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FORMULATION AND EVALUATION OF OFLOXACIN MICROSPHERES BY USING METHYL CELLULOSE AS A POLYMER AT DIFFERENT RATIO

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ABSTRACT

The present study aimed to formulate and evaluate ofloxacin microspheres employing methyl cellulose as a polymer at varying ratios. Microspheres were prepared by the emulsion solvent evaporation method. The effects of different ratios of methyl cellulose on the physicochemical properties of microspheres were investigated. The prepared microspheres were characterized for particle size, drug entrapment efficiency, surface morphology, and in vitro drug release behavior. The results indicated that the particle size and drug entrapment efficiency were influenced by the polymer-to-drug ratio. Scanning electron microscopy revealed spherical morphology of microspheres with smooth surfaces. In vitro drug release studies demonstrated sustained drug release profiles over a prolonged period. Statistical analysis indicated significant differences among formulations with different polymer ratios. Thus, the findings suggest that methyl cellulose can be effectively utilized to formulate ofloxacin microspheres with tailored drug release profiles, offering potential applications in controlled drug delivery systems

Keywords: Ofloxacin, Microspheres, Methyl Cellulose, Polymer Ratio, Drug Release

1. INTRODUCTION

Over the past 30 years as the expense and complications involved in marketing new drug entities have increased, with concomitant recognition of the therapeutic advantages of controlled drug-delivery, greater attention has been focused on development of sustained or controlled release drug delivery systems. There are several reasons for the attractiveness of these dosage forms[1,2]. It is generally recognized that for many disease states, a substantial number of therapeutically effective compounds already exist. The effectiveness of these drugs, however, is often limited by side effects or the necessity to administer the compound in a clinical setting. The goal in designing sustained or controlled delivery systems is to reduce the frequency of dosing or to increase the effectiveness of the drug by localized at the site of action, reducing the dose required, or providing uniform drug delivery.

Sustained release constitutes any dosage form that provides medication over extended time or these are designed so that the administration of a single dosage unit provides the immediate release of an amount of drug that promptly produces the desired therapeutic effect, gradually and continually release of additional amounts of the drug to maintain this level of effect over an extended period, usually 8 to 12 hours. In general the goal of a sustained release dosage form is to maintain therapeutic blood or tissue levels of the drug for an extended period. This is usually accomplished by attempting to obtain zero-order release from the dosage form. Zero-order release constitutes drug release from the dosage form that is independent of the amount of drug in the delivery system (i.e. A constant release rate). Sustained release systems generally do not attain this type of release and usually try to mimic zero-order release by providing drugs in as slow first order fashion (i.e. Concentration-dependent). Systems that are designated as prolonged release can also be considered as attempts at achieving sustained release delivery. Repeat action tablets are an alternative method of sustained release in which multiple doses of a drug are contained within a dosage form, and each dose is released at a periodic interval[3-5].

The application of microencapsulation might well include sustain-release or prolonged action medications, taste masking, chewable tablets, powders and suspensions, single layered tablets containing chemically incompatible ingredients and new formulation concepts for creams, ointments, aerosols, dressing, plasters, suppositories and injectables. Pharmaceutically related areas such as hygiene, diagnostic aids and medical equipment design are amenable to microencapsulation applications. Problems frequently encountered include incomplete or uneven coating deposition, clumping of microcapsules, unsatisfactory or non reproducible core release and scale up difficulties. Every microencapsulated product requires an individual design approach, and there is no one methodology that is suitable in all cases.

The reservation of persons in industry and drug regulatory agencies to accept new dosage forms, particularly when they involve the use of novel adjuvant and technologies.

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- Satisfactory toxicological data on polymers and other materials for use in microencapsulated medicines for use in humans must be available before being authorized for clinical trials and marketing.
- Microencapsulation method can be adopted for the following reasons and it has to be useful for novel drug therapy to mask the bitter taste drugs.
- It has been employed to provide protection to the core material against
- Environmental effects.

Drug delivery systems (DDS) that can precisely control the release rates or target drugs to a specific body site have had an enormous impact on the health care system. The ideal drug delivery system delivers drug at rate decided bythe need of the body throughout the period of treatment and it provides the active entity solely to the site of action [6]. So, carrier technology offers an intelligent approach for drug delivery by coupling the drug to a carrier particle such as microspheres, nanoparticles, liposomes, etc which modulates the release and absorption characteristics of the drug.

2. MICROEMULSIONS: AS DRUG DELIVERY SYSTEM

The term “microemulsion” refers to a thermodynamically stable isotropically clear dispersion of two immiscible liquids, such as oil and water, stabilized by an interfacial film of surfactant molecules. A microemulsion is considered to be a thermodynamically or kinetically stable liquid dispersion of an oil phase and a water phase, in combination with a surfactant. The dispersed phase typically comprises small particles or droplets, with a size range of 5 nm-200 nm, and has very low oil/water interfacial tension. Because the droplet size is less than 25% of the wavelength of visible light, microemulsions are transparent. The microemulsion is formed readily and sometimes spontaneously, generally without high-energy input. In many cases a cosurfactant or cosolvent is used in addition to the surfactant, the oil phase and the water phase. Three types of microemulsions are most likely to be formed depending on the composition: Oil in water microemulsions wherein oil droplets are dispersed in the continuos aqueous phase Water in oil microemulsions wherein water droplets are dispersed in the continuous oil phase; [7-12]. □ Bi-continuous microemulsions wherein microdomains of oil and water are interdispersed within the system.In all three types of microemulsions, the interface is stabilized by an appropriate combination of surfactants and/or co-surfactants.

The specific objectives are:

- To prepare and optimise w/o microemulsions using combinations of surfactants, organic and aqueous phases and to characterise the resulting microemulsions along two dilution lines within the monophasic region in ternary phase diagrams.
- To incorporate a model hydrophilic guest molecule (sodium chloride) into the water domains of oil-continuous microemulsions and to characterise these salt containing microemulsions along the two dilution lines within the monophasic region in the developed ternary phase diagrams.
- To test the efficiency of selected salt-containing microemulsion compositions for salt-release using conductivity and establish the mechanism of release.

2.1 METHOD OF PREPARATION

a. Phase Titration Method

Microemulsions are prepared by the spontaneous emulsification method (Phase titration method) and can be depicted with the help of phase diagrams. Construction of phase diagram is a useful approach to study the complex series of interactions that can occur when different componentare mixed. Microemulsions are formed along with various association structures (including emulsion, micelles, lamellar, hexagonal, cubic, and various gels and oily dispersion) depending on the chemical composition and concentration of each component. The understanding of their phase equilibria and demarcation of the phase boundaries are essential aspects of the study[12].

As quaternary phase diagram (four component system) is time consuming and difficult to interpret, pseudo ternary phase diagram is often constructed to find the different zones including microemulsion zone, in which each corner of the diagram represents 100% of the particular component . The region can be separated into w/o or o/w microemulsion by simply considering the composition that is whether it is oil rich or water rich. Observations should be made carefully so that the metastable systems are not included.

b. Phase Inversion Method

Phase inversion of microemulsions occurs upon addition of excess of the dispersed phase or in response to temperature. During phase inversion drastic physical changes occur including changes in particle size that can affect drug release both in vivo and in vitro. These methods make use of changing the spontaneous curvature of the surfactant. For non-ionic surfactants, this can be achieved by changing the temperature of the system, forcing a

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transition from an o/w microemulsion at low temperatures to a w/o microemulsion at higher temperatures (transitional phase inversion). During cooling, the system crosses a point of zero spontaneous curvature and minimal surface tension, promoting the formation of finely dispersed oil droplets [13]. This method isreferred to as phase inversion temperature (PIT) method. Instead of the temperature, other parameters such as salt concentration or pH value may be considered as well instead of the temperature alone. Additionally, a transition in the spontaneous radius of curvature can be obtained by changing the water volume fraction. By successively adding water into oil, initially water droplets are formed in a continuous oil phase. Increasing the water volume fraction changes the spontaneous curvature of the surfactant from initially stabilizing a w/o microemulsion to an o/w microemulsion at the inversion locus.

Microemulsions can be prepared by controlled addition of lower alkanols (butanol, pentanol and hexanol) to milky emulsions to produce transparent solutions comprising dispersions of either water-in-oil (w/o) or oil-in-water (o/w) in nanometer or colloidal dispersions (~ 100 nm). The lower alkanols are called cosurfactants, they lower the interfacial tension between oil and watersufficiently low for almost spontaneous formation. The miscibility of oil, water and amphiphile (surfactant plus cosurfactant) depends on the overall composition which is system specific.

When English chemist [14] J.H. Schulman introduced the term "microemulsion" in 1943 he described the transition from a stable oil-rich mixture to a stable water-rich mixture. Microemulsions contain a polar component, water, and a non polar component, oil, which makes them capable of solubilizing a wide spectrum of substances. They measure in size from 3 to 300 nanometers in droplet diameter, are transparent and thermodynamically stable. Due to these special properties microemulsions offer a high potential for numerous practical applications. Consequently, microemulsions may be used for enhanced oil recovery, cosmetic formulations, edible coatings for food, and for drug delivery systems as both transdermal or oral administrative vehicles for the controlled release of dosages. Microemulsions also have industrial applications, one of them being the synthesis of polymers. Microemulsion polymerization is a complex heterogeneous process where transport of monomers, free radicals and other species (such as chain transfer agent, co-surfactant and inhibitors) between 8the aqueous and organic phases, takes place. Compared with other heterogeneous polymerization processes (suspension or emulsion) microemulsion polymerization is a more complicated system. Polymerization rate is controlled by monomer partitioning between the phases, particle nucleation, and adsorption and desorption of radicals. Particle stability is affected by the amount and type of surfactant and pH of dispersing medium.

Several authors have reported preparation of microemulsions using alcohols of short or medium length chains (e.g., 9butanol, heptanol or pentanol) as co-surfactants. These substances limit the potential application of microemulsion due to their toxic and irritant properties [15]. A selection of components for microemulsions suitable for pharmaceutical use involves a consideration of their toxicity and, if the systems are to be used topically, their irritation and sensitivity 10properties. The ionic surfactants are generally too toxic to be used for preparation of lipid emulsions; therefore, non ionic surfactants, such as the poloxamers, polysorbates, polyMETHYLene glycol are preferred. Polysorbate 80 is widely applied to pharmaceutical preparations, including ophthalmicFormulary, the European Pharmacopoeia and the Japanese 11.Pharmacopoeia. . With the recent improvements in aseptic processing and the availability of new well-tolerated emulsifieres (polysorbate 80), emulsion technology is currently under evaluation for topical cyclosporine A 12delivery. Ding developed a castor oil in water microemulsion. This microemulsion is stabilized by polysorbate 80 where the active substance cyclosporine A remains stable over 9 months and causes only mild discomfort and slight hyperemia on the rabbit eyes applied 8 times per day during 7 days. This encouraging result allowed the formulations to undergo clinical trials of phase II and III in dry eye disease. The II phase trial performed on 162 patients 13demonstrated good tolerance of the emulsion.

3. LIPOSOMES(DDS)

Liposomes, sphere-shaped vesicles consisting of one or more phospholipid bilayers, were first described in the mid-60s. Today, they are a very useful reproduction, reagent, and tool in various scientific disciplines, including mathematics and theoretical physics, biophysics, chemistry, colloid science, biochemistry, and biology. Since then, liposomes have made their way to the market. Among several talented new drug delivery systems, liposomes characterize an advanced technology to deliver active molecules to the site of action, and at present, several formulations are in clinical use. Research on liposome technology has progressed from conventional vesicles to ‘second-generation liposomes’, in which long-circulating liposomes are obtained by modulating the lipid composition, size, and charge of the vesicle [1,10] .Liposomes with modified surfaces have also been developed using several molecules, such as glycolipids or sialic acid. This paper summarizes exclusively scalable techniques and focuses on strengths, respectively, limitations in respect to industrial applicability and regulatory requirements concerning liposomal drug formulations based on FDA and EMEA documents.

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Table 1: Advantages and disadvantages of liposome

Advantages of liposome	Disadvantages of liposome
Liposomes increased efficacy and therapeutic index of drug (actinomycin-D)	Low solubility
Liposome increased stability via encapsulation	Short half-life
Liposomes are non-toxic, flexible, biocompatible, completely biodegradable, and non-immunogenic for systemic and non-systemic administrations	Sometimes phospholipid undergoes oxidation and hydrolysis-like reaction
Liposomes reduce the toxicity of the encapsulated agent (amphotericin B, Taxol)	Leakage and fusion of encapsulated drug/molecules
Liposomes help reduce the exposure of sensitive tissues to toxic drugs	Production cost is high
Site avoidance effect	Fewer stables
Flexibility to couple with site-specific ligands to achieve active targeting	

It has been displayed that phospholipids impulsively form closed structures when they are hydrated in aqueous solutions. Such vesicles which have one or more phospholipid bilayer membranes can transport aqueous or lipid drugs, depending on the nature of those drugs. Because lipids are amphipathic (both hydrophobic and hydrophilic) in aqueous media, their thermodynamic phase properties and self assembling characteristics influence entropically focused confiscation of their hydrophobic sections into spherical bilayers. Those layers are referred to as lamellae. Generally, liposomes are definite as spherical vesicles with particle sizes ranging from 30 nm to several micrometers. They consist of one or more lipid bilayers surrounding aqueous units, where the polar head groups are oriented in the pathway of the interior and exterior aqueous phases. On the other hand, self-aggregation of polar lipids is not limited to conventional bilayer structures which rely on molecular shape, temperature, and environmental and preparation conditions but may self-assemble into various types of colloidal particles.[

Liposomes are extensively used as carriers for numerous molecules in cosmetic and pharmaceutical industries. Additionally, food and farming industries have extensively studied the use of liposome encapsulation to grow delivery systems that can entrap unstable compounds (for example, antimicrobials, antioxidants, flavors and bioactive elements) and shield their functionality. Liposomes can trap both hydrophobic and hydrophilic compounds, avoid decomposition of the entrapped combinations, and release the entrapped at designated targets.Because of their biocompatibility, biodegradability, low toxicity, and aptitude to trap both hydrophilic and lipophilic drugs and simplify site-specific drug delivery to tumor tissues, liposomes have increased rate both as an investigational system and commercially as a drug-delivery system. Many studies have been conducted on liposomes with the goal of decreasing drug toxicity and/or targeting specific cells [13].

Liposomal encapsulation technology (LET) is the newest delivery technique used by medical investigators to transmit drugs that act as curative promoters to the assured body organs. This form of delivery system proposal targeted the delivery of vital combinations to the body. LET is a method of generating sub-microscopic foams called liposomes, which encapsulate numerous materials. These ‘liposomes’ form a barrier around their contents, which is resistant to enzymes in the mouth and stomach, alkaline solutions, digestive juices, bile salts, and intestinal flora that are generated in the human body, as well as free radicals. The contents of the liposomes are, therefore, protected from oxidation and degradation. This protective phospholipid shield or barrier remains undamaged until the contents of the liposome are delivered to the exact target gland, organ, or system where the contents will be utilized.

4. PLAN OF WORK

- Exhaustive and update the review of literatures on Microspheres.
- Identification and confirmation of Drug.
- Identification and confirmation of Polymers.
- Performing preformulation study (physical evaluation of drug, drug-polymer compatibility study).
- Preparation of Microspheres by using the solvent evaporation technique.
- Conformation of Microspheres by SEM (Scanning Electronic Microscope) by CECRI.
- Study of Morphological character of Microspheres.

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- Evaluation of physicochemical properties.
- Bulk density
- Angel of repose
- Drug content
- Percentage of drug entrapped
- Particle size.
- In-vitro release study for prepared Microspheres.
- Zero order kinetics for Prepared Microspheres.
- Stability test for prepared Microspheres.

5. RESEARCH ENVISAGED

5.1 MATERIALS USED

1. Ofloxacin (Gifted sample from Vertex Pharma Chemicals, Pondicherry.
2. Methyl Cellulose (Nice chemicals, Mumbai)
3. n-Hexane (Merck chemicals, Mumbai)
4. Acetone (Nice chemicals, Cochin)
5. Distilled water
6. Sterile water
7. Ethanol (Loba chemicals, Mumbai)
8. Liquid Paraffin (Loba chemicals, Mumbai)
9. Methanol (Loba chemicals, Mumbai)
10. Chloroform (Nice chemicals, Mumbai)
11. Phosphate buffer (pH 7.4)

APPARATUS AND INSTRUMENTS

1. pH meter (Universal Biochemical's)
2. Hot air oven
3. Electronic Balance (Axis Corporation)
4. Dissolution Apparatus (LABINDIA DISSO – 8000)
5. UV-visible spectrophotometer (Shimadzu)
6. FTIR spectrophotometer (Nexus –670)
7. Differential scanning calorimeter (Mettler Toledo DSC 821)
8. Mechanical Stirrer (Remi Equipments, Mumbai)
9. Scanning Electron Microscope (Hitachi Model S-450).

5.2 PREFORMULATION STUDIES

5.2.1 Identification of Ofloxacin pure drug

Fig.1 show the I. R. spectrum of Ofloxacin.

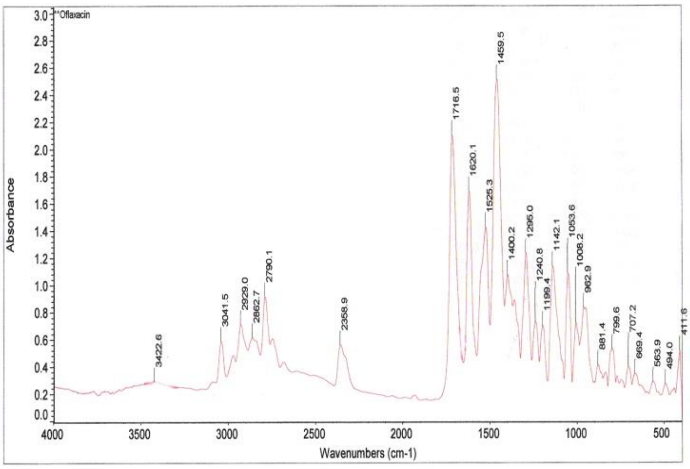

Fig 1 A U.V spectrum of Ofloxacin gives 3 peaks at 288,331 and 333nm respectively using phosphate buffer saline pH 7.4 as a solvent, which is shown in

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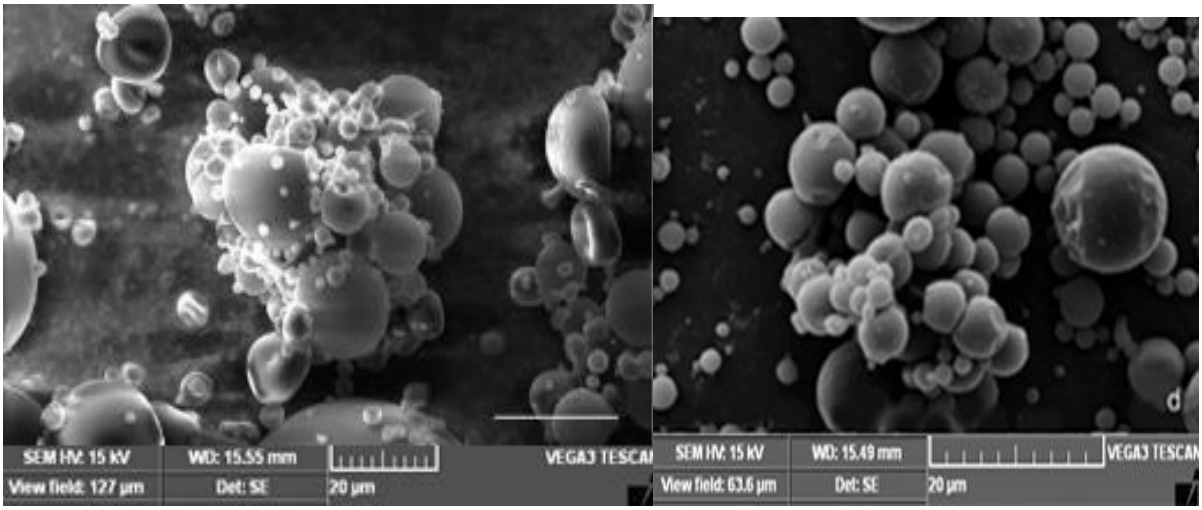
5.3 PREPARATION OF MICROSPHERES

The drug and polymer in different proportions (1:2, 1:3, 1:4, 1:5 and 1:6) were weighed & dissolved at room temperature into Methanol with vigorous agitation to form uniform drug polymer dispersion. This was slowly poured into the dispersion medium consisting of light liquid paraffin (200 ml) containing 0.1% Span 80.The system was stirred using Magnetic stirrer at 500 rpm, at room temperature over a period of 2-3 hours, to ensure complete evaporation of the solvent. The liquid paraffin was then decanted & the microspheres were separated by filtration through a Whatmann filter paper, washed thrice with 180 ml of n- hexane and air dried for 24 hours.

S.No	Formulation	Name of the Drug & Amount taken (in gm)	Name of the Polymer & Amount take (in gm)	Drug: Polymer Ra
1	Formulation I	Ofloxacin (1gm)	Methyl cellulose (1gm)	1:1
2	Formulation II	Ofloxacin (1gm)	Methyl cellulose (1.5gm)	1:1.5
3	Formulation III	Ofloxacin (1gm)	Methyl cellulose (2gm)	1:2

5.4 Morphological Study

The morphology of Methyl cellulose microspheres was observed by scanning electron microscopy (SEM). The microspheres were mounted directly onto the SEM sample stub, using double sided sticking tape and coated with gold film under reduced pressure (001 Torr). It's shown in (figure 3,4.5)



6. RESULTS AND DISCUSSION

- The solvent evaporation technique was used for preparation of Ofloxacin Microspheres with Methyl cellulose.
- The delayed release Microspheres of all batches were found to be discrete, spherical and free flowing (fig 4) the size range of different batches of Microspheres was in the range of 324.92 µm to 361.74 µm (table 5-7). Drug content analysis showed that the distribution of drug within IP limits.
- The packing properties of the drug and the formulation widely depend upon bulk density It has been stated that, bulk density values less than 1.2gm/cm3 indicate good flow and values greater than 1.5gm/cm3 indicate poor flow characteristic. It is seen from Table 4 that the bulk density values are less than 1.2gm/cm3 indicating good flow characteristics of the Microspheres. Angle of repose less than or equal to 400 indicate free flowing properties of the Microspheres. The Angle of repose for all the formulations table 9 is seen to be between 2103´ to 2507´ indicating good flow property.
- The formulation F1 showed better entrapment efficiency than other formulations.
- In-vitro drug release studies were carried out with formulation F1 to F3. All formulations showed the slow drug released initially, which may be ascribed to the low permeability of Methyl cellulose. At the end of 8hrs, drug release from the Microspheres prepared with drugs: Methyl cellulose ratios of 1:1, 1:1.5 and 1:2 were 61.71, 60.34 and 57.85 respectively. This stated the drug release retardation was directly proportional to the Methyl cellulose content of the particle. It has been documented that the most types of cellulosic membranes including Methyl cellulose swells in aqueous environments and thus in high concentration these retards the drug release by forming more barriers of thick gel around the drug particle. Furthermore, in this study the higher concentration of Methyl cellulose in formulation produced the large Microspheres.

7. CONCLUSION

The solvent evaporation method was found suitable to produce spherical Methyl cellulose Microspheres with smooth surface and better drug content. The formulation F1 was found to be the best formulation as is shown by the In-vitro studies and the evaluation of other formulations.From the result, it can be concluded that the ratio of 1:1 of Ofloxacin and Methyl cellulose produced the Microspheres with all desired characteristics like sieve analysis, bulk density, and sustained release of drug for an extended period of 8 hours. The Methyl cellulose formed the semi permeable membrane over the Ofloxacin to give sustained delivery of the Ofloxacin.

8. REFERENCES

[1] Albertsson, A.C., Donaruma, L.G., Vogl, O. Synthetic polymers as drugs, In Tirrell, D.A., Donaruma, L.G., Turek, A.B., (Eds.), Macromolecules as drugs and drug as carriers for biologically active material. Ann NY Acad Sci . 1985; 446: 105-115.

[2] Donaruma, L.G., Warner, R.J. Some biologically active (thiosemicarbazides). In Tirrell, D.A., Donaruma, L.G. and Turek, A.B. (Eds.), Macromolecules as drugs and drug as carriers for biologically active materials. Ann NY Acad Sci . 1985; 446: 116-133.

[3] Abra, R.M., Hunt, C.A. Liposome disposition in vivo . III. Dose and vesicle size effects, Biochim Biophys Acta . 1981; 666: 493-503.

[4] Tirrell, D.A., Heath, T.D., Colley, C.M., Ryman, B.E. New aspects of liposomes, Biochim Biophys Acta . 1976; 457: 259.

[5] Tirrell, D.A., Takigawa, D.Y., Seki, K. pH sensitization of phospholipid vesicles via complexation with synthetic poly (carboxylic acids). In Tirrell, D.A., Donaruma, L.G., Turek, A.B. (Eds.), Macromolecules as drugs and drug as carriers for biologically active materials. Ann NY Acad Sci . 1985; 446: 237- 248.

[6] Mozafari, M.R. Liposomes: an overview of manufacturing techniques. Cell Mol Biol Lett. 2005; 10: 711-719.

[7] Bangham, A.D., Horne, R.W. Negative Staining of Phospholipids and Their Structural Modification by Surface-Active Agents As Observed in the Electron Microscope. J Mol Biol .1964; 8: 660-668.

[8] Bangham, A.D., Hill, M.W., Miller, N.G.A. Preparation and use of liposomes as models of biological membranes, In Korn, E.D. (Ed.), Methods in Membrane Biology. Vol. 1. Plenum Press, New York. 1974; pp. l-68.

[9] Gregoriadis, G., Florence, A.T. Liposomes in drug delivery: Clinical, diagnostic and ophthalmic potential. Drugs , 1993; 45: 15-28.

[10] Wu. J., Liu. Q., Lee, R.J. A folate receptor- targeted liposomal formulation for paclitaxel. Int J Pharm . 2006; 316(1-2): 148-153.

[11] Pavelic, Z., Skalko-Basnet, N., Filippvic-Grcic, J., Martinac, A., Jalsenjak, I. Development and in vitro evaluation of a liposomal vaginal delivery system for acyclovir. J Control Release . 2005; 106: 34-43.

[12] Nagarsenker, M.S., Londhe, V.Y., Nadkarni, G.D. Preparation and evaluation of liposomal formulations of tropicamide for ocular delivery. Int J Pharm . 1999; 190(1): 63-71.

[13] Al-Angary, A.A., Al-Meshal, M.A., Bayomi, M.A., Khidr, S.H. Evaluation of liposomal formulations containing the anti-malarial agent arteether. Int J Pharm . 1996; 128(1-2): 163-168.

[14] Qiu, L., Jing, N., Jin, Y. Preparation and in vitro evaluation of liposomal chloroquine diphosphate loaded by a transmembrane pH-gradient method. Int J Pharm . 2008; 361(1-2): 56-63

[15] Agarwal, R., Katare, O.P., Vyas, S.P. Preparation and in vitro evaluation of liposomal/ niosomal delivery systems for anti-psoriatic drug dithranol. Int J Pharm . 2001; 228(1-2): 43-52.