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Design, Development and Evaluation of Topical Dosage Form of Naproxen for Pain Management

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ABSTRACT

The aim of our research work is to promote mixed solvency concept by formulating the topical solution (lotion) and topical gel of poorly water soluble drug naproxen by decreasing the individual solubilizer concentration in small proportion for expected enhancement of drug solubility in water. For poorly water soluble drug naproxen, solubilizers such as sodium benzoate, sodium citrate, sodium caprylate, arginine, valine, benzoic acid, poloxamer 407 and niacinamide has been used in combinations as mixed solvent systems. The enhancement of solubility in selected mixed solvent blend was more than 60 folds. The procured sample of naproxen was characterized by melting point, UV spectroscopy, IR and DSC studies. The formulation was designed, formulated and evaluated for various properties of solution and gels such as pH, freeze thaw study and thin layer chromatography, physical appearance and Invitro drug relaease studies were performed using franz diffusion cell. Mixed solvency concept was successfully utilized for formulation development of marketable product of Naproxen.

Keywords: NSAIDS, Naproxen, Pain, Solubilization, Solution, Gel.

INTRODUCTION

Solubilizing practically water insoluble drugs is a challenging factor and really vital issue in screening studies of new drug

moieties as well as formulation development research [1]. It leads to difficulties in several developmental, manufacturing and administrative processes. Furthermore, due to their poor pharmacokinetics, the clinical trials of these drugs have witnessed a great failure. Topical delivery of these drugs also offers challenges while formulating dosage forms. Pharmaceutical lotions and gels are the topical products meant to be applied on skin without friction. Drug penetration through topical route of administration is a most convenient and easy approach for local effect of drugs [2,3]. A topical solution is a monophasic system of two or more substances. Absorption of drugs from solution dosage is rapid and very high. The solution which is applied directly to skin is called topical solution. Major key pre formulation parameters that need to be taken under the consideration while formulating the solutions are solubility and stability. Topical solution acts locally and targets at the site of allergy and inflammation resulting in reduced side effects and toxicity to other organs. Low solubility in aqueous medium is the main problem for the formulation development of the various drugs which are used locally. Water is the major solvent used for liquid pharmaceutical formulations. Various solubility improvement techniques are used for solubility enhancement of poorly water soluble drugs. Mixed solvency concept is novel technique which used for the purpose of solubility enhancement. As per the mixed solvency concept proposed by Maheshwari each and every substance present on the earth has got solubilizing property *i.e.* all the liquids, gases and solids possess solubilizing power. As per his statement each substance is a solubilizer. Any substance is just solvent for some and non-solvent for another. The aqueous solution containing various water soluble substances may act as good solvent for poorly water soluble drugs. Such concentrated solutions may show synergistic or additive solubilizing actions on solubility of practically insoluble drugs. Each and every weaker solvent using various solid solubilizers [4-7].

MATERIALS AND METHODS

Chemicals

Naproxen drug sample was procured as gift sample form M/s Alkem Laboratories Ltd, Mumbai. All other chemicals and reagent was procured from Industrial Pharmacy research lab, Shri G.S institute of technology and sciences, Indore, M.P (Figure 1) [8].

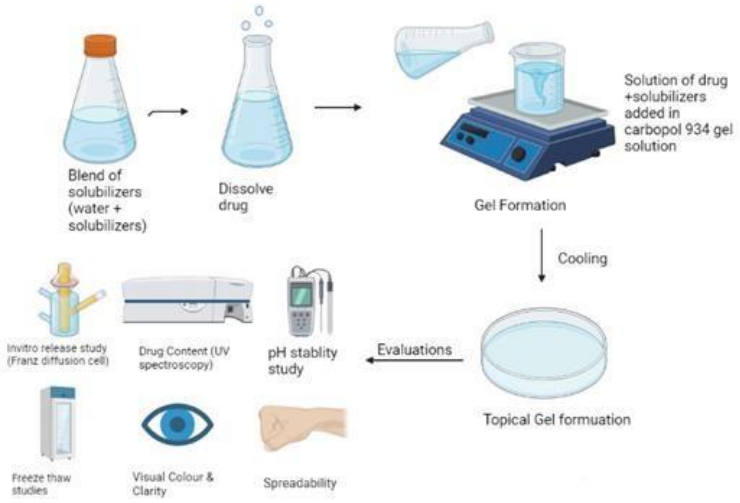

Figure 1: Graphical abstract.

Drug characterization

UV spectrophotometric analysis of naproxen in DM water: Fifty mg of naproxen drug powder was accurately weighed and transferred in a 50 ml volumetric flask. Twenty five ml of aqueous solution of 2 M sodium benzoate was added to dissolve the drug and the volume was made upto 50 ml with demineralised water, to obtain a stock solution of 1000 µg/ml. A dilution from the stock solution was made with demineralised water to obtain the drug solution of the concentration of 40 µg/ml. The UV spectrum of the resulting drug solution was scanned against reagent blank on a double beam UV/Visible spectrophotometer (Shimadzu 1700). The spectrum obtained is shown in Figure 2 (Table 1) [9].

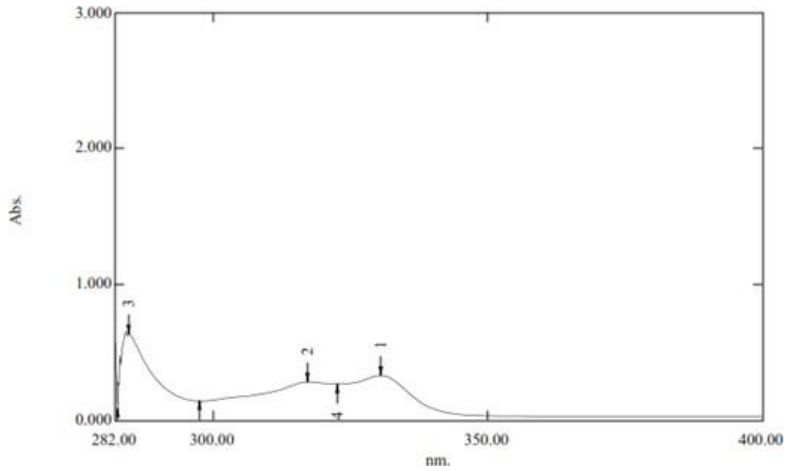

Figure 2: UV spectrum of naproxen in demineralised water at 330 nm.

S. no.	Wave no. (cm^{-1})	Interpretation
1	3001.24	Aromatic C-H stretching
2	1502.55	Aromatic C=C stretching
3	1724.3	Carboxylic stretching
4	1392.61	Methyl group bending
5	2904	Methyl C-H stretching
6	2839.22	Aliphatic C-H stretching
7	1267.23	Methoxy stretching

Table 1: Interpretation of the FTIR spectrum of naproxen drug sample.

DSC study of naproxen drug sample

A Pyris 6 DSC (Jade DSC) differential scanning calorimeter with thermal analyzer was used for the DSC investigation. Samples were accurately weighed (about 3 mg) and kept in a sealed aluminium pan before being heated at a scanning rate of 10°C per minute from 25 to 350°C under nitrogen flow (20 ml/min). As a reference, an empty aluminium pan was used. The data was analysed and compared to the literature. DSC spectrum of naproxen drug sample is shown in Figure 3 [10].

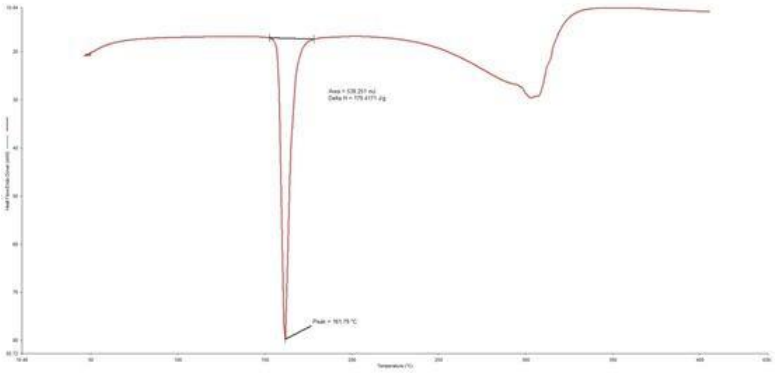

Figure 3: DSC analysis of drug naproxen.

Infrared spectroscopy of naproxen

The infrared spectroscopic analysis of naproxen drug sample was performed and the spectrum was recorded in the wave number region of 400-4000 cm^{-1} on FTIR spectrophotometer (Shimadzu affinity^{-1}) and shown in Figure 4.

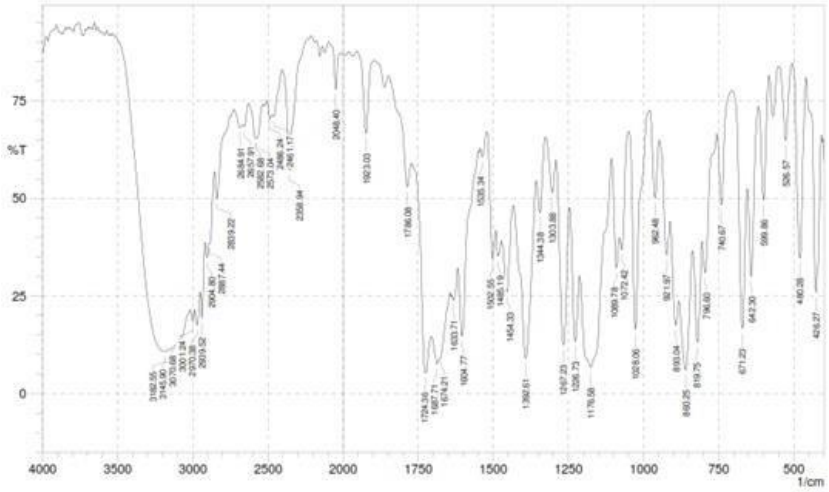

Figure 4: FTIR spectrum of naproxen.

Melting point determination of naproxen drug sample

The melting point of naproxen was determined using open capillary method. The powered drug sample was packed in capillary and the melting point was measured by Analog melting point testing apparatus. Results were shown in Table 2.

S. no.	Melting point (°C)	Average
1	152°C	
2	152°C	
3	153°C	152.33°C

Table 2: Melting point determination.

Preformulation studies

Preparation of calibration curve of naproxen using DM water

Accurately weighed quantity of Naproxen (50 mg) was dissolved in 25 ml aqueous solution of 2 M sodium benzoate in 50 ml volumetric flask and volume was made upto 50 ml by demineralised water. The concentration of this resulting solution (stock solution) was 1000 µg/ml. Aliquots of the above solution were taken and diluted with demineralised water to get naproxen concentration in the range of 40-200 µg/ml. The resulting dilutions were analysed at 330 nm on Shimadzu-1700 UV spectrophotometer against respective blanks. The absorbance data are shown in the Table 3 and graphically represented in Figure 5.

S. no.	Concentration (µg/ml)	Absorbance (mean ± S.D.) (N=3)
1	0	0 ± 0
2	40	0.346 ± 0.006
3	80	0.694 ± 0.006
4	120	1.024 ± 0.010
5	160	1.348 ± 0.007
6	200	1.642 ± 0.015

Table 3: Calibration curve data of naproxen in demineralised water at 330 nm.

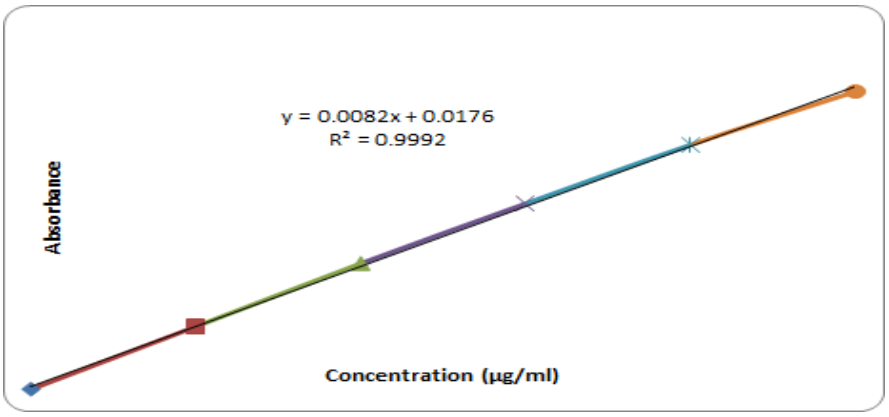

Figure 5: Calibration curve of naproxen in demineralised water at 330 nm.

Equillibirium solubility studies in different solvent systems

Equillibirium solubility studies in different solvent systems were achieved by adding excess amount of drug in 10 ml of respective mediums, it was then screw capped and kept on mechanical shaker for 24 hrs. It was centrifuged in centrifuge tubes at 2000 rpm for about 5 min and filtered using Whatman grade 41 filter then diluted with suitable respective medium. The absorbance was measured at 330 nm on a double beam UV/Visible spectrophotometer (Shimadzu-1700) against reagent blank and noted in Table 4 [11].

S. no.	Solvent system	Equilibrium solubility (mg/ml)	Description
1	DM water	0.0855	Practically insoluble
2	Hydrochloric acid buffer pH 1.2	0.01	Practically insoluble
3	Hydrochloric acid buffer pH 2.0	0.015	Practically insoluble
4	Acid phthalate buffer pH 3.0	0.019	Practically insoluble
5	Acid phthalate buffer pH 4.0	0.081	Practically insoluble
6	Neutralized phthalate buffer pH 5.0 0.340 Practically insoluble	0.111	Practically insoluble
7	Phosphate buffer pH 6.0	0.553	Practically insoluble
8	Phosphate buffer pH 7.0	0.583	Very slightly Soluble
9	Phosphate buffer pH 8.0	1.844	Very slightly Soluble
10	Alkaline borate buffer pH 9.0 1.632 slightly soluble	2.824	Slightly soluble
11	Alkaline borate buffer pH 10.0	3.366	Slightly soluble

Table 4: Equillibrium solubility of Naproxen in different solvent systems.

Approximate solubility of naproxen in different blends

Different concentrations of solubilizers in small quantity were used to prepare 10 ml blend of various composition and concentration and labelled as blend 1 to blend 20.

One ml of blend-A solution was taken in volumetric flask. Five mg of drug naproxen was added and shaken vigorously for about 15-20 minutes on vortex. When clear solution was formed then again the process was continued until turbidity appears. The approximate solubilities were noted in Table 5 [12].

S. no.	Blend code	Composition of blends	Approximate solubility
1	Blend 1	PVP K-30 (5%)	15 mg/ml
		Lignocaine HCl (5%)	
		Niacinamide (5%)	
		Sodium benzoate (5%)	
2	Blend 2	PVP K-30 (5%)	10 mg/ml
		Niacinamide (5%)	
		Sodium benzoate (5%)	
3	Blend 3	PVP K-30 (5%)	10 mg/ml
		Sodium citrate (5%)	
		Niacinamide (5%)	
		Sodium benzoate (5%)	
4	Blend 4	PVP K-30 (5%)	5 mg/ml
		Niacinamide (5%)	
		Sodium benzoate (10%)	
5	Blend 5	PVP K-30 (5%)	Less than 5

		Sodium citate (5%)	mg/ml
		Sodium acetate (5%)	
6	Blend 6	PVP K-30 (5%)	5 mg/ml
		Caffeine (5%)	
		Niacinamide (5%)	
		Sodium benzoate (5%)	
7	Blend 7	Caffeine (5%)	5 mg/ml
		Niacinamide (5%)	
8	Blend 8	Sodium citrate (2.5%)	55 mg/ml
		Sodium benzoate (5%)	
		L-Arginine (10%)	
		Benzoic acid (5%)	
		Niacinamide (2.5%)	
		HP-β cyclodextrin (5%)	
9	Blend 9	Sodium citrate (5%)	55 mg/ml
		Sodium benzoate (5%)	
		L-Arginine (10%)	
		Benzoic acid (5%)	
		Niacinamide (2.5%)	
10	Blend 10	Sodium citrate (2.5%)	55 mg/ml
		Sodium benzoate (5%)	
		L-Arginine (10%)	
		DL-Valine (5%)	
		Sodium caprylate (5%)	
		Benzoic acid (5%)	
		Niacinamide (2.5%)	
11	Blend 11	Sodium citrate (5%)	55 mg/ml
		Sodium caprylate (5%)	
		HP-β cyclodextrin (5%)	
		L-Arginine (10%)	
		Benzoic acid (5%)	
12	Blend 12	L-Arginine (10%)	30 mg/ml
		Poloxamer 407 (5%)	
		Sodium caprylate (5%)	
		Sodium benzoate (5%)	
		Sodium citrate (5%)	
		Benzoic acid (5%)	
13	Blend 13	Sodium caprylate (5%)	40 mg/ml
		L-Arginine (10%)	
		DL-Valine (5%)	
		Poloxmer 407 (5%)	

		Benzoic acid (5%)	
14	Blend 14	Sodium caprylate (5%) Sodium benzoate (5%) Sodium citrate (5%) L-Arginine (10%) Poloxamer 407 (5%) Lycine Hcl (10%)	30 mg/ml
15	Blend 15	Glycine (10%) Poloxamer 407 (5%) Sodium caprylate (5%) Sodium benzoate (5%) Sodium citrate (5%)	35 mg/ml
16	Blend 16	L-Arginine (10%) Glycine (10%)	10 mg/ml
17	Blend 17	Sodium caprylate (5%) Sodium benzoate (5%) Sodium citrate (5%) Niacinamide (2.5%)	15 mg/ml
18	Blend 18	Sodium acetate (5%) Sodium benzoate (5%) Sodium citrate (5%) Niacinamide (2.5%)	10 mg/m
19	Blend 19	Sodium acetate (5%) Sodium citrate (5%)	Less than 5 mg/ml
20	Blend 20	Sodium acetate (5%) Sodium benzoate (5%) Sodium citrate (5%) Niacinamide (5%)	5 mg/ml

Table 5: Approximate solubility of naproxen in different blends.

Selection of blends for formulation of topical solutions and gel

Two blends were considered as they provide great solubility to naproxen for formulation of topical solution. As a result, these mixtures were chosen for further research. These studies were conducted based on visual appearance, which included precipitation, crystal development, and clarity. Prepared blends with acceptable medication concentrations were visually observed in these experiments. For clarity and precipitation, these solutions were observed. Blend-9 and blend-11 were used for preparation of aqueous topical solution of drug as they showed maximum solubility. To prepare aqueous topical gels, same blends were chosen. Caropol 934 has been found as suitable gelling agent for formulations. The visual appearance of the samples was considered in the selection experiments, which included clarity, spreadability, and grittiness. Two blends, blend-9 and blend-11, with requied quantities of solubilizers were chosen for the production of aqueous topical gel formulations, and they were used in the preparation of aqueous topical gel formulations containing 5% naproxen [13].

Preperation of topical solutions using selected blends

About 1% Topical solution of naproxen using mixed solvency concept was prepared, for this initially all the solubilizers, were taken and weighed accurately according to quantities decided in a 100 ml clean and calibrated volumetric flask and sufficient amount of water was added to dissolve them. When drug dissolves totally, volume was made up with remaining water. This gave 100 ml of blend having 25%/30% concentrations of solubilizes. Now, 5 gm of naproxen drug was weighed and transferred to a 100 ml volumetric flask. After this about 60 ml of blend was added to dissolve the drug, when a clear solution was obtained, volume was made up using remaining blend solution. Hence, the topical solution using blend 9 and blend 11 was prepared and stored in an air tight container. The quantities required for formulation composition are shown in Tables 6 and 7 [14].

S. no.	Ingredients	Quantity for 100 ml	Uses
1	Naproxen	5 gm	Active ingredient
2	L-Arginine	10 gm	Solubilizer
3	Sodium citrate	2.5 gm	Solubilizer
4	Sodium benzoate	5 gm	Solubilizer
5	Benzoic acid	5 gm	Solubilizer
6	Niacinamide	2.5 gm	Stabilizer
7	Propylene glycol	10 ml	Humeactant
8	Water (milli-Q water)	q.s. 100 ml	Vehicle

Table 6: Formulation composition of topical solution F1.

S. no.	Ingredients	Quantity for 100 ml	Uses
1.	Naproxen	5 gm	Active ingredient
2.	L-Arginine	10 gm	Solubilizer
3.	Sodium caprylate	5 gm	Solubilizer
4.	Sodium citrate	5 gm	Solubilizer
5.	Cyclodextrin	5 gm	Solubilizer
6.	Benzoic acid	5 gm	Solubilizer
7.	Propylene glycol	10 ml	Humeactant
8.	Water (milli-Q water)	q.s. 100 ml	Vehicle

Table 7: Formulation composition of topical solution F2.

Preparation of topical gel

For preparation of gel using mixed solvency concept, firstly blend solution was prepared using decided quantity of solubilizers. All the solubilizes were taken in a 100 ml volumetric flask and 60 ml of milli-Q water was added to dissolve through shaking for about 10-15 minutes the solubilizers, now 5 g of naproxen was added to it with continues shaking until drug gets dissolve. Twenty ml of water was added and about 3.5 g of carbopol 934 was added gradually with a continuous stirring in a water bath at 40-50°C with avoidation of bubble formation. When transparent gel was formed, the blend solution was added gradually with continuous stirring. The gel was cooled completely using ice bath and the consistency was checked. Now the gel was stored in an air tight container [15].

The quantities required for formulation composition are shown in Tables 8 and 9.

S. no.	Ingredients	Quantity for 100 ml	Uses
1	Naproxen	5 gm	Active ingredient
2	L-Arginine	10 gm	Solubilizer
3	Sodium citrate	2.5 gm	Solubilizer
4	Sodium benzoate	5 gm	Solubilizer
5	Benzoic acid	5 gm	Solubilizer
6	Niacinamide	2.5 gm	Stabilizer
7	Propylene glycol	10 ml	Humeactant
8	Carbopol 934	3.5 gm	Gelling agent
9	Water (milli-Q water)	q.s. 100 ml	Vehicle

Table 8: Formulation composition of topical gel F3.

S. no.	Ingredients	Quantity for 100 ml	
1	Naproxen	5 gm	Active ingredient
2	L-Arginine	10 gm	Solubilizer
3	Sodium caprylate	5 gm	Solubilizer
4	Sodium citrate	5 gm	Solubilizer
5	Cyclodextrin	5 gm	Solubilizer
6	Benzoic acid	5 gm	Solubilizer
7	Propylene glycol	10 ml	Humeactant
8	Carbopol 934	3.5 gm	Gelling agent
9	Water (milli-Q water)	q.s. 100 ml	Vehicle

Table 9: Formulation composition of topical gel F4.

Evaluation of topical solutions and gels

pH determination of formulations

About 5 ml of topical solution was taken in a 25 ml dry and clean beaker and the pH determined using Cyberscan 510 pH meter fitted with electrode and data was recorded in Table 10.

S. no.	Selected topical solution	pH
1	F1	6.9
2	F2	6.82
3	F3	5.4
4	F4	5.23

Table 10: pH of selected topical solutions and gels.

About 5 g of topical gel was taken in 25 ml dry beaker and diluted up to 25 ml using milli-Q water, then was recorded using cyberscan 510 pH meter fitted with an electrode [16].

Drug content

About 1.0 ml of topical solution and 1.0 g for topical gel was placed in a 100 ml volumetric flask to determine the drug content. About 10 ml of 20% sodium caprylate solution was added, and the flask was sonicated for 15 minutes and the volume was make up to 100 ml with DM water. The resulting solution was filtered *via* Whatman filter paper no. 41. The filtrate was properly diluted and spectrophotometrically examined. The results are summarized in Table 11 [17].

S. no.	Topical solution formulation	Percent drug content (% w/v)
1	F1	0.0103
2	F2	0.0106
3	F3	0.0102
4	F4	0.0103

Table 11: Drug content of topical solutions and gels.

Freeeze thaw testing

Freeze thaw stress testing used to study the chances of precipitation in formulation. Both the selected topical solutions were filled in a vial and capped properly. The vials were stored at temperature of 2-8°C in a refrigerator for 24 hours and then in oven at temperature 40°C for another 24 hour. After oven, the vials were then placed in a room temperature. This is the first cycle of testing. Likewise 7-7 such cycles was performed alternately at 2-8°C then 40°C oven and then room temperature to observe the precipitation and turbidity [18].

TLC (thin layer chromatography) analysis of topical solutions

The analysis study was performed to find any possibility of interactions between the solubilizers and the drug. A plate of silica gel GF 254 was activated at the temperature 110°C for 1 hour. A spot of drug solution was made using 2% solution of drug in ethanol and on another side topical solution was spotted. Now, the plate was allowed to dry.

The aqueous solvent system was prepared using 20% solution (having 10% sodium benzoate, 10% sodium caprylate) in a beaker. After the drying of spot the plate was placed in a solvent medium and allowed to run for about 5 cm. The plate was dried and the spot was observed under UV light chamber. Rf values were recorded in Table 12 [19].

		R_f Value		R_f value	
Solvent system	**Absorbent**	**Pure drug**	**Drug in blend 9**	**Pure drug**	**Drug in blend 11**
20% blend solution (10% sodium benzoate, 10% sodium caprylate)	Silica gel GF 254	0.55	0.56	0.75	0.75

Table 12: TLC analysis of pure drug and selected topical solutions.

Physical evaluation of topical gels

By examining the gel against a white background, the clarity and color of the topical gels were determined visually. Small sized polythene bag were used to fill the prepared gels. The capability of the gel to extrude from the gel when pushing through the polythene bag determines the gel's extrudability. The prepared gels were applied to human skin, and the spreadability of the gels was investigated [20].

Physical evaluation studies were recorded in following Table 13.

Gel formulations	Color	Clarity	Spreadibility	Extrudibility
F3	White	Clear	Good	Good
F4	White	Clear	Good	Good

Table 13: Physical evaluation of topical gels.

***In-vitro* drug release study of topical solution of naproxen**

The *in-vitro* drug release studies were performed using dialysis membrane to measure amount of drug released in a respective medium. The dialysis membrane was firstly activated and humectant glycerol can be removed by washing the membrane with running water for 3-4 hours. The sulphate salts were removed by soaking the tubing in a 0.3 percent (w/v) sodium sulphide solution for 1 minute at 80°C. It was washed for 2 minutes with hot water (60°C), then acidified with a 0.2 percent (v/v) sulfuric acid solution, then rinsed with hot water to remove the acid. The experiment was performed under certain conditions like, the release medium having phosphate buffer pH 7.4 of volume 200 ml and rotated at 50 rpm at temperature 37°C [21].

Method used for *in-vitro* drug release study

The percent drug release of the developed topical solution was calculated by placing 1 ml of the developed topical solution in a dialysis membrane placed in a 250 ml beaker containing 200 ml of phosphate buffer of pH 7.4. Ten ml of sample was taken at regular intervals (1 hr, 2 hr, up to 7 hr) and replenished with an equal volume of phosphate buffer of 7.4 pH for maintaining sink condition. The samples were examined by a double beam UV-visible spectrophotometer (Shimadzu 1700) at 262 nm. The gel/solution's area of contact with the medium was 15 cm^2. Table 14 and 15 showing *in-vitro* release data of F1, F2 and graphically represented in Figures 6 and 7 [22].

S. n.o	Time (min)	% Cumulative drug release (%)
1	0	0
2	60	34.73
3	120	66.32
4	180	72.93
5	240	78.48
6	300	82.91
7	360	91.39
8	420	96.11

Table 14: *In vitro* drug release study data of topical solution (F1).

S. no.	Time (min)	% Cumulative drug release (%)
1	0	0
2	60	42.43
3	120	44.09
4	180	48.31
5	240	55.39
6	300	65.38
7	360	78.36
8	420	94.38

Table 15: *In vitro* drug release data study of topical solution (F2).

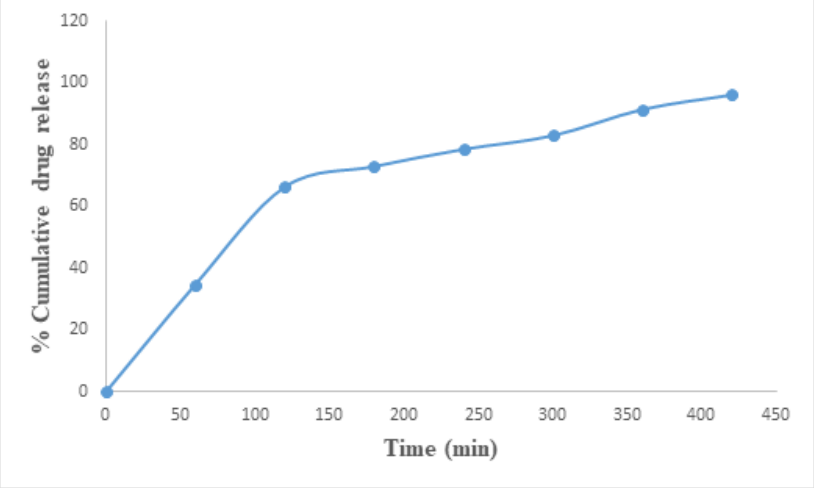

Figure 6: *In-vitro* release of topical solution F1.

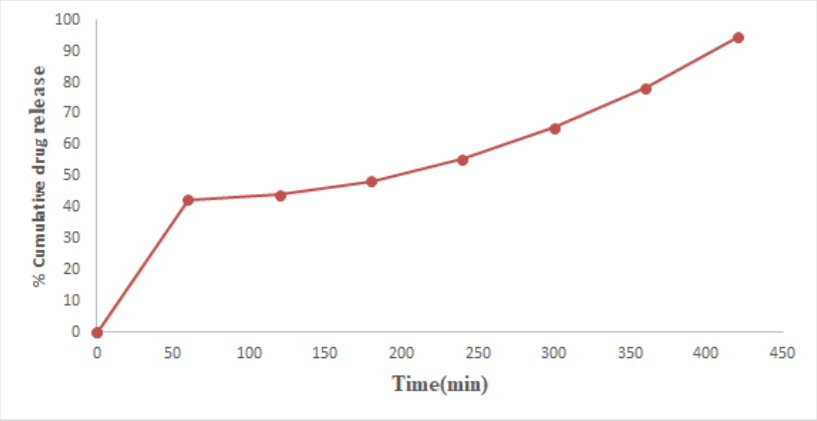

Figure 7: *In-vitro* release of topical solution F2.

***In-vitro* drug release study of topical gels**

The release studies were carried out by inserting 1 g of the formulated gel in the dialysis bag in a 250 ml beaker containing 200 ml of phosphate buffer 7.4 pH. 10 milliliters of sample were taken at 1, 2, 3, 4, 5, 6, and 7, hours. In order to keep the sink condition, this was replaced with an equal volume of buffer. Table 16 and 17 shows the drug release statistics and represented graphically in Figures 8 and 9 [23].

S. no.	Time (min)	% Cumulative drug release (%)
1	0	0
2	60	42.4
3	120	44.09
4	180	48.31
5	240	55.39
6	300	65.38
7	360	78.36
8	420	94.38

Table 16: *In vitro* drug release study data of topical gel (F3).

S. no.	Time (min)	%Cumulative drug release (%)
1	0	0
2	60	35.65
3	120	37.44
4	180	42.1
5	240	50.09
6	300	61.63
7	360	77.46
8	420	97.84

Table 17: *In vitro* drug release study data of topical gel F4.

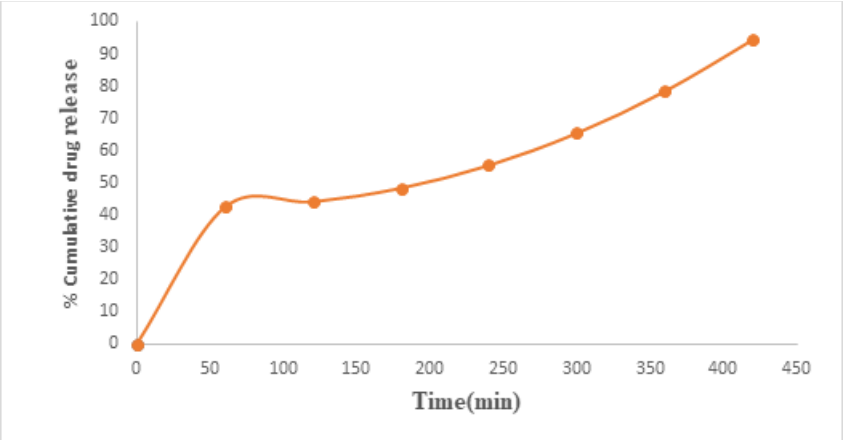

Figure 8: *In-vitro* release of topical gel F3.

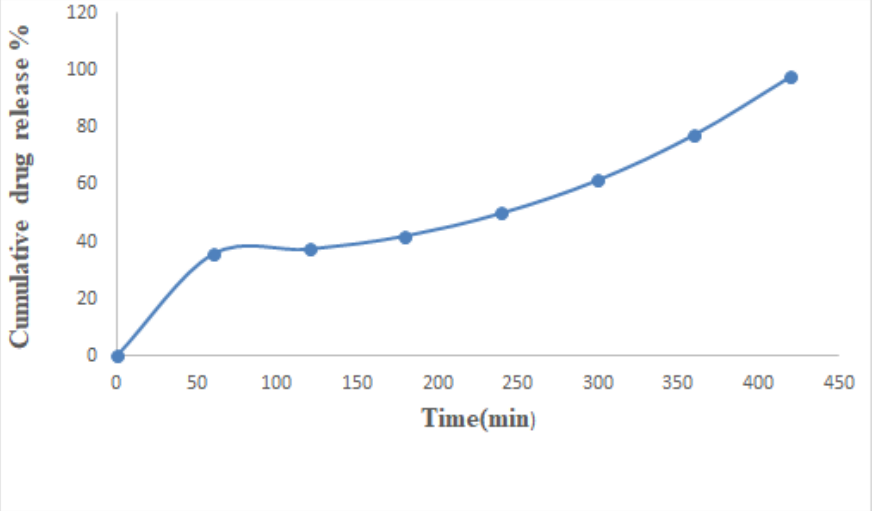

Figure 9: *In-vitro* release of topical gel F4.

RESULTS AND DISCUSSION

The motivation behind this investigation was to see if mixed solvency concept may help improve transdermal penetration and formulation of aqueous topical gels and solutions for a weakly water soluble medication. Naproxen is a non-selective cyclooxygenase inhibitor and Non-Steroidal Anti-Inflammatory Drug (NSAID) used to treat musculoskeletal problems, dysmenorrhea and postoperative pain. A sample of the bulk drug was obtained and characterized using UV, DSC, and melting point studies. The outcomes of the experiments were consistent with those described in official compendia, hence the sample obtained was employed for further research. In the current study, the naproxen drug sample was subjected to various characterization parameters. The characterization result of the drug sample obtained confirmed that it was naproxen and it was used for further research [24].

The calibration curve of the drug, Naproxen in DM water was developed during the preformulation studies. The absorbances at 330 nm of solution or pure drug and drug with solubilisers are nearly same therefore no interference was shown by the excipients in the UV visible estimation of 330 nm. Various aqueous solutions of mixed blend solubilisers were used to study the solubility of naproxen. The drug's calibration curve was made in an aqueous solution of sodium benzoate (2 M), the linearity of the calibration curve revealed that the Beer Lambert's law was obeyed in the concentration range of 40-200 µg/ml at a maximum wavelength of 330.0 nm [25].

CONCLUSION

The clarity and precipitation study of blends were used to choose solubilizers for the formulation creation of an aqueous topical solution and gel. For the formulation development of aqueous topical solutions, two blends with a minimum concentration of solubilizers were chosen. Gels using Carbopol 934 were formed in less concentration with good clarity and organoleptic properties than other gels. These gels were further evaluated. The final batches of topical solution and gels were made, as well as evaluation trials. Gels were made from batches of the above mentioned topical solution blends (Blend 9 and Blend 11). The aforementioned study discovered that several solubilizers from the hydrotropes and cosolvents can improve transdermal penetration of a poorly water soluble medication (propylene glycol). Carbopol as a gelling agent and sodium caprylate, sodium citrate, L-arginine, cyclodextrin, niacinamide and propylene glycol as solubilizers (all GRAS) can be used to make aqueous topical gels and solutions with good clarity, spreadability, extrudability and stability.

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