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Original Research Article

Development and Assessment of Transdermal Drug Delivery System for an Antiemetic Medication

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Abstract: ***Background:*** The Transdermal drug delivery system (TDDS) was created to enhance drug release sustainability, increase drug bioavailability, and improve patient compliance. Matrix dispersion transdermal patches distribute the drug in a solvent with polymers, and then the solvent evaporates to create a uniform drug-polymer matrix. The aim of this study was to create and develop transdermal drug delivery systems (TDDS) containing granisetron hydrochloride and assess its prolonged release in laboratory conditions. ***Materials and Methods:*** The study aims to develop a matrix-type transdermal treatment system that includes granisetron hydrochloride using different ratios of hydrophilic and hydrophobic polymer combinations through the solvent evaporation process. ***Results:*** Fourier transform infrared spectroscopy was employed to investigate the physicochemical compatibility of the drug with the polymers. The results showed that there was no physical-chemical incompatibility between the drug and the polymers. The patches were subjected to further physical evaluations and in-vitro permeation studies. ***Conclusions:*** The patches containing Carbopol 934P and ethylcellulose, along with span 80 as the penetration enhancer, were identified as the most effective formulations for transdermal delivery of granisetron hydrochloride based on physical evaluation and *in-vitro studies*.

Keywords: Carbopol 934P and ethylcellulose, span 80, penetration enhancers, permeation studies & granisetron hydrochloride.

INTRODUCTION

Transdermal therapy systems are distinct dose forms that administer medications through the intact skin at a controlled rate to the systemic circulation. The transdermal route is well-known for its ability to deliver medicines locally and systemically. Transdermal drug delivery systems (TDDS) provide benefits over traditional pharmaceutical dosage forms, including bypassing first-pass metabolism, continuous drug release, decreased need for frequent dosing, minimized side effects, and enhanced patient adherence. A transdermal drug delivery device is a mechanism that offers an alternate method for giving medication, and it can be either active or passive in design. These devices facilitate the transdermal delivery of medications. This drug delivery strategy provides numerous benefits compared to conventional ways [1]. Transdermal medication delivery can be used instead of oral administration to bypass gastrointestinal absorption, therefore avoiding issues like enzymatic and pH-related inactivation. This approach enables lower pharmacological dose by utilizing the shorter metabolization pathway of the Transdermal route compared to the stomach pathway. A transdermal medicine delivery system administers its active ingredient by passing it through the patient's skin, ensuring a consistent blood concentration. Furthermore, as the active ingredient is transported through the bloodstream directly to the specific organ, a lower effective dose may be required compared to standard drug formulations. The Transdermal Delivery System allows for consistent dosing, eliminating the fluctuations in medicine levels typically seen with oral administration. Extended treatment with one application, quick drug detection in emergencies, and the ability to stop drug effects promptly by removing the patch are additional benefits of this method [2].

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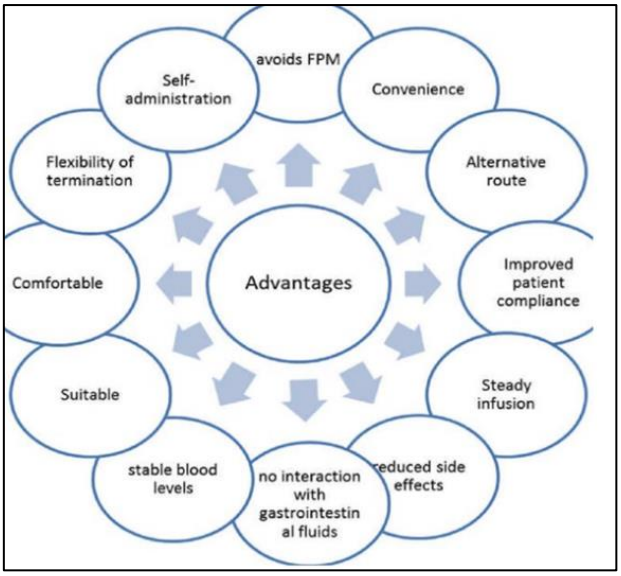
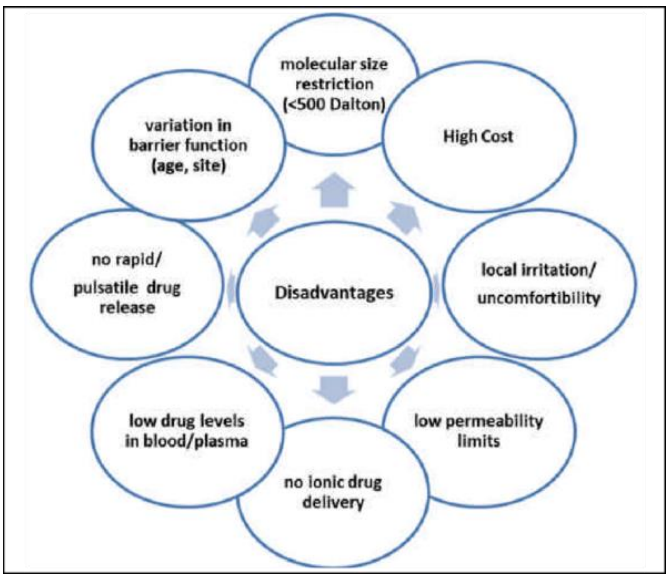




An indazole derivative with antiemetic qualities is called granisetron. Granisetron, a selective serotonin receptor antagonist, suppresses nausea and vomiting brought on by chemotherapy and radiation by competitively blocking serotonin's action at 5-HT3 receptors [3]. The current study generated a matrix-type transdermal therapeutic system has been created using different ratios of hydrophilic and hydrophobic polymers along with Granisetron HCl. This system aims to decrease dosing frequency and enhance the absorption of the antiemetic drug used for chemotherapy-induced vomiting, utilizing the solvent evaporation technique.

MATERIALS AND METHODS

Grainsetron hydrochloride was procured from Niksan Pharmaceutical Pvt. Ltd, Ancleshwer (India), Gujarat as a gift sample. Carbopol 934P and ethylcellulose was purchased from Renkem laboratory.

Preformulation studies

Prior to developing the drug ingredient into a transdermal patch, preformulation tests were conducted to determine the physical and chemical properties of the medication and its interaction with various excipients. [4-5].

Identification of drug

The identification of drug was carried out by ATR(Bruker), UV & HPLC analysis.

Calibration curve of grainsetron hydrochloride

The wavelength maximum of granisetron hydrochloride was determined to be 302 nm using ultraviolet-visible spectroscopy using a Shimadzu 1700 instrument. A standard solution with a concentration of 10 µg/ml was generated by diluting a stock solution with a concentration of 1 mg/ml using distilled water. Aliquots of a standard medication solution ranging from 1 to 8 ml were placed into a 10 ml volumetric flask and diluted with distilled water to reach the mark. The final concentration ranges from 1 to 8 µg/ml. The absorbance of each solution was measured at 302 nm using distilled water as a reference. A graph depicting the medication concentrations against absorbance was created. Linear regression analysis was conducted. [6].

Formulation of transdermal patch

Transdermal patches of Granisetron Hydrochloride were prepared by solvent evaporation technique. The matrix-type transdermal patches containing Granisetron Hydrochloride were prepared using different ratios of ethyl cellulose and carbopol 934P. Polymers in different ratios were dissolved in methanol then drug was added slowly to the polymeric solution. To the mixture, Propylene glycol (0.2 ml) as plasticizer and Span 80 (0.1 ml) as permeation enhancer were added and mixed. The dispersion was poured within a glass bangle in a glass plate previously lubricated with Light liquid paraffin. The plate was kept aside for drying at room temperature for 24 hrs. Inverted funnel was placed over the glass plates to prevent the current of air. After drying, the patches were peeled from glass plates, wrapped in aluminum foil and preserved in desiccator for further studies. Compositions of different formulations NEB1 to NEB6 are represented in Table.6 and photographs are shown below:

Table 1: Different formulation compositions of Granisetron Hydrochloride transdermal patches

Formulations	Granisetron Hydrochloride (mg)	EC: CP (mg)	Span 80 (ml)	Propylene glycol (ml)
NEB1	11	200:200	0.1	0.2
NEB2	11	133:267	0.1	0.2
NEB3	11	100:300	0.1	0.2
NEB4	11	267:133	0.1	0.2

Formulations	Granisetron Hydrochloride (mg)	EC: CP (mg)	Span 80 (ml)	Propylene glycol (ml)
NEB5	11	300:100	0.1	0.2
NEB6	11	320:80	0.1	0.2

Preliminary screening [7]

Physical Appearance

All the prepared patches were kept under visual observation for 7 days, it was observed that patches were found to be transparent, clear, soft & smooth. Film appearance showed that the uniform films were formed.

Thickness uniformity

Thickness of the prepared patches were measured in 3 different points by using a vernier caliper and determined the average thickness. The thickness of the patches was varied from 0.030 mm to 0.056 mm. The film shows increase in thickness was linear with polymer concentration.

Weight uniformity

For each formulation, three randomly selected patches were used. For weight variation test, 3 films from each batch were weighed individually by Digital electronic balance and the average weight was calculated. The weight of the patches was varied from 54 mg to 154 mg.

Tensile Strength

The tensile strength was determined by the apparatus. The instrument was designed such that it had horizontal wooden platform with fixed scale and attachments for two clips that holds transdermal patch under test. Out of the two clips one was fixed and other was movable. Weights were hanged to one end of pulley and the other end of pulley was attached with movable clip. The wooden platform was such fitted that it would not dislocate while the test is running. Three strips of patch were cut having 2cm length and 2cm breadth. The thickness and breadth of strips were noted at three sites and average value was taken for calculation. The rate of change of stress was kept constant with the increment of 0.5g per 2 minutes. The elongation was observed and the total weights taken were used for calculation.

Folding endurance

A strip of specific area (2×2 cm^2) was cut evenly and repeatedly folded at same place till it was broken. The number of times the films could be folded without breaking/ cracking gives the value of the folding endurance, and if the film shows any crack it was taken as end point.

Percentage Moisture Absorption Studies

The physicochemical studies like moisture absorption (uptake) provide information regarding the stability of the formulations. The accurately weighed films were kept in desiccators at room temperature for 24 hours, containing saturated solution of potassium chloride in order to maintain 80-90% RH. After 24 hours the films were taken out and reweighed. After 72 hours films are again weighed.

Percentage Moisture Loss Determination

The moisture loss studies provide information regarding the stability of formulations. The prepared films are to be weighed individually and to be kept in desiccators containing fused calcium chloride at room temperature for 72 hours. After 72 hours the films are taken out and reweighed. The percentage moisture loss was calculated from the formula mentioned below.

$$\% \text{ Moisture Loss} = [\text{Initial weight} - \text{Final weight}/ \text{Final weight}] \times 100$$

Water Vapour Transmission Rate (WVTR) Determination

WVRT is defined as the quality of moisture transmitted through unit area of the film in unit time. This is expressed as gm/hr cm^2. Glass vials of 5 ml capacity were washed, dried to a constant weight in oven. 1 gram of fused calcium chloride was taken in the vials and the polymer films of 2.25 cm^2 was fixed over a brim of each vial separately with the help of adhesive tape. Then the vials were weighed and stored in a humidity chamber of 80-90% RH condition for a period of 24 hours and 72 hours. Each vial were then removed and reweighed after 24 hours and 72 hours of the storage and weight gain was noted. Transmission rate was calculated by using formula given below.

$$\text{Water Vapour Transmission rate} = W \times L / S$$

Where, W= gram of water transmitted, L= thickness of the film in centimeter, S= exposed surface area of the film in cm^2.

Drug content

Drug content of the prepared transdermal patch was determined with slight modification. Specified area of patch (1cm^2) were cut and dissolved in 10 ml of methanol then volume was made up to 100 ml with phosphate buffer saline of pH 7.4. The medium was stirred with magnetic bead. The content was filtered using whatmann filter paper and the filtrate was

examined for the drug content against the reference solution consisting of plaNEBo films (containing no drug) with the UV spectrophotometer (Shimadzu 1700) at λ_{max} 302 nm and average was calculated.

***In vitro* drug release studies**

In vitro drug release studies were performed with slight modification. By using Franz diffusion cell with receptor compartment of capacity of 20 ml and by mounting the synthetic cellophane membrane between the donor & receptor compartment of the diffusion cell, *in vitro* drug release studies were performed. The formulated patches were cut into size of $1cm^2$ and placed over the drug releasing membrane and the receptor compartment of the diffusion cell was filled with phosphate buffer pH 7.4. The whole assembly was fixed on magnetic stirrer and the solution in the receptor compartment was constantly and continuously stirred using magnetic bead at 50 rpm; the temperature was maintained at 37^0C then sample of 5 ml was withdrawn at the time interval of 0, 0.25, 0.75, 1, 2, 3, 4 and 24 hours and analysed for the drug content spectrophotometrically at λ_{max} 302 nm against blank solution. The receptor compartment (phase) was replenished with an equal volume of phosphate buffer pH 7.4 at each time of the sample withdrawal. The cumulative amount of drug released per square centimeter of the patches was plotted against time [8].

RESULT AND DISCUSSION

A group of physicochemical technologies that can regulate the release and transport of pharmacologically active chemicals into cells, tissues, and organs such that these active substances can have the best possible effects are collectively referred to as drug delivery systems (DDS). Unlike the commonly utilized direct administration routes, which involve needle-based injections, TDDS has emerged as one of the most extensively researched noninvasive drug delivery methods via the skin. The distribution of numerous therapeutic substances has been greatly impacted by TDDS, particularly in the areas of pain management, hormone therapy, and the treatment of disorders affecting the central nervous system and cardiovascular system. Granisetron is an antiemetic medication used to treat nausea and vomiting after radiation and chemotherapy. It is a serotonin 5-HT 3 receptor antagonist. The goal of the current study was to develop a transdermal patch containing granisetron hydrochloride to lessen the frequency of doses when chemotherapy induces vomiting.

Prior to developing a pharmaceutical formulation, the inherent chemical and physical characteristics of each medicine were taken into consideration. This characteristic offers the structure for the drug's combination with medicinal components. Preformulation studies are carried out for recently synthesized or extracted compounds and provide information on the drug's bioavailability, pharmacokinetics, degradation process, toxicity, and any unfavorable conditions. Preformulation studies improve public safety standards, improve product quality in the fabrication of dosage form, reinforce the scientific basis of the guidelines, offer regulatory relief and conserve resources in the drug development and review process. Preformulation investigations on Granisetron hydrochloride were conducted. Granisetron HCl was found to be soluble in both water and methanol after the solubility of the chosen drug in several solvents was assessed (table 2). As reported in Table 3, the melting point of GSH was determined to be between 288^0 and 292^0C, which is the same as 291^0 C. ATR (Bruker) was used to identify the pure drug, and the results showed that the main peaks ranged from 756 to 3082 (fig 1 & table 4). Additionally, dist. water was used for UV scanning at λmax 302 nm (fig 2). The calibration curve was prepared which showed straight line having y= 1.9914x+ 0.006 & R^2= 1(fig 3). Partition (K) and diffusion (D) coefficients are important to measure for the modelling of skin penetration of chemicals through the stratum corneum (SC). The partition coefficient was found to be 2.6 (table 5). The drug – excipient interaction studies was carried out by using IR, which revealed that there was no interaction between drug and selected polymers (fig 4). Cyber Lab HPLC performed additional HPLC analysis utilizing a C-18 column and a water:acetonitrile mobile phase with a flow rate of 1.9 ml/min. 3.42 minutes was determined to be the RT (table 6).

Table 2: Solubility of Granisetron HCl in different solvent.

S. No.	Solvent	Observed Solubility
1.	Methanol	Soluble
2.	Ethanol	Sparingly soluble
3.	Water	soluble
4.	0.1 N HCL	Sparingly soluble
5.	0.1 N NaOH	Sparingly soluble
6.	Phosphate buffer saline (pH 7.4)	Sparingly soluble

Table 3: Melting point determination

Sample no.	Melting point (^{0}C)
1.	288-291
2.	288-292
3.	288-291

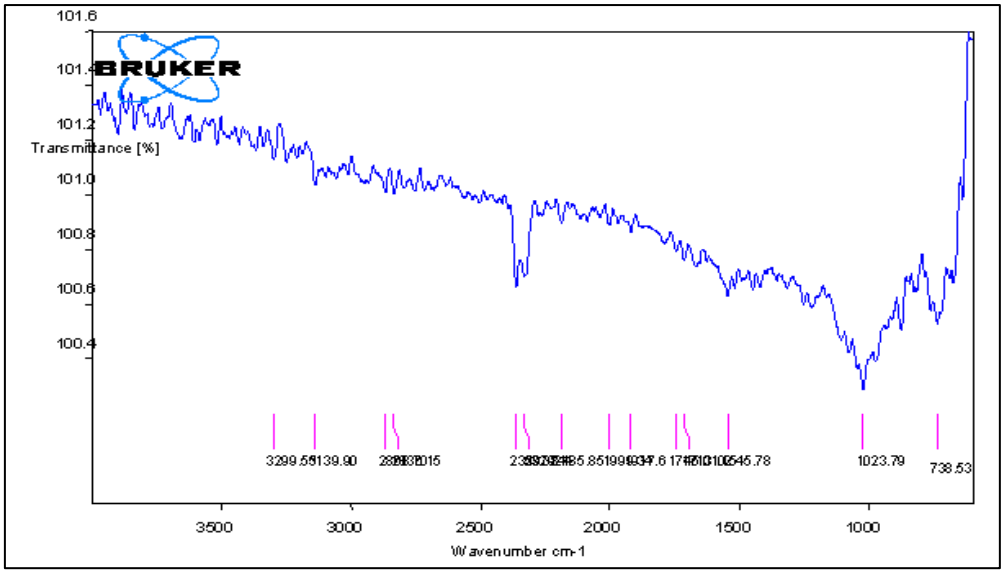


Fig. 1: IR spectra of pure drug Granisetron HCl

Table 4: Interpretation of IR of Pure drug

Major Peak	Peak
Aromatic peak	756
Amine(C-N)	1132,1228,1248,1308
C=O-NH-/O=NH	1609,1614,3232
Aromatic -C-C-	1413,1436,1474,1544
CH_3 (Alkanes)	2876,2937
C=C-H stretch	3082

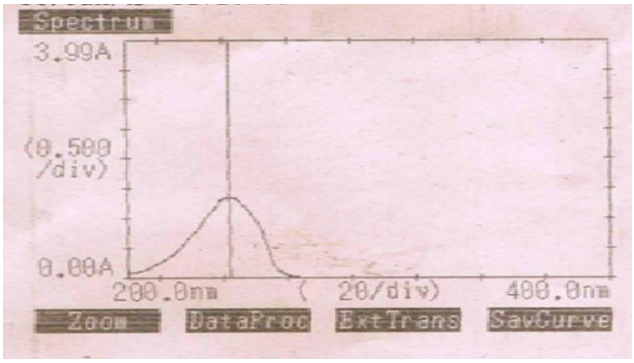


Fig. 2: UV spectrum analysis of Granisetron in Dist.water

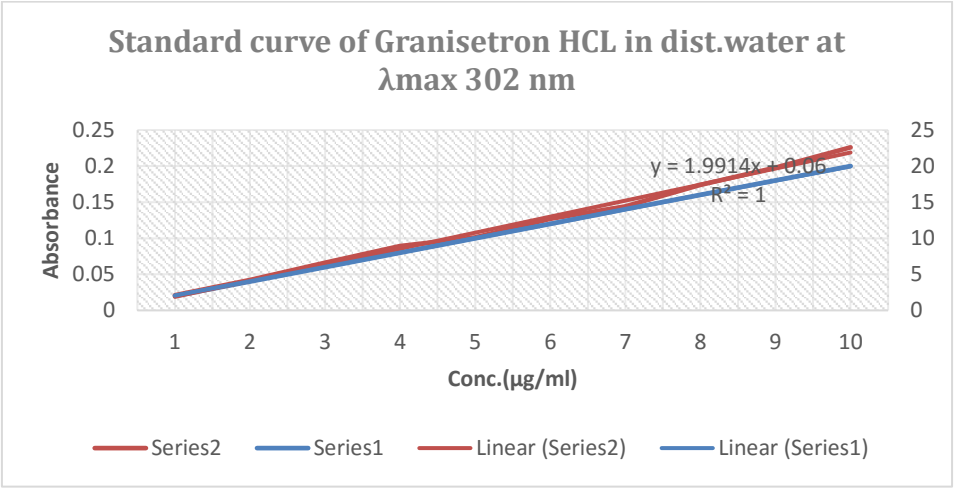


Fig. 3: Standard curve of Granisetron in dist.water at λ_{max} 302 nm

Table 5: Partition coefficient of Granisetron HCL

S. No.	Solvent system	Partition coefficient
1.	n-octanol:distilled water	2.6

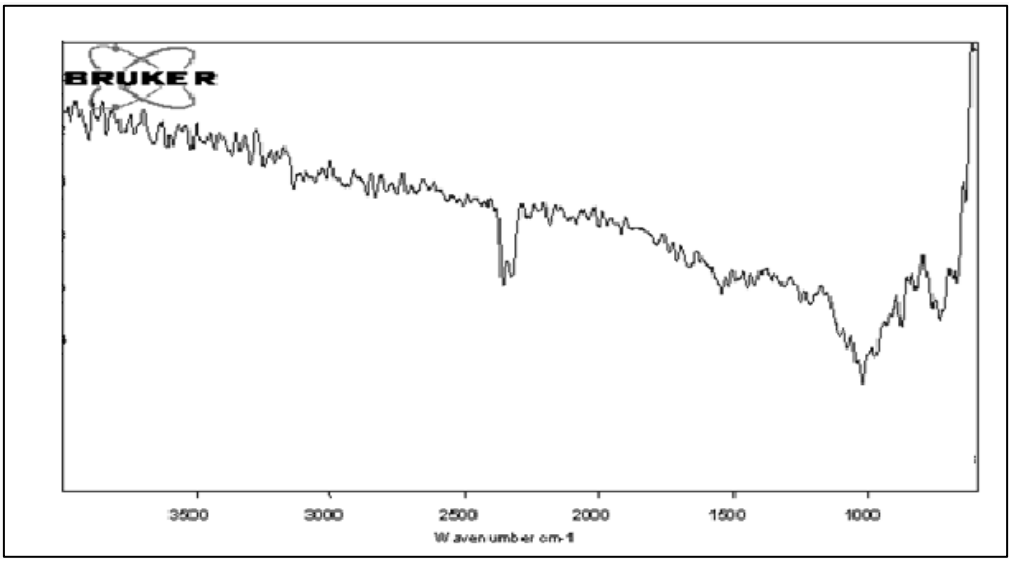
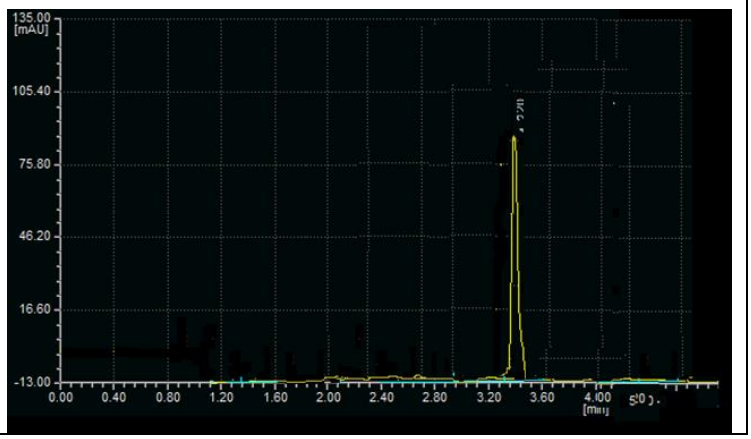


Fig. 4: IR spectra of Granisetron+Carbopol 934P+EC

Table 6: HPLC Analysis of Grainsetron hydrochloride

Chromatographic condition	Chromatogram
Mobile phase: dist.water and acetonitrile Column : C18, 250 × 4.6mm, 5µm or equivalent Flow Rate : 1.9 ml/min Injection Volume : 20µl Wavelength : 302 nm Run time : 40 minutes Retention time : Granisetron HCl peak about 3.42 min	

The Granisetron HCl loaded matrix type transdermal films were made *via* the "solvent evaporation method." Different ratios of lipophilic and hydrophilic polymers (such EC and Carbopol 934P, respectively) were dissolved in 5 milliliters of methanol and set aside to make clear solutions. The plasticizer employed was propylene glycol, while the permeation enhancer was span 80. 30 minutes were spent mixing the dissolved 11 mg of medication in the above clear solution (table 1).

The dispersion was added on a glass plate that had been previously greased with light liquid paraffin using a glass bangle. The plate was left out to dry for a full day at room temperature. Over the glass plates, an inverted funnel was used to stop the solvent from evaporating too quickly. Following drying, the patches were removed from the glass plates, coated in aluminum foil, and kept in a desiccator so that they could be examined in more detail. Since the pH of the skin is between 5.0 and 6.5, the medicine becomes soluble at the absorption site and absorbs quickly through the skin due to skin hydration and swelling. For this reason, span 80 was utilized as a penetration enhancer.

It was discovered by patch characterization that the uniform films had been made. It was discovered that patches were smooth, clear, soft, and transparent due to the use of propylene glycol, a plasticizer that aided in the creation of flexible films.

The patches' thickness was adjusted between 0.031 and 0.056 mm. indicates that the film's thickness increased linearly with polymer concentration. A low standard deviation in the measurements of film thickness guaranteed the homogeneity of the solvent-evaporation-

prepared patch. The patches' weight ranged from 0.054 gm to 0.154 gm. The movie demonstrates how weight increased linearly with polymer content. A low standard deviation value in the measurements of the film weight guaranteed the homogeneity of the solvent-evaporated patch. It was discovered that the tensile strength ranged from 0.72 to 0.58. The best tensile strength was demonstrated by formulation NEB3. It was discovered that the % elongation fell between 15.34% and 31.2%. Out of all the patches, the formulation NEB3 exhibited the lowest percentage of elongation at 15.34% (fig 5). Manual folding endurance testing revealed that formulation NEB3 had the highest folding endurance (157.8 folds), whereas formulation NEB6 had the lowest folding endurance (82 folds). The findings show that when films are applied, they have a maximum folding endurance and remain intact even when the skin folds normally. Information about the stability of the formulations is provided by the studies on moisture content. According to the observation of percentage moisture absorption, formulation NEB3 13.5 had the largest moisture absorption, whereas formulation NEB6 (1.813) had the lowest moisture uptake. At 80–90% relative humidity, it was discovered that the hydrophilic polymer Carbopol had a greater capacity to absorb water than the lipophilic polymer. This finding was explained by the hygroscopic characteristic of Carbopol. On the other hand, moisture absorbed did not alter film strength or integrity. Moisture uptake gives information about the stability of formulations. According to the moisture loss study observation, formulation NEB3 12.75 had the largest % moisture loss, while formulation NEB6 5.34 had the lowest percentage moisture loss (fig 6). Because of their hygroscopic nature, it was discovered that the formulations' moisture contents increased as the concentrations of the hydrophilic polymer (Carbopol 934P) and the lipophilic polymer (EC) decreased. However, the formulations' low moisture content kept the patches from becoming completely dry and brittle. According to the water vapor transmission rate (WVTR) values in gm/hr cm^2, formulation NEB6 had the highest water vapour transmission rate (0.0048) after 24 hours, whereas formulation NEB2 had the lowest water vapour transmission rate (0.00374). Within 72 hours, the same outcomes were observed. The casting solvent's vaporization rate, which may or may not depend on its boiling point and vapour pressure during the polymer's desolvation, could be the cause of the variance in WVTR (fig 7). The aforesaid finding was shown in Table 7. Granisetron HCl transdermal patches had a drug content that ranged from 81.2 % to 98.182 %, according to the drug content observation (table 8 & fig 9). The outcome demonstrated that the drug content was determined to be lowest for formulation NEB6 and to be maximal for formulation NEB2 (98.186%). The outcome shows minimal batch variability, indicating uniform drug distribution and providing confidence regarding the potency of slow-dosage medications.

Table 7: Physiochemical Screening of Patches

F. Code	Thickness (mm)	Wt. variation	Tensile strength	%elongation	Folding endurance	%moisture absorption	%moisture loss	WVTR studies (gm/ hr cm^2)	
								After 24hrs	After 72 hrs
NEB1	0.044	0.104	0.72	15.25%	133.6	7.072	10.33	0.00292	0.00388
NEB2	0.047	0.134	0.69	20.63%	145.6	9.232	10.12	0.00265	0.00374
NEB3	0.031	0.154	0.76	15.34%	157.8	13.53	12.75	0.0034	0.0048
NEB4	0.040	0.054	0.72	23.76%	111.6	5.54	6.26	0.0038	0.0052
NEB5	0.047	0.073	0.62	31.2%	93.6	2.88	5.78	0.0044	0.0072
NEB6	0.056	0.055	0.58	29.46%	81	1.83	5.34	0.0048	0.00844

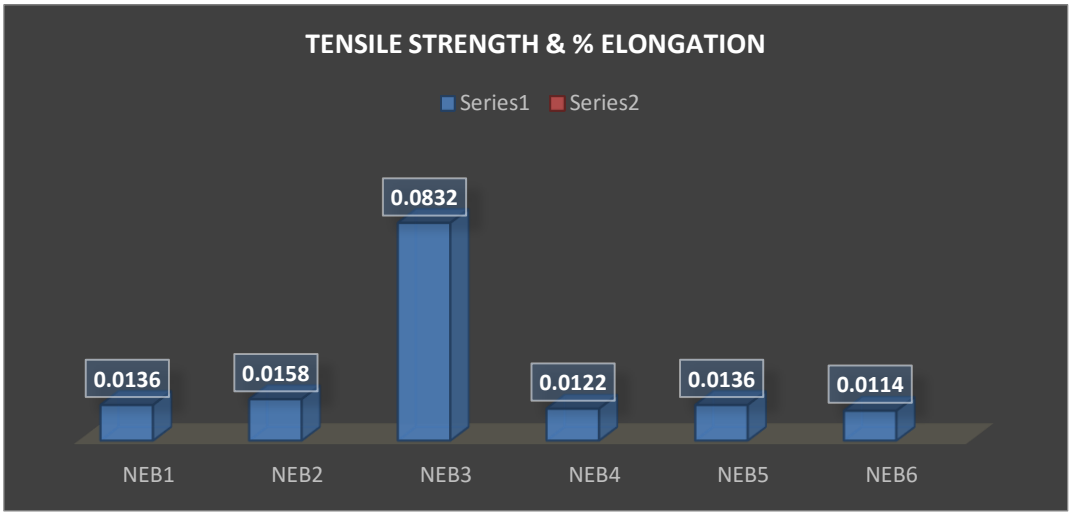


Fig. 5: Comparative Tensile strength & % Elongation studies of all Granisetron Hydrochloride matrix transdermal patch formulations

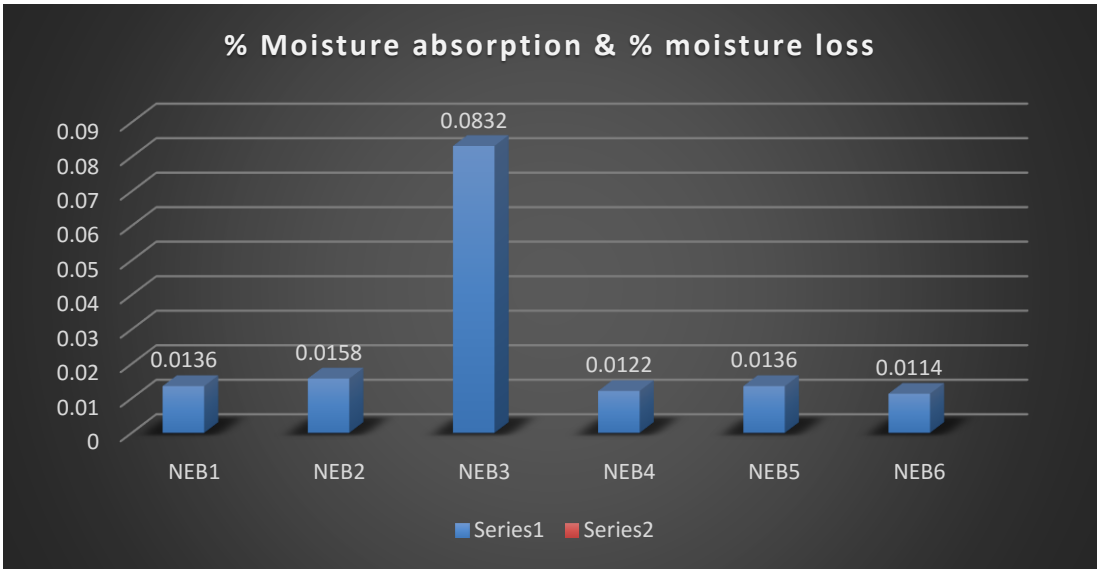


Fig. 6: Comparative percentage moisture content studies of all Granisetron Hydrochloride matrix transdermal patch formulations

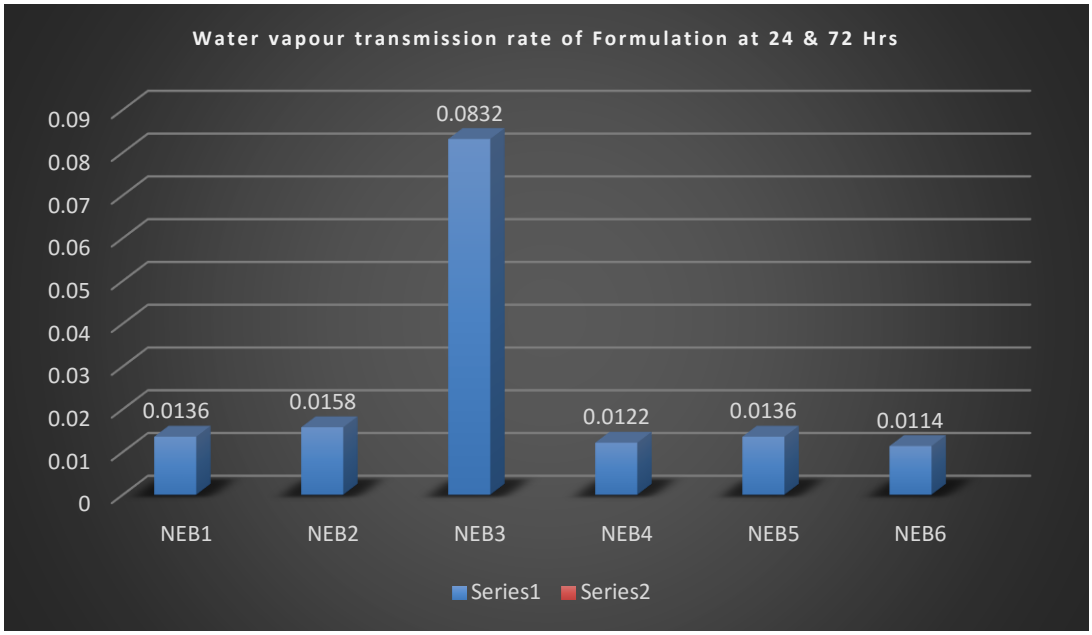


Fig. 7: Water vapour transmission rate (WVTR) studies of all Granisetron Hydrochloride transdermal patch formulations after 24 & 72 hours

Table 8: Percentage drug content profiles of Granisetron Hydrochloride transdermal patch formulations by using phosphate buffer pH 7.4

Formulation code	% Drug content
NEB1	92.6
NEB2	98.162
NEB3	96.182
NEB4	89.08
NEB5	86.45
NEB6	81.2

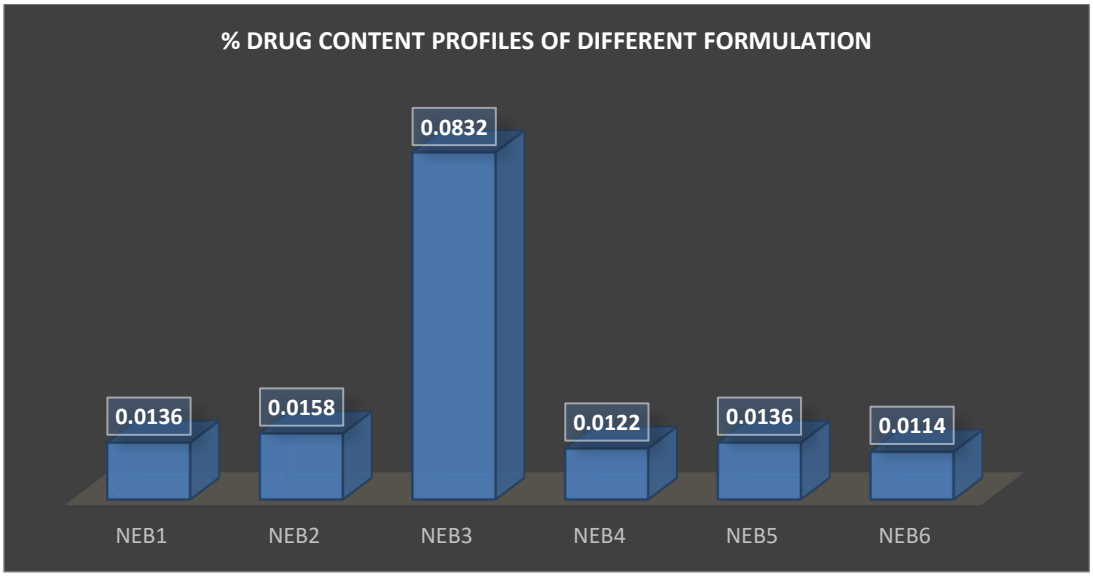


Fig. 8: % Drug content in different formulation

In-vitro drug release studies are necessary to anticipate the consistency of the rate and duration of drug release. Polymer breakdown significantly influences drug release from matrices to ensure sustained release performance. The study found that the granisetron HCl transdermal patches had the highest drug release in 4 hours for formulation NEB3 (92.86%) and in 24 hours for formulation NEB2 (89%). Conversely, the lowest drug release after 24 hours was observed for formulation NEB6 (67.25%). The release kinetics of different formulations were analyzed using zero order, first order, and Higuchi model. The results, presented in table 22, indicated that formulation NEB3 exhibited zero order release kinetics with R^2 = 0.993 and slope = 23.02. In contrast, formulations NEB1, NEB2, NEB4, and NEB5 displayed first order release kinetics with R^2 values ranging from 0.931 to 0.985. Formulation NEB6 followed the Higuchi model with R^2 = 0.912 and slope = 14.94. Formulation NEB3 exhibits zero-order kinetics, indicating that the drug dissolves from the dosage form without disaggregation, releasing the drug slowly. This means that the drug release rate is constant and not dependent on its concentration. The graphical representation of the fraction of drug dissolved versus time shows a linear relationship over a period of 4 hours. The NEB3 releases a consistent amount of drug per unit of time, making it an optimal method for achieving prolonged pharmacological effects. However, it only provides drug release for 4 hours, falling short of our goal for sustained release which requires drug release for at least 22-24 hours. Therefore, we have not chosen it for therapeutic use. The NEB1, NEB2, NEB4, and NEB5 formulations exhibit first-order kinetics, indicating that the rate of drug release is influenced by concentration. The graph of the decimal logarithm of drug release over time shows a linear relationship. The NEB1, NEB2, NEB4, and NEB5 dosage forms exhibit a specific release profile due to the presence of the lipophilic drug Granisetron HCl in porous matrices. The drug release is proportional to the amount released over time, with NEB2 showing an 89% release, making it suitable for sustained release over 24 hours for therapeutic purposes.

Cumulative Granisetron HCl permeation through animal cadaver skin was explored in vitro to observe the relationship between time and the amount permeated into a receptor solution from different patches. Various kinetic models were analyzed to understand the permeation mechanism. The study revealed that the in vitro drug permeation of Granisetron HCl transdermal patches was highest for formulation NEB3 (94.6%) within 4 hours and for formulation NEB2 (90.531%) within 24 hours. Conversely, after 24 hours, the in vitro drug permeation was lowest for formulation NEB6 (62.27%). NEB2 emerged as the optimal formulation as it met the criteria for improved and sustained release. Permeation mechanism kinetics were calculated. Formulation NEB6 exhibited the Higuchi mechanism with an R2 value of 0.846, while formulation NEB3 showed zero-order permeation kinetics with an R2 value of 0.996. Other formulations followed first-order permeation kinetics with R2 values ranging from 0.906 to 0.974. Formulation NEB6 is based on the Higuchi model, which proposes the penetration of the lipophilic medication Granisetron HCl when included in semisolid matrices. The dissolving behavior of a flat spherical heterogeneous matrix system is characterized by drug concentration below its solubility level and penetration through holes in the matrix. Higuchi explains that drug release follows a diffusion process according to Fick's rule, where penetration is dependent on the square root of time. Formulations NEB1, NEB2, NEB4, and NEB5 exhibit first-order kinetics, indicating that the pace of drug permeation is influenced by concentration. The graph of the logarithm of the remaining drug to be permeated against time shows a linear relationship. This formulation is designed to contain the lipophilic drug Granisetron HCl in porous matrices. The drug permeates through the matrices in a manner that is directly related to the rate at which the medication is released over time.

The drug penetration of 90.531% in NEB3 led to its selection for therapeutic purposes to sustain/control release for 24 hours. The drug release and permeation studies of matrix films indicated that increasing the concentration of hydrophilic polymer led to higher cumulative % drug release and cumulative % drug permeation, while decreasing the concentration of lipophilic polymer resulted in increased % cumulative drug release and % cumulative drug permeation. This was due to the highly hydrophilic nature of Carbopol 934P, which caused the dissolution of the aqueous soluble fraction of the polymer matrix, leading to polymer swelling and subsequent release of the drug from the gelatinous pores of the films, facilitated by adequate porosity and diffusivity. Creating these pores reduces the average distance drug molecules need to travel to be released and permeate into the surrounding medium, resulting in increased release and penetration rates. EC was attributed to the polymer's hydrophobic character, which had low affinity for water. This led to a decrease in the thermodynamic activity of the drug in the film, resulting in reduced drug release and permeation. EC can function as a more effective release retardant at higher concentrations than Carbopol 934P. Combining lipophilic and hydrophilic polymers allows for regulated release and penetration rates over an extended duration. The Permeability Coefficient of Granisetron Hydrochloride transdermal patches was measured. The NEB3 formulation exhibited a greater value compared to other formulations as shown in figure 9-11.

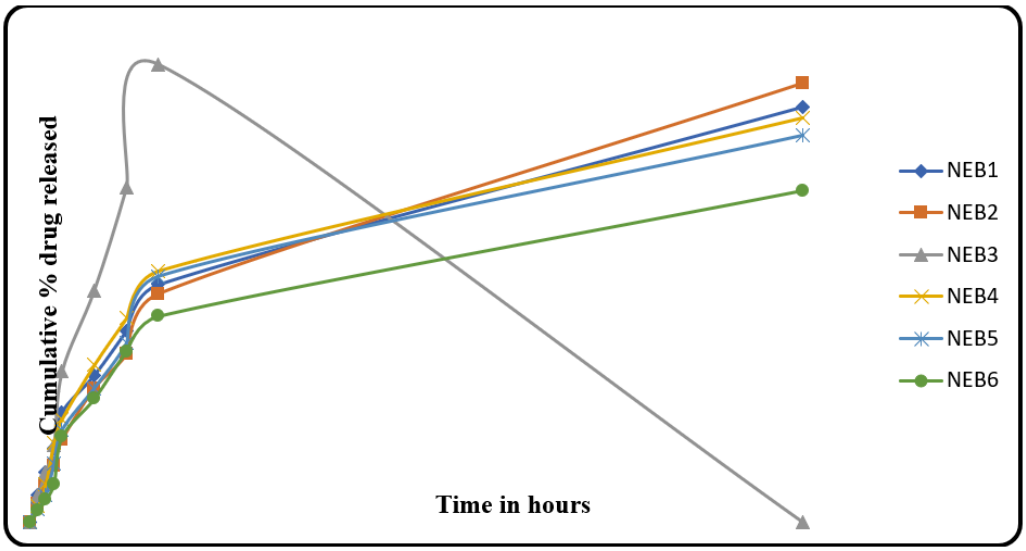


Fig. 9: Comparative in vitro drug release studies of various Granisetron Hydrochloride transdermal patches, for Zero order release kinetic model

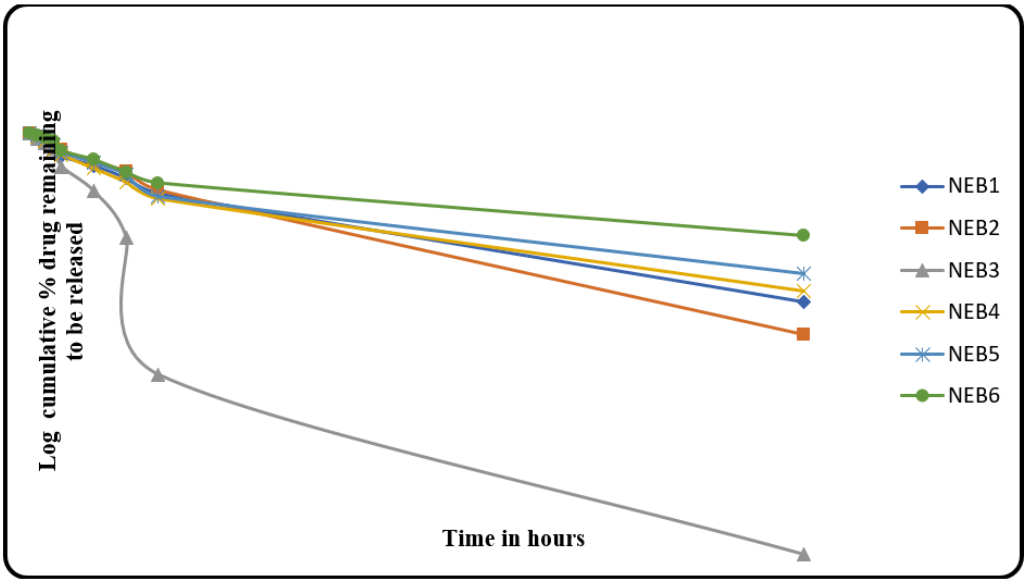


Fig. 10: Comparative in vitro drug release studies of various Granisetron Hydrochloride transdermal patches, for First order release kinetic model

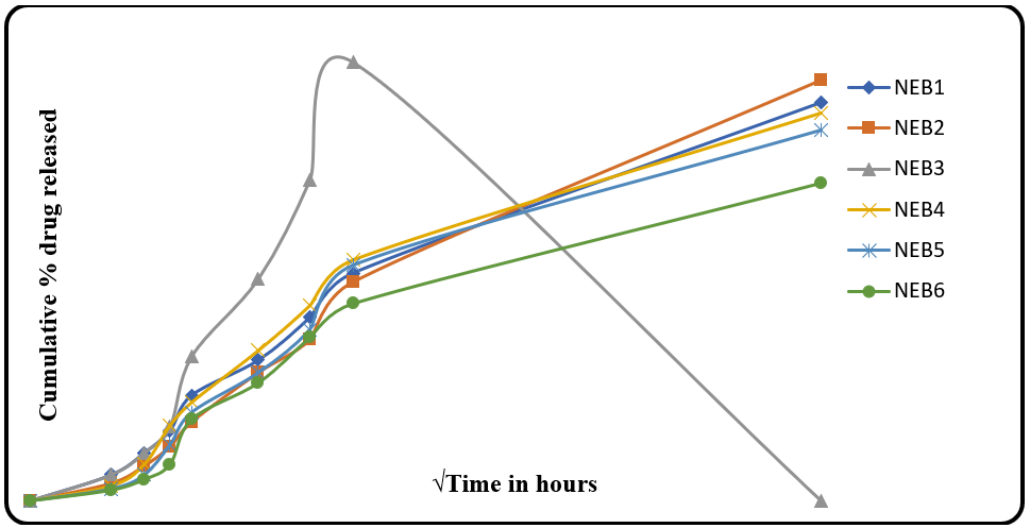


Fig. 11: Comparative in vitro drug release studies of various Granisetron Hydrochloride transdermal patches, for Higuchi release kinetic model

CONCLUSION

Grainsetron hydrochloride transdermal patches were created by the solvent evaporation process. The patches were made using a mixture of Carbopol 934 P and ethylcellulose in different ratios, with PG as plasticizers and span 80 as permeation enhancers. All formulations exhibited favorable physicochemical characteristics, including thickness, weight consistency, drug content, and folding endurance. The in-vitro release data indicated that the drug release from the patch was influenced by the kind and concentration of the polymer. Optimized formulations were evaluated using this data.

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