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Recent Trends in Niosomal Formulations for the Enhancement of Bioavailability

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ABSTRACT

Niosomes are the non-ionic surfactant-based vesicular drug delivery system used to improve the permeability of a hydrophilic drug. This vesicular approach enhances the bioavailability by preventing the enzymatic degradation and acidic degradation of the drug. Niosomes are ampiphilic in nature and can entrap both the hydrophilic and lipophilic drug. It can provide sustained and controlled drug release inside the body. This review article explains briefly about different formulations of niosomes available to enhance the drug bioavailability. To enhance the topical bioavailability niosomes can be formulated as niosomal creams, niosomal gels andniosomal patches. Fororal bioavailability enhancement niosomal tablets and suspensions are available and also niosomal formulations to enhance the bioavailability of the drug given via nasal, pulmonary and parenteral route. The niosomal formulation provides better stability, enhanced bioavailability, reduced toxicity and adverse effects by preventing the degradation and pre-systemic metabolism and also by maintaining a constant plasma drug concentration when compared to the conventional dosage form available in the market. The niosomal formulations are better than the liposomal formulations because niosomes are more stable and cost-effective and do not undergo leakage due to the absence of lipid content. They are used for the treatment of diseases locally and systemically. They are used widely in cosmetic industry too. Still researchers are focusing on commercializing these niosomal drug delivery.

INTRODUCTION

Niosomes are non-ionic surfactant-based vesicular novel drug delivery system (Figure: 1) helps to deliver the drug effectively to its site of action. They are bilayer vesicular structure made up of non-ionic surfactant (Figure: 2) and cholesterol (Vadlamudi H. C et al., 2012). Niosomes have better penetration property and effectively cross the biological membrane because of their ampiphilic nature. Niosomes are bilayer structured similar like liposome, but niosomes are more advantageous than liposomes because they are more stable and cost effective. Niosomes are microscopic in size ranging between 10nm-100nm. (Chandu V. P et al., 2012). As they are ampiphilic in nature that means they contain both hydrophilic and lipophilic portions due to this they can entrap both the hydrophilic and lipophilic drug. Drugs that are having poor aqueous solubility and low bioavailability can be incorporated into this niosomes to enhance the permeability and obtain better bioavailability (Katrolia A et al., 2019).

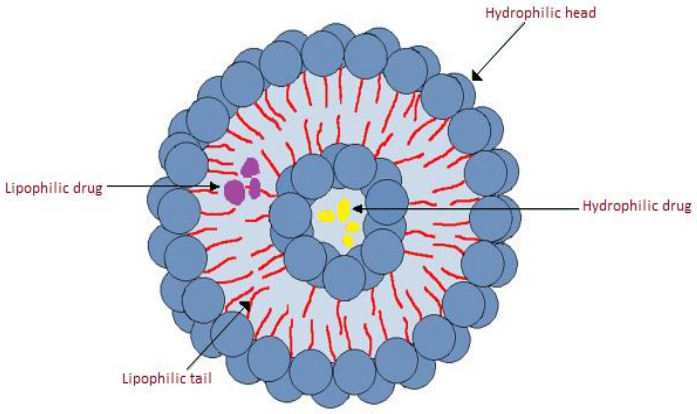

Figure: 1 (Ampiphilic structure of niosome)

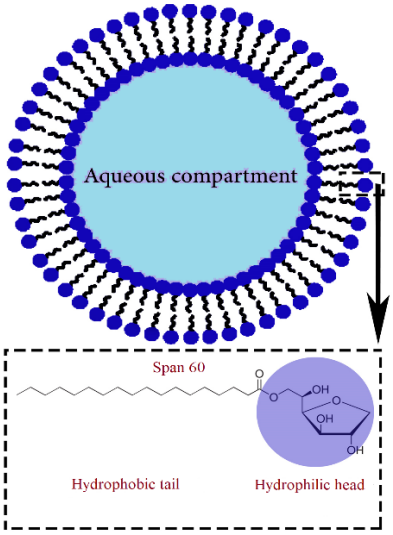

Figure: 2 (Span 60 surfactant-based niosome)

Advantages of niosome

- Niosomes are non-toxic, non-immunogenic, biodegradable and biocompatible in nature.
- Due to its ampiphilic nature it can entrap both the hydrophilic and lipophilic drugs.
- The storage of niosome is easier than liposome.
- They are more stable than the liposome.
- Niosomes helps to enhance the permeability of a poorly permeable drug.

- They are economical and cost-effective.
- Niosomes can release the drug in a controlled or sustained manner.
- It helps to improve the oral bioavailability of poorly aqueous soluble drugs.
- Helps to avoid the enzymatic and acidic degradation.
- Niosomes can help the drug to avoid presystemic metabolism.
- Niosomes possess stable structure even in emulsion form.

(Vadlamudi H. C et al., 2012).

Method of Preparation of Niosome

The size of niosome, entrapment efficiency and number of layers can be varied by using different preparation techniques for niosome.

The various methods are:

- Ether injection method
- Lipid injection method
- Handshaking method/thin film hydration method
- Multiple membrane extrusion methods
- Micro fluidization
- Emulsion method
- Reverse phase evaporation technique
- Sonication
- Transmembrane pH gradient drug uptake
- The bubble method
- Formation from pr-niosomes

(Vadlamudi H. C et al., 2012).

Drug-loaded niosomes are administered into the body via various route such as: topical, nasal oral, parenteral etc. The drug-loaded niosomal formulation can be administered into the body with the help of different formulation. These various niosomal formulations are: niosomal cream, niosomal gel, niosomal transdermal patches for topical drug delivery, niosomal tablet, niosomal suspension for oral drug delivery, niosomal inhaler, niosomal nebulizer for pulmonary drug delivery and niosomes for nasal and parenteral drug delivery etc. These drugs-loaded niosomes are incorporated into these conventional formulations to enhance the bioavailability by increasing the solubility and permeability of the drug and to prevent the dose-related and drug-related toxicity and adverse effects. These drug delivery systems of niosomes also helps to achieve controlled and prolonged drug release (Chen S et al., 2019).

A brief introduction of the various niosomal formulations is given below and some research work done by researchers on these formulations are mentioned.

Various niosomal carrier-mediated drug delivery systems

Niosomal cream

Niosomal cream is one of the types of topical drug delivery system used to treat the infection caused by bacteria, fungus, virus etc. It can be used to treat bacterial infection such as cellulitis, folliculitis, impetigo etc. Topical niosomal cream provides greater penetration and greater bioavailability than the conventional cream and it helps to improve the permeability of a poorly permeable drug. Niosomal cream helps us to achieve better drug entrapment efficiency, increase skin residence time, sustained or delayed release and better permeability of the drug on the upper layer of skin. They are biocompatible and non-toxic. One more advantage of this topical niosomal cream over oral route is that the systemic toxicity or side effect is less due to its lesser drug doses (Suresh R V et al., 2015).

Creams are used to treat various skin related problem such as hyperpigmentation, wrinkles, bacterial infection, fungal infection, rashes, itching etc. Sun burn is mainly caused due to the exposure of ultraviolet rays, this may also cause harmful side effects and leads to aging. This skin-related disorder and harmful effects of reactive oxygen species can be treated by this topical cream. It is possible to deliver the herbal extract into the body to treat several diseases by incorporating into novel approaches like niosome and can be delivered topically through this niosomal cream (Jadoon S et al., 2015).

Rice bran extract that contains antioxidative compounds such as y-oryzanol, ferulic acid, phytic acid etc. can be incorporated into niosomes and can be delivered topically by formulating into niosomal cream to provide better hydration enhancement and to improve some skin conditions such as skin lightening, roughness, thickness and elasticity in human being. This rice bran loaded niosomal cream is used as an anti-aging product (Manosroi J et al.,).

Niosomal cream of pentoxifylline shows greater wound healing properties. Pentoxifylline is hydrophilic and due to this hydrophilicity, their skin permeability is limited. So, this niosomal cream formulation of pentoxifylline helps this drug to cross the skin layer easily. This type of novel topical drug delivery provides greater wound healing property by increasing the therapeutic efficasy through various mechanisms such as : enhancing the localization of the active ingredients on the specific site or wound, facilitating the entry of the drug to the cytoplasmic space, improving the skin compatibility, by activating the transport mechanism through which the drug transport across the cell membrane, by enhancing the drug stability, and as well as by decreasing the toxic effects or adverse effects of the drug (Aghajani A et al., 2020).

Some of the drugs that can be incorporated into niosomal cream for the treatment of wound are soframycin, neosprine, silver nitrate, sulphadiazine, cetrimide, betadine etc. (Lalita C et al., 2020).

Niosomal Gel

There are various gel base or gelling agent available such as carbopol 940, HPMC, sodium alginate, sodium CMC etc. to prepare a topical gel. The gelling agent is dissolved in required amount of distilled water (Rupal J et al., 2010). Then the niosomes are added to the gel and the niosomes and the gel are stirred together until a homogenous mixture appears. To adjust the pH of the formulation to make it similar to the skin pH triethanolamine is added (Goyal G et al., 2015).

Niosomal gel is one of the topical formulations to and novel approaches to enhance the drug permeability and solubility of poorly soluble or poorly permeable drugs. Topical medication was invented a long back which helps to cure various types of skin related disorder. Niosomal gel provides greater stability, increase bioavailability and lesser side effect when applied topically (El-Say K. M et al., 2015). Hydrogel of niosome can be formulated with the help of

suitable polymer i.e., Carbopol. Compared to other semisolid dosage form niosomal gel provides better bioavailability due to their good rheological behavior, increased residence time (Jacob S et al., 2016).

Niosomal gel can be used to treat inflammation (Gharbavi M et al., 2018), fungal infection, bacterial infection, conjunctivitis etc.

The major drawback of the conventional ophthalmic formulation is its low bioavailability and reduced therapeutic action because of tear fluid.

Papain-loaded niosomal gel shows better efficacy than the ethosmal gel when it is given through transdermal route to treat scar. Fluconazole-loaded proniosomal gel also shows greater bioavailability when administered through topical route. Niosomal gel provides increased local bioavailability and prolonged duration of action due to higher drug accumulation into the skin (Bhardwaj P et al., 2020). Sustained release and prolonged release of niosomal gel helps to decrease the dose which prevents the first pass metabolism and GI toxicity (Asthana G S et al., 2016).

Diclofenac sodium is an analgesic used to reduce pain, also used to treat osteoarthritis, rheumatoid arthritis etc. Diclofenac sodium undergoes hepatic metabolism. So, this can be incorporated into niosomes and formulated as niosomal gel which acts as a controlled drug delivery system and delivers the in a controlled manner inside the body (Akbari J et al., 2021).

Drug like benzoyl peroxide which is used widely for the treatment of acne is having very less aqueous solubility. Thus, the bioavailability of this drug is also less when applied topically. But when the drug is formulated as niosomal gel after incorporating into niosomes and applied topically the permeability of the drug increases and a better bioavailability is achieved (Goyal G et al., 2015).

An anti-inflammatory drug like baclofen is a drug with narrow therapeutic index and short half-life. Oral administration of this drug may create various side effects like dizziness, nausea, vomiting, insomnia etc. So, to avoid these side effects the drug is administered into the body via topical route. And topical niosomal gel of this drug helps to achieve greater bioavailability and lesser toxicity or side effects (Nabarawi M. A. E et al., 2015).

Bovine serum albumin is a protein used in the field of tissue engineering as well as drug delivery system. This bovine serum albumin-loaded niosomal gel helps to obtain controlled drug delivery. Also, the stability of the drug is increased by this novel vesicular approach (Moghassemi S et al., 2016).

Farnesol is a drug of antifungal category used to treat candida infection. Niosomal formulation of farnesol helps this drug to achieve a sustained action inside the body. Also, by this formulation, the frequency of dose can be reduced. Thus, the side effects or toxic effects will automatically reduce (Barot T et al., 2021).

Niosomal transdermal drug delivery

Niosomal transdermal is a type of topical drug delivery system that are given or applied topically for both local as well as systemic effect. Niosomal transdermal drug delivery has several benefits over conventional drug delivery such as: painful intravenous drug delivery, hepatic first-pass metabolism, GI degradation, and drug food interaction can be overcome. This type of drug delivery provides increased drug permeation, sustained action by forming local depot etc. which helps achieve better bioavailability. Normal transdermal route has lesser penetration because of the stratum corneum, so to improve the penetration the drug can be incorporated into niosomes and formulated as niosomal transdermal patches (Muzzalupo R et al., 2015).

Niosomal transdermal drug delivery is an attractive, non-invasive, and a better alternative method when compared to oral conventional dosage form, which helps to reduce the dosing frequency, dosing number, reduce the systemic adverse effects etc. In case of transdermal drug delivery, the drug reaches to the site of action via various mechanisms such as: via transcellular route, through intracellular route, and through appendageal route. Niosomes improve the permeability by modifying or by loosening the stratum corneum. To administer a drug into the body via transdermal, route stratum corneum layer acts as major barrier which reduces the drug permeation. So, novel vesicular approach like niosome can play a vital role here to enhance the penetration. To prepare the niosomal patch components like polymer matrix, penetration enhancer, backing membrane, drug release rate controlling membrane, plasticizers, adhesives etc. can be used (Lakshmikanth G et al., 2018).

Methotrexate is a drug having low therapeutic index and less aqueous solubility due to this the bioavailability of this drug is less. So, to improve the bioavailability drug is incorporated

in niosomes and formulated as a niosomal transdermal patch. Where niosomes helps to improve the permeability of this drug (Bhavani D et al., 2020).

Buflomedil hydrochloride is a drug used to treat various disorders like: insomnia, dementia, ischaemic chest pain, disorientation, etc. But the problem associated with this drug is hepatic first-pass metabolism and also it also has various adverse effects. So, the niosomal transdermal drug delivery helps this drug to avoid the first-pass metabolism as well as helps to reduce those adverse effects by delivering the drug topically (Akhtar N et al., 2014).

Lacidipine is usedfor the treatment of hypertension, atherosclerosis etc. and also having antioxidant property. The major drawback of this drug is its oral bioavailability which is very less almost 10% and also the drug undergoes hepatic first-pass metabolism. These problems are due to it higher lipophilicity which makes this drug less soluble when given orally. So, to avoid those problems the is incorporated into niosome and given topically by formulating it as a transdermal product (Qumbar M et al., 2017).

An antiepileptic drug like midazolam which undergoes first-pass metabolism can be incorporated into niosome and then can be formulated as niosomal transdermal patches to overcome this problem. This niosomal transdermal patch of midazolam also helps to achieve sustained drug release (Shefrin S et al., 2019).

Celecoxib is a NSAIDS drug used to treat inflammation and also has analgesic action. The drug is highly lipophilic in nature and due to this the aqueous solubility of this drug is less. Thus, the oral bioavailability is also less when the drug is administered orally. And when the drug is administered orally due its higher doses it leads to an increase the risk of side effect. So, to overcome all these problems associated with the drug, this can be administered topically by formulating it as a niosomal transdermal patches. Which ultimately increase the bioavailability and reduce the side effect (Auda S. H et al., 2015).

Niosomal tablet

Niosomal tablet is an alternative approach of oral conventional tablet to enhance the drug bioavailability by overcoming the degradation, solubility, and permeability issue associated with conventional tablet. This formulation helps to avoid enzymatic degradation, degradation by acid present in stomach as well as helps to avoid presystemic metabolism.

Drug like ginkgo biloba extract can be incorporated into niosome and delivered orally as a tablet to improve oral bioavailability than the conventional one. Niosomal tablet also helps to enhance the oral stability by preventing enzymatic degradation or acidic degradation in stomach (Jin Y et al., 2013). The oral bioavailability of a class III or class IV drug can be enhanced by incorporating into niosomal tablet.

Drug like clarithromycin which is a broad-spectrum antibiotic and is a BCS class II drug that has low solubility leads to decrease in oral bioavailability due to its poor absorption. So, the drug is formulated as niosomal tablet to improve its solubility (Ullah S et al., 2016). Also, it is possible to achieve sustained action of drug when formulated as a niosomal tablet.

Ganciclovir is a drug of BCS class III with low permeability hence its oral bioavailability is less. So, to improve the bioavailability of this drug it can also be given through nasal route or intravenous route but at the same time cost is also increased up to 40%. Here oral niosomal formulation like niosomal tablet plays a major role which enhancing the bioavailability as well reduce the cost. This niosomal oral tablet behaves similar like liposomal oral tablet inside the body which is prolonging the drug release and circulation of the incorporated drug which alters the drug distribution in different organs. Niosomal tablet is chemically more stable, cost-effective than the liposomal tablet (Akhter S et al., 2012).

Niosomal tablet also plays a major role in case of treating type II diabetes, where metformin hydrochloride is used to treat this disorder. Metformin hydrochloride (MH) is a drug with short half-life and low bioavailability. To overcome this problems MH is incorporated in niosomes and formulated as a niosomal tablet which helps to achieve extended drug release. Thus, the frequency of the dose and the side effect is minimized, as well as the effective plasma drug concentration is maintained (Hasan A. A., 2013).

To achieve prolonged duration of action of several drug, sustained released drug delivery system plays a greater role whereby these problems like shorter half-life, dosing frequency, toxicity associated with dose and patient no-compliance etc. can be overcome. And to deliver drug with sustained-release pharmaceutical company mainly prefers oral sustained release tablet over any other formulation due to its ease of manufacturing. So, the drug like ketoprofen which is to be given as sustained release drug delivery is incorporated in niosomes and formulated as niosomal tablet to overcome some problems related to this drug like shorter half-life, less bioavailability, GI disturbance etc. (Raslan M. A et al., 2012).

Niosomal suspension

Suspension is the biphasic liquid dosage form of medicament administered orally to treat various disorder. This formulation is mainly for those drugs that are insoluble in aqueous medium. So, instead of solubilizing the drug is dispersed in the aqueous medium. In case of suspension, solid particle size plays a major role, lesser the particle size the surface area will be more and higher will be the drug absorption. Niosomal suspension prefers enhanced bioavailability and drug stability. Also helps to prevent enzymatic or acidic degradation when taken orally.

Niosomal suspension of cefixime drug that is used for the antibiotic activity provides better bioavailability and stability than the conventional one. This formulation of cefixime helps to achieve prolonged drug action inside body (Kumar B. S et al., 2017).

Ginkgo biloba extract is used to treat scavenging radicals, it also has antioxidant property, antitumor activity and acts as a protective agent. GbE also used to treat Alzheimer's disease, tinnitus etc. This GbE when administered orally as a conventional oral dosage form shows shorter half-life and poor bioavailability. To overcome this problem associated with the oral convention dosage form the drug is incorporated in niosomes and administered orally as a niosomal suspension. This niosomal suspension provides better drug entrapment efficiency and reduced particle size than the niosomal powder form (Jin Y et al., 2013).

Novel vesicular approach like niosome can be used to target a specific site, where the niosomal formulation of anticancer also helps to target the brain tumours. For some drug it is difficult to cross the Blood-Brain Barrier due to their less lipophilicity or higher molecular wight when targeted in brain. So, in this case this novel vesicular approach plays major role in drug transport across the BBB. Doxorubicin is an anticancer drug used for the treatment of malignant tumour. The drug is unable to cross the Blood-brain Barrier when used for brain targeting due to its poor lipophilicity. So, to cross the BBB and target the brain tumour effectively the drug can be incorporated into niosomes and given orally as a niosomal suspension (Bragagni M et al., 2012).

Treating the disease caused by various microbes maybe difficult sometimes because it requires chemotherapy which may produce toxicity, poor bioavailability, and is non-compliance by the patient. Antibiotics can be delivered effectively into the body by using this novel carrier system to reduce the adverse effect and to enhance the bioavailability. Isoniazid

is a drug used to treat tuberculosis, when this drug is incorporated in niosomes a sustained drug release is achieved at the targeted site. Thus, when the drug is given as oral niosomal suspension for targeted drug delivery it increases the bioavailability of the drug as well as reduces the toxicity (Singh G et al., 2011).

Candesartan is a drug used to treat hypertension. When this drug is taken orally as oral conventional dosage form, it fails to provide effective plasma drug concentration because of the poor aqueous solubility and poor oral absorption. Drug can be given by incorporating into liposomes but the main problem that may arise in this case is rancidity because the liposomes contain lipid constituents and due to this the susceptibility to rancidity is more. So, the niosomal formulation is perfect for this drug to overcome problems associated with oral conventional dosage from. The niosomal suspension of this drug enhances the oral drug absorption as well as enhances the bioavailability, this is because the hydrophilic drug is incorporated in niosomes due to this the particle size is very less and dispersed well in the liquid vehicle. It also helps to prevent the drug degradation and unwanted adverse effects by masking the drug into this vesicular system (Manvi S. R et al., 2012).

Oral niosomal suspension is a very effective oral drug delivery system that can also be used treat some fungal infection. So, the antifungal drug fluconazole can be administered orally to treat oropharyngeal candidiasis. This formulation provides better penetration and better bioavailability. Also, it is possible to achieve sustained drug action which can be beneficial in treatment of these fungal infections (Sharma S. K et al., 2009).

Carvedilol is a cardiovascular drug with low aqueous solubility, and it also undergoes hepatic first-pass metabolism, due to this the oral bioavailability of this drug is less. To enhance the oral bioavailability the drug given in the form of suspension by incorporating into niosomes which helps to increase the bioavailability and prevents the hepatic or pre-systemic metabolism. Suspension do not undergo disintegration like oral conventional tablet because the insoluble drug particles are suspended into the liquid system in a very minute form due to this the onset of action is also faster than the tablet form. Niosomal suspension provides greater membrane permeability than the conventional suspension and the degradation is also avoided because the drug is protected from the external environment (Arzani G et al., 2015).

Niosomes for nasal drug delivery

Nasal route is very effective when the drug is to be given systemically. Its onset of action is very fast. It has various advantages over oral drug delivery system such as: hepatic first-pass metabolism can be avoided; enzymatic degradation or acidic degradation can be avoided. This route is safer, non-invasive and also convenient.

In case of targeting the brain to treat various CNS disorder drugs can be delivered through nasal route. This route helps the drug to bypass the Blood-Brain Barriereffectively acts through the olfactory and trigeminal nerves route.

Bromocriptine Mesylate is a drug with very less oral bioavailability because of its first pass metabolism. So, to avoid this bioavailability issue instead of giving the drug orally, it can be delivered through nasal route by incorporating the drug into niosomes to enhance the bioavailability (Sita V.G et al., 2020).

Ondansetron HCL is an anti-emetic drug used to prevent nausea and vomiting related to cancer chemotherapy, anaesthesia, radiotherapy etc. To achieve a better anti-emetic property and increased residence time, the drug is incorporated into niosomes and formulated as thermoreversible in-situ gel and delivered via nasal route (Teaima M. H et al., 2020).

Loratadine is a drug used for the treatment of allergies and acts as an antihistaminic. Loratadine rapidly undergoes hepatic first pass metabolism due to this the oral bioavailability of this drug is less. So, to overcome this problem and to improve the bioavailability it can be administered through nasal route by incorporated into niosomes (Vyshnavi V et al., 2015).

Flibanserin is a drug with low aqueous solubility and undergoes presystemic metabolism. Thus, the bioavailability of this drug is less when administered orally. So, nasal route can be an alternative approach to avoid all these problems associated with this drug. When the drug is incorporated in niosomes its permeability also increases (Fahmy U. A et al., 2020).

One of the major disadvantages of this nasal route is bioavailability which is very less for drugs that are hydrophilic in nature. The bioavailability issue is due to lesser membrane penetration. So, to increase the permeability novel vesicular approach like niosomes can play a vital role here. Pentamidine is the drug having low permeability and also having a hepatotoxicity nature. To overcome this problem, it is coated with chitosan for increased

residence time and then formulated as niosomal formulation for nasal drug delivery (Rinaldi F et al., 2018).

Drug like olanzapine that acts as an antipsychotic drug and is having poor oral bioavailability due to its hepatic first-pass metabolism and aqueous insolubility. So, instead of giving this drug orally it can be administered into the body via nasal route to avoid those problems. To enhance the permeability when administered through nasal route the drug is incorporated into niosomes. And this is a very effective approach to bypass the Blood-Brain Barrier when the drug is used for brain targeting (Khallaf R. A et al., 2019).

Sumatriptan is the drug for acute migraine. The main problem associated with this drug is its less oral bioavailability which is 14%. This is mainly because of the presystemic metabolism or hepatic first pass metabolism. Nasal route is used as an alternative approach here to bypass this metabolism and to achieve better bioavailability, where the drug is delivered via this route after incorporating into niosomes (Devi S G et al., 2000).

Alzheimer is a brain related disorder which may causes due to an imbalance of acetylcholine neurotransmitters. Rivastigmine is a drug that acts as an acetylcholine inhibitor and by reducing the amount of acetylcholine it shows its action. This drug also undergoes hepatic first-pass metabolism if administered orally due to this the oral bioavailability of this is also less. So, to avoid this presystemic metabolism and to enhance the bioavailability, the drug is delivered to the body via nasal route by incorporating into niosomes and formulating a niosomal formulation (Kulkarni P et al., 2021).

Niosomes for pulmonary drug delivery

Pulmonary route of drug delivery is used over oral or other route when it is meant for targeting the lungs or respiratory tract to treat some respiratory tract infection. Because of the large surface area this drug delivery system is suitable for delivering the drug effectively. Drug can be delivered via this route with the help of device like inhalers and nebulizers. So, the novel carrier system or vesicular approaches are used to overcome some limitation like low therapeutic efficasy of the inhalation device and improper loading of drug, associated with this route. By the help of niosomal formulation the entrapment efficiency will be more and the drug loading can also be improved (Chen S et al., 2019).

Ciprofloxacin is an antibiotic, and it shows great antibacterial activity against both gram-positive and gram-negative bacteria when used for the pulmonary infection. Liposome is

good carrier for this drug when given via this route but due to some reason like hydrolysis, oxidation the non-ionic surfactant-based niosome is the best carrier for this. The niosomal carrier is used to enhance the drug penetration, enhance the drug loading capacity etc. thus, the bioavailability is also increases. By changing the ratio of span 40, span 60, tween 40 and tween 60 surfactants proper vesicular niosomes are prepared. Nebulizer is device use to deliver the aerosolized drug to the pulmonary region. When this ciprofloxacin-loaded niosomes are incorporated into this nebulizer and delivered to the lung or pulmonary region, the antibacterial activity of this drug increases (Moazeni E et al., 2010).

Drug loaded niosomes provides a controlled drug release when given as a pulmonary drug delivery system with the help of a metered dose inhaler. Salbutamol sulphate (SS), when entrapped into niosomes and delivered via pulmonary route the drug loaded niosomes, gets submersed into the alveoli layer and due to the ampiphilic nature of niosomes it easily crosses the layer. SS loaded niosomal controlled drug delivery shows increase plasma drug concentration than the sustained release formulation of salbutamol sulphate. Ultimately this formulation SS shows better pharmacokinetic properties than conventional one and also the dose related toxicity is reduced as it maintains a constant therapeutic level of drug (Arafa M. G et al., 2018).

Problem associated with glibenclamide is its plasma half-life which is very short due to this the frequency of dose administration is high. After oral administration glibenclamide undergoes hepatic first pass metabolism, the metabolism rate is almost 50%. To overcome these problems, glibenclamide is incorporated in niosomes and given as a pulmonary administration via nasal route. This niosomal formulation protects the drug from presystemic metabolism and when delivered in lung due to the larger surface area the drug absorption increases. Particle size plays a major role in case of pulmonary drug delivery for effective permeability, so the niosomes prepared here are of particle size lesser than 100 nm. The particle size of niosome is reduced by altering the surfactant ratio and by changing the preparation method. This lesser particle size of niosomes helps the drug to cross the biological layer easily and helps to achieve greater bioavailability (Rashid R. S.A et al., 2020).

Aerosolized niosomal drug delivery provides several advantages like prolongation in drug circulation, enhanced drug entrapment efficiency, alteration in organ distribution and also provides better metabolic stability. Retinoids are the analogs of vitamin A and they effective

in treatment of cancer. Like other anticancer drugs these derivatives also have some serious toxic effects on chronic administration. To treat disease like lung cancer and malignant disorder these retinoids derivatives are incorporated in niosomes and aerosolized to target lung. The dose is delivered with the help of nebulizer. When these drugs loaded niosomes are administered via pulmonary route, they effectively target the lung and deposit in alveoli and due to the lesser particles size and higher lipophilicity these niosomes easily crosses the layer, thus the toxicity associated with these derivatives are reduced and also the bioavailability increases (Desai T. R et al., 2002).

Niosomes for parenteral drug delivery

Drugs when administered parenterally it shows 100% bioavailability so there is no need of novel approaches to enhance the bioavailability. But some drugs that are used to target a specific site can be incorporated into niosomes and can be administered parenterally because niosome is the novel nano vesicular system that is very effective in targeting a specific site. Niosomal formulation also enhances the drug stability when administered parenterally.

Nystatin is an antifungal drug used for the treatment of various topical, vaginal and oral fungal infection. The bioavailability of this drug is less when administered orally or via topical route because the permeability of this drug is very less through the skin and gastrointestinal tract. Also, the drug when administered via these routes it causes severe toxicity like severe shaking, chills, fever, malaise etc. To avoid all these problems novel vesicular approaches are introduced. To prevent the toxicity associated with oral and topical route nystatin is delivered into the body via parenteral route by incorporated into niosomes (Ridy M. S. E et al., 2011).

In case of targeted drug delivery niosome plays a decent role to target a specific site which not only reduces the size but also the dosing frequency. Magnetic carrier is a very effective and useful tool for this targeted drug delivery than the other nanocarrier system. It shows several benefits like direct visualization with the help of magnetic resonance imaging. In this magnetic drug targeting the drug release is controlled by external magnetic field. Here doxorubicin is a drug incorporated in niosomes along with magnetic carrier for better drug targeting and by this the entrapment efficiency will be more and vesicular stability will also increase. This doxorubicin-loaded magnetic niosomes is delivered into the body via parenteral route which provides faster onset of action and better targeting (Tavano L et al., 2013).

Niosomes is a very effective carrier that can deliver vaccine and gene into the body via parenteral route. For sustained action of vaccine niosomes are used. This niosomal formulation of vaccine and gene helps to prevent degradation and enhances the stability. Vaccines are higher molecular weight compound due to which they are unable to cross the biological membrane or Blood-Brain Barrier in case of brain targeting, to increase their permeability they are incorporated into niosomes and given parenterally. This helps to increase the bioavailability of these vaccines and genes (Paradakhty A et al., 2013).

This novel vesicular nanocarrier is used in parenteral drug delivery for targeted drug delivery and to obtain a sustained drug release. With the help of this drug delivery system steady state plasma drug level can be reduced. Intravenous infusion of rifampicin loaded niosomes shows lung accumulation when used for the treatment of pulmonary disorder. This rifampicin-loaded niosome is used for the site-specific targeted drug delivery and it also shows better volume of distribution in different organs when compared to conventional drug delivery. Niosomes are very effective in chemotherapy for cancer treatment. Drug like 5-flurouracil can be incorporated into niosomes for tumour targeting (Chen S et al., 2019).

Local anaesthetics like lidocaine is incorporated in niosomes and given parenterally for anaesthesia. This is done because the skin permeability of this drug is less (Aditya S et al., 2019).

To achieve a better immunogenic response the adjuvants are delivered through niosomal carrier system. So, to get a better efficasy or bioavailability the ALM is incorporated in positively charged niosomes and delivered parenterally, thus the effectiveness of the drug will increase against this cutaneous leishmaniasis (Pardakhty A et al., 2012).

CONCLUSION

Niosomes have been extensively investigated in recent years for a variety of uses, including topical, transdermal, oral, and brain-targeted drug delivery. They are simple to prepare and have a lower cost than its analogue system liposomes, while also having a higher entrapment efficiency. In the fields of pharmaceutical and aesthetic sciences, this versatile drug delivery technology offers a lot of potential. Niosomes are promising delivery systems, and their potential can be further enhanced by novel preparation, modification, and formulation components that enable targeted distribution, improved drug entrapment efficiency, and the development of vesicles with unique structures.

Niosomes incorporated in a marketed formulation provide a stable and effective formulation than the marketed conventional dosage form with reduced toxicity and adverse effects and improved bioavailability. Thus, these novel drug delivery systems are better and effective formulations in case of treating various diseases when given topically, orally, parenterally and via pulmonary and nasal route.

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