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Formulation and Evalution of Floating Sustained Release Matrix Tablet of NSAIDs

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Abstract

To increase lornoxicam's stomach residence time, this study aims to develop floating sustained release matrix tablets. Because of its potent oxicam group of non-steroidal anti-inflammatory drugs' relatively short half-life of 2 to 3 hours and maximal absorption in the proximal gastro intestinal tract region, lornoxicam must be produced as floating sustained release matrix tablets. In the current investigation, gelatin and guar gum were preserved in a variable ratio along with high-grade hydroxyl propyl methyl cellulose K4M, a polymer with an apparent viscosity of 15,000 cps, and calcium carbonate and citric acid were used as a gas generator.

Keywords: Lornoxicam, FTIR, Guar gum, Xanthan gum, NSAIDs

1. Introduction

Controlled release medication administration has just been the norm in contemporary pharmaceutical design, and extensive study has been done to improve the efficacy, dependability, and safety of therapeutic products. The most common drug delivery method will continue to be oral sustained release medicine. In order to circumvent first pass metabolism and boost bioavailability, tablets were created in this study. [1] Given the above, it is clear that many medications are not suitable for conventional sustained release formulations that are retained in the stomach and release the medication in the intestine. It is also clear that such medications would benefit greatly from a sustained release formulation that is retained in the stomach and releases the medication slowly over an extended period of time. [2] After oral dosing, bioavailability is 20%. Silent design elements reduce the chance of dose dumping in sustained release pills. less variation between and within subjects. High degree of intestinal dispersion reduces the possibility of high local medication concentrations. Drug bioavailability is reproducible when it successfully reaches the optimal absorption location. Drug transport does not depend on stomach emptying. [3]

Nsaids for inflammation medicine (NSAID) lornoxicam, which belongs to the oxicams class, has strong analgesic and anti-inflammatory effects. Lornoxicam's painkilling and anti-inflammatory qualities, like those of other NSAIDs, are attributed to its reduction of prostaglandin synthesis through inhibition of cyclo-oxygenase (COX)

activity. The ratio of COX-1 to COX-2 inhibition is the same for both isoforms of COX when lornoxicam is used. It quickly reaches the synovial fluid. However, unlike several NSAIDs, Lornoxicam does not reduce 5-lipoxygenase activity and does not shunt arachidonic acid to the 5-lipoxygenase pathway or inhibit leukotriene production. The opioid neuropeptides system's activation may be a factor in how effective Lornoxicam is at relieving pain.[4]

The most popular method of medicine administration is via the oral route. the bulk of oral dosages are in tablet form [(19)]. They are widely used because they are simple to apply (patients are more likely to comply) and simple to prepare on an industrial scale. The majority of oral tablet formulation represents the so-called immediate release (IR) dosage form. Plasma concentration of drug with an IR dosage form generally raises quickly, peaks, and then declines. If the elimination of drug is fast this result in only a short period during which the plasma concentration of the drug is within the therapeutic window. In figure,

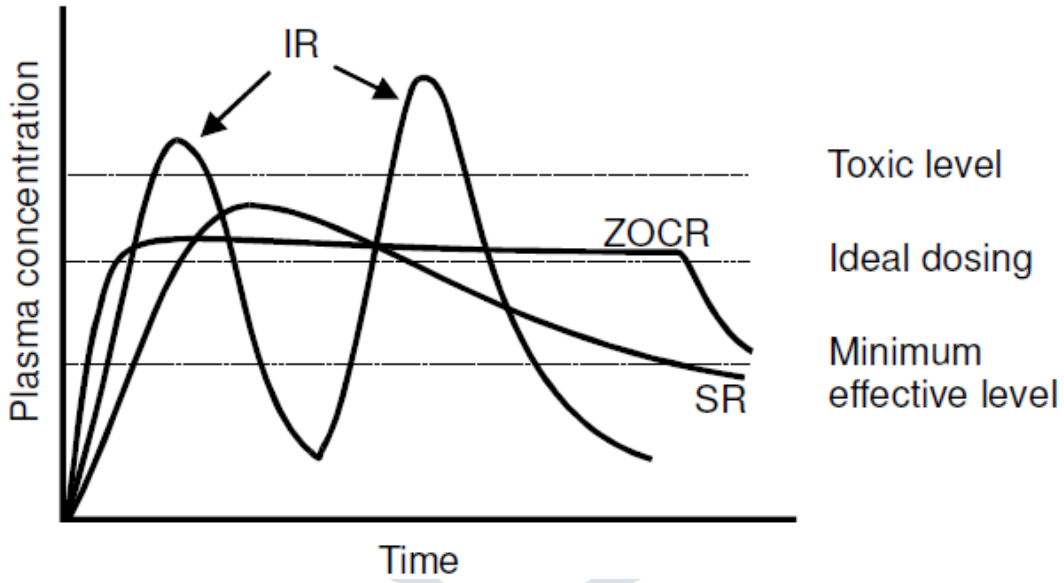


Fig-1.1 Plasma concentrations of an idealised zero order control release (zocr) dose form and a conventional immediate release dosage form are shown in a characteristic way (in combination with a start up dosage)

Material Profile & Method

List of Material & Apparatus which are used in preformualtion studies is presented in Tables 5.1 and 5.2.

Table 5.1 List of material used

Sr. No	Material	Manufacturer/Suppliers
1	Lornoxicam	Morden labs, Indore
3	Guar Gum	Titan Biotech, Bhivandi, Rajasthan.
4	Xanthane gum	HiMedia Laboratories Pvt Ltd., Mumbai
5	Ethanol	Jiangsu Huaxi International Trade Co. Ltd Made in China
6	Sodium bi carbonate	Thermo Fisher Scietific India Pvt. Ltd, Mumbai
7	Citric acid	Finar Chemical (India) Pvt Ltd., Ahmedabad.
8	Calcium carbonate	HiMedia Laboratories Pvt Ltd., Mumbai.
9	Magnesium stearate	HiMedia Laboratories Pvt Ltd., Mumbai.
10	Talc	HiMedia Laboratories Pvt Ltd., Mumbai.

Table 5.2 List of Apparatus

Sr. No	Instrument	Manufactures
1	Weigh Balance	Wensar
2	Melting Point	Khera Industries, Delhi
3	U.V.	Systronic double beam spectrophotometer 2203
4	FTIR	Bruker
5	DSC	

Method

Parameters for Preformulation Study:

- Physical appearance
- Solubility estimation
- Melting point
- Standard absorbance/calibration curve for UV estimate
- Partition coefficient
- FT-IR determination (Compatibility study)

1.Outer appearance: The powdered medication (lornoxicam) was tested for its organo-leptic characteristics, including colour and odour, which were somewhat yellowish.

2. Estimated solubility: The sample's solubility in various solvents was evaluated qualitatively. According to IP, it was determined by putting 10 mg of the drug sample in 10 ml of water, methanol, ethanol, pH buffer

6.8 and pH buffer 7.4 in test tubes and thoroughly blending it by shaking. Table 7.1 lists various solubility terms.

Table 7.1 Various Solubility Terms

Term for describing	parts of the solute needed for each part of the solvent
highly soluble	*< 1*
completely soluble	*1 - 10*
Soluble	*10 - 30*
minimally soluble	*30 - 100*
hardly soluble	*100 - 1000*
extremely hardly soluble	*1000 - 10000*
Insoluble or almost insoluble	*10,000 more*

3. Calculating the melting point:

The melting point was determined using the capillary method utilising a digital melting point apparatus. By gently pressing the open end into a pure drug sample and tapping the capillary's base on a hard surface to force the drug into the tube's bottom, the capillary tube was linked, filled, and packed. The gadget was switched on, the tube with the drug packed inside was put into the slot, and the temperature at which the medication melted was recorded.

4. Development of calibration curves: Acyclovir solution was scanned using a Systronic Double Beam UV Visible Spectrophotometer in the UV range of 200-400 nm (true wavelength about 251 nm to 390 nm).

4.1 Determination of the Maximum Absorbance Wavelength (λ max)

Accurately weighing 10 mg of the medication (aciclovir), it was then put to a 10 ml volumetric flask. After that, 0.1 N HCL was added to completely dissolve the medication. Solvent was used to increase the volume to 10 ml. A 1000 g/ml prepared sample was used. Then, 1 ml of the aforementioned solution was transferred to a second volumetric flask with a capacity of 10 ml and diluted therein. A 100 g/ml prepared sample was used. When 1 more millilitre of this solution was taken and diluted up to 10 millilitres, it produced a solution with a concentration of 10 g/ml. Now, scan the sample in the UV Spectrophotometer between 200 and 400 nm. The same steps were taken to prepare distilled water.

4.2 Making the Lornoxicam Calibration Curve

Between concentration and absorbance, the calibration curve was drawn. In 0.1 N HCL and distilled water, the calibration curve for 2-12 µg/ml was performed.

5. partition coefficient determination

For equilibration, 25 mg of the medication was divided among three separating funnels, which were shaken for two hours in a wrist action shaker. The partition coefficient of the drug in phases was estimated using the following formula after two phases were separated and the amount of the drug in the aqueous phase was spectrophotometrically analysed by using formula:

$$\text{Partition Coefficient, } K = \frac{\text{Amount of drug in organic layer}}{\text{Amount of drug in aqueous layer}}$$

6. A compatibility analysis of drugs and excipients

Drug – Excipient compatibility study done by FT-IR spectroscopy. The presence of characteristic peaks associated with specific structural characteristics of the drug molecule was noted.

Result and Discusion:

5.1 Solubility: Solubility profile of lornoxicam is shown in table 5.1

Table 5.1 Solubility Profile of Lornoxicam

Sr. No.	Medium	Solubility Profile	Parts of Solvent
1	Water	Slightly Soluble	100 - 1000
2	Methanol	Vey slightly soluble	10 – 30
3	Ethanol	Very slightly soluble	1000 – 10,000
4	0.1 N hydrochloric Acid	Soluble	10 - 30
5	0.1 N Sodium Hydroxide	Insoluble	>10,000
6	Acetone	Slightly Soluble	100 -1000
7	Simulated Gastric Fluid (pH 1.2)	Slightly Soluble	100 - 1000
9	Chloroform	Insoluble	>10,000

Where * The average of three determinations: easily soluble = 1–10 parts of solvent, soluble = 10–30 parts of solvent, sparingly soluble = 30–10 parts of solvents, little soluble = 100–1000 parts of solvent, and very slightly soluble = 1000–10000 parts of solvent.

5.2 Melting Point: Melting point of lornoxicam is shown in table 5.2

Table 5.2 Melting Point Range of lornoxicam

Sr. No.	Onset	Complete	Melting Point
1	225° C	230° C	220 ± 2°C
2	220° C	228° C	

5.3 Determination of λmax and Preparation of Calibraton Curve of lornoxicam in 0.1N HCl Solution

Between concentration and absorbance was plotted the calibration curve. It was done using the calibration curve of 2–10 g/ml. The calibration curve's slope and intercept were 0.053 and 0.027, respectively. The

computed value of the correlation coefficient, or "r2," was 0.990. Table 8.3, Figure 8.4, and the Statistical Parameters of Aciclovir demonstrate the calibration curve.

5.4 Determination of λmax and Calibration curve:

Using a Sistronic UV Visible spectrophotometer, the UV range of 200–400 nm was scanned on an acyclovir solution. It was discovered that the spectrophotometric method of examination of lornoxicam at max 370.4 nm was highly sensitive and reproducible. Acyclovir standard curves were created in distilled water and 0.1N HCl solution at a maximum wavelength of 370.4 nm. To generate the straight line, the data were regressed. In every instance, a correlation coefficient larger than 0.99 was found, indicating that the drug complies with Beer-rule Lambert's in the concentration range of 2–10 g/ml. Figures 8.1 and 8.2 display the determination max.

5.4.1. Preparation of Calibraton Curve of lornoxicam in 0.1N HCl Solution

The calibration curve was plotted between the concentration and absorbance. The calibration curve of 2-10µg/ml was carried out. The slope and intercept of the calibration curve were 0.053 and 0.027 respectively. The correlation coefficient 'r^2' values were calculated as 0.990. Calibration curve and Statistical parameters of lornoxicam is shown in table 8.3, 8.4 and figure 8.4.

5.4.2. Calibration Curve: Calibration curve and Statistical parameters of lornoxicam is shown in table 5.3 and 5.4

Table 5.3 Calibration Curve of lornoxicam in Different Medium at λ_{max} 370.4 nm

Sr. No.	Conc (µg/ml)	0.1 N Hydrochloric Acid
1	2	0.016
2	4	0.024
3	6	0.04
4	8	0.05
5	10	0.062

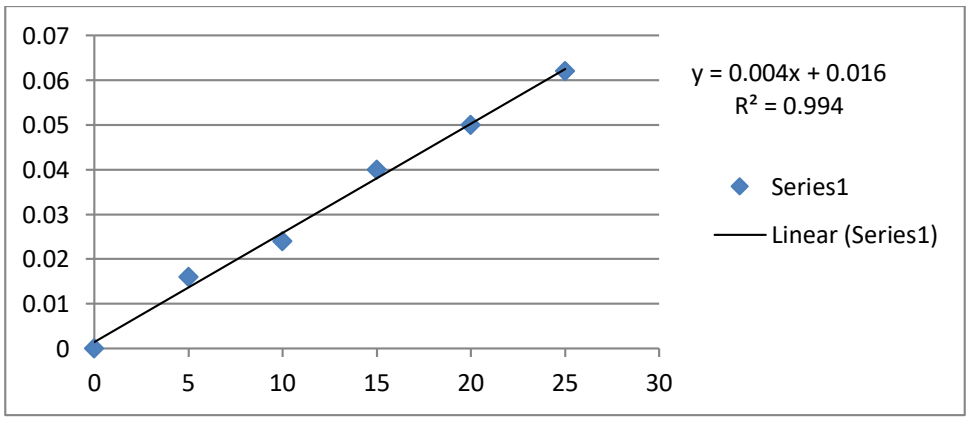


Fig 5.4 Standard curve in 0.1 N HCL of lornoxicam

Table 5.4 Statistical Parameter Related to Standard Curve of lornoxicam at λ_{max} 370.4 nm

		Regressed Line Eqaution (y = mx +c)	y = 0.05 x – 0.016
1	Standard Curve In 0.1 N Hydrochloric Acid (pH1.2)	Beer's Law Range	1 -10 µg/ ml
		Regression Coefficient	R^2 = 0.994
		Regressed Line Eqaution (y = mx +c)	y = 0.004x – 0.016

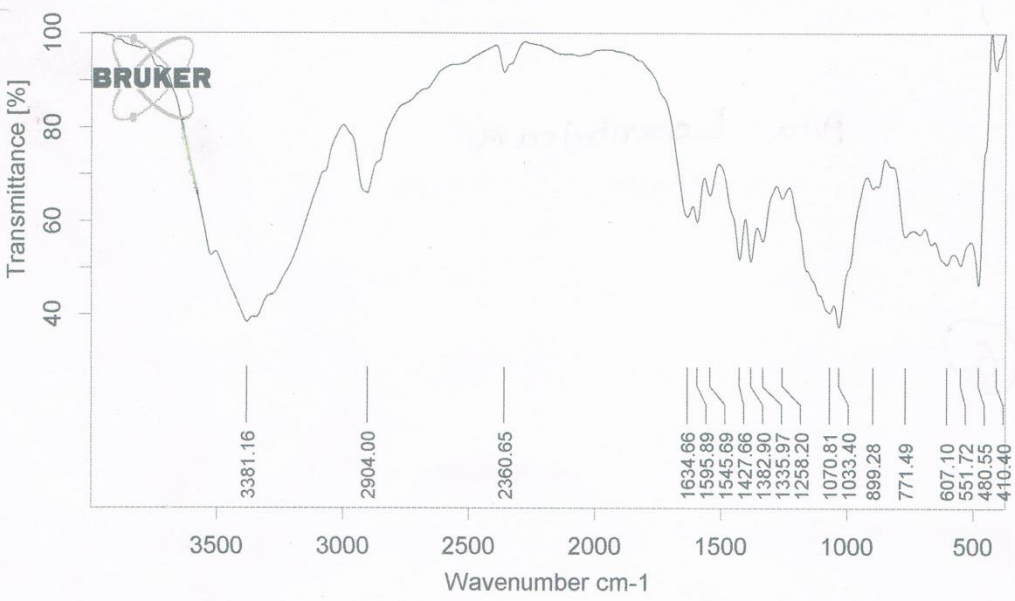
5.5 Partition Coefficient: partition coefficient of drug is shown in Table 5.5

Table 5.5 Partition Coefficient Values of Drug

Sr. No.	Medium	Partition Coefficient (Log P)
1	n – octanol : Water	-1.454
2	Cyclohexane : Water	-0.987

5.6 FTIR Study

Fig 5.5 FTIR Spectra of LORNOXICAM



Wavenumber	Abs. intensity	Rel. intensity	Width	Found if threshold <	Shoulder
3381.1589	0.385	0.610	498.7350	95.409904	0
2903.9983	0.660	0.168	100.1119	23.088863	0
2360.6481	0.917	0.060	54.6691	9.245365	0
1634.6612	0.610	0.033	65.9370	3.559894	0
1595.8876	0.599	0.152	82.5354	19.735245	0
1545.6933	0.655	0.049	29.9789	5.924603	0
1427.6580	0.519	0.096	25.1256	13.849420	0
1382.9016	0.515	0.193	91.2594	25.749250	0
1335.9673	0.558	0.055	426.0131	4.582465	0
1258.2032	0.649	0.025	24.5270	3.712591	0
1070.8115	0.405	0.025	68.4181	2.685994	0
1033.3962	0.374	0.627	551.1000	99.897705	0
899.2755	0.670	0.037	743.4982	3.872817	0
771.4862	0.567	0.091	348.5889	2.823827	0
607.0949	0.508	0.042	158.4399	3.495163	0
551.7215	0.507	0.070	107.0207	7.896163	0
480.5467	0.464	0.504	615.7487	43.012295	0
410.3979	0.923	0.076	33.0279	11.161976	0

Sample Name SBRL -F-1

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Drug

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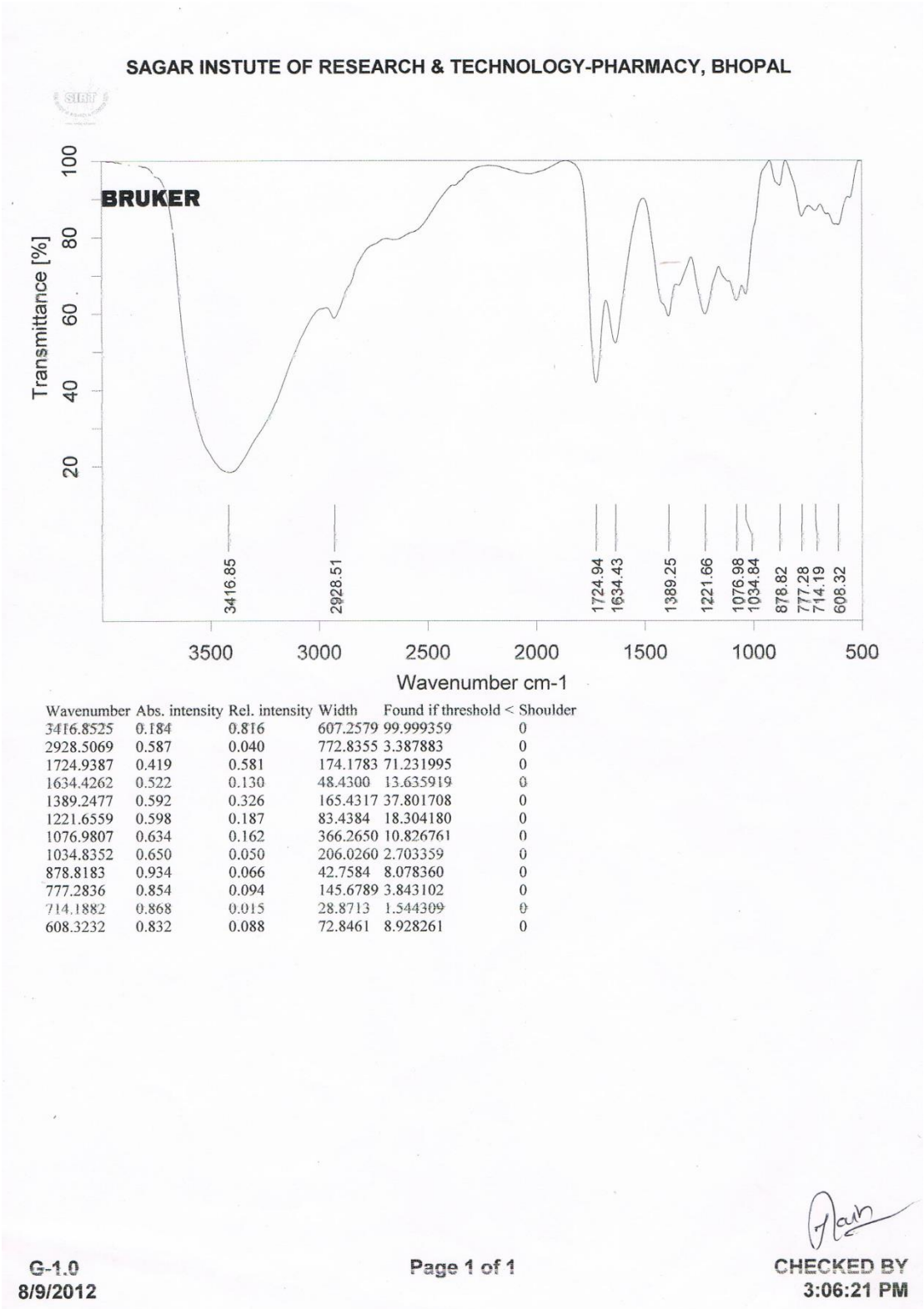
Fig 5.6 FTIR Spectra of Lornoxicam + Gaur gum



Wavenumber	Abs. intensity	Rel. intensity	Width	Found if threshold <	Shoulder
3416.8525	0.184	0.816	607.2579	99.999359	0
2928.5069	0.587	0.040	772.8355	3.387883	0
1724.9387	0.419	0.581	174.1783	71.231995	0
1634.4262	0.522	0.130	48.4300	13.635919	0
1389.2477	0.592	0.326	165.4317	37.801708	0
1221.6559	0.598	0.187	83.4384	18.304180	0
1076.9807	0.634	0.162	366.2650	10.826761	0
1034.8352	0.650	0.050	206.0260	2.703359	0
878.8183	0.934	0.066	42.7584	8.078360	0
777.2836	0.854	0.094	145.6789	3.843102	0
714.1882	0.868	0.015	28.8713	1.544309	0
608.3232	0.832	0.088	72.8461	8.928261	0

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Page 1 of 1

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Fig 5.7 FTIR Spectra of Lornoxicam xanthane gum

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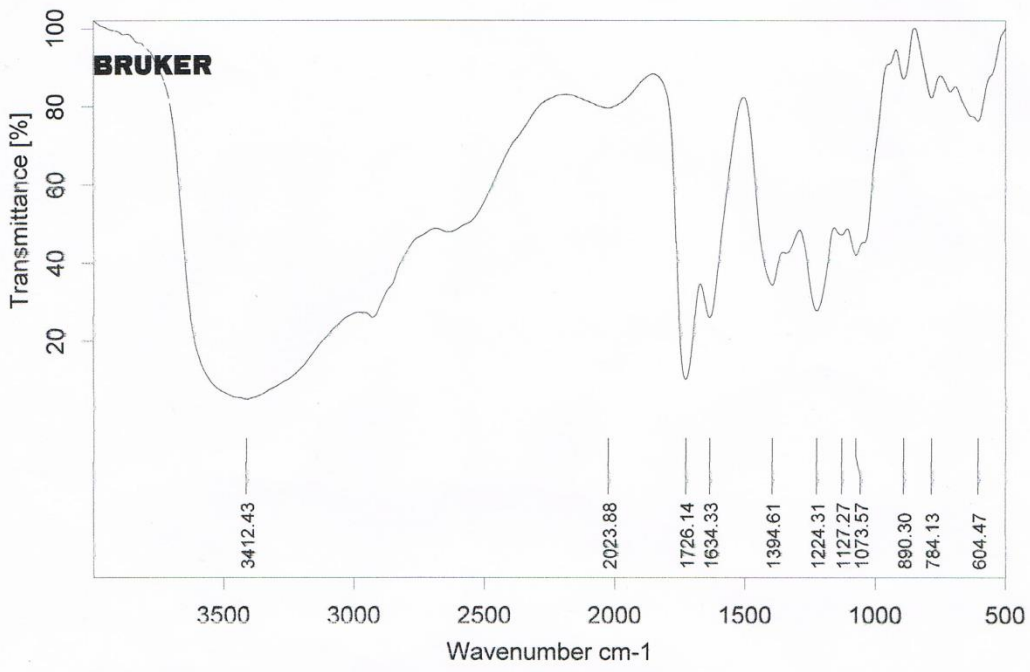

Wavenumber	Abs. intensity	Rel. intensity	Width	Found if threshold <	Shoulder
3412.4291	0.051	0.965	1149.1022	98.011040	0
2023.8813	0.796	0.060	2368.8502	3.579964	0
1726.1409	0.101	0.797	179.4434	80.627678	0
1634.3332	0.260	0.115	143.5423	8.824563	0
1394.6144	0.343	0.307	874.8401	14.445462	0
1224.3047	0.278	0.621	446.5795	56.203377	0
1127.2660	0.472	0.017	29.4585	1.609081	0
1073.5664	0.420	0.207	812.2064	7.213362	0
890.3044	0.871	0.098	40.8187	7.687604	0
784.1312	0.823	0.099	1023.5868	5.750502	0
604.4696	0.763	0.235	254.5537	24.086584	0

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Page 1 of 1

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