INTERNATIONAL RESEARCH JOURNAL OF PHARMACY
www.irjponline.com ISSN 2230 – 8407
Review Article

PRONIOSOME AS A SUSTAINED DRUG DELIVERY SYSTEM: A REVIEW

Singh Pankaj Kumar*, Niranjan Sunil Kumar, Irchhaiya Raghuveer
Department of Pharmacy, Bundelkhand University, Jhansi, India

Article Received on: 17/08/12 Revised on: 20/09/12 Approved for publication: 09/10/12

*E mail: pankajpharma07@rediffmail.com

ABSTRACT
Proniosome were prepared by slurry method with different surfactant to cholesterol ratio. An ideal or best formulation of proniosomes based niosome is said to be one which gives high entrapment efficiency with desirable sustained release. In this study entrapment efficiency is found to be cholesterol: surfactant ratio dependent. The release rate also found to be dependent of cholesterol: surfactant ratio. For effective proniosomes, it is essential that the surfactant coating be smooth and uniform to allow for rapid and consistent hydration. SEM study reveals that the coating of the surfactant on the maltodextrin powder is uniform. Angle of repose measurements indicated that the fluidity of proniosomes dry powder is equal to or better than that of maltodextrin powder, so further processing of proniosomes powder should be straightforward.
Key words: Proniosomes, span60, maltodextrin, cholesterol,

INTRODUCTION

The method by which a drug is delivered can have a significant effect on its efficacy. Some drugs have an optimum concentration range within which maximum benefit is derived, and concentrations above or below this range can be toxic or produce no therapeutic benefit at all. On the other hand, the very slow progress in the efficacy of the treatment of severe diseases, has suggested a growing need for a multidisciplinary approach to the delivery of therapeutics to targets in tissues. From this, new ideas on controlling the pharmacokinetics, pharmacodynamics, non-specific toxicity, immunogenicity, biorecognition, and efficacy of drugs were generated. These new strategies, often called drug delivery systems (DDS), are based on interdisciplinary approaches that combine polymer science, pharmaceutics, bioconjugate chemistry, and molecular biology.

The NDDS should ideally fulfill two prerequisites[1]

1) It should deliver the drug at a rate directed by the needs of the body, over the period of treatment.
2) It should channel the active entity to the site of action.

The main aim of novel drug delivery systems is to provide some control of drug release in the body, which is either of temporal or spatial nature, or both. It attempts to either sustain drug action at a predetermined rate, or maintains a relatively constant, effective drug level in the body with concomitant minimization of undesirable side effects. It also localizes drug action by spatial placement of control release systems adjacent to, or in the diseased tissue or organ; or target drug action by using carriers or chemical derivatization to deliver drug to particular target cell type. At present, no available drug delivery system behaves ideally for achieving all the lofty goals, but many attempts have been made to achieve them through novel approaches in drug delivery. Encapsulation of the drug in vesicular structures is one such system, which can be expected to prolong the duration of the drug in systemic circulation, and reduce the toxicity by selective up taking. Consequently a number of vesicular drug delivery systems such as liposomes, niosomes, transferosomes, and pharmacosomes and provesicular systems like proliposomes and proniosomes have been developed.

Conventional Drug Therapy

The short duration of action of conventional dosage form is due to its inability to control temporal delivery. If an attempt is made to maintain drug levels in the therapeutic range for extended period of time by increasing the dose of the drug initially, toxic levels may be produced at an early time which is undesirable & unsuitable[2]. There are several potential problems in it.

- If the dosing interval is not appropriate for the biological half- life of the drug, large peaks & valleys in the drug blood level may result. For example, drugs with short half -lives require frequent dosing to maintain constant therapeutic levels.
- The drug blood level may not be within therapeutic range at sufficiently early times, an important consideration for certain disease states.
- Patient non-compliance with multiple dosing regimens can result in failure of this approach.
- These problems are significant enough to make drug therapy with conventional dosage form less desirable than with controlled release drug therapy.

Controlled Drug Delivery System

An ideal dosage regimen[3] in the drug therapy of any disease is the one which immediately attains the desired therapeutic concentration of drug in plasma (or at the site of action) and maintain it constant for the entire duration of treatment. This is possible through administration of a conventional dosage form in particular dosage and at a particular frequency. The frequency of administration or the dosing interval of any drug depend upon its half-life or mean residence time and its therapeutic index. In most cases, the dosing interval is much shorter than half-life of the drug resulting in a number of *limitation* associated with such a conventional dosage form:[4]

Poor patient compliance; increased chances of missing the dose of a drug with short half life for which frequent administration is necessary.

1) A typical **peak-valley** plasma concentration-time profile is obtained which make attainment of steady state condition difficult.
2) The unavoidable fluctuation in the drug concentration may lead to **under medication** or **over medication** as the Cs value fall or rise beyond the therapeutic range.
3) The fluctuating drug level may lead to precipitation of adverse effect epically of a drug with small therapeutic index whenever overmedications.

There are two ways to overcome such a situation:

1) Development of new, better ,and safe drug with long half-lives and large therapeutic indices, and
2) Effective and safer use of existing drug through concept and techniques of controlled and targeted delivery systems.

The basic goal of any drug delivery system is to provide a therapeutic amount of drug to the proper site in the body to achieve promptly & then maintaining the desired drug concentration. That is why the drug delivery system should deliver drug at a state dictated by the needs of the body over a specified period of treatment. This idealized objective points to the two aspects most important to drug delivery, namely, spatial placement relates to targeting a drug to a specific organ or tissue while temporal delivery refers to the control of rate of drug delivery to the target tissue. An appropriately designed controlled release drug delivery system can be a major advance towards solving these two problems.

The advantage of controlled drug delivery system over a conventional dosage form are:

1) Improved patient compliance and convenience due to lesser frequent drug administration[5].
2) Reduction in fluctuation in steady-state levels and therefore better control of disease condition and reduced intensity of local or systemic side effects.
3) Increased safety margin of high potency drugs due to better control of plasma level.
4) Maximum utilization of drug enabling reduction in total amount of dose administered.
5) Reduction in health care cost through improved therapy, shorter treatment period.
6) A greater selectivity of pharmacological activity.

The disadvantage of controlled drug delivery system over a conventional dosage form are:

1) Decreased systemic availability in comparison to immediate release conventional dosage forms; this may due to incomplete release ,increased first pass metabolism ,increased instability, insufficient residence time for complete release, site specific absorption, ph-dependent solubility, etc.6Poor in vitro-in vivo correlation.
2) Possibility of dose dumping due to food, physiologic or formulation variable or chewing or grinding of oral formulation by the patient and thus, increased risk of toxicity.
3) Retrieval of drug is difficult in case of toxicity , poisoning or hypersensitivity reactions.
4) Reduced potential of dosage adjustment of drugs normally administered in varying strengths.
5) Higher cost of formulation.
6) Need for additional patient education and counseling.

Rationale of sustained/controlled drug delivery

The basic rationale for controlled drug delivery is to alter the pharmacokinetics and pharmacodynamics of pharmacologically active moieties by using novel drug delivery systems or by modifying the molecular structure and or physiological parameters inherent in a selected route of administration.[7]

- It is desirable that the duration of drug action become more a design property of a rate-controlled dosage form.
- The dosing interval may be increased either by modifying the drug molecule to decrease the rate of elimination or by modifying the release rate of a dosage form to decrease the rate of absorption. Both approaches seek to decrease fluctuations in plasma levels during multiple dosing, allowing the dosing interval to increase without either overdosing or under dosing.
- The purpose of a sustained action dosage form is to improve therapeutic management through assuring an uniform plasma concentration of drug at steady state and through reducing the ratio maximum and minimum plasma levels following each dose.

Potential advantages of controlled drug therapy

There are various advantages of controlled release system over with their non-controlled counterparts.[8]

(A) Improve efficiency in treatment: The most important advantage of controlled release is optimized therapy. The result of obtaining constant drug blood levels from a controlled release system is to promptly achieve the desired effect and maintain it for an extended period of time.

- Cure/ control condition more promptly.
- Reduction or elimination of fluctuations in the drug blood level allows better disease state management.
- The method by which controlled release is achieved can improve the bioavailability of certain drugs.
- Make use of special effects like sustained release Aspirin for morning relief of arthritis by dosing before bed time.

(B) Employ less total drug

Because of the nature of its release kinetics, a controlled release system should be able to use less total drug over the time course of therapy than a conventional preparation. Advantages[9] of these are:

- Minimize or eliminate local or systemic side effects.
- Obtain less potentiation or reduction in drug activity with chronic use.
- Minimize drug accumulation with chronic dosing

(C) Economy

Although the initial unit cost of most controlled drug delivery systems usually is greater than that of conventional dosage forms, the average cost of treatment over an extended time period may be lower. Economy may also result from a decrease in nursing time, hospitalization, less lost work time etc.[10]

- Reduction in health care cost reduction in dosing frequency.
- Avoids patient noncompliance.

(D) More consistent and prolonged therapeutic effect.

(E) Decreased incidence and/or intensity of adverse effect and toxicity.

Terminology

The general consensus is that controlled release denotes systems which can provide some control. Whether this is of a temporal or spatial nature or both, of drug release in the body. In other words, the system attempts to control drug concentrations in the target tissue or cells. Thus, prolonged release or sustained release systems, which only prolong therapeutic blood or tissue levels of the drug for an extended period of time. It can't be considered as controlled release systems by this definition. They are distinguished from rate controlled drug delivery systems.[11] Drug targeting; on the other hand, can be considered as a form of controlled release in that it exercises spatial control of drug release within the body. Since rate controlled release and drug targeting represent totally separate delivery approaches In general, controlled delivery attempts to:

- Sustain drug action at a predetermined rate by maintaining a relatively constant, effective drug level in the body with concomitant minimization of undesirable side effects associated with a saw tooth kinetic pattern.

- Localize drug action by spatial placements of a controlled release system (usually rate-controlled) adjacent to or in the diseased tissue or organ.
- Target drug action by using carriers or chemical derivatization to deliver drugs to a particular "target" cell type.
- In order to maintain a constant drug level in either plasma or target tissue, release rate from the controlled release system should be equal to the elimination rate from plasma or target tissue. The most conventional method to achieve a constant plasma level is the use of intravenous infusion.
- Comparative blood drug level profile obtained from administration of conventional, controlled as well as prolonged release dosage forms. Thus, the conventional tablet or capsule provides only a single and transient burst of drug. As long as the amount of drug is above the minimum effective conc., a pharmacological response is observed. Problem occurs when the therapeutic range is very narrow or when the peak is greater than the upper limit of this range. Indeed one of the main purposes of controlled is to improve safety and minimize side effect of the drug by reducing fluctuation in drug level. Prolonged release dosage form also reduced fluctuation in plasma drug level by slow in down the absorption rate due to slower drug release rate. In many cases, this is achieved by intermittently releasing a small burst of drug over a prolonged period of time as in the case of repeat action dosage forms.

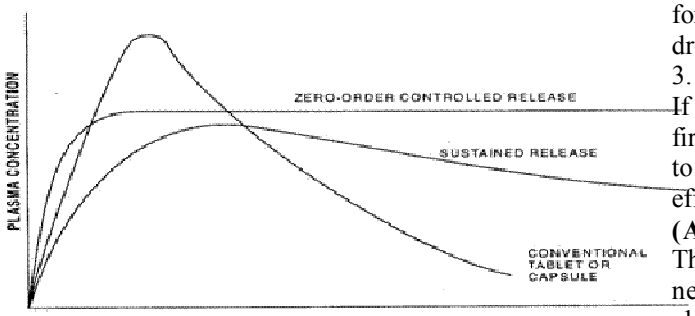


Figure 1.1: Plasma concentration-time curve

(A) Bioavailability of controlled release dosage forms

Ideally, the optimization of therapeutic efficacy and safety of controlled release dosage formulation is attained as a result of providing a nearly constant pharmacological response, thereby avoiding the normal peak and valley pattern associated with multiple dosing of conventional drug products. Therefore, in order to evaluate controlled release dosage forms, drug blood levels must be correlated with the claimed functional response to the particular delivery system under study. Usually the performance specifications consist of drug delivery rate Vs time profile.[12]

One of the critical limitations of controlled oral drug delivery systems is the transit time through the GI tract. The average time it takes for a solid dosage form, from the time of ingestion, to reach the lower end of the tract, is 10-12 hrs. This has restricted oral delivery systems to twice-daily administration, unless the drug has a long half-life. Recent attempts to overcome this limitation include the use of special drugs such as antihypertensive, use of modified density particles and most recently, the use of bioadhesives. However, a major problem which has to be taken into consideration during the design of these systems is the ability to localize such system in selected regions of the GI tract where absorption of the drug is optimum. Many drugs have narrow windows of absorption and if the delivery system releases its drug outside this window, low bioavailability and inferior therapeutic efficacy may result.

(B) Pharmacokinetic analysis of controlled delivery systems

The Pharmacokinetic analysis of controlled release delivery systems involves two primary processes. The first describes the initial diffusion of the drug through the special coating material or polymer membrane of the dosage form into the surrounding body tissue or fluids, and the second is subsequent absorption, distribution, metabolism and excretion of the drug. Since the absorption of the active ingredients is intentionally slowed, the distribution effects usually are obscured and in most cases, a simple one compartment open model can be used to calculate the in-vivo release rate constant, as long as the rates of elimination and metabolism are known.

Oral controlled drug therapy

In the oral controlled release drug administration, one encounters three areas of potential challenge:[13]

1. **Development of a drug delivery system***:* To develop a viable oral controlled release drug delivery system capable of delivering a drug at a therapeutically effective rate to a desirable site for duration required for optimal treatment.
2. **Modulation of gastro intestinal transit time:** To modulate the GI transit time so that the drug delivery system developed can be transported to a target site and reside there for prolonged period of time to maximize the delivery of a drug dose.
3. **Minimization of hepatic first pass elimination:** If the drug to be delivered is subjected to extensive hepatic first pass elimination, preventive measures should be devised to either bypass or minimize the extent of hepatic metabolic effect.

(A) Gastro-intestinal drug delivery system

The idea of proniosomal drug delivery began with the clear need to localize a drug at the GI tract. Therefore, a primary objective of using such drug delivery system orally would be achieved by obtaining a substantial increase in residence time of the drug for local drug effect and to permit once-daily dosing. [14]

(B) Merrits of gastro-intestinal mucosa as an administration site

Systemic delivery of drugs via absorption into the blood stream through the GI epithelium can be limited by drug degradation during the first pass through the liver; however the GI mucosa offers several advantages as an administration site over other mucous membrane. These include:

- The oral administration route is familiar, convenient and an accepted means of dosing for most people.
- The GI epithelium offers a large surface area for absorption.
- The GI epithelium provides a close connection with a vast blood supply.

(C) Potential advantages of oral controlled drug therapy

Convenience and ease of administration.

- Greater flexibility in dosage form design.
- Ease of production and low cost of such a system.

Factor influencing the design and performance of sustained/controlled release products

Drug properties:[15] The physiochemical properties of a drug, including stability, partitioning characteristic, charge and protein binding propensity, play a dominant role in the design and performance of controlled release systems.

Route of drug delivery: The area of the body in which drugs will be applied or administered can be restrictive on the basis of a controlled release mechanism. Certain route can exert a negative influence on drug efficacy, particularly during chronic administration, and hence other route of administration should be considered. Performance of the controlled release system may also be influenced by first pass metabolism, GI motility, blood supply and sequestration of small foreign particles by the liver and spleen.

Target sites: In order to minimize unwanted side effect, it is desirable to maximize the fraction applied dose reaching the target organ or tissue. This can be partially achieved by local administration or by the use of carrier. The absorptive surface of most route are impermeable to macromolecule or other targeted delivery system.

Acute or chronic therapy: Consideration of whether one expect to achieve cure or control of a condition and the expected length of drug therapy are important factors in designing controlled release systems. Long term toxicity of rate controlled drug delivery system is usually different from that of conventional dosage forms.

The disease: Pathological changes during the course of a disease can play a significant role in the design of a suitable drug delivery system. For example to design an ocular controlled release product for an external inflammation , the time courses of changes in protein content in ocular fluid and in the integrity of the ocular barrier would have to take into consideration.

The patient: whether the patient is ambulatory or bedridden, young or old ,obese or gaunt etc., can influence the design of a controlled release product. An implant or intramuscular injection of a drug to a bedridden patient with little muscle movement may perform in a function significantly different from that of an ambulatory patient. For example single unit controlled release products are particularly prone to intra-and inter- subject variation because of variability in individual GI motility.

Physicochemical properties of a drug influencing drug product design and performance

Molecular weight of the drug: The lower the molecular weight, the faster and more complete the absorption. For drugs absorbed by pore transport mechanism, the complete molecular size threshold is 150 dalton for spherical compound and 400 dalton for linear compound. However, more than 95% of drugs are absorbed by passive diffusion. Diffusivity[16]defined as the ability of a drug to diffuse through the membranes, is inversely related to molecular size. The upper limit of drug molecular size for passive diffusion is 600 daltons. Drugs with larger molecular size are poor candidates for oral controlled release systems e. g. peptides and proteins.

Aqueous solubility of the drug: A drug with good aqueous solubility, especially if pH-independent serve as a good candidate for controlled release dosage form e.g. pentoxifylline. Drug with pH –dependent aqueous solubility e.g. Phenytoin, or drug with solubility in non-aqueous solvent. Steroid, are suitable for parenteral (e.g. in depot) controlled release dosage form; the drug precipitate at the injection site and thus, its release is slowed down due to change in pH or contact with aqueous body fluids. Absorption of poorly soluble drugs is dissolution rate limited which means that the controlled release device does not control the absorption process; hence they are poor candidates for such systems.

Apparent Partition Coefficient of the Drug: Greater the apparent partition coefficient of a drug, greater is its rate and extent of absorption. Such a drugs have increased tendency to cross even the more selective barrier like BBB.

Drug pKa and Ionization at physiologic pH: The pKa range for acidic drugs whose ionization is pH sensitive is 3 to 7.5 and that for basic drug is 7.0 to 11.0. For optimum passive absorption, the drug should be ionized at that site at least to an extent0.1 to 5 % .Drugs existing largely in ionized forms are poor candidates for controlled delivery.

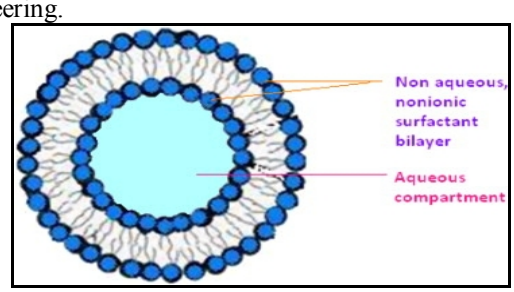
Drug Stability: Drugs unstable in GI environment cannot be administered as oral controlled release formulation because of bioavailability problems e.g. nitroglycerine. A different route of administration should then be selected such as the transdermal route.

Mechanism and Site of Absorption: Drug absorbed by carrier mediated transport process and those absorbed through a window are poor candidates for controlled release systems e.g. several B vitamins.

Vesicular drug delivery system

Vesicular systems are a novel means of drug delivery that can enhance bioavailability of encapsulated drug and provide therapeutic activity in a controlled manner for a prolonged period of time. Vesicle are colloidal particles in which a concentric bilayer made up of amphiphilic molecules surrounded an aqueous compartment. They are useful vehicle for drug delivery of both hydrophobic drug, which associated with the lipid bilayer and hydrophilic drugs, which are encapsulated in the interior aqueous compartment. In general vesicle made of natural or synthetic phospholipid are called liposome whereas those made of non- ionic surfactant (e.g. alkyl ethers and alkyl esters) and cholesterol constitute a nonionic surfactant vesicular system called niosomes.[17]

Encapsulation of a drug in vesicular structure can be predicted to prolong the existence of the drug in the systemic circulation and thus enhance penetration into target tissue and reduce toxicity. The phagocytic uptake of the systemic delivery of the drug loaded vesicular delivery system provides an efficient method of delivery of drug directly to the site of infection and hence reduces the drug toxicity. Vesicular delivery of the drug also improves the bioavailability of medications especially in the case of poorly soluble drug. They can incorporate both hydrophilic and lipophilic drug, this system also delay the elimination of rapidly metabolized drug and function as sustained release system. Now days vesicle as a carrier system have become the vehicle of choice in drug delivery and lipid vesicles were found to be of value in immunology , membrane biology and, diagnostic technique and most recently in genetic engineering.



Structure of niosome

Drawbacks associated with liposomes

- In a dispersed aqueous system liposomes show degradation of phospholipids by hydrolysis or oxidation.[18]
- In dispersed aqueous system it also have problem of sedimentation, aggregation or fusion during storage.
- Other problems associated with clinical application of liposome include difficulties in sterilization and in large scale production to obtain a product with adequate physical and chemical stability.
- Phospholipids are suitable for parenteral administration not for oral.
- Phospholipids are costlier one.
- To overcome these limitations various liposome like vesicles like proliposome, niosomes and proniosomes have been developed.

Niosomes: Better than liposomes

- Niosome are closed vesicles formed in aqueous media from nonionic surfactant with or without the presence of cholesterol or other lipids. Niosomes have unique advantages over liposomes. Niosomes are quite stable structures, even in the emulsified form. They require no special conditions such as low temperature or inert atmosphere for protection or storage, and are chemically stable. Relatively low cost of materials makes it suitable for industrial manufacture. A number of non- ionic surfactants have been used to prepare vesicles viz. polyglycerol alkyl ether, glucosyl dialkyl ethers, crown ethers, ester linked surfactants, polyoxyethylene alkyl ether, and a series of spans and tweens.[19]
- Niosomes possess an infrastructure consisting of hydrophilic and hydrophobic moieties together, and as a result, can accommodate drug molecules with a wide range of solubility. They exhibit flexibility in structural characteristics (composition, fluidity, size,), and can be designed according to the desired situation. Niosomes improve the oral bioavailability of poorly absorbed drugs, and enhance skin penetration of drugs.

Advantages of proniosomes over the other vesicular system

- Proniosomes required no special condition during their preparation storage as in the case of liposomes and niosomes.[20]
- Minimizes the problems of physical instability of niosomes on storage.
- In aqueous suspension liposomes have problems regarding degradation by oxidation and hydrolysis of phospholipids molecules
- Ease to transfer, distribution, measuring, and storage.
- Proniosomes is a dry product which could be easily hydrated immediately before use i.e. easy to use.
- Proniosomes is free flowing powder uniform in size.
- Cheap as compared to niosomes.
- Exhibit better purity than liposomes.
- Hydration is much easier than the long shaking process required in the case of liposome and niosomes.
- Proniosomes are dry powder, which makes further processing and packaging possible.
- The powder form provides optimal in capsules could be beneficial.

Components of proniosome

1. Non-ionic surfactant
2. Cholesterol
3. A polysaccharide carrier
4. Phospholipids
5. Charge inducers
   - Positive charge inducer
   - Negative charge inducer

Non-ionic surfactant

Non -ionic surfactant which are helping in formulation of vesicles. Non-ionic surfactants act as a main component in niosomal formulation .Generally they possess hydrophilic head group and a hydrophilic tail. Hydrophobic moiety consist of 1/2/3/ alkyl chain or in certain cases a single stearyl group. The alkyl group chain length is from C_{12} –C_{18} . The hydrophilic and hydrophobic variations determined by HLB number and balance between hydrophilic and hydrophobic interaction resulted from forces of attraction and repulsion are crucial in determining the types of aggregates which could form in aqueous environment, i.e. spherical or asymmetrical micelles, mesophase or vesicles. Like lipid non-ionic surfactants also orient in an aqueous medium as planner bilayer lattices wherein polar or hydrophilic heads align facing aqueous bulk while hydrocarbon segments are so aligned that their interaction with aqueous media is minimized. Every bilayer for thermodynamic reasons folds over itself to be a continuous membrane i.e. forms vesicles so that hydrocarbon/water interface remains no more exposed. The amphiphillic nature is an inexplicable prerequisite for molecules to form vesicles.[20, 21]

Cholesterol

Cholesterol is a waxy steroid metabolite found in the cell membranes. Cholesterol is is added usually to the non-ionic surfactant to give rigidity and give orientational order to the niosomal bilayer .Cholesterol is also known to abolish gel to liquid phase transition of niosomal system resulting in noisome that are less leaky. Steroids are important components of cell membrane and their presence in membrane brings about discernible changes in regard to bilayer fluidity and permeability. Cholesterol can be incorporated in bilayers at significantly higher molar ratios; however by itself it does not form bilayers. Thus, it could be used to manipulate the membrane characteristics. It is ampiphilic in nature[21] thus it aligns itself in a manner that OH group faces the aqueous phase while the aliphatic chain aligns parallel to hydrocarbon chain of surfactant. Cholesterol acts as a fluidity buffer, since below the phase transition temperature it makes the membrane less ordered while above it the membrane becomes more ordered.

Polysaccharides Carrier

In the formation of proniosomal powder polysaccharide carriers are used for loading of surfactants. As these carriers are biodegradable and non- toxic, they can be successfully be used in formation of proniosomal powder. The most commonly used carriers are sorbitol and maltodextrin.[22]

Maltodextrin

Maltodextrin is a synthetically manufactured long chain carbohydrate. Also known as a polysaccharide. It has minimal solubility in organic solvent. Thus it has possible to coat maltodextrin particle by simply adding surfactant in organic solvent .The use of maltodextrin as carrier in proniosome preparation permitted flexibility in the ratio of surfactant and other components which can be incorporated. Coating sorbitol results in solid cake like mass. It is produced from starch by partial hydrolysis and is usually found as a creamy-white hygroscopic spray dried powder. Maltodextrin is easily digestible, being absorbed as rapidly as glucose and might be either moderately sweet or almost flavorless. It is commonly used for the production of natural sodas and

candy. Maltodextrin consists of D-glucose units connected in chains of variable length. The glucose units are primarily linked with α(1→4) glycosidic bonds. Maltodextrin is typically composed of a mixture of chains that vary from three to nineteen glucose units long. Maltodextrin are classified by DE (dextrose equivalent) and have a DE between 3 to 20 (The higher the DE value, the shorter the glucose chains, the higher the sweetness and the higher the solubility). Maltodextrin do not go to the mailard reaction which leads to the browning and discoloration of product.

Phospholipid

Phospholipids are composed of phosphate groups, two alcohol, and one or two fatty acids. On one end of the molecule are the phosphate groups and one alcohol; this end is polar, i.e. has an electric charge, and is attracted to water. The other end Consist of fatty acids is neutral; it is hydrophobic and water insoluble but is fat soluble. The amphiphilic nature makes phospholipids important component of membrane. They form a two layer structure, called the lipid bilayer with polar head facing out on each surface to interact with water, and neutral tails driven inwards facing one another. The hydrophilic head contains the negatively charged phosphate group, and may contain other polar groups. The hydrophobic tail has long fatty acid hydrocarbon chain. When placed in water phospholipids form variety of structures depending on the specific properties of phospholipids.[24]

Charge Inducer

Non-ionic surfactant vesicles are also prepared with various ionic amphiphiles such as dicetylphosphate, stearylamine, etc, in order to achieve a stable vesicular suspension. The presence of charge inducer[25] avoids the aggregation that occurs among the vesicles in the isotonic saline solution. Aggregation is attributed to the shielding of the vesicle surface charge by the ions in the solution and thereby reducing the electrostatic repulsion. Two types of charge inducers are

- Positive charge inducer e.g. stearylamine
- Negative charge inducer e.g. dicetylphosphate

CONCLUSION

Proniosome is a better choice for oral drug delivery system to provide a better oral bioavailability. Proniosome are very promising drug carriers as compared to liposome and noisome. Compared to liposome and noisome suspension, proniosome represent a significant improvement by eliminating physical stability problems, such as aggregation or fusion of vesicles and leaking of entrapped drug during long term storage. They can easily be prepared and convenient to store, transport, and for unit dosing since proniosome's have similar release characteristic as conventional niosomes.

REFERENCES

1. Sudhamani. T, Priyadarisini N, Radhakrishnan M, promising drug carrier's proniosomes. Research International Journal of PharmTech 2010; 2(2): 1446-1454.
2. Chengjiu Hu, Rodes D.G, proniosomes. A novel drug carrier preparation. International journal of pharmaceutics.1999; 185:23-35.
3. Almira I, Blazek W, Rhodes D.G. SEM imaging predicts quality of niosomes from maltodextrin-based proniosome. Pharmaceutical Rearch. 200; 18(5): 656-661.
4. Agrawal R, Katare O.P, Vyas S.P. Preparation and in-vitro evaluation of liposome/niosomal delivery system for antipsoriatic drug dithanol. Int. J. pharm. 2001; 18(5): 656-661.
5. Perrett S, Golding M, Williams WP. A Simple Method for the Preparation of Liposomes for Pharmaceutical Applications: Characterization of the Liposomes. J. Pharm. Pharmacol. 1991, 43, 154-161.
6. Verma S, Singh S. K, Mathur Pooja. Nanoparticular vesicular system: aversetile tool for drug delivery. J. Chem. pharm. Res.2010; 2 (2):496-509.
7. Abubkar N.O. Recent progress in sustained/controlledora l delivery of captopril. Int. J. Pharm.2000; 194: 139-146.
8. Annakula Deepthi, Rao Madhukar Errabelli, Jukanti Raju. Provesticlular drug deliverys system: an overview and appraisal. Scholars research library. 2010; 2(4): 135-146.
9. Jain N. K. "Controllled and novel drug delivery 1st edition (1997) 101-106
10. Nasr Mohamed. In-Vitro and In-Vivo Evaluation of Proniosomes Containing Celecoxib for Oral Administration. AAPS Pharm SciTech, 2010; 11 (1) 85-89.
11. Rathi V. Formulation and evaluation of maltodextrin based proniosome loaded with indomethacin. International journel of pharmtech research. 2009; 1(3): 517-523.
12. Tank C. J, Borkhataria Chetan H, B. Ashok H. Formulation and evaluation of Aceclofenac loaded maltodextrin based proniosomes. Int. J. Chem Tech Res. 2009;1(3): 567-573.
13. Sharma P.K., Chandra A. Proniosome based drug delivery system of piroxicam. African Journal of pharmacy and pharmacology.2008; 2(9): 184-190.
14. Tripathi K.D."Essentials of medical pharmacology"; Fifth edition; jaypee brothers. medical publishers (p) Ltd. New Delhi, pp., 725, 730-731.
15. Gupta A, Prajapati S. K, Balamurugan M, Singh M, Bhatia D. Design and development of proniosomal transdermal drug delivery systems for captopril. Trop J Pharm Res. 2007; 6: 687-693.
16. Ibrahim A. Alsarra A.A. Proniosomes as a drug carrier for transdermal delivery of ketorolac. European Journal of phramceutics and biopharmaceutics. 2005; 59: 485-490.
17. Agarwal D, Pal D, Mitra A.K, and Kaur I.P. Study of the extent of ocular absorption of acetazolamide from a developed niosomal formulation humor. Int J Pharm. 2007; 338: 21-26.
18. Blazek-Welsh, Almera I. SEM imaging predicts quality of niosomes from maltodextrin-based proniosomes. Pharmaceuticals research. 2001; 18:5.
19. Vyas S. P, Khar R. "Targeted and controlled drug delivery and novel carrier system" 1st edition (2002) 173-75:149-51.
20. Lawrence M.J, Chauhan S, Lawrence S.M, Barlow D.J. The formation, characterization and stability of non-ionic surfactant vesicles. STP Pharm Sci 1996, 1, 49-60.
21. Sarpotdar P.P, Zatz J.L. Percutaneous absorption enhancement by non-ionic surfactants. Drug Dev Ind Pharm 1986, 12, 1625-1647
22. Rathi J. Chandra., Rathi V., Biradar S., Tamizharasi S:formulation and evaluation of maltodextrin based Proniosomes loaded with indomethacin. International J. of Pharm. Tech Res.2009: 1(3). 517-523
23. Mokhtar M, Sammour O.A, Hammad M.A, Megrab N.A. Effect of some formulation parameters on flurbiprofen encapsulation and release rates of niosomes prepared from proniosomes. Int J Pharm 2008, 361:104–111.
24. Kirby C, Clarke J, Gregoriadis G, Effect of the cholesterol content of small unilamellar liposomes on their stability in vivo and in vitro. Biochem J 1980, 186:591–598.
25. Navin K. Dahiya. Rekha Rao, Sanju Nandan ,Preparationand characterization technique in niosomal vesicular systems, Journal of pharmaceutical and biomedical science 2011.5{20},289-298

Source of support: Nil, Conflict of interest: None Declared

IRJP is an official publication of Moksha Publishing House. Website: www.mokshaph.com. All rights reserved.