infections and cancer. For sustained-release action of systemic antineoplastic drugs, hormones, corticosteroids, drug depot in the lungs in cancer and biotherapeutics.

LIPOSOMES AS DRUG DELIVERY VEHICLES

Enhanced drug solubilization, e.g., Amphotericin B, Minoxidil, Cyclosporine Protection of sensitive drug molecules, e.g., Cytosine arabinose, DNA, RNA Enhanced intracellular uptake, e.g., Anticancer drugs, Antiviral drugs, Antimicrobial drugs Altered pharmacokinetics and biodistribution i.e. prolonged or sustained release of drugs with short circulatory half lives. Increased therapeutic index, e.g., Antitumor drugs i.e. cytosine arabinoside tri-phosphate (ara-CTP), Actinomycin D.

LIPOSOMES AS A LYSOSOMOTROPIC CARRIER

Liposomes have been used as lysosomotropic carriers therapeutically in enzyme diseases like Gaucher's disease i.e. beta glycosidase deficiency and Pompe's disease i.e. alpha glycosidase deficiency. A variety of lysosomal enzymes can be entrapped in liposomes and administered to patients suffering from lysosomal storage disorders. Liposomes is also used in the treatment of metal poisoning, e.g., liposomal EDTA.

LIPOSOMES IN ANTICANCER THERAPY

DaunoXome®: Daunorubicin containing DSPC/chol liposomes is used in Advanced Kaposi's sarcoma Doxil®/Caelyx®: Doxorubicin containing HSPC/chol/PEG-DSPE liposomes is used in Metastatic ovarian cancer and advanced Kaposi's sarcoma MyocetTM: Doxorubicin containing EPC/chol liposomes is used in Metastatic breast cancer.

LIPOSOME AS ANTI-INFECTIVE AGENTS

Active Targeting Approach

Anamycin is used in treatment of Leishmianiasis

Asiaticoside is used in treatment of Tuberculosis and Leprosy

Rifampicin is used in treatment of Tuberculosis

Passive targeting approach Amphotericin B is used in treatment of Meningitis, Leishmianiasis, Candidiasis Praziquantal is used in treatment of Macrophage activation Gentamycin is used in treatment of Staphylococcal pneumonias

LIPOSOME IN EYE DISORDERS

Liposome has been widely used to treat disorder of both anterior and posterior segment. The disease of eye includes dry eyes; Keratitis, an inflammation of the cornea; Corneal transplant rejection; Uveitis, An inflammation of the middle layer of the eye; Endophthalmitis, an inflammation of the internal coats of the eye; and Proliferative vitreoretinopathy (PVR), a disease that develops as a complication of rhegmatogenous retinal detachment i.e. retinal separation associated with a break, a hole, or a tear in the sensory retina. The liposomal drugs currently approved are 'verteporfin' for the use in the eye.

LIPOSOMES AS RADIODIAGNOSTIC CARRIERS

Liposomes are used in different imaging modalities to locate the sites specifically. Their radio diagnostic applications include Liver and spleen imaging, Lymphatic imaging, Tumor

imaging, Blood pool imaging, Brain imaging, Imaging cardiovascular pathologies, Visualization of inflammation and infection sites, bone marrow and eye vasculature.[7]

MUCOADHESIVE DRUG DELIVERY SYSTEM

The term bioadhesion refers to any bond formed between two biological surfaces or a bond between a biological and a synthetic surface. In case of bioadhesive drug delivery, the term bioadhesion is used to describe the adhesion between polymers, either synthetic or natural and soft tissues or the gastrointestinal mucosa. In cases where the bond is formed with the mucus the term mucoadhesion may be used synonymously with bioadhesion. Mucoadhesion can be defined as a state in which two components, of which one is of biological origin, are held together for extended periods of time by the help of interfacial forces. Generally speaking, bioadhesion is a term which broadly includes adhesive interactions with any biological or biologically derived substance, and mucoadhesion is used when the bond is formed with a mucosal surface.[8]

ADVANTAGES OF ORAL MUCOADHESIVE DRUG DELIVERY SYSTEM

Mucoadhesive drug delivery systems offers several advantage over other oral controlled release systems by virtue of prolongation of residence time of drug in gastro intestinal tract.

- Improved patience compliance -ease of administration.
- Targeting and localization of dosage form at a specific site, rapid onset of action.
- Also, the mucoadhesive system-are known to provide intimate contact between dosage form and the absorptive tissue and improve the therapeutic performance of drug.
- Avoid of first pass metabolism
- The residence time of dosage form at the site of absorption is prolong, hence increase the bio-availability.[9]

DISADVANTAGES OF ORAL MUCOADHESIVE DRUG DELIVERY SYSTEM

- Occurrence of local ulcerous effect due to prolonged contact of the drug possessing ulcerogenic property.
- One of major limitation in the development of oral mucosal delivery is the lack of the good model for *in-vitro* screening to identify drug suitable for such administration.
- Patience acceptability in terms to taste, irritancy and mouth feel is to checked.[10]

RECENT APPLICATIONS IN ORAL MUCOADHESIVE DRUG DELIVERY

Oral mucoadhesive drug delivery has wide spread applications for many drugs which on oral administration result in poor bioavailability and are rapidly degraded by the oral mucoadhesive drug delivery provides advantages of high accessibility and low enzymatic activity.

Earlier the hydrophilic polymers like SCMC, HPC and polycarbophil were used for the treatment of periodontal diseases, but now the trend is shifting towards the effective utilization of these systems to the delivery of peptides, proteins and polysaccharides. The buccal cavity has additional advantages of high patient compliance. Orabase, a first generation mucoadhesive paste has been used as barrier system for mouth ulcers. Semisolids offer more ease in administration, but tablets have also been formulated. Table include matrix devices or multilayered systems containing a mucoadhesive agent. The tablet is kept under the upper lip to avoid clearance mechanism of the salivary gland. Buccastem, an adhesive antiemetic tablet containing Prochlorperazine is usually administered in this manner.

Buccal mucoadhesive dosage forms may be classified into three types,

- A single layer device with multidirectional drug release.
- An dosage form with impermeable backing layer which is super imposed on top of an drug loaded bioadhesive layer, creating a double layered device and preventing loss from the top surface of the dosage form into the oral cavity.
- Unidirectional release device, the drug is released only from the side adjacent to the buccal mucosa.[3]

Table No: 1 Recently reported Mucoadhesive liposomal drug delivery system.

SI No	Drug	Polymer	Method of preparations	Report
1	Riserdronate	Chitosan	Freezing drying method	In drug leakage from the chitosan coated liposomes was negligible, with the coated layer further protecting the liposomal membrane.[11]
2	Atenolol	Cabopol 974P	Ethanol injection method	Chitosan coated liposomes is attributing to the longer retention in intestinal tract. Increasing the concentration polymer used for coating the increases the thickness of coating layer.[12]
3	Pilocarpine nitrate	Egg phosphotidyl choline, cholesterol	Thin layer film hydration method	Delivery of liposome encapsulated drug as eye drops improved the extent of uptake and residence time campared to

				free drug solution. Prolong the residence time.[13]
4	Methotrexate	Soyabean lecithin, phosphotidyl choline.	Thin film hydration method.	Aimed develop a lipid based local delivery system for oral cancer.[14]
5	Celcoxib	Soyabean lecithin, cholesterol.	Thin film method	In the components such as lecithin and cholesterol, and vortex time in liposomal formulations have an essential role in the physic-chemical properties and celcoxib permeability through rat skin.[15]
6	Clotrimazole	Soya phosphotidyl choline	Rotary evaporation method	These is elastic liposomes in higher skin permeation and result indicated optimized elastic liposomes have higher anti-fungal activity.[16]
7	Mefenide acetate	Phosphotidyl choline, cholestrol	Solvent evaporation and micro encapsulation vesicular	Increasing the size of liposome decreasing in permeability. Liposomes provided sustained release vehicle that decreases the permeability.[17]
8	Itraconazole	Soya lecithin, cholestrol	Solvent injection method.	Clearly indicated that the liposomes are more efficient when compared to pure drug.[18]
9	Paracetamol	Lecithin,and cholesterol	Solvent evaporation method	These enhancing the potency of the drug and protecting the drug therapeutics efficacy till the desired period.[19]
10	Bromfenac	Chitosan	Calcium acetate gradient method	Rigid liposomes generally exhibit entrapped substances. Liposomal formulation that can deliver drugs to posterior segment of eye.[20]

REVIEW OF LITRETURE

Rajput GC *et al* (2010)., developed stomach-specific mucoadhesive tablets to increase gastric retention time of the dosage forms. Mucoadhesive tablets offer unique carrier system for many pharmaceuticals and can be tailored to adhere to any mucosal tissue, including those found in oral cavity and gastrointestinal tract. They concluded that mucoadhesive tablets could be used not only for controlled release of the drugs to specific sites in body. Recent advances in medicine have envisaged the development of polymeric drug delivery systems for protein/peptide drug sand gene therapy.[21]

P K karn *et al (2011).,* derveloped atenolol loaded mucoadesive liposomal prepared by modified ethanol injection method. Atenolol loaded liposomes were coated by different mucoadhesive polymer for example chitosan, cabopol 974P, Eudragit L 100 and Eudragit S 100, to optimize the choice of coating material.[13]

Shravya lakshmi (2017)., designed a mucoadhesive liposomal system of repaglinide for the treatment type of -2 diabetes mellitus that is capable of delivering entrapped drug over on extended period of time. Mucoadhesive liposomal formulation were prepared by thin film hydration method technique followed by coating liposomes by 0-1%w/v chitosan were evaluted for entrapment efficiently, particle size, zeta potential, surface morphology, and *invitro* drug release.[22]

Rao *et al* (2014)., developed mucoadhesive microspheres of Simvastatin. The microspheres were prepared by the orifice inotropic gelation method using polymers such as HPMC (K 100 M), Carbopol 940P, Sodium CMC, Guar gum, Sodium Alginate, Ethyl Cellulose, Methyl Cellulose, Xantham gum and 10% Calcium Chloride solution. The prepared batches of microsphere were evaluated for Micromeritic study such as tapped density, bulk density, Carr's index, Hausner ratio and angle of repose.[23]

Wu ZH *et al* (2004)., evaluated the hypoglycemic efficacy of Insulin liposomes coated by Chitosan with different molecular weights and concentrations. Insulin-liposomes were prepared by reversed-phase evaporation and Chitosan coating was carried out by incubation of the liposomal suspensions with the chitosan solution. They concluded that chitosan-coated liposomes could reduce tryptic digestion on insulin, and enhanced enteral absorption of insulin. They reported, the Insulin liposomes coated by 0.2% chitosan showed a better hypoglycemic efficacy as compared with the other liposomes coated by Chitosan.[24]

CONCLUSION

Liposomes are one of the unique drug delivery system, They can be use in controlling and targeting drug delivery. Now, in days the Liposomal topical formulations are more effectively and give the safe therapeutic efficacy. It was concluded from the review that liposomes have great potency in drug delivery system. Drug of both category (hydrophilic/lipophillic) easily embedded in the liposomes. The use of liposome in the delivery of drugs and genes are promising and is sure to undergo further development in future. mucoadhesive drug delivery systems like prolongation of the residence time of the drug which in turn increases the absorption of the drug are important factors in the oral bioavailability of many drugs. Mucoadhesive dosage forms extend from the simple oral mucosal delivery to the nasal, vaginal, ocular and rectal drug delivery systems. Recently the focus has been on the novel second generation polymers like the thiolated polymers, lectins and lecithins.

REFERENCES

1. Kumar V, Sharma A, Ashish S, Joshi G, Dhillon V. Recent advances in novel drug delivery system for delivery of Anti- Hypertensive drugs. Int J Drug Dev & Res**,** 2011; 3(1): 252-259.
2. Shashi K, kumar S, prashar B. A complex review on: liposomes. Int Res J Pharma, 2012; 3(7): 10-16.
3. Pranshu T, Satheesh NV. Recent advances in oral mucoadhesive drug delivery systems: a ssreview. Int J Pharma, 2011; 2(3): 151-162.
4. Mansoori MA, Agrawal S, Jawade S, Khan MI. A review on liposome. Int J Adv Res pharm Bio Sci, 2012; 2(4): 453-464.
5. Dua1 JS, Rana AC, Bhandari AK. Liposome: methods of preparation and applications. Int J Pharm Studies Res, 2012; 2(3): 14-20.
6. Loveleenpreet K, Kaur P, Khan MU**.** Liposome as a drug carrier – a review. Int J Res Pharm Chem, 2013; 3(1): 121-128**.**
7. Rabiya A, Abdul M. Liposomes as a novel drug delivery system. Int J Pharm Tech, 2017; 2(9): 29735-29758.
8. Pranshu T, Satheesh NV. Oral mucoadhesive drug delivery systems: a review. Int J Biopharm, 2011; 2(1): 36-46.
9. Harvinder KS, ujjwal N. Pioneering and encouraging approach mucoadesive drug delivery system. Int J Pharm Med Res, 2017; 5(3): 455-463.
10. Monoar L, kumar S, Anil B, Akanksha G, Navneet G. Muchoadhesive drug delivery system. Cri Rev Pharm Sci, 2014; 3(3): 2319-1082.
11. Jung IW, Han HK. Effective mucoadhesive liposomal delivery system for risedronate preparation and *in-vivo/in-vitro* characterization. Int J Pharm Res Dev, 2014; 9(1): 2299-2306.
12. Pankaj RK, Zehijka V, Ivan P, Natasa SB. Mucoadhesive liposomal delivery system; the choice of coating material. Drug Dev Ind Pharm, 2010; 37(4): 482-488.
13. Rathod SG, Deshpande. liposomal formulation of pilocarpine nitrate. Int J Pharm Sci, 2010; 72(2): 155-160.
14. Zhang BJ, Xiao QD, Xin X, Feng. Delevlopment and in-vitro evalution of mucoadesive pathes of MTX for targeted delivery to oral cancer. Spandidos Pub, 2017; 2541-2549.
15. Kandar M, Salami A, Mahsa M. Formulation and evalution of liposomes for transdermal delivery of celecoxib. Jun J Nat Pharm Prod, 2015; 10(1): e 17653.

16. Ravi K, Rana AC, Rajni B, Nirmarth S. Formulation and evalution of elastic liposomes of clotrimazole. Int J Drug Dev Res, 2012; 4(3): 348-355.
17. Behzad SM, Zahra AZ, Armita A. preparation and evalution mafenide acetate liposome formulation as eschar delivery system. Int J Drug Dev Res, 2011; 3(4): 129-140.
18. Srinivas LK, Vinaikumar T, Rajasri A. Preparation and evalution of liposomes formulation for poorly soluble drug itraconazole by complexation. Res Schlr Lib, 2015; 7(8): 1-7.
19. Kannaiyam S, Muthuprasanna P, Vardhareddy V. Asian J Pharm. 2009. DOI:104/03/0973-8398.56308.
20. Toshimash T, Hirofumi T. Preparation of bromfenac loaded liposomes modified with chitosan for opthalmic drug delivery and evalution of physico chemical properties and drug release profile. Asian J Pharm Sci, 2013; 8(2): 104-109.
21. Rajput G, Majmudar F, Patel J, Thakor R, Rajgor N. Stomach-specific mucoadhesive microsphere as a controlled drug delivery system. Sys Rev Pharm, 2010; 1(1): 70-78.
22. Rao DS, Reddy SH, Ramu S, Rambabu E. Preparation and Evaluation of Mucoadhesive Microspheres of Simvastatin by Ionic Gelation Technique. American J Adv Drug Deli, 2014; 2(5): 594-608.
23. Shravya Lakshmi S, Parthiban S, SenthilKumar GP, Tamizh Mani T. Development and evaluation of mucoadhesive liposomes of repaglinide for oral. W J Pharm Res, 2017; 6(4): 706-718.
24. Wu ZH, Ping QN, Wei Y, Lai JM. Hypoglycemic efficacy of chitosan-coated Insulin liposomes after oral administration in mice. Acta Pharmacol Sci, 2004; 25(7): 966-972.