EFFECT OF ADDED HYDROPHILIC AND HYDROPHOBIC POLYMERS ON THE RELEASE OF NAPROXEN FROM TABLETS FOR CONTROL RELEASE

DR.PURUSHOTHAM RAO.K*[1], ANILKUMAR REDDY[1], VIJAY HIREMATH[2], BABURAO NCK[1], MANJUNATH.P[1], SHARAN.SV[1], JHANSI.A[1], HARSHAVARDHAN.K[1].

[1]Dept. of Pharma. Tech., H.K.E.'s College of Pharmacy (MRMC Campus), Gulbarga-585 105

[2]P.D.A Engineering College. Gulbarga -585102, Karnataka.

ABSTRACT

The term arthritis means "joint inflammation" but is generally used to describe inflammatory and degenerative conditions of the joints. It can effect anyone at any age. There are several kinds of arthritis the most of which is the osteoarthritis (OA), rheumatoid arthritis (RA) and gout. To treat these conditions prolonged action dosage forms are very much needed. The aim of the present study was designed to develop novel sustained-release (SR) matrix tablet formulations of naproxen a non-steroidal anti-inflammatory drug. The release of naproxen from sustained release tablets based on hydrophilic matrices of hydroxy propyl methyl cellulose (HPMC) and Hydrophobic matrix polymer cetostearyl alcohol for controlled release. The fatty alcohol and cellulose derivative were used in the ratio of 3:1 along with usual tablet additives like lactose and talc. The compressed matrix tablets were evaluated for various parameters like hardness, friability, weight variation, drug content uniformity, IR spectral analysis, in-vitro drug release profiles and stability studies. The in-vitro release profiles showed sustained drug release from HPMC matrix tablets i.e. 41.48% at the end of 8th hour and was found to release the drug by anomalous (non-fickian) transport Probably due to its less hydration potential.

KEY WORDS: Hydrophilic & Hydrophobic matrix tablets, Sustained release, Naproxen, Formulation.

1.INTRODUCTION

The term arthritis literally means "Joint inflammation", but is generally used to describe inflammatory and degenerative conditions of the joints. Contrary to popular misconception, arthritis is not a diseases, which is inevitable with old age. It can affect anyone at any age. Also, there are a hundred different kinds of arthritis, the most common of which is the osteoarthritis (OA), rheumatoid arthritis (RA) and gout (Harshmohan,2000). The basic goal of therapy is to achieve a steady state drug in blood level for an extended periods of time. The design of proper dosage regimens is an important element in accomplishing this goal. In recent years considerable attention has been stressed on the development of controlled drug delivery system for convenience and patient compliance (Lachmman,1991; Herbert,1981; Chien,1992), Shivkumar (2001), have studied effect of added HPMC and HEC on the release of cetostearyl alcohol embedded diclofenac sodium from tablets for control release, Nath (2000), have worked on "Formulation and evaluation of sustained release dosage form of theophylline using a combined hydrophobic and hydrophilic matrix, Basak (2004), have worked on controlled release HPMC matrix tablets of propronalol hydrochloride. In the present work an attempt has been made to find the effect of hydrophilic component by selecting cellulose derivative HPMC with cetostearyl alcohol as matrix material using naproxen a NSAID drug with analgesic and antipyretic properties (British Pharmacopoeia,1993).

*** Address for correspondence:**
kprao369@rediffmail.com
kprao369@yahoomail.com

2.MATERIALS AND METHODS

Naproxen was a gift sample from Brown and Burk, Hosur (Tamil Nadu) Cetostearyl alcohol, lactose, talc, hydroxy propyl methyl cellulose . All other chemicals and reagents used were of analytical grade.

Method of Preparation of tablets

The Lactose and Naproxen were added to melted cetostearyl alcohol at 60°C and stirred until drug was uniformly dispersed. The HPMC was intimately mixed with talc and partially hydrated using three parts of water for each part of polymer. The cetostearyl alcohol embedded granules were mixed with the paste of cellulose polymers and passed through sieve no-8 and dried at room temperature for 40 min. the dried granules were than passed through and collected on sieve no-44.

As for the official standards10% of fines were included to bulk. The granules were lubricated with talc and magnesium stearate and compressed into tablets weighing 400mg using 10-mm flat punches to a hardness of 5-6 Kg/ cm². Formulae of naproxen matrix tablets shown in table-1. The hardness of tablets from each type of formulation was determined using a Roche friabilator, weight variation test was carried out as per official method (Indian Pharmacopoeia,1996), for the estimation of drug content. Five tablets were powdered in a mortar. From this powder equivalent to 100mg. of drug was taken in a 100 ml round bottom flask. It is extracted with 20ml. of methanol for ½ hour filtered and then filtrate was Made up to mark with methanol. Further appropriate dilutions are made and the absorbance was measured at 271.5 nm against blank.

IR spectral analysis for drug excipient interactions

The studies were carried out using IR method with the help of perkin-elmer 1615 spectrophotometer indicated that there are no drug excipient interaction.

In-vitro Dissolution Studies

In-vitro dissolution of naproxen tablets was studied in USP XXIII dissolution apparatus (Electrolab) employing a rotating basket. The in-vitro release of naproxen was studied for first two hours in pH 1.2 and for subsequent six hours in phosphate buffer of pH 7.4. An amount of 900 ml. of respective dissolution fluids were used at 37±1°C with a stirrer speed of 70 ± 02 rpm. One tablet was used in each test. 5 ml. of the sample of dissolution Medium was withdrawn by means of a syringe fitted with prefilter of known intervals of time (1 hour). The volume withdrawn of each interval was replaced with same quantities of fresh dissolution medium. The sample was analysed for drug release by measuring the absorbance at 272.5 nm in first two hours and 271.5 nm for subsequent six hours using UV-visible spectrophotometer, Shimadzu-1700.

3.RESULTS AND DISCUSSIONS

In the present study sustained release matrix tablets of naproxen were prepared by using HPMC, as an hydrophilic polymer and cetostearyl alcohol will be used as hydrophobic polymer. Here the fatty alcohol and cellulose derivative were used in the ratio of 3:1 along with usual tablet additives like lactose and talc. The granules prepared to compress the formulation in to the tablet dosage forms have the properties True density 1.77 gm/cm³, Bulk density (gm/cm³) and percent Porosity was 70.05 and the granules were formed to be free flowing (table 2,3). The compressed tablets were tested for various physical parameters such as the hardness of the tablets were found to be in the range of 5.2 Kg/cm². The friability of all the prepared tablets was found to be in the range of 0.29 % fulfilling the official requirement (not more than 1%). Drug content estimation was found to be in the range of 96.59% with low values of standard deviation indicates uniform drug content present in the tablets prepared. All the prepared tablets were evaluated for weight variation and the percent deviation from the average weight was found to be within the prescribed official limits. The tablets of naproxen were evaluated for drug excipient interaction by IR studies (fig-1&2), which confirms the undisturbed drug structure in the formulation. The in-vitro release of naproxen from all the formulations are shown in table 4. The results showed that tablets of HPMC (F) drug release was 41.48% at the end of 8th hour. This may probably due to less hydration potential. The in-vitro drug release data was subjected to goodness of fit test by linear regression analysis according to zero order. First order kinetic equations Higuchi's and Peppa's models in order to determine the mechanism of drug release. Since the plots of log cumulative percent drug remaining versus time are linear. The regression co-efficient was found to be 0.99. The release of drug from this matrix tablets was diffusion controlled process. Since the plots of cumulative percent drug release versus square root of time were found to be linear. when the data was treated according to Peppa's equation. The release exponents (n-value) for most of the formulations was found to be In the range of 0.45 to 0.89 indicating non-fickian release mechanism.

4.CONCLUSION

From the present study, the following conclusions can be drawn. Matrix tablets of Naproxen using a hydrophilic polymer i.e., HPMC and hydrophobic polymer cetostearyl alcohol were found to be good without chipping, capping and sticking. Thus it can be concluded from the results obtained that HPMC, showed differences in their behavior in controlling the release of the naproxen from cetostearyl alcohol embedded granular particulates.

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Table-1: Formulae of naproxen matrix tablet

Ingredients	Formula for one tablet	Formula for 50 Tablets.
Naproxen	100 mg	5 gm
Cetostearyl alcohol	90 mg	4.5 gm
HPMC	30 mg	1.5 gm
Lactose	90 mg	4.5 gm
Talc	45 mg	2.25 gm
Mg.stearate	45 mg	2.25 gm
Total weight	400 mg	20 gm

Table-2: physical properties of prepared granules

Formulation	True density	Bulk density	%porosity
F	1.77	0.53	70.05

Each reading is a mean of three replicates

Each matrix tablet contains 100mg. of Naproxen

Table-3: Physical properties of prepared formulation

Sl. No.	Formulation Code	Hardness (Kg/cm²)	Percent Friability	Weight variation		Drug Content in mg ± S.D.
				Average	% Deviation	
1	F	5.2	0.29	401.25	0.55	96.59±0.57

Each reading is a mean of three replicates

Table-4: in-vitro drug release profile naproxen matrix tablet formulation F

S. no	Time (hrs)	Square root of time	Log time	Cumulative % drug released ± S.D.	Log cumulative % drug released	Cumulative % drug remaining	Log cumulative % drug remaining
1.	0	-		0		100.0	
2.	1	1.000	0.000	3.23±0.28	0.509	96.77	1.985
3.	2	1.4142	0.3010	4.81 ± 0.26	0.682	95.19	1.978
4.	3	1.720	0.4771	10.87±0.20	1.036	89.13	1.950
5.	4	2.00	0.6020	13.84±0.27	1.141	86.16	1.935
6.	5	2.2326	0.6989	17.25±0.89	1.236	82.75	1.917
7.	6	2.4494	0.7781	19.70±0.24	1.294	80.30	1.904
8.	7	2.6457	0.8450	29.55±0.43	1.470	70.45	1.847
9.	8	2.8284	0.9030	41.48±0.20	1.617	58.52	1.767

Each reading is a mean of three replicates

Each matrix tablet contains 100mg. of Naproxen

Table-5: Kinetic Data of Naproxen Matrix Tablets

Formulation Code		Zero Order	First Order	Higuchi Model	Peppa's Euqation
F	r	0.9598	-0.9377	0.9242	0.9912
	a	5.016	2.036	-20.701	1.206
	b	4.981	-0.0278	18.801	0.4792

Figure-1: IR Spectrum of Naproxen Pure Drug

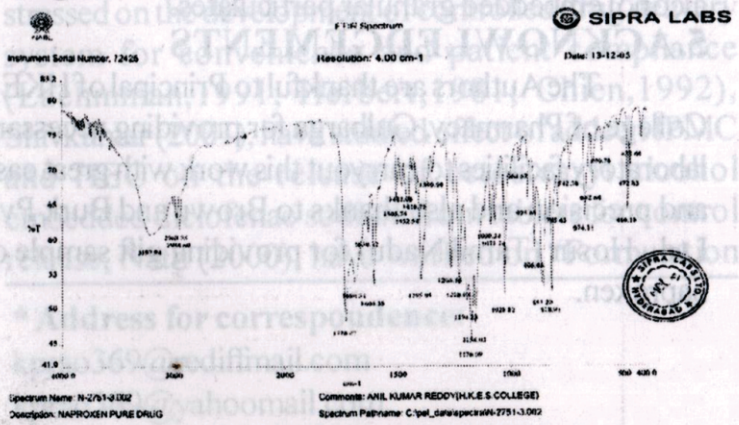
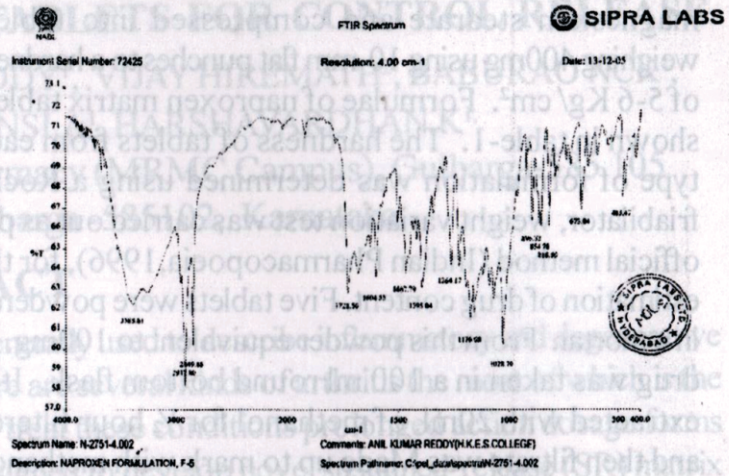


Figure-2: IR Spectrum of Naproxen Tablet Formulation-F



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