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ORIGINAL ARTICLE

Synthesis and Evaluation of Grafted Xanthan Gum as a Drug Carrier in Developing Lornoxicam Gel Formulations

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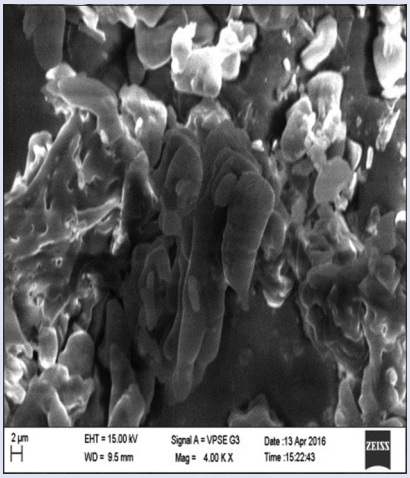
ABSTRACT

Background: In the medical and pharmaceutical fields, man has successfully used natural-origin things for millennia. Polymers obtained from plant sources have flashed much consideration in current eras owing to their various pharmaceutical properties, such as gelling agents in gels. Also incorporated in cosmo products, fabrics, dyes, and paper manufacture as binders, diluents, disintegrating agents, thickeners in oral fluids, protective colloids in suspensions, and bases in a suppository. **Objectives:** Natural polymers are chosen over semisynthetic and synthetic excipients due to their lack of toxicity, low cost, availability, soothing action, and nonirritant nature, as well as their ability to undergo a variety of chemical modifications. However, they have some drawbacks, including microbial contamination, lot to lot variation, reduced viscosity throughout storage, inappropriate mechanical properties, low storage, and an uninhibited rate of hydration. Current research work aims to chemically modify xanthan gum and study its impact on the formulation of topical gels. **Materials and Methods:** Chemical modification of xanthan gum is conceded by using a thiol-esterification reaction with thioglycolic acid (TGA) in the presence of hydrochloric acid. Microwave irradiated thiolated xanthan gum was also willing by further irradiation of thiolated xanthan gum by microwave using 750 W frequency. Topical drug delivery of lornoxicam release applications of thiolated and microwave irradiated xanthan gum are comparatively evaluated with pure xanthan gum polymer by formulating gel incorporated lornoxicam as a drug. **Results:** The physical properties of gel-like physical evaluation and viscosity results are within official limits. Formation of gel with idyllic properties. Determination of drug content, spreadability, and extrudability of modified xanthan gum was high compared with native xanthan gum. *In vitro* drug release study showed that prepared gel sustains the drug release for 24 h. **Conclusion:** Thiolation and irradiated xanthan gum sustain the release of lornoxicam over a prolonged period and might be a promising lornoxicam carrier in topical drug delivery to enhance antinociceptive and anti-inflammatory efficiency.

Key words: Gel, lornoxicam, microwave irradiation, thiolation, xanthan gum

SUMMARY

- Lornoxicam gel formulations prepared with crude and modified xanthan gum were evaluated for pH, viscosity, spreadability, extrudability, and *in vitro* diffusion studies. Formulation G6 prepared with irradiated xanthan gum exhibited highest drug release of 98.57% at the end of 24 h.



Abbreviations used: TGA- Thioglycolic acid; NSAID- Non steroidal anti-inflammatory drug; FTIR- Fourier Transform Infrared Spectroscopy; DSC- Differential scanning calorimetry; SEM - Scanning Electron Microscopy; XRD- X-ray diffractometry analysis

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INTRODUCTION

A polymer is a large molecule, or macromolecule, composed of several recurrent subunits.[1] A natural polymer plays a significant role an as excipient in a therapeutic dosage form as they stimulate drug release. Polysaccharides and cellulose are examples of natural polymers. They are non-toxic, cost-effective, biocompatible, and have no adverse side

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effects. Polymeric materials serve a variety of purposes, including as additives, medication release modifiers, and so on. A polymer's structure contains various functional groups, such as hydroxyl, amino, and carboxylic acid groups, which are responsible for chemical modifications.[2] To improve the stability and process ability of newly found gums, chemical changes were made.[1,3]

A variety of strategies can be used to change the molecular interactions between polymers. Physical and chemical techniques are also viable options.[4] Physical abilities to induce a molecular interaction between polymers, dry heat, water-logged steam, microwave, UV, and even gamma radiation can all be used.[5] In the chemical technique, polymers are processed with chemicals such as aldehydes, epichlorohydrin, borax, or glutaraldehyde. Temperature cross-linking is one of the most advantageous cross-linking processes since it eliminates the need for harsh organic compounds, as well as the accompanying equipment and methods, in large-scale production.[6]

Lornoxicam, an oxicam-family nonsteroidal anti-inflammatory drug (NSAID), has significant anti-inflammatory and analgesic actions. Commercially available forms include traditional instant release tablets (4 mg/8 mg), fast release 8 mg tablets, and dosage forms such as (4 mg/mL) for intravenous and intramuscular delivery. Lornoxicam is a drug that is often used to treat symptomatic soreness and infection in patients with osteoarthritis and rheumatoid arthritis, as well as pain from gynecological, orthopedics, gastrointestinal, and dental procedures. Lornoxicam a suitable for sustained release dosage forms because of its short half-life of 3–5 h and weak acid solubility.[7,8]

Gels are a highly dilute cross-linked system with no flow.[9-13] They are made up of a two-part semisolid structure with a lot of liquid. One of its distinguishing characteristics is a continuous structure with solid-like qualities.[14] Because of the biocompatibility, network structure, and molecular stability of the integrated bioactive ingredient, gels are the preferred medium for drug delivery formulations.[15] Topical formulations majorly have three purposes like to moisturize the skin through their emollient characteristics and protect against the external environment, to heal an entire or wounded area of the skin, and to administer drugs through the skin.[16-20]

MATERIALS AND METHODS

Material

Drugs and chemicals

Lornoxicam, xanthan gum, thioglycolic acid HCl, MCC, and Mg stearate were procured from Yarrow Chem. Products. All other used ingredients are of analytical grade.

Methods

Synthesis of thiolated xanthan gum

Xanthan gum (24 g) was liquefied in 110 mL of warm water and added to 15 mL. TGA (80%) and 3 mL 7 N HCL. This solution was heated at 80°C for up to 150 min. Then reaction blend was transferred into 500 mL of methanol. White precipitate of thiolated xanthan gum was obtained. Thiolated xanthan gum washes away two times with methanol and becomes dry at room temperature.[21]

Synthesis of microwave-irradiated xanthan gum

The approach was the same as for thiolated xanthan gum synthesis but the sample was then microwaved at 750 W frequency and for 30 s time intervals (LG microwave oven MC2886BLT, Black). After cooling for a while, the microwave-irradiated material was precipitated with a 4:1 acetone:ethanol ratio. The precipitate was washed away with 30% aqueous ethanol to eliminate unreacted polymer and additional chemicals. At 45°C, the precipitated material was dried to a uniform weight before being converted into fines. The final product is called grafted xanthan gum.[22]

Characterization of modified xanthan gum

Modified xanthan gum was characterized for Fourier transform infrared spectroscopy (FTIR),[23] thermal behavior by differential scanning calorimetry,[24] scanning electron microscopy (SEM), and X-ray diffractometry analysis (XRD).[24] The complete procedure for the characterization of modified xanthan gum was described in the Supplementary File.

Preparation of Lornoxicam gel formulation

First, boiled water was shifted to a chamber and the temperature was adjusted to 60°C, as well as weighed quantity (2% w/v) of gelling agents, namely, xanthan gum, cross-linked xanthan gum, irradiated Xanthan gum, where spread in hot water with continues stirring till gel is prepared. Then, air bubbles are removed by using the sonication method for 30 min. Then the addition of an appropriate quantity of Oleic acid and propylene glycol into the gel as a penetration enhancer and the required amount of sodium benzoate as a preservative. Lornoxicam solution (0.80% w/w), liquefied lornoxicam in triethanolamine, and added in small quantities with stirring till a consistent, transparent lornoxicam gel is prepared. The pH of the gel is adjusted to 5.0–6.5. Finally, the prepared lornoxicam gels Table 1 were left in the fridge until advanced analysis.[8,25]

Characterization studies

Physical evaluations and characteristics

Gels had been placed in a container for visual inspections of appearance, color, phase separation, and odor.

Determination of pH

In distilled water, 5 g of the gel was swirled until an even dispersion was achieved. The solution keeps away for 2 h. The volume was then increased to 100 mL, corresponding to a 5% solution of the product formulation. Then take a pH reading of the solution three times to complete the test (techno-scientific products Mumbai). The readings were taken for three samples on average.[26]

Viscosity measurements of gel

The viscosity of lornoxicam gel is determined with a Brookfield Viscometer (RV DV2T, USA) using spindle no 6. Temperature maintained to 25°C, the gel is tested at various angular velocities. Changing the angular velocity from 5 to 25 rpm was a typical run. The viscosity was calculated using the averages of three readings.

Table 1: Composition of different formulations of Lornoxicam gel

Formulation (% w/w)	G1	G2	G3	G4	G5	G6	G1
Lornoxicam	0.8	0.8	0.8	0.8	0.8	0.8	0.8
Xanthan gum	2.5	2.5	--	--	--	--	2.5
Cross-linked XG	--	--	2.5	2.5	--	--	--
Irradiated XG	--	--	--	-	2.5	2.5	--
Oleic acid	5	-	5	-	5	-	5
Propylene glycol	-	5	-	5	-	5	-
Sodium benzoate	0.25	0.25	0.25	0.25	0.25	0.25	0.25
Triethanolamine	2	2	2	2	2	2	2
Purified water q.s.	100	100	100	100	100	100	100

Cross-linked-XG=Cross-linked xanthan gum, Irradiated-XG=Irradiated xanthan gum, q.s. = quantity sufficient

Spreadability determination

The gel is placed in between the two glass slides then squeezed to uniform thickness by placing 1000 g weight up to 5 min to determine spreadability. The pan was filled with weight (50 g). Spreadability was measured by the time it took to separate the slides, i.e., the time it took for separation of slides from each other (S).[27,28]

Drug content analysis

Lornoxicam concentrations in prepared gel preparations were determined by dissolving 0.5 g of gels in phosphate buffer (pH 6.8). A 15-min sonication of the sample solution was performed. The solution was filtered through a 0.45 µ filter, then transferred 1 mL of the filtrate to a 50 mL volumetric flask, and phosphate buffer was added to bring it up to volume. After dilution, the sample was analyzed by UV-Vis spectrophotometer at 358 nm (Shimadzu, Japan). The linear regression analysis equation derived from the lornoxicam standard calibration curve was plotted to quantify the drug content.[29]

Extrudability

It is a test to determine how much force is required to extrude material from a tube. The method used to evaluate gel formulation for extrudability in this study is based on the amount of gel extruded in percentage from a collapsible tube after applying the weight in grams required to extrude at least 0.5 cm ribbon of gel in 10 s. Have to take a triplicate reading on each formulation's and the average of reading are reported.[30]

Homogeneity test

After the lornoxicam gel formulations were distributed into their containers, they were visually inspected for homogeneity. They were graded as homogeneous or non-homogenous.[31]

In vitro drug diffusion study

To carry out *in vitro* drug release investigations, Franz diffusion cell was used with a dialysis membrane with an 8000 Dalton molecular weight cut-off. The water-resistant receiver compartment held a total of 25 mL and had two arms, one for the sample and the other for the thermometer. The inside diameter of the donor chamber was 2 cm. The donor compartment was positioned so that it only comes in contact with the diffusion medium in the receptor compartment. The receptor compartment was filled with phosphate buffer (buffer solution) with a pH of 6.8, and the temperature of the receptor media was kept at 37°C. The donor compartment was then treated with 0.5 g of lornoxicam gel. At 1 h, 2 h, 4 h, 6 h, 12 h, 18 h, and 24 h, aliquots (1 mL) of the media were withdrawn and filled with a 1 mL medium to maintain volume constant throughout the experiment. After suitable dilution, the samples were filtered through 0.45 µ Whatman filter paper and examined by UV spectrophotometer (Shimadzu-1800, Japan) at 358 nm.[32]

Mathematical modeling of release kinetics

The *in vitro* release of drugs from all formulations was estimated by plotting graphs of mathematical modeling methods like Zero-order equation, First order equation, Higuchi model equation, and Korsmeyer–Peppas equation.[33]

Stability studies

The chosen formulations were packed in 15 g laminated tubes and subjected to 6 months of stability testing in a stability chamber (Lab Top, India) at 25°C/60% RH and 40°C/75% RH. In the beginning, third, and sixth months, samples were taken and tested for changes in color, pH, drug content, and drug release profile.[34]

RESULTS AND DISCUSSION

Thiolated xanthan gum

To accomplish the reaction of xanthan gum to thiolated xanthan gum, ester linkages were generated between the hydroxyl group of galacturonic acid [Figure 1] moieties of xanthan gum and the carboxyl group of thioglycolic acid. They are chemically converted into a yellow, odourless powder, which will be the esterified xanthan gum as a precept. After precipitation was purified with methanol and water for washing, keep aside precipitate overnight, the purification of thiolated xanthan gum was determined to be excellent. The grafted sample was then exposed to microwave irradiation for a predetermined time to produce irradiated xanthan gum.

Fourier transform infrared spectroscopy

Crude xanthan gum, thiolated, and microwave irradiated xanthan gum FTIR spectra are reported in Figures 2-4, and peeks summarized in Table 2.

The FTIR spectra of thiolated Xanthan gum show bands showing O-H stretching vibrations at 3556.85 cm^{-1}, as well as another peak at 29,29.97 cm^{-1} attributed to C-H stretching vibrations of $-CH_2$ groups. Peak 1668.48 cm^{-1} indicates the existence of C = O groups. There are no substantial changes in functional groups as a result of chemical alterations. When the same thiolated xanthan gum was microwave irradiated, and the spectrum was compared with that of crude xanthan gum, all of the peaks identified in crude xanthan gum were present in the microwave irradiated xanthan gum as well. In thiolated xanthan gum and microwave irradiated gum, additional peaks were discovered that were not present in crude xanthan gum. The presence of the thiol group's SH stretch may be noticed in the bands between 2503.60 cm^{-1} and 2636.69 cm^{-1}. According to FTIR studies, in modified xanthan gum, no change of any functional group's frequencies was found; hence as a result, the change plan may be successful.

Thermal analysis by DSC

The DSC curves of the tested materials are shown in Figures 5-7. Gum has a prominent endothermic peak between 90°C and 120°C. Despite the crude xanthan gum being dried at 120°C for half an hour before the research, Figure 5 indicates that the endothermic peak of moisture was still visible in the thermogram. The thermogram of crude xanthan

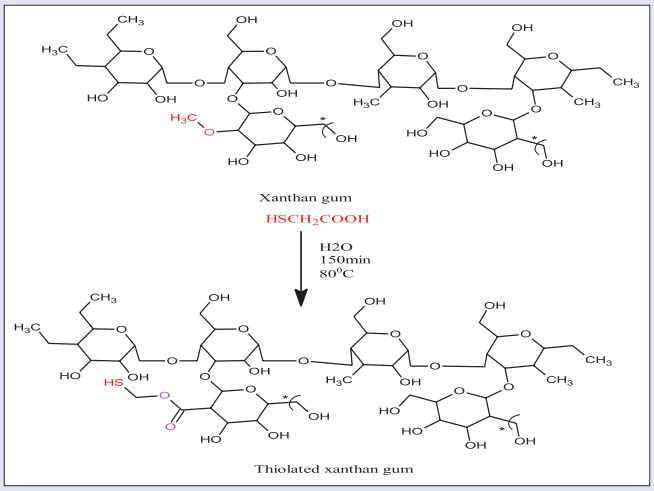

Figure 1: Reaction involved in the production of modified xanthan gum

Table 2: Result of FTIR

	Xanthan Gum			
Functional group	**IR Spectrum Standard range (cm^{-1})**	**Crude (cm^{-1})**	**Thiolated Xanthan gum (cm^{-1})**	**Microwave Irradiated (cm^{-1})**
OH (s, vib)*	3550–3200	3547.21	3556.85	3556.85
CH (s, vib)* of CH2	3000–2850	2928.04	2929.97	2928.04
C=O (s), of acetyl group	1710–1665	1670.41	1668.48	1668.48
COO- (s, vib)* of COOR	1760–1690	1629.90	1610.61	1614.47
CO (s, vib)* of C-O-C	1320–1000	1024.24	1035.81	1003.02
S-H (s)	2600–2500	--	2503.60	2636.69

* s, vib; stretching vibration * s; stretching

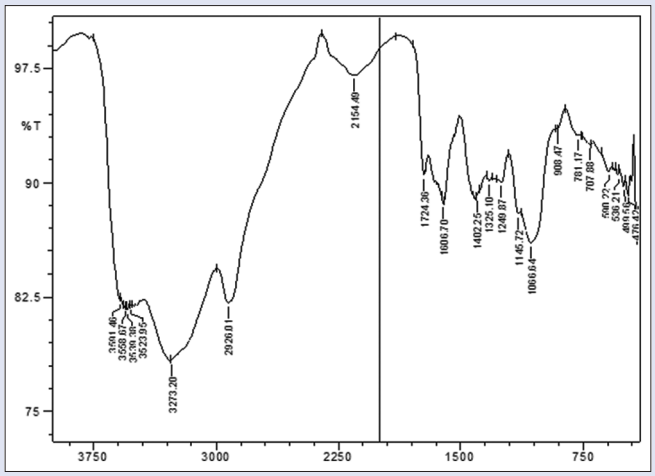

Figure 2: FTIR of crude xanthan gum

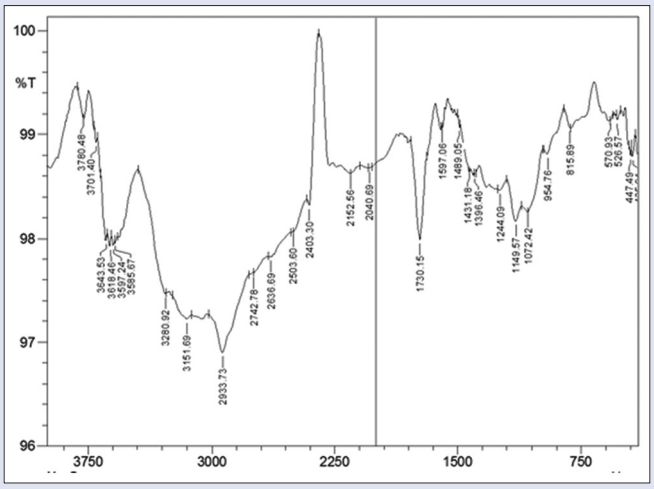

Figure 3: FTIR of thiolated xanthan gum

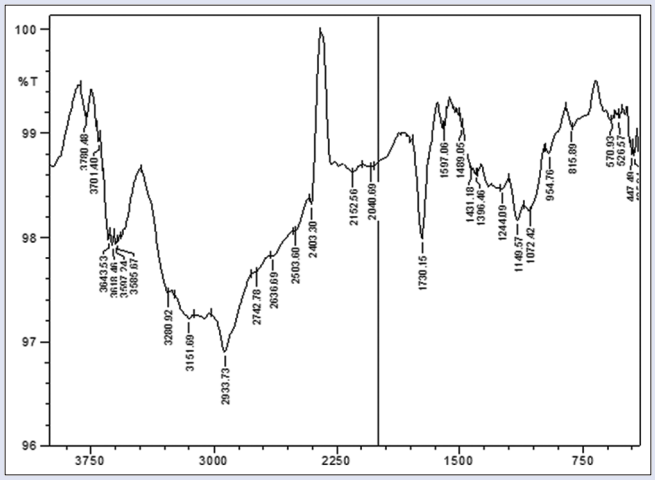

Figure 4: FTIR of microwave irradiated xanthan gum

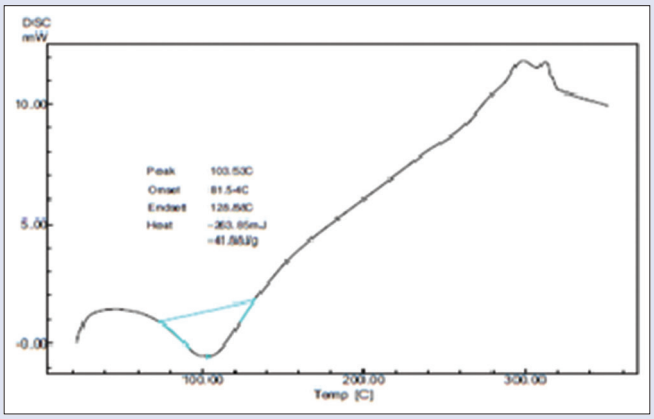

Figure 5: DSC of thiolated xanthan gum

gum indicated an endothermic peak at 103.53°C, which matched its melting point, with normalized energy of −41.88 J/g. The appearance of an endothermic peak at 103.53°C suggests that the xanthan gum in question is amorphous. In thiolated xanthan gum, Figure 6 exhibits four endothermic peaks. At 63.62°C, the first broad endothermic peak was noticed, which could be due to moisture loss in the sample. At 124.31°C, the two endothermic peaks were found, corresponding to a fusion enthalpy (Hf) of −69.73 J/g. The enthalpy value of thiolated xanthan gum increased somewhat when compared with that of its crude form. Thioglycolic acid had the fourth peak at 272.01°C (endothermic peak). Third endothermic peaks were identified during the understanding of DSC curves of microwave irradiated xanthan gum [Figure 7]. Furthermore, 77.27°C, 144.70°C, and 217.13°C for the 1, 2, and 3 endothermic peaks, respectively. Irradiated xanthan gum is similar to that of thiolated xanthan gum. The Tp value of thiolated as well as irradiated xanthan gum was more than crude gum. Tp value, in general, denotes thermostability, with higher Tp values indicating greater thermostability.

X-ray diffractometry analysis (XRD)

An X-ray diffractogram of crude, thiolated, as well as microwave irradiated xanthan gum, is reported in Figures 8-10. X-ray diffractometry was used to identify the sample's nature (crystallinity or amorphous). Figure 8 shows the diffractogram of crude xanthan gum, which is amorphous

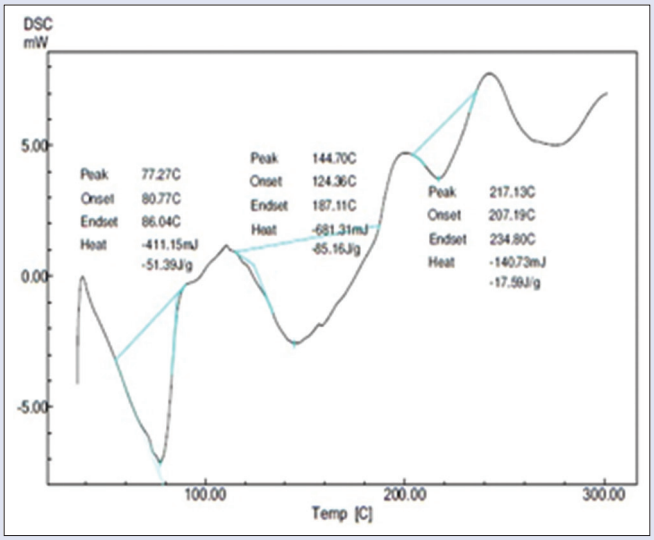

Figure 6: DSC of thiolated xanthan gum

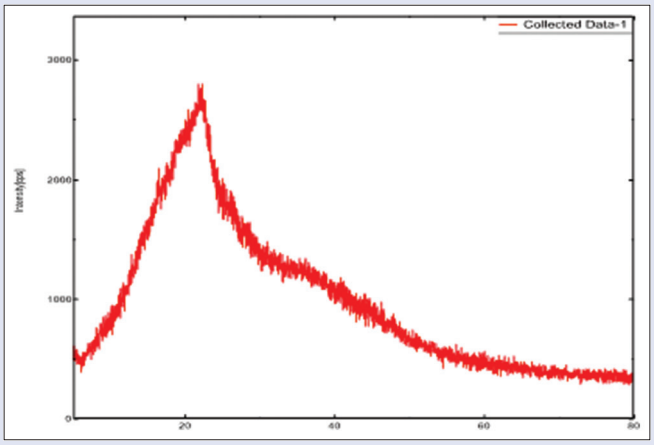

Figure 8: X-ray diffraction pattern of crude xanthan gum

in nature. The diffractogram of xanthan gum has just one crystalline peak with two values of 22.30° with relative intensity of 60.23%. The crystallinity of native xanthan gum is improved by thiolated xanthan gum Figure 9. The presence of nineteen distinct and apparent diffraction peaks in the grafted xanthan gum attests to this. 2θ values ranging from 11.873° to 75.18°. Peaks of thiolated xanthan gum are substantially higher than the only peak generated by crude xanthan gum. The extreme grafting ensued when the thio-group reacted with xanthan gum, yielding thiolated grafted xanthan gum as the final product, according to this data. It is possible that thioglycolic acid contributed to the increase in crystallinity of grafted gum. When thiolated xanthan gum is additionally exposed with microwave irradiation, its crystallinity is considerably amplified. Figure 10 shows diffraction peaks in the microwave-irradiated gum at two different values ranging from 11.90° to 75.35°.

Scanning Electron Microscopy analysis (SEM)

The surface morphology of xanthan gum, thiolated, and microwave irradiated xanthan gum are studied Figures 11-13. xanthan gum fibers appeared to be present in a cross-linked form. In scanning electron microscopy images of thiolated xanthan gum, thiolated xanthan gum appeared clumpy, and undulant acute edges. These strong breaking

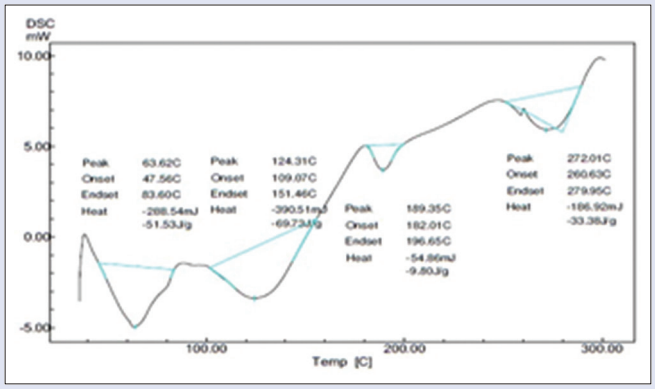

Figure 7: DSC of microwave irradiated xanthan gum

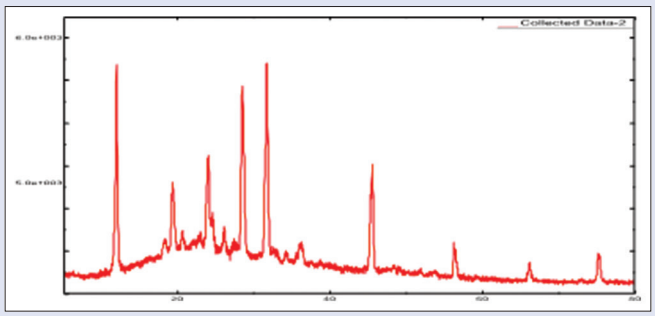

Figure 9: X-ray diffraction pattern of thiolated xanthan gum

points demonstrated the brittle character of the thiolated xanthan gum. The surface morphology of microwave irradiated xanthan gum was like that of thiolated xanthan gum; the clumpy mass that appeared in irradiated xanthan gum was the same as that of the thiolated form. Granules of thiolated gum and microwave-irradiated xanthan gum were bigger than pure xanthan gum.

Characterization of the prepared lornoxicam gels

Visual inspection and homogeneity

The observations of visual assessment of the formulated lornoxicam gels. Lornoxicam gels were opaque and yellowish in color in all of the batches that were made. All of the produced gels were homogeneous, with no lumps or syneresis. There is no evidence of grit. The gels were smooth, homogeneous, and glossy in appearance.

pH determination

The formulations' average pH was determined to be between 5.20 and 5.82. Summarizes the results. The pH of the skin varies from 4 to 6, depending on the gender, age, and location of the body.

Viscosity determination

The consistency of gel compositions is often reflected in their viscosity. At five revolutions per minute, the viscosity of the formulated hydrogels is between 48,100 to 62,800 cps. Hydrogels with crude xanthan gum (G2) had the lowest viscosity while hydrogels containing irradiated Locust bean gum had the highest (G6). The viscosity of this sample was the highest. The viscosity of the formulation generally reduces when the rate of shear is increased, indicating the formulation is shear-thinning pseudoplastic in nature. Formulations demonstrated pseudoplastic behavior, indicating a gel structure, conferring with the examination of the correlation among shear rate and share stress.

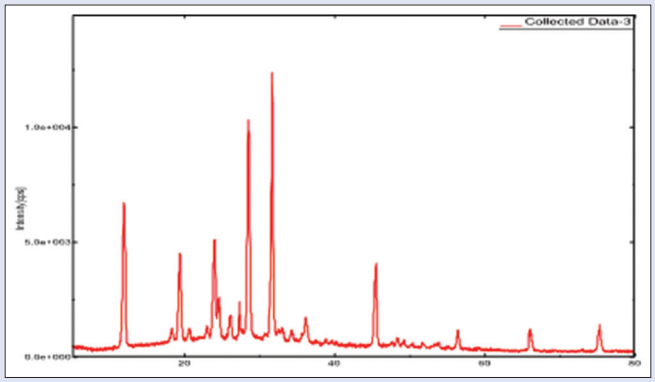

Figure 10: X-ray diffraction pattern of microwave irradiated xanthan gum

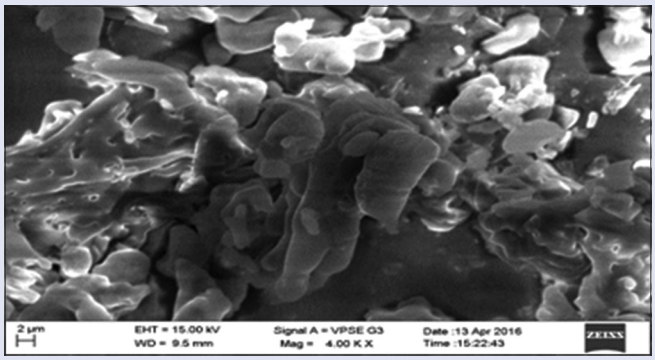

Figure 12: SEM image of thiolated xanthan gum

Because topical formulations must be applied as a thin layer to the skin, sample consistency is critical. As a result, non-Newtonian formulations are preferred due to minimal resistance to flow when applied at high shear rates. Figure 14 depicts the flow curves of produced gels Table 3.

Drug Content estimation

All formulations had drug content ranging from 98.40 to 99.70%, with an RSD of 1.13%. The assay values for content uniformity of topical semi-solid dosage form should range from 90 to 110% of the indicated amount of medicine with an RSD of not more than 6%, according to the USP 43-NF 38.

Spreadability

Spreadability and firmness are significantly connected. Firmness is defined as the highest force necessary to achieve a given deformation.

When modified gum was utilized as a gelling agent, the spreadability of formulations was shown to be lower than when crude gum was used. The spreadability of prepared gels is between 48.87 g.cm/s and 98.80 g.cm/s, showing that the gels may be spread easily with a gentle shear. From observations, the formulation is simple to apply and does not runoff. When applied to the site, this confirms that the formulation had a worthy wet contact period Table 3 displays spreadability results.

Extrudability

Extrudability was excellent in all of the gel compositions. Because it impacts spreadability and extrudability, viscosity is an essential characteristic for characterizing gels. Extrudability was determined to be in the range of 54.05 to 84.40 g/cm^2 in the study indicated in Table 3.

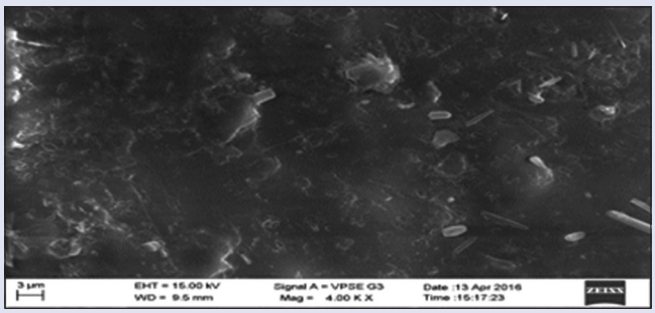

Figure 11: SEM image of crude xanthan gum

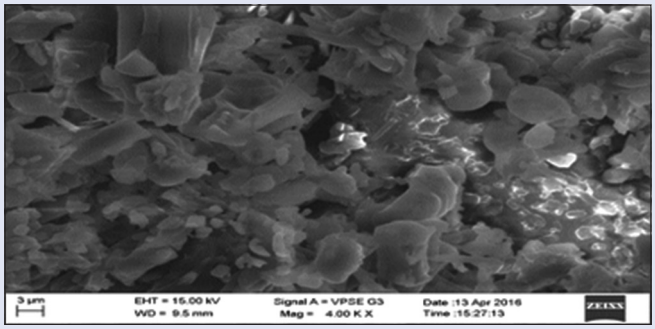

Figure 13: SEM image of microwave irradiated xanthan gum

Table 3: Determination of drug content, spreadability, and extrudability

Formulation	Drug content (% w/w)	Spreadability (g. cm/s)	Extrudability (g/cm^2)
G1	98.41±0.62	48.87±0.195	56.20±1.24
G2	99.22±0.79	50.42±0.243	54.05±1.28
G3	98.87±0.35	84.39±0.570	75.80±1.39
G4	98.40±0.44	86.82±0.698	79.68±1.90
G5	99.65±0.36	95.26±0.522	83.33±2.36
G6	99.70±0.28	98.80±0.478	84.40±2.46

When modified gum was utilized as a gelling agent, extrudability of prepared gels was slightly reduced due to the modified gum's increased viscosity, which resulted in a higher weight required to extrude gel from the tube.

In vitro drug diffusion studies

The effect of several gelling agents and permeability enhancers on drug release behavior was investigated. The concentration of gelling agents and permeation enhancers was kept constant across all batches. Xanthan gum and modified xanthan gum were utilized as gelling agents in formulations G1-G6. Permeation enhancers such as oleic acid and propylene glycol were utilized, as well as sodium benzoate used as a preservative.

The *in vitro* drug release characteristics of six formulations are compared in Figure 14. It can be seen that medication release remained very constant throughout the trial time. The t_{90} was 12 h in formulations G1 and G2, which used crude xanthan gum as gelling agents. The results indicate that the crude xanthan gum utilized insufficient to regulate lornoxicam release over a period of 24 h. Independently, in the following phase, and efforts are made to control the release of topical drugs using cross-linked and irradiated gum. The fact that the release profile of formulations G6 with irradiated xanthan gum revealed a drug release profile that was

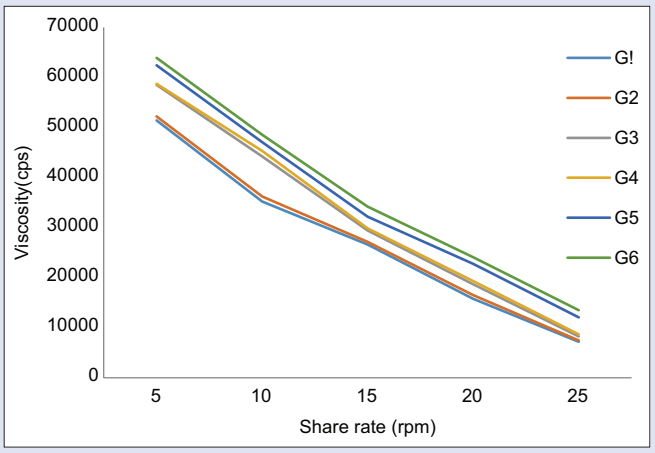

Figure 14: Viscosity of Lornoxicam gel formulations (G1-G6)

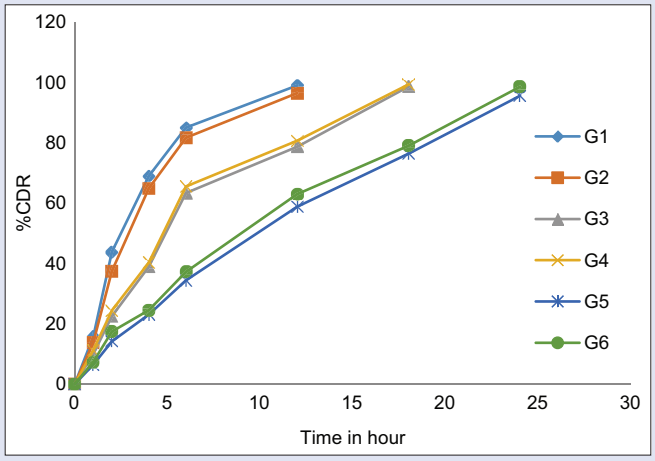

Figure 15: *In vitro* drug diffusion profile of prepared gel (G1-G6)

Table 4: Results of kinetic model fitted for Lornoxicam gel formulations.

Formulation code	Release Kinetics Models					Best Fit Model	Drug release mechanism
	Zero order	First order	Higuchi	Korsmeyer-Peppas			
	r^2	r^2	r^2	r^2	N		
G1	0.912	0.846	0.991	0.948	0.422	Higuchi	Fickian
G2	0.950	0.889	0.995	0.982	0.441	Higuchi	Fickian
G3	0.907	0.895	0.992	0.917	0.659	Higuchi	non-Fickian
G4	0.960	0.822	0.993	0.936	0.627	Higuchi	non-Fickian
G5	0.988	0.756	0.990	0.917	0.618	Higuchi	non-Fickian
G6	0.974	0.634	0.989	0.981	0.686	Higuchi	non-Fickian

*Drug diffusion profile of xanthan gum based gel formulations (G1-G6)

consistent throughout the trial period is of great importance. t_{90} was determined to be 24 h for G5 and significantly longer ($P = 0.05$) for G6 when compared with the other formulations. The increased viscosity of G5 and G6 formulations relative to basic gum may explain their sustained drug release behavior shown in Figure 15.

Drug release kinetics

The cumulative release data was submitted to a variety of kinetics models, and the results of the release kinetics investigations are shown in Table 4. Higuchi release kinetics may be used to represent the *in vitro* release profile of lornoxicam from prepared gels, as the graphs exhibit strong linearity ($r^2 = 0.989–0.995$) when compared with first order ($r^2 = 0.634–0.889$) and zero order ($r^2 = 0.907–0.988$). As a result, it was assumed that all formulations followed Higuchi's release kinetics. The data was entered into the Korsmeyer–Peppas model to confirm the diffusion mechanism.

During the dissolution investigation, the G1 ($n = 0.422$) and G2 ($n = 0.441$) underwent case I Fickian diffusion control, according to the diffusion control studies. The rate of drug release is substantially slower with polymer relaxation (swelling/erosion) in the Fickian release mechanism. As a result, drug release was primarily reliant on diffusion across the matrix. During the drug release investigation, the remaining batches of gel formulations (G3, G4, G5, and G6) Diffusion control was non-Fickian (anomalous), implying that polymer relaxation played a role. The combined effects of drug diffusion and polymer relaxation dictate the rate of drug release in the non-Fickian (anomalous) case II release. The nature of drug release from topical gels was determined using the correlation coefficients acquired from the plots of the kinetic models.

Short-term stability studies

Formulation G6 was chosen for stability test results *in vitro* drug diffusion investigations. The drug concentration, pH, and release profile were all evaluated, and the results were shown to be stable across a wide range of temperatures. Using the Student's *t* test at a 5% level of significance ($P < 0.05$), all of the results were found to be statistically significant. As a result, the generated formulation based on selected screened elements was shown to be stable in terms of the chosen replies.

CONCLUSION

An attempt was made in this study to manufacture and successfully optimize a lornoxicam-based gel utilizing crude and modified xanthan gum. Chemical and microwave irradiation methods were used to modify xanthan gum. *In vitro* diffusion investigations revealed sustained drug release for up to 24 h with the newly formulated gel formulations, including irradiation gum. According to the findings, for topical treatment of inflammation and pain, the implemented procedure was found to be a successful method for the creation of topical medication delivery methods that are safe, simple, repeatable, and cost-effective.

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Conflicts of interest

There are no conflicts of interest.

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