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RESEARCH ARTICLE

Formulation and *In–Vitro* Evaluation of Fast Disintegrating Tablets of Naproxen

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ABSTRACT

The demand of fast dissolving tablets has been growing, during the last decade especially for geriatric and pediatric patients because of swallowing difficulties. Naproxen is a Propanoic acid derivative related to the arylacetic acid group of Non-Steroidal Anti-Inflammatory Drugs. It is a selective Cox-2 inhibitor used in the treatment of rheumatoid arthritis and other rheumatic or musculo skeletal disorders, dysmenorrheal and acute gout. Fast dissolving tablets of Naproxen were prepared by Wet granulation method. The tablets were prepared by using Mannitol as filler, Crospovidone, Sodium Starch Glycolate as super disintegrants in different concentration (6-8-10 %). Total eighteen formulations were prepared and evaluated for Hardness, friability, weight variation, content uniformity, wetting time, water absorption ratio and disintegration time and in - vitro drug release. Optimized formulation CP10H1 was compared with control formulation for disintegration time and % drug release. The stability studies were performed as per ICH guidelines. The Optimized formulation (CP10H1) showed no significant variations for the tablets parameters and it was stable for the specified time period. It was concluded the FDT for Naproxen can be formulated for emergency treatment of rheumatoid arthritis and acute gout.

Keywords: Gout, Naproxen, Patient, Formulation, ICH guidelines

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CONTENTS

1. Introduction

Naproxen is a selective Cylco Oxygenase (Cox) – 2 inhibitor, comparatively have lesser side effects than Non-Steroidal Anti Inflammatory Drugs. Used in the treatment of rheumatoid arthritis and other rheumatic or acute musculo skeletal disorders, dysmenorrheal and acute gout.

Cyclo – Oxygenase:

Cyclo Oxygenase (Cox) is an enzyme involved in the synthesis of prostaglandins. Prostaglandins are known to have a cytoprotective function in gastro intestinal mucosa as well as play a major role in the body's response to inflammation.

Fast Disintegrating Tablets (FDT):

There are many different drug delivery systems in the market and many more sure to be developed. Among all the dosage forms, solid dosage forms (especially - Tablets) are more convenient and among them conventional Tablets like chewable Tablets, Lozenges, dispersible Tablets, effervescent Tablets, seems to be most popular because of greater advantages over others. Most of medicaments are prescribed to geriatrics and pediatric patients only, as they fell ill very frequently when compare to adults. It was found that these patients have certain difficulty in swallowing Tablets.

Technologies used for preparing fast disintegrating tablets:

Various technologies that are commonly used in production of fast disintegrating tablets are

- Freeze drying technique
- Tablets moulding technique.
- Spray drying technique
- Mass- extraction technique
- Direct Compression technique

Drug Profile

Drug: Naproxen

Chemical Name: (R)-2-(6-Methoxynaphthalen-2-yl) propanoic acid

Formula: $C_{14}H_{14}O_3$

Molar mass: 230.259 g/mol

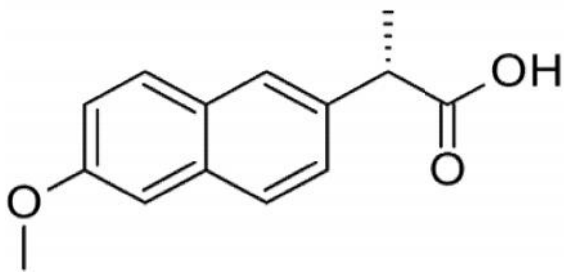

Fig 1: Structure of Naproxen

Description:

Naproxen is a nonselective COX inhibitor. It is in the propionic acid class of medications. As an NSAID, naproxen appears to exert its anti-inflammatory action by reducing the production of inflammatory mediators called prostaglandins. It is metabolized by the liver to inactive metabolites. An anti-inflammatory agent with analgesic and antipyretic properties. Both the acid and its sodium salt are used in the treatment of rheumatoid arthritis and other rheumatic or musculoskeletal disorders, dysmenorrhea, and acute gout.

Review of Literature:

- Sheetal malke *et al* 2007, Formulated and evaluated Oxcarbazepine fast dissolve Tablets.
- P.V. Swamy *et al* 2007., designed Orodispersible Tablets of Meloxicam using disintegrants blends for improved efficiency.
- Honey Goel *et al* 2008, designed a novel approach to optimize and Formulation fast disintegrating tablets of nausea and vomiting.

2. Materials and Methods

Table 1: List of Materials Used

Materials Used	Suplier
Naproxene	Gift sample from Aurobindo pharm Ltd, Hyderabad.
Crospovidone/ Sodium Starch Glycolate	Aurobindo pharm Ltd, Hyderabad, AP, India
Mannitol	Aurobindo pharm Ltd, Hyderabad, AP, India
Starch	Aurobindo pharm Ltd, Hyderabad, AP, India
Aspartame Powder	Aurobindo pharm Ltd, Hyderabad, AP, India
Orange Flavor	Aurobindo pharm Ltd, Hyderabad, AP, India
Colloidal Silicon Dioxide	Aurobindo pharm Ltd, Hyderabad, AP, India
Magnesium Sterate	Aurobindo pharm Ltd, Hyderabad, AP, India

Table 2: List of Equipment Used

Equipment	Manufacturer
Electronic weighing balance	Sartorious
Sieves	Saguras
Rapid mixer granulator	Anchor Mark Pvt Ltd
Fluidized bed dryer	Anchor Mark Pvt Ltd
Octagonal blender	Anchor Mark Pvt Ltd
Compression machine	Cadmach and Rimek
Hardness tester	Dr.Schleuniger pharmatron
Disintegrator tester	Electro lab USP
Dissolution apparatus	Electro lab USP
Friabilator	Electro lab USP
HPLC	Agilant 1100C
FTIR	Jasco
Bulk and tap density apparatus	Electro lab USP
Stability Walk in chamber	Newtronics

Experimental Methods

Formulation of Fast Disintegrating Tablets of Naproxen:

Formulation Design: Naproxen fast disintegrating tablets were prepared by wet granulation technique, as it is most convenient method of preparation. Tablets were to be prepared by using two different superdisintegrants varying on three types of concentrations and three types of hardness, keeping all other ingredients constant.

Evaluation of Fast Disintegrating Tablets of Naproxen:

Quality Control Tests: Tablets so prepared were evaluated in order to pass the specified quality control test in the USP. The quality control tests performed are

- Weight Variation Test
- Friability Test
- Hardness Measurement
- Disintegration Test
- Dissolution Test

3. Results and discussion

Weight Variation Test: No Tablets were outside the ±10 percentage of Tablet weight in weight variation test. Hence the tablets passed the weight variation test.

Friability:

Friability = ((W1-W2)/W1) × 100

W1-W2 = Weight loss

W1 - Initial weight of Tablet

W2 - Final weight of tablet

Percentage loss of Tablet weight is calculated.

Table 3: Standard Graph of Naproxen

Concentration	Absorbance
0	0
10	0.05
20	0.13
30	0.19
40	0.23
50	0.32
60	0.39
70	0.45
80	0.52
90	0.59

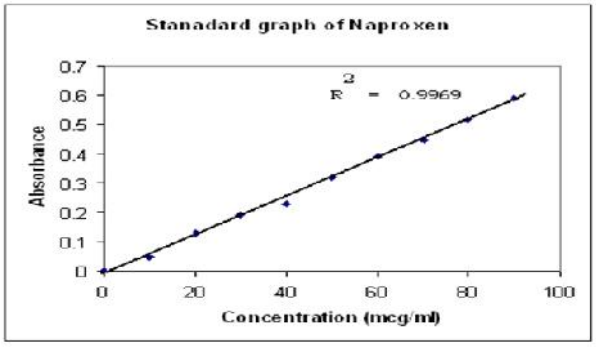

Fig 2: Standard Graph

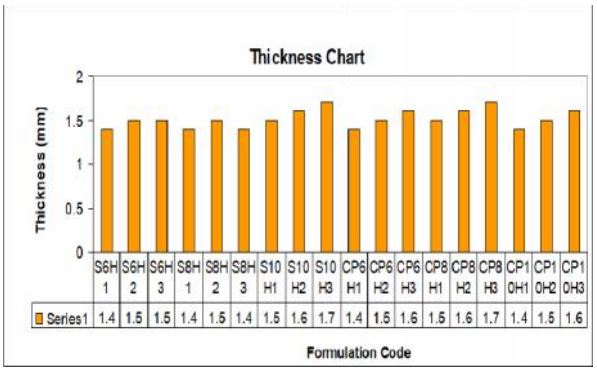

Fig 3: Thickness Graph

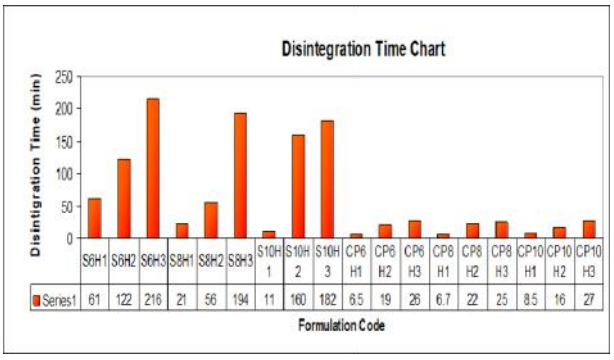

Fig 4: Disintegration Time Graph

Table 4: Assignment of codes to various Formulations

S.No	Disintegrant used	Concentration	Hardness (Kgs)	Formulation Code
1	Sodium Starch Glycolate	6	1	S6H1
2			2	S6H2
3			3	S6H3
4		8	1	S8H1
5			2	S8H2
6			3	S8H3
7		10	1	S10H1
8			2	S10H2
9			3	S10H3
10	Crospovidone	6	1	CP6H1
11			2	CP6H2
12			3	CP6H3
13		8	1	CP8H1
14			2	CP8H2
15			3	CP8H3
16			1	CP10H1

17		10	2	CP10H2
18			3	CP10H3

Table 5: Formula is set Using Ingredients

S.No	Excipients	PURPOSE / USE
1	NAPROXEN	API
2	Crospovidine/ Sodium Starch Glycolate	Disintegrants
3	Mannitol	Bulking Agent
4	Starch	Binding Agent
5	Aspartamate Powder	Sweetening Agent
6	Orange Flavor	Flavoring Agent
7	Colloidal Silicon Dioxide	Gliding Agent
8	Magnesium Stearate	Lubricant

Table 6: Disintegrant Concentration (%) Sodium Starch Glycolate

S.No	Ingredients	Disintegrant Concentration (%) Sodium Starch Glycolate		
		10	8	6
1	Naproxen	200	200	200
2	Mannitol	125.6	128.0	130.4
3	Disintegrants	12	9.6	7.2
4	Starch	3	3	3
5	Orange flavor	3	3	3
6	Magnesium Stearate	2	2	2
7	Colloidal Silicon Dioxide	2	2	2
8	Aspartame Powder	2.4	2.4	2.4

Table 7: Disintegrant Concentration (%) Crosspovidone

S.No	Ingredients	Disintegrant Concentration (%) Crosspovidone		
		10	8	6
1	Naproxen	200	200	200
2	Mannitol	125.6	128.0	130.4
3	Disintegrants	12	9.6	7.2
4	Starch	3	3	3
5	Orange Flavor	3	3	3
6	Magnesium Stearate	2	2	2
7	Colloidal Silicon Dioxide	2	2	2
8	Aspartame Powder	2.4	2.4	2.4

Table 8: Characteristics of various Naproxen Fast Disintegrating Tablets Formulation

Formulation Code	Friability	Thickness ± S.D(mm)	Disintegrating Time ± S.D (seconds)
S6H1	3.32	1.4mm	60.5 ± 9.2
S6H2	0.82	1.5mm	122 ± 1.5
S6H3	0.71	1.5mm	216 ± 0.31
S8H1	1.62	1.5mm	20.5 ± 0.30
S8H2	0.94	1.4mm	156 ± 0.61
S8H3	0.94	1.5mm	194 V 0.70
S10H1	0.96	1.4mm	0.7 V 0.54
S10H2	0.93	1.5mm	160 ± 0.26
S10H3	0.95	1.4mm	182 ± 0.30
Cp6H1	3.30	1.5mm	8.5 ± 0.28
Cp6H2	0.84	1.4mm	18.7 ± 0.30
Cp6H3	0.85	1.5mm	26.3 ± 0.32
Cp6H1	1.57	1.4mm	8.7 ± 0.54
Cp8H2	0.94	1.5mm	22.3 ± 0.68
Cp8H3	0.95	1.4mm	24.6 ± 0.89

Cp10h1	0.92	1.4mm	6.5 ±1.0
Cp10H2	0.93	1.5mm	15.6±2.2
Cp10H3	0.93	1.4mm	27 ± 1.22

Table 9: Dissolution Profile

S.No	Formulation Code	% Drug Release						
		Time (Min)	0	2	5	7	10	15
1	S6H1	-	0	56.04	71.52	90.12	92.58	94.25
2	S6H2	-	0	53.91	67.97	87.45	90.45	92.52
3	S6H3	-	0	51.99	64.92	87.12	89.12	92.58
4	S8H1	-	0	57.41	72.99	91.45	90.14	95.32
5	S8H2	-	0	54.82	68.99	88.54	93.12	95.47
6	S8H3	-	0	52.91	65.92	88.39	96.12	94.12
7	S10H1	-	0	62.58	78.97	94.52	94.45	96.12
8	S10H2	-	0	61.42	77.92	92.14	85.25	94.45
9	S10H3	-	0	59.14	75.91	89.99	87.45	96.98
1	Cp6H1	-	0	58.01	72.91	90.12	88.65	95.24
2	Cp6H2	-	0	57.01	71.90	89.12	94.25	94.25
3	Cp6H3	-	0	55.12	69.99	86.25	96.85	93.25
4	Cp8H1	-	0	59.99	74.25	92.25	89.12.	98.13
5	Cp8H2	-	0	58.12	73.21	91.45	96.25	95.15
6	Cp8H3	-	0	57.12	72.29	90.12	87.96	94.56
7	Cp10H1	-	0	61.12	78.25	94.25	95.12	99.97
8	Cp10H2	-	0	60.16	77.56	94.54	96.25	98.13
9	Cp10H3	-	0	59.12	76.89	93.12	89.25	98.17

4. Conclusions

The worldwide incidence all the formulations were released above 90% of the Naproxen within 15 minutes. When SSG is used as Superdisintegrant at 10% concentration the % release of drug was found to be above 96 percentages. Whereas in case of Crospovidone it is higher than the SSG 6,8,10 & the percentage release of CP10 is above 99%. Percentage release of S10 Formulations' was higher than the S6 & S8 Formulations. When Crospovidone 10% used as Superdisintegrant the percentage of drug release was found to be higher than 6 & 8 % of concentrations of Crospovidone. It was concluded that 10% concentration of Crospovidone used as Superdisintegrant is the best formulation. It was concluded that Cp10H1 is the best formulation when compared to all formulations. Cp10H1 disintegrated within 6.5 sec. in this formulation percentage of drug release was found to be 99.97 within 15 minutes.

5. References

[1] Radhakrishna.T, Srinivas Rao.D and Om Reddy. G "LC Determination of Rofecoxib in Bulk and Pharmaceutical Formulations". Journal of pharmaceutical and Biomedical analysis 26 (2001) 617 – 628.

[2] Robert. W.M.C, Murray. M.D, Kenneth.J, Hardy. M.D "Cox – 2 inhibitors: Today and Tomorro". The American Journal of Medical Sciences. April 2002 Vol: 323 P.P, 181–189.

[3] Slowson.M and Slowson.S "What to do when patients cannot swallow Their Medications". Pharmatimes 1985: 51:90-96.

[4] Johy.S, James.S and Shawn.A, "The Zydis® Drug delivery System" Pharmaceutical III Dr. Das April 1, 2001.

[5] Virley.P, Yarwood.R, "Zydis-a Novel, Fast Dissoving dosage forms", Manf.chem.1990; 61:36-37.

[6] Koizumi.K, Mastsui.J and Keneda.Y, Int. J. Pharm,(1997) 152 – 127.

[7] Habib.W, Khankari and Hontz.J, Critical reviews TM Therapeutic Drug Carrier Systems, 2000, 17, 61.

[8] Jaccard.T.T and J. Leyder, "One Nouvelle Forme Galenique Lelyo" Ann. Pharma. 1985, 432. 12 - 131.

[9] Blank.R.G.Mody, S.Kenny.R.J and M.C. Arenson. "US Patent No: 1990. "4,946,684".

[10] Koizumi.K, Mastsui.J and Keneda.Y, Int. J. Pharm, 1997, 152 – 127.

[11] Makino.T, Yamada.M and Kikuta.J (Takada Chemical Industrial) "Fast dissolving Tablets and Its product ion", European Patent 1993, 0.553,777 A2.

[12] Luca dobetti, "Fast melting Tablets; Devolopments and Technologies" Pharmaceutical technology Drug Delivery 2001 P 44-49.
[13] Humber.P, Scidel.M, and Matani.R (Novartis Consumer Health), "Fast Disintegration Oral Dosage Forms". PCT patent No; 1997, 97/38679 – A1.
[14] LAllen.L.V, Wang.B: Particulate support matrix for making rapidly dissolving tablets. US Patent No. 5,595,761, 1997
[15] Bhaskaran.S. and Narmada.G.V , Indian Pharmacist,2002, 1(2), 9 – 12
[16] Avani Gosai.R, Sanjay.B. Patil and Krutika.K, Sawant, "Formulation and evaluation of Oro Dispersible Tablets of Ondonsetron Hydrochloride by Direct Compression using Superdisintegrants", International Journal of Pharmaceutical Sciences and Nanotechnology, volume – I, april – June 2008, 106-111.
[17] Simore Schiermier, and Peter Christian Schmid (Germany). "Fast dispersible Ibuprofen Tablets". European Journal of pharmaceutical science, 15 (2002) p 295 – 305.
[18] Drug Delivery Report: Orally disintegrating dosage Forms. "Cima Labs:Orasolv® and Dura solv TM Technologies" Pharma Concepts GMBH and Co.KG ,2001.
[19] James Klancke Sr. Director, analytical devolpment CIMA LABS inc.Brooklyn park, MN. "Dissolution testing of Orally Disintegrating Tablets", Dissolution technologies – may 2003
[20] Johy.S, James.S and Shawn.A, "The Zydis® Drug delivery System" Pharmaceutical III Dr. Das April 1, 2001.
[21] Chrukuri.S.R et al., (Fuizy Technologies). "Quickly Dispersing Comestible Unit and Products". PCT patient no 95/34290 – A1, 1995.
[22] Mizumoto.T, Masuda.Y , Kukui.M, US Patent No. 5,576,014, 1996.
[23] European Pharmacopeia, Third Edition Supplement 2000 "Council of Europe, European Pharmacopeia, Strasbourg, France" P.1347.
[24] Misra.T.K, Currington, Kamath.J.W, Sanghi.S.V, Sisak.P.P, J.R, Raiden. M.G., US Patent No; 5869, F098 .1999.
[25] Manvi.F.V, hiremath.S.P, Nanjwade.B.K, Kulkarni.A.S and Chaljkwar.S.S, "Formulation & evaluation of Dispersible Tablets of Flurbiprofen", the Indian Pharmacist, - February 2005, 68 – 71.
[26] Chandra Shekar Rao.G, Nagoj. K.E.V and Bhanoji. Rao.M.E. "Formulation and evaluation of Nimesulide dispersible Tablets", Indian Journal of Pharmaceutical Sciences, Nov – dec 2002,598–599.
[27] Koizumi K.I: New method of preparing high porosity rapidly saliva soluble compressed tablets using mannitol with camphor, a subliming material. Int. J. Pharm., 152:127-131, 1997.
[28] Bi Y: Preparation and evaluation of a compressed tablet rapidly disintegrating in the oral cavity. Chem. Pharm. Bull., 1996, 44 (11): 2121-2127.
[29] Sheetal malke, Supriya Shidhaye and V.J. Kadam, "Formulation and Evaluation of oxcarbazepine Fast dissolve Tablets", Indian Journal of Phramaceutical sciences, March-April 2007, 211-214.
[30] P.V.Swamy, Areefulla S.H, Shirsand, Smitha S.B, Gandra and Prashanth.B, "Orodispersible Tablets of Meloxicam using Disintegrant Blends for improved efficacy", Indian Journal of Pharmaceutical sciences, November – December 2007, 836 – 839.
[31] Kucheker.B.S., Atual.C.Badhan, and Mahajan. H.S, "Mouth dissolving Tablets: "A Novel Drug Delivery System"Pharma Time vol.35, June 2003.
[32] Venkateshwarlu.V, 2000 "Fundamentals of Biopharmaceutics and pharmacokinetics". P.P, 243 – 262.