

DESIGN AND DEVELOPMENT OF NANOBIOCOMPOSITE OF ANTI-INFLAMMATORY DRUG**Shwetnisha Vyankatesh Mande^{1*}, Dr Manmeet Singh Saluja²**

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Abstract: To enhance the physicochemical properties of Soluplus® nanocomposites loaded with naproxen, this study's goal was to create and characterise them. In vitro percentage dissolving efficiency, nanocomposites' anti-inflammatory effectiveness, and the impact of polymer and surfactant concentration on particle size were also studied. Utilising the freeze-drying method, the nanocomposites were created. By using differential scanning calorimetry (DSC), Fourier transformation infrared spectroscopy (FTIR), X-ray powder diffractometry (XPRD), and scanning electron microscopy (SEM), the analytical evidence supporting the synthesis of lyophilized nanocomposites in the solid state was generated and confirmed. Comparing nanocomposites' in vitro drug release profile to that of Naproxen powder purified. The particle size and zeta potential of the naproxen nanocomposites were 64.6 nm and 47.6 mv, respectively, and they were all contained in the nano range. When compared to Naproxen alone, the nanocomposites' solubility and dissolution were significantly ($p < 0.001$) improved, as shown by their lowered log P values (1.90 ± 0.002). The results of the characterisation studies demonstrated that naproxen formed amorphous nanocomposites with the presence of physical contacts between the drug and polymer. The carrageenan-induced rat paw edoema model used to test the anti-inflammatory activity of nanocomposites revealed a non-significant ($p > 0.05$) increase in anti-inflammatory activity when compared to pure naproxen. Based on the findings, it can be inferred that using Soluplus® to create Naproxen nanocomposites could be a useful and different strategy for changing the physicochemical characteristics of Naproxen.

Keywords: Naproxen, Soluplus®, Nanocomposites, Physicochemical properties, Anti-inflammatory activity, etc.

Introduction

One of the most frequently used methods to increase the solubility and rate of dissolution of medications that dissolve slowly is the creation of a drug's nanocomposite^[1,2]. A multiphase solid substance called a nanocomposite has one of the phases and one, two, or three dimensions that are less than 100 (nm)^[3]. structures with nanoscale repetition spacing between the various phases that comprise the material. The last several decades have seen a rise in interest in polymer nanocomposites, which provide potential for improving the physicochemical characteristics of medications with poor water solubility.

Many compounds currently in development fit into the BCS (Biopharmaceutical Classification System) class II group, meaning they have low solubility and high permeability^[4] and typically exhibit dissolution rate-limited absorption. A member of the class of NSAIDs known as propionic acids is Naproxen (NPX), or (2S)-2-(6-methoxynaphthalen-2-yl) propanoate. Osteoarthritis, rheumatoid arthritis, injuries, tendinitis, bursitis, and psoriatic arthritis are among the conditions that it is typically utilised to treat when it comes to pain, pyrexia, inflammation, and stiffness^[5]. As a result, creating naproxen's formulation with a better controlled release pattern may have significant benefits in treating inflammatory and painful conditions of the body^[6].

NPX anti-inflammatory actions are mediated by the suppression of COX-1 and COX-2, which, when activated by inflammatory mediators such tumour necrosis factor and interleukins, produce prostaglandin E2^[7]. Peptic ulcers and haemorrhagic diseases can develop in the gastrointestinal system because of oral NSAID use^[8]. After oral ingestion, naproxen also produces gastrointestinal bleeding and ulcers, like other NSAIDs. Prostaglandin-mediated processes, increased stomach acid production, reduced mucus, bicarbonate secretion, and decreased mucosal cell proliferation and blood flow are some of the mechanisms behind these gastrointestinal injury events^[9].

A unique amphiphilic polymeric solubilizer, Soluplus® (polyvinyl caprolactam-polyvinyl acetate-polyethylene glycol grafted copolymer) has both hydrophilic and lipophilic characteristics. It is anticipated that because of its dual functionality, it will serve as a good matrix to dissolve the medication in an aqueous media. This new polymer, which was created specifically for fourth-generation solid solutions aimed at enhancing dissolution^[10], can

improve the solubility and bioavailability of pharmaceuticals that are not easily soluble. For creating new pharmacological compounds, Soluplus® is appropriate ^[11].

Despite having substantial analgesic and anti-inflammatory properties, naproxen has a delayed rate of absorption ^[12,13]. Because of this, efforts were undertaken to enhance the physicochemical characteristics of naproxen employing solid dispersion ^[14–16], drug amorphization ^[17–19], cyclodextrin complexation ^[20,21], and spherical crystallisation technology. In this study, Naproxen nanocomposites were created using Soluplus® to test their physicochemical makeup and anti-inflammatory effects.

The purpose of this study was to formulate naproxen into its nanocomposites with soluplus® in the presence of tween 80 to explore its physicochemical properties and anti-inflammatory activity. The goal was expanded to include research into how the amounts of polymer and surfactant affect the particle size and % dissolving efficiency of nanocomposites made of naproxen using the freeze-drying method. Differential scanning calorimetry (DSC), Fourier transformation infrared spectroscopy (FTIR), X-ray powder diffractometry (XPRD), scanning electron microscopy (SEM), saturation solubility, partition coefficient determination (log P), and uniform drug content were used to characterise the lyophilized nanocomposites. In phosphate buffer (pH 7.4), the dissolving capabilities of both pure drugs and nanocomposites were further investigated. The carrageenan-induced rat paw edoema model was used to assess the optimised batch and pure drug's anti-inflammatory efficacy.

Material and Method

Materials

The company selling Naproxen was Himedia laboratories Pvt. Ltd. (Mumbai), India. Methanol and tween 80 were bought from Loba Chemie Pvt., Ltd. in Mumbai, India. Throughout the experiment, glass distilled water and reagents of analytical grade were utilised. Without additional purification, the chemicals were used right away.

Preparation of Naproxen (NPX) loaded nanocomposites through freeze-drying technique

The freeze-drying technique was used to create the nanocomposites. First, a probe ultrasonicator was used to create a nanoemulsion of Naproxen in Soluplus®. To create the organic phase, the medication and polymer were dissolved in methanol at various polymer ratios. The aqueous phase was created using 20 ml of distilled water and various concentrations of Tween 80 surfactant. The two mixtures underwent 15 minutes of sonication. The organic phase was progressively injected into the aqueous phase using a syringe. Effective homogeneity of the two phases was achieved using a continuous probe ultrasonication in an ice bath. After the mixture was constantly magnetically agitated for 24 hours at room temperature ($25^{\circ}\text{C} \pm 2$) to remove the methanol, the mixtures were frozen for 25 hours at -80°C in a deep freezer (ELCOLD, Denmark). To create free-flowing powders, the frozen mixtures were lyophilized at -80°C and gently pulverised. Following this, the powders were sieved through mesh with a 100 m sieve size and kept in desiccators until additional examination^[22].

Determination of drug content

To determine the amount of drug present, produced nanocomposites containing 5 mg of a given substance were dissolved in 10 ml of methanol, and the volume was then increased to 50 ml with distilled water. 15 minutes of ultrasonic sonication and a 0.2 m membrane filtering were used to filter the solution. A UV-visible spectrophotometer (Shimadzu 1800, Japan) was used to measure absorbance at 273 nm after the aliquots had been appropriately diluted.

Saturation solubility studies

Studies on saturation solubility were carried out as follows: In solubility tubes, excess amounts of the pure medication naproxen and nanocomposites were introduced. The mixture was then agitated on a mechanical shaker at room temperature ($25 \pm 2^{\circ}\text{C}$) for 24 hours. Once equilibrium had been reached, the proper aliquots were taken out, filtered through a 0.2 m membrane filter, and the filtrate was then examined using a Shimadzu 1800 UV spectrophotometer (Shimadzu, Japan) at 273 nm^[23]. ANOVA (Instat, GraphPad software, Inc. Version 3.05) was used to statistically validate the results of solubility studies.

Particle size analysis

Using a Horiba nanoparticle size analyser (HORIBA SZ-100 for windows [Z-Types] Ver. 1.90, Kyoto, Japan), the nanocomposites' particle sizes were characterised. The particle size diameters at the 90th, 50th, and 10th percentiles of undersized particles, respectively, were $d(0.9)$, $d(0.5)$, and $d(0.1)$, which were used to represent the particle size distribution ^[24].

Zeta potential determination

Using a Horiba Nano particle size analyser (HORIBA SZ-100 for windows [Z-Types] Ver. 1.90, Kyoto, Japan), the electrophoretic mobility of nanocomposites was measured to estimate the surface charge. After diluting the sample with distilled water and allowing it to stand at room temperature, the zeta potential was measured ^[25].

Determination of partition coefficient (log *P*)

Glass tubes were filled with 10 ml of octanol and 10 ml of water apiece, and the mixture was let to stand at room temperature for 24 hours. Remini-CIS 24 plus Incubator Shaker, Mumbai, India) for 24 hours at 25°C with an excess amount (equal to 25 mg) of the pure drug and/or its nanocomposites added in glass tubes. The mixtures were then put to the separating funnel and left to stand for roughly 6 hours so that they could equilibrate. Separating the aqueous and organic phases allowed for the analysis of the drug concentration in the aqueous phase using UV spectrophotometry at 273 nm ^[26]. The partition coefficient was determined using the formula below,

The partition coefficient ($\log P$) = $\log (C_{\text{octanol}}/C_{\text{water}})$ (1)

Where C is the concentration of the drug in octanol and/or water phase.

***In vitro* drug release**

The USP type II-compliant Electrolab dissolution apparatus, located in Mumbai, India, was used to conduct dissolution investigations on naproxen and its nanocomposites in triplicate. According to US FDA recommendations, samples were put into the dissolution tank with 900 ml of phosphate buffer (pH 7.4), kept at 37±0.5 °C and 50 rpm. 900 cc of phosphate buffer

(pH 7.4) was mixed with 60 mg of naproxen or its equivalent in nanocomposites. At the appropriate times, 5 ml of samples were taken. By adding 5 ml of fresh phosphate buffer (pH 7.4) for each 5 ml of removed dissolution media, the volume of the dissolution media was increased to 900 ml^[27]. As soon as possible, the solution was filtered through membrane filter paper with a 0.2- μ m pore size, sufficiently diluted as needed, and then spectrophotometrically analysed at 273 nm (Shimadzu 1800, Japan). ANOVA (Instat, GraphPad software, Inc. Version 3.05) was used to statistically assess the data from the dissolution studies.

DSC analysis

Using a DSC analyser (TA Instruments, SDT Q600 USA), pure Naproxen, Soluplus®, and an improved batch of nanocomposites were all subjected to DSC analysis. Under a nitrogen environment, a sample (5 mg) was heated over a temperature range of 0-275 °C at a rate of 10 °C/min.

FTIR analysis

In conjunction with infrared spectroscopy, the sampling technique known as attenuated total reflectance (ATR) allows samples to be analysed immediately in their solid or liquid state without the need for any additional preparation. Utilising ATR (BRUKER-ECO-ATR-ALPHA, Germany), infrared spectra of all materials were acquired. With 24 scans, the samples were examined in the 600 to 4000 cm⁻¹ spectral range after being placed directly on a sample pan.

XRPD studies

X-ray diffractometer (BRUKAR-D2 PHA-SER, Germany) with tube anode Cu was used to record the XRPD patterns of pure Naproxen, Soluplus®, and an optimised batch of nanocomposites throughout the range of 10-90°/2. These were the operational data: 30 kV of generator tension and 10 mA of generator current.

SEM analysis

A scanning microscope (SEM-JOEL Instruments, JSM-6360, Japan) operating at an acceleration voltage of 20 kV was used to analyse the surface morphology of the drug and the optimised batch of nanocomposites. The generated micrographs were then inspected at 200 and 500 times their original magnification.

Anti-inflammatory activity of Naproxen nanocomposites

The CPCSEA (committee for the purpose of control and supervision of experiments on animals) guidelines were followed in all experiments after receiving approval from the institutional animal ethics committee. The present investigation used healthy Wistar albino rats of either sex, weighing 275-250 g, obtained from the National Institute of Biosciences. Six animals were snugly kept together in a single, spotless plastic cage that had a metal frame lid over the top. They were housed in a temperature- and humidity-controlled setting that was typical. There was a 12:12 h light-dark cycle. Free water and normal laboratory animal diet food were available to all the animals.

The rat paw edoema caused by carrageenan was used to test the anti-inflammatory efficacy of nanocomposites. Male Wistar rats used for the study were randomly assigned to one of six groups, each of which had six animals, depending on their body weight. Carrageenan (0.1 ml of 1% solution in normal saline) was injected into the plantar side of the left hind paw of the rats subcutaneously (S.C.). The lateral malleolus of the paw was marked with ink. All the animals had their paw volumes measured up to the mark using a digital Plethysmometer before (-1 h) and at 1, 2, 3, 4, and 6 h after receiving carrageenan injections. By deducting the relative paw volumes at 1, 2, 3, and 6 hours, the volume of the paw edoema was estimated [28-31].

Result and Discussion

Preformulation study

API characterization

Table: Organoleptic properties of Naproxen

Sr. No.	Name of property	Specification
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1.	Colour	White
2.	Odour	Unpleasant
3.	Nature	Crystalline

Identification of pure drug

a) Melting Point

Table: Melting point of Naproxen

Sr.no.	Melting point	Reference range	Average melting point
1	153°C		
2	150°C	152-155 °C	152.66°C
3	155°C		

Melting point of Naproxen was initiate to be 152.66 °C, that is in compass as given in literature (152-155°C). Consequently, the drug can be expressed as pure.

b) UV Spectroscopy

i) Determination of λ max

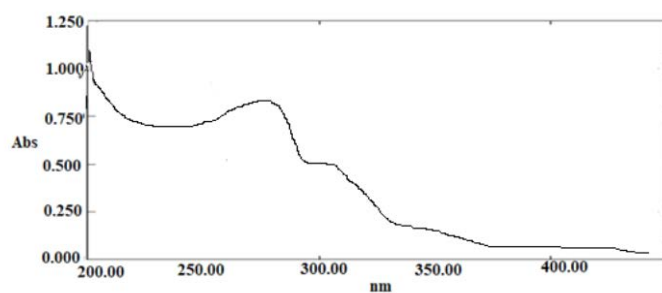


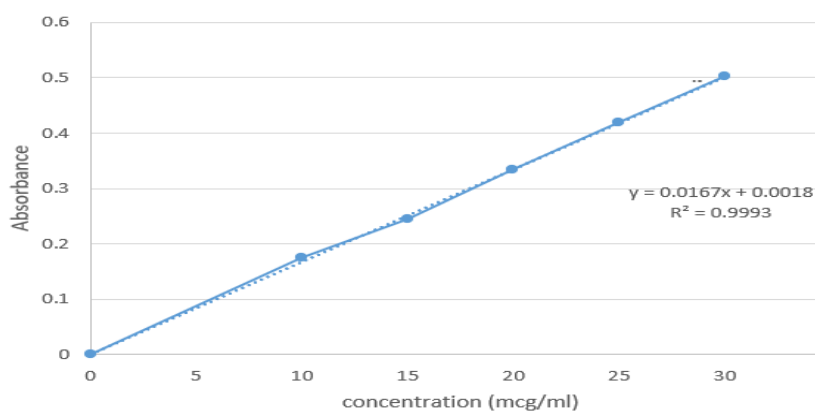
Fig. UV Spectra of pure Naproxen in methanol

Absorption maximum was found to be at 273 nm. Therefore, 273 nm was designate as λ max for additional studies.

ii) Calibration curve of Naproxen in methanol

Table: Different concentration & absorbance of Naproxen

Sr.no.	Concentration ($\mu\text{g/ml}$)	Absorbance
1	0	0
2	10	0.176
3	15	0.245
4	20	0.335
5	25	0.419
6	30	0.502

**Fig. Calibration curve of Naproxen in methanol****Table: Parameters of calibration curve**

Sr. No.	Parameter	Finding
1	Wavelength detection	273 nm
2	Correlation coefficient	$Y = 0.0167x - 0.0018$

3	Regression equation	$R^2 = 0.9993$

Optimization of batches

Based on its saturation solubility data, a batch of naproxen and various polymer: surfactant ratios were optimised.

Saturation solubility studies

Table 1 displays the findings of investigations on the saturation solubility of all Naproxen nanocomposites. It was clear that all batches' solubility had dramatically increased ($p < 0.001$) when compared to the pure medication alone. In comparison to pure naproxen, the optimised batch (F6)'s water solubility increased 6.90-fold. A significant rise in the solubility of formulations may have been caused by the polymer's hydrophilicity and a concurrent decrease in particle size.

Table 1: Particle size and solubility data of various batches for optimization

Batch code	Drug to polymer ratio (mg: mg)	Amount of surfactant added (ml)	Particle size (nm)	Saturation solubility ($\mu\text{g/ml}$)*
Naproxen	-	-	-	43.45 ± 0.21
F1	1:1	0.005	16.8	$255.67 \pm 2.31^{**}$
F2	1:3	0.005	4.4	$283.23 \pm 2.78^{**}$
F3	1:1	0.0095	150	$198.78 \pm 2.04^{**}$
F4	1:3	0.0095	30.0	$283.89 \pm 3.80^{**}$

F5	1:1	0.014	65.3	$275.65 \pm 2.67^{**}$
F6	1:3	0.014	64.6	$293.89 \pm 2.78^{**}$

Percent drug content

The freeze-dried optimised batch (F6)'s percentage drug content was discovered to be 98.2 ± 0.46 (w/w).

Particle size analysis

The nanocomposites of naproxen were discovered to be in the nano range, according to the particle size analysis (table 1). The polydispersity index (PI) of the pure naproxen particle, 3.32 μ m in size, was found to be 0.71. The optimised batch F6's particle size was found to be 64.6 nm (fig. 1). The dispersion of the particles, however, was not uniform. The size of the pure medication was dramatically decreased to a nano size using the freeze-drying method.

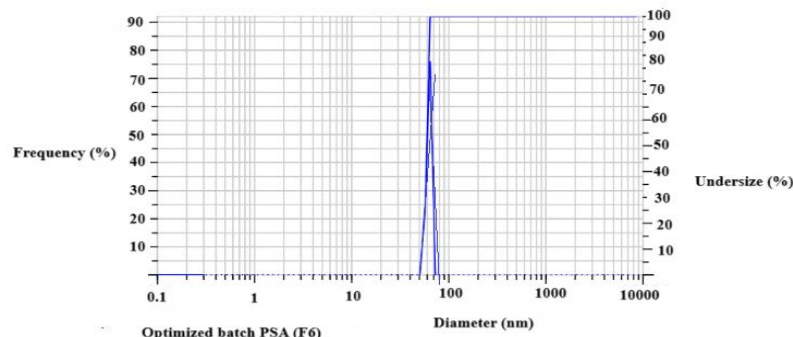


Fig. 1: The particle size distribution of optimized batch (F6); PSA: particle size analysis

Zeta potential determination

Zeta potential investigation was performed on the drug and the improved batch F6 (fig. 2). In general, stable particles are those with zeta-potential values more than +30 mV and less than -30 mV, respectively. The zeta potential was discovered to be -66.6 and -47.6 mV, respectively, according to the findings, indicating the development of stable nanocomposites. A negative charge on the droplets is shown by the negative zeta potential value.

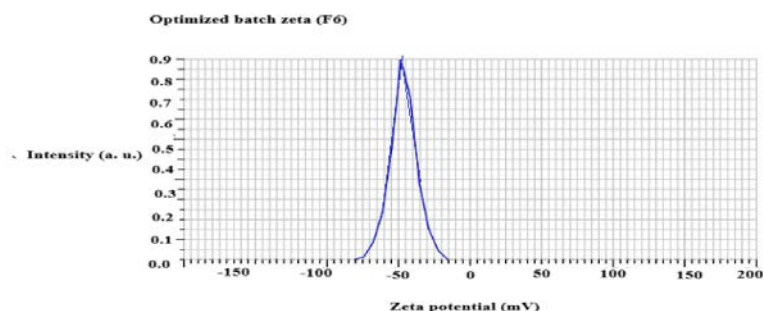


Fig. 2: Zeta potential of drug (Naproxen), optimized batch (F6)

Determination of partition coefficient (log P)

Naproxen and the optimised batch (F6) both had log P values of 3.38 ± 0.008 and 2.91 ± 0.003 , respectively ($p < 0.001$). The improved hydrophilicity of the optimised batch (F6) was evident from the optimised batch's (F6) lower log P value as compared to naproxen.

In vitro drug release

The percentage of drug released (vs.) time was used to express the release rate profiles (fig. 3). It was clear that nanocomposites dramatically accelerated naproxen's rate of dissolution. For Naproxen and its nanocomposites batches (F1 to F6), Table 2 displays the percentage of drug dissolved in 5 minutes (DP_5), 15 minutes (DP_{15}), 30 minutes (DP_{30}), and 45 minutes (DP_{45}). A statistical comparison and reporting of the dissolving efficiency values (DE_{45}) at 45 minutes has been done. The area under the dissolution curve up to time t expressed as a percentage of the area of the rectangle described by 100% dissolution at the same time is known as the dissolution efficiency (DE). Faster dissolution was seen with the optimised batch (F6) of naproxen compared with just pure naproxen. The percentage of naproxen released from the optimised batch (F6) within 15 minutes (DP_{15}) was 67.76 ± 0.61 . However, the amount of naproxen that was released within 15 minutes from pure naproxen was only 8.46 ± 0.07 . As a result, the pure Naproxen dissolving rate has been greatly increased by the optimised batch (F6) of Naproxen with soluplus® (DE_{45} : 60.66 ± 0.27 , $p < 0.001$).

Table 2: The dissolution data of pure Naproxen (NPX) and its nanocomposites batches in phosphate buffer (pH 7.4) at 37 ± 0.5 °C

Batch code	DP ₅ * ± SD	DP ₁₅ * ± SD	DP ₃₀ * ± SD	DP ₄₅ * ± SD	DE ₄₅ * ± SD
Naproxen	3.66 ± 0.09	8.46 ± 0.07	12.89 ± 0.06	16.82 ± 0.25	9.83 ± 0.07
F1	32.81 ± 0.31	46.81 ± 0.53	60.56 ± 0.16	63.86 ± 1.23	49.50 ± 0.33**
F2	27.56 ± 0.76	44.86 ± 1.28	59.41 ± 0.61	69.51 ± 0.61	49.35 ± 0.36**
F3	29.56 ± 0.83	36.86 ± 0.40	47.57 ± 0.41	49.81 ± 0.53	39.19 ± 0.15**
F4	38.51 ± 0.26	58.06 ± 0.53	68.21 ± 0.80	69.86 ± 0.99	56.62 ± 0.34**
F5	38.67 ± 0.97	51.86 ± 0.66	63.71 ± 0.61	67.76 ± 0.61	53.98 ± 0.20**
F6	38.11 ± 0.46	67.21 ± 0.53	69.61 ± 0.68	72.01 ± 0.63	60.29 ± 0.44**

DP: % drug dissolved; % DE: % dissolution efficiency; indicates *p* value compared to pure Naproxen ($p < 0.001$), i.e., **significant.

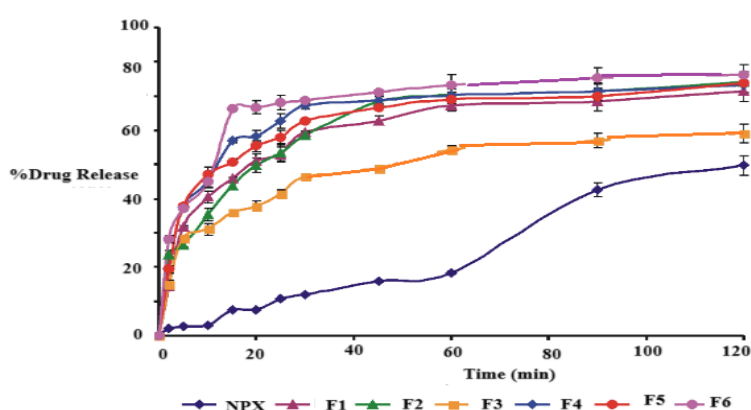


Fig. 3: The dissolution profile of Naproxen and F1 to F6 batches at 37 ± 0.5 °C; NPX: Naproxen

DSC analysis

Figure 4 depicts the DSC thermogram of the optimised batch (F6), polymer, and NPX. At 155 °C, NPX displayed a clear melting endotherm. At 63.59 °C, the polymer Soluplus® displayed a glass transition endotherm (T_g). The pure NPX melting peak has completely vanished from the nanocomposites of the optimised batch (F6), indicating a decrease in the drug's crystalline nature. It is known that changing the medication from its stable crystalline structure to an amorphous state in formulations leads to improved solubility and quicker drug dissolution rates.

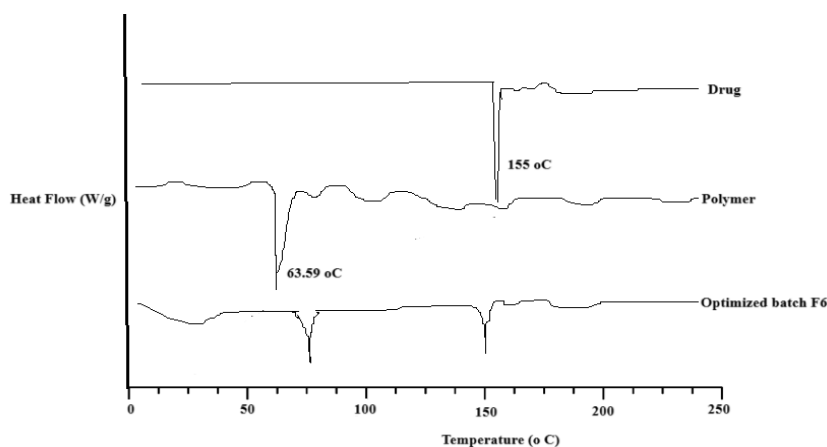


Fig. 4: DSC thermograms of drug (NPX), Soluplus® (polymer), optimized batch (F6); NPX: Naproxen

FTIR analysis

The FTIR spectra of NPX, polymer, and optimised batch (F6) investigated by ATR-IR spectroscopy are shown in Fig. 5. The main absorption peaks in the IR spectra of NPX are at 3153.90 cm^{-1} (C-H stretch), 2983.18 cm^{-1} (C-H stretch), 1770.76 cm^{-1} , 1696.08 cm^{-1} , and 1593.32 cm^{-1} (C=C aromatic), as well as 1670.76 cm^{-1} (C=N). The O-H stretching bands in the Soluplus® IR spectra were 3338.08 cm^{-1} and 3281.19 cm^{-1} , the aliphatic-CH stretching band was 2917.81 cm^{-1} , the C=O stretching band was 1733.16 cm^{-1} , and the O-H stretching band was 1635.94 cm^{-1} . The peak of NPX at 3053.90 cm^{-1} (C-H stretch) was totally lost in the IR spectrum of the optimised batch (F6), whereas other peaks were discovered to be diffused. The IR bands at 1085.40 cm^{-1} and 2891.82 cm^{-1} (C-H stretch) were moved towards

lower frequencies, respectively. The peaks of Soluplus® were shifted to 3324.60 cm^{-1} from 3338.08 cm^{-1} (O-H stretching). As a result of physical interactions, the intensity of the band at 1596.08 cm^{-1} (C=C aromatic) was also considerably reduced.

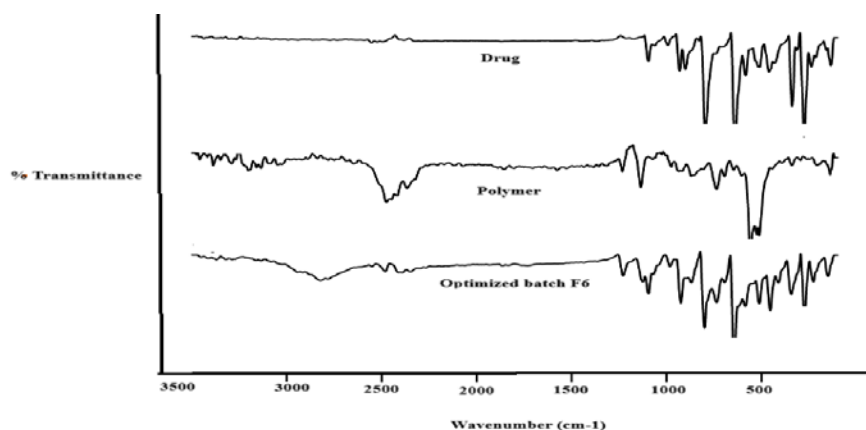


Fig. 5: FTIR spectra of drug (NPX), Soluplus® (polymer), optimized batch (F6); NPX: Naproxen

XRPD studies

The NPX's XRPD pattern showed strong and distinct peaks, demonstrating its crystalline structure. Peak intensities and 2θ values for NPX (fig. 6) were observed at 16.45° , 17.46° , 17.32° , 23.70° , and 30.17° . For Soluplus®, a characteristic halo-pattern was seen (fig. 6), indicating its amorphous nature. To calculate the relative drop in crystallinity (RDC) of NPX in the optimised batch (F6), the peak height at 17.75° (2) was utilised, as the peaks of NPX with the highest intensity (17.46°) vanished in these nanocomposites. Other NPX peaks, though, have also vanished. The loss of crystallinity and potential presence of some NPX amorphous entities in these nanocomposites were suggested by the removal of strong NPX peak intensities in the optimised batch (F6).

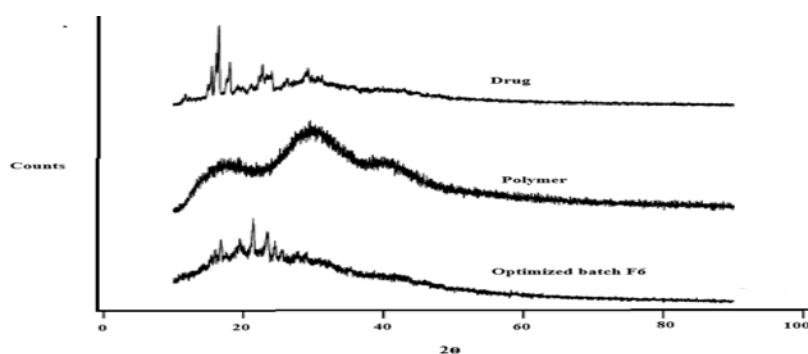


Fig. 6: XRPD patterns of drug (NPX), soluplus[®] (Polymer), optimized batch (F6); NPX: Naproxen

SEM analysis

Figure 7 depicts the surface morphology of pure NPX powder, a batch of nanocomposites that has been optimised (F6). The presence of rod-shaped, irregular, rough, and shattered particles was a defining characteristic of NPX. The original morphologies of pure NPX diminished, while the surface morphology of the freeze-dried nanocomposites (F6) batch revealed irregular particles of some amorphous aggregates with limited particle size distribution. The NPX nanocomposites significantly impacted the drug's solubility and dissolving rate by taking an amorphous shape and reducing particle size.

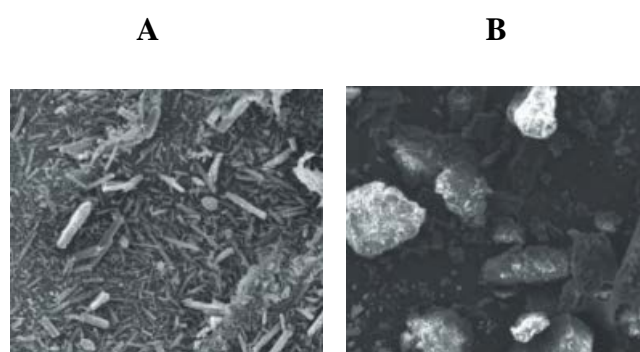


Fig. 7: SEM of drug (NPX) A; optimized batch (F6) B

Anti-inflammatory action of Naproxen nanocomposites

At 0 hours, the medication displayed negative% inhibition due to poor absorption, as seen in the histogram (fig. 8) and table 3. Due to the drug's reduced particle size and improved solubility, the F6 batch showed % inhibition at 0 h, indicating quicker absorption of

nanocomposites. Between medication and F6 at any hour, there was no discernible change. The outcome implied that the nanocomposites displayed the same activity.

Table 3: The anti-inflammatory action through carrageenin-induced hind paw edema in rat

Hours/ System	-	Control	Naproxen	F6
0	Increase in paw volume* ml	2.88 ± 0.008	2.07 ± 0.29	1.86 ± 0.17
	% inhibition	-	-11.17	2.07
1	Increase in paw volume* ml	3.51 ± 0.15	2.17 ± 0.27	1.98 ± 0.06
	% inhibition	-	14.7	22.3
2	Increase in paw volume* ml	3.65 ± 0.03	2.28 ± 0.33	2.09 ± 0.08
	% inhibition	-	15.67	22.81
3	Increase in paw volume* ml	3.81 ± 0.043	2.46 ± 0.38	2.37 ± 0.09
	% inhibition	-	15.65	16.36
4	Increase in paw volume* ml	3.99 ± 0.05	2.46 ± 0.38	2.37 ± 0.09
	% inhibition	-	18.29	21.81
6	Increase in paw volume* ml	4.02 ± 0.03	2.40 ± 0.40	2.35 ± 0.08
	% inhibition	-	21.60	23.26

* mean ± SD (n=6); SD standard deviation, **non-significant difference associated toward pure Naproxen ($p > 0.05$); NPX: Naproxen, F6: optimized batch F6

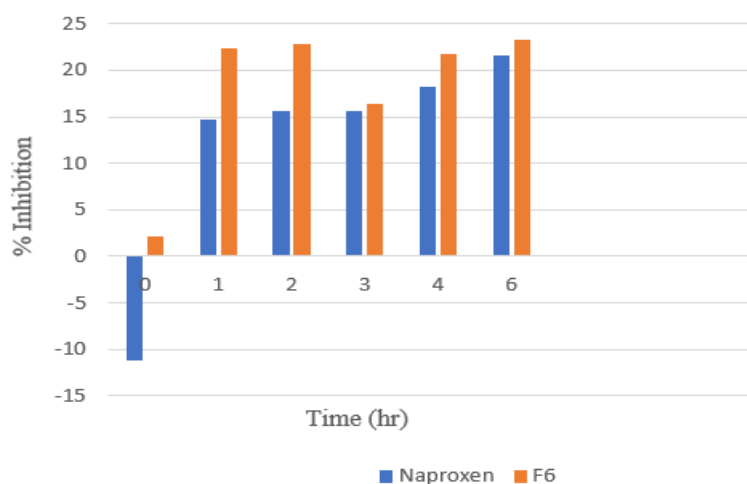


Fig. 8: Histogram of % inhibition of NPX; F6 (optimized batch nanocomposites); NPX: Naproxen

Conclusion

Using the amphiphilic polymer Soluplus® and the freeze-drying method, the current experiment successfully formed nanocomposites of naproxen. The solubility and dissolving rate of the medicine have improved thanks to the freeze-drying procedure, which has also significantly reduced particle size. It was discovered through the analysis of freeze-dried nanocomposites that the medication had changed into an amorphous form. To create nanocomposites with the specified particle size and % drug release within 45 minutes, a statistically methodical approach was used in conjunction with the freeze-drying technique. The formulation F6 batch, which produced negligible anti-inflammatory effect in rats, was chosen as an optimised batch with the desired qualities. Therefore, it may be inferred that creating polymeric nanocomposites using freeze-drying technology, amphiphilic carriers, and tween 80 could enhance the physicochemical properties of naproxen.

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