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Shruti Shukla
Advance Institute of Biotechnology and Paramedical Science, Kanpur, Uttar Pradesh, India

Manish Singh
Sai College of Pharmacy, Mau, Uttar Pradesh, India

Ajay Kumar Verma
Research Scholar, Maharishi School of Pharmaceutical Sciences, Maharishi University of Information Technology, Lucknow, Uttar Pradesh, India

Corresponding Author:
Ajay Kumar Verma
Research Scholar, Maharishi School of Pharmaceutical Sciences, Maharishi University of Information Technology, Lucknow, Uttar Pradesh, India

Formulation development and *in vitro* assessment of metronidazole emulgels prepared with natural polymers

Shruti Shukla, Manish Singh and Ajay Kumar Verma

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Abstract
In order to enhance topical drug delivery, the current study designed and assessed metronidazole emulgels using xanthan gum and guar gum, two natural gelling agents. FTIR analyses verified the drug-polymer compatibility. Metronidazole's λmax was determined to be 273 nm, demonstrating compliance with Beer-Lambert's law. The viscosity (603±15 cP) and pH (7.2±0.1) of the guar gum-based emulgel were higher than those of the xanthan gum-based formulation (497±15 cP, pH 6.8±0.1). The guar gum formulation demonstrated superior spreadability and extrudability (7.0±0.1 cm, 10.9±0.2 N) compared to xanthan gum emulgel (6.0±0.2 cm, 12.8±0.3 N). With xanthan gum emulgel releasing 97.2% guar gum emulgel releasing 94.7%, *in vitro* release studies using Franz diffusion cells demonstrated sustained drug release over eight hours. These results show that both formulations are appropriate for topical application, with guar gum offering better consistency and handling and xanthan gum favoring quicker drug diffusion.

Keywords: Metronidazole, emulgel, guar gum, xanthan gum, topical drug delivery, *in vitro* release

1. Introduction
The targeted administration method offered by topical drug delivery systems (TDDS) maximizes local therapeutic effects while reducing systemic side effects. By preventing first-pass metabolism and facilitating self-administration, they increase patient compliance [1, 2]. Because of their enhanced stability, regulated drug release, and patient acceptability, emulgels hybrid systems combining emulsions and gels have drawn a lot of interest among different topical dosage forms [3-6].

Il metronidazole, un derivato di nitroimidazole, è un efficace antimicrobial che combatte anaerobic bacteria e protozoa [7-9]. It is commonly used to treat bacterial vaginosis, rosacea, and dermatological infections [10, 11]. However, its traditional topical formulations, like lotions or creams, have inconsistent drug absorption, poor residence times, and restricted skin penetration [12-15]. Consequently, creating a stable, sustained-release topical emulgel provides a way to improve local bioavailability and sustain extended drug presence at the application site [16, 17].

Because of their rheological control, non-toxicity, and biocompatibility, natural polymers like xanthan gum and guar gum are being used more and more as gelling agents [18-20]. Guar gum, which comes from *Cyamopsis tetragonoloba*, produces more viscous gels that improve stability and prolong release, while xanthan gum, a polysaccharide made by *Xanthomonas campestris*, forms smooth gels that promote quick diffusion [21-23].

The formulation, assessment, and comparative performance of metronidazole emulgels made with xanthan gum and guar gum are the main topics of this study. pH, viscosity, spreadability, extrudability, FTIR compatibility, and *in vitro* drug release were important evaluation factors. The objective was to determine how the gelling agent affects drug release kinetics and formulation texture, thereby directing the creation of topical antimicrobial systems that are optimized.

2. Materials and Methods

2.1 Materials

Metronidazole (API) was purchased from a licensed pharmaceutical supplier and kept in amber containers with regulated humidity and temperature [24]. The gelling agents, guar gum and xanthan gum, came from reputable chemical suppliers. Additional excipients included mineral oil, distilled water, vitamin E (antioxidant), polysorbate 80 (emulsifier), and phenoxyethanol (preservative).

2.2 Determination of λmax: Metronidazole's maximum wavelength (λmax) was measured using an IGeneLabserve 100 UV-visible spectrophotometer. After dissolving a 100 mg drug sample in 100 mL of distilled water, the sample was sonicated for 15 minutes and scanned between 200 and 400 nm. The maximum absorbance was measured at 273 nm, which established linearity with concentration (Beer-Lambert's law) and confirmed λmax [25, 26].

2.3 Calibration Curve

Solutions of standard metronidazole (10-50 µg/mL) were measured at 273 nm. Plotting absorbance against concentration on a calibration curve revealed a linear correlation ($R^2 > 0.99$). A summary of the calibration data is provided in Table 1.

Table 1: Calibration data for Metronidazole at 273 nm

Concentration (mg/mL)	Absorbance (273 nm)
0.1	0.326
0.2	0.647
0.3	0.978
0.4	1.305
0.5	1.634

2.4 Formulation of Emulgels

Two emulgels were formulated:

- **F1:** Xanthan gum-based
- **F2:** Guar gum-based

Both included 80 g of distilled water, 0.5 g of phenoxyethanol, 0.2 g of vitamin E, 2 g of metronidazole, and 2 g of polysorbate 80. After dispersing the gelling agent (1.5 g xanthan or 0.75 g guar) in water, the medication was added and homogenized. The oil phase was added gradually while being constantly stirred until a homogenous emulgel was created (Table 2) [22, 27, 28].

Table 2: Composition of Metronidazole Emulgels

Ingredient	Xanthan gum Emulgel (F1)	Guar gum Emulgel (F2)
Metronidazole	2 g	2 g
Xanthan gum	1.5 g	—
Guar gum	—	0.75 g
Polysorbate 80	2 g	2 g
Phenoxyethanol	0.5 g	0.5 g
Vitamin E	0.2 g	0.2 g
Distilled water	80 g	80 g
Mineral oil	q.s.	q.s.

2.5 Evaluation Parameters

2.5.1 FTIR Compatibility

For pure metronidazole, xanthan gum, guar gum, and formulations, FTIR spectra (4000-400 cm^{-1}) were obtained. To identify potential chemical interactions, characteristic peaks were compared.

2.5.2 Ph Determination

Using a calibrated pH meter at room temperature, the pH of each emulgel was determined in triplicate.

2.5.3 Viscosity

A Brookfield viscometer was used to measure viscosity at 25 °C and the proper spindle speed. Three readings were used to calculate the mean ± SD.

2.5.4 Spreadability

Spreadability was evaluated for one minute between two glass plates with a fixed weight. The spread's diameter (in centimeters) was noted [21]

2.5.5 Extrudability

Tubes that could be folded were filled with emulgels. A force gauge was used to measure the force (N) needed to extrude the formulation.

2.5.6 *In vitro* Drug Release

A synthetic membrane-equipped Franz diffusion cell was employed. The receptor medium was phosphate buffer (pH 7.4), which was kept at 37±1 °C and constantly agitated. Samples were taken every hour for up to eight hours, and they were examined at 273 nm [29, 30].

3. Results

3.1 FTIR Analysis

The distinctive peaks of metronidazole were found at 1356 cm^{-1} (N=O), 1523 cm^{-1} (C=N), 1600 cm^{-1} (C=C), and 2924 cm^{-1} (C-H). Typical O-H, C-H, and C=O stretching bands (3400, 2920-3000, and 1650 cm^{-1}) were seen in xanthan and guar gums. Formulations showed no new or altered peaks, indicating that there was no drug-polymer interaction.

3.2 Physicochemical Properties

The pH values of both formulations were skin-compatible (6-7.5). The viscosity and spreadability of the guar gum emulgel were higher (Figure 1, Figure 2, and Table 3).

Table 3: Physicochemical Parameters of Emulgel Formulations

Parameter	Xanthan gum Emulgel (F1)	Guar gum Emulgel (F2)
pH	6.8±0.1	7.2±0.1
Viscosity (cP)	497±15	603±15
Spreadability (cm)	6.0±0.2	7.0±0.1
Extrudability (N)	12.8±0.3	10.9±0.2

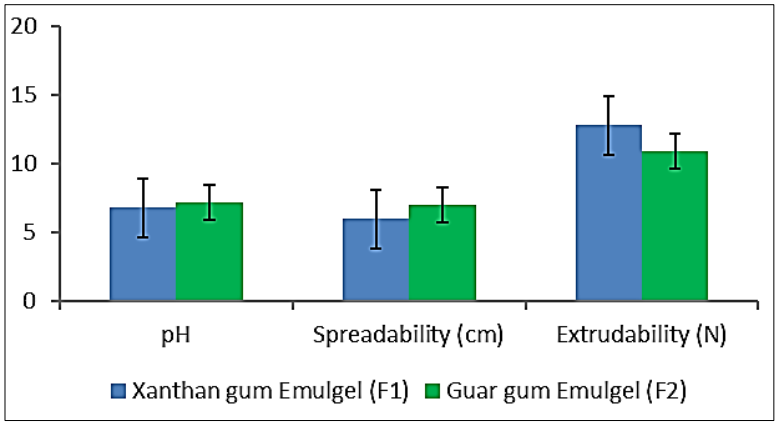

Fig 1: Comparison of physicochemical characteristics of Xanthan gum emulgel (F1) and Guar gum emulgel (F2), including pH, spreadability, and extrudability. Values are presented as mean±standard deviation (n =3).

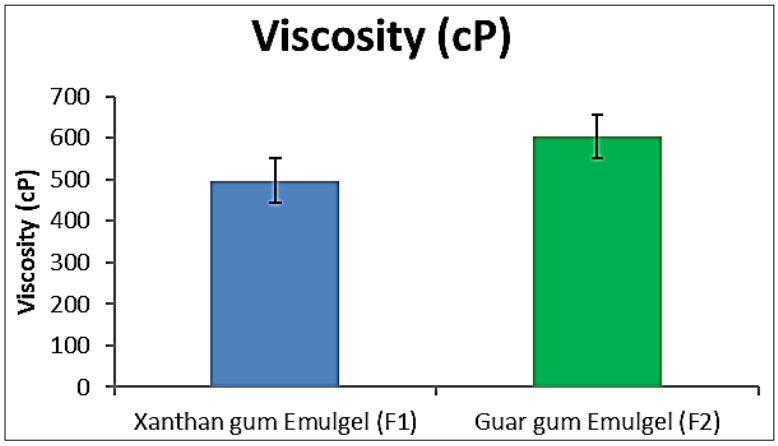

Fig 2: Comparison of viscosity between Xanthan gum emulgel (F1) and Guar gum emulgel (F2). Values are expressed as mean±standard deviation (n =3).

3.3 *In vitro* Drug Release: For eight hours, both emulgels showed sustained release (Figure 3, Table 4). Guar gum released 94.7% of metronidazole, while xanthan gum formulation released 97.2%.

Table 4: Cumulative Drug Release from Emulgels

Time (h)	F1 (Xanthan, %)	F2 (Guar, %)
1	15.2	12.6
2	29.5	25.1
4	57.8	50.2
6	79.3	74.1
8	97.2	94.7

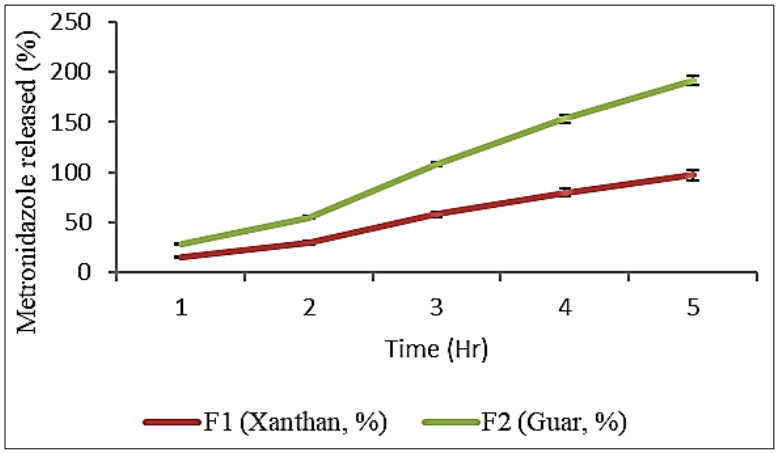

Fig 3: *In vitro* cumulative drug release profile of metronidazole from xanthan and guar gum emulgels (n = 3).

4. Discussion

Stable metronidazole emulgels were successfully created by the study using two natural polymers. FTIR spectra confirmed that the drug and excipients were chemically compatible, guaranteeing formulation stability.

Because of its high molecular weight galactomannan structure, which creates a denser gel network, the guar gum-based formulation showed higher viscosity [31, 32]. Drug diffusion was slowed by this higher matrix density, which led to a marginally lower cumulative release (94.7%). On the other hand, the less viscous matrix of the xanthan gum-based emulgel allowed for improved molecular mobility and quicker drug diffusion (97.2%).

For skin tolerance and to avoid irritation, the pH range of 6.8-7.2 was perfect [33]. Analysis of the guar gum emulgel's spreadability and extrudability revealed improved handling qualities; it spreads readily and requires less force during extrusion. These rheological properties affect application uniformity and patient compliance.

Previous research on xanthan-guar systems is supported by the sustained release pattern seen in both formulations, which shows that natural gums can effectively modulate release behaviour [22, 23, 27]. The findings imply that for the best topical performance, drug release rate and mechanical characteristics must be balanced by polymer concentration and molecular structure.

5. Conclusion

Guar gum and xanthan both worked well for making stable metronidazole emulgels. Compatibility was verified by FTIR analysis, and physicochemical analysis revealed that both formulations had the right pH and viscosity for topical application.

- **Xanthan gum emulgel:** Faster drug release (97.2%), smoother texture, better diffusion.
- **Guar gum emulgel:** Higher viscosity (603±15 cP), superior spreadability and handling.

Therefore, guar gum is preferred when improved consistency and a longer-lasting effect are sought, while xanthan gum is advised for formulations that need a faster release. Additional research on long-term stability and *in vivo* performance is necessary.

- **Conflict of Interest:** The authors declare no conflict of interest.
- **Funding:** No external funding was received for this study.

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