www.amlett.com, www.amlett.org, DOI: 10.5185/amlett.2012.ib.116
"Nanostructuring by electrons, photons and ions" Special Issue Published online by the VBRI press in 2013

Microstructural investigation of lipid solubilized microemulsions using laser light scattering

Suman Rana, Gunjan Verma, P. A. Hassan*

Chemistry Division, Bhabha Atomic Research Centre, Mumbai 400 094, India

*Corresponding author. Tel: (+91) 22 25595099; Fax: (+91) 22 25505151; E-mail: hassan@barc.gov.in

Received: 16 March 2012, Revised: 22 July 2012 and Accepted: 26 July 2012

ABSTRACT

Solubilization of solid lipids in oil-in-water microemulsion is an important step in the preparation of lipid nanoparticles. Oil in water microemulsion has been prepared using Tween-80 (T-80) as a surfactant and isopropyl myristate (IPM) as an oil phase with a view to utilize them for the preparation of Solid Lipid Nanoparticles (SLN). The microstructure of the microemulsions were evaluated using laser light scattering studies. From light scattering studies, it was observed that the intensity of scattered light increases on increasing the concentration of IPM at a fixed concentration of T-80 (15%), reflecting an increase in the size of the micelles. Dynamic light scattering studies show that the hydrodynamic diameter of the micelles increases on increasing the concentration of IPM. Phospholipon® 90 G (lipid) solubilized microemulsions were prepared using 1:1 w/w mixture of lipid and IPM as the oil phase. DLS studies suggest that addition of lipid did not alter the size of microemulsion droplets significantly. Copyright © 2013 VBRI press.

Keywords: Microemulsion; solid lipid nanoparticles; dynamic light scattering; micelle.

Suman Rana is a research scholar in Chemistry group under the supervision of Dr. P. A. Hassan at Bhabha Atomic Research Centre, Mumbai, India. She received her M.Sc. degree in Chemistry from Maharshi Dayanand University and M.Phil. degree from Chaudhary Devi Lal University, Haryana. Her research interests are in self-assembly of amphiphiles and investigation of their potential applications in biomedical field.

Gunjan Verma obtained her M.Sc. degree in Chemistry from Indian Institute of Technology, Roorkee and did Ph.D from Indian Institute of Technology, Delhi. She joined Bhabha Atomic Research Centre in the year 2005 as a scientific officer. Since then, she has been working on the microstructure and dynamics of association colloids such as micelles, their application in materials synthesis and rheological studies of complex fluids.

P. A. Hassan obtained his M.Sc. degree in Chemistry from Mahatma Gandhi University, Kottayam, Kerala and joined Bhabha Atomic Research Centre (BARC), Mumbai in 1993, as a Scientific Officer. Currently, he is Head of the Thermal & Interfacial Chemistry Section, Chemistry Division, BARC. He was a visiting researcher at the University of Louis Pasteur, France and pursued his post doctoral research at University of Delaware, USA. His current research interests include structural transitions in micelles, liposomes, polymers, polyelectrolyte-surfactant interactions and biotechnological applications of nanomaterials.

Introduction

Particulate drug carrier systems offer great promise to improve the therapeutic effectiveness and safety profile of various drugs. Incorporation of the drug into a particulate carrier can protect it against degradation (both in vitro and in vivo), control its release profile and also offers possibilities for targeted drug delivery [**1-8**]. Solid lipid nanoparticles (SLN, also referred to as solid lipid nanospheres or lipospheres) are a new field of drug carrier. They are colloidal systems providing controlled release profile for many lipid soluble substances. The use of solid lipids at the place of liquid oils is emerging as an attractive idea to achieve controlled drug release, because drug mobility in a solid is considerably lower compared to liquid oil [**1, 9-15**]. SLN can be made from solid lipids (or lipid blends) and are produced by one of the following techniques, namely, high pressure homogenization [**11,16**] microemulsion template technique [**11,17**] solvent emulsification evaporation technique [**11,18**] solvent displacement technique [**19**] solvent emulsification diffusion technique [**11,20**] phase inversion [**21**] and membrane contractor technique [**22**]. Among these techniques, we have focused our study on microemulsion

 Copyright © 2013 VBRI press.

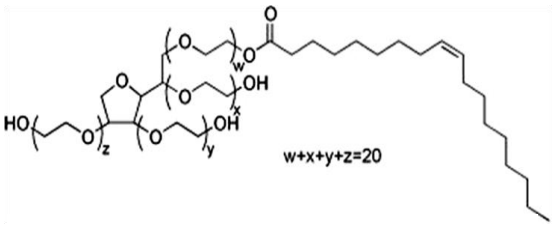
template technique for the preparation of SLN. Microemulsions are monophasic, thermodynamically stable, transparent (or slightly translucent) dispersions of oil and water. They are promising candidates to be used as a medium to prepare nanoparticles of controlled size. It is important to identify the solubilization of oil and lipids in surfactant solutions, in order to explore their potential in nanoparticle preparation. The focus of this study is to investigate oil solubilization in surfactant micelles and the effect of lipids on microemulsion structure with a view to utilize them for the preparation of SLN. These microemulsions were characterized using laser light scattering techniques.

A variety of lipids have been employed for the preparation of SLN in drug delivery applications. For example, lipid acids, mono, di or triglycerides, glyceride mixtures, waxes etc, stabilized by a biocompatible surfactant of choice (nonionic as well as ionic) have been reported [**10, 23, 24**]. In the present paper, we examine the microstructure of microemulsions formed by Tween-80 and isopropyl myristate (IPM) using laser light scattering. Polysorbate-80 or Tween-80 (polyoxyethylene-20-sorbitan monooleate) is a biocompatible non-ionic surfactant that is widely used as a solubilizer in pharmaceutical industry. A lot of surfactants have been explored to study their efficacy in drug delivery. Non-ionic surfactants are less toxic as compared to ionic surfactants and have a high hydrophilic-lipophilic balance (HLB) [**10, 23, 25**]. The nanoparticles coated with Tween -80 led to the uptake by the endothelial cells of the brain capillary. It has also been investigated that the nanoparticles coated with Tween-80 could get across the blood brain barrier and increases the brain drug concentration by many folds [**26, 27**]. It is one of the widely used excipients in pharmaceutical industry for various applications and is approved by the U.S. Food and Drug Administration for usage in injectable, oral and topical products. Isopropyl myristate is synthetic oil manufactured by condensing myristic acid with isopropyl alcohol. It readily gets absorbed in the skin and hence used as an emollient or moisturizer in creams and lotions and in pharmaceutical industries as a lubricant [**28-30**]. Phospholipon 90G is used for the preparation of mixed micelles, liposomes and microemulsions. It is used as a solubilizer and stabilizer for parenteral administration and is a phosphatidylcholine source for drugs and dietetics [**31-33**].

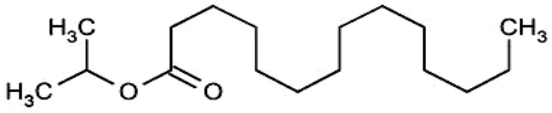
Experimental

Chemicals

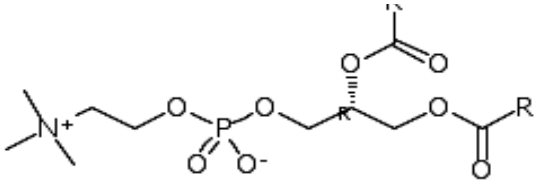
General ingredients include Tween-80 (Polyoxyethylene monooleate), as a surfactant, was obtained from E. Merck, Mumbai (India), IPM (isopropyl myristate) as an oil phase was obtained from Sisco Research Laboratories, Mumbai , Lipid (phospholipon®90G) was a gifted chemical from Bombay College of Pharmacy, Mumbai. All the chemicals were used as received. Deionized water from a Millipore Q system (resistivity ~ 18MΩcm) was used to prepare aqueous solutions. The chemical structures of Tween-80, IPM and Phospholipon® 90G used for the preparation of microemulsions are shown in **Fig. 1**.



Polyoxyethylene-20-sorbitan monooleate (Tween-80)



Isopropylmyristate (IPM)



Phospholipon 90G (R = long chain fatty acid)

Fig. 1. Chemical structures of (A) Tween-80, (B) Isopropyl myristate, (C) Phospholipon® (90G).

Dynamic light scattering

Light scattering measurements were performed using a Malvern 4800 Autosizer employing 7132 digital correlator. The light source was He-Ne laser operated at 632.8 nm with maximum power output of 15 mW. All measurements were carried out at 25.0±0.1°C using a circulating water bath. Cylindrical cells of 10 mm diameter were used in all of the light scattering experiments. The intensity of scattered light was measured five times for each sample at 130° angle. The correlation functions were analysed by the method of cumulants.

Preparation of microemulsions

Microemulsions are considered as two-phase systems composed of an inner and outer phase (e.g. o/w microemulsions, w/o microemulsion). Oil in water microemulsions were prepared using biocompatible ingredients, i.e. Tween-80 as a surfactant and isopropyl myristate (IPM) as an oil phase. All microemulsions were formulated with nanopure water to avoid surface-active impurities. In order to formulate o/w microemulsions an appropriate amount of Tween-80, isopropyl myristate (oil phase, IPM) and (water phase, W), was weighed into glass vials and homogenized completely by vortexing the mixtures vigorously. The solubility of IPM was checked for different concentration of Tween-80. A plot showing maximum solubility of IPM at different concentration of Tween-80 is shown in **Fig. 2**. With an aim to prepare SLN, the lipid, phospholipon®90G was solubilized in the above formulated microemulsions. Lipid solubilised microemulsions were prepared by solubilizing equimolar

Copyright © 2013 VBRI press.

quantity of IPM and a biocompatible lipid (Phospholipon 90G) in the surfactant solution.

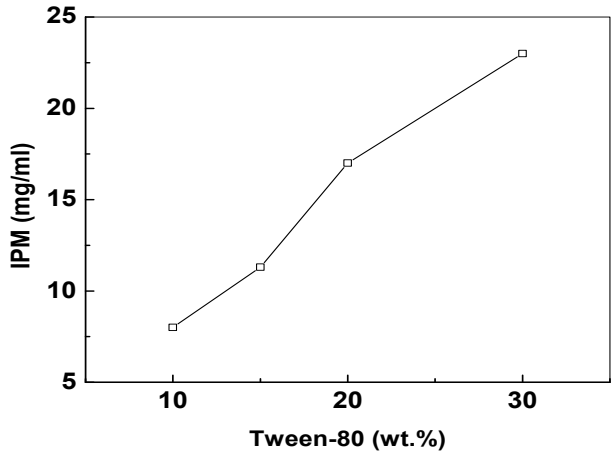


Fig. 2. Plot showing maximum solubility of IPM at different concentration of Tween-80.

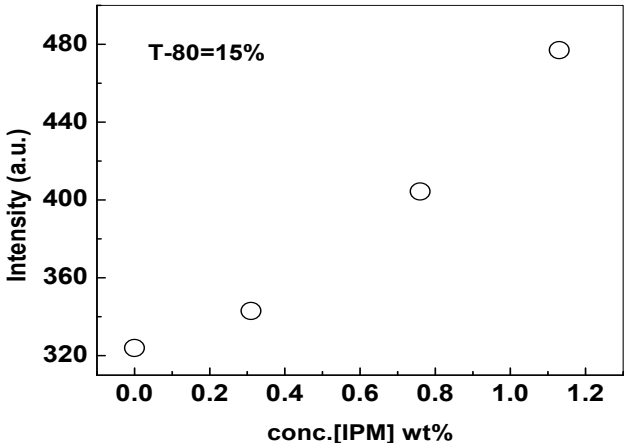


Fig. 3. Variation of the scattered intensity of light as a function of IPM concentration.

Results and discussion

Characterization of microemulsions

Static laser light scattering:

Laser light scattering studies were performed on (o/w) microemulsions prepared by addition of different concentration of IPM at fixed concentration of Tween-80 (15%). The variation in the scattered light intensity (at a scattering angle of 130^o) as a function of IPM concentration is depicted in **Fig. 3**. Backscatter geometry is chosen to minimize the interference from dust particles, if any. The scattering intensity increases noticeably on increasing the concentration of IPM. The absolute scattering intensity per unit concentration of surfactant aggregates depends on the volume of the aggregates as well as the nature and strength of the intermicellar interactions. Thus, the observed increase in the scattered intensity with an increase in the concentration of IPM is an indication of the growth of the micelles and/or changes in the intermicellar interaction. At such low volume fraction of oil, changes in the intermicellar interaction can be neglected and the observed increase in scattering can be attributed to increase in the micelle size. Quantitative analysis using complementary dynamic light scattering (DLS) measurements provides more insight into the morphological changes in these assemblies. DLS measurements were performed on these microemulsions at different concentrations of IPM keeping surfactant concentration constant.

Dynamic light scattering:

The variation in the hydrodynamic diameter of the micelles upon oil or lipid solubilisation has been monitored by dynamic light scattering. In colloidal range, suspended particles diffuse in a random walk fashion by a process known as Brownian motion. As a result of this, the phases of each of the scattered waves arriving at the detector will fluctuate in time due to random fluctuations in the relative positions of the particles which scatter the light. Since the net intensity measured by the detector is a result of superposition of all the waves scattered from the scattering volume, the intensity fluctuate randomly in time. This time dependence or the fluctuations in the net scattered intensity forms the basis of the Dynamic Light Scattering (DLS) experiment [**34**].

The key concept underlying in a basic DLS experiment is the fact that time scale of these fluctuations depends on the size of the diffusing particles. Small particles diffuse in the solution relatively rapidly resulting in a rapidly fluctuating intensity signal in contrast to the larger particles which diffuse more slowly.

The characteristic time scale of fluctuations in the scattering intensity can be obtained from the autocorrelation of scattered intensity.

A representative plot of the intensity correlation function for 15% Tween-80 with 2.25% IPM and at a scattering angle of 130° is shown in **Fig. 4**. Cumulants method of analysis of autocorrelation function is applied for a suspension of unimodal, rigid, spherical particles with small polydispersity undergoing Brownian diffusion, the correlation function decays exponentially and is given as [**35**]

$$g^{(1)}(\tau) = e^{(-\bar{\Gamma}\tau)}\left[1+\frac{\mu_2\tau^2}{2}\right] \qquad (1)$$

where Γ is the rate of relaxation of autocorrelation function and μ_2 is the variance in the relaxation rate distribution.

$$\Gamma = Dq^2 \qquad (2)$$

D is the translational diffusion coefficient and q is the magnitude of the scattering wave vector given by

$$q = (4\pi n/\lambda)\sin(\theta/2) \qquad (3)$$

The solid line in **Fig. 4** represents the theoretical fit to the experimental data by the method of cumulants and it reveals a reasonably good fit with this model.

Copyright © 2013 VBRI press

The average relaxation rate (Γ) value was obtained from cumulant analysis for different concentration of IPM and was used to calculate the diffusion coefficient of the micelles. A progressive decrease in the Γ value was observed with increasing concentration of IPM, which suggests a decrease in the apparent diffusion coefficient of the micelles. The variation of apparent diffusion coefficient, D_a, of T-80 micelles (15 %) at different concentration of IPM is depicted in **Fig 5.** A decrease in the diffusion coefficient suggests an increase in the hydrodynamic diameter of the micelles. For small dilute non-interacting spheres the hydrodynamic radius, R_h can be obtained from the translational diffusion coefficient using the Stokes-Einstein relationship [**35**].

$$D = kT / (6\pi\eta R_h) \quad (4)$$

where k is the Boltzmann constant, η is the solvent viscosity and T is the absolute temperature. If the particle is nonspherical then R_h is often referred as the apparent hydrodynamic radius. The variation of hydrodynamic radius, R_h of T-80 micelles (15 %) at different concentration of IPM is depicted in **Fig 8**.

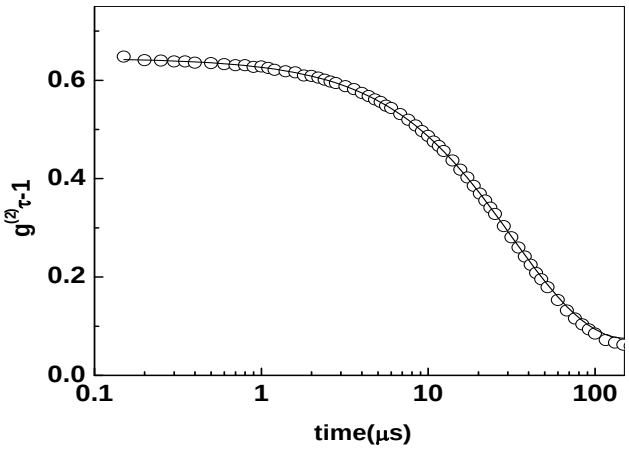


Fig. 4. Representative plot of the intensity correlation function for 15% T-80 at a maximum solubilised IPM. The solid line is a fit to the data using method of cumulants.

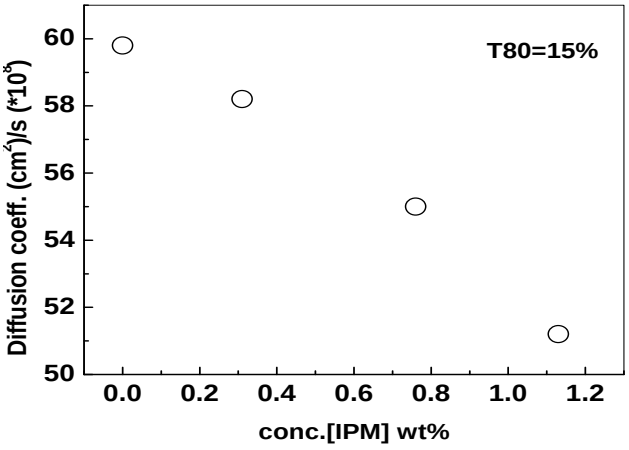


Fig. 5. Variation of diffusion coefficient of microemulsions at different concentration of IPM.

Hence, from SLS and DLS studies it is evident that with increase in the concentration of IPM the size of the micelles goes on increasing. Assuming a spherical aggregate and using simple geometric considerations, the surface area and volume of the micelles were calculated at each concentration of IPM added in T-80 micelles using the formula,

Surface area of the micelles = $4\pi R_h^2$

Volume of the micelles = $4/3\pi R_h^3$

Here R_h is the hydrodynamic radius obtained from DLS studies. The surface area as well as the volume of the aggregates increases on increasing the concentration of IPM. The aggregation number of the aggregates at different concentration of IPM was calculated using the formula:

$V = vN_{agg}$

here, V = volume of the micelles

$v = 27.4 + 26.9\ n$ ($Å^3$) (Tanford's formula)

N_{agg} = aggregation number
v = volume of the surfactant monomer obtained by Tanford formula.[36] The volume of surfactant monomer was found to be 484.7 $Å^3$.

The aggregation number of the micelles increases with increase in the concentration of IPM. The hydrodynamic radius, surface area of the micelles, corresponding volume of the aggregates and the aggregation number at different concentration of IPM are given in **Table 1**.

Table 1. Micellar parameters obtained from DLS studies.

S.No.	Concentration Tween-80 (%)	Concentration IPM (%)	R_h (nm)	Volume ($Å^3$)	Surface area ($Å^2$)	N_{agg}
S1	15	0	4.0	2.7×10^5	2.0×10^4	557
S2	15	0.31	4.3	3.2×10^5	2.3×10^4	660
S3	15	0.76	4.5	3.8×10^5	2.5×10^4	784
S4	15	1.13	4.8	4.5×10^5	2.8×10^4	928

Table 2. % increase in the volume of the micelles due to IPM solubilization.

S. No.	% (ΔV)	% (ΔA)	% (ΔV - ΔA)*
S2-S1	18.5	15	3.5
S3-S1	39.3	25	14.3
S4-S1	66.7	42	24.7

By assuming that IPM is evenly distributed among surfactant aggregates, and each droplet contains similar amount of IPM, we have calculated the % increase in the volume of the micelles due to addition of IPM. The percentage increase in the volume as well as surface area of the micelles by addition of IPM in the 15% T-80 solution were calculated at each concentration of added IPM corresponding to that of pure Tween-80 micelles (**Table 2**). The increase in the surface area with increase in the

Copyright © 2013 VBRI press.

concentration of IPM may be attributed to the increase in the number of T-80 molecules per micelle. Due to the solubilization of the IPM in the core of the micelles, the hydrophobic proportion of the micelles increases. In order to maintain the hydrophilic-lipophilic balance, more surfactant molecules are involved in the formation of micelles, i.e. the aggregation number of the micelles increases, which is in accordance to the results obtained from DLS studies. The corresponding increase in the volume of the aggregates occurs due to the combined effect of increase in the aggregation number of the micelles as well as the additional volume of the added IPM droplet. Thus by subtracting percentage increase in surface area % (ΔA) to that of percentage increase in volume % (ΔV) of the micelles at different concentration of IPM with respect to that of pure Tween-80 micelles, % increase in the volume of the aggregates due to IPM addition has been obtained at different concentration of IPM (**Table 2**). This increase in volume corresponds to the percentage volume occupied by IPM in the core of the micelles. In 15% Tween-80 micelles the maximum solubilized IPM is 1.13%, which corresponds to ~ 8% of the surfactant concentration, while the % increase in the volume of the micelles due to maximum IPM solubilization is ~ 25%. It indicates that due to addition of IPM the aggregation number of the micelles increases and swelling of the micelles occurs.

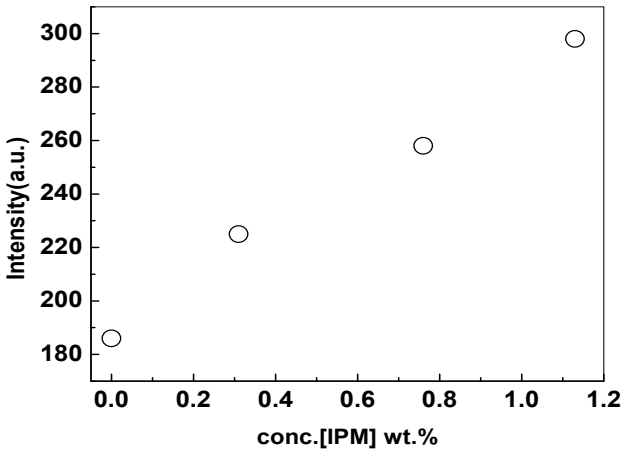


Fig. 6. Variation of the scattered intensity of light as a function of IPM = Lipid concentration.

Characterization of lipid solubilized microemulsions

With an aim to prepare solid lipid nanoparticles we have dissolved a lipid phospholipon®90G in these above prepared microemulsions. The concentration of phospholipon was kept equal to the concentration of IPM. These lipid solubilized microemulsions were characterized by light scattering techniques. The intensity of scattered light increases on increasing the concentration of IPM = phospholipon®90G that indicates an increase in the size of the micelles (**Fig. 6**). To investigate the effect of addition of phospholipon on morphology of Tween-80/IPM microemulsions, we performed dynamic light scattering studies on lipid solubilized microemulsions at different concentration. Similar methodology was employed for the analysis of the DLS data as mentioned above. The diffusion coefficient of micelles decreases on increasing the concentration of IPM = phospholipon® 90G (**Fig. 7**). The average hydrodynamic diameter calculated from diffusion coefficient using Stoke's Einstein relationship shows an increase with increasing concentration of IPM = phospholipon® 90G. The hydrodynamic diameters of the micelles in the presence as well as absence of phospholipon are compared in **Fig. 8**. From the figure it is evident that there is not much change in the size of the mcielles upon addition of lipid to the microemulsion comprised of Tween-80 and IPM. At all the concentration of IPM = phospholipon® 90G, the size of the micelles is more or less similar to that of the microemulsions in absence of the lipid only a little swelling of the micelles is taking place, which indicates that the lipid is getting solubilized in the micelles.

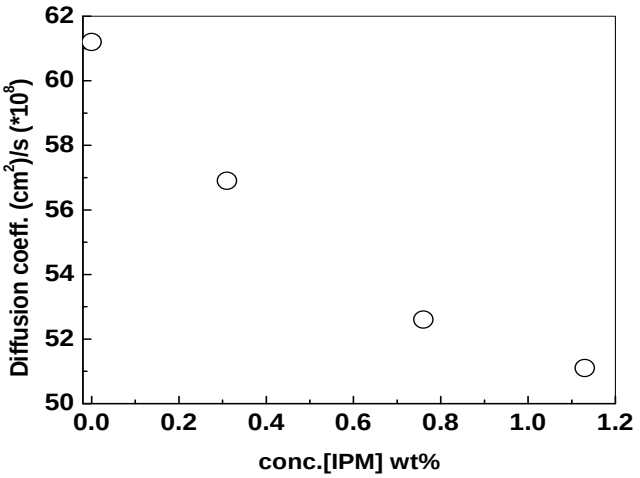


Fig. 7. Variation of diffusion coefficient of microemulsions at different concentration of IPM = Lipid.

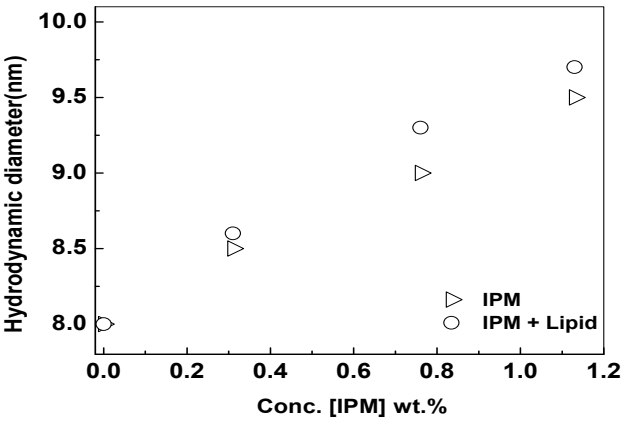


Fig. 8. Variation of hydrodynamic diameter of microemulsions in absence and presence of lipid.

Conclusion

Oil-in-water microemulsion were formulated using Tween-80 as a surfactant and IPM as an oil phase keeping the concentration of Tween-80 constant (15%) at variable concentration of IPM. The microstructure of these microemulsions has been evaluated using static and dynamic light scattering techniques. Analysis of the results showed that with increase in the concentration of IPM, the

Copyright © 2013 VBRI press

hydrodynamic size of the micelles increases. With a focus to prepare solid lipid nanoparticles, equal amount of phospholipon® 90G to that of IPM was solubilized in the microemulsions. DLS studies indicate that no significant changes occur in the size of the microemulsions upon addition of phospholipon.

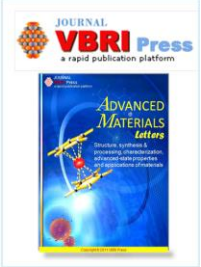
Reference

1. Wong, H. L.; Bendayan, R.; Rauth, A. M.; Li, Y.; Wu, X. Y. *Adv. Drug Deliv. Rev.* **2007**, *59*, 491-504. **DOI:** 10.1016/j.addr.2007.04.008
2. Torchilin, V. P. *J. Control. Rel.* **2001**, *73*, 137-172. **DOI:** 10.1016/S0168-3659(01)00299-1
3. Chandra, S.; Barick, K. C.; Bahadur, D. *Adv. Drug Deliv. Rev.* **2011**, *63*, 1267-1281. **DOI:** 10.1016/j.addr.2011.06.003
4. Hans, M. L.; Lowman, A. M. *Curr. Opin. Solid State Mat. Sci.* **2002**, *6*, 319-327. **DOI:** 10.1016/S1359-0286(02)00117-1
5. Dey, N. S.; Majumdar , S.; Rao, M. E. B. *Trop. J. Pharm. Res.* **2008**, *7*, 1067-1075. **DOI:** 10.1016/j.ymthe.2004.03.020
6. Li, X.; Li, H.; Liu, G.; Deng, Z.; Wu, S.; Li, P.; Xu, Z.; Xu, H.; Chu, P.K. *Biomaterials* **2012**, *33*, 3013-3024. **DOI:** 10.1016/j.biomaterials.2011.12.042
7. Hua, M. Y.; Yang, H. W.; Liu, H. L.; Tsai, R. Y.; Pang S. T.; Chuang, K. L.; Chang, Y. S.; Hwang, T. L.; Chang, Y. H.; Chuang, H. C.; Chuang, C. K. *Biomaterials* **2011,** *32*, 8999-9010. **DOI:** 10.1016/j.biomaterials.2011.08.014
8. Barick, K. C.; Nigam, S.; Bahadur, D. *J. Mater. Chem.* **2010**, *20*, 6446-6452. **DOI:** 10.1039/C0JM00022A
9. Muller, R. H.; Keck, C. M. *J. Biotech.* **2004**, *113*, 151-170. **DOI:** 10.1016/ j.jbiotec.2004.06.007
10. Mehnert, W.; Mader, K. *Adv. Drug Deliv. Rev.* **2001**, *47*, 165-196. **DOI:** 10.1016/ S0169-409X(01)00105-3
11. Wissing, S. A.; Kayser, O.; Muller, R. H. *Adv. Drug Deliv. Rev.* **2004**, 56, 1257-1272. **DOI:** 10.1016/j.addr.2003.12.002
12. Hsu, M. H.; Liao, C. Y.; Su, Y. C. Proceedings of 3rd IEE Int. Conf. on Nano/Micro Engineered and Mol. Systems, Sanya, China, **2008**.
13. Zur Muhlen, A.; Schwarz, C.; Mehnert, W. *Eurp. J. Pharm. Biopharm.* **1998**, *45*, 149-155. **DOI:** 10.1016/S0939-6411(97)00150-1
14. Pragati, S.; Kuldeep, S.; Ashok, S.; Satheesh, M. *Int. J. Pharm. Sci. Nanotech.* **2009**, *2*, 509-516.
15. Joshi, M.; Patravale, V. *Int. J. Pharm.* **2008**, *346*, 124-132. **DOI:** 10.1016/j.ijpharm.2007.05.060
16. ALHaj, N. A.; Abdullah, R.; Ibrahim, S.; Bustamam, A. *Am. J. Pharmacol. Toxicol.* **2008,** *3*, 219-224. **DOI:** 10.3844/ajptsp.2008.219.224
17. Gasco, M. R. *Pharm. Technol.* Eur. **1997**, *9*, 52-58.
18. Sjostrom, B.; Bergenstahl, B. *Int. J. Pharm.* **1992**, *88*, 53-62. **DOI:** 10.1016/0378-5173(92)90303-J
19. Hu, F. Q.; Yuan, H.; Zhang, H. H.; Fang, M. *Int. J. Pharm.* **2002**, *239*, 121-128. **DOI:** 10.1016/S0378-5173(02)00081-9
20. Trotta, M.; Debernardi, F.; Caputo, O. *Int. J. Pharm.* **2003**, *257*, 153-160. **DOI:**10.1016/S0378-5173(03)00135-2
21. Heurtault, B.; Saulnier, P.; Pech, B.; Proust, J. E.; Benoit, J. P. *Pharm. Res.* **2002**, *19*, 875-880. **DOI:** 10.1023/A:1016121319668
22. Charcosset, C.; Harati, A.E.; Fessi, H. *J. Controlled Release* **2005**, *108*, 112-120. **DOI:**10.1016/j.jconrel.2005.07.023
23. Fricker, G.; Kromp, T.; Wendel, A.; Blume, A.; Zirkel, J.; Rebmann H.; Setzer, C.; Quinkert, R.O.; Martin F.; Goymann, C.M. *Pharm. Res.* **2010**, *27*, 1469-1486. **DOI:** 10.1007/s11095-010-0130-x
24. Schott, H. *J. Pharm. Sci.* **1984**, *7*, 790-792. **DOI:** 10.1002/jps.2600730621
25. Gershanik, T.; Benita, S. *Eurp. J. Pharm. Biopharm.* **2000**, *50*, 179-188. **DOI:** 10.1016/S0939-6411(00)00089-8
26. Kreuter, J.; Shamenkov, D.; Petrov, V.; Ramge, P.; Cychutek, K.; Brandt, C. K.; Alyantdin, R. *J. Drug Target.* **2002**, *10*, 317-325. **DOI:** 10.1080/10611860290031877
27. Olbrich, C.; Gessner, A.; Schroder, W.; Kayser, O.; Muller, R. H. *J. Control. Release* **2004**, *96*, 425-435. **DOI:** 10.1016/j.jconrel.2004.02.024
28. Trotta, M.; Vgazio, E.; Peira, E.; Pulitano, C. *J. Control. Rel.* **2003**, *86*, 315-321. **DOI:** 10.1016/S0168-3659(02)00416-9
29. Chen, H.; Xiao, L.; Du, D.; Mou, D.; Xu, H.; Yang, X. *Nanotechnology* **2010**, *21*, 015101. **DOI:**10.1088/0957-4484/21/1/015101
30. Acharya, A.; Sanyal, S. K.; Moulik, S. P. *Cur. Sci.* **2001**, *81*, 362-370.
31. Fundueanu, G.; Constantin, M.; Esposito, E.; Nastruzzi, C.; Menegatti, E. *Biomaterials* **2005**, *26*, 4337-4347. **DOI:**10.1016/j.biomaterials.2004.10.036
32. Attama, A. A.; Schicke, B. C.; Paepenmuller, T.; Muller-Goymann, C. C. *Eur. J. Pharm. Biopharm.* **2007**, *67*, 48-57. **DOI:**10.1016/j.ejpb.2006.12.004
33. Barras, A.; Mezzetti, A.; Richard, A.; Lazzaroni, S.; Roux S.; Melnyk, P.; Betbeder, D.; Monfilliette-Dupont, N. *Int. J. Pharm.* **2009**, *379*, 270-277. **DOI:**10.1016/j.ijpharm.2009.05.054
34. Pecora, R. In *Dynamic Light Scattering: Application of Photon Correlation Spectroscopy;* Plenum Press: New York, **1985**.
35. Hassan, P. A.; Kulshrestha, S. K. *J. Coll. Interf. Sci.* **2006**, *300*, 744-748. DOI: 10.1016/j.jcis.2006.04.013
36. Tanford, C. In *The Hydrophobic Effect: Formation of Micelles and Biological Membranes*; Wiley: New York, **1980**.

Advanced Materials Letters

Publish your article in this journal

ADVANCED MATERIALS Letters is an international journal published quarterly. The journal is intended to provide top-quality peer-reviewed research papers in the fascinating field of materials science particularly in the area of structure, synthesis and processing, characterization, advanced-state properties, and applications of materials. All articles are indexed on various databases including DOAJ and are available for download for free. The manuscript management system is completely electronic and has fast and fair peer-review process. The journal includes review articles, research articles, notes, letter to editor and short communications.



Copyright © 2013 VBRI press.