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Formulation, Evaluation and Optimization of Orodispersible Tablets of Naproxen Sodium 250 Mg

[1] Ansari Mohd. Razi*, [2] Dr. Sumer Singh, [3] Dr. Quazi Majaz, [1] Ansari Yaasir Ahmed [1] Jameel Abbas,

[1] Research Scholar, School of Pharmacy and Medical Sciences, Singhania University, Pacheri Bari, Dist-Jhunjhunu

[2] Asso. Professor, School of Pharmacy and medical Sciences, Singhania University, Pacheri Bari, Dist-Jhunjhunu

[3] Asso. Professor, Ali Allana College of Pharmacy, Akkalkuwa, North Maharashtra University, Jalgaon.

ABSTRACT

Among the different type of route of administration oral route for drug administration is most common route in which Orodispersible tablet is preferred for the patient which are unconscious, week or for immediate control. The tablet gets dispersed in mouth cavity without water, present study deals with formulation of Naproxen sodium mouth dissolving tablets using super disintegrants. Naproxen sodium is analgesic and NSAID, used for the treatment of pain and inflammation caused by different condition such as osteoarthritis, rheumatoid arthritis and menstrual cramps. However gastric discomfort caused by naproxen sodium result in poor patient compliance associated with it conventional doses form but now days Naproxen sodium MDTs produces rapid onset of action and minimise gastric discomfort associated with it. Thus improves patient compliance, enhance bioavailability and reduces the dose of drug. MDTs are formulated by direct compression method using super disintegrants in different proportion. The powder blend is subjected to pre-compression evaluation parameters like bulk density, true density, and tapped density and angle of repose. Formulations are evaluated for weight variation, hardness, wetting time, water absorption time, disintegration time. And in vitro dissolution studies and all formulations complies Pharmacopoeias standards. The tablets are evaluated and result compared for all five formulations the most efficacious super disintegrants for MTDs of Naproxen sodium as suggested by the dispersion time, disintegration time and drug dissolution profiles.

Keywords: Mouth Dissolve Tablet, Naproxen Sodium, crosscarmellose Sodium, Sodium starch glycolate.

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***Address for Correspondence:**

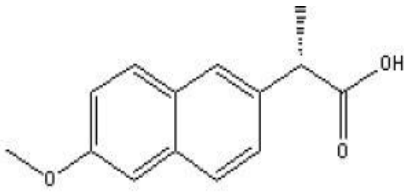
Ansari Mohd. Razi, Research Scholar, School of Pharmacy and Medical Sciences, Singhania University, Pacheri Bari, Dist-Jhunjhunu

1. INTRODUCTION:

Naproxen Sodium is a non-steroidal anti-inflammatory agent useful for the treatment of pain inflammation and fever caused by the conditions such as arthritis, migraine and menstrual cramps. It has a good solubility in water and saliva and inherent ability to permeate through oral mucosal tissue, drug moiety is weak acidic so remains in partially non ionised form at oral pH which favour pre gastric absorption. These parameter makes the drug ideal character for MTD. These tablets display a fast and spontaneous de-aggregation in mouth, soon after the contact with saliva, the active agent can thus rapidly dissolved in the saliva and be absorbed through whatever membrane it encounters, during deglutition, unless it is protected from pre-gastric absorption. To fulfil these requirements tablets must be highly porous, incorporating hydrophilic excipients, able to rapidly absorb water for a rapid de-aggregation of the matrix. Different technological techniques, such as freeze drying, moulding and direct compression currently employed to prepare the formulation of this type present in the pharmaceutical market. The aim and objective of the present study is to develop and evaluate orodispersible tablet of Naproxen sodium and enhance the onset of action of Naproxen and also to study the influence of excipients on the physical characteristics of the tablets by applying two level three factor factorial designs taking Naproxen as model drug.

2 MATERIALS AND METHOD

2.1 API Structure Characterisation:
Molecular Formula: $C_{14}H_{14}O_3$
Molecular mass: 230.26
Melting point: 154^0C to 158^0C
State/ Form: White Powder.
Description: Naproxen is an odourless, White to off white crystalline powder.



Structure and IPUAC Name of Naproxen

Chemical Name: (+)-2-(6-methoxy-2-naphthyl)-propionic acid**.**

2.2 Pre formulation Study:

Drug Solubility: As per research study from the Naproxen Sodium Wikipedia

The Drug is soluble in lipid, practically insoluble in water at low pH and freely soluble in water at high pH. It is soluble in ethanol (95%) and in methanol. Solubility of drug in different solvent given in below table.

S. No.	Solvent	Solubility
1	Lipid	Soluble
2	Water	Insoluble at low pH
3	Water	Freely Soluble at high pH
4	Ethanol	Soluble
5	Methanol	Soluble

2.3 Drug and Excipients study:

S. No.	Drug + Excipient	Duration (Months)	Result
1	Naproxen Sodium	6 Months	Stable
2	SSG	6 Months	Stable
3	CCS	6 Months	Stable
4	Crospovidone	6 Months	Stable
5	Aspartame	6 Months	Stable
6	Sodium CMC	6 Months	Stable
7	Mannitol	6 Months	Stable
8	Starch DC grade	6 Months	Stable
9	Magnesium stearate	6 Months	Stable
10	Talc	6 Months	Stable
11	Lactose	6 Months	Stable
12	MCC	6 Months	Stable

2.4 Material: Material and their use with obtained sources:

S. No.	Material	Duration (Months)	Result
1	Naproxen Sodium	Active Ingredients	Iosis Pharma
2	Lactose	Diluent	Pacific India. A Pharmaceutical exporter, Village-Dhana, Bagbania Nalagarh, Solan, (H.P.)
3	Microcrystalline cellulose	Diluent	
4	SSG	Disintegrants	
5	CCS	Super Disintegrants	
6	Crospovidone	Disintegrants	
7	Aspartame	Diluents	
8	Sodium CMC	Diluents	
9	Mannitol	Diluents	
10	Starch DC grade	Antiadhrants	
11	Magnesium stearate	Glidant	
12	Talc	Lubricants	

2.5 Preparation of Naproxen tablet by direct compression method:

Formulation Table:

Serial No.	Ingredients	C1 (mg)	C2 (mg)	C3 (mg)	C4 (mg)	C5 (mg)
1	Naproxen Sodium	250	250	250	250	250
2	SSG	10	10	10	10	10
3	CCS	20	15	10	5	--
4	Crospovidone	10	10	10	10	10
5	Lactose	10	10	10	10	10
6	Aspartame	5	5	5	5	5
7	Sodium CMC	10	10	10	10	10
8	Mannitol	50	50	50	50	50
9	Starch DC grade	57.5	62.5	67.5	72.5	77.5
10	MCC	15	15	15	15	15
11	Magnesium stearate	5	5	5	5	5
12	Talc	7.5	7.5	7.5	7.5	7.5
13	Total weight	450	450	450	450	450

All the ingredients of formulation i.e. Active ingredients and additives were passed through 60 # sieve separately, Magnesium stearate and talc through 40 #, The ingredient were mixed by geometrical mixing and Tablet were compressed on 9 mm sizes of biconvex round punch to get tablet by using Rimeck Single rotary compression machine.

3. Post compression parameters:

3.1 Thickness of compressed tablets:

The thickness of the compress tablets of Naproxen Sodium was determined using a Digital Vernier calliper. Ten tablets from each type of formulation were measure and average values were calculated in mm.

3.2 Hardness:

The crushing strength of 10 tablets of each formulation was measured using Monsanto hardness tester and Pfizer harness tester. The tablet was hold along its oblong axis in Between the two jaws of the tester. At this point, reading should be zero kg/cm2. Then constant force was applied by rotating the knob in Monsanto tester and in case of Pfizer directly force applied until the tablet breakdown in the pieces. The reading the both cases at this point was noted.

3.3 Friability Test:

Friability Test is generally used to measure of tablet strength. Roche Friability tester was used for testing the friability using. In This test subjects a number of compressed tablets to the combined effect of shock abrasion by utilizing a circular plastic chamber which revolves at a speed of 25 revolutions per minutes for 4 minutes i.e. 100 rpm, dropping the compressed tablets to a distance of 6 inches in each revolution. A sample of Pre weighed 10 compressed tablets was placed in Roche friability chamber which was then operated for 100 revolutions i.e. 4 minutes. The tablets were then de-dusted and reweighed. A loss of less than 1 % in weight is generally considered and acceptable according to Pharmacopeia. Percentage friability (% F) was calculated as follows:

$$\% \text{ Friability} = \frac{\text{Initial Weight} - \text{Final Weight}}{\text{Initial Weight}} \times 100$$

3.4 Weight variation test:

As per the limitation of Pharmacopeia to find out weight variation test, 20 tablets of each type of formulation were weighed individually using single pan balance or an electronic balance, average weight was calculated and individual tablet weight was then compared with average value to find the deviation in weight.

Specifications for tablets as per Indian pharmacopoeia 1996:

S. No.	Average Weight of Tablet (mg)	Percentage Deviation
1	80 mg or less	10
2	More than 80 mg but less than 250 mg	7.5
3	250 mg or more	5

3.5 Uniformity of Drug content:

Five tablets of each compressed formulation are weighed and crushed in mortar Pastel and powdered, A quantity of powder equivalent to one tablets i.e. 450 mg was weighed and dissolved in 100 ml of 0.1 N Hydrochloric acid (pH 1.2). This was the stock solution from which 0.2 ml sample was withdraw and diluted to 10 ml with the help of 0.1N Hydrochloric acid. The drug content was estimated by recording the absorbance 272 nm by using UV- visible spectrophotometer. Content uniformity of the drug was calculated using formula.

% Purity of the Drug = 10 C (Au / As) -------

Where, C = Concentration,

Au and As=Absorbance's obtained from unknown preparation and standard Preparation.

3.6. Wetting time:

This method is applied to calculate tablet wetting time. A piece of tissue paper or absorbent folded twice was placed in a small Glass Petri dish having the diameter 6.5 cm, containing 10 ml of water. Compressed tablet was placed on the paper, and the time record or note for complete wetting.

Three trials for each batch were performed and standard deviation calculated.

3.7. In vitro disintegration time:

The process of breakdown or convert the tablet into pieces or into smaller particles is called as disintegration. The in vitro Disintegration time of a tablet was determined using disintegration test apparatus as per Indian Pharmacopeia specifications. Place one tablet in each of the 6 tubes of the basket. Add a disc to each tube and run the apparatus using distilled water maintained at 37° ± 2°C which is similar to body temperature. The assembly should be raised and lowered between 30 cycles per minute in the 0.1 N HCL or Distilled water maintained at 37° ± 2°C. Time taken in second for complete disintegration of the tablet. In this disintegration test if the tablets are adhere to the 10 # sieve then continue the test till all tablets are completely disintegrated.

3.8. In vitro dissolution test:

Rate of dissolution are studied by using USP type-II apparatus having 50 rpm, using 900ml of 0.1 N Hydrochloric acid as dissolution solvent. Temperature of the dissolution medium was maintained at 37 ± 0.5°C. The sample of dissolution medium was withdrawn at every 5 min interval and first filtered. The absorbance of filtered solution was measured by using Ultra Violet spectro photometric method at 272 nm and concentration of the drug was determined from standard calibration curve.

4. RESULT AND DISCUSSION:

4.1 Pre compressed parameter and studies:

S. No.	Formulation code	Angle of Repose	Bulk Density (Weight/ml)	Taped Density (weight/ml)
1	C1	25.74±0.45	0.41±0.02	0.48±0.02
2	C2	27.92±0.70	0.41±0.02	0.49±0.04
3	C3	27.40±0.69	0.42±0.03	0.48±0.02
4	C4	28.36±0.63	0.42±0.03	0.49±0.04
5	C5	26.10±0.56	0.41±0.02	0.48±0.02

4.2 Post compression parameter Studies:

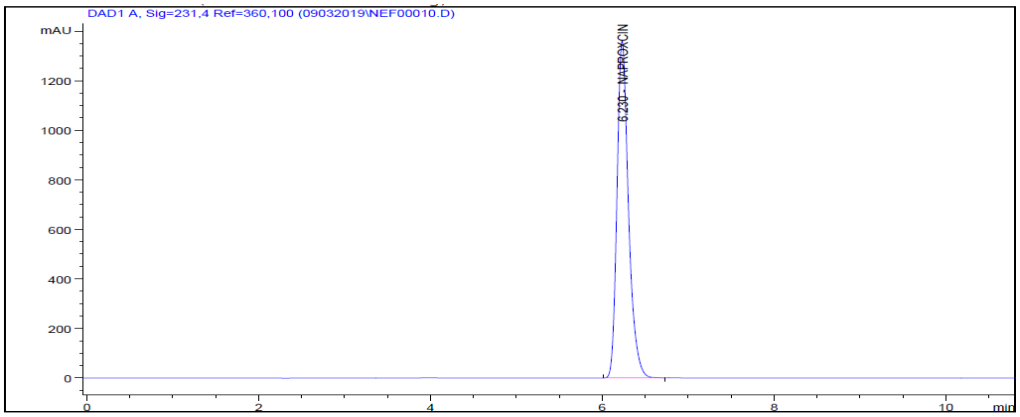
Formulation code	Hardness (Kg/cm2)	Friability (%)	Thickness (mm)	Diameter (mm)	Weight (mg)
C1	8.0	0.08	4.54	9.02	452
C2	8.5	0.09	4.55	9.03	448
C3	9.0	0.15	4.51	9.01	454
C4	7.7	0.31	4.48	9.02	446
C5	8.5	0.01	4.53	9.03	456

4.3 Post compression Studies:

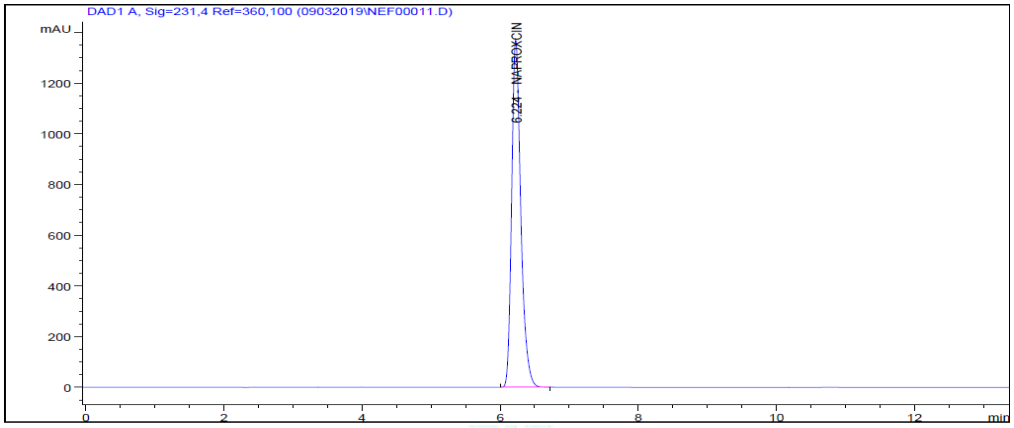
Formulation code	Assay of Drug (%)	Disintegration Time (Sec)	Dissolution (%)	Water Intake Time (Sec)
C1	101.13	8 to 12	98.92	8
C2	100.39	9 to 24	95.68	13
C3	101.84	16 to 30	93.76	12
C4	98.59	22 to 38	90.86	20
C5	99.30	31 to 55	86.89	23

4.4 Post compression studies of graphs:

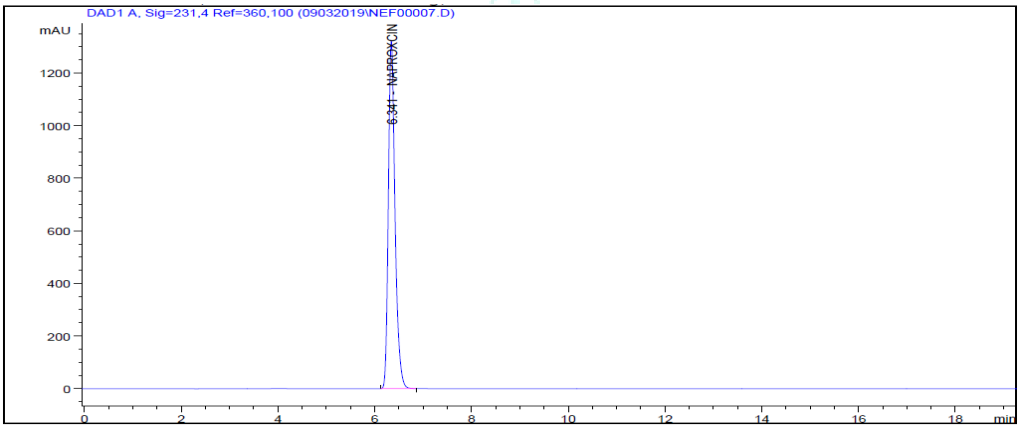
4.4.1 Graph of C1 formulation: Naproxen 250 mg orodispersible tablet.



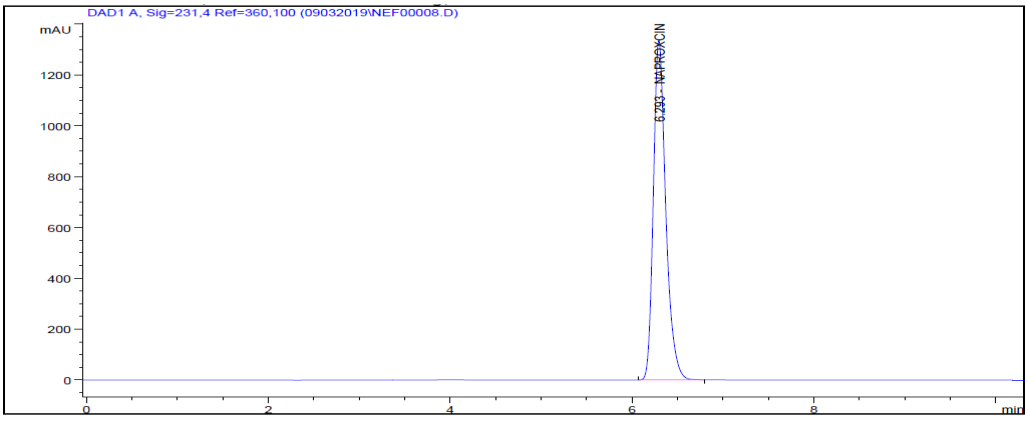
4.4.2 Graph of C2 formulation: Naproxen 250 mg orodispersible tablet.



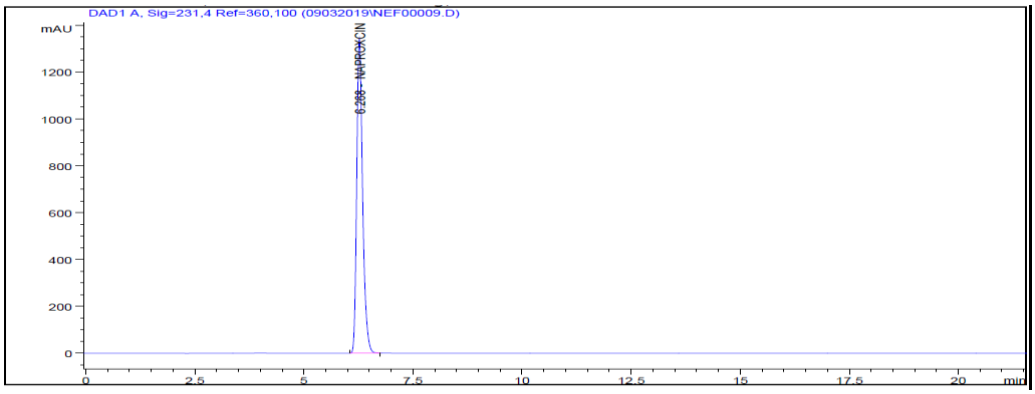
4.4.3 Graph of C3 formulation: Naproxen 250 mg orodispersible tablet.



4.4.4 Graph of C4 formulation: Naproxen 250 mg orodispersible tablet.



4.4.5 Graph of C5 formulation: Naproxen 250 mg orodispersible tablet



5. CONCLUSION:

After completion of this experiment the results obtained and conclude that development of orodispersible tablet of Naproxen sodium formulation by using super disintegrants i.e. Cross carmillose sodium gives the result of dissolution more than mentioned in the Pharmacopeia. Some results are mentioned below:

1. Naproxen Sodium Active drug stable with different excipients.
2. Fast Disintegrating tablets of Naproxen Sodium were successfully prepared by direct compression method.
3. The flow property of the granules of three batches (C1,C3,C5) are better than two other formulation (C2,C4) and uniformity of the compressed tablets are also better.
4. The angle of repose of prepared granules are found less than 30º.
5. The hardness of compressed tablet by direct compression method found in the rage of 7.7 to 9.00 kg/cm2.
6. The Thickness of the prepared tablets of all 5 formulations was found between 4.48 mm. to 4.55 mm.
7. The Friability of the compressed tablet found within the range i.e. less than 1%.
8. The in vitro disintegration studies are found to be in 8 to 55 seconds. Formulation C1 show in vitro disintegration time i.e. 8 seconds.
9. On the basis of disintegration time formulation C1 which facilitate the faster disintegration in the mouth. The *in-vitro* percentage drug releases from fast dissolving tablets of Naproxen Sodium prepared by direct compression method were found to be in the range of 98.59 to 101.84%. Hence, finally it was concluded that the prepared orodispersible tablets of Naproxen Sodium 250 mg may prove to be potential candidate for effective fast disintegrating tablet dosage form.

REFERENCES:

1. Neha vishal et al. Formulation and Evaluation of orodispersible Tablets of Naproxen Sodium, International journal of Pharmaceutical Science and Research, 2011; 2(II):2983-2990.
2. Vijay Kumar Volity et al. Formulation and Evaluation of mouth dissolving Tablets of Naproxen Sodium International journal of Pharmacy and Industrial Research, 2013;03(01):64-69.
3. D. Bhowmik et al. Fast Dissolving Tablet: An over view, Journal of chemical and Pharmaceutical Research, 2009: 163-177.
4. Tripathi KD. Essential of Medical Pharmacology. Jaypee Broters Medical Publishers, 5th Edition, New Delhi, 2003: pg.177.
5. Marshall K, Lachman L, Liberman HA, The Theory and practice of industrial Pharmacy, 3rd ed. Mumbai: Varghese Publishing house; 1987: pp.66-69.
6. Mahaveer Pra. Khinchi, orally disintegrating tablets: A future prospectus. Int J Pharm, Sci Boi., 2010: 71-79.
7. Neha VD Khadabadi SS Angadi SS, Formulation and evaluation of orodispersible tablets of Naproxen Sodium using three super disintegrants at Different concentration. International Journal of Pharmaceutical Science and Research, 2011: 2983-2990.
8. Hardman JG, Libird LE. Goodman and Gilman's The Pharmaceutical Basis of Therapeutics. Mc Graw-Hill Medical Publishing Division, 10th Edition: pp.710-712.
9. Jekku NSR Nagaraja TS Bharthi Devi Reddy M, formulation and evaluation of naproxen sodium rapimelt by direct compression method using different super disintigrant in formulation, IJPLCP, 2013; 2615-2620.
10. Jejveerkaur, Bhawandeep Gill, Sandeep, D.G. Gupta, Mouth dissolving tablets: A novel approach to drug delivery, Int J Curr Pharm Res, 2011;3(1): 1-7.