J Integral Sci, 2019, Volume 2, Issue 1, 06-16. ISSN: 2581-5679

www.jisciences.com

Research Article

Journal of Integral Sciences

Formulation and evaluation of Naproxen sustained release matrix tablet

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Received: 13th Jan 2019; Revised: 23rd Jan 2019; Accepted: 29th Jan 2019

Abstract

The present study was carried out to formulate sustained release matrix tablet of naproxen and to evaluate its drug release and stability. Formulation and evaluation of oral sustained release matrix tablets of naproxen were prepared by wet granulation technique by employing different concentration of HPMC-K4M, HPMC-K100 and DCP polymers to achieve sustained release of drug. The formulated batches were evaluated for physicochemical parameters and dissolution profiles as per pharmacopial methods. The physical parameters like weight variation, thickness, hardness, friability and assay of all formulations were evaluated. The results of formulated tablets complied with pharmacopoeial specifications and formulated combination F7 was well optimized and its stability data was found to be stable for three months at accelerated stability conditions at a temperature (40±2°C) and relative humidity 75±5% as per ICH norms.

Key words: Naproxen, Tablets, Physiological parameters, Assay and Stability.

1. Introduction

The oral route of administration has by far received the most attention because there is more flexibility in dosage form design, more patient acceptance and relatively easy route of administration than parental route and also constraints of sterility and potential damage at the site of administration are minimal (Sandeep *et al.*, 2013). Some drugs are inherently long lasting and require only once-a-day oral dosing to sustain adequate drug blood levels and the desired therapeutic effect (Rogers and Kwan, 1979; Madan, 1985). These drugs are formulated in the conventional manner in immediate-release dosage forms. However, many other drugs are not inherently long lasting and require multiple daily dosing to achieve the desired therapeutic results. Multiple daily dosing often is inconvenient for the patient and can result in missed doses, made up doses and patient noncompliance with the therapeutic regimen (Natanya Civijan, 2012; Maulik *et al.*, 2012). When conventional immediate release dosage forms are taken on schedule and more than once daily, there are sequential blood level peaks and valleys associated with the taking of each dose. However, when doses are not administered on schedule, the resulting peaks and valleys reflect less than optimal drug therapy (Sathish *et al.*, 2013). So this can be overcome by using sustained release formulation. These forms will produce therapeutic action for a prolonged period of time.

Naproxen is a non steroidal anti-inflammatory, weekly acidic, drug has low aqueous solubility at acidic pH. It is used in the treatment of rheumatoid arthritis, osteoarthritis, dysmenerorheal, tendontotis, and ankolysoing spondylitis and also used as pain reliever and analgesic. It exhibits gastric toxicities, mucosal ulceration and hemorrhage due inhibition of production. Biological half-life of naproxen is 12 h but due to its extensive protein binding (90%), it leads to nonlinear pharmacokinetics, resulting in an increase in urinary excretion of naproxen and its metabolites (Vree *et al.*, 1993). Due to these properties it will be more effective to deliver the drug as a sustained release dosage form. So, the purpose of the present investigation was to formulate sustained release matrix tablet of naproxen and to evaluate its drug release and stability.

2. Materials and Methods

2.1 Chemicals and Instruments

Naproxen, HPMC- K4M, HPMC-K100M, DCP, Ethylcellulose, Polyvinylpyrrolidone (PVP-K-30) were received as Gift sample from Ajantha Pharmaceutical Ltd, Cadila Pharma, Glenmark Pharmaceuticals Ltd, Talc and Magnesium stearate were purchased from Qualikems Fine Chemicals Pvt. Ltd, Pottasium dihydrogen orthophosphate purified LR from S.D. Fine Chemical Pvt. Ltd, Sodium hydroxide pellets from Finar Chemicals Ltd, Tweens 80 and Isopropyl alcohol purchased from RFCL Ltd.

Electronic weighing balance from Shimadzu, Eight station rotary tableting machine from Cemach Machinery Co, Tap density tester (USP) from Electrolab, Hardness tester from Cmach Machinery Co, Digital vernier caliper from Mitutoyo Corp, Sieves from Rolex standard sieves, Dissolution apparatus (USP), Infrared spectrophotometer from FTIR 8400S from Shimadzu, Hot- air oven from Sisco Pvt. Ltd, Friability test apparatus from Electrolab Pvt Ltd. pH meter from Elico Pvt. Ltd, Stability chamber from Sisco.

2.2 Drug authentication

Drug (Naproxen) authentication was carried out by determining its melting point using capillary method, solubility analysis, Infrared spectrum of naproxen was determined on Fourier Transform Infrared Spectrometer using KBr pellet (John R. Dyer, 2007; Robert M. Silverstein and Francis, 2014).

2.3 Development of analytical method

The absorbance of solutions containing 6 µg/mL was determined in UV range 200-400 nm using pH 7.2 phosphate buffer (containing 0.5% v⁄v of TWEENS 80) as blank (Hokanson, 1994).

2.3.1 Preparation of calibration curve

Various concentrations of naproxen (1 to 12 µg⁄ mL) solutions absorbance of solutions were determined in UV range between 200-400 nm using pH 7.2 phosphate buffer as blank. The λ_{max} was found to be 273 nm. At this wavelength maximum calibration curve was drawn by plotting graph between absorbance (on Y-axis) and concentration (on X-axis).

2.4 Formulation and development studies

2.4.1 Preparation of naproxen matrix tablets

Naproxen matrix tablets were prepared by wet granulation method. First sift drug and polymers HPMC-K100M, HPMC-K4M through sieve no # 40 in order to form uniform particles. First take small quantity of drug and polymers and mix it properly, then repeat the process to the remained quantity of drug and polymers to ensure uniform mixing. Naproxen was dry blended with various polymers and granulated using isopropyl alcohol. The wet mass was passed through sieve no #10. The wet granules were dried at 50ºC for half an hour and passed through sieve no #18. The drug granule mixture were blended with magnesium stearate and talc and blended for five minutes. Tablet formulations containing 365 mg of naproxen, binder agents, fillers, and lubricants were prepared by wet granulation followed by compressing the blended powders, using an eight-station compression machine *Cmach* (Ahmadabad, India), and 10-mm diameter flat beveled punches. Tablet compositions were given in Table 1.

2.4.2 Evaluation of precompression blend

The physical characterization of selected API and powder blend such as bulk density, tapped density, Hausner's ratio, angle of repose and compressibility index were determined as per official procedures (Lachmman *et al.,* 1991; Gibson *et al.,* 2004; Khan and Meidan, 2007; Harun-Or-Rashid, Zakir Hossain, 2009; Faiyaz Shakeel *et al.,* 2007; Shabaraya and Narayanacharyulu, 2000).

2.4.3 Evaluation of tablet

The formulated tablets were evaluated by measuring their physical appearance, hardness using Monsanto hardness tester, friability using friability test apparatus (Roche friabilator), drug content (by Assay) and dissolution and drug release studies were carried out as the US Pharmacopoeia Paddle method II.

2.4.3.1 Physical appearance

The physical appearance such as thickness, diameter, shape and uniformity of a tablet are very for consumer acceptance. So, they were be dimensionally described, monitored, and controlled.

Table 1. Composition of naproxen sustained release matrix formulations.

Ingredients (in mg)	FORMULATION CODE										
	F1	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**	**F10**	**F11**
Naproxen	365	365	365	365	365	365	365	365	365	365	365
Ethyl Cellulose	80	-	-	-	-	-	-	-	-	-	-
HPMC-K100M	-	30	50	100	-	50	50	-	100	100	-
HPMC-K4M	50	20	20	20	50	-	50	100	-	-	100
Di-Calcium Phosphate	20	100	80	30	100	100	50	50	50	-	-
PVP K30	30	30	30	30	30	30	30	30	30	30	30
Magnesium stearate	10	10	10	10	10	10	10	10	10	10	10
Talc	10	10	10	10	10	10	10	10	10	10	10
Total weight	565	565	565	565	565	565	565	565	565	515	515

2.4.3.2 Thickness

Twenty tablets from the representative sample were randomly taken and individual tablet thickness was measured by using digital vernier caliper

2.4.3.3 Hardness

From each batch ten tablets were measured for the hardness and average of ten values were noted along with standard deviation.

2.4.3.4 Friability

From each batch, twenty tablets were accurately weighed and placed in the friability test apparatus (Roche friabilator). Apparatus was operated at 25 rpm for 4 minutes and tablets were observed while rotating. The friability was calculated as the percentage weight loss.

Note: No tablet should stick to the walls of the apparatus. So, the walls brushed with talcum powder. There should be no capping also.

2.4.3.5 Weight variation test

To study weight variation individual weights (W_I) of 20 tablets from each formulation were noted using electronic balance. Their average weight (W_A) was calculated. Percent weight variation was calculated as follows. Average weights of the tablets along with standard deviation values were calculated. % weight variation = $(W_A–W_I) \times 100/ W_A$.

2.4.3.6 Assay calculation

An accurately weighed portion of the powder equivalent to about 100 mg of naproxen was transferred to a 100mL volumetric flask of pH 7.2 phosphate buffer (containing 0.5%v⁄v of TWEENS 80). It was shaken by mechanical means for 1 h. Then it was filtered through a Wattman filter paper (No.1) and diluted to 100mL with same phosphate buffer solution. From this resultant solution was diluted to 10mL with same medium and absorbance was measured against blank at 278nm.

2.4.3.7 In-vitro dissolution studies

For dissolution and drug release studies, the US Pharmacopoeia Paddle method II was used. The dissolution medium consisted of 900mL of pH 7.2 phosphate buffer solution, maintained at 37.5ºC ± 0.5ºC and stirred at 100rpm. Samples (5mL) were withdrawn at predetermined time intervals for 24 h and immediately replaced with equal volumes of dissolution medium. Samples were filtered to remove suspended, insoluble tablet components and assayed by UV-Visible spectrophotometer at 278 nm.

2.4.3.7.1 Kinetic analysis of dissolution data

To analyze the *in-vitro* release data various kinetic models were used to describe the release kinetics. The zero order rate describes the systems where the drug release rate is independent of its concentration. The first order describes the release from system where release rate is concentration dependent.

2.5 Stability studies

Developed tablet formulations were wrapped in aluminum foils individually and placed in stability chamber. Conditions were set at 40ºC, 75% RH, room temperature (25ºC, 60% RH) and 2-8 ºC as per ICH guidelines. Stability studies were carried out for three months. Samples were withdrawn at an interval of 1, 2 and 3 months, analyzed for *in-vitro* dissolution.

3. Results and Discussion

3.1 Drug authentication studies

The drug authentication is important to study its pharmacokinetic and pharmacodynamic

performance. In this purity studies are important parameter and it play a vital role in drug affects.

The melting point of drug was found to be 15˚C which correlates with that of standard reference value (Table 2).

Table 2. Melting point analysis of naproxen.

S. No.	Melting Point (˚C)		
	Experimental	Average	Reference
1	150-153	151	
2	152-154	152	149-153
3	150-152	151	

Naproxen was found to be sparingly soluble in phosphate buffer pH 7.4 as well as in solvents like methanol, ethanol and acetone. The solubility performed in various solvents and results were presented in Table 3.

Table 3. Solubility analysis of naproxen.

S. No.	Solvent	Solubility
1	Purified water	insoluble
2	Phosphate buffer (pH 7.4)	Sparingly soluble
3	Methanol	Soluble
4	Ethanol	Sparingly soluble
5	Chloroform	Soluble

In FTIR, sharp distinct peak of naproxen was observed at 1215cm^{-1} (Fig 1). The infra-red spectrum analysis of naproxen and combination of various excipients were done using KBr pellets (Fig 2 to 4). The IR spectra of pure naproxen drug showed the characteristic absorption bands are as follows: COO^- at 1585 cm^{-1}, aromatic CH_3-CH stretching at 2957 cm^{-1}, aliphatic CH_3O stretching at 2904 cm^{-1}, C-H stretching of aromatic ring at 3058 cm^{-1}, carboxyl keto group showed absorption band at 1631 cm^{-1}. No shift of either drug or excipient peaks were occurred indicating compatibility of all excipient with drug. This data was verified and confirmed from pharmacopeial specifications and available literature information. Hence drug was found to be pure.

The possible drug and excipient interactions of blends were also analyzed. No drug-polymer interaction was observed in the FTIR spectra of the powder mixture of optimized formulation. Since the absorption peaks of the drug still could be detected in the mixture. In the entire FTIR spectrum these peaks are observed indicating the stable nature of naproxen with various excipients (Fig 5 and 6).

T he FT-IR spectrum of pure drug and FT-IR spectra of the formulations showed that there is a negligible difference in the position of characteristics of absorption bands of the functional groups of the drug and the drug has remained in its normal form even when the formulations were prepared from it without undergoing any chemical interaction with the different polymers and other excipients used during the study. Thus, it is clear from FT-IR study that there is no interaction of the drug with the polymer and other excipients.

3.2 Analytical method development and validation

The λ_{max} of the drug for analysis was determined by taking scans of the drug sample solutions in the entire UV region. It was found to be that only one peak was observed in this method at the wavelength of 273nm (Fig 7). From scan it was confirmed that the addition of suitable surfactant increased solubility of drug. At this wavelength maximum calibration curve was drawn by plotting graph between absorbance (on Y-axis) and concentration (on X-axis).

The aliquots of concentrations ranging from 1-20 µg/mL were prepared in triplicate, but linearity was found to be between 1-12 µg/mL. Statistical parameters like slope, intercept, coefficient of correlation, standard deviation and relative standard deviation were determined (Fig 8).

3.3 Formulation and development studies

3.3.1 API and formulation characterization (Pre-formulation)

The physical characterization of selected API and powder blend such as bulk density, tapped density, Hausner's ratio, angle of repose and compressibility index were determined as per official procedure and presented in Table 4 and 5**.** The bulk density was 0.37± 0.2 to 0.39±0.11 g/mL, tapped density was found to be in the range of 0.47±0.11 to 0.49±0.13 g/mL, Hausner's ratio less than 1.25 indicating better flow properties, and the compressibility index was in range of 18.0±0.15 to 20.0±0.13% for API. The bulk density was 0.40±0.09 to 0.52±0.03 g/mL, tapped density was found to be in the range of 0.45±0.09 to 0.62±0.05 g/mL, Hausner's ratio values was in the range of 1.12±0.84

to 1.22±0.99 better flow properties, and the compressibility index was in range of 11.11±0.05 to 18.53±0.04% for powder blend. The value for compressibility index below 21% indicates a powder having fair flow characters, whereas a value above 25 % indicates poor flow ability.

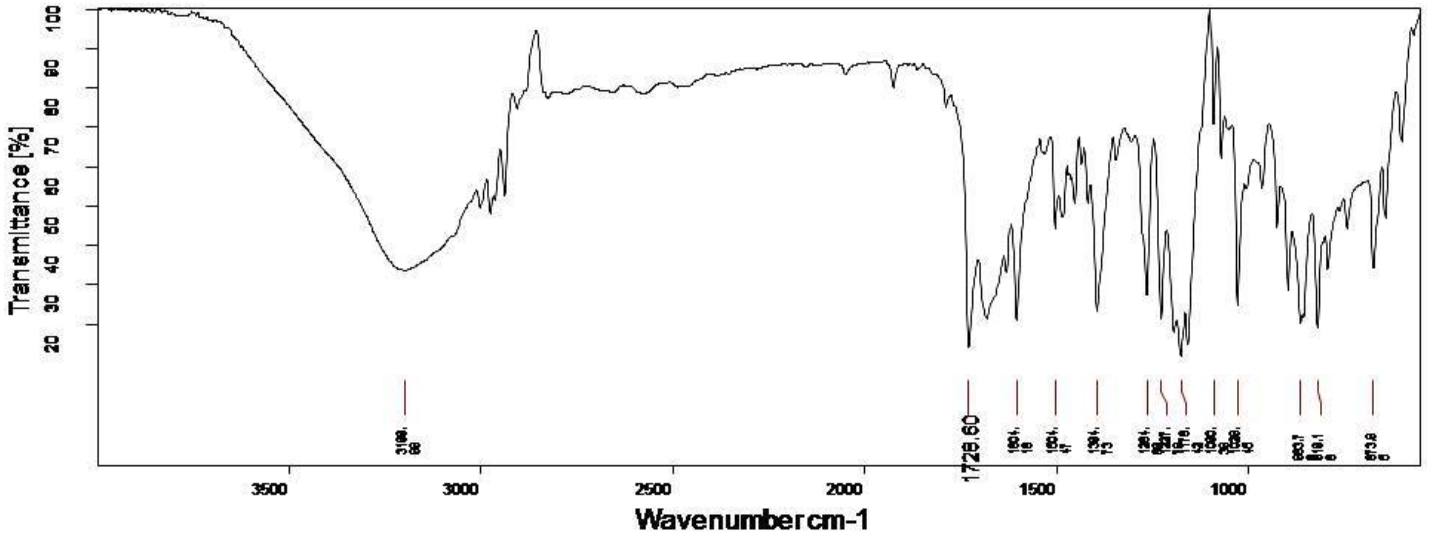

Fig. 1. FTIR spectrum of Naproxen pure drug.

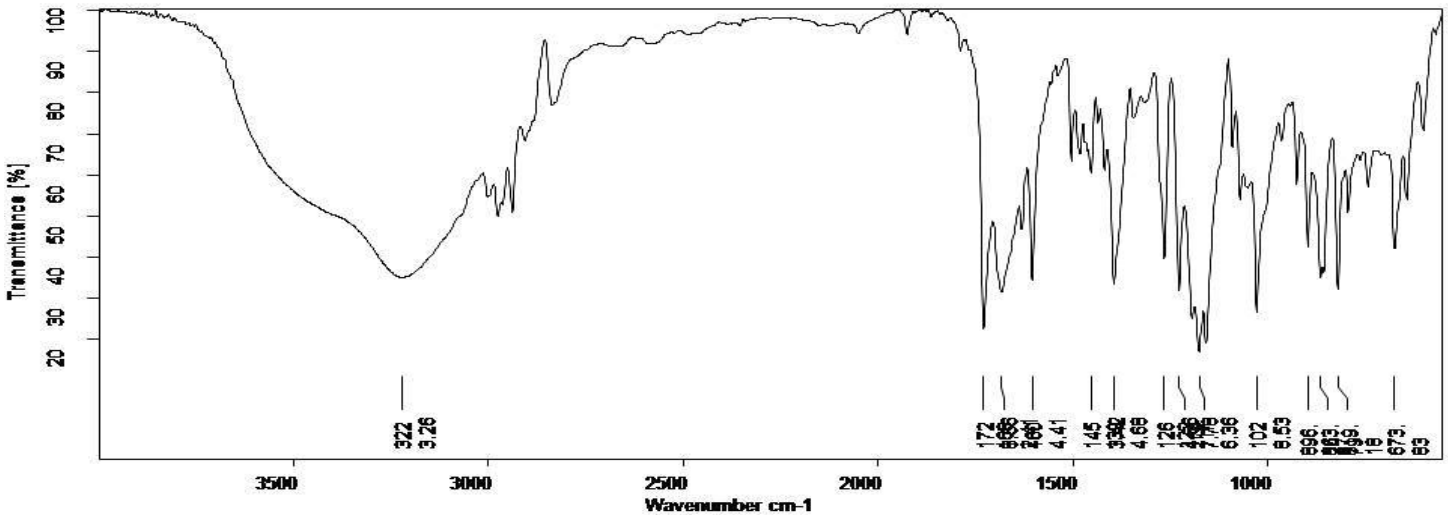

Fig. 2. FTIR spectrum of Drug + HPMC-K100M.

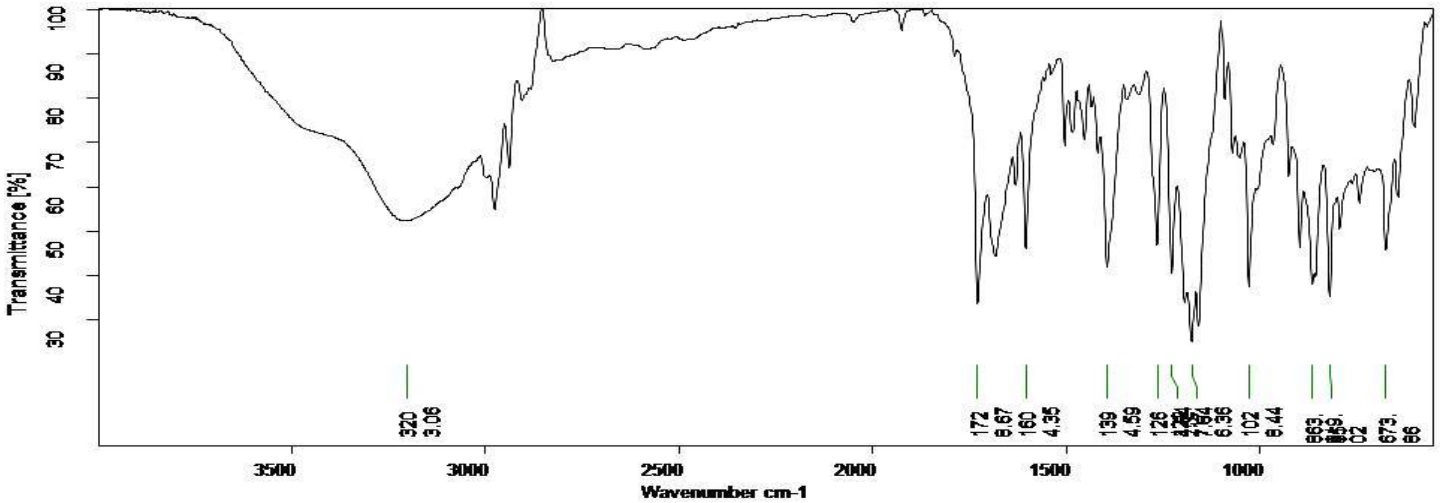

Fig. 3. FTIR spectrum of Drug + Ethyl Cellulose**.**

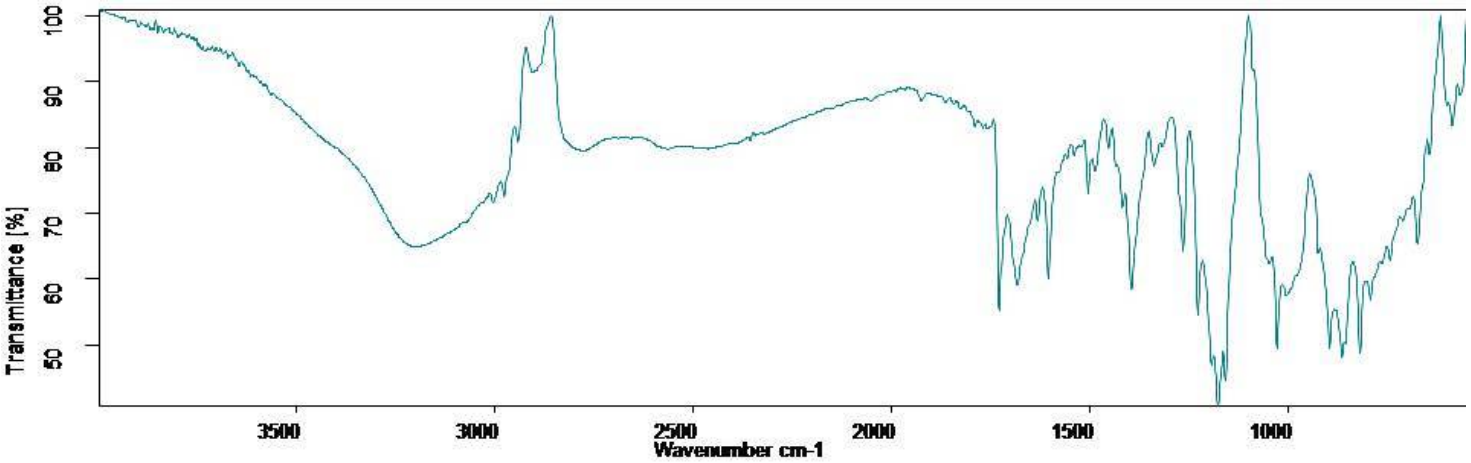

Fig 4. FTIR spectrum of Drug + Di-Calcium Phosphate.

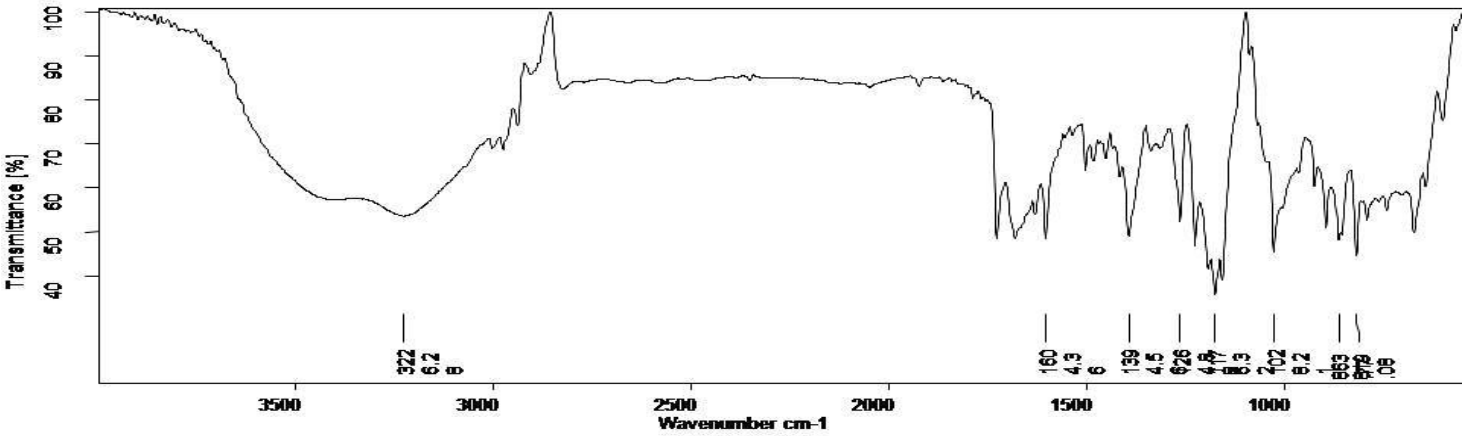

Fig 5. FTIR spectrum of optimized formulation (F-7).

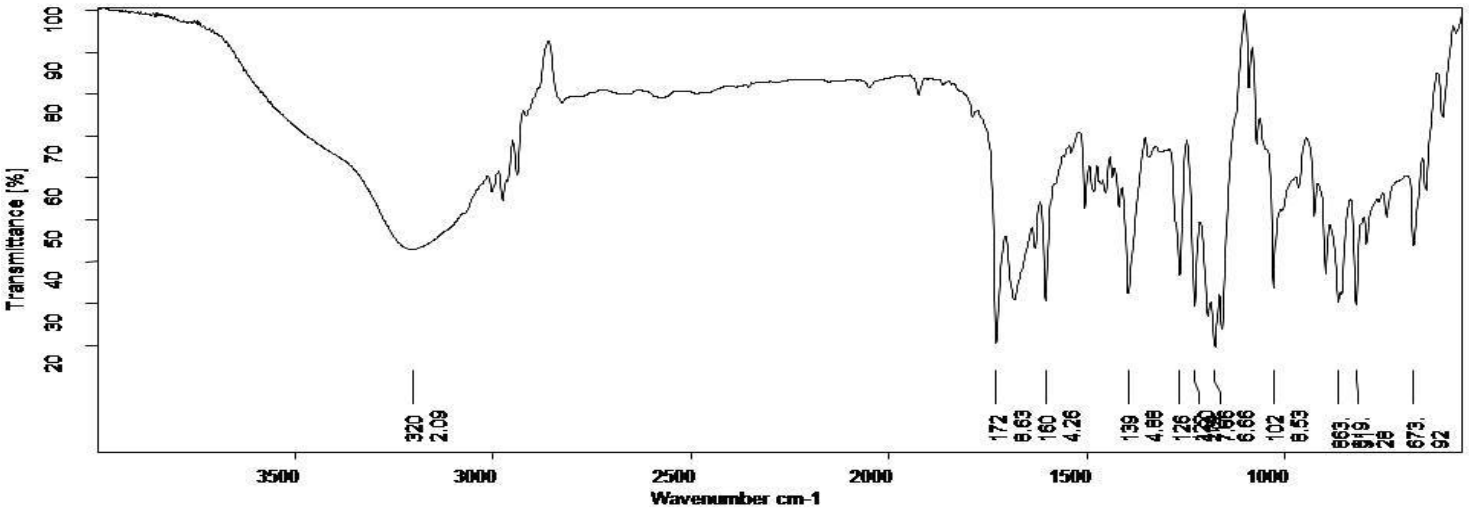

Fig 6. FTIR spectrum of optimized formulation (F-1).

Table 4. Physical characterization of API.

S. No.	Parameter	Value (± SD)
1.	Bulk density (g/mL)	0.38 ± 0.11
2.	Tap density (g/mL)	0.48 ± 0.14
3.	Compressibility index (%)	20.0 ± 0.07
4.	Hausner's ratio	1.13 ± 0.19
5.	Angle of repose (º)	27.47 º ± 0.04

Table 5. Physical parameters of powder blend of formulations F-1 to F-11.

S. No.	Formulation code	Parameter				
		Bulk density (g/mL)	Tapped density (g/mL)	Compressibility index (%)	Hauser's ratio	Angle of repose (º)
1	F-1	0.45±0.07	0.55±0.03	18.18±0.03	1.22±0.92	30.1±0.03
2	F-2	0.51±0.06	0.58±0.05	13.79±0.07	1.16±0.90	29.68±0.06
3	F-3	0.52±0.03	0.62±0.05	16.12±0.09	1.19±0.89	29.68±0.05
4	F-4	0.43±0.05	0.51±0.04	14.0±0.05	1.16±0.94	31.39±0.01
5	F-5	0.40±0.09	0.45±0.09	11.11±0.05	1.12±0.84	29.68±0.09
6	F-6	0.43±0.08	0.52±0.04	17.3±0.06	1.12±0.95	33.42±0.07
7	F-7	0.51±0.03	0.58±0.08	12.06±0.08	1.20±0.96	26.56±0.08
8	F-8	0.44±0.02	0.50±0.07	12.0±0.04	1.13±0.93	27.7±0.06
9	F-9	0.49±0.05	0.60±0.05	18.53±0.04	1.13±0.97	29.24±0.05
10	F-10	0.45±0.02	0.53±0.06	15.09±0.05	1.22±0.99	30.11±0.04
11	F-11	0.44±0.04	0.52±0.04	15.38±0.09	1.17±0.92	29.21±0.08

Table 6. Physical parameter data of naproxen matrix tablets.

S. No.	Formulation code	Weight variation(mg)	Thickness (mm)	Hardness (kg/cm^2)	Friability (%)	Assay
1	F1	565.3±0.6	5.3±0.02	10 ± 0.15	0.52±0.01	100.11±0.36
2	F2	564.5±0.7	5.4±0.04	9.2 ± 0.12	0.53±0.02	98.5±0.45
3	F3	563.4±0.5	5.3±0.02	10 ± 0.15	0.52±0.01	99.89±0.38
4	F4	565.3±0.6	5.4±0.04	9.8 ± 0.14	0.54±0.03	100.21±0.47
5	F5	564.6±0.7	5.3±0.04	11± 0.25	0.52±0.01	100.16±0.46
6	F6	565.3±0.6	5.3±0.02	12± 0.30	0.54±0.03	99.21±0.33
7	F7	564.5±0.7	5.4±0.04	10± 0.15	0.52±0.01	100.07±0.43
8	F8	563.4±0.5	5.3±0.02	11± 0.25	0.54±0.03	100.05±0.42
9	F9	565.3±0.6	5.4±0.04	12 ± 0.30	0.52±0.01	100.21±0.47
10	F10	514.6±0.7	5.2±0.04	10± 0.15	0.54±0.03	100.21±0.50
11	F11	514.4±0.5	5.2±0.04	12± 0.30	0.54±0.03	99.21±0.33

Table 7. *In-vitro* dissolution of formulations F-1 to F-11.

Time (in Hours)	Cumulative percentage of drug release										
	F-1	F-2	F-3	F-4	F-5	F-6	F-7	F-8	F-9	F-10	F-11
0.5	22.84 ±0.28	15.36 ±0.21	21.85 ±0.15	16.79 ±0.26	13.75 ±0.28	12.15 ±0.21	12.05 ±0.15	21.03 ±0.26	17.73 ±0.28	22.02 ±0.21	20.58 ±0.15
1	25.79 ±0.34	25.04 ±0.31	24.43 ±0.22	20.20 ±0.37	18.26 ±0.34	15.40 ±0.31	15.18 ±0.22	22.37 ±0.37	20.58 ±0.34	23.58 ±0.31	25.89 ±0.22
2	32.57 ±0.37	35.54 ±0.34	29.41 ±0.19	27.49 ±0.32	26.44 ±0.37	21.97 ±0.34	20.47 ±0.19	29.78 ±0.32	26.79 ±0.37	27.35 ±0.34	33.60 ±0.19
4	44.4± 0.45	51.75 ±0.32	43.71 ±0.14	35.59 ±0.25	36.87 ±0.45	34.92 ±0.32	26.79 ±0.14	39.08 ±0.25	39.21 ±0.45	35.71 ±0.32	43.03 ±0.14
6	56.67 ±0.21	68.10 ±0.25	55.15 ±0.42	47.46 ±0.17	50.88 ±0.21	44.26 ±0.25	34.48 ±0.42	48.80 ±0.17	46.41 ±0.21	42.15 ±0.25	53.86 ±0.42
8	67.44 ±0.43	84.33 ±0.16	67.39 ±0.15	53.08 ±0.19	63.62 ±0.43	53.85 ±0.16	41.61 ±0.15	58.65 ±0.19	56.67 ±0.43	50.67 ±0.16	60.57 ±0.15
10	78.32 ±0.26	96.84 ±0.29	75.11 ±0.43	61.11 ±0.33	76.66 ±0.26	61.84 ±0.29	49.14 ±0.43	68.25 ±0.33	65.15 ±0.26	57.62 ±0.29	71.91 ±0.43
12	91.29 ±0.23	-	82.95 ±0.14	71.24 ±0.16	84.63 ±0.23	71.61 ±0.19	56.75 ±0.14	80.25 ±0.16	72.31 ±0.23	65.63 ±0.19	80.76 ±0.14
14	100.0 ±0.31	-	96.6± 0.25	81.8 ±0.11	96.9 ±0.31	85.5 ±0.14	68.5 ±0.25	91.1 ±0.11	82.1 ±0.31	77.1 ±0.14	92.0 ±0.25
18	-	-	-	97.3 ±0.17	-	98.1 ±0.33	79.0 ±0.1	99.4 ±0.17	98.7 ±0.14	97.1 ±0.33	99.1 ±0.1
24	-	-	-	-	-	-	99.0 ±0.5	-	-	-	-

3.3.2 Physical evaluation of matrix tablets

The results of the uniformity of weight, thickness, hardness, friability, and drug content of the tablets are given in Table 6. All the tablets of different batches complied with the official requirements of uniformity of weight as their weights of the formulations F-1 to F-9 varied between 563.4±0.5 mg to 565.3±0.6 mg and the weights of the formulations F-10 and F-11 varied between 514.4±0.5 mg to 514.6±0.7 mg. The thickness of the tablets ranged from 5.3±0.02 mm to 5.4±0.04 mm. The hardness of the tablets ranged from 9.2±0.12 to 12 ± 0.30 kg/cm^2 and the friability values were less than 0.8 % indicating that the matrix tablets were compact and hard. All the formulations satisfied with content uniformity of the drug as they contained 98.5 to 100.21±0.47 % of naproxen. Thus all the physical attributes of the prepared tablets were found to be practically within control.

3.4 In-vitro dissolution studies

In-vitro drug release depends on several factors, such as the manufacturing process, the type of excipient, and the amount of drug. In this work the effect of matrix forming polymers on naproxen release was studied (Table 7, Fig 9, Fig 10). Naproxen is a weak acid with greater solubility in alkaline than in acidic media, therefore, its release profiles are pH dependent and its solubility is higher when is increased.

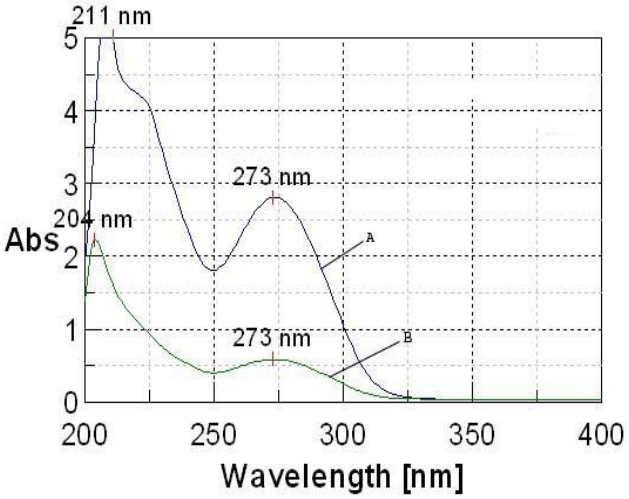

Fig 7. UV-scan of naproxen in phosphate buffer with (A) and without Tweens 80 (B).

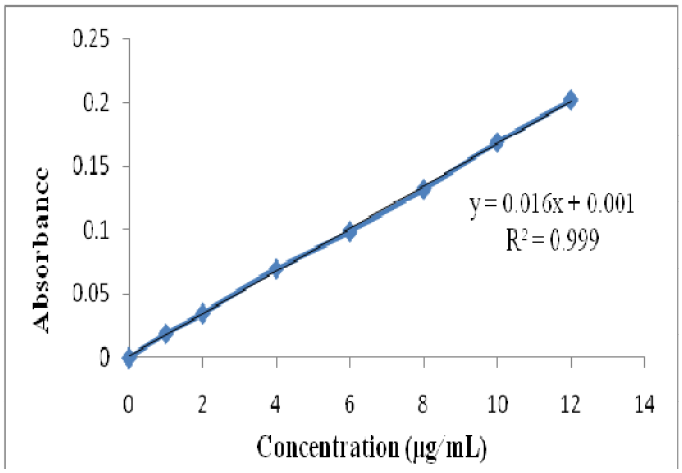

Fig 8. Standard calibration curve of naproxen.

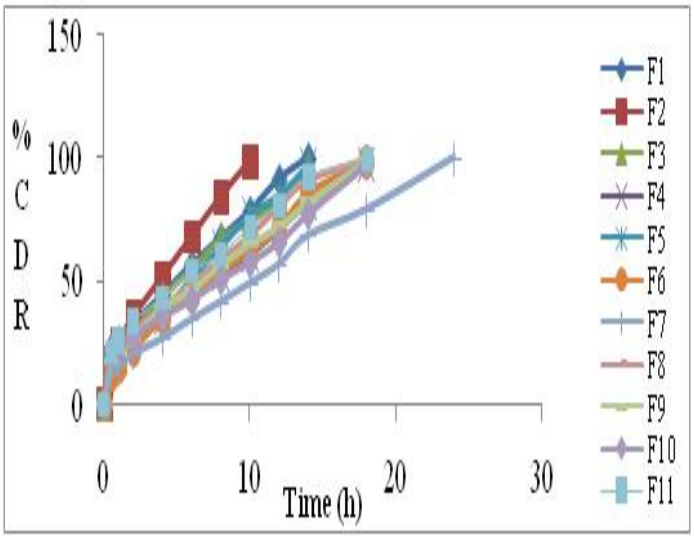

Fig 9. Comparative dissolution of formulations F-1 to F-11.

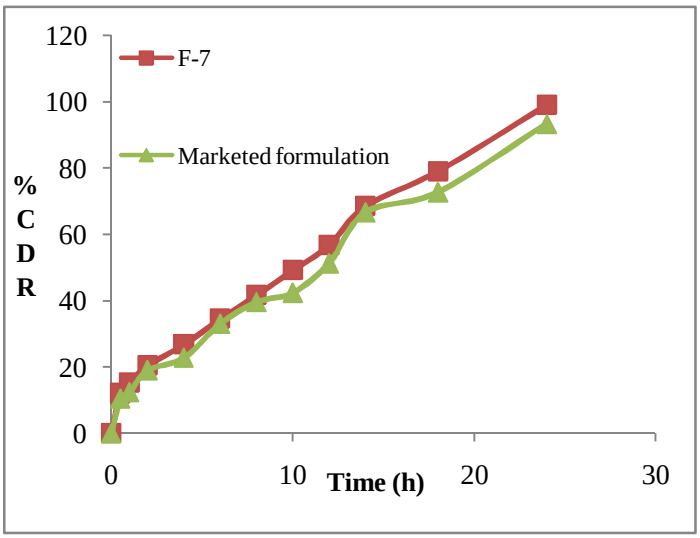

Fig 10. Comparison of optimized formulation with marketed formulation.

Effect of matrix forming polymers on *In-vitro* dissolution was studied using two polymers with different grades of HPMC. The use of HPMC-K4M

and HPM-K100M matrices in different concentrations where in di-calcium phosphate, insoluble filler, in combination with matrix forming agent, formulations F-10 and F-11 with tablet formulated without filler was studied. Formulation F-1 containing ethyl cellulose and moderate amount of HPMC-K4M (low viscosity matrix forming agent) was able to sustain release only for 14h. As combinations of low and high viscosity forming agents were formulated, release was sustained with respect to compositions in formulations F-2, F-3 and F-4.

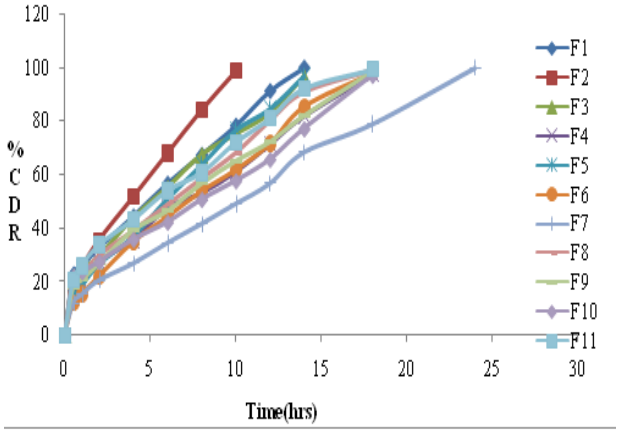

Fig 11. Zero order release graph of formulations F1-F11.

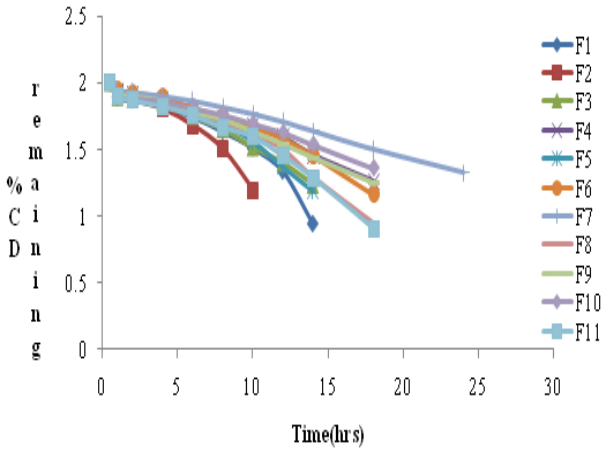

Fig 12. First order release graph of formulations F1-F11.

Trails were also performed to study effect of these matrix forming agents with combinations. In this study release was sustained only for 12-16 h, as these matrix forming agents failed to control rate and extent of release. Hence, trail containing equal amount of both polymers in moderate concentrations was done and found to be sustaining and controlling release for 24 h.

It could be rationalized from this optimized formulation that, initially due to low viscosity of HPMC-K4M, it starts to form matrix rapidly but could not retain its integrity longer than 10-14h. On other side, HPMC-K100M forms matrix at relatively slower rate but could last for 24h. The effect of insoluble filler was also studied in present work. In last two formulations efforts were made to formulate tablets with highest possible matrix forming agents and without insoluble filler DCP. These formulations showed good physical characters, but *In-vitro* dissolution was not able to sustain longer than 16h. This indicates that if we use insoluble fillers with matrix forming agents, it helps to maintain not only integrity of formulation but also provide positive deviation on release from formulation (Fig 11 and 12).

Table 8. Accelerated stability study data of optimized formulation (F-7).

S.No.	Parameters	Time in months			
		0 (initial)	1st month	2nd month	3rd month
1	Weight variation (mg)	564.5 ±0.7	564.3 ±0.6	563.5 ±0.6	563.3 ±0.5
2	Thickness (mm)	5.4 ±0.04	5.4 ±0.04	5.4± 0.02	5.4± 0.03
3	Hardness (kg/cm^2)	10.0 ±0.15	10.0 ±0.15	9.8 ±0.15	9.5± 0.14
4	Friability (%)	0.52 ±0.01	0.52 ±0.01	0.53 ±0.01	0.53 ±0.03
5	Assay	99.0 ±0.3	99.20 ±0.4	99.35 ±0.4	98.0 ±0.38
6	*In-vitro* drug release (%)	99.0 ±0.5	99.0 ±0.5	98.85 ±0.9	97.56 ±0.8

3.5 Accelerated stability studies

The optimized formulation, F7 was found to be stable for three months at accelerated stability conditions at a temperature (40 ± 2^0 C) and relative humidity 75 ± 5% as per ICH norms. Prominent changes in physical evaluation parameters like weight variation, thickness, hardness, friability, assay and *in-vitro* drug release were not noticed and the formulation F7 was found to be stable even after exposing to accelerated temperature and humidity conditions and gives the results (Table 8) of

accelerated stability study data of optimized formulation (F-7).

In the present study, formulation and evaluation of oral sustained release matrix tablets of naproxen were prepared by wet granulation technique by employing different concentration of HPMC-K4M, HPMC-K100 and DCP to achieve sustained release of drug. The effect of insoluble filler was also studied in present work. The results indicate that if we use insoluble filler with matrix forming agents, it helps to maintain not only integrity of formulation but also provide positive deviation on release from formulation (Vinay *et al.,* 2011; Ali Kadivar *et al.,* 2015). From the pre-formulation studies for drug excipient compatibility, it was observed that the selected excipients used in this study were not involved in any physical changes of the drug. FT-IR studies confirmed that no chemical interaction and indicating stability of drug in tablets

The formulated batches were evaluated for physicochemical parameters and dissolution profiles. The physical parameters like weight variation, thickness, hardness, friability and assay of all formulations complied with the pharmacopoeial specifications.

4. Conclusion

It may be concluded from the present study that slow, sustained release of naproxen matrix tablets over a period of time 24 h was obtained by formulating equal amount of both polymers (HPMC-K100, HPMC-K4M) along with insoluble filler (DCP). Increase in viscosity of the polymer caused decrease in the release of the drug from the polymer matrix. The mechanism of drug release for optimized tablet formulation (F7) was found to be non-Fickian diffusion controlled. Optimized tablet formulation (F7) were compared with marketed formulation and in these study it was found that it, has got better drug release profile than marketed formulation.

Acknowledgments

The authors are thankful to LEE Pharma Ltd., Hyderabad, India for their help in completion of research work and Ganapathy PAV, Production manager, LEE Pharma Ltd., Hyderabad, India for his encouragement during the research work.

Conflict of Interest

Authors declare none.

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