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Review Article

Niosomes: A novel drug delivery system and its Therapeutic uses

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Abstract

Administration of medications to specific targets with minimal affinity to other organs is a challenge during treatment of disease conditions. Drug-delivery systems which are Target-specific enable the localization of drugs to their site of action. These Targeted drug delivery systems utilize various carriers, such as serum proteins, liposomes, synthetic polymers, and microspheres. Niosomes, are a type of drug delivery system which has a bilayer structure made of non-ionic surfactants. Niosomes are amphiphilic hence they can encapsulate both lipophilic or lipophobic drugs and increase their bioavailability. This review describes the structure, methods of preparation and applications of niosomes in various diseases.

Keyword: Niosomes, Drug Delivery, Therapeutic Uses

Introduction:

Drugs are used for cure as well for palliative treatment in many diseased conditions. Nevertheless they are also associated with systemic adverse effects because of their non-specific action on all organs. Drug concentration attained in tissues which are not the site of action is responsible for their side and toxic effects[1]. A number of drug delivery systems have been introduced among which liposomes and niosomes are proved to be effective. They have the advantage of delivering the drug molecule to the site of action thereby increasing the bioavailability and decreasing the side effects[2]. Niosomes are made up of amphiphilic surfactants which can accommodate both hydrophilic and lipophilic drugs. Liposomes acquired a lot of attention after their discovery as drug transporters but niosomes have certain advantages compared to liposomes such as low cost, good physical and chemical stability due to non-ionic surfactants and ease of synthesis[3]. Niosomes have the ability to carry both hydrophilic and lipophilic drugs in the same vesicle with higher bioavailability and low toxicity. The cholesterol present in the niosomes provides stability to the vesicle thus restrains degradation of the drug within it before it reaches the site of action[4].

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Structure of niosomes

Niosomes have unilammelar or bilammellar vesicular structure. They are made up of non-ionic surfactants and other additives[3]. The vesicles have both hydrophilic as well hydrophobic components, thus they encapsulate and deliver hydrophilic and hydrophobic drugs to the target (Fig – 1). The non-ionic surfactants and additive used in formation of niosomes are listed in Fig – 2. The non-ionic surfactant forms a bilayer and continues on itself forming a vesicle in such a way that the membrane will be hydrophobic and the centre of vesicle will be hydrophilic. The cholesterol in the niosomes will enable rigidity and maintain permeability of the vesicle while the charged molecule helps to prevent aggregation of the vesicles[4].

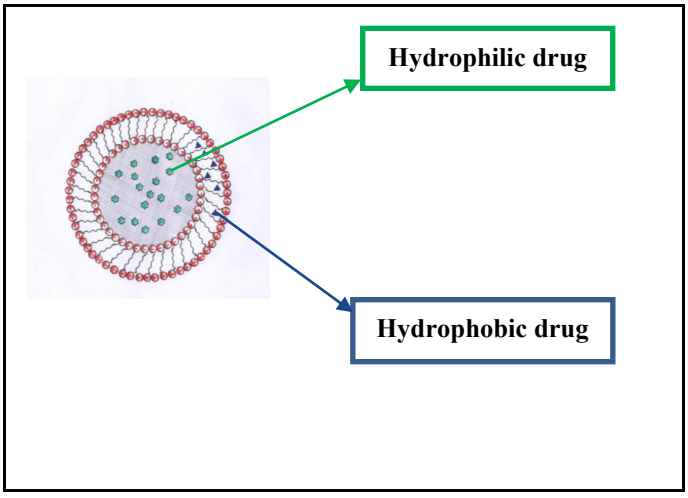

Figure 1 : Showing composition of niosomes – Bilammellar structure

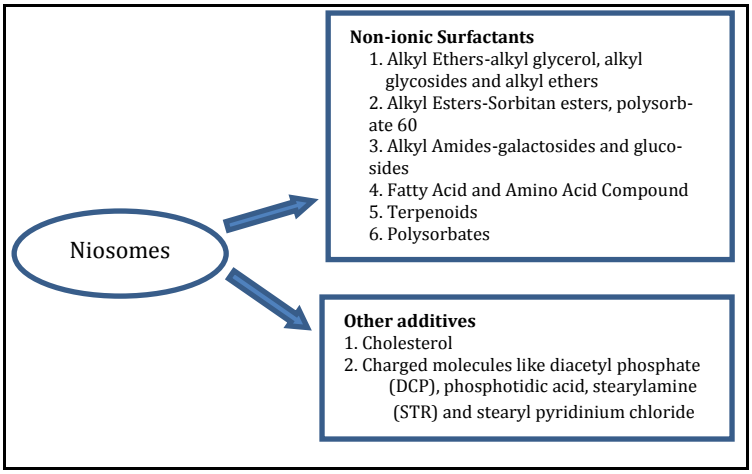

Fig 2 : Composition of niosomes

Preparation methods for niosomes

Niosomes are prepared commonly by hydration of non-ionic surfactants. The other methods by which they are formed are - bubbling of nitrogen, transmembrane pH gradient method, sonication, the enzymatic method, lipid layer hydration, reversed-phase evaporation, ether Injection and microfluidization [2,5]. The details of these methods are explained in Table – 1

Table 1 : Techniques for preparation of niosomes

	Technique of niosome preparation	Description of the technique
1.	Bubbling of Nitrogen	Cholesterol and surfactant at pH7.4 and 70°C in round-bottomed flask - nitrogen gas was passed through the homogenate to from large unilamellar vesicles
2.	Transmembrane pH Gradient Method	Surfactant and cholesterol in chloroform are evaporated under reduced pressure and stream of N2 - lipid film is hydrated with an acidic compound
3.	Sonication	Surfactant cholesterol combination in water phase is distributed along with the drug in flax - subjected to probe sonication for 3 minutes at 60°C
4.	The Enzymatic Method	Ester bond in cholesterol and polyoxyethylene is cleaved by esterases - combined with dicetyl phosphate and other lipids to form multilamellar niosomes
5.	Lipid Layer Hydration	Surfactant and cholesterol in chloroform are evaporated under reduced pressure and stream of N2 – lipid film is hydrated with an aqueous solution of drug
6.	Reversed-Phase Evaporation	Surfactants dissolved in a mixture of ether and chloroform - added into water phase - emulsified - mixture is homogenized
7.	Ether Injection	Surfactant, cholesterol and drug, is dissolved in diethyl ether -injected gradually into an aqueous phase
8.	Microfluidization	It is based on the submerged jet principle - two fluidized streams are connected at ultrahigh speeds - inside the interface chamber - thin-liquid sheet was set up to deliver the energy of the system for the formation of niosomes

Clinical applications of niosomes

1. **Cancer chemotherapy** – The niosomal drugs for cancer chemotherapy are listed in Table 2 [1,11]. Most the niososmal drug preparations showed good activity against cancer cells compared to their normal counterparts and also had less toxic effects.

Table 2: Noisome drug preparations used in treatment of cancer

Niosomal drug	Indication
Doxorubicin	Showed increased life span and decreased proliferation of sarcoma
Daunorubicin	Destroyed lymphoma cells in peritoneum within 3 days of treatment
5-fluorouracil	Effective in treatment of Skin cancer
Tocotrienol	2-fold increase in cytotoxic effect and 2.5-fold increase in drug uptake by breast cancer cells
Artemisinin	Cytotoxic to melanoma cells with very minimal toxicity to normal skin cells
Tamoxifen citrate	Greater cytotoxicity against MCF-7 breast cancer cell line and reduction in tumour volume
Mitoxantrone	showed greater cytotoxicitythan conventional niosomes on the cancer cells but a lower cardiotoxicity and other systemic side effects
Cisplatin	Increased cytotoxicity toward breast cancer cells

2. Antiinflammatory agents

Diclofenac sodium, nimesulide, flurbiprofen exhibited good anti-inflammatory activity compared to free drugs[12]. Topically used niosomal serratiopeptidase showed comparably better efficacy than diclofenac in gel formulation[1]. Naproxen proniosomes (NAPRNs) transdermal preparation showed faster release of naproxen and better anti-inflammatory property compared to normal naproxen in rat models done by Mohanty D et al[7]

3. Anti microbials

Cefpodoxime Proxetil combined with span 20 and cholesterol reduced its toxicity whereas rifampicin was combined with span 85 and cholesterol for lung targeting[4].Similarly itraconazole, fluconazole and miconazole niosomal preparations showed better efficacy in treatment of fungal infections[1]. Sodium stibo-gluconate niosomal formulation showed higher levels of antimony in liver as compared to free drug thus enabling higher efficacy[11].

4. Other applications

Niosomes loaded with vancomycin instilled into the eye of MRSA-infected rabbits showed 2.5-fold increase in antibacterial efficacy compared with animals treated with vancomycin free drug solution[9]. Drugs used as niosomes for ophthalmic use are- brimonidine tartarate, gentamycin sulphate, timolol maleate and cyclopentolate[10]. Eid RK et al found that use of olive oil and clove oil to noisome containing felodipine increased its efficacy by improving skin penentration[6]. Tetanus toxoid and New castle disease vaccine have been formulated as niosome for better delivery of vaccine antigens[5]. The niosomal glipizide and metformin hydrochloride release experiments using buffers were performed at different pH values mimicking the normal blood pH showed that the drug release lasted for 12–14 hrs[13]. Other drugs developed as transdermal niosomes are anti-inflammatory drugs like flurbiprofen and piroxicam, sex hormones like estradiol and levonorgestrel[8].

Conclusion

Niosomes are newer novel drug delivery system made of amphiphilic vesicular structure capable of transporting both lipophilic and hydrophilic drugs to their target tissues. They have the advantage of higher bioavailability, stability, efficacy and less toxicity compared to free drugs. In recent future niosomes can be the choice drug delivery system for treatment of cancers, immunocompromised states as well as end diseases.

References

1. Yeo PL, Lim CL, Chye SM, Ling APK, Koh RY. Niosomes: a review of their structure, properties, methods of preparation, and medical applications. Asian Biomed 2017;11: 301–14.
2. Sharma D, Ali AAE, Aate JR. Niosomes as Novel Drug Delivery System: Review Article. Pharma Tutor 2018; 6: 58-65.
3. Ge X, Wei M, He S, Yuan WE. Advances of Non-Ionic Surfactant Vesicles (Niosomes) and Their Application in Drug Delivery. Pharmaceutics 2019; 11: 55-71.
4. Rajera R, Nagpal K, Singh SK, Mishra DN. Niosomes: A Controlled and Novel Drug Delivery System. Biol Pharm Bull 2011; 34: 945-53.
5. Gharbavi M, Amani J, Kheiri-Manjili H, Danafar H, Sharafi A. Niosome: a promising nanocarrier for natural drug delivery through blood-brain barrier. Adv Pharmacol Sci 2018; 2018: 1–15.
6. Eid RK, Essa EA, El Maghraby GM. Essential oils in niosomes for enhanced transdermal delivery of felodipine. Pharm Dev Technol 2018; 24:157-65.
7. Mohanty D, Rani MJ, Haque MA, Bakshi V, Jahangir MA, Imam SS et al. Preparation and evaluation of transdermal naproxen niosomes: formulation optimization to preclinical anti-inflammatory assessment on murine model. J Liposome Res 2019:1-11.
8. Kazi KM , Mandal AS, Biswas N, Guha A, Chatterjee S, Behera M et al. Niosome: A future of targeted drug delivery systems. J Adv Pharm Technol Res 2010; 1: 374–80.
9. Allam A, El-Mokhtar MA, Elsabahy M. Vancomycin-loaded niosomes integrated within pH-sensitive in-situ forming gel for treatment of ocular infections while minimizing drug irritation. J Pharm Pharmacol 2019; 71: 1209-21.
10. Chavda VP. Niosome: A vesicular weapon for targeted and controlled drug delivery. Indian Journal of Novel Drug Delivery 2016; 8: 133-56.
11. Keshav J. Niosomes as apotential carrier system: A review. International Journal of Pharmaceutical, Chemical & Biological Sciences 2015; 5: 947-59.
12. Sharma R, Dua JS, Prasad D, Hira S, Monika. Advancement in Novel Drug Delivery System: Niosomes. JDDT [Internet]. 15 Jun.2019 [cited 22 Oct 2019]; 9(3-s): 995-001. Available from: http://jddtonline.info/index.php/jddt/article/view/2931
13. Samed N, Sharma V, Sundaramurthy A. Hydrogen bonded niosomes for encapsulation and release of hydrophilic and hydrophobic anti-diabetic drugs: An efficient system for oral anti-diabetic formulation. Applied Surface Science 2018; 449: 567-73.