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Research Article

Formulation and Evaluation of Topical Thermosensitive Gel Containing Tapentadol for Pain Management

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Abstract

An innovative centrally acting analgesic, tapentadol works by inhibiting norepinephrine reuptake and agonising mu-opioid receptors. Tapentadol's oral use is restricted by gastrointestinal adverse effects and first-pass metabolism. We used Poloxamer 407 and Carbopol 934 to create a topical thermosensitive gel formulation in order to get around these restrictions. In order to give long-lasting and targeted pain relief, the goal was to create an in-situ gelling system that stays liquid at room temperature and turns into a gel at skin temperature. pH, viscosity, gelation temperature, spreadability, drug content, in vitro drug release, ex vivo skin penetration, and stability were all assessed for the produced gel. The improved formulation showed good penetration properties, a gelation temperature of 32±0.5°C, and sustained drug release of up to 89.2% after 8 hours. According to these results, thermosensitive gel filled with tapentadol presents a viable substitute for regional pain management.

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KEYWORDS: topical administration, in situ gel, pain management, thermosensitive gel, poloxamer 407, and tapentadol

INTRODUCTION

1.1 Pain Management: Clinical Relevance

One of the most common and incapacitating symptoms of many different medical disorders is pain. Particularly, neuropathic and chronic pain severely reduce quality of life and frequently necessitate long-term medication [1,2]. Despite their effectiveness, traditional opioid analgesics have a number of drawbacks, such as tolerance, dependence, and adverse gastrointestinal consequences.

1.2 Role of Tapentadol in Analgesia

A synthetic, centrally acting analgesic, tapentadol has a special dual mode of action that involves both inhibition of norepinephrine reuptake (NRI) and agonism of the mu-opioid receptor (MOR) [3]. Its strong analgesic effects and lower frequency of frequent opioid-related side effects are a result of its dual activity [4]. Oral administration of Tapentadol is linked to hepatic first-pass metabolism, which reduces its bioavailability and may cause systemic adverse effects, despite its pharmacodynamic benefits [5].

1.3 Limitations of Oral Delivery and Need for Alternative Systems

First-pass metabolic loss, gastrointestinal issues, and variations in plasma drug concentration are among the disadvantages of oral Tapentadol formulations. Due to these restrictions, alternate drug delivery methods must be investigated, especially those that provide regulated drug release and localized activity [6,7].

1.4 Topical and Transdermal Drug Delivery Systems

There are many benefits of topical drug delivery, including focused therapy, non-invasiveness, ease of application, and prevention of first-pass metabolism [8]. Transdermal methods decrease systemic toxicity, enhance patient compliance, and provide continuous medication release [9]. One novel class of topical delivery techniques is thermosensitive gels.

1.5 Thermosensitive Gels: An Overview

Semi-solid compositions known as thermosensitive gels experience a reversible sol-to-gel phase transition when their temperature changes [10]. The most widely used thermosensitive polymer is polxamer 407, a triblock copolymer (PEO–PPO–PEO). It is perfect for in situ gelling formulations because of its temperature-dependent micellization and gelation [11,12]. Poloxamer by itself, however, has mechanical strength limitations that can be addressed by mixing it with bioadhesive compounds like Carbopol 934 [13,14].

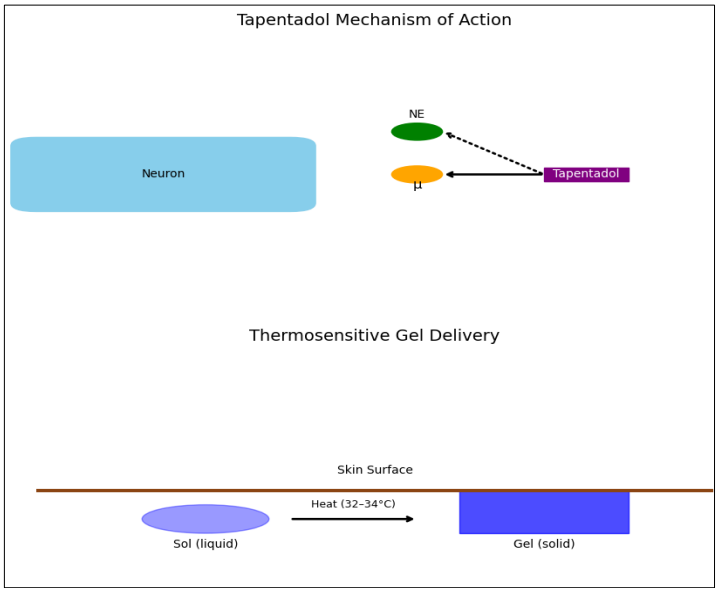
1.6 Rationale of the Study

To overcome the drawbacks of oral administration, this study intends to develop and assess a novel topical thermosensitive gel containing Tapentadol. The objective is to guarantee sustained drug release, improved drug penetration via the skin, decreased systemic adverse effects, and localized analgesic activity.

Table 1: Advantages of Topical Thermosensitive Gel Delivery

Parameter	Conventional Oral Delivery	Thermosensitive Topical Gel
First-Pass Effect	Present	Absent
Localized Action	No	Yes
Systemic Side Effects	High	Minimal
Patient Compliance	Moderate	High
Dose Frequency	Higher	Lower
Onset of Action	Variable	Rapid

Figure 1: Mechanism of Action of Tapentadoland hermosensitive Gel Delivery Concept



2. MATERIALS AND METHODS

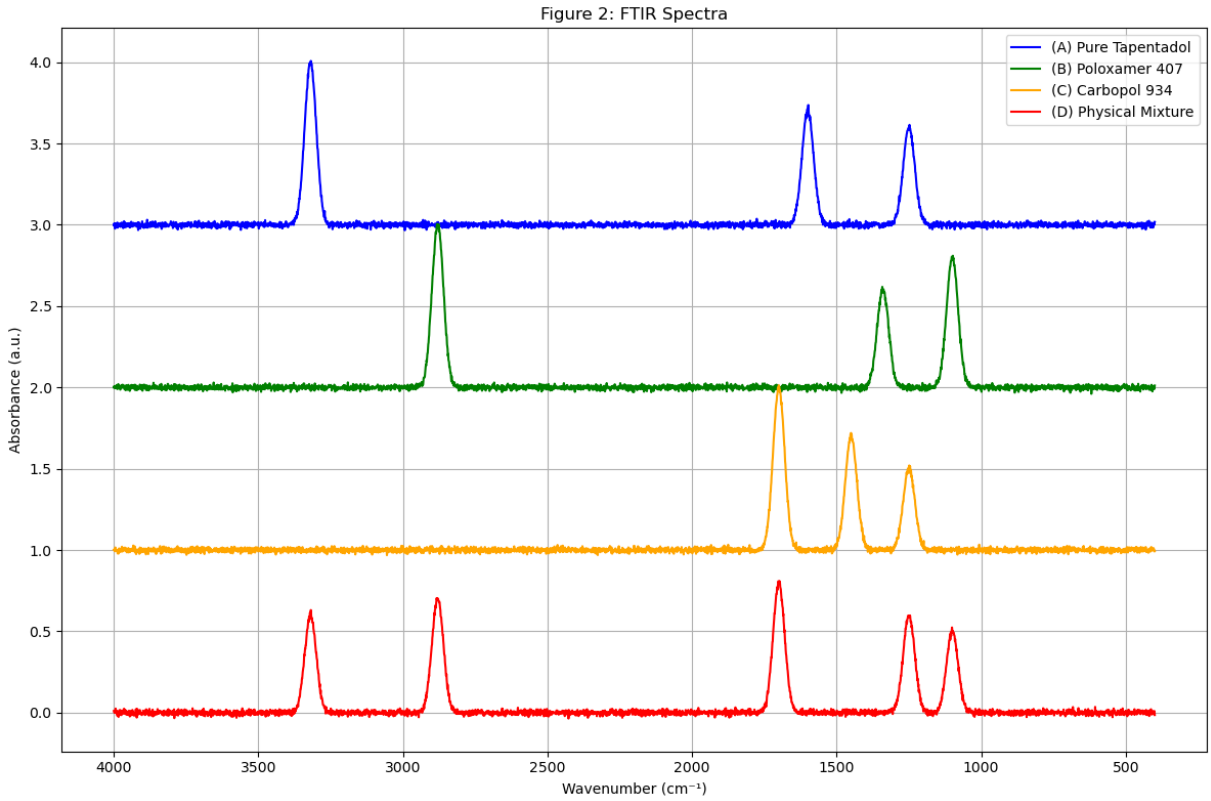
2.1 Materials

Cipla Ltd. (India) provided a complimentary sample of tapentadol hydrochloride. HiMedia Laboratories (Mumbai, India) provided the poloxamer 407, carbopol 934, triethanolamine, propylene glycol, and analytical grade solvents.

2.2 Preformulation Studies

- **Solubility Study:** To identify appropriate solvents for gel formulation, tapentadol's solubility in distilled water, ethanol, propylene glycol, and PEG 400 was assessed.
- **FTIR Compatibility Study:** FTIR spectroscopy employing the KBr pellet method was used to evaluate drug-polymer compatibility. To look for any changes or disappearances that would indicate interaction, peaks corresponding to functional groupings were analysed.

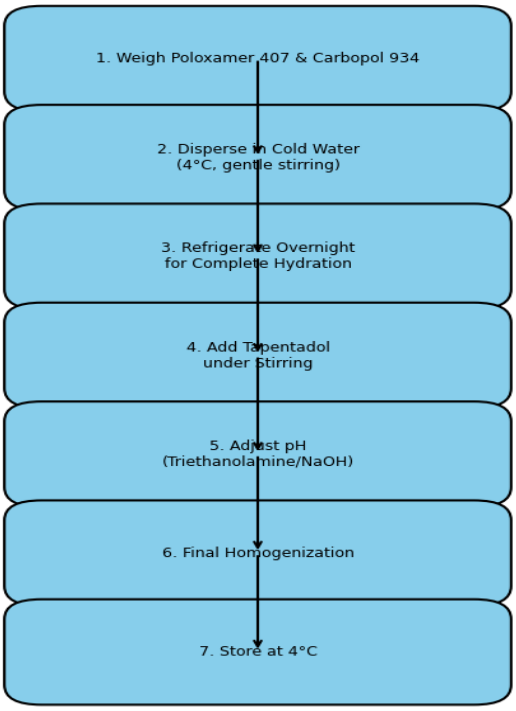
Figure 2: FTIR Spectra of (A) Pure Tapentadol, (B) Poloxamer 407, (C) Carbopol 934, (D) Physical Mixture



2.3 Formulation of Thermosensitive Gel

They used the cold technique. To ensure full dissolution, poloximer 407 (18–22% w/w) was progressively added to cold distilled water (4°C) and chilled overnight. Triethanolamine was used to neutralize carbopol 934 (0.3–0.5% w/w) after it had been distributed in water separately. An ethanol and propylene glycol (1:1) co-solvent mixture was used to dissolve 1% w/w tapentadol. To avoid early gelation, all ingredients were mixed together in a cool environment.

Figure 3: Schematic Representation of Gel Formulation Process



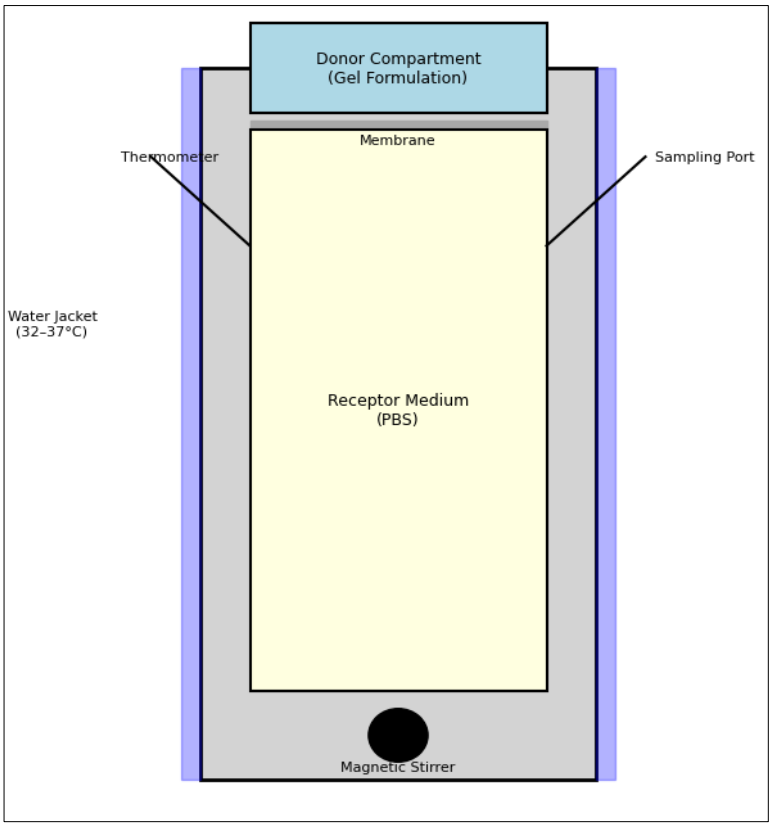
2.4 Evaluation Parameters

The following assessment criteria were applied to the prepared gel:

Table 2: Evaluation Parameters and Test Conditions for Gel Formulations

Parameter	Methodology
pH	Measured using a calibrated digital pH meter
Viscosity	Determined at 25°C and 37°C using Brookfield viscometer (Spindle No. 64)
Gelation Temperature	Determined by gradual heating and recording sol-to-gel transition point
Spreadability	Evaluated by slip and drag method (glass slide and weights)
Drug Content	Analyzed using UV spectrophotometry at 272 nm after dilution in phosphate buffer (pH 7.4)
In Vitro Drug Release	Franz diffusion cell using cellulose acetate membrane in phosphate buffer (pH 7.4) at 37°C
Ex Vivo Skin Permeation	Goat abdominal skin mounted on Franz cell; samples analyzed over 8 hours
Stability Studies	Conducted at 4°C, 25°C, and 40°C/75% RH for 3 months per ICH guidelines (Q1A-R2)

Figure 4: Franz Diffusion Cell Setup for In Vitro Studies



3. RESULTS AND DISCUSSION

3.1 Compatibility Studies

Compatibility was confirmed by FTIR spectra, which showed no discernible interaction between Tapentadol and the excipients. As shown in Figure 2, the peaks in the physical mixture spectra that corresponded to important functional groups did not alter.

3.2 Physical Characteristics

Every formulation showed good clarity and uniformity. All batches had pH values between 6.1 and 6.4, which is appropriate for topical use. With a gelation temperature of 32±0.5°C, the optimised batch (F3) was perfect for the sol-to-gel transition when it came into contact with skin.

3.3 Viscosity and Spreadability

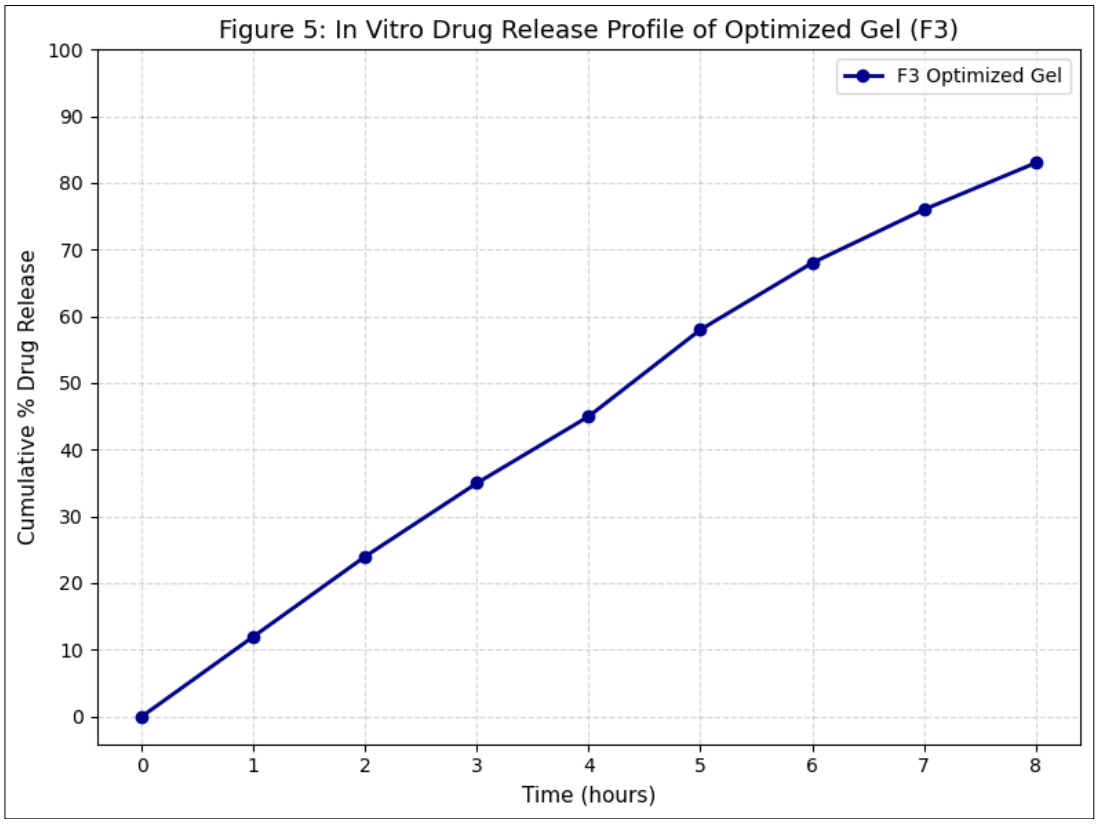
Thermoresponsive gelation was confirmed by viscosity analysis, which revealed a notable rise at 37°C (8200 cps) in comparison to 25°C (3500 cps). Good spreadability is crucial for patient compliance and simplicity of application, as evidenced by the measured spreadability of 22.5 g·cm/sec.

3.4 In Vitro and Ex Vivo Studies

The improved formulation (F3) demonstrated a sustained drug release of 89.2% over 8 hours in the in vitro release testing, suggesting the possibility of long-lasting analgesic activity. The viability of transdermal drug delivery was supported by the ex vivo permeation investigation that used goat abdomen skin, which showed notable dermal penetration without rupturing the stratum corneum barrier.

Table 3: Evaluation Parameters of Optimised Formulation (F3)

Parameter	Result
pH	6.2 ± 0.05
Gelation Temp	32 ± 0.5°C
Viscosity @25°C	3,500 cps
Viscosity @37°C	8,200 cps
Spreadability	22.5 g•cm/sec
Drug Content	99.3 ± 0.4%
In vitro release	89.2%



4. CONCLUSION

Tapentadol's thermosensitive topical gel, which was made using Poloxamer 407 and Carbopol 934, had a high drug concentration, enhanced permeability, and sustained release. While reducing systemic exposure, this administration method may improve local pain relief. To prove its therapeutic effectiveness in patients, more clinical research is needed.

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