https://doi.org/ 10.33472/AFJBS.6.Si2.2024.3150-3164

African Journal of Biological Sciences

Journal homepage: http://www.afjbs.com

Research Paper Open Access

Potential of Granisetron Hydrochloride for Transdermal Drug Delivery: Comprehensive Characterization, Preformulation studies and Compatibility Analysis

Geeta[1], Sharda Sambhakar[1]*, Geeta Saroha[2], Dolly[3], Sangeeta[3], Swati Rana[4], Sonia Narwal[5]

[1]Banasthali Vidyapith, Vanasthali Road, Aliyabad, Rajasthan 304022, India

[2]School of Pharmacy, RIMT University, Mandi Gobindgarh, Punjab, India-147301

[3]Puran Murti College of Pharmacy, Kami Road, Sonepat, Bhuri, Haryana-131001

[4]Laureate Institute of Pharmacy, Kathog, Tehsil Jawlamukhi, District Kangra, Himachal Pradesh-176031 [5]Departmant of Pharmacy, Panipat Institute of Engineering and Technology, Samalkha, Panipat, Haryana, India-132102

*** Corresponding author**

Sharda Sambhakar

Banasthali Vidyapith, Vanasthali Road Aliyabad, Rajasthan 304022, India

Email: **shardasambhakar@banasthali.in**

ARTICLE INFO:

Volume 6,Issue Si2, 2024

Received:14 Apr 2024

Accepted : 03 May 2024

doi: 10.33472/AFJBS.6.Si2.2024.3150-3164

Abstract

Transdermal drug delivery systems offer a promising alternative to conventional administration routes by enabling non-invasive, controlled, and sustained drug release. Granisetron hydrochloride, used primarily to prevent chemotherapy-induced nausea and vomiting, was extensively characterized for potential transdermal application. Physical characterization confirmed its crystalline nature, high melting point (301±1°C), and specific functional groups through FTIR and DSC analyses, indicating purity .Preformulation studies showed excellent solubility in water, phosphate buffer, methanol, and chloroform, while the partition coefficient indicated low lipophilicity. Compatibility studies revealed no significant interactions with excipients. A standard calibration curve in phosphate buffer saline (pH 7.4) was developed for quantitative analysis. Overall, Granisetron hydrochloride demonstrates potential for transdermal delivery, offering improved therapeutic outcomes for chemotherapy-induced nausea and vomiting.

Keywords: Granisetron hydrochloride, Phospholipon 90 G, Physical compatibility, partition coefficient, FTIR etc

Introduction

Transdermal drug delivery systems have gained considerable attention in the pharmaceutical industry due to their potential to overcome various limitations associated with conventional routes of drug administration. Unlike oral or injectable routes, transdermal delivery offers a non-invasive, controlled, and sustained release of therapeutic agents through the skin, directly into the systemic circulation. This approach bypasses the gastrointestinal tract and hepatic first-pass metabolism, thereby enhancing bioavailability, reducing systemic side effects, and improving patient compliance (1).

The skin, being the largest organ of the human body, serves as a formidable barrier against external threats while also providing an attractive route for drug delivery. Its unique structure, comprising the stratum corneum, epidermis, and dermis layers, presents both challenges and opportunities for transdermal drug permeation. Overcoming these barriers necessitates innovative formulation strategies, such as the use of permeation enhancers, nano formulations, and microneedle technologies, to facilitate drug transport across the skin barrier (2).

In recent years, transdermal drug delivery systems have found applications across a wide range of therapeutic areas, including pain management, hormone replacement therapy, cardiovascular diseases, and neurological disorders (3). The development of transdermal patches, gels, creams, and other delivery platforms has enabled the targeted and sustained delivery of drugs, leading to improved therapeutic outcomes and patient convenience (4).

Despite the numerous advantages offered by transdermal drug delivery, several challenges remain, including skin irritation, limited drug permeability, and formulation stability issues. Addressing these challenges requires a multidisciplinary approach, integrating principles from pharmacology, chemistry, materials science, and engineering (5).

MATERIAL AND METHODS

Instruments and Apparatus

A double beam UV-Visible spectrophotometer, spectral band width of 1nm, wavelength accuracy ± 0.5nm and a pair of 1cm matched quartz cells was used to measure absorbance of the resulting solution and connected with computer loaded UV Probe software. Calibrated electronic single pan balance Shimadzu AY 220, Sonicator, pH Meter, Heating Mantle, Filter Paper 0.45 microns. All the glasswares were calibrated before use.

Chemicals and Reagents

Granisetron hydrochloride was received as a gift samples from Health biotech Ltd. Phospholipon 90 G was purchased from Lipoid Gmbh, Ludwighafen, Germany .All the solvents and chemicals like sodium chloride, hydrochloric acid, Methanol, n-octanol, Chloroform, Sodium dihydrogen phosphate, Di-sodium hydrogen phosphate etc. were gifted by Qualigens fine chemicals, Mumbai, India All other ingredients used were of analytical grade.

Granisetron

Granisetron is a medication primarily used to prevent nausea and vomiting caused by chemotherapy or radiation therapy. It belongs to a class of drugs known as serotonin 5-HT3 receptor antagonists (6). These medications work by blocking the action of serotonin, a neurotransmitter involved in triggering nausea and vomiting.

Mechanism of Action

It selectively blocks serotonin receptors called 5-HT3 receptors. These receptors are located in the chemoreceptor trigger zone (CTZ) of the brain and in the gastrointestinal tract. By blocking these receptors, granisetron inhibits the signals that induce nausea and vomiting.

The dosage of granisetron varies depending on the patient's age, weight, the severity of symptoms, and the type of treatment. Generally, for chemotherapy-induced nausea and vomiting in adults, the typical oral dose is 1-2 mg once daily or as directed by the physician. The injectable form may be administered intravenously or intramuscularly at a dose of 10 mcg/kg (7).

It should be used with caution in patients with a history of cardiac arrhythmias, electrolyte abnormalities, or liver dysfunction (8). It may prolong the QT interval on electrocardiogram, so it should be used cautiously in patients with pre-existing cardiac conditions or those taking other medications that affect cardiac conduction.

Characterization of Drug

The gift sample of Granisetron hydrochloride procured from Health biotech Ltd. was characterized for the standard parameters, physical as well as chemical parameters as below:

Physical characterization

The drug sample underwent rigorous characterization to ascertain its physical attributes. Further organoleptic studies were conducted to assess its color and odor.

Melting Point

The melting of drug was determined by Thieles tube method using melting point apparatus. Glass capillary tube previously fused from one end was filled with Granisetron hydrochloride with tapping. The capillary was introduced into the melting point apparatus (Multitech Instrument Co. (P) Ltd., India) along with a thermometer and heated slowly and evenly. The temperature at which, drug starts melting, was recorded. The procedure was repeated in triplicate (9).

Fourier Transforms Infrared spectrophotometric analysis (FTIR)

FTIR analysis of drug was done to identify the presence of specific functional groups in its structure (10). The FTIR spectra of Granisetron hydrochloride was obtained by placing small quantity of drug directly on the crystal of FTIR(Cary-630, Agilent technologies) and running the spectra at 4000-400 cm^{-1}.

Differential Scanning calorimeter (DSC)

Differential scanning colorimetry (DSC) measures the heat loss or gain resulting from physical or chemical changes within a sample as a function of temperature. Examples of endothermic processes are fusion, boiling, sublimation, vaporization, desolvation, solid-solid transition, and chemical degradation. Crystallization and degradation are usually exothermic processes. DSC helps in assessment of purity and excipients compatibility (11).

Preformulation Studies

Preformulation studies focus on those Phyisco-chemical parameters of the drug that could affect drug performance and development of an efficacious dosage forms

Determination of absorption maxima (λ_{max}) using UV spectrophotometer

Preparation of phosphate buffer saline of pH 7.4

2.38 gm of disodium hydrogen orthophosphate, 0.19 gm of potassium dihydrogen phosphate and 8.0 gm of sodium chloride was dissolved in carbon dioxide free distilled water and finally make up the volume up to 1000ml with distilled water and checked the pH.

Preparation of stock solution

25 mg of drug was dissolved in small amount of phosphate buffer saline of pH 7.4 and volume was made up to 25 ml, resulting into stock solution of 1000µg/ml. From this solution 2.5 ml is further diluted to 25 ml resulting into conc. of 100µg /ml, which is further diluted in order to obtain a concentration of 5, 10, 15, 20, 25µg/ml and spectra measurement was done using UV-Vis spectrophotometer (Jasco, V-630, Japan) in the region of 200 nm to 400 nm.

Determination of solubility

The solubility of a substance is defined as the concentration at which the solution phase is in equilibrium with a given solid phase at a stated temperature and pressure. It is a critical factor in determining its usefulness, since aqueous solubility dictates the amount of compound that will dissolve and therefore, available for absorption. Solubility experiments should have all factors defined, including pH, temperature etc. Solubility values that are generally useful in early development are in: distilled water, buffer of pH7.4, all at room temperature (12).

Solubility study was carried out in water, phosphate buffer pH 7.4, methanol and chloroform. 1 ml of each of solvent was taken in separate glass vials and an excess amount of drug was added to each of them in order to obtain a saturated solution (13). The solutions were kept on mechanical shaker at 25^{o}C for a period of 24 hrs. After 24 hrs., the saturated solutions were subjected to centrifugation, and the supernatant thus obtained was suitably diluted and then analyzed spectrophotometrically at 302 nm for drug concentration.

Determination of partition coefficient

A measurement of drugs lipophilicity and an indication of its ability to cross cell membranes is the oil/water partition coefficient. The partition coefficient, log P, is defined as the ratio of un-ionized drug distributed between the organic and aqueous phases at equilibrium.

$$\mathbf{P_{o/w} = (C_{oil}/C_{water})\ equilibrium}$$

The partition coefficient of drug was determined using n-Octanol: Phosphate buffer saline (pH-7.4) system. The n-Octanol-aqueous phase partition coefficient serve as a parameter of lipophilicity. N-Octanol and phosphate buffer were pre saturated with each other for at least 24 h before the experiment. An accurately weighed quantity of drug was dissolved in 10 ml of n-Octanol phase and shaken at 37^{o}C against 10 ml aqueous phase in a separating funnel and kept undisturbed for 24 hrs. The separated n-Octanol phase was assayed after appropriate dilution with 0.01M methanolic HCL by UV spectrophotometer at 302 nm, to determine its residual concentration and hence the amount partitioned into the aqueous phase (14).

Compatibility study of drug and excipients

The drug excipients compatibility is an important Preformulation parameter used in the development of a dosage form as their incompatibility can alter the stability and/or bioavailability of drug thereby, affecting safety and/or efficacy of a formulation. There are two types of incompatibilities i.e. physical and chemical.

Physical Incompatibility

In order to determine the possible interaction between Granisetron hydrochloride and excipients, drug and excipients were physically mixed in the ratio of 1:1. The drug alone and mixture was then subjected to different experimental conditions of temperature and humidity i.e. 25^{o}C /60% RH, and 40^{o}C /75% RH for 28 days. Then these samples were inspected for any visual changes such as discoloration, and liquefaction etc. at specified time intervals of 0, 7, 14, 21 and 28 days (15).

Physicochemical incompatibility study

The sample prepared for Physical compatibility study was also evaluated for chemical incompatibility after 28 days of physical evaluation using FTIR analysis (16).

Analytical Methodology

Development of analytical method is an important technique for quantitative estimation of drug present in a solution (17). A developed analytical method for Granisetron hydrochloride was used for its quantitative analysis, using saline phosphate buffer as blank in double beam UV Visible Spectrophotometer (JASCO V 530).

Preparation of Buffer solution

2.38 g disodium hydrogen orthophosphate, 0.19 g potassium dihydrogen orthophosphate and 8 g sodium chloride were dissolved in small amount of distilled in 1000ml volumetric flask

and volume made up to the mark with distilled water to prepare PBS pH 7.4

Determination of lambert Beer's range

Aliquots of 1 ml, 2 ml, 3 ml and 4 ml were drawn from the stock solution and volume was made up to 10 ml with phosphate buffer saline pH 7.4 in order to obtain concentration of 10, 20, 30 and 40 mcg/ml respectively (18). The dilutions thus obtained were analyzed spectrophotometrically from 200 to 400 nm in order to obtain Lambert-beer's range (19).

Preparation of calibration curve in saline phosphate buffer pH 7.4

25 mg of drug was dissolved in SPB and volume was made up to 25 ml, from this solution 2.5ml is further diluted to 25ml with SPB to get the stock solution of conc. 100 mcg/ml. Aliquots of o.5, 1.0, 1.5, 2.0, 2.5, and 3.0 ml were drawn from the stock solution and volume was made up to 10 ml with SPB in order to obtain solution with conc. 5, 10, 15, 20, 25, and 30 mcg/ml respectively (20). Absorbance was measured spectrophotometrically at 302 nm using SPB as blank and the calibration curve was obtained by plotting the concentration vs absorbance.

Results and discussion

Characterization of Drug

The physical characterization of the drug reveals that it is crystalline in nature. Organoleptic studies show that the drug is almost white in color and is odourless.

Identification

Melting point

The melting point of Granisetron hydrochloride was determined by Thieles tube method was found to be 301±1^{o}C (Reported value is 301-306^{o}C). It confirms the identity and purity of the drug.

Fourier Transform Infrared spectrophotometric analysis

The FTIR spectra of Granisetron hydrochloride is shown in figure 1.It is observed that, FTIR spectra of test drug retained their characteristics peaks at 3232cm^{-1}, 1645 cm^{-1} and 1557 cm^{-1} due to –NH, C=O and –CN stretching's respectively, at 400-4000cm^{-1}. The FTIR spectra of test drug (fig.1) was compared with the standard spectra (fig.2) and it was found that as there was no shift in principal peak position of Granisetron hydrochloride in the sample drug, it could be concluded that drug sample procured was pure.

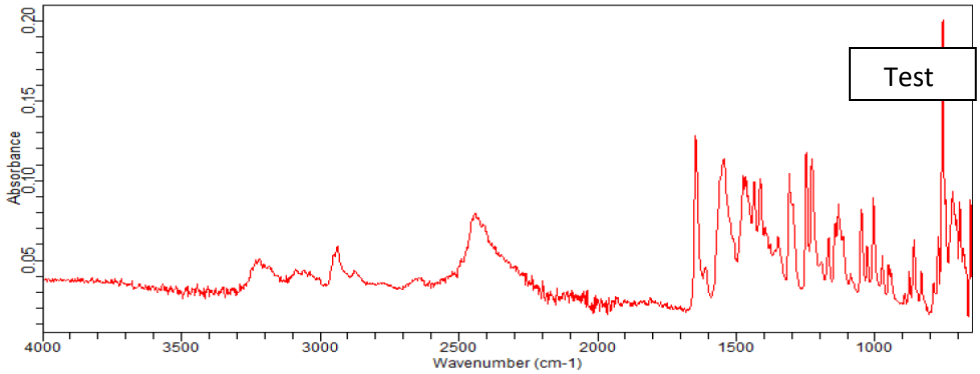

Figure 1: FTIR spectra of Granisetron hydrochloride Test

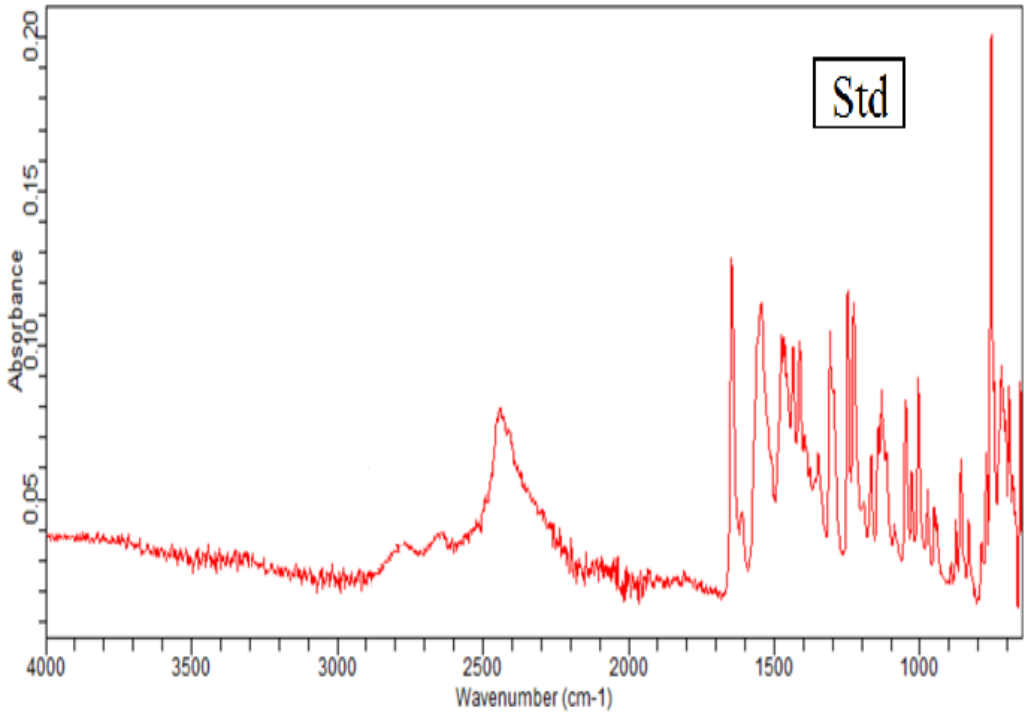

Figure 2: FTIR spectra of Granisetron hydrochloride Standard

Differential Scanning Calorimetery (DSC)

Granisetron hydrochloride exhibited an endothermic peak at 308.94±3.4^{o}C. The Granisetron hydrochloride (2mg) was hermetically sealed in an aluminum pan and heated at a constant rate of 10^{o}C/min over a temperature range of 50-350^{o}C. As the value is in accordance to the reported value as shown in fig. 3, it is inferred that drug is pure and authentic. Area under the DSC-curve for melting endotherm, gives the heat of fusion.

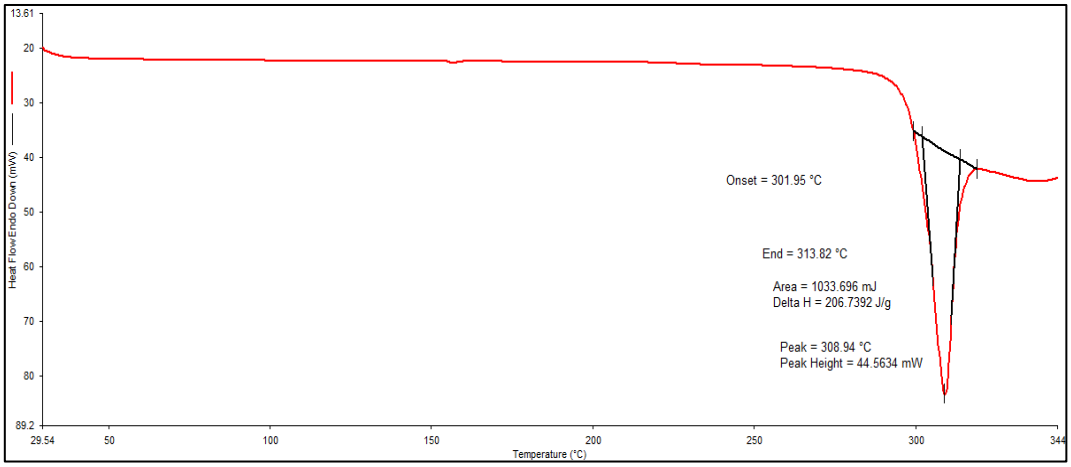

Figure 3: DSC thermograph of Granisetron hydrochloride

The DSC confirms the identity of Granisetron hydrochloride.

Preformulation Studies

Determination of UV absorption maxima of Granisetron hydrochloride

The absorption maximum of Granisetron hydrochloride in phosphate buffer saline pH 7.4 was determined by scanning 10µg/ml concentration solution in the wavelength range of 200-400nm using UV-VIS spectrophotometer. The spectra observed are shown in the fig.4.

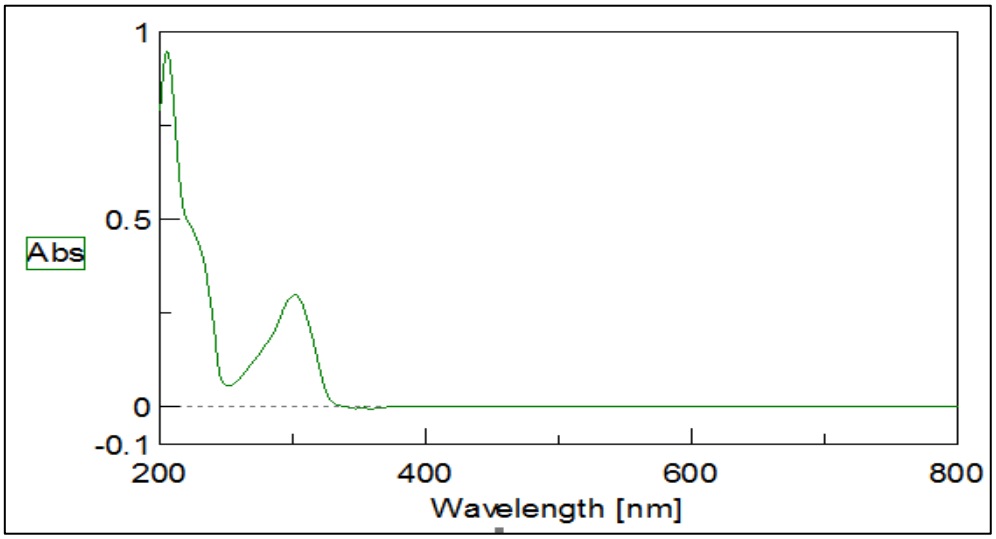

Figure 4: Absorption maxima of Granisetron-Hydrochloride in phosphate buffer saline pH 7.4

The absorption maxima ($\lambda_{max.}$) for Granisetron hydrochloride came out to be 302±0.8 nm as can be seen in fig .4.

Determination of solubility in different solvents

It is a critical factor in determining its usefulness, since aqueous solubility dictates the amount of compound that will dissolve and therefore, available for absorption.

Solubility values that are generally useful in early development are in: Distilled water, buffer of pH7.4, all at room temperature. As the drug is hydrophilic and very soluble in water and phosphate buffer, solubility study was carried out in different solvents like methanol and chloroform which were to be used in formulation and *In-Vitro* drug release etc. Drug is freely soluble in methanol and chloroform.

Determination of Partition Coefficient

The partition coefficient, log P, is defined as the ratio of un-ionized drug distributed between the organic and aqueous phases at equilibrium. Determination of log P in a realistic biological medium is virtually impossible. The Octanol-water partition coefficient has been widely adopted.

The apparent partition coefficient studies were performed in triplicate. The value of apparent partition coefficient of Granisetron hydrochloride in n-Octanol and PBS (7.4) was found to be 0.1903±0.004**.**It indicates the less lipophilicity of the drug. So by means of transethosomal formulation we can increase the drug permeation through the skin.

Compatibility study of drug and excipients

Physical compatibility

The drug and excipients were physically mixed in the ratio of 1:1 and this physical mixture was then observed for any visual changes at different temperatures and humidity levels i.e. 4^{o}C/55% RH and 25^{o}C/60 % RH for 4 weeks as shown in Table1. This temperature and humidity condition was selected because phospholipid is stable at lower temperature.

Ingredients	**4±2ºC/55%RH**										**25±2ºC/60%RH**							
	Physical appearance										**Physical appearance**							
	0 day		**7days**		**14 days**		**21 Days**		**28 days**		**7 days**		**14 days**		**21 Days**		**28 Days**	
	Colour	**LF**	**Colour**	**LF**	**Colour**	**LF**	**Colour**	**LF**	**Colour**	**LF**	**Colour**	**LF**	**Colour**	**LF**	**Colour**	**LF**	**Colour**	**LF**
Granisetron hydrochloride	Almost white powder	**NO**	**NC**	**NC**	**NC**	**NC**	**NC**	**NC**	**NC**	**NC**	**NC**	**NC**	**NC**	**NC**	**NC**	**NC**	**NC**	**NC**
Granisetron hydrochloride+ PC-90 G+SDC	Off white mixture	**NO**	**NC**	**NC**	**NC**	**NC**	**NC**	**NC**	**NC**	**NC**	**NC**	**NC**	**NC**	**NC**	**NC**	**NC**	**NC**	**NC**

NC: No change, LF: Liquefaction, PC-90G: Phospholipon -90G, SDC: Sodium deoxycholate

Table 1: Physical compatibility of drug-excipients mixture (1:1)

From the table 1, it can be concluded that there was no change in the physical state of the drug and the physical mixture of drug and excipients, at different temperature conditions**.** No interaction was found between drug and excipients. Thus the excipients selected for the formulation was found to be compatible with drug.

Physicochemical Compatibility

The physicochemical compatibility of drug and excipients was evaluated by FTIR. The FTIR spectrum of the lipid (fig.5) and physical mixture of Granisetron hydrochloride and excipients in the ratio of 1:1 has been shown in fig.6.The principle peaks in FT-IR spectra of pure drug is compared with those of FTIR spectra of drug and excipients. It was observed that, there was no disappereance of principal peak of Granisetron hydrochloride in the FTIR spectra of mixture. The results shows no sign of incompatibility between Granisetron hydrochloride and excipients.

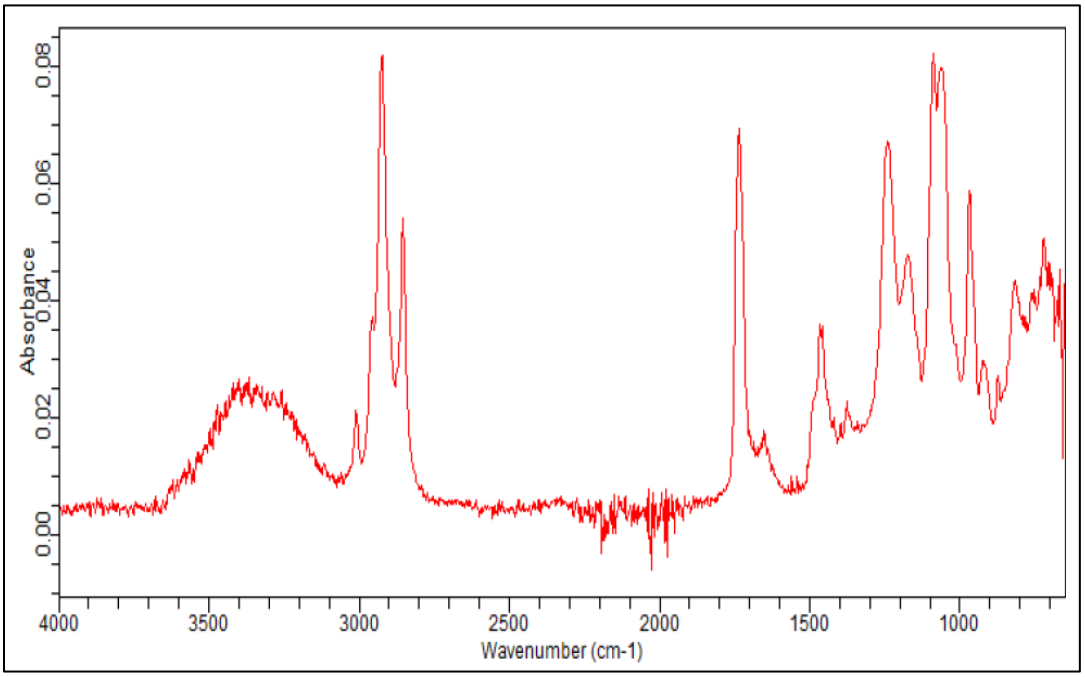

Figure 5: FTIR spectra of Phospholipon 90-G

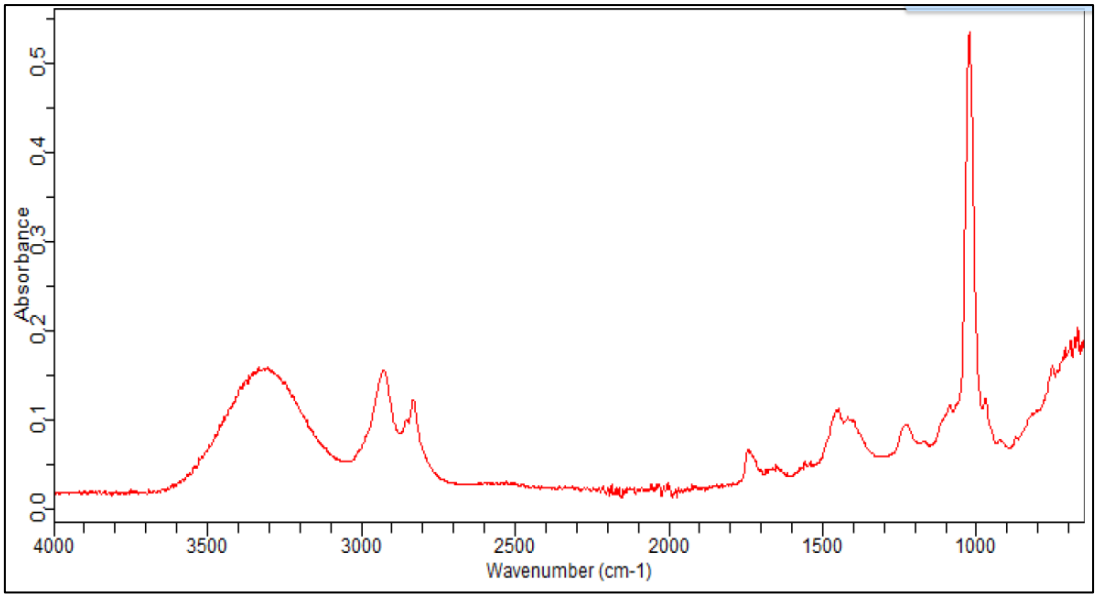

Figure 6: FTIR spectra of drug-excipients mixture (1:1)

FTIR spectra of excipient and mixture of drug and excipients shows no sign of incompatibility between drug and excipients.

ALYTICAL METHODOLOGY

Preparation of standard calibration curve in phosphate buffer saline pH 7.4

A series of concentrations ranging from 5--25µg/ml were prepared after diluting 0.5-2.5 ml of stock solution (100µg/ml) in 10 ml volumetric flask using phosphate buffer saline pH 7.4. Absorbance was measured at 302 nm against phosphate buffer saline pH 7.4 as blank. Calibration curve was constructed by plotting absorbance (nm) vs. conc. (µg/ml), and correlation coefficient was calculated.

S.No.	Concentration(µg/ml)	Absorbance(in nm), mean ±SD, n=3	Regressed absorbance
1	5	0.142±0.01	0.1310
2	10	0.318±0.01	0.3263
3	15	0.5101±0.02	0.5216
4	20	0.7208±0.03	0.7169
5	25	0.9171±0.01	0.9122

Table 2: Absorbance at different concentration of Granisetron hydrochloride

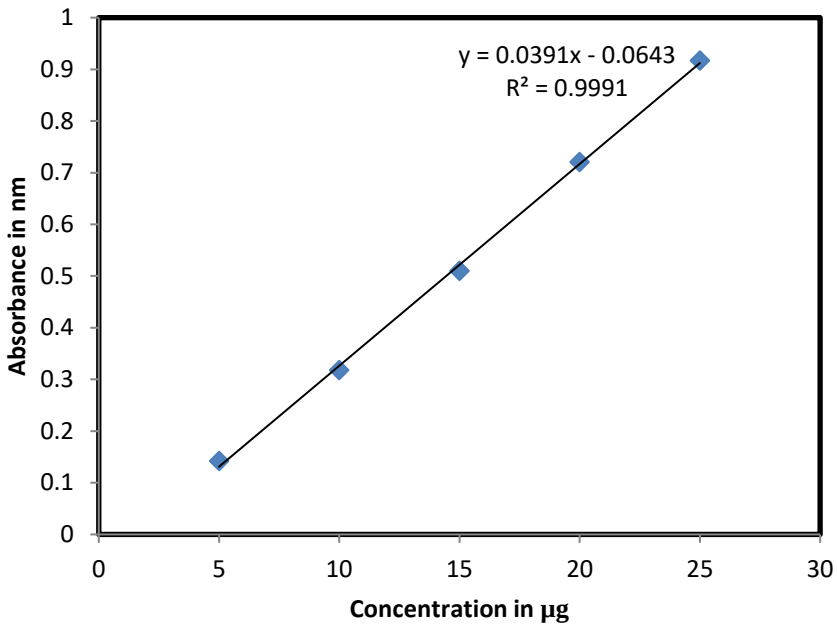

Figure 7: Calibration curve of Granisetron hydrochloride in phosphate buffer saline pH 7.4

A linear relationship was observed between absorbance and concentration at a conc. range of 5-25 µg/ml. The regression (R^2) was found to be 0.9991

Standard plot will be further used in determination of entrapment efficiency, drug release and drug content etc.

Conclusion:

The comprehensive analysis of Granisetron hydrochloride demonstrates its potential for effective transdermal drug delivery. The drug's physical and chemical properties were accurately characterized, revealing its crystalline nature, high melting point (301±1°C), and specific functional groups through FTIR and DSC analyses, confirming its purity and authenticity. Preformulation studies indicated that Granisetron hydrochloride exhibits excellent solubility in water, phosphate buffer, methanol, and chloroform, making it suitable for various formulations. The partition coefficient of 0.1903±0.004 reflects its lower lipophilicity, suggesting the need for formulation strategies to enhance skin permeation. Compatibility studies with selected excipients showed no significant physical or chemical interactions, ensuring stability and efficacy in the final formulation. The development of a standard calibration curve in phosphate buffer saline (pH 7.4) facilitated accurate quantitative analysis of the drug. These findings emphasize the feasibility of Granisetron hydrochloride as a candidate for transdermal delivery systems, potentially offering improved therapeutic outcomes and patient compliance in managing chemotherapy-induced nausea and vomiting.

References:

1. Narwal, S., Saini, V., & Kaushik, V. (2016). Evaluation of anti-ulcer activity of esomeprazole magnesium trihydrate film in wistar rats with gastric ulceration induced by Indomethacin. *EJPM*, *3*(10), 443-447.
2. Thakur, R. R., & Narwal, S. (2012). Formulation and Evaluation of orally disintegrating tablet of niacinamide. *Res J Pharm Biol Chem Sci 2012; 3 (3): 292*, *302*.
3. Thakur, R. R., Rathore, D. S., & Narwal, S. (2012). Orally disintegrating preparations: recent advancement in formulation and technology. *Journal of Drug Delivery and Therapeutics*, *2*(3).
4. Rathore, S. D., Thakur, R. R., & Narwal, S. (2012). Solid dispersion a new horizon in novel drug delivery system. *JPR*, *5*(2), 1007-1014.
5. Kumari, B., Upadhyay, P. K., Kumar, M., Narwal, S., Pandurangan, A., & Malik, A. (2020). An updated overview of recent advances on formulation development for colon targeting. *IJPSR*, *11*(4), 1571-1580.
6. Narwal, S., Kumar, A., Chaudhary, M., & Budhwar, V. (2021). Formulation of eutectic mixture of curcumin with salicylic acid for improving its dissolution profile. *Research Journal of Pharmacy and Technology*, *14*(4), 1875-1879.
7. Upadhyay, P. K., Kumar, M., Vishwakarma, V. K., Yadav, M. K., Yadav, V. K., Narwal, S., & Singh, M. P. (2021). An Overview on Underlying Concepts and Mechanisms of Wound Healing. *Annals of the Romanian Society for Cell Biology*, *25*(6), 6714-6736.
8. Sangeeta, P. C., & Narwal, S. (2023).Formulation and evaluation of mucoadhesive microspheres of dolasetron for nasal delivery. *Acta Biomed*. 94(1), 1091-1100.
9. Ghildiyal, P., Bhatt, A., Chaudhary, N., Narwal, S., & Sehgal, P. (2022). Study of various biochemical parameters on atrazine induced glucose-6-phosphate dehydrogenase deficiency in brain. *International Journal of Health Sciences*, 6(S7), 2552–2558.
10. Sehgal, P., Bhatt, A., Narwal, S., Bhagwat, D. P., Chaudhary, N., Berwal, A., & Nawani, M. (2022). Formulation Characterization Optimization and In Vitro Evaluation of Aceclofenac Topical Emulgel. *Neuroquantology*, *20*(14), 1027.
11. Bhatt, A., Kumar, A., Ghildiyal, P., Maithani, J., Chaudhary, N., Nawani, M., & Narwal, S. (2022). Performance of Data Security and Privacy Requirements in Edge Computing. *NeuroQuantology*, *20*(9), 2426.
12. Ritu, P. D., Priya, M., Agarwal, G., & Sangeeta, S. N. (2023). Current developments in Nano-based technology for Ocular Disease: Recent evidence, Barriers and Translational opportunities. *Latin American Journal of Pharmacy: A Life Science Journal*, *42*(7), 74-88.
13. Preeti, N., Ajay, R., Renu Sehrawat, B. S., Minkal Tuteja, S. N., & Deepak, P. B. (2023). Formulation, Development, and Characterization of Tadalafil Ethosomes for Transdermal Delivery: In Vitro Evaluation of Ethosomes Pharmaceutical Potentia. *Latin American Journal of Pharmacy: A Life Science Journal*, *42*(3), 755-765.

14. Sambhakar, S., Saharan, R., Narwal, S., Malik, R., Gahlot, V., Khalid, A., & Mohan, S. (2023). Exploring LIPID's for their Potential to Improves bioavailability of lipophilic drugs candidates: a review. *Saudi Pharmaceutical Journal*, 101870.
15. Rani, N., Singla, R. K., Redhu, R., Narwal, S., & Bhatt, A. (2022). A Review on Green Synthesis of Silver Nanoparticles and its Role against Cancer. *Current Topics in Medicinal Chemistry*, *22*(18), 1460-1471.
16. Rani, N., Kumar, S., Narwal, S., & Redu, R. (2024). A Review on Green Synthesis of Nanoparticles Using Natural Gums. *International Journal of Pharmaceutical Sciences and Nanotechnology (IJPSN)*, *17*(2), 7299-7312.
17. Narwal, S., Rohilla, S., Rohilla, A., & Bhagwat, D. P. (2023). Role of Herbal Drugs in Treatment of Dermatologic Disorders: A Review. *International Journal of Pharmaceutical Sciences and Nanotechnology (IJPSN)*, *16*(3), 6562-6570.
18. Rani, N., Singla, R. K., Narwal, S., Kumar, N., & Rahman, M. M. (2022). Medicinal plants used as an alternative to treat gingivitis and periodontitis. *Evidence-Based Complementary and Alternative Medicine*, *2022*.
19. Rohilla, S., Rohilla, A., Narwal, S., Dureja, H., & Bhagwat, D. P. (2023). Global Trends of Cosmeceutical in Nanotechnology: A Review. *Pharmaceutical Nanotechnology*, *11*(5), 410-424.
20. Rathore, S. D., Thakur, R. R., & Narwal, S. (2012). Solid dispersion a new horizon in novel drug delivery system. *JPR*, *5*(2), 1007-1014.