Preparation and Evaluation of Paroxetine Hydrochloride Drug as Nasal Gel For Effective Management of Depression

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ABSTRACT

Depression is a psychological disorder affecting different age groups belonging to different countries and cultures. It was estimated that around 264 million individuals of all ages suffer from depression globally. Thus, much research is carried on establishing significant advancement in diagnosis and treatment of the depression. The purpose of this study is to prepare and evaluate nasal gel formulation containing paroxetine hydrochloride and establishing the effect of different excipient on drug release and nasal absorption, evaluation of physiochemical properties of nasal gel and evaluating their stability during storage condition thereof.

Pre-formulation investigations were carried out for paroxetine hydrochloride which lead to preparation of optimised formulation with drug and excipient compatibility. Nasal gel were prepared by using cold technique, where drug along with mucoadhesive polymers are mixed with distilled water. Four different nasal gel formulations were prepared and are evaluated.

The nasal gel formulated with Paroxetine hydrochloride possess a clear appearance and exhibit gelling temperatures ranging from 34.56°C to 35.34°C with an average gelling time of 7.85 to 10.2 seconds. The viscosities of prepared nasal gel formulation range from 145.25 Cp to 199.25 Cp. The drug content in these formulations varies from 97.42% to 99.25%. with an average gel strength of 50.12 s to 64.22 s. The pH of the formulations ranges from 5.7 to 6.0, indicating a slightly acidic to neutral environment and spreadability of 8.65 mm to 10.21 mm. Thus, these results lead to a conclusion, a prepared nasal gel with Paroxetine hydrochloride as active constituent deliver a potential to be developed as marketed formulation for treatment depression.

Key words: Nasal gel, Depression, Paroxetine hydrochloride, Optimised, Mucoadhesive polymers, Physiochemical properties, stability study.

DOI: 10.48047/ecb/2023.12.Si8.526

INTRODUCTION

Depression is a mental health disorder characterized by persistent feelings of sadness, loss of interest or pleasure in activities, and a range of emotional and physical symptoms. It affects a person's thoughts, feelings, and behaviors, and can significantly impact their daily life.[1]

Depression is a widespread condition that affects millions of people worldwide. It is estimated that around 264 million individuals of all ages suffer from depression globally. The prevalence varies across different countries and cultures, but it is a significant public health concern in every region.[2]

Depression is characterized by a range of symptoms that affect a person's thoughts, emotions, and behaviors. Common symptoms include [8,9]

1. Persistent feelings of sadness, emptiness, or hopelessness.
2. Loss of interest or pleasure in activities once enjoyed.
3. Significant changes in appetite and weight (either weight gain or weight loss).
4. Sleep disturbances, such as insomnia or excessive sleeping.
5. Fatigue or loss of energy, leading to decreased productivity.
6. Feelings of worthlessness or excessive guilt.
7. Difficulty concentrating, making decisions, or remembering things.

8. Recurrent thoughts of death or suicidal ideation.
9. Physical symptoms such as headaches, digestive problems, or chronic pain

Diagnostic criteria according to Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5)

The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) is widely used by mental health professionals to diagnose mental disorders, including depression. The DSM-5 outlines the following criteria for a major depressive episode [10,11]

Presence of five or more symptoms during the same two-week period.
At least one of the symptoms is either a depressed mood or loss of interest or pleasure.
Symptoms cause significant distress or impairment in social, occupational, or other important areas of functioning.
The symptoms cannot be better explained by another medical condition or substance use.

Some Treatment Approaches :

Psychotherapy

Psychotherapy, also known as talk therapy or psychological therapy, involves the use of therapeutic techniques to help individuals with depression understand their thoughts, emotions, and behaviors, and develop effective coping strategies. One widely used form of psychotherapy for depression is cognitive-behavioral therapy (CBT). CBT focuses on identifying and changing negative thought patterns and behaviors that contribute to depression. It helps individuals develop more positive and adaptive ways of thinking and promotes the development of healthy coping skills. Other types of psychotherapy used for depression include interpersonal therapy (IPT), which focuses on improving interpersonal relationships and social functioning, and psychodynamic therapy, which explores unconscious processes and unresolved conflicts.[19-20]

Pharmacotherapy

Pharmacotherapy involves the use of medications to treat depression. Antidepressant medications are commonly prescribed for moderate to severe depression. The most commonly prescribed class of antidepressants is selective serotonin reuptake inhibitors (SSRIs), which increase the availability of serotonin, a neurotransmitter involved in mood regulation, in the brain. Other classes of antidepressants include serotonin-norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants (TCAs), and monoamine oxidase inhibitors (MAOIs). Medication selection is based on various factors, including the individual's symptoms, medical history, and response to previous treatments. It is important to note that medication should be prescribed and monitored by a qualified healthcare professional.[21-22]

Alternative and Complementary Treatments

Alternative and complementary treatments are often used as adjuncts to traditional treatments for depression, although their effectiveness may vary. Some examples include:

1. Mindfulness-based therapies: Practices such as mindfulness meditation and mindfulness-based cognitive therapy (MBCT) can help individuals cultivate present-moment awareness and develop skills to manage negative thoughts and emotions.[23]

2. Exercise: Regular physical exercise, such as aerobic exercises or yoga, has been found to have mood-enhancing effects and can serve as a complementary treatment for depression.[24]

3. Herbal supplements: Certain herbal supplements, such as St. John's wort, have been studied for their potential antidepressant effects. However, it is important to consult with a healthcare professional before using any herbal supplements as they can interact with other medications and have potential side effects.[25]

4. Electroconvulsive therapy (ECT): ECT is a medical procedure that involves passing electric currents through the brain to induce controlled seizures. It is typically used for severe depression that has not responded to other treatments and can be highly effective in relieving symptoms.[26]

The role of nasal gel in depression management

The use of nasal gel in depression management is a relatively novel approach that is being explored as a potential alternative or adjunct treatment method. Nasal gel formulations offer a unique delivery route for medications and therapeutic agents, bypassing the

gastrointestinal system and directly targeting the nasal mucosa. Here is an explanation of the potential role of nasal gel in depression management:

1. Direct Delivery to the Brain: The nasal cavity provides direct access to the central nervous system, including the brain. Administering medications via nasal gel allows for direct absorption into the bloodstream through the highly vascular nasal mucosa. This route can potentially facilitate the rapid and efficient delivery of therapeutic agents to the brain, enhancing their therapeutic effects.[34]

2. Enhanced Drug Bioavailability: Nasal gel formulations can enhance the bioavailability of drugs by increasing their absorption and reducing their metabolism and first-pass effect. This can result in higher drug concentrations reaching the brain, leading to improved therapeutic outcomes. By maximizing drug delivery efficiency, nasal gel may offer advantages over traditional oral administration, where some medications may undergo significant degradation or have poor bioavailability.[35]

3. Potential for Targeted Drug Delivery: Nasal gel formulations can be designed to release therapeutic agents in a controlled manner, allowing for sustained drug release and prolonged therapeutic effects. This controlled release feature may be particularly beneficial in depression management, where consistent drug levels are desired to stabilize mood and alleviate symptoms.[36]

   Non-Invasive and Patient-Friendly: Nasal gel administration is generally non-invasive and well-tolerated by patients. It eliminates the need for injections or invasive procedures, making it a more patient-friendly approach. Nasal gel can be self-administered by patients, reducing the need for healthcare provider intervention and enabling convenient at-home use.[37]

4. Potential for Combination Therapy: Nasal gel formulations can be designed to deliver multiple therapeutic agents simultaneously, allowing for combination therapy. This opens up the possibility of targeting different mechanisms of depression simultaneously, such as neurotransmitter modulation, neurotrophic support, or anti-inflammatory effects. Combination therapy has the potential to enhance treatment response and address the complex nature of depression.[38]

5. Improved Treatment Adherence: Depression is often associated with low treatment adherence, especially with oral medications. Nasal gel formulations may offer an alternative for individuals who struggle with oral medication compliance. The ease of administration and potential for improved drug delivery efficiency may enhance treatment adherence and overall treatment outcomes.[39]

Understanding Nasal Gel Therapy

Nasal gel therapy refers to the use of gel formulations that are specifically designed for administration through the nasal cavity. It involves applying a gel-based formulation to the nasal mucosa, allowing for direct absorption of therapeutic agents into the bloodstream. Nasal gel therapy offers a unique route of drug delivery that bypasses the gastrointestinal system and provides direct access to the central nervous system.[40]

The nasal gel formulation typically consists of a gel matrix that contains the active drug or therapeutic agent. The gel matrix provides a viscous and adherent consistency, allowing it to adhere to the nasal mucosa and facilitate prolonged contact with the nasal tissues. The gel can be formulated to release the drug in a controlled manner, ensuring sustained drug delivery over a specified period.[41]

The nasal mucosa is highly vascularized, meaning it contains an extensive network of blood vessels. This vascularization allows for efficient absorption of drugs directly into the bloodstream. Upon application of the nasal gel, the therapeutic agents present in the gel are absorbed through the nasal mucosa and enter the systemic circulation. From there, they can reach the target sites in the body, including the brain, where they exert their pharmacological effects.[42]

Nasal gel therapy offers several advantages over other routes of drug administration. It provides a non-invasive and patient-friendly method of drug delivery, eliminating the need for injections or invasive procedures. It also bypasses the first-pass metabolism in the liver, resulting in improved bioavailability and potentially reducing systemic side effects. Moreover, the direct delivery of drugs to the nasal mucosa allows for rapid onset of action and enhanced therapeutic outcomes.[43]

It is important to note that nasal gel therapy is a specialized form of drug delivery and is typically used for specific applications or formulations. It is extensively studied in areas such as neurology, psychiatry, and pain management, where direct drug delivery to the brain or central nervous system is desired. However, not all medications or therapeutic agents are suitable for nasal gel formulation, and the use of nasal gel therapy should be determined on a case-by-case basis.[44]

MATERIAL & METHOD

Table 1: Instrument List

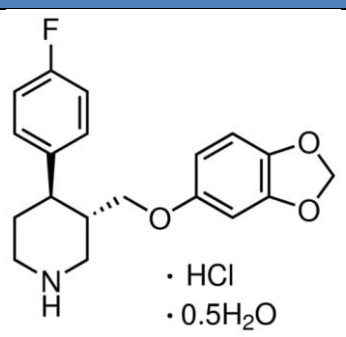
INSTRUMENT	INSTRUMENT DETAIL
pH metre	Zeiss
Centrifuge	Ohaus
Anton Paar Rheometer	Ohaus
Electric heater	Yamato Scientific
Digital pH meter	Mettler Toledo
Optical microscope	Zeiss
Zetasizer	Zeiss
Refrigerator	Thermo Fisher Scientific
Digital balance	Ohaus
Magnetic stirrer	Corning
Dissolution Apparatus	Yamato Scientific
Graduated cylinder	Corning
Volumetric pipette	Corning
Brookfield viscometer	Brookfield Engineering Labs.
Shimadzu 8400S (FTIR Spectrometer)	Ohaus
Test tubes	Corning

Table 2 : Chemicals List

Chemical Name	Company Name
Paroxetine Hydrochloride	Thomas Baker (Chemicals)
Hydrochloric acid	Thomas Baker (Chemicals)
Polyvinylpyrrolidone (PVP)	Changshu Hongsheng Fine Chemical
Sodium alginate	Honeywell
Carbopol	Honeywell
Hydroxypropyl methylcellulose (HPMC) K 100	SD Fine Chemicals
Distilled water	Thomas Baker (Chemicals)
Magnesium stearate	Fisher Scientific
n-octonol	Changshu Hongsheng Fine Chemical

Methanol	SD Fine Chemicals
Xanthan gum	SD Fine Chemicals
Mannitol	SD Fine Chemicals
Polyethylene glycol (PEG)	Fisher Scientific
Benzalkonium chloride	Fisher Scientific
Other chemicals used were of analytical grade	

Table 3: Drug Profile

DRUG	PAROXETINE HYDROCHLORIDE
Chemical Structure	
Chemical formula	$C_{19}H_{20}FNO_3.HCl$
Solubility	Paroxetine hydrochloride is soluble in water
Density	The density of Paroxetine hydrochloride is approximately 1.29 g/cm³
Molecular Weight	The molecular weight of Paroxetine hydrochloride is approximately 365.83 g/mol
Color	Paroxetine hydrochloride is a white to off-white crystalline powder.
Appearance	Paroxetine hydrochloride appears as a crystalline solid
Odor	Paroxetine hydrochloride is odorless.
Taste	The taste of Paroxetine hydrochloride is not readily available.
Melting Point	The melting point of Paroxetine hydrochloride is approximately 120-122°C.
Stability/Shelf Life	Paroxetine hydrochloride should be stored in a tightly closed container, protected from light and moisture. It has a shelf life of about 3-5 years when stored properly.

Pre- formulation study of Paroxetine Hydrochloride

Paroxetine Hydrochloride pre-formulation studies look at its physicochemical characteristics, stability, compatibility, and formulation factors. The physicochemical characteristics of the pharmacological material, such as solubility, polymorphism, and particle size, are revealed through pre-formulation investigations. This knowledge aids in the formulation of acceptable dose forms, the choice of appropriate excipients, and the optimisation of the drug release and bioavailability.

Identification of drug Paroxetine Hydrochloride : Melting point method

Determine the melting point of a material, such as paroxetine hydrochloride, using the melting point method. Here is a broad description of how the melting point calculation is carried out:

1. **Sample Preparation**: Obtain a tiny quantity of paroxetine hydrochloride, making that it is crystalline or finely powdered. The sample needs to be dry and impurity-free.
2. **Melting Point Apparatus**: A Mel-Temp device or a capillary tube melting point apparatus should be set up as an appropriate melting point equipment. The equipment normally consists of a magnifying glass or a microscope, a heating block or hot plate, and a thermometer.
3. **Capillary Tube Filling**: The sample of paroxetine hydrochloride should be placed in a capillary tube. Using a spatula or other suitable filling tool, the sample is placed into the capillary tube's open end, which has one end capped. Make sure the sample is well sealed and devoid of air bubbles.
4. **Melting Point Determination**: Make sure the sealed end of the capillary tube is placed closer to the heat source as you insert it into the melting point device. Heat the sample slowly and steadily while keeping a close eye on it under the microscope or a magnifying glass. The melting point range is the range of temperatures at which the sample begins to liquefy and full melting takes place.
5. **Recording the Melting Point**: Note the range of temperatures at which the sample melts. The range of the melting point, from the temperature at which the first evidence of melting is seen to the temperature at which total melting occurs, is how the melting point is commonly stated.

Preparation of Gels : Material Preparation

Paroxetine Hydrochloride Gel Preparation and Optimisation

The gels were made using the cold technique, both plain and drug-loaded.

For drug-loaded gels, the drug was mixed with an adequate amount of distilled water and refrigerated at 4°C overnight. After then, paroxetine hydrochloride was gradually added while being constantly stirred.

After obtaining a clear solution, the dispersions were refrigerated while the volume was finally adjusted. By adjusting the concentration of paroxetine hydrochloride and comparing them for gelation temperature, plain and drug-loaded gels were optimised.

To further investigate the impact of mucoadhesive polymers on gelation temperature and mucoadhesive strength, a batch containing an optimised concentration of paroxetine hydrochloride was employed.

Four different concentrations of 5 polymers were screened. Carbopol 934P (0.1% to 0.4%), HPMC K_4M (0.5% to 2.0%), PVP (0.1% to 0.5%), Sodium alginate (0.1% to 0.5%).

Table 4 : Composition of Paroxetine Hydrochloride Loaded Gel Formulation (F)

S.No	Ingredients % w/w	F1	F2	F3	F4
1.	Paroxetine Hydrochloride	2	2	2	2
2.	Carbopol	0.1	0.2	0.3	0.4

3.	Hydroxypropyl methylcellulose (HPMC)	1.5	1.0	1.5	1.5
4.	Sodium alginate	0.1	0.3	0.4	0.5
5.	Polyvinylpyrrolidone (PVP)	0.1	0.5	0.4	0.3

Preparation of in situ nasal gels A 24 factorial design was used for optimization of the process parameters. The drug was dissolved in methanol and 10 ml of distilled water (Milli-Q) was added. The solution was mixed by constant stirring. To the above drug solution, mannitol, PEG, and benzalkonium chloride were added..

The polymeric solution of HPMC K 100 and xanthan gum were prepared separately in distilled water and thoroughly mixed with the above mixture. The resultant mixture was stirred for 15 min on a magnetic stirrer and phosphate buffer solution was added. The final volume was made up to the desired quantity with distilled water.

The sublingual tablets of Paroxetine HCl were formulated by Direct Compression method with a total weight of 100mg for each tablet in all the formulation batches. The drug API is mixed with various excipients. Kyron t - 314 was used as super disintegrating agent in the concentration 2 -10%. It is a cation exchanger which facilitates tablet compression prompting greater hardness and improving the permeability of anionic drugs. It increases drug potential for rapid absorption and improved bioavailability.[8] It also exhibits taste masking property and is derived from cross linked polymer of poly-carboxylic acid as per USP/NF and has a K+ ionic form.[9]

F - Melt Type - M was selected as a diluent; it is a co -processed excipient composed of Magnesium alumino - metasilicate Neusilin (2-9%), D – mannitol (55-70%), Microcrystalline cellulose (10- 25%), Xylitol (2- 9%), Crospovidone (5- 13%). It improves the quality of granules imparting better flow properties and enhances overall quality of tablet.[10]

Pregelatinized starch was incorporated as a binder in the formulation. It is composed of 15% free amylo - pectin, 5% free amylase and 80% unmodified starch. When used in the conc. of 5 - 10%, it enhances flow and compression properties [11] . It is self-lubricating, bland, odorless, capable of digestion and can also be used as a diluent (5-75%) as well as a disintegrant (5-10%). Sweetening agent, sodium saccharin was added to mask the bitter taste of drug (1-2%) Talc and Aerosil act as a lubricant and a glidant respectively [12].

Aerosil is a moisture absorbent and a thickening agent when used in concentration of 0.125 -0.5%.[13] Less than 2% of talc (also known as a clay mineral), composed of hydrated magnesium silica, prevents the cake formation, thereby, further improving the property of the formulation [14]. Gelling temperature refers to the temperature when the meniscus of the formulation would no longer move upon slanting the test tubes at 90 ° [15].

Miller and Donovan's technique [15] was used to determine the gelation studies. The gelling temp. was determined by placing the test tube, containing sufficient quantity of the prepared solutions, in a water bath at 4 °C. The temperature of water bath was increased slowly at a constant rate of 1 °C every 2 min. Gelling time of formulations was determined using the procedures described by Miller and Donovan.

The delivery systems exist in sol form before administration, however, once they are administered; they undergo gelation to form a gel. Gelling time was recorded as the time for first detection of gelation. The sol-gel transition temp. (Tsol-gel) of the prepared in situ gel formulations was evaluated by transferring 2 ml of the prepared formulation to a test tube (10 ml), with a diameter of 1.0 cm. After sealing with a parafilm, the tube was kept in a circulation water bath at 37 °C. Following each temperature setting, equilibration was allowed for 10 min. Finally, the test tube was placed horizontally to observe the state of the sample and to examine the gelation.

Viscosity of solution & Viscosity of the in situ gel systems was determined using Brookfield Viscometer DV-II+ Pro coupled with S-94 spindle (Brookfield Engineering Laboratories Inc., MA, USA) .The prepared gel formulations were transferred to the

beaker. The spindle was lowered perpendicularly into the gel at l00 rpm and temperature was maintained at 37 ± 0.5°C. The viscosity was determined during the cooling of the system [12].

Drug - excipient compatibility studies is done by Fourier transform infrared (FTIR) & Differential Scanning calorimetry (DSC). By using FTIR and DSC, compatibility studies were carried out to find out any interactions between drug and excipients.The FTIR spectroscopy study of pure Paroxetine HCl was performed using Shimadzu 8400S and characterization of the drug and excipients was accomplished using DSC study.

Evaluation of Formulations

Clarity

By visual inspection against a black and white backdrop, the clarity of several formulations was assessed and classified as follows: muddy, +; clear, ++; and extremely clear (glassy), +++.

pH of Formulation

With the use of a pH metre (Equiptronics, Model EQ-610), the pH of each composition was measured. First, pH 4.5 and pH 7 solutions were used to calibrate the pH metre.

Gelation Temperature

A. Visual Observation Method

A test tube with a water bath was filled with a two millilitre aliquot of gel. From room temperature to the point at which gel formed, the temperature of the water bath was gradually raised over the course of two minutes at a steady rate of 1°C. The sample was next tested for gelation, which was thought to have happened when the meniscus stopped moving while the test tube was tilted through a 90° angle.

B. Anton Paar Rheometer (MCR52) Method

1-m l aliquot of the material was used to measure the gelation temperature using an Anton Paar Rheometer (model: Gmbh, 3ITT) and probe (PP25-SN 17002). Measurements were made while utilising the temperature sweep mode in oscillation mode. The temperature was raised steadily from 10°C to 60°C. Rheoplus software was used to automatically plot the storage modulus and loss modulus vs temperature to calculate the gelation temperature.

Drug Content

1ml of formulation was taken in 10 ml volumetric flask, diluted with distilled water and volume adjusted to 10 ml. 1ml quantity from this solution was again diluted with 10 ml of distilled water. Finally the absorbance of prepared solution was measured at 261 nm by using UV visible spectro-photometer.

Viscosity

The viscosity measurements were carried out by using Brookfield DV Pro II model with spindle no. 62. The instrument was equipped with the temperature control unit and the sample were equilibrated for 10 min before the measurement. The viscosity was measured against increasing shear rate. Measurement was taken at 4-34 degree respectively.

Spreadability

Spreadability is expressed in terms of time in seconds taken by two slides to slip off from gel and placed in between the slides under the direction of certain load, lesser the time taken for separation of two slides, better the spreadability.

Gel Strength

A sample of the nasal gel weighing 50 g was placed in a graduated cylinder with a volume of 100 ml, and it gelled at 37 °C in a thermostatically controlled water bath. 35 g of weight were applied to the gel. The time in seconds needed by the weight to pierce the gel 5 cm deep was used to determine the gel strength, which is a measure of the nasal gel's viscosity at physiological temperature.

RESULT & DISCUSSION

Nasal gel refers to a gel-like substance that is designed to be applied inside the nostrils. It is commonly used for various purposes, such as nasal moisturization, nasal congestion relief, and nasal irrigation. Nasal gels can be over-the-counter products or prescribed by a healthcare professional.

Nasal gel products may contain ingredients like saline solution, which can help moisturize and soothe the nasal passages, or decongestants, which can provide temporary relief from nasal congestion. Some nasal gels may also include ingredients to alleviate symptoms associated with allergies or sinus issues.

Paroxetine hydrochloride is a medication that belongs to the class of selective serotonin reuptake inhibitors (SSRIs). It is commonly prescribed for the treatment of various mental health conditions, including major depressive disorder, generalized anxiety disorder, panic disorder, obsessive-compulsive disorder, and social anxiety disorder.

Paroxetine hydrochloride is typically available in oral tablet or capsule form, and it is taken by mouth. It works by increasing the levels of serotonin, a neurotransmitter in the brain, which helps regulate mood, emotions, and anxiety.

The study focuses on developing a nasal gel formulation of Paroxetine Hydrochloride, which offers an alternative route of administration for the treatment of depression. Nasal delivery bypasses the gastrointestinal tract, potentially providing rapid drug absorption and avoiding first-pass metabolism, thus improving therapeutic outcomes.

Nasal gel formulations have the potential to improve drug delivery to the brain due to the rich vasculature and proximity to the central nervous system. This study aims to optimize the formulation to enhance the nasal absorption and permeation of Paroxetine Hydrochloride, thereby potentially increasing drug bioavailability and efficacy.

Depression is a complex psychiatric disorder that often requires long-term treatment. By developing a nasal gel formulation, this study aims to provide a sustained and controlled release of Paroxetine Hydrochloride, which may lead to improved therapeutic effect and better patient compliance.

Nasal delivery can potentially minimize systemic side effects associated with oral administration, such as gastrointestinal disturbances and liver metabolism-related issues. By delivering the drug directly to the nasal cavity, this study seeks to minimize systemic exposure and related adverse effects.

The study aims to compare the pharmacokinetic profile of Paroxetine Hydrochloride following nasal administration of the gel formulation with that of the oral dosage form. This comparison will provide valuable insights into the potential advantages and disadvantages of nasal delivery in terms of drug absorption, distribution, metabolism, and elimination.

Preformulation studies

Preformulation studies are essential preliminary investigations conducted before the formulation development of a drug product. These studies provide valuable information about the physicochemical properties of the drug substance and guide the formulation process. Here is an outline of preformulation studies for the preparation and evaluation of Paroxetine Hydrochloride nasal gel:

Physico-chemical properties of Paroxetine Hydrochloride

Paroxetine Hydrochlorideis a pharmaceutical compound used primarily as a non-selective beta-adrenergic antagonist. It belongs to the class of drugs known as beta-blockers and is commonly used for the management of various cardiovascular conditions, including hypertension, angina, and arrhythmias. Here, we will discuss the physicochemical properties of Propranolol hydrochloride

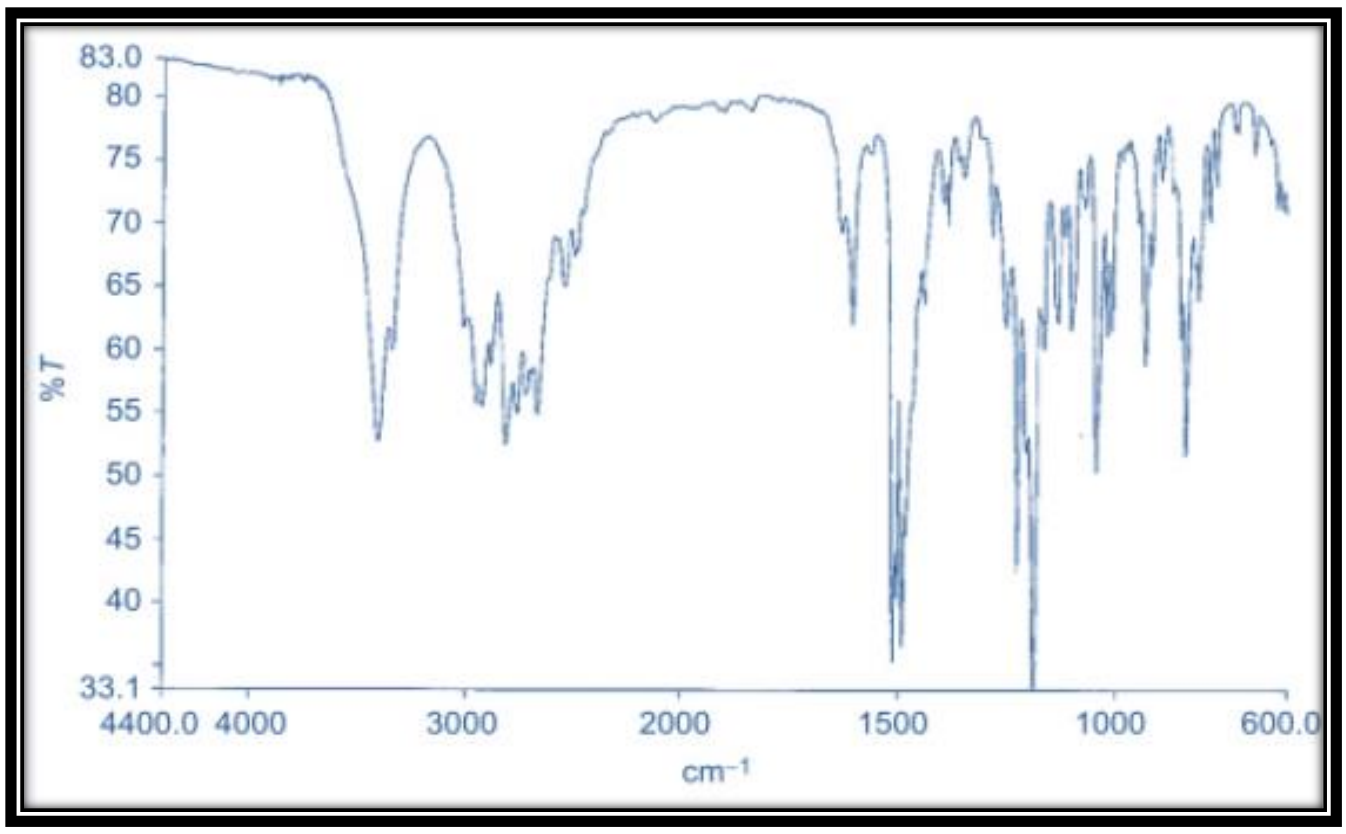
Table 5 : Physico-chemical Properties of Paroxetine Hydrochloride

S.No	Parameter	**Observed**
1.	Physical appearance	Paroxetine hydrochloride is a white or off-white crystalline powder

2.	Melting point	The melting point of Paroxetine hydrochloride ranges from approximately 120-125°C.
3.	Solubility	Paroxetine hydrochloride is slightly soluble in water and freely soluble in methanol and ethanol
5.	Stability	Paroxetine hydrochloride is generally stable under normal storage conditions but can degrade upon exposure to light, moisture, and elevated temperatures.

Table-6 : The Peaks observed in the FTIR spectrum of Paroxetine hydrochloride along with their corresponding wavenumbers and functional group assignments

Wavenumber (cm^-1)	**Functional Group Assignment**
3375-3430	Broad peak corresponding to the stretching vibrations of the N-H bond in the primary amine group.
2980-3100	Strong peaks associated with the stretching vibrations of C-H bonds in the aromatic and aliphatic groups.
1730-1760	Strong peak related to the stretching vibrations of the carbonyl group (C=O) in the amide moiety.
1570-1620	Strong peaks corresponding to the stretching vibrations of the aromatic C=C bonds.
1450-1500	Medium peaks associated with the bending vibrations of the C-H bonds in the aromatic groups.
1320-1380	Medium peaks attributed to the stretching vibrations of C-N bonds in the amine groups.
1110-1150	Strong peak related to the stretching vibrations of C-O bonds in the ether group.
720-800	Medium peaks associated with the bending vibrations of C-H bonds in the aromatic groups.



Graph-1 : FTIR spectrum of Paroxetine Hydrochloride

Properties of nasal gel of Paroxetine Hydrochloride

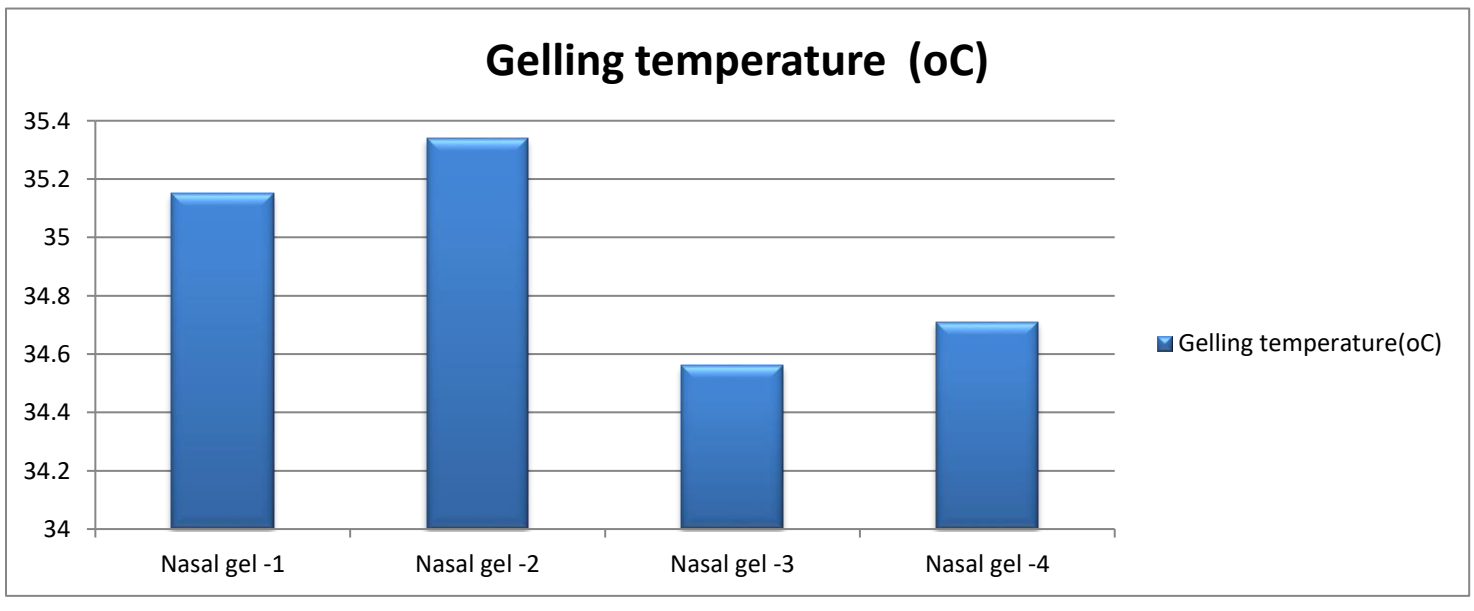
The nasal gels formulated with Paroxetine hydrochloride exhibit a clear appearance, indicating transparency and visual clarity.

The gelling temperature of the formulations ranges from 34.56°C to 35.34°C, suggesting the temperature at which the gel transitions from a liquid to a gel-like state.

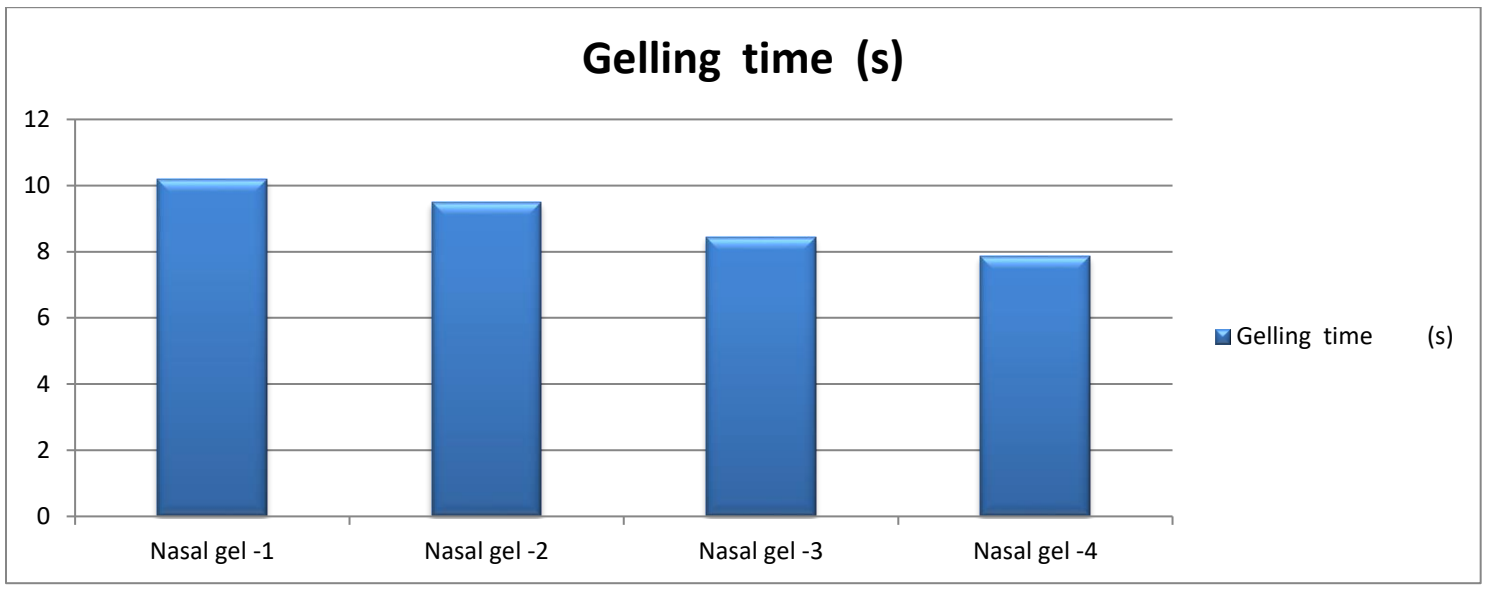
The gelling time, measured in seconds, varies from 7.85 to 10.2 seconds, indicating the time required for the gel to fully form after reaching the gelling temperature.

Table- 7 : Properties of nasal gel of Paroxetine Hydrochloride

Formulation	Appearance	Gelling temperature(°C)	Gelling time (s)
Nasal gel -1	Clear appearance	35.15	10.2
Nasal gel -2	Clear appearance	35.34	9.5
Nasal gel -3	Clear appearance	34.56	8.45
Nasal gel -4	Clear appearance	34.71	7.85



Graph- 2: Graph showing gelling temperature (oC)



Graph- 3: Graph showing gelling time(s)

Properties of nasal gel formulations of Paroxetine hydrochloride

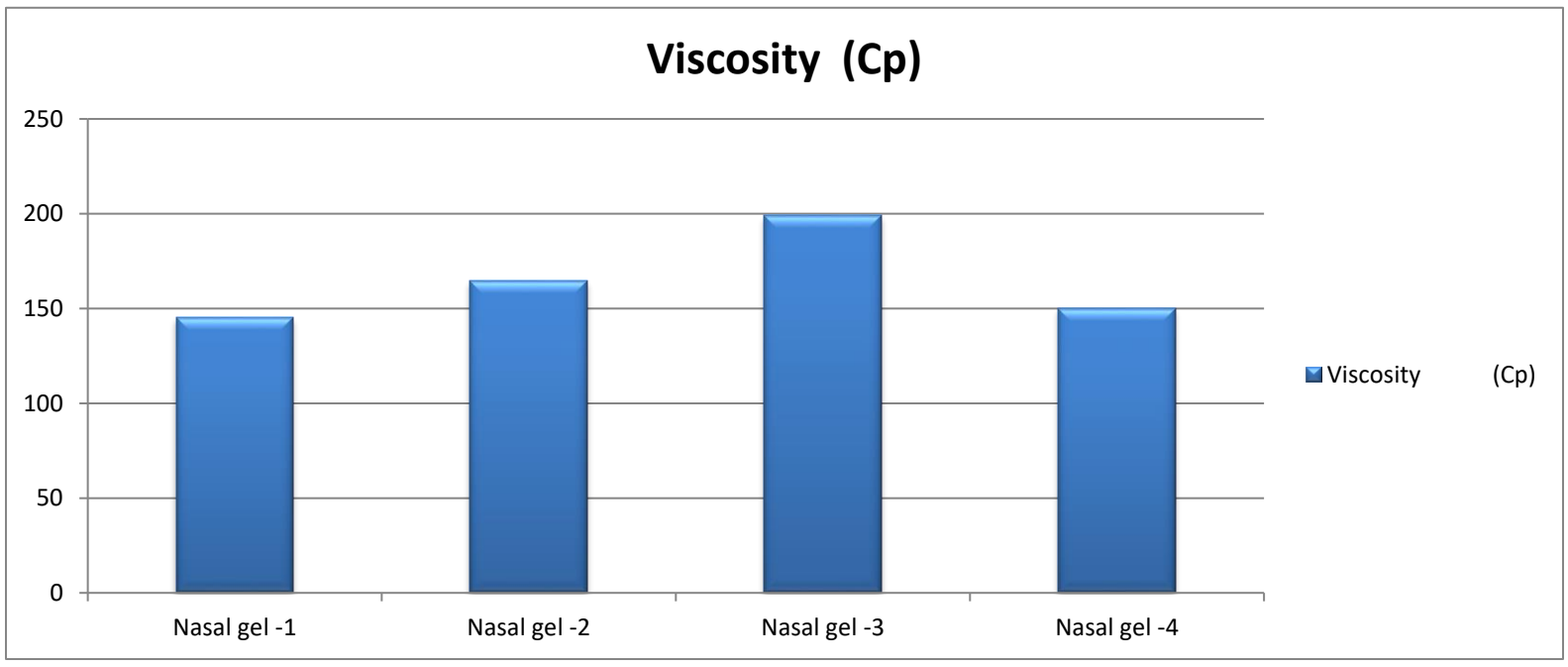
Viscosity, measured in centipoise (Cp), represents the resistance to flow of the nasal gel. The formulations have viscosities ranging from 145.25 Cp to 199.25 Cp, indicating variations in their flow properties.

The drug content of the nasal gels is expressed as a percentage. The formulations contain Paroxetine hydrochloride at levels ranging from 97.42% to 99.25%, ensuring consistent and accurate dosing of the active ingredient.

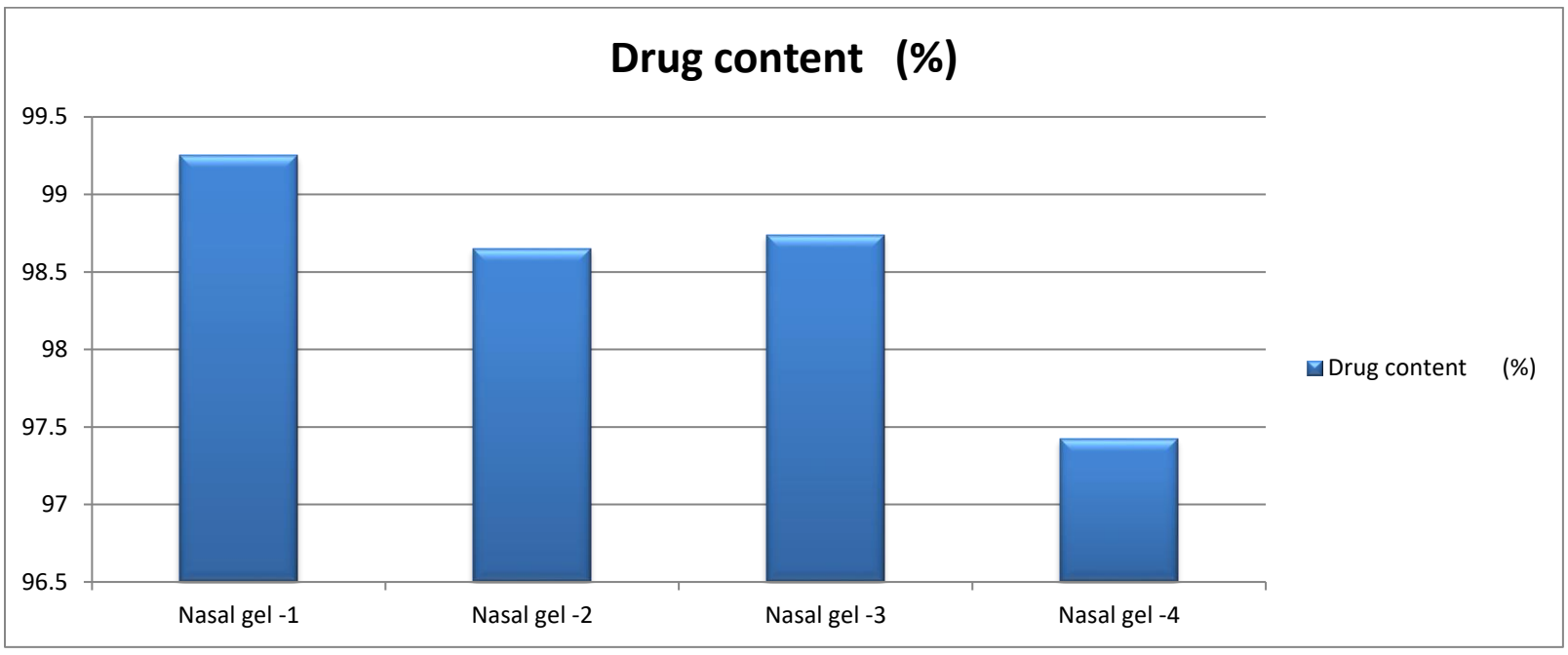
Gel strength, measured in seconds (s), reflects the ability of the gel to maintain its structure and resist deformation. The nasal gel formulations exhibit gel strengths ranging from 50.12 s to 64.22 s, indicating their ability to retain their gel-like consistency.

Table-8 : Properties of nasal gel of Paroxetine Hydrochloride

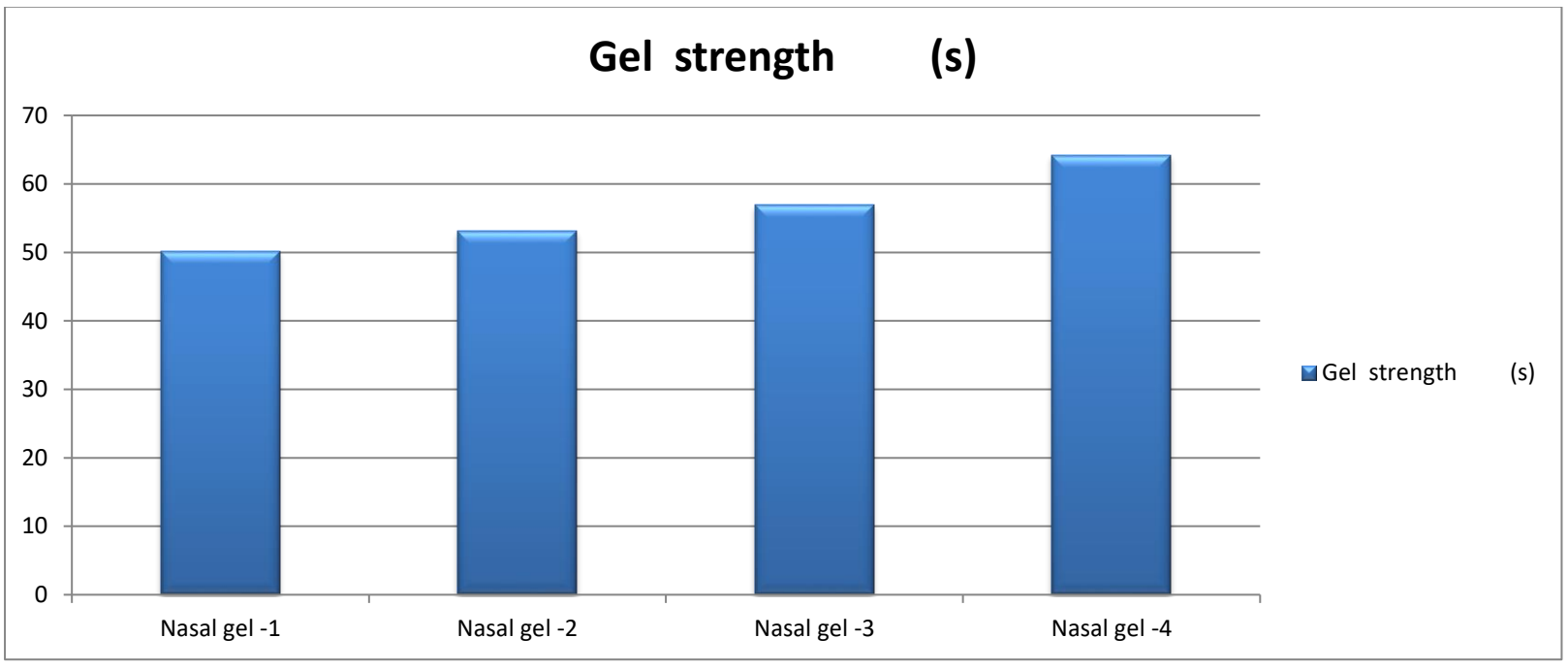
Formulation	Viscosity (Cp)	Drug content (%)	Gel strength (s)
Nasal gel -1 (F1)	145.25	99.25	50.12
Nasal gel -2 (F2)	164.52	98.65	53.14
Nasal gel -3 (F3)	199.25	98.74	56.98
Nasal gel -4 (F4)	150.25	97.42	64.22



Graph- 4: Viscosity of solution of nasal gel of Paroxetine Hydrochloride



Graph- 5 : Drug content of nasal gel of Paroxetine Hydrochloride



Graph- 6: Gel Strength of nasal gel of Paroxetine Hydrochloride

Properties of nasal gel of Paroxetine Hydrochloride

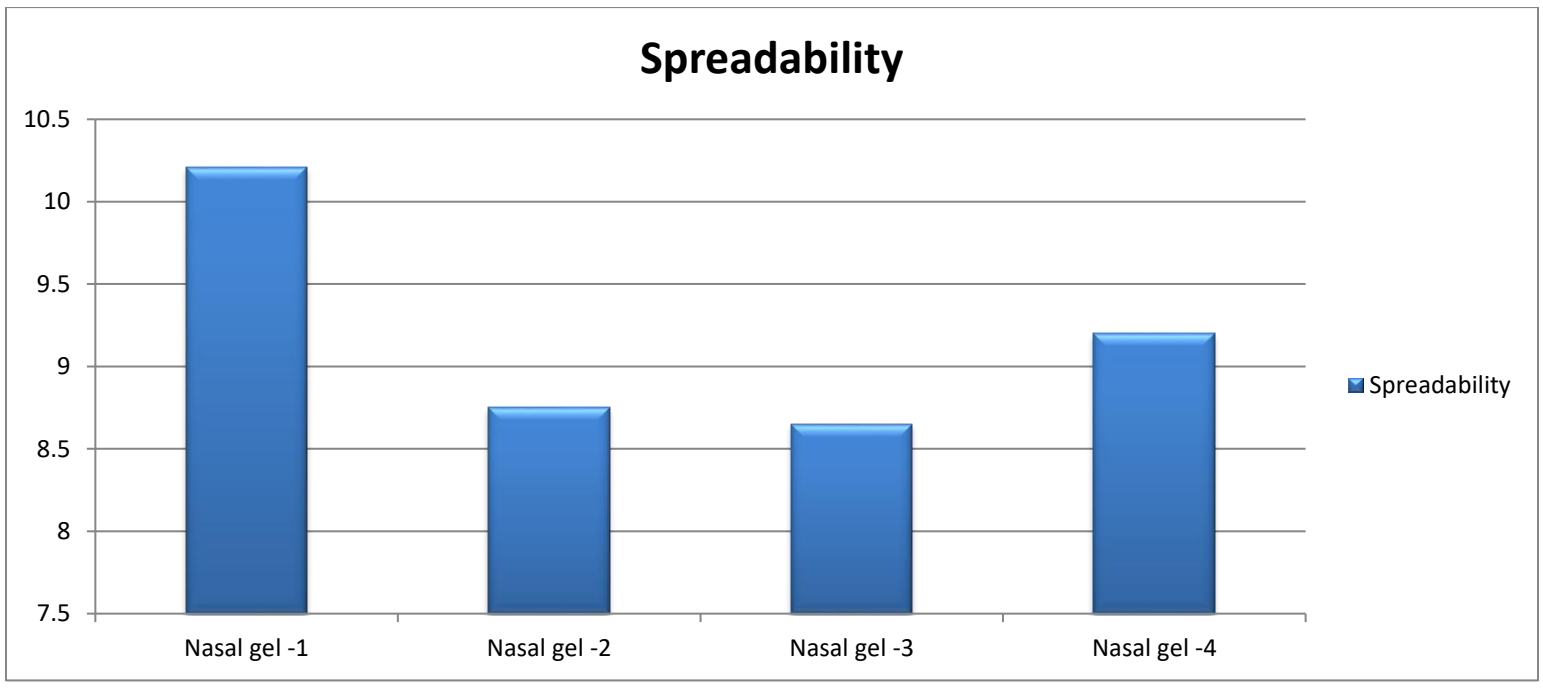
The nasal gel formulations of Paroxetine hydrochloride exhibit different properties related to spreadability and pH.

Spreadability is measured in millimeters (mm) and represents the ability of the gel to spread over a surface. The formulations show spreadability values ranging from 8.65 mm to 10.21 mm, indicating variations in their ability to spread.

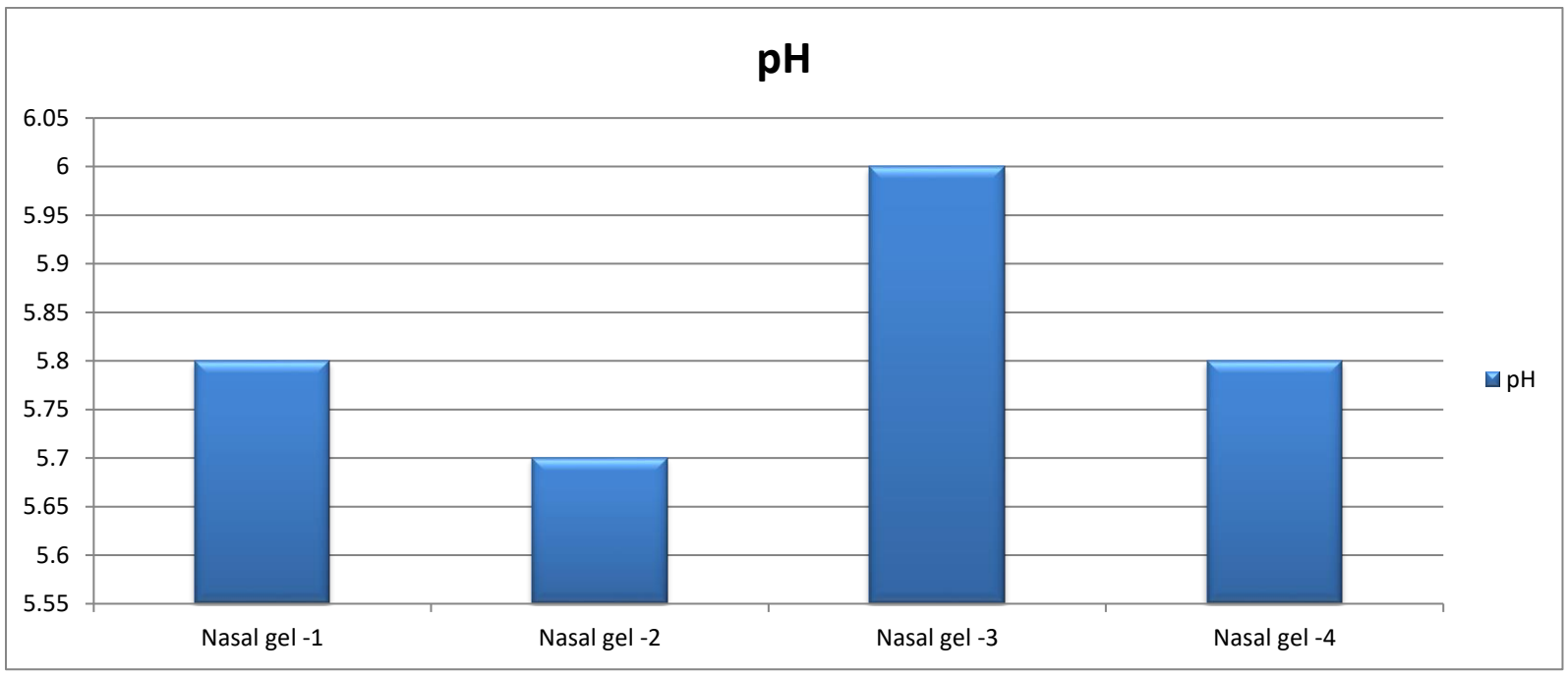
pH is a measure of the acidity or alkalinity of a solution. The nasal gel formulations have pH values ranging from 5.7 to 6.0. These values indicate the formulations are slightly acidic to neutral.

Table- 9: Properties of nasal gel of Paroxetine Hydrochloride

Formulation	Spreadability	pH
Nasal gel -1 (F1)	10.21	5.8
Nasal gel -2 (F2)	8.75	5.7
Nasal gel -3 (F3)	8.65	6.0
Nasal gel -4 (F4)	9.20	5.8



Graph- 7: The physicochemical properties, such as spreadability



Graph- 8: The physicochemical properties, such as pH

CONCLUSION

Paroxetine hydrochloride is a white or off-white crystalline powder with a melting point range of approximately 120-125°C. It is slightly soluble in water but freely soluble in methanol and ethanol. While it is generally stable under normal storage conditions, precautions should be taken to prevent its exposure to light, moisture, and high temperatures, which may cause degradation.

The flow properties analysis of Paroxetine hydrochloride reveals that it has a bulk density of 0.40 gm/ml, a tapped density of 0.55 gm/ml, a % Carr's Index of 27.27%, and a Husnar's Ratio of 1.37. These findings suggest that the drug possesses relatively good flowability, which can be advantageous for its formulation and manufacturing processes.

The nasal gels formulated with Paroxetine hydrochloride possess a clear appearance and exhibit gelling temperatures ranging from 34.56°C to 35.34°C. The gelling time for these formulations ranges from 7.85 to 10.2 seconds. These properties are important considerations for the formulation and application of the nasal gel in delivering Paroxetine hydrochloride for nasal administration.

The nasal gel formulations of Paroxetine hydrochloride possess viscosities ranging from 145.25 Cp to 199.25 Cp. The drug content in these formulations varies from 97.42% to 99.25%. The gel strength of the nasal gels ranges from 50.12 s to 64.22 s. These properties play a crucial role in the formulation, administration, and effectiveness of the nasal gel in delivering Paroxetine hydrochloride for nasal use.

The nasal gel formulations of Paroxetine hydrochloride exhibit different spreadability values ranging from 8.65 mm to 10.21 mm. The pH of the formulations ranges from 5.7 to 6.0, indicating a slightly acidic to neutral environment. These properties are important considerations for the formulation, application, and overall effectiveness of the nasal gel in delivering Paroxetine hydrochloride for nasal administration.

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