Sharma et al., J Pharm Drug Deliv Res 2012, 1:3
http://dx.doi.org/10.4172/2325-9604.1000109

Journal of Pharmaceutics & Drug Delivery Research

Research Article

A SCITECHNOL JOURNAL

Formulation, Optimization and Evaluation of Atorvastatin Calcium Loaded Microemulsion

Bhumika Sharma[1], Arvind Sharma[1*], Sandeep Arora[1], Shriya Gupta[1] and Manila Bishnoi[1]

Abstract

Atorvastatin calcium is a HMG-CoA inhibitor having an Anti-hyperlipidemic effect. It belongs to the II class of BCS classification hence formulating a microemulsion will increase its solubility/dissolution and thus improves the oral bioavailability. Microemulsion formulation is prepared by water titration method using Labrafil M1944CS, Cremophor RH 40 and Transcutol HP as oil, surfactant and co-surfactant respectively. A single isotropic region, which is considered to be a bicontinuous microemulsion, is found in the pseudoternary phase diagrams developed at various ratios of Labrafil M1944CS, Cremophor RH 40 and Transcutol HP. The prepared microemulsion formulations are characterised for their thermodynamic stability, drug content, pH, percent transmittance, viscosity, conductivity, particle size determination, TEM analysis and *in vitro* release. The formulation is optimized in terms of clarity, percent transmittance, percent drug content, particle size, viscosity and *in vitro* drug release. The optimized formulation is found stable over a period of 2 months. Drug release from the optimized formulation is high, i.e. 92.47 ± 1.53% (3 folds) in 7 hrs as compared to the pure drug suspension which is very low i.e. 30.13 ± 1.57% in the same time. The high release may be due to the solubility enhancing components of surfactant and co-surfactant. The result is also attributed to the fact that the optimized formulation has comparatively smaller size of oil droplets and hence larger surface area for dissolution as justified by droplet size distribution and TEM photomicrograph.

Keywords: Atorvastatin calcium; Solubility; Microemulsion

Introduction

Oral route is the simplest and easiest way to administer drug for reasons of convenience of administration, greater stability, smaller bulk, accurate dosage, ease of production and easy compliance [1]. Therefore, most of the new chemical entities (NCE) which are under development these days, are intended to be used orally that reproduces an effective *in vivo* plasma concentration after oral administration [2,3].

Hypercholesterolemia is a condition characterized by very high levels of cholesterol in the blood. People with hypercholesterolemia have a high risk of developing a form of heart disease called coronary artery disease. More than 34 million American adults have elevated blood cholesterol levels (higher than 240 mg/dL). Atorvastatin calcium is the drug used for treating hypercholesterolemia [4]. Most of the potential drug candidates exhibit a problem of low oral bioavailability. Orally taken drugs have poor bioavailability because of poor drug dissolution and solubility rather than limited permeation through the epithelia of gastrointestinal tract.

Hence, together with permeability, the solubility and dissolution behaviour of a drug are key determinants of its bioavailability when administered orally. Atorvastatin calcium belongs to BCS class II category and the problem with this potentially useful hypolipidemic agent is that it is very slightly soluble in water (0.21 mg/ml at 37°C), thus it has poor bioavailability (14%) due to its poor aqueous solubility and poor absorption [5]. The drug delivery industry scientists are used a wide range of methods to improve the dissolution rate of poorly water-soluble drugs, including formulations containing nanoparticles, a solid solution formulation or self emulsifying drug delivery system (SEDDS), and stable amorphous form of the drug [6-10]. Microemulsions are used as edge as potential drug delivery vehicles because of their thermodynamic stability, reversibility, simple manufacturing, and scale up feasibility, and do not require any special equipment. Oil-in-water (o/w) microemulsion is the most suitable formulation, which is expected to increase the solubility by dissolving the compounds with low water solubility into an oil phase. Thus, Atorvastatin calcium is considered to be a good candidate for microemulsion drug delivery system to enhance its oral bioavailability by reducing the droplet size, hence increasing the rate of absorption due to surfactant induced permeability changes.

Materials

Atorvastatin calcium was a gift sample from Alkem Laboratories, Baddi Ltd. Labrafil M1944CS, Labrafac CC and Transcutol HP were obtained as gift samples from Gattefosse, Mumbai, India. Tween 60, Propylene glycol, Isopropyl Myristate and Methanol were purchased from Loba Chemie Pvt. Ltd Mumbai, India. Cremophor EL, Cremophor RH40 were obtained from Hi Media Laboratories Pvt. Ltd Mumbai, India.

Methods

Preformulation studies

Solubility studies: The solubility of the drug was determined in different oils i.e. olive oil, sunflower oil, oleic acid, Labrafil M 1944CS, Isopropyl myristate; surfactants i.e. Cremophor RH 40, Cremophor EL, Labrafac CC, Tween 60 and co-surfactants i.e. Transcutol HP, Propylene glycol.

Pseudo-ternary phase diagram study

The ratio of surfactant to co-surfactant was fixed at different ratios of 1:1, 2:1, 3:1 and 4:1 on the weight basis for each phase diagram. The mixture of surfactant and co-surfactant is referred to as "surfactant phase" in the following discussion.

***Corresponding author:** Arvind Sharma, Chitkara College of Pharmacy, Chitkara University, Chandigarh-Patiala National Highway (NH-64) Punjab 140401, India, Tel: + 01762505084; Fax: 01762505085; E-mail: arvind.sharma@chitkara.edu.in

Received: October 09, 2012 **Accepted:** November 23, 2012 **Published:** November 26, 2012

The oil phase was mixed with the surfactant phase in the ratios (volume basis) of 1:9, 2:8, 3:7, 4:6, 5:5, 6:4, 7:3, 8:2 and 9:1. A water titration technique was employed for the preparation of the pseudo ternary phase diagrams. Distilled water was added drop by drop to the mixture of oil/surfactant phase at room temperature.

After each water addition, the mixture was stirred in a beaker for 2-3 min using a stirring rod until homogenous solution was obtained. After each addition, the system was examined for appearance and flow property. The end point of the titration was the point in which the solution becomes cloudy or turbid. The quantity of aqueous phase required to make the mixture turbid was noted.

The pseudo-ternary phase diagram consisted of two regions: biphasic emulsion region and monophasic microemulsion region. In each of the titration runs, several end points were noted down as critical points between the two regions. The critical point was a specific composition where a significant change in the appearance (turbidity) of the mixture occurred. The boundaries between these regions were drawn on the phase diagram by joining together the critical points. Four such phase diagrams were constructed taking ratio of surfactant/co-surfactant as 4:1, 3:1, 2:1, and 1:1 respectively.

Preparation of drug loaded microemulsion

Microemulsion was prepared by using water titration method keeping constant ratio of surfactant/cosurfactant (i.e. ratio selected from phase diagram studies). Seven formulations from the monophasic area of the phase diagram were prepared using various concentrations of oil, surfactant/cosurfactant and water. The water was added dropwise, after addition of each drop, the mixture was stirred and observed. In microemulsion system distilled water was used as external phase (Table 1).

Optimization of microemulsion

Various batches of microemulsions were prepared by water titration method and optimization was done in terms of clarity,% transmittance, particle size, viscosity,% drug content and% drug release.

The optimized microemulsion drug delivery system was then characterised and later subjected to the stability study.

Characterisation of microemulsion formulation

Percent drug content: The drug content of the microemulsion formulation was determined by dissolving 1 ml (equivalent to 10 mg drug) of the formulation in 10 ml of methanol. After suitable dilutions with methanol, absorbance was determined using the UV spectrophotometer (AU-2701 Systronic, Mumbai, India) keeping blank microemulsion as control at wavelength 246 nm.

Table 1: Composition of various microemulsion formulations containing drug (ATV).

Formulation code	Oil	S_{mix}	Water	Amount of drug (mg/ml)
F1	10%	40%	50%	10
F2	12%	45%	43%	10
F3	13%	61%	26%	10
F4	19%	44%	37%	10
F5	22%	48%	30%	10
F6	26%	60%	14%	10
F7	38%	56%	6%	10

Determination of pH: The pH values of the samples were measured by a pH meter (Digital Systronics, Mumbai, India) at ambient temperature with glass electrode.

Thermodynamic stability: Microemulsions are thermodynamically stable formulations and are formed at particular concentration of oil, surfactant and water, with no phase separation, creaming and cracking. It is the thermo stability that differentiates microemulsions from emulsions that have kinetic stability and eventually phase separate. Thus, the selected formulations were subjected to different thermodynamic stability by using heating cooling cycle, centrifugation and freeze thaw cycle stress tests [11].

Dispersibility test [12]: The thermodynamically stable microemulsions were further taken for the dispersibility test for visual assessment and were assessed using following grading system:

Grade A: Rapidly forming (within 1 min) microemulsion, having a clear or bluish appearance.

Grade B: Rapidly forming, slightly less clear microemulsion, having a bluish white appearance.

Grade C: Fine milky microemulsion that formed within 2 min.

Robustness to dilution: Microemulsions resulting from dilution with dissolution media must be robust to all dilutions and should not show any separation even after 24 hours of storage.

Particle size distribution, Polydispersity index and Zeta potential: Physical characteristics of microemulsion (particle size distribution, polydispersity index and zeta potential) were determined by using dynamic light scattering (DLS) method using Malvern Zetasizer 2000 HS (Malvern Instruments, NIPER, SAS Nagar, Punjab).

Viscosity measurements: Microemulsions are generally low viscosity systems. The viscosity measurement of the prepared microemulsion was performed using Brookfield's viscometer (Brookfield DV-2+ pro viscometer) at single mode using spindle # CPE40 at 32 ± 0.5°C.

Percent transmittance: Transparency of microemulsion formulation was determined by measuring the percentage transmittance at 650 nm with purified water taken as blank through UV spectrophotometer.

Transmission electron microscopy: TEM characterised the microstructure of the prepared Atorva microemulsion (TEM Hitachi (H-7500). Microemulsions were prepared at ambient conditions. Morphology and structure of oil globules were determined with the aid of TEM at CIL, Punjab University, and Chandigarh. The microemulsion systems were dried on a microscopic carbon coated grid and viewed under microscope after staining at suitable magnification. Photo-Micrographs of the globules were then taken.

Conductance: Electrical conductivity (s) has been traditionally used as a standard technique to study the phase behaviour. The

underlying principle for phase determination by conductivity is the ability of water to conduct an electric current, which is measured in Scm^{-1} or μScm^{-1}. The conductive measurements were taken by a conductivity meter. The microemulsion prepared with addition of water was measured after thorough mixing and temperature equilibration at 25°C, the electrode was dipped in the microemulsion sample until equilibrium was reached, and reading becomes stable. Reproducibility was checked for certain samples and no significant differences were observed.

***In vitro* drug release by membrane diffusion technique:** *In vitro* drug release studies of Atorvastatin calcium from microemulsions were carried out using the membrane diffusion technique. *In vitro* diffusion cell was made using dialysis membrane as a semi-permeable membrane. The diffusion cell consists of a test tube with both ends open. One end of the test tube was closed using pre-soaked dialysis membrane and the other end was open to introduce the formulation. An accurately measured amount of formulation equivalent to 10 mg (1 ml) was introduced into the test tube having a diameter of 2.5 cm that was covered with dialysis membrane (12,000-14,000 molecular wt cut off). The test tube was suspended in the dissolution flask of a USP dissolution apparatus containing 250 ml phosphate buffer (pH 6.8). The temperature of the buffer solution was maintained at 37 ± 0.5°C and the glass tube was allowed to rotate at a constant speed (50 rpm). Aliquots of the medium were withdrawn every hour and replaced with fresh phosphate buffer (pH 6.8). The samples were analysed by using UV/Vi spectrophotometer (AU-2701 Systronic, Mumbai, India) at 246 nm. The same method was used for the suspension containing 10 mg of ATV in 1 ml distilled water. The release of drug from different selected microemulsion formulations was compared with drug suspension and finally formulation showing the best release was selected.

Stability studies: The optimized microemulsion formulation was selected for stability study on the basis of its in vitro performance and stored in tightly closed glass vials at 4°C, ambient temperature and 40°C. During stability studies various parameters like transparency, particle size and drug content were observed periodically for a period of 8 weeks (2 months).

Results and Discussion

Preformulation studies

Solubility studies: Solubility studies were carried out to identify the potential ingredients for the formulation of microemulsion.

Table 2: Solubility studies of different potential vehicles.

S. No.	Vehicles	Solubility (mg/ml ± SD)
1	Sunflower oil	24.9 ± 2.2
2	Isopropyl Myristate	34.9 ± 1.8
3	Oleic acid	20.1 ± 1.1
4	Labrafil M 1944CS	57.7 ± 1.3
5	Olive oil	8.4 ± 1.2
6	Labrafac CC	26.5 ± 2.7
7	Tween 60	5.56 ± 0.9
8	Cremophor EL	11.4 ± 1.2
9	Cremophor RH 40	28.2 ± 1.1
10	Transcutol HP	23.4 ± 1.6
11	Propylene glycol	8.20 ± 1.4

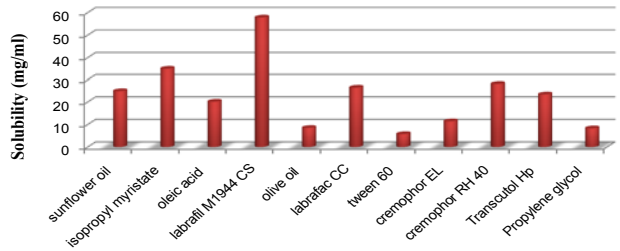

Figure 1: Graphical representation of solubility studies of different potential vehicles.

Amongst oils that were screened, Labrafil M1944CS (unsaturated polygylcolysed glycerides) exhibited the highest solubilising potential for Atorvastatin calcium and it was selected as an oily phase for further studies. Accordingly, Cremophor RH 40 (polyethoxylated castor oil) and Transcutol HP (highly purified diethylene glycol monoethyl ether) were selected as surfactant and co-surfactant respectively (Table 2) and the graphical representation of solubility studies is given in figure 1.

Phase diagram: From the results of the pseudo-ternary phase diagram, 3:1 ratio of S_{mix} was selected for microemulsion preparation. Optimum microemulsion formula was selected using phase studies employing Labrafil M1944CS as oily phase, Cremophor RH40 as surfactant and distilled water as aqueous phase. Phase studies help finding out the concentration range of the components for the formation of clear and stable microemulsion systems. Suitable formulas were hence selected from the phase diagram. The phase diagrams are shown in figures 2a-2d.

Characterisation of microemulsion formulation

Drug content: The drug content of microemulsion preparations of Atorvastatin calcium was found to be in the range of 98.60 ± 0.32 to 99.81 ± 0.25. Data indicates uniform distribution of drug throughout the microemulsion (Table 3).

pH Determination: The pH values of microemulsion formulations of Atorvastatin calcium were found to be between 7.26 to 7.41 which is suitable for oral administration. pH range of the formulations is shown in table 3.

Thermodynamic stability studies

Microemulsions are thermodynamically stable systems and are formed at a particular concentration of oil, surfactant and water with no phase separation, creaming or cracking. It is the thermo stability that differentiates microemulsions from emulsions that have kinetic stability and eventually phase separate. Thus, the selected formulation was subjected to different thermodynamic stability by using heating cooling cycle, centrifugation and freeze thaw cycle stress tests. After the thermodynamic stability study, the formulation further tested for dispersibility.

It was observed that formulation (F6) did not pass the thermodynamic stability test and thus was dropped for further studies. The results of thermodynamic stability study and dispersibility test are shown in table 4.

Percentage transmittance

The percentage transmittance of the microemulsion formulations ranged from 93.46% to 97.20% table 5.

Viscosity

Viscosity studies are necessary determinations for microemulsions to characterize the system physically and to control its physical stability (Table 5).

Particle size, size distribution, polydispersity index (PDI) and zeta potential

It is known that particle size distribution is one of the most important characteristics of an emulsion for evaluation of its stability and the bioavailability of drug from an emulsion. Various parameters which can affect globule size of a microemulsion include the type of surfactants and co-surfactants, amount of dispersed phase and rate of stirring. Particle size characterisation of the resulting microemulsion is essential in ensuring stability and efficient dosage. The average diameter of selected formulation is shown in figure 3, as observed the mean diameter was found to be 28.27 nm. The polydispersity index was found to be 1. The statistical representation of particle size distribution curve is shown in figure 4. The zeta potential of prepared microemulsion was measured using Malvern Zetasizer ™ was found to be -0.312 mV (Figure 5).

Conductivity

The conductivity of the microemulsion formulation (F1) was found to be 88.5 µS cm^{-1}. The conductivity owes to the conductance of water in o/w microemulsion.

Table 3: Evaluation parameters of microemulsion formulations.

Formulation code	Clarity	Percent drug content	pH
F1	✓	99.81 ± 0.25	7.38
F2	✓	99.20 ± 0.18	7.39
F3	✓	99.18 ± 0.14	7.41
F4	✓	99.10 ± 0.12	7.32
F5	✓	98.64 ± 0.54	7.30
F6	✓	98.60 ± 0.32	7.26
F7	×	-	-

Table 4: Thermodynamic stability study and dispersibility test results.

Formulation code	Thermodynamic Stability			Dispersibility test	Inference
	Heat/ cooling cycle	Centrifugation	Freeze thaw	grades	
F1	✓	✓	✓	A	Passed
F2	✓	✓	✓	A	Passed
F3	✓	✓	✓	B	Passed
F4	✓	✓	✓	A	Passed
F5	✓	✓	✓	B	Passed
F6	✓	✓	×	×	Failed

Table 5: Evaluation parameters of prepared microemulsion.

Formulation code	Viscosity (cP)	% Transmittance	Particle size (nm)
F1	27.51	97.20%	28.27
F2	35.32	96.10%	35.76
F3	28.22	95.32%	48.80
F4	37.30	94.67%	152.32
F5	40.63	93.46%	117.46

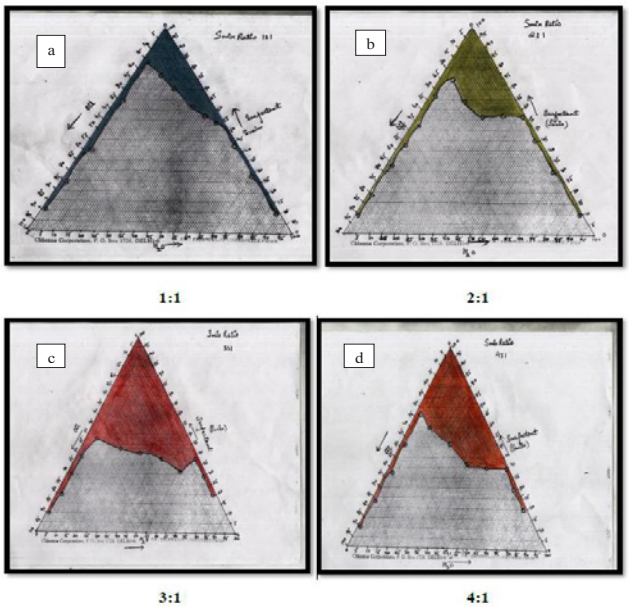

Figure 2: Ternary phase diagrams of microemulsion using different ratios of S_{mix} (1:1, 2:1, 3:1 and 4:1 respectively).

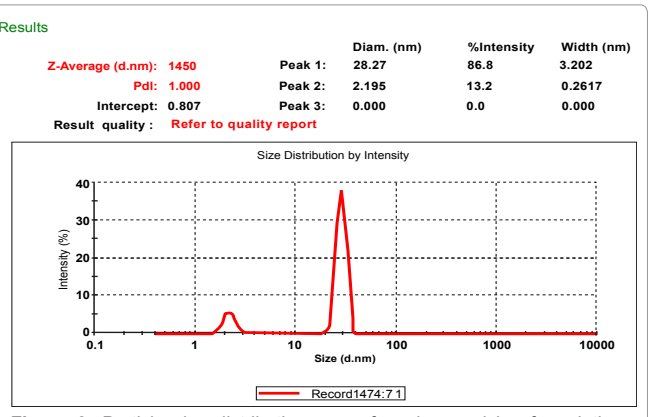

Figure 3: Particle size distribution curve for microemulsion formulation (F1).

Characterization of microemulsion by TEM

The transmission electron microscopic picture of selected microemulsion reveals that the microemulsified droplets were almost spherical in shape (Figure 6).

In vitro drug release study

Dissolution study was performed by membrane diffusion technique in phosphate buffer 6.8 for the final selection of microemulsion formulation. The dissolution study was performed for 24 hrs. Drug dissolution from formulation F1 was very fast as 92.15 ± 0.53% of drug released in 7 hrs; while formulations F2, F3, F4 and F5 showed comparatively slow release i.e. 86.33 ± 0.11, 80.21 ± 0.73, 77.01 ± 0.45 and 78.76 ± 0.18 in 7 hrs. In contrast to this drug

released from API suspension was found to be very low i.e. 30.13 ± 0.57% in 7 hrs. This result was attributed to the fact that formulation F1 is having comparatively smaller size (28.27 nm) of oil droplets and hence the larger surface area for dissolution as justified by droplet size distribution and by TEM photograph. Comparative *in vitro* dissolution data of prepared ATV microemulsion formulations is given in figure 7 and table 6.

Stability studies

Stability studies of selected formulation were carried out at ambient temperature, 4 ± 2°C and 40 ± 5°C. The results of stability are shown in table 7. These results indicate that selected microemulsion remained stable for a period of 8 weeks at ambient temperature, 4 ± 2°C and 40 ± 5°C. Microemulsion formulation maintained its clarity at all the temperatures for a period of 8 weeks. The pH of the formulation remained almost same during the study period of 8 weeks and was observed in the range of 7.38 to 7.41 at the start of study, while after completion of study it was in the range of 7.26 to 7.34. Also, a slight decline in the drug content was observed over a period of 8 weeks: 0.6% decrease at 4°C, 1.2% decrease at ambient temperature and 1.5% decrease in drug content at 40°C.

There was a slight increase in particle size ranging from 28.27 nm to 28.42 nm over a period of 8 weeks (Table 7).

Conclusion

Oral microemulsion of Atorvastatin calcium was prepared and evaluated with an objective to improve the solubility/dissolution and hence improve the oral bioavailability. Microemulsion formulation was prepared by water titration method using Labrafil M 1944 CS, Cremophor RH 40 and Transcutol HP as oil, surfactant and cosurfactant as per the solubility studies. From the Pseudo ternary phase diagrams, 3:1 ratio of surfactant: cosurfactant was chosen as the best ratio for microemulsion formulation. The prepared microemulsion formulations were characterised for their thermodynamic stability, drug content, pH, percent transmittance, viscosity, particle size determination and in-vitro release. The formulation was optimized on the basis of percent drug content, thermodynamic stability, percent transmittance, particle size, zeta potential, conductivity, TEM analysis and *in vitro* release studies. The amount of the drug content in the optimized formulation was around 99.81 ± 0.25% of the added amount indicating the suitability of the system for high entrapment in the internal phase. The high value of percentage transmittance (97.20%) indicates that the system

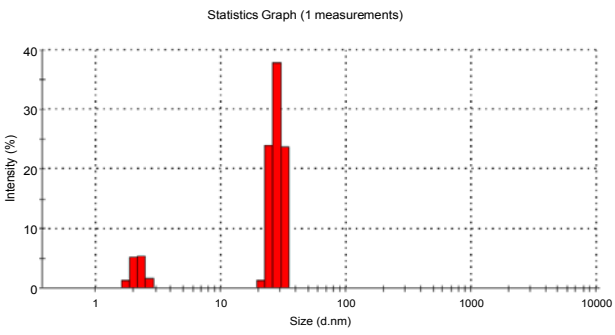

Figure 4: Graphical representation of particle size distribution curve for microemulsion formulation (F1).

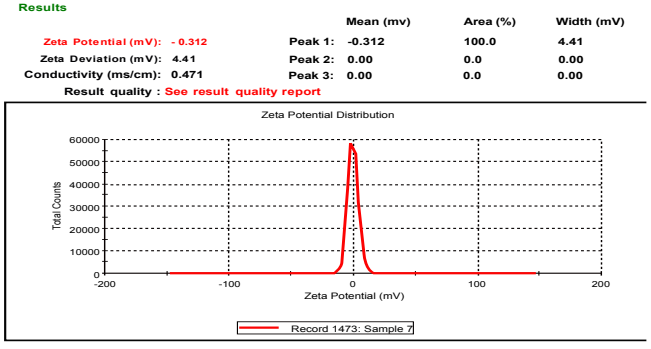

Figure 5: Zeta potential distribution curve for microemulsion formulation (F1).

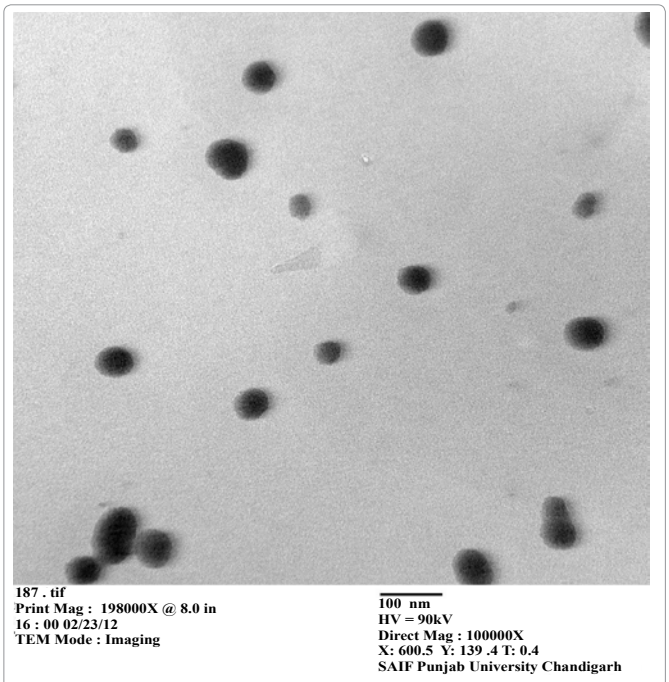

Figure 6: Transmission electron photograph of microemulsion formulation (F1).

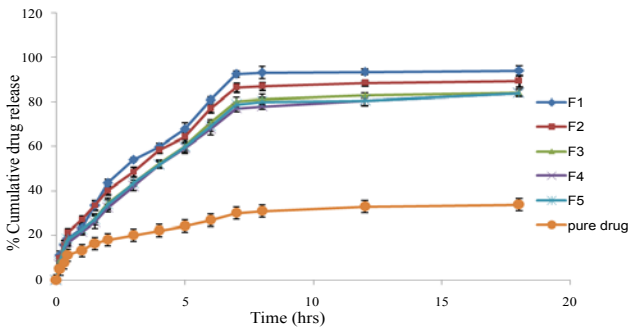

Figure 7: Comparative cumulative amount of drug released from the different ATV microemulsion formulations.

Table 6: Comparative *In vitro* dissolution data of prepared ATV microemulsion formulations.

Time (Min)	F1	F2	F3	F4	F5	Pure drug
0	0	0	0	0	0	0
0.15	11.21 ± 1.79	10.05 ± 1.24	8.88 ± 1.69	6.84 ± 1.31	8.01 ± 1.82	5.09 ± 2.90
0.3	15.87 ± 1.98	15.87 ± 2.19	14.41 ± 1.59	13.83 ± 2.48	14.41 ± 1.66	7.71 ± 1.73
0.45	18.78 ± 2.75	21.69 ± 1.47	18.19 ± 2.94	17.03 ± 1.43	18.49 ± 1.79	11.21 ± 1.17
1	23.44 ± 1.48	27.22 ± 1.57	22.56 ± 1.70	21.69 ± 1.38	22.85 ± 1.81	13.24 ± 1.86
1.5	33.64 ± 2.20	33.63 ± 2.22	27.51 ± 1.69	26.06 ± 2.72	27.22 ± 2.52	16.45 ± 1.21
2	43.54 ± 1.54	40.32 ± 1.85	34.50 ± 2.59	32.46 ± 1.74	33.92 ± 2.34	18.19 ± 2.77
3	54.03 ± 0.98	48.48 ± 2.17	43.53 ± 1.29	42.07 ± 1.77	43.53 ± 1.34	20.23 ± 1.60
4	59.85 ± 1.54	58.38 ± 1.19	52.26 ± 1.70	51.68 ± 1.54	51.68 ± 1.42	22.27 ± 1.40
5	67.72 ± 2.85	64.20 ± 2.05	60.12 ± 2.71	59.25 ± 2.35	59.83 ± 1.62	24.31 ± 1.22
6	80.82 ± 1.27	77.01 ± 1.73	70.61 ± 1.37	67.69 ± 2.73	68.86 ± 2.23	26.93 ± 1.27
7	92.47 ± 1.53	86.33 ± 2.11	80.21 ± 1.73	77.01 ± 1.45	78.76 ± 1.18	30.13 ± 1.57
8	93.05 ± 2.78	86.90 ± 1.64	81.08 ± 2.38	77.88 ± 1.12	79.91 ± 1.94	31.00 ± 1.73
12	93.34 ± 1.31	88.36 ± 1.28	82.83 ± 1.13	80.50 ± 2.29	80.50 ± 2.12	33.04 ± 1.62
18	93.93 ± 2.35	89.23 ± 2.57	83.99 ± 1.54	83.70 ± 1.59	83.70 ± 1.59	33.91 ± 1.87

* Values are mean ± SD (*n* = 3)

Table 7: Stability study parameters for selected microemulsion formulation.

S. No.	Time	Temperature conditions	% Drug content	Transparency/ Clarity	Particle size (nm)
1	1st day	4°C Ambient Temp. 40°C	99.80% 99.80% 99.80%	✓ ✓	28.27 28.27 28.27
2	15th day	4°C Ambient Temp. 40°C	99.74% 99.46% 99.35%	✓ ✓	28.29 28.27 28.26
3	4th week	4°C Ambient Temp. 40°C	99.41% 98.80% 98.56%	✓ ✓	28.33 28.28 28.28
4	8th week	4°C Ambient Temp. 40°C	99.21% 98.75% 98.30%	✓ ✓	28.42 28.30 28.31

is optically clear which is prerequisite for microemulsions. The size of the globule is also found to be in the desirable size range (10-100 nm) indicating the possibility of enhanced permeation through the biological membrane. Drug release from the optimized formulation was found to be very fast as 92.47 ± 1.53% of drug released in 7 hrs. In contrast to this drug released from the API suspension was found to be very low i.e. 30 ± 1.57% at the same time. The zeta potential of the formulation was found to be slightly negative in spite of the non-ionic nature of the surfactant, co-surfactant and the oil. This indicated that the formulation would remain physically stable on storage, which was further confirmed by stability study. The optimized formulation showed conductivity of 88.5 µS/cm which indicated that the type of the emulsion formed was oil in water (o/w).

Acknowledgement

The authors are grateful to M/S Alkem Laboratories, Baddi (India) for their kind gift samples of the drug, Atorvastatin calcium.

References

1. Anguiano-Igea S, Otero-Espinar FJ, Vilajato JL, Blanco-mendez J (1995) The properties of solid dispersions of clofibrate in polyethylene glycols. Int J Pharm 70: 57–66.
2. Serajuddin AT (1999) Solid dispersion of poorly water-soluble drugs: early promises, subsequent problems, and recent breakthroughs. J Pharm Sci 88: 1058–1066.
3. Craig DQ (2002) The mechanisms of drug release from solid dispersions in water-soluble polymers. Int J Pharm 231: 131–144.
4. Hypercholesterolemia- (2011).
5. Bobe KR, Subrahmanya CR, Suresh S, Gaikwad DT, Patil MD, et al. (2011) Formulation and evaluation of solid dispersion of atorvastatin with various carriers. Int J Comp Pharm 1: 1-6.
6. Kumar M, Misra A, Babbar AK, Mishra AK, Mishra P, et al. (2008) Intranasal nanoemulsion based brain targeting drug delivery system of risperidone. Int J Pharm 358: 285-291.
7. Teixeira H, Dubernet C, Rosilio V, Laigle A, Deverre JR, et al. (2001) Factors influencing the oligonucleotides release from O-W submicron cationic emulsions. J Control Release 70: 243-55.
8. Dixit N, Kohli K, Baboota S (2008) Nanoemulsion system for the transdermal delivery of a poorly soluble cardiovascular drug. PDA J Pharm Sci Technol 62: 46-55.
9. Rao SV, Shao J (2008) Self-nanoemulsifying drug delivery systems

(SNEDDS) for oral delivery of protein drugs: I. Formulation development. Int J Pharm 362: 2-9.

10. Mason TG, Wilking JN, Meleson K, Chang CB, Graves SM (2006) Nanoemulsions: formation, structure, and physical properties. JPhys Condens Matter 18: R635.
11. Patel AR, Vavia PR (2007) Preparation and in vivo evaluation of SMEDDS (Self-microemulsifying drug delivery system) Containing fenofibrate. AAPS J 9: E344-E352.
12. Paolino D, Ventura CA, Nistico S, Puglisi G, Fresta M (2002) Lecithin microemulsions for the topical administration of ketoprofen: percutaneous absorption through human Skin and in vivo human skin tolerability. Int J Pharm 244: 21-31.

Author Affiliation Top

[1]FChitkara College of Pharmacy, Chitkara University, Chandigarh-Patiala National Highway (NH-64) Punjab 140401, India