AMERICAN JOURNAL OF PHARMTECH RESEARCH

Journal home page: http://www.ajptr.com/

Formulation and Evaluation of Escitalopram Nanoparticles by Employing Cutina As Lipid

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ABSTRACT

Nanoparticles are submicron nano sized particles having the size range of about 1-100nm range. Because of their sub-microscopic size, they have unique material characteristics, and manufactured nanoparticles may find practical applications in a variety of areas, including medicine, engineering, catalysis, and environmental remediation. Escitalopram (ETP), an SSRI (selective serotonin reuptake inhibitor), and s-enantiomer of citalopram is exclusively used as an antidepressant. The drug shows extensive hepatic metabolism, reduced drug efficacy and potential side effects, which reduces its therapeutic index. So, the present study is focused on increasing the solubility and thus the bioavailability. The nanoparticles were prepared by using hot homogenization method by using Cutina as lipid, soya lecithin as lipophilic surfactant and PEG as hydrophilic surfactant. The prepared solid lipid Nanoparticles were evaluated for Drug content, entrapment efficiency and dissolution studies and stability studies and found that the Drug content (90.7%), Entrapment efficiency (86.1 %) and Drug release of (82.4%), Particle size(796nm) and Zeta potential (-29.4mV)

Keywords: Escitalopram, Hot Homogenization method, Solid lipid Nanoparticles

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Received 20 September 2019, Accepted 29 September 2019

Please cite this article as: Sai Ch *et al*., Formulation and Evaluation of Escitalopram Nanoparticles by Employing Cutina As Lipid. American Journal of PharmTech Research 2019.

INTRODUCTION

Solid lipid nanoparticles is one of the most widely spreading field in the nanotechnology with several different applications in the drug delivery, clinical medicine and research.

Solid lipid nanoparticles are submicron carriers ranging from 50-1000nm, which are composed of a physiological lipid dispersion in water or in a aqueous surfactant solution[1]. Solid lipid nanoparticles were discovered by Gasco and Muller in 1991. These are mainly designed to overcome the disadvantages associated with the liquid state of oil droplets.

Significance of Lipid Based Systems:

1. Lipids enhance the oral bioavailability of the drugs.
2. They have better release over the drug release kinetics.
3. They are much easier to manufacture than the biopolymer nanoparticles.
4. Wider range of base materials(lipids).
5. Chemical protection of liable incorporated compounds.
6. No special solvents required.
7. Application versatility.

MATERIALS AND METHOD

Escitalopram obtained as a gift sample from Hetero labs. Soya lecithin and Cutina were purchased from Himedia Laboratories, Mumbai, India. Methanol and all the chemicals used were of analytical grade. Dialysis membrane was from Hi media, Mumbai.

Preparation of Escitalopram nanoparticles:

This solid lipid nanoparticles were prepared by using hot homogenization method.

Hot homogenization method: Hot homogenization method is best suited method for the preparation of solid lipid nanoparticles as it can be performed at elevated temperatures to that of lipids melting point[2]. In hot homogenization technique the drug was dispersed in the lipid (Cutina) and Soya lecithin (surfactant) by melting them to their melting point and it is taken as lipid phase. The aqueous phase was prepared by adding hydrophilic surfactant (PEG 400) in the distilled water and heated to the temperature of oil phase. The above lipid phase was added drop wise to the aqueous phase through continuous stirring for 3hrs. This formulation was further sonicated for 30min and cooled to room temperature and this was stored for further evaluation. Formulations prepared by Hot homogenization was coded as F1 to F6. (Table 1)

Table 1: Composition of Nanoparticles by using Cutina as lipid:

Ingredients	F1	F2	F3	F4	F5	F6
Drug	10mg	10mg	10mg	10mg	10mg	10mg
Cutina	1gm	1gm	1gm	1gm	1gm	1gm
Soya lecithin	0.05mg	0.1mg	0.2mg	0.3mg	0.4mg	0.5mg
PEG 400	0.35ml	0.35ml	0.35ml	0.35ml	0.35ml	0.35ml
Water	10ml	10ml	10ml	10ml	10ml	10ml

EVALUATION TESTS:

Drug content:

Nanoparticle preparation was separately taken in 10ml volumetric flask and the volume was made up with methanol and to disperse the nanoparticles thorough shaking should be done for 10min and from this 1ml of the solution was taken to another volumetric flask and added upto the mark with buffer and the concentration of the drug was analysed using UV Spectrophotometer at 238nm.

Encapsulation Efficiency:

The drug Encapsulation Efficiency (EE) of the prepared Nanoparticles was determined by centrifuging the Nanoparticles at 12750g for 40 min and analyzing the supernatant at 238nm. Then Encapsulation Efficiency (EE) was calculated using the following equation:

Encapsulation Efficiency (%)[3]: $\frac{\text{Total amount of drug loaded} - \text{Free drug in supernatant}}{\text{Total amount of drug loaded}} \times 100$

Particle Size Determination:

The mean diameter of SLNs in the dispersion was determined by using instrument Nano Particle analyzer (HORIBA SZ-100) which works on the principle of dynamic light scattering.

Measurement of Zeta Potential The zeta potential is a physical property, which is exhibited by all the particles in the preparation. The magnitude of the zeta potential gives an indication of the potential stability of the system[5]. The zeta potential was determined by Nano Partica analyzer (HORIBA SZ100).

Fourier transform infrared spectroscopy (FTIR):

Fourier transform infrared spectroscopy spectra of Escitalopram drug, Cutina without drug and Escitalopram loaded nanoparticles were scanned. The samples were prepared by potassium bromide disc method and scanned for absorbance from the range of 400 – 4000 cm-1.

In-vitro drug release:

In vitro release profiles of escitalopram were obtained by a dissolution test apparatus using USP Ⅱ in phosphate buffer solution (USP Phosphate buffer pH7.2)[6]. Regenerated cellulose membrane (Dialysis membrane50, Hi-Media) was used. Escitalopram nanoparticles dispersion was placed

into a dialysis bag and sealed. This is immersed into 900 ml phosphate buffer solution and the system was maintained at 37±2℃ under mild agitation of 50 RPM/min. Aliquotes were collected for every hour upto 24hrs and the same was replaced with the fresh buffer. The samples were further analysed using UV spectrophotometer and absorbance was measured at 238nm.

Stability Studies

Stability studies were carried out for the formulations having high entrapment efficiency by storing the formulation at two different temperatures, in refrigerated condition and at room temperatures.

RESULTS AND DISCUSSION

Drug content:

The Drug content of all the three formulations were evaluated by hot homogenization method. The drug content for the prepared escitalopram nanoparticles was found in the range of 42.9% to 90.7%. Among all the 6 formulations F3 showed the maximum drug content (F1 to F6). (Table 2), (Figure 1)

Table 2: The Drug content of Escitalopram Nanoparticles by Employing Cutina as lipid:

S.No	Formulation	%Drug Content
1	F1	62.3
2	F2	74.8
3	F3	90.7
4	F4	68.7
5	F5	55.7
6	F6	49.5

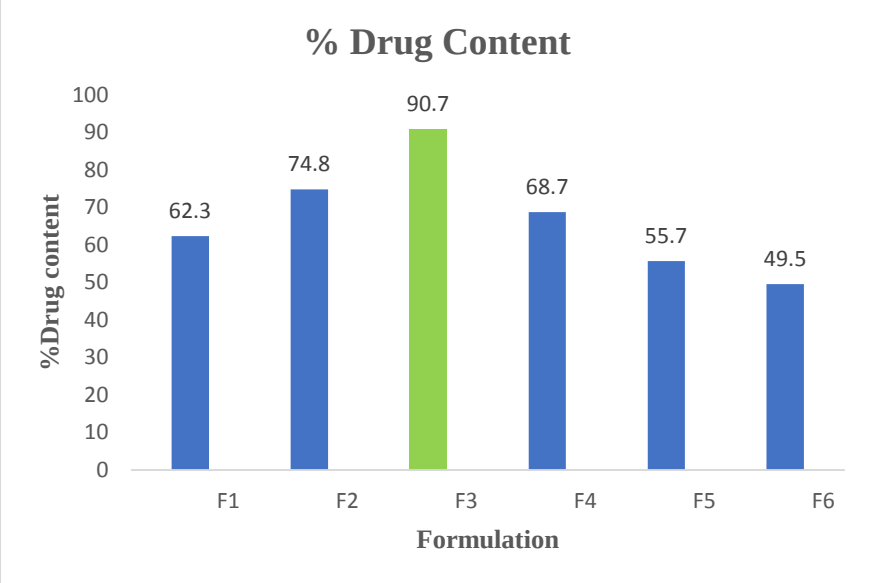

Figure 1: Drug Content of Prepared Formulations of Escitalopram loaded Solid lipid Nanoparticles by employing Cutina as a Lipid

Entrapment efficiency:

The Entrapment efficiency of the prepared formulation by hot homogenization was given in 3. The entrapment efficiency of the prepared SLNs by hot homogenization method was found to be in the range of 47.6% to 86.1%. The best entrapment efficiency was shown by F3 formulation. The ratio of lipid and surfactant concentration was optimum in F3 and showed good entrapment of the drug. (Table 2), (figure 2)

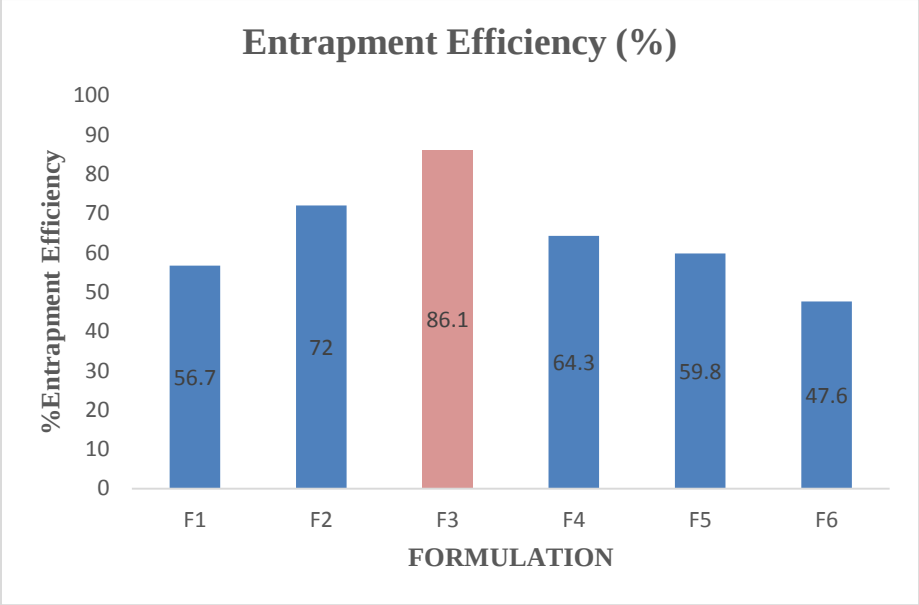

Figure 2: Entrapment Efficiency of Prepared Escitalopram loaded nanoparticles by Employing Cutina as a lipid

Determination of Particle size:

Among all the six prepared formulations, the particle size of the F3 was considered as the best formulation with the particles of size of 796 nm. Particle size analysis was determined by

HORIBA SZ 100 Z nanoparticle analyser. Thus it was observed that found in the nano range.

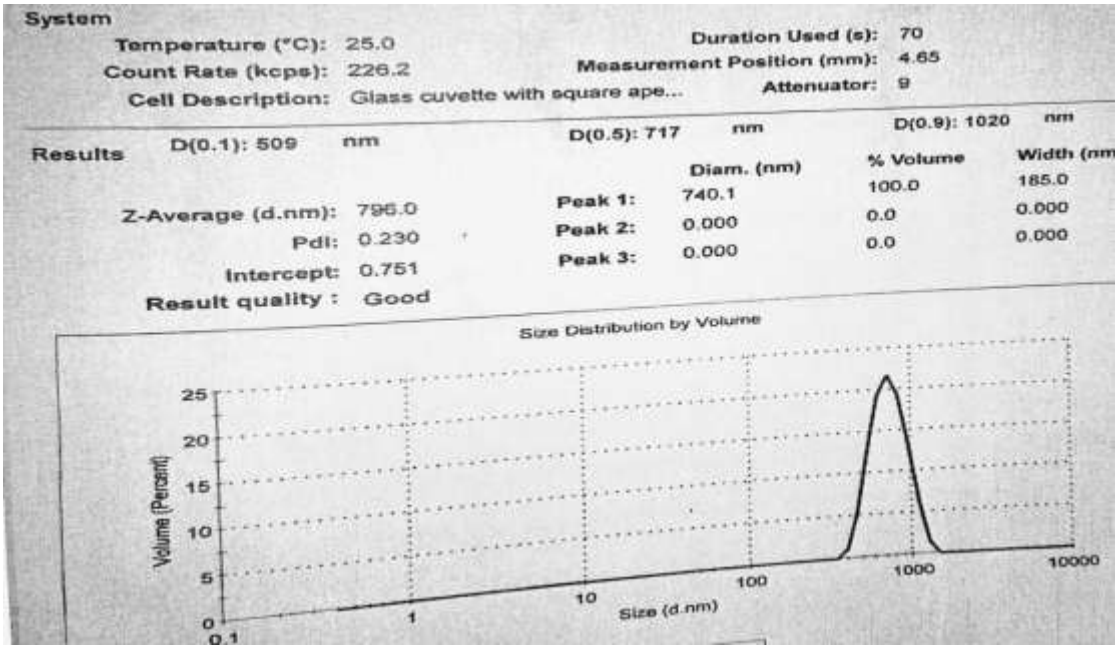

Figure 3: Particle size report of F3 formulation of Escitalopram loaded SLN by Hot Homogenization Method.

Determination of Zeta potential:

The zeta potential values indicates the stability of nanoparticles. It was determined by HORIBA SZ 100 Z nanoparticle analyser. And the best formulation F3 showed the zeta potential value of -29.4 mV. Thus it was found that the formulation was stable. (Figure 4).

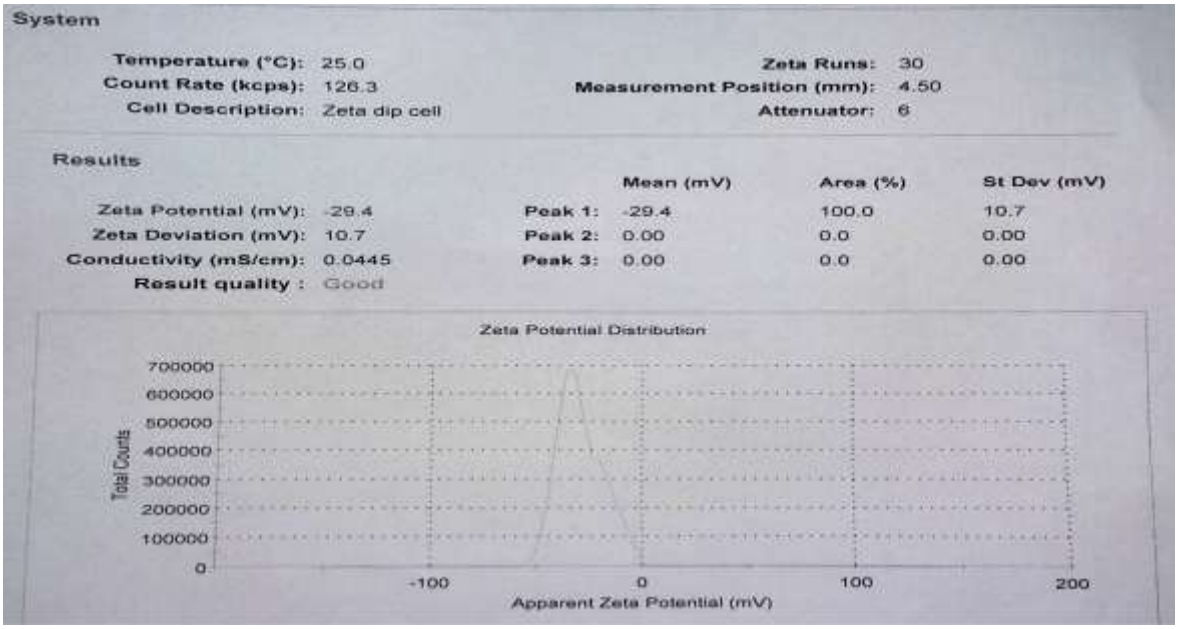

Figure 4: Zeta potential report of F3 formulation of Escitalopram loaded solid lipid nanoparticles by employing cutina as a lipid.

FTIR :

Fourier transform infrared spectroscopy spectra of Escitalopram drug, Cutina without drug and escitalopram loaded nanoparticles were scanned. The samples were prepared by potassium bromide disc method and scanned for absorbance from the range of 400 – 4000 cm-1. (Figure 5,6,7)

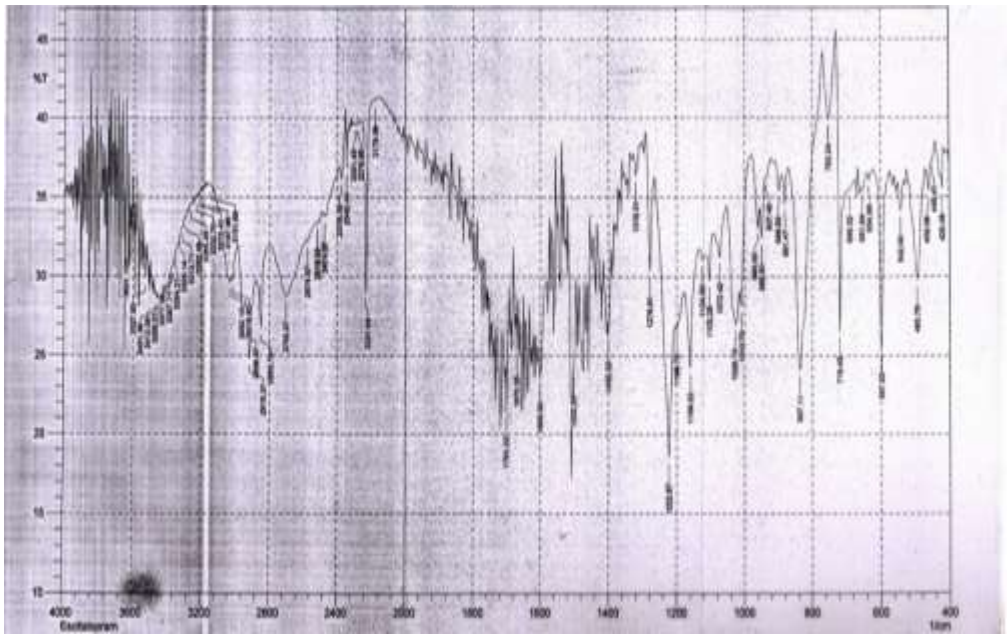

Figure 5: FTIR spectra of Escitalopram

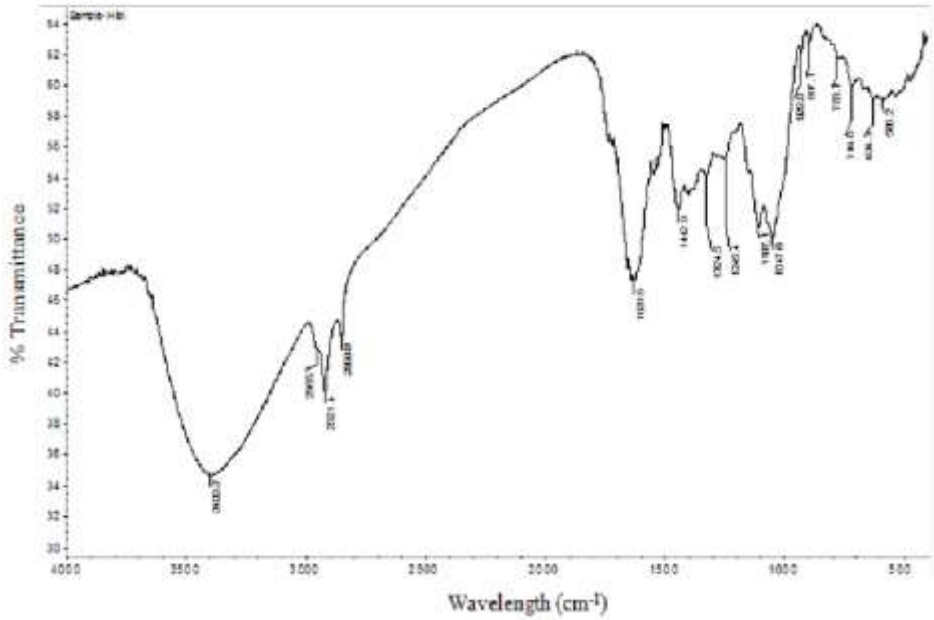

Figure 6: FTIR Spectra of Cutina

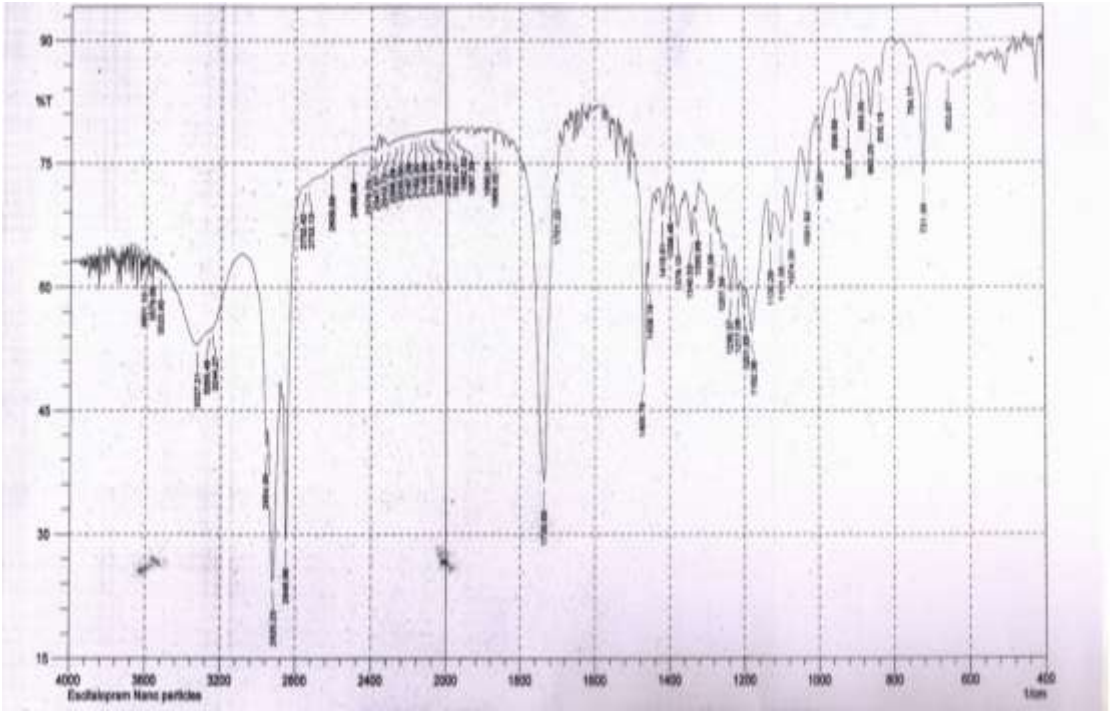

Figure 7: FTIR spectra of the Escitalopram loaded Nanoparticles.

The FTIR spectra shown by the Ecitalopram pure drug and Escitalopram loaded Nanoparticles are compared and found that the C ≡ C is present in the wavelength region 2374nm and C=O groups in the 1650nm and OH group in wavelength region of 3200nm. It also shows all the prominent peaks that are present in the escitalopram loaded nanoparticles are quite similar with the drug and lipid suggesting that less possibility of incompatability between drug and excipients.

In-vitro Drug release studies:

In-vitro drug release studies were carried by dissolution apparatus using USP Ⅱ (Paddle). Samples were collected at every one hour interval upto 24hrs. Medium used for dissolution was pH 7.2 at 37±2℃ and wavelength at 238nm. (Table 6) In-vitro drug release studies were performed for a period for a period for 24hrs. the percentage drug release for prepared formulation was calculated. The drug release of prepared formulation was found in the range 39.2% to 82.4%. Among all the formulations F3 was found to have highest drug release of 82.4 % in 24hrs. (Figure 8).

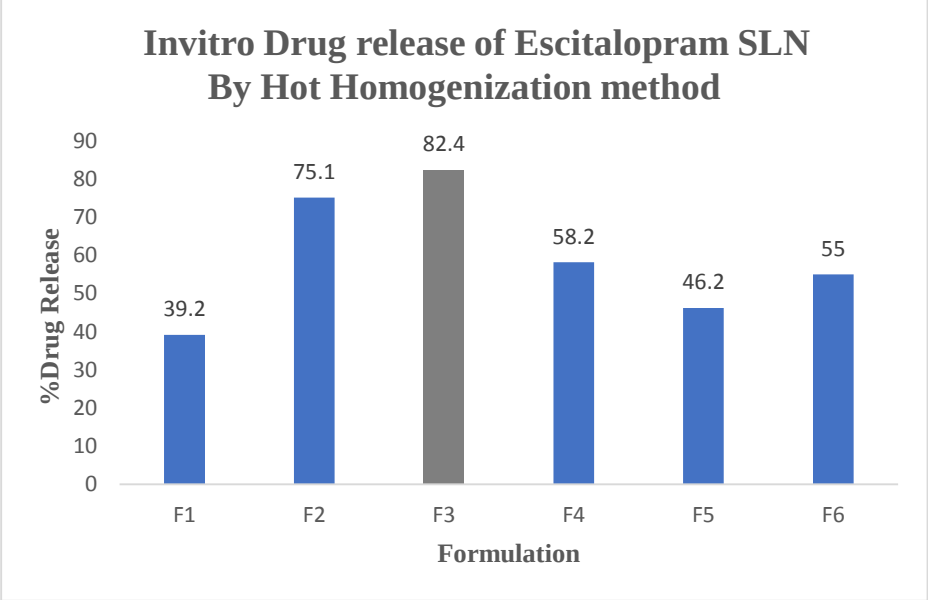

Figure 8: In-vitro release of Prepared Formulations of Escitalopram loaded Solid Lipid Nanoparticles by Employing Cutina as a lipid.

Table 3: Entrapment Efficiency of Escitalopram loaded nanoparticles with different lipid to surfactant ratio by Employing Cutina as a lipid.

Formulation	Entrapment Efficiency (%)
F1	56.7
F2	72.0
F3	86.1
F4	64.3
F5	59.8
F6	47.6

Stability studies:

The F3 formulation was kept for stability studies for 3 months at room temperature and Refrigerated temperatur**e (**Table 7), **(**Figure 9) then (Table 8), (figure 10) The finalized formulation based on entrapment efficiency and drug release of the SLN which were kept for stability studies at room temperature and refrigerated conditions and found that the formulation stored at refrigerated temperature was more compared to the room temperature. This was may be due to more drug expulsion from lipid matrices at higher temperature.

Table 6: In-vitro drug release of Escitalopram loaded nanoparticles by Employing Cutina as a Lipid.

Time (hrs)	F1 (Mean±SD) (n=3)	F2 (Mean±SD) (n=3)	F3 (Mean±SD) (n=3)	F4 (mean±SD) (n=3)	F5 (mean ± SD)(n=3)	F6 (mean±SD) (n=3)
1	6.21±0.27	15.7±0.51	15.7±0.10	19.2±0.35	4.3±0.45	16.2±0.30
2	9.86±0.24	22.8±0.30	18.1±0.18	23.2±0.51	5.86±0.45	18.2±0.35
3	11.3±0.55	26.6±0.55	22.7±0.56	26.5±0.53	9.03±0.56	24.8±0.61
4	14.7±0.35	35.7±0.40	36.3±0.32	26.0±0.20	9.4±0.45	35.3±0.35
5	19.2±0.30	44.3±0.55	45.8±0.15	27.1±0.86	19.4±0.40	42.3±0.58
6	20.7±0.73	64.2±0.65	59.7±0.45	47.3±0.90	23.6±0.25	44.0±0.62
7	29.7±0.40	70.1±0.45	74.8±0.45	47.8±0.90	31.8±0.40	48.3±0.75
24	39.2±0.85	75.1±2.05	82.4±0.40	58.2±0.40	46.2±0.81	55.0±0.62

Table 7 : Stability studies of Escitalopram Nanoparticles at Room Temperature

F3	0 Month	1 month	2 month	3 month
Drug content	90.7%	89.5%	89.2%	89.0%
Entrapment efficiency	86.1%	86.1%	85.8%	85.3 %
% Drug release(24hrs)	82.4%	82.2%	81.9%	81.5%

Table 8: Stability studies of prepared Nanoparticles at Refrigerated Temperature

F3	0 Month	1 month	2 month	3 Month
Drug content	90.7%	91.5%	92.7%	93.3%
Entrapment efficiency	86.1%	87.2%	88.6%	89.1%
% Drug release	82.4%	82.9%	83.5%	84.3%

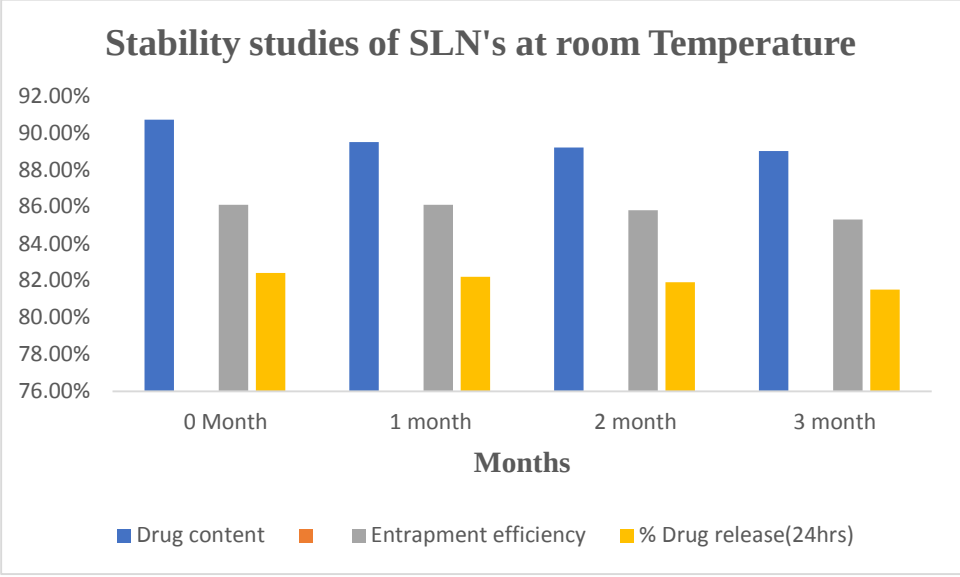

Table 9 : Stability study of best formulation F3(% Entrapment Efficiency, Drug content and % Drug release at room temperature) by employing Cutina as lipid.

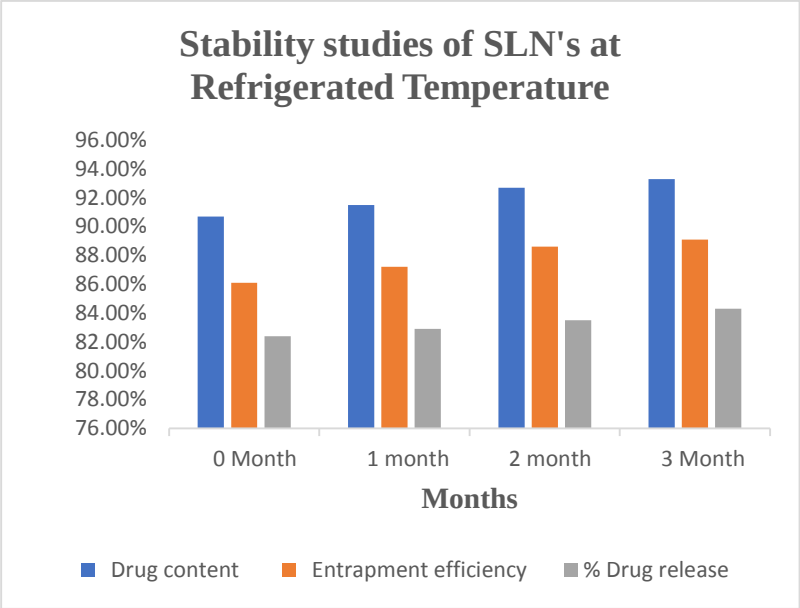

Figure 10: Stability studies of Escitalopram Solid Lipid Nanoparticles at Room Temperature by employing Cutina as lipid

CONCLUSION:

In the present study Escitalopram SLNs were prepared by Hot Homogenization method by employing cutina as a lipid.The Drug content and Entrapment Efficiency are dependend on the concentration of the lipid that is used in the formulation. Among the the formulation F3 formulation (0.3mg surfactant) show better Drug content(90.7%), Entrapment efficiency(86.1 %) and In vitro Drug release(82.4 %), Particle size of 796nm with zeta potential of -29.4 mV. It was observed that this preparation was found to be cost effective and can be scaled up when compared with other preparation methods.

ACKNOWLEDGEMENT

The authors thank M. SUMAKANTH principal of RBVRR Women's college of pharmacy, for providing required facilities to carry out this research work.

REFERENCES:

1. Kashanian S, Azandaryani AH, Derakhshandeh K. New surface-modified solid lipid nanoparticles using N-glutaryl phosphatidylethanolamine as the outer shell. Int J Nanomedicine. 2011;(6):2393–2401.
2. Baby B, Harsha NS, Nano Composix, Nano Composix's Guide to Dynamic Light Scattering Measurement and Analysis. NanoComposix, San Diego, Calif, USA; 2012;1(1)
3. Jayaveera KN, Abraham A. Formulation and Evaluation of Levofloxacin Nanoparticles by Ionic Gelation Method. J. Pharmacy and Pharmaceutical Sciences, 2012; 1(1):34-36.

4. Verma VK, Ram A. Preparation, Characterization and in vitro release of Piroxicam-loaded Solid Lipid Nanoparticles. Int. J. Pharmaceutical Sciences and Nanotechnology, 2010; (3):234-242.
5. Sandhiya Jatwani, Avtar chand Rana, Gurpreet singh and Geeta Aggarwal, "An overview on solubility enhancement techniques for poorly soluble drugs and solid dispersion as an eminent strategic approach" International journal of Pharmaceutical Sciences and research, 2012; 3(4): 942-956.
6. S. Mukherjee, S. Ray and R. S Thakur, "Solid lipid nanoparticles: A Modern Formulation Approach in Drug Delivery System" Indian journal of Pharm Sci., 2009; 71(4): 349-358.