CONCLUSIONS

A simple, specific, selective and precise method was developed for the determination of anti-viral drugs valacyclovir. The mobile phase was easy to prepare with little or no variation with-out the involvement of buffers and was economical. The analysis time was found to be less than 4 min. The recovery from formulations and rat plasma were in good agreement and they suggested no interference in the estimation. Hence, this method can be easily and conveniently used for the routine quality control of the drugs in pharmaceutical dosage forms, can also be applied to clinical studies and pharmacokinetic study of the drug valacyclovir.

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REFERENCES

[1] Martindale - The Complete Drug Reference, 33rd Edition. London, Pharmaceutical Press, 1999; p.643

[2] ICH, Stability Testing of New Drug Substances and Products; International Conference on Harmonization, IFPMA, Geneva, 2003.

[3] A.S. Jadhav, D.B. Pathare, M.S. Shingare, J. Pharmaceutical Biomedical Analysis, 2007; 43, supplement 4: 1568-72.

[4] M.L. Palacios, G. Demasi, M.T. Pizzono, A.I. Seall, J. Liquid chromatography Related Technology 2005; 28, supplement 5: 751-62.

[5] D.N. Fish, V.A. Vidaurri, R.G. Deeter, American Journal of Health system pharmacy1999; 56(19):1957-1960.

[6] L. Jan, M. Clas. Antimicrobial Agents. Chemotherapy 2003; 47: 2438-41.

[7] G. Srinu Babu, I. Sarat babu, N. Kiran kumar, N.M. Yurandhar, CHAI. Raju, Asian J. Chem 2007; 19 (2):1642-44.

[8] E.G. Gladys, L.A. Gordon, International Journal of Pharmaceutics 2006; 317: 14-18.

[9] K. Srinivasa Rao, M. Sunil, International Journal of Chem Tech Research 2009; 1(3): 702-708.

[10] M.M. Ayad, H.E. Abdellatef, M.M. El-Henawee, H.M. El-Sayed, Spectrochimica Acta Part A 66 (2007) 106.

[11] I.A. Darwish, A.S. Khedr, H.F. Askal, R.M. Mahmoud, II Farmaco, 60 (2005) 555.

[12] K. Basavaiah, H.C. Prameela, U. Chandrashekar, II Farmaco 58 (2003) 1301.

[13] K. Basavaiah, H.C. Prameela, II Farmaco 57 (2002) 443.

[14] M. Sultan, II Farmaco 57 (2002) 865.

[15] D. Teshima, K. Otsubo, T. Yoshida, Y. Itoh, R. Oishi, Biomed. Chromatogr. 17 (2003) 500.

[16] J.M. Poirier, N. Radembino, P. Jaillon, Ther. Drug Monitoring 21 (1999) 129.

[17] M. Fernandez, J. Sepulveda, T. Aranguiz, C. von Plessing, J. Chromatogr. B 791 (2003) 357.

NIOSOME: A NOVEL APPROACH FOR TARGETED DRUG DELIVERY

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ABSTRACT

The main goal of a site specific drug delivery system is not only to increase the selectivity but also to reduce the toxicity of the drug. Over the past several years, treatment of infectious diseases and immunisation has undergone a revolutionary shift. With the advancement in biotechnology and genetic engineering, not only a large number of disease-specific biologicals have been developed, but also emphasis has been laid on effective delivery of these biologicals. Different carriers like liposomes, niosomes, microspheres, resealed erythrocytes, dendrimers, aquasomes, transfersomes, ethosomes, phytosomes, nanoparticles etc. are used in novel drug delivery system. Vesicular systems are 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. Niosomes are vesicles composed of non-ionic surfactants, which are biodegradable, relatively nontoxic, more stable and inexpensive, an alternative to liposomes. We review the current deepening and widening interest of niosomes in many scientific disciplines and, particularly its application in medicine. We also present an overview of the techniques of preparation of noisome, types of niosomes, characterisation and their applications.

KEYWORDS: Target cells, drug therapeutic index, lamellar, surfactants.

INTRODUCTION

The concept of drug targeting or site specific drug delivery was introduced for the first time by Paul Elrich in 1909, when he reported 'magic bullet' to deliver a drug to the desired site of action without affecting the non target organs or tissues (Juliano, 1980) by associating the drug with a pharmacologically 'inactive carrier' capable of conveying the drug selectivity towards the target cells. Target oriented drug delivery systems are the areas of major interest in modern pharmaceutical research. Selective drug delivery to the target tissues increases the therapeutic efficacy of the drug and reduces its undesirable effect to non target tissues. The main goal of a site specific drug delivery system is not only to increase the selectivity, but also to reduce the toxicity of the drug.

The concept of targeted drug delivery is designed for attempting to concentrate the drug in the tissues of interest while reducing the relative concentration of the medication in the remaining tissues. As a result, drug is localised on the targeted site. Hence, surrounding tissues are not affected by the drug. In addition, loss of drug does not happen due to localisation of drug, leading to maximum efficacy of the medication. Different carriers have been used for targeting of drug, such as immunoglobulin, serum proteins, synthetic polymers, liposomes, microspheres, erythrocytes and niosomes [1].

Niosomes are one of the best among these carriers. The self-assembly of non-ionic surfactants into vesicles was first reported in 1970s by researchers in the cosmetic industry. Niosomes (non-ionic surfactant vesicles) obtained on

hydration are microscopic lamellar structures formed upon combining non-ionic surfactant of the alkyl or dialkyl polyglycerol ether class with cholesterol[2]. The non-ionic surfactants form a closed bilayer vesicle in aqueous media based on its amphiphilic nature using some energy for instance heat, physical agitation to form this structure. In the bilayer structure, hydrophobic parts are oriented away from the aqueous solvent, whereas the hydrophilic heads remain in contact with the aqueous solvent. The properties of the vesicles can be changed by varying the composition of the vesicles, size, lamellarity, tapped volume, surface charge and concentration. Various forces act inside the vesicle, e.g., van der Waals forces among surfactant molecules, repulsive forces emerging from the electrostatic interactions among charged groups of surfactant molecules, entropic repulsive forces of the head groups of surfactants, short-acting repulsive forces, etc. These forces are responsible for maintaining the vesicular structure of niosomes. But, the stability of niosomes is affected by type of surfactant, nature of encapsulated drug, storage temperature, detergents, and use of membrane spanning lipids, the interfacial polymerisation of surfactant monomers *in situ,* inclusion of charged molecule. Due to presence of hydrophilic, amphiphilic and lipophilic moieties in the structure, these can accommodate drug molecules with a wide range of solubility [3]. These may act as depot, releasing the drug in a controlled manner. The therapeutic performance of the drug molecules can also be improved by delayed clearance from circulation, protecting the drug from biological environment and restricting effects to target cells [4]. Niosome made of α, ω-hexadecyl-bis-(1-aza-18-crown-6) (Bolo-surfactant)-Span 80-cholesterol (2:3:1 molar ratio) is named as Bola- surfactant containing noisome [5]. The surfactants used in noisome preparation should be biodegradable, biocompatible and non-immunogenic. A dry product known as proniosomes may be hydrated immediately before use to yield aqueous niosomes dispersions. The problems of niosomes such as aggregation, fusion and leaking provide additional convenience in transportation, distribution, storage and dosing [6].

ADVANTAGES OF NIOSOMES [7]

- The vesicle suspension is water-based vehicle. This offers high patient compliance in comparison to oily dosage forms.
- They possess an infrastructure consisting of hydrophilic, amphiphilic and lipophilic moieties together and as a result can accommodate drug molecules with a wide range of solubilities.
- The characteristics of the vesicle formulation are variable and controllable. Altering vesicle composition, size, lamellarity, tapped volume, surface charge and concentration can control the vesicle characteristics.
- The vesicles may act as a depot, releasing the drug in a controlled manner.
- They can reduce drug toxicity because of their non-ionic nature.

DISADVANTAGES OF NIOSOMES

- Physical instability [8],[9]
- Aggregation
- Fusion
- Leaking of entrapped drug
- Hydrolysis of encapsulated drugs which limits the shelf-life of the dispersion[10,11]

COMPOSITION OF NIOSOME

Cholesterol and non-ionic surfactants are the two major components used for the preparation of niosomes. Cholesterol provides rigidity and proper shape. The surfactants play a major role in the formation of niosomes. Non-ionic surfactants like spans (Span 20, 40, 60, 80, 85), Tweens (Tween 20, 40, 60, 80) and Brij (Brij 30, 35, 52, 58, 72, 76) are generally used for the preparation of niosomes[8]. Few other surfactants that are reported to form niosomes are as follows

- Ether linked surfactant
- Di-alkyl chain surfactant
- Ester linked Surfactant
- Sorbitan Esters
- Poly-sorbates

TYPES OF NIOSOMES

Based on vesicle size, there are 3 categories:

- Smaller unilamellar vesicles (SUV, Size=0.025-0.05µm)
- Mutilamellar vesicles (MLV, size=>0.05µm)

Large unilamellar vesicles (LUV, size=>0.10µm)

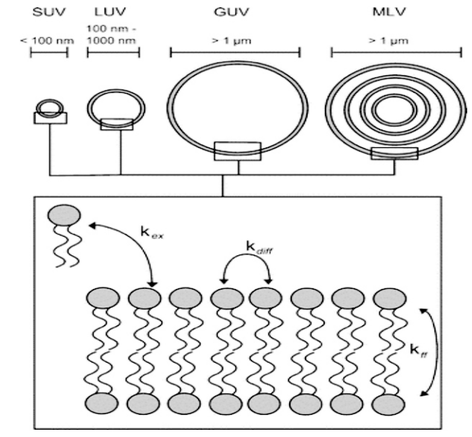

Figure 1 : Types of Niosomes [31]

METHODS OF PREPARATION

Niosomes are prepared by different methods based on the size of the vesicles and their distribution, number of double layers, entrapment efficiency of the aqueous phase and permeability of vesicle membrane.

PREPARATION OF SMALL UNILAMELLAR VESICLES

Sonication

The aqueous phase containing drug is added to the mixture of surfactant and cholesterol in a scintillation vial [12]. The mixture is homogenized using a sonic probe at 60°C for 3 minutes. The vesicles are small and uniform in size.

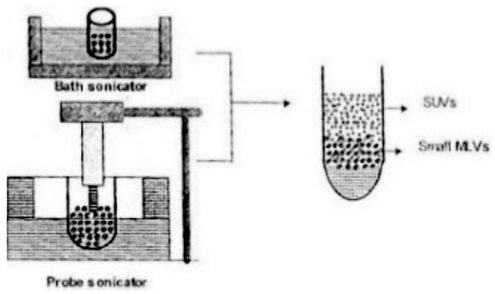

Figure 2 : Sonication method [31]

Micro fluidization

Two fluidized streams move forward through precisely defined micro channels and interact ultra-high velocities within the interaction chamber [13]. Here, a common gateway is arranged such that the energy supplied to the system remains within the area of noisome formation. The result is a greater uniformity, smaller size and better reproducibility.

PREPARATION OF MUTILAMELLAR VESICLES

Hand shaking method (Thin film hydration technique)

Surfactant and the other vesicle forming ingredients like cholesterol are blended and the mixture is dissolved in a volatile organic solvent like diethyl ether, chloroform or methanol in a round bottom flask. Using rotary evaporator, the organic solvent is removed at room temperature (20°C), by this method a thin layer of solid mixture is deposited on the wall of the flask. The dried surfactant film can be rehydrated with aqueous phase at 60°C with gentle agitation resulting in formation of multilamellar niosomes [12]

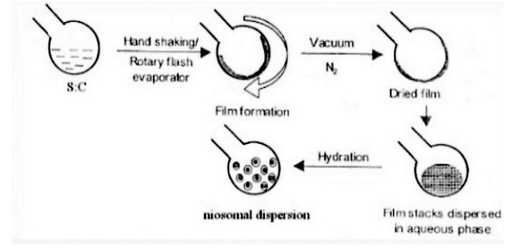

Figure 3 : Hand shaking method [31]

Trans-membrane pH gradient (inside acidic) drug uptake process (Remote Loading)

In a round-bottom flask, a blend of surfactant and cholesterol is dissolved in chloroform and the chloroform is then evaporated under reduced pressure to obtain a thin film on the wall of the flask. The film is hydrated by vortex mixing with 300mM citric acid (pH 4.0). The multilamellar vesicles are frozen and thawed three times and then sonicated. Aqueous solution containing 10mg/ml of drug is added to this niosomal suspension and vortexed. The pH of the sample is then raised to 7.0-7.2 with 1M disodium phosphate.The mixture is then heated at 60° C for 10 minutes to produce the desired multilamellar vesicles [14],[15].

PREPARATION OF LARGE UNILAMELLAR VESICLES

Reverse phase evaporation technique (REV)

In this method, cholesterol and surfactant (1:1) are added in a mixture of ether and chloroform. An aqueous phase containing drug is added to this and the resulting two phases are sonicated at 4-5°C. A small amount of phosphate buffer saline is then added to the clear gel formed above and is further

sonicated. Under low pressure and at 40°C, the organic phase is removed. Phosphate buffer saline is added to dilute the resulting viscous noisome suspension and heated in a water bath at 60°C for 10 min to yield niosomes [14].

Ether injection method

This method provides a means of making niosomes by slowly introducing a solution of surfactant dissolved in diethyl ether into warm water maintained at 60°C. The surfactant mixture in ether is injected through 14-gauge needle into an aqueous solution of material. Vaporization of ether leads to formation of single layered vesicles. Depending upon the conditions used, the diameter of the vesicles ranges from 50 to 1000nm^2.

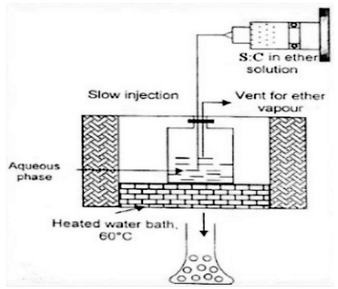

Figure 4 : Ether injection method [31]

MISCELLANEOUS

Multiple membrane extrusion method

A mixture of surfactant, cholesterol and dicetyl phosphate in chloroform is made into thin film by evaporation. The film is hydrated with aqueous drug solution and the resultant suspension extruded through polycarbonate membranes, which are placed in series for up to 8 passages. It is good method for controlling noisome size.

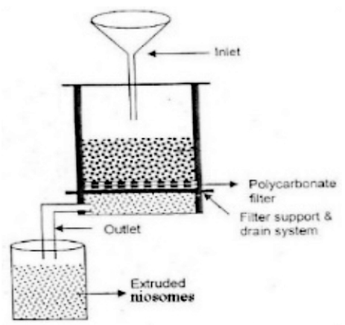

Figure 5 : Extrusion method [31]

The Bubble method

It is one step technique by which liposomes and niosomes are prepared without the use of organic solvents. A round bottom flask is used as bubbling unit with its three necks positioned in water bath to control the temperature. A water cooled reflux and thermometer are positioned in the first and second neck and nitrogen supply through the third neck. At 70°C, cholesterol and surfactant are dispersed together in the buffer (pH 7.4) and mixed with high shear homogenizer for 15 seconds and immediately afterwards 'bubbled' at 70°C using nitrogen gas [15].

Formation of niosomes from proniosomes

In this method of producing niosomes, a water- soluble carrier such as sorbitol is coated with surfactant resulting in the formulation of dry formulation in which each water-soluble particle is covered with a thin film of dry surfactant. This preparation is termed 'proniosomes''. Then, the proniosomes powder is filled in a screw capped vial, and mixed with water or saline at 80°C by vortexing, followed by agitation for 2 min resulting in the niosomal suspension [16].

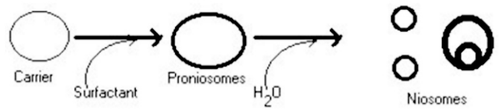

Figure 6 : Formation of niosomes from proniosome [32]

Emulsion method

The oil in water (o/w) emulsion is prepared from an organic solution of surfactant, cholesterol, and an aqueous solution of the drug [17],[18]. The organic solvent is then evaporated leaving niosomes dispersed in the aqueous phase.

Lipid injection method

In this process, either mixture of lipids and surfactants is first melted and then injected into a highly agitated heated aqueous phase containing dissolved drug, or the drug can be dissolved in molten lipid and the mixture will be injected into agitated, heated aqueous phase containing surfactant. This method does not require an expensive organic phase [15].

Niosome preparation using micelle

Niosomes may also be formed by the use of enzymes in a mixed micellar solution. A mixed micellar solution of C16 G2, dicalcium hydrogen phosphate (DCP), polyoxyethylene cholesteryl subacetate diester (PCSD) when incubated with esterases converts to a noisome dispersion. PCSD is cleaved by the esterases action to yield polyoxyethylene, Sebacic acid and then cholesterol in combination with C16 G2 and DCP then yields C16 G2 niosomes [15]

Niosome preparation using polyoxyethylene alkyl ether

Characteristics like size and number of bilayers of polyoxyethylene alkyl ethers and cholesterol consisting vesicles can be changed in an alternative way. Small unilamellar vesicles transform into large multilamellar vesicles by a temperature rise above 600°C, while multilamellar vesicles transform into unilamellar ones by vigorous shaking at room tempearature. It is a characteristics for the polyoxythylene alkyl ether surfactant to transform from unilamellar to multilamellar vesicles at higher temperature since it is known that polyethylene glycol (PEG) and water at higher temperature unmix due to a breakdown of hydrogen bonding between water and PEG moieties[19]

CHARACTERISATION OF NIOSOMES

Particle size analysis and surface morphology

Size, shape of niosomal vesicles is to be spherical, and their mean diameter is determined by using laser scattering method [20]. Also, diameter of these vesicles can be determined by using electron microscopy, molecular sieve chromatography, ultracentrifugation, photon correlation microscopy and optical microscopy [21],[22] and freeze fracture electron microscopy. Freeze thawing of niosomes increase the vesicle diameter, which might be attributed to a fusion of vesicles during the cycle.

Entrapment efficiency

After preparing niosomal dispersion, unentrapped drug is separated by dialysis, centrifugation or gel filtration and or complete vesicle disruption using 50% n-propanol or 0.1% triton X-100 is done for the estimation of the drug remained entrapped in niosomes and then analysing the resultant solution by appropriate assay method for the drug [23]. It can be represented as:

Entrapment efficiency (EF) = (amount entrapped/total amount) x 100

In-Vitro RELEASE STUDY

Dialysis tubing

The *in-vitro* release rate study can be performed with the help of dialysis tubing [24]. A dialysis sac is washed and soaked in distilled water. The vesicle suspension is transferred into a bag made up of the tubing and sealed. The bag containing the vesicles is then placed in 200ml buffer solution in a 250ml beaker with constant shaking at 25°C or 37°C. At various time intervals, the buffer is analysed for the drug content by an appropriate assay method.

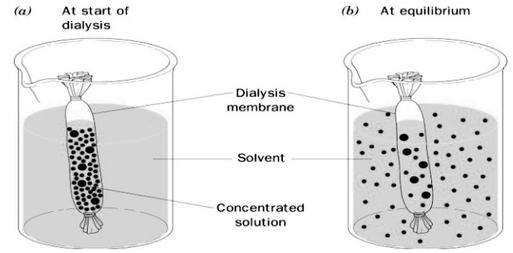

Figure 7 : Dialysis bag method [33]

Franz diffusion cell

This franz diffusion cell has a donor chamber fitted with a cellophane membrane. The niosomes are placed in it and dialysed against a suitable dissolution medium at room temperature. The drug content is analysed using suitable method (UV spectroscopy, HPLC). Maintenance of sink conditions is essential.

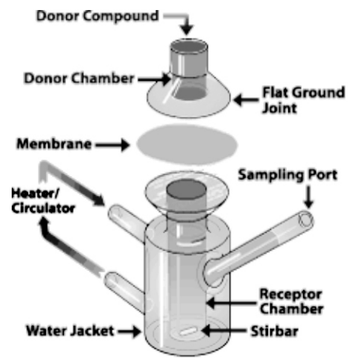

Figure 8 : Franz diffusion cell [33]

STABILITY STUDIES

Physical stability study is carried out to investigate the degradation of drug from noisome during storage. Stability studies carried out by storing the prepared niosomes at various temperature conditions like refrigeration on (2-8 °C), room temperature (25 °C ± 0.5°C) and elevated temperature (45°C ±0.5°C) from a period of one month to 3 months. Drug content and variation in the average vesicle diameter are periodically monitored. ICH guidelines suggest stability studies for dry proniosomes powder meant for reconstitution should be studied for accelerated stability at 75% relative humidity as per international climatic zones and climatic conditions.

ZETA POTENTIAL ANALYSIS

Zeta potential analysis is done for determining the colloidal properties of the prepared formulation. The suitably diluted niosomes is analysed for zeta potential based on electrophoretic light scattering and laser Doppler velocimetry method. The temperature is set at 25°C. Charge on vesicles and their mean zeta potential values with standard deviation of 5 measurements are obtained directly from the measurement [25].

APPLICATIONS OF NIOSOMES [26], [27], [28]

The applications of niosomal technology widely vary and can be used to treat a number of diseases.

NIOSOMES AS DRUG CARRIERS

Niosomes have also been used as carriers for iobitridol, a diagnostic agent used for X-ray imaging. Topical niosomes may serve as solubilisation matrix, as a local depot for sustained release of dermally active compounds, as penetration enhancers, or as rate-limiting membrane barrier for the modulation of systemic absorption of drugs.

DRUG TARGETTING

One of the most useful aspects of niosomes is their ability to target drugs. Niosomes can be used to target drugs to the reticuloendothelial system. The reticuloendothelial system (RES) preferentially takes up niosome vesicles. The uptake of niosomes is controlled by circulating serum factors called opsonins. These opsonins mark the niosomes for clearance. Such localized drug accumulation has, however, been exploited in treatment of animal tumours known to metastasize to the liver and spleen and in parasitic infestation of liver.Niosomes can also be utilized for targeting drugs to organs other than the RES. A carrier system (such as antibodies) can be attached to niosomes (as immunoglobulins bind readily to the lipid surface of the noisome) to target them to specific organs.

ANTI- NEOPLASTIC TREATMENT

Most antineoplastic drugs cause severe side effects. Niosomes can alter the metabolism, prolong circulation and half-life of the drug, thus decreasing the side effects of the drug. The niosomes decrease the rate of proliferation of tumour and higher plasma levels accompanied by slower elimination

LEISHMANIASIS

Leishmaniasis is a disease in which a parasite of the genus *Leishmania* invades the cells of the liver and spleen. Use of niosomes in tests conducted showed that it was possible to administer higher levels of the drug without triggering side effects, and thus allowed greater efficacy and safety in treatment.

DELIVERY OF PEPTIDE DRUGS

Oral peptide drug delivery has long been faced with a challenge of by passing the enzymes which would breakdown the peptide. Use of niosomes to successfully protect the peptides from gastrointestinal peptide breakdown is being investigated. In an *in-vivo* study conducted, the stability of the peptide drug significantly increased.

USE IN STUDYING IMMUNE RESPONSE

Due to their immunological selectivity, low toxicity and greater stability, niosomes are being used to study the nature of the immune response provoked by antigens. Non- ionic surfactant vesicles have clearly demonstrated their ability to function as adjuvant following parenteral administration with a number of different antigens and peptides.

NIOSOMES AS CARRIERS FOR HAEMOGLOBIN

Niosomes can be used as carriers for haemoglobin within the blood. The niosomal vesicle is permeable to oxygen and hence can act as a carrier for haemoglobin in anaemic patients.

OTHER APPLICATIONS [29], [30]

Sustained release

Sustained release action of niosomes can be applied to drugs with low therapeutic index and low water solubility since those could be maintained in the circulation via niosomal encapsulation.

Localized drug action

Drug delivery through niosomes is one of the approaches to achieve localized drug action, since their size and low penetrability through epithelium and connective tissue keeps he drug localized at the site of administration.

CONCLUSION

Niosomal drug delivery system is one of the examples of great evolution in drug delivery technologies. The concept of drug incorporation in the niosomes and to target the niosomes to the specific site is widely accepted by researchers and academicians. Niosomes represent a promising drug delivery technology and much research has to be inspired in this area to unveil all the potential of this novel drug delivery system.

REFERENCES

[1] T.M. Allen, Liposomal drug formulations, Rationale for development and what we can expect for the future, Drugs. 56(1998) 747–56.

[2] M. Malhotra, N.K.Jain, Niosomes as drug carriers, Indian Drugs. 31(1994) 81–6.

N. Udupa, Niosomes as drug carriers, In: Jain NK, editor, Controlled and novel drug delivery, New Delhi, CBS Publishers and Distributors, 2002.

[3] A.J. Baillie, A.T. Florence, L.R. Hume, G.T. Muirhead, A. Rogerson, The Preparation and propereties of Niosomes-Non ionic surfactant vesicles, J Pharm Pharmacol. 37(1985) 863–8.

[4] I.P. Kaur, A. Garg, A.K. Singla, D. Aggarwal, Vesicular systems in ocular drug delivery, Int J Pharm. 269(2004) 1–14.

[5] C. Hu, D.G. Rhodes, Proniosomes: A Novel Drug Carrier Preparation, Int J Pharm. 185(1999) 23–35.

[6] P. Gadhiya , S. Shukla, D. Modi, P. Bharadia, A Review-Niosomesin Targeted Drug Delivery, International Journal for Pharmaceutical Research Scholars. 2(2012) 61.

[7] S.S. Biju, S. Talegaonkar, P.R. Misra, R.K. Khar, Vesicular systems: An overview, Indian J. Pharm. Sci. 68(2006) 141-153.

[8] F. Ijeoma, Uchegbu, P. Suresh, Vyas, Non-ionic surfactant basedvesicles (niosomes) in drug delivery, Int. J. Pharm. 172(1998) 33–70.

[9] M. Malhotra, N.K. Jain, Niosomes as Drug Carriers. Indian Drugs, 1994, : 81-866.

[10] A. Alsarra, A. Bosela, S. M. Ahmed, G.M. Mahrous, Proniosomes as adrug carrier for transdermal delivery of ketorolac, Eur. J. Pharm. And Biopharm. 2(2004) 1-6.

[11] A.J. Baillie, G.H. Coombs, T.F. Dolan, J. Laurie, Non-ionic surfactant vesicles, niosomes, as delivery system for the anti-leishmanial drug, sodium stibogluconate, J Pharm Pharmacol. 38(1986) 502–5.

[12] K. Masud Karim, A. SattwaMandal, N. Biswas, A. Guha, S. Chatterjee, M. Behera, Niosome: A future of targeted drug delivery systems. J Adv Pharm Tech Res. 62(2011) 122

[13] R.A. Raja Naresh, G. Chandrashekhar, G.K. Pillai, N. Udupa, Antiinflammatory activity of Niosome encapsulated diclofenac sodium with Tween -85 in Arthitic rats, Ind J Pharmacol. 26(1994) 46-48

[14] S. Chauhan, M.J. Luorence, The preparation of polyoxyethylene containing non-ionic surfactant vesicles. J Pharm Pharmacol. 41(1989) 6.

[15] A.I. Blazek Welsh, D.G. Rhodes, SEM Imaging Predicts Quality of Niosomes from Maltodextrin-Based Proniosomes, Pharm Res. 18(2001) 656-661.

[16] Y. Hao, F. Zhao, N. Li, Y. Yang, Li K, Studies on a high encapsulation of colchicines by a noisome system, Int J Pharm. 244(2002) 73–80

[17] I.F. Uchegbu, S.P. Vyas, Non-ionic surfactant based vesicles (niosomes) in drug delivery, Int J Pharm. 172(1998) 33–70.

[18] S. Kaneshina, O. Shibata, M. Nakamura, The effect of pressure on the mutual solubility of anionic surfactant water system, Bull Chem Soc Japan. 55(1982) 951-952.

[19] I. Almira, I.A. Blazek-welsh, G.D. Rhodes, Maltodextrin – Based proniosomes, AAPS Pharm Sci Tech. 3(2001)1–8.

[20] S. Biswal, P.N. Murthy, J. Sahu, P. Sahoo, F. Amir, Vesicles of Non-ionic Surfactants (Niosomes) and Drug Delivery Potential, Int J Pharm Sci Nanotech. 1(2008) 1–8.

[21] M.N. Azmin, A.T. Florence, R.M. Handjani-Vila, J.F. Stuart, G. Vanlerberghe, J.S. Whittaker, The effect of non-ionic surfactant vesicle (niosome) entrapment on the absorption and distribution of methotrexate in mice, J Pharm Pharmacol. 37(1985)237–42.

[22] T. Yoshioka, B. Stermberg, A.T. Florence, Preparation and properties of vesicles (niosomes) of sobitan monoesters (Span 20, 40, 60, and 80) and a sorbitan triester (Span 85), Int J Pharm. 105(1994) 1–6.

[23] R. Karki, G.C. Mamatha, G. Subramanya, N. Udupa, Preparation, characterization and tissue disposition of niosomes containing isoniazid, Rasayan J Chem. 1(2008) 224–7.

[24] D. Akhilesh, G.Hazel, J.V. Kamath, Proniosomes- A propitious provesicular Drug carrier, Int J Pharm Sci Res. 1(2011) 98-103.

[25] A. Mehta, Pharma X Change_info - Articles – Niosomes. 1(2011) 33-43.

[26] K. Ruckmani, B. Jayakar and S.K. Ghosal, Drug Development and Industrial Pharmacy. 26(2000) 217-222.

[27] M. Conacher, J. Alexanderand, J.M. Brewer, M. Conacher and J. Alexander, Niosomes as Immunological Adjuvants, In"Synthetic Surfactant Vesicles" (Ed. I.F. Uchegbu).

Publishers Distributors Ltd. Singapore, 2000: 185-205.

[28] M.N. Azmin, A.T. Florence, R.M. Handjani-Vila, J.B. Stuart, G. Vanlerberghe and J.S. Whittaker, J. Pharm. Pharmacol. 37(1985) 237.

[29] B.M. Mithal, A text book of Pharmaceutical formulation, Vallabhan prakashan. 6: 306-307

[30] K.B. Makeshwar, R.W. Suraj, Niosome: A Novel Drug Delivery system, Asian. J. Pharm. Res. 3(2013)16-20.

[31] D. Akhilesh, G.Hazel, J.V. Kamath, Proniosmes-A propitious Provesicular Drug Carrier, Int. J. Pharm. Pharmaceu. Sci. Res. 1(2011) 98-103.

ENHANCED DISSOLUTION RATE OF DICLOFENAC BY SOLID DISPERSION METHOD

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ABSTRACT

The objective of this work was to improve aqueous solubility of poorly water soluble drugs by a modified porous starch as solid dispersion carrier. The yield of the porous starch was found to be 80%. The flow property of the prepared porous starch was found to be good, with good compressibility index. Drug content of all the formulations were found to be in the range between 90-100%. The dissolution profile showed that in solid dispersions prepared by physical mixing process and solvent evaporation method, the dissolution of pure diclofenac is high in comparison with the solid dispersion samples. Whereas in solid dispersions prepared by solvent evaporation method, dissolution of pure diclofenac is very low in comparison with the solid dispersion samples of drug with porous starch due to co-habitation of carriers with diclofenac that improved the dissolution rate of the drug. The predicted drug release mechanism for solvent evaporation method where the drug release could be by first order release model. Thus this study confirmed that a porous starch can be developed and utilized as a carrier to improve the aqueous solubility of poorly water soluble BCS class II drugs thereby improving its dissolution rate and bioavailability.

Keywords : Porous starch, diclofenac, solid dispersion, solubility.

INTRODUCTION

Solid dispersion technique can be used to increase the dissolution and absorption characteristics of several water insoluble drugs[1,2]. Lately, a number of drugs are not showing complete therapeutic response due to their poor solubility and dissolution rate, which in turn leads to poor bioavailability of the drug[3,4]. So, in the modern days, a lot of effort is given to improve the dissolution rate of poorly soluble drugs, to enhance their bioavailability. Among many other techniques, Solid Dispersion (SD) technology has been successfully applied to increase the dissolution rate of highly lipophilic drugs thereby improving their bioavailability [5, 6, 7, 8]. Usually, solid dispersions are two component systems consisting of a hydrophilic carrier in which the drug is incorporated. The drug that is incorporated in the hydrophilic carrier may be molecularly dispersed or may occur as nanocrystals or may be amorphous nanoparticles. The improved dissolution rate of the drug may be attributed to (i) an increased solubility of the drug because of its amorphous state or small particle size (Kelvin's law) [9, 10, 11, 12] (ii) an increasing surface area available for drug dissolution because of the small size of the drug particles [13, 14] and (iii) an improved wetting of the drug caused by the hydrophilic carrier [15, 16].

Drug release profiles from such mixtures are driven by the carrier properties [11]. Various hydrophilic carriers employed in preparation of solid dispersions include polyethylene glycols, carbohydrates (lactose), poloxamers, polyvinyl pyrollidone K-25, polyols (such as sorbitol and mannitol), organic acid (citric acid) and hydrotopes (urea) [19-21].