Research Article
CODEN (USA): IJPLCP

[Jekku *et al.*, 4(4): April, 2013]
ISSN: 0976-7126

INTERNATIONAL JOURNAL OF PHARMACY & LIFE SCIENCES

Formulation and evaluation of naproxen sodium rapimelts by direct compression method

Naga Subba Reddy Jekku[1], T.S Nagaraja[1], Bharathi[1] and M. Devi Reddy[2]

1, Department of Pharmaceutics, SJM College of Pharmacy, Chitradurga, (Karnataka) –India

2, Department of Pharmaceutics, Krishna Teja College of Pharmacy, Thirupathi, (Andhra Pradesh) -India

Abstract

Naproxen sodium is an analgesic NSAID (non steroidal anti inflammatory drug) used for the treatment of pain, inflammation, fever and stiffness caused by conditions such as osteoarthritis, rheumatoid arthritis, juvenile arthritis, gout, migraine and dysmenorrhea. However, the gastric discomfort caused by drug results in poor patient compliance associated with its conventional dosage forms. Hence the present investigation was undertaken with a view to develop Rapimelt tablet of naproxen, which offers quick onset of action of drug and minimizes the problem of gastric discomfort associated with it. Thus improves patient compliance, generates rapid response, enhances bio-availability and also reduces the dose of drug. In this study, rapimelt tablets were prepared by direct compression method using three different superdisintegrants e.g. sodium starch glycolate, croscarmellose sodium and crospovidone in three different concentrations e.g. 2%, 4% and 6% along with other excipients. The prepared tablets were evaluated for weight variation, hardness, friability, disintegration time, wetting time and dissolution rate. In the present work efforts have been made to prepare and evaluate Rapimelt tablets of Naproxen with different concentrations of superdisintegrants sodium starch glycolate, CCS and Crospovidone by direct compression technique. Release profile of F-9 having 6% Crospovidone in direct compression method was found to have maximum release of 97.56 % at the end of 30 minutes. The drug release from all batches was found to be concentration dependent. Hence the formulation of F-9 fulfills the objective of the present study. of F-12 fulfills the objective of the present study.

Key-Words: Rapimelts, Naproxen sodium, Sodium starch glycolate, Crosscarmellose sodium

Introduction

With the increase in the average human life, drug administration for elderly patients has become more important. Due to a decline in swallowing ability with age, a great many elderly patients complain that it is difficult to take medication in the form of tablets. Recently, useful dosage forms, such as rapimet tablets or rapidly disintegrating or dissolving tablets have been developed and applied clinically. This dosage form can also improve compliance in children, as well as, for local action within oral cavity as local anesthetics for toothache, cold sore or teething product. Rapimelt tablets may also be another option in emergency. Naproxen is a non-steroidal anti-inflammatory drug (NSAID), with analgesic and antipyretic properties. Naproxen sodium is an odourless crystalline powder, white to creamy in color. It is soluble in methanol and water..

*** Corresponding Author**
E.mail: subbu.naga14@gmail.com

The basic approach used in the development of the Rapimelt tablets is the use of superdisintegrates. The main objective of this research is to study the effect of concentration of different superdisintegrants on drug release of Naproxen Sodium by direct compression method.

Material and Methods

Tablets containing 250 mg of Naproxen Sodium were prepared by direct compression method and the various formulae used in the study[6]. Total nine formulations with different concentration of CCS (F1, F2, F3), SSG (F4, F5, F6) and Crospovidone (F7, F8, F9) were prepared. The drug, diluents, superdisintegrants and sweetener are passed through sieve #60.All the above ingredients were properly mixed together (in a poly-bag). Talc and magnesium stearate were passed through sieve #30, mixed and blended with initial mixture in a poly-bag.[7]The powder blend was compressed in to tablets on ten station rotary punch-tableting machine(Rimek mini press-1, Model RSB-4, Karnavati Engineering, Ahmedabad). The prepared tablets were evaluated for various parameters like

hardness, friability, weight variation, thickness, wetting time, disintegration time, dissolution study and dissolution efficiency.[8]

Compression of tablets by using direct compression technique:

To the blended powders finally magnesium stearate and talc were added. The mixed blend of drug and excipients was compressed into tablets weighing 250 mg using a flat faced punches of 8 mm diameter in a rotary tablet press (Rimek mini press- 1, Model RSB-4, Karnavati Engineering, Ahmedabad). A minimum of 50 tablets were prepared for each batch.

Evaluation of naproxen sodium rapimelt tablets

Pre compression parameters

Angle of Repose: [9]

Angle of repose was determined using funnel method4. The blend was poured through funnel that can be raised vertically until a maximum cone height (h) was obtained. Radius of the heap (r) was measured and angle of repose was calculated using the formula

$$\theta = \tan^{-1}\frac{h}{r}$$

Where, θ is the angle of repose, h is height of pile; r is radius of the base of pile.

Bulk Density [10]

Apparent bulk density (ρb) was determined by pouring the blend into a graduated cylinder4. The bulk volume (Vb) and weight of powder (M) was determined. The bulk density was calculated using the formula

$$\rho b = \frac{M}{Vb}$$

Tapped Density [10]

The measuring cylinder containing known mass of blend was tapped for a fixed time. The minimum volume (Vt) occupied in the cylinder and weight (M) of the blend was measured. The tapped density (ρt) was calculated using the following formula

$$\rho t = \frac{M}{Vt}$$

Compressibility Index [11]

The simplest way of measurement of free flow of powder is compressibility, an indication of the ease with which a material can be induced to flow is given by compressibility. The compressibility index of the granules was determined by Carr's or compressibility index (I), which is calculated by using the following formula

$$I = \frac{pt - pb}{pt} \times 100$$

Post compression parameters

All prepared Rapimelts were evaluated for its uniformity of weight, hardness, friability and thickness, *in vitro* disintegration time, wetting time, *in vitro* drug release according to official methods shown in Table 3.

Hardness[12]

The crushing strength of the tablets was measured using a Monsanto hardness tester. Three tablets from each formulation batch were tested randomly and the average reading noted.

Friability [13]

Ten tablets were weighed and placed in a Roche friabilator and the equipment was rotated at 25 rpm for 4 min. The tablets were taken out, dedusted and reweighed. The percentage friability of the tablets was measured as per the following formula,

$$\text{Percentage friability} = \frac{\text{Initial weight} - \text{Final weight}}{\text{Initial weight}} \times 100$$

Weight Variation[14]

Randomly, twenty tablets were selected after compression and the mean weight was determined. None of the tablets deviated from the average weight by more than ±7.5% (USP XX).

Disintegration time [15]

The *in vitro* disintegration test was carried out at 37ººC in 900ml of distilled water. The *in vitro* disintegration time of 5 tablets from each formulation was determined using disintegration test apparatus. One tablet was placed in each of the six tubes of the apparatus containing distilled water. One disk was added to each tube. The time taken in seconds for complete disintegration of the tablet with no mass remaining in the apparatus was measured.

Wetting time [16, 17]

Wetting time is an important step in the disintegration process. Wetting is closely related to the inner structure of tablet and to the hydrophilicity of excipients. The method reported by Yunexia was used to measure tablet wetting time.[8] A piece of tissue paper folded twice was placed on the distilled water (6ml) which was taken in a small petridish (6.5cm diameter).One tablet was placed on the paper and the time for complete wetting of the tablet was measured.

***In vitro* drug release studies[18]**

In Vitro dissolution studies for all the prepared tablets were carried out using USP paddle method at 50 rpm in 900 ml of 6.8 pH phosphate buffer as dissolution media, maintained at 37 ± 0.5º. 5 ml of samples, were

withdrawn from the dissolution medium at the specified regular intervals, filtered through Whatmann filter paper and release of the drug was determined spectrophotometrically at 272nm. An equal volume of pre warmed (37ºC) fresh medium was replaced into the dissolution medium after each sampling, to maintain the constant volume of the dissolution medium throughout the test. Then the cumulative percentage of drug release was calculated and represented graphically (Figure-2 and 3).

Results and Discussion

Nine formulations of Naproxen Sodium were prepared with concentration of three superdisintegrants: Sodium Starch glycolate, Croscarmellose sodium, Crospovidone and Avicel 101 were used as a direct compressible vehicle. For each formulation, blend of drug and excipients were prepared and evaluated for various parameters as explained earlier. The powder blend was compressed using direct compression technique. Bulk density was found in the range of 0.50-0.56 g/cm3 and the tapped density between 0.61-0.66g/cm^3. Using these two density data compressibility index was calculated. The Hausner's ratio was found between 1.17-1.23 and the compressibility index was found between 15.152 and 19.048 % and the compressibility -flowability correlation data indicated a fairly good flowability of the blend. The good flowability of blend was also evidenced with angle of repose (range of 26 – 31º), which is below 40º indicating good flowability. Tablets were prepared using direct compression technique. Precompression parameters shown in table no: 2.

The hardness of the tablets between 3.1–3.5kg/cm^2. The weight variation of the tablets between 248–251 mg. The thickness of the tablets between 2.56 – 3.42 mm. Friability of the tablets was found below 1 % indicating a good mechanical resistance of tablets. Wetting time is closely related to the inner structure of the tablet. This showed that wetting process was very rapid in almost all formulations. This may be due to ability of swelling and also capacity of water absorption and causes swelling. The *in vitro* disintegrating time is measured by the time taken to undergo complete disintegration of the tablets. Rapid disintegration within the seconds was observed in all the formulations. Comparision of disintegration time and wetting time done by drawing graph shown in figure no: 1. The results showed that tablet containing Crospovidone having low disintegrating time as compare to other superdisintegrants. The concentration of superdisintegrantsincreases as the disintegrating time decreases. The *in vitro* disintegration time of the tablets was found to be less than 50 sec. Post compression parameters shown in table no: 3. All the formulations showed enhanced dissolution rate as compared to superdisintegrants. The maximum increase in the dissolution rate was observed with Crospovidone amongst the three superdisintegrants. In the present work release profile of F-9 having 6% Crospovidone in direct compression method was found to have maximum release of 97.56 % at the end of 30 minutes. The drug release from all batches was found to be concentration dependent. Hence the formulation of F-9 fulfills the objective of the present study.

Conclusion

The use of superdisintegrants for preparation of Rapimelt tablets is highly effective and commercially feasible. These superdisintegrants accelerate disintegration of tablets by virtue of their ability to absorb a large amount of water when exposed to an aqueous environment. The absorption of water results in breaking of tablets and therefore faster disintegration. This disintegration is reported to have an effect on dissolution characteristics as well. Prepared Rapimelt tablets gets dispersed in the mouth quickly and releases the drug fast. Fig. 3 show the cumulative percentage of Naproxen Sodium Sodiumsodium released from formulated tablet with different concentration of Sodium Starch Glycolate and Croscarmellose sodium, and Crospovidone. It is clear that the dissolution and disintegration of Naproxen Sodium Sodiumsodium has improved considerably in batch F9 as compared to other formulations, Batch F9 tablet showed good dissolution efficiency and rapid dissolution. The study shows that the dissolution rate of Naproxen Sodium Sodiumsodium can be enhanced to a great extent by direct compression technique with the addition of superdisintegrants and no extreme changes in formulation F9 during stability studies.

Acknowledgement

The authors are thankful to Dr.Shivamurthy Murugha Sharanaru, President, S.J.M Vidya Peetha for providing all necessary facilities through the Principal and HOD, Dept. of pharmaceutics, S.J.M college of Pharmacy, Chitradurga and also thankful to Dr Reddy's laboratories for providing the gift sample of Naproxen Sodium.

References

1. Valleri M, Mura P, Maestrelli F, Cirri M, Ballerini R, Development and evaluation of glyburide fast dissolving tablets using solid dispersion technique. *Drug DevInd Pharm*, 30 (5): 525-34, (2004).
2. Hanawa T, Watanabe A, Tsuchiya T, Ikoma R, Hidaka M, Sugihara M, New Oral dosage form

for elderly patients: Preparation and characterization of silk fibroin gel. *Chem Pharm Bull*, 43 (2): 284-88, (1995).
3. Mallet L, Caring for the Elderly Patient. J. Am. Pharm. Assoc, 36 (11): 628-35, (1996).
4. Porter SC, Novel drug delivery: Review of recent trends with oral solid dosage forms. *Am Pharm Rev*, 85: 28-35, (2001).
5. Dollo G, Chevanne F, Le Corre P, Chemtob C, Le Verge R. Bioavailability of phloroglucinol in man. *J Pharm Belg*, 1999; 54:75-82.
6. Clarke A, Brewer F, Johnson ES, Mallard N, Hartig F, Taylor S, *et al.* A new formulation of selegiline: Improved bioavailability and selectivity for MAO-B inhibition. *J Neural Transm*.2003; 110:124-5.
7. Avani R. Gosai, Sanjay B.Patil and Krutika K .Sawant. Formulation and Evaluation of orodispersible tablet of ondansetronHCl by direct compression using super disintegrants. *IJPSN*. 2008;1(1):106-111.
8. TejveerKaur , Bhawandeep Gill, Sandeep Kumar, G.D. Gupta. Mouth Dissolving Tablets : A Novel Approach to Drug delivery. *Int J Curr Pharm Res*. 2011;3(1):1-7.
9. Ishikawa T., Watanabe Y., Utoguchi N., Matsumoto M., Preparation and evaluation of tablets rapidly disintegrating in saliva containing bitter taste masked granules by compression method, *Chem Pharm Bull (Tokyo*), 1999; Vol 47:1451-54.
10. Shagufta K., Prashant K., Premchand N., PramodY.,"Taste Masking of Ondansetron Hydrochloride by Polymer Carrier System and Formulation of Rapid-Disintegrating Tablets", *AAPS Pharm Sci Tech*, 2007; Vol 8 (2), E1-E7.
11. Reeta R T., MridulK.,"An unlimited scope for novel formulations as orally disintegrating systems: Present and future prospects", *Journal of Applied Pharmaceutical Science*, 2011; Vol 01 (01): 13-19.
12. Lachman L, Lieberman A, Kinig JL. The Theory and Practice of Industrial Pharmacy. 2nd edn. Varghese Publishing House, Bombay. 1991.
13. Bi Y, Sunada H, Yonezawa Y, Danjo K, Otsuka A, Iida K. Preparation and evaluation of a compressed tablet rapidly disintegrating in the oral cavity. Chem Pharm Bull (Tokyo).
14. 1996; 44: 121-127.
15. Swamy PA, Areefulla SH, Shrisand SB, Gandra S, Prashanth B. Orodispersible tablets of
16. meloxicam using superdisintegrant blends for improved efficiency. Ind J Pharm Sci. 2007; 69: 836-40.
17. Aulton, M.E. and Wells, T.I. Pharmaceutics The Science of Dosage Form Design, Churchill Livingstone,Vingstone, London, 1988, 168.
18. Vijaya, K.S.G. and Mishra, D.N. Rapidly Disintegrating Oral Tablets of Meloxicam, Indian Drugs.2006; 43(2):117-21.
19. Pharmacopoeia of India, Ministry of Health and Family Welfare, Govt. of India Controller of Publications, New Delhi; 1996; 2:736; A-80-83.
20. Mohapatra A, Parikh KR, Gohel CM. Formulation, development and evaluation of patient friendly dosage forms of metformin, Part- I: Orally disintegrating tablets. *Asian J Pharma* 2008; 167-71.

Table1: Composition of Rapimelt tablets of Naproxen Sodium

Ingredients (mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9
Naproxen Sodium	100	100	100	100	100	100	100	100	100
CCS	5	10	15	-	-	-	-	-	-
SSG	-	-	-	5	10	15	-	-	-
Crospovidone	-	-	-	-	-	-	5	10	15
Lactose	18	18	18	18	18	18	18	18	18
Sodium saccharine	5	5	5	5	5	5	5	5	5
Aerosol	5	5	5	5	5	5	5	5	5
Mg. stearate	3	3	3	3	3	3	3	3	3
Talc	2	2	2	2	2	2	2	2	2

Avicel 101	112	107	102	112	107	102	112	107	102
Total weight	250	250	250	250	250	250	250	250	250

Table 2: Pre compression parameters of Naproxen Sodium Rapimelts

Formulation code	Bulk density (g/cc) ±SD, n=3	Tapped density(g/cc) ±SD, n=3	Angle of repose (degree) ±SD, n=3	Carr's index (%) ±SD, n=3	Hausner's Ratio ±SD, n=3
F1	0.52 ± 0.004	0.62 ± 0.01	26.28 ± 1.26	16.12 ± 0.80	1.19 ± 0.04
F2	0.50 ± 0.003	0.61 ± 0.01	28.53 ± 1.20	18.03 ± 0.90	1.22 ± 0.02
F3	0.56 ± 0.002	0.66 ± 0.02	29.39 ± 1.27	15.15 ± 1.55	1.17 ± 0.7
F4	0.51 ± 0.007	0.63 ± 0.02	28.43 ± 1.46	19.04 ± 1.13	1.23 ± 0.06
F5	0.50 ± 0.009	0.61 ± 0.02	30.38 ± 1.31	18.03 ± 0.93	1.22 ± 0.07
F6	0.53 ± 0.002	0.63 ± 0.31	31.03 ± 1.40	15.87 ± 1.42	1.18 ± 0.11
F7	0.53 ± 0.002	0.64 ± 0.01	28.32 ± 1.52	17.18 ± 1.0	1.20 ± 0.02
F8	0.52 ± 0.005	0.62 ± 0.01	29.08 ± 1.20	16.12 ± 1.52	1.19 ± 0.04
F9	0.55 ± 0.003	0.66 ± 0.02	30.21 ± 1.70	16.66 ± 1.20	1.20 ± 0.03

Table 3: Post compression parameters of Naproxen Sodium Rapimelts

Formulation code	Weight variation ±SD, n=3	Hardness (Kg/cm^2) ±SD, n=3	Friability (%) ±SD, n=3	Thickness (mm) ±SD, n=3
F1	250±1.05	3.8±0.14	0.65±0.03	3.42±0.12
F2	251±1.02	3.8±0.11	0.64±0.07	3.39±0.09
F3	250±0.99	3.6±0.16	0.59±0.05	2.70±0.05
F4	250±1.15	3.7±0.15	0.70±0.03	2.96±0.08
F5	248±1.32	3.5±0.13	0.74±0.01	2.72±0.05
F6	249±1.10	3.4±0.15	0.58±0.06	2.68±0.02
F7	249±1.32	3.4±0.12	0.64±0.05	2.65±0.09
F8	250±1.14	3.3±0.13	0.75±0.06	2.60±0.10
F9	250±1.15	3.1±0.12	0.48±0.08	2.56±0.06

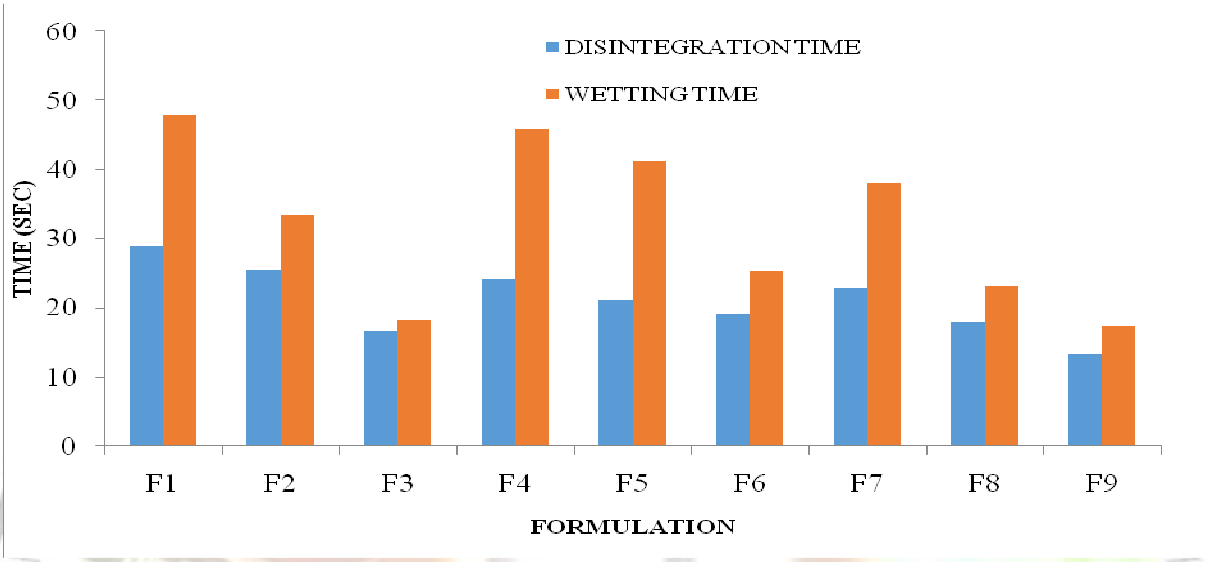

Fig. 1: Comparision of disintegration time and wetting time done by drawing graph

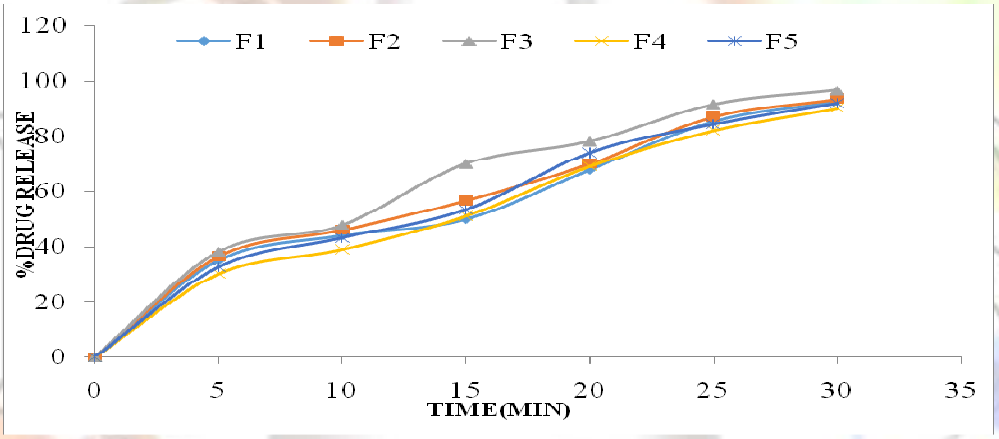

Fig. 2: Cumulative % drug Release Vs Time in min from prepared batches F-1, F-2, F3, F-4 & F-5 of Rapimelts of Naproxen Sodium prepared by direct compression method

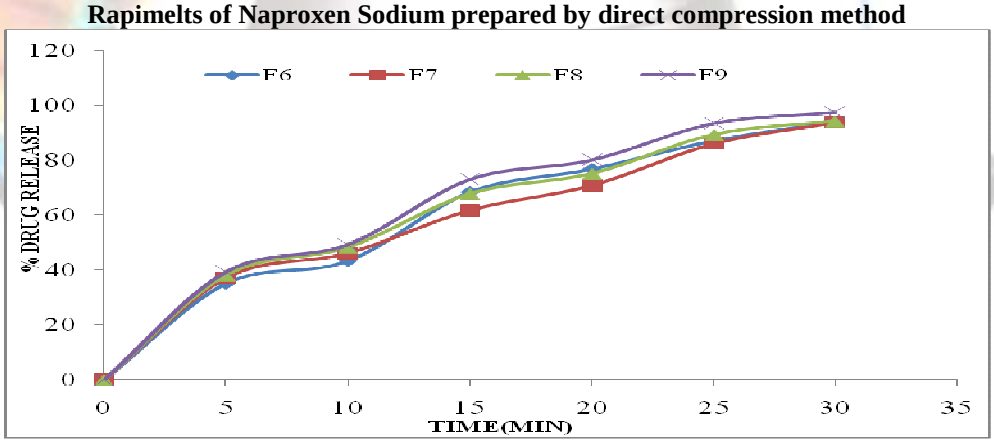

Fig. 3: Cumulative % drug Release Vs Time in min from prepared batches F6, F-7, F-8 & F-9 of Rapimelts of Naproxen Sodium prepared by direct compression method