CHAPTER-6 RESULTS AND DISCUSSION

Different type of studies from the physicochemical to in vitro assay were performed as to optimize and also to assess the potential of the delivery system developed. The same has been represented in the previous chapters. Results and detailed discussion are being given here to convince the rationale for development of delivery system.

PreformulationStudies

Organoleptic evaluation: The drugs were examined for its organoleptic properties like colour and odour and it was observed that *B. lanzan* was light yellow and *S. Chinesis* Pale yellow colored liquid.

Table 6.1: Organoleptic property of *Buchananialanzan* and *Simmondiachinesis*

Parameter	*Buchananialanzan*	*Simmondiachinesis*
Colour	Light yellow	Pale yellow
Odor	Odorless	Odorless
Taste	Tasteless	Tasteless

Preparation of standard curve of Colchicine

100 mg of Colchicine was accurately weighed and transferred to a 100 ml volumetric flask containing 100 ml of 7.5 pH phosphate Buffer and shaken to dissolve. The solution resulted is ≈1000 µg/ml. Then 1 ml of this solution is transferred to another 10 ml volumetric flask to obtain solution of 100µg/ml as stock. From this stock solution 1 ml was pipette out in 10 ml calibrated volumetric flask and dilution was made with buffer and from this serial dilutions were done. The absorbance was taken on double beam U.V. spectrophotometer using λmax at 350.0 nm for Colchicine. The absorbance values were plotted against concentration (µg/ml) to obtain the standard calibrationcurve.

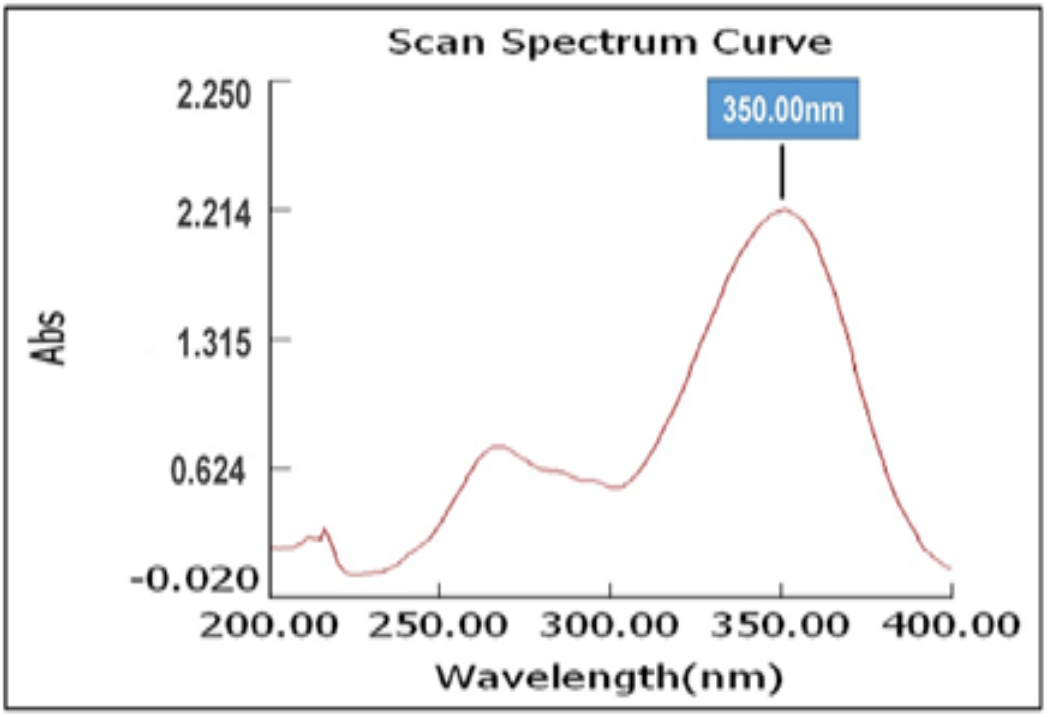


Figure No 6.1: Wavelength scan of Colchicine in PBS pH 7.5.

Calibration curve of Colchicine in PBS (pH 7.4)

The calibration curve was plotted between concentration and absorbance. The correlation coefficient 'r^2' values were calculated as 0.999 and 0.998 for colchicine the parameters are listed in Table 6.3.

Table 6.2: Calibration curve of the proposed method for the estimation of colchicine

Conc. (µg/ml)	**Colchicine (350nm)**
	Absorbance*
10	0.624±0.014
20	1.315±0.009
30	2.214±0.012

*Average of three readings

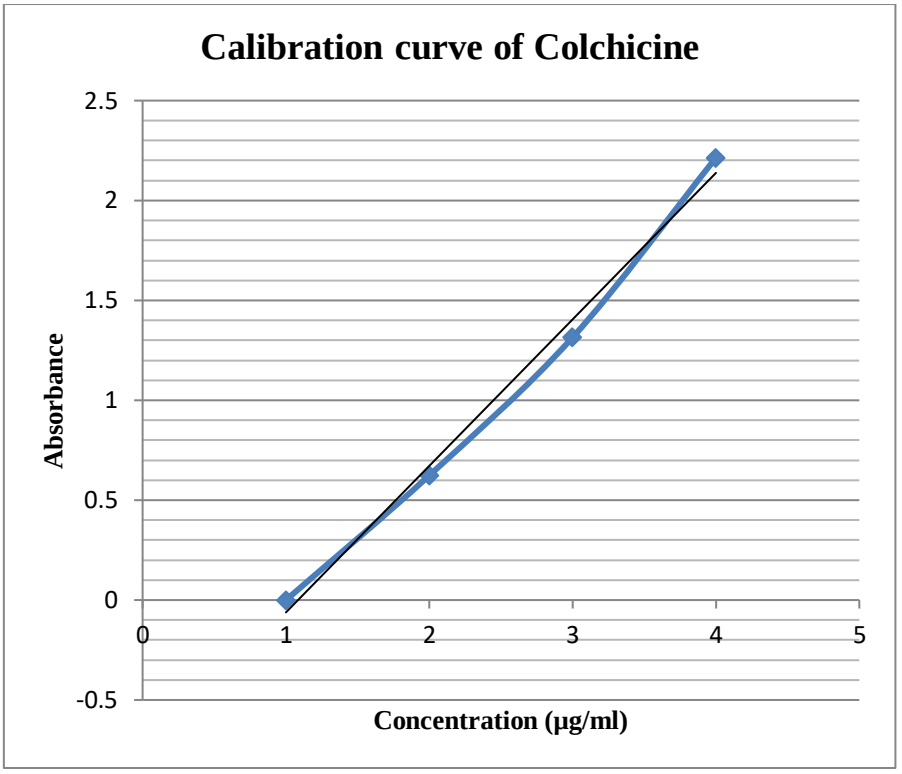


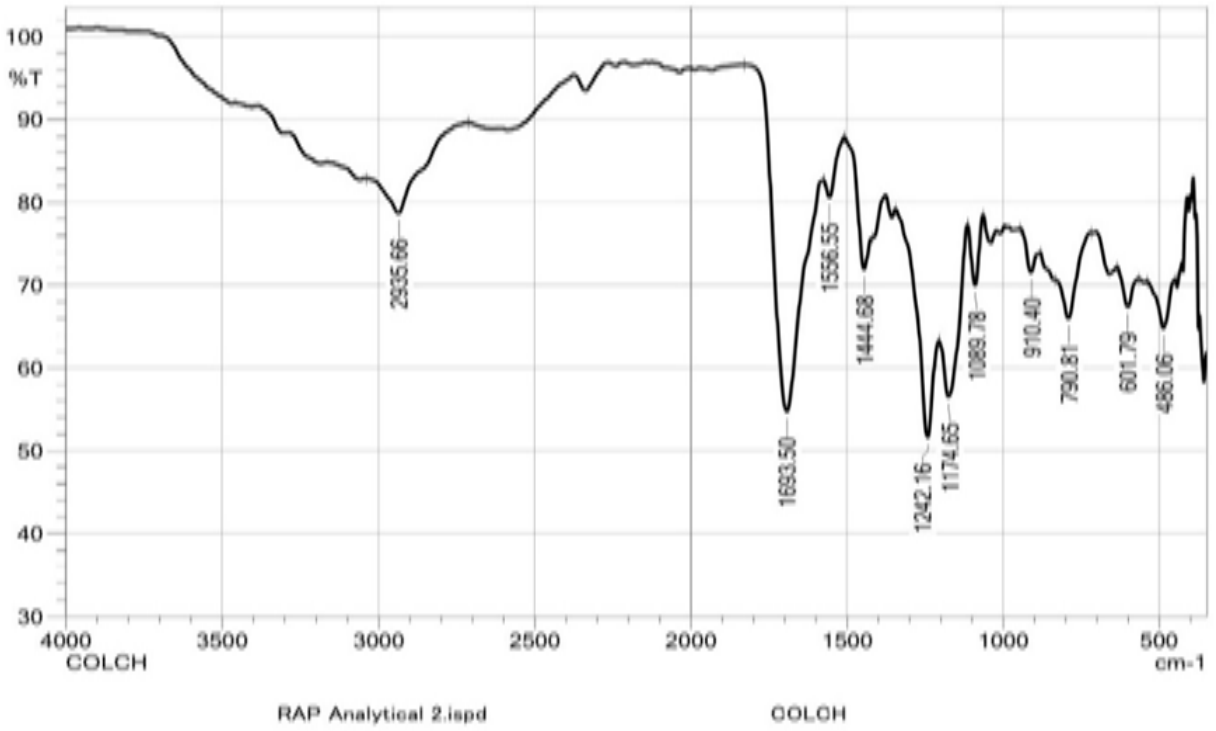
Figure 6.2: Calibration curve of Colchicine in PBS (pH 7.4) at 350 nm

Table: 6.3: Statistical parameters related to standard curve of colchicine

Drug	Parameters	Values
Colchicine	Concentration Range	1-5µg/ml
	Regression Coefficient	$R^2 = 0.9927$
	Equation of line (y = mx + c)	y = 0.7333x -0.795

Where y is the response, x is the concentration, m is the slope and c is the intercept of a best fit line to the data.

Fourier-Transform Infra-Red Spectroscopy (FTIR): the spectrums of drug along with other ingredients were authenticated by FTIR spectroscopy. The characteristic peaks present were obtained due to specific structural characteristics of the molecules were noted. The FTIR scan of drug and other ingredients are shown in Figure 6.3 and 6.4 and the wave numbers are listed in Table 6.4 and6.5.



	Peak	Intensity	Corr. Intensity	Base (H)	Base (L)	Area	Corr. Area	Comment
1	486.06	64.79	5.78	540.07	451.34	2835.448	223.206	
2	601.79	67.37	4.11	636.51	567.07	2107.197	127.061	
3	790.81	65.97	6.85	835.18	719.45	3367.659	299.054	
4	910.40	71.52	3.69	947.05	881.47	1714.115	99.510	
5	1089.78	69.95	7.90	1114.86	1064.71	1314.510	203.836	
6	1174.65	56.54	11.49	1205.51	1114.86	3324.452	626.263	
7	1242.16	51.63	15.83	1344.38	1205.51	4676.404	678.397	
8	1444.68	71.87	7.24	1508.33	1419.61	1797.764	178.957	
9	1556.55	80.59	3.52	1575.84	1508.33	1088.395	91.516	
10	1693.50	54.72	34.42	1828.52	1575.84	5761.919	3139.073	
11	2935.66	78.70	6.29	3037.89	2711.92	5118.741	633.371	

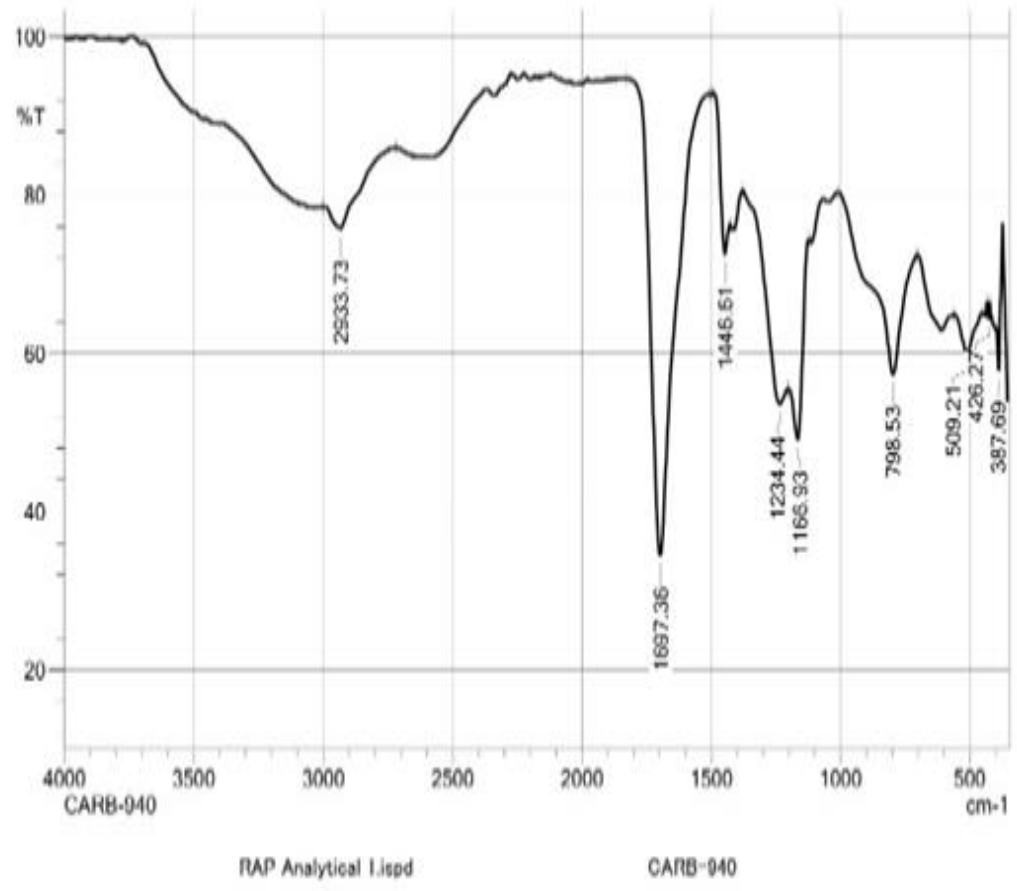
Figure No 6.3: FT-IR of Colchicine

Major peaks observed in the FTIR spectrum of Colchicine

Transmittance [%]
95.5 96.0 96.5 97.0 97.5 98.0 98.5

s. no.	Wave number(cm^{-1})	Inference
1.	2935.66	-NH
2.	1693.50	-C=O
3.	1242.16	-CH3
4.	1174.65	-CH2

Table No 6.4: Major peaks observed in the FTIR spectrum of Colchicine



	Peak	Intensity	Corr. Intensity	Base (H)	Base (L)	Area	Corr. Area	Comment
1	387.69	57.85	7.66	397.34	383.83	534.071	58.986	
2	426.27	64.23	2.09	433.98	422.41	309.989	10.678	
3	509.21	59.80	5.09	563.21	463.27	4099.620	240.776	
4	798.53	57.30	17.56	1010.70	704.02	9510.108	2262.330	
5	1166.93	49.09	14.93	1203.58	1122.57	3404.696	562.973	
6	1234.44	53.51	6.39	1379.10	1203.58	5786.168	172.675	
7	1446.61	72.54	8.59	1492.90	1427.32	1209.236	198.153	
8	1697.36	34.48	59.40	1830.45	1506.41	8094.283	6053.373	
9	2933.73	75.75	4.54	3001.24	2717.70	5400.550	366.559	

Figure No 6.4: FT-IR of Carbopol

s. no.	Wave number(cm^{-1})	Inference
1.	3829.67	-OH
2.	3122	-Aromatic
3.	1511.88	-C=O

Table No 6.5: Major peaks observed in the FTIR spectrum of Carbopol

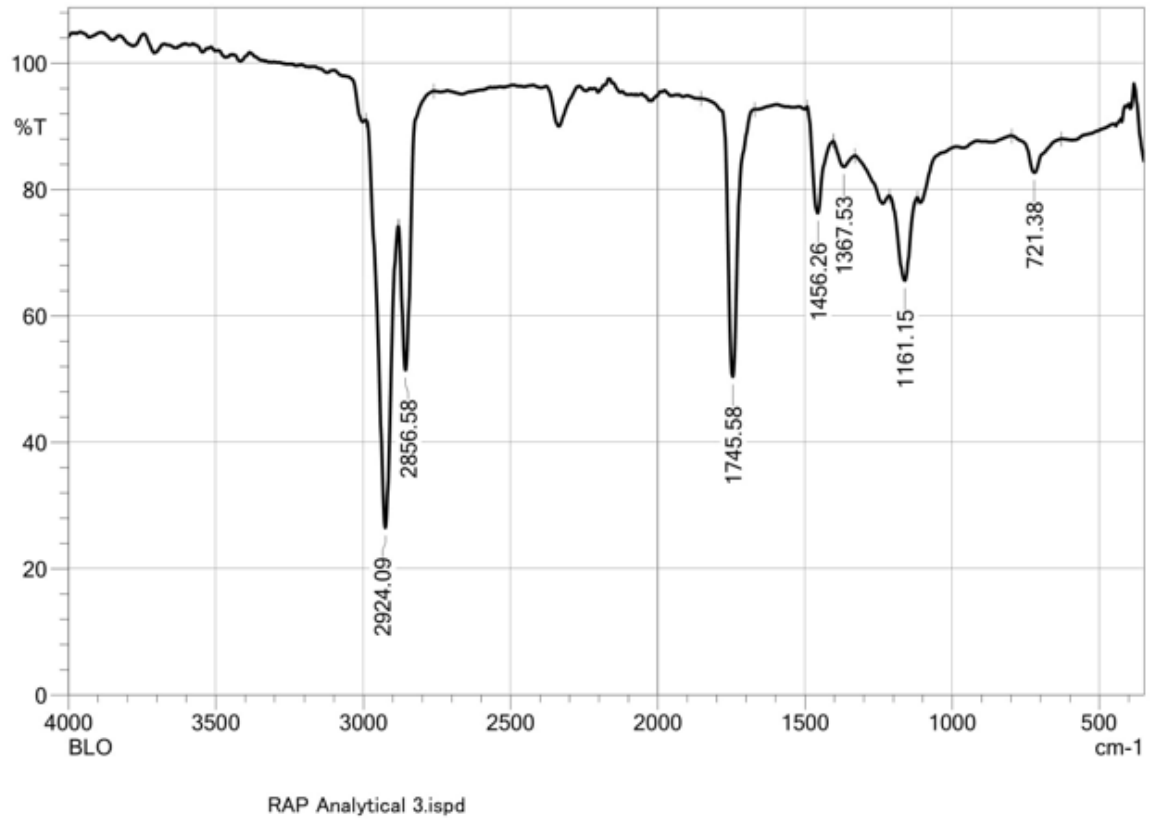


Figure No 6.5: FT-IR of BLO

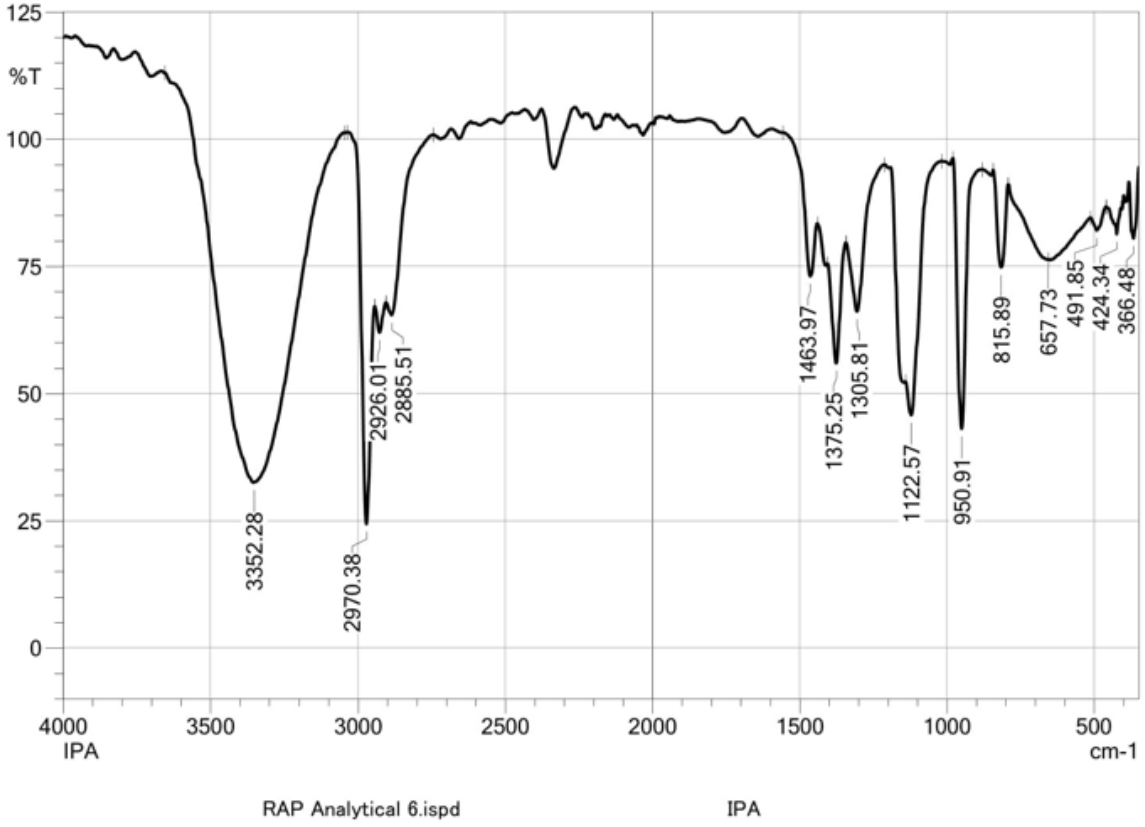


Figure No 6.6: FT-IR of IPA

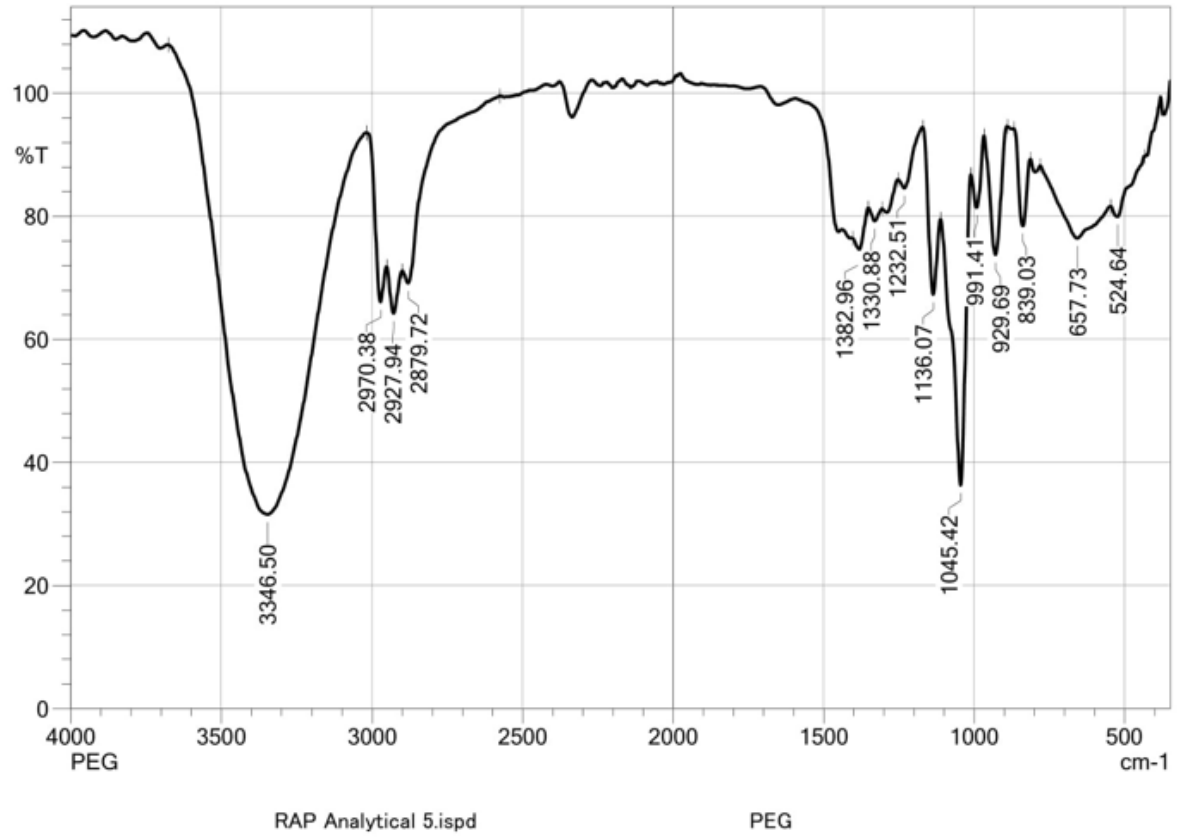


Figure No 6.7: FT-IR of PEG

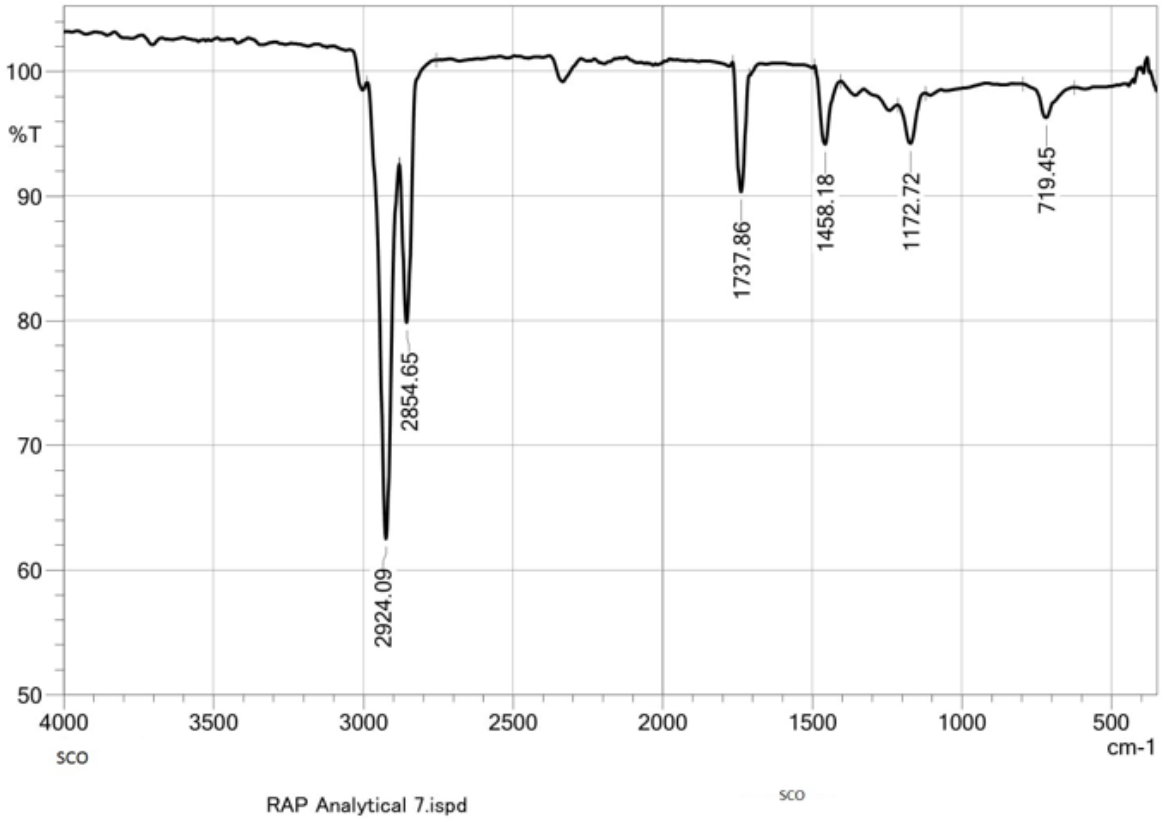


Figure No 6.8: FT-IR of SCO

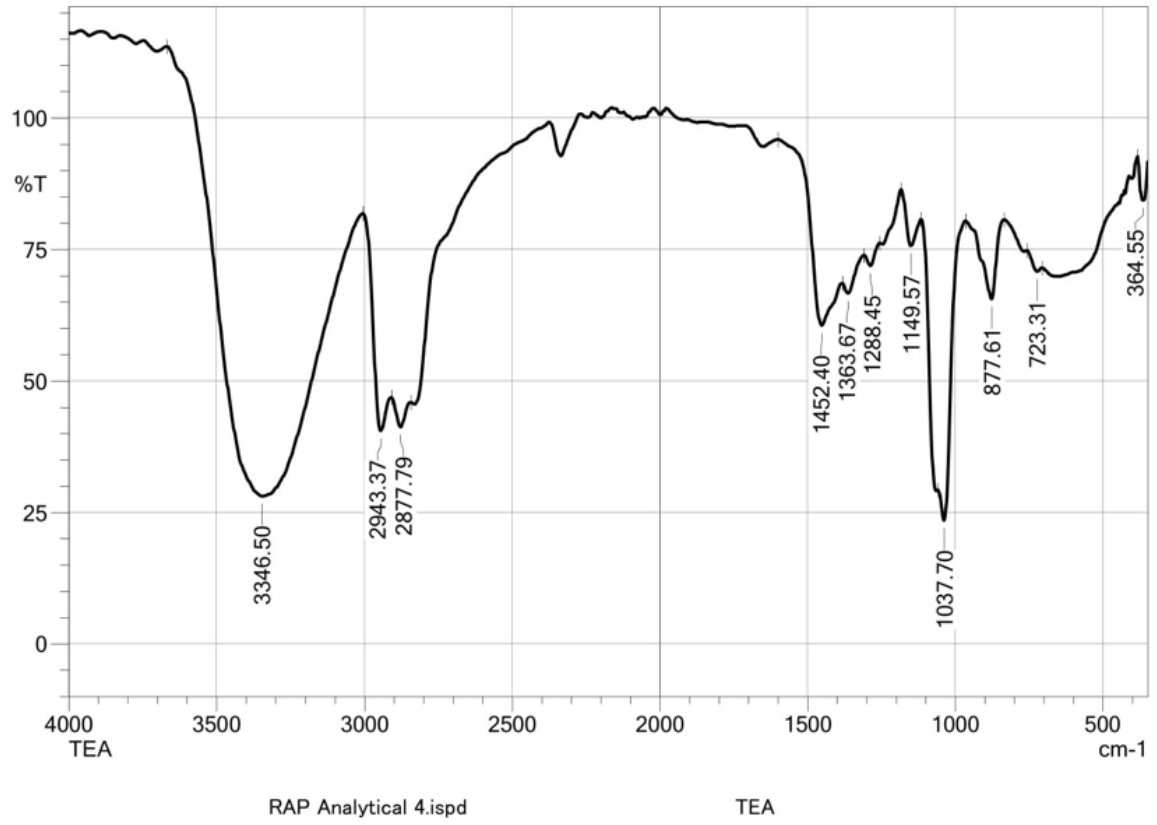


Figure No 6.9: FT-IR of TEA

Discussion: The peak obtained indicates characteristic groups and the bonds present in the compound. Hydroquinone shows the characteristic peak at3829.67cm^{-1}due to OH stretching, 3122 cm^{-1} was due to CH stretching vibration and peak at 1511.88 cm^{-1}C=C stretching vibration. Similarly for Colchicine shows the characteristic peak at 817.49 cm^{-1}for C=S stretching, 2956.55 cm^{-1}for C-H aromatic stretch and 1711.04 cm^{-1}for C=O stretch were obtained.

FTIR spectrum for both the drugs was compared with the standard spectrum. It was observed that there are similar peaks for functional groups in the standard spectrum which was reported in pharmacopeia and the spectrum was found to be compatible for each other. This shows that the drugs are pure.

LOD:

To determine LOD firstly weight of empty dish was recorded. Then 1.5gm of sample placed in dish and again weighed. The total weight was recorded. The dishes with sample of seeds were kept on an oven for 2hrs and weight of dish was recorded intermittently. The final weight was taken after 2hrs. The last value was considered as the final value of LOD. The procedure was done in triplicate to obtained precise reading.

Ash value:

The ash value determination done by given procedure and performed in triplicate to get **standard deviation**

The obtained result represented as follows.

The presented data shown that the oil shows acceptable range of values which ultimately shows that the seeds are enrich in their contents and free from any inorganic matter (Although it may present but in negligible quantity)

Table No.6.6 Estimation of total ash in *BLO and SCO*

Sr.no	**Drug**	total ash	acid insoluble ash	water soluble ash value	**Alcohol soluble extractable matter**	**water soluble extractable matter**	**Unsaponifiable matter**
1.	*BLO*	**3.3±0.17**	**1.00±0.01**	**2.36±0.11**	**0.31±0.017**	**1.11±0.012**	**0.32±0.017**
2.	*SCO*	**4.96±0.15**	**1.63±0.115**	**7.36±0.23**	**0.42±0.005**	**1.47±0.017**	**2.97±0.023**

Physicochemical Evaluation of BLO and SCO:

Parameter	***SCO***	***BLO***
Saponification value (mg/g)	167 ± 1.52	262 ±0.58
Iodine value	167.88 ± 1.45	249.9 ±1.12
Acid value (mg)	5.50 ± 0.04	2.04 ±0.05
Ester value (mg)	161.50 ± 0.25	259.96 ± 0.78
% FFA	2.76 ± 0.11	8.83 ±0.06
% of Glycerol	1.02 ± 0.05	14.2 ± 0.10

Table No 6.7: Physicochemical Evaluation of BLO and SCO

From above analysis it was found that the saponification values obtained for both the oils were within the range of their standard values. It can be said that the saponification value of *Buchananialanzan*posseses high saponification value. The lower acid value shows low rancidity of oil. But higher value which was found in the case of *simmondsiachinesis*shows

more rancid than other one. The percent free fatty acid and glycerol varied from 2.26% to 8.83% . and 1.02% to 14.2% respectively.

Acute Pharmacological study:

Acute toxicity of oil was determined according to the OECD (TG 423) test guide line for testing of chemical. Albino mice (either sex) fasted over night, but allowed access to water *ad libitum*. Animals were randomly divided in to three groups. The control received water. Group I-III were orally treated with test material (OBL and OSC) at dose of 5g/kg

Clinical observation

Assessment of the behavior of animals was carried out by general observations of each animal on alternative basis from the stage of dosing to the end of the study. Any changes or abnormalities recorded could be an indication of toxicity. The test animals at all dose levels showed no significant changes in behavior before and after the administration of oral dose of oil. The clinical observation for two oil under investigation detailed in Table no 6.8

Table No 6.8 .Evaluation of LD_{50} of oil obtained from seeds of *Buchananialanzan* and *Simmondsiachinesis* (*linn*.)Dose 2000mg/kg BW, Species: Albino mice: Male and Female Date 23/03/2018, duration:15 days, TRE- Tremor, CON- Convulsion, SALI-Salivation, Diah- Diarrhea, LET-Lethargy) (×= Negative, √= Positive),BLO= Oil of *Buchananialanzan*

Sr. no.	**Oil**	**Toxicity study**		**Time of death**	**Skin**	**Resp.**	**Eyes**	**CNS**	**Observation**					
		Onset	Stop						Tre	Sali	Diarh	Let	Com	Sleep
1	BLO	×	×	×	×	×	×	×	×	×	×	×	×	×
2	SCO	×	×	×	×	×	×	×	×	×	×	×	×	×

Table No 6.8: clinical observation of oils

and SCO=oil of *Simmondsiachinesis*

Body Weight Changes

Body weight is an important factor to monitor the of health of the animal. The loss of body is

frequently the first indicator of the onset of an adverse effect. A dose, which causes 10 % or more reduction in body weight, is considered to be a toxic dose. It is considered to be the dose, which produces minimum toxic effect, irrespective of whether or not it is accompanied by any other changes. All the animals from treated groups did not show any significant decrease in body weight for all the 14 days as compared with the 0 day it thus indicating no signs of toxicity.

Loss on drying:

Drug-Excipients compatibility study:

Sr. No.	**Ingredients**	**Ratio**	**Days**	**Observation**
1	Carbopol 934 + BLO	1:1	30days	No change observe in mixture
2	Carbopol 934+ SCO	1:1	30days	No change in mixture
3	Carbopol 934+ IPA	1:1	30days	No change in mixture
4	Carbopol 934+ TEA	1:1	30days	No change in mixture
5	Carbopol 934+ PEG	1:1	30days	No change in mixture
6	IPA+ TEA	1:1	30days	No change in mixture
7	IPA + BLO	1:1	30days	No change in mixture
8	IPA + SCO	1:1	30days	No change in mixture
9	IPA + PEG	1:1	30days	No change in mixture
10	TEA+ BLO	1:1	30days	No change in mixture
11	TEA + SCO	1:1	30days	No change in mixture
12	TEA + PEG	1:1	30days	No change in mixture
13	PEG + BLO	1:1	30days	No change in mixture
14	PEG + SCO	1:1	30days	No change in mixture
15	Methyl paraben + Carbopol 934	1:1	30days	No change in mixture
16	Methyl paraben + IPA	1:1	30days	No change in mixture
17	Methyl paraben + TEA	1:1	30days	No change in mixture
18	Methyl paraben + PEG	1:1	30days	No change in mixture
19	Methyl paraben + BLO	1:1	30days	No change in mixture
20	Methyl paraben + SCO	1:1	30days	No change in mixture
21	Propyl paraben + IPA	1:1	30days	No change in mixture

22	Propyl paraben + TEA	1:1	30days	No change in mixture
23	Propyl paraben + PEG	1:1	30days	No change in mixture
24	Propyl paraben + BLO	1:1	30days	No change in mixture
25	Propyl paraben +SCO	1:1	30days	No change in mixture
26	Colchicine + Carbopol 934	1:1	30days	No change in mixture
27	Colchicine + IPA	1:1	30days	No change in mixture
28	Colchicine + TEA	1:1	30days	No change in mixture
29	Colchicine + PEG	1:1	30days	No change in mixture
30	Colchicine +BLO	1:1	30days	No change in mixture
31	Colchicine + SCO	1:1	30days	No change in mixture
32	Colchicine + Methyl paraben	1:1	30days	No change in mixture
33	Colchicine + Propyl paraben	1:1	30days	No change in mixture

Table No 6.9: Comparative data of Preformulation studies

Discussion:

Drug excipient compatibility study was performed at laboratory level by keeping above combinations in desiccator in the presence of saturated solution of KCL for 30 days. After said periods the sample were observed and data have been shown in above table as there was no significant changes observed in the studies.

Evaluation offormulations

Various different gel formulation was developed and in order to optimize factorial design was utilized wherein 3^2 design was employed for screening of significant formulation and process variables which were involved in the development of gel which is 3 level 2 factor design. Independent variable selected amount of Carbopol940, amount of permeation enhancer.

Design of experiment yielded out 09 formulations with different values of the independent variables to be selected at both low and high level.

The evaluation of formulation was done by evaluating their pH, Spreadability, viscosity, Drug content, skin irritation study and organoleptic characters such as appearance.

Determination of pH:

Formulation	pH
BL1	6.70±0.04
BL2	7.25±0.06
BL3	6.85±0.03
BL4	7.5±0.015
BL5	6.90±0.045
BL6	7.25±0.053
BL7	7.30±0.05
BL8	7.2±0.04
BL9	7.10±0.02

Table No 6.10. pH values of gel formulations containing *Buchananialanzan* oil

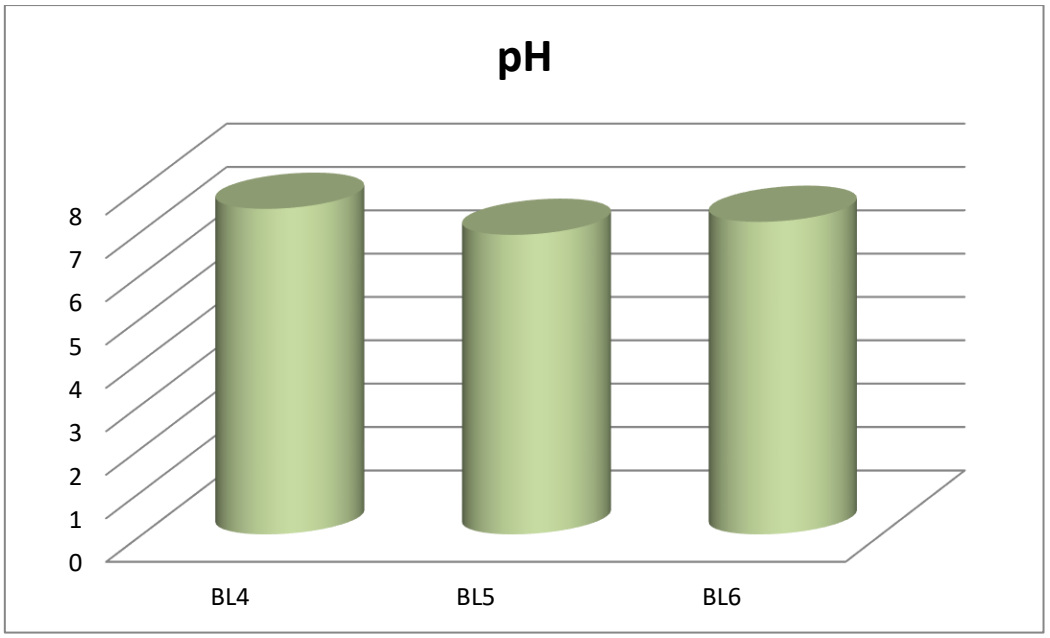


Figure No 6.10. pH values of gel formulations containing *Buchananialanzan* oil

Formulation	pH
SC1	7.79±0.012
SC2	7.95±0.02

SC3	7.79±0.017
SC4	7.50±0.011
SC5	7.65±0.012
SC6	7.79±0.017
SC7	7.65±0.02
SC8	7.65±0.02
SC9	7.50±0.05

Table No. 6.11: pH values of gel formulations containing *Simmondisiachinesis* oil

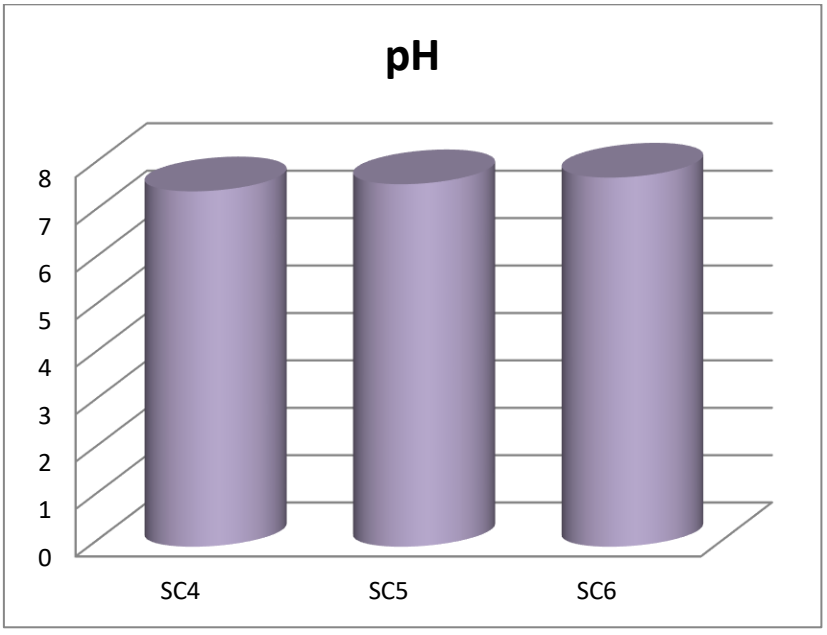


Figure No. 6.11: pH values of gel formulations containing *Simmondisiachinesis* oil

The above table shows values obtained for the different gel formulations. It was found that the pH of formulations fall under range of 6.70 to 7.95 which shows its acceptability

towards application to skin as all the values are close or near neutral pH.

Determination of Spreadability:

:

Formulation	Spreadability
BL1	0
BL2	0
BL3	12.94±0.06
BL4	12.05±0.05
BL5	11.84±0.04
BL6	11.33±0.04
BL7	11.46±0.05
BL8	10.52±0.02
BL9	10.43±0.04

Table No. 6.12: Spreadability values of gel formulations containing *Buchananialanzan* oil

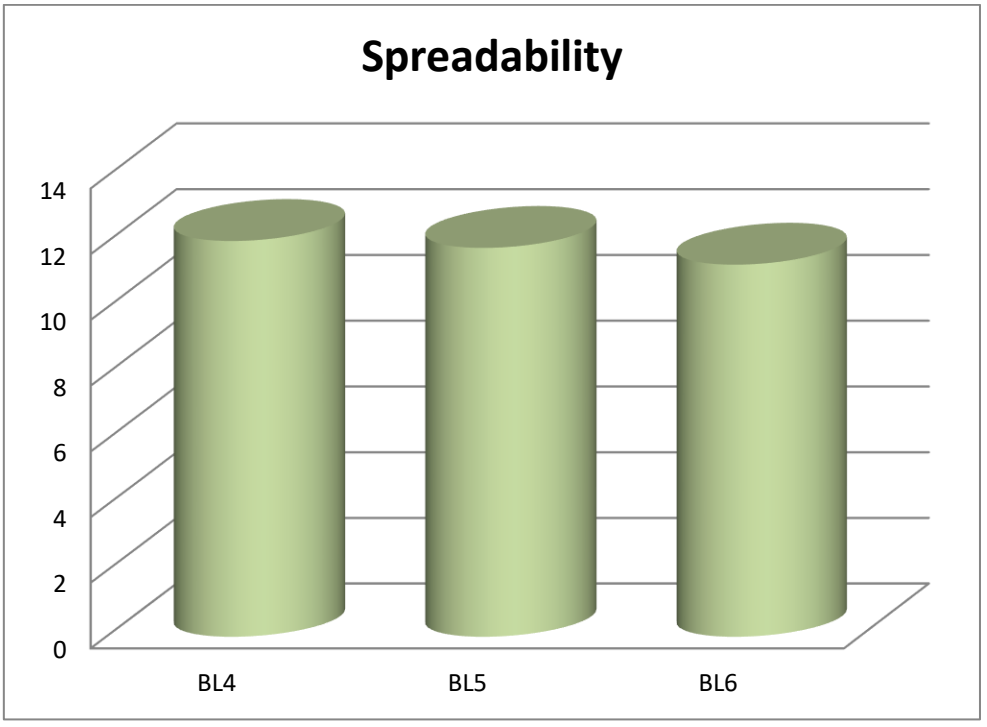


Figure No. 6.12: Spreadability values of gel formulations containing *Buchananialanzan* oil

Formulation	Spreadability
SC1	0
SC2	0
SC3	21.39±0.04
SC4	18.69±0.07
SC5	16.89±0.02
SC6	16.79±0.05
SC7	16.35±0.03
SC8	11.01±0.06
SC9	9.65±0.03

Table No. 6.13:Spreadability values of gel formulations containing *Simmondisiachinesis* oil

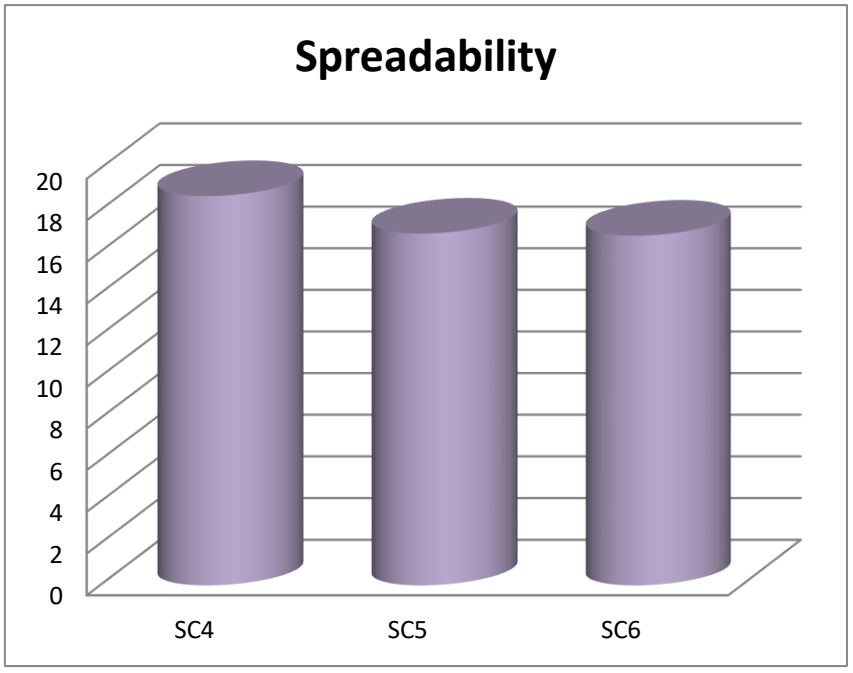


Figure No. 6.13: Spreadability values of gel formulations containing *Simmondisiachinesis* oil

The value of Spreadability shows that the prepared formulations are easily spreadable except formulation 1 and 2 of respective oil. Higher the value of carbopol shows the resistance in

application to the skin hence higher concentration of carbopol gel formulations may not be suitable to apply on skin. In short Spreadability decrease with the increase in the concentration of the polymer The Spreadability is considered as one of the important as shows the behavior of gel which comes out from the tube.

Determination of Drug content:

Formulation	Drug content (%)
BL1	98± 0.58
BL2	98± 0.76
BL3	97± 0.5
BL4	97.5± 0.29
BL5	98± 0.58
BL6	98.5±0.30
BL7	97±0.76
BL8	97.5± 0.28
BL9	96±0.57

Table No 6.14. Drug content values of gel formulations containing *Buchananialanzan* oil

Formulation	Drug content (%)
SC1	98±0.76
SC2	97± 0.5
SC3	97.5± 0.29
SC4	98± 0.58
SC5	98± 0.59
SC6	97.5± 0.77
SC7	97± 0.29
SC8	98.5± 0.28
SC9	98± 0.57

Table No 6.15: Drug content values of gel formulations containing *Simmondisiachinesis* oil

Drug content of formulated gels shows acceptable range as it may be consider that the

formulations contents equal amount of drug in it. Which shows that the drug s present near about 100% in each formulation

Skin irritation test:

Formulation Code	Skin irritation score
BL1	1
BL2	1
BL3	0.5
BL4	0.5
BL5	0
BL6	0
BL7	2
BL8	1.5
BL9	1.5

Table No. 6.16: Skin irritation study of gel formulations containing *Buchananialanzan* oil

Formulation Code	Skin irritation score
SC1	0
SC2	1.5
SC3	1
SC4	0.5
SC5	0
SC6	0.5
SC7	1.5
SC8	2
SC9	2

Table No 6.17: Skin irritation study of gel formulations containing *Simmondisiachinesis* oil

Prepared gel formulations were subjected to skin irritation test and allotted score depending on the reaction shown on the skin of volunteers the score below 2 shows

acceptability of gel formulations to be applied on skin.

AFM-Carbopol control gel-without drug (F1)

Area Roughness --

Area 2.52nm^2

Sa 330.26nm

Sq 410.79nm

Sy 2136.9nm

Sp 1013.5nm

Sv -1123.4nm

Sm -18.626fm

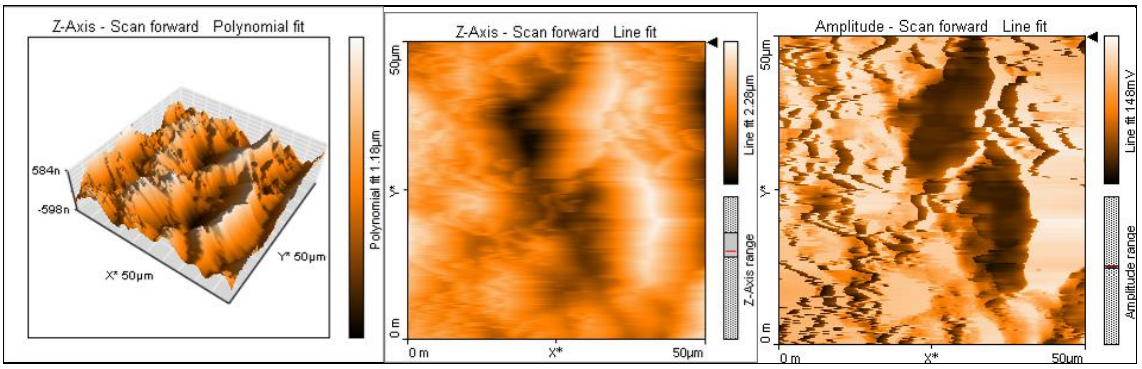


Figure No: AFM-Carbopol control gel-without drug (F1)

AFM-Carbopol control gel-without drug (F2)

Area 2.52nm^2

Sa 205.25nm

Sq 254.79nm

Sy 1611.8nm

Sp 866.97nm

Sv -744.86nm

Sm -18.626fm

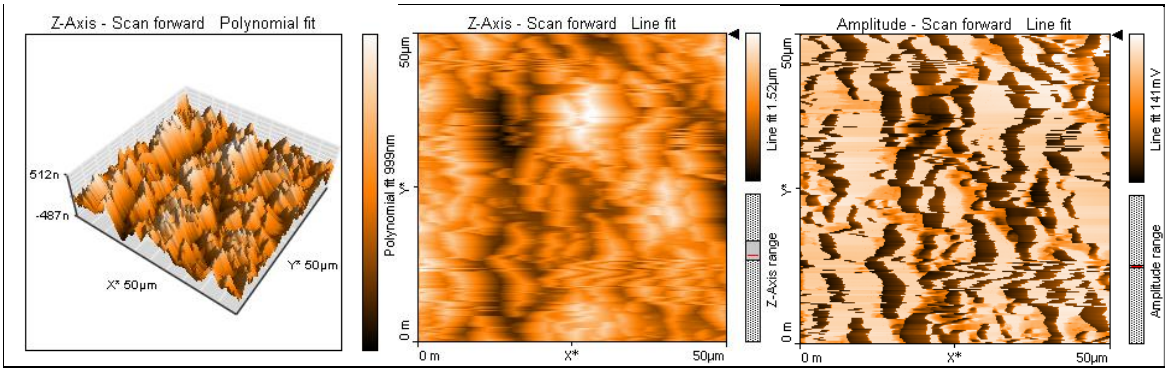


Figure No: AFM-Carbopol control gel-without drug (F2)

AFM-Carbopol control gel-without drug (F3)

Area	2.52nm^2
Sa	247.07nm
Sq	312.08nm
Sy	1754.3nm
Sp	875.95nm
Sv	-878.3nm
Sm	-18.626fm

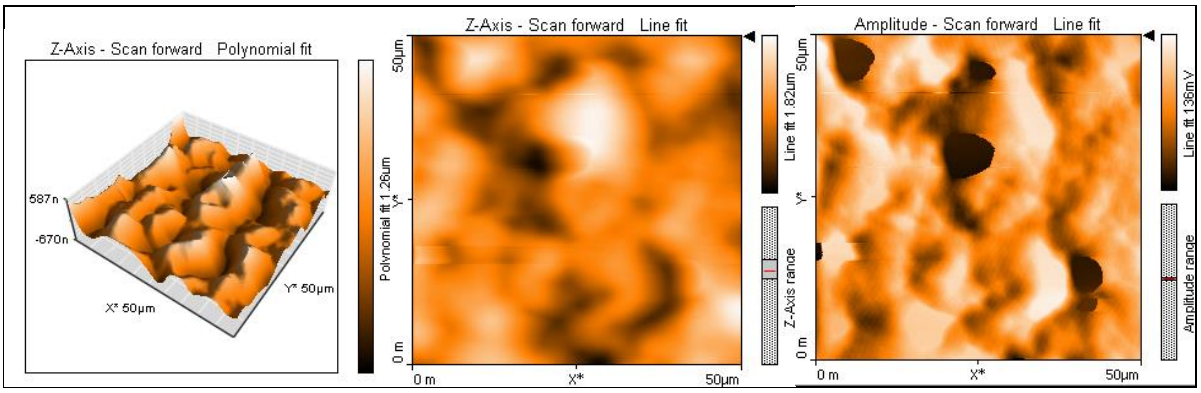


Figure No: AFM-Carbopol control gel-without drug (F3)

AFM-Carbopol gel(F1)

Area	2.52nm^2
Sa	397.01nm
Sq	502.88nm
Sy	4.7877µm
Sp	1962.6nm
Sv	-2825.1nm
Sm	-18.629fm

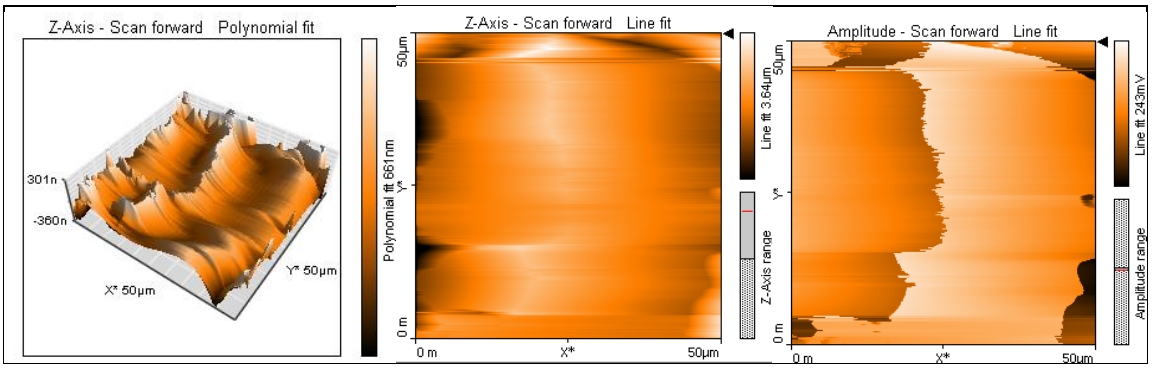


Figure No: AFM-Carbopol gel (F1)

AFM-Carbopol gel(F2)

Area	2.52nm^2
Sa	609.05nm
Sq	766.5nm
Sy	5.4884µm
Sp	2646.9nm
Sv	-2841.5nm
Sm	-20.339fm

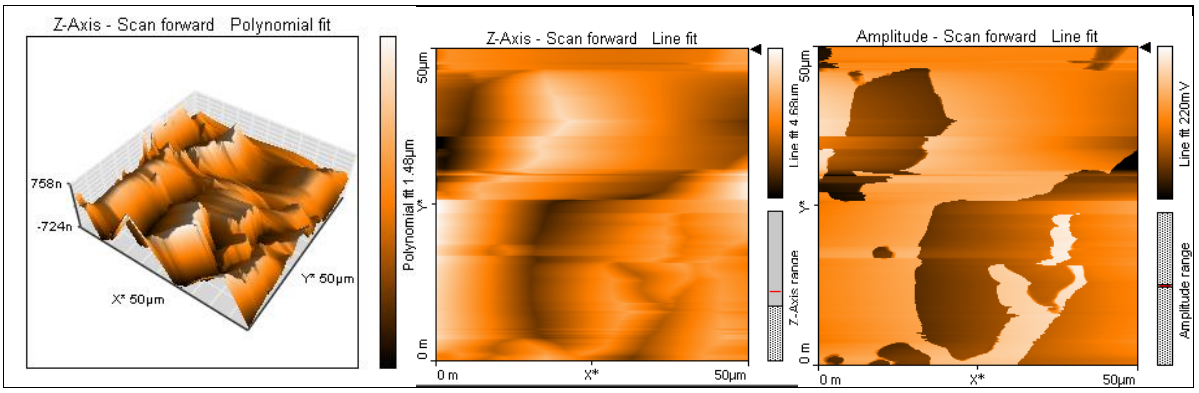


Figure No: AFM-Carbopol gel (F2)

AFM-Carbopol gel(F3)

Area	2.52nm^2
Sa	892.29nm
Sq	1298.7nm
Sy	7.5323µm
Sp	3.4495µm
Sv	-4.0828µm
Sm	-18.626fm

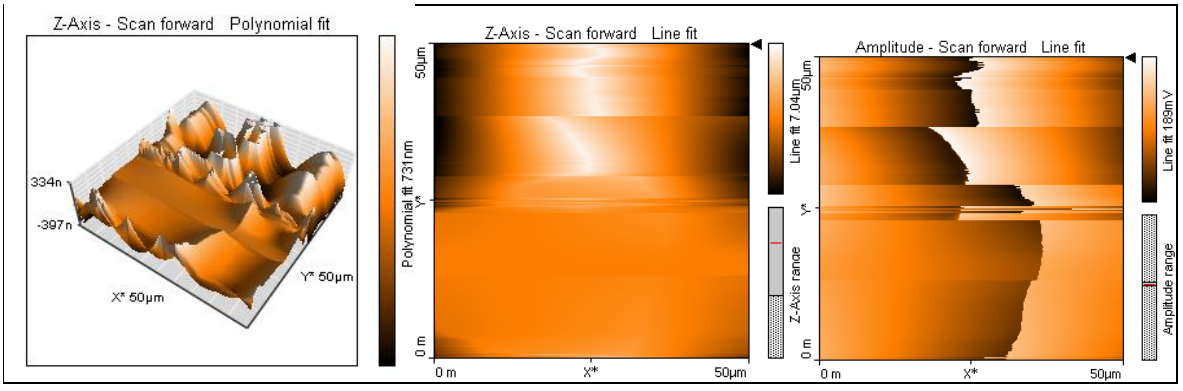
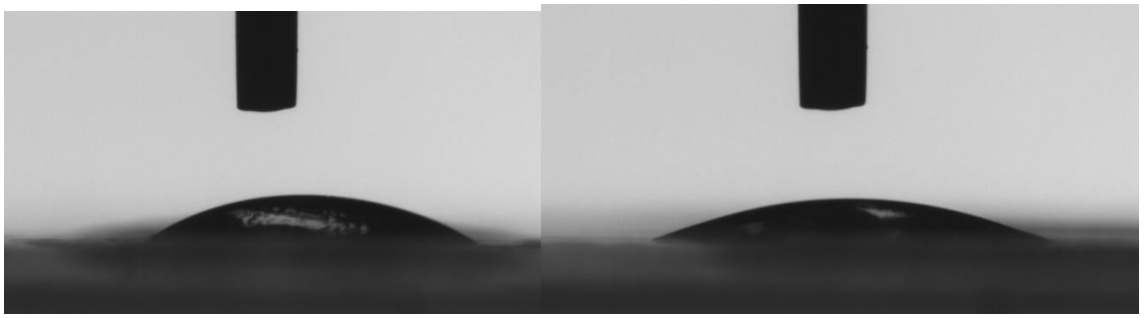


Figure No: AFM-Carbopol gel (F3)

CONTACT ANGLE

Three methods for modeling and predicting water contact angle for a heterogeneous series of pharmaceuticals using computed molecular descriptors and statistical analysis were developed. A number of theoretical molecular descriptors that were related to the structure and physicochemical properties were computed for compounds (n=34) whose experimental water contact angle was known. Thereafter, the descriptors were subjected to partial least squares projections to latent structures analysis. Three multivariate models were derived that allowed theoretical prediction of water contact angle for structurally heterogeneous materials. The R^2 and Q^2 values of the models ranged from 0.57 to 0.80 and 0.42 to 0.66, respectively. The models had moderate predictive ability and provided useful information about the molecular and physicochemical properties that affect material water contact angle.

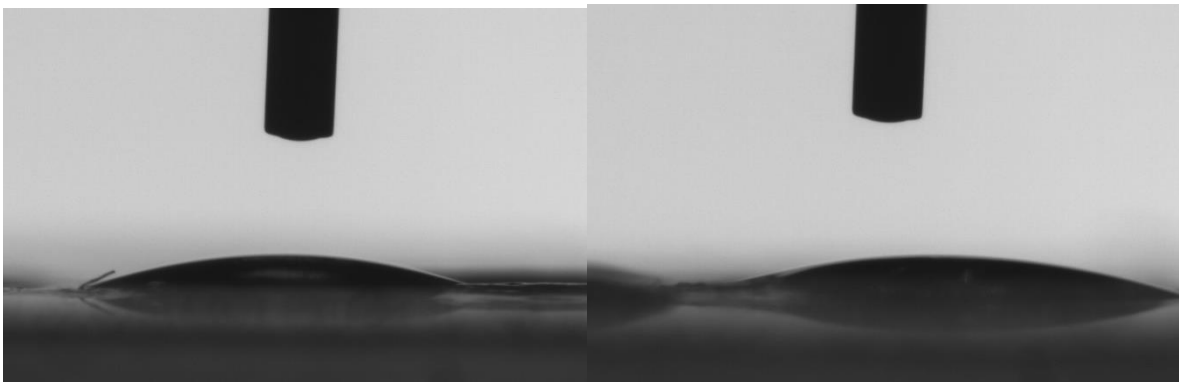
Contact angle of DI



Contact angle of Drop 1 and 5

Run-No	CA(M)[°]	IFT[mN/m]	Err[µm]	Vol[µL]
1	34.5929298	0	-999	-999
2	29.2261944	0	-999	-999

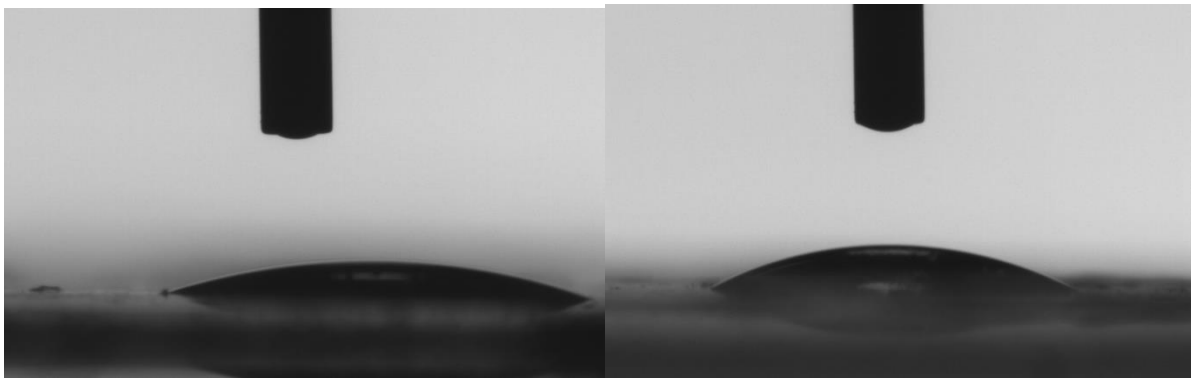
Contact angle of E



Contact angle of Drop 10 and 11

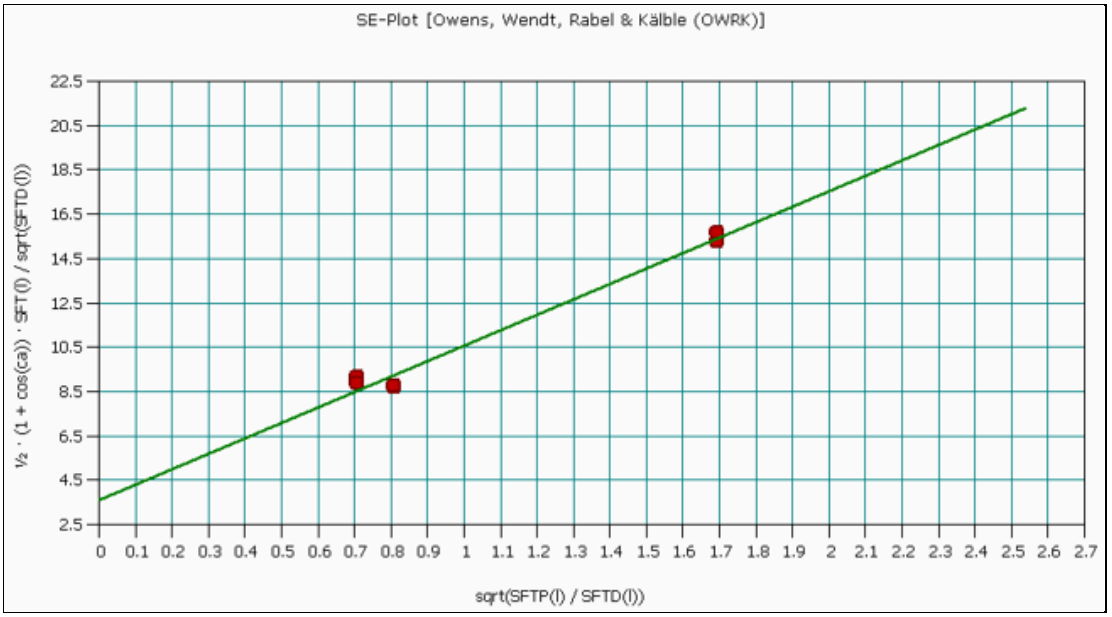
Run-No	CA(M)[°]	IFT[mN/m]	Err[µm]	Vol[µL]
1	18.4725018	0	-999	-999
2	17.5838318	0	-999	-999

Contact angle of F



Contact angle of Drop 8 and 9

Run-No	CA(M)[°]	IFT[mN/m]	Err[µm]	Vol[µL]
1	19.1353989	0	-999	-999
2	27.5673218	0	-999	-999



DESIGN EXPERIMENT

To enhance comprehension of the intricate relationships between the independent and dependent variables, 3D response surface plots, 2D contour plots, and perturbation graphs were generated using the Design Expert® software. These graphical representations provided an insightful depiction of how changes in variables influence the responses.

3D response surface plots, 2D contour plots, and perturbation graphs of BLO

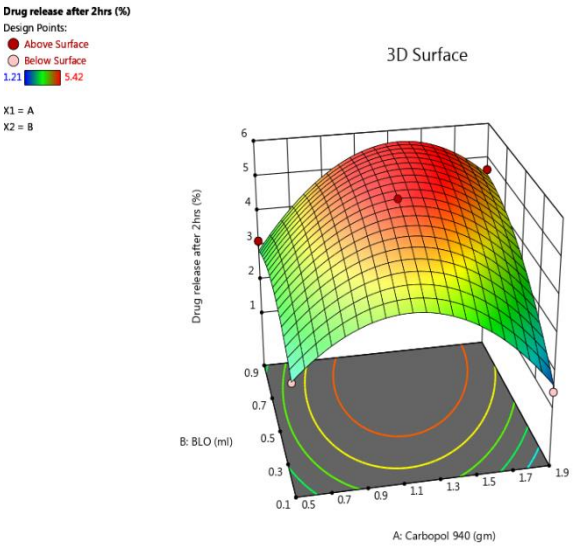


Figure No: 3D Image of BLO after 2 hrs.

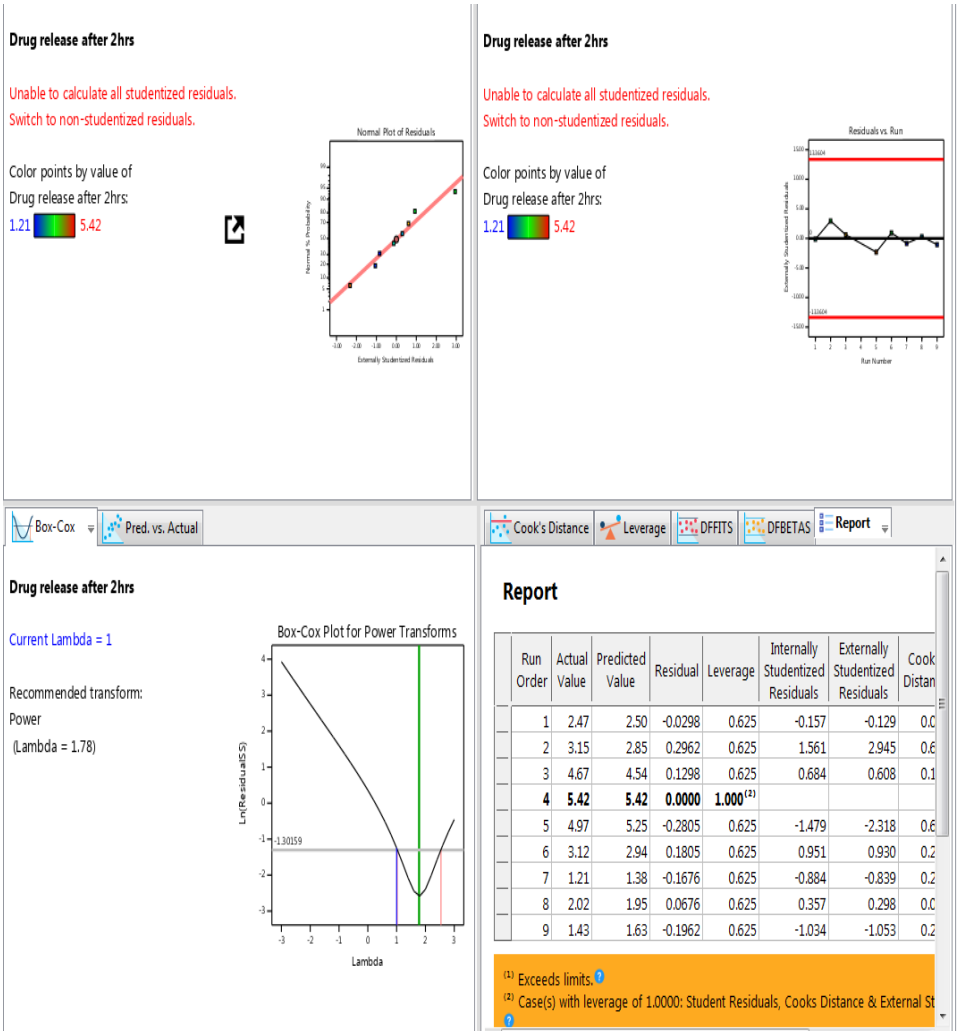


Figure No: Diagnostic analysis of BLO after 2 hrs.

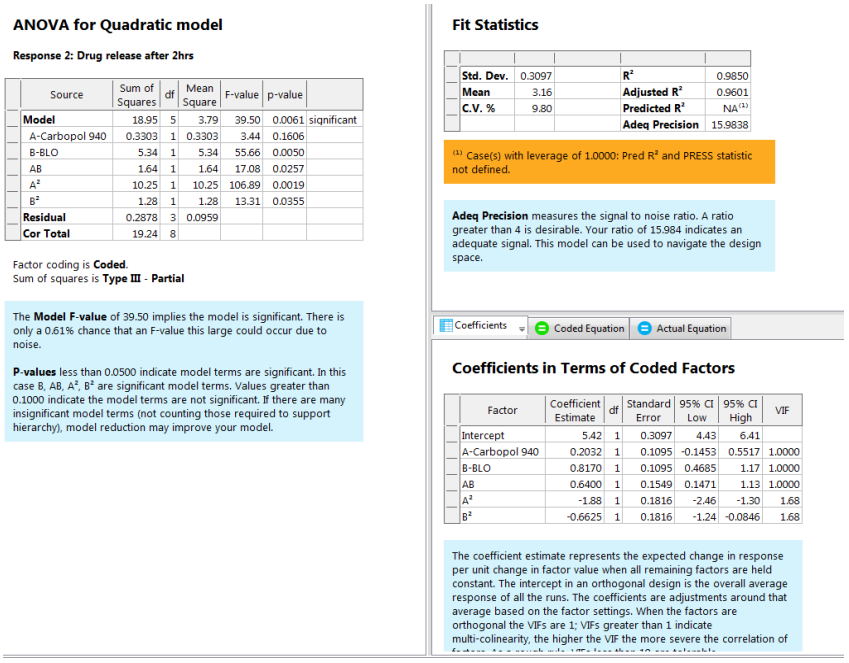


Figure No: ANOVA of BLO after 2 hrs.

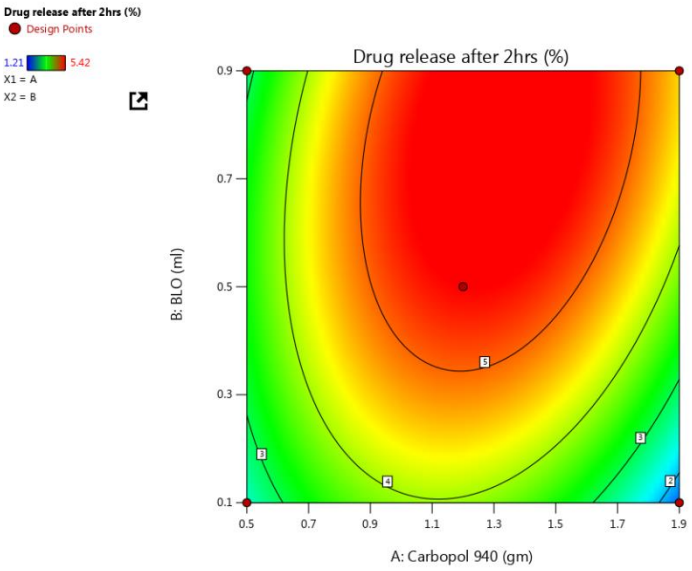


Figure No: Conour of BLO after 2 hrs.

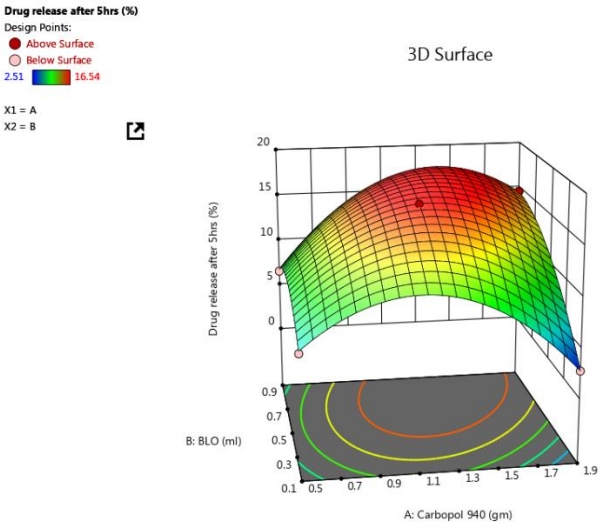


Figure No: 3D Image of BLO after 5 hrs.

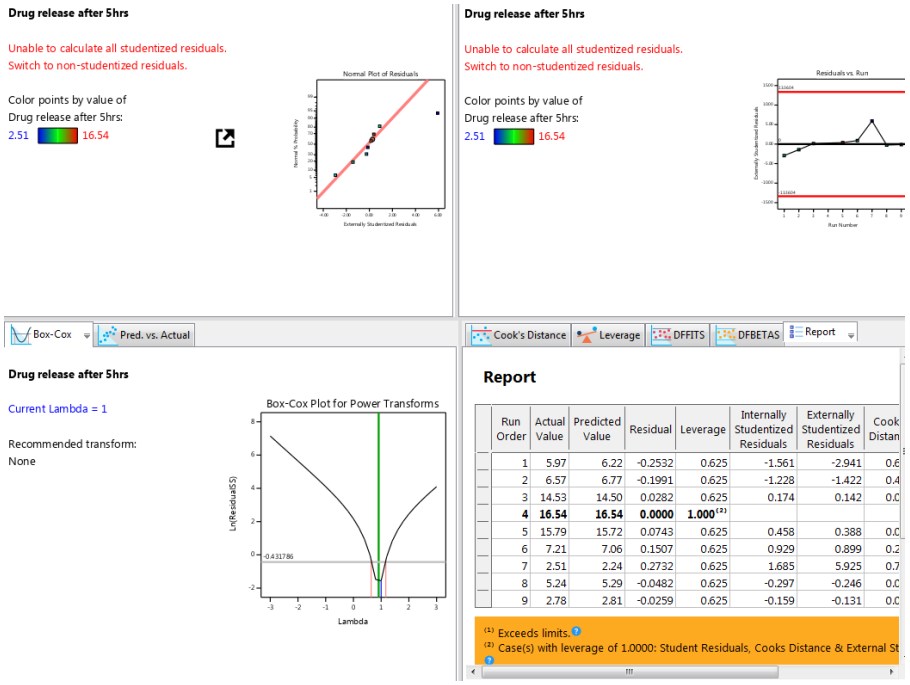


Figure No: Diagnostic analysis of BLO after 5 hrs.

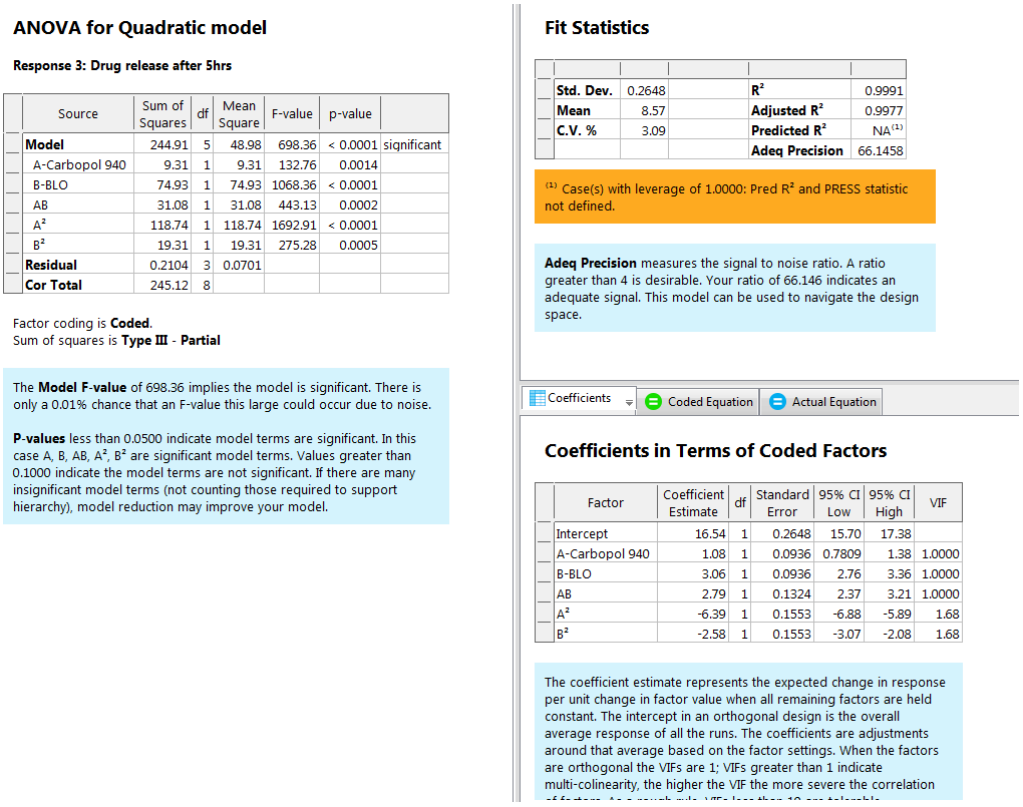


Figure No: ANOVA of BLO after 5 hrs.

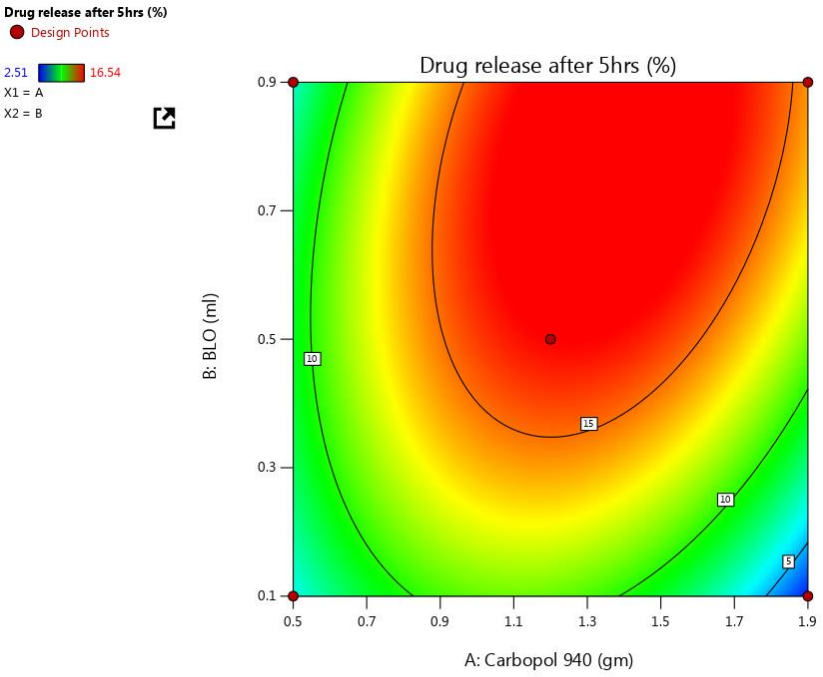


Figure No: Conour of BLO after 5 hrs.

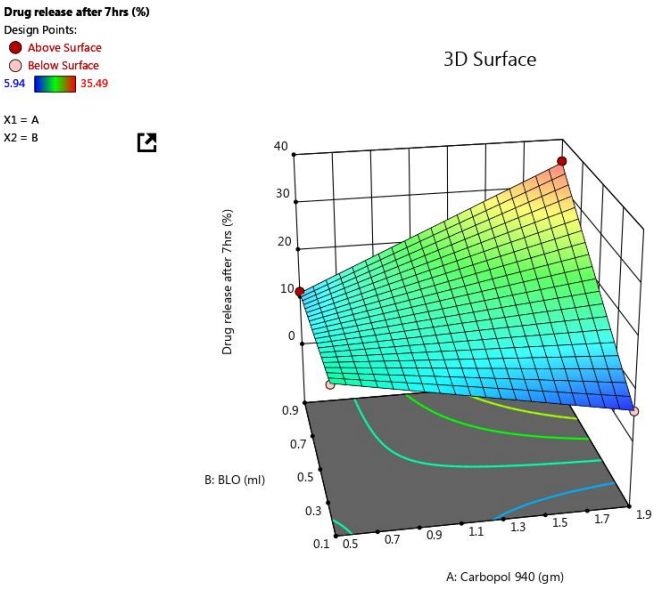


Figure No: 3D Image of BLO after 7 hrs.

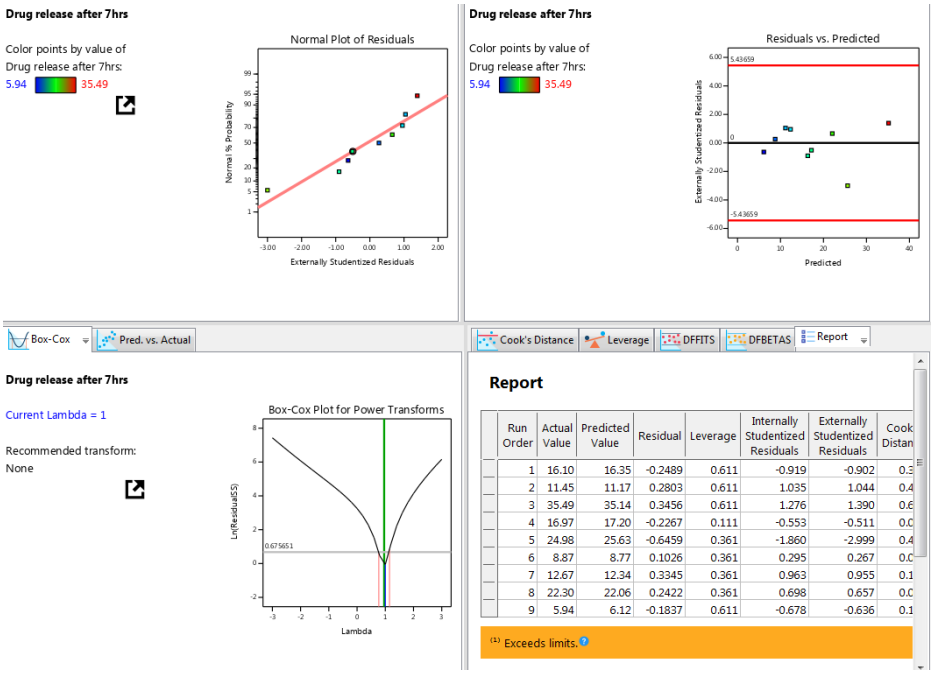
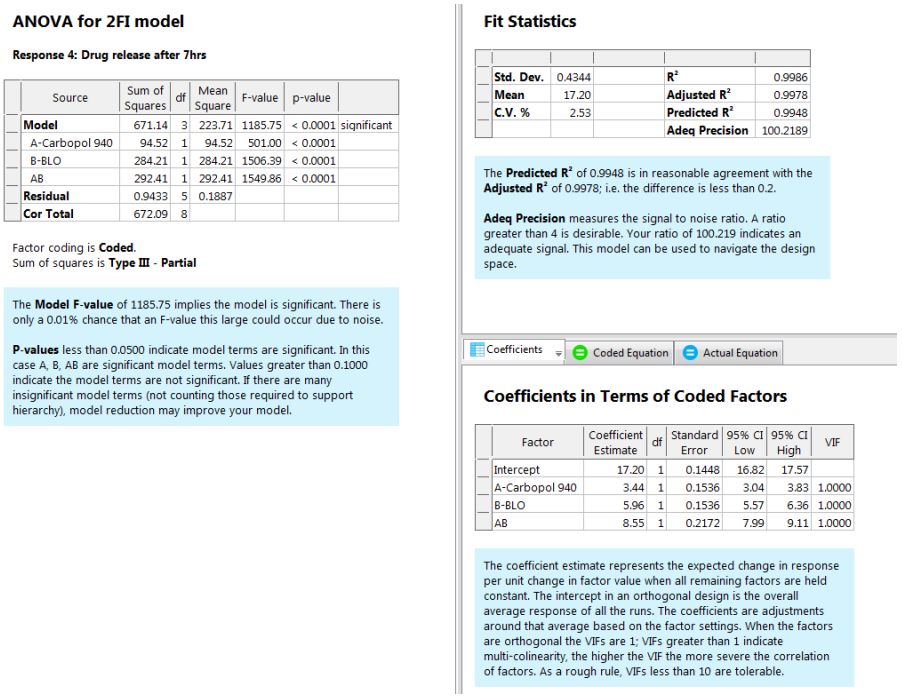


Figure No: Diagnostic analysis of BLO after 7 hrs.



ANOVA for 2FI model

Response 4: Drug release after 7hrs

Source	Sum of Squares	df	Mean Square	F-value	p-value	
Model	671.14	3	223.71	1185.75	< 0.0001	significant
A-Carbopol 940	94.52	1	94.52	501.00	< 0.0001	
B-BLO	284.21	1	284.21	1506.39	< 0.0001	
AB	292.41	1	292.41	1549.86	< 0.0001	
Residual	0.9433	5	0.1887			
Cor Total	672.09	8				

Factor coding is **Coded**.
Sum of squares is **Type III - Partial**

The **Model F-value** of 1185.75 implies the model is significant. There is only a 0.01% chance that an F-value this large could occur due to noise.

P-values less than 0.0500 indicate model terms are significant. In this case A, B, AB are significant model terms. Values greater than 0.1000 indicate the model terms are not significant. If there are many insignificant model terms (not counting those required to support hierarchy), model reduction may improve your model.

Fit Statistics

Std. Dev.	0.4344	R^2	0.9986
Mean	17.20	**Adjusted R^2**	0.9978
C.V. %	2.53	**Predicted R^2**	0.9948
		Adeq Precision	100.2189

The **Predicted R^2** of 0.9948 is in reasonable agreement with the **Adjusted R^2** of 0.9978; i.e. the difference is less than 0.2.

Adeq Precision measures the signal to noise ratio. A ratio greater than 4 is desirable. Your ratio of 100.219 indicates an adequate signal. This model can be used to navigate the design space.

Coefficients | Coded Equation | Actual Equation

Coefficients in Terms of Coded Factors

Factor	Coefficient Estimate	df	Standard Error	95% CI Low	95% CI High	VIF
Intercept	17.20	1	0.1448	16.82	17.57	
A-Carbopol 940	3.44	1	0.1536	3.04	3.83	1.0000
B-BLO	5.96	1	0.1536	5.57	6.36	1.0000
AB	8.55	1	0.2172	7.99	9.11	1.0000

The coefficient estimate represents the expected change in response per unit change in factor value when all remaining factors are held constant. The intercept in an orthogonal design is the overall average response of all the runs. The coefficients are adjustments around that average based on the factor settings. When the factors are orthogonal the VIFs are 1; VIFs greater than 1 indicate multi-colinearity, the higher the VIF the more severe the correlation of factors. As a rough rule, VIFs less than 10 are tolerable.

Figure No: ANOVA of BLO after 7 hrs.

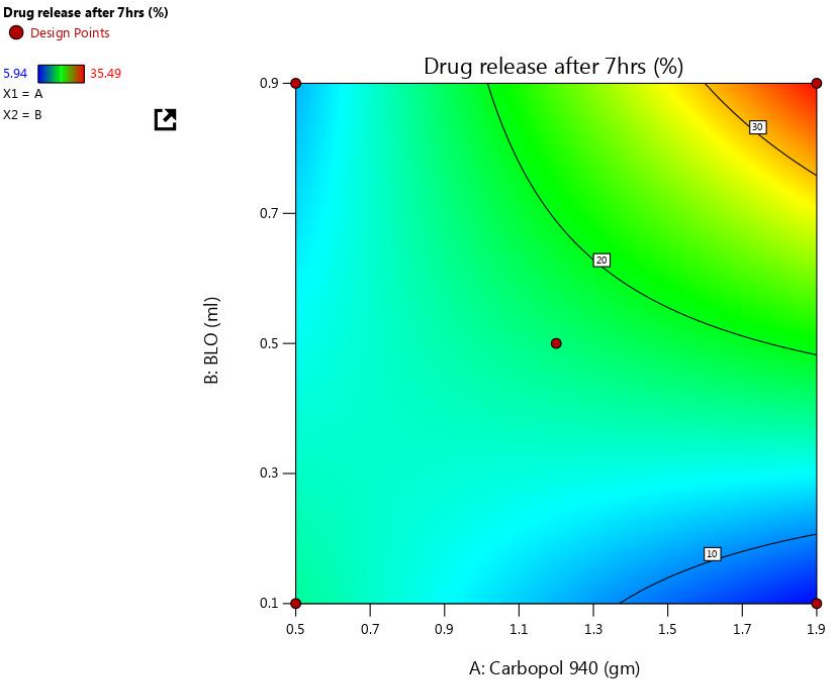


Figure No: Conour of BLO after 7 hrs.

3D response surface plots, 2D contour plots, and perturbation graphs of SCO

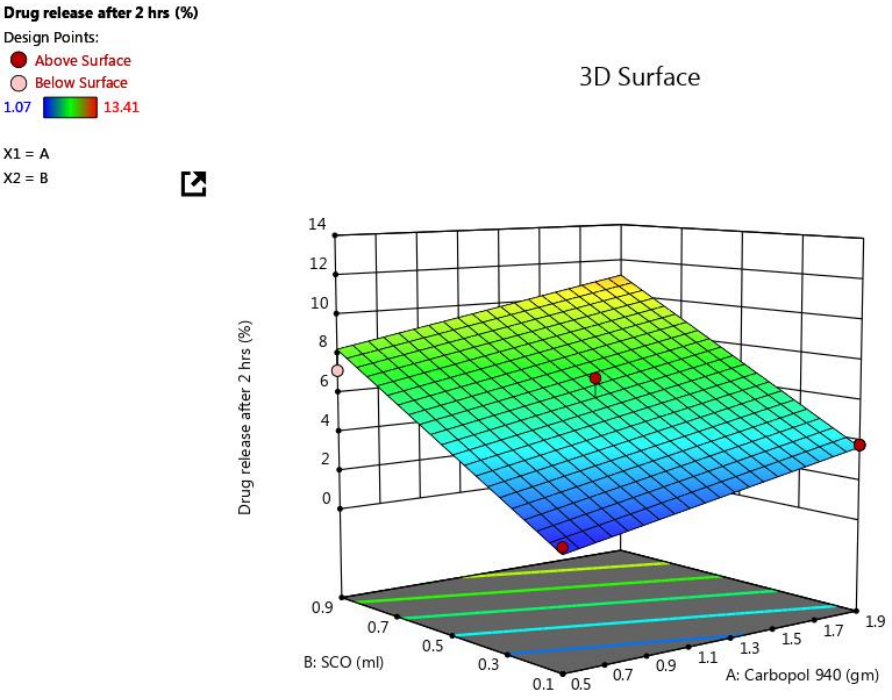


Figure No: 3D Image of SCO after 2 hrs.

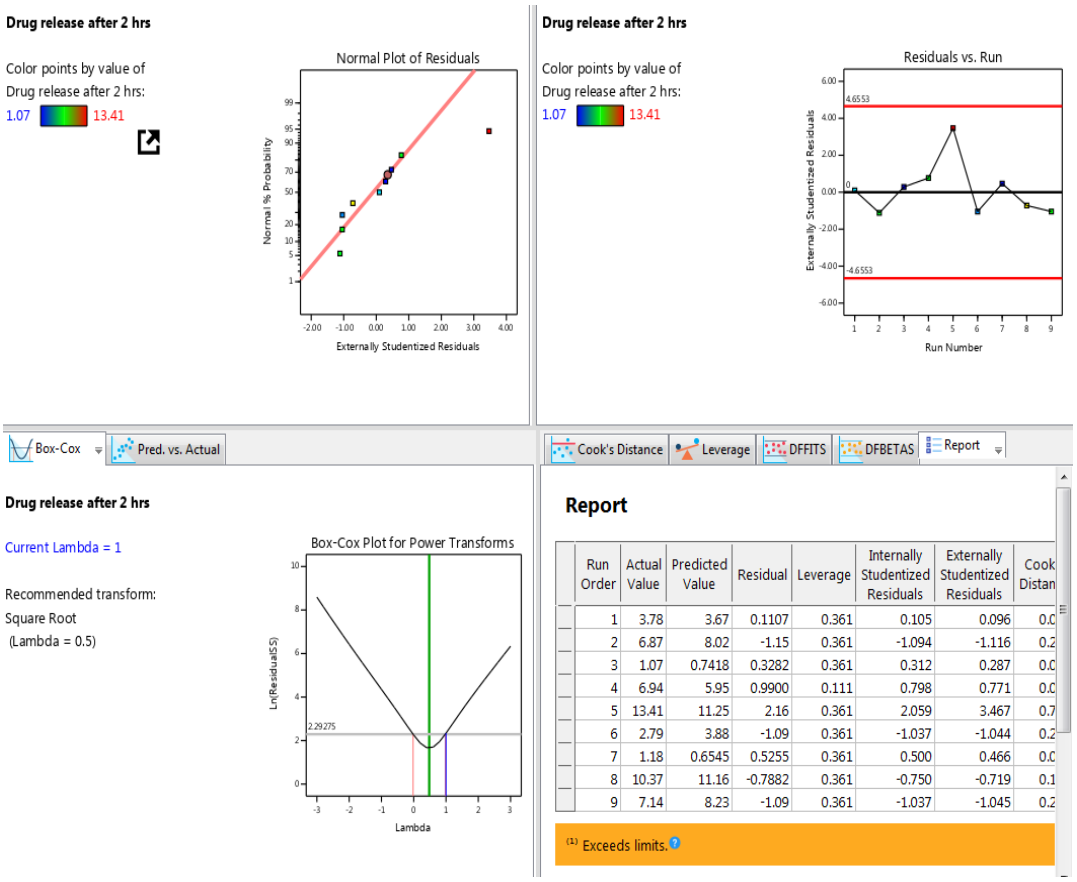


Figure No: Diagnostic analysis of SCO after 2 hrs.

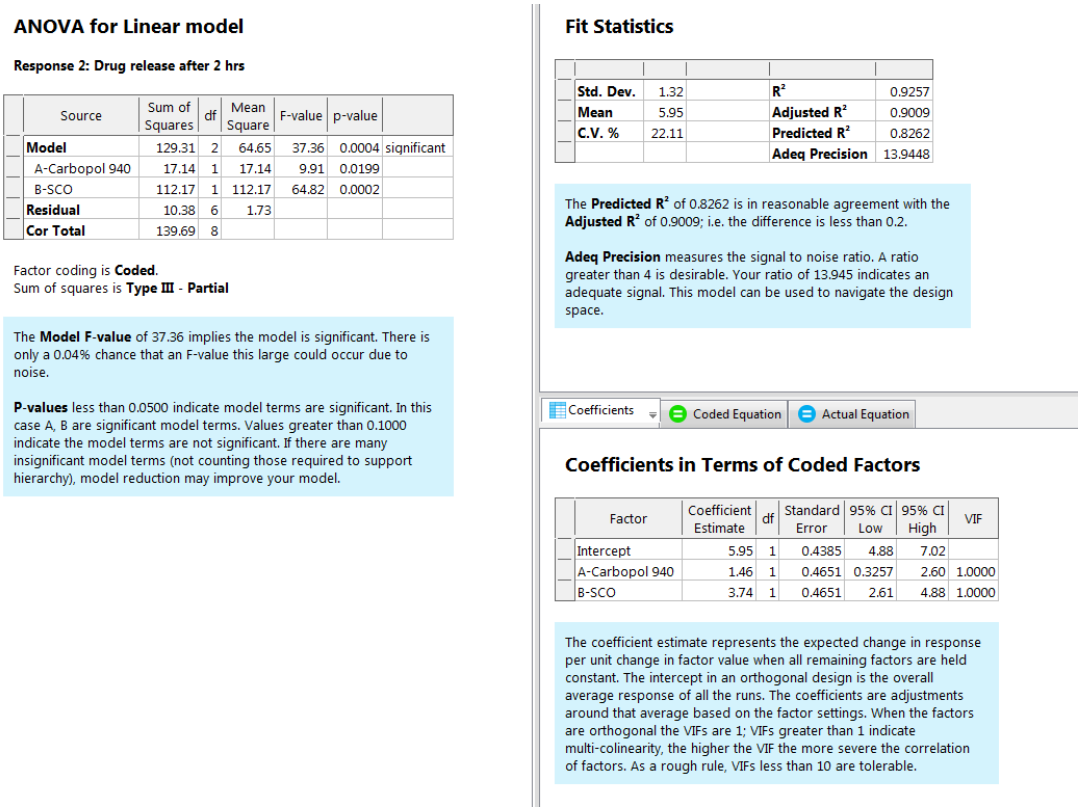


Figure No: ANOVA of SCO after 2 hrs.

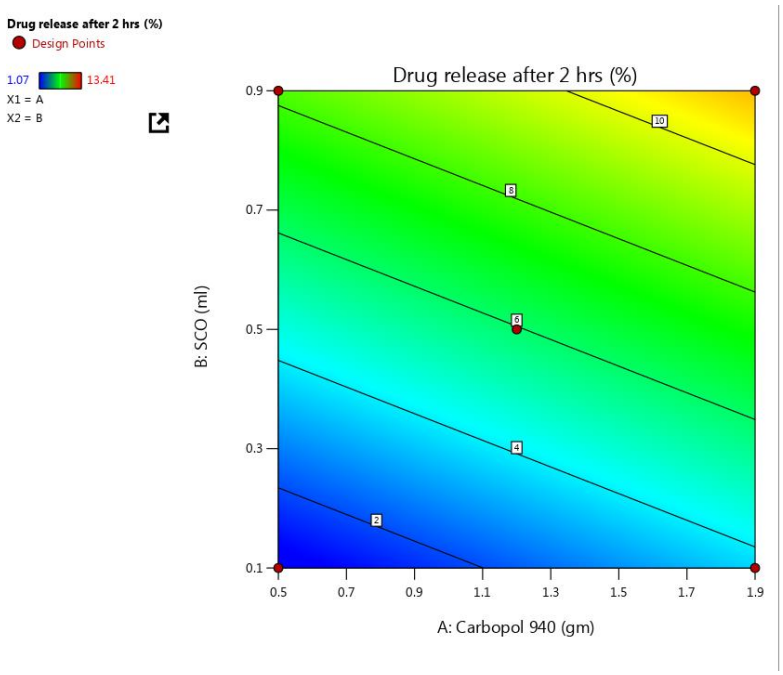


Figure No: Conour of SCO after 2 hrs.

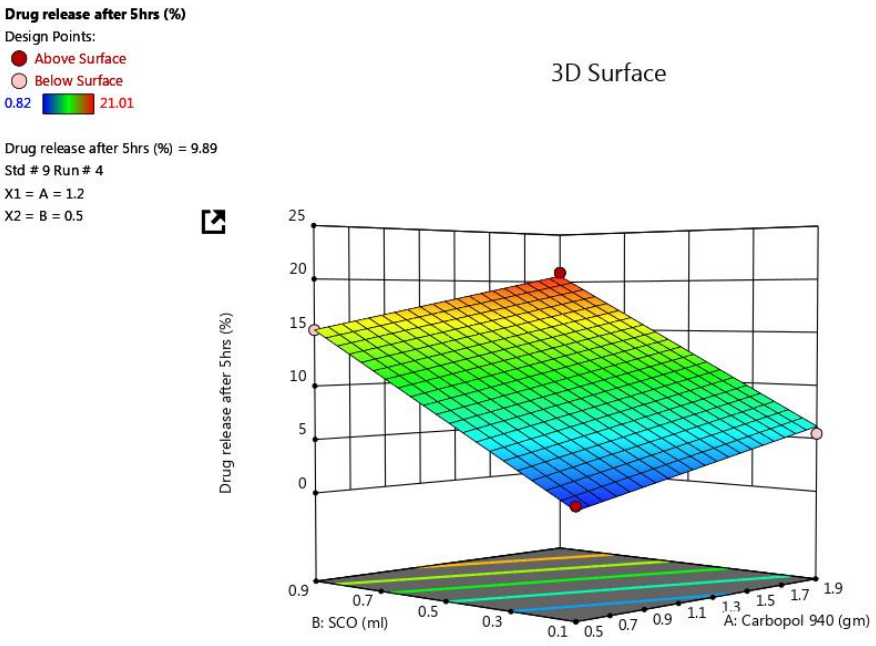


Figure No: 3D Image of SCO after 5 hrs.

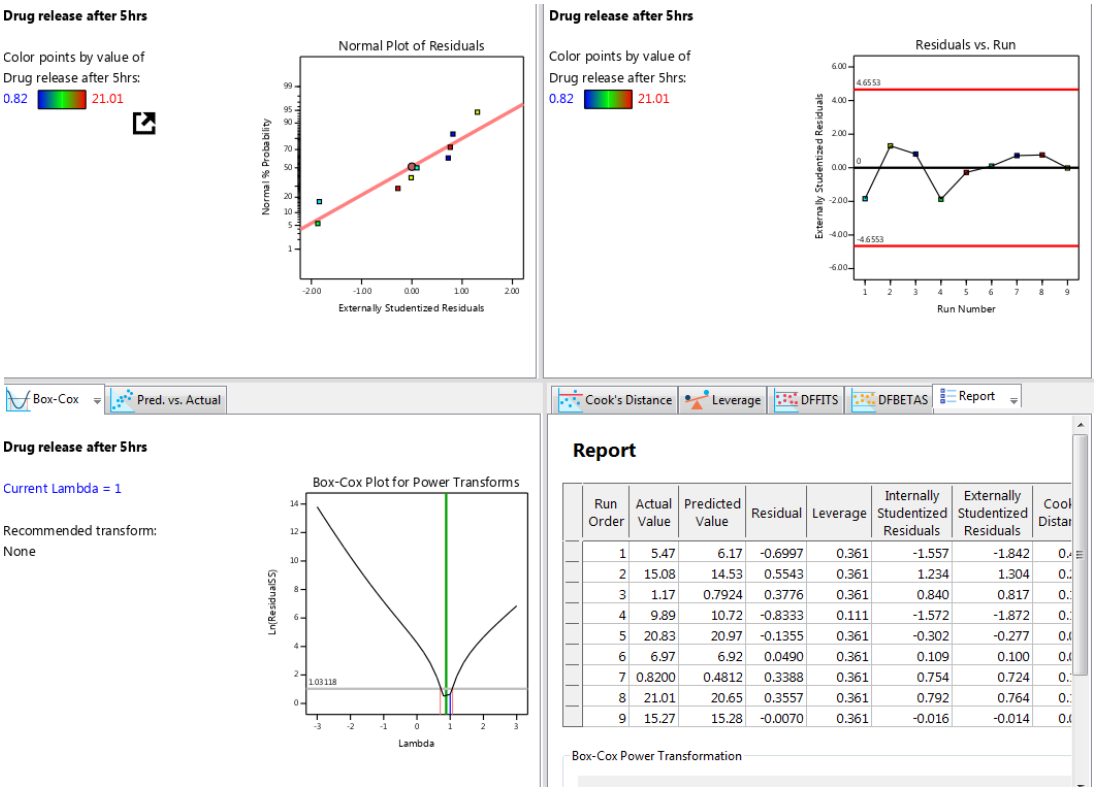


Figure No: Diagnostic analysis of SCO after 5 hrs.

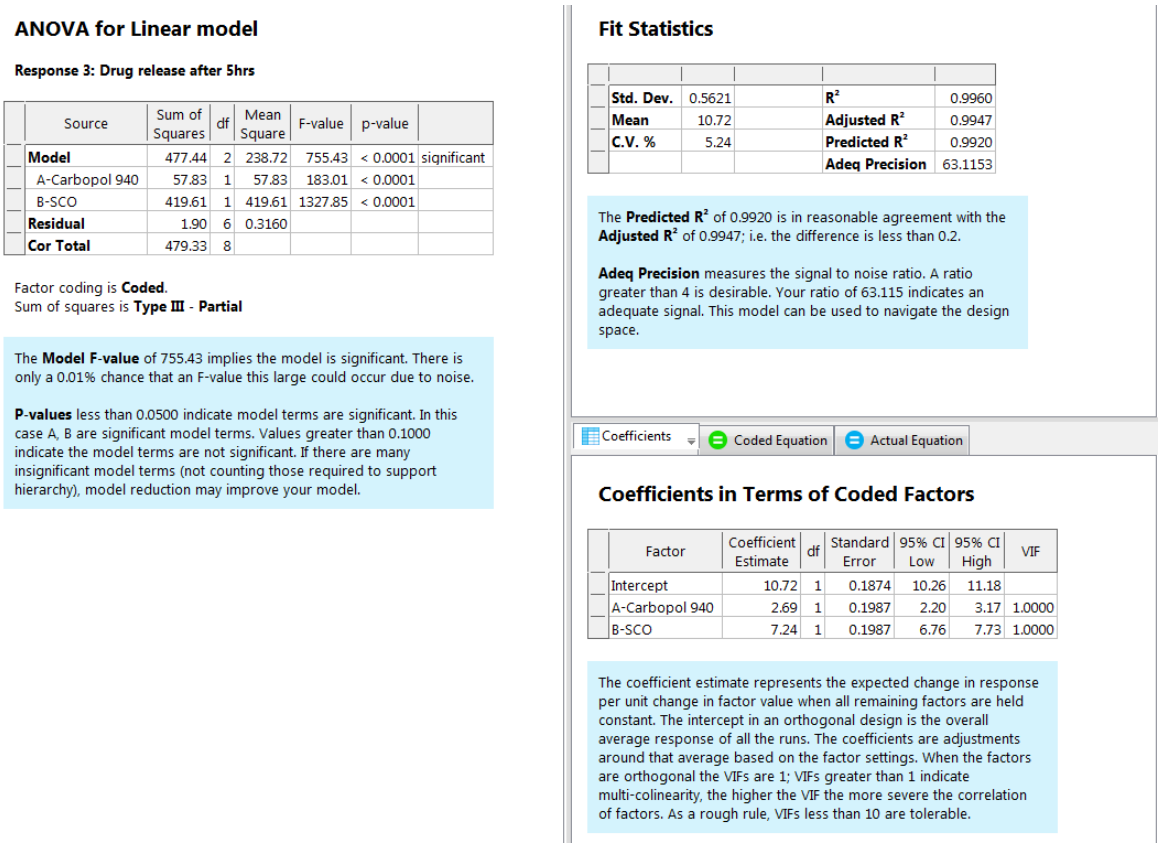


Figure No: ANOVA of SCO after 5 hrs.

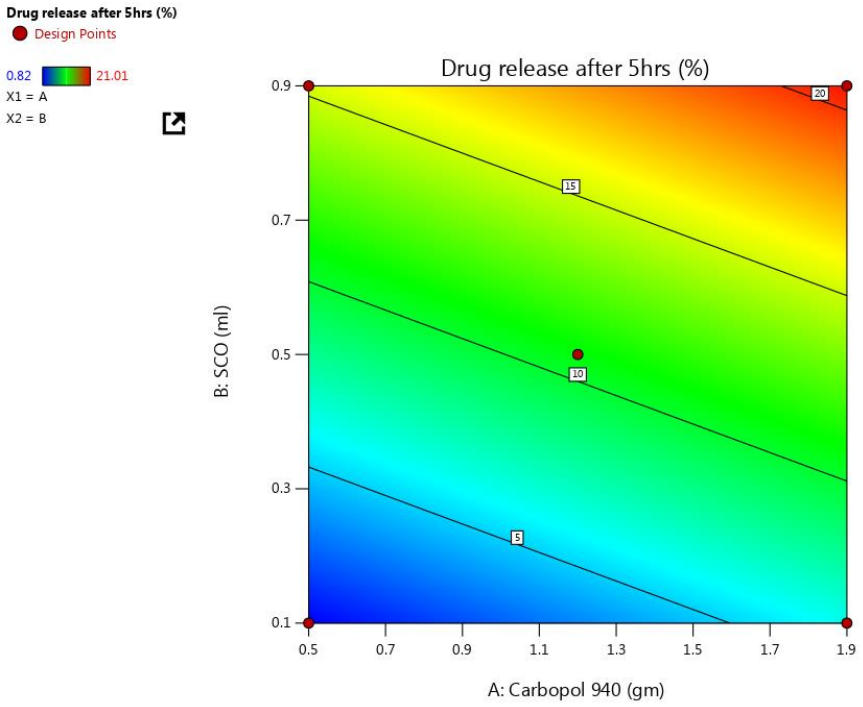


Figure No: Conour of SCO after 5 hrs.

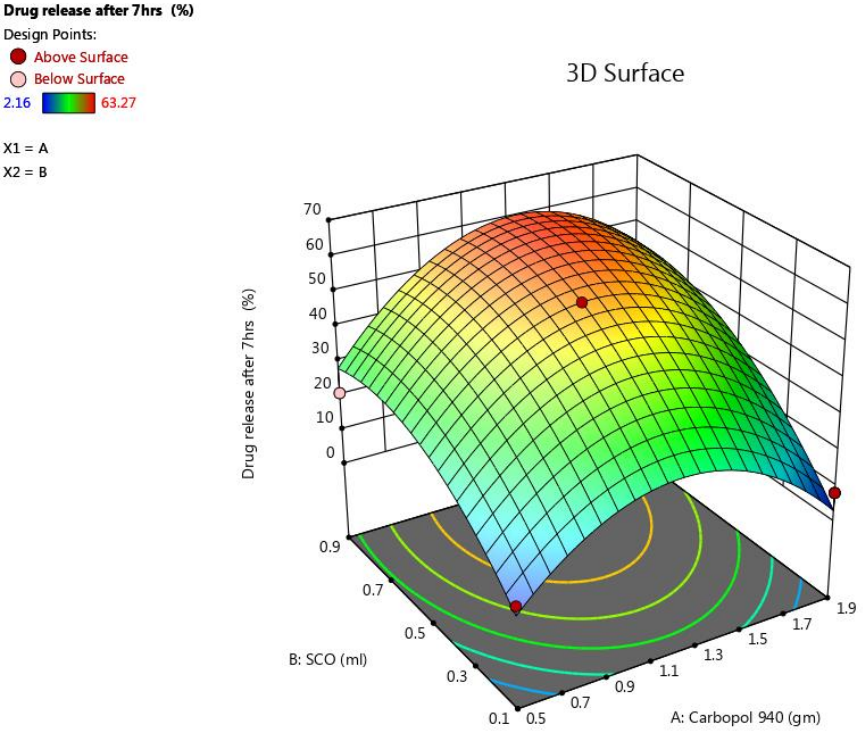


Figure No: 3D Image of SCO after 7 hrs.

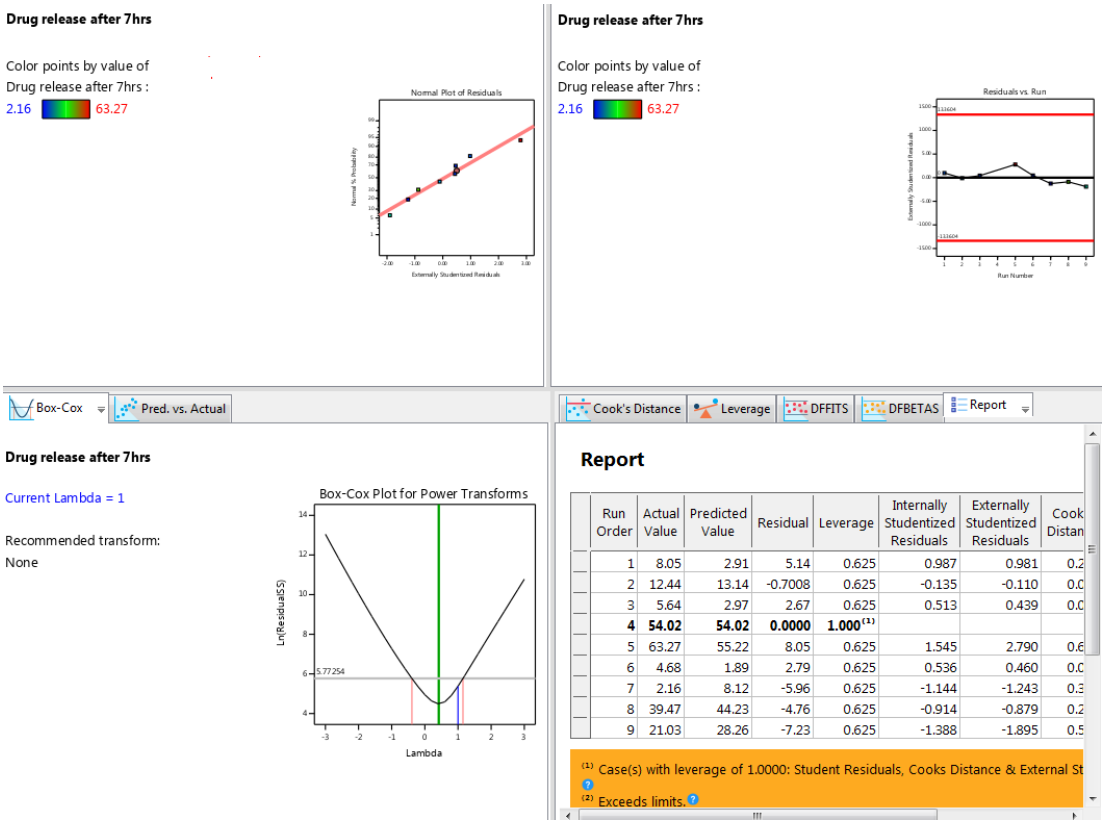


Figure No: Diagnostic analysis of SCO after 7 hrs.

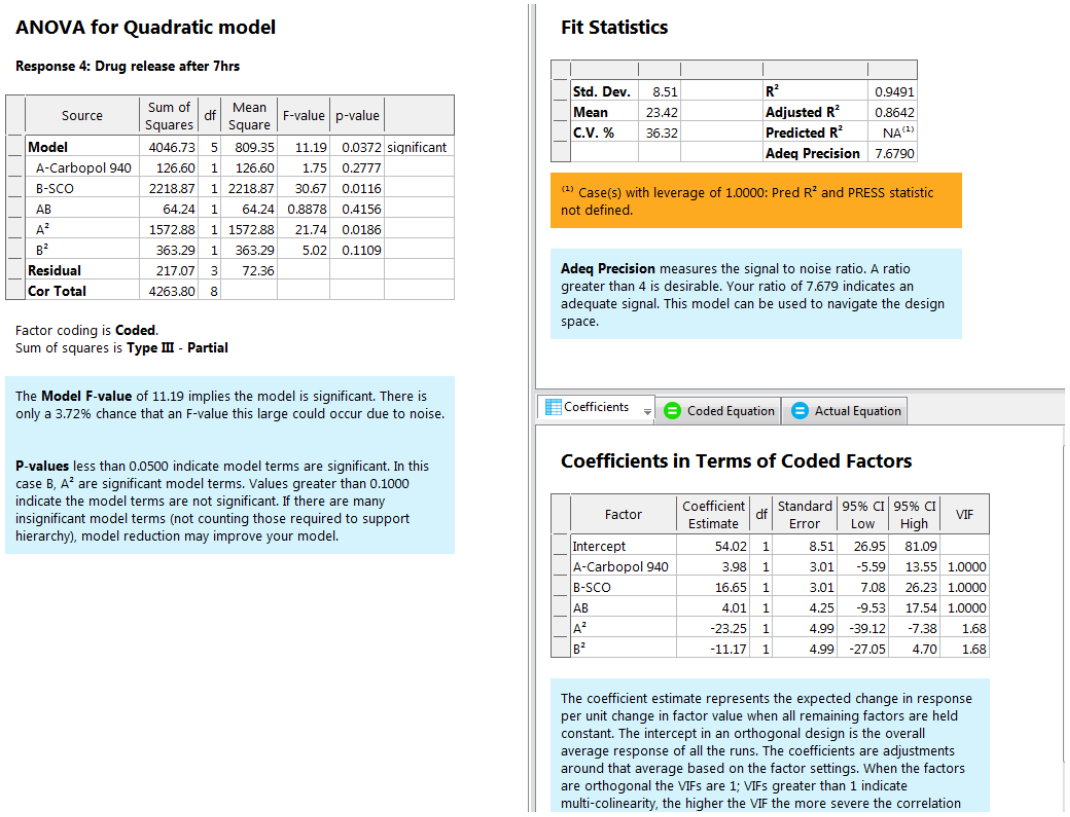


Figure No: ANOVA of SCO after 7 hrs.

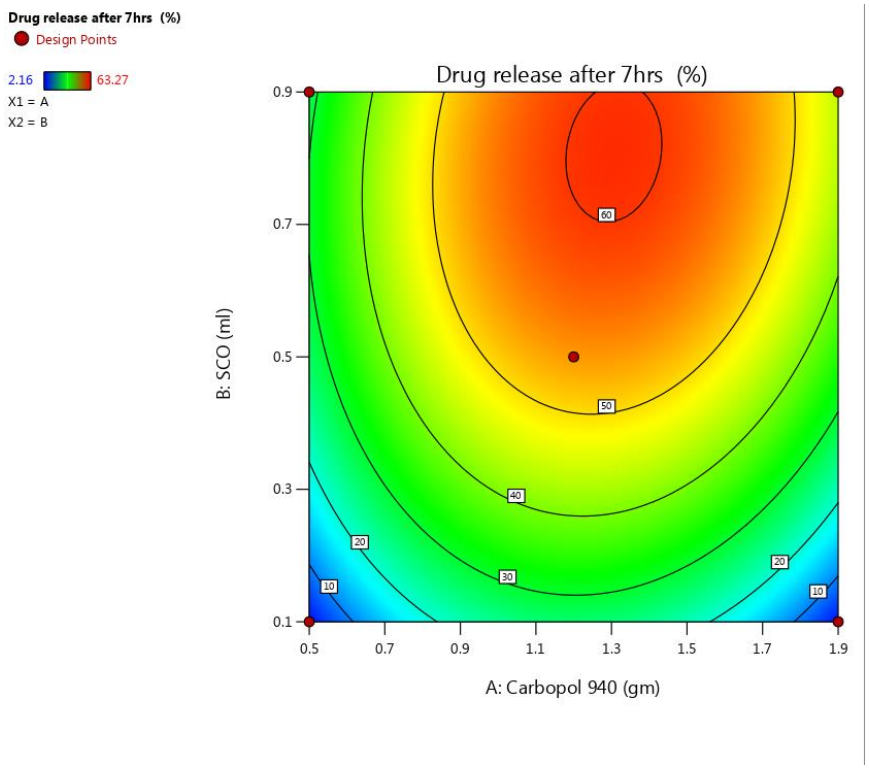
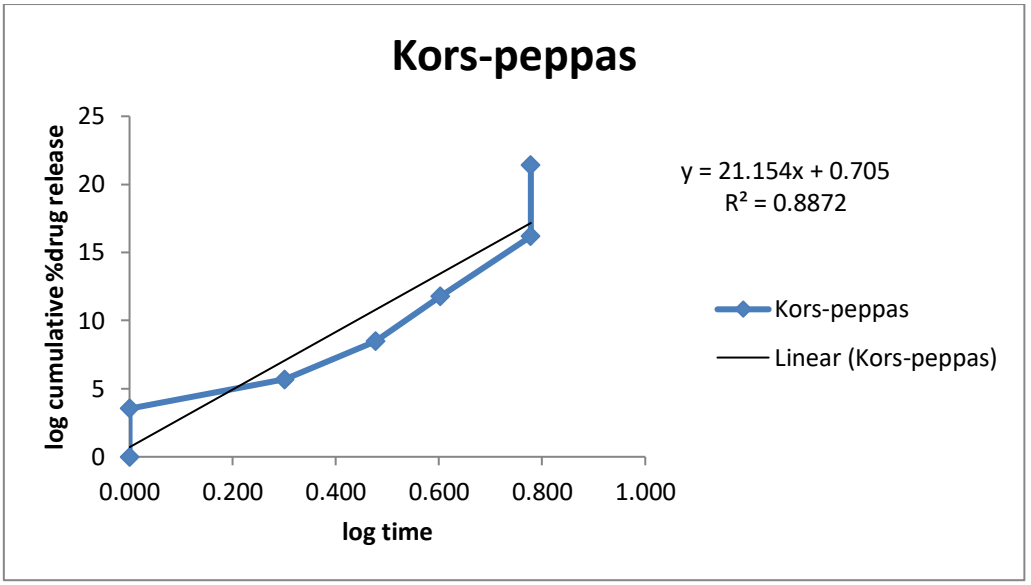
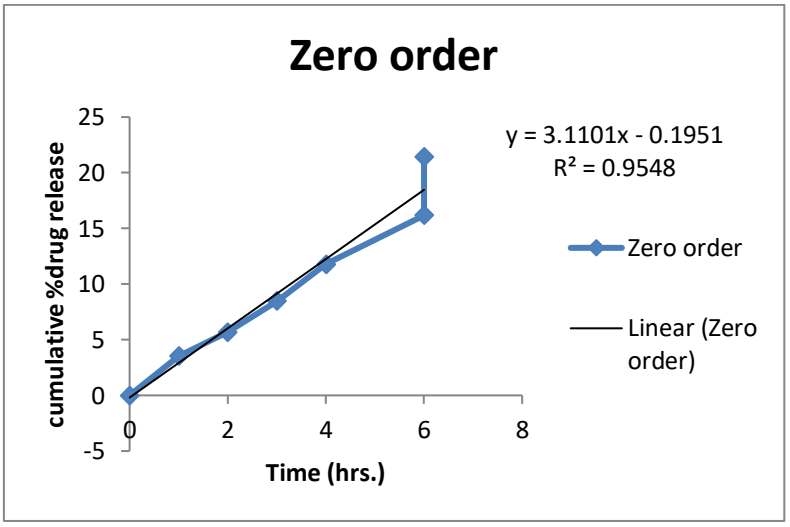


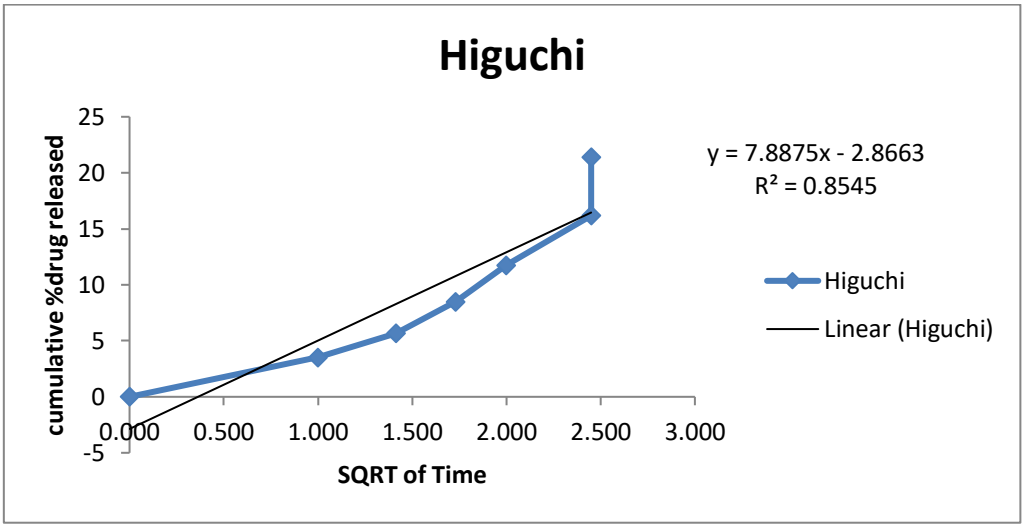
Figure No: Conour of SCO after 7 hrs.

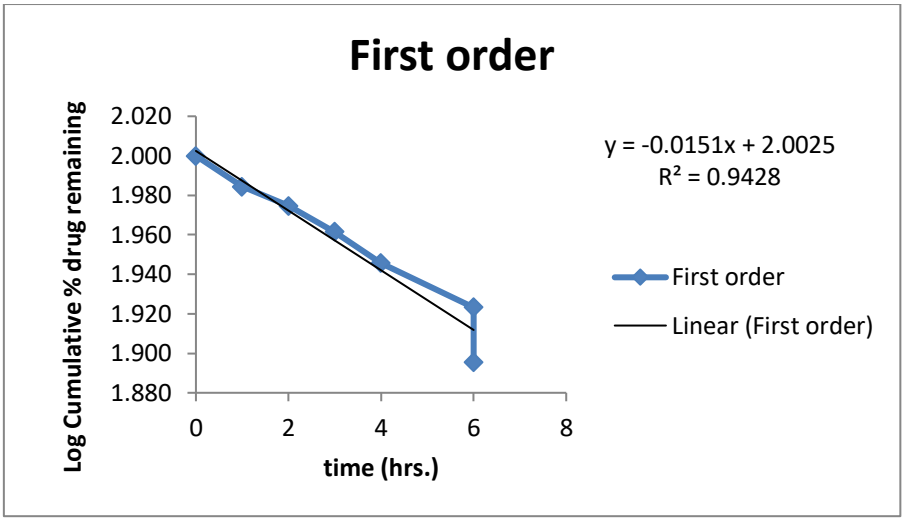
GOAT SKIN DRUG RELEASE OF FORMULATION BL4

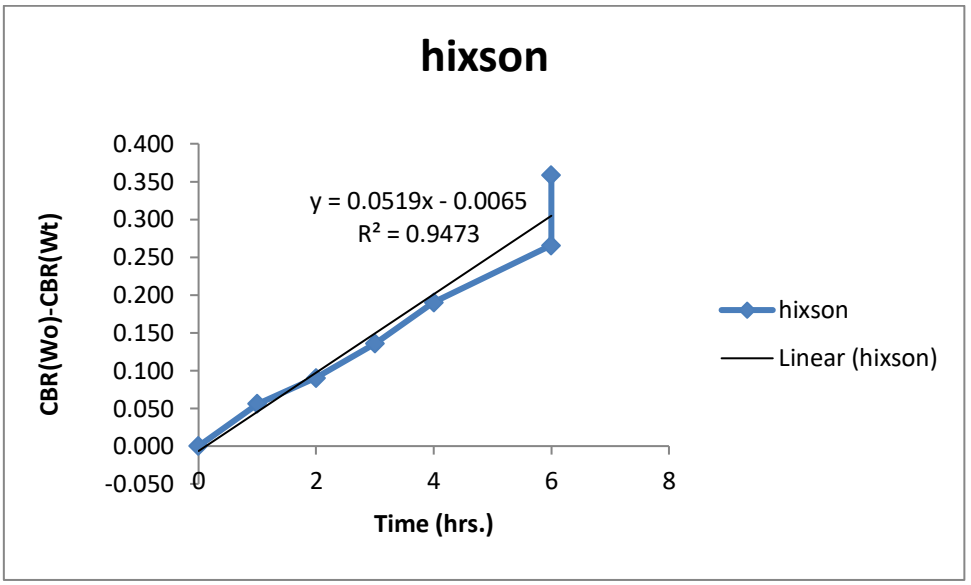
Time (Hr)	cumulative % drug released	% drug remaining	Square root time	log Cumu % drug remainining	log time	log Cumu % drug released	% Drug released	Cube Root of % drug Remaining(Wt)	Wo-Wt
0	0	100	0.000	2.000	0.000	0.000	100	4.642	0.000
1	3.5374	96.4626	1.000	1.984	0.000	0.549	3.5374	4.586	0.056
2	5.681425	94.31858	1.414	1.975	0.301	0.754	2.144025	4.552	0.090
3	8.48515	91.51485	1.732	1.961	0.477	0.929	2.803725	4.506	0.136
4	11.76533	88.23468	2.000	1.946	0.602	1.071	3.280175	4.452	0.190
6	16.18165	83.81835	2.449	1.923	0.778	1.209	4.416325	4.376	0.266
6	21.40428	78.59573	2.449	1.895	0.778	1.331	5.222625	4.284	0.358
7	27.10335	72.89665	2.646	1.863	0.845	1.433	5.699075	4.177	0.465


Kors-peppas
log cumulative %drug release
25
20
15
10
5
0
0.000
0.200
0.400
0.600
0.800
1.000
log time
y = 21.154x + 0.705
R² = 0.8872
Kors-peppas
Linear (Kors-peppas)

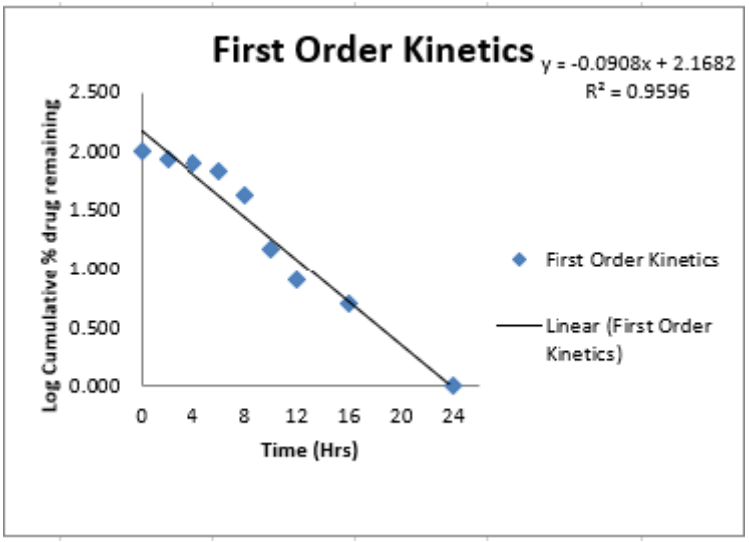

Zero order
cumulative %drug release
25
20
15
10
5
0
-5
0
2
4
6
8
Time (hrs.)
y = 3.1101x - 0.1951
R² = 0.9548
Zero order
Linear (Zero order)

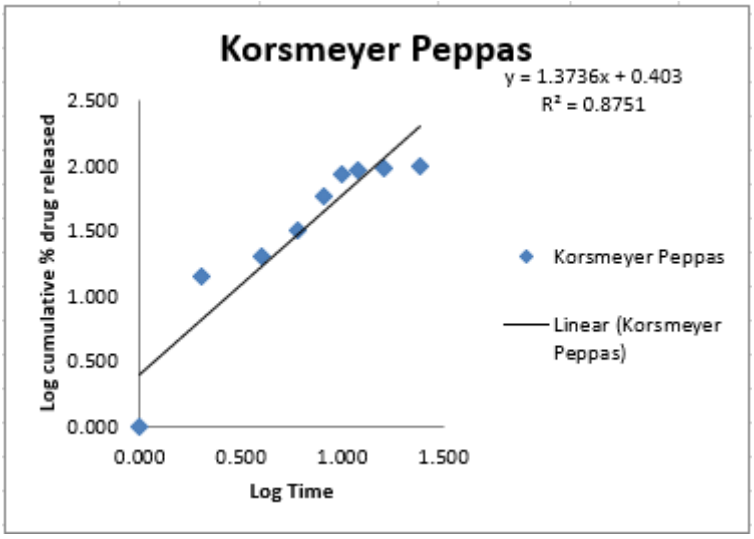

Higuchi
cumulative %drug released
25
20
15
10
5
0
-5
0.000
0.500
1.000
1.500
2.000
2.500
3.000
SQRT of Time
y = 7.8875x - 2.8663
R² = 0.8545
Higuchi
Linear (Higuchi)

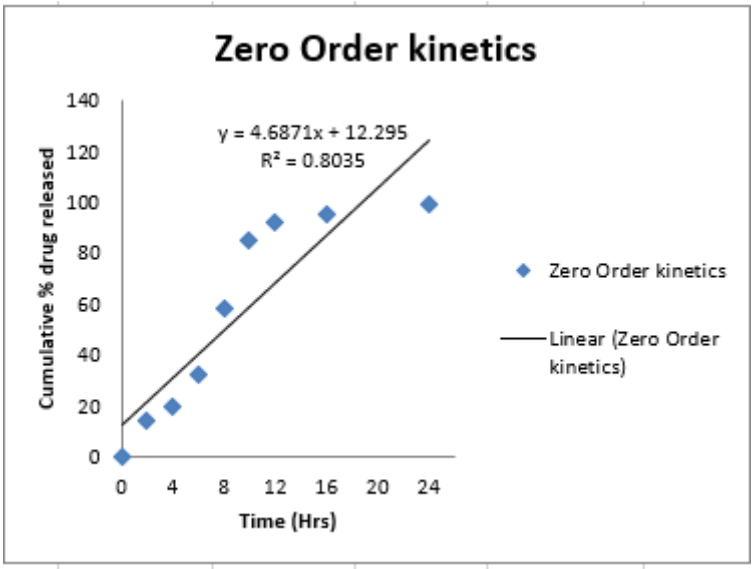


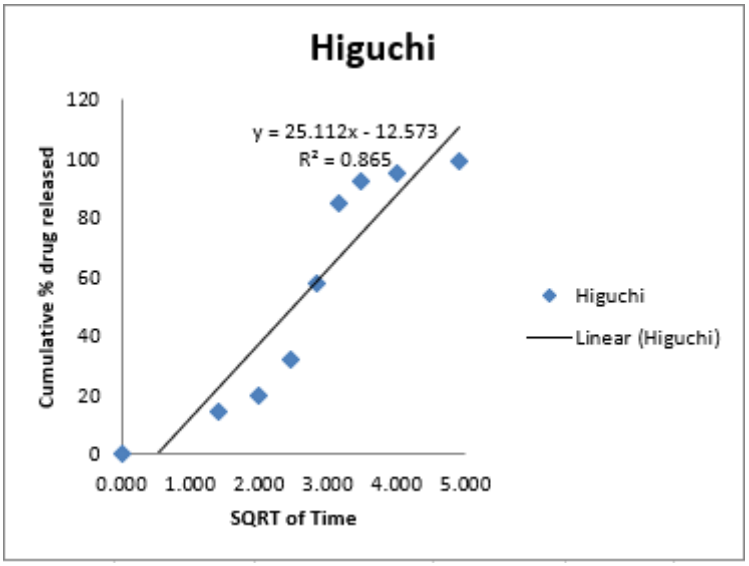


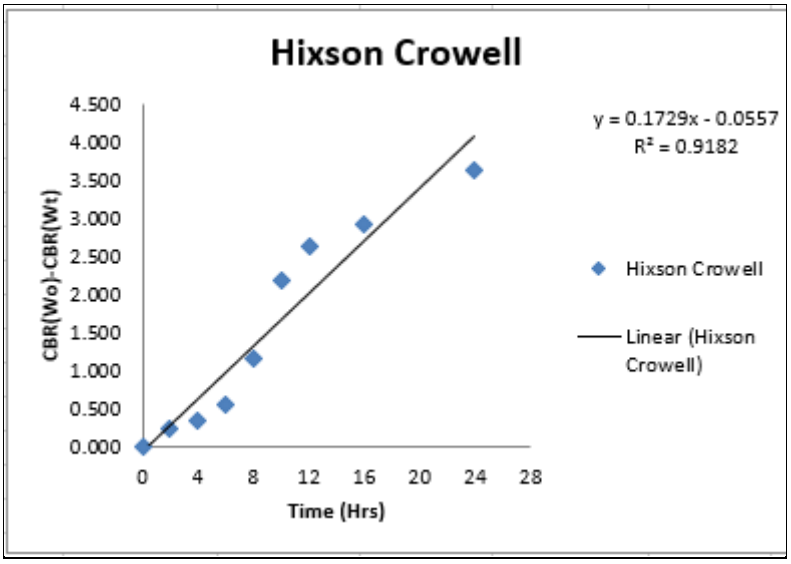
Time (Hr)	cumulative % drug released	% drug remaining	Square root time	log Cumu % drug remaining	log time	log Cumu % drug released	% Drug released	Cube Root of % drug Remaining(Wt)	Wo-Wt
0	0	100	0.000	2.000	0.000	0.000	100	4.642	0.000
2	14	86	1.414	1.934	0.301	1.146	14	4.414	0.228
4	20	80	2.000	1.903	0.602	1.301	6	4.309	0.333
6	32	68	2.449	1.833	0.778	1.505	12	4.082	0.560
8	58	42	2.828	1.623	0.903	1.763	26	3.476	1.166
10	85	15	3.162	1.176	1.000	1.929	27	2.466	2.176
12	92	8	3.464	0.903	1.079	1.964	7	2.000	2.642
16	95	5	4.000	0.699	1.204	1.978	3	1.710	2.932
24	99	1	4.899	0.000	1.380	1.996	4	1.000	3.642


First Order Kinetics
y = -0.0908x + 2.1682
R² = 0.9596
Log Cumulative % drug remaining
2.500
2.000
1.500
1.000
0.500
0.000
0
4
8
12
16
20
24
Time (Hrs)
First Order Kinetics
Linear (First Order Kinetics)


Korsmeyer Peppas
y = 1.3736x + 0.403
R² = 0.8751
Log cumulative % drug released
2.500
2.000
1.500
1.000
0.500
0.000
0.000
0.500
1.000
1.500
Log Time
Korsmeyer Peppas
Linear (Korsmeyer Peppas)


Zero Order kinetics
y = 4.6871x + 12.295
R² = 0.8035
Cumulative % drug released
140
120
100
80
60
40
20
0
0
4
8
12
16
20
24
Time (Hrs)
Zero Order kinetics
Linear (Zero Order kinetics)

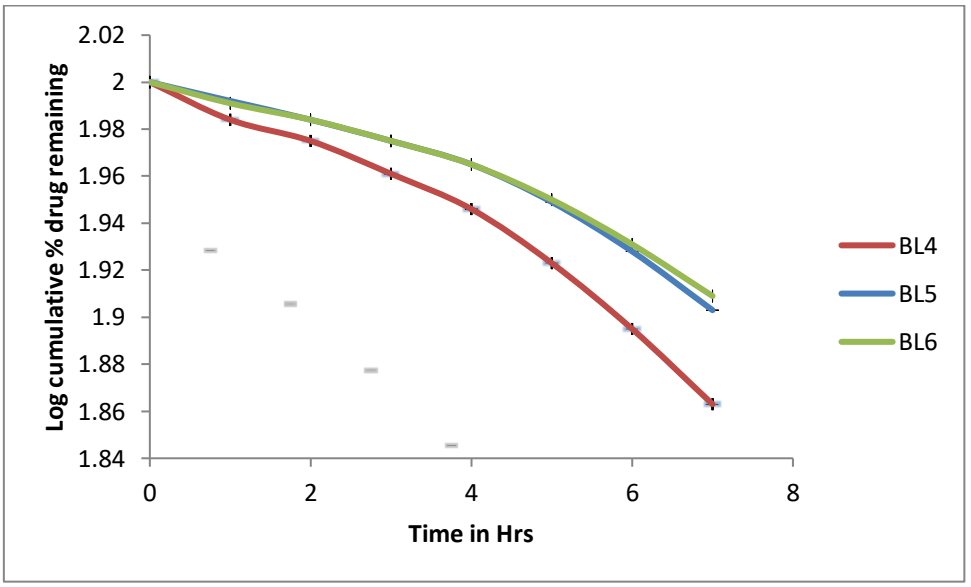




Mathematical models play a vital role in the interpretation of mechanism of drug release from a dosage form. It is an important tool to understand the drug release kinetics of a dosage form. The drug release was found to be best fitted by Higuchi square root model r2 =0.865 for BL4 which implies that release of drug as a square root of time dependent process and diffusion controlled. The dissolution data was also plotted according to Hixson –Crowell model r2 =0.9182 for BL4 which describes that change in surface area and diameter of the formulation with the progressive dissolution as a function of time. Also, the model Korsmeyer-Peppas power law equation states the type of diffusion, which was evaluated by value, n (Release exponent) which is higher than 0.875 which implies that the drug release from the system follow Super case II transport

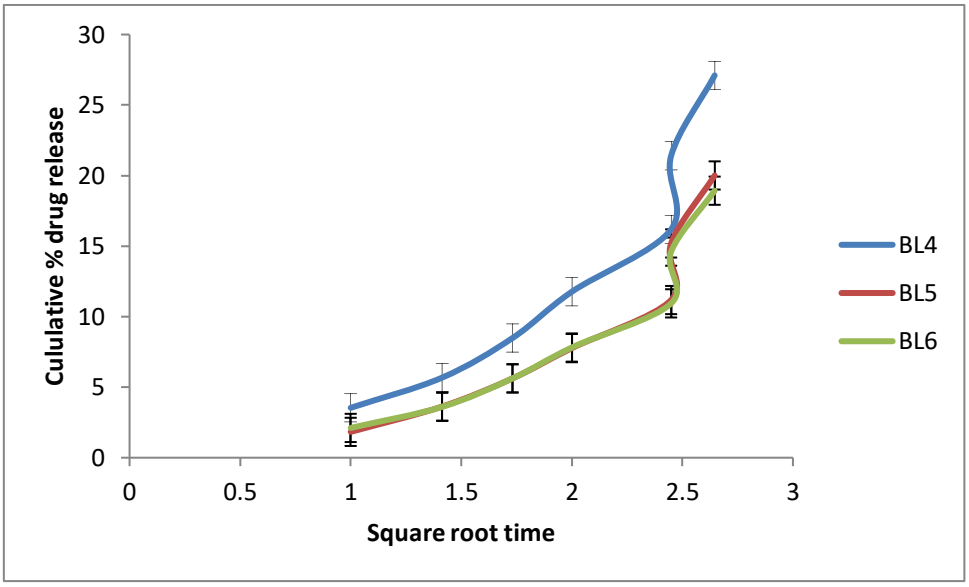
GOAT SKIN DRUG RELEASE OF FORMULATION BL5

Time (Hr)	log Cumu % drug remainining		
0	2	2	2
1	1.984	1.992	1.991
2	1.975	1.984	1.984
3	1.961	1.975	1.975
4	1.946	1.965	1.965
5	1.923	1.949	1.95
6	1.895	1.928	1.931
7	1.863	1.903	1.909

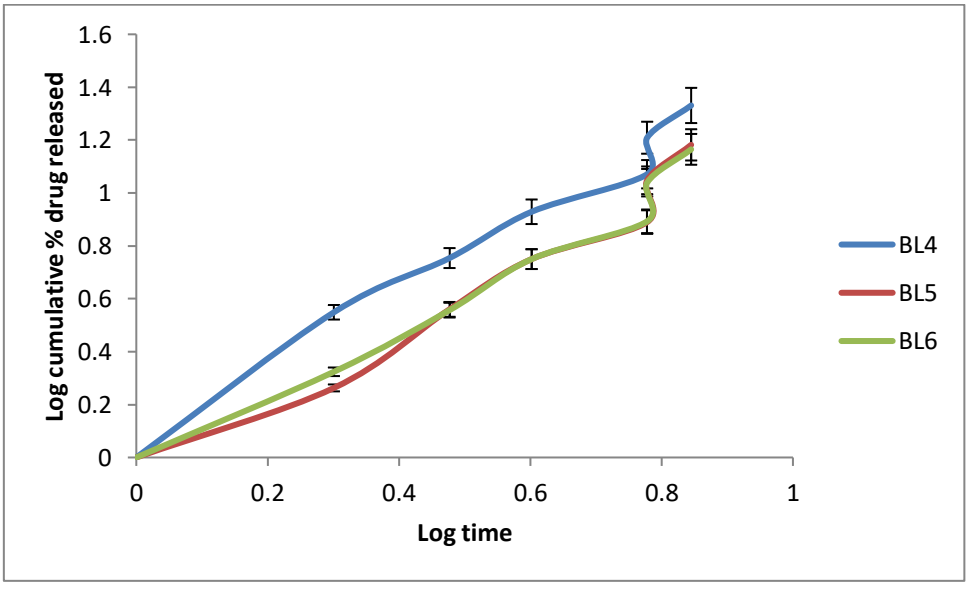


Square root time	cumulative % drug released		
0	0	0	0
1	3.5374	1.83195	2.1102
1.414	5.68143	3.6278	3.6078
1.732	8.48515	5.625225	5.6238
2	11.7653	7.76925	7.8126
2.449	16.1817	11.1777	10.942
2.449	21.4043	15.19088	14.609

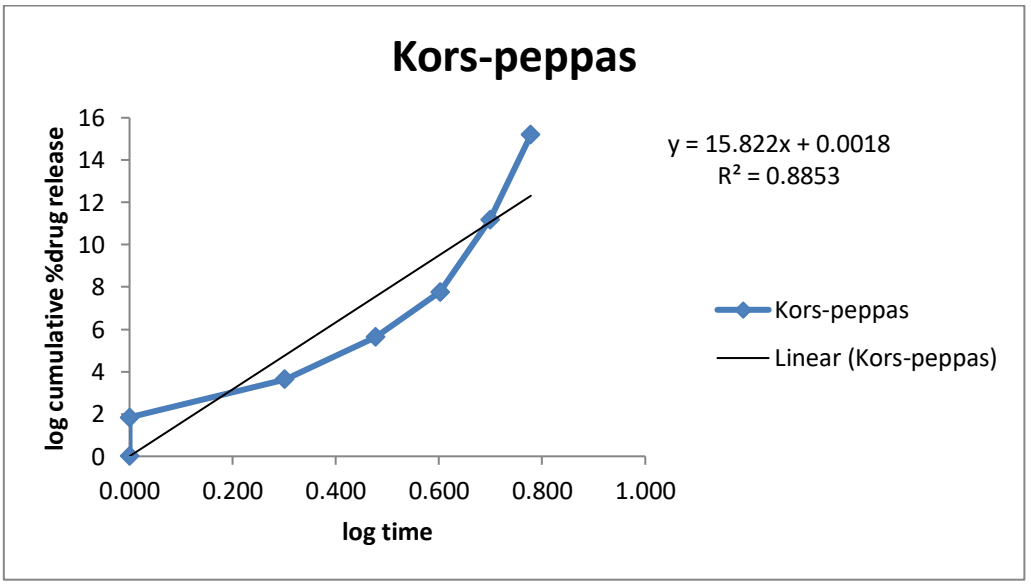
2.646	27.1034	20.01035	18.929

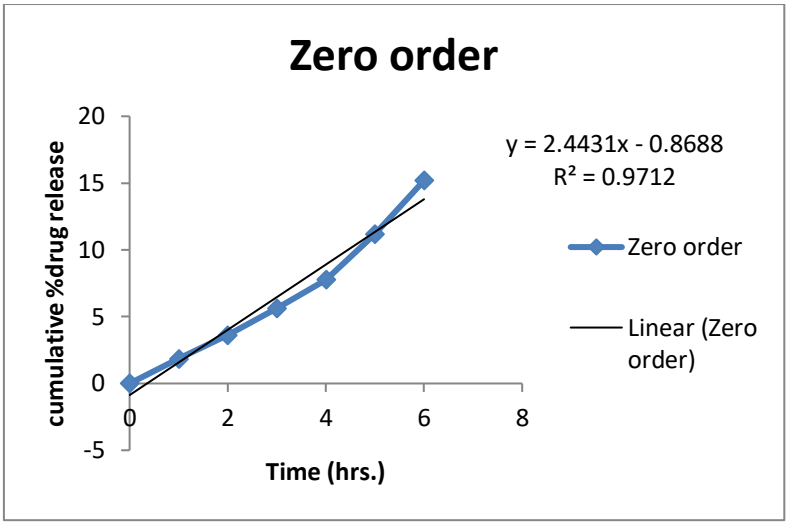


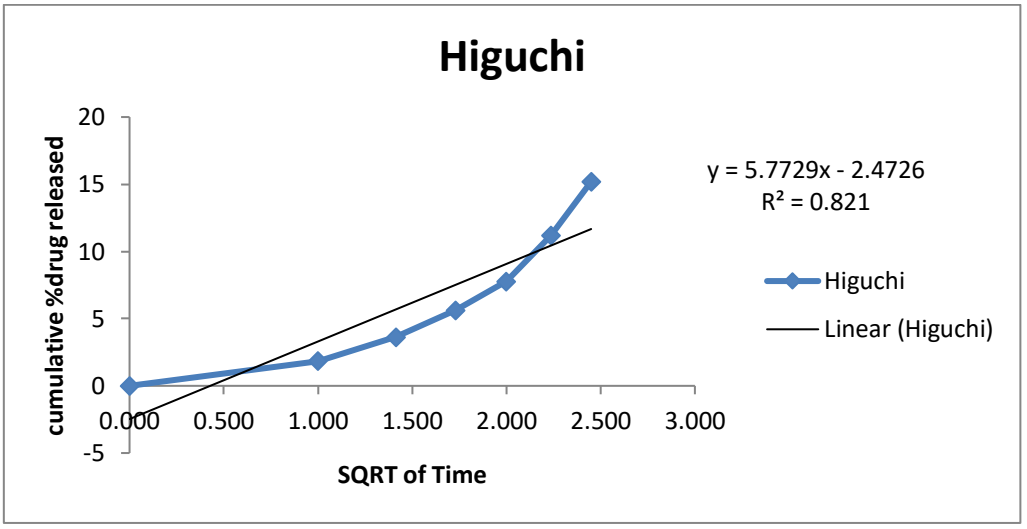
Log time	Log cumulative % drug released		
0	0	0	0
0	0.549	0.263	0.324
0.301	0.754	0.56	0.557
0.477	0.929	0.75	0.75
0.602	1.071	0.89	0.893
0.778	1.209	1.048	1.039
0.778	1.331	1.182	1.165
0.845	1.433	1.301	1.277

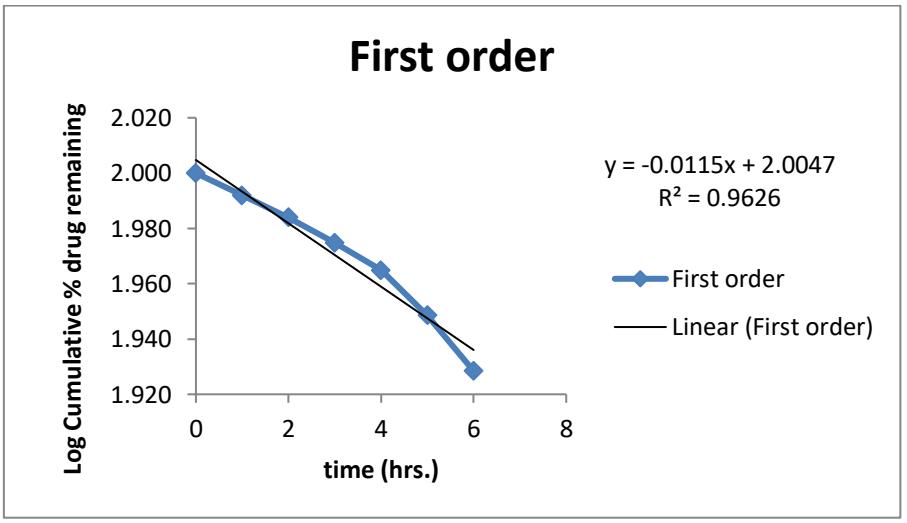


Time (Hr)	cumulative % drug released	% drug remaining	Square root time	log Cumu % drug remainining	log time	log Cumu % drug released	% Drug released	Cube Root of % drug Remaining(Wt)	Wo-Wt
0	0	100	0.000	2.000	0.000	0.000	100	4.642	0.000
1	1.83195	98.16805	1.000	1.992	0.000	0.263	1.83195	4.613	0.029
2	3.6278	96.3722	1.414	1.984	0.301	0.560	1.79585	4.585	0.057
3	5.625225	94.37478	1.732	1.975	0.477	0.750	1.997425	4.553	0.089
4	7.76925	92.23075	2.000	1.965	0.602	0.890	2.144025	4.518	0.124
5	11.1777	88.8223	2.236	1.949	0.699	1.048	3.40845	4.462	0.180
6	15.19088	84.80913	2.449	1.928	0.778	1.182	4.013175	4.394	0.248
7	20.01035	79.98965	2.646	1.903	0.845	1.301	4.819475	4.309	0.333

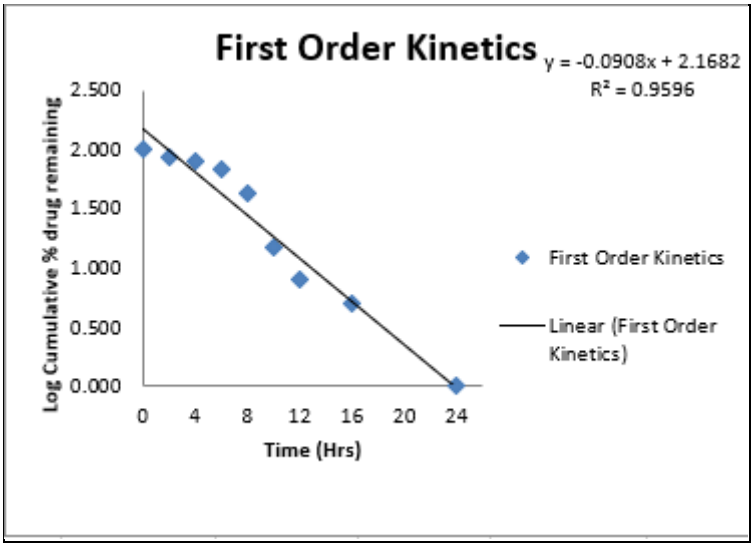


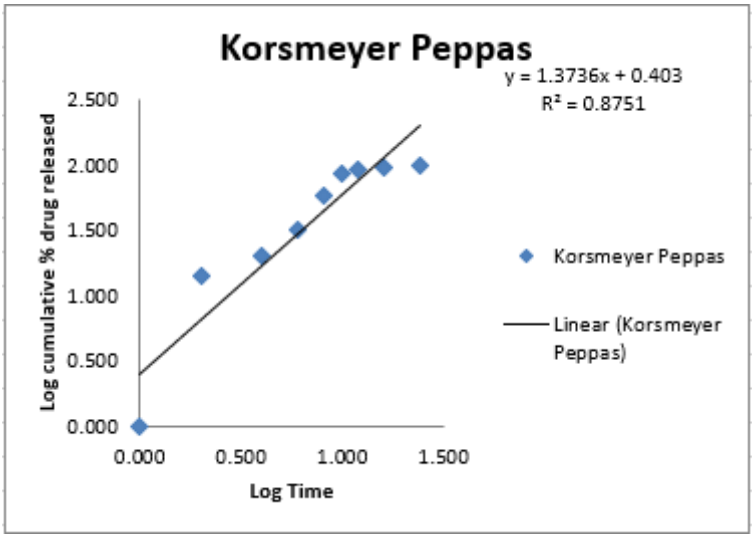

Zero order
cumulative %drug release
Time (hrs.)
y = 2.4431x - 0.8688
R² = 0.9712
Zero order
Linear (Zero order)

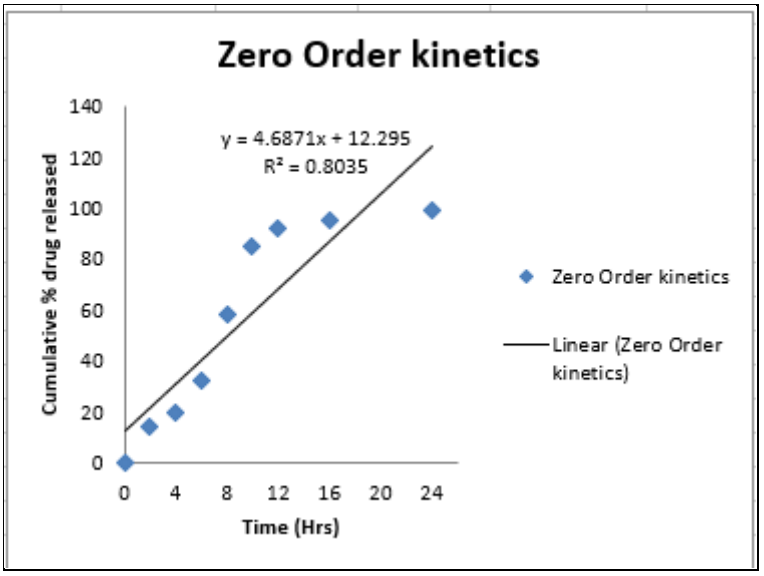

Higuchi
cumulative %drug released
SQRT of Time
y = 5.7729x - 2.4726
R² = 0.821
Higuchi
Linear (Higuchi)

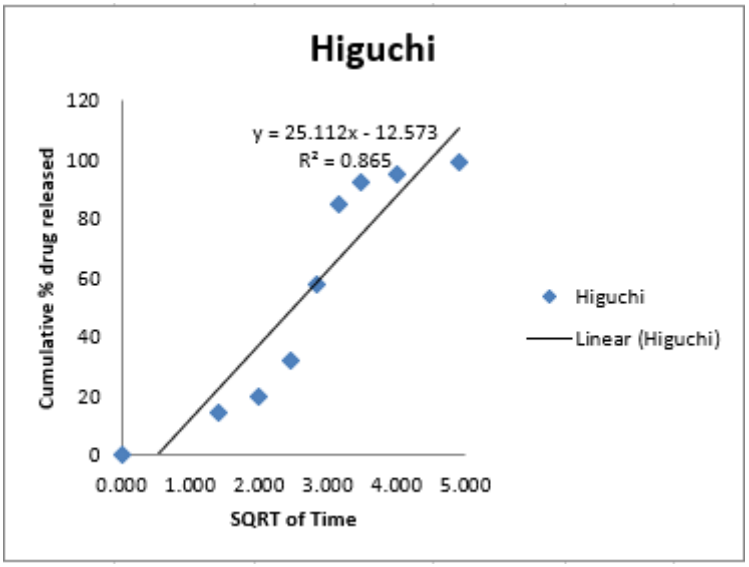

First order
Log Cumulative % drug remaining
time (hrs.)
y = -0.0115x + 2.0047
R² = 0.9626
First order
Linear (First order)

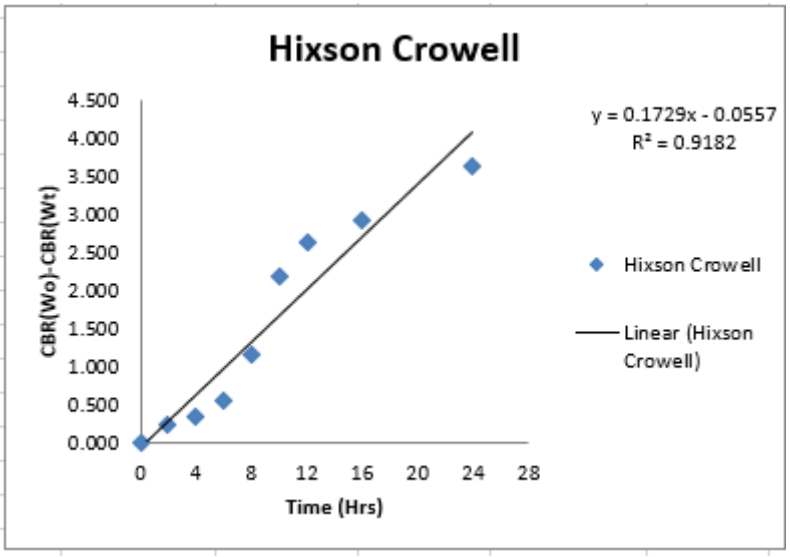
Time (Hr)	cumulative % drug released	% drug remaining	Square root time	log Cumu % drug remaining	log time	log Cumu % drug released	% Drug released	Cube Root of % drug Remaining(Wt)	Wo-Wt
0	0	100	0.000	2.000	0.000	0.000	100	4.642	0.000
2	14	86	1.414	1.934	0.301	1.146	14	4.414	0.228
4	20	80	2.000	1.903	0.602	1.301	6	4.309	0.333
6	32	68	2.449	1.833	0.778	1.505	12	4.082	0.560
8	58	42	2.828	1.623	0.903	1.763	26	3.476	1.166
10	85	15	3.162	1.176	1.000	1.929	27	2.466	2.176
12	92	8	3.464	0.903	1.079	1.964	7	2.000	2.642
16	95	5	4.000	0.699	1.204	1.978	3	1.710	2.932
24	99	1	4.899	0.000	1.380	1.996	4	1.000	3.642





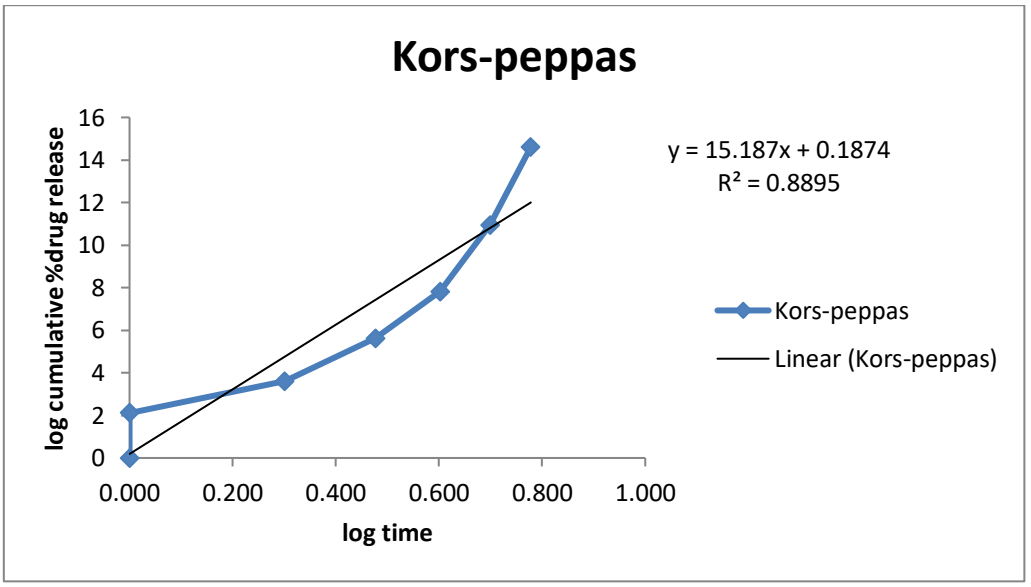

Zero Order kinetics
y = 4.6871x + 12.295
R² = 0.8035
Cumulative % drug released
Time (Hrs)
Zero Order kinetics
Linear (Zero Order kinetics)

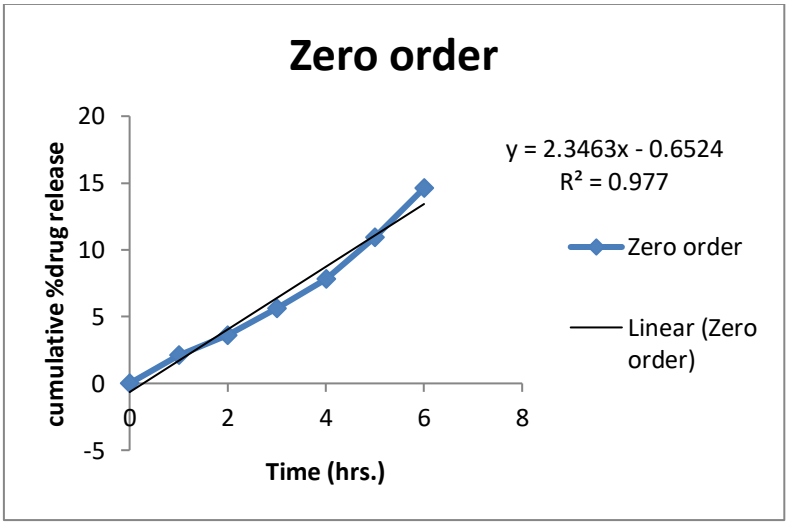

Higuchi
y = 25.112x - 12.573
R² = 0.865
Cumulative % drug released
SQRT of Time
Higuchi
Linear (Higuchi)

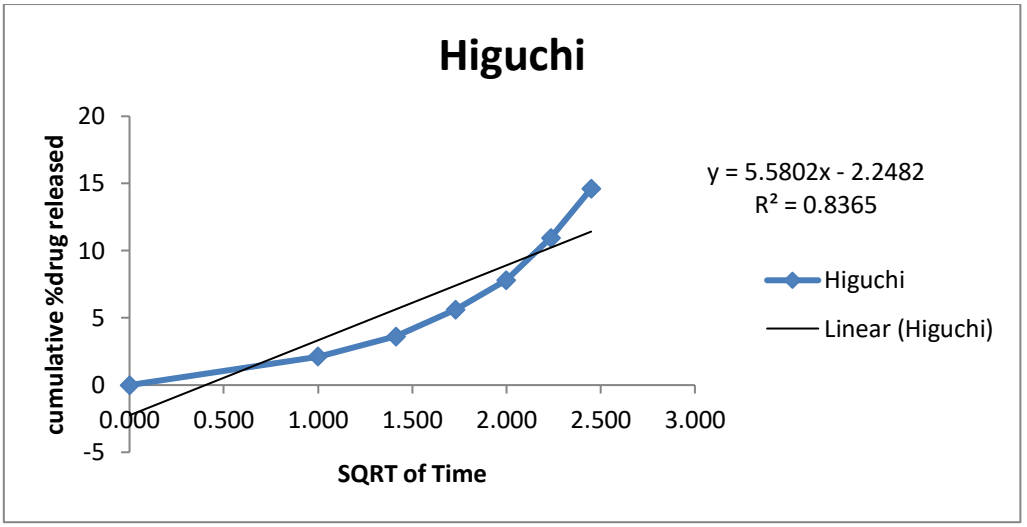

Hixson Crowell
y = 0.1729x - 0.0557
R² = 0.9182
CBR(Wo)-CBR(Wt)
Time (Hrs)
Hixson Crowell
Linear (Hixson Crowell)

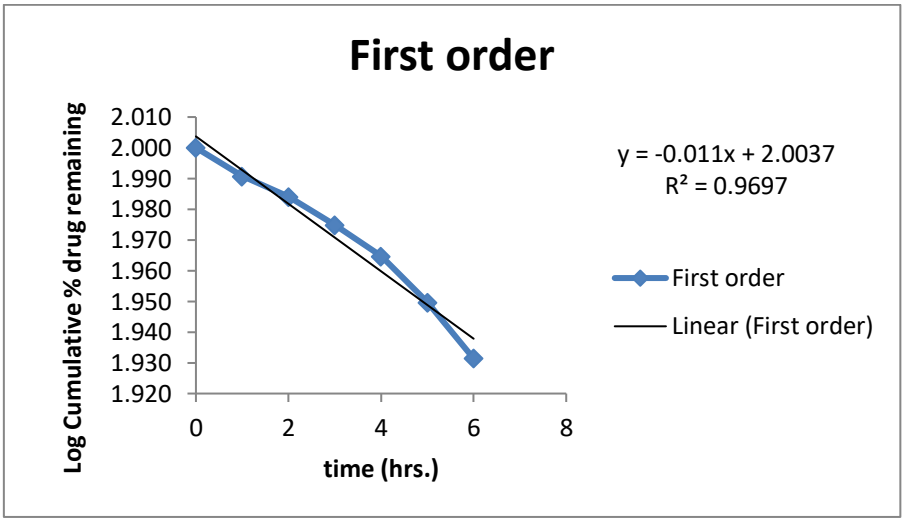
GOAT SKIN DRUG RELEASE OF FORMULATION BL6

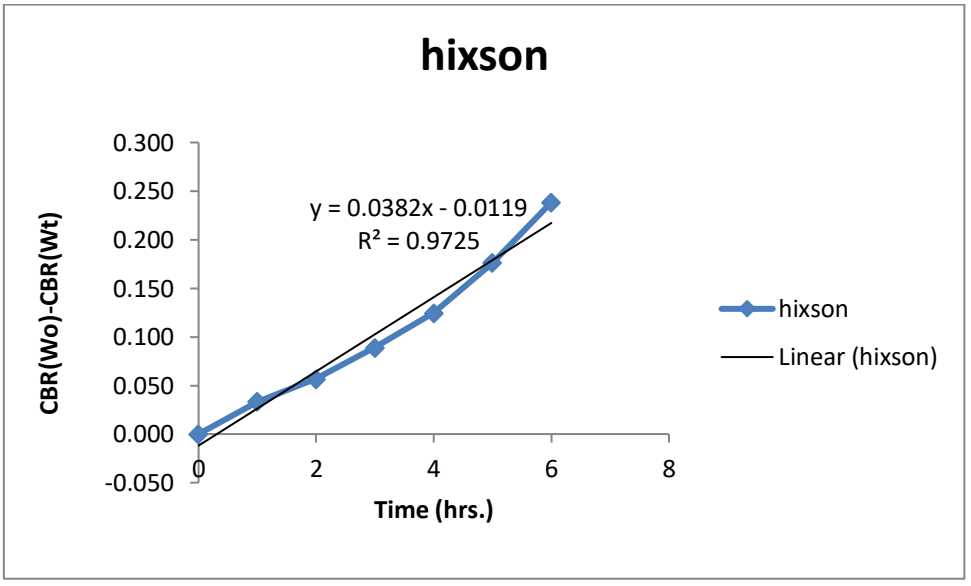
Time (Hr)	cumulative % drug released	% drug remaining	Square root time	log Cumu % drug remainining	log time	log Cumu % drug released	% Drug released	Cube Root of % drug Remaining(Wt)	Wo-Wt
0	0	100	0.000	2.000	0.000	0.000	100	4.642	0.000
1	2.1102	97.8898	1.000	1.991	0.000	0.324	2.1102	4.609	0.033
2	3.6078	96.3922	1.414	1.984	0.301	0.557	1.4976	4.585	0.057
3	5.6238	94.3762	1.732	1.975	0.477	0.750	2.016	4.553	0.089
4	7.8126	92.1874	2.000	1.965	0.602	0.893	2.1888	4.517	0.125
5	10.9422	89.0578	2.236	1.950	0.699	1.039	3.1296	4.466	0.176
6	14.6094	85.3906	2.449	1.931	0.778	1.165	3.6672	4.404	0.238
7	18.9294	81.0706	2.646	1.909	0.845	1.277	4.32	4.328	0.314



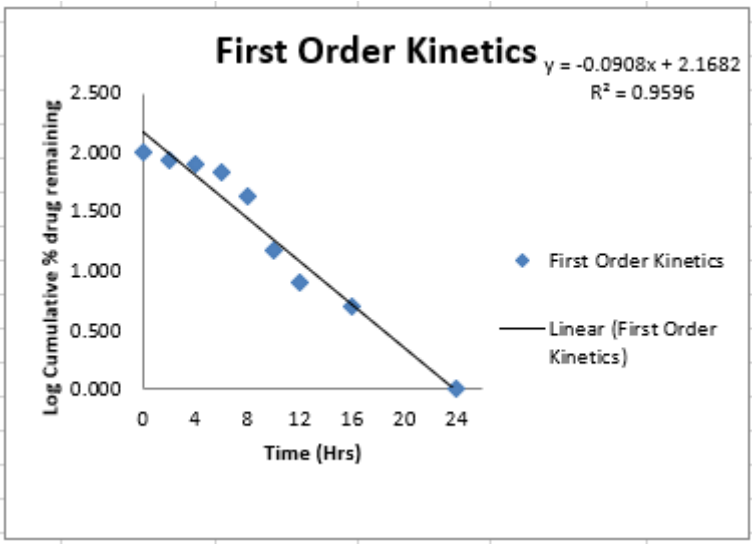


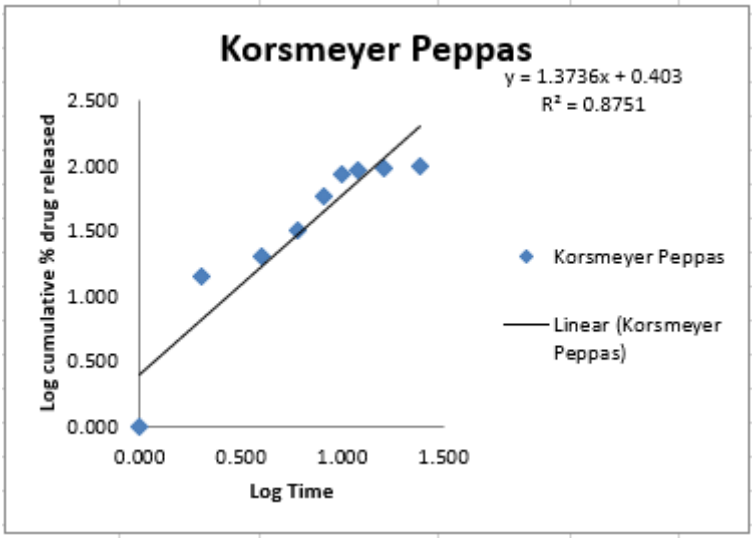

Higuchi
cumulative %drug released
20
15
10
5
0
-5
0.000
0.500
1.000
1.500
2.000
2.500
3.000
SQRT of Time
y = 5.5802x - 2.2482
R² = 0.8365
Higuchi
Linear (Higuchi)

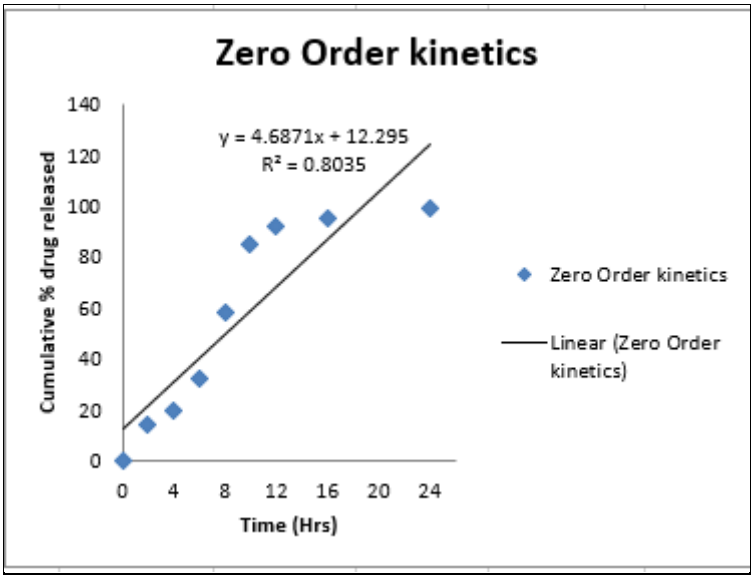

First order
Log Cumulative % drug remaining
2.010
2.000
1.990
1.980
1.970
1.960
1.950
1.940
1.930
1.920
0
2
4
6
8
time (hrs.)
y = -0.011x + 2.0037
R² = 0.9697
First order
Linear (First order)

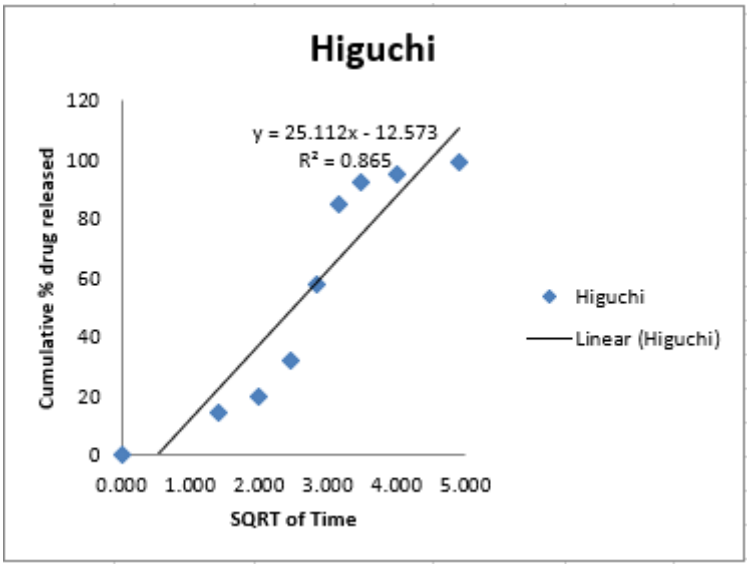

hixson
CBR(Wo)-CBR(Wt)
0.300
0.250
0.200
0.150
0.100
0.050
0.000
-0.050
0
2
4
6
8
Time (hrs.)
y = 0.0382x - 0.0119
R² = 0.9725
hixson
Linear (hixson)

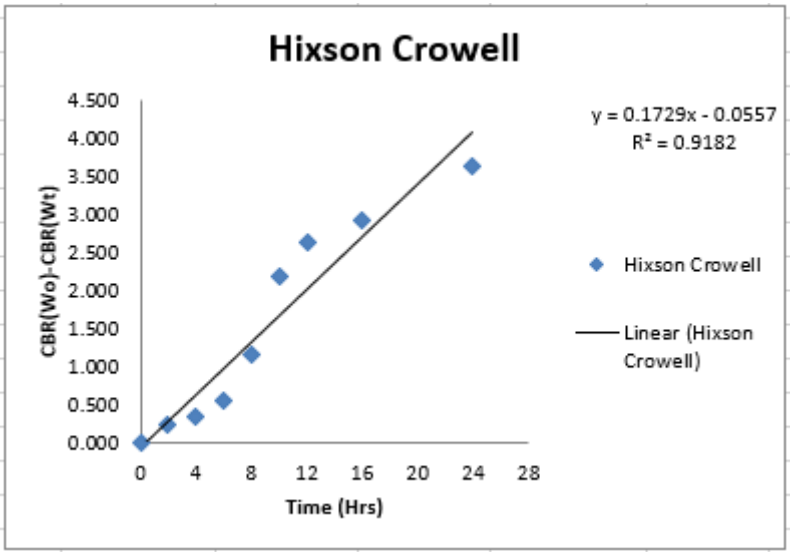
Time (Hr)	cumulative % drug released	% drug remaining	Square root time	log Cumu % drug remaining	log time	log Cumu % drug released	% Drug released	Cube Root of % drug Remaining(Wt)	Wo-Wt
0	0	100	0.000	2.000	0.000	0.000	100	4.642	0.000
2	14	86	1.414	1.934	0.301	1.146	14	4.414	0.228
4	20	80	2.000	1.903	0.602	1.301	6	4.309	0.333
6	32	68	2.449	1.833	0.778	1.505	12	4.082	0.560
8	58	42	2.828	1.623	0.903	1.763	26	3.476	1.166
10	85	15	3.162	1.176	1.000	1.929	27	2.466	2.176
12	92	8	3.464	0.903	1.079	1.964	7	2.000	2.642
16	95	5	4.000	0.699	1.204	1.978	3	1.710	2.932
24	99	1	4.899	0.000	1.380	1.996	4	1.000	3.642











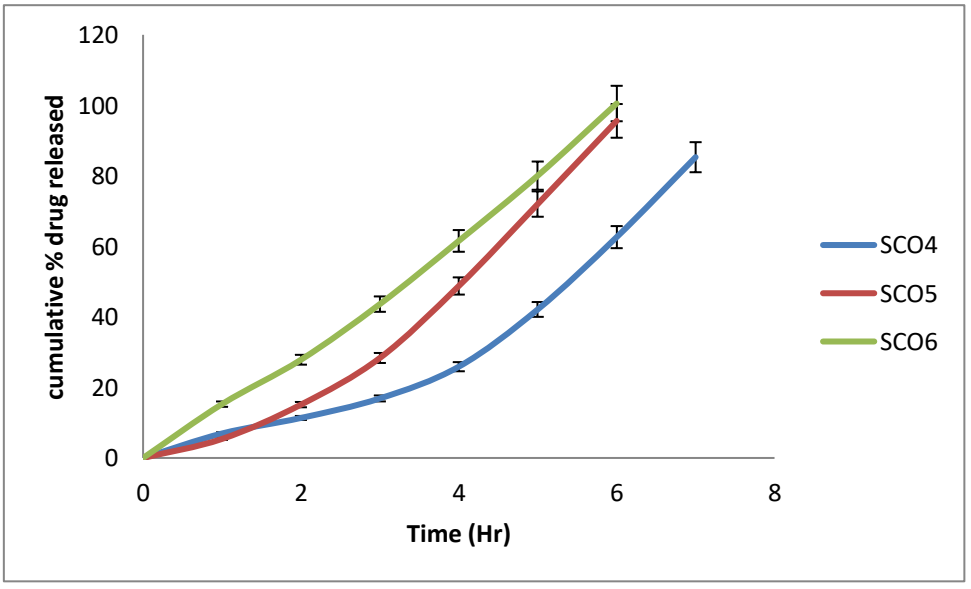
Mathematical models play a vital role in the interpretation of mechanism of drug release from

a dosage form. It is an important tool to understand the drug release kinetics of a dosage form. The drug release was found to be best fitted by Higuchi square root model r2 =0.865 for BL5 and r2 =0.8365 for BL6 which implies that release of drug as a square root of time dependent process and diffusion controlled. The dissolution data was also plotted according to Hixson –Crowell model r2 =0.9182 for BL5 and r2 =0.9725 for BL6 which describes that change in surface area and diameter of the formulation with the progressive dissolution as a function of time. Also, the model Korsmeyer-Peppas power law equation states the type of diffusion, which was evaluated by value, n (Release exponent) which is higher than 0.875 which implies that the drug release from the system follow Super case II transport

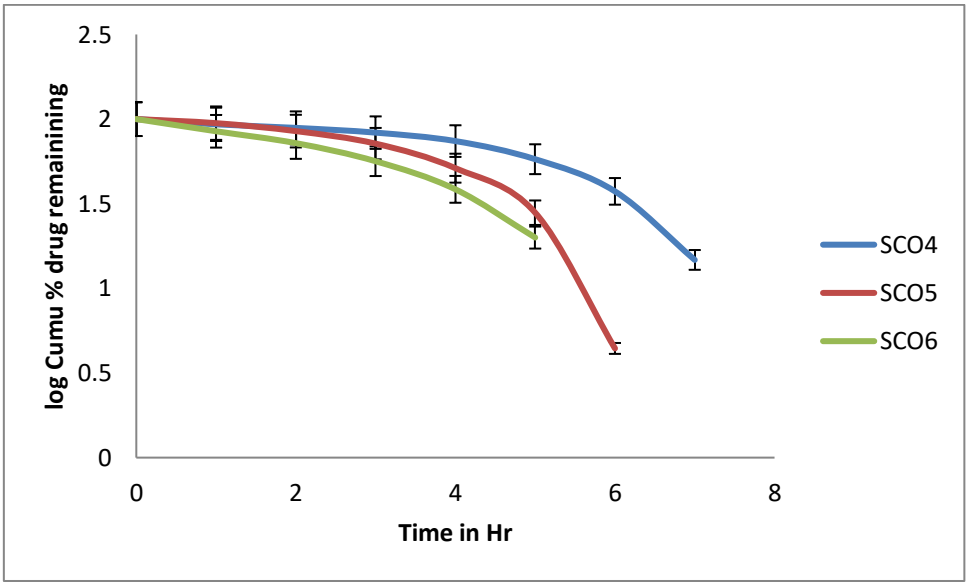
Goatskin is used instead of rat-skin to study the permeation and the results are compared. The percentage of permeation is double in goatskin. Comparative study shows that there is twofold increases in the percentage of permeation.

GOAT SKIN DRUG RELEASE OF FORMULATION SCO4

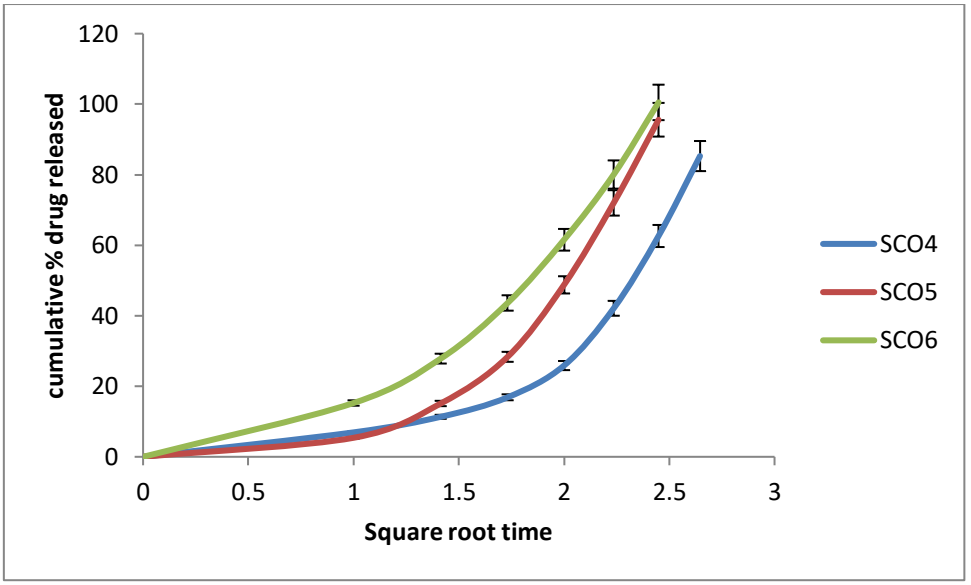
Time (Hr)	cumulative % drug released		
0	0	0	0
1	6.93145	5.392025	15.26
2	11.347775	15.1226	27.849
3	16.881925	28.35325	43.627
4	25.8795	48.7673	61.549
5	42.11545	72.0034	80.057
6	62.621125	95.587675	100.51
7	85.28915		



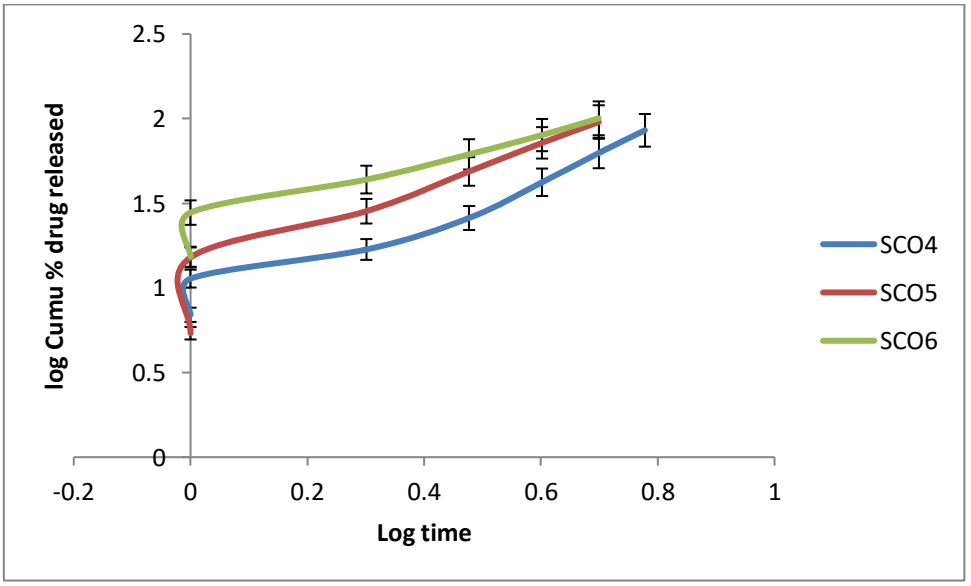
Time (Hr)	log Cumu % drug remainining		
0	2	2	2
1	1.969	1.976	1.928
2	1.948	1.929	1.858
3	1.92	1.855	1.751
4	1.87	1.71	1.585
5	1.763	1.447	1.3
6	1.573	0.645	
7	1.168		



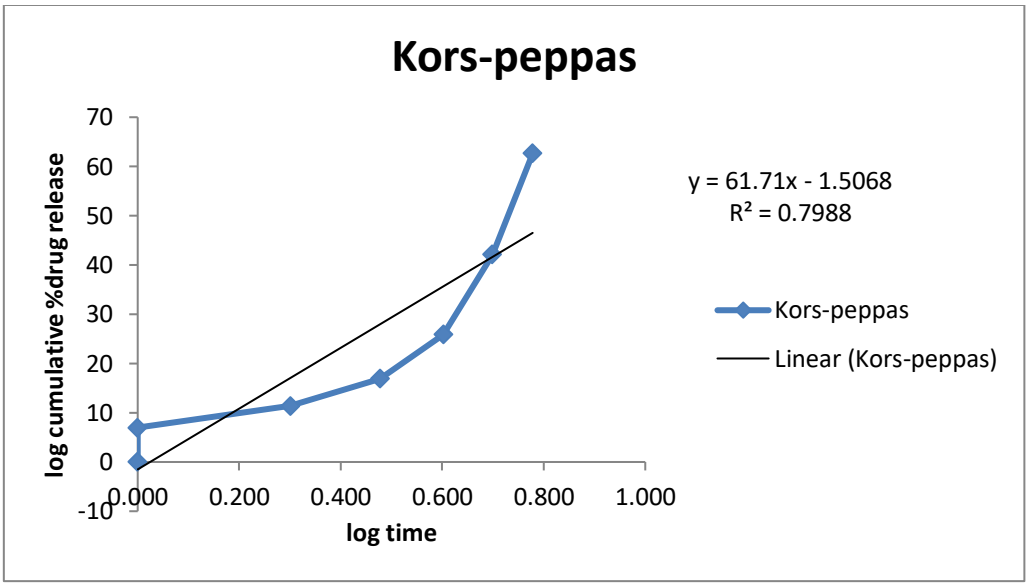
Square root time	cumulative % drug released		
0	0	0	0
1	6.93145	5.392025	15.26
1.414	11.34778	15.1226	27.849
1.732	16.88193	28.35325	43.627
2	25.8795	48.7673	61.549
2.236	42.11545	72.0034	80.057
2.449	62.62113	95.58768	100.51
2.646	85.28915		

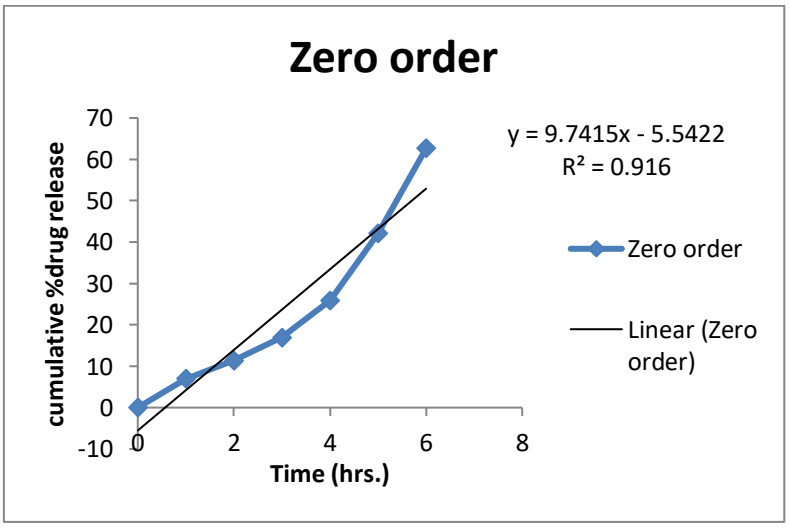


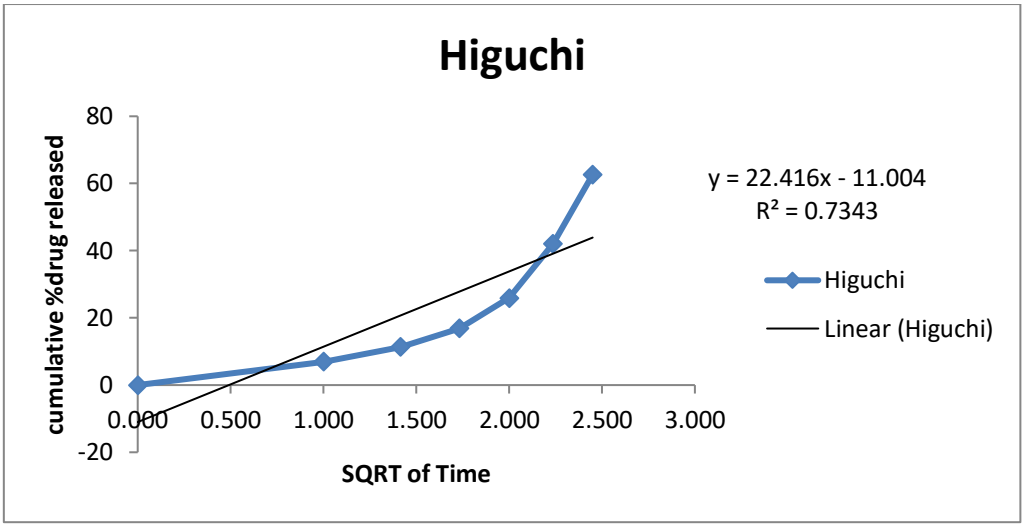
Log time	log Cumu % drug released		
0	0	0	0
0	0.841	0.732	1.184
0.301	1.055	1.18	1.445
0.477	1.227	1.453	1.64
0.602	1.413	1.688	1.789
0.699	1.624	1.857	1.903
0.778	1.797	1.98	2.002
0.845	1.931		

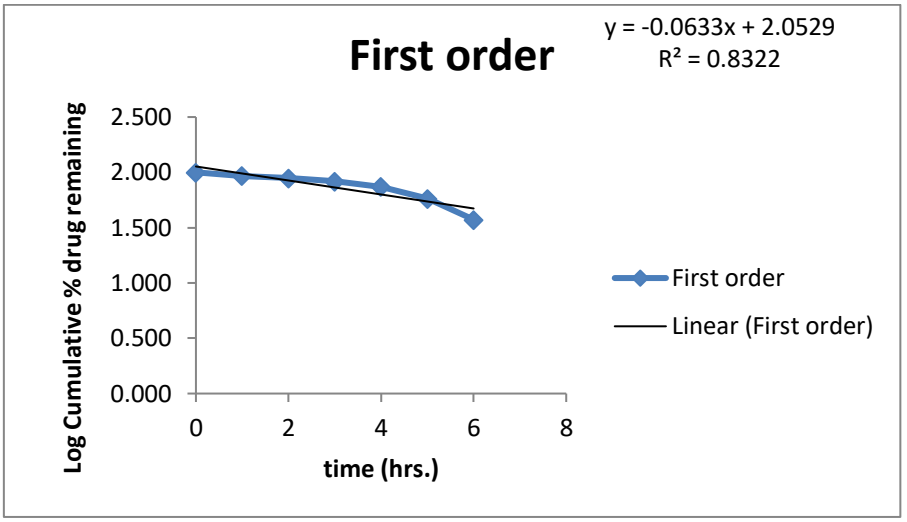


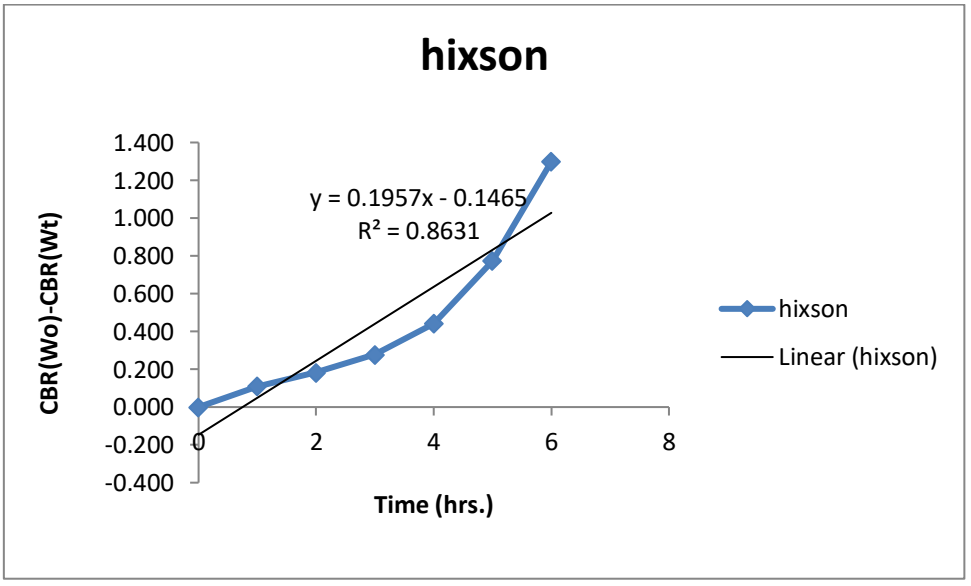
Time (Hr)	cumulative % drug released	% drug remaining	Square root time	log Cumu % drug remainining	log time	log Cumu % drug released	% Drug released	Cube Root of % drug Remaining(Wt)	Wo-Wt
0	0	100	0.000	2.000	0.000	0.000	100	4.642	0.000
1	6.93145	93.06855	1.000	1.969	0.000	0.841	6.93145	4.532	0.110
2	11.34778	88.65223	1.414	1.948	0.301	1.055	4.416325	4.459	0.183
3	16.88193	83.11808	1.732	1.920	0.477	1.227	5.53415	4.364	0.278
4	25.8795	74.1205	2.000	1.870	0.602	1.413	8.997575	4.201	0.441
5	42.11545	57.88455	2.236	1.763	0.699	1.624	16.23595	3.868	0.774
6	62.62113	37.37888	2.449	1.573	0.778	1.797	20.50568	3.344	1.298
7	85.28915	14.71085	2.646	1.168	0.845	1.931	22.66803	2.450	2.192



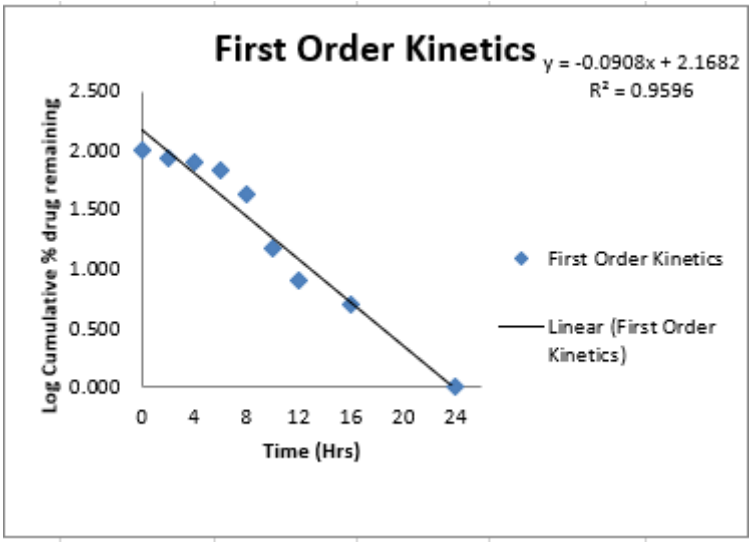


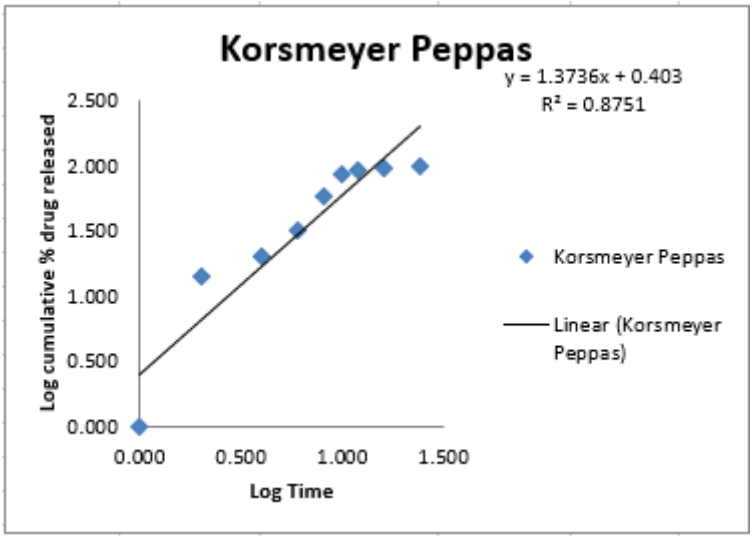

Higuchi
cumulative %drug released
80
60
40
20
0
-20
0.000
0.500
1.000
1.500
2.000
2.500
3.000
SQRT of Time
y = 22.416x - 11.004
R² = 0.7343
Higuchi
Linear (Higuchi)

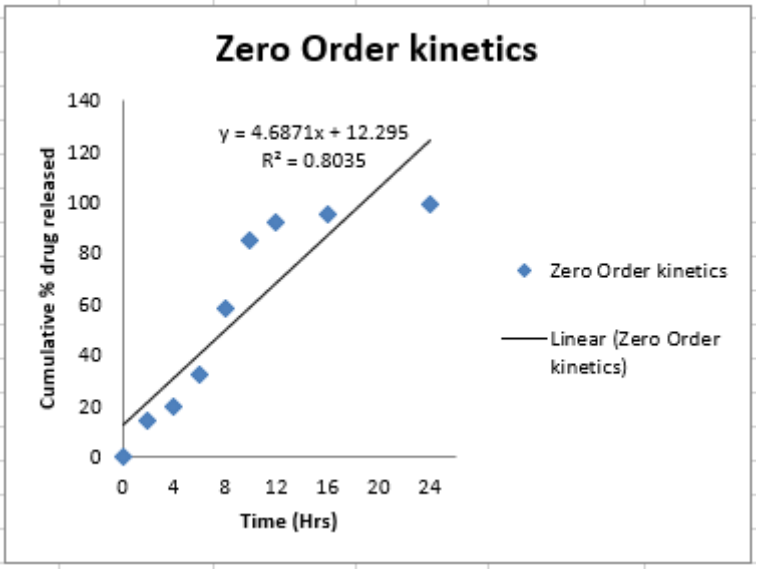

First order
y = -0.0633x + 2.0529
R² = 0.8322
Log Cumulative % drug remaining
2.500
2.000
1.500
1.000
0.500
0.000
0
2
4
6
8
time (hrs.)
First order
Linear (First order)

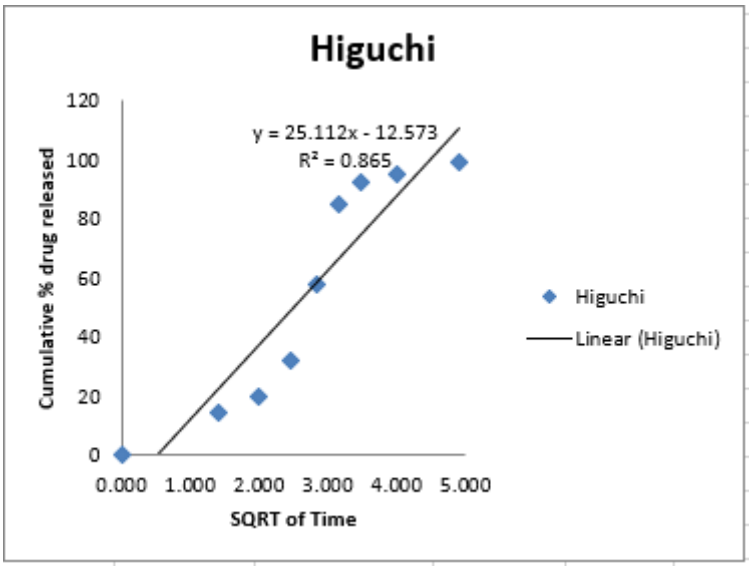

hixson
CBR(Wo)-CBR(Wt)
1.400
1.200
1.000
0.800
0.600
0.400
0.200
0.000
-0.200
-0.400
0
2
4
6
8
Time (hrs.)
y = 0.1957x - 0.1465
R² = 0.8631
hixson
Linear (hixson)

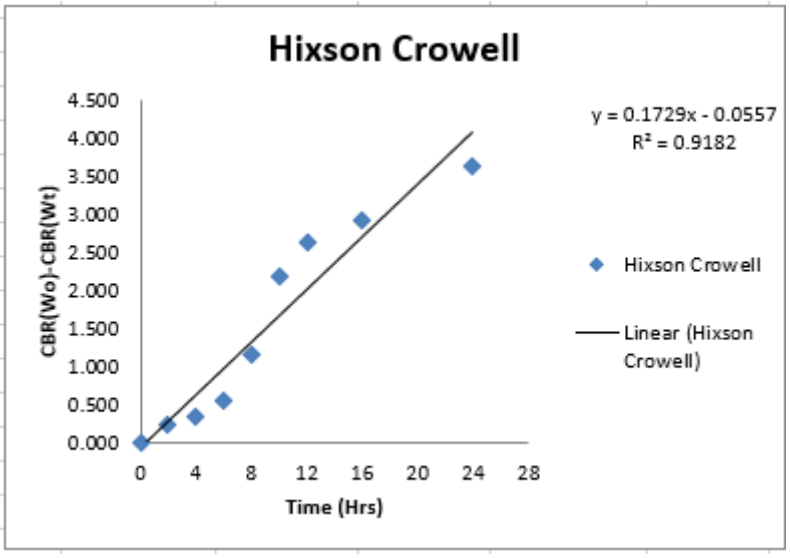
Time (Hr)	cumulative % drug released	% drug remaining	Square root time	log Cumu % drug remaining	log time	log Cumu % drug released	% Drug released	Cube Root of % drug Remaining(Wt)	Wo-Wt
0	0	100	0.000	2.000	0.000	0.000	100	4.642	0.000
2	14	86	1.414	1.934	0.301	1.146	14	4.414	0.228
4	20	80	2.000	1.903	0.602	1.301	6	4.309	0.333
6	32	68	2.449	1.833	0.778	1.505	12	4.082	0.560
8	58	42	2.828	1.623	0.903	1.763	26	3.476	1.166
10	85	15	3.162	1.176	1.000	1.929	27	2.466	2.176
12	92	8	3.464	0.903	1.079	1.964	7	2.000	2.642
16	95	5	4.000	0.699	1.204	1.978	3	1.710	2.932
24	99	1	4.899	0.000	1.380	1.996	4	1.000	3.642





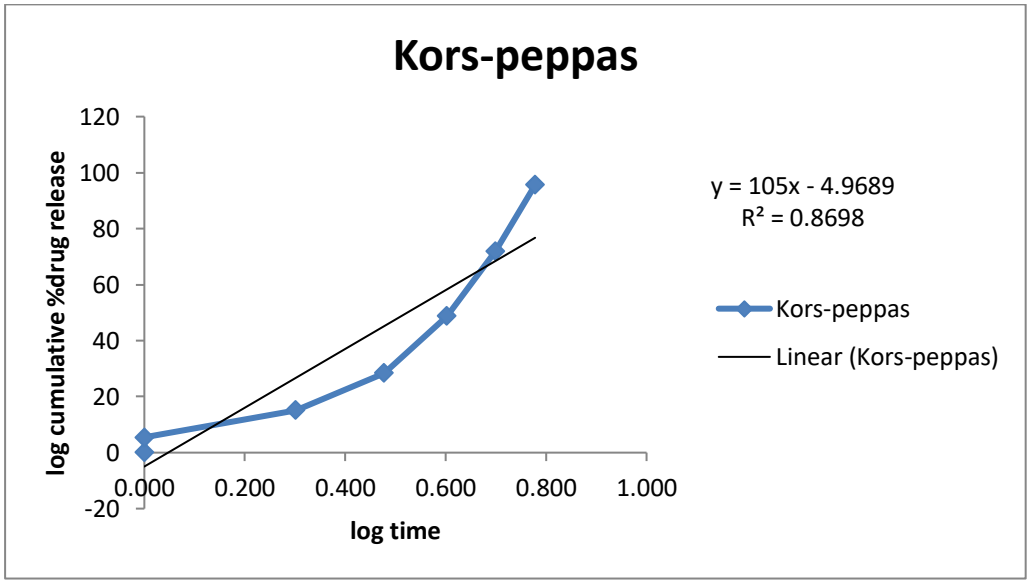


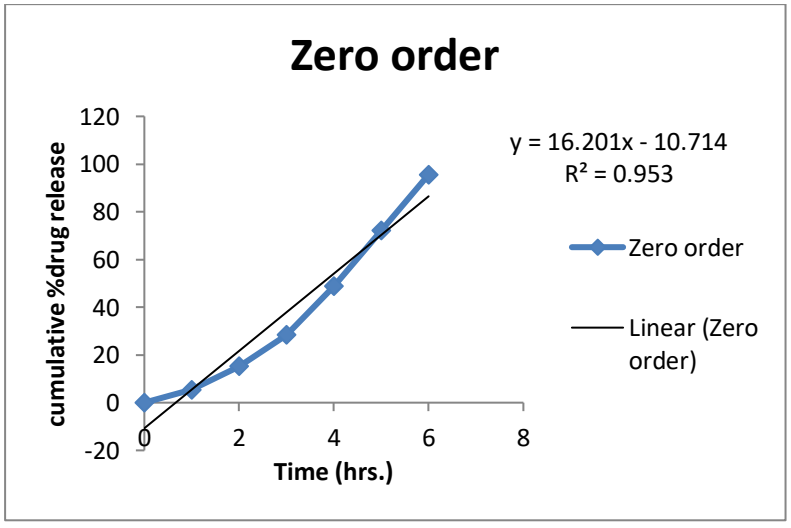


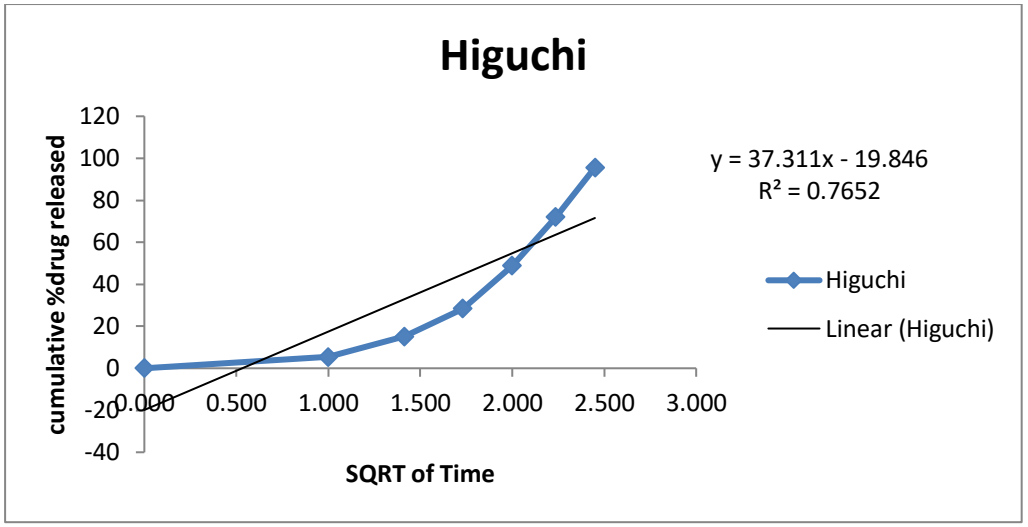


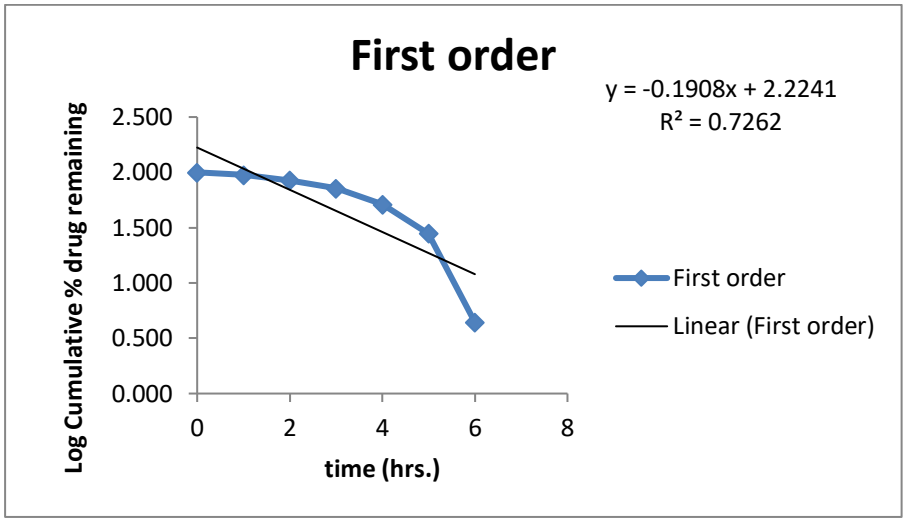
GOAT SKIN DRUG RELEASE OF FORMULATION SCO5

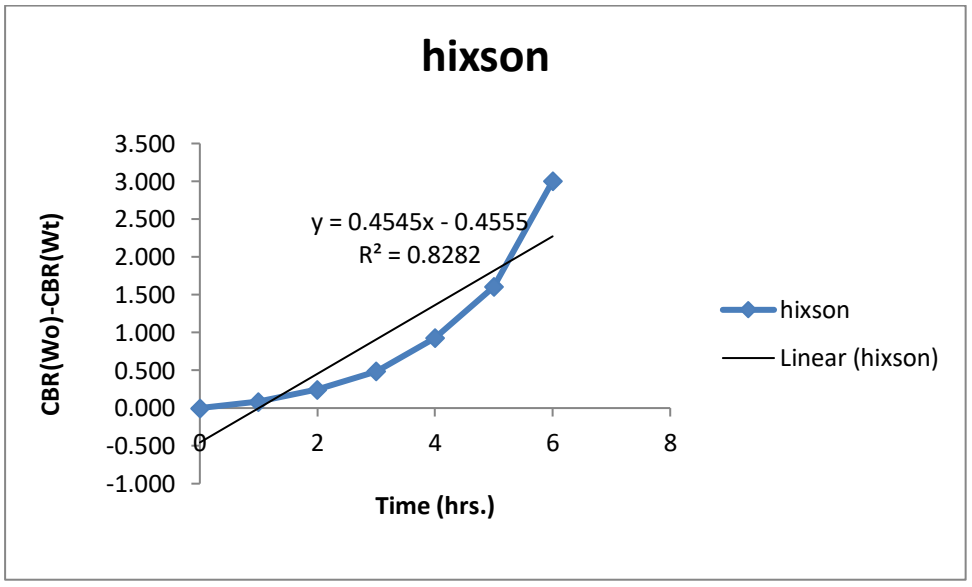
Time (Hr)	cumulative % drug released	% drug remaining	Square root time	log Cumu % drug remainining	log time	log Cumu % drug released	% Drug released	Cube Root of % drug Remaining(Wt)	Wo-Wt
0	0	100	0.000	2.000	0.000	0.000	100	4.642	0.000
1	5.392025	94.60798	1.000	1.976	0.000	0.732	5.392025	4.557	0.085
2	15.1226	84.8774	1.414	1.929	0.301	1.180	9.730575	4.395	0.247
3	28.35325	71.64675	1.732	1.855	0.477	1.453	13.23065	4.153	0.489
4	48.7673	51.2327	2.000	1.710	0.602	1.688	20.41405	3.714	0.928
5	72.0034	27.9966	2.236	1.447	0.699	1.857	23.2361	3.036	1.606
6	95.58768	4.412325	2.449	0.645	0.778	1.980	23.58428	1.640	3.002
7	-	#VALUE!	2.646	#VALUE!	0.845	#VALUE!	#VALUE!	#VALUE!	#VALUE!



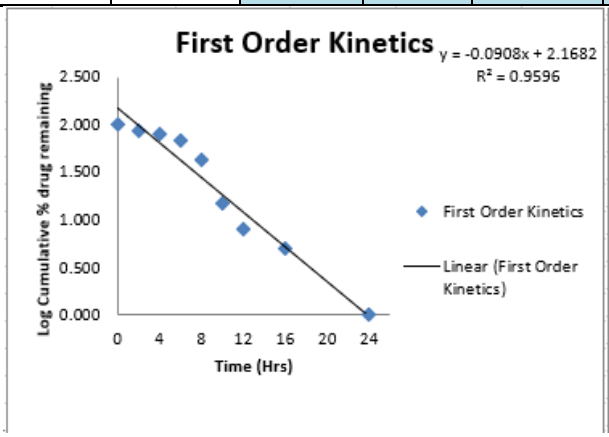


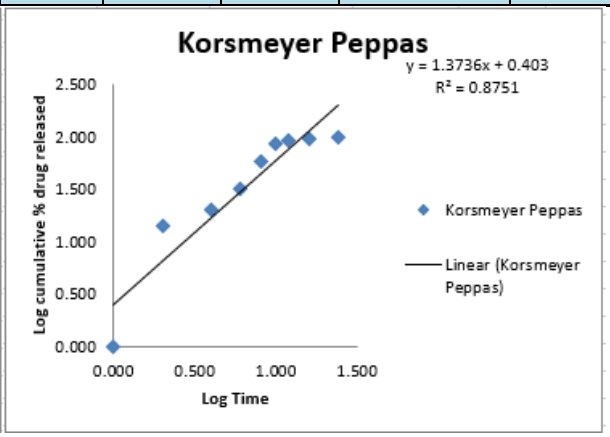

Higuchi
cumulative %drug released
120
100
80
60
40
20
0
-20
-40
0.000
0.500
1.000
1.500
2.000
2.500
3.000
SQRT of Time
y = 37.311x - 19.846
R² = 0.7652
Higuchi
Linear (Higuchi)

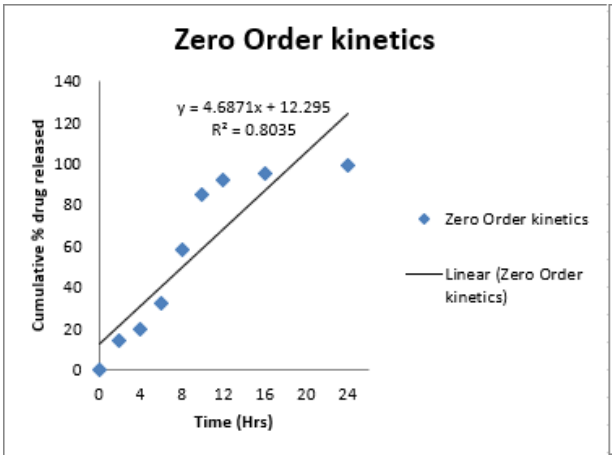

First order
Log Cumulative % drug remaining
2.500
2.000
1.500
1.000
0.500
0.000
0
2
4
6
8
time (hrs.)
y = -0.1908x + 2.2241
R² = 0.7262
First order
Linear (First order)

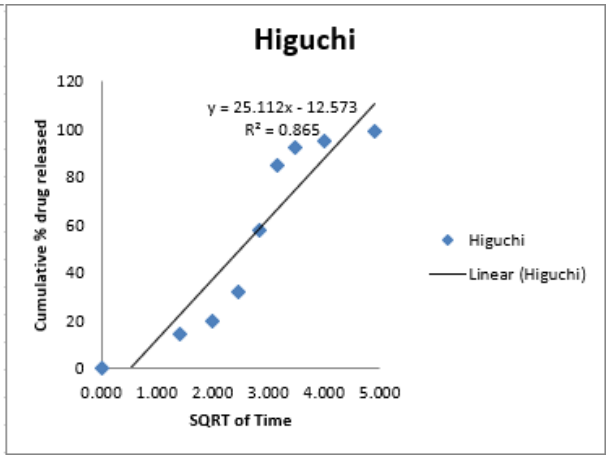

hixson
CBR(Wo)-CBR(Wt)
3.500
3.000
2.500
2.000
1.500
1.000
0.500
0.000
-0.500
-1.000
0
2
4
6
8
Time (hrs.)
y = 0.4545x - 0.4555
R² = 0.8282
hixson
Linear (hixson)

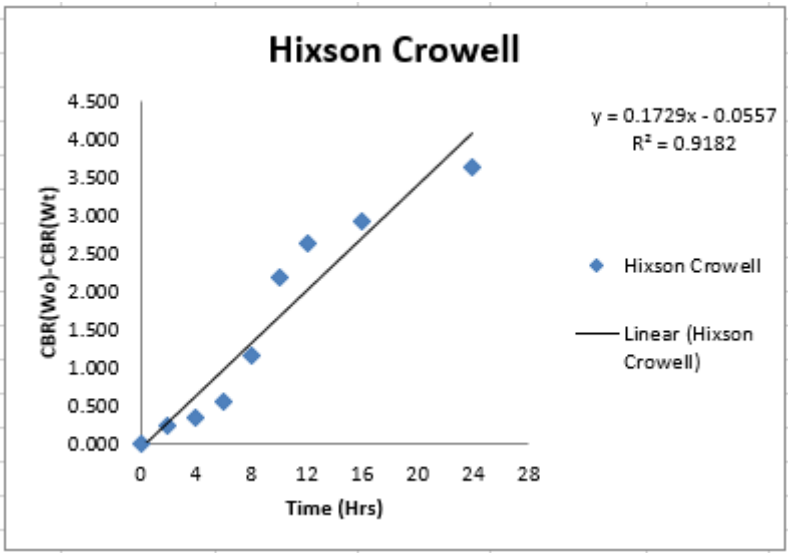
Time (Hr)	cumulative % drug released	% drug remaining	Square root time	log Cumu % drug remaining	log time	log Cumu % drug released	% Drug released	Cube Root of % drug Remaining(Wt)	Wo-Wt
0	0	100	0.000	2.000	0.000	0.000	100	4.642	0.000
2	14	86	1.414	1.934	0.301	1.146	14	4.414	0.228
4	20	80	2.000	1.903	0.602	1.301	6	4.309	0.333
6	32	68	2.449	1.833	0.778	1.505	12	4.082	0.560
8	58	42	2.828	1.623	0.903	1.763	26	3.476	1.166
10	85	15	3.162	1.176	1.000	1.929	27	2.466	2.176
12	92	8	3.464	0.903	1.079	1.964	7	2.000	2.642
16	95	5	4.000	0.699	1.204	1.978	3	1.710	2.932
24	99	1	4.899	0.000	1.380	1.996	4	1.000	3.642





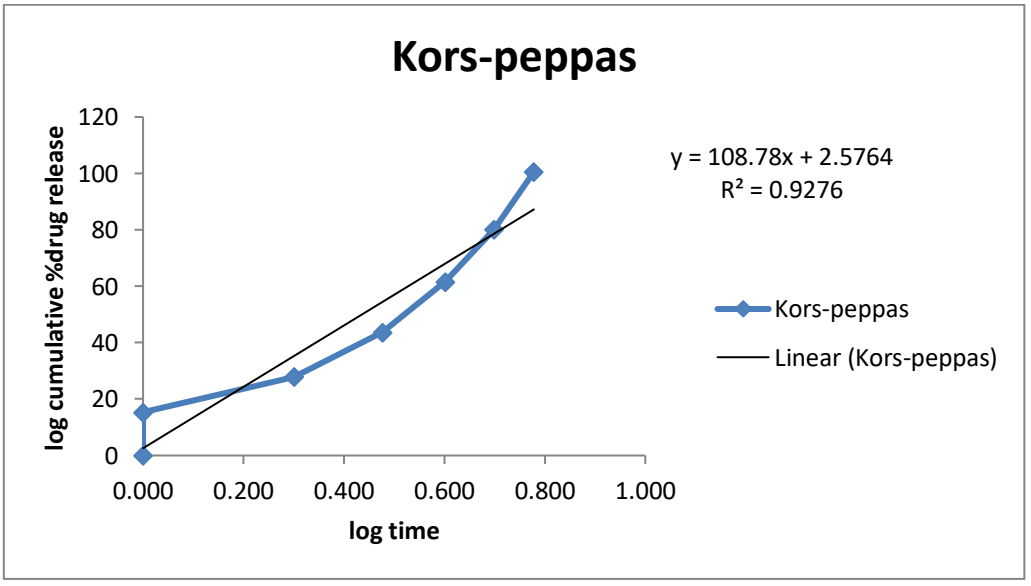


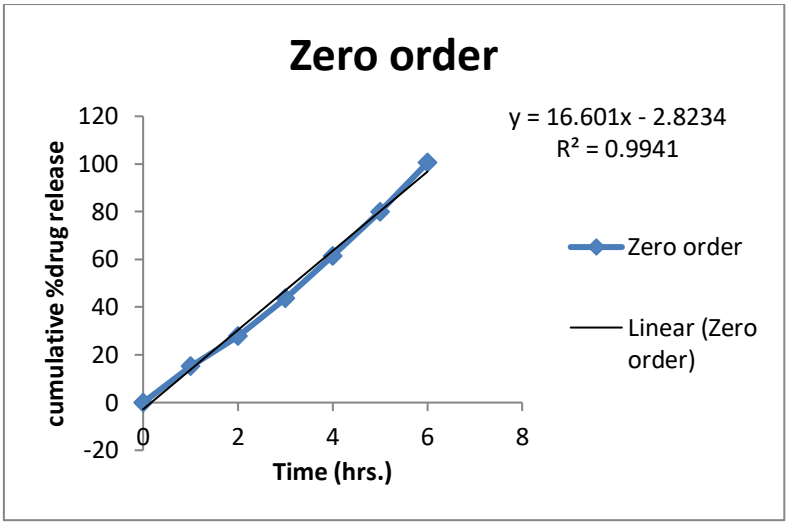


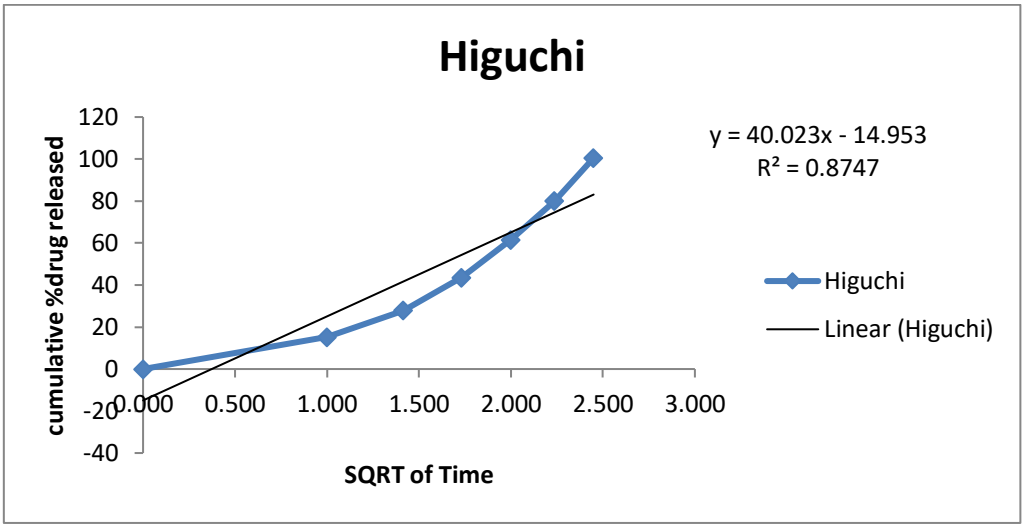


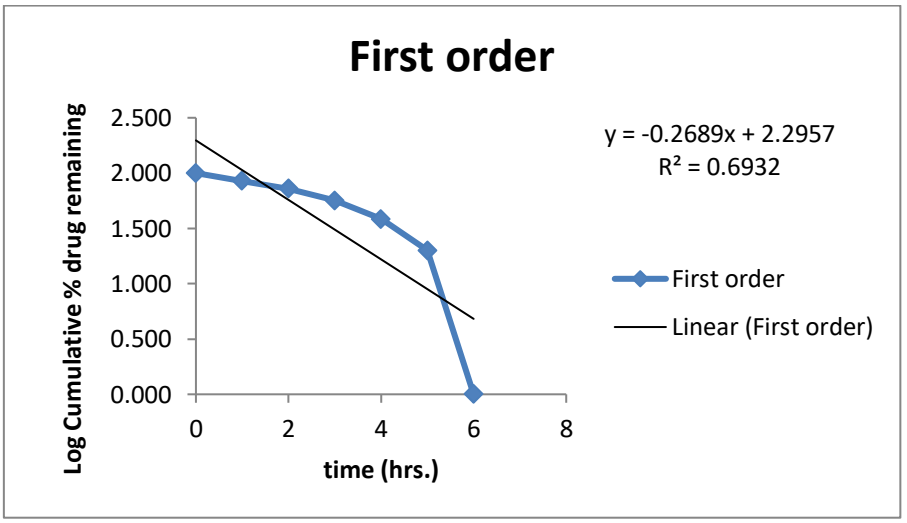
GOAT SKIN DRUG RELEASE OF FORMULATION SCO6

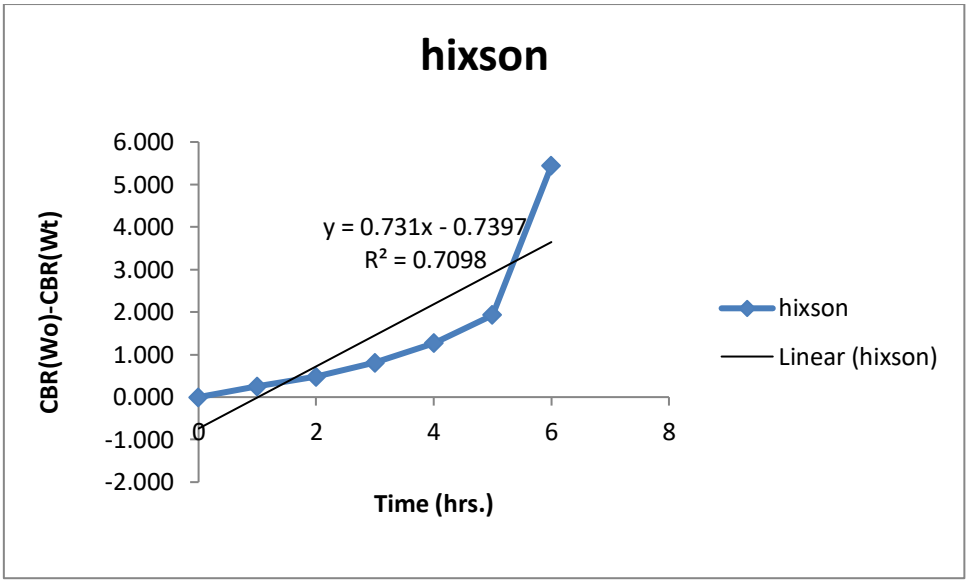
Time (Hr)	cumulative % drug released	% drug remaining	Square root time	log Cumu % drug remainining	log time	log Cumu % drug released	% Drug released	Cube Root of % drug Remaining(Wt)	Wo-Wt
0	0	100	0.000	2.000	0.000	0.000	100	4.642	0.000
1	15.2597	84.7403	1.000	1.928	0.000	1.184	15.2597	4.392	0.250
2	27.84898	72.15103	1.414	1.858	0.301	1.445	12.58928	4.163	0.479
3	43.6268	56.3732	1.732	1.751	0.477	1.640	15.77783	3.834	0.808
4	61.54865	38.45135	2.000	1.585	0.602	1.789	17.92185	3.375	1.267
5	80.0569	19.9431	2.236	1.300	0.699	1.903	18.50825	2.712	1.930
6	100.5076	-0.5076	2.449	#NUM!	0.778	2.002	20.4507	-0.798	5.440
7	-	#VALUE!	2.646	#VALUE!	0.845	#VALUE!	#VALUE!	#VALUE!	#VALUE!



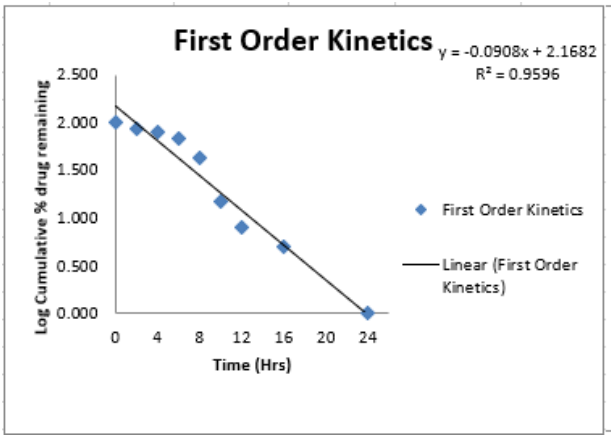

Zero order
y = 16.601x - 2.8234
R² = 0.9941
cumulative %drug release
Time (hrs.)
Zero order
Linear (Zero order)

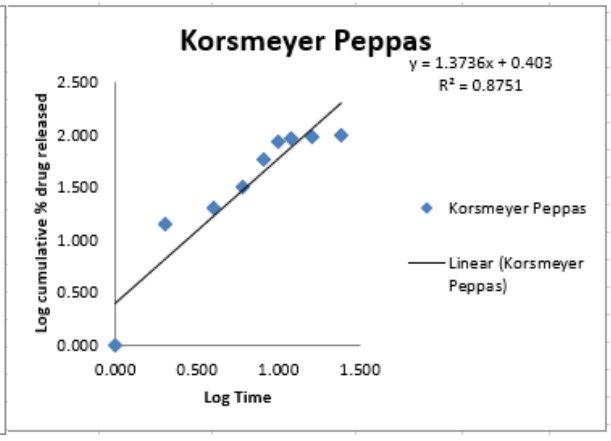

Higuchi
y = 40.023x - 14.953
R² = 0.8747
cumulative %drug released
SQRT of Time
Higuchi
Linear (Higuchi)

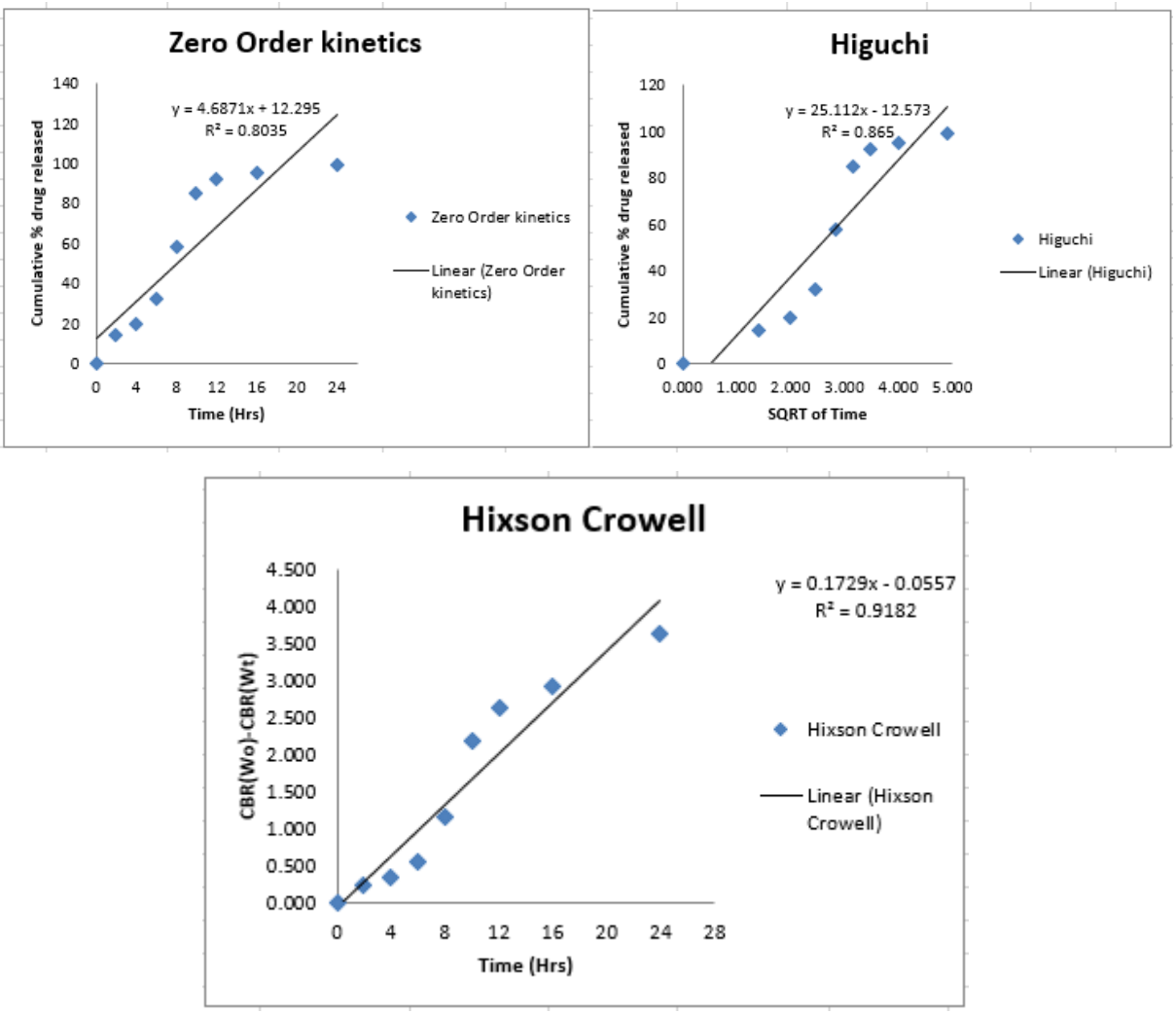

First order
y = -0.2689x + 2.2957
R² = 0.6932
Log Cumulative % drug remaining
time (hrs.)
First order
Linear (First order)



Time (Hr)	cumulative % drug released	% drug remaining	Square root time	log Cumu % drug remaining	log time	log Cumu % drug released	% Drug released	Cube Root of % drug Remaining(Wt)	Wo-Wt
0	0	100	0.000	2.000	0.000	0.000	100	4.642	0.000
2	14	86	1.414	1.934	0.301	1.146	14	4.414	0.228
4	20	80	2.000	1.903	0.602	1.301	6	4.309	0.333
6	32	68	2.449	1.833	0.778	1.505	12	4.082	0.560
8	58	42	2.828	1.623	0.903	1.763	26	3.476	1.166
10	85	15	3.162	1.176	1.000	1.929	27	2.466	2.176
12	92	8	3.464	0.903	1.079	1.964	7	2.000	2.642
16	95	5	4.000	0.699	1.204	1.978	3	1.710	2.932
24	99	1	4.899	0.000	1.380	1.996	4	1.000	3.642



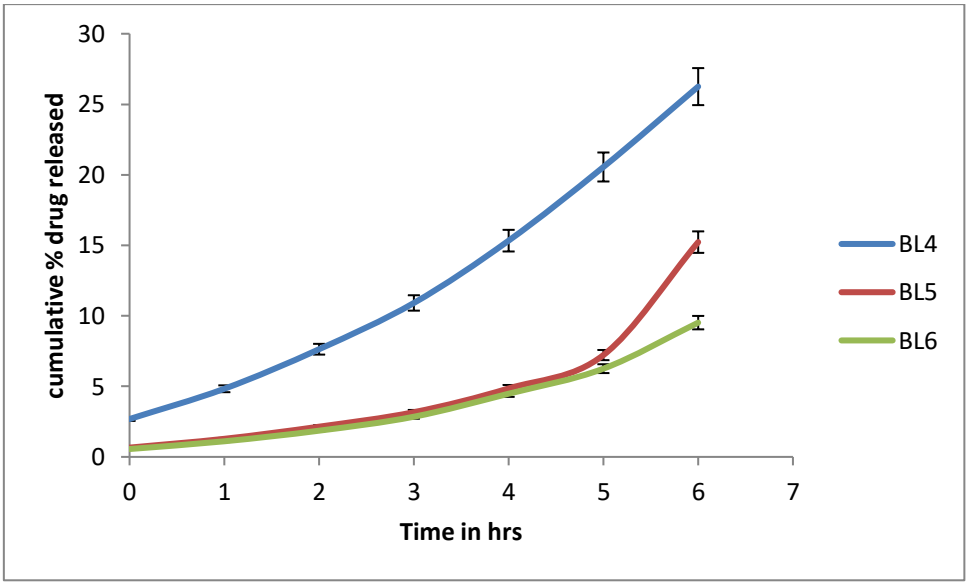




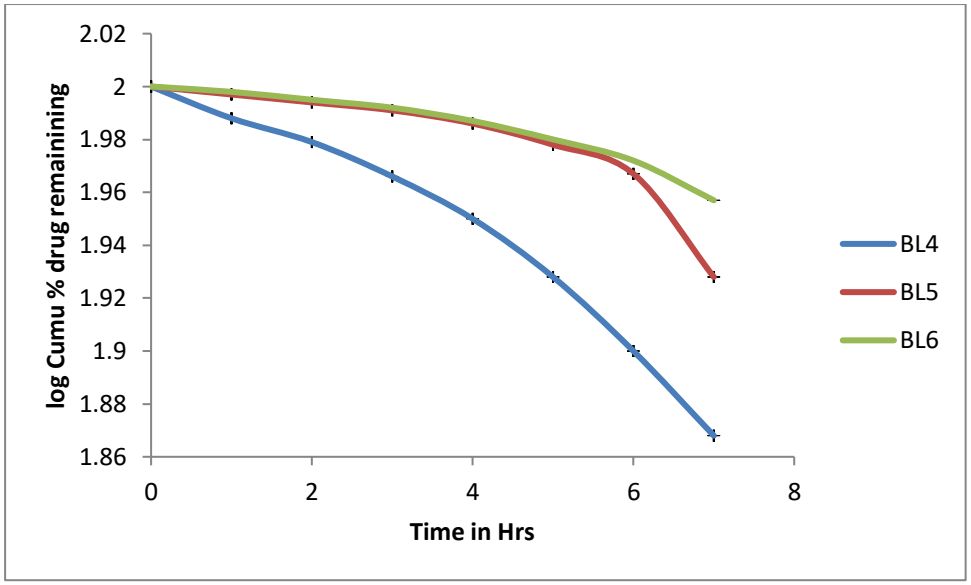
Mathematical models play a vital role in the interpretation of mechanism of drug release from a dosage form. It is an important tool to understand the drug release kinetics of a dosage form. The drug release was found to be best fitted by Higuchi square root model r2 =0.7343 for SCO4 and r2 =0.865 for SCO5and r2 =0.7652 for SCO6 which implies that release of drug as a square root of time dependent process and diffusion controlled. The dissolution data was also plotted according to Hixson –Crowell r2 =0.8631 for SCO4 and r2 =0.8282 for SCO5 and r2 =0.9182 for SCO6 which describes that change in surface area and diameter of the formulation with the progressive dissolution as a function of time. Also, the model Korsmeyer-Peppas power law equation states the type of diffusion, which was evaluated by value, n (Release exponent) which is higher than 0.79 which implies that the drug release from the system follow Super case II transport

SNAKE SKIN DRUG RELEASE OF FORMULATION BL4

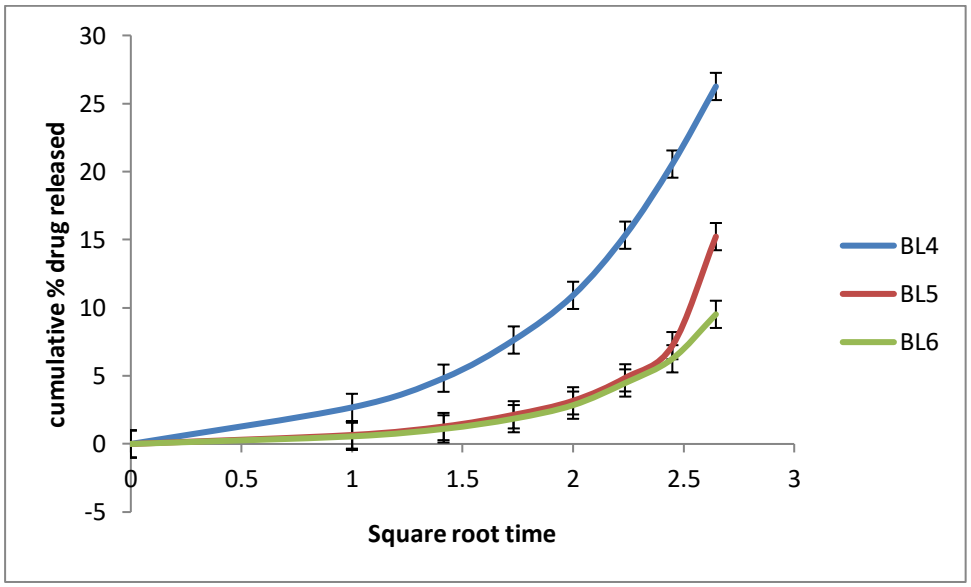
Time (Hr)	cumulative % drug released		
0	0	0	0
1	2.685625	0.658475	0.5574
2	4.82965	1.281525	1.1071
3	7.633375	2.1428	1.8584
4	10.91355	3.169	2.848
5	15.329875	4.8549	4.4789
6	20.5525	7.218825	6.2564
7	26.251575	15.22685	9.5183



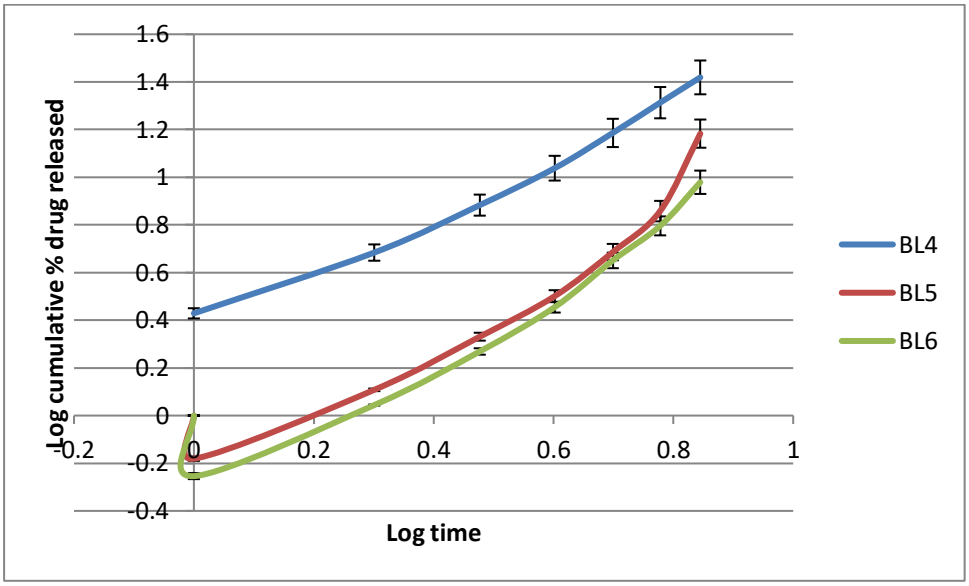
Time (Hr)	log Cumu % drug remainining		
0	2	2	2
1	1.988	1.997	1.998
2	1.979	1.994	1.995
3	1.966	1.991	1.992
4	1.95	1.986	1.987
5	1.928	1.978	1.98
6	1.9	1.967	1.972
7	1.868	1.928	1.957



Square root time	cumulative % drug released		
0	0	0	0
1	2.685625	0.658475	0.5574
1.414	4.82965	1.281525	1.1071
1.732	7.633375	2.1428	1.8584
2	10.91355	3.169	2.848
2.236	15.32988	4.8549	4.4789
2.449	20.5525	7.218825	6.2564
2.646	26.25158	15.22685	9.5183

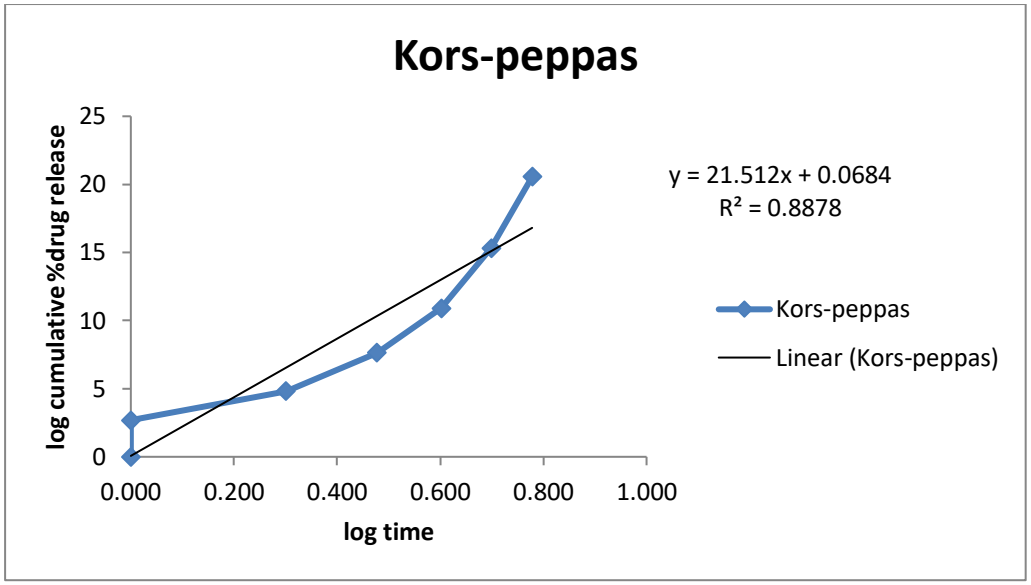


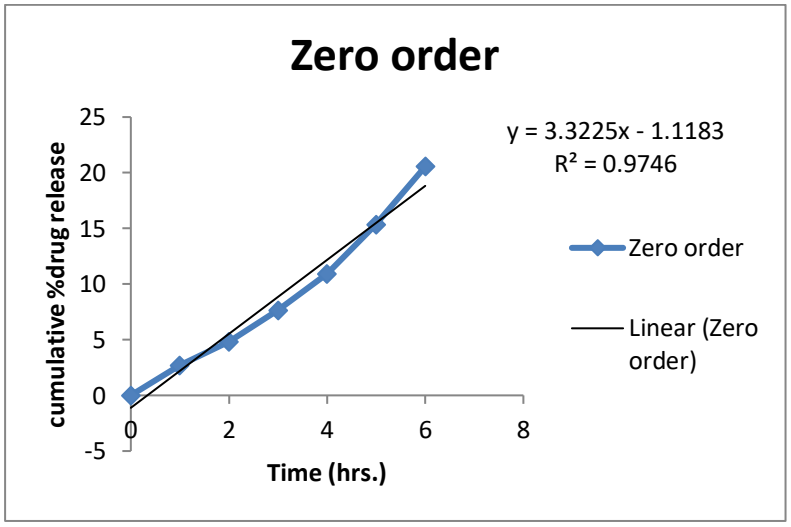
Log time	Log cumulative % drug released		
0	0	0	0
0	0.429	-0.181	-0.254
0.301	0.684	0.108	0.044
0.477	0.883	0.331	0.269
0.602	1.038	0.501	0.455
0.699	1.186	0.686	0.651
0.778	1.313	0.858	0.796
0.845	1.419	1.183	0.979

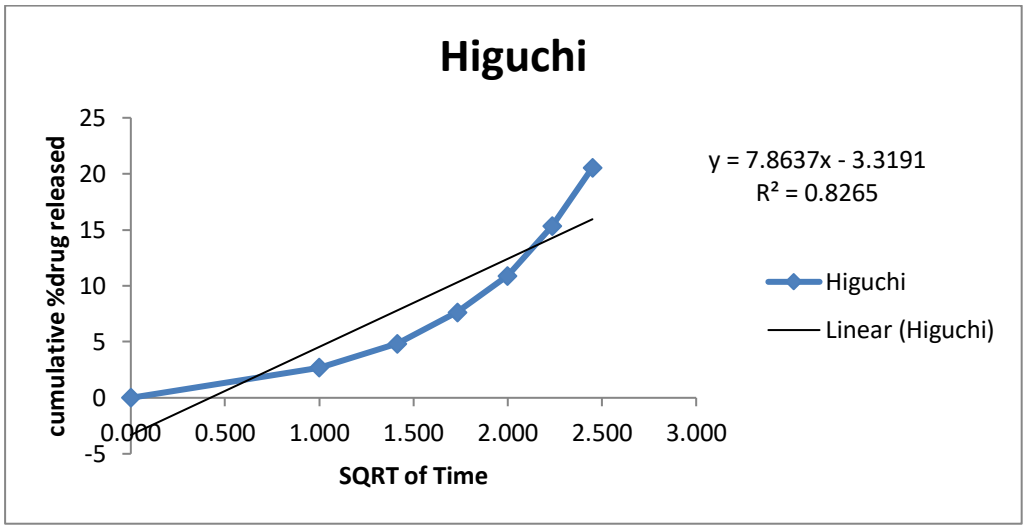


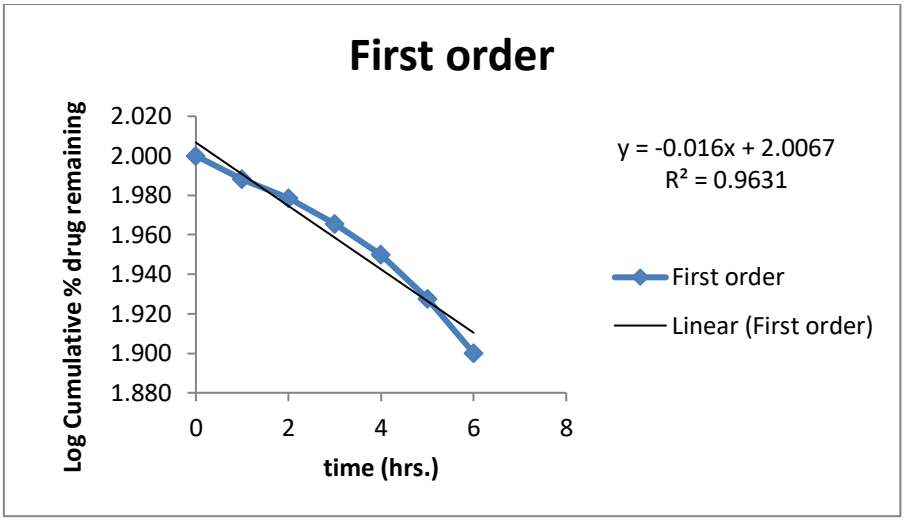
To investigated the utilities of a shed snake skin as a model membrane for preclinical studies of transdermal drug delivery, in shed snake skin was greater than that reported in human skin, and shed snake skin had excellent drug release properties

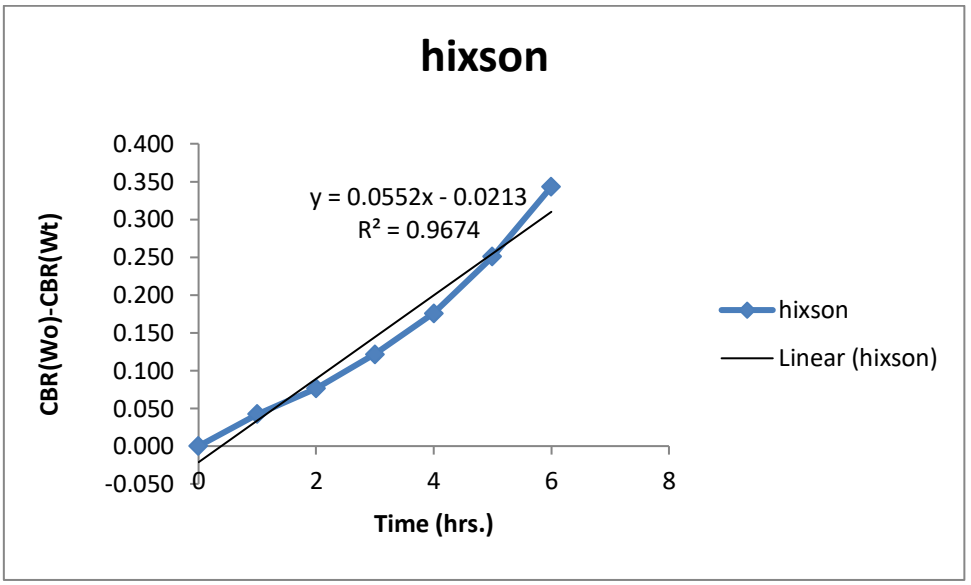
Time (Hr)	cumulative % drug released	% drug remaining	Square root time	log Cumu % drug remainining	log time	log Cumu % drug released	% Drug released	Cube Root of % drug Remaining(Wt)	Wo-Wt
0	0	100	0.000	2.000	0.000	0.000	100	4.642	0.000
1	2.685625	97.31438	1.000	1.988	0.000	0.429	2.685625	4.600	0.042
2	4.82965	95.17035	1.414	1.979	0.301	0.684	2.144025	4.566	0.076
3	7.633375	92.36663	1.732	1.966	0.477	0.883	2.803725	4.520	0.122
4	10.91355	89.08645	2.000	1.950	0.602	1.038	3.280175	4.466	0.176
5	15.32988	84.67013	2.236	1.928	0.699	1.186	4.416325	4.391	0.251
6	20.5525	79.4475	2.449	1.900	0.778	1.313	5.222625	4.299	0.343
7	26.25158	73.74843	2.646	1.868	0.845	1.419	5.699075	4.194	0.448


Kors-peppas
log cumulative %drug release
25
20
15
10
5
0
0.000
0.200
0.400
0.600
0.800
1.000
log time
y = 21.512x + 0.0684
R² = 0.8878
Kors-peppas
Linear (Kors-peppas)

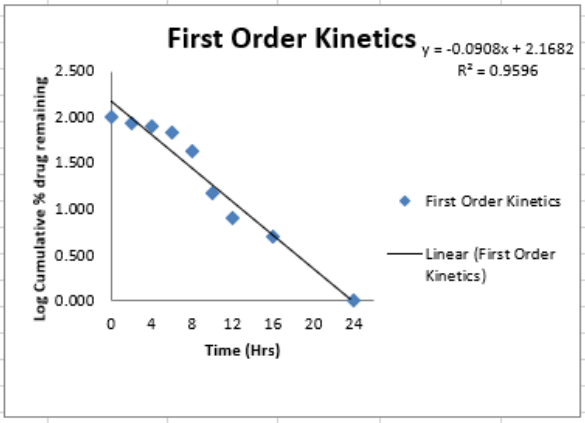

Zero order
cumulative %drug release
25
20
15
10
5
0
-5
0
2
4
6
8
Time (hrs.)
y = 3.3225x - 1.1183
R² = 0.9746
Zero order
Linear (Zero order)

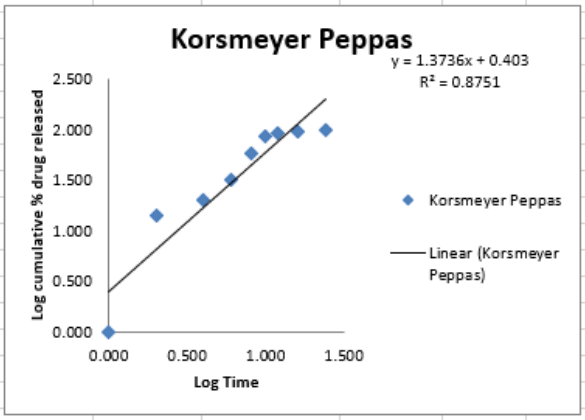

Higuchi
cumulative %drug released
25
20
15
10
5
0
-5
0.000
0.500
1.000
1.500
2.000
2.500
3.000
SQRT of Time
y = 7.8637x - 3.3191
R² = 0.8265
Higuchi
Linear (Higuchi)

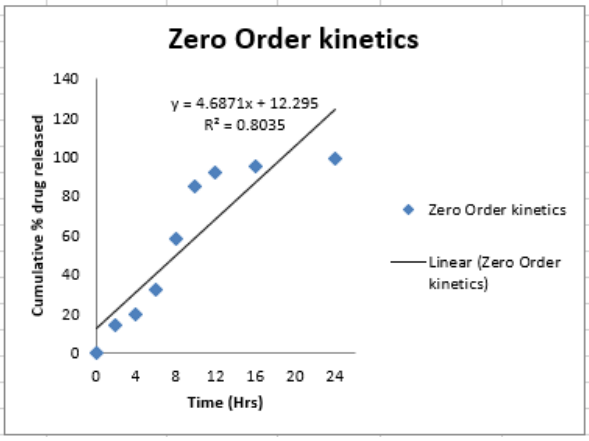


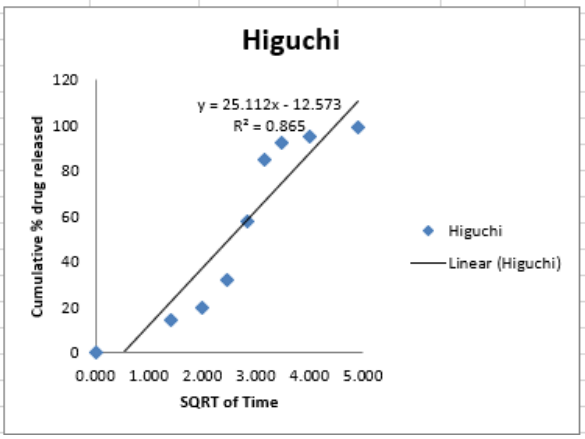


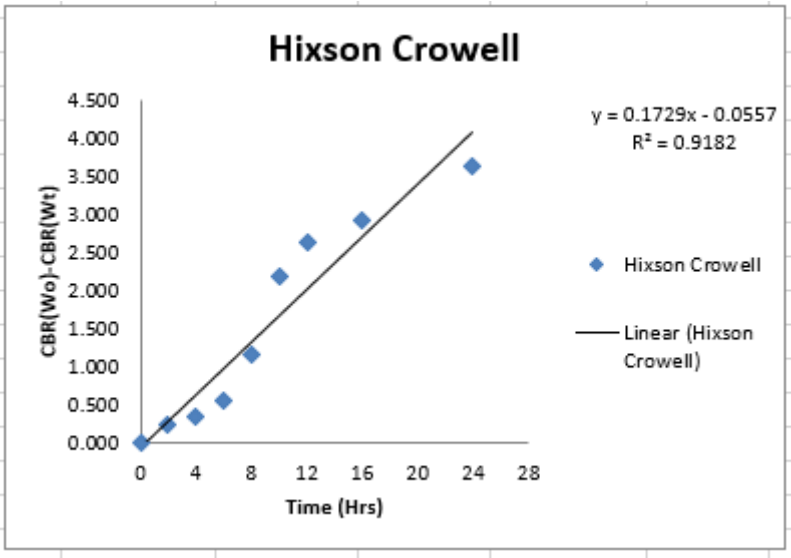
Time (Hr)	cumulative % drug released	% drug remaining	Square root time	log Cumu % drug remaining	log time	log Cumu % drug released	% Drug released	Cube Root of % drug Remaining(Wt)	Wo-Wt
0	0	100	0.000	2.000	0.000	0.000	100	4.642	0.000
2	14	86	1.414	1.934	0.301	1.146	14	4.414	0.228
4	20	80	2.000	1.903	0.602	1.301	6	4.309	0.333
6	32	68	2.449	1.833	0.778	1.505	12	4.082	0.560
8	58	42	2.828	1.623	0.903	1.763	26	3.476	1.166
10	85	15	3.162	1.176	1.000	1.929	27	2.466	2.176
12	92	8	3.464	0.903	1.079	1.964	7	2.000	2.642
16	95	5	4.000	0.699	1.204	1.978	3	1.710	2.932
24	99	1	4.899	0.000	1.380	1.996	4	1.000	3.642







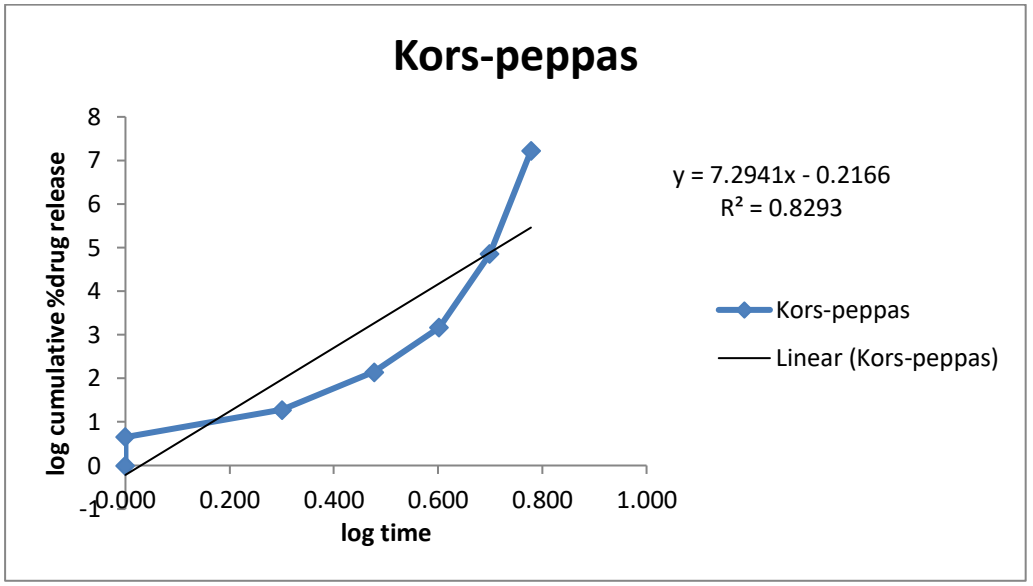


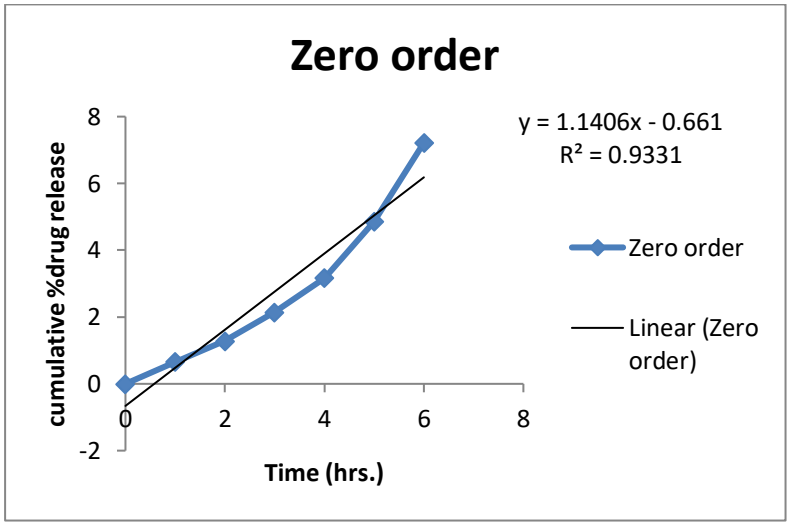


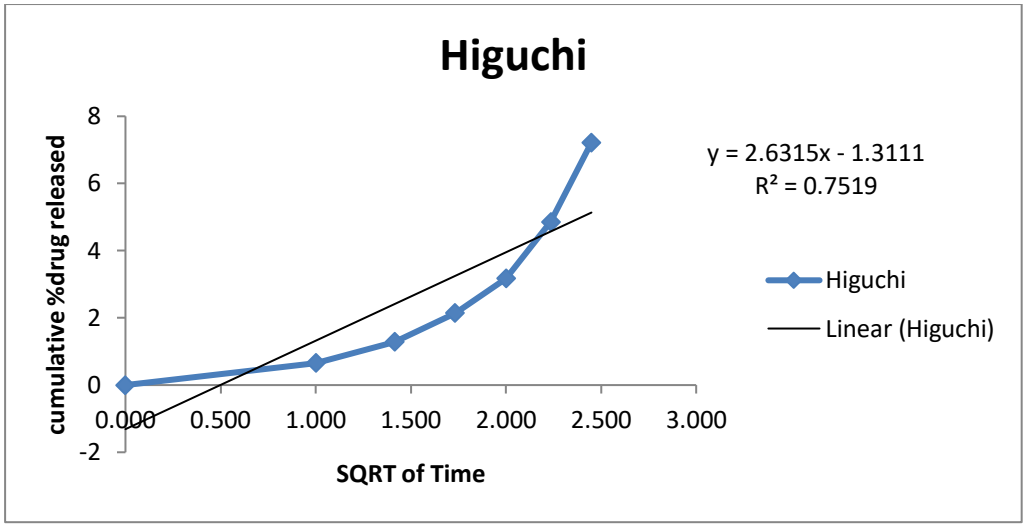
SNAKE SKIN DRUG RELEASE OF FORMULATION BL5

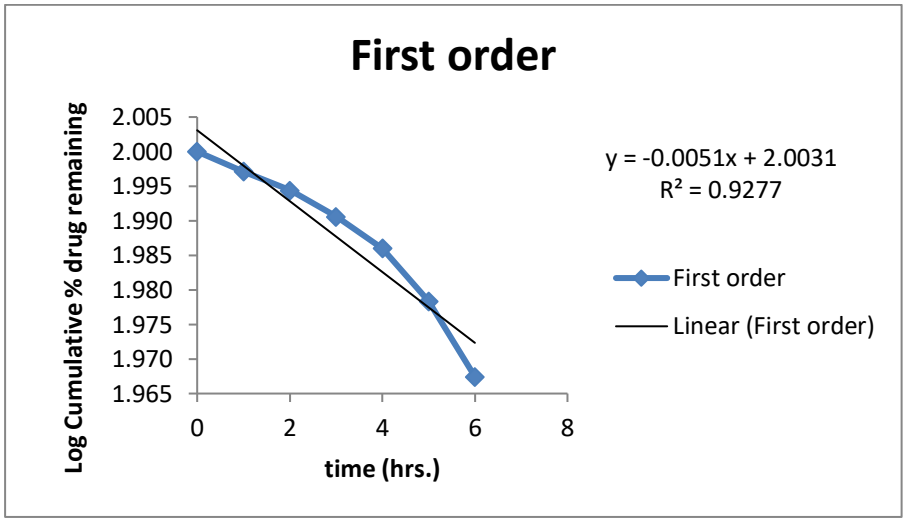
Time (Hr)	cumulative % drug released	% drug remaining	Square root time	log Cumu % drug remainining	log time	log Cumu % drug released	% Drug released	Cube Root of % drug Remaining(Wt)	Wo-Wt
0	0	100	0.000	2.000	0.000	0.000	100	4.642	0.000
1	0.658475	99.34153	1.000	1.997	0.000	-0.181	0.658475	4.631	0.011
2	1.281525	98.71848	1.414	1.994	0.301	0.108	0.62305	4.622	0.020
3	2.1428	97.8572	1.732	1.991	0.477	0.331	0.861275	4.608	0.034
4	3.169	96.831	2.000	1.986	0.602	0.501	1.0262	4.592	0.050

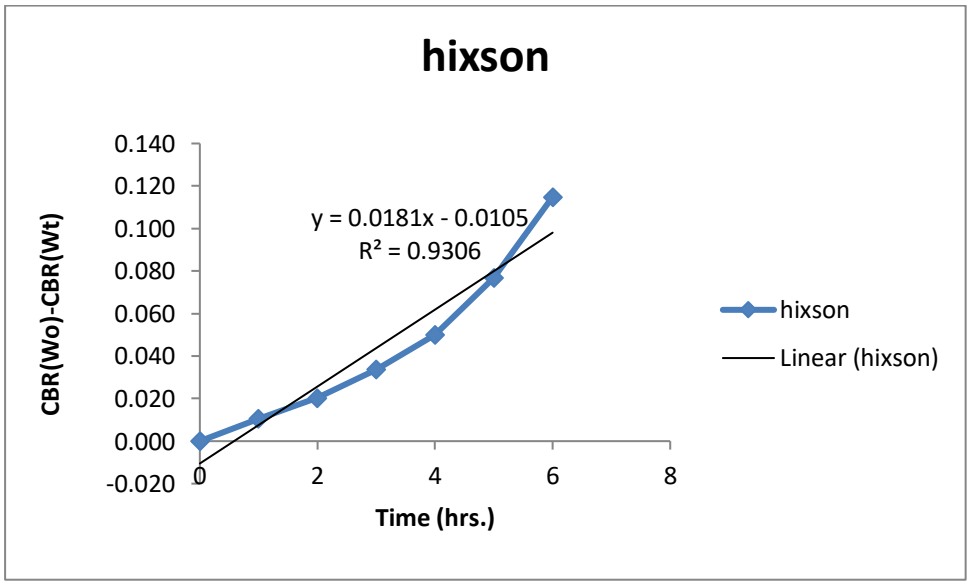
5	4.8549	95.1451	2.236	1.978	0.699	0.686	1.6859	4.565	0.077
6	7.218825	92.78118	2.449	1.967	0.778	0.858	2.363925	4.527	0.115
7	15.22685	84.77315	2.646	1.928	0.845	1.183	8.008025	4.393	0.249



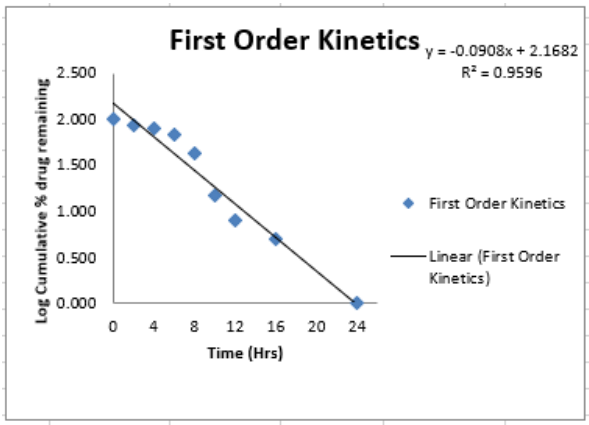


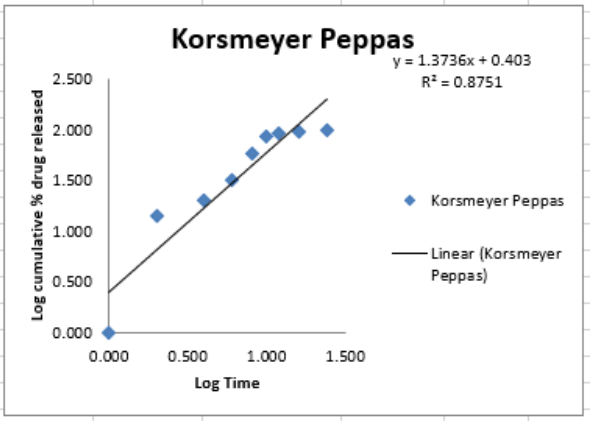

Higuchi
cumulative %drug released
8
6
4
2
0
-2
0.000
0.500
1.000
1.500
2.000
2.500
3.000
SQRT of Time
y = 2.6315x - 1.3111
R² = 0.7519
Higuchi
Linear (Higuchi)

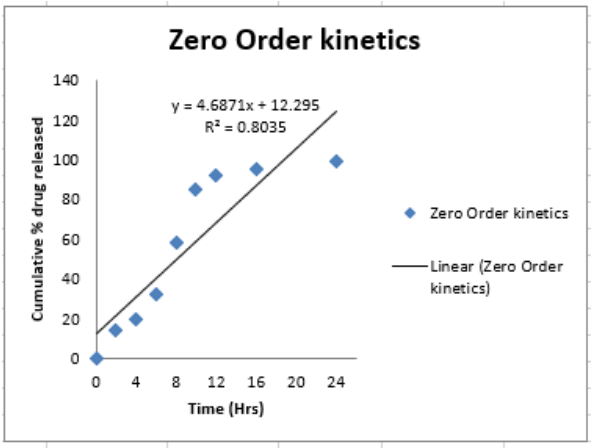

First order
Log Cumulative % drug remaining
2.005
2.000
1.995
1.990
1.985
1.980
1.975
1.970
1.965
0
2
4
6
8
time (hrs.)
y = -0.0051x + 2.0031
R² = 0.9277
First order
Linear (First order)

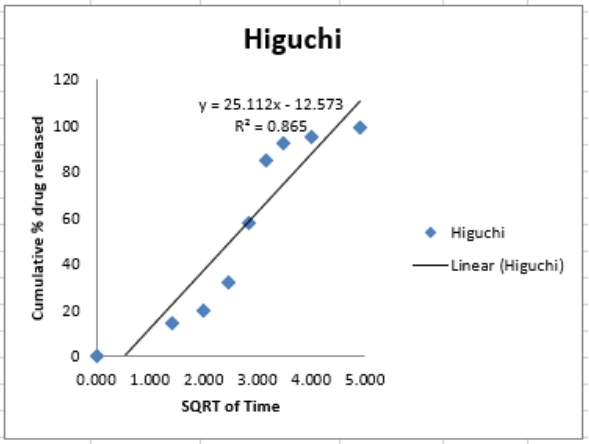

hixson
CBR(Wo)-CBR(Wt)
0.140
0.120
0.100
0.080
0.060
0.040
0.020
0.000
-0.020
0
2
4
6
8
Time (hrs.)
y = 0.0181x - 0.0105
R² = 0.9306
hixson
Linear (hixson)

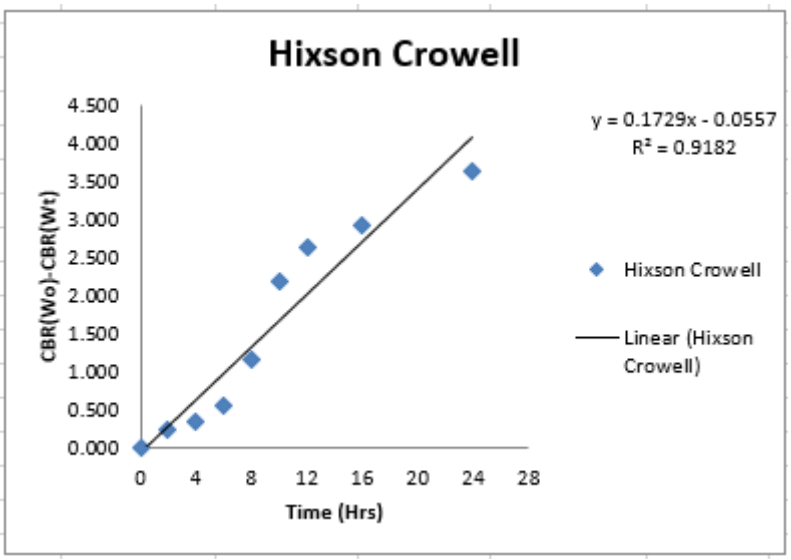
Time (Hr)	cumulative % drug released	% drug remaining	Square root time	log Cumu % drug remaining	log time	log Cumu % drug released	% Drug released	Cube Root of % drug Remaining(Wt)	Wo-Wt
0	0	100	0.000	2.000	0.000	0.000	100	4.642	0.000
2	14	86	1.414	1.934	0.301	1.146	14	4.414	0.228
4	20	80	2.000	1.903	0.602	1.301	6	4.309	0.333
6	32	68	2.449	1.833	0.778	1.505	12	4.082	0.560
8	58	42	2.828	1.623	0.903	1.763	26	3.476	1.166
10	85	15	3.162	1.176	1.000	1.929	27	2.466	2.176
12	92	8	3.464	0.903	1.079	1.964	7	2.000	2.642
16	95	5	4.000	0.699	1.204	1.978	3	1.710	2.932
24	99	1	4.899	0.000	1.380	1.996	4	1.000	3.642





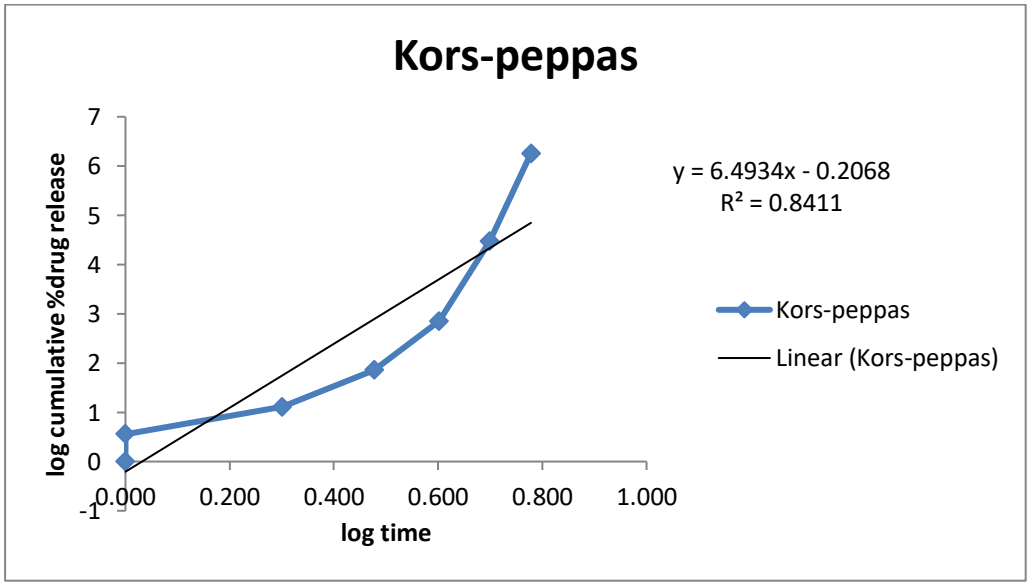


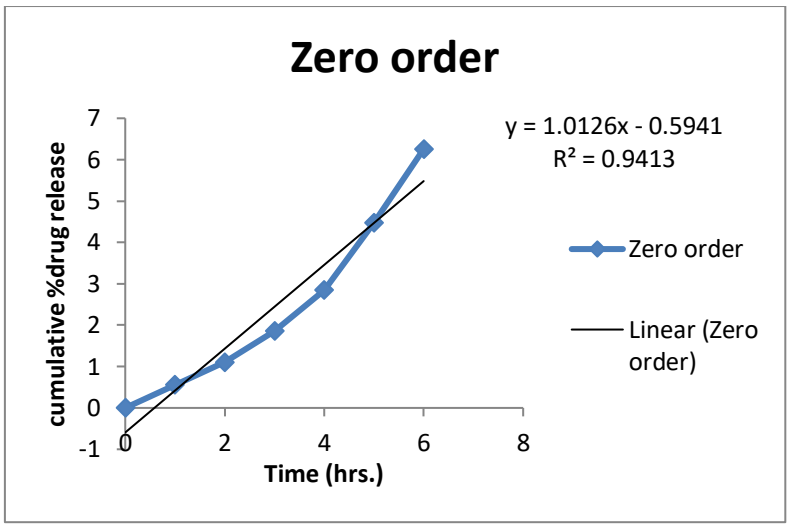


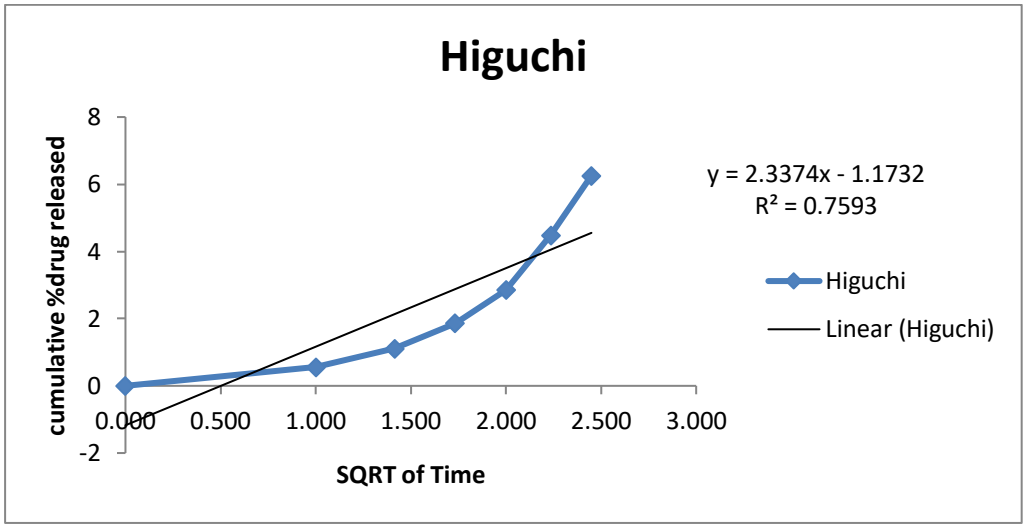


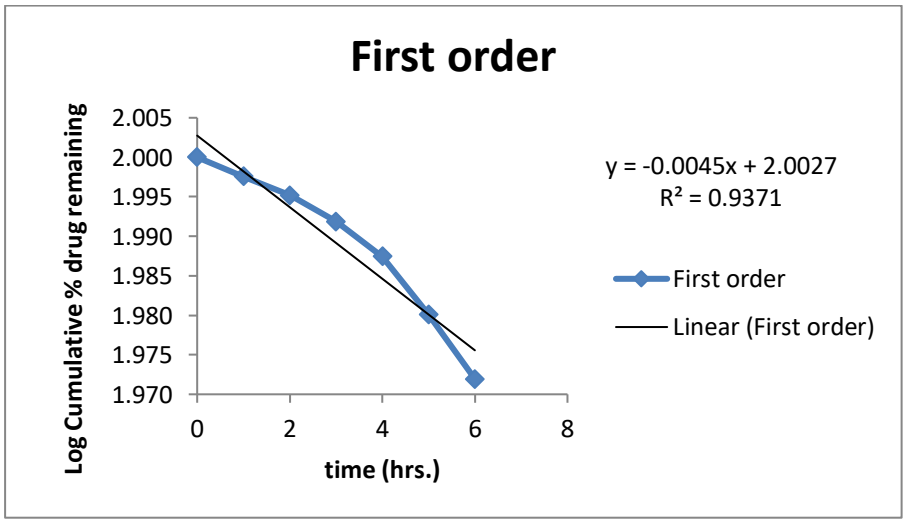
SNAKE SKIN DRUG RELEASE OF FORMULATION BL6

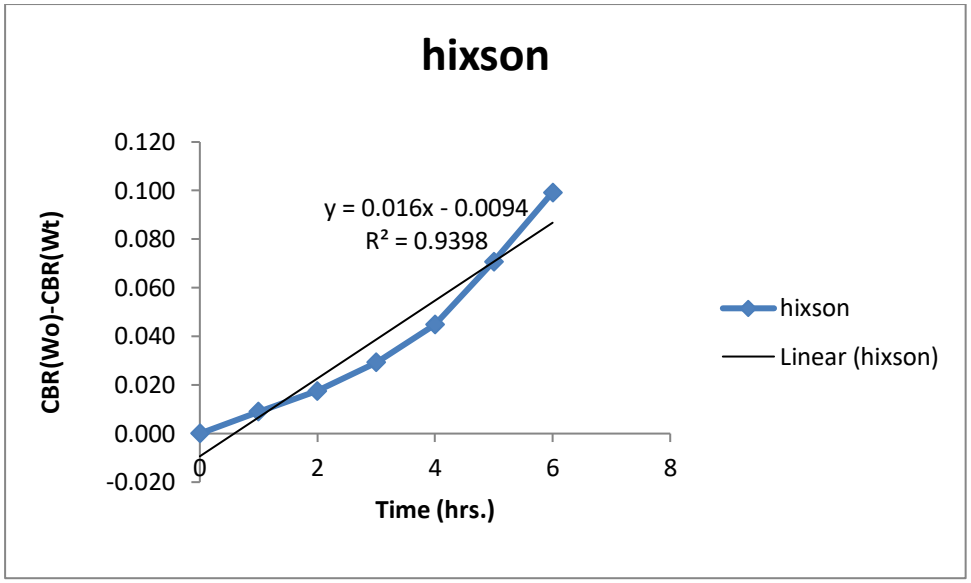
Time (Hr)	cumulative % drug released	% drug remaining	Square root time	log Cumu % drug remainining	log time	log Cumu % drug released	% Drug released	Cube Root of % drug Remaining(Wt)	Wo-Wt
0	0	100	0.000	2.000	0.000	0.000	100	4.642	0.000
1	0.55735	99.44265	1.000	1.998	0.000	-0.254	0.55735	4.633	0.009
2	1.1071	98.8929	1.414	1.995	0.301	0.044	0.54975	4.624	0.018
3	1.858425	98.14158	1.732	1.992	0.477	0.269	0.751325	4.613	0.029
4	2.847975	97.15203	2.000	1.987	0.602	0.455	0.98955	4.597	0.045
5	4.4789	95.5211	2.236	1.980	0.699	0.651	1.630925	4.571	0.071
6	6.256425	93.74358	2.449	1.972	0.778	0.796	1.777525	4.543	0.099
7	9.518275	90.48173	2.646	1.957	0.845	0.979	3.26185	4.489	0.153



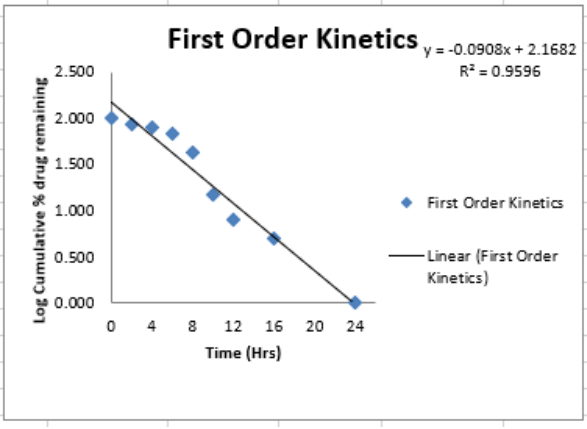

Zero order
y = 1.0126x - 0.5941
R² = 0.9413
Zero order
Linear (Zero order)
cumulative %drug release
Time (hrs.)
7
6
5
4
3
2
1
0
-1
0
2
4
6
8

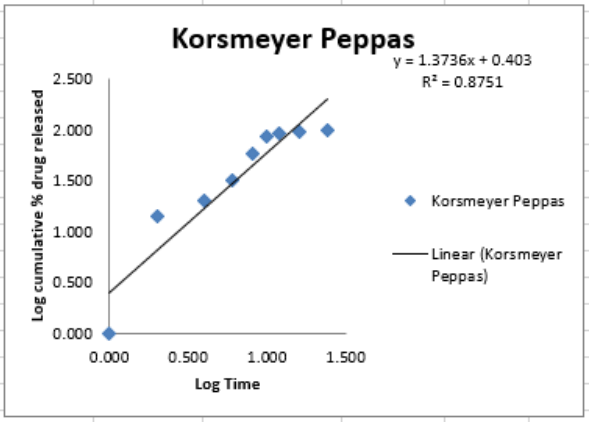

Higuchi
y = 2.3374x - 1.1732
R² = 0.7593
Higuchi
Linear (Higuchi)
cumulative %drug released
SQRT of Time
8
6
4
2
0
-2
0.000
0.500
1.000
1.500
2.000
2.500
3.000

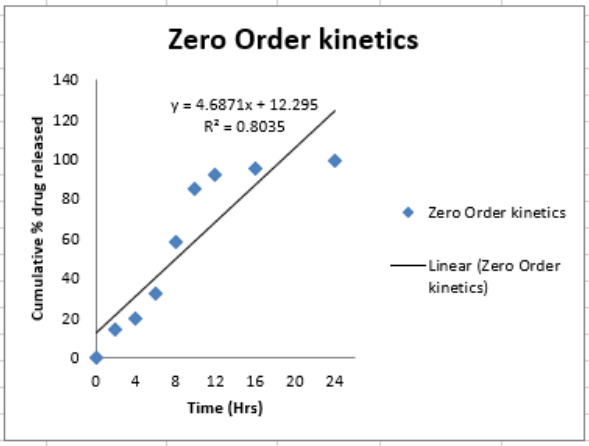

First order
y = -0.0045x + 2.0027
R² = 0.9371
First order
Linear (First order)
Log Cumulative % drug remaining
time (hrs.)
2.005
2.000
1.995
1.990
1.985
1.980
1.975
1.970
0
2
4
6
8

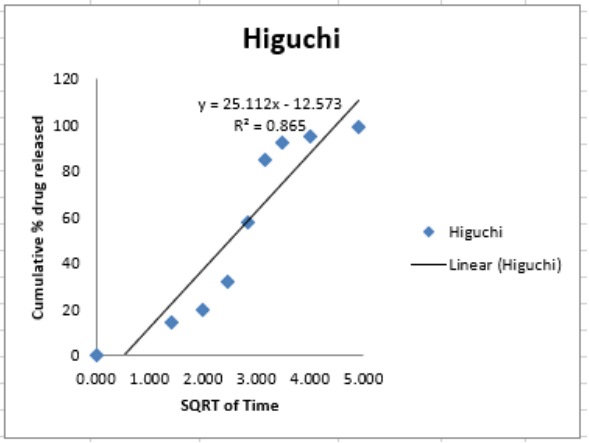


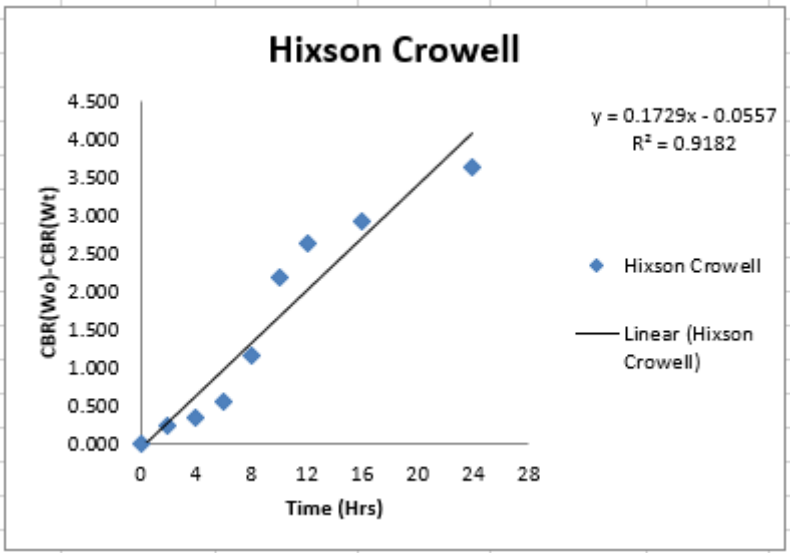
Time (Hr)	cumulative % drug released	% drug remaining	Square root time	log Cumu % drug remaining	log time	log Cumu % drug released	% Drug released	Cube Root of % drug Remaining(Wt)	Wo-Wt
0	0	100	0.000	2.000	0.000	0.000	100	4.642	0.000
2	14	86	1.414	1.934	0.301	1.146	14	4.414	0.228
4	20	80	2.000	1.903	0.602	1.301	6	4.309	0.333
6	32	68	2.449	1.833	0.778	1.505	12	4.082	0.560
8	58	42	2.828	1.623	0.903	1.763	26	3.476	1.166
10	85	15	3.162	1.176	1.000	1.929	27	2.466	2.176
12	92	8	3.464	0.903	1.079	1.964	7	2.000	2.642
16	95	5	4.000	0.699	1.204	1.978	3	1.710	2.932
24	99	1	4.899	0.000	1.380	1.996	4	1.000	3.642





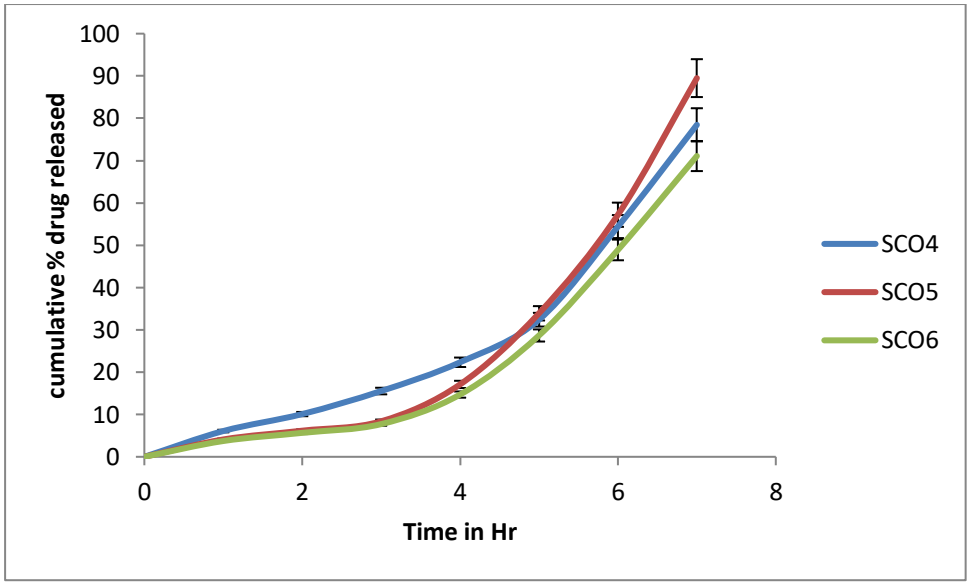




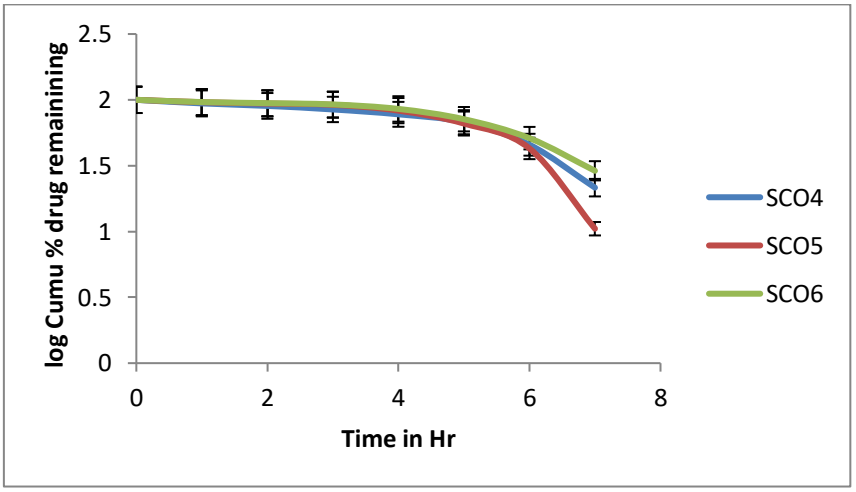


SNAKE SKIN DRUG RELEASE OF FORMULATION SCO4

Time (Hr)	cumulative % drug released		
0	0	0	0
1	6.0885	4.101125	3.7365
2	10.101675	6.17185	5.6607
3	15.5442	8.389175	7.7314
4	22.342775	17.111875	14.713
5	32.4032	33.9159	28.677
6	54.411525	57.206975	48.889
7	78.453925	89.495625	71.081

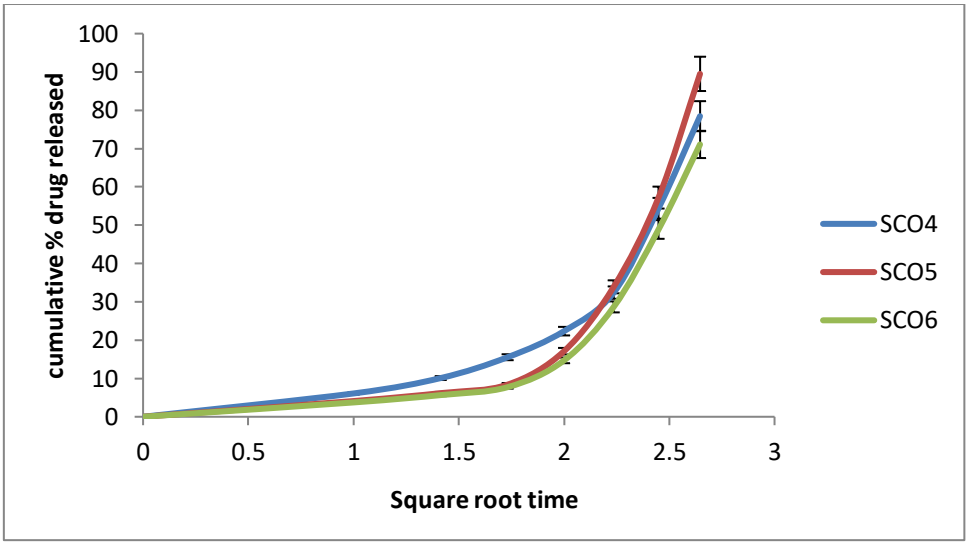


Time (Hr)	log Cumu % drug remainining		
0	2	2	2
1	1.973	1.982	1.983
2	1.954	1.972	1.975
3	1.927	1.962	1.965
4	1.89	1.918	1.931
5	1.83	1.82	1.853
6	1.659	1.631	1.709
7	1.333	1.021	1.461

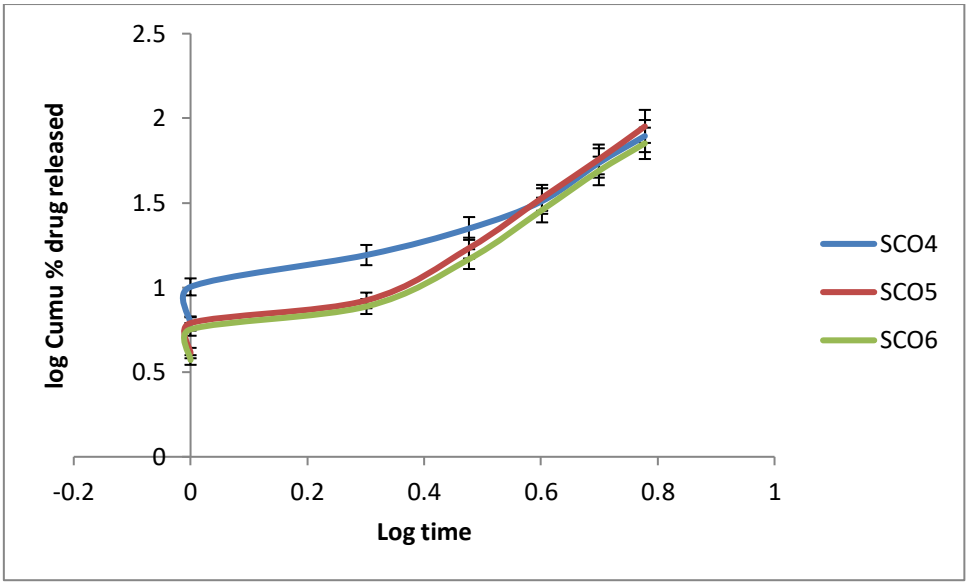


Square root time	cumulative % drug released		
0	0	0	0

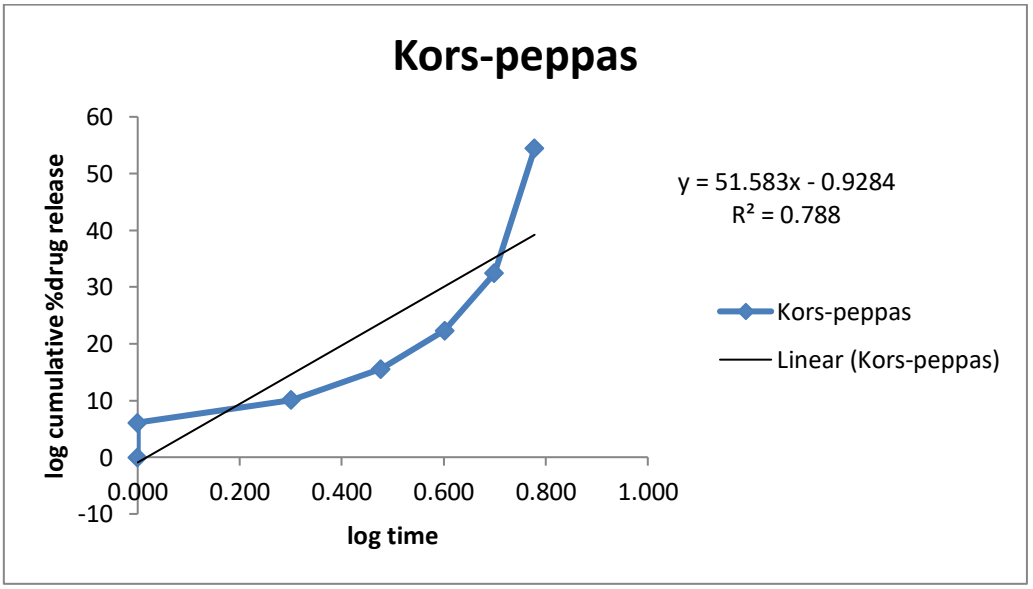
1	6.0885	4.101125	3.7365
1.414	10.10168	6.17185	5.6607
1.732	15.5442	8.389175	7.7314
2	22.34278	17.11188	14.713
2.236	32.4032	33.9159	28.677
2.449	54.41153	57.20698	48.889
2.646	78.45393	89.49563	71.081

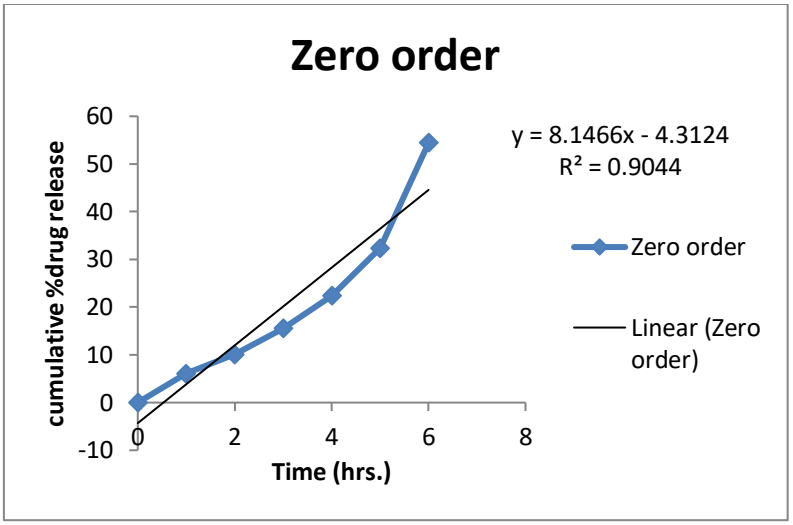


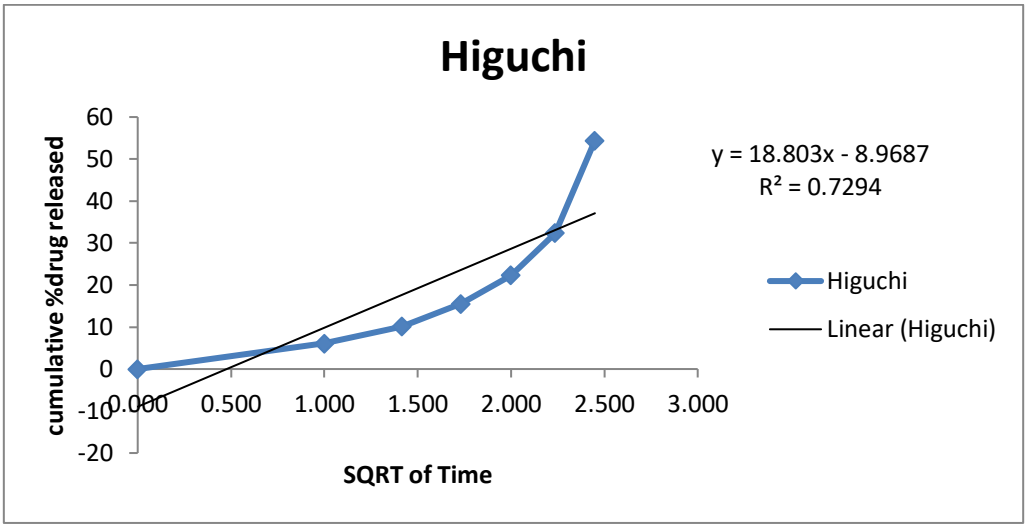
Log time	log Cumu % drug released		
0	0	0	0
0	0.785	0.613	0.572
0.301	1.004	0.79	0.753
0.477	1.192	0.924	0.888
0.602	1.349	1.233	1.168
0.699	1.511	1.53	1.458
0.778	1.736	1.757	1.689
0.845	1.895	1.952	1.852

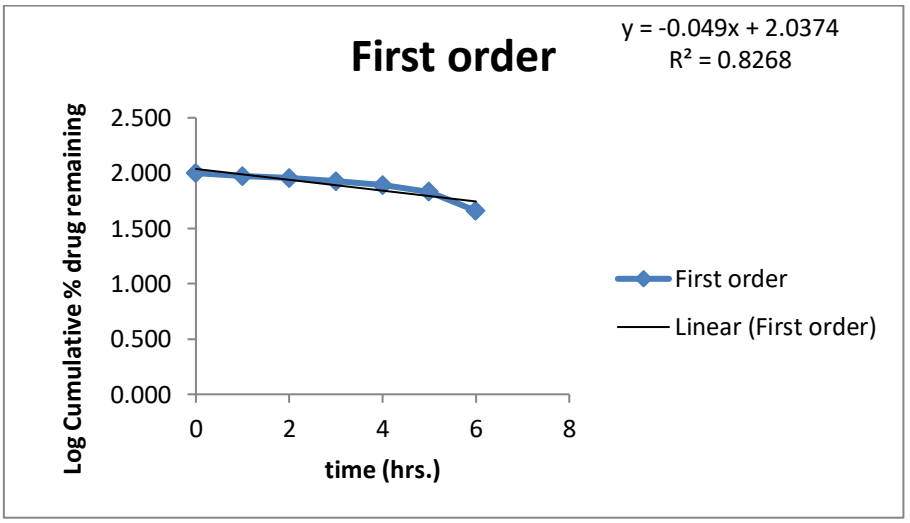


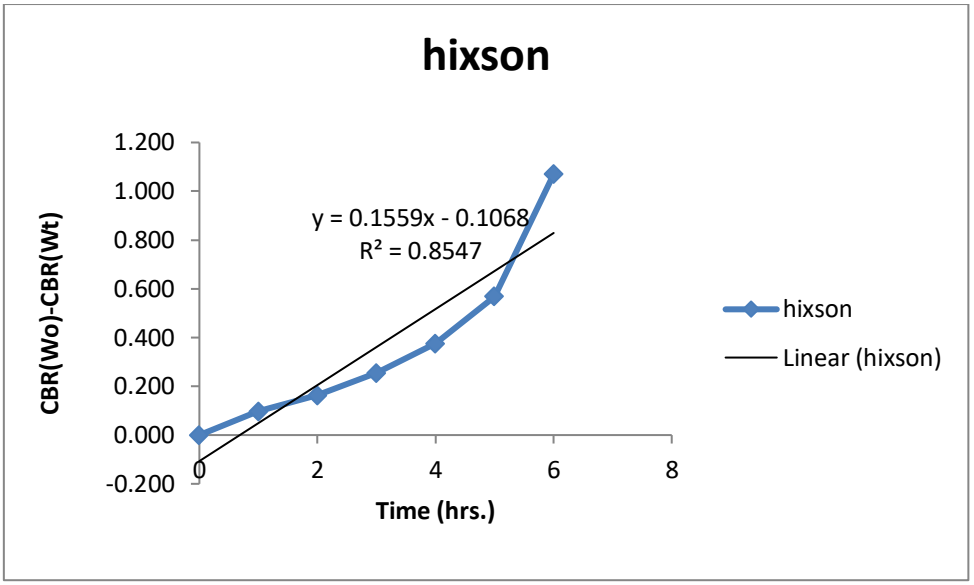
Time (Hr)	cumulative % drug released	% drug remaining	Square root time	log Cumu % drug remainining	log time	log Cumu % drug released	% Drug released	Cube Root of % drug Remaining(Wt)	Wo-Wt
0	0	100	0.000	2.000	0.000	0.000	100	4.642	0.000
1	6.0885	93.9115	1.000	1.973	0.000	0.785	6.0885	4.545	0.097
2	10.10168	89.89833	1.414	1.954	0.301	1.004	4.013175	4.480	0.162
3	15.5442	84.4558	1.732	1.927	0.477	1.192	5.442525	4.387	0.255
4	22.34278	77.65723	2.000	1.890	0.602	1.349	6.798575	4.266	0.376
5	32.4032	67.5968	2.236	1.830	0.699	1.511	10.06043	4.074	0.568
6	54.41153	45.58848	2.449	1.659	0.778	1.736	22.00833	3.572	1.070
7	78.45393	21.54608	2.646	1.333	0.845	1.895	24.0424	2.783	1.859



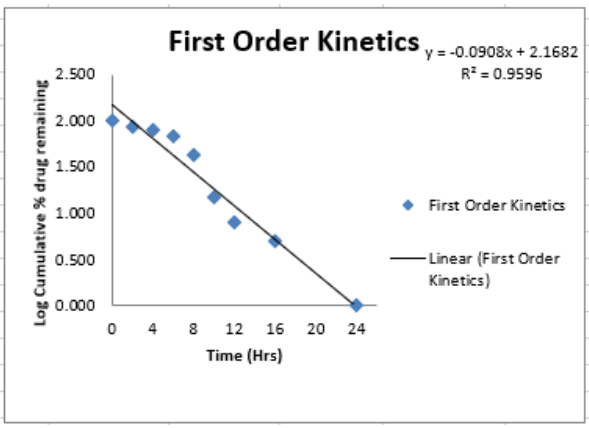

Zero order
cumulative %drug release
Time (hrs.)
y = 8.1466x - 4.3124
R² = 0.9044
Zero order
Linear (Zero order)

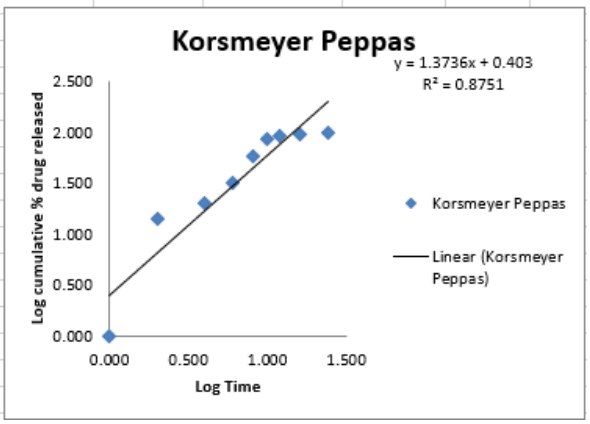

Higuchi
cumulative %drug released
SQRT of Time
y = 18.803x - 8.9687
R² = 0.7294
Higuchi
Linear (Higuchi)

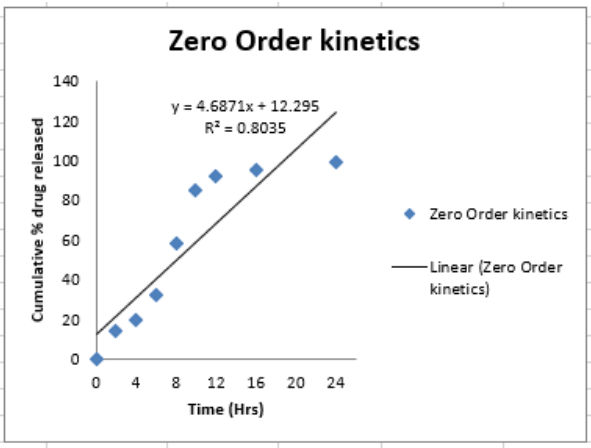

First order
Log Cumulative % drug remaining
time (hrs.)
y = -0.049x + 2.0374
R² = 0.8268
First order
Linear (First order)

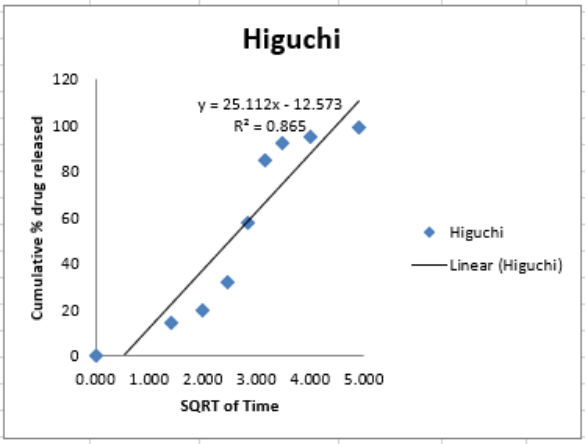


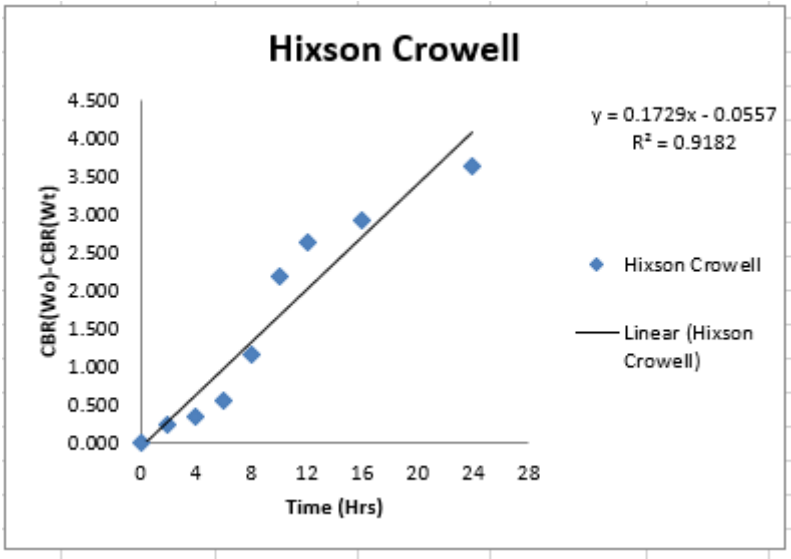
Time (Hr)	cumulative % drug released	% drug remaining	Square root time	log Cumu % drug remaining	log time	log Cumu % drug released	% Drug released	Cube Root of % drug Remaining(Wt)	Wo-Wt
0	0	100	0.000	2.000	0.000	0.000	100	4.642	0.000
2	14	86	1.414	1.934	0.301	1.146	14	4.414	0.228
4	20	80	2.000	1.903	0.602	1.301	6	4.309	0.333
6	32	68	2.449	1.833	0.778	1.505	12	4.082	0.560
8	58	42	2.828	1.623	0.903	1.763	26	3.476	1.166
10	85	15	3.162	1.176	1.000	1.929	27	2.466	2.176
12	92	8	3.464	0.903	1.079	1.964	7	2.000	2.642
16	95	5	4.000	0.699	1.204	1.978	3	1.710	2.932
24	99	1	4.899	0.000	1.380	1.996	4	1.000	3.642





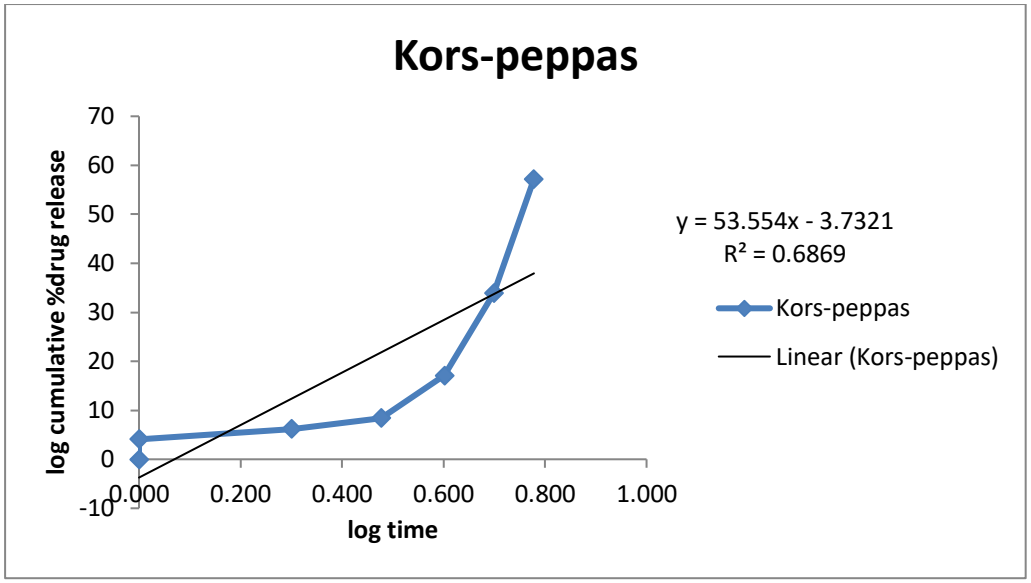


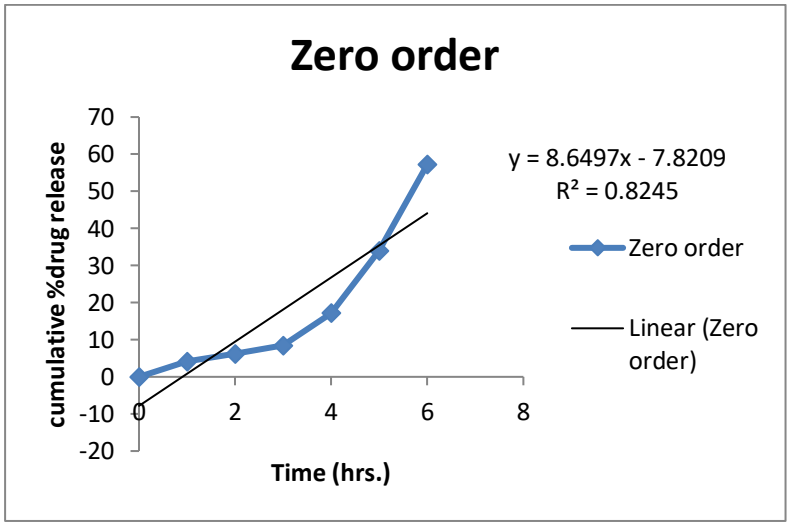


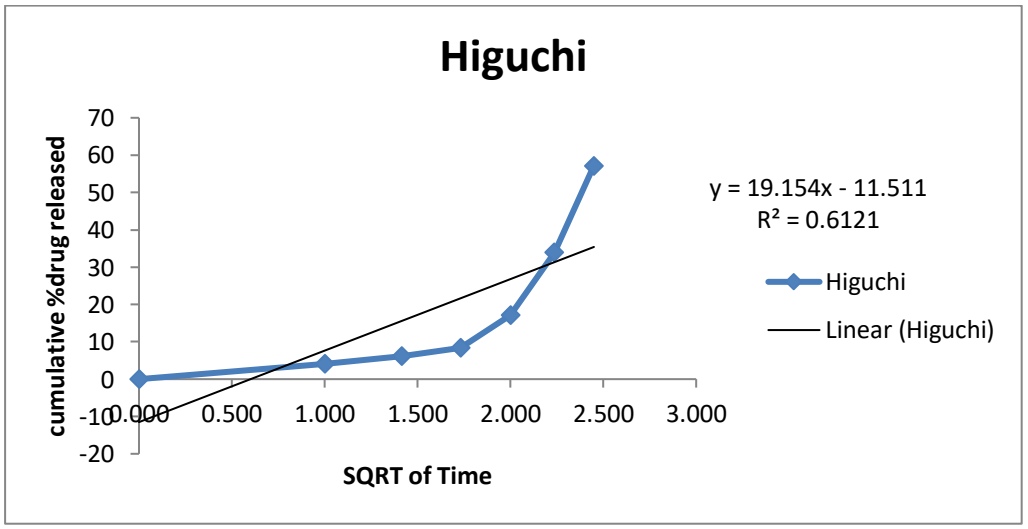


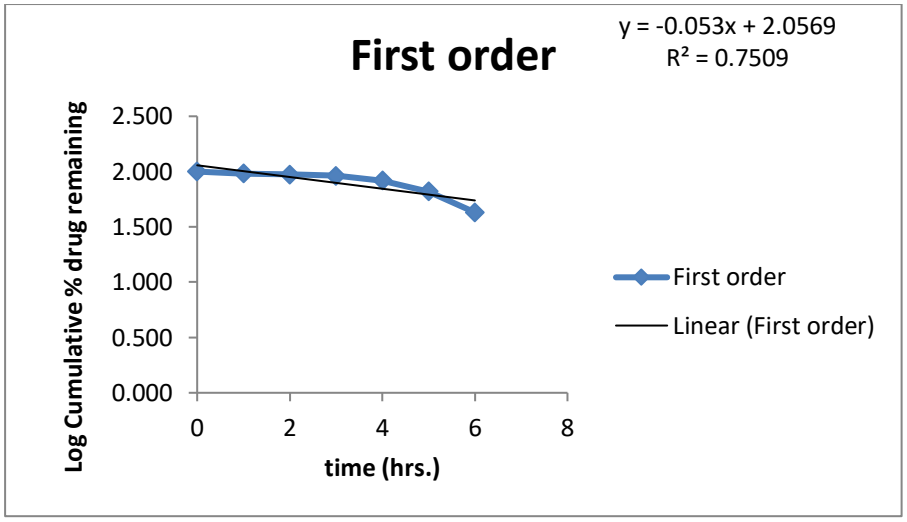
SNAKE SKIN DRUG RELEASE OF FORMULATION SCO5

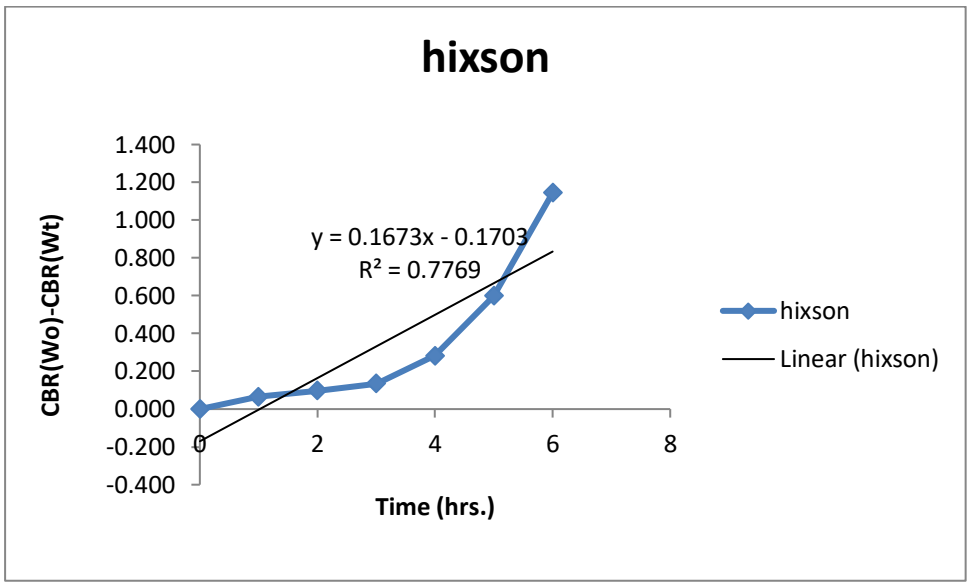
Time (Hr)	cumulative % drug released	% drug remaining	Square root time	log Cumu % drug remainining	log time	log Cumu % drug released	% Drug released	Cube Root of % drug Remaining(Wt)	Wo-Wt
0	0	100	0.000	2.000	0.000	0.000	100	4.642	0.000
1	4.101125	95.89888	1.000	1.982	0.000	0.613	4.101125	4.577	0.065
2	6.17185	93.82815	1.414	1.972	0.301	0.790	2.070725	4.544	0.098
3	8.389175	91.61083	1.732	1.962	0.477	0.924	2.217325	4.508	0.134
4	17.11188	82.88813	2.000	1.918	0.602	1.233	8.7227	4.360	0.282
5	33.9159	66.0841	2.236	1.820	0.699	1.530	16.80403	4.043	0.599
6	57.20698	42.79303	2.449	1.631	0.778	1.757	23.29108	3.498	1.144
7	89.49563	10.50438	2.646	1.021	0.845	1.952	32.28865	2.190	2.452


Kors-peppas
log cumulative %drug release
70
60
50
40
30
20
10
0
-10
0.000
0.200
0.400
0.600
0.800
1.000
log time
y = 53.554x - 3.7321
R² = 0.6869
Kors-peppas
Linear (Kors-peppas)

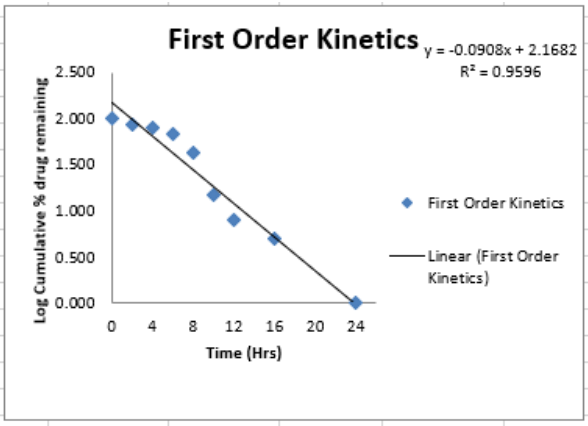

Zero order
cumulative %drug release
70
60
50
40
30
20
10
0
-10
-20
0
2
4
6
8
Time (hrs.)
y = 8.6497x - 7.8209
R² = 0.8245
Zero order
Linear (Zero order)

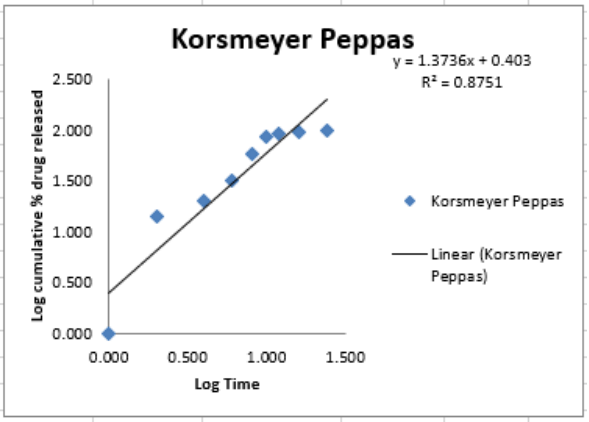

Higuchi
cumulative %drug released
70
60
50
40
30
20
10
0
-10
-20
0.000
0.500
1.000
1.500
2.000
2.500
3.000
SQRT of Time
y = 19.154x - 11.511
R² = 0.6121
Higuchi
Linear (Higuchi)

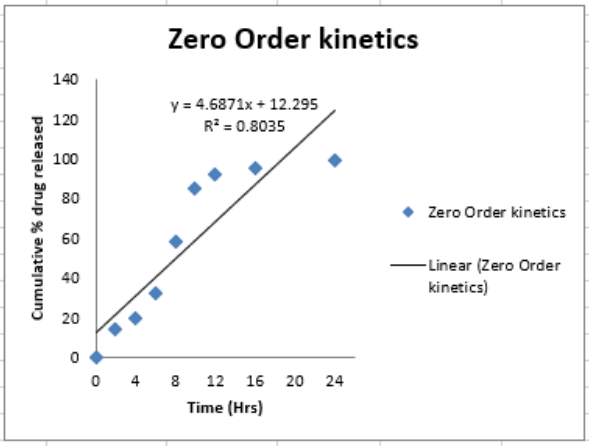


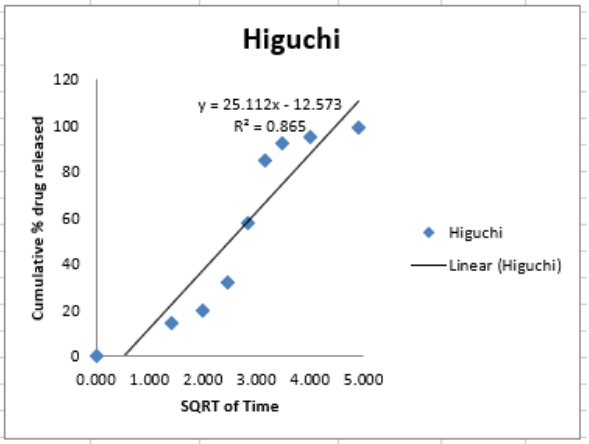


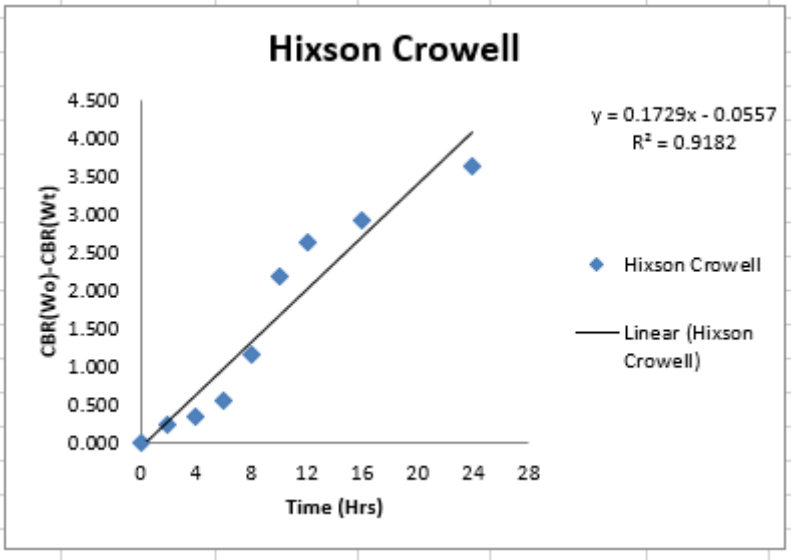
Time (Hr)	cumulative % drug released	% drug remaining	Square root time	log Cumu % drug remaining	log time	log Cumu % drug released	% Drug released	Cube Root of % drug Remaining(Wt)	Wo-Wt
0	0	100	0.000	2.000	0.000	0.000	100	4.642	0.000
2	14	86	1.414	1.934	0.301	1.146	14	4.414	0.228
4	20	80	2.000	1.903	0.602	1.301	6	4.309	0.333
6	32	68	2.449	1.833	0.778	1.505	12	4.082	0.560
8	58	42	2.828	1.623	0.903	1.763	26	3.476	1.166
10	85	15	3.162	1.176	1.000	1.929	27	2.466	2.176
12	92	8	3.464	0.903	1.079	1.964	7	2.000	2.642
16	95	5	4.000	0.699	1.204	1.978	3	1.710	2.932
24	99	1	4.899	0.000	1.380	1.996	4	1.000	3.642







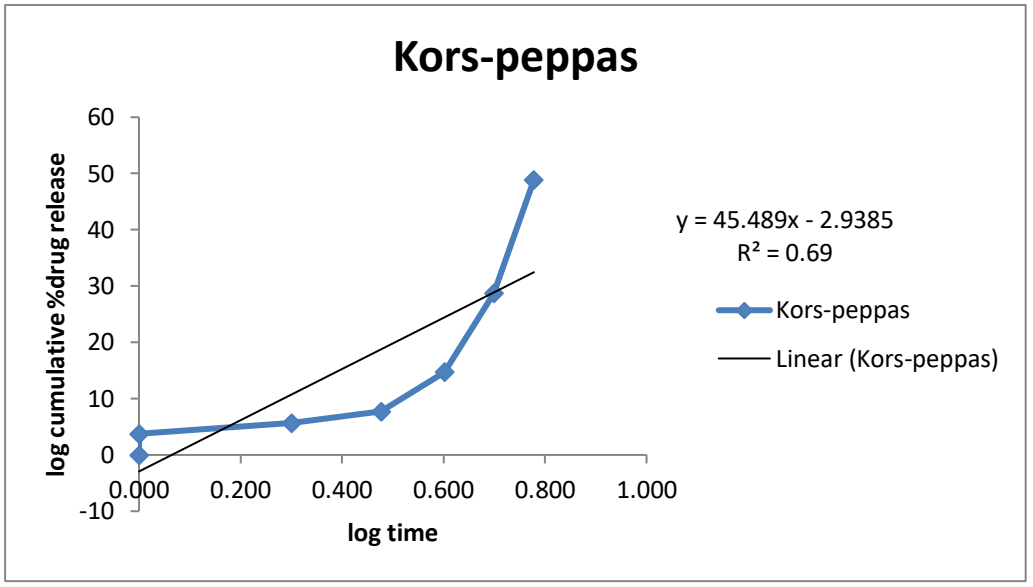


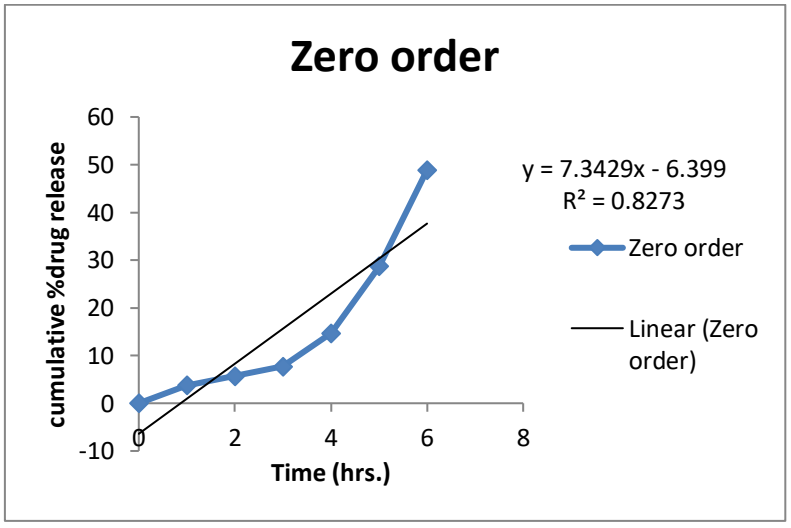


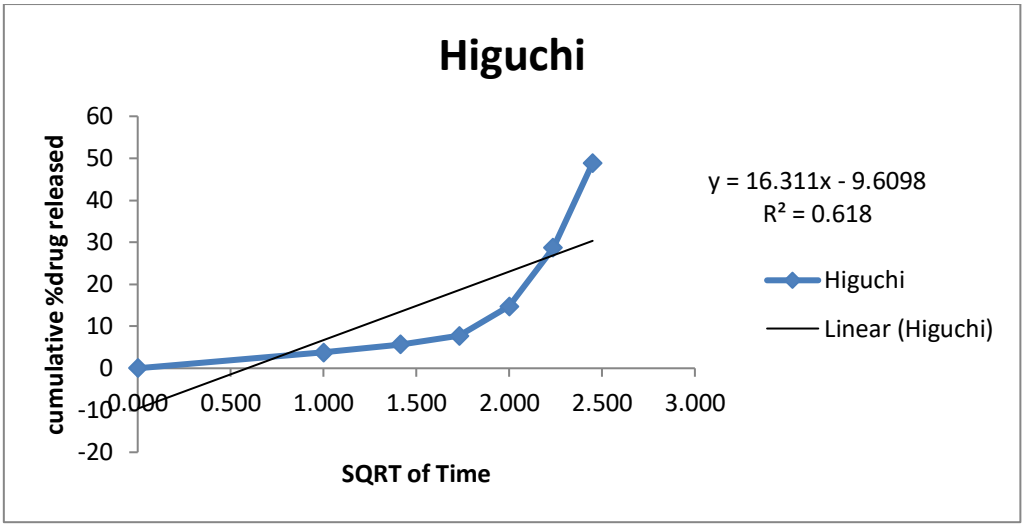
SNAKE SKIN DRUG RELEASE OF FORMULATION SCO6

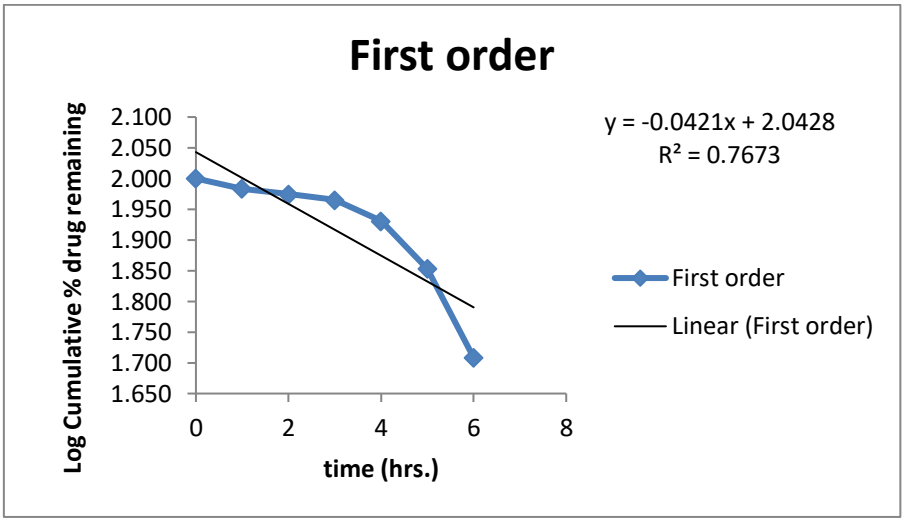
Time (Hr)	cumulative % drug released	% drug remaining	Square root time	log Cumu % drug remainining	log time	log Cumu % drug released	% Drug released	Cube Root of % drug Remaining(Wt)	Wo-Wt
0	0	100	0.000	2.000	0.000	0.000	100	4.642	0.000
1	3.736525	96.26348	1.000	1.983	0.000	0.572	3.736525	4.583	0.059
2	5.66065	94.33935	1.414	1.975	0.301	0.753	1.924125	4.552	0.090
3	7.731375	92.26863	1.732	1.965	0.477	0.888	2.070725	4.519	0.123

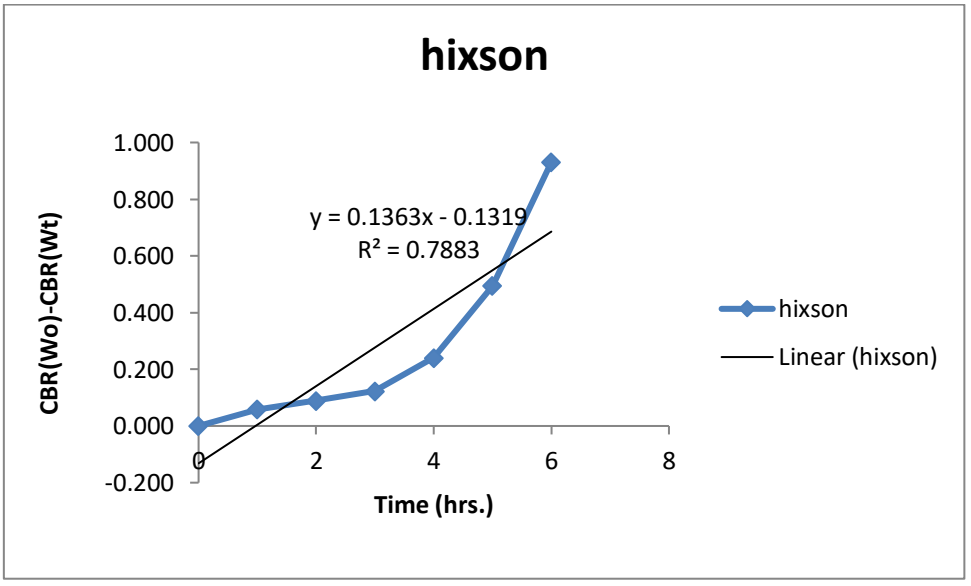
4	14.7132	85.2868	2.000	1.931	0.602	1.168	6.981825	4.402	0.240
5	28.67685	71.32315	2.236	1.853	0.699	1.458	13.96365	4.147	0.495
6	48.88933	51.11068	2.449	1.709	0.778	1.689	20.21248	3.711	0.931
7	71.0809	28.9191	2.646	1.461	0.845	1.852	22.19158	3.069	1.573



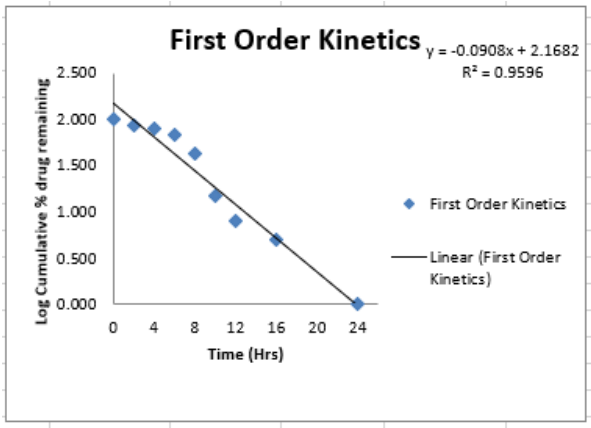


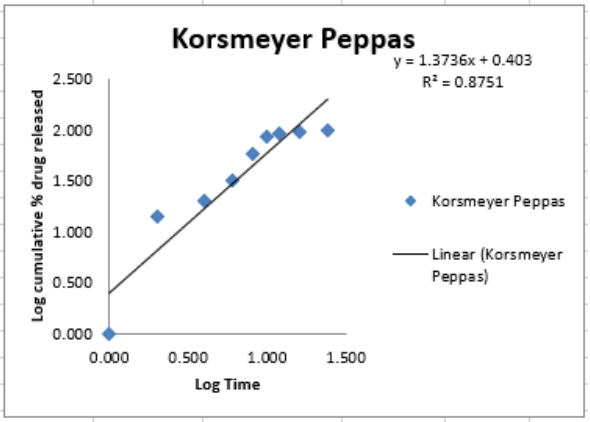

Higuchi
cumulative %drug released
60
50
40
30
20
10
0
-10
-20
0.000
0.500
1.000
1.500
2.000
2.500
3.000
SQRT of Time
y = 16.311x - 9.6098
R² = 0.618
Higuchi
Linear (Higuchi)

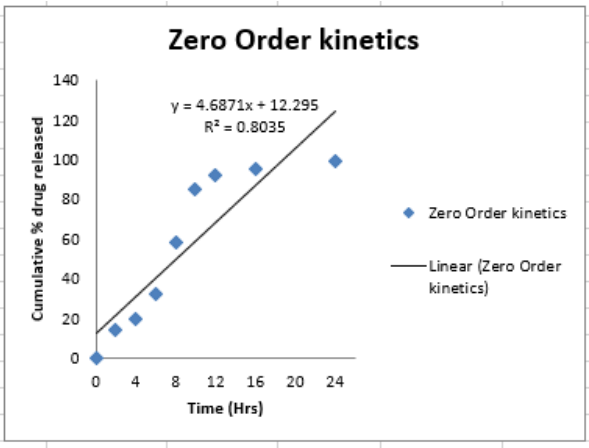

First order
Log Cumulative % drug remaining
2.100
2.050
2.000
1.950
1.900
1.850
1.800
1.750
1.700
1.650
0
2
4
6
8
time (hrs.)
y = -0.0421x + 2.0428
R² = 0.7673
First order
Linear (First order)

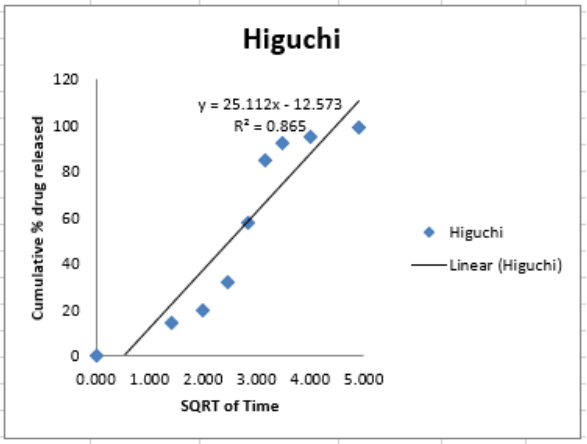

hixson
CBR(Wo)-CBR(Wt)
1.000
0.800
0.600
0.400
0.200
0.000
-0.200
0
2
4
6
8
Time (hrs.)
y = 0.1363x - 0.1319
R² = 0.7883
hixson
Linear (hixson)

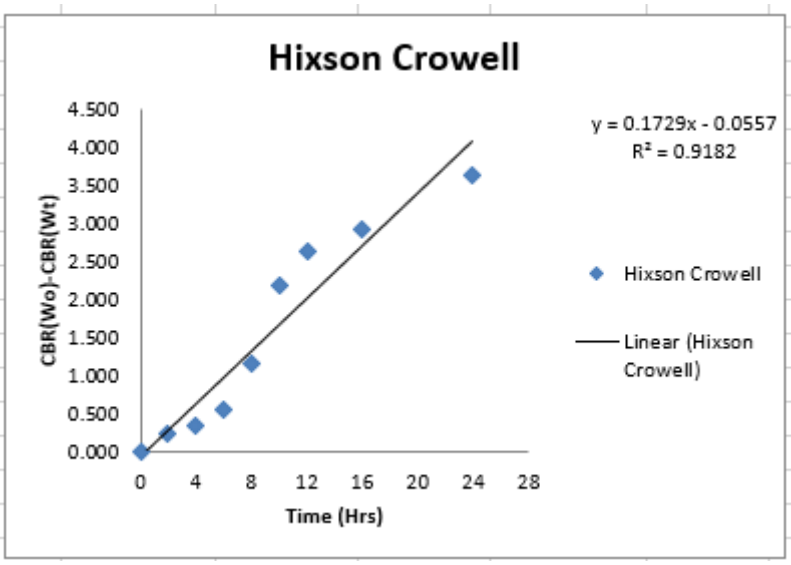
Time (Hr)	cumulative % drug released	% drug remaining	Square root time	log Cumu % drug remaining	log time	log Cumu % drug released	% Drug released	Cube Root of % drug Remaining(Wt)	Wo-Wt
0	0	100	0.000	2.000	0.000	0.000	100	4.642	0.000
2	14	86	1.414	1.934	0.301	1.146	14	4.414	0.228
4	20	80	2.000	1.903	0.602	1.301	6	4.309	0.333
6	32	68	2.449	1.833	0.778	1.505	12	4.082	0.560
8	58	42	2.828	1.623	0.903	1.763	26	3.476	1.166
10	85	15	3.162	1.176	1.000	1.929	27	2.466	2.176
12	92	8	3.464	0.903	1.079	1.964	7	2.000	2.642
16	95	5	4.000	0.699	1.204	1.978	3	1.710	2.932
24	99	1	4.899	0.000	1.380	1.996	4	1.000	3.642











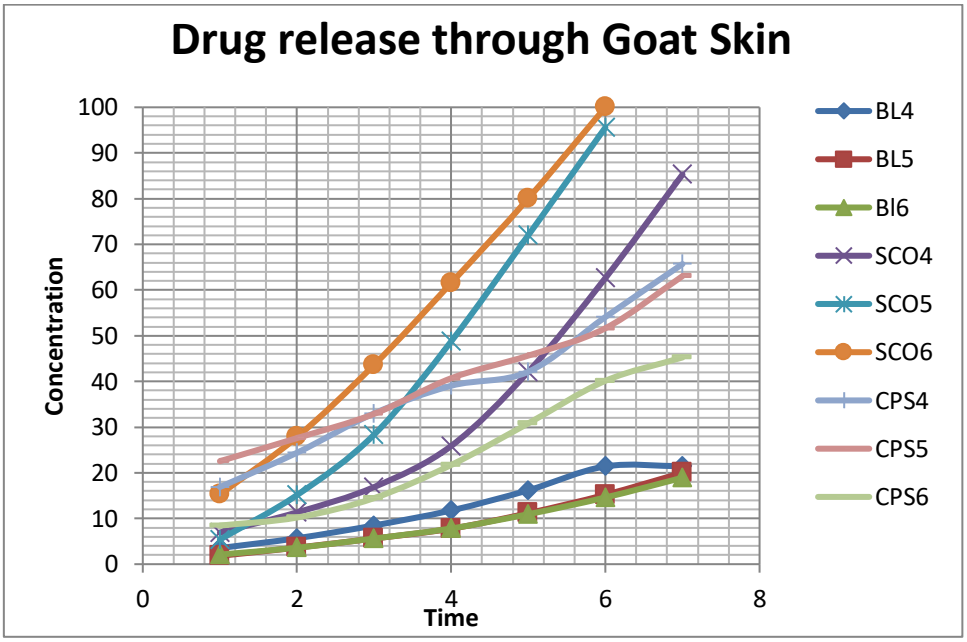
Mathematical models play a vital role in the interpretation of mechanism of drug release from a dosage form. It is an important tool to understand the drug release kinetics of a dosage form. The drug release was found to be best fitted by Higuchi square root model r2 =0.865 for BL4 and SCO4 and r2 =0.865 for BL5 and SCO5 and r2 =0.865 for BL6 and SCO6 which implies that release of drug as a square root of time dependent process and diffusion controlled. The dissolution data was also plotted according to Hixson –Crowell r2 =0.9182 for BL4 and SCO4 and r2 =0.9182 for BL5 and SCO5 and r2 =0.0.9182 for BL6 and SCO6 which describes that change in surface area and diameter of the formulation with the progressive dissolution as a function of time. Also, the model Korsmeyer-Peppas power law equation states the type of diffusion, which was evaluated by value, n (Release exponent) which is higher than 0.8751 which implies that the drug release from the system follow Super case II transport

DRUG RELEASE GOAT SKIN

Goat skin final graph

Time	BL4	BL5	BL6	SCO4	SCO5	SCO6	CPS4	CPS5	CPS6
0	0	0	0	0	0	0	0	0	0
5	1	1	1	0.0779	0.0513	0.0532	0.35	0.3515	0.3515
15	1	1	1	1.672175	1.022525	0.914475	0	0	0
30	1	1	1	3.834525	2.3236	5.78	0	0	0
1	3.53	1.83	2.1102	6.93	5.39	15.25	16.88	22.53975	8.447825
2	5.68	3.62	3.6	11.34	15.12	27.84	24.39	27.59745	10.20703
3	8.48	5.62	5.62	16.88	28.35	43.62	33	32.89338	14.45843

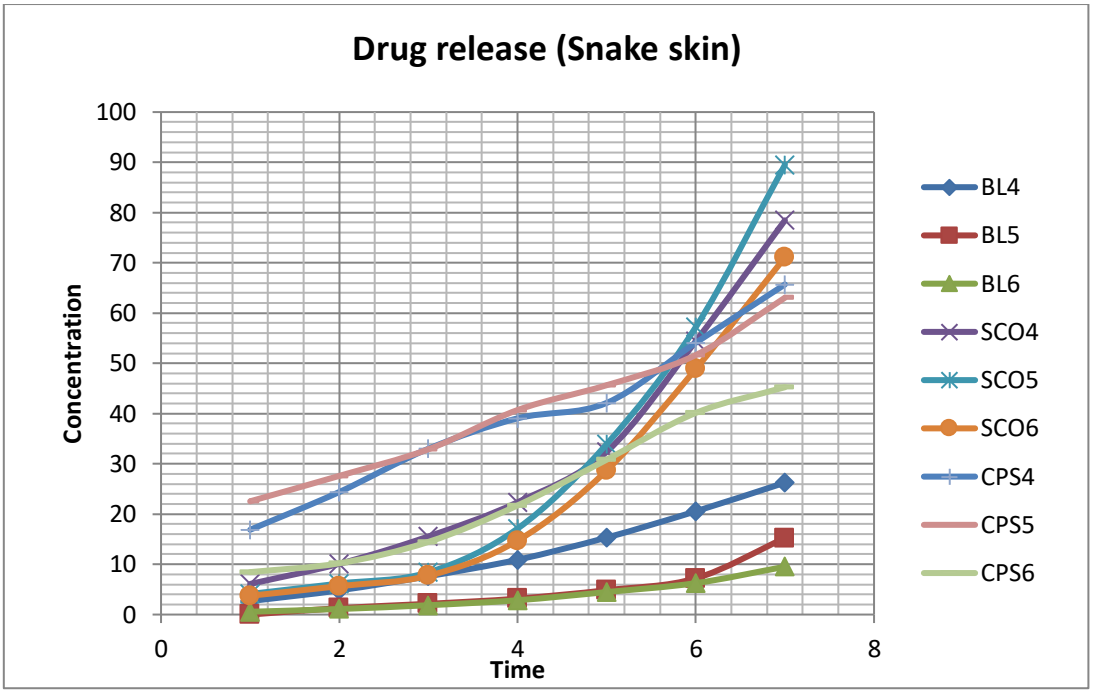
4	11.76	7.77	7.81	25.87	48.76	61.54	39.05	40.69983	21.71513
5	16.18	11.17	10.94	42.11	72	80.05	42.12	45.64758	30.82265
6	21.4	15.19	14.6	62.62	95.58	100	54.09	51.63985	40.13175
7	21.43	20.01	18.92	85.28			65.69	63.05633	45.24443



DRUG RELEASE SNAKE SKIN

SNAKE SKIN final graph

Time	BL4	BL5	BL6	SCO4	SCO5	SCO6	CPS4	CPS5	CPS6
0	0	0	0	0	0	0	0	0	0
5	1	1	1	0.0779	0.0513	0.0532	0.35	0.3515	0.3515
15	1	1	1	1.672175	1.022525	0.914475	0	0	0
30	1	1	1	3.834525	2.3236	2.06895	0	0	0
1	2.68	0	0.55735	6.0885	4.101125	3.736525	16.88	22.53975	8.447825
2	4.82	1.281	1.1071	10.10168	6.17185	5.66065	24.39	27.59745	10.20703
3	7.63	2.14	1.858425	15.5442	8.389175	7.731375	33	32.89338	14.45843
4	10.91	3.169	2.847975	22.34278	17.11188	14.7132	39.05	40.69983	21.71513
5	15.32	4.85	4.4789	32.4032	33.9159	28.67685	42.12	45.64758	30.82265
6	20.55	7.21	6.256425	54.41153	57.20698	48.88933	54.09	51.63985	40.13175
7	26.25	15.22	9.518275	78.45393	89.49563	71.0809	65.69	63.05633	45.24443



Antibacterial activity of liposomalgel

Bacterial cultures: For the studies of antibacterial effect of antibacterial gel formulation, MCC bacterial strains procured from Microbial Culture collection (MTCC), National Centre for Cell Science, Pune, Maharashtra, India. The lyophilized cultures of bacterial strain upon culturing in nutrient broth for 24 hours at 37°±0.5 ° C in an incubator resulted into turbid suspension of activated live bacterial cell ready to be used for antibacterial study. From the broth of respective revived cultures of microorganism loop full of inoculums was taken and streaked on to the nutrient agar medium and incubated again at same culture conditions and duration that yielded the pure culture colonies on to the surface of the agar culture that were successfully stored in refrigerated conditions at 4°C as stock culture to be used for furtherexperimentation.

Antibacterial studies: The lawn cultures were prepared with the pathogenic bacterium used under present study by plating the culture onto the solidified agar plates under aseptic hood and potential of the anti-bacterial liposomal gel formulation against the bacterium was studied at the concentration of 25, 50 and 100 µg/ml using disc diffusion method.

Antibacterial activity: Anti-bacterial activity of the developed formulation was studied evaluated through zone of inhibition study by applying the optimized Liposomal gelat three different concentration (25, 50 and 100 µg/ml) and these were compared with marketed Tazarotene gel at same concentration. The results of anti-bacterial activity are shown inTable No 6.39

Table No 6.39: Antibacterial activity of Marketed and optimized gel formulations againstPropionibacterium acnes

Sample	Zone of Inhibition (mm)		
	25µg/ml	50 µg/ml	100µg/ml
Marketed Gel	15±0.22	20±0.12	22±0.11
Liposomal Gel (LF2)	18±0.12	24±0.10	26±0.20

In present work, liposomal, and marketed gels showed antibacterial activity against *Propionibacterium acnes* with maximum zone of inhibition lying after 24 hours in the range of 18 to 26 mm (Figure 6.28).

Figure No 6.28: **Photograph showing antibacterial activity**

Liposomalgel showed greater percentage of inhibition of microbial infection against *Propionibacterium acnes*- On comparison of formulated gels with marketed gel of Tazarotene, Liposomal gel showed greater percentage of inhibition of bacterial infection against *Propionibacterium acnes.* This may be due to the fact that the liposomal gel released the drug in more efficientmanner.

Results of *In - Vivo* anti acne activity

Table No 6.40: Effect of Clindamycin (standard), formulation I & II on acne

Sr. No	Group	Mean Thickness± SEM(excisedskin)
1	Normal	1.18 ± 0.09
2	Clindamycin	0.30 ± 0.09***
3	Formulation I (Marketed formulation)	0.65 ± 0.06 **
4	Formulation II (Liposomal gel)	0.45 ± 0.06***

*Values expressed as mean ± SEM*P<0.05, **P<0.01, ***P<0.001 as compared to normal*

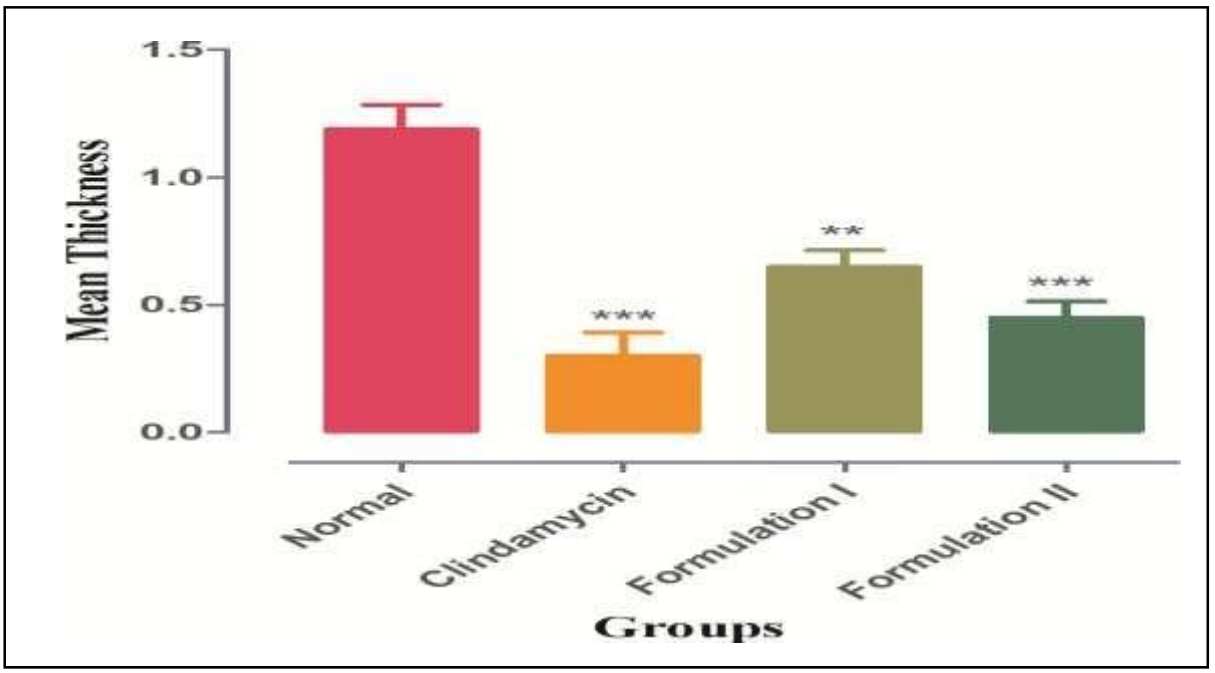


Figure No 6.29: Effect of Clindamycin (standard), formulation I & II on acne

Photo Plates of *In - Vivo* anti acne activity

AcneInduction **Standard Drug**

FormulationI **FormulationII**

Figure No 6.30: Photo Plates of *In - Vivo* anti acne activity

Application of gel **Standard Drug administration**

Formulation I **Formulation II**

Figure No 6.31: Photo Plates of *In - Vivo* diffusion study

In present in-vivo anti acne activity Clindamycin was selected as a standard drug and showed the effect of Clindamycin, Formulation- I (marketed Tazarotene gel) and formulation

II(liposomal gel LF2) on acne and mean thickness compared to the normal. Results showed in table 6.40 and figure6.30-6.31.

It was observed that formulation-I(marketed Tazarotene gel) and formulation-II (liposomal gel LF2) showed a significant reduction in the acne without necrosis as compared with the standardClindamycin.

Various antibiotics like tetracycline, Clindamycin, and erythromycin etc and other drugs like benzoylperoxide are used for acne treatment. The various drawbacks of synthetic drugs are different side effects and resistant developed towards these drugs. Formulation therapy is required to overcome the above drawbacks and treat the acne. The formulation-I showed a reduction in the acne as compared to the Clindamycin formulation but the marked reduction in the acne was found in case of Formulation II. This shows that most effective reduction in the acne cold be have had by the developed formulation which is due to the fact that the developed formulation consisted on liposomes loaded with colchicine. The liposomes penetrated to deeper layer of the skin thereby providing enhanced reduction in the bacterial population of the bacterium located deeper within the acne. Also since the formulation released the drug in a controlled fashion owing to controlled release nature of the delivery system which ensured the gradual delivery of drug for a longer period of time and hence the therapeutic concentration of drug was maintained at the infection site for more longer period of time. All the features resulted in efficient delivery there by leading to marked reduction in the infection. Also since the gel contains hydroquinone which also aids in the reduction of the acne and protects the skin from any untoward effects and therefore the combination therapy as is evident result in efficient drug delivery leading to enhanced treatment foracne.

Reportson

EstimationofPharmacokineticsparametersofstandcolchicine,topicalformulationBL6andSL06 aftertopicalskinapplicationinwistarrats

Pharmacokineticstudyparameters

Sr no	Parameters	Standard Colchicine	Testsample BL6	Testsample SL06
1.	slope	-0.06	-0.011	-0.016
2.	intercept	3.69	3.050	3.356
3.	Kel(perhour)	0.14	0.025	0.037
4.	t1/2(hours)	4.98	27.651	18.908
5.	C0(pg/ml)	4910.52	1121.877	2268.132
6.	Vd(Liters)	101822.27	445681.550	220445.739
7.	clearnce(liters/hours	14183.45	11169.664	8079.497
8.	AUC0-t(pg.hr/ml)	3545.99	2792.541	2019.999
9.	AUC1-t(pg.hr/ml)	44583.17	31590.000	62347.325
10.	AUC1-∞(pg/ml)	71.79	11902.490	10460.911
11.	AUC(TOTAL)(pg.hr/ml)	48200.95	46285.031	74828.235
12.	Cmax(pg/ml)	12000.67	2993.300	7086.200
13.	Tmax(hour)	1.00	1.000	1.000

Pharmacokineticstudy

Standard:Colchicine

Srno	**Time(hours)**	**Concentration (pg/mL)**	**logconc. (pg/ml)**	**AUC**
1.	0.5	4000.59	3.602124045	4000.315
2.	1	12000.67	4.079205493	25502.12
3.	4	5000.74	3.699034275	6200.74
4.	6	1200	3.079181246	4800
5.	12	400	2.602059991	3000
6.	24	100	2	1320
7.	48	10	1	-240

Testformulation:BL06

Srno	Time(hours)	Concentration (pg/mL)	logconc.	AUC
1.	0.5	143.3	2.16	784.15
2.	1	2993.3	3.48	7787.25
3.	4	2198.2	3.34	3652.4
4.	6	1454.2	3.16	6685.2
5.	12	774.2	2.89	8517
6.	24	645.3	2.81	11323.2
7.	48	298.3	2.47	-7159.2

SL06

Srno	Time(hours)	Concentration (pg/mL)	logconc.	AUC
8.	0.5	178.9	2.25261	1816.275
9.	1	7086.2	3.85041	19388.55
10.	4	5839.5	3.76638	9941.6
11.	6	4102.1	3.61301	15267.9
12.	12	987.2	2.99441	10793.4
13.	24	811.7	2.90940	14341.2
14.	48	383.4	2.58365	-9201.6