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FORMULATION AND EVALUATION OF TRANSDERMAL PATCH LOADED WITH ONDANSETRON

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Abstract:

The purpose of this research was to develop and design a matrix-type transdermal therapeutic system that contains the drug Ondansetron along with different ratios of Xanthan Gum and Guar Gum forming hydrophilic polymer systems by film casting technique, using 15% v/w of Propylene Gylcol to the polymer weight, incorporated as plasticizer and DiMethyl Sulfoxide was used to enhance the transdermal permeation. These formulated transdermal patches were physically evaluated with regard to thickness, moisture content, moisture uptake, tensile strength, folding endurance, flatness and drug content. All prepared formulations indicated good physical stability. Ex-vivo permeation studies of formulations were performed by using Franz-Diffusion cells. It was observed that the formulation F8 shows better extended release when compared with other formulations and followed Higuchi model in dissolution study. The release rate found to follow Zero-Order rate kinetic. Primary irritation study shows that the prepared transdermal films are non-irritant. Transdermal delivery is a potential route for the administration of Ondansetron.

***KEYWORDS**: Ondansetron, Hydrophilic polymers, Transdermal Patch, Antiemetic.*

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INTRODUCTION:

"TDDS" is an abbreviated version for Transdermal Drug Delivery System, which is known to be the structures dissembling underneath the class of managed drug transport, where consequently the intention is to furnish the drug thru the pores and skin at a pre-decided and managed rate. The chosen drug is applied to the inside of the patch in a partially high dosage form and then applied to the skin for a prolonged period. The selected drug then enters the bloodstream directly through the skin, by using the process of diffusion. The drugs will keep entering into the blood for a long period and in turn providing a steady concentration of this drug in the blood flow.

1. **Advantages: -**
   - Cancellation of first-pass metabolism and gastrointestinal incompatibility
   - Anticipated and outstretched continuance of activity
   - Minimizing repulsive side effects

2. **Limitations: -**
   - The drug that needs higher blood levels cannot be dispensed.
   - Those drugs that have a higher level of molecular weight and also those that undergo metabolism in the passages through the skin are not suitable.
   - TDDS cannot deliver ionic drugs and also the drugs that possess pulsatile fashion.

3. **Basic components of TDDS:** The components of transdermal devices consist of the following components;
   i) Polymer matrix
   ii) Drug
   iii) Permeation enhancers
   iv) Others

1. Polymer matrix: -

The preparation of the polymer matrix is usually done by dispersing the present drug in a liquid or solid- state polymer base. Certain criteria should be contented for a polymer to be beaded and used in a transdermal system:

1. Polymers should have biocompatibility & chemical compatibility with drugs & other components of the system such as penetration enhancers and PSAs.
2. They should provide consistent & effective delivery of a drug throughout the product's intended shelf life and should be of safe status.

The polymers employed for TDDS can be classified as,

Natural Polymers:

e.g., Cellulose derivatives, Zein, Gelatin, Natural rubber, Starch, etc.

Synthetic Elastomers:

e.g., Hydrin rubber, Silicone rubber, Nitrile, Butyl rubber, Neoprene, etc.

Synthetic Polymers:

e.g., Polyvinyl alcohol, Polyvinyl chloride, Polyethylene, Polypropylene, Polyacrylate, etc.

2. Drug

To develop the transdermal drug delivery system successfully, the selection of drugs should be done with utmost care. The following are some of the many desirable properties of a drug for transdermal delivery.

Physicochemical properties

1. Substances having a molecular weight of fewer than 1000 Daltons are suitable.
2. The drug shall have some degree of solubility in both oil and water (ideally greater than 1 mg/ml).
3. The substance must have a melting point of < 200 °C.
4. A saturated aqueous solution of the drug should have a pH value between 5 and 9. Drugs highly acidic or alkaline in solution are not appropriate for TDD; because they get ionized quickly at physiological pH & ionized materials generally penetrate the skin poorly.

3. Permeation Enhancers.

These are compounds that enhance the permeability of skin by altering it as a barrier to the flux of the desired penetrant.

Ideal characteristics of chemical penetration enhancers

- They should be non-toxic, non-irritating and non-allergenic.
- They should have no pharmacological activity within the body.
- The penetration enhancers should work unidirectionally.
  - o When removed from the skin, barrier properties must return both rapidly & fully to normal.

2. AIM OF THE STUDY:

The present study had been designed in such a way that it develops suitable type transdermal drug delivery systems of Ondansetron, using two different

natural polymers Xanthan Gum & Guar gum in different proportions.

2.1. OBJECTIVES OF THE WORK.

The present work is planned by considering the following objectives:

To develop a matrix-type transdermal patch containing Ondansetron, we have to use a blend of polymers; Guar gum & Xanthan gum in different ratios with 6% Propylene Glycol as a plasticizer.

1. The physical appearance of transdermal systems, moisture content, moisture uptake, thickness, area, etc., is evaluated only to produce such economical patches that are available for the poor people It is done by using simple and economical polymers.
2. To study In-vitro drug release, we have to ensure drug release was controlled and prolonged over a while.
3. To lessen the side effect.

2.2. PLAN OF WORK

To meet the above aim and objectives:

1) To develop Patches for drugs Ondansetron using polymers Xanthan Gum & Guar gum in different ratios
2) To estimate the dosages forms for the following:
   - Weight variation
   - Thickness variation
   - Folding endurance
   - Estimation of drug content
   - Moisture content
   - In vitro release study

3. REVIEW OF LITERATURE

-**Pravin. Gavalis et al.** reported the design and development of HPMC-based polymeric films of enalapril maleate. Patches have been prepared using various concentrations and grades of HPMC (K4M, K15 M, K 100M) and evaluated for their physicochemical characterization.

-**Ahuruhuru J et al.,** developed Granstrom transdermal films using the solvent evaporation technique. Patches were prepared using HPMC and ERS 100/ ERL 100 in different ratios, with 15% v/w of propylene glycol as a plasticizer.

- **J. R. D Gupta et al.** formulated & evaluated transdermal patches of Glibenclamide. Patches were formulated using HPMC and PVP K-30/ ERS 100 in different ratios, PEG 400 (36%) as a plasticizer and DMSO (12%) as a penetration enhancer.

-**Mamatha T et al.** formulated monolithic matrix-type drug delivery systems of atomoxetine hydrochloride. Eight formulations carrying E RL100, HPMC, and E RS100 were prepared. All formulations carried 10%w/w of propylene glycol as penetration enhancer and 10% w/w of Di butyl phthalate as a plasticizer.

-**Anil J Shinde et al.** developed transdermal matrix patches of tramadol hydrochloride using HPMC, E RL100, and E RS100 in different ratios with tri ethyl citrate as the plasticizer and dimethyl sulfoxide as the penetration enhancer. The batch containing E RL100: HPMC (8:2) showed 79.65% release within 12hrs and the batch containing E RS100: HPMC (2:8) showed only 58.30% release within 12hrs. This is because the eudragit produces a crystallization-free patch.

- **Ramesh Gannu et al.,** prepared matrix type TDDS of nitrendipine by solvent evaporation technique. Ten formulations composed of E RL100, E RS100 and HPMC in different ratios were prepared. All formulations carried 6%v/w of carvone as a penetration enhancer and 15% v/w of propylene glycol as the plasticizer.

-**Gattani S.G. et al.,** formulated monolithic Transdermal films of ondansetron hydrochloride using various polymer combinations such as PVA: PVP, E RLPM: RSPM, and EC: PVP. Limonene & oleic acid were used as penetration enhancers.

-**Sadhana P. Guptha et al.** formulated and evaluated metoprolol tartrate TDDS for controlled release of the drug for an extended period. E RL and HPMC were used for the fabrication of TDDS and evaluated for thickness, tensile strength, drug content, *in vitro release kinetics & drug* permeation kinetics.

4. DRUG PROFILE

Identification	
Name	**Ondansetron**
Description	A competitive serotonin type 3 receptor antagonist. It is effective in treating of nausea and vomiting caused by cytotoxic chemotherapy drugs, including cisplatin, & has reported anxiolytic and neuroleptic properties. [PubChem]
Chemical Formula	C18H19N3O
Pharmacology	
Indication	For the prevention of nausea and vomiting related to emetogenic cancer chemotherapy, post-operation, and radiation. Also utilized for the treatments of postoperative nausea and vomiting.
Pharmacodynamics	Ondansetron is a highly specific & selective serotonin 5-HT3 receptor antagonist, not shown to have activity at other known serotonin receptors & with low affinity for dopamine receptors. The serotonin stimulates the vagal & splanchnic nerve receptors that project to the medullary vomiting center, as well as the 5-HT3 receptors in the area postrema, thus initiating the vomiting
Mechanism of action	Ondansetron is known to be a selective serotonin 5-HT3 receptor antagonist. The inhibition of 5-HT3 receptors in turn inhibits that visceral afferent stimulation of the vomiting center.
Absorption	Ondansetron undergoes limited first-pass metabolism.
Protein binding	70%-76% (Plasma protein binding)

Metabolism	Hepatic
Half-life	5.7 hours
Clearance	• 0.38 L/h/kg [Normal Adult Volunteers (19-40 yrs.)] • 0.32 L/h/kg [Normal Adult Volunteers (61-74 yrs.)] • 0.26 L/h/kg [Normal Adult Volunteers (>=75 yrs.)]
Toxicity	Low blood pressure and fainting, sudden blindness, severe constipation
Drug Interactions	Drug Interaction Asenapine Additive QTc-prolongation may occur. Concomitant therapy should be avoided. Crizotinib Concurrent use with crizotinib may reduce QTc interval. Consider alternative therapy. Ezogabine Concurrent use of ezogabine and ondansetron can increase QTc interval. Consider alternate therapy.

5. POLYMER PROFILES:

5.1. GUAR GUM

Nonproprietary Names:
BP, Ph. Eur: Guar Galactomannan
***Synonyms*:** Galactosol, Guar flour, Jaguar gum, Meyprofin.
***Chemical name*:** Galactomannan polysaccharide.
Molecular Formula: (C6H12O6) n
Molecular Weight: 220 000
Solubility: Practically insoluble in organic solvents. In cold or hot water, disperses and swells almost immediately to form a highly viscous, thixotropic solution.
Functional category: Suspending agent, binder, disintegrator, and viscosity agent.

MATERIALS	MANUFACTURER / SUPPLIERS
Ondansetron	Cipla Ltd.
Xanthan gum	Degussa, Germany
Guar Gum	Alfha Chemica
Propylene Glycol	S.D. Fine chem.
Dimethyl Sulfoxide	S.D Fine chem

5.2. XANTHAN GUM

Nonproprietary Names:
BP, USP-NF: Xanthan Gum
Synonyms: Corn sugar gum, Xanthani gummi.
Chemical Name: Xanthan Gum ***Molecular Formula: (***C35H49O29) n ***Molecular Weight:*** 1×106
Functional Category: Thickening agent, stabilizer, and suspending agent.
Solubility: Soluble in water and ethanol.

6. MATERIALS AND METHOD:

6.1Chemical Table: - Table 1

MATERIALS	MANUFACTURER / SUPPLIERS
Ondansetron	Cipla Ltd.
Xanthan gum	Degussa, Germany
Guar Gum	Alfha Chemica
Propylene Glycol	S.D. Fine chem.
Dimethyl Sulfoxide	S.D Fine chem

6.2Equipment Table: - Table 2

EQUIPMENT	MANUFACTURER
Digital weigh balance	Shimadzu, Japan
Glassware.	Borosil.
Magnetic Stirrer	Remi equipment, Mumbai
pH Meter	Elico Limited, Hyderabad
UV-Vis Spectrophotometer	Shimadzu, Japan

6.3 DETERMINATION OF LINEARITY PLOT OF ONDANSETRON

Formulation of the phosphate buffer pH 6.8"

Di-hydrogen phosphate 28.80 gm and potassium di-hydrogen phosphate 11.45 gm were dissolved in distilled water & volume was then made up to 1000 ml with distilled water.

Formulation of the standard stock solution:

Weigh accurately 10mg Ondansetron working standard into a 100ml clean, dry volumetric flask. Add about 10ml of solution medium (PH 6.8 buffer) and dissolve by shaking the volumetric flask.

Formulation of the working stock solution:

From the above solution, 1ml is pipetted out and made up to 10ml to m
ake 100ppm.

Formulation of the working solution:

From the above solution dilutions are made to prepare the concentrations of 0.2, 0.4, 0.6, 0.8 and1.0µg/ml (2,4,6,8,10ppm respectively) and analysis done in UV- double beam spectrophotometer absorbance at 242nm.

6.4. COMPATIBILITY STUDIES

IR spectroscopy can be used for investigating and predicting any physicochemical interactions between different components that are present in a formulation. This is the reason why it can be applied to the selection of suitable chemically compatible excipients.

The present study was aimed to test, whether there is an interaction between the carriers & drugs.

One part of the sample & three parts of potassium bromide was taken in a mortar and triturated. A small amount of triturated sample was taken into a pellet maker & was compressed at 10kg/cm2 using a hydraulic press. The pellet was kept on to the sample holder and scanned from 4000cm-1 to 400cm-1 in the Bruker IR spectrophotometer. Then it was compared with the original spectra.

IR spectra were compared & checked for any shifting in functional peaks and non-involvement of a functional group. From the spectra, there is no interaction between the selected carriers, drugs, and mixtures. Therefore, the selected carrier was found to be compatible in entrapping the selected Ondansetron along with carriers without any mutual interactions.

6.5 FORMULATION OF TRANSDERMAL PATCHES CONTAINING ONDANSETRON

Transdermal patches consisting of Ondansetron were prepared by solvent evaporation technique, using different ratios of Xanthan Gum (F2, F4, F6, F8) and Guar gum (F1, F3, F5, F7). The polymers were weighed in critical ratios & allowed for swelling for about 24 hours in a solvent mixture (1:1 ratio of dichloromethane, and methanol). 15%v/w propylene glycol was incorporated as the plasticizer. Then the drug solution was then added to the polymeric solution and cast onto anumbra Petri plate with a surface area of about 69.42sq.cm, permitted for air- drying overnight followed by vacuum drying for 8-10 hr. It is cut into individualpatches with an area of 6.9cl that is with a diameter of 2.9cm. About 7 patches have been obtained from each sheet. All formulations carried with 1ml Dimethyl Sulfoxide as a penetration enhancer and Propylene glycol as the plasticizer.

Table 3. List of materials.

Formulation code	Drug (mg)	Guar Gum(%)	Xanthan gum (%)	Propylene Glycol (%)	DMSO	Water
F1	8	1	-	6	0.5ml	20ml
F2	8	--	1	6	0.5ml	20ml
F3	8	1.5	-	6	0.5ml	20ml
F4	8	--	1.5	6	0.5ml	20ml
F5	8	2	-	6	0.5ml	20ml
F6	8	--	2	6	0.5ml	20ml
F7	8	2	--	8	0.5ml	20ml
F8	8	--	2	8	0.5ml	20ml

6.6 Characterization of Transdermal Patches Containing Ondansetron

- **Physicochemical -properties**

The Patches prepared by general procedure have been evaluated for the following properties

- **Thickness**

The thickness of the film was measured at ten different points on one film using vernier calipers. For each formulation, three selected Patches were used and the average thickness was recorded.

- **Weight variation**

Six selective patches from each batch were weighed individually & then the average weight was taken.

- **Folding endurance**

This feature of the patch was fixated by persistently overlapping a small strip of this medicated patch at the same place until it showed a crack.

Assessment of drug content in the polymeric Patches:

The formulated polymeric patches were checked thoroughly to measure the present drug content in each one of them. After selecting three of those polymeric patches from each formulation, they were evaluated to check the present drug content.

Procedure:

Patches from each formulation was precisely selected, incised into small pieces & then proceeded to dissolve in a 100 ml solution made up of 50 ml of methanol and 50 ml of dichloromethane. The solution was diluted appropriately and the absorbance of the solution was deliberated using a UV-Vis spectrophotometer, set at a wavelength of 242 nm against methanol dichloromethane mixture (1:1) as unmarked.

- **Evaluating The Moisture Content**

These patches are subjected to precisely calculating the percentage weight, after placing them in a desiccator that contains calcium chloride at 40oC for 24hr.

The weight of every individual patch was secured when there was no further change of weight seen in every listed patch. Then the probability of the lost moisture was calculated by using the difference between the initial weight & final weight as regards with the final weight.

$$\% \text{ Moisture Content} = \frac{\text{Initial weight} - \text{Final weight}}{\text{Initial weight}} \times 100$$

- ***In-vitro* Release Studies.**

After using the Franz diffusion cell theory, the drug release studies from Ondansetron transdermal patches were executed. The donor and receptor compartments were used to drug-containing patches were added in between the donor and receptor compartments. They were then separated by using a Cellophane membrane. The receptor compartment containing the diffusion medium was stirred with a magnetic bead operated by a magnetic stirrer, to prevent the formation of a concentrated drug solution layer below the Cellophane membrane. At appropriate time intervals, 5ml of samples were collected simultaneously & replaced by using 6.8 pH phosphate buffer. Analysis was conducted by using a UV-Visible spectrophotometer adjusted at 242 nm with opposite to phosphate buffer pH 6.8 as a reference.

6.7. DATA ANALYSIS

To evaluate the dosage form for its mechanism of release & release rate kinetics, the data acquired was befitting into Higuchi matrix, Zero-order as well as First-order, and Peppas model. Considering the R-value, the most accurate model was selected.

- **ZERO-ORDER KINETICS.**

Any drug that is dissolute in a dosage form that does not disarticulate and releases the drug slowly, predicting that with no change in equilibrium conditions are obtained when the area does not change & can be represented by the following equation,

$$Q\,t = Q\,o + K\,o\,t$$

Where Q t = amount of drug dissolved in time t

.

Q o = initial amount of drug in a solution.

K o = zero- order release constant.

- **FIRST-ORDER KINETICS**

To study first-order release rate kinetics, the release rate data have been applicable to the following equation,

$$\text{Log Qt} = \log \text{Qo} + \text{K1t} / 2.303$$

Where Qt is the amount of drug released in time t, Qo is the initial amount of drug in the solution and K1 is the first-order release constant.

- **HIGUCHI MODEL**

Higuchi has always focused on developing numerous theoretical models to investigate the unleashing of water-soluble & less soluble drugs blended in semisolids and/or solid matrices. Drug molecules present in a uniform matrix and also reacting as the diffusion media were used to prepare mathematical equations. And the equation is,

$$Qt = K\,H \cdot t1/2$$

Where Qt = amount of drug released in time t,

K H = Higuchi dissolution constant.

- **PEPPAS AND KORSMEYER RELEASE-MODEL**

To examine such a model the release rate data have been fitted to the following equation,

$$\text{Mt} / \text{M} \infty = \text{K} \cdot \text{t n}$$

Where 'Mt / M' is the fraction of drug release, 'K' is derived as the release constant, and 'n' the diffusional coefficient for the drug releases that is dependent on the shape of the matrix dosage form.

7. RESULTS AND DISCUSSION:

7.1. PREFORMULATION STUDIES

Table.4: Ondansetron preformulation studies

S.NO	PARAMETERS	REPORT
1	Physical appearance	Off-white fine crystalline powder.
2	Solubility	Slightly soluble in ethanol and isopropanol, freely soluble in dimethyl soapboxed .
3	Melting point	179°C

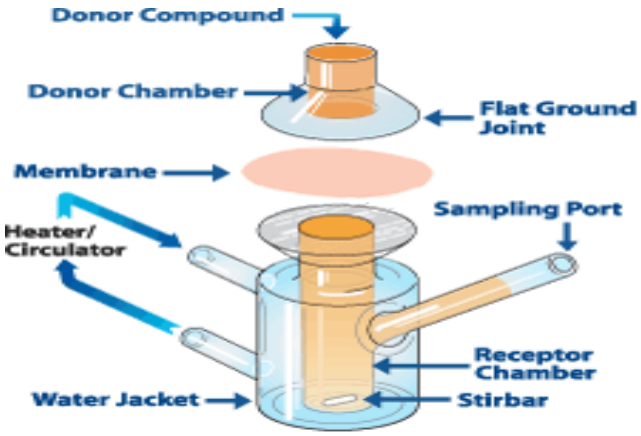


Fig. 1: Franz diffusion cell

In Preformulation studies drug characteristics were performed and results were complying with pharmacopeial values.

7.2. DETERMINATION OF LINEARITY PLOT OF ONDANSETRON

Ondansetron solutions were prepared and then the absorbance of those resulting solutions was measured by using a UV spectrophotometer adjusted at 310 nm. The absorbance is noted and given in table.2. The standard graph between concentration vs absorbance was given in figure no-1

Table 5: Determination of Linearity plot of ondansetron

CONCENTRATION(µg/ml)	ABSORBANCE
2	0.113
4	0.215
6	0.339
8	0.452
10	0.565

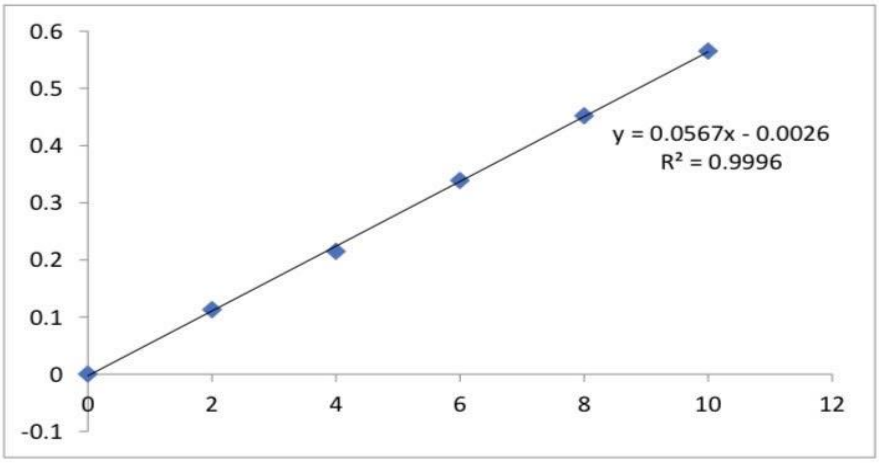
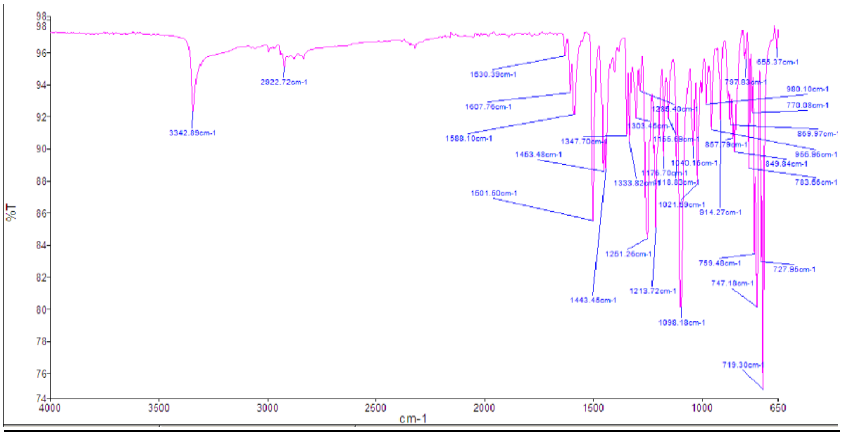


Figure No 2: Concentration (x-axis) and Absorbance (y-axis)

DRUG EXCIPIENT COMPATIBILITY STUDY.



FigureNo 3: Ondansetron Pure Drug FT - IR

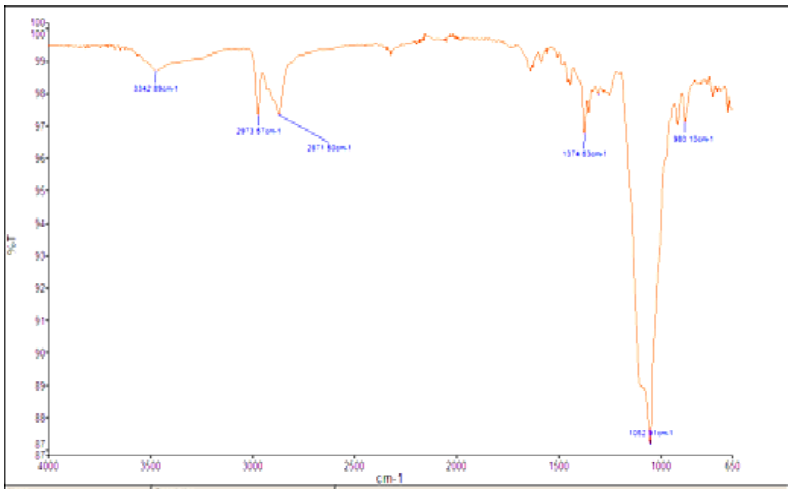


Figure No.4: Ondansetron Final Optimized FT-IR

Table 6: FT-IR Spectra data of Ondansetron and polymer

S no	Functional group	Characteristic peak cm^{-1}	The observed peak for drug cm^{-1}	Peaks for the transdermal patch formulation
1	N-H	3500-3300	3342.89	3342.89
2	C-H	2950-2800	2922.72	2973.57,2871.5
3	C=O	1260-1000	1098.28	1052.91

7.3. DISTINCTIVE CHARACTERS OF ONDANSETRON TRANSDERMAL PATCHES

Physicochemical properties.

The Patches prepared by the general method have been estimated for the listed properties mentioned below:

- **Weight Variation Test:**

The results of this test on several transdermal Patches were shown in Table. 7. Uniformity in the weight of patches was concluded.

- **Thickness Variation Test:**

The thickness variation test results for several transdermal Patches were shown in Table.7. In the thickness variation test, the thickness was found to be uniform.

- **Folding endurance number:** ``

The folding endurance numbers of formulations are presented in Table.7. These patches didn't display any cracks even after folding the patch more than 50 times. This number provides the mechanical property of the patches. A high folding endurance number suggested that it has high mechanical properties. The folding endurance number was enhanced with increasing the ratio of Xanthan gum. These conclusions indicated that patches couldn't break & would maintain their integrity when applied on the skin with its general folding.

- **Evaluation of drug content in polymeric Patches:**

The results of drug content for various transdermal Patches were shown in Table.8. Eventually, content uniformity results indicated that the drug was equally dispersed in all the tested transdermal patches. A comprehensive drug content analysis of the prepared formulation showed that the process engaged to prepare patches in this study was capable of delivering patches with systemic drug content & minimal batch flexibility.

- **Moisture Content study:**The conclusion of moisture content was mentioned in Table.8. They suggested that the moisture content was amplified with building up the polymer concentration. Very less moisture content found in the formulations helps them to remain stable & also to avoid complete dryness and formation of brittle films.

Table 7: Weight, thickness, and folding endurance of Ondansetron transdermal patches

Formulation	Weight (mg)	Thickness (mm)	Folding endurance
F1	47±0.2	0.155±0.6	**159**±1.3
F2	48±0.6	0.145±0.4	**159**±3.2
F3	47±0.8	0.135±0.4	**156**±2.0
F4	45±0.1	0.175±0.4	**171**±2.8
F5	48±0.6	0.135±0.2	**179**±2.3
F6	46±0.8	0.165±0.3	**141**±1.2
F7	45±0.8	0.155±0.6	**110**±1.4
F8	47±0.1	0.165±0.7	**130**±1.8

Table 8: Drug content and % Moisture content of Ondansetron transdermal patches

Formulation	Drug content **(%)**	**% Moisture content**
F1	**94.6**±0.9	**1.34**±0.3
F2	**96.8**±0.6	**1.44**±0.2
F3	**97.5**±0.7	**1.34**±0.5
F4	**96.0**±0.8	**1.44**±0.9
F5	**97.3**±0.5	**1.24**±0.7
F6	**98.1**±0.2	**1.54**±0.8
F7	**97.8**±0.5	**1.34**±0.3

Table 9: Swelling Index of Ondansetron transdermal patches

TIME (Hrs)	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**
0	0	0	0	0	0	0	0	0
1	39±0.9	48±0.6	49±0.7	73±0.2	34±0.7	71±0.8	31±0.5	61±0.5
2	59±0.3	79±0.9	78±0.6	101±0.9	64±0.5	100±0.5	71±0.6	96±0.7
4	99±0.3	111±0.6	104±0.8	136±0.9	82±0.2	132±0.2	84±0.7	140±0.9
8	--	--	126±0.9	154±0.7	106±0.9	170±0.1	102±0.9	160±0.8
16	--	--	--	179±0.5	132±0.7	184±0.2	141±0.2	190±0.2
24	--	--	--	--	--	190±0.8		195±0.9

- ***In-vitro* Release Studies**

Table 10: Cumulative percent release of Ondansetron from transdermal patches

TIME (Hrs)	F1	F2	F3	F4	F5	F6	F7	F8
0	0	0	0	0	0	0	0	0
1	26±0.2	23±0.1	17±0.3	14±0.7	16±0.6	7±0.5	21±0.2	11±0.6
2	50±0.3	46±0.5	38±0.4	30±0.8	33±0.7	18±0.5	34±0.5	22±0.3
3	77±0.8	74±0.6	62±0.6	54±0.9	49±0.9	31±0.2	49±0.2	34±0.5
4	84±0.9	83±0.8	71±0.2	67±0.9	60±0.6	48±0.6	58±0.3	48±0.9
6	97.7±0.7	100±0.2	84±0.6	75±0.6	68±0.5	60±0.3	68±0.2	58±0.7
8	98.3±0.5	100±0.6	100.7±0.5	82±0.7	81±0.2	73±0.2	77.6±0.3	71±0.9
12	98.3±0.1	100±0.9	100.7±0.5	90±0.5	91.7±0.3	78±0.5	88.4±0.8	79±0.5
16			100.6±0.7	99.5±0.2	99.6±0.5	85±0.2	99.6±0.9	89±0.6
20				99.5±0.3	99.6±0.4	99±0.9	99.6±0.7	91±0.3
24				99.5±0.2	99.5±0.6	100.1±0.7	99.6±0.6	99±0.7

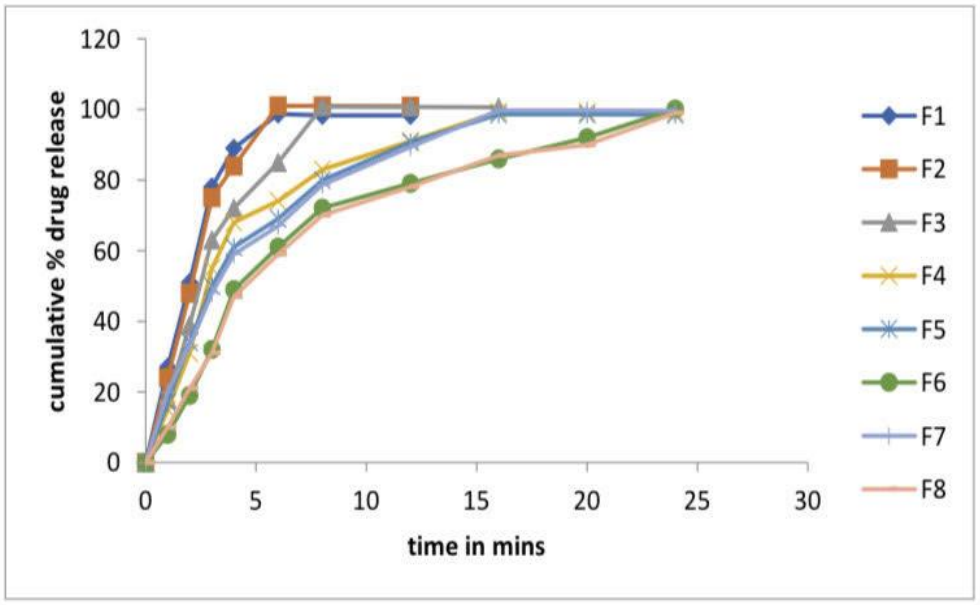


Fig. 5 Cumulative percent release of Ondansetron from transdermal patches F1-F8

- ***In-vitro* Drug Releases Studies from Transdermal Patches**

The cumulative amount of drug released from Transdermal patches is shown in Table.7. The results indicate that there was an increase in the number of drugs released with an increase in Xanthan gum.

Formulations F8 exhibited the greatest (99%) a percentage of drug released values when compared with other formulations. In the present study it was observed that as the concentrations of Xanthan Gum increased in the formulations, the drug release rate improved substantially.

KINETIC STUDIES FOR AN OPTIMIZED FORMULATION F8:

Table no 11: Release kinetics for an optimized formulation

	ZERO	FIRST	HIGUCHI	PEPPAS
	% CDR Vs T	Log % Remain, Vs T,	%CDR Vs √T	Log C Vs Log T
Slope	3.867891156	-0.06840852	21.99618526	1.023725946
Intercept	20.06204082	2.048044008	-2.69081455	0.787881927
Correlation	0.920969087	-0.95336667	0.980131134	0.853125637
R 2	0.84818406	0.908908011	0.96065704	0.727823353

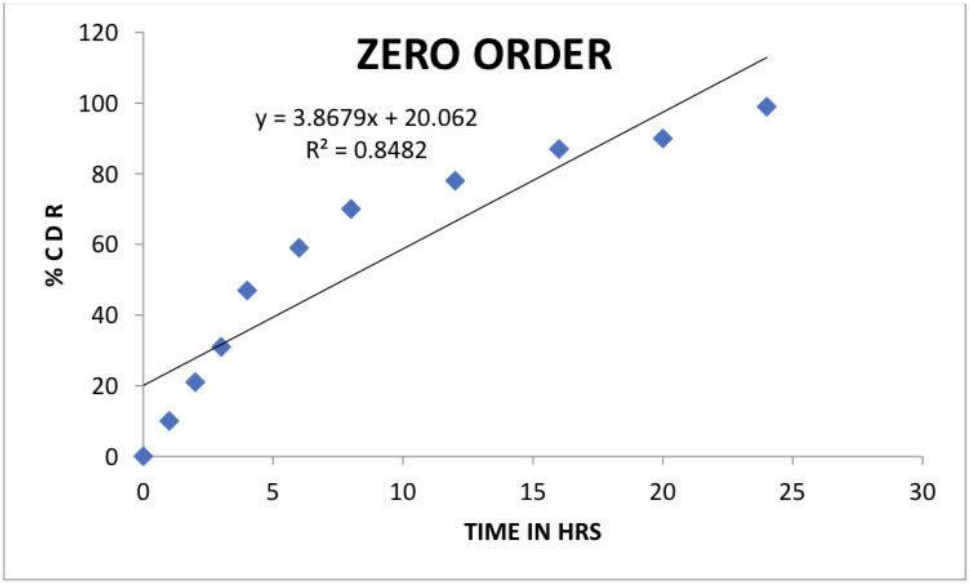


FIG NO 6: Zero-order plot for an optimized formulation

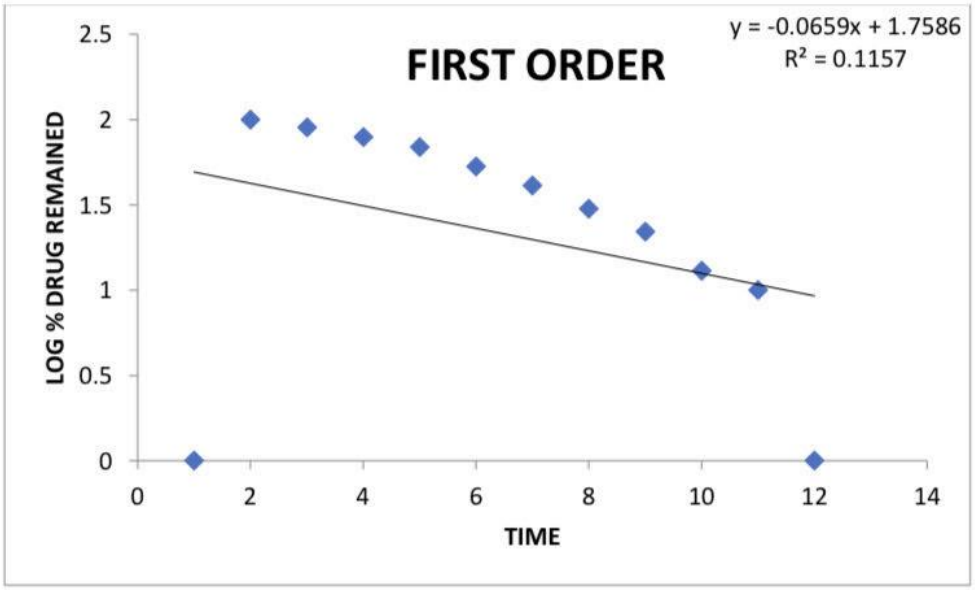


FIG NO 7: First Order plot for optimized formulation

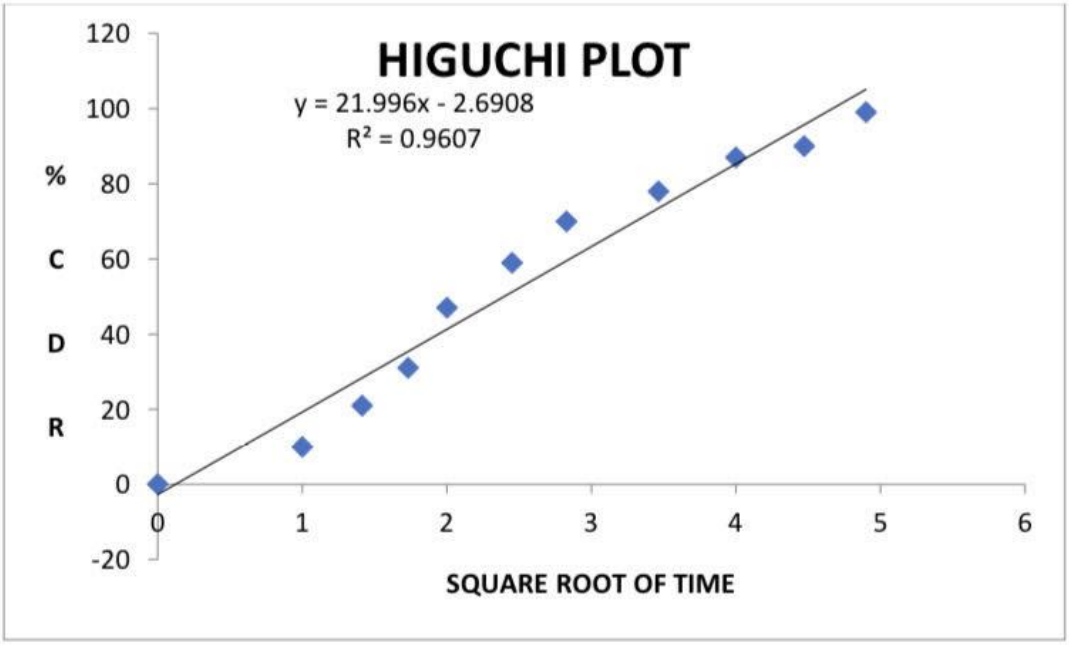


FIG NO 8: Higuchi plot for optimized formulation

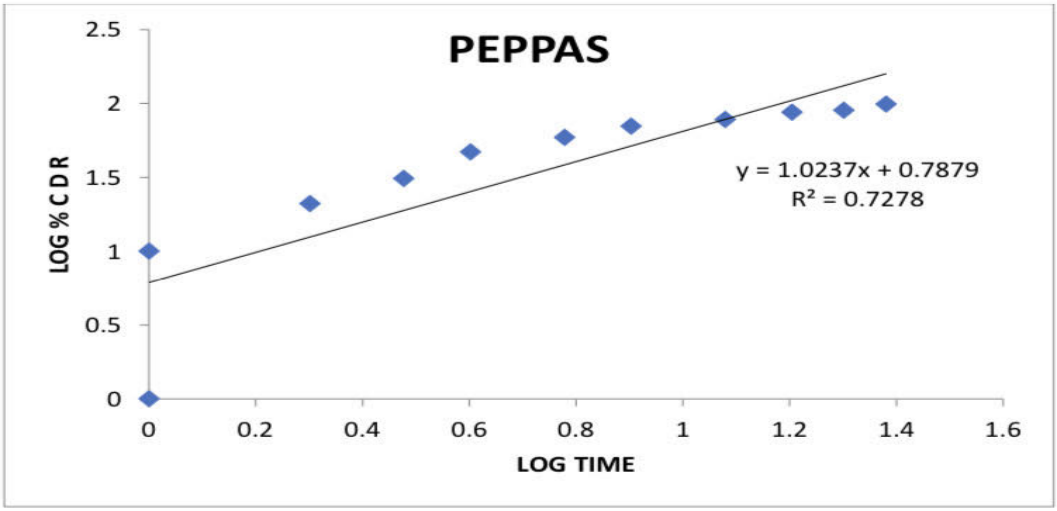


FIG NO 9: Peppas plots for an optimized formulation

8. SUMMARY AND CONCLUSIONS:

- Many polymeric Patches that possess Ondansetron were formulated & evaluated for physicochemical, in vitro drug release & Kinetic studies.
- When Ondansetron was evaluated to determine the IR spectral analysis and revealed the principal peaks and for the mixture of Ondansetron in addition to principal peaks and with different polymers in addition to the principal peaks, some additional peaks have been observed with physical mixtures, which could be due to the presence of polymers. The presence of all characteristic features shown due to the presence of functional groups in polymer mixtures indicates that there is no interaction between the drug & polymers that is used in the present study.
- The successfully formulated patches were evaluated for their physicochemical characteristics such as weight uniformity, physical appearance, thickness, folding endurance; moisture content, and drug content was suitable.
- Transdermal patches that were formulated with Xanthan gum indicated better release than patches with Guar Gum. It was observed that whenever Xanthan Gum content was increased, the release rate in the patch was increased.
- The release kinetics of the optimized formulations followed the Higuchi and the release mechanism was evaluated to be a non-fictional yet diffusion rate-controlled mechanism.
- This research gave a guideline for formulating a controlled release transdermal delivery system F8 for effective therapy.

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