International Journal of Pharmaceutical Science and Research
www.pharmacyjournal.net
ISSN: 2455-4685
Received: 23-03-2024, Accepted: 13-04-2024, Published: 07-05-2024
Volume 9, Issue 2, 2024, Page No. 30-36

Development and evolution of a mouth-dissolving tablet incorporating naproxen sodium

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Abstract
Naproxen sodium is an analgesic NSAID intended for the treating fever, pain, stiffness, as well as inflammation which may have multiple causes such as dysmenorrhea, gout, migraine, rheumatoid arthritis, osteoarthritis, and juvenile arthritis. However, the drug is known to cause gastric discomfort leading to poor compliance amongst patient with the conventional dosage form. Hence, it was thought worthwhile to develop Oro dispersible tablet of naproxen sodium, which serves the dual function of quickening the onset of action and minimizing the gastric issues associated with it so that patient compliance can be improved, bio-availability can be enhanced and drug's dose can be reduced.

Keywords: Evolution, oro dispersible, naproxen, development, incorporating

Introduction

The oral delivery of drug is one of the oldest and most utilized routes for drug's administration. Although, a variety of routes such as parenteral, nasal, rectal, ocular, as well as transdermal are available for the delivery of drugs. Yet, oral route is predominately used because of the numerous advantages associated with it. The advantages of an oral drug delivery system over other conventional dosage forms are higher patient compliance, ease of administration.

Drug Delivery Systems (DDS) are tools which can be used strategically for such purposes as expansion of markets/indications, extension of life cycles of products, and generation of opportunities. DDS are rapid moving tools which, by such strategies as market segmentation, affect sales of pharmaceuticals globally. With an increase in knowledge and understanding amongst pharmaceutical scientists of the parameters (biochemical as well as physicochemical) affecting their performance, DDS are going through continuous sophistication. Although, delivery of the drug to patients has gone through incredible advancements, yet the oral route of drug administration remains as the most preferred route because of ease of administration, avoidance of pain, accurate dosage, and versatility, which in turn results into high patient compliance. From amongst the variety of dosage forms which can be administered orally, tablets and capsules come with highest popularity. However, 'Dysphasia' or difficulty in swallowing is one of the most important drawbacks that presents itself with these dosage forms especially in such conditions as

- Children
- Elderly patients
- Parkinsonism
- Unconsciousness
- Motion sickness
- Mentally challenged persons
- Water unavailability.

Materials and Methodology

Table 1: List of Materials

S. No.	Ingredients	Category
1	Naproxen Sodium	NSAID (API)
2	Urea	Sublimating agents
3	Cross Carmellose sodium	Super Disintegrants
4	Sodium starch glycolate	Super Disintegrants
5	Crospovidone	Super Disintegrants
6	Aspartame	Sweetener
7	Magnesium stearate	Lubricant
8	Talc	Glidant
9	Micro crystalline cellulose	Diluent/binder/disintegrant
10	Mannitol (q. s.)	Diluent (sugar-based excipient)

Table 2: List of Equipment

S. No	Instrument Used	Manufacturer
1	Electronic weighing balance	Mettler, Switzerland
2	Max mixer	Innofab India pvt.ltd, Hyderabad
3	Fluidized bed dryer	Alliance, Bombay
4	Cadmill	Cadmach, Ahemedabad
5	Tablet Compression Machine 45 station double rotary	Cadmach, Ahemedabad
6	Friability Tester	Veego, Mumbai
7	Tablet Hardness Tester	Electrolab, Mumbai
8	Bulk density apparatus	Electrolab, Mumbai
9	Blender	Bhuvaneswari, Mumbai
10	Dissolution Apparatus	Veego, Mumbai
11	Tablet Disintegeration Apparatus	Veego, Mumbai
12	FT-IR Spectrophotometer	Perkin Elmer, USA

Results and Discussion

Identification of Drug

UV- Spectrophotometric study

UV- spectrophotometric study was carried out for the determination of λ_{max} and observed λ_{max} was found to similar with literature value. Absorbance observed at about 230 nm is 0.280 for a solution of 10µg/ml.

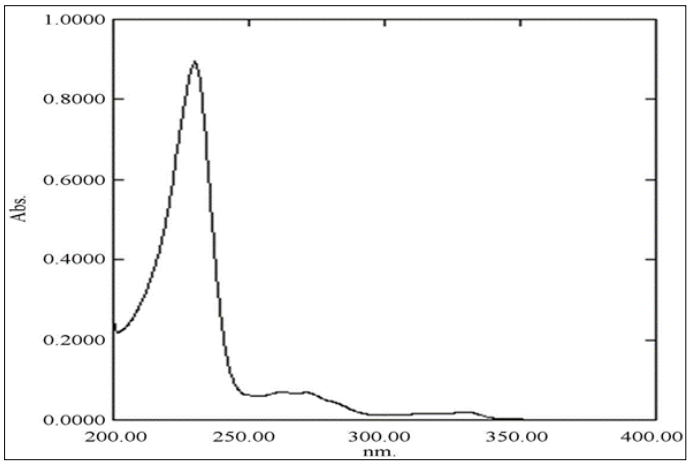


Fig 1: UV Absorption Spectrum of Naproxen Sodium

Melting Point Determination

The melting point of Naproxen Sodium was found to be 156° C, which is same as that reported in the literature (155-159° C). Thus, purity as well as identity of drug is established.

Solubility studies

The solubility was found to be same as that reported in literature values. This proves the identity of Naproxen Sodium.

FTIR Spectra

Table 3: Characteristics IR Peaks of Naproxen Sodium

S. No.	Wave number in cm-1	Characteristics
1	3078.18 - 2935.46	Aromatic C-H stretching
2	2850.59 – 2358.78	Overtone
3	1683.74	C= O stretching
4	1577	Presence of C-O stretching
5	1504.37 – 1396.37	CH_3, CH_2 bending
6	1182.28	C-O bending
7	958.59 – 640.32	CH_2 bending

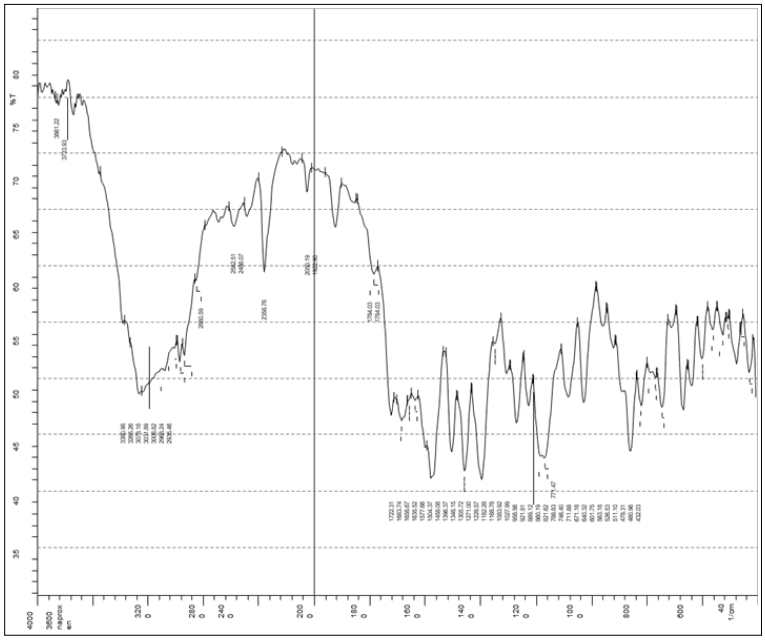


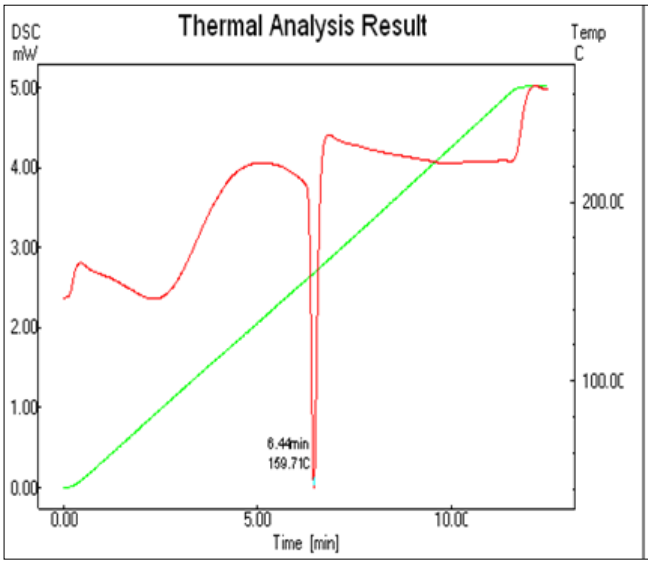
Fig 2: FT-IR Spectrum of Naproxen Sodium

All the above peaks are found to be similar as in the literature findings thus FTIR data identity and purity of Naproxen sodium.

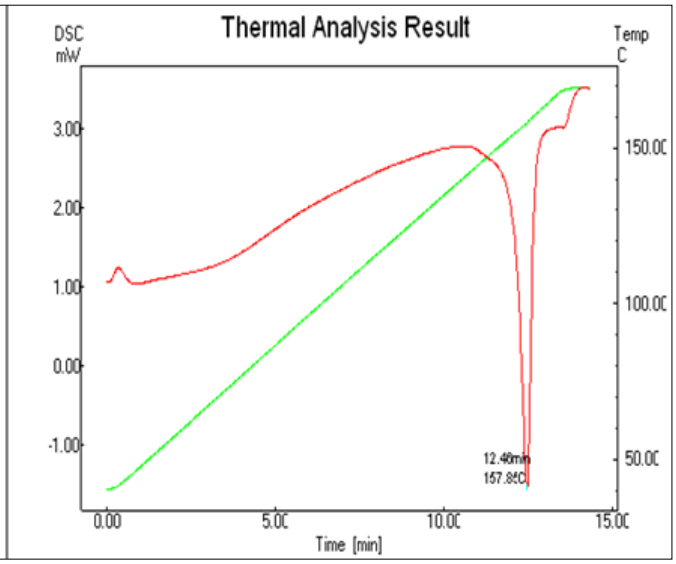
Compatibility Study

DSC spectra of following sample

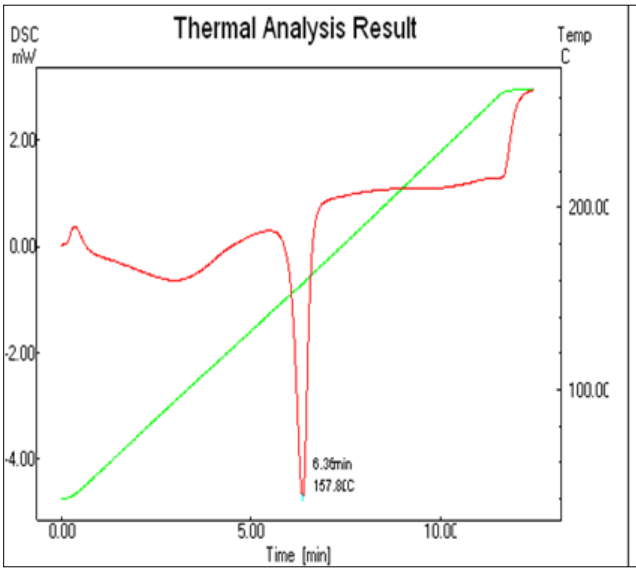
- Drug- Naproxen sodium
- Drug+Croscarmellose sodium
- Drug+Sodium starch glycolate
- Drug+Crospovidone



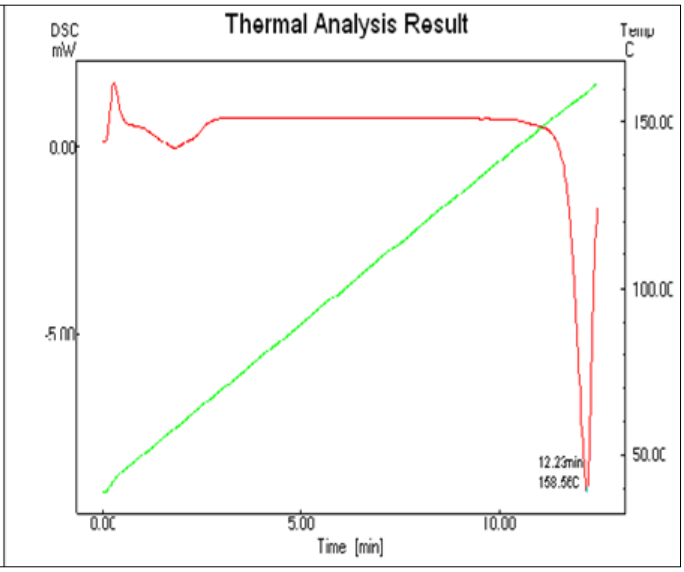
DSC spectra of Naproxen Sodium



DSC spectra of Drug+Croscarmellos sodium



DSC Spectra of Drug+Sodium starch glycolate

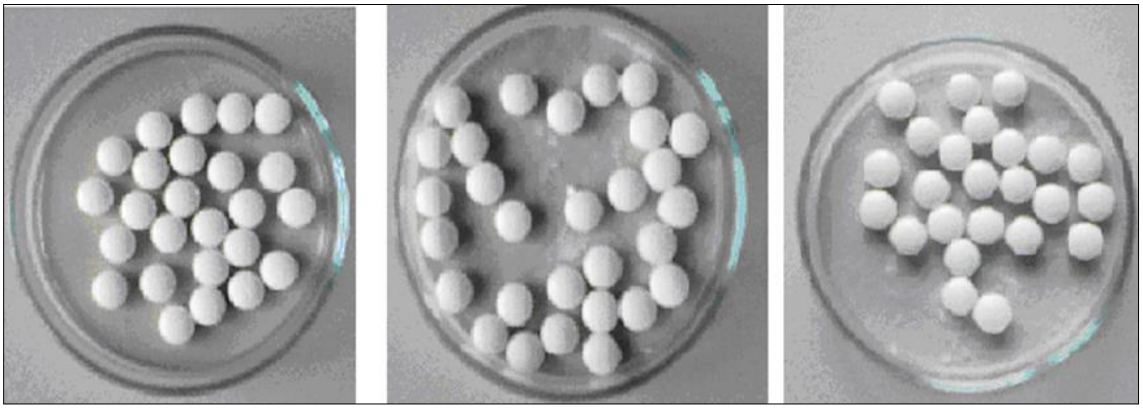


DSC Spectra of Drug+Crospovidone

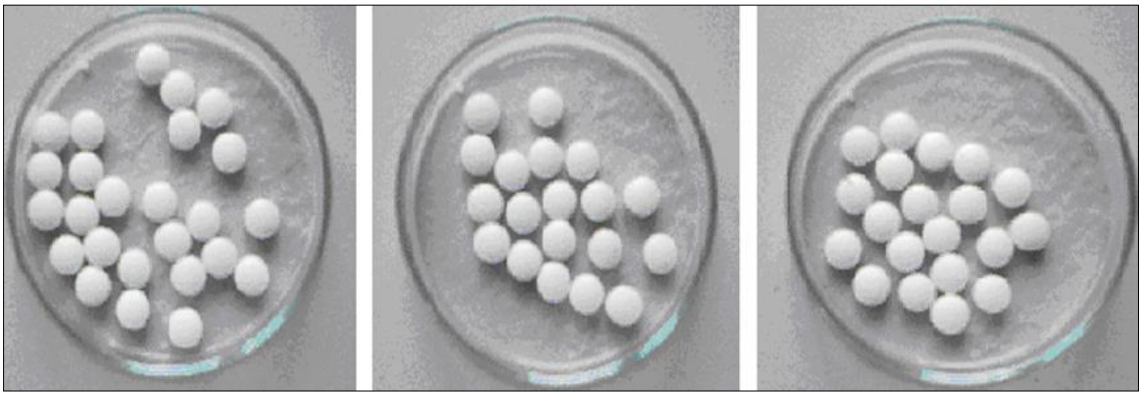
Fig 3: DSC Spectra of drug and super disintegrant

Formulation development of MDT

MDT of Naproxen sodium were formulated by using different type of super disintegrants by the employment of method of direct compression while MCC was used as diluent. Magnesium stearate was incorporated as lubricant. All ingredients were mixed and passed through a mesh ≠40. All ingredients were weighed accurately according to formula given in table no.7.2 and blended. The lubricated blend was compressed in to tablet of average weight of 220 mg in eight station rotatory tablet machine. Nine different formulation were prepared by the method of direct compression by using different type of superdisintegrator.



F1 Croscarmellose sodium (2%) F2 Croscarmellose sodium (3%) F3 Croscarmellose sodium (4%)



F4 Sodium starch glycolate (2%) F5 Sodium starch glycolate (3%) F6 Sodium starch glycolate (4%)

F7 Crospovidone (2%) F8 Crospovidone (3%) F9 Crospovidone (4%)

Fig 4: Photographs of different formulations containing different type of super disintegrators

Characterization of Blend

The dried blends of different formulations were subjected for evaluation for micrometric properties i.e. Bulk density, Angle of repose, Tapped density, % compressibility, Hausner ratio. The results are as follows.

Table 4: Result of evaluation

Formulation Blend	Angle of Repose	Bulk Density	Tapped Density	% Compressibility	Hausner Ratio
F1	28.002±0.623	0.540±0.004	0.822±0.002	30.30%	1.53
F2	30.034±0.765	0.535±0.007	0.852±0.006	31.20%	1.4
F3	27.056±0.543	0.561±0.002	0.857±0.003	34.53%	1.52
F4	26.074±0.645	0.583±0.006	0.845±0.008	31.00%	1.44
F5	25.02±0.456	0.545±0.007	0.801±0.012	31.96%	1.46
F6	24.17±0.234	0.567±0.002	0.834±0.004	32.01%	1.47
F7	27.45±0.342	0.540±0.015	0.869±0.008	29.85%	1.60
F8	26.74±0.368	0.535±0.005	0.823±0.003	34.99%	1.53
F9	28.65±0.356	0.540±0.014	0.846±0.007	29.17%	1.56

(values are mean ±SD, N=3)

Evaluation of Mouth Dissolving Tablets of Naproxen Sodium prepared by Direct Compression Method

Evaluation of physical parameters

The Prepared Mouth Dissolving Tablets of Naproxen Sodium were subjected to a variety of physical parameters as discussed below. The results are as follows

Table 5: Characteristics of Mouth Dissolving Tablets of Naproxen sodium

Formulation code	Thickness(mm)	Weight variation	Hardness(kg/cm^2)	Friability	Content Uniformity(%)
F1	4.1±0.004	PASS	3.0±0.267	0.679±0.135%	96.27±0.654
F2	4.1±0.003	PASS	2.7±0.345	0.826±0.245%	97.65±0.576
F3	4.0±0.008	PASS	2.8±0.567	0.606±0.541%	99.01±0.634
F4	4.2±0.007	PASS	3.0±0.654	0.755±0.326%	95.67±0.234
F5	4.1±0.003	PASS	2.8±0.734	0.687±0.256%	97.45±0.276
F6	4.1±0.001	PASS	3.0±0.392	0.823±0.412%	98.45±0.134
F7	4.0±0.005	PASS	2.5±0.437	0.954±0.264%	97.60±0.463
F8	4.1±0.002	PASS	2.6±0.649	0.755±0.321%	96.00±0.865
F9	4.2±0.004	PASS	2.7±0412	0.603±0.348%	97.34±0.768

(value is mean ± SD, N=3)

Evaluation of other parameters

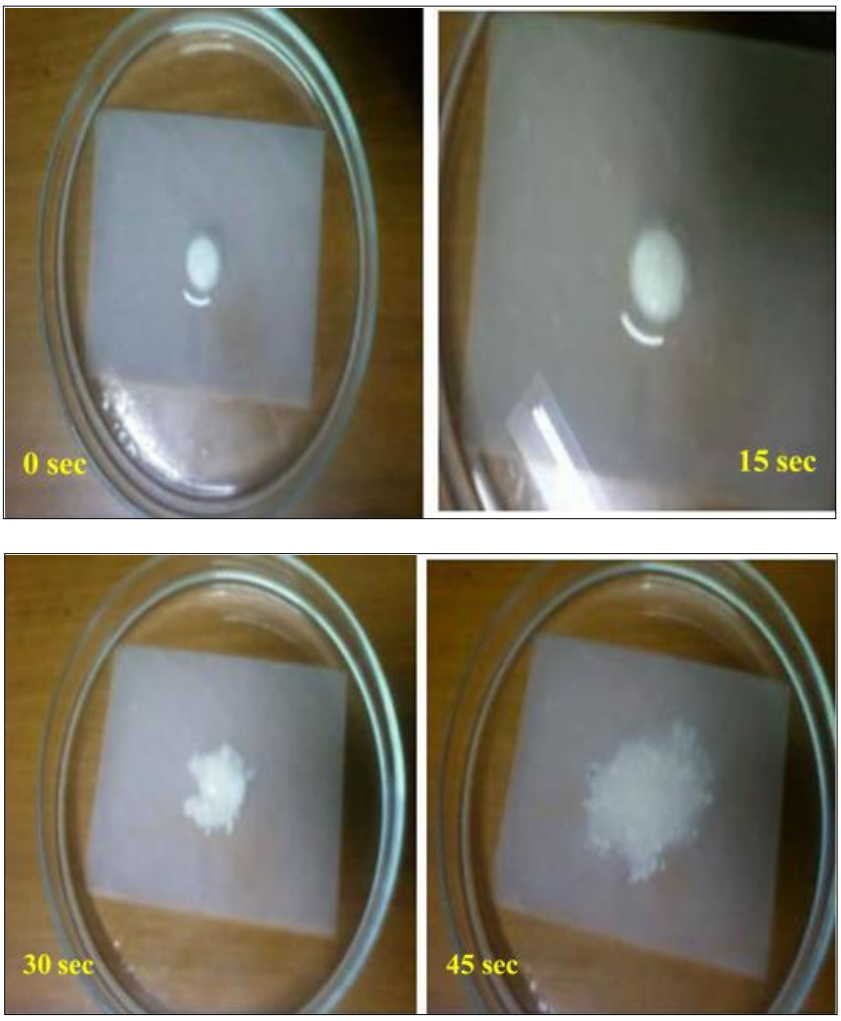


Fig 5: Wetting of tablet at different time

Table 6: Other evaluation tests of tablets

Formulation code	Wetting time(sec)	Water absorption ratio(%)	Disintegration Time (sec)	In-vitro Dispersion time(sec)
F1	85	69	28	75
F2	79	71	26	70
F3	75	81	25	68
F4	65	73	23	48
F5	60	75	22	46
F6	60	73	22	40
F7	52	80	19	30
F8	48	92	17	25
F9	45	85	16	23

In-vitro release study

Calibration curve of Naproxen Sodium in pH 6.8 phosphate buffer

Table 7: Calibration curve of Naproxen Sodium in pH 6.8 phosphate buffer

S.No.	Concentration in µg/ml	Absorbance at 232 nm
1	5	0.185
2	10	0.285
3	15	0.396
4	20	0.494
5	25	0.594
6	30	0.687
7	35	0.826
8	40	0.989
9	45	1.165
10	50	1.235

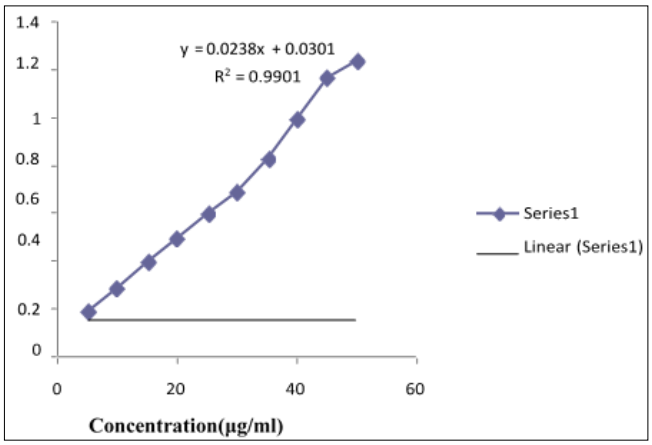


Fig 6: Calibration Curve of Naproxen Sodium in pH 6.8 Phosphate Buffer

Table 8: Drug release study of the Mouth Dissolving Tablets in simulated salivary fluid pH 6.8

S.No.	Time (min)	% cumulative drug release								
		F1	F2	F3	F4	F5	F6	F7	F8	F9
1	2	44.73	45.66	46.17	45.30	46.89	46.67	46.10	47.10	47.75
2	5	55.49	56.00	56.51	55.78	56.37	56.80	57.08	57.81	58.17
3	10	64.72	65.74	66.11	65.02	65.60	66.25	67.12	67.85	69.08
4	20	70.12	70.78	71.29	71.06	71.80	72.45	72.74	73.63	73.99
5	30	76.63	77.43	77.88	76.56	77.23	77.89	79.48	80.36	81.17
6	40	82.80	83.40	83.10	83.10	83.85	84.43	88.19	88.79	89.60
7	50	91.53	92.35	91.98	91.98	92.94	93.75	95.58	96.55	97.36
8	60	94.94	95.33	96.39	97.39	98.42	98.44	98.41	99.52	99.36

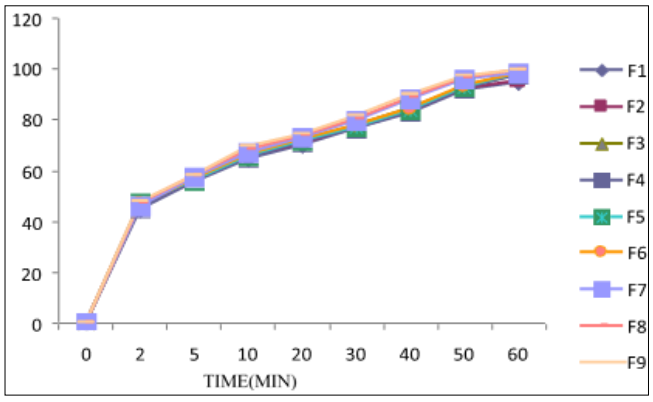


Fig 7: Drug release study of the MDT in simulated salivary fluid pH 6.8

Conclusion

Formulation of Mouth Dissolving Tablets has been done by superdisintegrant addition method. Three superdisintegrant CrosCarmellose Sodium, Crospovidone, and Sodium starch

glycolate are used to prepare nine batches of Mouth Dissolving Tablets of Naproxen Sodium by direct compression and sublimation method. Tablets prepared from crospovidone shows best results out of all batches of tablet formulated that is prepared by using sublimating agent urea. Optimum tablets such pass in general appearance, Thickness 4.1±0.004, Avg. of weight 221 mg, Hardness 2.7±0.412, Friability 0.603%, Content uniformity 97.34±0.768, Wetting Time 45 sec, Water Absorption Ratio 85%, Disintegration time 16 sec, *In-vitro* Dispersion Time 23 sec. Optimized Formulation (F9) of Naproxen Sodium shows very better release in 2-60 min in comparison conventional tablets of Naproxen Sodium that comes in market.

Acknowledgments
Firstly, I would like to express my heartfelt gratitude to my project guide and co-guide Dr. Monika Maan and Mrs. Shikha Shrivastava, for guiding me throughout the course of the major project, extend my thanks all the teaching and non-teaching staff members so on.

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