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NOVEL TECHNOLOGIES OF TRANSDERMAL DRUG DELIVERY SYSTEMS

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COMMENTARY

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INTRODUCTION

Transdermal drug delivery systems (TDDS) are controlled-release devices that contain the drug either for localized treatment of tissues underlying the skin [1, 2]. Topical or transdermal drug delivery is challenging because the skin acts as a natural and protecting barrier. Many strategies are examined to extend thepermeation of therapeutic molecules into and through the skin and one such approach is use of nanoparticulate delivery system [3 - 5].

Human skin encompasses multifunctional role primary among which that its role as a barrier against each the egress of endogenous substances like water and therefore the ingress of xenobiotic material (chemicals and drugs). This barrier function of the skin is mirrored by its multilayered structure. The highest or top layer of the skin referred to as the corneum (SC) represents the tip product of the differentiation method at first started within the basal layer of the cuticle with the formation of keratinocytes by mitotic division. The Sratum corneum, thus it is comprised of dead cells (corneocytes) interdispersed among a lipid rich matrix. It is the "brick and mortar" design and lipophilic nature of the SC, that primarily accounts for the barrier properties of the skin [1, 2]. The SC is is additionally legendary to exhibit selective permeability and permits solely comparitively lipophilic compounds to diffuse into the lower layers. As a result of the dead nature of the Sratum corneum substance transport across this layer is primarily by passive diffusion (3) in accordance with Fick's Law (4) and no active transport processes are known. Typical delivery systems will be utilized to attain percutaneous drug delivery or dermal drug delivery. The previous involves the delivery of medication to explicit the skin barrier in order that they exert a systemic effect [4 - 6].

NOVEL TECHNOLOGIES FOR TRANSDERMAL DELIVERY SYSTEMS

Nanoparticles for transdermal applications such liposomes, ethosomes as well as other types of nanosized drug carriers have been developed. Different carrier systems have been proposed in an attempt to favor the transport

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of drugs through the skin, faculatative drug retention and in some cases permitting a sustained release. Skin penetration is crucial variety of current considerations [7 - 10].

Physicochemical properties of Nano vesicular systems confirm the interaction with biological systems and nanocarrier cell acquisition. The main physicochemical properties have an effect on cellular uptake are size, shape, rigidity, and charge in the surface of particles. The foremost used and investigated nanocarriers for transdermal drug delivery in the pharmaceutical field include liposomes, transfersomes, ethosomes, niosomes, dendrimers, nanoparticles-lipid and polymer nanoparticles and nanoemulsions [11 - 15].

MICROEMULSIONS

Microemulsions are dispersions with droplet size from 10 to 100 nm with non-coalesce nature. Microemulsions form spontaneously with appropriate amounts of a lipophilic and a hydrophilic ingredient, as well as a surfactant and a co-surfactant. Microemulsions have several specific physicochemical properties such as transparency, optical isotropy, low viscosity and thermodynamic stability [16 - 18].

Most of the microemulsions have terribly low viscosity, which can limit their application to the transdermal delivery field use. The main mechanisms to explain the advantages of microemulsions for the transdermal delivery of drugs include the high solubility capacity for hydrophilic drugs of microemulsion systems, permeation effect of the ingredients of microemulsions, and the increased thermodynamic activity of the drug in the carriers [19 - 22].

NANOEMULSIONS

Nanoemulsions are isotropic dispersed systems of two nonmiscible liquids. It consists of an oily system dispersed in an aqueous system, or an aqueous system dispersed in an oily system by forming droplets. Nanoemulsions are thermodynamically unstable and are susceptible to incorporate Hydrophobic and hydrophilic drugs. They are nontoxic and nonirritant systems so that they have been utilized in the cosmetic field. Currently, transdermal nanoemulsion formulations are not developed due to the stability problems [23 - 29].

LIPOSOMES

Liposomes are spherical, selfclosed vesicles of colloidal dimensions. Liposomes have become one of the pharmaceutical nanocarriers of choice for many applications. Liposomes were also proposed as drug carriers that reduce toxicity and increase efficacy. The nature of liposomes makes them one of the best alternatives for drug delivery because they are nontoxic and remain inside the bloodstream for a long time [30 - 33].

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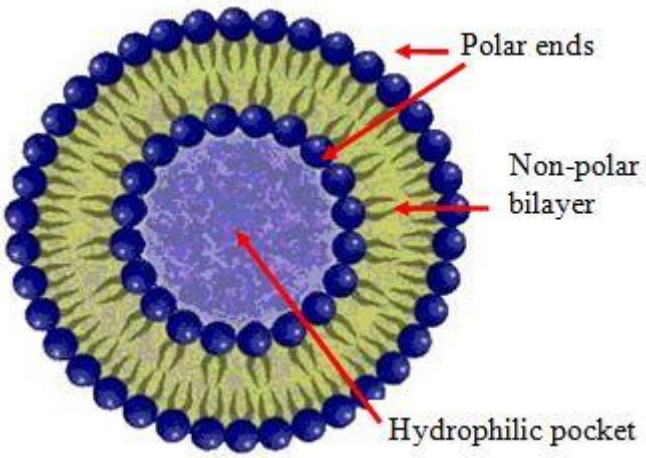

Figure 1: Structure of a Liposome

NIOSOMES

Niosomes are non-ionic surfactant vesicular novel drug delivery system in which the medication is encapsulated in a vesicle. Niosomes are unilamellar or multilamellar vesicles capable of entrapping hydrophilic and hydrophobic solutes. Niosome surfactants are biodegradable, biocompatible and non-immunogenic [34 - 36].

Niosomes are versatile carrier systems that can be administered via transdermal delivery. In the treatment of dermatological disorders, niosomes are considered as an interesting drug-delivery system [37 - 43].

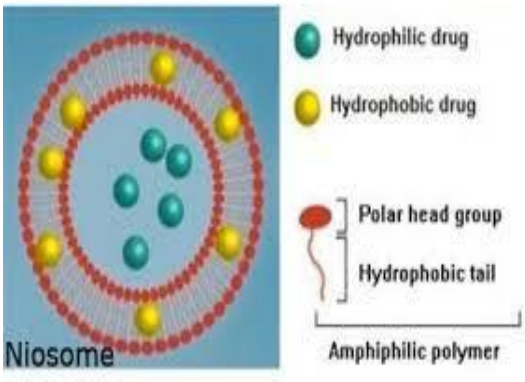

Figure 2: Structure of a Niosome

TRANSFERSOMES

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Transfersomes are vesicular particles, consisting of an inner liquid compartment surrounded by a lipid bilayer. A Transfersome carrier is an artificial vesicle mainly suitable for sustained and targeted drug delivery. Transfersomes have high deformability nature. Due to its adaptability vesicles can accommodate to a confining pore [44 - 49].

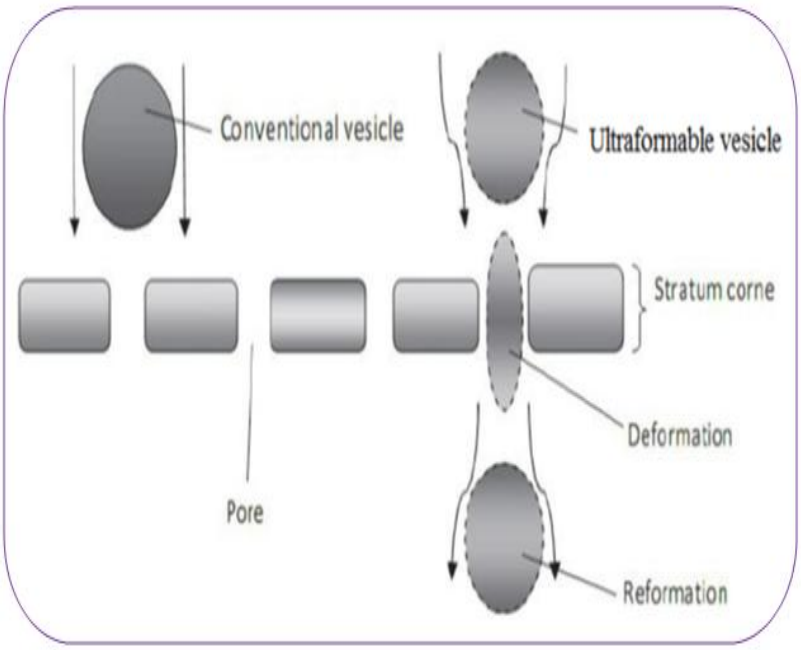

Figure 3: Structure of a Transfersomes

ETHOSOMES

Ethosomes are lipid vesicular carriers embodying high concentrations of alcohol i.e. ethanol that is beneficial for the permeation of medicine through the skin. They are composed primarily of phospholipids, ethanol and water [50, 51].

Structurally, an ethosomal vesicle is composed a phospholipid bilayer and an aqueous inner core containing the entrapped active ingredient. They are soft and malleable. The size of an ethosome vesicle lies within the nanometer range. In addition, the size of ethosome vesicle is smaller than that of a liposome when prepared under the same conditions, due to the high alcohol content. The size decreased as alcohol increased from 20 to 45 %. This reduction in size was attributed to the conferment of a net negative charge on the vesicle surface by ethanol. Other excipients usually added in ethosome formulation include cholesterol, for vesicle membrane stabilization; permeation enhancers, marker dyes (if required) such as rhodamine, for characterization study. The stabilizing effect of cholesterol is due to prevention of vesicle aggregation and enlargement during storage the small size and malleability of ethosomes enable them to pass through the skin or membrane barrier and also influence the extent of transdermal permeation. The smaller the size, the greater will be the extent of penetration [52 - 57].

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Ethosomes permeate through the stratum corneum barrier and possess significantly high transdermal flux unlike classical liposomes. These effects of combined phospholipids and high concentration of ethanol in vesicular formulations have been suggested to be responsible for deeper distribution and penetration in the skin lipid bilayers. Application of ethosomes in drug delivery has numerous advantages: simplicity of the technology, non-invasive means of application (e.g., topical), enhanced transdermal drug delivery, and avoidance of first-pass effect. Non-invasiveness enhances patient's compliance hence, better therapeutic outcome. Ethosomes have been shown to exhibit high encapsulation efficiency for a wide range of molecules including lipophilic drugs due to the multilamellarity of the vesicles as well as the presence of ethanol, which allows for better solubility of many drugs. Unlike liposomes and transfersomes, ethosomes were able to improve skin delivery of drugs both under occlusive and non-occlusive conditions [58 - 60].

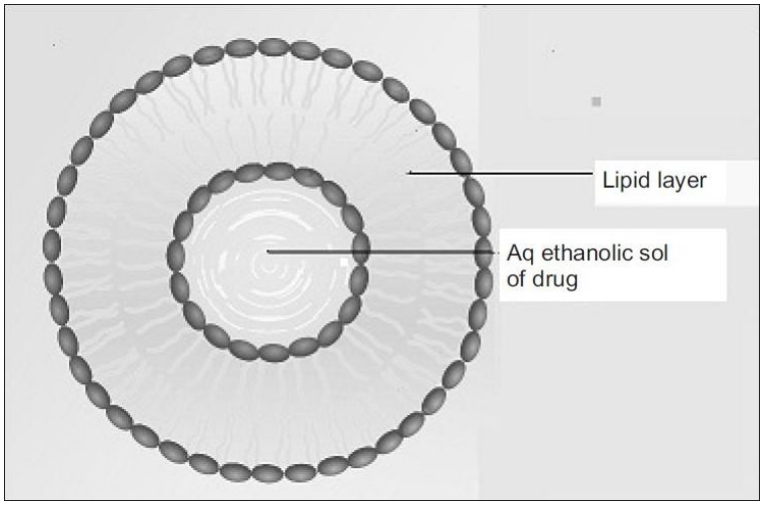

Figure 4: Structure of an Ethosome

DENDRIMERS

Dendrimers are nonpeptidic fractal 3-D structures made from various tiny molecules. The structure of those molecules leads to comparatively uniform shapes, sizes, and molecular weights. The porosity of dendrimers through the skin depends on physicochemical characteristics like generation size, molecular weight, surface charge, composition, and concentration. These nanocarriers will be used to transport photosensitizers for photochemical therapy and antifungal molecules [61].

Dendrimers are utilized for transdermic drug delivery system. The main issues with this type of transdermal carrier are their poor biodegradation and inherent cytotoxicity. The foremost advantage of dendrimers is that they need multivalency and it is possible to precisely control the functional groups on the surface. Due to their form and size, these molecules can carry drugs, imaging agents, etc. Dendrimers interact with lipids present in membranes, and

they show better permeation in cell cultures and intestinal membranes. Dendrimers additionally act like solubility enhancers, increasing the permeation of lipophilic medication. However, they are not sensible carriers for hydrophilic drugs. Examples of medicine delivered throughout the skin by using dendrimers are tamsulosin, indomethacin, ketoprofen, diflunisal, 5-fluorouracil and peptides [62].

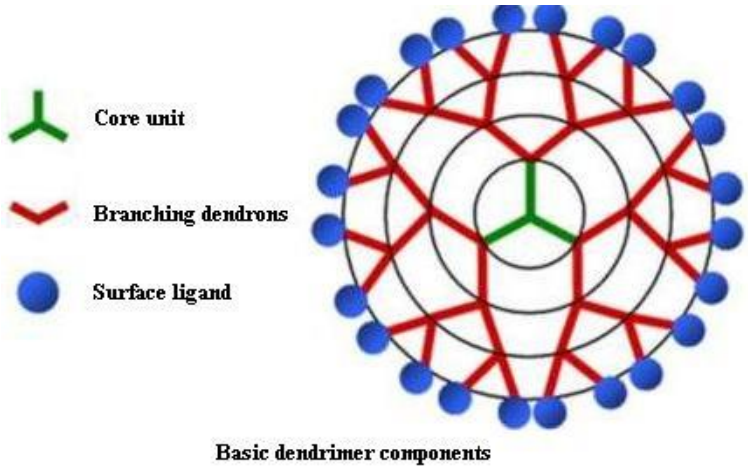

Figure 5: Structure of a Dendrimer components

REFERENCES

1. Chein YW. Transdermal drug delivery & delivery systems. Novel drug delivery systems. New York: Marcel Dekker, 1992; 301-380.
2. Chein YW. Transdermal controlled systemic medications. New York: Marcel Dekker, Inc. 1987.
3. Vyas SP, Khar RK. Transdermal drug delivery. Controlled drug delivery-concepts and advances. New Delhi, India: VallabhPrakashan, 2002; 411-447.
4. Rise of transdermal drug delivery technologies. In pharmatechnologist.com,2003.
5. Rein H. Experimental electroendosmotic studies on living human skin. Z Biol. 1924; 81: 124-128.
6. Champion RH, Burton JL, Burns DA, Breathnach SM. Textbook of Dermatology London: Blackwell Science.1998.
7. Walker RB, Smith EW. The role of percutaneous penetration enhancers. Adv Drug Deli Rev. 1996; 18: 295-301
8. Paudel KS, et al. Challenges and opportunities in dermal/transdermal delivery. Ther Deliv. 2010; 1: 109-131.
9. Vyas SP, Khar RK.Controlled Drug Delivery: Concepts and Advances, 1st edition, Vallabh Prakashan, New Delhi. 2002.
10. Bouwstra JA, Honeywell-Nguyen PL, Gooris GS, Ponec M. Structure of the skin barrier and its modulation by vesicular formulations. Prog Lipid Res. 2003; 42: 1-36.
11. Alexander A, et al. Approaches for breaking the barriers of drug permeation through transdermal drug delivery. J Control Release. 2012; 164: 26-40.
12. Cevc G. Transfersomes, liposomes and other lipid suspensions on the skin: permeation enhancement, vesicle penetration, and transdermal drug delivery. Crit Rev Ther Drug Carrier Syst. 1996; 13: 257-388.

13. Lopez RF, Seto JE, Blankschtein D, Langer R. Enhancing the transdermal delivery of rigid nanoparticles using the simultaneous application of ultrasound and sodium lauryl sulfate. Biomaterials. 2011; 32: 933-941.
14. Chaudhary H, Kohli K, Kumar V. Nano-transfersomes as a novel carrier for transdermal delivery. Int J Pharm. 2013; 454: 367-380.
15. Benson HA. Transfersomes for transdermal drug delivery. Expert Opin Drug Deliv. 2006; 3: 727-737.
16. Schatzlein A, Cevc G. Characterization, metabolism, and novel biological applications. Champaign, AOCS Press, 1995; 191-209.
17. Agyralides GG, Dallas PP, Rekkas DM. Development and in vitro evaluation of furosemide transdermal formulations using experimental design techniques. Int J Pharm. 2004; 281: 35-43.
18. Giannakou SS, Dallas PP, Rekkas DM, Choulis NH. Development and in vitro evaluation of nitrendipine transdermal formulations using experimental design techniques. International Journal of Pharmaceutics. 1995; 125: 7-15.
19. Chaudhary H, et al. Optimization and formulation design of gels of Diclofenac and Curcumin for transdermal drug delivery by Box-Behnken statistical design. J Pharm Sci. 2011; 100: 580-593.
20. Chaudhary H, Rohilla A, Rathee P, Kumar V. Optimization and formulation design of carbopol loaded Piroxicam gel using novel penetration enhancers. Int J Biol Macromol. 2013; 55: 246-253.
21. Gupta A, Gaud RS, Ganga S. Development of Buccal adhesive formulations using in-situ formation of inter-polymer complex and optimization using box-benhken design. International Journal of Advances Pharmaceutical Sciences. 2010; 1: 86-95.
22. Trotta M, Peira E, Carlotti ME, Gallarate M. Deformable liposomes for dermal administration of methotrexate. Int J Pharm. 2004; 270: 119-125.
23. Ali A, Trehan A, Ullah Z, Aqil M, Sultana Y. Matrix type transdermal therapeutic systems of glibenclamide: Formulation, ex vivo and in vivo characterization. Drug Discov Ther. 2011; 5: 53-59.
24. Mishra MK, Ray D, Barik BB (2009) Microcapsules and transdermal patch: a comparative approach for improved delivery of antidiabetic drug. AAPS PharmSciTech 10: 928-934.
25. Mutalik S, Udupa N. Glibenclamide transdermal patches: physicochemical, pharmacodynamic, and pharmacokinetic evaluations. J Pharm Sci. 2004; 93: 1577-1594.
26. Mutalik S, Udupa N. Formulation development, in vitro and in vivo evaluation of membrane controlled transdermal systems of glibenclamide. J Pharm Pharm Sci. 2005; 8: 26-38.
27. Sheo DM, et al.Transfersomes-a novel vesicular carrier for enhanced transdermal delivery of Stavudine: Development, characterization and performance evaluation. Journal of Science and Speculations Research. 2010; 1: 30-36.
28. Jain S, Jain P, Umamaheshwari RB, Jain NK. Transfersomes--a novel vesicular carrier for enhanced transdermal delivery: development, characterization, and performance evaluation. Drug Dev Ind Pharm. 2003; 29: 1013-1026.
29. Hiruta Y, et al. Novel ultra-deformable vesicles entrapped with bleomycin and enhanced to penetrate rat skin. J Control Release. 2006; 113: 146-154.

30. Zheng WS, Fang XQ, Wang LL, Zhang YJ. Preparation and quality assessment of itraconazole transfersomes. Int J Pharm. 2012; 436: 291-298.
31. Vinod KR, et al. Developing ultra deformable vesicular transportation of a bioactive alkaloid inpursuit of vitiligo therapy. Asian Pacific Journal of Tropical Disease. 2013; 2: 301-306.
32. Malakar J, Sen SO, Nayak AK, Sen KK. Formulation, optimization and evaluation of transferosomal gel for transdermal insulin delivery. Saudi Pharm J. 2012; 20: 355-363.
33. Jain A, Ghosh B, Nayak S, Soni V. A study of transdermal delivery of Glibenclamide using Iontophoresis. International Journal of Health Research. 2009; 2: 85-87.
34. Singh HP, Utreja P, Tiwary AK, Jain S. Elastic liposomal formulation for sustained delivery of colchicine: in vitro characterization and in vivo evaluation of anti-gout activity. AAPS J. 2009; 11: 54-64.
35. Aggarwal N, Goindi S. Preparation and evaluation of antifungal efficacy of griseofulvin loaded deformable membrane vesicles in optimized guinea pig model of Microsporum canis--dermatophytosis. Int J Pharm. 2012; 437: 277-287.
36. ICH Harmonised Tripartite Guideline Q1A [R2] International conference on harmonisation of technical requirements for registration of pharmaceuticals for human use: stability testing of new drug substances and products. 2003; 1-18.
37. Ahad A, et al. Formulation and optimization of nanotransfersomes using experimental design technique for accentuated transdermal delivery of valsartan. Nanomedicine. 2012; 8: 237-249.
38. Mishra D, Garg M, Dubey V, Jain S, Jain NK. Elastic liposomes mediated transdermal delivery of an anti-hypertensive agent: propranolol hydrochloride. J Pharm Sci . 2007; 96: 145-155.
39. Bavarsad N, Fazly Bazzaz BS, Khamesipour A, Jaafari MR. Colloidal, in vitro and in vivo anti-leishmanial properties of transfersomes containing paromomycin sulfate in susceptible BALB/c mice. Acta Trop. 2012; 124: 33-41.
40. Shah M, Pathak K. Development and statistical optimization of solid lipid nanoparticles of simvastatin by using 2(3) full-factorial design. AAPS PharmSciTech. 2010; 11: 489-496.
41. Vult von Steyern F, Josefsson JO, TÃ¥gerud S. Rhodamine B, a fluorescent probe for acidic organelles in denervated skeletal muscle. J Histochem Cytochem. 1996; 44: 267-274.
42. Naik A, Kalia YN, Guy RH. Transdermal drug delivery: overcoming the skin's barrier function. Pharm SciTechnolo Today. 2000; 3: 318-326.
43. Hosmer J, et al. Microemulsions containing medium-chain glycerides as transdermal delivery systems for hydrophilic and hydrophobic drugs. AAPS Pharm Sci Tech. 2009; 10: 589-596.
44. Herai H, Gratieri T, Thomazine JA, Bentley MV, Lopez RF. Doxorubicin skin penetration from monoolein-containing propylene glycol formulations. Int J Pharm. 2007; 329: 88-93.
45. Holmqvist P, Alexandridis P, Lindman B. Modification of the microstructure in poloxamer block copolymer-water-â€œoilâ€ systems by varying the â€œoilâ€ type. Macromolecules. 1997; 30: 6788-6797.
46. Fanun M. A study of the properties of mixed nonionic surfactants microemulsions by NMR, SAXS, viscosity and conductivity. J Mol Liquids. 2008; 142: 103-110.
47. Williams AC. Transdermal and topical drug delivery. Pharmceutical Press, London, UK. 2003.

48. Scheinfeld N. Topical treatments of skin pain: a general review with a focus on hidradenitissuppurativa with topical agents. Dermatol Online J. 2014; 20.
49. Ghosh TK. Permeation enhancement. In Transdermal and Topical Delivery Systems (Ghosh T, Yum S and Pfister W, eds) Inter pharm Press, Buffalo Grove, IL, USA, 21â€"22. 1997.
50. Barry BW. Lipid-protein-partitioning of skin penetration enhancement. J Control Release 15: 237â€"248. 1991.
51. Sarpotdar R, Zatz JL. Percutaneous absorption enhancement by nonionic surfactants. Drug Devlnd Pharm. 1986;12: 1625-1647.
52. Cappel MJ, Kreuter J. Effect of nonionic surfactants on transdermal drug delivery: I. Polysorbates. Int J Pharm. 1991; 69: 143-153.
53. Iwasa A, Irimoto K, Kasai S, Okuyama H, Nagai T. Effect of nonionic surfactants on percutaneous absorption of diclofenac sodium. Yakuzaigaaku. 1991; 51: 16-21.
54. Park ES, Chang SY, Hahn M, Chi SC. Enhancing effect of polyoxyethylene alkyl ethers on the skin permeation of ibuprofen. Int J Pharm. 2000; 209: 109-119.
55. Shin SC, Cho CW, Oh IJ. Effects of non-ionic surfactants as permeation enhancers towards piroxicam from the poloxamer gel through rat skins. Int J Pharm. 2001; 222: 199-203.
56. Shokri J, et al. The effect of surfactants on the skin penetration of diazepam. Int J Pharm. 2001; 228: 99-107.
57. Rhein LD, Robbins CR, Fernee K, Cantore R. Surfactant structure effects on swelling of isolated human stratum corneum. J SocCosmetChem. 1986; 37: 125-129.
58. Mitragotri S. Synergistic effect of enhancers for transdermal drug delivery. Pharm Res. 2000; 17: 1354-1359.
59. Benson HA. Transdermal drug delivery: penetration enhancement techniques. Curr Drug Deliv. 2005; 2: 23-33.
60. Ancel HC, Allen LV, Popovich NG. Pharmaceutical dosage forms and drug delivery systems. 5th edition, New Delhi: Lippincott Williams & Wilkins. 2005; 311-312.
61. James-Smith MA, Shekhawat D, Shah DO. Importance of micellar lifetime and sub-micellar aggregates in detergency processes. Tenside Surf Deterg. 2007; 44: 142-154.
62. Patist A, Kanicky JR, Shukla PK, Shah DO. Importance of micellar kinetics in relation to technological processes. J Colloid Interface Sci . 2002; 245: 1-15.