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Research Article

Formulation and Evaluation of Nefopam Topical Gel

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ABSTRACT

Introduction: Gels are semisolid mixtures in which a liquid is confined inside a network of three-dimensional polymers composed of either synthetic or natural gums and stabilized by strong chemical or physical cross-linking. In order to treat localized skin diseases, topical drug administration entails applying a treatment directly to the skin. Psoriasis and other underlying systemic disorders may also be indicated by symptoms relating to the skin. Objective: The main objective of this study was to make and test an Nefopam Topical Gel drug identification test (Nefopam Topical Gel); Gel formulation; evaluation of gel, assessment of physicochemical properties; and evaluation of drug release. Method: Triethanolamine was added to neutralize the gel and maintain its pH while stirring constantly. The gel was then treated with the proper amount of DMSO (dimethyl sulfoxide), which acts as a penetration enhancer, and the necessary amount of methyl paraben, which servesasapreservative. Result: evaluate the all parameter of Nefopam Topical Gel. All parameter such as colour, Spreadability, pH, drug content, Viscosity in the limit. Their result such as colour is pale yellow, Spreadability, 11.16, pH 6.5, Drug content 99.1, Viscosity is 8950. And releasing time is 94.64 all parameter in limit. Conclusion: The study sought to enhance the medication release of API by formulating the fast-dissolving tablet Verapamil hydrochloride with super disintegrating agents such as dried banana powder or Hispanic salvia. The study's employment of super disintegrates agents improved the API mod peen's drug release, which could lead to a serious and substantial improvement in therapeutic results.

INTRODUCTION

1.1 Topical gels:

Gels are semisolid formulations where a liquid is trapped within a three-dimensional polymer network made from natural or synthetic gums, stabilized through significant physical or chemical cross-linking. Topical drug delivery involves applying a medication directly to the skin to treat local skin conditions Skin-related symptoms can also indicate underlying systemic conditions such

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as psoriasis. The aim is to confine the drug's action to the surface or within layers of skin. Among various systems to topical administration, semisolid formulations are the most prevalent. However, Traditional topical formulations, including lotions, creams, and ointments, powders—pose certain limitations. These include inadequate drug release and poor skin penetration. Creams and lotions often show low bioavailability due to rapid removal from the skin surface and insufficient drug release from their base. Non-hydrophilic ointments, being greasy and oleaginous, are inconvenient for patients. Medicated powders, meanwhile, tend to have a short duration of adherence to the skin. Gels offer an alternative semisolid system where the mobility The movement of the dispersion medium is limited by a three-dimensional network formed by interconnected particles or solvated macromolecules., resulting in improved retention and drug delivery performance. Topical gels typically made Organic polymers like carbomers contribute to the transparent appearance, appealing look and make them easy to wash off the efficacy of a topical dermatological product heavily depends on the base it uses, particularly when that base is water-based. Bases rich in oleaginous substances help moisturize and soothe dry, irritated skin. In particular, Oil-based, non-volatile bases, like those using hydrocarbons, create a barrier on the skin to block moisture from escaping. and promoting hydration by trapping moisture between the skin and the ointment layer. This retained moisture hydrates The skin's surface is composed of the stratum corneum, which in turn opens up intra- and intercellular pathways, facilitating enhanced drug permeation. The moisture layer also acts as a solvent medium, aiding in the dissolution of the drug, which may otherwise remain in a finely dispersed state within the ointment base. The structural integrity of a gel is primarily determined by the affinity between the polymer and the solvent. According to classical gel theory, solvents within a gel can be categorized into three types:

• Free solvent, which remains highly mobile;

• Bound solvent, which forms a solvation layer typically through hydrogen bonding;

Entrapped solvent, which is immobilized within the gel's network structure.

1.2 Desirable Properties of Gels:

• Gels Needs to be unreactive, harmless, and work well with other formulation components.
• They must remain stable under standard storage conditions.
• The formulation must be free of microbial contamination.
• Gels should retain their rheological (flow-related) characteristics.
• Cost-effectiveness is essential.
• They should be water-washable and non-staining.
• The gel base must not interfere with the drug's biological activity.
• It should be easy to handle and apply.
• Ideal gels exhibit desirable characteristics such as thixotropy, being non-greasy, emollient, and non-staining.

1.3 Advantages of Gels

• Non-greasy texture makes for comfortable application.
• Simple and straightforward to formulate.
• Easily washable and non-toxic.
• Exhibit good long-term stability.
• Allow targeted delivery to the affected area for quick therapeutic action.
• Minimize systemic side effects by avoiding gastrointestinal absorption.
• Spread easily on the skin.

• Demonstrate good skin adherence and retention.

1.4. Methods for Gel Formulation One of the following methods is used to prepare gels:

• Fusion method
• Cold method
• Dispersion method

1.4.1 Fusion Method: In this approach, waxy substances used as gelling agents in non-polar media are melted through heating. The drug is incorporated during the melting stage, the mixture of gently stirred until a smooth, uniform gel achieved.

1.4.2 Cold Method: Cold water, maintained between 4–10°C, is added to Prepare a mixing container. Gradually add the gelling agent sprinkled in with continuous stirring, keeping the temperature below 10°C until the gel forms completely. The drug, already dissolved, is then added gradually with gentle mixing.

1.4.3 Dispersion Method : The Under continuous stirring at 1200 rpm, the gelling agent was dispersed in water approximately 30 minutes. In a separate step, Dissolving the drug in a non-aqueous, preservative-containing solvent created a stable solution.. was gradually incorporated into the gel base under constant stirring to obtain a uniform and stable formulation.

1.5 Nefopam: Nefopam represents a non-narcotic analgesic with a distinct structural composition compared to other pain relievers. Research indicates it produces analgesic effects comparable to oral medications such Including aspirin, dextropropoxyphene, and pentazocine, along with the moderate doses of injectable pethidine, morphine and pentazocine, administered at suitable doses. proportions were assessed in brief clinical evaluations. However, in comparisons involving 'higher' dosage ratios, morphine and pethidine frequently demonstrated superior efficacy to Nefopam. This discrepancy potentially reflects a 'ceiling effect' on analgesia that manifests with increased Nefopam dosages, similar to other fundamental analgesics. While Nefopam administration has occurred in limited cases of chronic pain patients over extended periods of several weeks, additional investigation remains necessary to establish its enduring efficacy and safety profile. Nefopam functions as a non-opioid, non-steroidal, centrally actings analgesic medication utilized for postoperative pain prevention, mainly within multimodal analgesia approaches. Combined therapies of nefopam with NSAIDs In all instances, either Clinical studies have demonstrated that combining paracetamol with aspirin, nimesulide, or ketoprofen results in a stronger pain-relieving effect than using either drug alone. diverse surgical procedures involving varying pain intensities. Nefopam represents a less commonly employed centrally acting agent, administered for nociceptive pain management and potentially applicable in neuropathic pain treatment. The limited instances of pain mitigation nanomedicine via predominantly oral administration have sought to enhance the bioavailability of ibuprofen and nefopam.

1.6 Mode of Action: Nefopam's analgesic action mechanism remains unclear. Unlike narcotic analgesics, it does not exhibit significant opiate receptor binding. While nefopam inhibits the synaptosome uptake the of norepinephrine, dopamine and serotonin, the relevance of these findings to its pain-relieving properties is uncertain. Nefopam effectively prevents shivering during or after surgical procedures. Regarding potency, twenty milligrams of nefopam hydrochloride is approximately as effective for pain relief as 12 milligrams of morphine, demonstrating similar efficacy to both morphine

and oxycodone. Nefopam generally produces lower incidence of side effects, no risk of respiratory depression, presents substantially lower abuse potential, making it valuable either as an opioid alternative or as a complementary treatment along with opioids or other pain relievers. It is also utilized in treating severe hiccups. Cases of overdose and fatality have been documented with nefopam. Management typically involves supportive care, addressing Beta-blockers can lead to heart-related issues reducing absorption through activated charcoal administration.

1.7 Therapeutic Trails: Nefopam has mainly been studied in short-term or single-dose trials involving Postoperative or musculoskeletal pain patients. Most comparative studies have shown tha t typical challenges in assessing pain relief. When taken orally at doses between 30 and 90 mg, nefopam showed similar effectiveness to equivalent The capacity of aspirin, dex tropes pen. oral pentajo is less noticeable. Similarly, NEFOPAM is provided in muscles (15 or 30 mg) or intravenous (10 or 15 mg) pain relief comparable to moderate, Morphine, pethidine, and pentazocine provided similar pain relief at comparable doses, but morphine and pethidine proved more effective at higher doses. With 8 mg of morphine and 100 mg of pethidine offering stronger pain relief than 30 mg of nefopam—though nefopam sometimes delivered longer-lasting effects at those doses. Nefopam Hydrochloride Each film-coated tablet contains 30 mg of the specified ingredient. active ingredient of nefopam hydrochloride tablet. These tablets are white, round, biconvex, and measure approximately 7.1 mm in diameter. Nefopam 30 mg is used for the symptomatic relief of both This medication helps manage acute and chronic pain stemming from various sources, including post-operative discomfort, dental pain, musculoskeletal conditions, traumatic injuries, and cancer. The typical dose is 1 to 3 tablets, administered three times per day. The specific dosage Depends on severity of the pain how the patient responds to the medication. A starting dose of 1 to 2 tablets three times daily is recommended.

2. MATERIALS AND METHODS

Sr. No	Material Used	Description
1	Carbopol-940	A transdermal gel formulation containing Glibenclamide, prepared using Carbopol-940 as a carrier via direct dispersion method
2	Propylene Glycol	It's a clear, syrupy liquid that tastes slightly sweet. and little to no odor, and it mixes easily with solvents such as water, acetone, and chloroform.
3	Triethanolamine	A viscous organic compound, colorless but may appear yellow due to impurities. It functions as both a triol and a tertiary amine.
4	Propylparaben	A preservative, synthetically produced It is utilized in the cosmetic, pharmaceutical, and food industries. It occurs naturally in plants and insects and belongs to the paraben class.
5	HPMCK4M	A semi-synthetic, non-reactive, viscoelastic polymer commonly used in eye drops and as a controlled-release component in oral medications. various commercial products.
6	Linseed Oil	A colorless to yellowish oil derived from flax plant seeds, obtained through pressing and sometimes solvent extraction
7	Menthol	A naturally occurring compound in mint plants, also synthetically produced. First added to tobacco in the 1920s and 1930s.

8	Hydroxypropyl Methylcellulose	A semi-synthetic, non-reactive, and flexible polymer utilized in eye drops and as an excipient and sustained-release agent in oral drug formulations.
9	Sodium Alginate	Extracted from brown seaweed, With alginic acid making up 30 to 60 percent of its content, converting it into sodium alginate makes it more water-soluble, making it easier to extract.
10	Nefopam Hydrochloride	A painkiller used for moderate pain relief after surgery, injury, or related to conditions like cancer. It's also used for long-term pain when other painkillers are ineffective.

A prospective, non-randomized study comparing outcomes at a single center. was conducted, involving a control group and a nefopam group, with Patients receiving total hip arthroplasty (THA)During general anesthesia. Each participant was administered Patient-controlled analgesia was administered using paracetamol, ketoprofen, ketamine, and morphine/droperidol. Additionally, For 48 hours, Patients in the nefopam group were given a continuous infusion of nefopam., with a daily dosage of 120 mg. Pain levels were assessed daily over a seven-day period, with the primary outcomes being total Morphine consumption was analyzed in relation to pain intensity, which was measured using a numerical rating scale as well as a validated pain questionnaire.

2.1 Procedures for Making Nefopam Topical Gel

The cold mechanical approach was used to make the gels.

Step 1: Weighing the necessary amount of polymer (natural and synthetic), it was then gradually sprinkled over the surface of the cleansed water for two hours.
A mechanical stirrer was then used to continually agitate it until the polymer had soaked in the water.
Step 2: Triethanolamine was added to neutralize the gel and maintain its pH while stirring constantly. The gel was then treated with the proper amount of DMSO (dimethyl sulfoxide), which acts as a penetration enhancer, and the necessary amount of methyl paraben, which servesasapreservative.

2.3 Nefopam Topical Gel evaluation preformulation studies

2.3.1 Determination of the melting point

A little amount of Nefopam Topical Gel is obtained, put in a capillary tube with thin walls that is 8–10 cm long and 1 mm in diameter, and sealed at one end. It is then connected to a thermometer and suspended in an oil bath-containing Thiele tube. The melting point is the range of temperatures across which the sample is observed to melt, and the equipment can be heated gradually.

2.3.2 Determination of λ max

A 10 µg/ml concentration of Nefopam Topical Gel was made in methanol. A UV spectrophotometer was used to scan the solution between 200 and 400 Nm, and a spectrum was examined for absorption maxima.

2.3.3 Standard calibration curve of Nefopam Topical Gel

As a stock, 100 milliliters of methanol were used to dissolve 100 milligrams of precisely weighed nefopam. answer.100 ml of methanol was made by diluting 10 ml of the stock solution mentioned above. Using a UV spectrophotometer set to λ max, µg/ml of the aforementioned solutions 6, 12,

18, 24, and 30 were created. The linearity of the absorbance against concentration was checked by plotting the absorbance concentration graph in µg/ml and calculating.

2.4 Post formulation studies

2.4.1 Physical evaluation

All the formulations of econazole nitrate were evaluated for organoleptic characteristics, occlusive ness and washability.

2.4.2 Measurement of pH

A digital pH meter was used to measure the prepared gels' pH. The gel was submerged in the electrode and the pH meter's readings were noted.

2.4.3 Spreadability

A 0.1 g sample of each formula was sandwiched between two slides that were separated into squares with sides of 5 mm. The slides were then left for roughly five minutes, during which time no further spreading was anticipated. The spreadability comparison values were calculated using the diameters of the spread circles, which were measured in centimeters. Three calculations were averaged to produce the findings.

2.4.4 Viscosity studies

A Brookfield viscometer was used to measure the viscosity of the formulations. Using spindle number 64, the gels were spun at 10 and 20 rpm. The matching dial reading was recorded for every speed.

2.4.5 Drug content studies

500 mg of econazole nitrate gel was collected and dissolved in 50 milliliters of pH 7.4 phosphate buffer. To ensure appropriate mixing, the volumetric flasks were shaken vigorously in a shaker for two hours. The filtrates were subjected to spectrophotometric analysis for drug content at 285 nm using the corresponding gel concentration as a blank after the solution was run through Whatman filter paper.

2.4.6 In vitro drug release studies

Diffusion investigations of the produced gels were conducted in a hollow tube diffusion cell utilizing a prehydrated cellophane membrane and phosphate buffer pH 7.4 (100 ml) as the receptor compartment after the cellophane membrane had been cleaned under running water before to the experiment. The membrane was evenly coated with 500 mg of each formulation (Yamaguchi et al., 1996). The temperature was maintained at 37±0.5°C, and the donor and receptor compartments were kept in touch. Teflon-coated magnetic bars that were driven externally agitated the solution on the receptor side. Five milliliters of solution from the receptor compartment were pipetted removed and promptly replaced with new five milliliters of phosphate buffer at prearranged intervals. Using spectrophotometry, the drug concentration in the receptor fluid was measured at 285 nm in relation to the suitable blank. The formula was used to calculate the medication release percentage.

3. RESULT AND DISCUSSION

3.1 Preformulation studies

Table 3.1 Melting point determination

Reported	Method	Observed
244-250°C	Thiel's tube method	237°C

3.2 FTIR of verapamil hydrochloride

The FTIR of the medication showed that the indicated feature peaks of Nefopam hydrochloride were retained. Nefopam hydrochloride was recognized as the medicine.

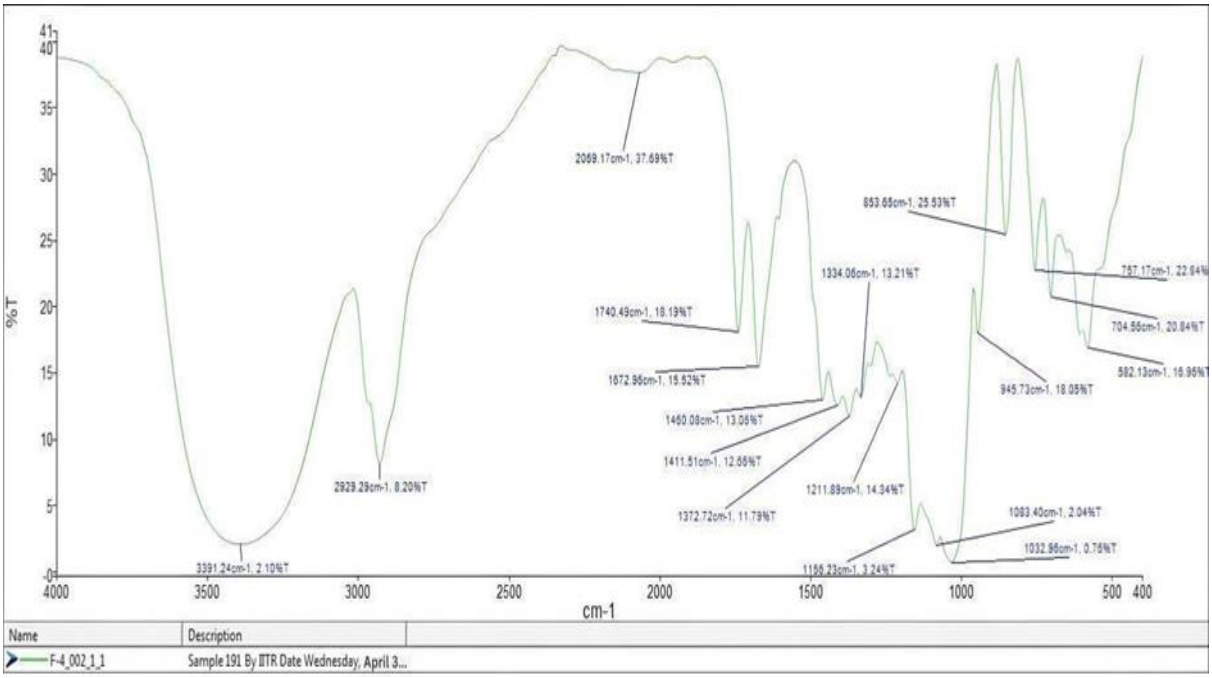

Fig.3.1 FTIR of Nefopam hydrochloride

3.3 Calibration Curve of NEFPAM hydrochloride: Method is described in section The standard plot of Nefopam in Solution of 6.8 pH Phosphate Buffer indicates that the standard curve of Nefopam followed Beer's law.

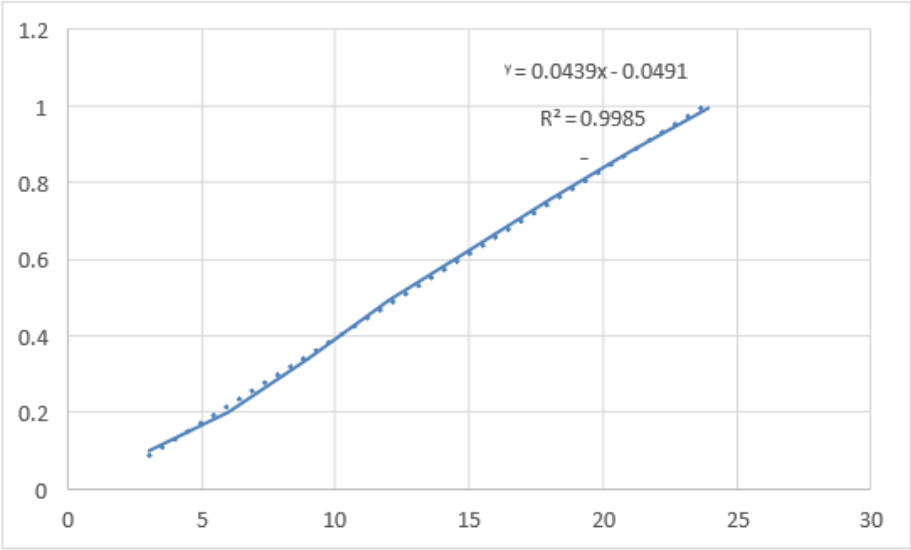

Fig.3.2 Abosorbtion Rate of Nefopam

3.5 Post evaluation test

3.5.1 Physical evaluation

The prepared gel formulation was inspected visually for their colour and appearance. The developed formulations

Table 3.2 Evaluation of Nefopam Gel

S. No	Parameter	Result
1	Colour	Pale yellow
2	Spreadability (gm.cm2)	11.16
3	pH	6.5
4	Drug content (%)	99.1
5	Viscosity	8942

3.5.3 Measurement of pH: The pH of gels was determined using digital pH meter. The Formulation shows 6.5 pH. The pH results are given in table no.3.2

3.5.4 Viscosity: study The formulation shows 8942 cps of viscosity. The viscosity results are given in table no.3.2

3.5.4 Spreadability

The value of spreadability indicates the degree of shear required to apply the gel. The spreadability results are shown in table no.3.2

3.5.5 Drug content

The drug content of formulations were in the range of 99.1%. The drug content determination showed that the drug was uniformly distributed throughout the gel. The drug content results are given in table no.3.2

3.5.6 In vitro diffusion studies

Nefopam topical gel formulations containing shows drug release of 94.64% . The drug content results are given in table no.3.3

In vitro diffusion study of Nefopam hydrochloride

Table 3.3 In Vitro Diffusion Studies

S.no	Time	formulation
1	5	18.04
2	15	24.06
3	30	38.26
4	45	46.83
5	60	56.05
6	90	65.08
7	120	72.78
8	150	78.54
9	180	84.60
10	210	89.89
11	240	94.64

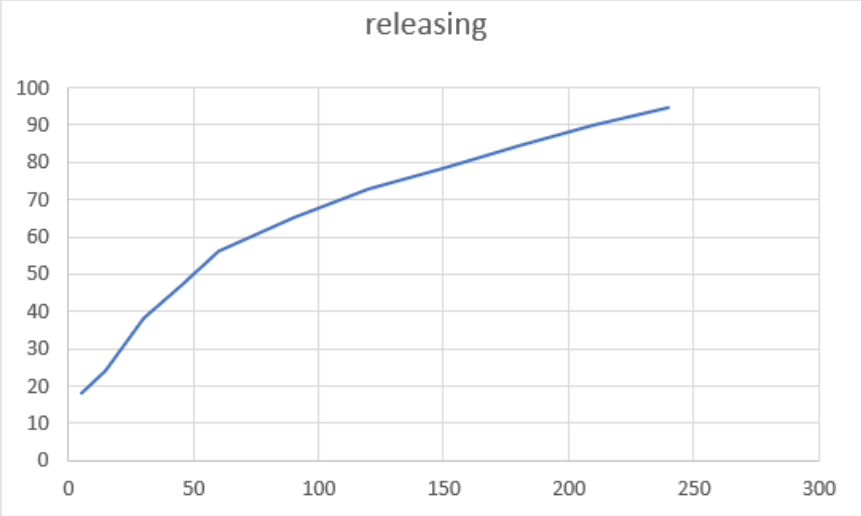

Fig 3.3 In vitro diffusion studies

CONCLUSION:

The development and use of Nefopam topical gel have become increasingly important in the medical

field. Topical formulations are designed for direct application to the skin or mucous membranes. to deliver localized effects by allowing the drug to penetrate the underlying layers. A key benefit of this delivery method is that it bypasses first-pass metabolism. Optimizing gel formulations is essential, as they can improve drug efficacy, enhance tolerability, and boost patient compliance. Topical delivery also avoids the risks and discomfort associated with intravenous therapy, as well as challenges like pH variations, enzymatic degradation, and gastric emptying time. In essence, topical drug delivery involves applying a pharmaceutical product to the skin to treat local skin conditions or skin-related symptoms of systemic diseases, aiming to keep the drug's action limited to the surface area.

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