WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.074
Volume 7, Issue 6, 576-594. Research Article ISSN 2277– 7105

DESIGN AND EVALUATION OF COMPRESSION COATING PULSATILE DRUG DELIVERY SYSTEM WITH NATURAL AND SYNTHETIC POLYMERS

M. Swetha*[1], B. Mohan[2], Dr. J.N. Suresh Kumar[3], Dr. R. Narshimha Rao[1], Dr. B. Rama[4] and G. Natesh[5]

*[1]Hits College of Pharmacy.

[2]Sanofi ltd.

[3]Narsaraopet Institute Of Pharmaceutical Sciences.

[4]Malla Reddy College of Pharmacy.

[5]Prasthista College of Pharmacy.

Article Received on
21 Jan. 2018,

Revised on 11 Feb. 2018,
Accepted on 04 March 2018,

DOI: 10.20959/wjpr20186-11394

***Corresponding Author**
M. Swetha
Hits College Of Pharmacy.

ABSTRACT

Aim of the present work is to formulate &evaluate an oral; time controlled pulsatile drug delivery system of Aceclofenac, based on chronotherapeutic approach for the treatment of Rheumatoid arthritis. Aceclofenac is a class of NSAID which is poorly water soluble, used by elders/ Rheumatoid arthritis patients, who may get morning stiffness and joint pains early in the morning. It generally affects the joints and their synovial membranes, cartilages, capsules and the muscles supplying them. Patients with rheumatoid arthritis have pain that usually peaks in the morning and decreases during the day. Chrono therapy for all forms of arthritis using NSAIDs should be timed to ensure the highest levels of drug coincide with peak pain. In present study an attempt made to develop Chrono therapeutic drug delivery system of Aceclofenac with natural super disintegrates in core tablet and natural and synthetic polymers in different ratios as a coating. With pre-determined lag time of 6 hours by compression coating technique.

KEYWORD: Time controlled pulsatile drug delivery system, Aceclofenac, Rheumatoid arthritis, NSAID, Chrono therapy, super disintegrants, core tablet, natural and synthetic polymers, compression coating.

INTRODUCTION

PULSATILE DRUG DELIVERY SYSTEM[1,5]

A Pulsatile drug delivery system delivers drug in rapid and burst manner within a short time period instantaneously after a programmable lag phase[1]. Pulsatile Drug Delivery Systems (PDDS) are time-controlled drug delivery systems in which the drug is released over a definite pause time which is independent of environmental factors like pH, enzymes, gastrointestinal mobility, etc.

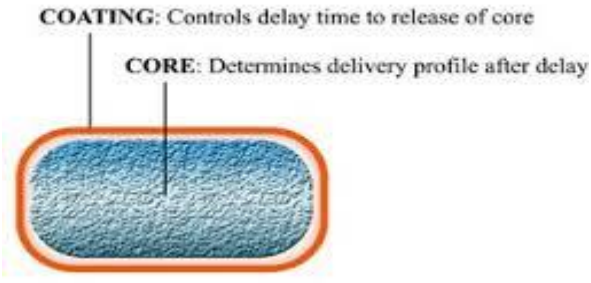


Fig. 1: Pulsatile drug delivery.

Circadian time structure[1,5]

Circadian rhythms are controlled by an inbred master clock network composed of the paired supra chiasmatic nuclei (SCN) that are sited in the hypothalamus and the pineal gland. This master clock network arranges the period and phase of the multitude of submissive peripheral circadian clocks located in cells, tissues, and organ-systems. The end effect is a rather exquisite temporal organization of biological processes and functions.

Circadian rhythms are self-sustaining, endogenous oscillations that occur with a periodicity of about 24 hours.

Circadian rhythms are synchronized according to internal biologic clocks related to the sleep-wake cycle. Our circadian rhythm is based on sleep activity cycle and is influenced by our genetic makeup and thereby affects our bodies' function throughout day and night (24-hour period).

Circadian rhythm regulates many body functions in humans like breakdown, physiology, behavior, sleep pattern, hormone production.

There are number of conditions which show circadian pattern and advantage could be taken by timing and adjusting the administration of drugs according to the circadian rhythm of the disease.

Compression coating is the absolute dry coating without solvent and heat use. The compression coated tablet dosage form (tablet –in-tablet design) is a time and rate-controlled drug delivery device, which consist of a core tablet and an outer layer that is considerably thicker than typical tablet core tablet and which completely, surrounds the core tablet. This method has no limitation for the cores & coating.[6,7]

This method can be used to protect hygroscopic, light sensitive, oxygen –labile or acid labile drugs, to combine and separate different drugs and to modify drug release pattern.

MATERIALS AND METHODS

ACECLOFENAC was purchased from Yarrow chemicals, Micro crystalline cellulose And Eudragit L 100 obtained as a gift sample from Sanjay chemicals (Chennai) remaining all chemicals were laboratory reagents.

METHODS

SATURATION SOLUBILITY STUDIES

Saturation solubility was determined by the shake-flask method. Plain Aceclofenac in excess quantity were placed in glass-stoppered flasks containing 10 ml of distilled water, pH1.2, pH6.8, pH7.4 respectively. The samples were placed in a mechanical shaker (Technico, thirumudivakam) at 37 °C and 100 rpm until equilibrium was achieved (24 h). The aliquots were filtered through Whatman No. 41 filter paper. The filtrates were diluted appropriately in distilled water and assayed spectrophotometric ally at 273 nm. The results were shown in Table no 4 and figure no. 2

CALIBRATION CURVE

25mg of Aceclofenac was weighed and transferred to a volumetric flask containing 2 ml of Methanol as a solvent. This was sonicated for 5 min to dissolve it and the solution obtained was diluted to 100 ml with Phosphate buffer pH 7.4. 10ml of this standard preparation was transferred to another volumetric flask and then diluted to 100 ml with buffer. From these suitable dilutions were made to get concentration of 1,4,6,8,10 µg/ml. Absorbance of these solutions was measured spectrophotometric ally at 273 nm. The same procedure was

followed with Phosphate buffer pH 6.8 and 7.4 and the absorbance was measured spectrophotometric ally. The results were shown in table no 5, 6&7. and figure no 3,4, &5.

Drug- Excipient Compatibility Studies

The compatibility between drug and polymers was evaluated using Fourier Transmitted Infrared spectroscopy (FTIR). Physical mixtures were prepared to study the effect of sample manipulation. In addition, the samples of physical mixture were heated at 55°C for three weeks to obtain more reliable conclusions[70]. The IR shows that all peaks are present in Aceclofenac spectra are present in the physical mixture. The results were shown in figure no 6,7,8,9, &10.

Methods Of Pre-Formulation Studies

Bulk Density Apparent bulk density was determined by placing prepared powders into a graduated cylinder and measuring the volume and weight as it is

Bulk density =weight / bulk volume

Tapped Density The accurately weighed blend was filled in 100 ml graduated cylinder of tap density tester which was operated for fixed number of taps until the powder bed volume has reached a minimum. The result was shown in Table no.8. That was calculated by formula

Tapped density =weight / tapped volume

Compressibility Index

Carr's compressibility index = (Tapped density – Bulk density / Tapped density) X 100

Hausner 's ratio = bulk density / tapped density.

Angle of Repose: The angle of repose is the angle formed by the horizontal base of the bench surface and the edge of a cone like pile of granules.

$\Phi = \tan^{-1} h/r$

Isolation of mucilage from psyllium seed

The Psyllium seeds were socked in distilled water for 48 hours and then boiled for 10 min. The resulting mass was squeezed through the muslin cloth. To the filtrate an equal volume of acetone was added to precipitate the mucilage. The isolated mucilage was dried in an oven at 40^0C for 4 hours. Powered, passed through sieve no 80 and stored in desiccator.[8]

Preparation Of Modified Agar

Modification of natural Agar was done by suspending 5 grams of agar-agar in 100mi distilled water. The suspension is stirred at 500 RPM using magnetic stirrer for 24 hours. Obtained swollen mass is dried at 40^0C for 72 hours. Dried product is collected and crushed in mortar pestle and passed through sieve no 100.[8]

Preparation Of Core Tablet[10]

- STEP1: All ingredient was weighed accurately and blend it for 15 min and MCC was used as direct compression agent.
- STEP 2: Modified agar, Psyllium seed mucilage was used as super disintegrant
  And Magnesium stearate and talc was used as lubricant
- STEP 3: Tablet was compressed using mini press compression using 6mm diameter
- Formulation was shown in table no 1

Table -1 Formulation of Core Tablet.

Ingredients (mg)	CT_1	CT_2	CT_3	CT_4	CT_5	CT_6	CT_7	CT_8	CT_9	CT_{10}	CT_{11}	CT_{12}
Drug	100	100	100	100	100	100	100	100	100	100	100	100
Microcrystalline cellulose	10	10	10	10	10	20	10	10	10	10	10	20
Modified Agar	10	12	15	15	15	15	-	-	-	-	-	-
Psyllium gum	-	-	-	-	-	-	10	12	15	12	12	12
Magnesium stearate	1	1	1	1	1	1	1	1	1	1	1	1
Starch	12	12	10	07	7	-	10	12	10	07	7	-
Lactose	19	17	17	20	20	17	21	1	17	20	10	07
Total wt.	150	150	150	150	150	150	150	150	150	150	150	150

Coating Of Core Tablet By Compression Coating Method

The accurate quantity of pH sensitive polymer or gums was weighed Half quantity of weighted coating material was placed in the die cavity. Than the core tablet was placed Over this remaining half part of coating polymer was poured. Than at optimum speed the tablet was compressed using 9 mm punch. [10] composition was shown in Table no2

Table No. 2: Formulation Of Compression Coated Tablet With Synthetic Polymers.

Ingredients(mg)	SF_1	SF_2	SF_3	SF_4	SF_5	SF_6	SF_7	SF_8	SF_9	SF_{10}	SF_{11}	SF_{12}
Core tablet	CT 1	CT 2	CT 3	CT 4	CT 5	CT 6	CT 7	CT 8	CT 9	CT10	CT11	CT12
Ethyl Cellulose	50	50	50	100	75	75	50	50	50	100	75	75
Eudrajit L 100	100	100	100	50	75	75	100	100	100	50	75	75
Total weight	300	300	300	300	300	300	300	300	300	300	300	300

Table No. 3: Formulation Of Compression Coated Tablet With Natural Gums.

Ingredients(mg)	NF_1			NF_4	NF_5	NF_6	NF_7	NF_8	NF_9	NF_{10}	NF_{11}	NF_{12}	
Core tablet	CT 1	CT 2	CT 3	CT 4	CT 5	CT 6	CT 7	CT 8	CT 9	CT10	CT11	CT12	
Xanthum gum	50		50	50	100	75	75	50	50	50	100	75	75
Guar gum	100		100	10	50	75	75	100	100	10	50	75	75
Total weight	300		300	300	300	300	300	300	300	300	300	300	300

Evaluation Studies[10,11.12]

- **Hardness test**

The crushing strength kg/cm^2 of prepared tablets was determined for tablets by using Monsanto hardness tester. A tablet is placed between the anvils and the crushing strength, which causes the tablet to break, is recorded. Average of three readings was taken and noted. The result was shown in Table no.9&10.

- **Thickness of coated tablet**

Tablet thickness is an important characteristic in reproducing appearance; average thickness of coated tablet is calculated and presented with deviation using vernier caliper .The result was shown in Table no 9&10.

Weight Variation

Individually coated tablets were weighed and average weight was calculated, not more than 2 tablets from this average weight should not be deviate. The test was performed according to the Indian Pharmacopoeia 2010. Weight variation was calculated by using following formula. The result was shown in Table no 9&10.

$$\text{Percentage weight variation} = \frac{\text{Weight of single tablet} - \text{average tablet}}{\text{Average weight of tablet}} \times 100$$

Friability Testing

20 tablets were taken, it is weighed and initial weight was noted then it was placed into the Roche friabilator and test was performed for 4 min by using 25 rpm after that tablets were weighed and friability was calculated by using following formula. The result was shown in Table no 9&10.

$$\text{Percentage friability} = \frac{\text{Initial Weight of tablet} - \text{final weight of tablet}}{\text{Initial weight of tablet}} \times 100$$

Disintegration test for compressed coated tablet

Disintegration test on coated tablet of simvastatin was performed by using phosphate buffer pH-7.4, the tablets of simvastatin were taken and placed in 6 respective tubes of disintegration apparatus and disintegration time of the tablet was measured. The result was shown in Table no 9&10.

- **Drug Content**

The tablet was tested for their drug content, randomly 10 tablets were weighed and powered. The powder equivalent to 100mg was weighed accurately and transferred to 100ml of volumetric flask then dissolved with 5ml of methanol then the flask is sonicated for 5 min. The Volume was then made up to 100ml with phosphate buffer pH 7.4. Above solution was filtered through Whatman paper and absorbance was measured at 273 nm. The result was shown in Table no 9&10.

In- vitro dissolution studies of core tablet

The in vitro release pattern of core tablets was studied as visually by taking images of the core tablets in a petri dish containing dissolution medium (Phosphate buffer pH7.4) at the specific time intervals of 10 min up to 1hr.

IN- VITRO DISSOLUTION STUDIES[17,18]

Dissolution test of coated tablet of aceclofenac was performed by using pH1.2, 6.8 and 7.4 phosphate buffers for 10 hrs, 2hrs in pH-1.2 (HCL) followed by 3hrs in 6.8 pH and 5 hrs. in pH-7.4, The Dissolution study was carried out at 37^0C and 50 rpm by using USP type II

apparatus. 1ml sample were withdrawn from dissolution medium at every 1 hr up to 10hr and diluted to 10ml with respective pH medium, the absorbance was measured by using UV spectroscopy at the range of 273-275 nm. The withdrawn sample was immediately replaced by equal volume of fresh buffer. The dissolution data obtained were plotted as percentage drug release versus time. The result was shown in Figure no.11, 12, 13, and 14.

Rupture Test[19]

The rupture test on coated tablets was carried out using USP paddle 2 apparatus. Here all other Parameters were same as *In-Vitro* dissolution method. The rupture time was carried out in pH 1.2 6.8 and 7.4.The time at which the outer coating layer starts to rupture is called as lag time. This was determined by rupture test. The results are shown in Figure no. 14.

- **Swelling Studies**[20,21]

The percentage swelling capacity of tablets was determined in the containers filled with 10 ml of pH 1.2 and pH 7.4 phosphate buffers. Tablets were removed from containers at predetermined regular intervals, blotted with tissue paper, weighed and again placed in medium till the outer coating of tablet started to rupture. The % swelling was calculated using the formula. The result was shown in Table no.15 and Figure no.11

% swelling = ((Wt -Wo)/Wo) ×100

Where, Wt is weight of wet tablet at time

Wo is weight of dry tablet.

RESULTS AND DISCUSSION

SOLUBILITY STUDIES

Table No-4: solubility studies.

Pure drug	Solubility(µg/ml)
Distilled water	1.29
pH1.2	14.8
pH6.8	19.6
pH7.4	26.4

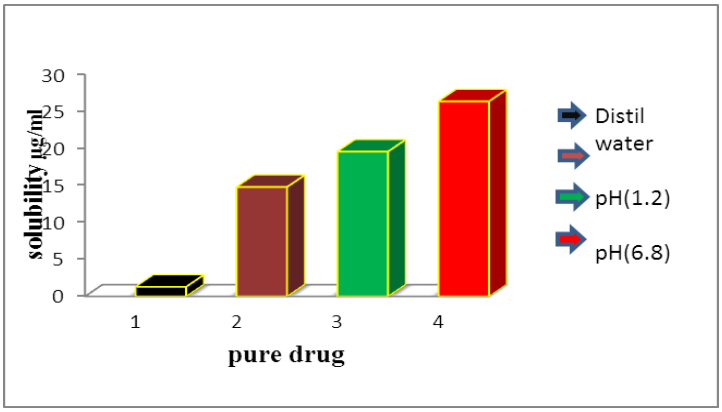


Fig. no. 2: Solubility studies of pure drug in different pH.

Calibration Curve Of Aceclofenac

Table no. 5: Calibration curve with pH 1.2.

Sl.no	Concentration	Absorbance
1	0	0
2	2	0.108
3	4	0.263
4	6	0.396
5	8	0.543
6	10	0.708

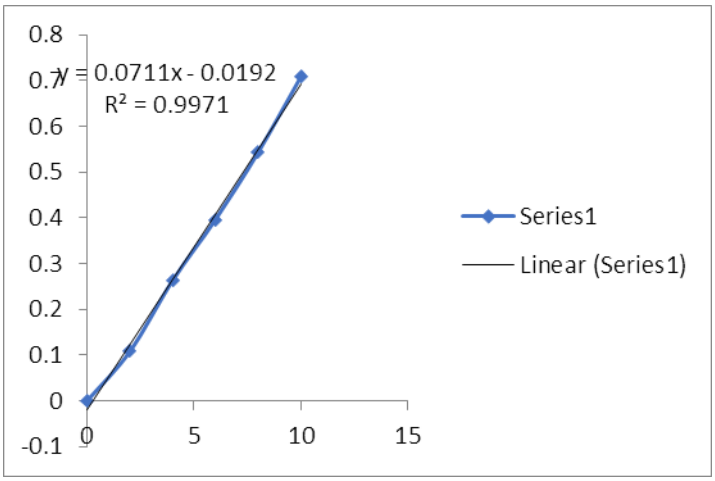


Fig. No. 3: Calibration curve with pH 1.2.

Table No. 6: Calibration curve with Phosphate buffer pH 6.8.

Sl.no	Concentration	Absorbance
1	0	0
2	2	0.136
3	4	0.315
4	6	0.474
5	8	0.656
6	10	0.826

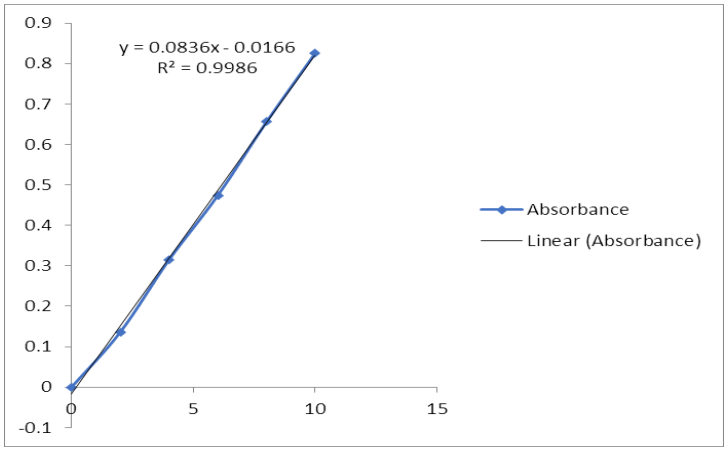


Fig. No. 4: Calibration curve with Phosphate buffer pH 6.8.

Table No: 7: Calibration curve with Phosphate buffer pH 7.4.

Sl.no	Concentration	Absorbance
1	0	0
2	2	0.224
3	4	0.432
4	6	0.636
5	8	0.818
6	10	1.034

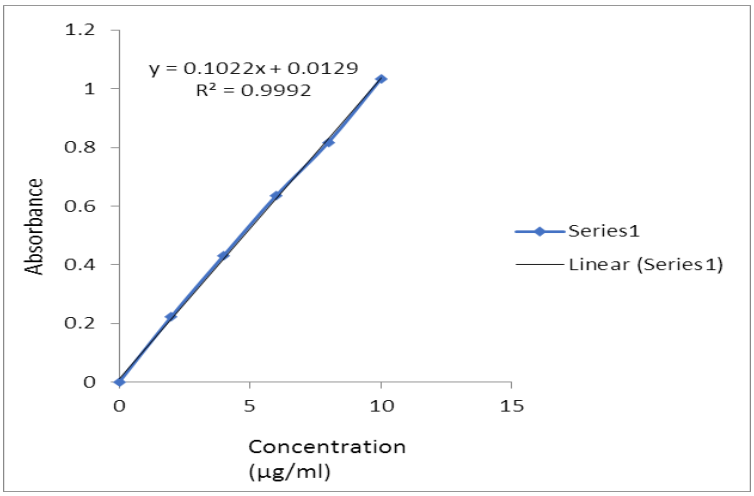


Fig. No. 5: Calibration curve with Phosphate buffer pH 7.4.

DRUG EXCIPIENT COMPATABILITY STUDIES

FTIR SPECTRUM

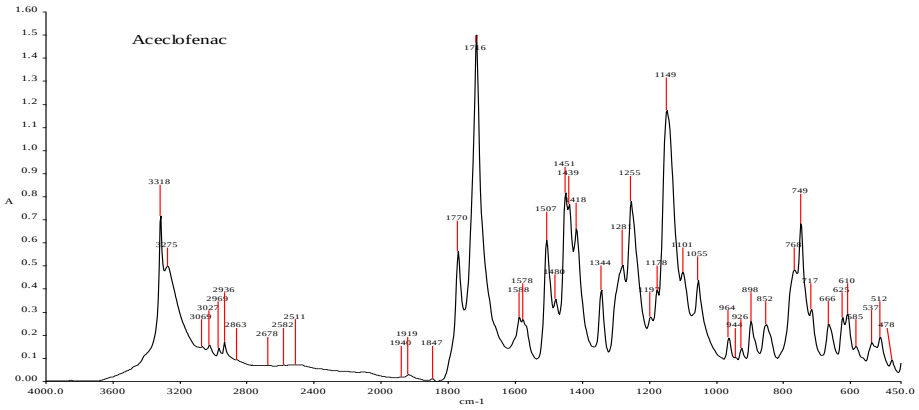


Fig. No. 6: FTIR SPECTRUM of Drug (Aceclofenac).

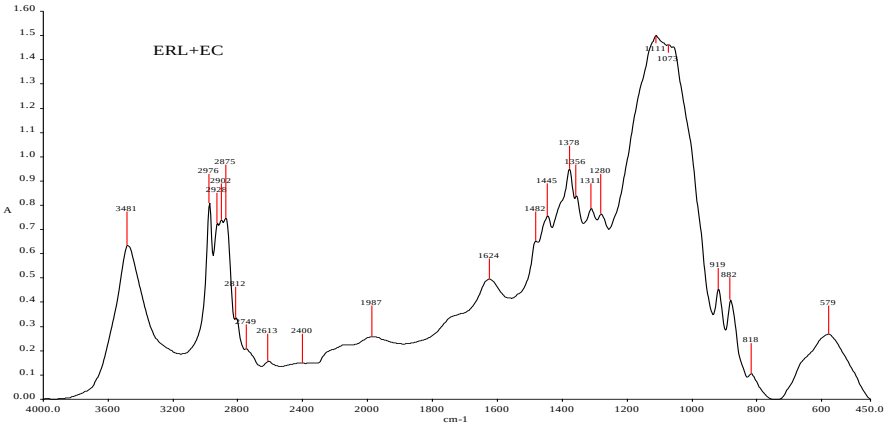


Fig. no. 7: FTIR SPECTRUM OF Eudrajit RL 100 +Ethyl cellulose.

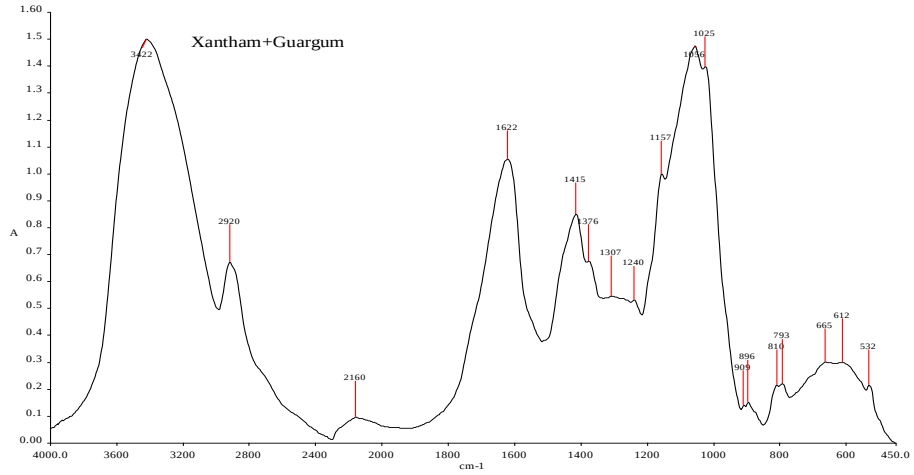


Fig. No. 8: Ftir Spectrum Of Xantam Gum+ Guar Gum.

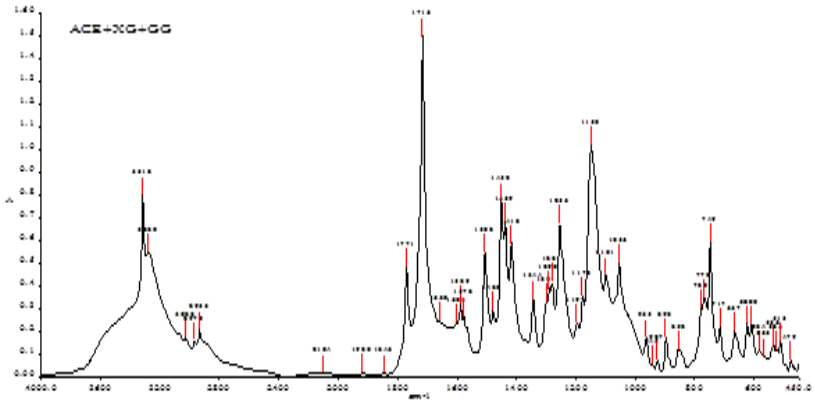


Fig. No. 9: Ftir Spectrum Of Aceclofenac + Xantam Gum+ Guar Gum.

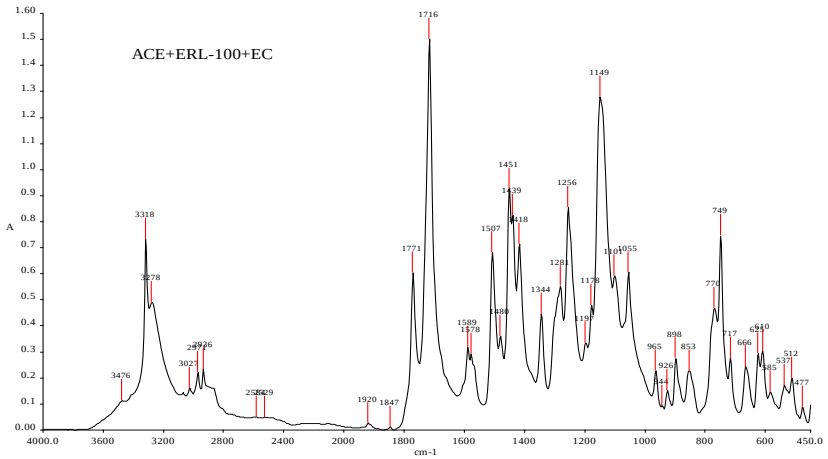


Fig No. 10: Ftir Spectrum Of Aceclofenac+Erl100+Ec.

PRE-COMPRESSION PARAMETERS

Table No: 8. Pre-compression parameters of prepared granules.

Formulation code	Bulk density (gm/ml)	Tapped density (gm/ml)	Hauser's ratio	Carr's index	Angle of Repose (θ)
F1	0.287±0.038	0.330±0.028	1.12±0.020	8.28± 2.16	25.92±0.4
F2	0.323±0.017	0.378±0.005	1.18±0.054	14.26±1.78	24.95±0.1
F3	0.292±0.010	0.330±0.015	1.16±0.040	13.79±2.37	24.56±0.10
F4	0.298±0.022	0.348±0.098	1.16±0.01	13.12±1.16	23.89±0.3
F5	0.301±0.014	0.367±1.018	1.18±0.020	15.21±3.42	25.17±0.1
F6	0.281±0.035	0.342±0.031	1.19±0.014	12.20±1.36	23.15±0.41
F7	0.315±0.026	0.372±0.021	1.16±0.05	15.23±1.32	26.16±0.51

Table no. 9: Post- compression parameter for compressed coated tablet.

Formulation Code	Thickness (mm)	Weight variation(mg)	Hardness (Kg/cm²)	Friability (%)	%drug content	Disintegration Time(min)
SF1	4.39±0.12	299± 0.12	5.0±0.12	0.69±0.015	99.2±0.12	15.6± 0.12
SF2	4.36±0.08	298±0.1	5.36±0.24	0.51±0.017	100.2±0.1	18.26± 0.1
SF3	4.33±0.2	301±0.14	5.61±0.08	0.48±0.014	00.6.8±0.7	14.38± 0.2
SF4	4.29±0.1	299±0.1	5.62±0.15	0.64±0.015	99.4±0.32	11.48± 0.15
SF5	4.35±0.3	299±0.2	5.73±0.25	0.71±0.016	99.6±0.2	19.32± 0.1
SF6	4.38±0.13	302±0.18	5.66±0.17	0.54 ± 0.02	99.7±0.16	20.54± 0.2
SF7	4.38±0.11	297±0.17	5.70 ± 0.24	0.494± 0.2	100.5±0.18	23.12± 0.1
SF8	4.29±0.1	297±0.17	5.77± 0.24	0.77±0.015	99.2±0.12	15.6± 0.12
SF9	4.35±0.3	297±0.17	6.7 ± 0.22	0.56±0.015	100.2±0.1	18.26± 0.1
SF10	4.35±0.3	297±0.17	6.29 ± 0.12	0.78±0.015	100.6.8±0.7	14.38± 0.2
SF11	4.35±0.3	297±0.17	6.25 ± 0.17	0.49±0.015	99.4±0.32	11.48± 0.15
SF12	4.35±0.3	297±0.17	6.27 ± 0.25	0.55±0.015	99.6±0.2	19.32± 0.1

Table No. 10: Post Compression Parameter For Compressed Coated Tablet.

Formulation Code	Thickness (mm)	Weight variation(mg)	Hardness (Kg/cm²)	Friability (%)	%drug content	Disintegration Time(min)
NF1	**4.39±0.12**	**299± 0.12**	**5.80±0.12**	**0.69±0.015**	**99.2±0.12**	**15.6± 0.12**
NF2	**4.36±0.08**	**298±0.1**	**5.56±0.24**	**0.51±0.017**	**100.2±0.1**	**18.26± 0.1**
NF3	**4.33±0.2**	**301±0.14**	**5.63±0.08**	**0.48±0.014**	**100.6.8±0.7**	**14.38± 0.2**
NF4	**4.29±0.1**	**299±0.1**	**4.93±0.15**	**0.64±0.015**	**99.4±0.32**	**11.48± 0.15**
NF5	**4.35±0.3**	**299±0.2**	**5.73±0.25**	**0.71±0.016**	**99.6±0.2**	**19.32± 0.1**
NF6	**4.38±0.13**	**302±0.18**	**5.66±0.17**	**0.54 ± 0.02**	**99.7±0.16**	**20.54± 0.2**
NF7	**4.38±0.11**	**297±0.17**	**5.6 ± 0.24**	**0.49 ± 0.2**	**100.5±0.18**	**23.12± 0.1**
NF8	**4.32±0.1**	**300±0.12**	**4.38±0.11**	**4.38±0.11**	**100.5±0.18**	**23.12± 0.1**
NF9	**4.31±0.12**	**299±0.17**	**5.52 ± 0.14**	**0.71±0.016**	**99.6±0.2**	**11.12± 0.1**
NF10	**4.35±0.11**	**296±0.2**	**6.01± 0.17**	**0.54 ± 0.02**	**99.7±0.16**	**19.60± 0.2**
NF11	**4.38±0.11**	**297±0.12**	**6.1 ± 0.13**	**0.49 ± 0.2**	**100.5±0.18**	**21.2± 0.17**
NF12	**4.28±0.11**	**300±0.12**	**6.2 ± 0.14**	**4.38±0.11**	**4.38±0.11**	**20.12± 0.18**

INVITRO DRUG RELEASE

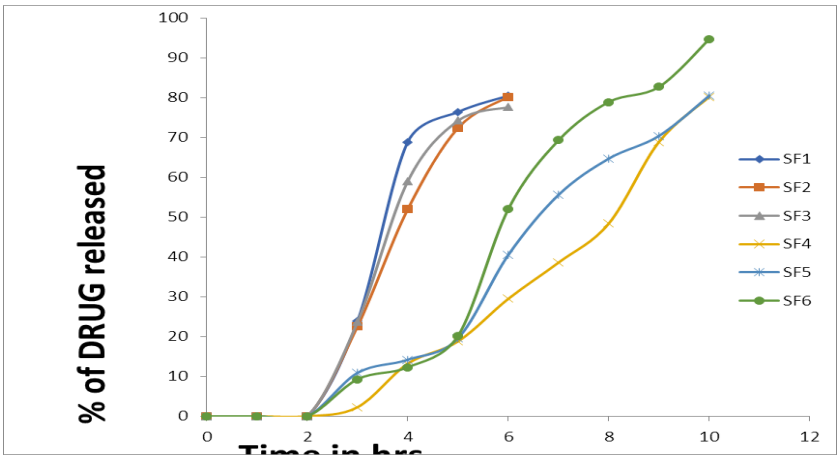


Fig No. 11: Invitro Drug Release Sf^1- Sf^6.

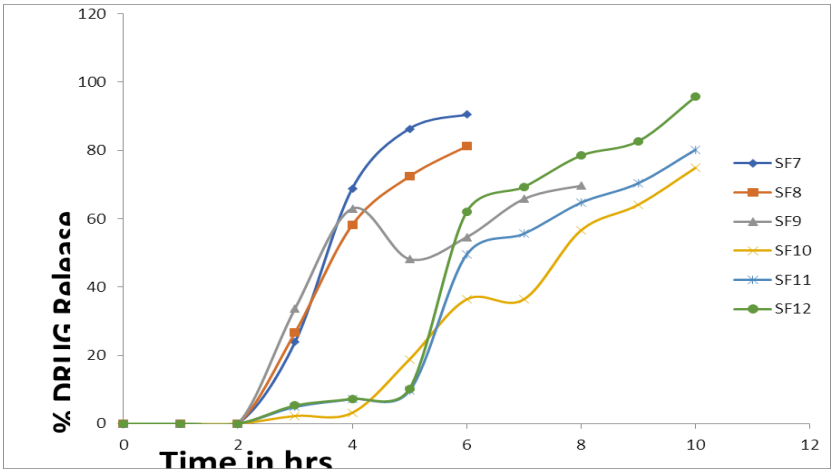


Fig. No. 12: Invitro Drug Release Sf^7- Sf^1.

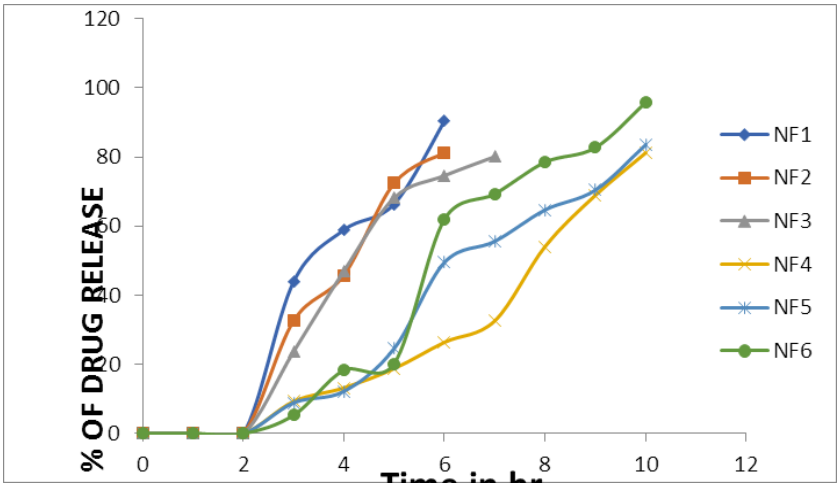


Fig. no. 13: I*n vitro* release of NF1-NF6.

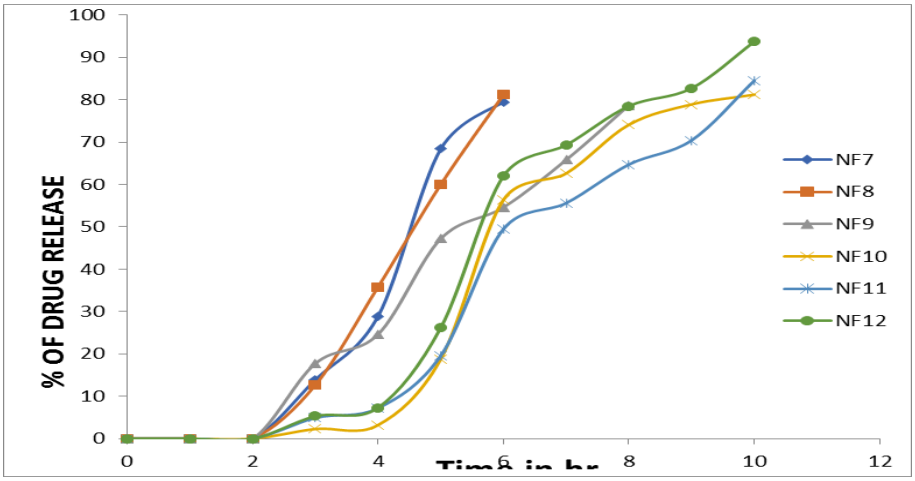


Fig. No. 14: I*n vitro* release of NF7-NF12.

RUPTURE TEST

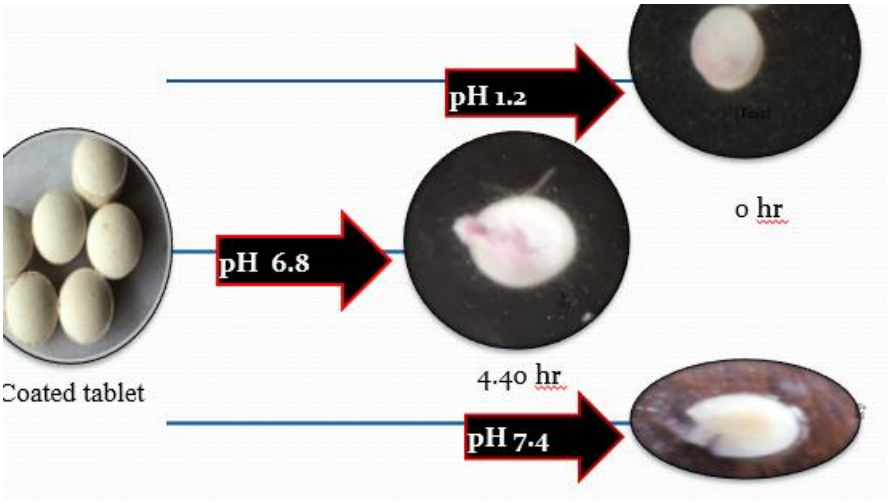


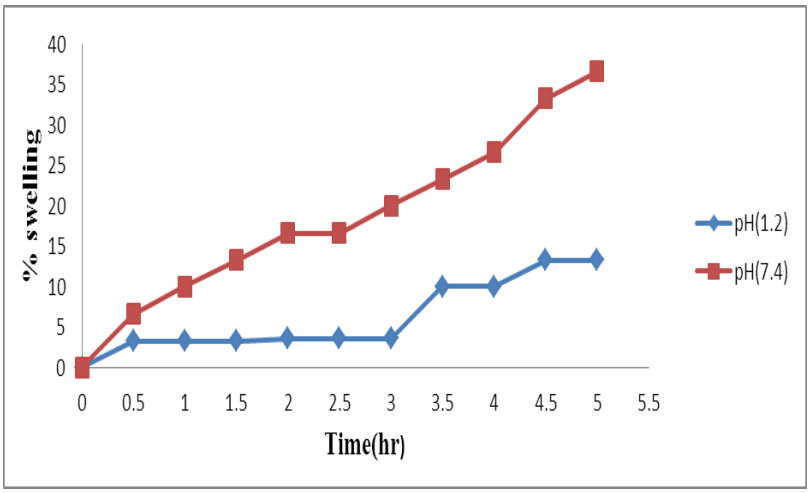
Figure No. 15: Rupture Test

SWELLING STUDIES

Table No. 11: swelling studies.

Time (hr)	Formulation code (F7)	
	pH (1.2)	pH(7.4)
0.5	3.3	6.6
1	3.3	10
1.5	3.3	13.3
2	3.6	16.6
2.5	3.6	16.6
3	3.6	20
3.5	10	23.3
4	10	26.6
4.5	13.3	33.3
5	13.3	36.6

Figure no- %swelling



SUMMARY AND CONCLUSION

Pulsatile drug delivery system is the most promising system, to deliver the drug after a pre-determined lag time according to circardian rhythm means drug deliver when the symptoms are more.

Aceclofenac tablets were prepared by pulsatile drug delivery system in this system the mechanism of increasing the lag time by using different pH sensitive synthetic & natural polymers in different concentration, thereby based on the solubility nature of the polymer the drug release will occur after a pre-determined lag time. The study shows that the solubility of Aceclofenac is very less in water and hence the various buffers having more solubility than the water like pH 1.2, pH 6.8, and pH 7.4. Compared to pH 1.2 and 6.8 solubility was more in pH 7.4. The micro crystalline cellulose, magnesium stearate and starch was added as the wetting agent, psyllium mucilage & modified agar is added as a super disintegrant, and diluents for the preparation of core tablet. Then Ethyl cellulose, Eudragit RL 100 as a synthetic polymers & xanthum gum, guar gum as a natural polymers are selected as coating polymers .The FTIR show no interaction between drug and excipients.

The pre-compression studies like bulk density, tap density, angle of repose, Hauser's ratio and Carr's index was performed all the formulations shows good flow properties. The post compression evaluation like thickness, hardness, weight variation, disintegration time, friability was performed.

In SF1 core tablet formulation modified Agar was added as a super disintigrant. CT1has shown less hardness and DT. So different concentrations of modified Agar were used in core tablet preparation (CT1- CT6).

In SF2, formulation Hardness and DT was within the limit but lag time was very less, around 3 hrs after coating. So, to increase the release concentration of modified Agar was increased to 10%. It shown good results after coating.

In SF3hardness and DT was within the limit but Lag time was less.

In SF4 Ethyl cellulose: Eudrajit RL100 (2:1). Due to the concentration of Ethyl Cellulose it shown more lag time (8 hrs). So in the next formulation Ethyl Cellulose: Eudrajit ratio was reduced to 1:1, it shown good results.

In SF5 lag time was good, but dissolution at the end of 10 hrs was found to be 80%. So concentration of MCC was changed from 10 to 20. The resulted SF6 was the best formulation. All the values were with in the limit.

In SF7 –SF12 Psyllium seed mucilage is used as a super disintegrant. Same like SF1- SF3 here also, the concentration of Psyllium Mucilage was changed in core tablet formulation SF7, SF8 and SF9 shown good hardness and disintegration time but it shown less lag time (<3.5 hrs).

In SF10 2:1 ratio of EC:ERL 100 was used as a coating material but lag time was more than 8 hrs. In SF11coating ratio was reduced to 1:1. It shown good lag time below 7 hrs but in dissolution studies at the end of 10 hrs drug release was 85% to improve drug release concentration of MCC was increased in core tablet preparation. SF12 shown good hardness, lag time and % of drug release at the end of 10 hrs, was 95.7%.

In synthetic polymer compression coating SF6 and SF12 were selected as best batches.

For same core tablet natural gums with same ratios mentioned in SF1 to SF12 was compression coated In NF1 to NF12, NF6-NF12 selected as best batches, due to good lag time and % of drug release was 95.3 and 95.7 respectively.

REFERENCE

1. Arinrindersingh* et al, Elsevier INTERNATIONAL JOURNAL OF INSTITUTIONAL PHARMACY &LIFE SIECNCES "Development And Evaluation of Pulsatile drug delivery system of Aceclofenac sodium., 2013.
2. Smolensky M H, Alonzo G E D, Biologic rhythms and medicine. Am. J. Med., 1988; 85: 34– 46.
3. Kumar Ami, RangaSonam. INTERNATIONAL JOURNAL OF DRUG DEVELOPMENT & RESEARCH. Pulsatile Drug Delivery System: Method And Technology Review., 2012; 4(4): 95-107.
4. Gothoskar A V, Joshi A M, Joshi N H DRUG DELIVERY TECHNOLOGY. Pulsatile drug delivery systems: a review., 2004; 4(5): 1-11.
5. Geest B G D, Mehuys E, Laekeman G, Demeester J, Smedt S.C.D. Pulsed drug delivery, Expert Opinion. Drug Delivery., 2006; 3: 459-462.
6. B k garg, G Gnanarajan, P. Kothiyal. 2012 THE PHARMA INNOVATION; Formulation and Evaluation Of Pulsatile Drug Delivery System Of Rosuvastatin calcium using different swelling polymers., 1(7): 61-67.
7. Parag A,*et al. SCHOLARS RESEARCH LIBRARY.2010; Development and evaluation of press coated tablets for chrono pharmaceutical drug delivery using gellable and permeable polymers., 2(4): 4IO82-497.
8. kamatAkshay Ramesh *et al; INTERNATIONAL RESEARCH JOURNAL OF PHARMACY ISSN2230-840. Formulation and evaluation of pulsatile drug delivery system containing indomethacin using natural polymers.
9. Shivampatel *etal 2015; INNOVATIONS IN PHARMACEUTICAL AND PHARMACOTHERAPY Formulation And Evaluations Of Colon Specific Microbially Dissolvable Matrix Aceclofenac Tablets.
10. Swati C.gagdale*et al 2013, BIO MED RESEARCH INTERNATIONAL VOLUME Optimization studies on compression coated floating pulsatile drug delivery system of BISOPROLOL.
11. V. kamalakanna*et al 2013 SCHOLAR RESEARCH LIBRARY ARCHIVES OF APPLIED SCIENCES. Formulation &In vitro evaluation of Aceclofenac potassium Tablets as a Oral time Controlled Drug Delivery System.
12. N. Guyen Thach Tung *et al. JOURNAL OF DRUG DELIVERY SCIENCE &TECHNOLOGY, Pectin/HPMC dry powder coating formulation for Colon specific targeting tablets of metronidazole.

13. ShajiJessy *et al INTERNATIONAL RESEARCH JOURNAL OF PHARMACY .ISSN NO: 2230-8407., Formulation &optimization of floating pulsatile Aceclofenac Microsphere's using Response Surface Methodology.
14. Michale *et al. ELSEVIER ADVANCED DRUG DELIVERY REVIEWS CHRONOBIOLOGY DRUG DELIVERY AND PHARMACOTHERAPEUTUCS., 2007.
15. PatelVipul P*et al ELSEVIER INTERNATIONAL JOURNAL OF DRUG DEVELOPMENT & RESEARCH. A Review Pulsatile drug delivery system for treatment of Various disorders., 2012.
16. Transber Tangi *et al 2011, INTERNATIONAL JOURNAL OF DRUG FORMULATION & RESEARCH .Pulsatile drug delivery system: methods & Advances.
17. B.k garg *et al THE PHARMA INNOVATION ISSN NO 2277-7695, .Formulation and evaluation of pulsatile drug delivery system of Rosuvastatin calcium using different swelling polymers., 2012.
18. M.P. Venkata Raju, ASIAN JOURNAL OF PHARMACEUTICAL SCIENCES; xanthum & locust bean gum (from elaterin siligue) Matrix tablets for Oral controlled delivery of propranolol., 2007.
19. Krishnaveni .G* et al INTERNATIONAL JOURNAL OF ADVANCED PHARMACEUTICAL SCIENCE RESEARCH Development and evaluation of pulsatile drug delivery system containing Montelukast sodium by press coated Tablet by using Natural poly saccharides., 2013.
20. Dr. S S KHADABADI, NAHID H, CHISHTI* et al, 2013, INTERNATIONAL JOURNAL OF PHARMACY AND PHARMACEUTICAL SCIENCES, Formulation evaluation of press coated tablet of Ketoprofen a Chronotherapeutic approach.
21. Mayee RV, Shinde PV. Jan 2013, ASIAN JOURNAL OF BIOMEDICAL& PHARMACEUTICAL SCIENCES. Development of pulsatile release of Aceclofenac tablets with swelling and rupturable layers of ethyl cellulose.