WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 9, Issue 11, 378-391. Review Article ISSN 2277– 7105

AN OVERVIEW OF NOVEL DRUG DELIVERY SYSTEM WITH ITS TYPES AND DIFFERENT DRUG CARRIERS

Aishwarya B. Deshpande*[1], Dayanedeo B. Sumbre[2], Poonam M. Bachhav[3] and Rupali V. Nirmal[4]

[1]Department of Pharmaceutical Chemistry, Government College of Pharmacy, Aurangabad, Babasaheb Ambedkar Marathwada University, Aurangabad. (M.S.) India.

[2,4]MVPs College of Pharmacy, Nashik-422 002, Department of Pharmaceutical Chemistry, Savitribai Phule Pune University, Pune (M.S) India.

[3]MVPs College of Pharmacy, Nashik-422 002, Department of Quality Assurance Techniques, Savitribai Phule Pune University, Pune (M.S) India.

Article Received on
27 July 2020,

Revised on 17 August 2020,
Accepted on 08 Sept. 2020

DOI: 10.20959/wjpr202011-18668

***Corresponding Author**
Aishwarya B. Deshpande
Department of Pharmaceutical Chemistry, Government College of Pharmacy, Aurangabad, Babasaheb Ambedkar Marathwada University, Aurangabad. (M.S.) India.

ABSTRACT

In Pharmaceuticals Different Drug delivery systems (DDS) are used as a formulation or a device that enables a therapeutic substance to selectively reach its site of action without reaching the non-target cells, organs, or tissues. Varieties of drug delivery systems are developed and many are in developing stages which are used for enhancing therapeutic action of drug as compared to conventional drug delivery system. In this review mainly focus on novel drug delivery system with its advantages and disadvantages. in NDDS mainly four types of drug delivery system are gives such as Sustained/ controlled- drug delivery, Localized drug delivery, Rate- pre-programmed drug delivery, Targeted drug delivery with its description, for these methods different types of drug carriers are used for preparation of dosage form in novel drug delivery system such as niosomes, microspheres, phytosomes, dendrimer, chitoson nanopartilces, emulgel and ethosomes with its different methods of preparation and advantages and disadvantages of each carrier.

KEYWORDS: Novel drug delivery system, Niosomes, emulgel, Ethosomes, controlled release, sustained release.

INTRODUCTION

In Recent years, varieties of drug delivery systems are developed and many are in developing stages. In this main motto for development of various drug delivery systems includes to reduce degradation, minimize or to avoid side effects as well as to enhance bioavailabity of drug and to attain the site specificity. The novel drug delivery systems useful in sustain as well as control drug delivery systems.It is essential to censoriously assess diverse terms used under the various broad categories of novel drug delivery system.[1]

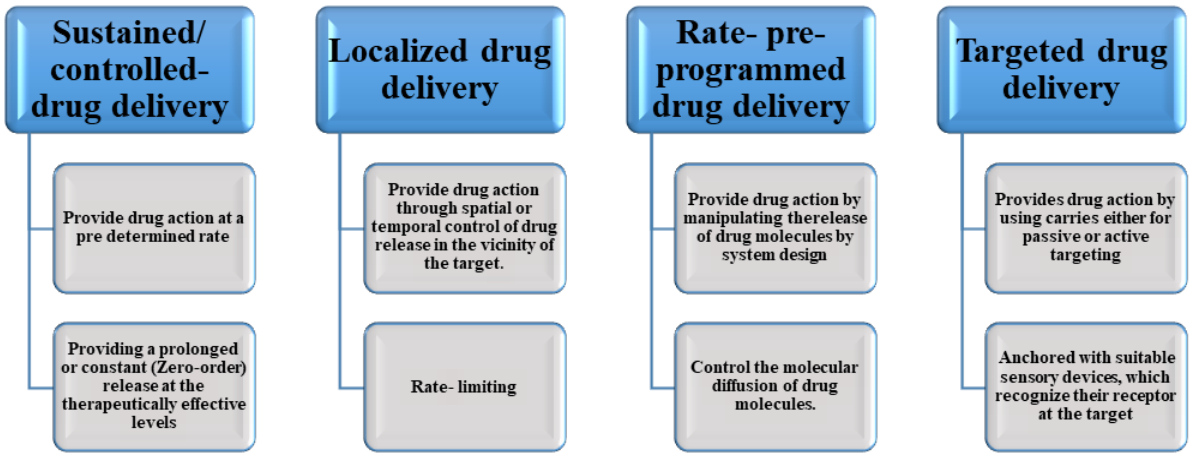

Fig. 01: Different types of Novel Drug Delivery Systems.

Table no. 1: Comparison of different drug delivery systems.[2]

Sr. No.	Conventional delivery systems	Novel drug delivery system
1	An appropriate dosage form that transports drug into body.	Improvement of various nano carrier based drug delivery system to progress cell specificity as well as targeted drug delivery.
2	After administration the release mechanisms of drug from dosage form to the targeted organ.	Higher control over the duration of drug release such as extended drug release system.
3	For formulation of dosage form proper use of medical device or technique.	Exploitation of novel manufacturing techniques.

Advantages of Ndds[3]

1. Raised Bioavailabity.
2. Good therapies for severe diseases such as Cancer.
3. Targeted drug delivery achieved through target specific affected part of body with less toxic effect.
4. By using lesser doses maintenance therapeutic response which is required and having better patient compliance.

5. By sustained drug delivery, dose release occurred over longer period of time.
6. Reduction in local as well as systemic side effects occurred due to drug dose.
7. Avoidance from first pass metabolism as well as gastrointestinal tract degradation.
8. Increased Biocompatibility.
9. Lesser expenditures are made from improved disease managing attained with this system.

Disadvantages[4]

Nevertheless, there are several advantages of NDDS but there are also some limitations in its usage.

Physiological parameters such as gastrointestinal degradation, food as well as other diseases, rate of intestinal transits which can affect the conventional drug delivery can also affect the controlled release of drug along with the absorption of drug.

Drugs having half- life of one hour or less are problematic to be manufacture as sustained release dosage form. The high rate of elimination of such drugs from the body requires a highly large maintenance dose which provides 8-12 hrs of continuous release.

The products which remain integral may become accommodates at some sites results slow release of drug from the dosage form may produce a high localized concentration of drug

DRUG CARRIERS FOR NOVEL DRUG DELIVERY SYSTEMS

1) Niosomes

Niosomes are defined as the vesicles having nonionic nature which is similar to liposomes, bilayer structure and it is formed by cholesterol incorporation as an excipient for improving rigidity and also other excipient. Niosomes are substitute tool for the liposomes. In case of neosomes various surfactant are use in formation of vesicles as well as they are having capacity to entrapment of hydrophilic as well as hydrophobic drugs. Niosomes are prepared by hydration of nonionic surfactant which formed dehydrated film which encapsulated hydrated solution. Niosomes are involve of two types of constituents that are non-ionic surfactant which gives advantage of being stable and additives or excipients. Penetration capacities of neosomes are higher than the emulsion. The existence of non-ionic surfactant overcomes the problems associated with liposomes such as oxidation susceptibility and stability. The sizes of the particles of niosomes are microscopic which ranges from 10nm to 100nm.[5,6,7]

Method of preparation

There are various methods of preparation from some are listed below.

Ether Injection Method

In this method by using specific gauze needle solution comprising a specific proportion of cholesterol in ether is gradually inserted into preheated aqueous solution of drugs whose temperature maintained at 60°C. Due to heating the vaporization of ether occurs which leads to formation of unilameller vesicles having surfactant contains drug. In case of thermo labile drugs, fluorinated hydrocarbons are used as an alternative to the ether because also at lower temperature they vaporized. By this method the size of niosomes obtained in the range between 500nm to 1000hm which is depends upon experimental conditions.[5]

Hand Shaking Method

In this method cholesterol as well as surfactant dissolved organic solvent involves ether, benzene or chloroform then by using vacuum evaporator under the reduced pressure the solvent is evaporated in round bottom flask. On the walls of round bottom flask deposited a mixture of solid surfactant and cholesterol. Further this layer of mixture is rehydrated using liquid solution containing drug with proper continuous shaking. This shaking resulted in the swelling of layer of surfactant. This enlarged amphiphles ultimately folds and made vesicles which entraps the drug. The volume of liquid entangled is in small quantity about 5-10%.

Sonication Method

Add dispersion of surfactant and cholesterol over the aqueous phase

↓

Then dispersion sonicated at 60 °C up to 10 min.

↓

Formation of multilameller vesicles

↓

Ultrasonicated by using probe Sonicator

↓

Formation of unilameller vesicles**.**

Advantages[7]

1. Niosomes are stable as well as osmotically active.
2. In case of handling of surfactant as well as storage do not need somewhat distinct conditions.
3. The properties of surfactants involves they are biodegradable, biocompatible as well as non-immunogenic.

4. Improve the therapeutic performance of the drug by protecting it from the biological environment and restricting effects to target cells, thereby reducing the clearance of the drug.
5. The niosomal dispersions in an aqueous phase could be emulsified in a non-aqueous phase to control the release rate of the drug and administer normal vesicles in external non-aqueous phase.
6. Niosomes are having better patient acquiescence as well as improved therapeutic result than other conventional oily preparations.
7. Niosomes can enhance the infusion of drugs over the skin.
8. Niosomes can be utilized in the delivery of wide variety of drugs as it has capability to entrap hydrophilic, lipophilic as well as amphiphilic drugs.

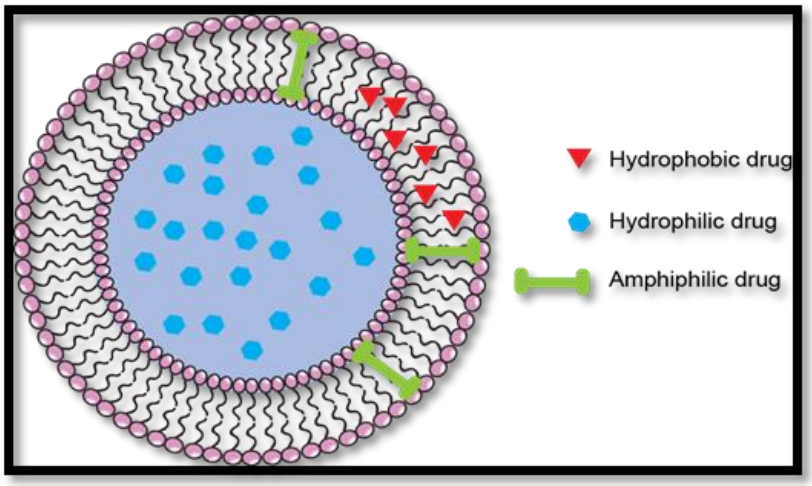

Fig 02: Structure of Neosomes.

2) MICROSPHERES

A microsphere are defined as the free flowing particles which are spherical in shape and includes particle size ranges from 1-50 microns. Microspheres consist of synthetic polymers or else proteins. Important application of development of microspheres as carrier for drug is to boost therapeutic efficacy of the drug and deliver the drug properly with site specificity along with maintenance of proper concentration of drug at the site of action with minimal side effect.

By using this system, it is possible to target the specific area in the body such as specific organ, group of cells as well as intracellular structure involves cell nucleus. The therapeutic efficacy of microspheres determined according to the rate of drug release. According to the

microencapsulation process the internal structure differs. This system is based on controlled release drug delivery in which drug release occurs through polymeric excipient in which entrapped drug released through pores.[8]

METHOD OF PREPARATION

Double emulsion technique

For the preparation of microspheres various techniques used which involves double emulsion method or multiple emulsion method. The emulsion type used is w/o/w. The technique is mainly useful in case of water soluble drugs, vaccines, proteins as well as for peptides. Both the polymers are used in this technique. In this method, the aqueous protein solution that might contain active constituents dispersed over lipophilic organic continuous phase. Continuous phase is generally contained of the polymer solution which eventually encapsulates of the protein containing in dispersed aqueous phase. Before the adding of aqueous solution of poly vinyl alcohol the primary emulsion is exposed for sonication otherwise homogenization. Which is further resulted in the formation of double emulsion. Further the emulsion is exposed to removal with either solvent evaporation or solvent extraction method. By using this technique of double emulsion various hydrophobic drugs which include vaccines as well as proteins are successfully incorporated into microspheres.

Advantages

1. They enable correct delivery of minor amounts of potent drug as well as lowered concentration of drug at location other than the target tissue or organ.
2. They afford shield for unstable drug previously as well as later administration, preceding to their convenience at the place of action.
3. They afford the capability to handle the in vivo action of the drug, pharmacokinetic profile, tissue dissemination and cellular interface of the drug. They permit controlled discharge of drug. Examples: Narcotic, Antagonist, Steroid hormones.

3) PHYTOSOME

Phytosomes are defined as the construction of the lipid compatible molecular complexes by incorporation of standardized plant extract as well as water soluble Phytoconstituents into phospholipids. It developed for the purpose of increase bioavailability and absorption. In case of phytosomes to protect the important compounds of herbal extract from deterioration due to digestive juices or secretions as well as gut bacteria the phytosomes are produced in small

cells. Phytosomes are good property of changeover from hydrophilic nature into lipid lovable nature of cell membrane and at the end into blood.[9]

In recent year there in great development and promotion of benefits from plant products. In case of Phytoconstituents, mainly they are water soluble and large size so they are not permeable through cell membrane also because of low lipid solubility limitations comes to cross lipid rich biological membrane which results in low bioavailability. Phytosomes are enhanced pharmacokinetic as well as various pharmacological parameters, which is effective in use in liver diseases as well as having anti-inflammatory property. Phytosomes are complex compounds prepared by reaction of preferably 1 mole of a natural as well synthetic phospholipids with one mole of component such as flavolignans, single or in complex form in dioxane solvent. The greatest superior ratio of phospholipid as to flavonoids is 1:1.

Method of preparation

Phytosomes are the complexes prepared by reaction of one mole of natural otherwise synthetic phospholipid (phosphatidylcholine, phosphatidylethanolamine or phosphatidyiserine) with one mole of other component (flavolignanans) in which they are either mixed alone otherwise in natural mixture in solvents (aprotic) such as either dioxane or acetone. And then from this complex can be isolated by method of precipitation along with non-solvent (aliphatic hydrocarbons) or other Methodes used such as lyophilization or spray drying. The best desirable ratio of phospholipid as to flavonoids is 1:1.

Advantages

1. They improve the absorption of lipid insoluble polar Phytoconstituents through oral as well as topical route show improved bioavailability, hence expressively greater therapeutic advantage.
2. Dose prerequisite is also reduced, as the absorption of active constituent(s) is enhanced.
3. Chemical bonds are formed among phosphatidylcholine particle and phytoconstituents, thus the phytosomes indicates improved stability profile.[10]

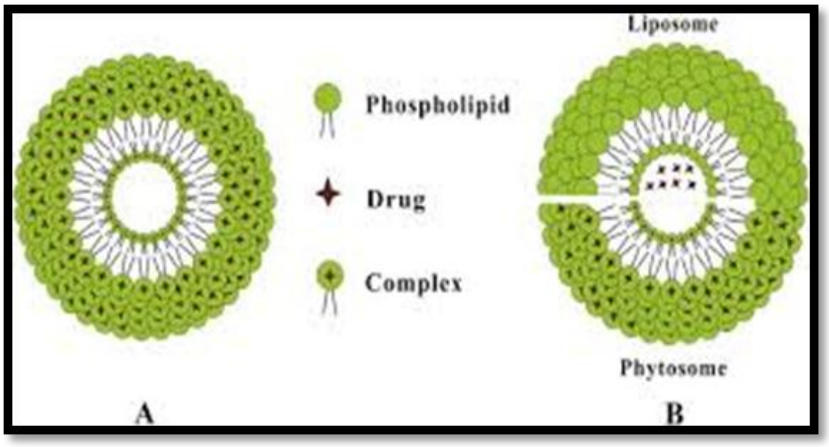

Fig 03: Structure of Liposome.

4) DENDRIMER

Dendrimers are defined as the nano size particles which involves size range from 1 to 15 nanometres consist of various properties includes they are synthetic and cost effective as well as well tolerated. They are easily uptake by cells due to their small size. Dendrimers are having branched structure with a central core unit which is having high degree of uniformity, narrow molecular weight and distribution as well as specific size and shape characters. The process of production involves series of repetitive steps. They are having cellular uptake process through endocytosis which causes drug binding to dendrimers into cell. The main application in development of dendrimers is to accelerate pharmacokinetic as well as pharmacodynamics properties as well as enhance bioavailability. Also attain the site specificity in case of drug release at proper area.[11]

Method of preparation

There are different methods of synthesis of dendrimers from which first two Methods are important.

1] Divergent growth method

This method involves the dendrimers growth originates from the core site and this process is continued tillthe described size dendrimers obtained.

2] Convergent growth method

In this method, growth of dendrimers start and end at the surface of dendrimers and then by linking surface units together it works inward. When the growing wedges are large enough, several are attached to an appropriate core to offer an entire dendrimer. A plus point of convergent growth rather than divergent growth stem is it includes two simultaneous reactions are essential for somewhat generation-adding phase.

3] Double Exponential' growth- monomers are produced from one starting for divergent and convergent growth which is further resulted two products reacted to offer orthogonally protected trimer, which may be used to repeat growth again.

Advantages

1. Drug to the affected part inside a patient's body directly.
2. Dendrimers are appropriate for targeting solid tumours due to improved permeability, partial drainage in tumour vasculature which will lead to accretion of macromolecules in tumour.
3. Controlled as well as sustained discharge of medicines are too attained.
4. Raise in therapeutic efficacy, reduction in side effects, reduced clearance of drug through changed spreading of drug in organs at place of localization and transport due to controlled as well as sustained release of the drug.

5) CHITOSON NANOPARTICLES

In recent years, nanoparticles are emerging trend and gain more attention of scientist in development of drug delivery system. They find advantageous due to their properties such as property of targeting various tissues, to access deep molecular target as well as control of drug release.

Nanoparticles are defined as the solid colloidal drug particles which size ranges from 10-10 nanometre in diameter and which is composed of polymers such as natural, synthetic or semi synthetic that encapsulating the drug compound. In case of chitosan it became advantageous over the other polymers carrier for nanoparticle drug delivery because of their biodegradable nature, easier formulation methods and vast applications. Due the versatile properties of chitosan it become advantageous in preparation of nanoparticles as well as micro particles in controlled release form. Chitosan have ability to control release of active ingredients so it becomes useful property.[12]

Method of preparation

Preparation method used for preparation of chitosan nanoparticles is isotropic gelation technique in which electrostatic interaction occurs between amino group of chitosan negatively charge group of tripolyphosphate (polyanion). By changing the proportion of chitosan and stabilizer the size as well as surface charge of nanoparticles can be changed. For the better yield the critical process parameter which is concentration of tripolyphosphate

should be maintained properly. As the solution temperature increases in ultrasonic radiation sample the particle size of nanoparticles decreased.

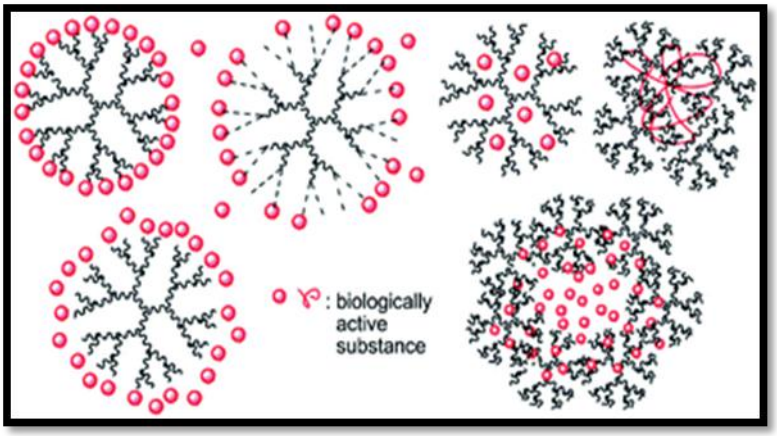

Fig 04: Structure of Chitosan Nanoparticles.

6) EMULGEL

Emulgel is defined as it is type of topical drug delivery system, they are either oil in water or water in oil type emulsion in which gel formation carry out by using gelling agent. Emulgel are mainly used in cosmetic preparations and skin care products. In case of Emulgel the conversion of emulsion into gel form enhances stability as well as efficacious as dual control release system. Because of absence of oily bases as well as excipients which are insoluble it shows better topical drug delivery as compared to other systems. Due to presence of gel phase it becomes non greasy and so that having favoured to patient compliance.[13]

Method of preparation

Various formulations were manufactured with use of differentquantity of gelling agent as well as penetration enhancers in which the method only diverged in procedure of production gel in diverse formulation. The same method is used for preparation of gel in all products. In the preparation of formulation gel phase were formulated by using mechanical stirrer in which Carbopol 940 was spread in water which is purified water with moderate stirring speed. After that the pH was attuned in range 6–6.5 by using triethanolamine (TEA). In this by means of liquefying span 20 in light liquid paraffin the oil phase of that emulsion was formulated though the aqueous phase were formulated by dissolving tween 20 with purified water. By dissolving methyl as well as propyl parabens in propylene glycol however then dissolved mefenamic acid in ethanol. After this both solutions were mixed with the aqueous phase. Clove oil as well as mentha oil were mixed in oil phase. Equally the oily as well as

aqueous phases were independently heated at 70–80°C and then the oily part was add to the aqueous part with nonstop stirring till it got cooled till room temperature. The formed emulsion was mixing with the gel with 1:1 proportion with minor stirring to attain the Emulgel.[14]

Advantages

1. Most of the topical dermatological preparation such as creams or ointments have drawback of less dissemination coefficient, tacky nature and also requirements rubbing throughout application. These restrictions are overcome in gel formulation.
2. Various other topical preparation show less stability than emulgel. As creams Show phase inversion, ointments show rancidity due to oily base and powders are hygroscopic in nature.
3. Production of emulgel is easy and done in short steps and no specialized instruments are needed thus low cost is needed for its formulation.
4. Emulgel act as a dual governed preparation and consequently is worthy for release of drugs with small half-life.[15]

7) ETHOSOMES

Ethosomes are defined as they are slight modification of liposomes which are lipid vesicles containing phospholipid, alcohol (in high concentration) as well as water. Ethosomes are mostly used for transdermal drug delivery system. The size of ethosomes varies from nanometres to microns. The synergistic possessions of mixture of phospholipids with high concentration of ethanol in vesicular preparations have been recommended to be liable for deeper delivery as well as diffusion in the skin lipid bilayers.[16,17,18]

Methods of preparation

1] Cold method

This is the common method for preparation of ethosomes which involves, in covered vessel containing ethanol components such as phospholipid, Drug as well as other lipid material dissolved and kept at room temperature by vital stirring with using mixer. Other components such as propylene glycol or other polyol are added during stirring. Then the mixture heated in water bath at 30°C and then heated water added to this mixture and then in covered vessel the mixture stirred for 5 min. Using sonication method the size of ethosomes can be reduced at required extent. The formulation is require store in refrigerator.

2] Hot method

In this method dispersion method used which involves phospholipid is dispersed over water with heating water bath at 40°C until colloidal solution obtained. In another vessel the ethanol along with propylene glycol are mixed and heated up to 40°C. After individually mixtures reaching at 40°C then the organic phase is added to the aqueous phase. According to property of drug (hydrophilic or hydrophobic) the drug either dissolved in water or ethanol. Using probe sonication method the size of ethosomes can be reduced at required extent.

Advantages

1. Improved infusion of drug over skin aimed at transdermal drug distribution.
2. Delivery of big molecules such as peptides, protein molecules is promising.
3. It comprises non-toxic raw material in preparation.
4. The ethosomal drug is managed in semisolid form therefore creating high patient obedience.
5. The Ethosomal system is passive, non-invasive as well as it is obtainable for instant commercial market.

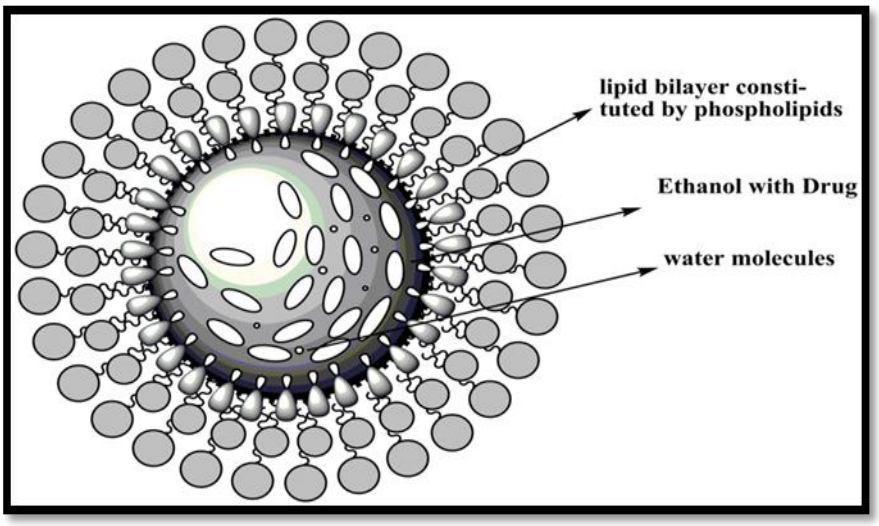

Fig 05: Structure of Ethosomes.

CONCLUSION

Novel drug delivery system is mainly used for the enhancing therapeutic effect of drugs. NDDS is mainly categorised into different types of system each system was plays an important role as compared to conventional drug delivery. For NDDS different type of carriers are used for preparation of dosage form and form these review it is cleared that niosomes, microspheres and emulgel are widely used and suitable carrier for a drug also they

required less time and easy method of preparation. Also each carrier having benefits and limitations for a drug delivery with its specific characteristics.

REFERENCES

1. Khan MG. The novel drug delivery system. *World journal of pharmacy and pharmaceutical science*, 2017; 7(6): 477-487.
2. Seyfoddin A, Dezfooli SM, & Greene CA. *Engineering Drug Delivery Systems* 2019. Woodhead Publishing.
3. Bhagwat RR, Vaidhya IS. Novel drug delivery systems: an overview. *International Journal of pharmaceutical sciences and research,* 2013; 4(3): 970.
4. Bhatia S. Nanoparticles types, classification, characterization, fabrication methods and drug delivery applications. *In Natural polymer drug delivery systems* 2019, (pp. 33-93). Springer, Cham.
5. Rajera R, Nagpal K, Singh SK, Mishra D. Niosomes: A Controlled and Novel Drug Delivery System. *Biol. Pharm. Bull.*, 2011; 34(7): 945-953.
6. Sankhyan A, Pawar P. Recent trends in niosome as vesicular drug delivery system. *Journal of Applied Pharmaceutical Science*, 2012; 2(6): 20-32.
7. Arunachalam A, Jeganath S, Yamini K, Tharangini K. Niosomes: a novel drug delivery system. *International journal of novel trends in pharmaceutical sciences,* 2012; 2(1): 25-31.
8. Patel NR, Patel DA, Bharadia PD, Pandya V, Modi D. Microsphere as a novel drug delivery. *International Journal of Pharmacy & Life Sciences*, 2018; 2(8).
9. Jain N, Gupta BP, Thakur N, Jain R, Banweer J, Jain DK, & Jain S. Phytosome: a novel drug delivery system for herbal medicine. *Int J Pharm Sci Drug Res.*, 2010; 2(4): 224-228.
10. Choubey A. Phytosome-A novel approach for herbal drug delivery. *International Journal of Pharmaceutical Sciences and Research*, 2011; 2(4): 807.
11. Mishra I. Dendrimer: a novel drug delivery system. *Journal of Drug Delivery and Therapeutics*, 2011; 1(2).
12. Nagpal K, Singh SK, Mishra DN. Chitosan nanoparticles: a promising system in novel drug delivery. *Chemical and Pharmaceutical Bulletin*, 2010; 58(11): 1423-1430.
13. Alexander A, Khichariya A, Gupta S, Patel RJ, Giri TK, Tripathi DK. Recent expansions in an emergent novel drug delivery technology: Emulgel. *Journal of Controlled Release*, 2013; 171(2): 122-132.

14. Khullar R, Kumar D, Seth N, Saini S. Formulation and evaluation of mefenamic acid emulgel for topical delivery. *Saudi pharmaceutical journal*, 2012; 20(1): 63-67.
15. Upadyay S, Chaunhanbist S, Kothiyal P. Emulgel: A Novel Approach for Topical Delivery of Hydrophobic Drugs. *International Journal of Pharmacy and Biological Sciences*, 2017; 7(3): 43-60.
16. Bhalaria MK, Naik S, Misra AN. Ethsomes: A novel drug delivery system for antifungal drugs in the treatment of topical fungal diseases. *Indian Journal of experimental Biology*, 2009; 47: 367-385.
17. Satyam G, Shivani S, Garima G. Ethosomes: A novel tool for drug delivery through the skin. *J Pharm Res*., 2010; *3*(4): 688-691.
18. Jain H, Patel J, Joshi K, Patel P, Upadhyay UM. Ethosomes: A novel drug carrier. *International Journal of Clinical Practice*, 2011; *7*(1): 1-4.