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FORMULATION AND*IN VITRO* CHARACTERIZATION OF MATRIX TABLETS CONTAINING DICLOFENAC SODIUM USING NATURAL POLYMERS

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ABSTRACT

Oral sustained drug delivery system is one of the most effective form to hold the drugs in biological system for a desired duration and thereby improve their biological half-life of the drug. Diclofenac sodium belongs to class of NSAIDs used extensively in the treatment of various diseases (Rheumatoid arthritis, ankylosing spondylitis, dental pain etc). The present study is focused to formulate Diclofenac sodium matrix tablets by direct-compression using natural polymers (Xanthan gum, Guargum). Formulated tablets were taken to pre-compression and post compression parameters analysis. Reports of pre-compression study shows granules prepared were free following with good compressibility. Post-compression parameters such as hardness, friability, weight variation, thickness and drug content were found in the range of 3-5 kg/cm^2, less than 1%, 295 to 305 mg, 2 to 3 mm and 97 to 99% respectively. Among various formulations (F1-F12), F12 showed 98% of drug release during 12hrs of release study.

KEYWORDS

Diclofenac sodium, Xanthan gum, Guargum, Matrix tablet and FTIR.

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INTRODUCTION

Among many NSAIDs, Diclofenac sodium selected in present study. Hence, Diclofenac sodium has low to moderate preference to block Cox-2 is coenzymes approximately by 10 fold and lower incidence of gastrointestinal compliance than aspirin and indomethacin[1].

In this study, Diclofenac sodium were dispersed homogeneously throughout soluble matrix of rigid non-swellable hydrophobic or swellable hydrophilic materials, is prepared by dispersing the drug in molten

fat followed by congealing[2]. The granules are then compressed into tablets by direct-compression method. Materials used for the rigid matrixes are insoluble plasticizer such as PVC and fatty materials like stearic acid, beeswax etc[3]. Matrix system is one of the least complicated approaches to manufacture the sustained release dosages forms. Moreover, advantage of the system includes release of short half-life drug is possible and incorporation of drugs which have a low aqueous solubility is possible, so that controlled release can be achieved[4].

MATERIAL AND METHODOLOGY

Material

Diclofenac sodium was obtained from Nacto Labs Ltd., Hyderabad, India. Microcrystalline cellulose 200 and 102 was obtained from Stride Arcolab Pvt. Ltd., Bangalore. Xanthan gum and Aerosil were obtained from Titan Biotech, Bhiwadi, Rajasthan, India. Guargum was obtained from Central drug house Pvt. Ltd., New Delhi, India. Magnesium stearate was obtained from S. D. Fine Chem. Ltd., Mumbai, India.

Formulation of matrix tablets of Diclofenac sodium

Diclofenac sodium matrix tablets were prepared using guargum and xanthan gum as rate controlling polymers. The concentration of polymer and ingredients were optimized on the basis of trial and error method[5]. Drug and excipients were weighed accurately and the granules for compression were prepared as per mention below and the hardness of tablet was adjusted to 4-5 kg/cm^2 using a Pfizer hardness tester[6].

FTIR spectroscopy

Infrared spectroscopy is a useful analytical method utilized to verify the chemical interactions in the functional group level between drug and excipients. In this study pellets (Drug + KBR) were prepared. The prepared pellets were examined within the wavelength region of 4000-400 cm^{-1} by Fourier Transform Infra-red spectroscopy (Bruker, Tensor 27, Netherlands)[7,8].

Pre-compression properties

Pre-compression properties of the final blend were characterized by bulk density, tapped density, angle of repose, Carr's index, Hausner's ratio were reported in Table No.2.

Bulk density, Tapped density

10 gm of powder was introduced into dried and clean 100ml measuring cylinder, the cylinder was tapped for 100 times from a constant height and the tapped volume (gm/cc) was read in the case of tapped density determination and the bulk density was determined from the bulk volume using the formula given below[9,10].

$D_b = M/V_o$

Where, D_b = Bulk density (gm/cc)
M = mass of the powder (g)
V_o = bulk volume of powder (cc)

$D_t = M/V_o$

Where, D_t = Tapped density (gm/cc)
M = mass of the powder (g)
V_o = bulk volume of powder (cc)

Compressibility index and Hausner's ratio

The compressibility of powder was determined by the Carr's compressibility index[11].

Carr's index (%) = [(TBD-LBD) x 100] / TBD

Where,

TBD = Tapped bulk density

LBD = Loose bulk density

Hausner's ratio was calculated by using following formula,

Hausner's ratio = Tapped density/Bulk density

Angle of repose (Θ)

It is defined as the maximum angle possible between the surface of pile of the powder and the horizontal plane. Fixed funnel method was used. A funnel was fixed with its tip at given height (h), above a flat horizontal surface on which a graph paper was placed. The powder were allowed to flow through the funnel freely onto the graph paper[12]. The angle of repose was then calculated using formula,

$\Theta = \tan^{-1}(h/r)$

Where, Θ = angle of repose
h = height of pile
r = radius of the base of the pile

Post-compression properties

The prepared matrix tablets were evaluated for their hardness (Monsanto hardness tester), friability, thickness, weight variation, drug content and *in vitro* drug release studies. The values were mentioned in Table No.3.

Hardness and Friability

The hardness of 10 tablets were found using Pfizer hardness tester. It is expressed in kg/cm^2. Mean and standard deviation were computed and reported in Table No.3. The friability of the tablets was determined using Roche friabilator (Remi Electronics, Mumbai, India). It is expressed in percentage[13]. 10 tablets were initially weighed and transferred into the friabilator. The friabilator was operated at 25 rpm/min for 4 minutes. After 4 minutes the tablets were weighed again[14]. The % friability was then calculated using the formula.

% Friability = (Initial weight - Final weight/Initial weight) X 100

Weight variation

From each formulation 20 tablets were weighed individually using electronic balance (Shimadzu electronic balance) and their average weight were calculated[15].

% Deviation = (Average weight - Tablet weight/Average weight) X 100

Thickness

The thickness of the tablets was determined using Vernier Calipers. Six tablets from each batch were used. The extent to which the thickness of each tablet deviated (±5%) from the standard value were determined[16].

Drug Content

For the determination of drug content, 3 tablets from each formulation were weighed individually, crushed and a quantity of powder equivalent to 100 mg weighed and it is dissolved in 100 ml of 6.8 pH buffer to give a solution of 1mg/ml. 1 ml of this solution was further diluted up to 10 ml with 6.8 pH buffer to give a solution of concentrations 100µg/ml. Then the aliquots of the filtrate was diluted suitably and analyzed spectrophotometrically at 276 nm against blank[17,18].

Amount of drug release =(Conc. x dilution factor x wt of tablet) / (5t1000 x wt of sample)

% Drug release = (Amount of drug release x 100) / Label claim

***In vitro* drug release and release kinetics study**

The *In vitro* release of Diclofenac from formulated tablets was carried for 12 hrs in 6.8 pH buffer. The studies were performed in USP type-II dissolution apparatus (Electrolab, Mumbai, India) at 37ºC±0.5ºC and 50 rpm speed. Samples were taken at every 1 hr interval and diluted with buffer and analyzed for at 276 nm by using UV-Visible spectrophotometer[19]. The release kinetics of all the dosage forms were evaluated kinetically using zero-order, first-order, Higuchi and Korsemayer-peppas[20]. The results of kinetic equations applied to dissolution profiles of each tablets were determined and shown in Table No.6.

DISCUSSION

FTIR study suggests that there was no specific shifting of peaks in the functional group levels in the drug-excipients mixture and formulation. 'It shows that there was no specific chemical interaction between the drug molecules and excipients used in the formulations. The pre-compression parameters and the post-compression parameters analysis data reveals that the formulated tablets were within the range as per mentioned in specified monograph, like weight variation and thickness were found to be 295±5.0 to 304±6.0 and 2.95±0.03 to 3.03±0.06 respectively. The hardness and friability of prepared matrix tablets were found to be 3.1±0.15 to 4.63±0.30 and 0.44 to 0.16 respectively. Drug content of prepared matrix tablets were reported in the ranges of 96.33±0.862 to 99.3±0.503. The % CDR of prepared tablets were reported in Table No.4 and 5. From the drug release and drug kinetics studies, formulation F12 showed prolonged release rate of Diclofenac for 12 hours.

RESULTS

FTIR studies

Table No.1: Composition of formulation (F1-F12) by direct compression method

S.No	Ingredients (mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
1	Diclofenac sodium	100	100	100	100	100	100	100	100	100	100	100	100
2	Xanthan gum	-	-	-	-	-	57	72	87	102	117	30	15
3	Guargum	15	30	45	60	75	-	-	-	-	-	15	30
4	MCC 102	135	120	105	90	75	93	78	63	48	33	105	105
5	MCC 200	36	36	36	36	36	36	36	36	36	36	36	36
6	Magnesium stearate	6	6	6	6	6	6	6	6	6	6	6	6
7	Aerosil	8	8	8	8	8	8	8	8	8	8	8	8
8	Total weight of each tablet (mg)	300	300	300	300	300	300	300	300	300	300	300	300

Pre-compression parameters data

Table No.2: Data for pre-compression parameters of formulations F1-F12

S.No	Formulation code	Bulk density (g/cc)	Tapped density (g/cc)	Angle of repose (Ɵ)	Carr's index (%)	Hausner's Ratio
1	F1	0.432±0.004	0.464±0.003	26.52±0.015	6.89	1.074
2	F2	0.421±0.002	0.453±0.002	27.45±0.01	7.06	1.078
3	F3	0.414±0.003	0.444±0.003	24.25±0.065	6.75	1.072
4	F4	0.404±0.002	0.433±0.003	27.77±0.120	6.69	1.071
5	F5	0.434±0.003	0.462±0.001	24.06±0.04	6.06	1.064
6	F6	0.439±0.001	0.475±0.003	28.61±0.09	6.73	1.082
7	F7	0.41±0.002	0.442±0.005	27.26±0.066	7.23	1.078
8	F8	0.429±0.002	0.455±0.003	28.45±0.070	5.71	1.06
9	F9	0.442±0.004	0.475±0.004	26.56±0.14	6.94	1.07
10	F10	0.428±0.003	0.462±0.002	25.33±0.200	7.35	1.07
11	F11	0.451±0.004	0.464±0.001	27.64±0.180	10.5	1.11
12	F12	0.423±0.003	0.481±0.002	25.65±0.127	12.0	1.13

Post-compression parameters data

Table No.3: Data for post compression parameters of formulation F1-F2

S.No	Formulation Code	Thickness (mm)	Hardness (Kg/cm^2)	Friability (%)	Weight variation (mg)	Drug content (%)	Content uniformity
1	F1	2.96±0.05	4.53±0.15	0.34	295±5	97.93±0.472	96.4±0.77
2	F2	2.95±0.03	4.63±0.30	0.21	296±1.52	96.33±0.862	97.5±0.65
3	F3	3.02±0.06	3.63±0.15	0.44	295±5.68	96.33±0.862	97.8±0.45
4	F4	2.96±0.02	4.13±0.25	0.18	299±5.56	98.76±0.305	97.5±0.85
5	F5	2.99±0.01	4.46±0.30	0.24	298±6.02	98.4±0.624	97.6±0.86
6	F6	2.97±0.02	3.16±0.30	0.16	304±6	98.1±0.4	96.4±0.62
7	F7	3.02±0.06	3.4±0.2	0.31	299±4.5	97.9±0.2	98.4±0.55
8	F8	2.96±0.02	4.1±0.3	0.36	294±4	98.86±0.472	97.4±0.90
9	F9	3.03±0.06	3.1±0.15	0.23	297±5.5	99.3±0.4	97.1±0.45
10	F10	2.98±0.05	3.53±0.15	0.26	295±3.6	99.2±0.404	97.7±0.60
11	F11	2.97±0.02	4.1±0.2	0.42	302±5.13	99.3±0.503	98.2±0.56
12	F12	2.97±0.01	4.46±0.25	0.36	300±5.13	98.9±0.351	98.4±0.45

In vitro drug release data

Table No.4: *In vitro* dissolution profile data of formulation F1-F5

Time (hrs)	F1	F2	F3	F4	F5
1	33.9±0.28	39.1±0.28	27.6±2.87	20.9±1.66	10.3±2.87
2	36.3±0.28	41.5±0.28	34.8±0.29	33.4±0.29	24.7±2.88
3	40.7±0.2	42.4±0.29	36.6±0.28	39.5±0.28	33.4±0.288
4	45.7±0.2	46.5±0.28	40.7±0.29	44.5±0.29	39.3±0.45
5	50.6±0.16	52.4±0.27	42.7±0.44	49.6±0.16	43.1±0.30
6	57.1±0.28	57.1±0.28	48.1±0.29	53.3±0.28	50.2±0.44
7	62.1±0.28	61.3±0.28	52.3±0.27	57.2±0.29	52.8±0.30
8	66.8±0.2	65.4±0.28	58.4±0.29	61.0±0.29	54.9±0.30
9	74.2±0.28	68.7±0.28	62.9±0.44	63.5±0.28	57.2±0.34
10	77.9±0.33	72.6±0.2	70.5±0.27	66.9±0.29	61.8±0.30
11	83.5±0.44	78.6±0.28	76.1±0.29	71.4±0.17	65.4±0.45
12	90.9±0.44	83.1±0.16	80.6±0.29	74.1±0.44	69.2±0.27

Table No.5: *In vitro* dissolution profile data of formulation F6-F12

Time (hrs)	F6	F7	F8	F9	F10	F11	F12
1	10.3±2.8	13.1±0.43	18.7±0.2	17.8±0.28	19.2±0.28	7.96±0.43	6.71±0.43
2	32.2±0.29	31.9±0.28	33.7±0.3	34.2±0.28	36.2±0.3	21.8±0.28	20.7±0.28
3	34.9±0.29	38.3±0.28	39.5±0.28	39.5±0.28	41.2±0.2	30.0±0.44	28.2±0.28
4	41.3±0.3	42.4±0.29	45.6±0.28	46.5±0.28	47.6±0.28	45.3±0.29	42.6±0.44
5	44.5±0.2	47.4±0.28	52.0±0.2	52.8±0.16	52.9±0.28	56.3±0.28	54.5±0.43
6	48.9±0.29	51.8±0.2	58.5±0.28	58.8±0.29	59.7±0.28	65.9±0.49	64.6±0.44
7	53.4±0.29	58.9±0.3	62.9±0.3	63.8±0.29	64.7±0.29	71.3±0.44	69.8±0.29
8	59.8±0.3	61.5±0.4	69.4±0.2	70.3±0.3	70.9±0.28	78.9±0.29	76.0±0.28
9	64.5±0.27	67.9±0.16	73.9±0.29	74.5±0.029	73.3±0.29	82.8±0.29	82.5±0.28
10	68.4±0.29	71.6±0.28	76.6±0.28	78.6±0.29	75.9±0.16	86.1±0.29	90.7±0.29
11	70.9±0.27	75.8±0.28	78.1±0.91	84.4±0.29	80.3±0.29	91.5±0.29	95.6±0.29
12	77.3±0.16	79.2±0.29	81.5±0.16	84.9±0.2	83.6±0.29	93.4±0.29	98.2±0.16

Drug release kinetics data

Table No.6: Kinetic profile data of formulation F1-F12

S.No	Formulation code	Zero-order	First-order	Higuchi	Korsemayer-peppas	
		Regression coefficient (R^2)	Regression coefficient (R^2)	Regression coefficient (R^2)	Slope (N)	Regression coefficient (R^2)
1	F1	0.900	0.962	0.975	0.385	0.919
2	F2	0.813	0.933	0.948	0.289	0.887
3	F3	0.893	0.942	0.968	0.384	0.931
4	F4	0.892	0.972	0.996	0.487	0.990
5	F5	0.917	0.972	0.980	0.717	0.948
6	F6	0.934	0.983	0.978	0.723	0.926
7	F7	0.932	0.985	0.984	0.662	0.948
8	F8	0.940	0.994	0.994	0.591	0.989
9	F9	0.943	0.993	0.993	0.611	0.984
10	F10	0.921	0.990	0.993	0.568	0.979
11	F11	0.971	0.988	0.945	1.02	0.975
12	F12	0.983	0.951	0.937	1.09	0.976

Comparative *in vitro* drug release profile data

Drug + Rate retarding polymers and excipients (MCC 102, Drug, Xanthan gum, Guargum)

↓

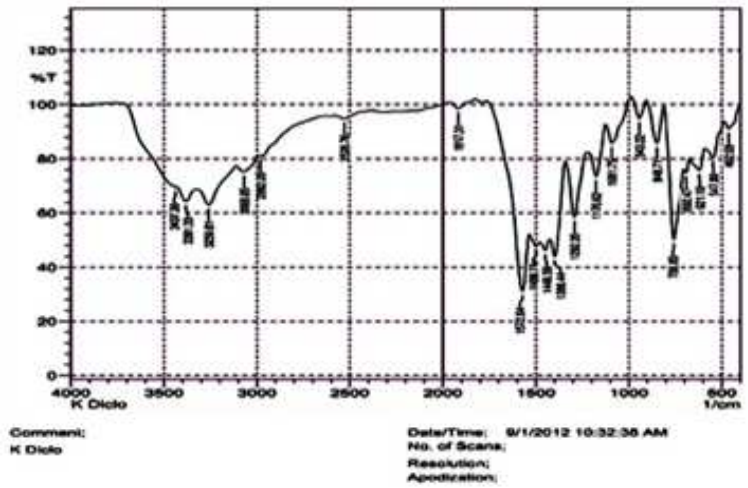
(For 20 mins) Mixing

↓ (For 1 Min)

Add magnesium stearate and alcohol

↓

300 mg of powder mixture was compressed (Direct compression method using 8 mm round surface punch)



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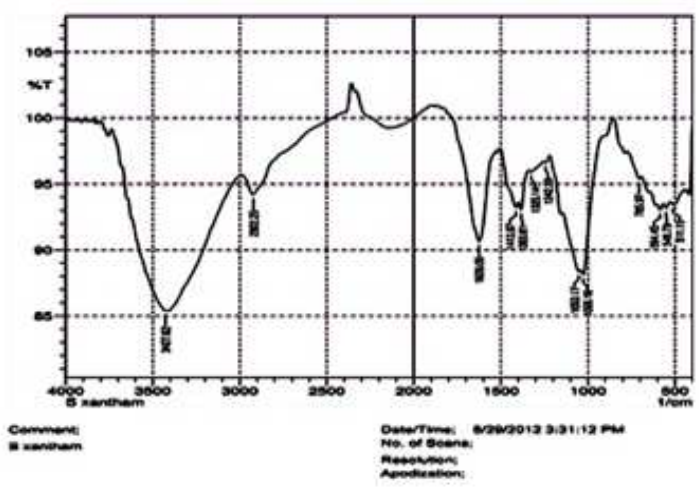

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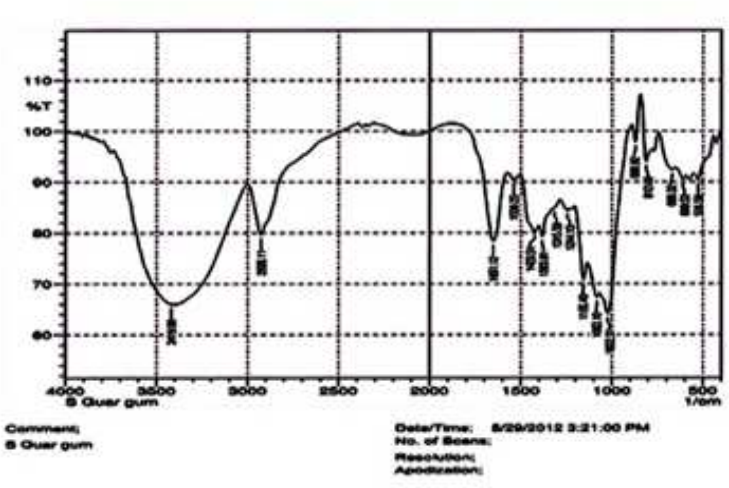

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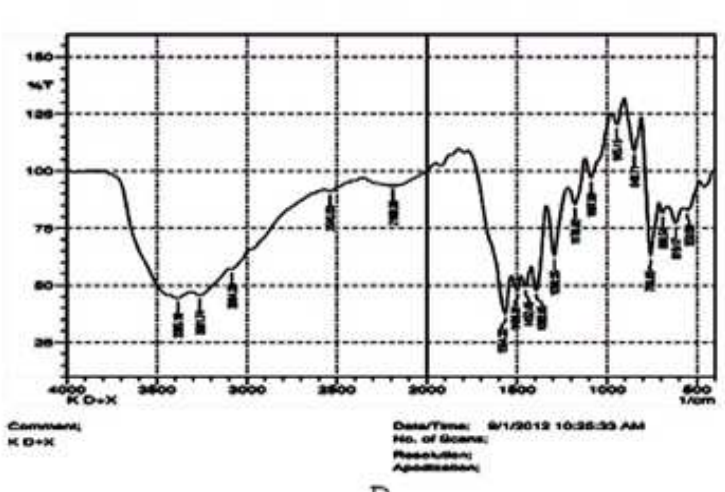

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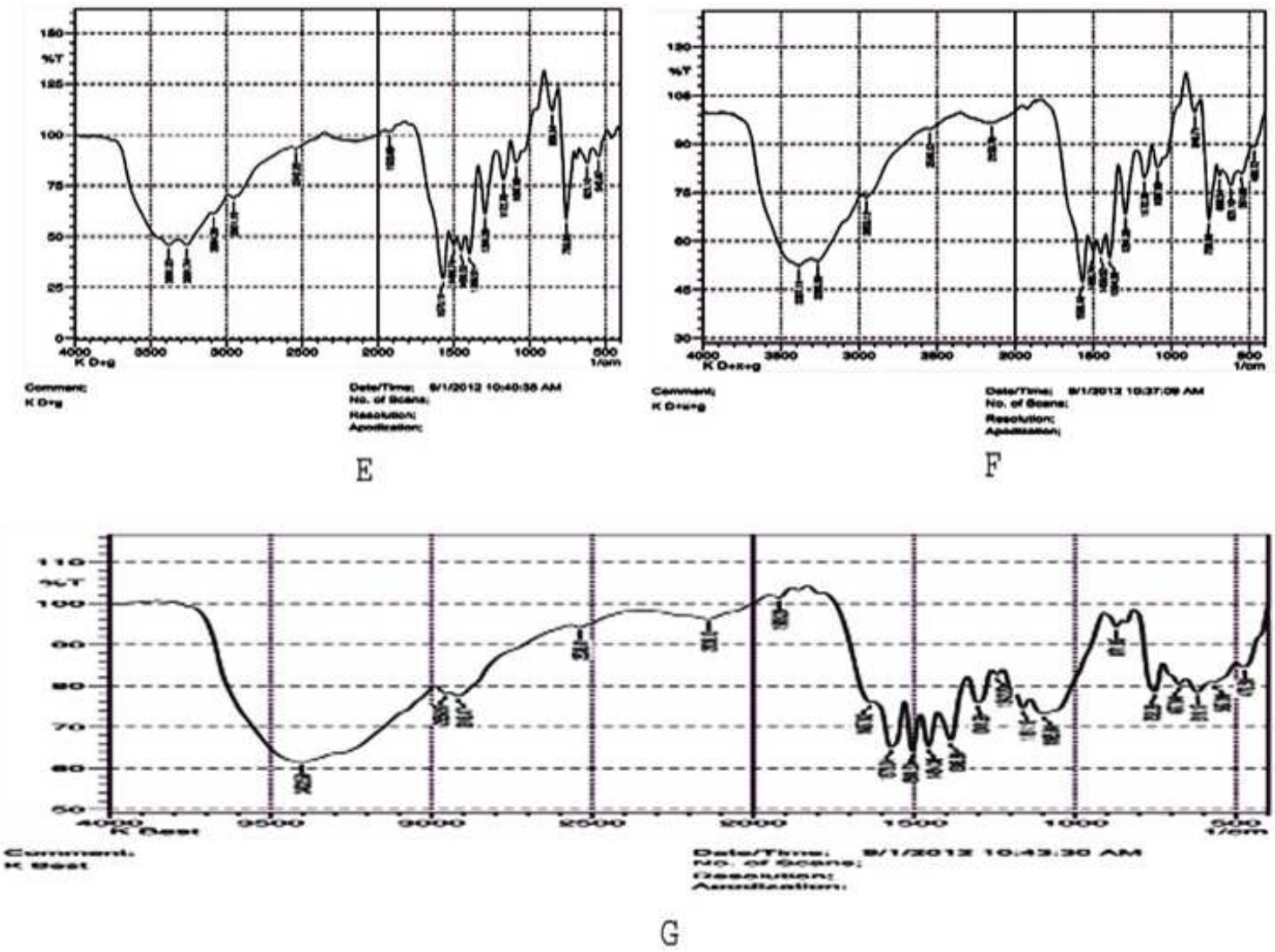

FigureNo.1: Fourier transform infrared (FTIR) spectra of (A) pure drug, (B) xanthan gum, (C) guargam, (D) Diclofenac sodium and xanthan gum physical mixture, (E) Diclofenac sodium and guargum physical mixture, (F) Diclofenac sodium, xanthan gum and guargum physical mixture, (G) Formulation (F12)

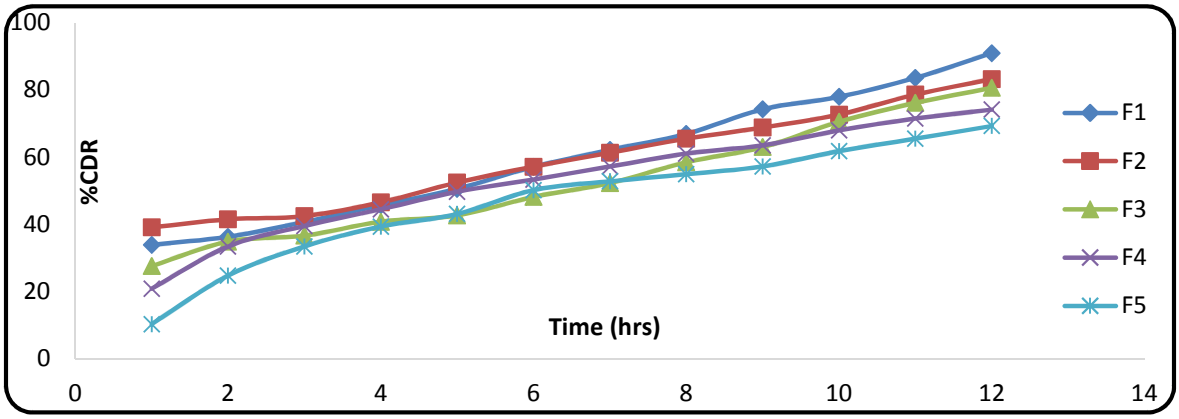

Figure No.2: Comparative *in vitro* drug release profile of formulation F1-F5

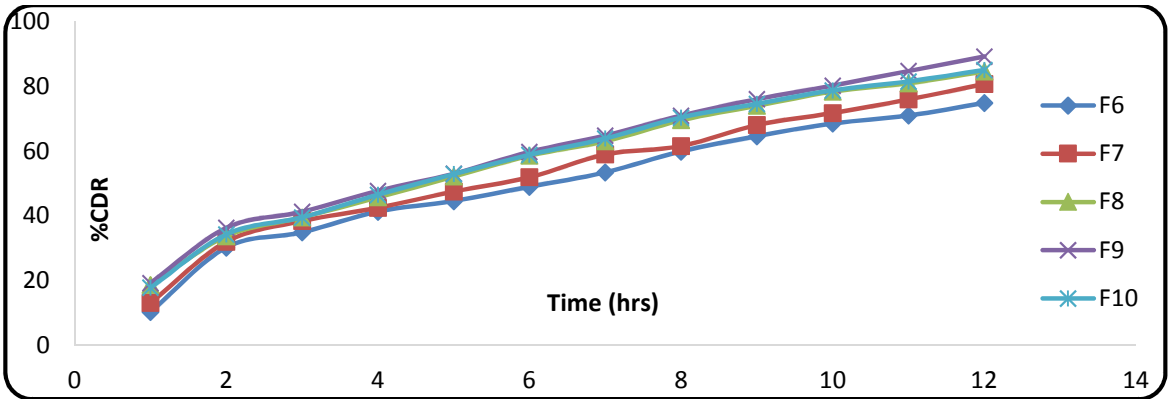

Figure No.3: Comparative *in vitro* drug release profile of formulation F6-F10

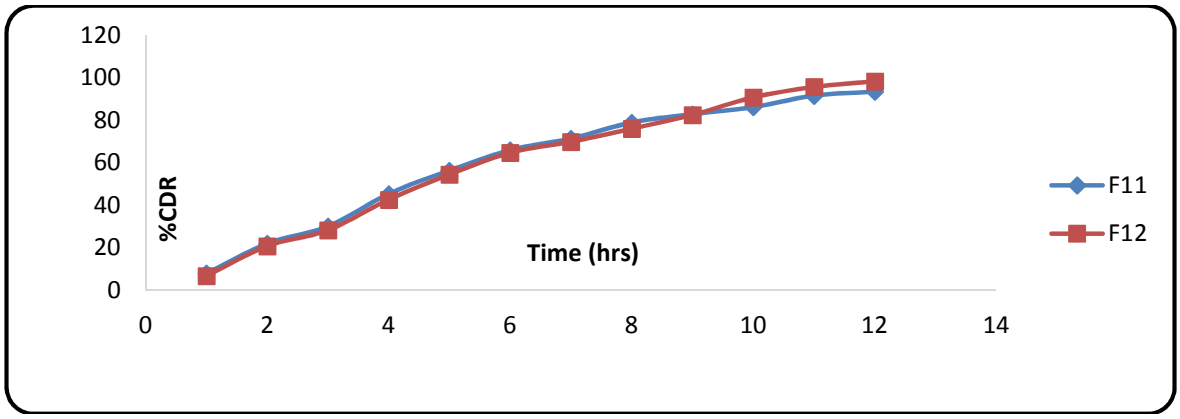

Figure No.4: Comparative *in vitro* drug release profile of formulation F11-F12

CONCLUSION

From the FTIR analysis, it was found that there was no drug-polymer interaction and showed good compatibility in the formulation. The pre-compression and post-compression parameters of all formulations were found to be satisfactory. As a result of this study, it was concluded that the matrix tablets using a combination of Xanthan gum, Gaurgum in optimized concentration in formulation (F12) can be used to increase the release rate of Diclofenac for 12 hours to deliver the drug in a sustained manner.

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CONFLICT OF INTEREST

We declare that we have no conflict of interest.

BIBILIOGRAPHY

1. Chein Y W, Lin S, Swarbrick J and Boylan J. Drug Delivery-Controlled Release In Encyclopedia of Pharmaceutical technology, *Marcel Dekker, NY*, 2nd edition, 2002, 193-199.
2. Chein Y W. Novel drug delivery system, *Marcel Dekkar, Inc*, 2nd edition, 1992, 269-300.
3. Banker G S, Rhodes C T. Modern Pharmaceutics, *Marcel Dekkar, INC*, 2nd edition, 1996, 333-394.
4. Alkhalidi B, Aiedeh K M, Bustanji Y, Hamed S, Mohammad M K, Njjar S *et al.* Modulation of buspirone HCL release from hypromellose matrices using chitosan succinate: Implications for pH-independent release, *Eur J Pharm Biopharm*, 70(3), 2008, 804-12.
5. Abdel-Rahman S I, Mahrous G M, Mahmoud El-Badry. Preparation and comparative evaluation of sustained release metoclopramide

HCl matrix tablets, *Saudi Pharm. J,* 17(4), 2009, 283-288.

6. Yogesh J, Ratendra K C, Teotia U V S. Formulation and evaluation of Diclofenac sodium sustained release matrix tablets using *Marmelos* gum. *Intl. J. of current trends in pharm, Res,* 1(3), 2013, 174-180.
7. Manasadeepa R, Paramita paul, Biswajit Mukherjee. Pressure-sensitive mucoadhesive polymer-based dental patches to treat periodontal diseases: an *In vitro* study, *Drug Deliv.*, 20(6), 2013, 258-267.
8. Prasanna Desu, Manoranjan Sahu. Formulation and evaluation of fast dissolving films of Zolmitriptan, *Intl. Res. J. of pharm,* 3(5), 2012, 373-376.
9. Tanwar Y S, Rana A C, Jaimini M. Formulation and evaluation of famotidine floating tablets, *Curr Drug Deliv,* 4(1), 2007, 51-55.
10. Mourao S C, Silva C D, Bersolin T M B, Serra C H R, Porta V. Dissolution parameters for sodium diclofenac containing hypromellose matrix tablet, *Int J Pharm,* 386(1-2), 2010, 201-07.
11. Pawar S D, Pawar R G, Gadhave M V, Jadhav S L, Gaikwad D D. Formulation and evaluation of pregabalin sustained release matrix tablet, *IJPRD,* 4(02), 2012, 153-159.
12. Ramadevi K, Padmavathi K, Sravani N, Chandra Sekhara Rao G. Formulation and evaluation of Diclofenac sodium sustained release tablets using seed powder of *Strychnos Potatorum, Intl. J. of Biopharmaceutics,* 4(2), 2013, 110-114.
13. The United States Pharmacopoeia, The National Formulary, *The United States Pharmacopoeial Convention, Rockville,* 10(1), 2009, 21-26.
14. Mura P, Mennini N, Maestrelli F, Cirri M, Corti G. Sustained-release matrix tablets of metformin hydrochloride in combination with triacetyl-β-cyclodextrin, *Eur. J. Pharm Biopharm*, 68(2), 2008, 303-309.
15. Bani-Jaber A K, Alkawareek M Y, Al-Gousous J J, Helwa A Y A. Floating and sustained-release characteristics of effervescent tablets prepared with a mixed matrix of eudragitl-100-55 and eudragit EPO, *Chem. Pharm Bull*, 59(2), 2011, 155-60.
16. Bodmeier R, Krogel I. Floating or pulsatile drug delivery systems based on coated effervescent cores, *Int. J. Pharm,* 187(2), 1999, 175-84.
17. Government of India, Ministry of Health and Family Welfare. *The pharmacopoeia of India*, *Controller of Publication,* 4th edition, 1996, 93-94.
18. Park SH, Chun MK, Choi HK. Preparation of an extended-release matrix tablets using chitosan/carbopol inter polymer complex, *Int J Pharm*, 347(1-2), 2008, 39-44.
19. Debajyoti Ray, Amresh K Prusty. Designing and *in vitro* studies of gastric floating tablets of Tramadol HCl, *Intl. J. of Applied Pharmaceutics,* 2(4), 2010, 12-16.
20. Sobhita Rani P, Neelima Rani T, jayanth V, Lavanya Reddy. Formulation and evaluation of HPMC and Physilliumhusk based floating tablets of Curcumin for ulcer, *J. Adv. Pharm. Edu. and Res*, 4(1), 2014, 80-92.

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