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Fabrication and evaluation of Lornoxicam matrix tablets with natural gums

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Abstract

The aim of the proposed work is to study the effect of natural gums like *Xanthan* gum, *Acacia nilotica* and *Buteamonosperma* on drug release. The present plan of work includes the preparation of matrix tablets by using three different natural gums with four varying concentrations and its comparison with marketed tablets. Lornoxicam was took as a model drug in the present study. The formulated tablets were tested for mechanical properties, friability, swelling behaviour, in vitro drug release pattern and the dissolution data was treated with mathematical modelling and the optimized formulation drug release was compared with marketed sample was tested for accelerated stability studies. The formulated tablets were found to have good mechanical properties, good swelling properties. The in vitro dissolution data was perfectly fitting to zero order release. The stability studies revealed that the tablets retain their characteristics even after stressed storage conditions. From this study it was concluded that the dried *Xanthan* gum, *Acacia nilotica* and *Buteamonosperma*gums can be used as a matrix forming material for making sustained release matrix tablets
Keywords: *Xanthan* gum, *Acacia nilotica* and *Buteamonosperma*

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1. Introduction

Lornoxicam is a NSAID, used to relieve inflammation, which has 90% bioavailability and elimination half-life of 3-5 h [1-3]. Xanthan gum is a polysaccharide, derived from the bacterial coat of *Xanthomonascampestris* [4]. *Buteamonosperma* gum (Family: Fabaceae) is a slow growing tree, young trees have a growth rate of a few feet per year. The gum is used in treatment of diarrhoea and dysentery [5]. *Acacia nilotica*has already known and proved as release retardant [6]. So, an attempt has been made to prepare sustained release matrix tablets with these gums in varying concentrations.

2. Materials and Methods

Materials

Lornoxicam was a gift sample from Dr. Reddy's Labs, Hyderabad, AP, India. Micro Crystalline Cellulose 101, Lactose, Xanthan Gum, *Buteamonosperma*gum, *Acacianiloticа*gum, Talc and Magnesium Stearate were procured from SD Fine chemicals, Mumbai, India. Double distilled water was used throughout the experiment.

Preformulation studies of Lornoxicam

The pure Lornoxicam was tested for colour, solubility, melting point (capillary tube method) and pH (1% w/v aqueous solution) [7].

Method development

Preparation of standard stock solution

Standard stock solution was prepared by dissolving 50mg of Lornoxicam in 50 ml of 0.1 N HCl to get concentration of 1 mg/ ml [8].

Preparation of working standard solution and construction of calibration curve

The prepared stock solution was further diluted with 0.1 N HCl to get working standard solution of 1, 2, 4, 6, 8 and 10 µg of Lornaxicam to construct Standard plot for the pure drug, the absorbance was measured at λ_{max} 373 nm, against mobile phase as blank [9]. The standard graph was plotted by taking concentration of drug on X-axis and absorbance on Y-axis in the concentration range of 1-20 µg. Similarly the standard graph is plotted with the results in 6.8 pH phosphate buffer as and the absorbance measured at λ_{max} 378 nm.

Characterisation of Lornoxicam by FTIR

The pure Lornoxicam was taken in mortar (1-2%) and triturated well to get a particle size of around 1-2 µm to that KBr was added and triturated well. The powder mixture was transferred into the puncher and pellets was prepared and kept in the instrument.

Preformulation studies of Gums

The dried Xanthan gum,*Buteamonosperma*and *Acacia nilotica* were tested for colour, solubility, viscosity (for 1% w/v aqueous solution with Brookefield viscometer, pH and swelling index [10, 11].

Interaction studies

The interaction between the Lornoxicam, Gums and other excipients are evaluated. The sample was placed on the crystal area and pressure arm was applied such that the sample fallen on the diamond surface.

Formulation

Preparation of tablets

Tablets of Lornoxicam were prepared by conventional wet granulation method. Natural gums of varying concentrations were also included in the formulation. The granules were compressed into tablets on a rotary tablet punching machine. Lornoxicam, MCC and Lactose were weighed accurately on electronic balance. Then the above mixture is transfer to V cone bender for 15min.Dissolve specified amount of gum in water(q.s). Then the above solution is slowly added to the mixture prepared in the step 2 with trituration to form dough.Then the dough is passed through sieve no #40 to produce granules. Later the granules are dried at 45^0Cfor about 6 h in ahot air oven [12-14].Then the dried granules are once again passed through sieve no #60. Later talc is mixed properly and evenly. Then the granules are weighed and then punched with a punching machine.

Evaluation

Evaluation of pre-compression parameters

The prepared granules were tested for flow properties [15-16].

Angle of repose

The flow properties of granules is given as follows

$$\text{Tan } \theta = h/r$$

Where, h = height of the powder pile,

r = radius of the powder pile

Bulk density

LBD = weight of the powder/volume of the packing

TBD = weight of the powder/tapped volume of the packing

Carr's consolidation index

Carr's index is expressed in % and given by the following formulas

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

Hausner's ratio

It is defined as the ratio of the tapped density to bulk density It is expressed as follows.

Hausner's ratio=(ρ_{tapped})/ρ_{bulk}

Evaluation of post-compressional parameters

The prepared tablets were tested for post compression parameters viz., Hardness, Thickness, Friability, Weight variation and Uniformity of drug content [17-19].

Swelling Studies: The extent of swelling was measured in terms of % weight gain by the tablet. The swelling behaviour of all formulation were studied. One tablet from each formulation was kept in a petridish containing pH 6.8 phosphate buffer. At the end of 1 h, the tablet was withdrawn, soaked with tissue paper, and weighed [20]. Then for every 2 h, weights of the tablet were noted, and the process was continued till the end of 12 h.
% weight gain by the tablet was calculated by formula;
S.I = {(Mt-Mo) / Mo} X 100,
Where, S.I = swelling index,
Mt = weight of tablet at time t
Mo = weight of tablet at time t = 0.

***In vitro* Dissolution studies**
The release rate of Lornoxicam from sustained release matrix tablets were determined using USP dissolution testing apparatus II (paddle type) at 50 rpm. Dissolution test was carried out for a period of 12 h using 0.1N HCl (pH 1.2) for first 2 h and then the pH is adjusted to 6.8 for the rest of the period. The temperature of the dissolution medium is maintained at 37±0.5°C. 10 ml of the sample was withdrawn at regular intervals and replaced with the same volume pre-warmed with fresh dissolution medium [21]. After filtration, the amount of drug release was determined from the standard calibration curve of pure drug.

Kinetic modeling of drug dissolution profile
The dissolution profile of most satisfactory formulation was fitted to zero order, first order, higuchi model and Korsmeyer Peppas model to ascertain the kinetic modeling of the drug release [22-25].

Stability studies for the most satisfactory formulation of sustained release matrix tablets of Lornoxicam
Stability testing of drug products begins as a part of drug discovery and ends with the demise of the compound or commercial product. To assess the drug and formulation stability, stability studies were done according to ICH guidelines. The stability studies were carried out of the most satisfactory formulation as per ICH guidelines. The most satisfactory formulation sealed in aluminum packaging and keptin humidity chamber maintained at 30 ± 2 °C / 65 ± 5 % RH and 40 ± 2 °C / 75 ± 5 % RH for three months. At the end of studies, samples were analyzed for the *in vitro* dissolution for sustained behavior [26].

3. Results and Discussion

Preformulation studies of Lornoxicam
Lornoxicam wasyellow in colour. Its solubility invarious solvents was tested and the solubility nature of Lornoxicam is listed in the table 1.

Table 1: Solubility of Lornoxicam in different solvents

Solvent	Solubility
Water	Hardly soluble
Methanol	Very lightly soluble
Chloroform	Slightly soluble
Acetonitrile	Very lightly soluble

Melting point
The melting point of Lornoxicam was found to be 237±2^{o}C.

pH:
The pH of 1% w/v aqueous solution of pure drug was found to be 8.7.
The standard graph of Lornoxicam in 0.1N HCl and 6.8 pH phosphate buffers were shown in fig. 1 and 2.

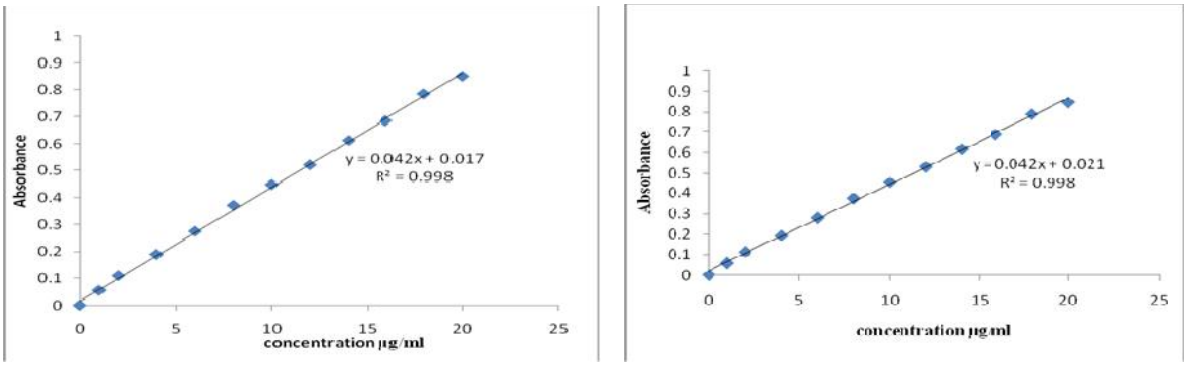
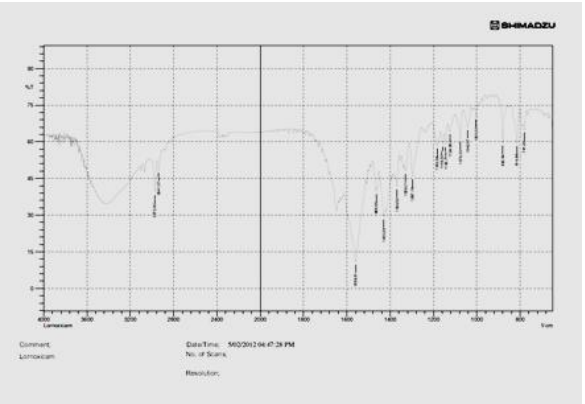


Figure 1: Calibration curvein 0.1N HCl; Fig.2Calibrarion curve in 6.8 pH PBS

Characterisation of Lornoxicam by FTIR

FTIR graph of pure Lornoxicam and that of reference are as follows in the fig. 3 and 4.



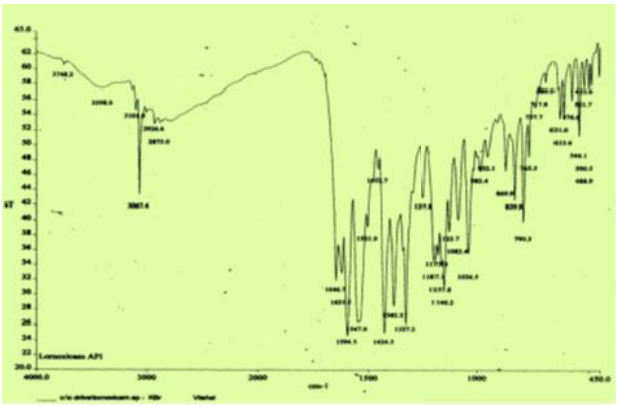


Figure 3: FTIR spectrum of procured drug; Fig.4. FTIR of reference Lornoxicam

Preformulation studies of Gums

Xanthan gum

It was in white to cream in colour. It was soluble both in hot and cold water. But, insoluble in most organic solvents. The viscosity of the 1% w/v aqueous solution of gum was performed using Brooke field viscometer. The value was found to be 1252 cps. The swelling index was found to be 92%.The pH of the gum was found to be 7.5.

Buteamonosperma

Buteamonosperma was reddish brown in colour. It was soluble both in hot and cold water. But, insoluble in most organic solvents. The viscosity of the 1% w/v aqueous solution was found to be 548cps. The swelling index is found to be 96%. The pH of the gum was found to be 7.2

Acacia nilotica

The gum was yellowish-white in colour. It was soluble both in hot and cold water. But, insoluble in most organic solvents. The viscosity of the 1% w/v aqueous solution of gum was found to be 686cps. The swelling index is found to be 57%. The pH was found to be 4.9.

Interaction studies

The resultant spectra of drug and the natural gums were shown in fig. 5-7.

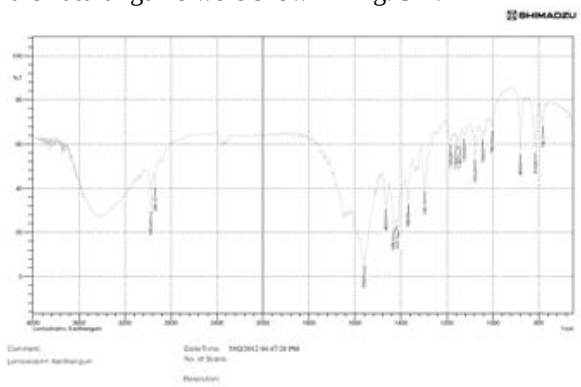


Figure 5: FTIR graph of Lornoxicam and Xanthan gum

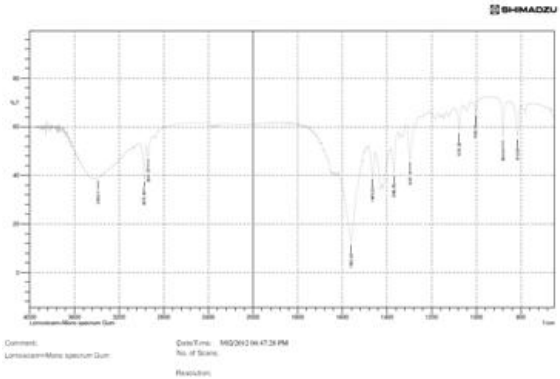


Figure 6: FTIR graph of Lornoxicam and *Buteamonosperma* gum

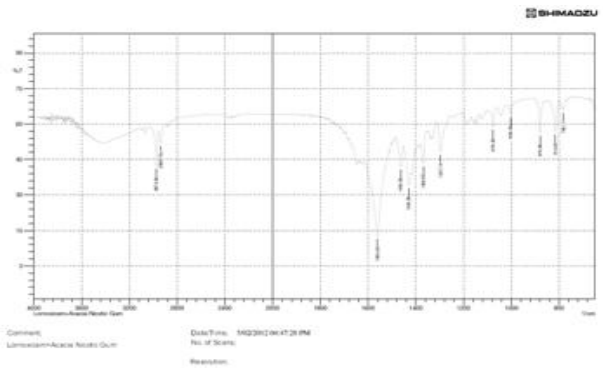


Figure 7: FTIR graph of Lornoxicam and *Acacia nilotica* gum

Granulation and tablet preparation was based on the formulation given in the below table 2.

Table 2: Master formula for Lornoxicam SR tablets

Ingredients (mg)	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**	**F10**	**F11**	**F12**
Lornoxicam	10	10	10	10	10	10	10	10	10	10	10	10
MCC 101	71	66	61	56	71	66	61	56	71	66	61	56
Lactose	96	86	76	66	96	86	76	66	96	86	76	66
Xanthan Gum	15	30	45	60	-	-	-	-	-	-	-	-
Buteamonosperma Gum	-	-	-	-	15	30	45	60	-	-	-	-
Acacia Nilotica Gum	-	-	-	-	-	-	-	-	15	30	45	60
Talc	5	5	5	5	5	5	5	5	5	5	5	5
Magnesium Stearate	3	3	3	3	3	3	3	3	3	3	3	3
Total Tab Wt	200	200	200	200	200	200	200	200	200	200	200	200

The results of Angle of repose and LBD, TBD Carr's index (%) and Hausner's ratio were shown in table 3.

Table 3: Flow properties of formulation blends

Formulation	**Angle of repose (θ)**	**Bulk density (g/ml)**	**Tapped density (g/ml)**	**Carr's index (%)**	**Hausner's ratio**
F1	23.452 ± 0.51	0.441 ± 0.0023	0.512 ± 0.0084	13.21 ± 0.086	1.13 ± 0.043
F2	29.113 ± 0.62	0.423 ± 0.0031	0.472 ± 0.003	13.23 ± 0.057	1.14 ± 0.037
F3	24.957 ± 0.50	0.419 ± 0.0056	0.535 ± 0.023	14.22 ± 0.069	1.16 ± 0.032
F4	26.740 ± 0.97	0.381 ± 0.001	0.497 ± 0.015	13.68 ± 0.013	1.12 ± 0.016
F5	24.808 ± 0.93	0.407 ± 0.0025	0.533 ± 0.0087	14.62 ± 0.008	1.18 ± 0.039
F6	25.811 ±1.34	0.496 ± 0.0031	0.556 ± 0.0023	13.29 ± 0.018	1.13 ± 0.032
F7	27.563 ± 0.86	0.429 ± 0.0025	0.530 ± 0.0074	14.21 ± 0.089	1.12 ± 0.045
F8	26.229 ± 0.73	0.454 ± 0.0023	0.538 ± 0.069	14.21 ± 0.057	1.13 ± 0.047
F9	24.781 ± 0.64	0.491 ± 0.0035	0.568 ±0.0059	14.32 ± 0.059	1.16 ± 0.032
F10	26.251 ± 0.82	0.436 ± 0.004	0.496 ± 0.0068	13.68 ± 0.023	1.14 ± 0.036
F11	27.125 ±0.92	0.421 ± 0.0035	0.519 ± 0.039	14.32 ± 0.008	1.18 ± 0.039
F12	29.456 ± 0.76	0.442 ± 0.0018	0.516 ± 0.0086	13.29 ± 0.058	1.13 ± 0.032
All values mentioned as mean ±S.D; Number of trials (n)=3					

The hardness, thickness, friability, weight variation, drug content (%) of tablets in the table 4.

Table 4: Results of post compression parameters for prepared tablets

Formulation	**Hardness (kg/cm^2)**	**Thickness (mm)**	**Friability (%)**	**Weight variation (%)**	**Drug content (%)**
F1	4.36 ± 0.022	3.14 ± 0.108	0.32 ± 0.06	1.032 ± 0.004	99.48 ± 0.055
F2	4.05 ± 0.023	3.62 ± 0.160	0.46 ± 0.03	1.043 ± 0.009	99.60 ± 0.048
F3	4.12 ± 0.018	3.12 ± 0.132	0.29 ± 0.04	1.028 ± 0.003	99.86 ± 0.023
F4	4.31 ± 0.028	3.18 ± 0.096	0.53 ± 0.09	1.034 ± 0.008	99.21 ± 0.041
F5	4.14 ± 0.053	3.23 ± 0.162	0.74 ± 0.03	1.084 ± 0.006	99.68 ± 0.052
F6	4.19 ± 0.038	3.17 ± 0.037	0.82 ± 0.12	1.049 ± 0.006	99.84 ± 0.081

F7	4.22 ± 0.012	3.12 ± 0.108	0.42 ± 0.06	1.032 ± 0.006	99.14 ± 0.057
F8	4.05 ± 0.021	3.62 ± 0.146	0.56 ± 0.02	1.040 ± 0.009	99.61 ± 0.058
F9	4.11 ± 0.018	3.23 ± 0.132	0.29 ± 0.03	1.038 ± 0.005	99.82 ± 0.036
F10	4.31 ± 0.018	3.18 ± 0.086	0.63 ± 0.06	1.030 ± 0.006	99.51 ± 0.045
F11	4.22 ± 0.053	3.43 ± 0.162	0.66 ± 0.03	1.074 ± 0.008	99.63 ± 0.052
F12	4.19 ± 0.068	3.17 ± 0.067	0.75 ± 0.12	1.039 ± 0.006	99.89 ± 0.072
All values mentioned as mean ±S.D; Number of trials (n)=6 for Hardness, 20 for Friability = 20 and 3for Thickness, 20 for Weight variation and 10 for Drug content					

Values of swelling studies of all the formulations was shown in fig.8.

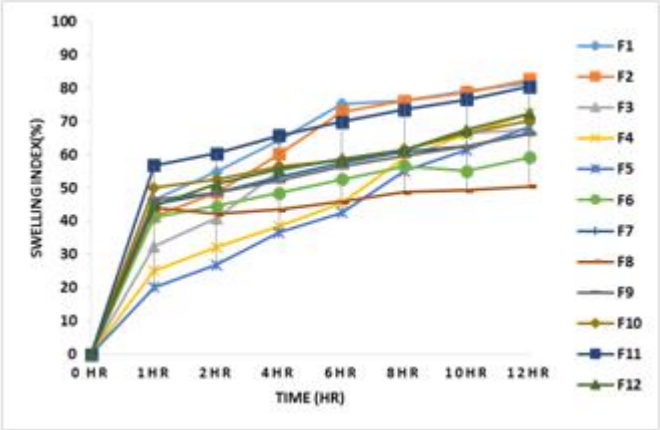


Figure 8: Swelling behaviour of Formulations

The drug release profile plots are depicted in the fig. 9. The zero order plots of best formulations F1,F5, F9 and marketed samples were shown in fig.10.

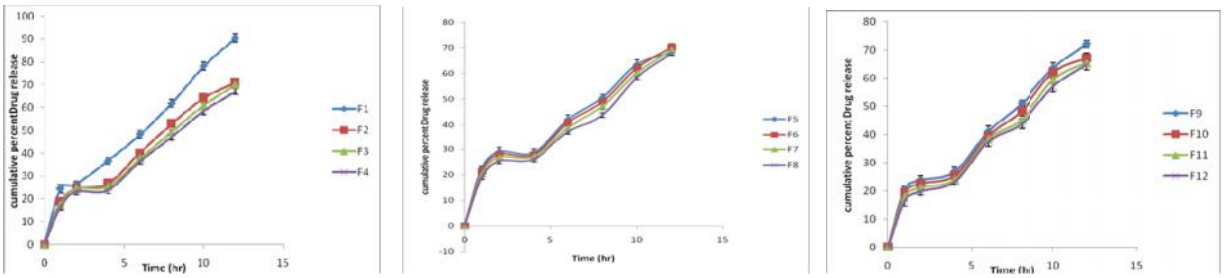


Figure 9: *In vitro* dissolution profile of Formulations F1-F12

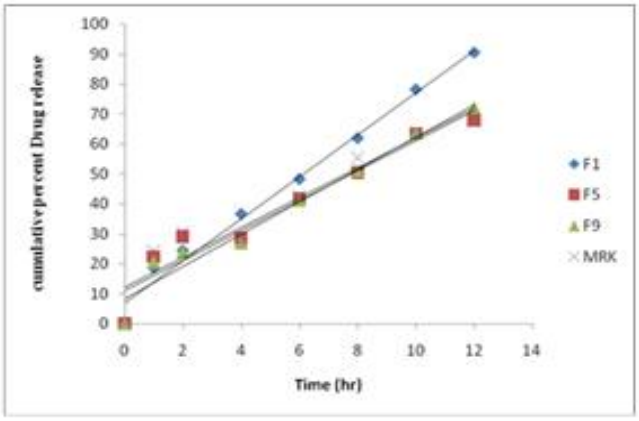


Figure 10: Zero order plots of FormulationsF1, F5, F9 & MRK

The Drug release profile after stability studies was shown in table 5. The tablets showed no change in the colour, shape even after stressed storage cnditions.

Table 5: Drug release after stability studies

Time (h)	After 30 days		After 60 days		After 90 days	
	30^0C ±SD	**40^0C ±SD**	**30^0C ±SD**	**40^0C ±SD**	**30^0C ±SD**	**40^0C±SD**
0	0.00±0.00	0.00±0.00	0.00±0.00	0.00±0.00	0.00±0.00	0.00±0.00
1	18.59±0.05	17.59±0.03	17.90±0.03	16.59±0.07	17.59±0.57	15.69±0.01
2	24.39±0.46	23.29±0.40	24.17±0.40	22.22±0.32	23.89±0.46	22.21±0.42
4	26.56±0.53	25.32±0.30	26.56±0.40	24.20±0.78	25.96±0.73	24.02±0.37
6	40.23±0.42	39.30±0.22	39.23±0.30	37.30±0.39	39.13±0.43	36.86±0.22
8	51.90±0.04	50.30±0.01	51.20±0.01	49.33±0.01	50.23±0.00	48.72±0.04
10	63.15±0.25	61.47±0.20	62.15±0.75	60.47±0.37	61.95±0.23	60.23±0.63
12	93.22±0.04	91.92±0.14	92.92±0.34	91.22±0.13	92.22±0.05	90.92±0.69

4. Conclusion

Various formulations were developed by using release rate controlling and gel forming gums like xanthan gum, *Buteamonosperma* and *Acacia nilotica*. Higher proportion of gums was associated with decrease in the overall cumulative drug release rate. The lower concentration of gum had been seen to produce extended release of Lornoxicam. Thus, we conclude that from among all the developed formulations, F1 formulation with 15 mg of xanthan gum sustained the drug release for longer period of time over 12 h when compare to other formulations.

5. References

1. Sweetman SC, Martindale, the Complete Drug Reference 34th ed., Pharmaceutical Press, London, **2005**, 324–348.
2. Tripathi KD. Essential of medical pharmacology. 4th ed. Delhi: Jaypee Brothers Medical Publishers (p) Ltd; **1998**.
3. Theodore WR, Alan SN, Taylor P, Gilman AG, eds. Goodman and Gilman's The Pharmacological Basis of Therapeutics, 8thed, New York, NY: McGraw-Hill; **1991**; 1484.
4. Yassin El-Said Hamza1 and Mona Hassan Aburahma: Design and In Vitro Evaluation of Novel Sustained-Release Double-Layer Tablets of Lornoxicam: Utility of Cyclodextrin and Xanthan Gum Combination: *AAPS PharmSciTech*, **2009**, 10 (4),1357-1367.
5. Davidson, Robert L. Handbook of Water-soluble Gums and Resins. McGraw Hill, **1980**.
6. Baveja SK, Rao KV and Arora J. Examination of Natural Gums and Mucilages as Sustaining Agents in Tablet Dosage Forms, *Indian J. Pharm. Sci*. **1988**, 50 (2), 89-92 .
7. Phadke DS, Collier JL. Effect of degassing temperature on the specific surface area and other physical properties of magnesium stearate. *Drug Dev Ind Pharm*, **1994**; 20:853–858.
8. Mohammed Ishaq B, Hindustan Abdul Ahad, ShaikMuneer and Praveena S, Colourimetric Assay of Atomoxetine Hydrochloride by Simple Aurum Coupling Reaction in Bulk and Tablet Dosage Form, *Global Journal of Medical research Pharma, Drug Discovery, Toxicology and Medicine*, **2013**, 13 (7), Version 1.0.
9. Martin A. Micromeritics. In: Martin A, ed. Physical Pharmacy. Baltimore, MD: Lippincott Williams & Wilkins; **2001**; 423-454.
10. Abdul Ahad H, Sreeramulu J, HimaBindu, Fabrication of Glimepiride Aloe barbadensis Miller Leaves Mucilage and Povidone Sustained Release Matrix Tablets: In Vitro and In Vivo Evaluation,*Journal of Pharmacy Research*, **2011**,4(3),748-752
11. Rajeev Garg. Pre-formulation: A need for dosage form design; *pharmainfo. Net*; **2008**; 6.
12. NareshGorantla, Sambasivarao A, Hindustan A Ahad, Fabrication and Characterization of Bilayer Sustained Release Tablets Using Ibuprofen and Methocarbamol as Model Drugs, *Int. J. Chem. and Life Sciences*, **2013**, 02 (03), 1132-1135.
13. Ahad HA, Probable Use Of ProsophisCumanensis Fruit Mucilage As Release Retardant With Povidone: Taking Nimesulide As A Model Drug, *International Journal of Institutional Pharmacy and Life Sciences*, 2012, 2(1), 147-155.
14. Pharmacopoeia of India. New Delhi: Ministry of Health and Family Welfare, Government of India, Controller of Publications; **2007**
15. Martin. Micromeritics. In: Martin A, ed. Physical Pharmacy. Baltimore, MD: Lippincott Williams & Wilkins; **2001**; 423-454.
16. Narasimha Reddy D, Srinath MS, Sudharani MV, Hindustan Abdul Ahad, Glipizide and Valdecoxib Combination Mucoadhesive Tablets: Formulation, In Vitro and In Vivo Evaluation, *International Journal of Institutional Pharmacy and Life Sciences*, **2012,** 2(1), 169-181.

17. Narasimha RD, Hindustan AA, Formulation and in vitro Evaluation Glimepiride and Parecoxib Mucoadhesive Tablets for diabetics associated with pain and inflammation, *Der Pharmacia Sinica*, **2011**, 2 (2): 101-109
18. Killedar SG, Bhagwat DA, Adnaik RS, More HN and D'souza JI, optimization of method for determination of swelling factor of Ispaghula husk seeds," *Indian Drugs*, **2008**, 45 (4), 310–313.
19. Boudreau MD, Beland FA, An evaluation of the biological and toxicological properties of Aloe barbadensis (miller), Aloe vera, Journal of environmental science and health. Part C, *Environmental carcinogenesis & ecotoxicology reviews*, **2006**, 24 (1), 103–54.
20. The United State Pharmacopoeia 24, NF 19, United State pharmacopoeial convention, Rockville, M.D. Asian Edi. **2000**, 1462-5, 1913-4.
21. Abdul HA et al., Probable use of Prosophiscumanensis fruit mucilage as release retardant with povidone: taking Nimesulide as a model drug, *International Journal Of Institutional Pharmacy and Life Sciences*, **2012**, 2(1), 147-155.
22. Korsmeyer RW, Gunny R, Doelker EM, Buri P and Peppas NA. Mechanisms of solute release from porous hydrophilic polymers. *Int. J. Pharm*, **1983**, 15, 25-35.
23. The British Pharmacopoeia. Department of health/by stationary office on behalf of the medicine and health care product regulatory agency, crown copy right, 5thEd. **2005**, 1303-1304, 2588-2589, A133.
24. Higuchi T. Mechanism of sustained action medication. Theoretical analysis of rate of release of solid drugs dispersed in solid matrices. *J. Pharm. Sci*. **1963**, 52, 1145-1149.
25. Muschert S, Siepmann F, Leclercq B. Drug release mechanism from ethyl cellulose: PVA-PEG graft copolymer coated pellets; *European journal of pharmaceutics and bio pharmaceutics*, **2009**, 72 (1), 130-137.
26. Remunan C, Bretal M, Nunez A, BilaJato JL. Accelerated stability of sustained release tablet prepared with Gelucire, *Int J Pharm*, **1992**, 80: 151-159.