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PREPARATION AND EVALUATION OF POVIDONE IODINE CONTAINING FILM FORMING GEL

Lala Moinuddin[1], Dr. Vishnu Patel[2], Dr. Maulik Mehta[3]

Student[1], Professor[2], Principal[3]

A.P.M.C. College of Pharmaceutical Education and Research, Motipura, Himatnagar-383001

Abstract

The Film-forming gels containing povidone iodine can create a protective barrier over the wound, promoting a moist environment conducive to healing while preventing infection. The experimental work done to carry out organoleptic properties, UV spectroscopy, FTIR study and melting point determination for drug determination and then trial batches were prepared for determining the concentration and selection various polymers. Based on that factorial batches were prepared and evaluation is performed. The povidone iodine gel was prepared using different ratios of PVA and PVP K-30, PEG 400 used as a plasticizer. Formulations (F1-F9) were prepared and evaluated for their physicochemical properties. Based on that 3^2 full factorial designs were applied to optimize the final formulation and check the impact of independent variables. The optimized (F6) Formulation (Ratio of PVA: PVP K-30 and PEG 400) exhibited % drug release 93.59% in 360 minutes. F6 formulation found stable for 1 month during stability study.

Key Words: Film forming gel, povidone iodine, antiseptic, wound healing.

Introduction

A new method in this field called film-forming gels may offer a substitute to the common dose forms applied to the skin, such ointments, lotions, gels, or patches. When the liquid polymeric solution gets applied to the skin, solvent evaporation creates a virtually undetectable film that develops there. In comparison to traditional pharmaceutical dosage formulations, transdermal drug delivery systems (TDDS) and dermal drug delivery system can offer some desirable performances, such as preventing gut and hepatic initial metabolism, increasing drug bioavailability, lowering dose frequency, and stabilizing drug delivery profiles. This review's objective was to find substitutes for the traditional forms that would lessen skin irritation, increase skin adherence, and improve drug release.

Film-forming preparations are characterized as non-solid formulations that, when applied to skin or any other surface of the body, form a significant film in situ. These mixtures can be liquids or semisolids, with the primary matrix ingredient being a film-forming polymer. The resulting coating is substantial enough to give the skin a continuous medication release.

Materials and methods

Povidone Iodine, Pulse Pharma, , himmatnagar,(Gujarat), PVP K30, HPMC 15CPS, Eudragit RL, Polyvinyl alcohol, Chemdyes Corporation, Rajkot-360001.(Gujarat) PEG 400, Alliedchemicalscorporation,Vadodra,Gujarat.

Method of Preparation of povidone iodine containing film forming gel

The polymeric solutions of PVP K30 and Polyvinyl alcohol were prepared in water using dispersion method. Heat the polymeric solution till the proper uniform paste is form. Then in another beaker take ethanol and plasticizer (PEG-400) were added and mix properly to uniform solution. Both solutions allow mixing properly with continuous stirring. Accurately weight the drug povidone iodine was dissolved into the water. Drug solution is added into polymeric dispersion mix properly with continuos stirring. Prepared gel formulation is filled under air tight container.

Table 1 Formulation Table of Trial Batches of povidone iodine film forming gel

Ingredient	B1	B2	B3	B4	B5	B6	B7	B8	B9
Povidone iodine (%w/v)	5%	5%	5%	5%	5%	5%	5%	5%	5%
PVA (%w/v)	8%	10%	12%	8%	10%	12%	8%	10%	12%
PVP K-30 (%w/v)	2%	2%	2%	3%	3%	3%	4%	4%	4%
PEG400 (%v/v)	3%	3%	3%	3%	3%	3%	3%	3%	3%
Ethanol (%v/v)	20%	20%	20%	20%	20%	20%	20%	20%	20%
Distilled water	upto 100%	upto 100%	upto 100%	upto 100%	upto 100%	upto 100%	upto 100%	upto 100%	upto 100%

Table 2 Layout of Factorial Design

3^2 Full Factorial Designs			
Formulation no.	X1 Amount of PVA	X2 Amount of PVP K30	
F1	-1	-1	
F2	0	-1	
F3	1	-1	
F4	-1	0	
F5	0	0	
F6	1	0	
F7	-1	1	
F8	0	1	
F9	1	1	
Independent Variables	Level		
	Low(-1)	Medium(0)	High(1)
PVA	10%	11%	12%
PVP K-30	2%	2.5%	3%
Response Variables			
Response Y1: Viscosity			
Response Y2: drying time			
Response Y3: % drug released			

Table 3 Formulation Table of Trial Batches of povidone iodine film forming gel

Ingredient	F1	F2	F3	F4	F5	F6	F7	F8	F9
Povidone iodine (%w/v)	5%	5%	5%	5%	5%	5%	5%	5%	5%
PVA (%w/v)	10%	11%	12%	10%	11%	12%	10%	11%	12%
PVP K-30 (%w/v)	2%	2%	2%	2.5%	2.5%	2.5%	3%	3%	3%
PEG400 (%v/v)	3%	3%	3%	3%	3%	3%	3%	3%	3%
Ethanol (%v/v)	20%	20%	20%	20%	20%	20%	20%	20%	20%
Distilled water	upto 100%	upto 100%	upto 100%	upto 100%	upto 100%	upto 100%	upto 100%	upto 100%	upto 100%

Methodology

Organoleptic property

The drug is colour and state is considered in this terminology.

Melting point determination of drug

Melting point is convenient method to examine the purity Determination of metling point done by capillary method.

Procedure: povidone iodine was filled in the capillary and tied with the thermometer. The thermometer with the capillary was placed in the Sunbim instrument. The instrument was subjected to the external heat and the point at which povidone iodine melts is recorded from the thermometer.

Compatability study of drug with Excipients

Povidone iodine calibration curve determination

Preparation of standards stock solution

Standard stock solution A: 100 mg of drug sample (povidone iodine) was accurately weighed and transfer to 100 ml stoppered iodine flask and diluted upto the mark with water (1000 µg/ml).

Standard working solution: from stock solution A pipette out 10 ml and diluted upto 100 ml with water in stoppered iodine flask (100 µg/ml).

Preperation of working solution

Povidone iodine in water with different concentration of standard solution ranging from 5 – 25 µg/ml. Further dilution with water works done of 0.5, 1, 1.5, 2, 2.5 µg/ml concentration of working stock solution of povidone iodine (100 µg/ml) into the series of 10 ml stoppered iodine flask and the volume was adjust to the mark with water to make 5, 10, 15, 20 and 25 µg/ml solution of povidone iodine.

Selection of analytical wavelength

Standard drug working solution with appropriate dilution, the solution containing 25 µg/ml of povidone iodine in range of 250 – 600 nm was scanned.

FTIR spectroscopy [Fourier transform infrared spectroscopy]

Physical and chemical interaction of drug and excipent resolved by FTIR technique. Instrument quickly evident in spectral quality and data collection speed. For the study of drug-polymer interaction, the infrared absorption spectra of the pure drug sample and the physical mixture of the drug with different polymers were carried out.

Evaluation Parameters of povidone iodine film forming gel

1. pH

The pH of optimized gel was determined using digital pH meter. Standardized using pH 7 buffers before use. The measurement of pH of each formulation was done in triplicate and mean values were calculated.

2. Film appearance

All prepared film are evaluated basis of uniformatiy of the film after drying, it should given range from average, good and best.

3. Folding endurance

The folding durability of the prepared film was measured manually. A small piece of film (4 X 3 cm) is sliced uniformly and folded repeatedly at the same point until it broke. The amount of times the film was able to be folded in the same spot without breaking determined the precise amount of folding endurance.

4. Spreadability

Spreadability was determined using slides of glass and a wooden block, and it was quantified using the gel's "slip" and "drag" qualities. A horizontal glass slide was mounted on this block. An excess much gel (about 1gm) from several formulations was put on the bottom slide. The gel was then placed over that slide and a second glass slide that had the same dimensions as the fixed ground slide. Excess gel was scraped off the edges. The plate on top was then exposed to a pull of 50mgs, which reduced the time required to separate two slides and demonstrated acceptable spreadability. The spreadability was then determined using a new formula:

$S = M \times L / T$

Where, S = spreadability, M = weight, L = length moved by the glass slide T = time taken to separate the slide completely from each other.

5. Viscosity

The viscosity of formed batches was measured using a viscometer manufactured by Brookfield (digital a viscometer version DV-II+, Stoughton in MA, USA) using spindle S96. To assess viscosity, the formulation was put to a beaker and allowed to settle for 30 minutes at 25° ± 1°C before measuring. The spindle was dropped perpendicularly into the middle of the gel, ensuring that it did not contact the bottom of beaker, and revolved at 50 rpm for 5 minutes. The intensity of reading was written down. The gel viscosity was calculated using the average three observations given over a 5-minute period.

6. Tensile Strength

The tensile strength was determined by tensile strength tester. 2 x 2 centimeter film strip free from air bubbles was cut and held longitudinally in tensile grip on the tester. The weights were added to the pan till the film broke. All measurements were performed in triplicate. Tensile strength was calculated by the applied load at the rupture devided by cross sectional area of the film strip as given in the equation below:

Tensile Strength = load of failure (kg) / Cross sectional area (cm^2)

7. Drying time

The film forming gel was put on a glass slide in order to figure out drying time. After 3 minutes, another glass slides was placed over the film with no pressure. If there was no liquid left on a glass slide upon

removal, the film had been considered dry. If any liquid remained on the glass slide, the experiment was carried out until the layer of film was fully dried.

8. In-vitro drug diffusion study of film

The drug diffusion investigation via film was carried out using a vertical diffusion cell (Franz type) with a receptor compartment of 20 mL capacity and 2 cm2 area. The receptor compartment was filled with 20ml of pH 7.4 phosphate buffer, and the activated dialysis membrane was installed on the diffusion cellreceptor compartment's flange. The produced film was put in the center of the membrane with an adequate amount of medication, the donor compartment then inserted, and the cell's two valves were clamped together. The entire assembly was placed on a magnetic stirrer, and the solution in receptor compartment was continually swirled with a magnetic bead at 32^{o}C. To maintain the sink condition, 1 ml of sample was taken from the receptor compartment's sampling port at one-hour intervals using a micropipette and replenished with receptor fluid solution. The samples were extracted, and the drug content was determined using the technique described above.

9. Drug content determination

In a stoppered iodine flask, add 1.5 mL of film-forming solution corresponding to 50 mg or iodine and enough water to make at least 30 mL. The resulting solution was filtered using watman paper and promptly tritrated with 0.02 M thiosulphate of sodium, with 3 ml of start solution added at the conclusion of the titration as an indicator. Perform a blank titration.

1 ml of 0.02M sodium thiosulphate is equivalent to 0.002538g of I.

10. STABILITY STUDY

During stability testing, the product is subjected to normal temperature and humidity levels. However, the studies will require longer, thus it would be more practical to conduct rapid stability experiments in which the product is held at severe temperatures. Stability studies were conducted to examine the stability of the medication and its formulation. The optimized formulation was packaged in aluminum packaging covered with polyethylene. Replicates were housed in a humidity room at 40±2°C and 75±5% RH over 30 days. The sample was examined for physical changes, drug content percentage, gel characteristics, film mechanical properties, and an in vitro diffusion profile.

Results & discussion

Organoleptic Property

Color: brownish crystalline powder.

Odour: Odourless

Texture: Crystalline

Melting point determination

Melting point of Povidone iodine drug is determined by using Sunbim.

Drug (API)	Reported Melting Point Range	Experimental Melting Point Range
Povidone Iodine	298-300 ℃	297-299 ℃

Compatability study of drug with excipients

By UV- Spectroscopy

Wavelength maxima of Povidone Iodine were determined by using UV- Vis 1700 Spectroscopy by Shimadzu. The UV spectrum of Povidone iodine (25 µg/ml) was taken in mixture distilled water.

Drug (API)	Reported λ_{max}
Povidone Iodine	355 nm

Figure 1 Wavelength Scan of povidone Iodine

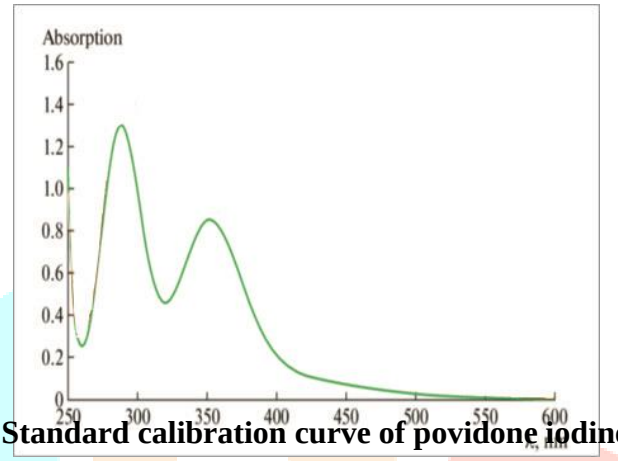


Table 4 Standard calibration curve of povidone iodine film forming gel

Concentraion (µg/ml)	Absorbance			Average	SD
5	0.161	0.166	0.165	0.164	0.00265
10	0.362	0.362	0.361	0.361	0.00057
15	0.558	0.555	0.556	0.556	0.00158
20	0.728	0.727	0.724	0.726	0.00208
25	0.927	0.927	0.922	0.925	0.00288

Figure 2 Standard calibration curve of povidone iodine film forming gel

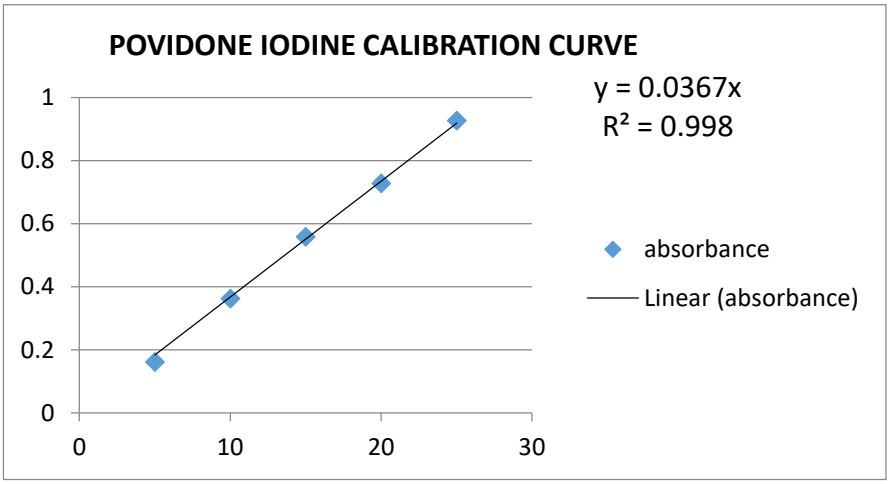


Figure 3 FTIR spectra of povidone iodine

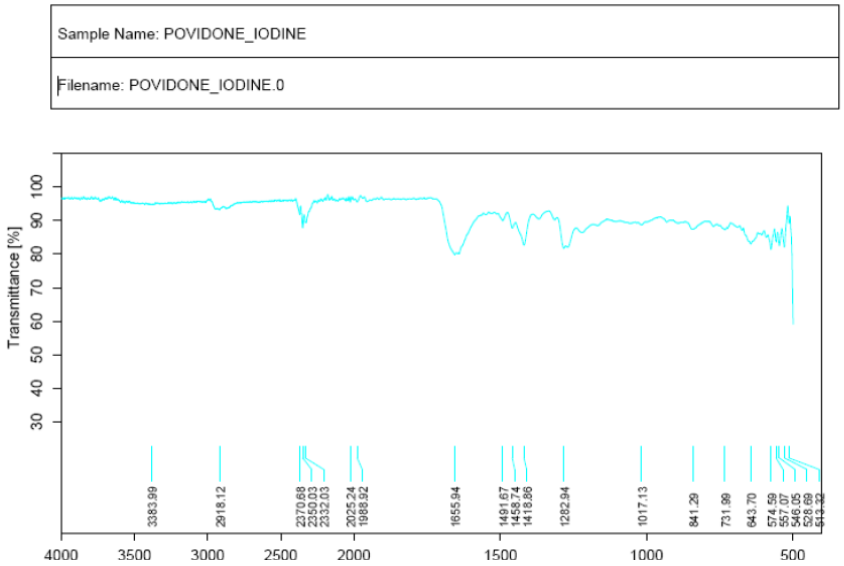


Figure 4 FTIR spectra of povidone iodine + excipients

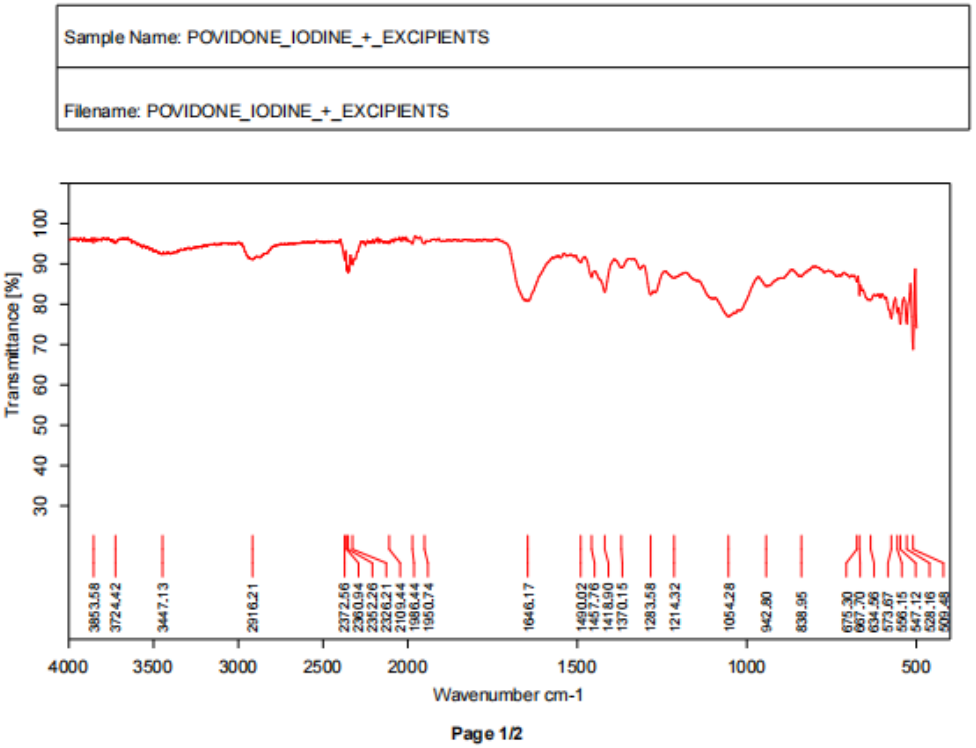


Table 5 Interaction studies through IR spectroscopy

Functional group	Drug	Drug-excipent mixture
C-H aromatic stretch	1018.45	1018.45
C ≡ N stretch	1319.37	1319.35
C=C aromatic stretch	1219.00	1219.26
C-I stretch	1292.40	1292.42

Frequencies of the functional groups of pure drug were intact in comparison, so it was concluded that there were no interaction occurred between the drug and polymer used in the present study.

Table 6 Result of trial batch povidone iodine film forming gel

Formulation	Viscosity(cps)	pH of the solution	Spredability (gm/cm sec^{-1})	Drying time	Folding endurance
B1	1217±7.1	5.87±0.015	19.32±0.21	4 min 10 sec ± 6 sec	39±2.17
B2	1326±5.4	5.31±0.024	17.61±0.13	5 min 31 sec ± 4 sec	51±1.94
B3	1421±4.2	5.90±0.032	16.75±0.25	5 min 74 sec ± 2 sec	45±2.51
B4	1577±2.5	5.52±0.011	15.29±0.20	5 min 98 sec ± 8 sec	41±2.40
B5	1617±7.3	5.84±0.023	14.16±0.30	6 min 06 sec ± 3 sec	58±1.82
B6	1624±2.0	5.70±0.031	13.90±0.22	6 min 32 sec ± 4 sec	56±1.97
B7	1459±5.0	5.86±0.022	18.83±0.12	6 min 52 sec ± 5 sec	38±2.76
B8	1698±6.1	6.01±0.024	18.01±0.32	7 min 29 sec ± 2 sec	35±2.95
B9	1727±7.2	5.93±0.033	17.38±0.11	7 min 40 sec ± 7 sec	43±1.53

NOTE: For, n=3 (All observations are average of three determinations)

INTERPRETATON:

Preliminary study 2 was carried out to determine the polymer concentration necessary for drug delivery. To study effect of polymer concentration on parameters such as Gel viscosity, pH, folding endurance, drying time and Ex Vivo physical property of film, Batches B1 to B9 were prepared as shown in Table .The concentration of PVA was ranged from 8 to 12% (w/v). The concentration of PVP K 30 was ranged from 2 to 4% (w/v).

In the batches B1 to B3 (Containing 2% PVP K30), the viscosity was less and drying time was found more than B4 to B9 batches, but batch B1 was found to less flexible as cracks were observed on film and dermal adhesion was found also less as the concentration of PVA less.

The characteristic of film formation was found to decent in the batches B4 to B6 (containing 3% PVP K30), but in B4 batch the viscosity is less due to which gel were observed less viscous and folding endurance was also found poor in this batch.

While the solution's viscosities were very high in the batches B7 to B9 (containing 4% PVP K30) due to higher concentration of PVP K30 due to which gel is containing more viscosity and drying time is also more. Preliminary study 2 was performed to determine the higher and lower value for PVA and PVP K 30 for further optimization of formulation.

From the result of preliminary study 2, it was observed that batch formulated using PVA at concentration of 10 to 12 percent w/v and PVP K30 at concentration of 2 to 3 percent w/v showed Satisfactory / Good viscosity, pH of the gel, folding endurance, drying time, and spredability. So, for PVA 11% was selected as lower concentration and 12% as higher concentration. And for PVP K30 2% was selected as lower concentration and 3% as higher concentration. With the selected high and low value further optimization was performed.

Table 7 Result of formulation povidone iodine film forming gel

Formulation	Viscosity(cps)	pH of the solution	Spredability (gm/cm sec^{-1})	Drying time	Folding endurance
F1	1337±5.1	5.82±0.021	16.32±0.25	5 min 24sec ± 4 sec	53±1.52
F2	1352±5.7	6.21±0.049	16.62±0.18	5 min 14sec ± 2 sec	54±1.84
F3	1486±4.1	5.89±0.031	15.85±0.21	5 min 21 sec ± 8 sec	50±2.31
F4	1487±3.3	5.81±0.029	15.70±0.23	6 min 18 sec ± 2 sec	54±1.63
F5	1457±2.8	5.75±0.036	16.13±0.39	6 min 16 sec ± 7 sec	55±1.63
F6	1632±3.9	5.86±0.032	16.81±0.16	5 min 50 sec ± 5 sec	58±1.72
F7	1659±1.7	5.69±0.024	15.83±0.10	6 min 22 sec ± 6 sec	56±2.43
F8	1695±4.1	6.08±0.021	15.46±0.25	6 min 27 sec ± 9 sec	54±2.61
F9	1721±1.2	5.52±0.035	15.92±0.33	5 min 58 sec ± 3 sec	52±1.94

Table 8 Result of formulation povidone iodine film forming gel

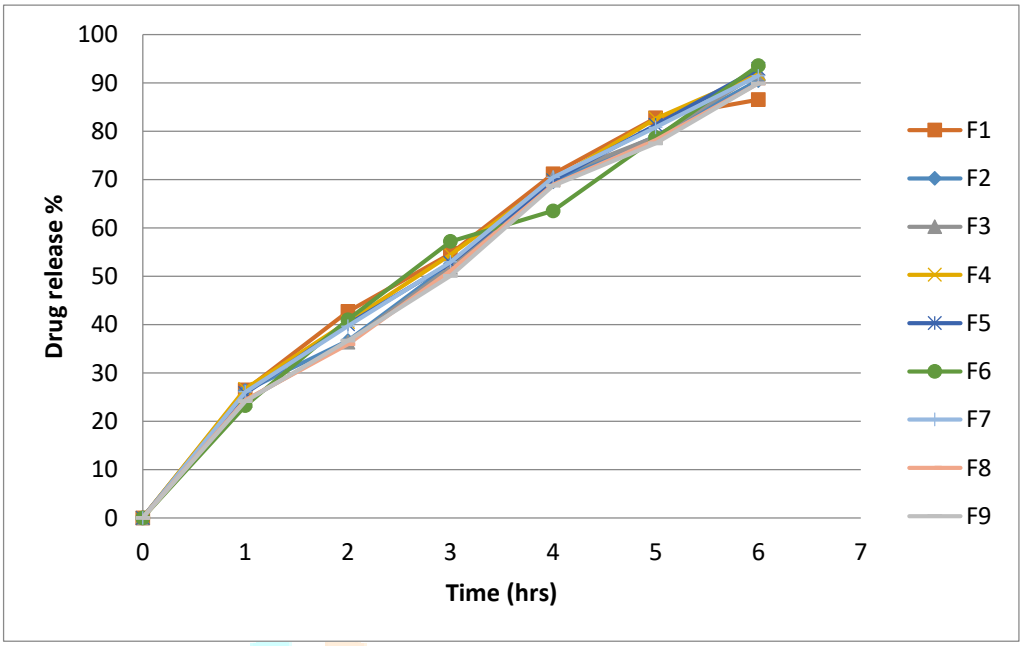
Formulation	% drug content	% drug release	Tensile strength (kg/cm^2)
F1	98.55±0.10	86.55±0.19	0.24 ±0.7
F2	98.67±0.21	90.50±0.20	0.25±0.2
F3	98.86±0.51	92.00±0.31	0.28 ±0.2
F4	99.55±0.14	91.93±0.39	0.31±0.1
F5	99.76±0.22	92.91±0.25	0.29±0.3
F6	99.78±0.19	93.59±0.30	0.36 ±0.1
F7	99.45±0.20	91.50±0.48	0.34±0.5
F8	99.89±0.46	89.90±0.53	0.36 ±0.2
F9	99.45±0.72	89.81±0.67	0.33 ±0.6

Table 9 Drug release of the povidone iodine formulation batch

Time (hours)	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0± 0.0	0± 0.0	0± 0.0	0± 0.0	0± 0.0	0± 0.0	0± 0.0	0± 0.0	0± 0.0
1	26.49± 0.10	26.33 ± 0.32	24.25± 0.34	26.69 ± 0.25	25.82± 0.10	25.22± 0.60	26.06 ± 0.45	24.42± 0.35	24.15± 0.59
2	42.71± 0.12	36.67 ± 0.23	36.34± 0.30	40.55 ± 0.39	40.04± 0.20	41.00± 0.034	39.68 ± 0.52	35.95± 0.47	36.67± 0.39
3	54.70± 0.19	52.52 ± 0.35	51.85± 0.37	54.49 ± 0.42	52.77± 0.29	57.21± 0.51	52.98 ± 0.49	51.20± 0.42	50.09± 0.52
4	71.19± 0.21	69.55 ± 0.26	70.49± 0.43	69.85 ± 0.35	69.85± 0.21	73.53± 0.34	70.45 ± 0.48	68.93± 0.500	68.74± 0.650
5	82.80± 0.01	79.01 ± 0.20	78.88± 0.359	82.66 ± 0.30	81.31± 0.027	78.69± 0.046	80.83 ± 0.49	78.19± 0.43	77.51± 0.48
6	86.55± 0.19	90.5± 0.20	92.0± 0.31	91.93 ± 0.39	92.91± 0.25	93.59± 0.30	91.5 ± 0.48	89.9± 0.53	89.81± 0.67

NOTE: For, n=3 (All observations are average of three determinations)

Figure 5 Drug release of Batch F1-F9 of formulation Batches



INTERPRETATON:

Formulation F6 was selected for further study as, it has best viscosity and film forming in less time and folding endurance more which show more flexible.

ANOVA for Quadratic model for Viscosity:

Response 1: Viscosity

Source	Sum of Squares	df	Mean Square	F-value	p-value	
Model	1.640E+05	5	32805.21	22.25	0.0141	significant
A-PVA	21122.67	1	21122.67	14.33	0.0323	
B-PVP K-30	1.350E+05	1	1.350E+05	91.56	0.0024	
AB	1892.25	1	1892.25	1.28	0.3396	
A^2	5477.56	1	5477.56	3.71	0.1495	
B^2	533.56	1	533.56	0.3619	0.5899	
Residual	4423.53	3	1474.51			
Cor Total	1.684E+05	8				

Fit Statistics

Std. Dev.	**38.40**	**R^2**	**0.9737**
Mean	1536.22	**Adjusted R^2**	0.9300
C.V. %	2.50	**Predicted R^2**	0.7509
		Adeq Precision	13.3534

Coefficients in Terms of Coded Factors

Factor	Coefficient Estimate	df	Standard Error	95% CI Low	95% CI High	VIF
Intercept	1490.44	1	28.62	1399.36	1581.53	
A-PVA	59.33	1	15.68	9.44	109.22	1.0000
B-PVP K-30	150.00	1	15.68	100.11	199.89	1.0000
AB	-21.75	1	19.20	-82.85	39.35	1.0000
A^2	52.33	1	27.15	-34.08	138.74	1.0000
B^2	16.33	1	27.15	-70.08	102.74	1.0000

- **Polynomial equation of dependent variable of film forming spray**

Viscosity (Y1): $1490.44 + 59.33X_1 + 150.00X_2 - 21.75X_{12} + 52.33X_{11} + 16.33X_{22}$

Result of 3^2 factorial design of Viscosity:

Figure 6 Contour Plot of Viscosity

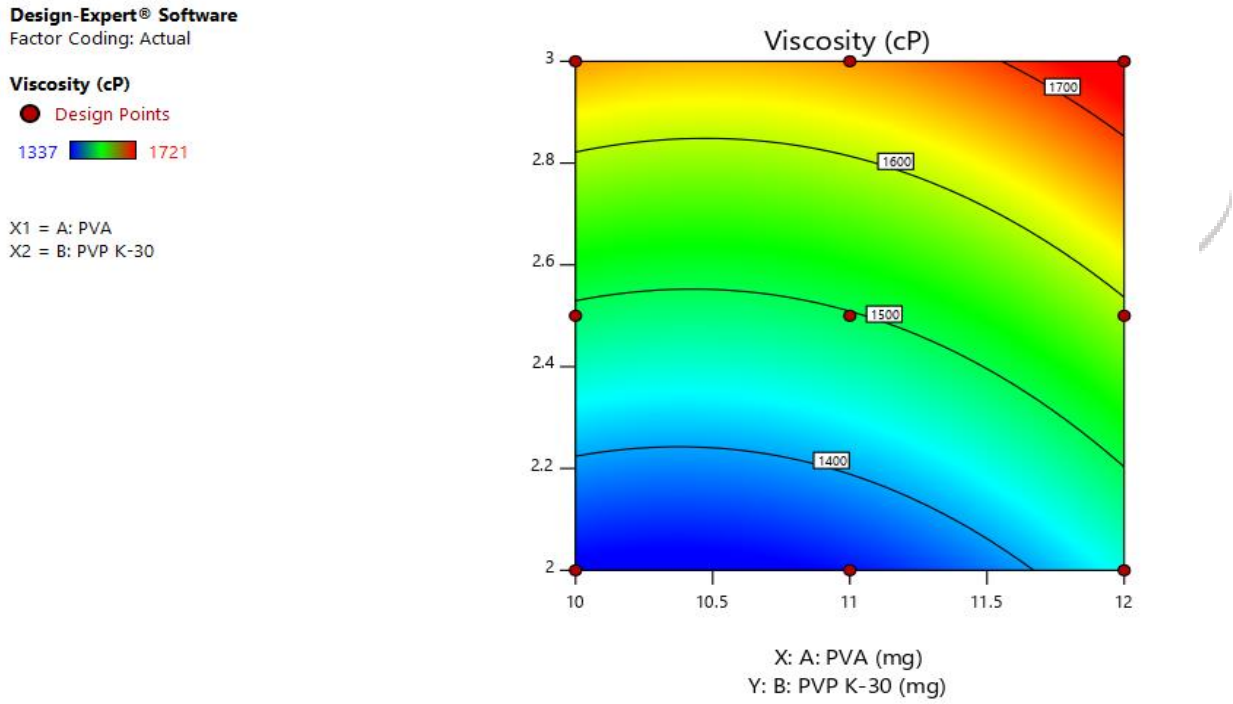
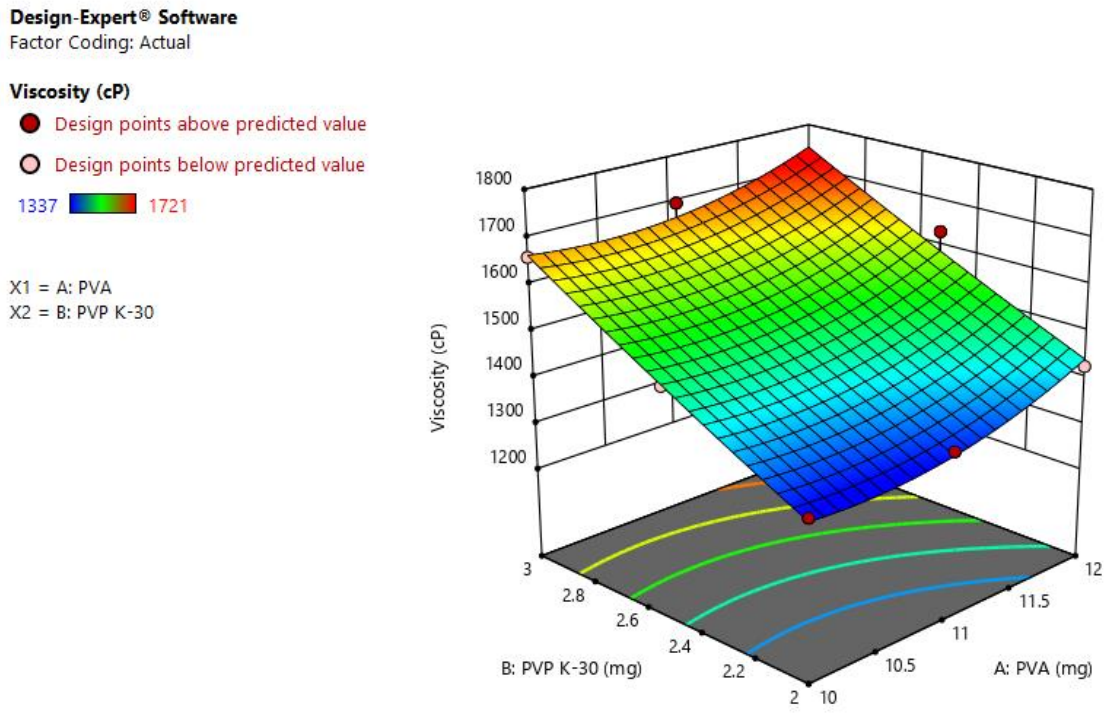


Figure 7 Response Surface Plot of Viscosity



ANOVA for Quadratic model for Drying time:

Response 2: Drying time

Source	Sum of Squares	df	Mean Square	F-value	p-value	
Model	1.93	5	0.3854	10.02	0.0433	significant
A-PVA	0.2321	1	0.2321	6.03	0.0911	
B-PVP K-30	1.17	1	1.17	30.44	0.0117	
AB	0.1521	1	0.1521	3.96	0.1409	
A^2	0.1058	1	0.1058	2.75	0.1958	
B^2	0.2665	1	0.2665	6.93	0.0782	
Residual	0.1154	3	0.0385			
Cor Total	2.04	8				

Fit Statistics

Std. Dev.	**0.1961**	**R^2**	**0.9435**
Mean	5.70	**Adjusted R^2**	0.8494
C.V. %	3.44	**Predicted R^2**	0.3301
		Adeq Precision	7.9734

Coefficients in Terms of Coded Factors

Factor	Coefficient Estimate	df	Standard Error	95% CI Low	95% CI High	VIF
Intercept	6.10	1	0.1462	5.63	6.57	
A-PVA	-0.1967	1	0.0801	-0.4514	0.0581	1.0000
B-PVP K-30	0.4417	1	0.0801	0.1869	0.6964	1.0000
AB	-0.1950	1	0.0981	-0.5070	0.1170	1.0000
A^2	-0.2300	1	0.1387	-0.6713	0.2113	1.0000
B^2	-0.3650	1	0.1387	-0.8063	0.0763	1.0000

- **Polynomial equation of dependent variable of Drying time**

Drying time (Y2): $6.10 - 0.1967X_1 + 0.4417X_2 - 0.1950X_{12} - 0.2300X_{11} - 0.3650X_{22}$

Figure 8 Contour Plot of Drying time

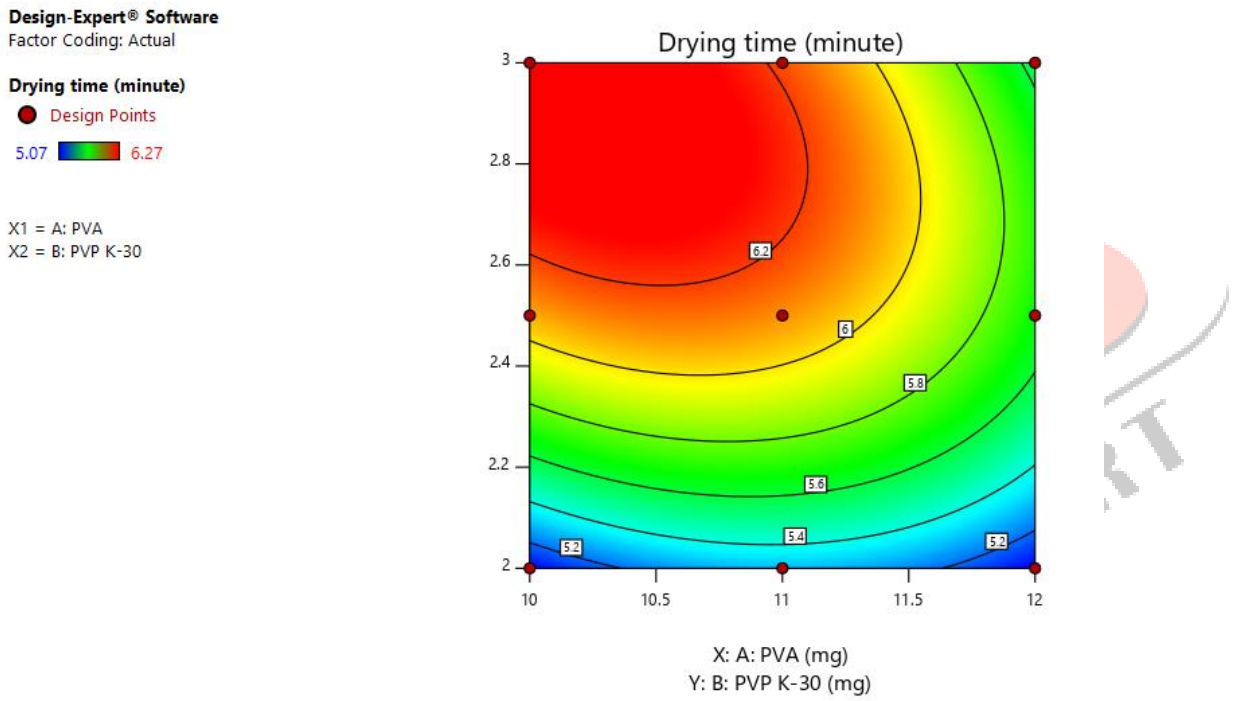
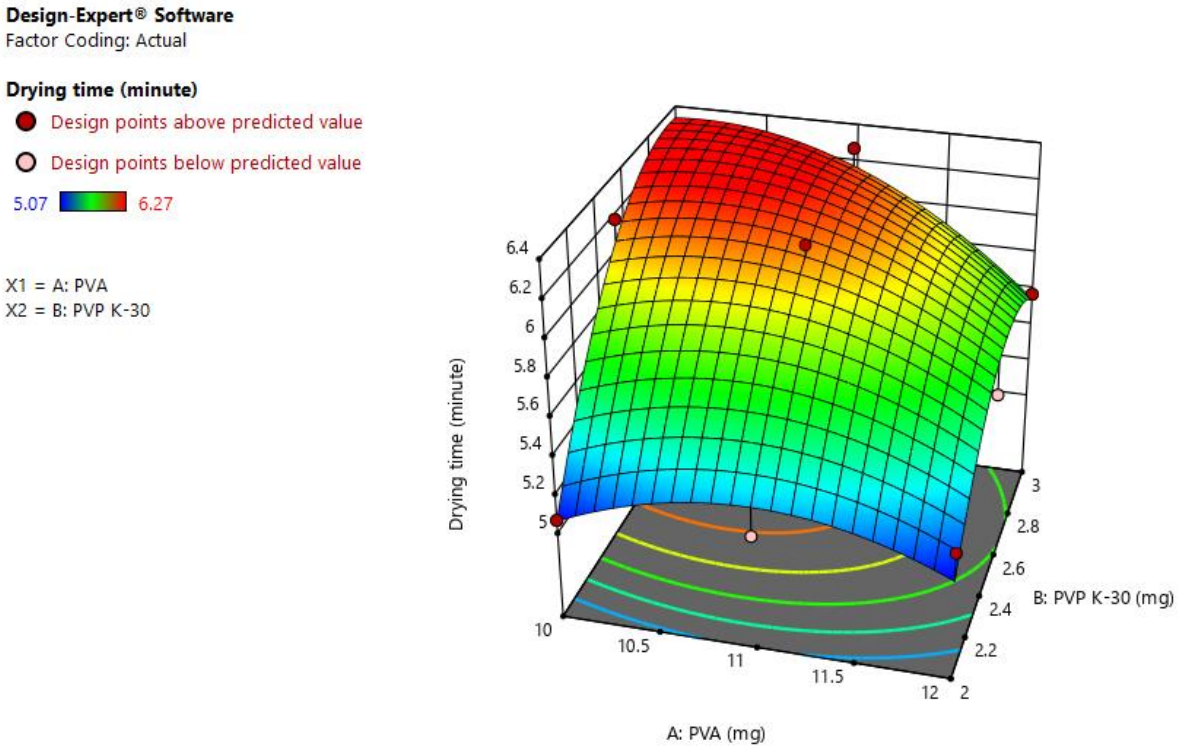


Figure 9 Response Surface Plot of Drying time



ANOVA for Quadratic model of Permeation study of % drug release:

Response 3: drug release

Source	Sum of Squares	df	Mean Square	F-value	p-value	
Model	33.81	5	6.76	15.30	0.0241	significant
A-PVA	4.90	1	4.90	11.08	0.0448	
B-PVP K-30	0.7776	1	0.7776	1.76	0.2767	
AB	12.74	1	12.74	28.83	0.0126	
A^2	0.0854	1	0.0854	0.1932	0.6900	
B^2	15.31	1	15.31	34.63	0.0098	
Residual	1.33	3	0.4420			
Cor Total	35.14	8				

Coefficients in Terms of Coded Factors

Factor	Coefficient Estimate	df	Standard Error	95% CI Low	95% CI High	VIF
Intercept	92.95	1	0.4956	91.37	94.52	
A-PVA	0.9033	1	0.2714	0.0395	1.77	1.0000
B-PVP K-30	0.3600	1	0.2714	-0.5038	1.22	1.0000
AB	-1.78	1	0.3324	-2.84	-0.7270	1.0000
A^2	-0.2067	1	0.4701	-1.70	1.29	1.0000
B^2	-2.77	1	0.4701	-4.26	-1.27	1.0000

- **Polynomial equation of dependent variable of film forming spray**

% Drug release (Y3): $92.95+ 0.9033X_1 + 0.3600X_2 -1.78 X_{12} - 0.2067X_{11} - 2.77X_{22}$

Figure 10 Contour Plot of % Drug release

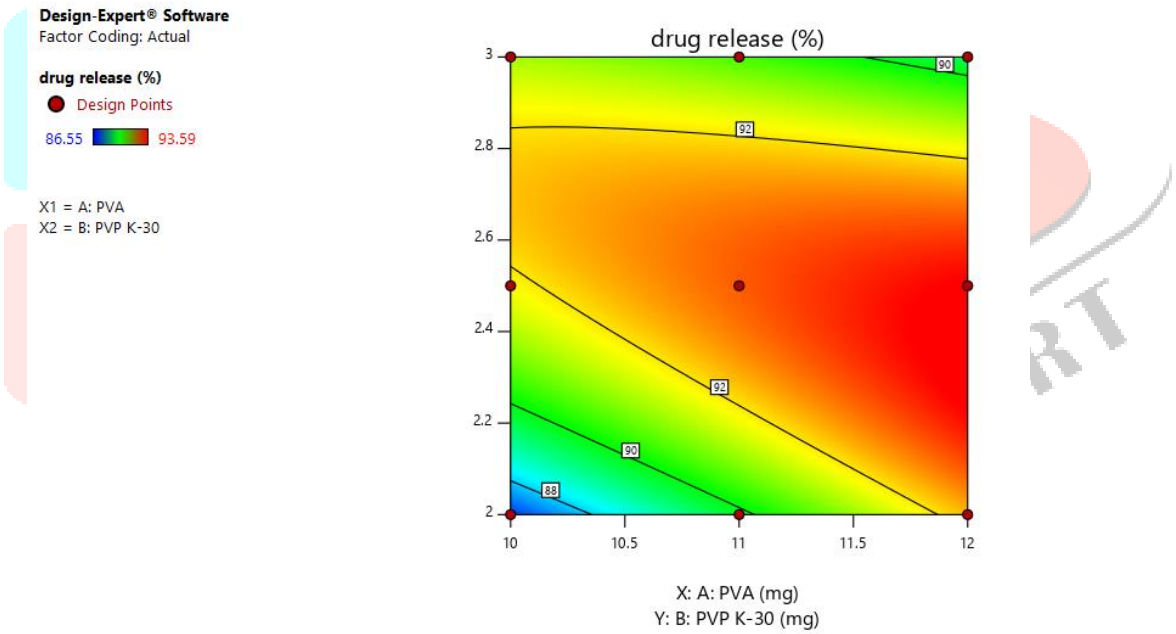
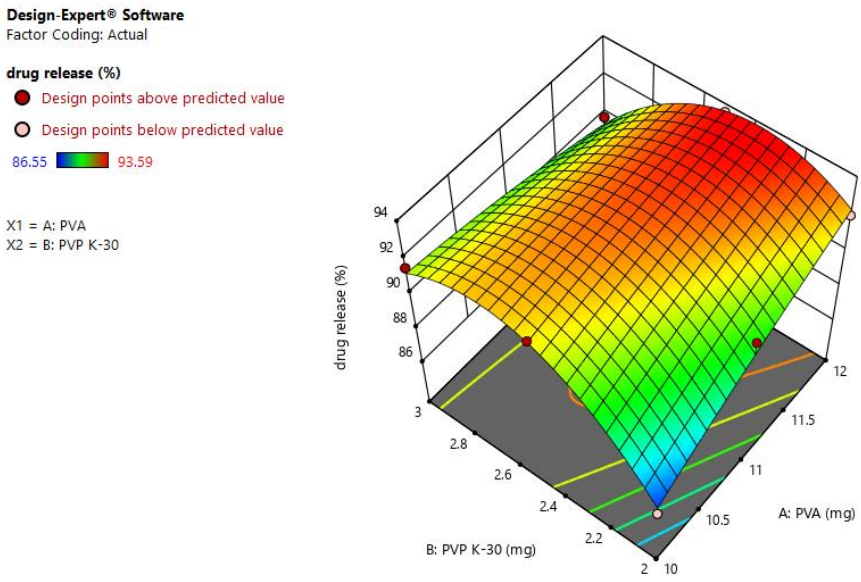


Figure 11 Response Surface Plot of Drying time



Discussion of factorial study

Optimization:

Based on preliminary trials, a factorial design of 3^2 factors was employed to develop Povidone iodine film forming gel. The design was used to study the effect of independent variables, i.e. PVA (X1) concentration and PVP K-30 (X2) concentration on the dependent variables viscosity (Y1), Drying time (Y2) and % drug release (Y3).

All factors were studied at all possible combinations in a 3^2 factorial design, as it is considered to be most efficient in estimating the influence of individual variables using minimal experimentation. In this analysis, the influence on dependent variables of independent variables such as concentration of PVA (X1) and concentration of PVP K-30 (X2) viz. Viscosity (Y1), Drying time (Y2) and % drug release (Y3) have been studied and are shown. The influence of independent variables on response variables is shown in three-dimensional surface plots, as shown in above all figures.

Polynomial equation

Viscosity (Y1): $1490.44+ 59.33X_1 + 150.00X_2 -21.75X_{12} + 52.33X_{11} +16.33X_{22}$

Drying time (Y2): $6.10 -0.1967X_1 + 0.4417X_2 -0.1950X_{12} -0.2300X_{11} -0.3650X_{22}$

% Drug release (Y3): $92.95+ 0.9033X_1 + 0.3600X_2 -1.78 X_{12} - 0.2067X_{11} - 2.77X_{22}$

Effect of formulation variables on viscosity,drying time and %Permeation study of drug released.

The R^2value for viscosity was found 0.9737 which is indicating the adequate fitting of quadratic model. From the polynomial equation, coefficients with either positive or negative signs are obtained which indicate the effect on variables. The P-value of the X1 (0.0033) < 0.05 and X2 (0.0024) < 0.05. Thus it indicates that X1 and X2 variables have significant effect on viscosity.

The R^2 value for drying time was found 0.9435 which is indicating the adequate fitting of quadratic model. From the polynomial equation for drug content it was found that as P- value for X1 is (0.0119) < 0.05 indicates that it has nosignificant effect on drying time and p value for X2 is (0.0117) < 0.05 it has significant effect on drying time.

The R^2 value for drug release was found 0.9623 which is indicating the adequate fitting of quadratic model. From the polynomial equation it was found that as P- value of X1 is 0.0448 < 0.05 and the p value for X2 is 0.2767 < 0.05. Thus it indicates that X1 and X2 has significant effect on drug release.

Kinetic Study:

Plots Showing Rate Kinetics Study of Factorial Batch F6:

In order to investigate the mode of release from the film formed by formulations F1-F9, the release data were analyzed as shown.

Formulations	Higuchi	Zero-order	Kros-peppas	First-order
F1	0.9878	0.9947	0.9973	0.9600
F2	0.9916	0.9913	0.9923	0.9794
F3	0.9959	0.9921	0.9952	0.9759
F4	0.9977	0.9955	0.9980	0.9764
F5	0.9984	0.9942	0.9977	0.9779
F6	0.9978	0.9917	0.9963	0.9782
F7	0.9970	0.9945	0.9972	0.9762
F8	0.9962	0.9924	0.9948	0.9769
F9	0.9965	0.9921	0.9957	0.9773

Figure 12 Formulation F6 - Zero order rate kinetics study (%Cumulative Drug Release vs Time)

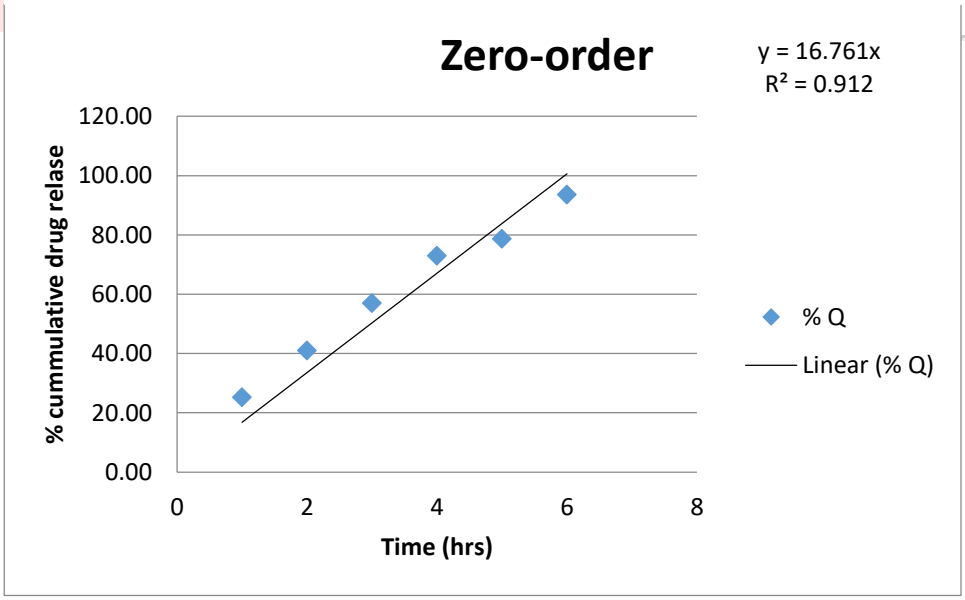


Figure 13 Formulation F6 - First order rate kinetics study (Log %Cumulative Drug Retained vs Time)

Figure 14 Formulation F6 - Higuchi model (%Cumulative Drug Release plotted against square root of time)

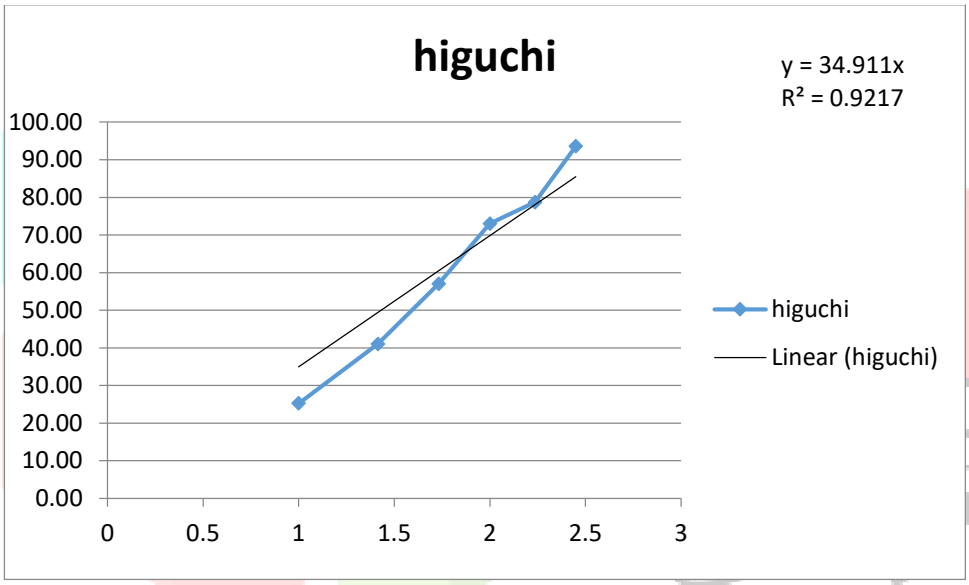
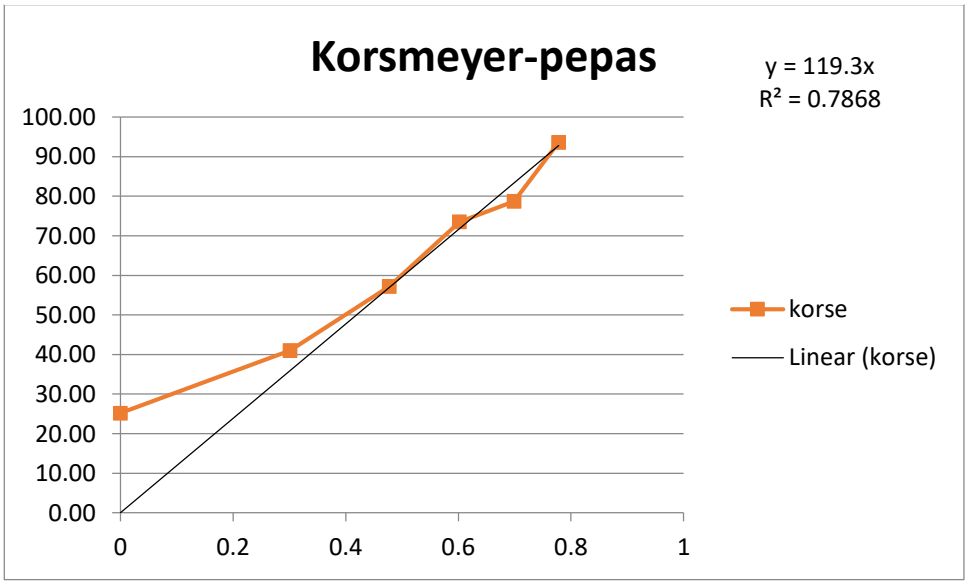


Figure 15 Formulation F6 - Korsmeyer-Peppas exponential equation model (Log %Cumulative Drug Release plotted vs Log Time)



The result of Permeation study of drug released by all the batches (F1 to F9) were best fitted by **Higuchi model kinetics**, as the **highest linearity (R^2)** of plot observed in Higuchi order kinetic plot. As our formulation drug release was **best fitted in Higuchi** we can say that the drug is released from the matrix of the film at a period of time.

Validation of factorial batch:

Factorial design gives the information about expected result of responses. Before taking it into consideration, need to validate the design. Hence, checkpoint batch was designed, as shown in below figure. To assess the validity of prediction, a checkpoint batch was prepared and evaluated under the same conditions as outlined for the other batches. The observed response data was compared with that of predicted data.

Interpretation of Check Point Batch:

From the Design-ExpertR 11 (Software developed by Stat- Ease R)

Figure 16 Overlay plot of check point batch

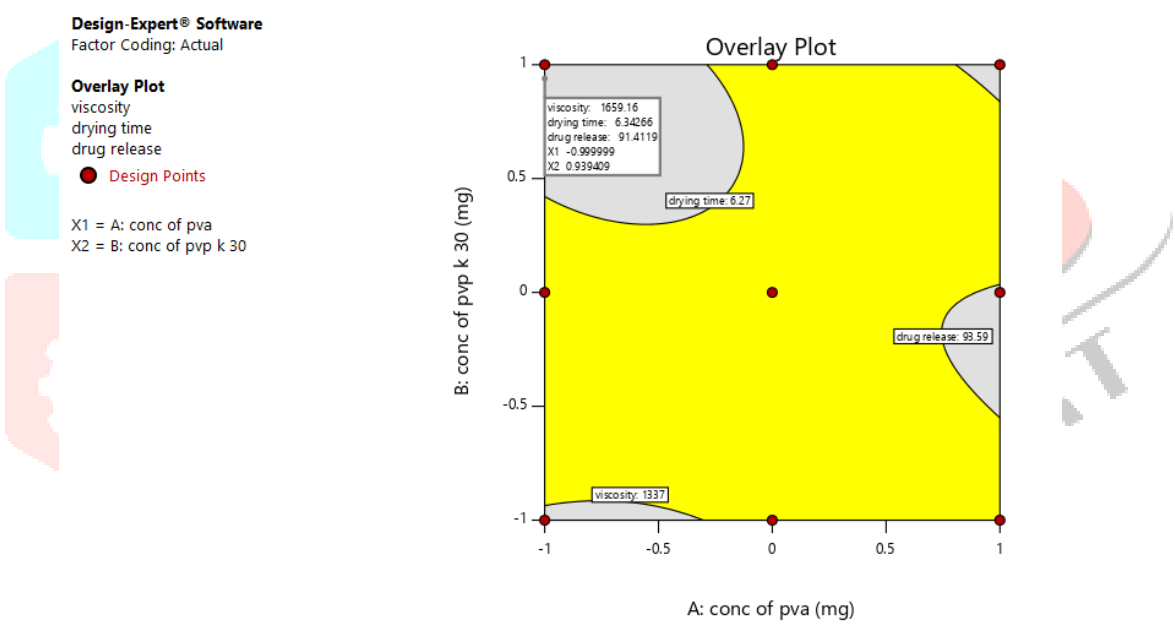


Table 10 Results of Dependent Variables of Checkpoint Batch

Test Parameters	**Results**
Viscosity(cps)	1659.16
Drying time (min)	6.3
% drug release	91.41

Comparison between observed and predicted results of checkpoint batch

In order to assess the Reliability of the equation that describes he influence of factors on the Viscosity, Drying time and Permeation study of % Drug Release of povidone iodine Film forming gel. Predicted results of Optimized batch are shown in table. The Experimental values and Predicted values of each

response are shown in table. The %Relative error petween Predicted values and Experimental Values of each response was calculated using the following equation,

% Relative error = |(Predicted values –Experimental values)/Predicted values X 100

Response Parameter	Predicted Value	Observed Value	% Relative error
Viscosity(cps)	1659	1621	2.29
Drying time (min)	6.3	6.22	1.26
% drug release	91.41	90.81	0.66

The results in the table illustrate a good relationship between the experimental values and predicted values, which confirms the practicability and validity of model.

Selection of optimized batch:

The optimized batch was selected on the basis of deisgn expert software. From which the formulation contains HPMC E5: HPMC K4M as 50:106 mg and concentration of PEG 400 as 143 mg was considered as optimized batch among all the formulation of transdermal patch of vildaglitpin among all batches from F1 to F9.Considering all these parameter F10 was selected as optimized formulation and renamed as OP1 and is selected for further stability study.

Table 11 Formulation of OP1

Ingredients	Quantity
Povidone Iodine	2.5 g
PVA	6 g
PVP K-30	1.25 g
PEG 400	1.5 ml
Ethanol	10 ml
Distilled water	Upto 50 ml

Table 12 Optimized batch result

Evaluation parameters	Results
Folding endurance	56±1.84
Viscosity	1621±4.3
Drying time	6 min 22sec ± 4 sec
pH	5.63±0.026
Drug content (%)	98.07±0.48
Spredability	16.43±0.13
Tensile strength	0.095±0.0006
% drug release	**Time (mins.)** / **Drug release (%)**: 1 / 22.14±0.20; 2 / 34.12± 0.19; 3 / 50.81±0.34; 4 / 68.93±0.61; 5 / 80.89±0.02; 6 / 90.01±0.38

Stability Study:

Table 13 Result of stability study

Parameter	Initial	After 30 days
Viscosity(cP)	1621±4.3	1615±1.5
Drying time (minutes)	6 min 22sec ± 6 sec	6 min 43sec ± 2 sec
Drug content (%)	99.07±0.48	97.95±0.37
Folding endurance	56±1.84	52±1.38
Spredability	16.43±0.13	15.78±0.41
Tensile strength	0. 35±0. 6	0.32±0. 6
pH	5.63±0.026	5.61±0.082
% Drug release	90.81±0.38	89.63 ± 0.67

Storage at 40°C and 75% RH for 1 month

For, n =3(average of three determinations)

The sample subjected to stability studies was then analyzed. The results of the stability studies indicated that the formulation OP1 was able to retain its stability for a period of 1 month at 40°C/75% RH. Stability

study revealed that no any major changes taken place throughout the stability study period of 1 month so we could say that formulation OP1 had good stability.

The factor F2, known as the similarity factor, measures the closeness between the two profiles.To check the similarity between drug release profiles for optimized batch at different time interval that is 0 month and 1 month. Similarity factor for this drug release was calculated using equation:

F2 =50×log {[1+ (1/n) ∑ (*R*i-*T*i) 2]-0.5 × 100}

$$F2=50 \times \log\{1 + \left(\frac{1}{n}\right) \sum_{T=t}^{n=1} (Ri - Ti) - 0.5 \times 100\}$$

Where, n is the number of dissolution time and Ri and Ti are the reference and test dissolution values at time t. Two dissolution profiles are considered similar when the F2 value is 50 to 100.

F2 = 71.25

Similarity factor of the patch was 71.25 which indicate the patch is stable.

CONCLUSION

The study aimed to develop Povidone iodine containing film forming gel, focusing on antiseptic properties. Polymers, including PVA and PVP K-30 were employed via dispersion method. Infrared spectrum analysis confirmed no drug-polymer interactions. Factorial batches were made using 3^2 full factorial designs. Formulation F6 was found to be best fitted formulation, considering evaluation parameter such Film forming gel met all the parameters like drying time, viscosity, spreadability and tensile strength. Their pH indicated safe skin use, In-vitro release extended to 6 hours, with formulation F6 exhibiting 93.59% drug release, optimization using factorial design. The drug content of the prepared formulation was within the acceptable range and ensures dose uniformity. Higuchi order model fit best (R^2 = 0.9984). Stability assessment over a month confirmed formulation stability. The desired system will improve compliance of patients and reduce the limitation of current therapy. So, Film forming gel can become an alternative to the current conventional dosage form. Model also found significant and validation of design was done which was well within acceptable limits.

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