FORMULATION AND CHARACTERIZATION OF SOLID LIPID NANOPARTICLES LOADED WITH RISPERIDONE

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ABSTRACT

Nanotechnology is the science of matter and material which deals with the particle size ranging from 1-1000nm. The solid lipid nanoparticles are novel submicron colloidal carriers which ranges from 50-1000nm which contains physiological lipid, dispersed in water or aqueous surfactant solution. In the current research, studies were carried out to design and characterize solid lipid nanoparticulate delivery systems to enhance the therapeutic efficacy of Risperidone and minimized adverse effects. Risperidone is used in the treatment of Schizophrenia. Risperidone SLNs were prepared by Solvent Injection Method by the use of different lipids, solvents, polymers and distilled water as aqueous phase. The resultant solid lipid nanoparticles of Risperidone were characterized by drug content, encapsulation efficiency, *in-vitro* drug release, particle size, zeta potential, Fourier transform infrared spectroscopy (FTIR) and Scanning electron microscopy (SEM). SEM photographs of formulations F3 revealed that nanoparticles were discrete particles with smooth, rigid surface. The drug content was found to be in the range of 30.22±0.24 to 45.24±0.42 and the encapsulation efficiency in the range of 48.50±0.62 to 77.73±0.54. The % cumulative of the formulation ranged from 19.91% to 96.01%. FT-IR study confirmed the drug-lipid compatibility. Best formulation (F3) showed a maximum drug release of 96% in 9 hrs, particle size of 348.6 nm and zeta potential of - 0.898mV. Risperidone solid lipid nanoparticles were best suited with the glyceryl monostearate as a lipid and acetone was used as a solvent. Structural characterization of SLNs by Fourier transform infrared spectroscopy (FTIR) analysis revealed that, there was no interaction of risperidone with lipid and was well dispersed in the lipid matrix without any crystallization.

KEYWORDS

Solid lipid nanoparticles, SLNs, Colloidal carriers and Solvent injection method.

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INTRODUCTION

During last two decades, considerable attention has been given to the development of Novel Drug Delivery System (NDDS). The rational for novel controlled drug delivery is to alter the pharmacokinetics and pharmacodynamics of a drug substance in order to improve the therapeutic efficacy and safety through the use of novel drug delivery system[1]. Nanotechnology is a newer

development technology expected to bring revolutionary changes in the field of life sciences. Nanotechnology, as defined by the National Nanotechnology Initiative (NNI), is the study and use of structures roughly in the size range of 1-100nm. Nanotechnology is the science of matter and material that deal with the particle size in nanometers. Nanoparticles are those in which the active principles are dissolved, entrapped, and or to which the active principle is adsorbed. These are small scale colloidal particles that are made of non biodegradable and biodegradable polymers and their diameter is about 200nm[2]. Nanoparticles offer several advantages in drug delivery owing to their small particle size, large surface area and the capacity of changing their surface properties. In general, nanoparticles can be used to target the delivery of drugs, to improve its bioavailability, to sustain its effect, to solubilize it for intravascular delivery and to improve its stability against enzymatic degradation[3]. The shortage of safe polymers and their high cost have limited the wide spread application of nanoparticles to clinical medicine. These lipid nanoparticles are known as solid lipid nanoparticles (SLN), which are attracting wide attention of formulator's world-wide[4]. Risperidone is a benzisoxazole derivative atypical antipsychotic indicated for treatment of schizophrenia, bipolar mania, and irritability associated with autistic disorder. Among the second-generation antipsychotics, risperidone conforms the least to the typicality criteria. According to its molecular characteristics, Risperidone belongs to the BCS class II, which means that it has poor water solubility and high intestinal permeability[5-7].

MATERIAL AND METHODS
Materials
Risperidone was obtained from Yarrow chem products, Mumbai. PVA (Poly vinyl chloride) was obtained from Yarrow chem. Products, Mumbai. Glyceryl monostearate was obtained from Loba Chemie. All the other reagents and chemicals used are of analytical grade.

Characterization of risperidone solid lipid nanoparticle prepared by solvent injection method:
Percentage yield[11]
Solid lipid nanoparticles were dried, collected and weighed to determine percentage yield (PY) from the following formula:
Percentage yield = (Practical yield)/ (Theoretical yield) × 100
Particle Size and Zeta Potential
Value of Particle size and Zeta Potential prepared Solid lipid nanoparticles determined by using Malvern Zetasizer.
Zeta potential[12,13]
The Zeta-potential and particle size of drug loaded solid lipid nanoparticles was measured by Zeta sizer (Malvern Zeta sizer). To determine the zeta potential and particle size nanoparticles samples were diluted with water (0.1ml) and placed in electrophoretic cell where an electrical field of 15.2 V/cm was applied.
Surface morphology study[14]
Scanning electron microscopy (SEM) of drug loaded solid lipid Nanoparticle was performed to examine the surface morphology. The solid lipid nanoparticles were mounted on metal stubs and the stub was then coated with conductive gold with sputter coater attached to the instrument. The photographs were taken using a Jeol scanning electron microscope under magnification of 20kv×25000.
Drug content and Entrapment efficiency[15]
Solid lipid Nanoparticles equivalent to 100mg of risperidone were crushed in a glass mortar and the powdered nanoparticles were suspended and diluted suitably with 7.4 pH Phosphate buffer and analyzed for drug content. The drug content was analyzed by measuring absorbance in UV spectrophotometer at 280nm using 7.4 pH Phosphate buffer as blank.
***In-Vitro* Drug Release study**[16-18]
In-vitro dissolution study on solid lipid nanoparticles (equivalent to 100mg) filled in capsules were carried out using dissolution test apparatus in pH 7.4 buffer solution at 37±0.5°C with 75rpm rotating speed. Samples of 5ml were

withdrawn at regular time interval of 1hour for 12hours. To maintain the sink condition an equal amount of dissolution medium was added. Drug content from sample was analyzed using UV-spectrophotometer at 280nm. All measurements were done in triplicate from three independent samples.

Stability studies[19]

Stability studies of prepared solid lipid nanoparticles determined by storing optimized formulation at 30°C ± 2°C in stability chamber for 90 days. The samples were analyzed at interval of 0, 1, 2, and 3 months for their drug content, drug release rate.

RESULTS AND DISCUSSION

Determination of λmax

The spectrum of Risperidone (10µg/ml) in 7.4 pH phosphate buffer showed the peak at 280nm.

Calibration Curve for Risperidone

The absorbance value remained linear and obeyed Beer's Lamberts Law in the range of 10 -50µg/ml with the R^2 value of 0.998.

The FT-IR spectra showed that all the peaks of pure drug were also visible in their drug and physical mixtures of excipients. Thus, it confirmed that combination of pure drug and the used polymers in the formulations are suitable for designing a formulation intended for its desired therapeutic purpose.

Evaluation of Risperidone solid lipid nanoparticles

Particle Size

The particle size and Polydispersity index of prepared Solid lipid nanoparticles determined by using Malvern Zetasizer.

Shape and Surface morphology

The shape and surface morphology of the prepared nanoparticles were observed by scanning electron microscopy.

Drug content and Encapsulation efficiency

The drug content was found to be in the range of 30.22±0.24mg to 45.24±0.42mg and Entrapment efficiency in the range of 48.50±0.62% to 77.73±0.54%. Entrapment efficiency was found to increase with increase in polymer concentration due to increase in viscosity. *In vitro* drug release.

All the formulations released more than 90% of the drug at the end of 9 hours in pH 7.4 buffer.

Stability Studies

The results of the stability studies indicated that the formulation (F3) did not show any changes in the drug content during the stability study period. The percentage cumulative drug release after 60 days study showed no significant change.

Preformulation studies of Risperidone

Table No.1: Preformulation studies of Risperidone

S.No	Properties	Reported	Observed
1	Appearance	White Amorphous powder	White to off-white Amorphous powder
2	Odour	Odourless	Odourless
3	Melting point	170ºC	170ºC - 172 ºC
4	Identification (UV)	280nm	280nm

Calibration Curve for Risperidone

Table No.2: Calibration curve of Risperidone

S.No	Concentration (µg/ml)	Absorbance
1	0	0
2	10	0.1462 ± 0.017
3	20	0.2651 ± 0.015
4	30	0.3845 ± 0.045
5	40	0.5292 ± 0.028
6	50	0.6791 ± 0.012

Table No.3: Comparision of FT-IR spectra of Risperidone and various excipients used

S.No	Functional Group	Reported Frequency (cm^{-1})	Observed Frequency (cm^{-1})
1	-OH Stretching	2939	2941
2	-CH Stretching	2804	2800
3	C=C Stretching	1642	1645
4	-CH-O-CH Stretching	1128	1124
5	-CH$_2$ Scissoring	1531	1533
6	-OH Bending	1349	1348
7	-C=O	1651	1645
8	-C-F Stretching	1130	1124
9	-C-N (Amines)	1060	1065

Percentage Yield

Table No.4: Percentage yield of Risperidone Solid lipid nanoparticles

S.No	Formulation Code	Percentage Yield (% w/w)
1	F1	84.96
2	F2	86.33
3	F3	88.23
4	F4	71.54
5	F5	70.21
6	F6	75.20
7	F7	80.23
8	F8	82.41
9	F9	84.22

Table No.5: Particle size and Polydispersity index of prepared Solid lipid nanoparticles

S.No	Formulation Code	Particle size (nm)	Polydispersity index
1	F1	311.7	0.323
2	F2	353.8	0.228
3	F3	278.6	0.342
4	F4	315.7	0.354
5	F5	309.5	0.282
6	F6	324.6	0.312
7	F7	348.6	0.286
8	F8	285.6	0.237
9	F9	305.4	0.334

Table No.6: Drug content and Encapsulation efficiency of the prepared solid lipid nanoparticles

S.No	Formulation code	Drug content (mg)	Encapsulation efficiency (%)
1	F1	35.65±0.39	55.00±0.19
2	F2	44.15±0.75	62.40±0.65
3	F3	45.24±0.42	77.73±0.54
4	F4	33.45±0.34	71.27±0.15
5	F5	34.33±0.45	63.41±0.18
6	F6	40.55±0.52	53.33±0.13
7	F7	30.22±0.24	48.50±0.62
8	F8	32.66±0.44	51.08±0.55
9	F9	35.14±0.65	63.41±0.40

Table No.7: *In vitro* drug release data of all formulations (F1-F9)

Time (in hours)	% Cumulative Drug Release								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
1	19.183	17.522	9.912	18.798	19.233	10.158	20.767	17.536	11.575
2	29.956	28.680	20.226	29.747	31.057	22.356	30.752	29.052	22.348
3	40.93	39.931	33.524	39.397	43.331	34.961	42.049	41.113	35.365
4	51.506	50.650	45.449	50.369	55.619	48.804	54.783	53.394	47.585
5	63.125	61.381	56.397	60.260	66.609	59.821	65.441	64.443	58.803
6	74.137	72.930	67.357	71.255	76.737	70.850	76.323	74.055	69.224
7	83.510	81.873	77.734	80.951	84.472	81.485	87.853	82.018	79.495
8	89.176	88.006	85.151	88.909	90.029	87.259	91.129	90.197	86.624
9	94.849	93.542	96.001	93.160	94.564	92.228	90.105	94.029	91.813

Stability Studies

Table No.8: Drug content and *in vitro* drug release of risperidone solid lipid nanoparticles formulation (F3) after stability studies

| S.No	Time (Days)	Drug content (mg)	Cumulative drug release (%)
1	0	45.04	90.246
2	30	44.78	90.342
3	60	44.38	90.481

Methodology: Solvent Injection Method[8-10]
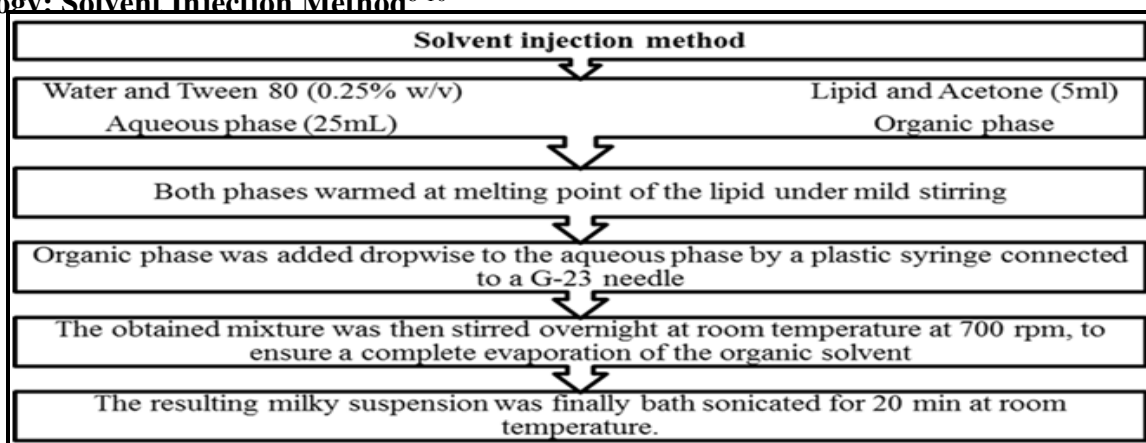
Figure No.1: Prepared Solid Lipid Nanoparticles Containing Risperidone

Batch Codes / Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
Risperidone (mg)	100	100	100	100	100	100	100	100	100
Glyceryl monostearate (mg)	100	200	300	--	--	--	--	--	--
Stearic Acid (mg)	--	--	--	100	200	300	--	--	--
Glceryl tripalmitate (mg)	--	--	--	--	--	--	100	200	300
Acetone (ml)	5	5	5	5	5	5	5	5	5
Distilled water	25	25	25	25	25	25	25	25	25
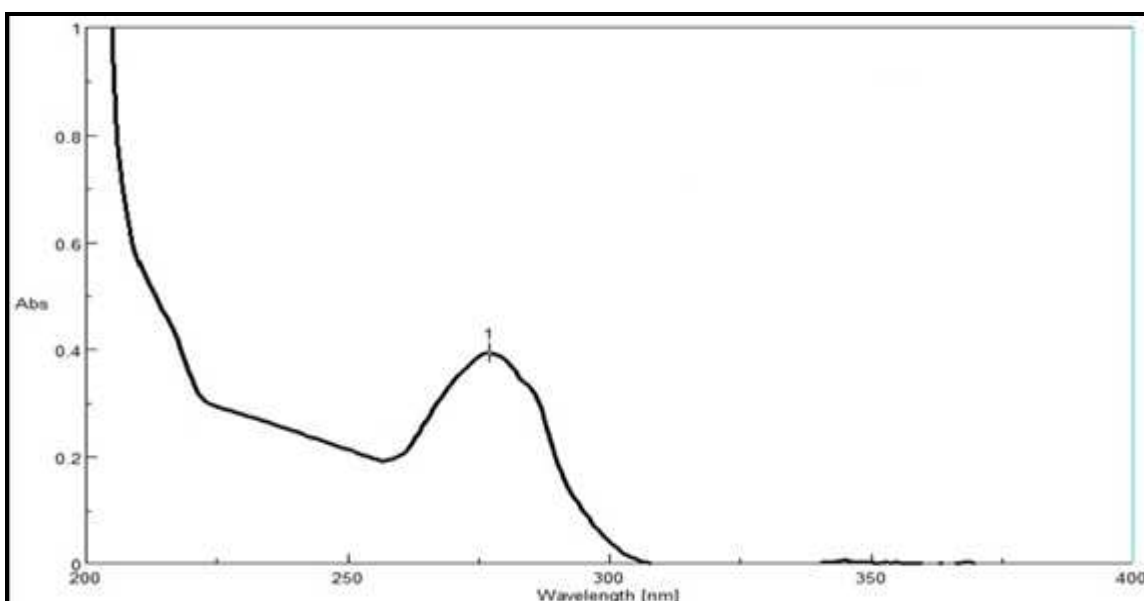
Figure No.2: UV-Spectra of Risperidone
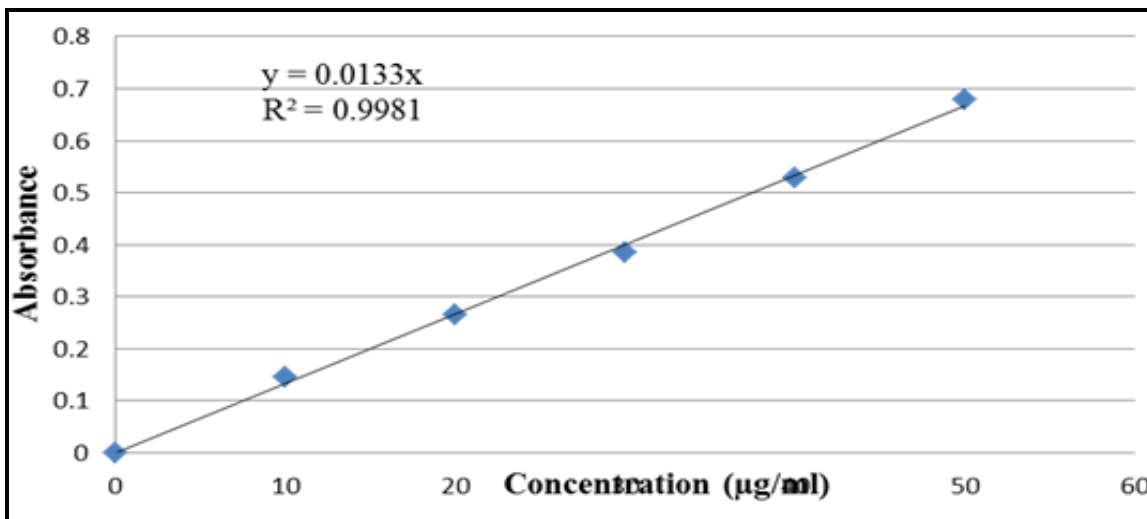
Figure No.3: Calibration curve of Risperidone

Drug Excipient Compatibility Study by FTIR
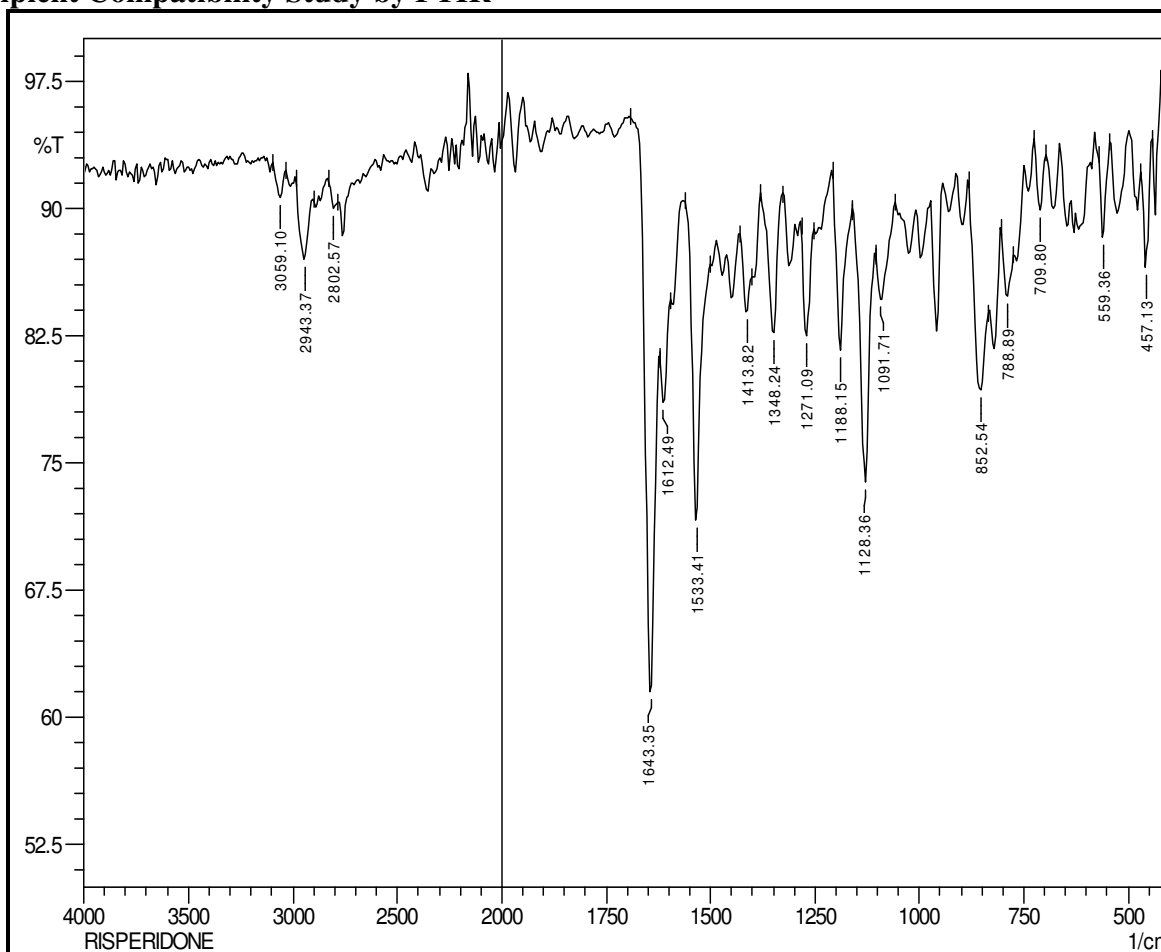
Figure No.4: FT-IR Spectra of Risperidone
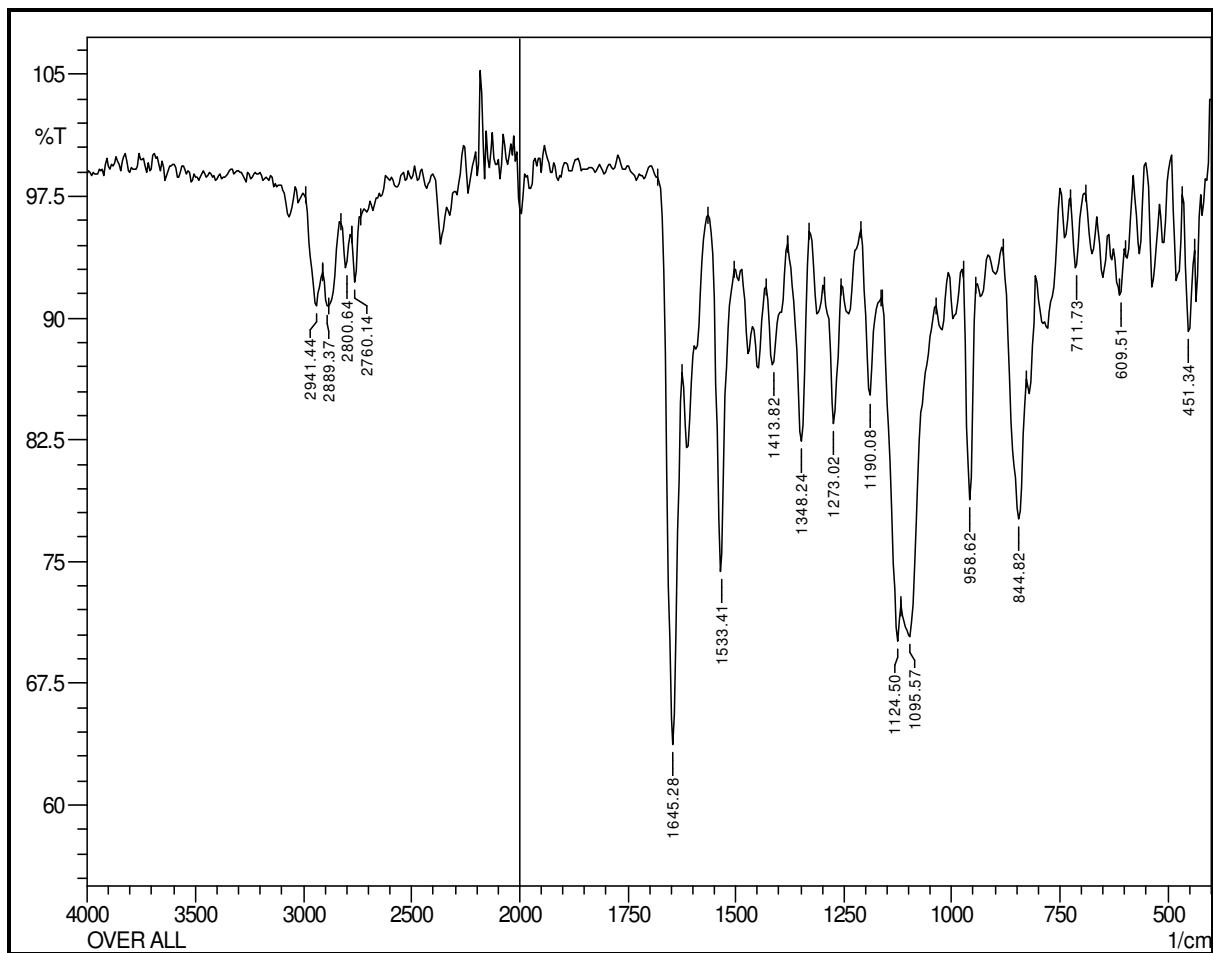
Figure No.5: FT-IR Spectra of Risperidone and other excipients used in the formulation

Particle Size and Zeta Potential
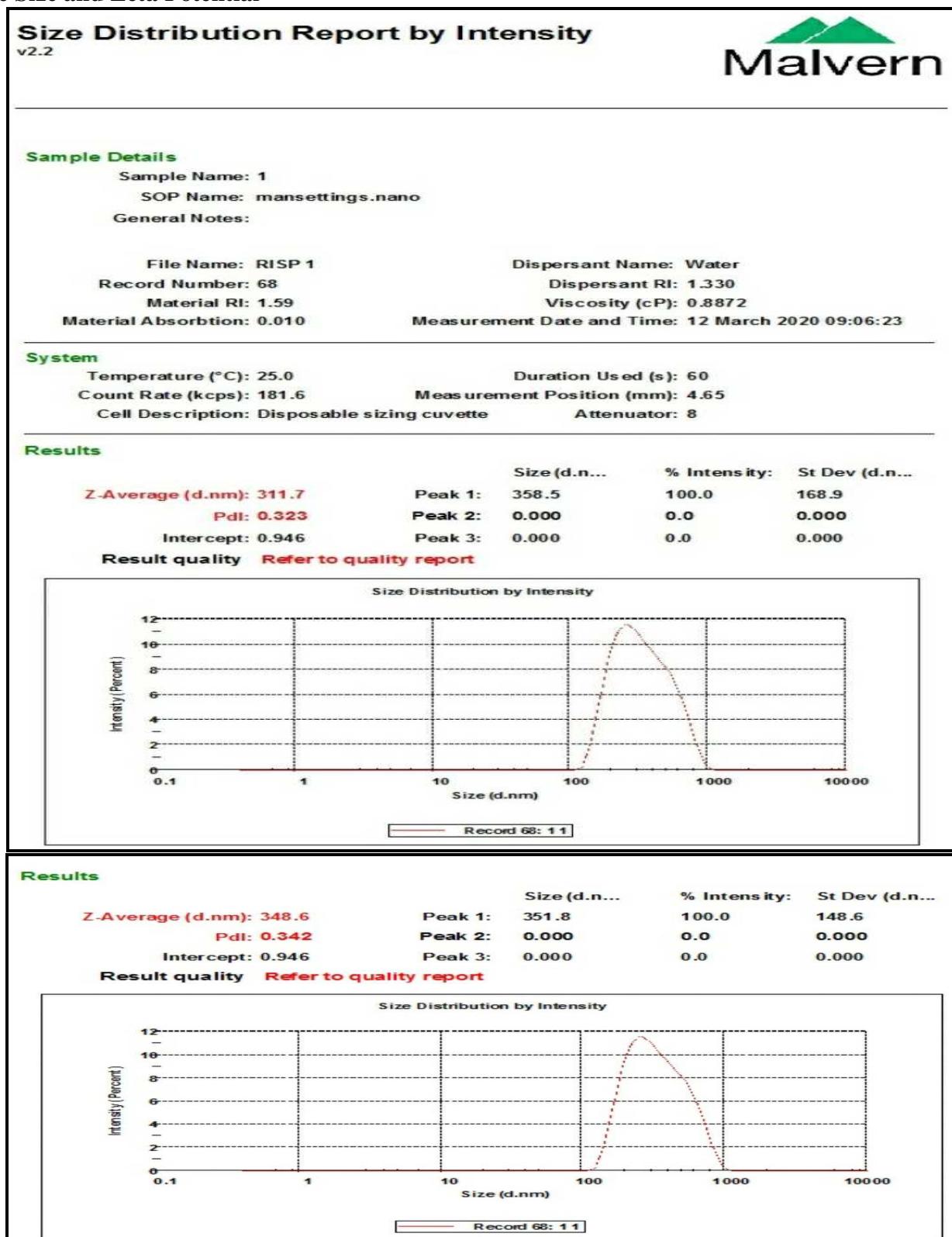
Figure No.6: Particle Size and Polydispersity Index of prepared Solid lipid nanoparticles (F3)
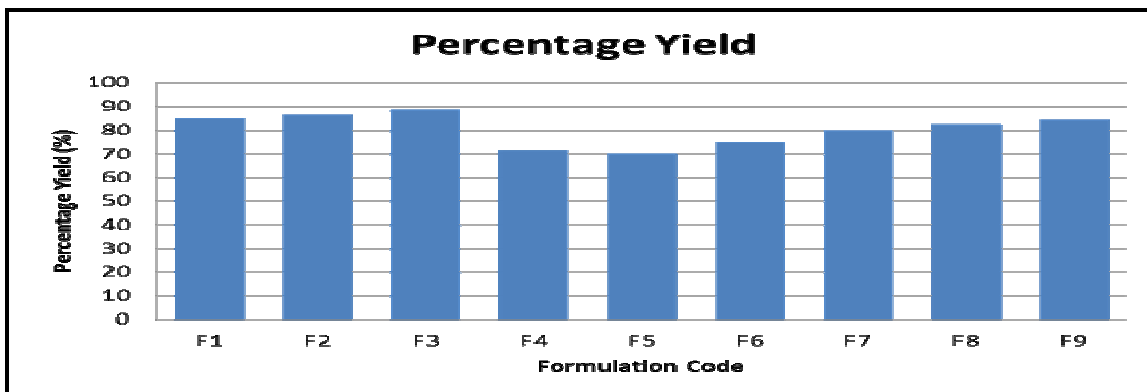
Figure No.7: Percentage yield of Risperidone Solid lipid nanoparticles
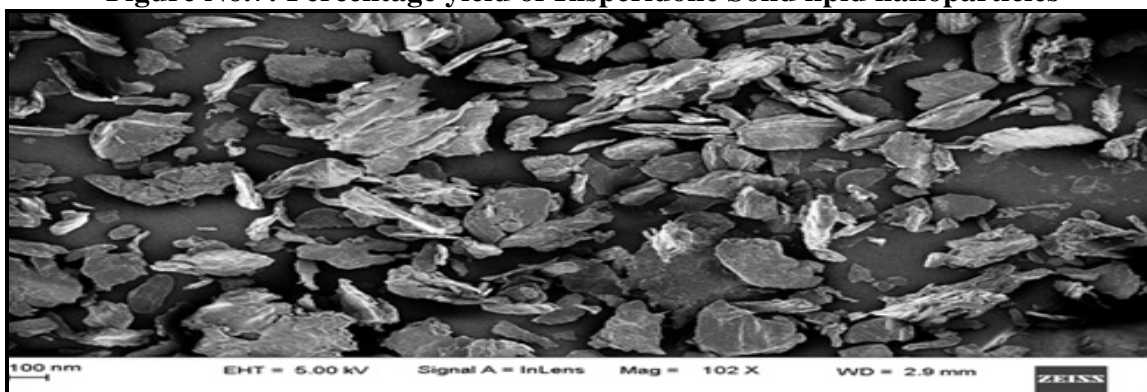
Figure No.8: SEM photographs of the prepared formulation (F3)
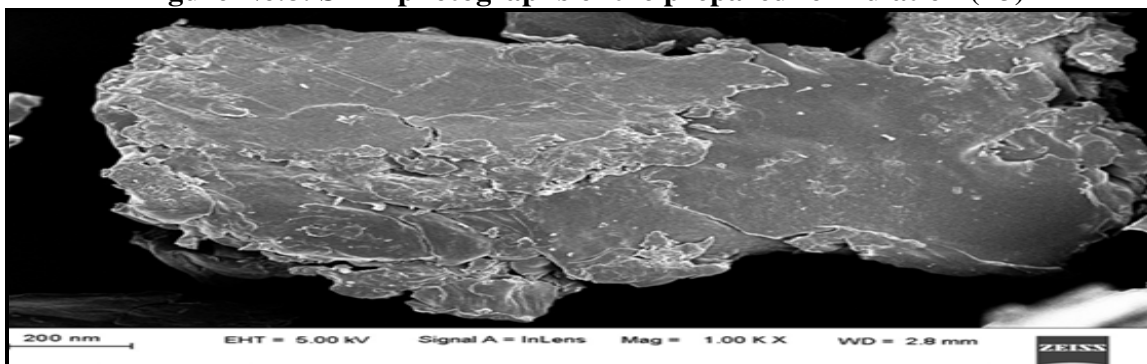
Figure No.9: SEM photographs of the prepared formulation (F6)
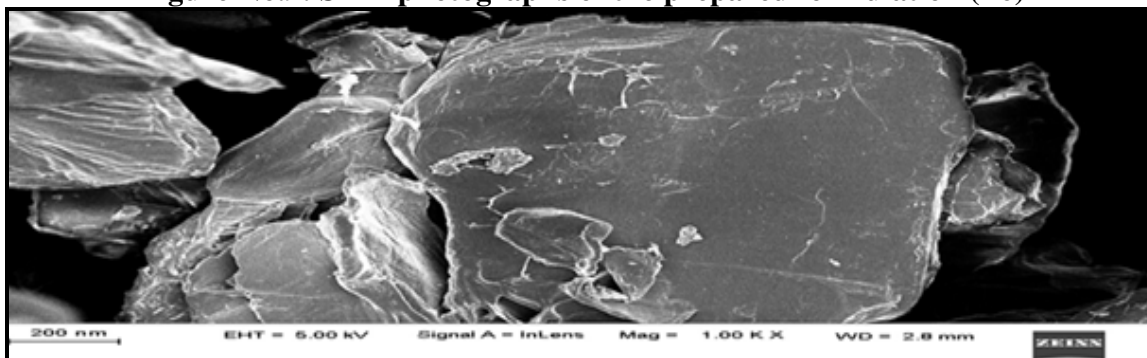
Figure No.10: SEM photographs of the prepared formulation (F9)
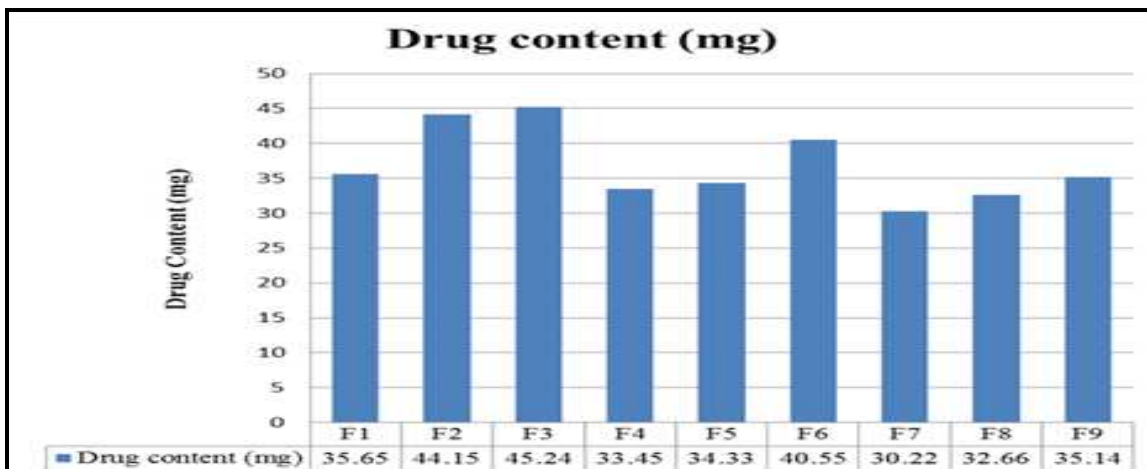
Figure No.11: Drug content of the prepared solid lipid nanoparticles

	F1	F2	F3	F4	F5	F6	F7	F8	F9
Drug content (mg)	35.65	44.15	45.24	33.45	34.33	40.55	30.22	32.66	35.14
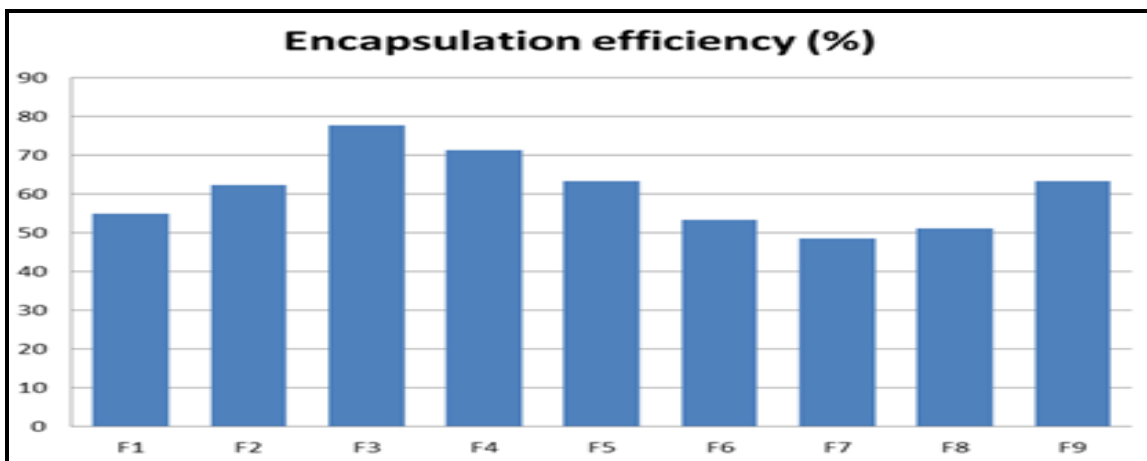
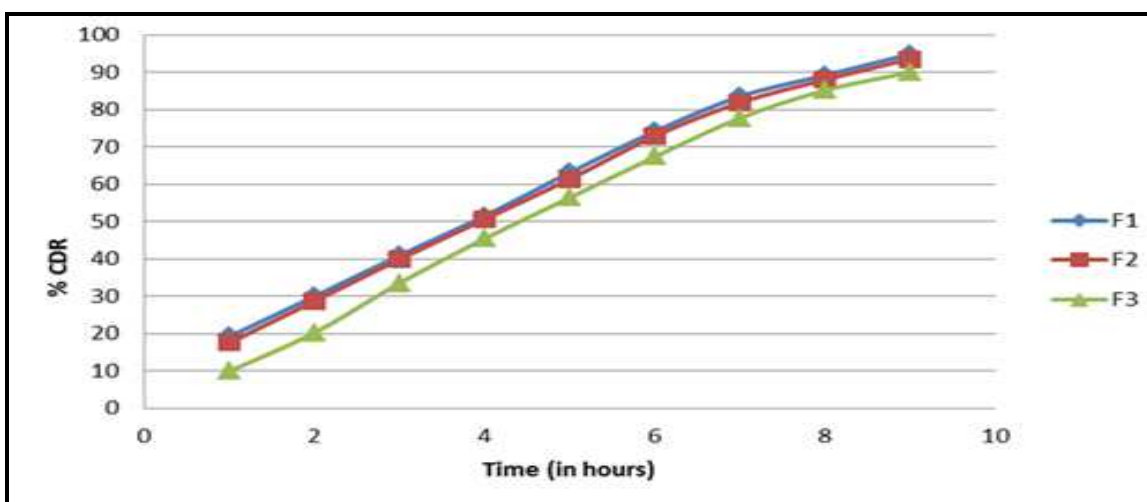**Figure No.12: Encapsulation efficiency of the prepared solid lipid nanoparticles**

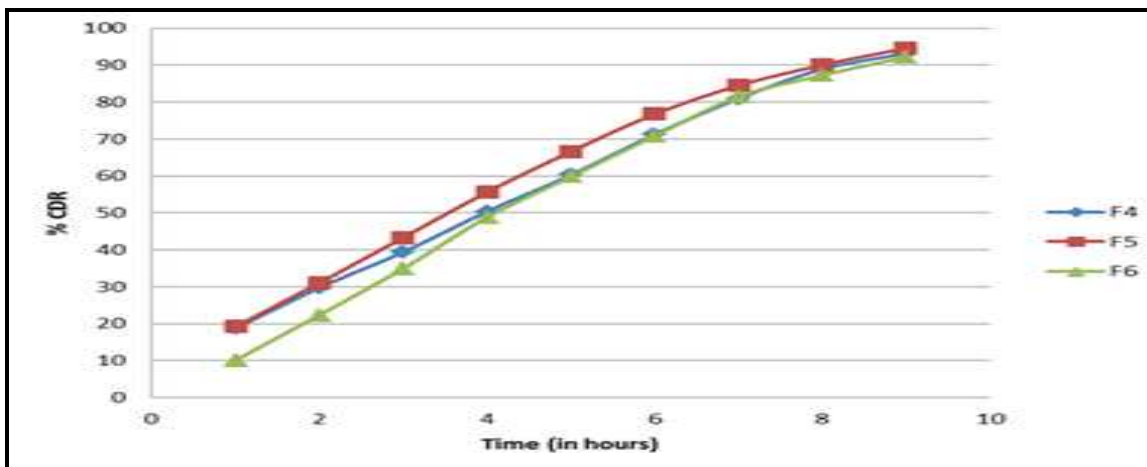**Figure No.13: Percentage CDR of prepared SLN formulation (F1, F2, F3)**

Figure No.14: Percentage CDR of prepared SLN formulation (F4, F5, F6)
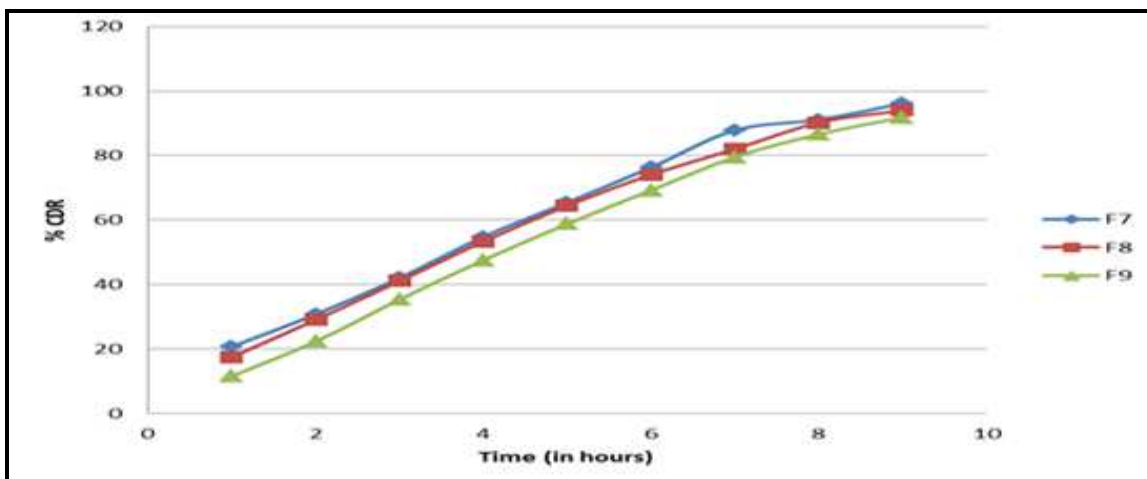

Figure No.15: Krosmayer - Peppas plot for prepared SLN formulation

CONCLUSION
The present study has been a satisfactory attempt to formulate Risperidone solid lipid nanoparticles using lipid system and polymer. From the reproducible results of the executed experiments, it can be concluded that: The IR spectra revealed that, there was no interaction between Risperidone and polymer, thus indicating the compatibility of Risperidone with the polymer used.

The Risperidone solid lipid nanoparticles were prepared by solvent injection method based on the emulsification of glyceryl monostearate (lipid system) and tween 80 (surfactant) mixtures in water.

The entrapment efficiency of the prepared solid lipid nanoparticles increased as the concentration of lipid increases. Formulation F3 was showed $77\pm0.3\%$ entrapment efficiency. The particle size determination of formulated risperidone solid lipid nanoparticles shows that the particles in all formulations were in nano range. From result F3 showed the smallest particle size that is 278.6nm.

In-vitro drug release study showed that the amount of the lipid increases the extent of drug dissolution also increases. Result of dissolution study contended the ability of solid lipid nanoparticles to control release rate of the drug Risperidone.

The cumulative drug release from formulation F3 showed the desired release rate, compared to other formulations showed desired drug release of about 90% after 9 hours.

Stability studies were carried out for the best formulation F3. The results of drug content and *in-vitro* drug release studies showed no significant changes indicating the formulation is stable.

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CONFLICT OF INTEREST

We declare that we have no conflict of interest.

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