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STUDIES ON EVALUATION OF EFFECT ON NOVEL EXCIPIENTS ON IN- VITRO DISSOLUTION, RHEOLOGY AND STABILITY OF OIL BASED SUSPENSION OF PROGESTERONE

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ABSTRACT

Progesterone is one of the most important hormone in our body and regulates numerous functions Extensive first pass metabolism of progesterone by liver limits its oral administration. Intramuscular administration improves absorption of progesterone but is uncomfortable, sincedaily injections may cause pain, inflammation and redness at the site of injection. There is need to find some other oily vehicle and suspending agent so that prepared formulation can have enhanced solubility, dissolution, bioavailability, stability and be devoid of allergenicity. Previous works in our laboratory have indicated that Moringa oil and Neusilin meets all the attributes as vehicle and suspending agent respectively. So there is need to compare performance of Moringa oil and Neusilin with other oils and novels excipients, so as to optimize best formula. Performance of each selected oil and novel excipient can be further explained by on the basis of molecular interactions using computational studies so as to establish solid background to practical findings.

KEYWORDS: Progesterone, Moringa oil, Neusilin, Sesame Oil, in- vitro dissolution.

INTRODUCTION

Chemistry Progesterone was independently discovered by four research groups. Willard Myron Allen co-discovered progesterone with his anatomy professor George Washington Corner at the university of Rochester Medical School in 1933 (LLC Books, 2010). Allen first determined its melting point, molecular weight, and partial molecular structure. He also gave it a name Progesterone (Pregn-4-ene-3, 20-dione) derived from progestational steroidal ketone (New World Encyclopedia). Progesterone contains four inter connected rings similar to other steroids. It is hydrophobic in nature and contains ketone, oxygenated functional group and two methyl branches.

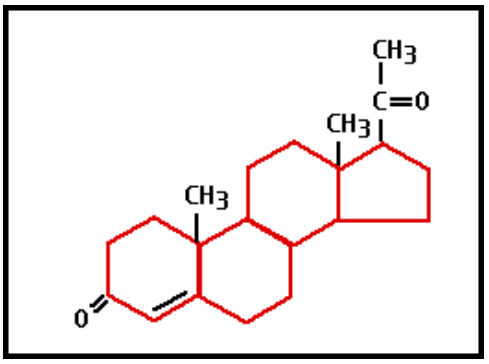

Figure No. 1.1: Structure of Progesterone.

Table No. 1.1: Physical and Chemical properties of progesterone.

Sr. No.	Parameter	Values
1	Molecular Weight	314.5
2	Specific Gravity	1.166 at 23^0 C
3	Melting Point	126^0 C - 131^0 C
4	Log Ko/w	3.87
5	Water Solubility	0.00881 g/L at 25^0 C
6	Vapor Pressure	1.3 × 10-6 mmHg at 25^0 C

Table No. 1.2: Dosage forms of Progesterone.

Dosage Form	Route of Administration
Capsule	Oral
Liquid	Intramuscular
Gel & Pessaries	Intravaginal

- Its poor aqueous solubility accounts for its poor bioavailability
- It undergoes extensive first pass hepatic metabolism which limits its administration byoral route.
- Intramuscular administration of progesterone is associated with pain, swelling, rashes etc, at the site of injection
- Oil based suspension of progesterone suffers issues likes allergenicity, poordissolution and stability.

Novel Excipients

Novel excipient is a new chemical entity, a new innovation that has not been used in any drug approved by regulatory authorities. They can be utilized for improving performance of oil based suspension of progesterone in terms of solubility, dissolution, bioavailability as well as stability in order to establish an efficacious formulation (Tachnical Newsletter, 2007).

Moringa oil

Moringa seed contains significant amount of oil that is commercially called as 'Ben oil' or 'Behen oil'. It is rich in palmitic, stearic, behenic and oleic acids. It is non drying oil, contains high amount of polyunsaturated triaglyceroles which makes it liquid at ambient temperature (Njoku et. al., 1997). The extracted oil is degummed to reduce its cloudiness and smoke point. Degumming oil changes its colour to pale and imparts characteristic odour.

Composition of moringa oil

- It is rich in monounsaturated fatty acids, especially oleic acid (75.39%), behenic acid (6.73%) and palmitic acid (6.04%).
- It has high levels of β- sitosterol, stigmasterol, campesterole, tocopherols (Anwar et.al., 2003).

Characteristics of moringa oil

1. Ben oil is sweet non- sticking, non- drying oil that resists rancidity.
2. Romans used moringa oil extensively in perfumery and egyptians used it to protect their skins from desert conditions.
3. Healing power of moringa oil were reported by ancient
4. Moringa oil has exceptional oxidative stability and has a shelf life upto 5 years (Delaveau et. al., 1980).

Uses of moringa oil

1. It is used in cosmetic and soaps.
2. Moringa oil is rich is behenic acid, Behenic acid is exceptionally moisturizing to skinand hair.
3. Moringa oil is highly valued by perfumers for its power of absorbing and retainingodours.
4. It possesses antifungal, purgative, antioxidant action (Fahey, 2005)

Computational prediction of effect of novel excipients on progesterone suspensions

Potential physical and chemical interactions between drug and excipients can affect the chemical nature, stability and bioavailability of drugs, and consequently, their safety and efficacy (Bharate, 2010).Computational modelling techniques can be applied to predict effect of excipients on performance of dosage form on the basis of molecular interactions taking place between drug and excipients which is function of their chemical structure.

MATERIAL AND EQUIPMENTS

Materials Used

Table No. 5.1: List of Drug, Excipient and Reagent.

Sr. No.	Material Name	Supplier
1	Progesterone	Puremed Biotech, Baddi.
2	Neusilin	Gangwal Chemicals, Mumbai
3	Fujicalin	Gangwal Chemicals, Mumbai
4	Syloid	Grace Division Pvt Ltd, Germany
5	Soya lecithin	Lipoid, Germany
6	Sunflower Oil	Bavdekar Ayurvedic Suppliers, Kolhapur
7	Sesame Oil	Bavdekar Ayurvedic Suppliers, Kolhapur
8	Moringa Oil	NA
9	n- Hexane	SD Fine Chemicals, Mumbai
10	Methanol	SD Fine Chemicals, Mumbai
11	2- propanol	SD Fine Chemicals, Mumbai
12	Iso-octane	SD Fine Chemicals, Mumbai
13	Sodium Lauryl Sulphate	West Coast Lab, Mumbai

Equipment's

Table No. 5.2: List of Equipments.

Sr. No.	Equipment	Company
1.	Digital Analytical Balance	Shimadzu BL 220-H
2.	Bath Sonicator	Spectralab UCB 70
3.	Hot Air Oven	Sai Enterprises Work, Mumbai
4.	Digital pH meter	MK-6, Systronics
5.	Centrifuge	Remi-R-8C
6.	Refractometer	Abbe Refractometer
7.	Orbital Shaker	Remi Instruments, Mumbai
8.	Rotary Evaporator	Heidolph G3, Germany
9.	UV- Visible Double BeamSpectrophotometer	Shimadzu, Jasco V630
10.	Viscometer	Brookfield
11.	Rheometer	Stress -Tech, Rheologica, Sweden
12.	Zeta Potential Analyzer	Malvern Zetasizer, Nano- ZS, UK
13.	Particle Size Analyzer	Malvern Zetasizer, Nano- ZS, UK
14.	Stability Chamber	Aditi Associates, Mumbai.
15.	Molecular docking software	V-life MDS
16.	Dissolution Apparatus	Electrolab TDT- 08L

RESULT AND DISCUSSION

Computational Studies

Computational studies were carried out to investigate molecular interactions taking place between drug, suspending agents and oils. Results for different batches of interaction studies are as follows,

BATCH I: INTERACTION BETWEEN EXCIPIENTS AND PROGESTERONE

Neusilin, Fujicalin, Syloid and Lecithin were computationally interacted with progesterone. Neusilin showed highest Van Der Waals and Hydrophobic interactions with progesterone. Lecithin was second most in terms interactions. Fujicalin and Syloid showed only Van der waals interaction with progesterone. Fujicalin forms on hydrogen bond with progesterone in contrast to other excipients.

Table No. 7. 1: Excipient- Progesterone Interactions.

Excipient	H- Bonding Score	VDW Score	Hydrophobic Interaction Score
Neusilin	NA	293	90
Lecithin	NA	133	19
Fujicalin	1	46	NA
Syloid	NA	19	NA

Neusilin is chemically Magnesium aluminometasilicate, it has tetrahedron or octahedron of aluminium, tetrahedron of magnesium and octahedron of Si, these atoms randomly arranged to form complex three dimensional network which could contribute to Van der waals and hydrophobic interactions between Neusilin and progesterone.

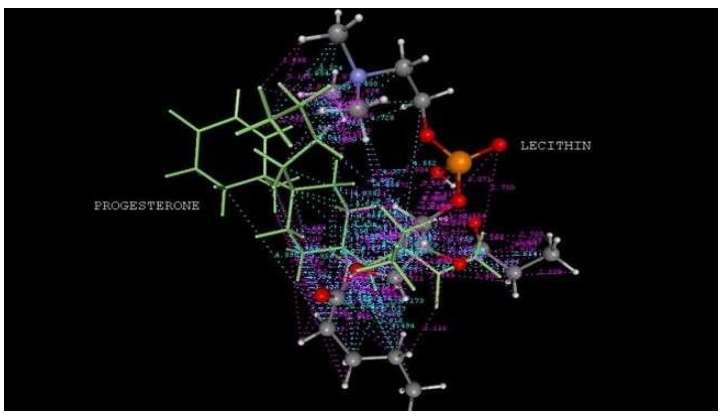

Figure No. 7.2: Lecithin - Progesterone Interactions.

BATCH II: INTERACTIONS BETWEEN OILS AND PROGESTERONE

Virtual interactions among drug and oils were investigated by computationally interacting fatty acids of Moringa oil, Sesame oil and sunflower oil with progesterone. It was found that Moringa oil shows more van der waals and hydrophobic interactions with progesterone than sesame oil and sunflower oil.

Table No. 7.2: Interactions between Moringa oil and Progesterone.

Fatty Acid	H- Bond Score	VDW Score	Hydrophobic Interaction Score
Oleic Acid	NA	132	100
Behenic Acid	NA	221	182
Palmitic Acid	NA	94	62

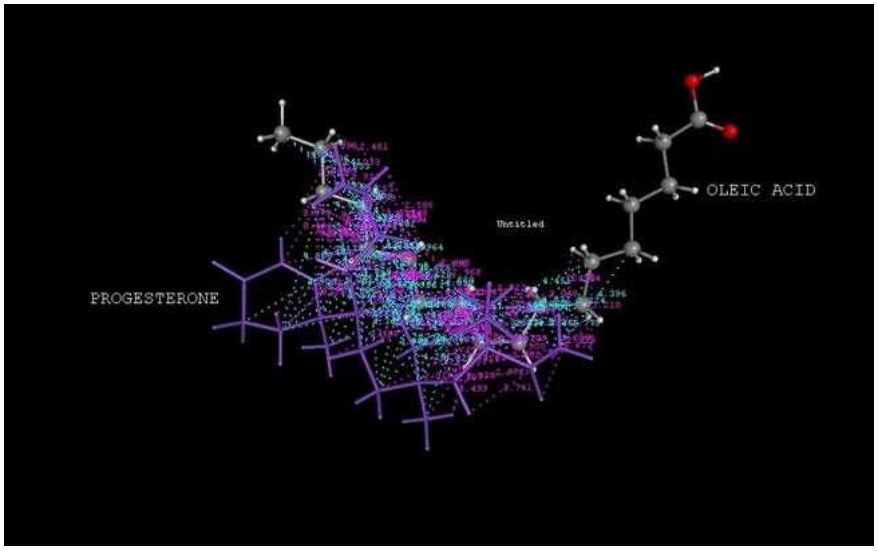

Figure No. 7. 6: Interaction between Oleic acid – Progesterone.

Table No. 7. 5: Net interactions between oils and progesterone.

OIL	H- Bonding Score	VDW Score	Hydrophobic Interaction Score
Moringa Oil	NA	447	344
Sesame Oil	NA	281	198
Sunflower Oil	NA	187	136

BATCH III: INTERACTION BETWEEN OILS AND EXCIPIENTS

Interaction studies between fatty acids of oils and excipients showed that, moringa oil shows highest interactions with selected excipients. Neusilin and Lecithin undergo Van der Waals and hydrophobic interactions with moringa oil to the greater extent than with sesame oil and sunflower oil.

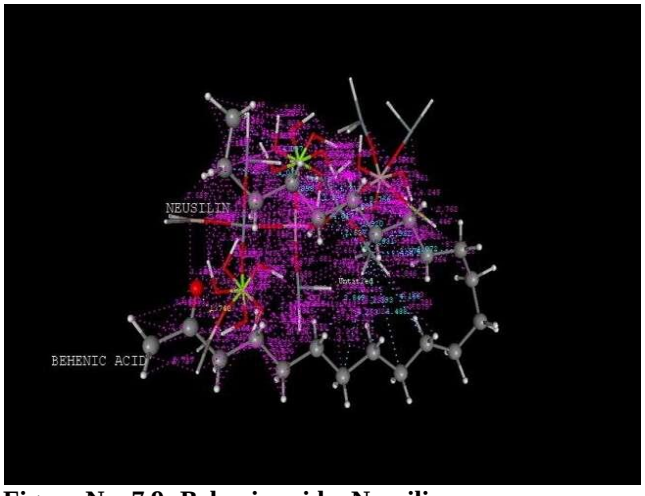

Figure No. 7.9: Behenic acid – Neusilin.

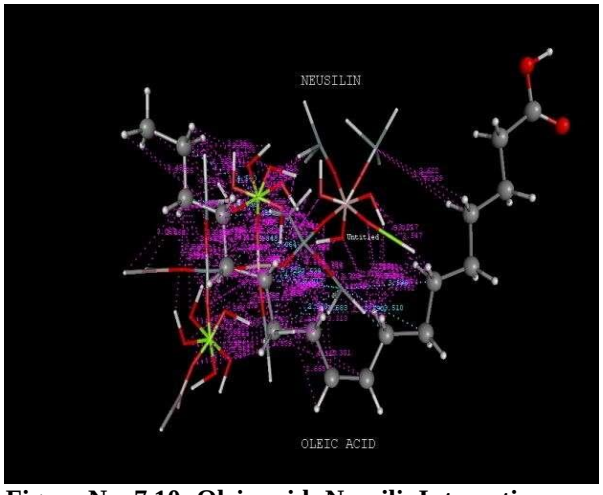

Figure No. 7.10: Oleic acid -NeusilinInteraction Interaction

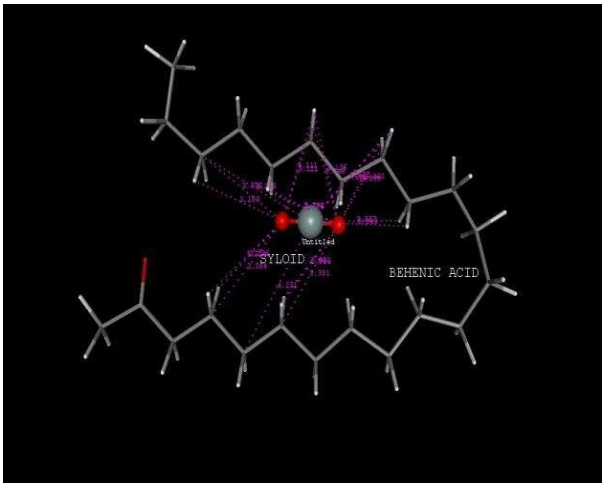

Figure No. 7.21: Behenic acid - Syloid Interactions.

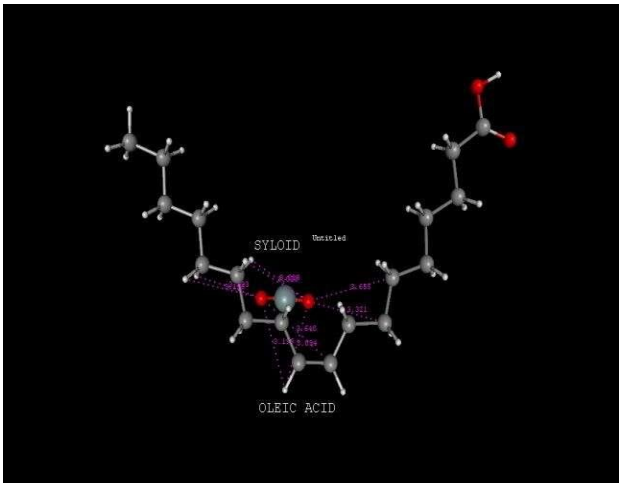

Figure No. 7. 22: Oleic acid - syloid Interactions.

Table No. 7.6: Net interactions in formulated suspension batches.

Oil	Excipient	H- Bond Score	VDW Score	Hydrophobic Interaction Score
MoringaOil	**Neusilin**	1	509	181
	Lecithin	NA	354	43
	Fujicalin	NA	111	NA
	Syloid	NA	41	NA
SesameOil	**Neusilin**	NA	336	91
	Lecithin	NA	253	51
	Fujicalin	NA	77	NA
	Syloid	NA	23	NA
SunflowerOil	**Neusilin**	NA	272	83
	Lecithin	NA	196	21
	Fujicalin	NA	61	NA
	Syloid	NA	13	NA

Net interactions were found to be more in Moringa oil batches than Sesame and Sunfloweroil batches. Neusilin and Lecithin showed more hydrophobic and van der waals interactions with oils and drug.

Extraction of Moringa Oil

Total seeds = 190 Weight of total powdered seeds = 179.3 gmOil obtained after extraction = 65ml

Analysis of all oils

Physicochemical analysis of oil samples

Characterisation of oil samples i. e Moringa, Sesame and Sunflower oil was carried out;results are as follows,

Table No. 7. 7: Physicochemical characteristics of oils.

Parameter	Sunflower Oil	Sesame Oil	Moringa Oil
Color	Yellowish- green	Yellowish- Brown	Yellow
R. I at 30^{0}C	1.485 ± 0.002	1.449 ± 0.01	1.454 ± 0.002
Sap Value	183 ± 0.2	198 ± 0.23	171 ± 1.02
Density(gm/ml)	0.90 ± 0.03	0.835 ± 0.002	0.868 ± 0.2
Iodine Value	120 ± 1.26	120.41 ± 1.1	65.63 ± 0.1
Acid Value	2.9 ± 0.9	2.7 ± 1.2	4.65 ± 1.26
PeroxideValue	1.8 ± 0.21	0.76 ± 0.23	4.9 ± 0.17
Viscosity(mPas. S)	37.17 ± 0.02	35.12 ± 0.1	44.11 ± 0.02

7. 3. 2 Determination of λmax

The λmax of Moringa oil was found to be 269nm, whereas of Sesame oil and Sunflower oilwas found to be 281nm and 269nm respectively. (fig. 7.- 7.).

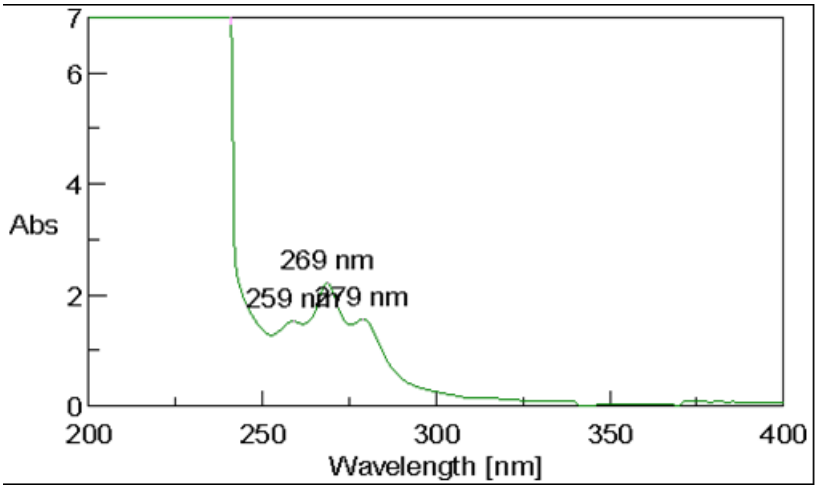

Figure No. 7. 25: λmax of Moringa oil.

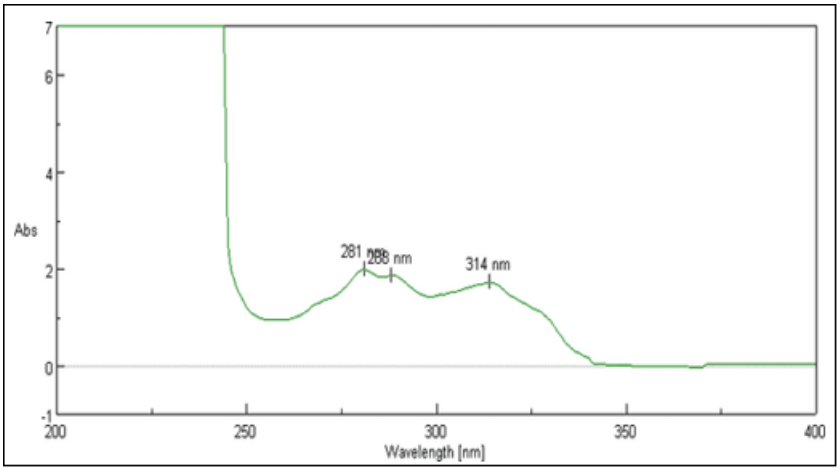

Figure No. 7. 26: λmax of Sesame oil.

Preformulation study of Progesterone

Description

The progesterone is white, crystalline powder.

Melting point

Melting point of progesterone was found to be 128^0-130^0 C.

λmax Determination

λmax of progesterone was found to be 240 nm in methanol.

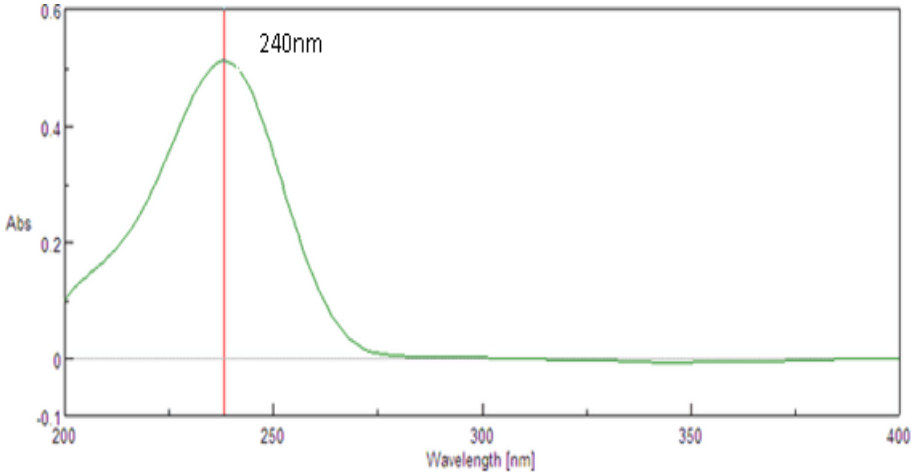

Figure No. 7.28: λmax of progesterone in methanol.

Analytical Study

1 UVspectroscopy

Preparation of standard calibration curve of Progesterone in Methanol.

Table No. 7. 8: Calibration data of Progesterone in methanol.

Concentration(µg/ml)	Absorbance
2	0.1097± 0.002
4	0.1965 ± 0.04
6	0.2587 ± 0.030
8	0.343 ± 0.31
10	0.4443 ± 0.01

Table No. 7.9: Statistical data for analysis of Progesterone in methanol.

Regression equation data	y = mx+ C
Slope (m)	0.040
Intercept (c)	0.025
Correlation coefficient (R^2)	0.994

Solubility of Progesterone in various oils

Solubility study of Progesterone in Moringa oil, Sesame oil and Sunflower oil was carried out. It has showed that Progesterone is more soluble in Moringa oil as compared to other oils this could be attributed to van der waals and hydrophobic interactions among Moringa oil and progesterone (Table No. 7.10)

Table No. 7. 10: Solubility study of Progesterone in various oils.

Oil	Conc. at saturation (mg/ml)
Moringa Oil	21.84 ± 0.02
Sesame Oil	15.23 ± 0.01
Sunflower Oil	19.98 ± 0.02

All the values are average ± S. D. (n=3)

Characterization of Progesterone oily suspension

Table No. 7. 11: pH of formulated suspension.

Batch Code	PH
MN	4.2
ML	4.4
MF	4.2
MS	4.6
SN	4.3
SL	4.3
SF	4.4
SS	4.5
SuN	4.1
SuL	4.3
SuF	4.3
SuF	4.2

pH

Rheological studies

Viscosity Measurement

Viscosity of plain Moringa oil samples was found to be more than Sesame oil and Sunflower oil.

Among all the formulation batches, Moringa oil bathes showed more viscosity than Sesame oil and Sunflower oil batches. In case of excipients Neusilin and Lecithin batches showed highest viscosity than Syloid and Fujicalin batches in all oils.

Table No. 7. 12: Viscosity of Progesterone suspension batches.

Batch Code	Viscosit(Pa.S)
MN	0.8665
ML	0.832
MF	0.7998
MS	0.7122
SN	0.6792
SL	0.5777
SF	0.573
SS	0.4548
SuN	0.4371
SuL	0.3426
SuF	0.2773
SuS	0.2537

Highest viscosity of Neusilin and Lecithin batches could be due to more hydrophobic and van der waals interactions. Moringa oil shows more hydrophobic and van der waals interactions that could be responsible for viscosity of Moringa oil batches.

Preparation of standard calibration curve of progesterone in 2 % SLS andAcetate Buffer pH 4.7.

Table No. 7. 17: Calibration data of Progesterone in 2 % SLS & Acetate buffer pH 4.7.

CONCETRATION (µg/ml)	ABSORBANCE
1	0.0885 ± 0.02
2	0.1079 ± 0.001
3	0.1492 ± 0.05
4	0.1877 ± 0.03
5	0.2378 ± 0.001
6	0.2747 ± 0.06
7	0.3088 ± 0.06
8	0.3536 ± 0.004
9	0.3871 ± 0.01
10	0.4262 ± 0.1

All the values are average ± S.D .(n=3)

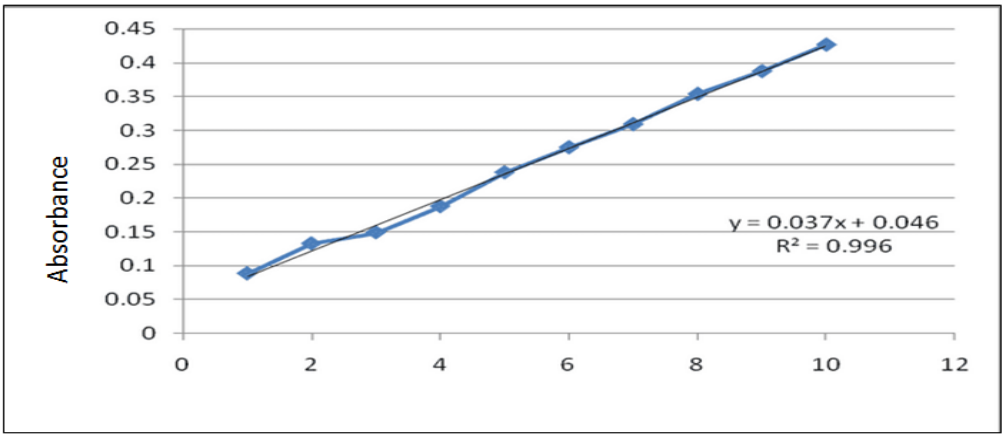

Figure No. 7.39: Calibration curve of Progesterone in 2 % SLS & acetate buffer pH 4.7.

Table No. 7. 18: Statistical data for analysis of Progesterone & acetate buffer pH 4.7.

Regression equation data	y = mx + c
Slope (m)	0.037
Intercept (c)	0.046
Correlation coefficient (R^2)	0.996

Table No. 7.7.2 Preparation of standard calibration curve of Progesterone in 2 % SLS Table No. 7. 19: Calibration data of Progesterone in 2 % SLS.

Concentration(µg/ml)	Absorbance at238nm
1	0.0522 ± 0.02
2	0.0907 ± 0.01
3	0.1058 ± 0.003
4	0.1369 ± 0.001
5	0.1485 ± 0.01
6	0.1665 ± 0.2
7	0.1963 ± 0.3
8	0.2243 ± 0.4
9	0.2520 ± 0.001
10	0.2590 ± 0.02

All the values are average ± S. D. (n=3)

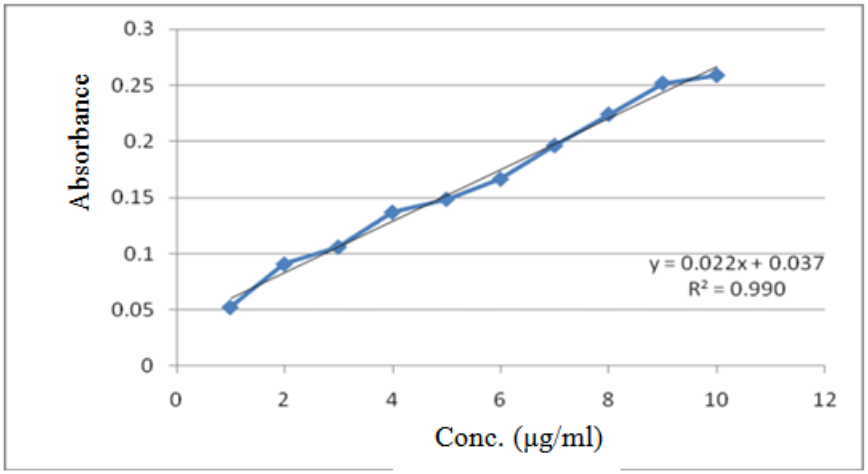

Figure No. 7.40: Clibration curve of Porgesterone in 2 % SLS.

Table No. 7.20: Statistical data for analysis of Progesterone in 2% SLS.

Regression Equation Data	y = mc + c
Slope	0.022
Intercept (c)	0.037
Correlation coefficient (R^2)	0.990

In- vitro release study

In- vitro release study of Moringa oil batches in Acetate buffer pH 4.7 and 2%SLS

Drug release from Moringa oil batch containing Neusilin, Syloid, Fujicalin and Lecithin as suspending agent was found to be 73.60%, 70.23%, 49.68% and 47.19% respectively.

Table No. 7.21: In- vitro release study of Moringa oil batches in Acetate buffer pH 4.7 and 2% SLS.

Time(min)	% Cumulative Release (Moringa oil)			
	MN	MS	MF	ML
30	4.663 ± 0.001	0.253 ± 0.001	0.091 ± 0.001	0.278 ± 0.19
60	9.571 ± 0.003	2.375 ± 0.002	1.024 ± 0.003	4.937 ± 0.13
90	13.24 ± 0.003	12.61 ± 0.003	4.272 ± 0.139	5.175 ± 0.15
120	21.27 ± 0.004	17.03 ± 0.003	5.249 ± 0.161	13.045 ± 0.16
180	22.14 ± 0.005	20.17 ± 0.003	17.22 ± 0.17	20.298 ± 0.17
240	28.38 ± 0.006	20.64 ± 0.004	19.95 ± 0.18	21.157 ± 0.15
300	31.43 ± 0.043	29.13 ± 0.004	24.58 ± 0.16	23.08 ± 0.06
360	34.42 ± 0.002	35.50 ± 0.006	26.36 ± 0.06	24.51 ± 0.008
420	36.82 ± 0.012	36.80 ± 0.004	27.71 ± 0.10	27.89 ± 0.08
480	45.23 ± 0.009	43.26 ± 0.004	29.59 ± 0.093	35.12 ± 0.19
540	51.51 ± 0.2	47.36 ± 0.012	31.85 ± 0.198	37.70 ± 0.24
600	57.22 ± 0.001	54.21 ± 0.007	33.62 ± 0.256	39.91 ± 0.08
660	66.08 ± 0.001	62.34 ± 0.01	43.83 ± 0.319	45.36 ± 0.30
720	73.60 ± 0.2	70. 23 ±0.022	49.68 ± 0.205	47.19 ±0.012

All the values are average ± S. D (n=3)

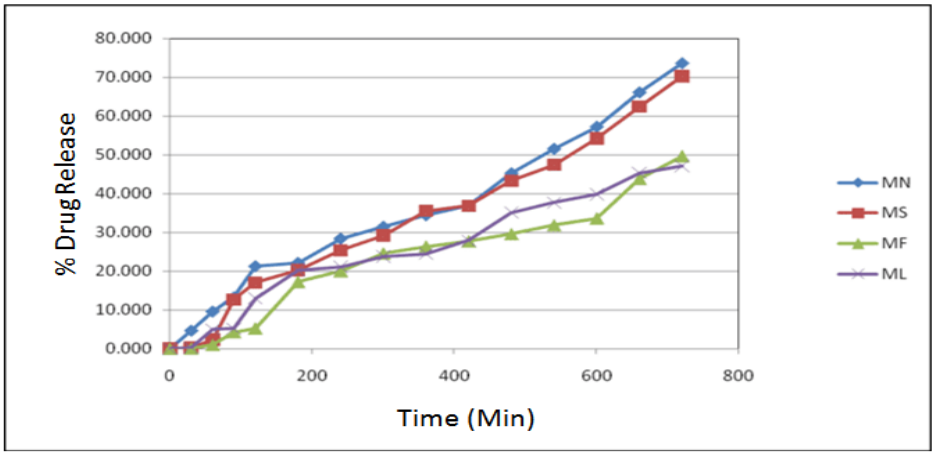

Figure No. 7.41: Dissolution profile of Moringa oil based suspension batches.

In- vitro release study of Sesame oil batches in Acetate buffer pH 4.7 and 2%SLS

Drug release from Sesame oil batch containing Neusilin, Syloid, Fujicalin and Lecithin as suspending agent was found to be 71.89%, 69.00%, 45.11% and 43.97% respectively.

Table No. 7. 22: In- vitro release study of Sesame oil batches in Acetate buffer pH 4.7 and 2% SLS.

Time(min)	% Cumulative Release (Sesame oil)			
	SN	SS	SF	SL
30	0.53 3 ± 0.0032	0.622 ± 0.002	0.668 ± 0.001	0.009 ± 0.0039
60	2.039 ± 0.0021	0.711 ± 0.002	2.307 ± 0.002	0.648 ± 0.0030
90	2.098 ± 0.0010	2.447 ± 0.002	3.104 ± 0.007	1.341 ± 0.0001
120	2.629 ± 0.0010	3.636 ± 0.003	5.229 ± 0.004	3.879 ± 0.0009
180	13.456 ± 0.0021	6.533 ± 0.001	5.574 ± 0.005	6.920 ± 0.004
240	19.636 ± 0.0057	9.692 ± 0.001	6.023 ± 0.006	10.158 ± 0.003
300	19.907 ± 0.0034	12.515 ± 0.02	8.759 ± 0.003	10.214 ± 0.006

360	25.230 ± 0.018	24.069 ± 0.07	15.075 ± 0.08	12.774 ±0.0015
420	35.397 ± 0.010	27.571 ± 0.09	26.613 ± 0.18	13.567 ± 0.006
480	38.415 ± 0.013	33.676 ± 0.04	29.900 ± 0.02	14.155 ± 0.009
540	50.627 ± 0.0233	38.579 ± 0.01	32.182 ± 0.03	24.601 ± 0.013
600	65.416 ± 0.066	44.260 ± 0.10	40.688 ± 0.01	29.437 ± 0.019
660	68.084 ± 0.058	48.778 ± 0.04	42.496 ± 0.05	35.769 ± 0.032
720	71.892 ± 0.098	69.006 ± 0.24	45.116 ± 0.01	43.972 ± 0.006

All the values are average ± S. D (n=3)

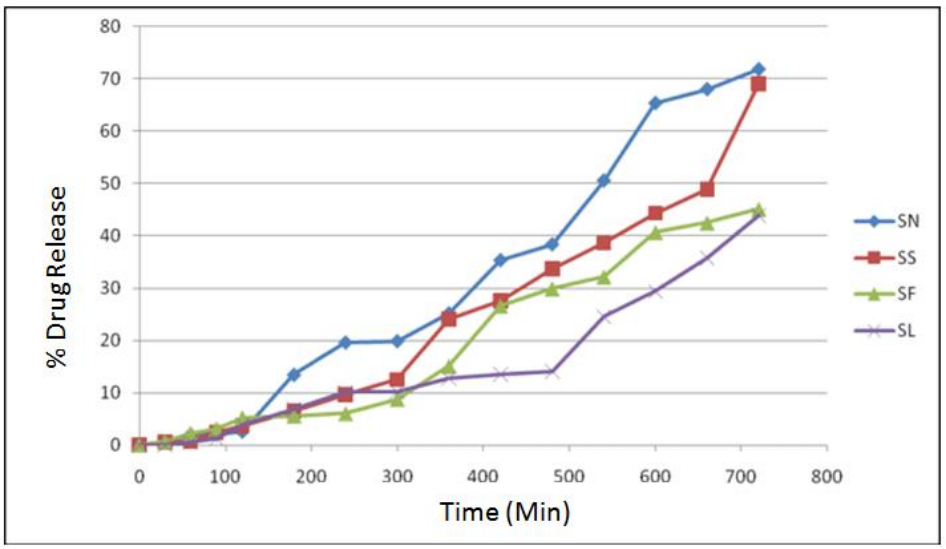

Figure No. 7.42: Dissolution profile of Sesame oil based suspension batches.

In- vitro release study of Sunflower oil batches in Acetate buffer pH 4.7 and 2%SLS

Drug release from Sunflower oil batch containing Neusilin, Syloid, Fujicalin and Lecithin as suspending agent was found to be 58.89%, 52.56%, 41.52% and 37.43% respectively.

Table No. 7. 23: In- vitro release study of Sunflower oil batches in Acetate buffer pH 4.7 and 2% SLS.

Time(min)	% Cumulative Release			
	SuN	SuS	SuF	SuL
30	1.75 ± 0.004	3.42 ± 0.005	2.83 ± 0.004	2.25 ± 0.005
60	3.40 ± 0.005	4.18 ± 0.002	3.01 ± 0.005	2.97 ± 0.005
90	6.58 ± 0.005	7.47 ± 0.007	5.25 ± 0.006	3.82 ± 0.005
120	7.57 ± 0.007	9.80 ± 0.006	4.56 ± 0.002	4.34 ± 0.004
180	12.90 ± 0.010	14.95 ± 0.008	10.58 ± 0.006	9.26 ± 0.006
240	17.65 ± 0.009	18.65 ± 0.010	14.61 ± 0.007	11.44 ± 0.006
300	22.37 ± 0.011	19.24 ± 0.010	18.11 ± 0.009	17.08 ± 0.016
360	25.20 ± 0.013	23.61 ± 0.012	19.21 ± 0.009	18.71 ± 0.01
420	36.30 ± 0.021	26.91 ± 0.013	26.38 ± 0.012	26.04 ± 0.014
480	39.20 ± 0.025	34.04 ± 0.018	29.63 ± 0.014	28.63 ± 0.016
540	47.34 ± 0.040	41.68 ± 0.026	32.16 ± 0.016	34.34 ± 0.019
600	49.78 ± 0.016	42.46 ± 0.02	37.32 ± 0.015	35.30 ± 0.058
660	50.54 ± 0.11	51.78 ± 0.011	39.61 ± 0.007	36.75 ± 0.014
720	58.89 ± 0.032	52.56 ± 0.003	41.52 ± 0.035	37.43 ± 0.006

All the values are average ± S. D (n=3)

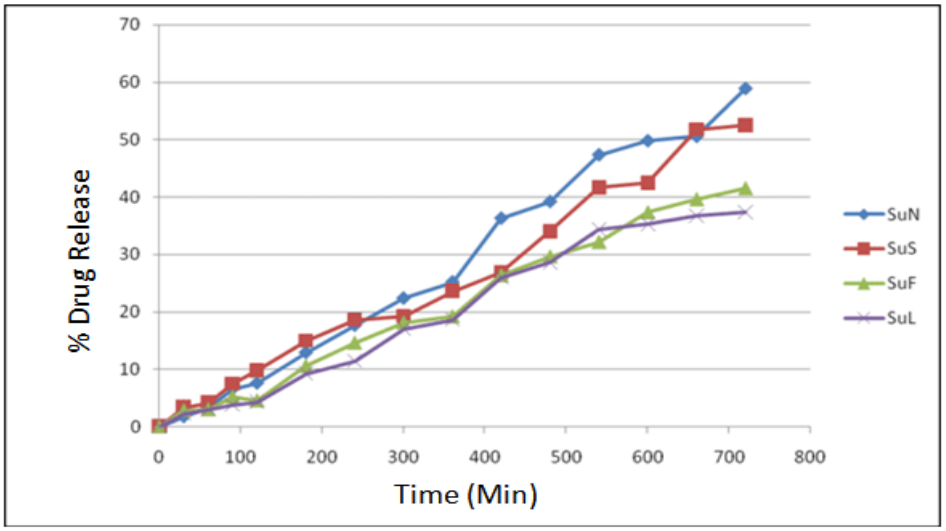

Figure No. 7.43: Dissolution profile of Sunflower oil based suspension batches.

In- vitro release study of Moringa oil batches in 2% SLS

Drug release from Moringa oil batch containing Neusilin, Syloid, Fujicalin and Lecithin as suspending agent was found to be 94.82%, 92.43%, 88.25% and 84.68% respectively.

Table No. 7.24: In- vitro release study of Moringa oil batches in 2% SLS.

Time (min)	% Cumulative Release (Moringa oil)			
	MN	MS	MF	ML
30	21.816 ± 0.001	7.545 ± 0.001	13.156 ± 0.001	3.169 ± 0.19
60	27.735 ± 0.003	8.969 ± 0.002	15.308 ± 0.002	6.209 ± 0.13
90	30.071 ± 0.003	10.932 ± 0.003	15.572 ± 0.13	6.635 ± 0.15
120	32.294 ± 0.004	11.958 ± 0.003	16.609 ± 0.16	7.260 ± 0.16
180	38.373 ± 0.005	14.268 ± 0.004	18.502 ± 0.17	9.325 ± 0.17
240	54.228 ± 0.006	18.582 ± 0.004	21.077 ± 0.18	11.975 ± 0.15
300	58.395 ± 0.04	20.769 ± 0.006	22.786 ± 0.16	19.680 ± 0.06
360	59.104 ± 0.002	25.061 ± 0.004	24.517 ± 0.06	26.520 ± 0.008
420	60.039 ± 0.012	25.765 ± 0.004	26.538 ± 0.01	32.564 ± 0.08
480	62.064 ± 0.004	40.265 ± 0.012	27.245 ± 0.09	34.799 ± 0.19
540	71.340 ± 0.008	50.278 ± 0.007	47.862 ± 0.19	53.223 ± 0.24
600	84.587 ± 0.01	71.141 ± 0.010	69.899 ± 0.25	65.573 ± 0.30
660	94.217 ± 0.023	92.118 ± 0.022	86.353 ± 0.31	75.502 ± 0.19
720	94.827 ± 0.001	92.431 ± 0.026	88.254 ± 0.20	84.687 ± 0.01

All the values are average ± S. D (n=3)

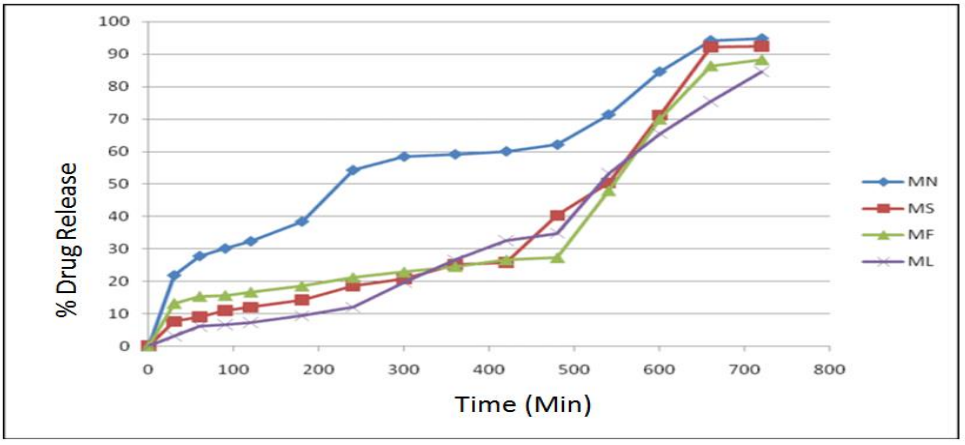

Figure No. 7.44: Dissolution profile of Moringa oil based suspension batches In- vitro release study of Sesame oil batches in 2% SLS.

Drug release from Sesame oil batch containing Neusilin, Syloid, Fujicalin and Lecithin as suspending agent was found to be 93.36%, 67.64%, 66.60% and 61.19% respectively.

Table No. 7.25: In- vitro release study of Sesame oil batches in 2% SLS.

Time(min)	% Cumulative Release (Sesame Oil)			
	SN	SS	SF	SL
30	3.48 ± 0.003	18.35 ± 0.004	18.19 ± 0.06	12.56 ± 0.006
60	16.65 ± 0.005	16.70 ± 0.05	18.36 ±0.052	14.93 ± 0.005
90	18.35 ± 0.005	22.58 ± 0.013	18.77 ± 0.001	15.04 ± 0.004
120	21.67 ± 0.005	27.72 ± 0.004	20.61 ± 0.004	17.29 ± 0.004
180	29.61 ± 0.006	24.63 ± 0.004	29.63 ± 0.13	22.40 ± 0.004
240	33.66 ± 0.006	33.99 ± 0.004	35.60 ± 0.006	32.53 ± 0.004
300	46.42 ± 0.005	34.50 ± 0.007	39.33 ± 0.07	34.54 ± 0.001
360	56.16 ± 0.007	39.44 ± 0.004	45.45 ± 0.14	38.73 ± 0.004
420	67.82 ± 0.008	44.91 ± 0.005	51.41 ± 0.16	44.25 ± 0.005
480	82.36 ± 0.014	52.55 ± 0.03	57.04 ± 0.16	50.11 ± 0.005
540	86.61 ± 0.013	63.61 ± 0.012	61.42 ± 0.12	56.91 ± 0.01
600	89.79 ± 0.016	64.94 ± 0.008	64.44 ± 0.09	58.58 ± 0.007
660	91.63 ± 0.005	65.48 ± 0.04	65.86 ± 0.08	59.68 ±0.005
720	93.56 ±0.0005	67.64 ± 0.004	66.60 ± 0.08	61.19 ± 0.001

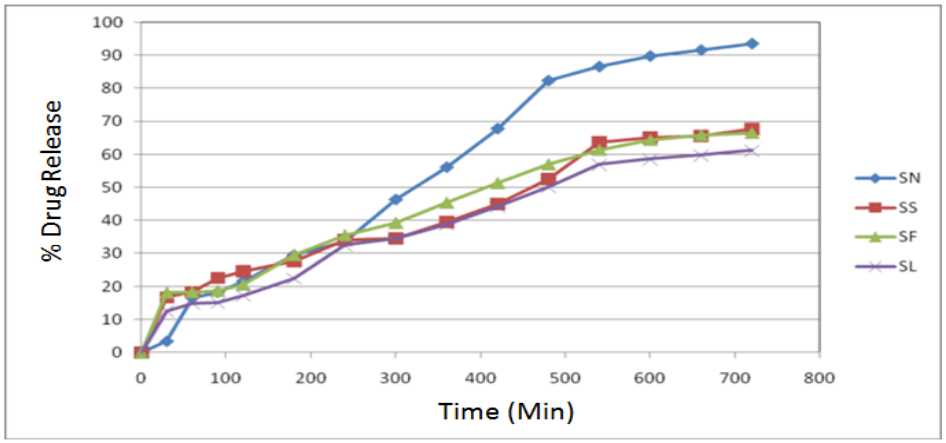

Figure No. 7.45: Dissolution profile of Sesame oil based suspension batches In- vitro release study of Sunflower oil batches in 2% SLS.

Drug release from Sunflower oil batch containing Neusilin, Syloid, Fujicalin and Lecithin as suspending agent was found to be 69.42%, 62.28%, 60.99% and 60.11% respectively.

Table No. 7. 26: In- vitro release study of Sunflower oil batches in 2% SLS.

Time(min)	% Cumulative Release			
	SuN	SuS	SuF	SuL
30	3.48 ±0.003	5.211 ± 0.002	1.041 ± 0.012	6.123 ± 0.002
60	4.34 ± 0.003	5.991 ± 0.006	2.027 ± 0.023	7.952 ± 0.002
90	6.967 ± 0.002	7.083 ± 0.006	4.561 ± 0.002	9.163 ± 0.002
120	15.24 ± 0.001	12.99 ± 0.001	7.88 ± 0.002	10.92 ± 0.003
180	16.54 ± 0.001	15.62 ± 0.001	19.51 ± 0.007	12.86 ± 0.001
240	19.87 ± 0.001	19.50 ± 0.0065	28.61 ± 0.008	13.60 ± 0.012
300	23.02 ± 0. 001	22.35 ± 0.12	33.23 ± 0.008	14.81 ± 0.006
360	30.76 ± 0.001	23.90 ± 0.005	39.51 ± 0.001	16.69 ± 0.006
420	36.57 ± 0.002	30.77 ± 0.002	48.31 ± 0.001	18.65 ± 0.004
480	52.33 ± 0.32	32.17 ± 0.0036	49.54 ± 0.002	25.93 ± 0.001
540	56.20 ±0.45	47.74 ± 0.001	52.25 ± 0.012	27.78 ± 0.004
600	64.86 ± 0.12	50.62 ± 0.002	54.23 ± 0.012	33.68 ± 0.001
660	68.66 ± 0.009	56.89 ± 0.002	57.25 ± 0.063	52.62 ±0.002
720	69.42 ± 0.009	62.28 ± 0.002	60.99 ±0.002	60.11 ± 0.002

Figure No. 7.46: Dissolution profile of Sunflower oil based suspension batches

In- vitro release indicates that all the suspension batches shows more release in 2% SLS than in Acetate buffer pH 4.7. Moringa oil batches shows higher release than sesame and sunflower oil batches. In case of excipients, Neusilin and Syloid containing batch of all oils shows maximum release than Lecithin and Fujicalin containing batches, this could be attributed to higher surface area of these excipients than later two Stability studies at Different Conditions of Temperature and Relative Humidity asper ICH Guidelines.

Accelerated stability studies were carried out at 40^0 C ± 2^0 C & 75% RH ± 5% for three months. In- vitro drug release and Zeta potential analysis was carried out to ensure stability offormulated batches. Table (7.27-7.32) shows In-vitro drug release and Table (7.33) shows Zeta potential analysis results for three months. It was found that Moringa oil batches are most stable than Sesame and Sunflower batches.

Table No. 7. 27: In- vitro drug release of Moringa oil batches in Acetate Buffer after stability studies.

BatchCode	Initial (%DR)	30 Days(%DR)	60 Days(%DR)	90 Days(%DR)
MN	76.71 ±0.1	74.07 ±0.001	71.26 ±0.01	71.23 ± 0.01
MS	72.42 ±0.02	72.01 ± 0.02	70.86 ± 0.001	70.86 ± 0.01
MF	68.19 ±0.05	67.52 ± 0.03	66.79 ± 0.26	66.78 ± 0.01
ML	47.19 ±0.02	47.11±0.001	46.04 ±0.02	46.03 ± 0.1

All the values are average ± S. D (n=3)

Table No. 7. 28: In- vitro drug release of Moringa oil batches in 2% SLS after stability studies.

Batch Code	Initial (%DR)	30 Days (%DR)	60 Days (%DR)	90 Days (%DR)
MN	94.82 ±0.001	93.167 ±0.002	92.80±0.006	92.77 ±0.01
MS	92.43±0.026	90.89 ±0.006	89.62 ± 0.05	89 ± 0.01
MF	88.25 ±0.20	87.27±0.001	86.83 ± 0.01	86.82 ± 0.02
ML	84.68 ±0.01	83.43 ±0.22	82.68±0.04	82. 68 ± 0.01

All the values are average ± S. D (n=3)

Table No. 7.29: In- vitro drug release of Sesame oil batches in Acetate Buffer after stability studies.

BatchCode	Initial (%DR)	30 Days (%DR)	60 Days (%DR)	90 Days (%DR)
SN	71.82 ± 0.02	71.17 ± 0.21	70.47 ± 0.001	69.23 ± 0.002
SS	69.00 ± 0.001	67.74 ± 0.33	66.98 ± 0.002	63.26 ± 0.23
SF	45.11 ± 0.01	44.64 ± 0.30	43.29 ± 0.6	40.26 ± 0.001
SL	43.97 ± 0.01	43.74 ± 0.2	44.53 ± 0.02	40.26 ± 0.01

All the values are average ± S. D (n=3)

Table No. 7. 32: In- vitro drug release of Sunflower oil batches in 2% SLS after stability studies.

BatchCode	Initial	30 Days	60 Days	90 Days
SuN	69.42 ± 0.001	68.56 ± 0.3	68.54 ± 0.31	60.21 ± 0.014
SuS	62.28 ± 0.12	61.75 ± 0.6	61.30 ± 0.87	59.36 ± 0.001
SuF	60.99 ± 0.20	59.94 ± 0.14	58.65 ± 0.14	55.21 ± 0.21
SuL	37.43 ± 0.1	37.33 ± 0.001	36.93 ± 0.2	30.21 ± 0.11

Table No. 7.33: Zeta Potential analysis of suspension batches after stability studies.

Oil	Batch Code	Zeta Potential (mV)			
		Initial	30 Days	60 Days	90 Days
Moringaoil	**MN**	-39.8	-39.7	-39.7	-39.7
	MS	-34.1	-33.2	-33.2	-33.1
	MF	-30.6	-30.6	-29.3	-29.3
	ML	-36.9	-36.9	-36.6	-36.5
Sesame oil	**SN**	-26.9	-26.8	-26.8	-26.8
	SS	-23.2	-23.2	-23.2	-23.1
	SF	-22.9	-22.9	-21.4	-21.3
	SL	-25.3	-25.2	-25.3	-25.3
Sunfloweroil	**SuN**	-24.8	-24.6	-24.5	-24.5
	SuF	-20.8	-20.8	-20.7	-19.3
	SuS	-20.6	-20.6	-20.4	-20.3
	SuL	-19.5	-19.2	-18.2	-18.2

CONCLUSION

Moringa oil and Neusilin can become a promising replacement to currently used allergic Pea nut oil and Lecithin respectively. Moringa oil and Neusilin shows more hydrophobic and van der waals interactions with the drug and thus improves solubility and bioavailability of the progesterone. Moringa oil and Neusilin has potential to stabilize progesterone oily suspension since they impart high viscosity, less sedimentation and less zeta potential values. Our studies concluded that, Computational investigation of virtual interactions between drug, oil and excipients explains excellence of Moringa oil and Neusilin over other oil and excipients respectively.

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