International Standard Serial Number (ISSN): 2249-6807

International Journal of Institutional Pharmacy and Life Sciences 5(1): January-February 2015

INTERNATIONAL JOURNAL OF INSTITUTIONAL PHARMACY AND LIFE SCIENCES

Pharmaceutical Sciences **Review Article……!!!**

Received: 25-01-2015; Revised: 29-01-2015; Accepted: 30-01-2015

LIPOSOMAL OCCULAR DRUG DELIVERY- AN OVERVIEW

Ranju R. Kondekar*[1], Gajanan Panpatte[2]

1. HI-Tech College of Pharmacy, Chandrapur
2. Gurunanak College of Pharmacy, Nagpur

Keywords:

Ophthalmic formulation, lipophillic component, lipophobic component, Liposomal drug delivery

For Correspondence:

Ranju R. Kondekar

HI-Tech College of Pharmacy, Chandrapur

E-mail:

ranjukon12@gmail.com

ABSTRACT

The present ophthalmic formulation play vital role to control & lower IOP in Anti -glaucoma therapy which relates to sustained release, prolong residing ophthalmic formulation show better absorption, having small particle size, hydrogel properties & thermosensitivity. The said formulation comprising at least one lipid bilayer, Basic active & the random block copolymer having lipophillic component & lipophobic component.

INTRODUCTION

This century has witnessed incredible advances in the field of medicine. Pharmaceuticals have primarily consisted of simple, fast-acting chemical compounds that are dispensed orally, as inject able or applied externally. During the past three decades, however, formulations that control the rate and period of drug delivery (i.e., time-release medications) and target specific areas of the body for treatment have become increasingly common and complex. Because of researchers' ever-evolving understanding of the human body and the explosion of new and potential treatments resulting from discoveries of bioactive molecules and gene therapies, pharmaceutical research hangs on the precipice of yet another great advancement. However, this next leap poses questions and challenges to not only the development of new treatments but also the mechanisms with which to administer them. The current methods of drug delivery exhibit specific problems. For example, many drug 'potencies and therapeutic effects are limited or otherwise reduced because of the partial degradation reaching the desired target site. The goal of all sophisticated drug delivery systems, therefore, is to deploy medications intact to specifically targeted parts of the body through a medium that can control the therapy's administration by means of either a physiological or chemical trigger. To achieve this goal, researchers are turning to advances in the worlds of micro- and nanotechnology. In addition, new ideas on controlling the pharmacokinetics, pharmacodynamics, non-specific toxicity, immunogenicity, biorecognition and efficacy of drugs were generated. The clinical utility of most conventional chemotherapeutics is limited either by the inability to deliver therapeutic drug concentrations to the target tissues or by severe and harmful toxic effects on normal organs and tissues. To minimize drug degradation and loss, to prevent harmful side-effects and to increase drug bioavailability by enhancing drug targeting specificity, various drug delivery and drug targeting systems are currently under development. In the recent years considerable attention has been focused on the development of new drug delivery systems. The therapeutic efficacy and safety of drugs administered by conventional methods can be improved by more precise spatial and temporal placement with in the body through a controlled drug delivery. Basically, there are three modes of drug delivery i.e. Targeted Delivery, Controlled Delivery and Modulated Delivery.

1) Targeted delivery refers to the systemic administration of drug carrier with the goal of delivering the drug to specific cell types, tissues or organ. 2) Controlled release refers to the use of delivery device with the objective of releasing the drug into the patient's body at a predetermined rate, or at a specific time or with specific release profiles.

3) Modulated release of a drug delivery device refers to release of drug at a variable rate, controlled by environmental conditions, biofeedback, sensor input/an external control device.

ANATOMY AND PHYSIOLOGY OF THE EYE

Eye is the most marvelous of the sense organs as it makes us aware of various objects all around us, near and far away. Eye is nearly spherical in shape except that its front portion i.e. transparent cornea bulges a bit forward. The eye is protected by the eyelashes, eyelids, tears and blinking. The eyelashes catch foreign materials as the blink reflex prevents injury by closing the lids, blinking occurs frequently during waking hours to keep the corneal surface free of mucous and moistened by the tears secreted by the lacrimal glands. Tears wash away irritating agents and are bactericidal, preventing infections. The protective operations of the eye lids and lacrimal system are such that, there is a rapid removal of material instilled into the eye unless the material is suitably small in volume, chemically and physiologically compatible with surface tissues. The eye is one of the most delicate and yet most valuable of the sense organs and is a challenging subject for topical administration of drugs to the eye [1].

Accessory structures of the eye

The accessory structures of the eye include the eyelids, eyelashes, eyebrows, the lacrimal (tearing) apparatus and extrinsic eye muscles. The lacrimal apparatus is a group of structures that produces and drains lacrimal fluids or tear [2].

Anatomy of the eyeball

The eyeball measures about 2.5 cm in diameter, only a small portion (about 1/6Th part) of the globular eye is exposed in front, the rest is hidden in bony socket of the orbit on a cushion of fat and connective tissue. The wall of the human eyeball consists essentially of three layers: Fibrous tunic, vascular tunic and Retina [2, 3].

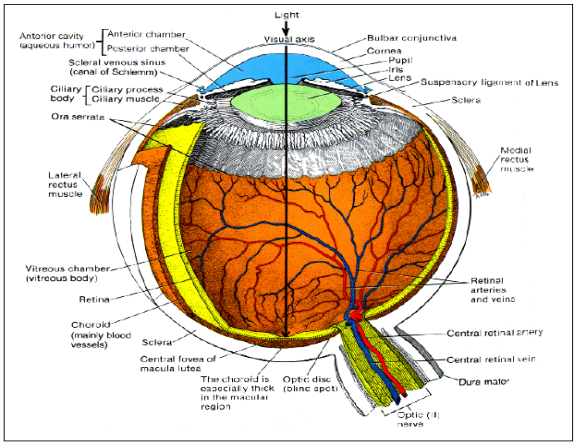

Figure 1.1: Anatomy of the eye [4]

Fibrous tunic

Fibrous tunic, the outermost coat of the eyeball, consists of the anterior cornea and posterior sclera. The **cornea** is a transparent coat that covers the colored iris. Cornea mainly consists of the following structures from the front to back, (I) Epithelium, (II) Bowman's membrane, (III) Stroma, (IV) Decrement's Membrane, and (V) Endothelium. The cornea is 0.5 to 1mm in thickness and normally it possesses no blood vessels except at the corneosclerar junction. The **sclera**, the "white" of the eye, is a layer of dense connective tissue made up densely of collagen fibers and fibroblasts. The sclera covers the entire eyeball except the cornea. At the junction of the sclera and cornea is an opening known as the sclera venous sinus (canal of Schelm).

Vascular tunic

This middle layer is mainly vascular, consisting of the choroid, ciliary body and iris. **Choroid** lines the posterior five-sixths of the inner surface of the sclera. It is very rich in blood vessels. **Ciliary body** is the anterior continuation of the choroids consisting of ciliary muscle and secretary epithelial cells. The major function of the ciliary body is the production of aqueous humor. Systemic drugs enter the anterior and posterior chambers largely by passing through the ciliary body vasculature and then diffusing in to the iris where they can enter the aqueous humor. The ciliary body is one of the major ocular sources of drug-metabolizing enzymes, responsible for drug detoxification and removal from the eye.

Iris is the visible colored part of the eye and extends interiorly from the ciliary body lying behind the cornea and in front of the lens. The pigment granules of the iris epithelium absorb light as well as lipophillic drugs. This type of binding is characteristically reversible, allowing release of drug overtime. As a result, the iris can serve as a reservoir for some drugs, concentrating and then releasing them for longer than otherwise expected [2, 4].

Retina

The innermost layer is the retina, consisting of the essential nervous system responsible for vision. Retina lines the posterior three quarters of the eyeball and is the beginning of the visual pathway. The retina is situated between the clear vitreous humor in its inner surface and choroids on its outer surface. Retina consists of two distinct chambers, anterior and posterior [5].

Lens

Behind the pupil and iris, within the cavity of the eyeball, is the lens. Protein called crystalline, arranged like the layers of an onion, make up the lens. The lens is held in place by

the zonules, which run from the ciliary body and fuse into the outer layer of the lens capsule. The lens tends to develop cataract or opacities with age, interfering with vision [5].

Interior of the eyeball

The lens divides the interior of the eyeball into two cavities; anterior cavity and Vitreous chamber. The **anterior cavity** consists of two chambers. The anterior chamber that lies between the cornea and the iris. The posterior chamber that lies behind the iris and in front of the lens. Aqueous humoris formed by ciliary bodies and occupies the posterior and anterior chambers, having a volume of about 0.2mL. The fluid is constantly generated by pigmented and non- pigmented epithelium of ciliary body [2, 4]. The **Vitreous chamber** is filled with a viscous fluid, vitreous humor, which is a viscoelastic connective tissue composed of small amounts of glycosaminoglycans, including of hyaluronic acid and proteins such as collagen[5].

Conjunctiva

The conjunctiva membrane covers the outer surface of the white portion of the eye and the inner surface of the eyelids. In most places it is loosely attached and thereby permits free movement of the eyeball, this makes possible subconjunctival injection. The conjunctiva forms an inferior and a superior sac except for the cornea, the conjunctiva is the most exposed portion of the eye[5].

COMMON EYE DISORDERS

A number of disorders can affect the structure of the eye, with outcomes ranging from moderate discomfort to significant loss of vision. The health care provider should be familiar with the signs and symptoms of common eye disorders and understand the decision making process behind treatment [6].

1.3.1 Inflammatory conditions

1. Hordeolum and Chalazion
2. Blepharitis
3. Dacryocystitis
4. Conjunctivitis
5. Trachoma
6. Anterior Uveitis

Glaucoma

Glaucoma is a group of diseases of the eye characterized by damage to Ganglion cells and the optic nerve. If left untreated, these effects may lead to various degrees of loss of vision and

blindness. Increased intraocular pressure (IOP) remains the most important risk factor for the development of glaucoma. Glaucoma is typically classified as either open angle or angle closure (closed angle), based upon causes of increased intraocular pressure[7].

Glaucoma classify according to etiology [8]

A) Primary glaucoma

1. Open angle glaucoma
2. Angle-closure glaucoma

B) Congenital glaucoma

1. Primary congenital glaucoma
2. Glaucoma associated with other
3. Glaucoma associated with extra Development ocular abnormalities

C) Absolute glaucoma:

D) Secondary glaucoma

1. Pigmentary glaucoma
2. Exfoliation syndrome
3. Due to lens changes (photogenic)
4. Due to uvula tract changes
5. Iridocorneoendothelial (ICE) syndrome
6. Trauma
7. Postoperative
8. Nonvascular glaucoma
9. Raised episcleral venous pressure
10. Steroid-induced

Etiology (Study of causes of disease)

Optic nerve damage caused by the different types of glaucoma is a result of a variety of initiating factors. Genetic predisposition, physical changes, systemic diseases, or medications may increase a person's risk of developing damage that may be broadly classified as intraocular pressure dependent (most commonly) or intraocular pressure independent. Increased intraocular pressure remains the major etiologic risk factor for the development of glaucoma. Myopia may be an additional risk factor, especially in younger patients. Glaucoma can occur as a secondary manifestation of systemic disorders or trauma.

Pathogenesis

There are five stages in the pathogenesis of glaucoma: (1) a variety of initial events, causing (2) Changes in aqueous outflow, resulting in (3) Increased IOP, which leads to (4) Optic nerve atrophy, and finally, (5) Progressive loss of vision. This description highlights the importance of aqueous humor production and elimination in the progression of glaucoma and subsequent complications.

Open-angle glaucoma

In open-angle glaucoma, a physical blockage occurs within the trabecular meshwork that retards elimination of aqueous humor. The obstruction is presumed to be between the trabecular sheet and the episcleral veins, into which the aqueous humor ultimately flows. The impairment of aqueous drainage elevates the intraocular pressure to between 25 and 35 mm Hg(Normal intraocular pressure is 10 to 20 mm Hg), indicating that the obstruction is usually partial. This increase in intraocular pressure is sufficient to cause progressive cupping of the optic disk and eventually visual field defects.

Angle-closure glaucoma

In angle-closure glaucoma, increased intraocular pressure is caused by papillary blockage of aqueous humor outflow and is more severe. The basic requirements leading to an acute attack of angle closure are a papillary block, a narrowed anterior chamber angle and a convex iris. When a patient has a narrow anterior chamber or a pupil that dilates to a degree where the iris comes in greater contact with the lens, there is interference with the flow of aqueous humor from the posterior to the anterior chamber. Because aqueous humor is continually secreted, pressure from within the posterior chamber forces the iris to bulge forward. This may progress to complete blockage. The pathologic complications of angle closure and open angle glaucoma include the formation of cataracts, adhesion of the iris to the cornea, atrophy of the optic nerve and retina, complete blockage of aqueous outflow, and ultimately, blindness.

Congenital glaucoma

Congenital glaucoma is a rare disorder in which intraocular pressure is increased as a result of developmental abnormalities of the ocular structures in the newborn or infant. It may occur in association with other congenital abnormalities and anomalies such as homocystinuria and Marfa's syndrome.

Normal-tension glaucoma

The etiology and pathogenesis of normal tension glaucoma remain to be completely understood. Normal tension glaucoma is thought to be related, at least in part, to decreased blood flow to the optic nerve. This may eventually cause neuronal damage. In addition, these eyes appear to be more susceptible to pressure related damage within the normal or high normal range, a pressure lower than normal is often necessary to prevent further visual loss.

Drug-induced glaucoma

Several therapeutic classes of drugs, such as those with anti-cholinergic, adrenergic, or corticosteroid effects, have been implicated in inducing or worsening glaucoma. Medications

affect open angle and closed angle glaucoma differently. Drugs that dilate the pupil, for instance, may precipitate an acute attack of angle closure glaucoma but usually do not produce harmful. Effects in those with open angle glaucoma. Dilation of the pupil in angle closure glaucoma may cause the peripheral iris to bulge forward, blocking the trabecular meshwork. The aqueous humor is prevented from reaching the outflow channels, which results in increased IOP. Because excessive resistance to outflow in open angle glaucoma is caused primarily by changes within the trabecular outflow channels, dilation of the pupil usually will not increase the intraocular pressure.

NOVEL OPHTHALMIC DELIVERY SYSTEMS

To overcome the drawbacks of conventional ophthalmic dosage form, many progresses have been done to improve the pre-corneal drug absorption and minimize pre-corneal drug loss.

Mucoadhesives

Mucoadhesives are retained in the eye by virtue of non-covalent bonds established with the corneal conjunctival mucin for extending pre-ocular residence time[10, 11].

Niosomes

Niosomes are the vesicles, containing non-ionic surfactants, that can entrap both hydrophilic and lipophillic drugs either in aqueous layer or in vesicular membrane made of lipid materials [12]. It helps in preventing metabolism of the drug by enzymes present at the tear or corneal surface[13].

Liposomes

Liposomes are microscopic vesicles composed of membrane like lipid layers surrounding aqueous compartments. The lipid layers are comprised mainly of phospholipids[14]. They have the ability to entrap hydrophilic compound in the aqueous compartment and to incorporate hydrophobic molecule in the lipid bilayers[15].

Nanoparticles

Nanoparticles are solid particles of polymeric nature ranging in size from 10-1000 nm. The drugs are bound to small particles, which are then dispersed into aqueous vehicle[16]. Due to very small in size these are not washed away with tears quickly[17].

Contact lenses

Contact lenses are substitutes for spectacles and are enjoying a certain degree of popularities. Use of soft contact lenses soaked in drug solution has been suggested for slow but prolonged drug delivery but particularly to corneal tissue[18].

Pharmacosomes

They are the vesicles formed by the amphiphilic drugs. Any drug possessing a free carboxyl group can be esterified to the hydroxyl group of a lipid molecule thus generating an amphiphilic prodrug. These are converted to pharmacosomes on dilution with tear[19].

Ophthalmic inserts

Inserts are defined as a thin disks or small cylinders made with appropriate polymeric material and fitting into the lower or upper conjunctival sac. Their long persistence in preocular area can result in greater drug availability with respect to liquid and semisolid formulation[20].

LIPOSOMES

The name liposome is derived from two Greek words: 'Lipos' meaning 'fat' and 'Soma' meaning 'body'. Liposomes were first produced in England in 1961 by Alec D. Bangham, who was studying phospholipids and blood clotting [21]. Alec Bangham first described how membrane molecules, e.g. phospholipids, interact with water to form unique structures now recognized as liposomes & 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. Water soluble medications added to the water trap inside the aggregation of the hydrophobic ends; fat-soluble medications are incorporated into the phospholipids layers.Liposomes are a form of vesicles that consist either of many, few or just one phospholipids bilayers. The polar character of the liposomal core enables polar drug molecules to be encapsulated. Amphiphilic and lipophillic molecules are solubilized within the phospholipids bilayer according to their affinity towards the phospholipids. Participation of non-ionic surfactants instead of phospholipids in the bilayer formation results in niosomes. Channel proteins can be incorporated without loss of their activity within the hydrophobic domain of vesicle membranes, acting as a size-selective filter, only allowing passive diffusion of small solutes such as ions, nutrients and antibiotics. Thus, drugs that are encapsulated in a nanocage-functionalized with channel proteins are effectively protected from premature degradation by proteolytic enzymes. The drug molecule, however, is able to diffuse through the channel, driven by the concentration difference between the interior and the exterior of the nanocage.

Liposomes can be formulated as a suspension, as an aerosol or in a semisolid form such as a gel, cream or dry powder. In-vivo, they can be administered topically or parent rally. After systemic (usually intravenous) administration, this seems to be the most promising route for

this carrier system. Liposomes typically recognized as foreign particles and consequently endocytosis by cells of the mononuclear phagocytic system (MPS), mostly fixed Kupffer's cells in the liver and spleen [22]. Liposomes as a drug delivery system can improve the therapeutic activity and safety of drugs, mainly by delivering them to their site of action and by maintaining therapeutic drug levels for prolonged periods of time. Liposomes also facilitate intracellular delivery via fusion with the plasma membrane, receptor-mediated endocytosis and phagocytosis [23]. As a promising delivery system liposomes are becoming more and more favorable in drug administration to the human body. This is due to many distinct advantages of these lipid vesicles which include: 1) biocompatibility, 2) biodegradability, 3)target ability, 4) nontoxicity, 5) flexible and non-immunogenic for systemic and non-systemic administrations, 6) ideal specific gravity and possibility of producing them in different size ranges, 7) carry both water and oil soluble payloads, 8) reduce exposure of sensitive tissues to toxic drugs, 9) protein stabilization, and 10) controlled hydration [24]. Despite the enormous research and development works on liposomes, only a small number of liposomal products got approval for human use, so far. This may be due to many reasons including: 1) toxicity of some liposomal formulations, 2) low entrapment of molecules and compounds into liposomes, 3) instability of the liposomal carriers, 4) leakage and fusion of encapsulated drug/molecules, 5) sometimes phospholipids undergoes oxidation and hydrolysis like reaction, 6) low solubility, and 7) high cost of liposome production especially on large scales etc.

TYPES OF LIPOSOMES

1. Noisome

2. Transfersomes

3. Ethosomes

4. Proliposomes

CLASSIFICATION OF LIPOSOMES

The liposome system has a major advantage over competing colloidal carrier systems: it allows almost infinite possibilities to alter structural and physicochemical characteristics. This feature of flexibility enables the formulation scientist to modify liposome behavior in vivo and to tailor liposome formulations to specific therapeutic needs. In an attempt to classify the plethora of possible liposome versions, it can be broadly distinguished on the basis of structural parameters and on the basis of composition and application [25, 26].

Based on structural parameters

MLV, Multilamellar large vesicles->0.05µm

LUV, Large unilamellar vesicles-0.1µm

SUV, Small unilamellar vesicles-0.025-0.05µm

UV, Unilamellar vesicles (all size range)

OLV, Oligolamellar vesicles-0.1-1 µm

MUV, Medium sized unilamellar vesicles

GUV, Giant unilamellar vesicles (vesicles with diameters>1 µm

MVV, Multivesicular vesicles

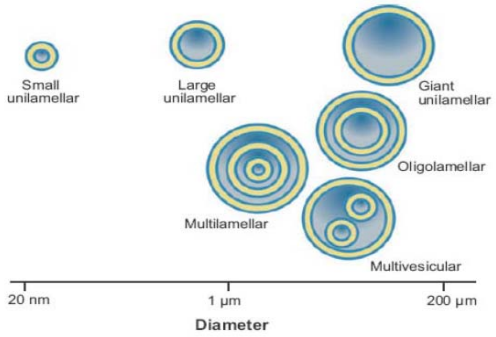

Fig.1.2 Schematic classification scheme of Liposomes[27]

LIPOSOME PREPARATION [28]

a) Handshaking / Thin Film Hydration Method

In order to produce liposomes, lipid molecules must be introduced into an aqueous environment. When dry lipid layer film is hydrated the lamellae swell and grow into myelin figures. Only mechanical agitation provided by vortexing, shaking, swearing or pip petting causes myelin figures to break and reseal the exposed hydrophobic edges resulting in the formation of liposomes made by hand shaken method.

b) Sonication Method

This method is probably the most widely used method for the preparation of small unilamellar vesicles. There are two sonication techniques:

I) Probe Sonication

In this method the dissipation of energy at the tip results in local overheating and therefore the vessel must be immersed into an ice bath. During the sonication up to one hour more than 5% of the lipids can be de-esterified. Also, with the probe sonicator, titanium will Slough off and generally contaminate the solution.

II) Bath Sonicator

In this method the liposome dispersion in a test tube is placed into a bath sonicator. Controlling the temperature of the lipid dispersion and sonicating for few minutes, are usually easier methods to produce small unilamellar vesicles. Material being sonicated can be kept in a sterile container, unlike the probe units, or under an inert atmosphere.

c) Reverse Phase Evaporation Method

Historically this method provided a breakthrough in liposome technology, since it allowed for the first time the preparation of liposomes with a high aqueous space-to-lipid ratio and able to entrap a large percentage of the aqueous material presented. Reverse phase evaporation is based on the formation of inverted micelles. These inverted micelles are formed upon sonication of a mixture of a buffered aqueous phase, which contains the water soluble molecules to be encapsulated into the liposomes and an organic phase in which the amphiphilic molecules are solubilized. The slow removal of the organic solvent leads to transformation of these inverted micelles into a gel like and viscous state. At a critical point in this procedure, the gel state collapses and some of the inverted micelles disintegrate. The excess of phospholipids in the environment contributes to the formation of a complete bilayer around the remaining micelles, which results in formation of liposomes. Liposome made by this method can be made from various lipid formulations and have aqueous volume to lipid ratios that are four time higher than multi lamellar liposomes or hand shaken method.

d) Freeze Dried Rehydration Method

Freeze dried liposomes are formed from preformed liposomes. Very high encapsulation efficiencies even for macromolecules can be achieved using this method. During the dehydration the lipid bilayers and the material to be encapsulated into the liposomes are brought into close contact. Upon reswelling, the chances for encapsulation of the adhered molecules are much higher. The rehydration is a very important step and should be done very carefully. The aqueous phase should be added in very small portions with a micropipette to the dried materials. After each addition the tube should be vortexes thoroughly. As a general rule the total volume used for rehydration must be smaller than the starting volume of the liposome dispersion.

APPLICATION OF LIPOSOMES[28]

A. Medical Application:

1) As model membrane system to deliver micro molecules as well as macromolecule such as proteins, DNA, etc.

2) Site specific targeting:

In certain cases liposomes with surface attached ligands can bind to target cells ('key and Lock' mechanism), or can be delivered into the target tissue by local anatomical conditions such as leaky and badly formed blood vessels, their basal lamina, and capillaries. Examples include anticancer, anti-inflammatory, antimonial drugs etc.

3) Site avoidance delivery:

Some drugs used in several treatments usually exhibit a narrow therapeutic index causing high toxicity to normal tissues. This toxicity could be minimized by decreasing delivery to normal tissues. Thus the distribution of a variety of antineoplastic drugs using liposome formulations can reduce considerably the toxicity to heart, liver or gastrointestinal tract. For example a) liposomal doxorubicin to reduce the cardiac toxicity and b) liposomal amphotericin B to reduce nephrotoxicity.

4) Sustained / controlled release:

Drugs which are rapidly excreted or metabolized 'saw tooth' pattern of plasma drug levels are often observed. Thus the concentration of drug in blood stream oscillates between toxic and sub-therapeutic level, e.g. many antitumor drugs are cleared from blood stream, while same agents, encapsulated in liposome persists in blood for hours. These drug encapsulated liposomes as an intravascular sustained release system would be enhanced by increasing life time of circulation and to reduce liposome uptake by fixed phagocyte cells of reticuloendothelial system. The use of liposomal sustained release preparation may be of most value for drugs of low therapeutic index. Another application would be the intravascular use of drugs with low water solubility, since these could be maintained in the circulation via liposome encapsulation. Examples are: a) Inhalation of bronchodilator b) Ocular delivery of antibiotic c) Topical delivery

5) Intravenous delivery of radio imaging agent:

Actively or passively targeted liposomes can be used as carriers for contrast agents to increase the signal difference between areas of interest and background, and to specifically localize the contrast moieties in the target tissues or organs. The versatility of liposomal vesicles to carry different types of compound in the bilayers or in the aqueous compartment makes them suitable for all contrast procedures, including gamma-scintigraphy, magnetic resonance imaging (MRI), computed tomography imaging (CTI), and sonography. Using liposomes in diagnostic imaging leads to several advantages, owing to their capability to incorporate multiple contrast moieties, to specifically deliver the agent to the target area, and

to enhance the contrasting signal. Scintigraphic techniques using 99mTc are useful tools for the noninvasive analysis of the in vivo behavior of liposomes. Using these techniques, quantitative information regarding the in vivo movement, distribution, and fate of the liposomes becomes readily available.

6) Gene therapy:

Conventional liposomes have also been tried as delivery system to deliver DNA into cells. The rationality was the ability of liposomes to enhance intracellular accumulation i.e.

Facilitate transfer of these large and heavily changed molecules across rather impermeable

Cell membrane. Cationic liposomes are the most suitable transecting vectors. Gene encapsulation in liposomal vesicles allows condensation of DNA plasmid into a structure, and protects DNA against degradation during storage and in the systemic circulation of the gene encoding a therapeutic protein. Moreover, structural organization of the gene-delivery system must bypass the cell membrane and facilitate escape, avoiding DNA degradation in lysosomal compartment.

7) Now the herbal products like flavonoids are given orally through liposomal delivery system. These herbal products containing liposomes are known as herbosomes.

8) Liposomes also improved transfer of hydrophilic and charged molecules such as chelators, antibiotics, plasmids and genes into cells.

B. Non-medical application of liposomes:

1. Liposomes make very useful model for studying biomembranes and membrane proteins.

2. In addition to application in basic sciences and medical application, their properties can be used in the food and cosmetics industry.

3. The ability of liposomes to solubilize compounds with demanding solubility properties, sequester compounds from potentially harmful milieu, and release of incorporated molecules in a sustained predictable fashion can be used also in the food processing industry..

4. Liposomes can be utilized also in the delivery of ingredients in cosmetics. In addition, liposome as a carrier itself offers advantages because lipids are well hydrated and can reduce

The dryness of the skin which is a primary cause for its ageing. Also, liposomes can act as a

Supply which acts to replenish lipids and, importantly, linolenic acid.

CONCLUSION

Glaucoma treatment with traditional dosage forms i.e. eye drops have poor bioavailability because of rapid precorneal elimination, Conjunctival absorption, Solution drainage by gravity, Induced lacrimation, Normal tear turnover.Frequent instillation of concentrated

medication is required to achieve a therapeutic effect. Systemic absorption of the drug and additives drained through nasolacrimal duct may result in undesirable side effects. The amount of drug delivered during external application may vary. The drop size of ocular Medication is not uniform and those delivered is generally not correct.

Presence of viscous vehicles can cause blurred vision. Some novel drug delivery systems like ocuserts, liposomes, Niosomes, Pharmacosomes, Contact lenses etc have advantages for comforts to patients, fulfill their needs, good penetrate of drug. The existing NDDS with some modification may more beneficial to patients. Sometime synergistic drugs or co administered drugs give wonderful results in glaucoma therapy.

REFERENCES

1. Chien YW. Novel drug delivery systems. 2nd ed. New York: MarcelDekker; 1992.
2. Gennaro AR. Remingtons pharmaceutical sciences. 18th ed.Pennsylvania: Mack Publishing Co.; 1990. p. 1581.
3. Tortora GJ, Derrickson B. "The special senses". In:Principles of anatomyand physiology 11th edition. New York: Wiley International; 2006. p. 579-86.
4. Avis KE, Lieberman HA, Lachman L. "Development of ophthalmic formulations". P'ceutical dosage forms: Parenteral medications. 2nd ed. New York: Marcel Dekker Inc.; 1993. p. 542-7.
5. Wilson KJW, Ross WA. "The special senses",. In; anatomy and physiologyin health and illness. 10th ed: Edinburgh: Churchill Lingstone; 2006. p.195- 7.
6. Phate RP. "The eye and vision". In; anatomy, physiology and healtheducation. 2nd ed. Nasik: career publication; 2003. p. 248.
7. Fulcher EM, Soto CD, Fulcher RM. "Medications for disorders of the eyeand ear". In; pharmacology: Principles and applications. Philadelphia PA:Saunders; 2003. p. 461-2.
8. Guptha SK, Jingan S. Eastern Pharmacist. 1998;31:71.
9. Jain NK. "Ocular drug delivery" In; controlled and novel drug delivery. 1st ed. New Delhi: CBS Publishers & Distributors; 2004. p. 86.
10. Ceulemans J, Vermeire A, Adriaens E, Remon JP, Ludwig A. Evaluation of a mucoadhesive tablet for ocular use. Journal of controlled release.2001; 77(3):333-42.
11. Malhotra M, Jain NK. Niosomes as drug carriers. Indian Drugs.1994; 31(3):81-6.
12. Guinedi AS, Mortada ND, Mansour S, Hathout RM. Preparation and evaluation of reverse-phase evaporation and multilamellar niosomes asophthalmic carriers of acetazolamide. International journal of pharmaceutics. 2005;306(1):71-82.

13. Biju SS, Talegaonkar S, Mishra PR, Khar RK. Vesicular systems: An overview. Indian journal of pharmaceutical sciences. 2006;68(2):141.
14. Nagarsenker MS, Londhe VY, Nadkarni GD. Preparation and evaluation ofliposomal formulations of tropicamide for ocular delivery. International journal of pharmaceutics. 1999;190(1):63-71.
15. Swarbrick J, Boylan JC. Ocular drug formulation and deliveryIn;encyclopedia of pharmaceutical technology. 2nd ed: InformaHealthcare; 2001. p. 43-75.
16. Gupta AK, Madan S, Majumdar DK, Maitra A. Ketorolac entrapped inpolymeric micelles: Preparation, characterisation and ocular anti-inflammatory studies. International journal of pharmaceutics.2000;209(1):1-14.
17. Ansel HC. "Opthalmic preparation". In; introduction to pharmaceutical dosage form. 4th ed. Philadelphia: Lea and Febiger; 1985. p. 330.
18. Mithal BM. "Ocular dosage forms" In;a textbook of pharmaceutical formulation. 6th ed. Delhi: Vallabh Prakashan; 1997. p. 271.
19. Saettone MF, Burglousi S, Chetoni P. In: Mathiowitz W, Lehr C, editors. Bioadhesive drug delivery systems, fundamental novel approaches and development. New York: Marcel Dekker Inc.; 1999. p. 621-5.
20. Bangham AD. Liposomes. (Ed. 1), Marcel Dekker. NewYork. (1983) 1-26.
21. Gregoriadis G. Engineering liposomes for drug delivery: progress and problems. Rev article. Trends Biotechnol. (1995) 13: 527–537.
22. Gregoriadis G, Florence AT. Liposomes in drug delivery, clinical, diagnostic andophthalmic potential. Drugs (1993)45: 15-28.
23. Mozafari, M.R. Construction of stable anionic liposome-plasmid particles using the heating method: investigation. Cellular & Molecular Letters, (2002) 7 (3): 923-927.
24. Hu C, Rhodes DG. Proniosomes: a novel drug carrier preparation. Int. J. Pharm. (2000) 206: 110-122.
25. Song KH, Chung SJ, Shim CK. Preparation and evaluation of proliposomes containing Salmon calcitonin. J. Control. Rel. (2002) 84: 27-37.
26. Jesorka A. and Orwar O. Liposomes: Technologies and Analytical Applications. Annual Rev. Anal. Chem. (2008) 1: 801-832.
27. Tapaswi Rani Dash, "Development and Characterization of Liposomal Delivery System Containing Diuretic drug Torsemide "Faculty of Engineering and Technology Jadavpur University Kolkata.

28. Rawle, A., Basic principles of particle size analysis, Surf Coatings Intl Part A. Coatings J 86 (2),58–65, 2003.
29. Kulkarni S, Sandeep N, Shankar S, Ranjit P, Someshwara B, Ramesh B, Ashok P. Effect of A Single drop Latanoprost Opthalmic Gel On Intra Ocular Pressure In The Treatment of Glaucoma. Int. J Ph Sci. Jan-April 2010;2(1): 429-435.
30. E Mohan, J Kandukari, V Allenki. Preparation and Evaluation Of In-Situ Gels For Ocular Drug Delivery. J Pharm Res.2009; 2(6):1089-1094.
31. Swamy P.H, Mulla J S. Formulation and Evaluation of Novel In-Situ Gum Based Opthalmic Drug Delivery System Of Linezolid. Sci Pharm.2008; 76:515-532.
32. Mohanambal E, Arun K.A, Sathali A. Formulation and Evaluation of pH- triggered in situ Gelling System of Levofloxacin. Ind. J Pharm Edu Res 2011; 45/Issue 1.
33. Wu Cj, Qi HY, Chen WW, Huang CY, Su C, Li WM, et al. (2007). Preparation and Evaluation of Carbopol/HPMC –Based in situ gelling ophthalmic system for Puerarin. Yakugaku Zasshi, 127:183-191
34. Upendra C. Galgatte, Praveen D. Chaudhari. Preformulation Study of Poloxamer 407 Gels: Effect of Additive. International Journal of Pharmacy and Pharmaceutical Sciences, ISSN- 0975-1491 Vol 6, Issue 1, 2014.