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Formulation And Evaluation Of Karanj Silver Nanoparticle Gel

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Abstract

Pongamia pinnata Linn.(Aka Karanja in Ayurveda) is a rough tree and a traditionally used medicinal factory set up throughout the India. It's generally used in Ayurveda and has an immense eventuality in treating colorful skin conditions like eczema, psoriasis, itchy skin, infections of skin. The end of present study was to prepare tableware nanoparticle herbal gel expression containing methanolic excerpt of Karanj on psoriasis. Topical gel expression was designed by using methanolic excerpt of seeds of pongamia pinnata in varied attention. The gel was prepared by using tableware nitrate, chitosan, carbopol 934, Pongamia Pinnata Extract(KARANJ), Methanol, propylene glycol, methyl paraben, propyl paraben,triethanolamine, glycerin and needed quantum of distilled water. The set gels were estimated for medicine content, pH, spread capability, physical appearance, density, swelling indicator, prolixity study, unity and grit. The results prove that gel phrasings were good in appearance and unity.

Keywords: Pongamia pinnata, Karanjin, Nanoparticle gel, Identification, Wound healing, Skin diseases

INTRODUCTION

Psoriasis is a common T- cell intermediated vulnerable complaint characterized by red, thickened, circumscribed, sturdy pillars with an overlying tableware-white scale. The name of the complaint is deduced from Greek word ‘ psora ’ which means itchy. Psoriasis is anoncontagious, dry, seditious and unhealthy skin complaint, which can involve entire system of person. It's substantially inherited and substantially characterized by sprucely marginated scaled, erythematous pillars that develop in fairly symmetrical distribution. Psoriasis an autoimmune complaint in which inheritable and environmental factors have a significant part. The most generally affected spots are the crown, tips of toes and fritters, soles, triumphs, umbilicus, gluteus, pins and sacrum, under the guts and genitals, elbows, knees. Gel supposed circumfluous, being either dormancies of small inorganic patches or large organic motes transfused with liquid. A gel is a circumfluous system of at least two percolating phases a gelatinizing agent and a liquid. Gels that contain water are called hydrogels, Development and Evaluation of Herbal Gel for Treatment of Psoriasis Hydrogels, in the broad sense, include the matrix of water-answerable accoutrements similar as natural epoxies and cellulose derivations. Nanoparticle technology is used to increase rapid-fire immersion of medicine into the

skin. Nanotechnology is rapid-fire growing point due to its faster functionality and wide range of uses. Nanotechnology for forestallment, treatment, opinion and control of complaint. gray nanoparticle gel are the stylish for seditious skin, that get absorbed into the skin briskly.
Pongamia pinnata have anti seditious parcels therefore in combination with tableware nanoparticle gel they give better results on skin. The combination of tableware nanoparticle gel and pongamia pinnata gives briskly action and relive for seditious and dry skin.

Pongamia pinnata(karanj) also known as Karanja is an important medicinal factory and it has been used from ancient time. It's a medium sized tree of height up to 18 measures and it's native in tropical and temperate regions of Asia. Dinghy, flowers, Root, leaves and seeds of this factory exhibition medicinal parcels. The seed of Pongamia pinnata reported to have Karanjin, pongamol, pongagalabrone, pongapin, pinnatin, kanjone, Glabrachalcone, isopongachromene. The major active element of Pongamia pinnata is Karanjin. The seed oil painting contains 5- 6 flavonoids in which the main element is karanjin(5), Chemically, Karanjin is a Furanoflavonoid.

MATERIALS AND METHODS

MATERIALS

KARANJ was gift sample from Klsalaya Herbals LTD. Gujrat, India. Other excipients similar as Chitosan, Silver nitrate, Carbopol 934, Propylene glycol, Methyl paraben, Propyl paraben, Glycerin, Triethanolamine were carried fromDr.D.Y. Patil College Of Pharmacy, Pune, Maharashtra, India.
Preparation of Formulation

SILVER NANOPARTICLES PREPARATION

The tableware nanoparticles was prepared by dissolving karanj in methanol as solvent and in another teacup dissolve tableware nitrate in 40 ml of water. Add tableware nitrate result in(karanj methanol) result with nonstop shifting,(glamorous shifting). This tableware ions reacts with medicine patches and forms gray nanoparticles by chemical reduction system. also dissolve chitosan in 10 ml of water and in below result as stabilizer, continue stirring for 30 mins on glamorous stirrer.
expression OF HERBAL GEL 50 ml of nanoparticle result were placed in teacup, also add counted quantum of Carbopol 934 in below result, kept it for mechanical shifting. Methyl paraben and Propyl paraben were dissolved in small volume of water, kept it to sonication for 10 mins.
Added glycerin and triethanolamine volume sufficient to maintain density.
Kept the formulation in well closed container with proper label and the prepared formulation batches of herbal gel were then further evaluated on different parameters.

• **FORMULATION TABLE:** Formulation of Silver Nanoparticles.
Table 1. Formulation table for silver nanoparticles.

Batch no.(N)	drug conc (mg)	AgNO3(mg)	stabilizer	RPM	Stirring time	solvent
1	150	7.5	0.75	1000	-32.0286	Methanol
2	100	3	1	1500	30	Acetone
3	100	3	1	500	120	Methanol
4	150	7.5	0.75	1000	75	Methanol
5	100	12	1	500	120	Methanol
6	100	12	0.5	1500	30	Methanol
7	100	3	0.5	1500	30	Acetone
8	200	12	1	500	30	Methanol

9	100	12	1	500	120	Acetone
10	200	12	1	1500	30	Methanol
11	100	3	1	1500	30	Methanol
12	200	3	1	500	30	Methanol
13	150	7.5	1.3446	1000	75	Methanol
14	100	3	0.5	500	120	Acetone
15	150	7.5	0.75	1000	75	Acetone
16	200	3	0.5	500	30	Methanol
17	100	3	0.5	500	30	Acetone
18	100	12	0.5	500	120	Acetone
19	200	12	1	1500	30	Acetone
20	200	3	0.5	1500	30	Acetone
21	31.0793	7.5	0.75	1000	75	Methanol
22	200	3	0.5	1500	30	Methanol
23	200	12	1	500	120	Methanol
24	200	3	1	1500	120	Methanol
25	200	12	0.5	500	30	Acetone
26	200	12	0.5	1500	30	Acetone
27	150	7.5	0.155396	1000	75	Acetone
28	100	3	1	500	30	Methanol
29	100	3	0.5	500	120	Methanol
30	150	7.5	0.155396	1000	75	Methanol
31	200	3	1	500	120	Acetone
32	200	12	1	1500	120	Methanol
33	150	7.5	0.75	1000	75	Acetone
34	150	-3.20286	0.75	1000	75	Methanol
35	200	12	0.5	1500	120	Methanol
36	200	12	0.5	500	30	Methanol
37	150	7.5	0.75	1000	182.029	Acetone
38	200	12	1	500	30	Acetone
39	150	7.5	0.75	1000	75	Acetone
40	200	12	1	1500	120	Acetone
41	150	7.5	0.75	1000	75	Acetone
42	100	3	1	500	120	Acetone
43	268.921	7.5	0.75	1000	75	Methanol
44	200	3	0.5	500	120	Methanol

45	100	12	0.5	1500	120	Methanol
46	150	7.5	0.75	1000	75	Methanol
47	150	7.5	0.75	1000	75	Acetone
48	150	18.2029	0.75	1000	75	Acetone
49	200	12	0.5	1500	120	Acetone
50	150	7.5	0.75	1000	75	Acetone
51	150	7.5	0.75	1000	75	Methanol
52	150	7.5	0.75	1000	182.029	Methanol
53	150	7.5	0.75	1000	75	Methanol
54	200	3	1	500	30	Acetone
55	100	3	0.5	1500	30	Methanol
56	100	12	0.5	500	30	Methanol
57	100	3	0.5	500	30	Methanol
58	150	7.5	0.75	-189.207	75	Methanol
59	150	7.5	0.75	1000	75	Methanol
60	100	12	0.5	1500	30	Acetone
61	100	3	1	500	30	Acetone
62	100	12	1	500	30	Acetone
63	150	7.5	0.75	-189.207	75	Acetone
64	150	7.5	0.75	1000	75	Methanol
65	100	12	1	1500	30	Methanol
66	100	12	0.5	500	30	Acetone
67	200	3	0.5	1500	120	Methanol
68	200	3	1	1500	120	Acetone
69	150	7.5	0.75	2189.21	75	Acetone
70	200	3	1	1500	30	Acetone
71	100	3	1	1500	120	Methanol
72	100	3	0.5	1500	120	Acetone
73	200	3	0.5	1500	120	Acetone
74	150	7.5	0.75	1000	75	Methanol
75	200	12	0.5	500	120	Methanol
76	150	7.5	0.75	2189.21	75	Methanol
77	100	3	0.5	1500	120	Methanol
78	150	-3.20286	0.75	1000	75	Acetone
79	200	12	1	500	120	Acetone
80	100	3	1	1500	120	Acetone
81	150	7.5	0.75	1000	-32.0286	Acetone
82	200	12	0.5	500	120	Acetone
83	200	3	1	1500	30	Methanol
84	31.0793	7.5	0.75	1000	75	Acetone
85	200	3	0.5	500	30	Acetone
86	100	12	1	1500	120	Acetone
87	150	7.5	0.75	1000	75	Acetone
88	100	12	0.5	500	120	Methanol

89	100	12	1	1500	120	Methanol
90	100	12	0.5	1500	120	Acetone
91	200	12	0.5	1500	30	Methanol
92	150	18.2029	0.75	1000	75	Methanol
93	268.921	7.5	0.75	1000	75	Acetone
94	150	7.5	1.3446	1000	75	Acetone
95	150	7.5	0.75	1000	75	Acetone
96	150	7.5	0.75	1000	75	Methanol
97	100	12	1	500	30	Methanol
98	100	12	1	1500	30	Acetone
99	200	3	1	500	120	Methanol
100	200	3	0.5	500	120	Acetone

The optimized batch is used for the preparation of herbal antipsoriatic gel; the optimized batch was found to be is as follows:-

Conc. of drug (mg)	Conc. of $Agno_3$ (mg)	Conc. of stabilizer (mg)	Stirring speed (RPM)	Time for stirring (mins)	Type of solvent
161.314	3.0001	0.500033	595.588	119.999	Methanol

Thus by using this batch of silver nanoparticles the herbal antipsoriatic gel was prepared and evaluated.

Table 2: Formulation of silver nanoparticle herbal antipsoriatic gel

Name of the content → / Batch no. ↓	Nanoparticles (ml)	Carbopol 934(%)	Propylene glycol (%)	Methyl paraben (gm)	Propyl paraben(gm)	Glycerin(ml)	Triethanolamine
F1	50	0.655025	2.75	0.3	0.2	-	2 drops
F2	50	1.15	-	0.3	0.2	5.93	2 drops
F3	50	1.5	5	0.3	0.2	-	2 drops
F4	50	1.15	2.75	0.3	0.2	-	2 drops
F5	50	1.15	-	0.3	0.2	2.75	2 drops
F6	50	1.15	5.93	0.3	0.2	-	2 drops
F7	50	0.655025	-	0.3	0.2	2.75	2 drops
F8	50	0.8	-	0.3	0.2	-	2 drops
F9	50	1.5	-	0.3	0.2	0.5	2 drops
F10	50	1.15	-	0.3	0.2	-0.4319	2 drops
F11	50	1.64497	-	0.3	0.2	2.75	2 drops
F12	50	1.64497	2.75	0.3	0.2	-	2 drops
F13	50	0.8	0.5	0.3	0.2	-	2 drops
F14	50	1.15	-0.4319	0.3	0.2	-	2 drops
F15	50	1.5	-	0.3	0.2	5	2 drops
F16	50	1.5	0.5	0.3	0.2	-	2 drops
F17	50	0.8	-	0.3	0.2	5	2 drops
F18	50	0.8	5	0.3	0.2	-	2 drops

18 batches of herbal antipsoriatic gel was preaperd and evaluated for viscosity, spreadability and drug release.

PREFORMULATION STUDIES

Characterization of medicine pongamia pinnata excerpt

1) Appearance and colour

The sample of pongamia pinnata Excerpt was examined visually for its appearance, colour, odour and nature

2) Melting point

Melting point of karanj was determined using capillary system. 3 mm of capillary tube which was sealed at one end was filled with karanj. Capillary was kept into the digital melting point outfit. Melting point was noted from the temperature at which medicine starts melting to the temperature at which entire sample melts.

3) FTIR gamuts analysis

A FT- IR diapason of karanj was recorded by potassium platitude(KBr) palletization system. medicine was mixed with KBr and was compressed into small thin bullet, which was latterly anatomized by FT- IR spectrophotometer. attained gamuts were anatomized for characteristic peaks corresponding to specific functional groups present in the medicine patch. These peaks attained from FTIR were considered as a reference for farther medicine- excipient comity studies.

4) UV-Visible spectroscopy

Directly counted volume(10.0 mg) of dried Karanj was placed in each 100 ml volumetric beaker containing 100 ml detergent(water, acetone, methanol) sonicated for 20 min. This stock result(100 µg/ ml) was also adulterated with separate detergent to get attention of 10 µg/ ml. The result was scrutinized in a spectrometric range of 800 and 200 nm on UV- spectrophotometer(Shimadzu- 1800) using separate detergent as blank.

5) Estimation wind of Karanj

The stock result of karanj(100 µg/ mL), in methanol were prepared as mentioned over. The stock result was further adulterated with separate detergents to get 5 consecutive direct attention of each detergent(µg/ ml.) The UV absorbances of these results were recorded spectrophotometrically at preliminarily determined λmax values and also estimation wind was colluded.

6) Solubility

The achromatism solubility of the medicine was measured in Phosphate buffer pH7.4, water, ethanol and methanol. 5 mL of these was taken in each of free glass vials of 5 mL capacity. medicine is added up to achromatism. These glass vials were kept at 250C/ 100 rpm in a temperature controlled Mechanical Shaker for 48 hrs. The performing result was filtered by Whatman sludge paper, adulterated and absorbance was recorded at λmax of separate detergent by using UV spectrophotometer.

1.1. Evaluation of silver nanoparticles: -

A. Physicochemical characterization of silver nanoparticle formulation:

Particle size: flyspeck size flyspeck size determined with help of optical microscopy. The nanoparticle result is weakened with water and sonicate for 5 beats. Place on glass slide and cover with cover slip and observe under optical microscope. flyspeck size distribution, polydispersity index(PDI) of nanoparticles were determined by DLS(Dynamic light scattering) by using horiba SZ 100 at room temperature. Zeta implicit were measure by instrument Horiba SZ 100. The sample were fitted into a cell and a dimension of the flyspeck electrophoretic mobility results in the evaluation of zeta eventuality.

Entrapment efficiency: 10 ml of nanoparticle expression was placed in centrifuge tube. also it's centrifuged in Remi centrifuge(R- 8C) at 12000 rpm for 2 hours. also0.1 ml from supernatant liquid were pipette out and weakened up to 10 ml. Take absorbance at 255 nm.

Ruse effectiveness calculated by following Formula,

Entrapment Efficiency = [{Total drug – Drug in Supernatant}/ Total drug] × 100

- **Stability Studies:** Optimized expression at cooled temperature(4- 8 ± 1ºC) and room temperature(25 ± 2 °C) for 30 days. After 30 days, shape, drug remain and drug ruse effectiveness of nanoparticles were determined. The results were compared with original shape, drug remaining and ruse effectiveness of both samples.
- **Study of lyophilized formulation of silver nanoparticles.**

Liquid tableware nanoparticle expression was kept for lyophilization(- LDplus) for about 34 days. Dried lyophilized cream was attained That lyophilized cream was studied for Fourier Transform Infrared Spectroscopy, Differential, surveying colorimetry, Scanning Electron Microscope.

A. Polydispersity Index: The polydispersity index(PI) is a measure of the diversity of a sample rested on size. Polydispersity can do due to size distribution in sample or agglomeration or aggregation of the sample during sequestration or analysis. The polydispersity index may be attained from instruments that use dynamic light scattering(DLS) or determined from electron micrographs.

B. Zeta Potential: Zeta eventuality can be used to gain further perceptivity into the stability of the attained colloidal AgNps. The magnitude of zeta implicit gives implicit stability of colloid. Zeta eventuality in between 40 to 60 shows good stability.

C. FTIR Study: Study FTIR of lyophilized expression was taken and checked for the bond conformation occurs in tableware nanoparticles and compared it with the FTIR of drug expression. A FT- IR spectrum of tableware nanoparticles of Karanj was recorded by potassium bromide(KBr) palletization system. Nanoparticles was mixed with K Br and was compressed into small thin pellet, which was subsequently analyzed by FT- IR spectrophotometer. attained spreads were analyzed for characteristic peaks corresponding to specific functional groups present in the nanoparticles. These peaks attained from FTIR were considered for further check emulsion of tableware nanoparticles. Comparison of FTIR results of pure drug and lyophilized nanoparticles were done.

D. Differential scanning colorimetry: DSC of lyophilized cream were done and compared the melting point of that with the melting point of pure drug sample.

E. Scanning Electron Microscope: The high- resolution, three- dimensional images produced by SEMS give topographical, morphological and compositional information makes them invaluable in operations. A Seanning Electron Microscope provides detailed face data of solid samples. It. Takes incidental electrons and focuses them onto a case; the electrons that scatter off the face following this commerce can be analyzed with a variety of detectors that give topographical, morphological. and compositional in conformation regarding the face of a sample.

• Calibration curve of Karanj

Development and standard curve of drug using UV- spectrometer Karanj dilutions were scanned in the range of 400 nm – 200 nm showed maximum absorption at wavelength 253 nm. Absorbance of prepared solution was measured at 253 nm using UV spectrophotometer.

Drug followed Beers and Lamberts law in the range of 0 to 10 µg/ml.

Table.no 3: Absorbance value of Karanj.

Sr.No.	Concentration (µg/ml)	Absorbance (nm)
1	2	0.1178
2	4	0.2113
3	6	0.3172
4	8	0.4575
5	10	0.5597

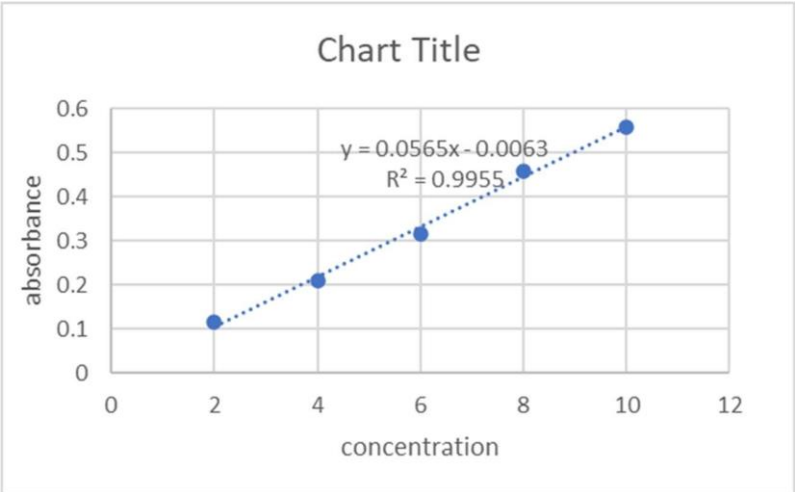


Fig No.8.3: Calibration curve of Karanj

1) FTIR OF PURE DRUG

Infrared spectrum of karanj on Fourier Transform Infrared Spectrophotometer. The sample was scanned over wavelength region 200 to 400 nm and compared with literature data.

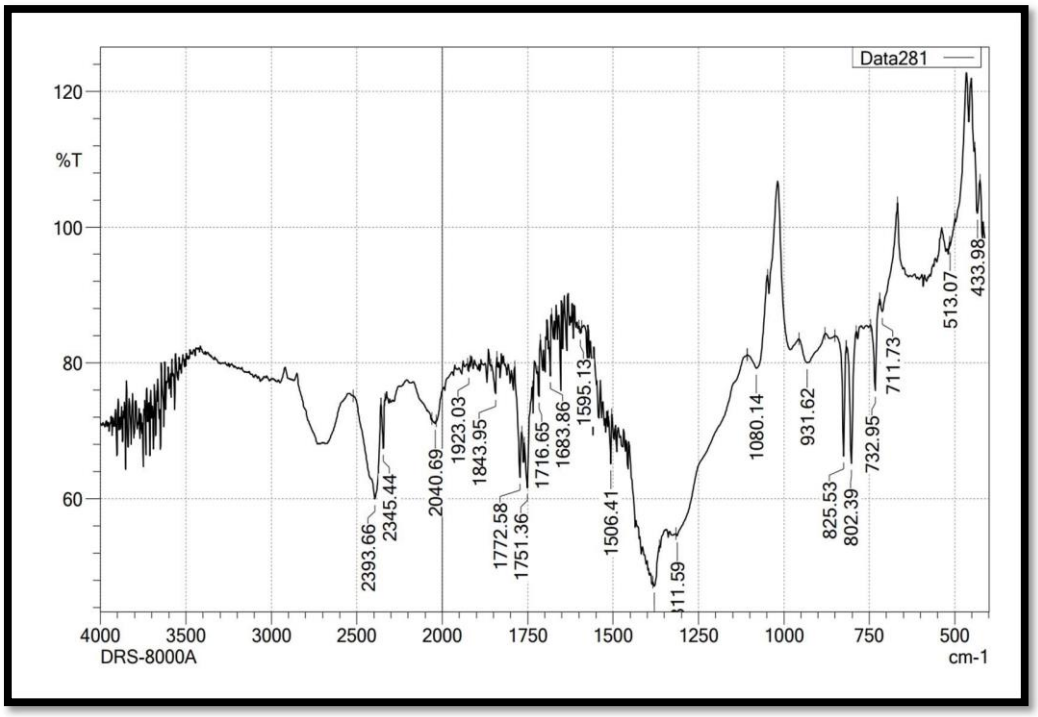
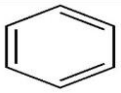


Fig 1: Infrared – Spectra of Karanj

Wave Number Range(cm-1)	Wave Number(cm-1)	Bonds
700- 1000	931.62	
1700- 1750	1716.65	C=O
1500- 1600	1595.13	C=C
1200- 1180	1180.14	C-O-C

2) Solubility Study

The solubility of karanj was found to be very soluble in methanol. It is poorly soluble in water and it is slightly soluble in ethanol and acetone.

3) Infrared spectrum of Silver Nanoparticles:

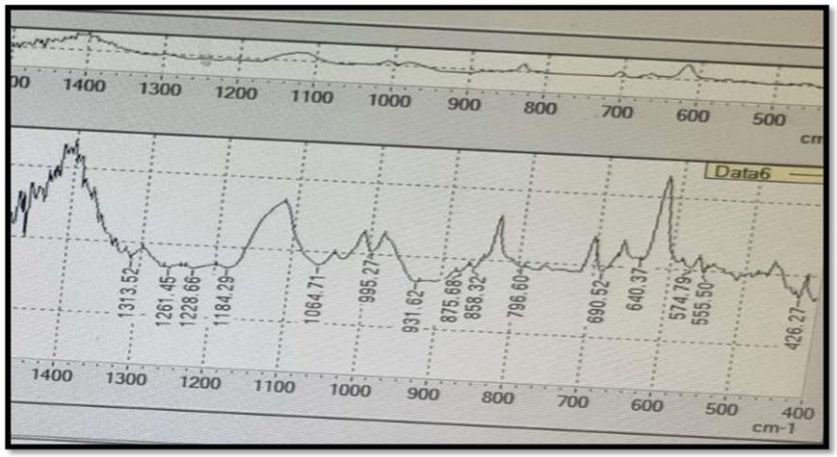
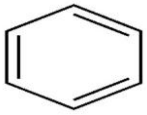


Fig no.2: Infrared- spectra of Silver Nanoparticles

Table No. 8.20: IR peaks of Silver Nanoparticles

Functional Group	Observed Range cm^{-1}
N-H Bond	640.37
C-N Bond	1261.45
C-O-C Bond	1184.29
	995.27

4) Differential Scanning Calorimetery (DSC)

A differential scanning calorimeter was used for thermal analysis of drug. Individual sample (drug) as well as the optimized formulation was weighed directly in the pierced DSC aluminum pan and scanned in the temperature range of 30-350°C under atmosphere of dry nitrogen. A heating rate of 10°C/min was used and the obtained thermograms were observed for any interaction. Samples with weight 1-2 mg were employed for testing.

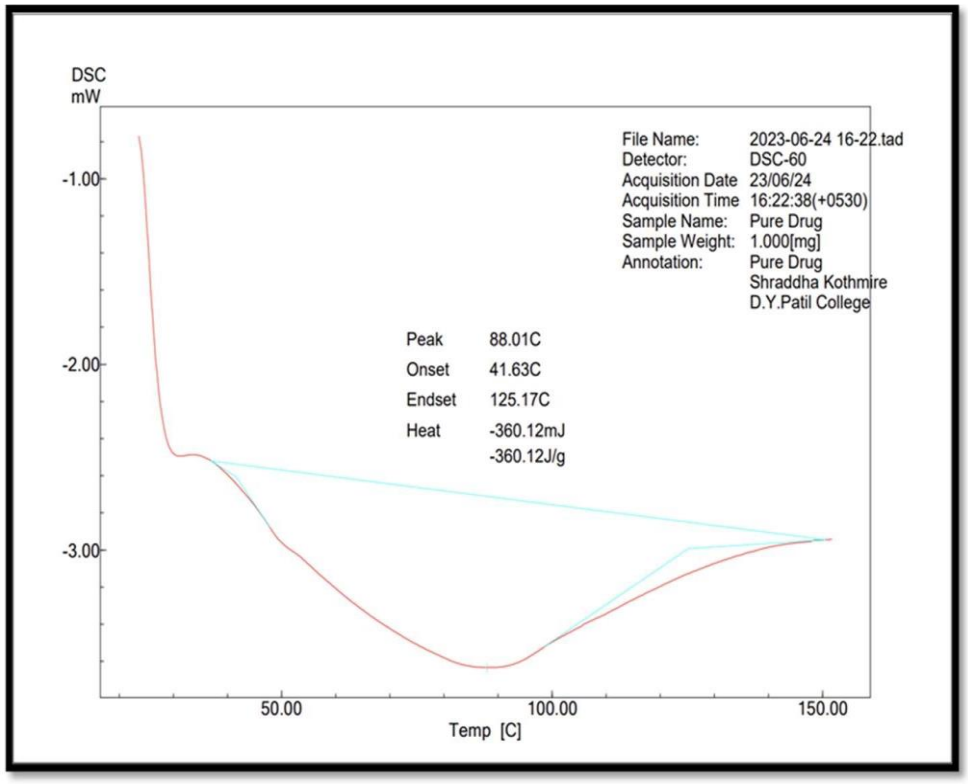


Fig 4. DSC characterization of Karanj

DSC studies were performed to observe thermal properties and intermolecular reaction between Karanj and excipients used in formulation of nanoparticulate dispersion. Pure karanj showed exothermic peak at 88.01C. The presence of sharp endothermic peak primarily indicates the crystalline nature of drug.

5) Effect of variables on Particle size of silver nanoparticle:

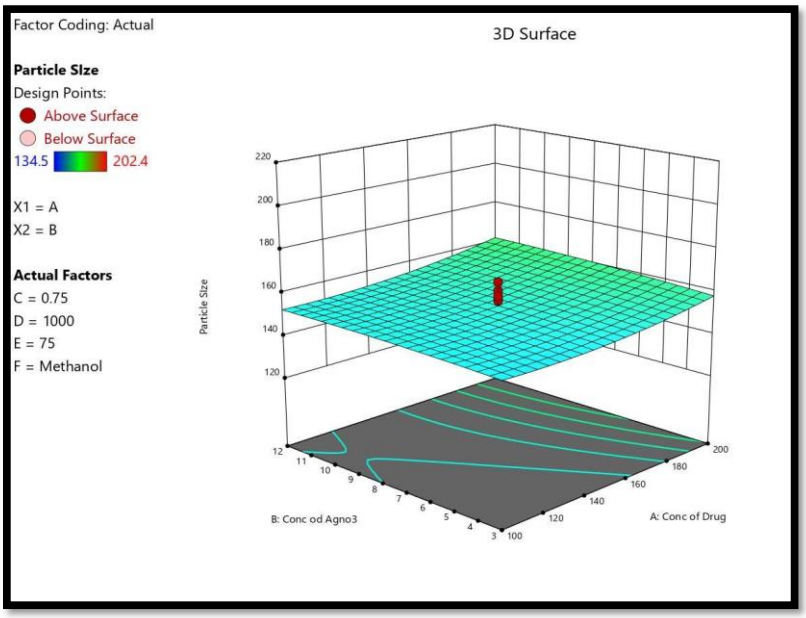


Fig 8.9: 3D Response Surface Plot for Particle Size

3D response surface plot and counter plot explains the particle size of nanoparticles. Response were constructed based on the model polynamial functions. The particle size of nanoparticles N1 to N100 ranges from 134.5 nm to 202.4 nm as shown in (Table no 8.5). On increasing the concentration of chitosan from 0.5 to 1 % and silver nitrate from 5 mM to 9mM, the particle size was increased. As of chitosan affects more the particle size than silver nitrate. The increase in particle size is due to the chitosan, causes a modification of the net charge of the system and some degree of stearic stabilization causes increase particle size. Increase in concentration of silver nitrate causes increase in particle size this could be due to higher concentration of silver causes destabilization of ionic strength of solution that destabilizes particles. This shows surface reduction occurs that reduces silver size and makes particle bigger.
From the point of experiment, it is concluded that variables have a significant contribution on particle size. Particle shape of all nanoparticulate formulation was found to be spherical with smooth surface as observed in optical microscope.

6) Effect of variables on % Entrapment Efficiency:

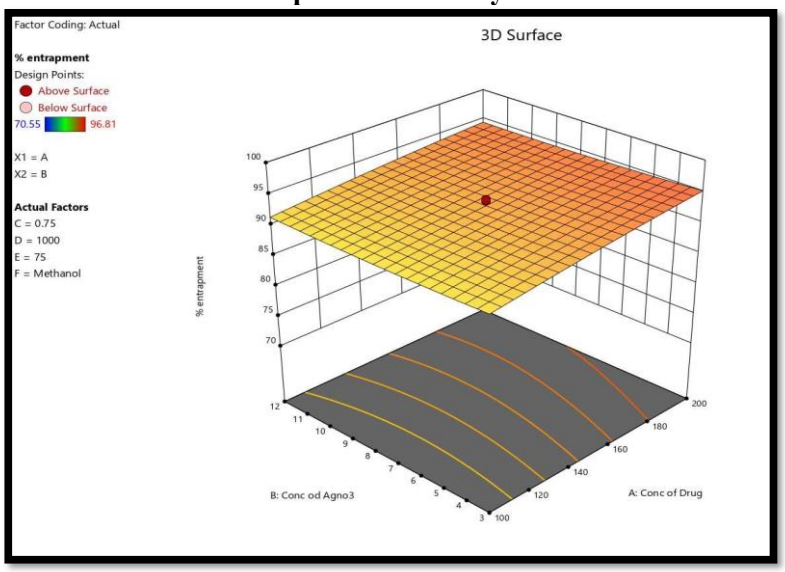


Fig 8.11: 3D Response Surface Plot for % Entrapment

The entrapment efficiency of Karanj of all the formulation waas found in range between 70.55 to 96.81. The entrapment efficiency of N43 was found to be maximum while N84 shows less entrapment efficiency. From this it clearly shows that high concentration of silver nitrate shows highest entrapment efficiency compared to low concentration. Chitosan also affect the entrapment efficiency. The more the silver nitrate more the entrapment efficiency. In 3D response surface plot, as the chitosan concentration increases drastically entrapment efficiency also increased which is due to the presence of hydroxyl and amino group in chitosan which acts as stabilizer of silver nanoparticle.

The entrapment efficiency of karanj increases as we increase the concentration of pure drug. As the concentration of silver nitrate increases results in decrease in entrapment efficiency of drug. As stirring speed increases will increase in entrapment efficiency as well as if stirring time increases will results in increase concentration of drug. Use of solvent also affect the entrapment efficiency as we used methanol will increase drug concentration; increases entrapment efficiency and use of acetone increases drug concentration and decreases entrapment efficiency.

1) Zeta potential

Zeta potential study is also based on the stearic stabilization and modification in net charge due to Chitosan. The observed zeta potential of optimized batch with electrophoretic mobility So according to table no 8.7 below the nanoparticles have excellent stability

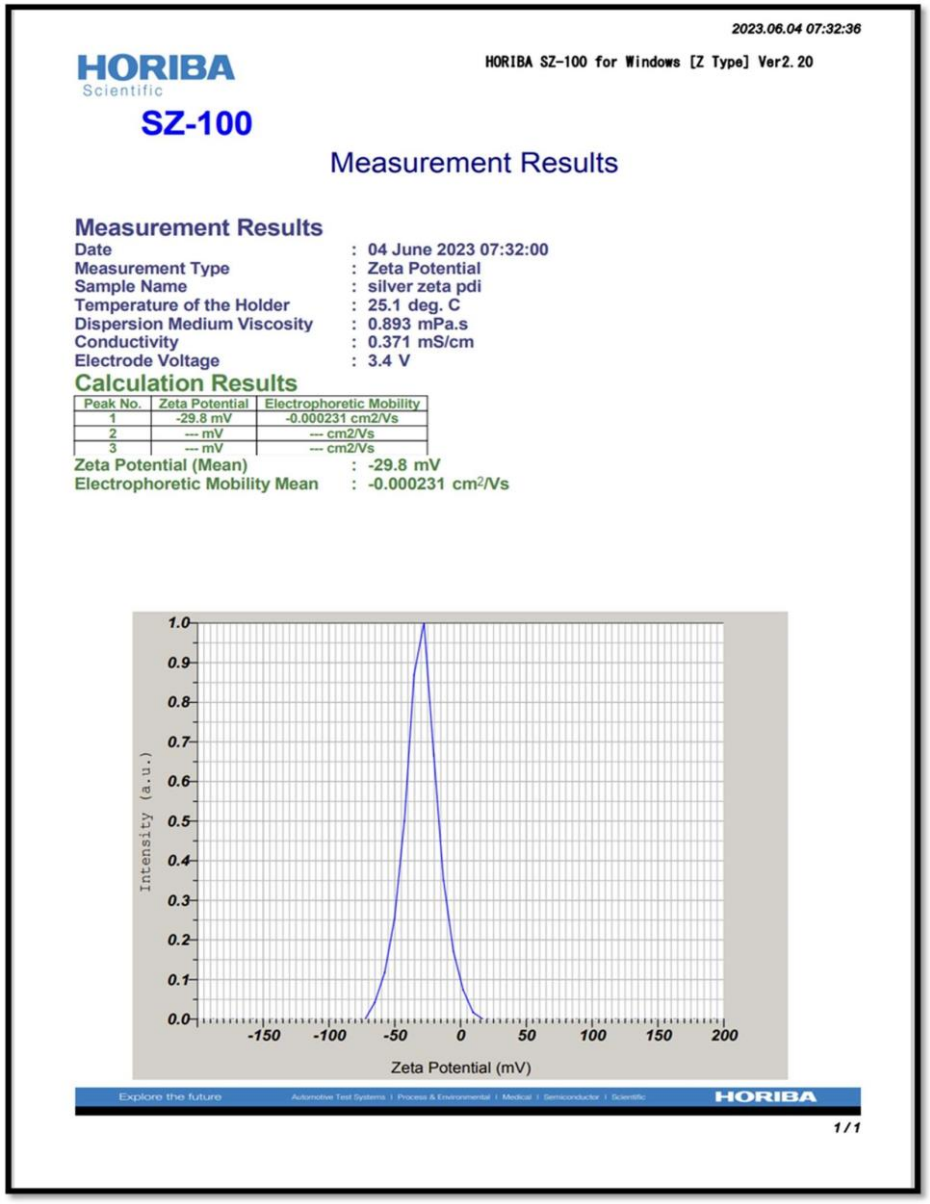


Fig no.5 Zeta potential of Silver nanoparticles

8) Polydispersity Index (PDI):

Polydispersity index of optimized batch is determined by Dynamic Light Scattering method by Horiba SZ-100 and computerized inspection system.

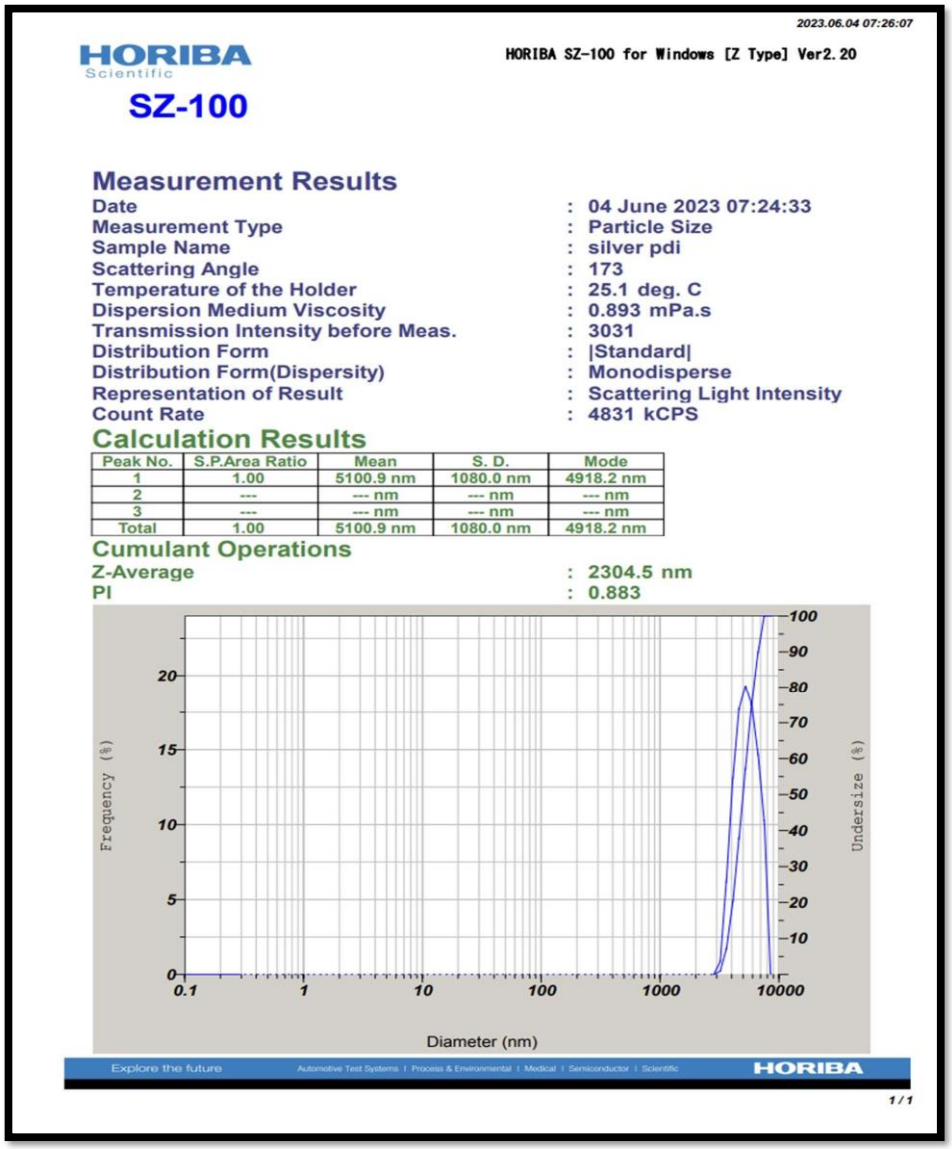


Fig 8.9: Data for Polydispersity index

9) Differential Scanning Colorimetry of Nanoparticles:

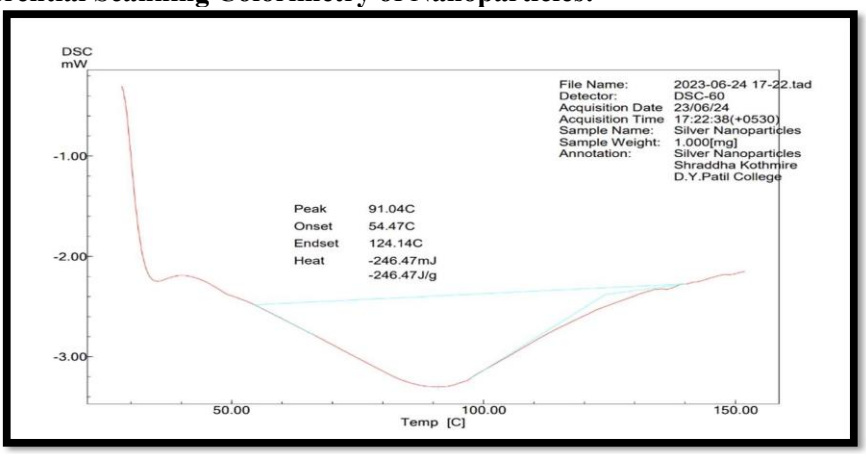


Fig. 8.16: DSC characterization of nanoparticle formulation

DSC studies were performed to observe the thermal properties and intermolecular reaction between silver nitrate, Karanj and chitosan in the nanoparticle formulation. Pure Karanj shows exothermic peak which corresponds to its melting point. The presence of sharp exothermic peak indicates the crystalline nature.of drug. In DSC thermogram of optimized formulation the exothermic peak showed .This might be due to no change in thermal properties of nanoparticles.

10) Scanning Electron Microscopy of Nanoparticles:

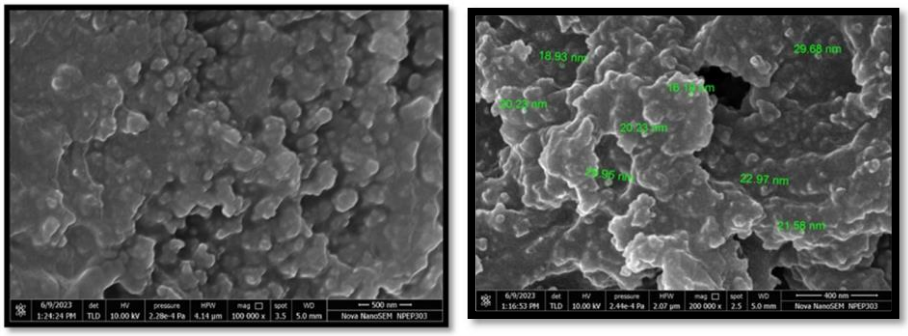


Fig 8.17: Microscopic image of Nanoparticles

Scanning Electron Microscopy of nanoparticles were performed and the particle size was found in between 16.19- 29.95 nm. This shows that the nanoparticle formed are in the range of 1-
100 nm.

11) pH herbal skin Gel:
Readings are in triplicates.

Table 8.9: pH of herbal Gel

Formulation	pH(± SD)	Formulation	pH(± SD)
F1	1.49 ± 0.08	F10	6.60 ± 0.021
F2	6.52 ± 0.014	F11	6.50 ± 0.11
F3	6.66 ± 0.029	F12	6.52 ± 0.12
F4	6.50 ± 0.10	F13	6.66 ± 0.029
F5	6.53 ± 0.03	F14	6.50 ± 0.10
F6	6.52 ± 0.014	F15	6.62 ± 0.020
F7	6.41 ± 0.07	F16	6.53 ± 0.02
F8	6.44 ± 0.05	F17	6.50 ± 0.10
F9	6.50 ± 0.10	F18	6.44± 0.02
			6.45

A. The formulation of nanoparticle gel was evaluated for % drug release, spread ability and Viscosity study.

Table 8.23: statistical analysis for spread ability, Viscosity and % drug release study

Response	Model	P value	F value	R^2 Value	Predicted R^2 Value	Remark
% Drug release	Quadratic	0.9830	0.0172	0.7387	0.6450	Significant
Spreadability	Quadratic	0.0019	9.22	0.7315	0.3381	Significant
Viscosity	Quadratic	0.0044	7.60	0.4979	-0.2206	Significant

8.9: Optimization of nanoparticle gel:

A. Effect of variables on Viscosity:

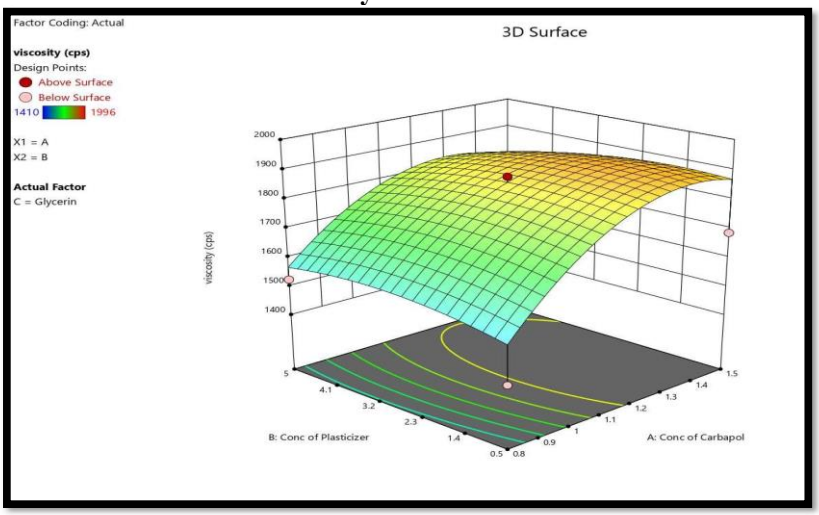


Fig. 8.18: 3D Response Surface Graph for Viscosity

Through preliminary experiments, amount of Carbopol 934 and propylene glycol are the most significant variables which affects viscosity, spread ability and % drug release. There were 13 experimental batches were obtained from response surface methodology based on Central State Ease Design- Expert v13. Based on the experimental design, factor combination yielded 13 different responses as shown table no 8.20. After formulation of 18 batches of herbal gels, the results of viscosity, spread ability and % drug release were analyzed using Stat Ease Design- Expert v13 to obtain ANOVA, regression coefficient and regression equation. Mathematical equations were generated using multiple linear regression analysis for particle size and entrapment efficiency. These equations represent quantitative effect of concentration and interaction of Carbopol 934 and propylene glycol on viscosity, spread ability and % drug release.

The viscosity of herbal gel F1 to F18 ranges from 1410-1996 cPs as shown in (Table no 8.20). Viscosity increases as the amount of Carbopol 934 increases but it is affected by propylene glycol. As shown in following perturbation plot and 3D surface graph fig. no 8.12. In perturbation the Carbopol 934 (A) amount increases causes increase the viscosity but when propylene glycol (B) is added viscosity reduces drastically. As presence of triethanolamine (viscosity enhancer) in gel which reacts with Carbopol 934 to give viscosity to gel on contrarily propylene glycol is humectant and responsible for reducing the viscosity.

B. Effect of variables on spreadability:

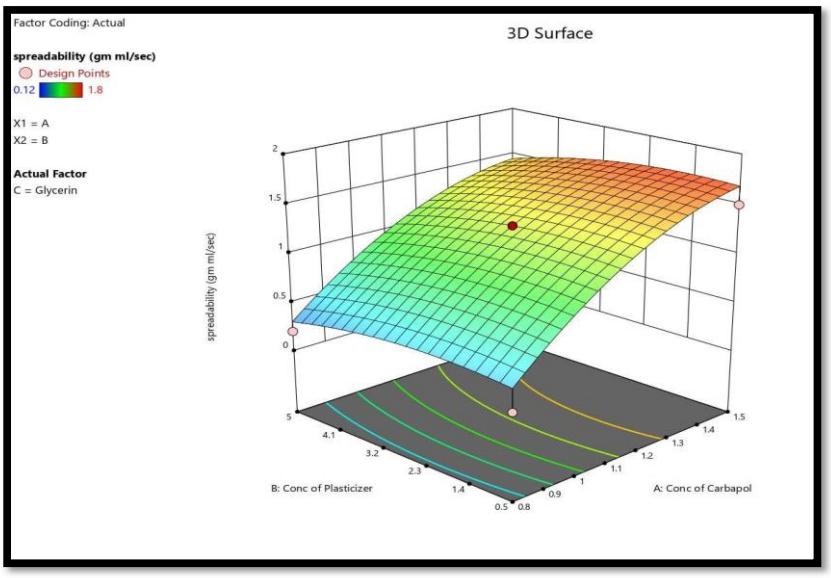


Fig 8.19: 3D Response Surface Graph for Spreadability

The spreadability of nanoparticulate gel F1 to F18 ranges from 0.12 gm.cm/sec to 1.8 gm.cm/sec as shown in (Table no 8.11). Spredability increases as the amount of Carbopol 934 increases but it is affected by propylene glycol. As shown in following perturbation plot and 3D surface graph fig. no. 8.19. In perturbation as the amount of Carbopol (A) and propylene glycol (B) increases the spreadability increases. When the concentration of Carbopol 934 and propylene glycol increases results in increase in spredability. It might be due to Carbopol 934 is well known compound for its excellent gel property such as sparkling clarity and spreadability.

C. Effect of variables on drug diffusion

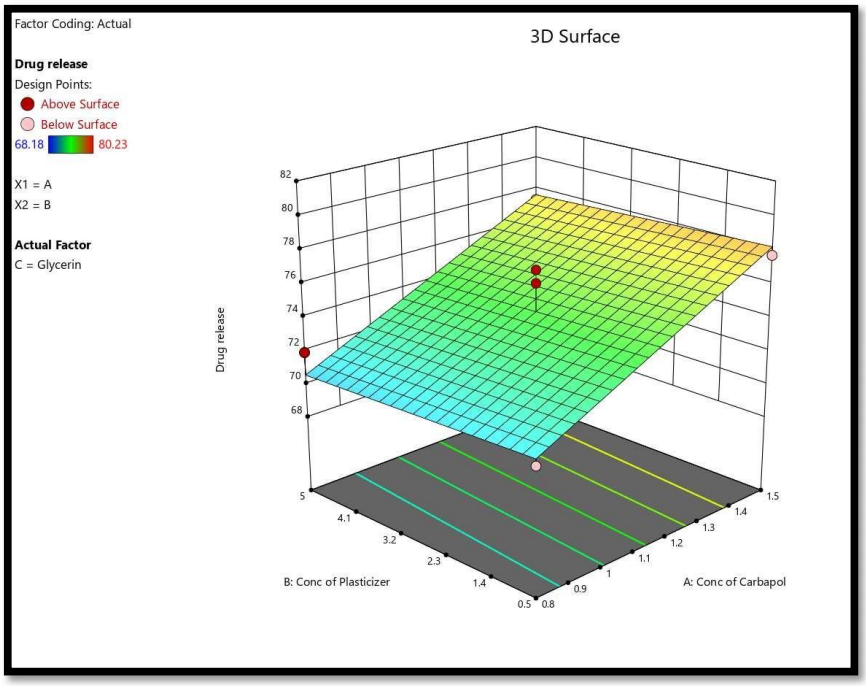


Fig 8.20: 3D Response Surface Graph for Drug Release

The % drug release of nanoparticulate gel F1 to F18 ranges from 68.18% to 80.23% as shown in table no.8.20. As we increase in Carbopol 934 content was associated with a corresponding just slight increase in drug permeation of drug. This could be due to extensive swelling property of polymer which created a thick gel barrier for drug diffusion. The permeation of drug was slightly increased with increasing concentration of propylene glycol this may be due to fact that dissolution of aqueous soluble fraction of polymer matrix leads to formation of gelaneous pores. The formation of such kind of pores leads to decrease the mean diffusion path length of drug molecule to release into the diffusion medium and hence higher drug release rate.

Table No. 8.24: Dependent and independent factors for formulation of gels

Run	Factor 1 A: Conc of Carbopol	Factor 2 B: Conc of Plasticizer	Factor 3 C: Type of plastisizer	Response 1 Drug release	Response 2 viscosity cps	Response 3 spreadability gm ml/sec
1	0.655025	2.75	propylene glycol	69.75	1440	0.12
2	1.15	5.93198	Glycerin	72.48	1868	1.02
3	1.5	5	propylene glycol	77.36	1656	1.42
4	1.15	2.75	propylene glycol	73.98	1855	1
5	1.15	2.75	Glycerin	71.08	1797	1.29
6	1.15	5.93198	propylene glycol	74.09	1824	1.02
7	0.655025	2.75	Glycerin	68.18	1456	0.16
8	0.8	0.5	Glycerin	70.77	1410	0.2
9	1.5	0.5	Glycerin	77.722	1687	1.5

10	1.15	-0.431981	Glycerin	76.63	1996	1.45
11	1.64497	2.75	Glycerin	80.038	1950	1.8
12	1.64497	2.75	propylene glycol	80.23	1985	0.2
13	0.8	0.5	propylene glycol	70.29	1501	0.2
14	1.15	-0.431981	propylene glycol	75.04	1908	1.24
15	1.5	5	Glycerin	77.31	1654	1.39
16	1.5	0.5	propylene glycol	76.48	1644	1.47
17	0.8	5	Glycerin	71.93	1524	0.2
18	0.8	5	propylene glycol	71.02	1577	0.21

B. Optimizing Formula of the gel as per Design Expert and Desirability plot:

After generating the model polynomial equation to relate the dependent and independent variables the process was optimized for responses. The final optimal experimental parameters were calculated using canonical analysis which allows the compromise among various responses and searches for a combination of factor levels that jointly optimize a set of response by satisfying requirements for each responsible test. The optimally calculated parameters are shown in table no 8.11 as per the Central Composite Stat Ease® Design- Expert V13 the optimized batch found to be containing Carbopol 934 is 1.15% and Glycerine 2.75%.

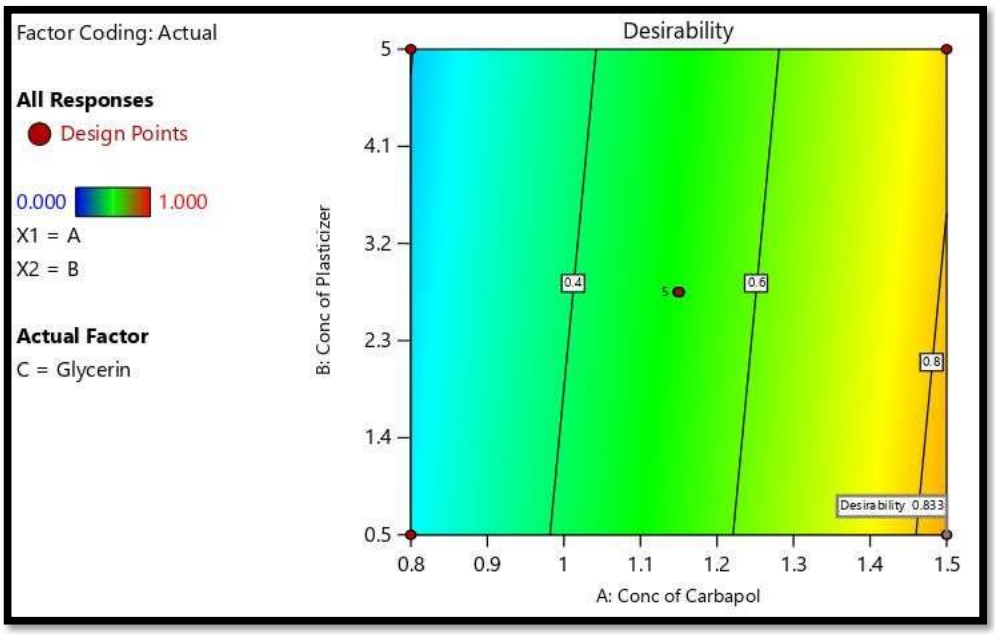


Fig No. 8.22: Desirability plot for gel

Table no 8.12: Optimized batch of nanoparticle gel

Factor	Name	Level
A	Carbopol 934	1.15
B	Glycerine	2.75

8.1.1 Stability study of gel formulation:

Table No. 8.26: Stability data for 30 days

Sr.No.	Parameters	Initial days	After 30 days
1	Drug release	71.08	71.04
2	Viscosity	1797	1867
3	Spreadability	1.29	1.25

This formulation was found to be more stable at refrigerated temperature.

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