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FORMULATION & DEVELOPMENT OF COX-2 INHIBITORS IN TREATMENT OF OSTEOARTHRITIS & RHUMATIOD ARTHRITIS

D. R. Nagesh, Likhith H. M.*, Prakash G. and B. Ramesh

Sri Adhichunchanagiri College of Pharmacy, Adhichunchanagiri University, B G Nagara, Mandya.

***Corresponding Author: Likhith H. M.**

Sri Adichunchanagiri College of Pharmacy. B. G. Nagara.

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ABSTRACT

Point of present examination work was attempted to figure bilayer tablets of Lornoxicam/Ketoprofen through its joining of oral measurements frame that can discharge Lornoxicam/Ketoprofen promptly in addition maintained arrival of Nateglinide for 24 hours to improve oral bioavailability of Lornoxicam/ Ketoprofen. Primary target of this work was plan of bilayer tablets utilizing superdisintegrant Kyron 314 for smart discharge layer Polyox 303 for supporting discharge layer made out of two unique classes of medications by utilizing straightforward simple to-scale-up definition system.

KEYWORDS: Bilayer Tablets, Ketoprofen, Lornoxicam, Superdisintegrant.

INTRODUCTION

Disturbing (Latin, īnflammō, "I trip, set territory") is touch of advanced basic reaction of vascular tissues to harming under pains, for occasion, pathogens, hurt cells or aggravations. Common place indications of uncommon aggravation area unit torment, heat, redness, swelling and loss of function. In intensive sense aggravations area unit of two sort's. Uncommon disturbance begins quickly (brisk onset) a space finds chance to amaze.

Signs responses area unit on the market for few days, none the less once in for a while could proceed for couples weeks a pair of endless aggravation - this proposes entire arrangement annoying, which may keep going for quite for a while even years. It will calculate needless to say as consequence of failure to eliminate no matter was creating real bothering.

An immunized structure reaction to self-antigen-safe framework ambushes solid tissue, mixing up it (them) for precarious pathogens.

A perpetual bothering of low drive that perseveres case of sicknesses conditions with enduring aggravation includes asthma attack, endless ulceration, infectious disease, unhealthy joint misery, diligent periodontal disease, colitis, crohn's affliction, endless rubor, perpetual part liver disease.

Lornoxicam is in a position non-steroidal opposing to inflammatory drug that's as usually as potential utilized for treatment of alleviating, extraordinary steady unhealthy joint exacerbation.

Lornoxicam produces unfavorable impact. to stay up essential detachment from these reactions to touch to alter plausibleness, arrangement may be controlled in style of robust super molecule nanoparticles as development structure.

METHODS

Method of Preparation of Lornoxicam bilayer tablets

Prepared granules of both layers were compressed on Double Rotary Bilayer compression machine on round shaped punch bottom layer was first compressed with lower pressure, which was then followed by filling of die cavity by upper layer granules. Final compression was done only after both granules occupied die cavity one on top of other. Both layers were identified on basis of color since immediate release layer had pink color sustain release layer has white color.

RESULTS AND DISCUSSIONS

A) The melting point of lornoxicam was found to be 231°C.

B) Solubility of lornoxicam

Very slightly soluble in water slightly in ethanol, partially in methanol.

C) Calibration curve of lornoxicam.

Preparation of standard calibration curve in pH=6.8 Phosphate buffer

From the solution (Stock-C), appropriate serial dilutions were prepared (5-25 mcg/ml) the absorbance were recorded at 364nm. The standard curve was obtained by plotting absorbance v/s concentration (in mcg/ml) graph.

Table no: 01. Calibration curve of lornoxicam

Sl. No.	Concentration (mcg/mL)	Absorbance(nm)
1	**0**	**0**
2	5	0.182±0.02
3	10	0.394±0.043
4	15	0.578±0.032
5	20	0.752±0.054
6	25	0.976±0.037

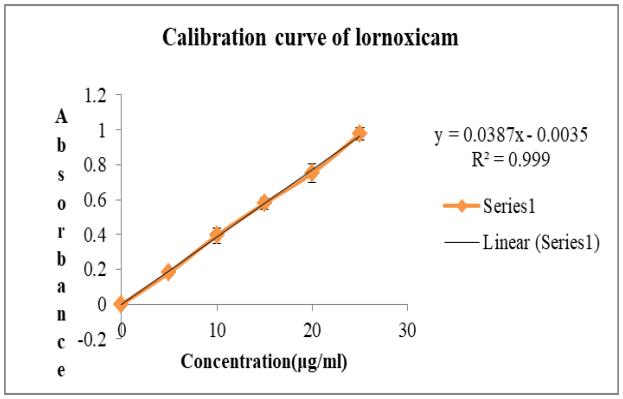

Fig: 01. Calibration curve of lornoxicam.

D) Identification of Drug- Lornoxicam by FT-IR Spectroscopy.

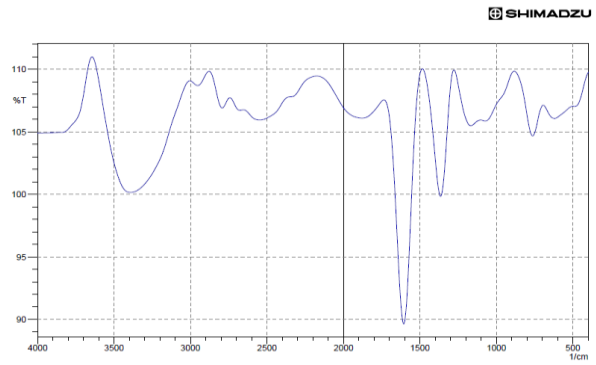

Fig: 02. FT-IR Spectrum of sample Drug Lornoxicam.

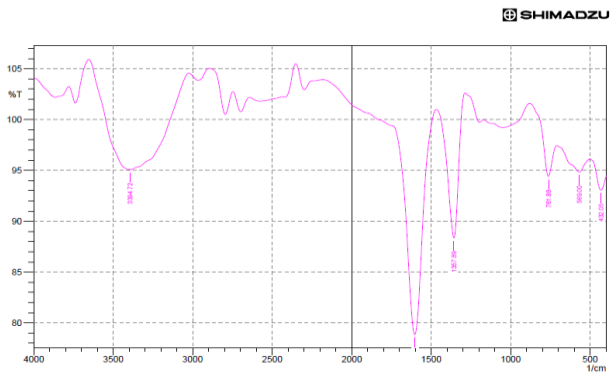

Fig: 03. FT-IR Spectrum Formulation.

E) Drug-Excipients Compatibility Studies by DSC.

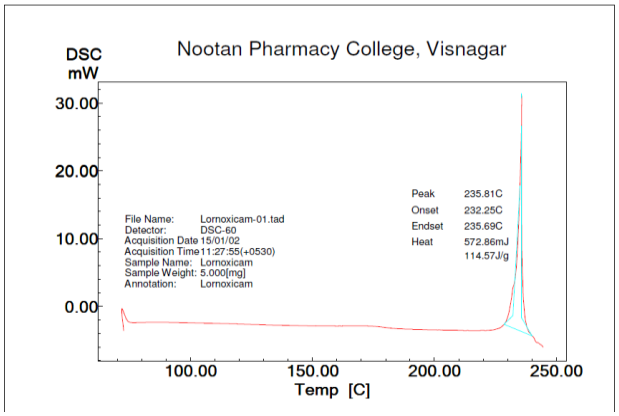

Fig: 04. DSC graph of Lornoxicam.

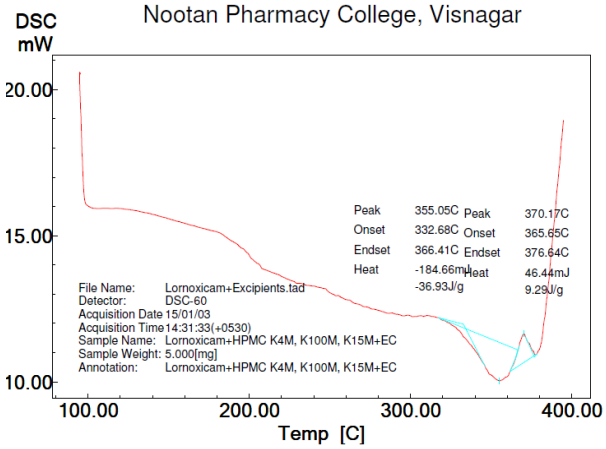

Fig: 05. DSC graph of Lornoxicam Formulation.

Composition of Lornoxicam Orodispersible Layer Tablet (1 TABLET)

Table no: 02. Composition of Lornoxicam Orodispersible Layer Tablet.

Tablet composition	Weight (mg)
Lornoxicam	4
Kyron 314	8
Microcrystalline cellulose	37
Amaranth	4
Aspartame	2
Talc	3
Magnesium stearate	2
Total	60

Formulation Characterization of Lornoxicam bilayer tablets Method of Preparation.

Table no: 03. Pre-compression Evaluation of powder blend.

Batch Code	Pre-compression Evaluation of powder blend				
	Bulk density (gm/cm^3) (n=3)	Tapped Density (gm/cm^3) (n=3)	Carr's Index (%)	Hausner's Ratio	Angle of Repose (θ)
LSB1	0.519±0.010	0.558±0.005	10.25	1.12	23º

Table no: 04. Pre-compression Evaluation of Orodispersible blend.

Batch Code	Pre-compression Evaluation of powder blend				
	Bulk density (gm/cm^3) (n=3)	Tapped Density (gm/cm^3) (n=3)	Carr's Index (%)	Hausner's Ratio	Angle of Repose (θ)
LOB1	0.552±0.005	0.677±0.012	11.64	1.04	21º

Table no: 05. Pre-compression Evaluation tests.

Formulation	Hardness (kg/cm^2)	Thickness(mm)	%Friability	Weight variation (g)	Drug Content (%)
LSOBT1	4.12±0.1	4.38±0.15	0.112±0.016	0.204±0.005	96.17±0.005
LSOBT2	4.42±0.2	4.49±0.15	0.124±0.008	0.210±0.010	97.41±0.010

Evaluation data for % drug release of formulated tablets

Table no: 06. Evaluation data for % drug release.

Time(min)	LSOBT1	LSOBT2
0	0	0
5	19.09 ± 1.12	20.89±1.09
10	34.16 ± 1.95	39.98±1.21
15	57.78 ± 1.23	59.78±1.12
20	79.45±1.25	80.56±1.35
25	98.12±1.45	99.02±1.45

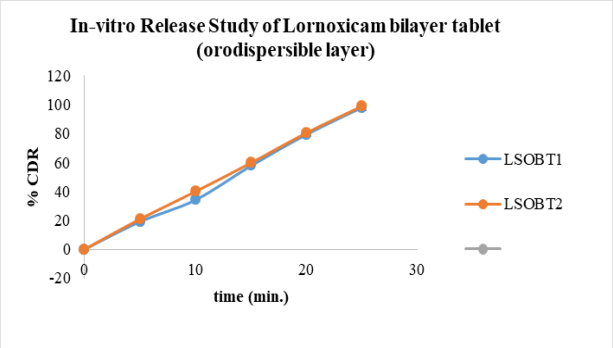

Fig.06 In-vitro Release Study of Lornoxicam bilayer tablet (orodispersible layer).

Drug Release Profile

Table no: 07. Release Kinetic of Batches LSOBT1-LSOBT2.

Model	Parameter	LSOBT 1	LSOBT 2
Zero Order	R^2	0.929	0.927
	Slope	8.496	8.421
	Intercept	13.27	12.89
First Order	R^2	0.9904	0.9747
	Slope	-0.162	0.158
	Intercept	4.51	4.5
Higuchi Model	R^2	0.9974	0.9913
	Slope	26.82	26.61
	Intercept	1.34	1.63
Hixon Crowell	R^2	0.8729	0.8647
	Slope	0.88	0.85
	Intercept	2.96	2.97
Corsmeyer Peppas	R^2	0.4298	0.4114
	Slope	0.57	0.55
	Intercept	-0.67	-0.62

Table No: 08. Stability Study.

Formulation	Parameters	After 30 days	After 60 days	After 90 days
LSOBT1	Physical appearance	No change	No change	No change
	Weight Variation (%± SD)	0.148 ± 2.31	0.151 ± 1.23	0.152 ± 1.89
	Thickness (mm ± SD)	4.48 ± 1.23	4.46 ± 1.89	4.40 ±1.89
	Hardness (kg/cm^3 ± SD)	4.12 ± 0.15	4.05 ± 0.45	4.01 ± 0.85
	Friability (%± SD)	0.112 ± 0.15	0.136 ± 0.62	0.15 ± 0.21
	Drug content(% ± SD)	98.02 ± 1.20	97.85 ± 1.01	97.52 ± 1.23
	Disintegration time (sec ± SD)	10	10	11
	Drug release (h)	98.56	98.12	97.97

Ketoprofen

Melting point of Ketoprofen 92°C ±0.001- 95°C±0.001

Table No: 09. Calibration curve of 6.8 pH phosphate buffer.

Conc.	Absorbance			Avg.
0	0	0	0	0
10	0.111	0.113	0.112	0.111 ±0.011
20	0.249	0.250	0.248	0.249 ±0.021
30	0.349	0.345	0.349	0.349 ±0.03
40	0.45	0.452	0.450	0.450 ±0.032
50	0.542	0.546	0.542	0.542 ±0.042
60	0.652	0.651	0.652	0.652 ±0.021
70	0.751	0.721	0.721	0.751 ±0.035
80	0.845	0.845	0.875	0.845 ±0.035

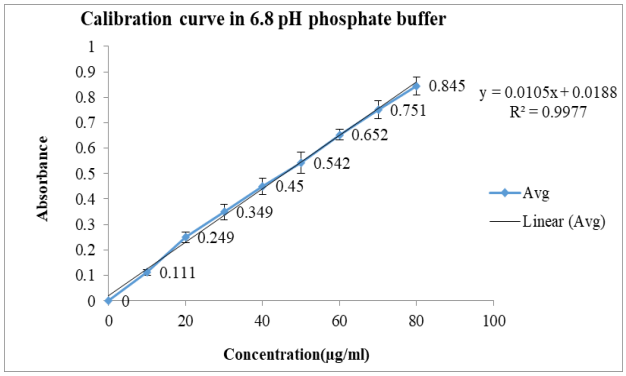

Fig: 07. Calibration curve of 6.8 pH phosphate buffer.

FTIR

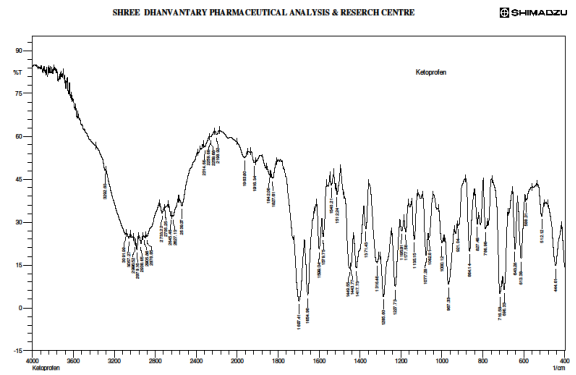

Fig: 08. FT-IR spectra for Ketoprofen.

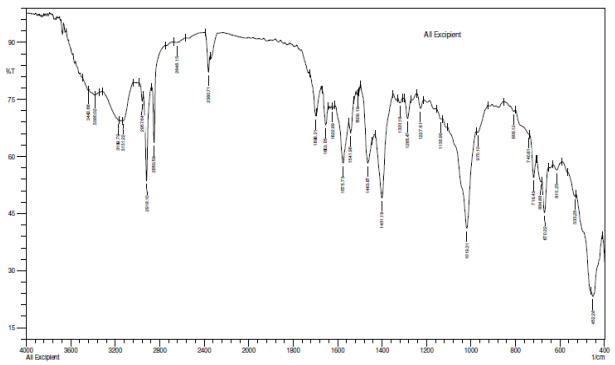

Fig: 09. FT-IR spectra for Ketoprofen +All excipients.

DSC

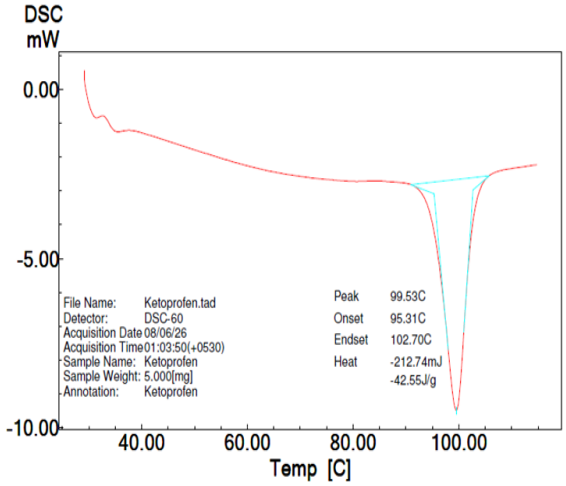

Fig: 10. DSC spectra of Ketoprofen.

By observing DSC spectra of Ketoprofen it can be concluded that endotherm peak at 99.53°C is observed it is comparable to standard drug Ketoprofen sample. So it could be said that sample is Ketoprofen.

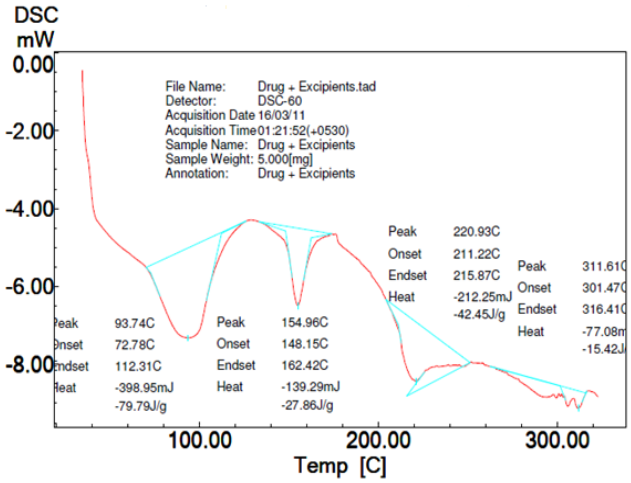

Fig: 11. DSC thermograph for Ketoprofen + all excipients.

Formulation Characterization of Ketoprofen Orodispersible Layer Tablet of KPOBT10:

Table 10: Composition of Ketoprofen Orodispersible Layer Tablet (1 TABLET)

Tablet composition	Weight (mg)
Ketoprofen	5
Kyron 314	9.6
MCC	36.4
Amaranth	3
Aspartane	2
Talc	3
Magnesium Stearate	2
Total	60

Table No: 11. Pre-compression Evaluation of powder blend.

Batch Code	Pre-compression Evaluation of powder blend				
	Bulk density (gm/cm3) (n=3	Tapped Density (gm/cm3) (n=3	Carr's Index (%	Hausner's Ratio	Angle of Repose (θ)
KPSBT1	0.529±0.010	0.568±0.005	10.35	1.04	25º

Table No: 12. Pre-compression characterization of Orodispersible blend.

Batch Code	Pre-compression Evaluation of powder blend				
	Bulk density (gm/cm^3) (n=3)	Tapped Density (gm/cm^3) (n=3)	Carr's Index (%)	Hausner's Ratio	Angle of Repose (θ)
LOB1	0.542±0.005	0.677±0.012	10.54	1.14	24º

Table No. 13 Pre-compression evaluation tests.

Formulation	Hardness (kg/cm^2)	Thickness(mm)	%Friability	Weight variation (g)	Drug Content (%)
KPSOBT1	3.12±0.1	4.38±0.15	0.112±0.016	0.206±0.005	96.17±1.56
KPSOBT2	3.42±0.2	4.49±0.15	0.124±0.008	0.212±0.010	97.41±1.5

Table no: 14. Evaluation data for % drug release of formulated tablets.

Time(min)	KPSOBT1	KPSOBT2
0	0	0
5	20.09 ± 1.12	21.89±1.09
10	35.16 ± 1.95	40.98±1.21
15	58.78 ± 1.23	60.78±1.12
20	80.45±1.25	81.56±1.35
25	98.42±1.45	99.74±1.45

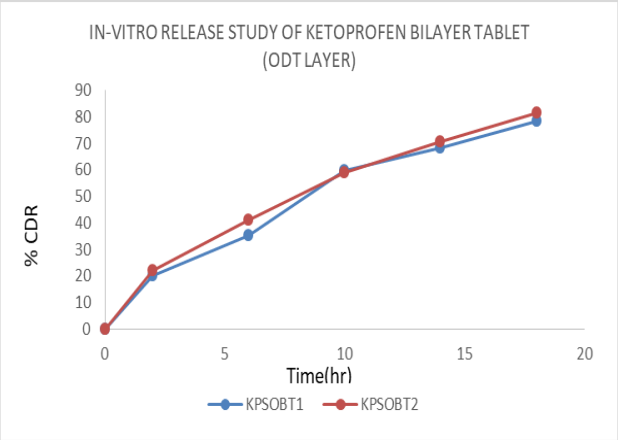

Fig: 12. in-vitro release study of ketoprofen bilayer tablet (ODT).

Table no: 15. Evaluation data for % drug release of formulated tablets.

Time(min)	KPSOBT1	KPSOBT2
0	0	0
2	20.09 ± 1.12	21.89±1.09
6	35.16 ± 1.95	40.98±1.21
10	59.78 ± 1.23	58.78±1.12
14	68.45±1.15	70.56±1.25
18	78.42±1.45	81.56±1.35
22	87.95±1.45	89.59±1.45
24	97.12±1.45	98.02±1.45

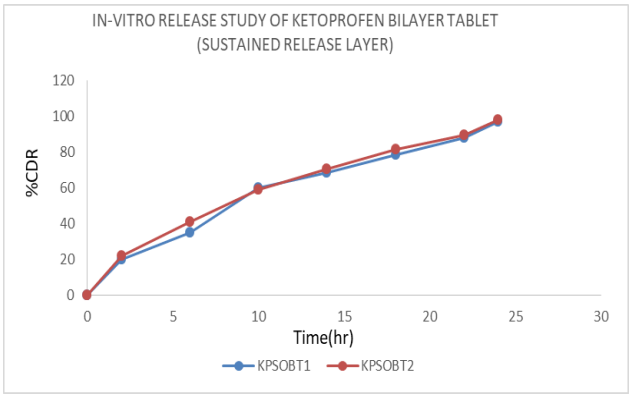

Fig: 13. in-vitro release study of ketoprofen bilayer tablet (Sustained release layer).

Tablet No: 16. Release Kinetic of Batches KPSOBT1-KPSOBT2.

Model	Parameter	KPSOBT1	KPSOBT2
Zero order	R^2	0.919	0.917
	Slope	8.486	8.411
	Intercept	13.26	12.88
First Order	R^2	0.9914	0.9947
	Slope	-0.152	0.157
	Intercept	4.52	4.41
Higuchi Model	R^2	0.9774	0.9713
	Slope	26.72	26.41
	intercept	1.34	1.66
Hixon Crowell	R^2	0.8739	0.8857
	slope	0.87	0.84
	intercept	2.95	2.96
Corsmeyer Peppas	R^2	0.4218	0.4144
	slope	0.54	0.54
	Intercept	-0.66	-0.61

Table No: 17. Staibility Study.

Formulation	Parameters	After 30 days	After 60 days	After 90 days
KPSOBT1	Physical appearance	No change	No change	No change
	Weight Variation (%±SD)	0.206 ±2.31	0.206 ±1.23	0.203 ±1.89
	Thickness (mm ± SD)	3.48 ±1.23	3.47 ±1.89	3.47 ±1.89
	Hardness (kg/cm3 ±SD)	4.42 ±0.15	4.40 ±0.45	4.39 ±0.85
	Friability (%± SD)	0.110 ±0.15	0.111 ±0.62	0.115 ±0.21
	Drug content(% ± SD)	98.12 ±1.20	98.06 ±1.01	98.11 ±1.23
	Disintegration time(sec ± SD)	9.15 ±1.20	9.12 ±1.20	9.16 ±1.20
	Drug release (h)	98.76 ±1.20	99.52 ±1.20.	98.34 ±1.20

CONCLUSION

Development of bilayer tablet of Lornoxicam/ Ketoprofen using superdisintegrant Kyron 314 for snappy release layer Polyox 303 for supporting release layer. Tablets exhibited fundamental burst release to give stacking estimation of pharmaceutical took after by kept up release up to 24 hrs. This balanced release bilayer tablets moreover diminished dosing repeat, manufacture bioavailability gives better patient consistence. Bi-layer tablet is upgraded valuable development to vanquish obstruction of single layered tablet. It is proper for progressive entry of medicines for bolstered release tablet in which one layer is snappy release as starting dose second layer is upkeep estimations. Course of action of tablets as multi layers is used to offer structures to association of meds, which are opposite to give controlled release tablet game plans by giving incorporating or various swelling layers.

From the research work this can be concluded that this is possible to design Bilayer Polymeric Tablets formulation for Lornoxicam Ketoprofen may increase efficacy patient compliance which are of prime importance. However, in – vivo experiments are essential to establish actual usefulness of these Tabs.

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