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Research Article

Formulation and Evaluation of Antiemetic Patch comprising Ondansetron Hydrochloride

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Abstract
The Transdermal patch of ondansetron was prepared by using combination of HPMC, PVP, PVA and Eudragit in various ratios using Dibutyl phthalate and propylene glycol as plasticizers and oleic acid as a permeation enhancer. The prepared Transdermal of ondansetron were evaluated for Thickness, moisture uptake,tensile strength, percent elongation, folding endurance, drug content, diffusion studies, percentage of drug release and compatibility. As compared to other formulae OND-1 shows best diffusion through the skin.
Keyword : Transdermal, plasticizers, plasticizers, incompatibility.

Introduction
Chemotherapy-induced nausea and vomiting (CINV) is a common side effect encountered by cancer patients during chemotherapy treatment. Ondansetron is a serotonin subtype 3 (5-HT3) receptor antagonists used in CINV management. Ondansetron hydrochloride (OS) is commercially available in oral and injectable forms. Orally administered OS undergoes extensive hepatic first pass metabolism, which accounts for its low bioavailability and short half-life [1-3]. The chemotherapeutic agents produce nausea and vomiting by releasing serotonin from the enterochromaffin cells of the small intestine, and that the released serotonin then activates 5-HT3 receptors located on vagal efferents to initiate the vomiting reflex. Therefore Ondansetron HCl works by blocking the reception of serotonin at these 5-HT3 receptors.

In the advent of modern era of pharmaceutical dosage forms, transdermal drug delivery system (TDDS) established itself as an integral part of novel drug delivery system[4]. Transdermal patches are polymeric formulations which when applied to skin deliver the drug at a predetermined rate across dermis to achieve systemic effects. Transdermal dosage forms, though a costly alternative to conventional formulations, are becoming popular because of their unique advantages. Controlled absorption, more uniform plasma levels, improved bioavailability, reduced side effects, painless and simple application and flexibility of terminating drug administration by simply removing the patch from the skin are some of the potential advantages of transdermal drug delivery[5].

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Ondansetron is a potent antagonist of Serotonin (5 HT_3) receptor which has been proved effective in prevention of chemotherapy and radiotherapy-induced nausea and vomiting. Ondansetron hydrochloride has been used by oral and injectable administration. Ondansetron hydrochloride is rapidly absorbed orally, but extensively metabolized by the liver. It should be administered 30 min before chemotherapy, and the orally administered antiemetic drug tends to be discharged by vomiting. On the contrary, intravenous administration renders rapid effect to a patient, but the onset of effect is too rapid to cause undesirable effects. In addition, it gives a local pain, and may cause an unexpected accident when it is not perfectly prepared[6]. In this work an attempt was made to formulate and evaluate TDDS for sustained release OSH by solvent casting method. Low molecular weight, good permeability, poor bioavailability (60%) and shorter half-life (5-6 h) of OSH made it a suitable drug candidate for the development of Transdermal patches[7]. The main objective of formulating the Transdermal system was to prolong the drug release time, reduce the frequency of administration and to improve patient compliance.

Advantages [9,10,11,12]

1. They can avoid gastrointestinal drug absorption difficulties.
2. They can substitute for oral administration of medication when that route is unsuitable, as with vomiting and diarrhea.
3. They avoid the *first-pass effect*,
4. They are noninvasive, avoiding the inconvenience of parenteral therapy.
5. They provide extended therapy with a single application, improving compliance over other dosage forms requiring more frequent dose administration.
6. The activity of a drugs having s short half-life is extended through the reservoir of drug in the therapeutic delivery system and its controlled release.
7. Drug therapy may be terminated rapidly by removal of the application from the surface of the skin.
8. They are easily and rapidly identified in emergencies.
9. They are used for drugs with narrow therapeutic window.

Technologies for developing transdermal drug delivery systems [8,14]

The technologies can be classified in four basic approaches.

A. Polymer membrane partition-controlled TDD systems:

In this type of systems, the drug reservoir is sandwiched between a drug-impermeable backing laminate and a rate controlling polymeric membrane. (Fig.1)

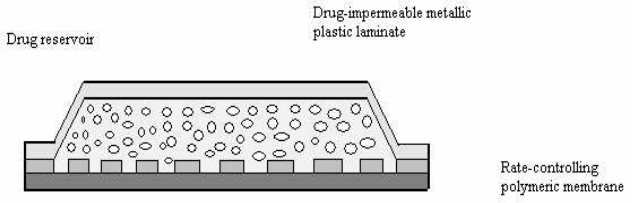

Figure. 1: Cross-sectional view of polymer membrane permeation-controlled TDD systems

The drug is allowed to permeate only through the rate controlling membrane. The drug solids are homogeneously dispersed in a solid polymer matrix, suspended in an unleachable, viscous liquid medium e.g. silicone fluid, to form a paste like suspension, or dissolved in a releasable solvent e.g. alkyl alcohol, to form a clear drug solution. The rate controlling membrane can be either a micro porous or a nonporous polymeric membrane e.g. ethylene-vinyl acetate copolymer, with specific drug permeability. On the external surface of the polymeric membrane a thin layer of drug- compatible, hypoallergenic pressure sensitive adhesive polymer e.g. silicone adhesive, may be applied to provide intimate contact of TDD system with the skin surface. Varying the composition of drug reservoir formulation and the permeability coefficient and thickness of rate controlling membrane can alter the drug release rate. E.g. Some FDA approved systems – Transderm-Nitro for angina pectoris,

B. Polymer matrix diffusion-controlled TDD systems:

In this system, the drug reservoir is formed by homogeneously dispersing the drug solids in a hydrophilic or lipophilic polymer matrix, and then the medicated polymer formed is molded into medicated disks with defined surface area and thickness. This drug reservoir containing polymer disk is then mounted on occlusive base plate in a compartment fabricated from a drug-impermeable plastic backing.

Instead of coating adhesive polymer directly on the surface of medicated disk, it is applied along the circumference of the patch to form a strip of adhesive rim surrounding the medicated disk. E.g. Nitro-Dur system and NTS system for angina pectoris.

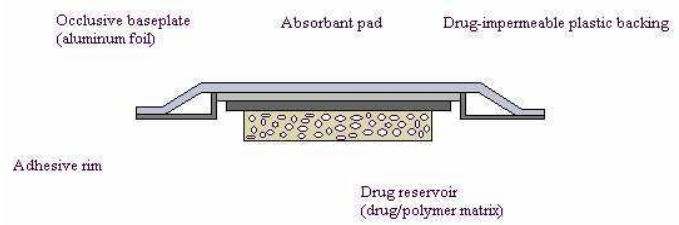

Figure. 2: Cross-sectional view of polymer matrix diffusion-controlled TDD systems.

The rate of release from polymer matrix drug dispersion-type is:-

$$\frac{dQ}{dt} = \left(\frac{L_d C_P D_P}{2t} \right)^{1/2}$$

Where, *Ld is* drug loading dose initially dispersed in polymer matrix

CP is solubility of drug in polymer matrix

DP is diffusivity of drug in polymer matrix

Only drug is dissolved in polymer matrix can release, *CP* is practically equal to *CR.*

Alternately, the polymer matrix drug dispersion-type TDD system can be fabricated by directly dispersing drug in a pressure-sensitive adhesive polymer, e.g. poly acrylate, and then coating the drug-dispersed adhesive polymer by solvent casting or hot melt onto a flat sheet of a drug-impermeable backing laminate to form a single layer of drug reservoir. this yields a thinner patch.E.g. Minitran system, Nitro-Dur II system for angina pectoris.

C. Drug reservoir gradient-controlled TDD systems:

Polymer matrix drug dispersion-type TDD systems can be modified to have the drug loading level varied in an incremental manner, forming a gradient of drug reservoir along the diffusion path across the multi laminate adhesive layers. The drug release from this type of drug reservoir gradient- controlled TDD systems can be expressed by:-

$$\frac{dQ}{dt} = \left(\frac{KF_{d/r} D_a}{h_a(t)} \right) L_d(h_a)$$

In this system the thickness of diffusion path through which drug molecules diffuse increases with time, i.e. ha (t). The drug loading level in the multi laminate adhesive layer is designed to increase proportionally i.e. Ld (ha) so as to compensate time dependent increase n diffusion path as a result of drug depletion due to release. Thus, theoretically this should increase a more constant drug release profile.

E.g. Deposit system containing nitroglycerine for angina pectoris.

D. Micro reservoir dissolution-controlled TDD systems:

A hybrid of reservoir- and matrix dispersion-type drug delivery systems, which contains dug reservoir formed by first suspending the drug solids in an aqueous solution of water-miscible drug solubilizer e.g. propylene glycol, then homogeneously dispersing the drug suspension, with controlled aqueous solubility, in a lipophilic polymer, by high shear mechanical force, to form thousands of unleachable microscopic drug reservoirs.

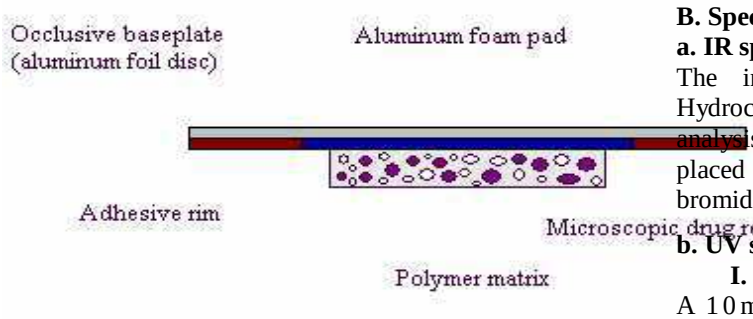

Figure.3: Cross-sectional view of a drug micro reservoir dissolution-controlled TDD system.

E.g. Nitro disk system for angina pectoris.

The rate of drug release from this system is defined by:-

$$\frac{dQ}{dt} = \frac{D_p D_s A K_p}{D_p h_d + D_s h_p A K_p} \left(B S_p \frac{K F_{d/r} D_1 S_1 (1 - B)}{h_1} \left[\frac{1}{K_1} - \frac{1}{K_m} \right] \right)$$

`

2. MATERIALS AND METHODS

Ondansetron hydrochloride (OS) was a gift from Sun Rise Pharma, India. Dibutylpthalate (DBP) and Oleic Acid were purchased from Ranbaxy Fine Chemicals Ltd, New Delhi. Ethyl Cellulose Pharma grade was a gift sample from Colorcon Goa, India. Poly Vinyl Pyrrolidone (PVP) and Poly Vinyl Alcohol (PVA) was a gift sample from Hi-Media Pharma Ltd, India. Chloroform were purchased from Merck Pharma Ltd, Mumbai. Menthol was a gift sample from Rankem fine chemicals Ltd, Mumbai. All other chemicals used in the study were of analytic reagent grade.

Methods

Polymer matrix diffusion-controlled TDD systems:

Preformulation studies:

Preformulation testing is the first step in the rationale development of dosage forms of a drug. It can be defined as an investigation of physical and chemical properties of drug substance, alone and when in combined with excipients. The overall objective of the Preformulation testing is to generate information useful to the formulator in developing stable and bio availability dosage forms which can be mass produced.

The goals of Preformulation studies are:

- To establish the necessary physicochemical characteristics of a drug substance.
- To determine its kinetic release rate profile.
- To establish it's compatibility with different excipients.

Hence, Preformulation studies on the obtained sample of drug include color, taste, solubility analysis, melting point determination and compatibility studies.

Characterization of Ondansetron Hydrochloride:

A. Melting point determination:

The melting point of Ondansetron hydrochloride was determined by using melting point apparatus.

B. Spectroscopic studies:

a. IR spectrum interpretation:

The infrared spectrum of the pure Ondansetron Hydrochloride sample was recorded and the spectral analysis was done. The dry sample of drug was directly placed after mixing and triturating with dry potassium bromide.

b. UV spectroscopy [15] :

I. Determination of λmax

A 10mg of Ondansetron Hydrochloride was accurately weighed and was first dissolved in 35ml methanol solution. The solution was then diluted using phosphate buffer (pH- 7.4) to 100 ml. UV spectrums was recorded in the wavelength range 200-600 nm.

II. Preparation of calibration curve for Ondansetron hydrochloride

A standard curve was prepared by dissolving 10 mg of Ondansetron hydrochloride in 50ml of methanol. It was further diluted with phosphate buffer pH – 7.4 to get solutions in concentration range of 4 to 16 µg /ml. The absorbance of these solutions were determined spectrophotometrically at 305 nm.

C. Determination of solubility of Ondansetron hydrochloride [16]

The Ondansetron hydrochloride has very low aqueous solubility. Its solubility is not reported in any official book, so determination of solubility is important. The solubility was determined in distilled water and phosphate buffer pH 7.4. The procedure can be detailed as follows.

Saturated solution of Ondansetron hydrochloride prepared using 10 ml. of distilled water/ phosphate buffer pH 7.4 in 25 ml volumetric flasks in triplicate. Precaution was taken so that the drug remains in medium in excess. Then by using mechanical shaker, the flasks were shaken for 48 hours. The sampling was done on 24th & 48th hour. The sample withdrawn (1 ml after

filtration) was diluted with appropriate medium and analyzed by using UV spectrophotometer at 305 nm and 303.5 nm for phosphate buffer and distilled water respectively.

FORMULATION OF TRANSDERMAL PATCHES [17,18]

Preparation of blank patches:

Polymers of single or in combination were accurately weighed and dissolved in respective solvent and then casted in a Petri-dish with mercury as the plain surface. The films were allowed to dry overnight at room temperature.

Formulation of Drug Incorporated Transdermal Patches:

The matrix-type transdermal patches containing Ondansetron HCl were prepared using different ratios of Hydroxy Propyl Methyl Cellulose (HPMC) , Polyvinyl Pyrrolidone (PVP), Eudragit and Polyvinyl Alcohol (PVA). The polymers in different ratios were dissolved in the respective solvents. Then the drug was added slowly in the polymeric solution and stirred on the magnetic stirrer to obtain a uniform solution. Di-N-Butyl Phthalate (DBP) and Poly Ethylene Glycol (PEG) were used as plasticizers. Oleic acid was used as the penetration enhancer. Then the solution was poured on the Petri dish having surface area of 78.5 cm^2 and dried at the room temperature. Then the patches were cut into 2x2 cm^2 patches. Drug incorporated for each 2x2 cm^2 patch was 14.5 mg. the formulation table is given in table no. 1.

D. Evaluations of films

a. Physical evaluations

1. Thickness [19]

The thickness of films was measured by digital Vernier calipers with least count 0.001mm. The thickness uniformity was measured at five different sites and average of five readings was taken with standard deviation.

2. Moisture uptake [18]

The percent moisture absorption test was carried out to check the physical stability and integrity of the films at high humid conditions. In the present study the moisture absorption capacities of the films were determined in the following manner. The films were placed in the desiccators containing saturated solution of aluminium chloride, keeping the humidity inside the desiccators at 79.5 % R.H. After 3 days the films were taken and weighed the percentage moisture absorption of the films was found.

3. Tensile Strength [20]

The tensile strength was determined by the apparatus designed as shown in fig 13 . 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. The tensile strength was calculated by using following formula:-

$$\text{Tensile stress (S)} = \frac{\text{Applied force}}{\text{Cross sectional area}} = \frac{m \times g}{b \times t}$$

where, S = tensile stress in 980 dynes/cm^2

m = mass in grams

g = acceleration due to gravity (980 dynes/cm^2)

b = breadth of strip in centimeters

t = thickness of strip in centimeters

The strain is change resulting in size of strip after the force was applied to its original

size. Therefore, the strain can be given as,

$$\text{Strain (E)} = \frac{\text{Total elongation}}{\text{Original length}} = \frac{L - L_0}{L_0}$$

Where, L = length after force was applied

L0 = original length

4. Percent elongation

The percent elongation at break was measured by formula given below:

$$\text{Strain (E)} = \frac{\text{Total elongation}}{\text{Original length}} \times 100 = \frac{L - L_0}{L_0} \times 100$$

where, L = length after force was applied

L0 = original length

5. Folding endurance [21]

Using an apparatus designed in laboratory, folding endurance test for films was performed. The disintegration apparatus was modified as a folding endurance apparatus. The apparatus consists of two clamps for holding the film. Out

of two clamps, one clamp was fixed while other was moving. The clamps were able to move 5cm distance from each other at speed of 30 rpm. The film was attached in such a way that when clamps were at maximum distance the film will be slightly stretched. The apparatus was put on and allowed to run until film broke into two pieces. The folding were counted by rpm.[22]

6. Drug content

The patch of area 2x2 cm^2 was cut and dissolved in distilled water. Then solvent ethanol and dichloromethane, to make polymer soluble, were added to the mixture and the remaining volume was made up with distilled water to 100ml in 100ml volumetric flask. Then 1 ml was withdrawn from the solution and diluted to 10ml. The absorbance of the solution was taken at 303.5nm and concentration was calculated. By correcting dilution factor, the drug content was calculated.

7. Weight variation[17]

The three disks of 2*2 cm^2 was cut and weighed on electronic balance for weight variation test. The test was done to check the uniformity of weight and thus check the batch- to- batch variation.

D. Diffusion studies[23]

Preparation of skin

A full thickness of skin was excised from dorsal site of dead rat and skin was washed with water. The fatty tissue layer was removed by using nails of fingers. The outer portion with hairs was applied with depilatory and allowed to dry. With the help of wet cotton the hairs were scrubbed and washed with normal saline solution. The skin was kept in normal saline solution in refrigerator until skin was used for diffusion study. Prior to use, the skin was allowed to equilibrate with room temperature. Then skin was mounted between donor and receptor compartment of cell. The skin was clamped in such a way that the dermal side will be in contact with receptor medium.

Diffusion cell

The diffusion studies were done to get an idea of permeation of drug through barrier from the transdermal system. In vitro studies are also done for TDDS development. Usually, two types of diffusion cells are used as horizontal and vertical. The Franz and Keshary Chien (K-C) type of diffusion cells are of horizontal type of cells. In this work, K-C type of diffusion cell was used. Diffusion cells generally comprise two compartments, one containing the active Compartment (donor compartment) and the other containing receptor solution (receptor compartment), separated by barrier i.e. rat abdominal skin. The cell consisted of sampling port and temperature maintaining jacket. The outlet and inlet was connected with latex tube so the jacket had stagnant water inside and heat was provided by hot plate. The stainless steel pin was used to stir the receptor solution using magnetic stirrer. The rat abdominal skin was placed on receptor compartment and both compartments held tight by clamps

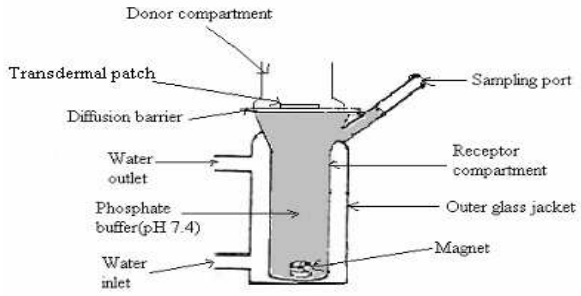

Figure 4 : Keshary Chein diffusion cell

Phosphate buffer pH 7.4 was used as receptor solution. The volume of diffusion cell was 10 ml and stirred with bent stainless steel pin. The temperature was maintained at 37 ± 1°C with the help of hot plate. The diffusion was carried out for 10 hours and 1 ml sample was withdrawn at an interval of 1 hour. The same volume of phosphate buffer pH 7.4 was added to receptor compartment to maintain sink conditions and the samples were analyzed at 305.5nm. Other designs of diffusion cells that are in existence include Valia-Chien (V-C) cell, Ghannam-Chien (G-C) cell, Jhawer-Lord (J-L) Rotating disc system, etc.

3. Results and Discussion

Six formulations of Ondansetron HCl transdermal patches were formulated using different polymer ratios, the composition of which is shown in table 2. The prepared formulations are shown in figure. the formulations are subjected to evaluation parameters like thickness, drug content, folding endurance, tensile strength, % elongation, % moisture absorption, IR studies, ex-vivo permeation studies.

A. **Preformulation studies**

a. Melting point determination: The melting points were found to be in the range of 178° to 179°C. The reported melting point is 178.5° to 179.5°C.

b. Spectroscopic Studies:

1. The spectra showed no incompatibility between the polymer and Ondansetron HCl drug. The spectra of the formulation F1 and the pure drug is given in the spectra 1 and 2 respectively.

2. Determination of λ_{max}

The spectrum obtained is shown in the figure 5. The peak showed in the figure is much similar to the reported peak.

3. Calibration curve of Ondansetron HCl

The absorbance values obtained, are shown in table 2. Using concentration and absorbance data, a beer and Lambert's plot was obtained. The plot is given the figure 6.

c. Solubility determination:

The solubility of Ondansetron hydrochloride was determined and found very less as 78.94 µg/ml in phosphate buffer. The solubility in distilled water was found more than that in phosphate buffer.

B. Physical evaluation:

1. Thickness:

The thickness of the films varied from 0.025 to 0.049 mm. The values obtained for all the formulations is given in the Table 11.

2.Moisture uptake: The formulation OND 5 (HPMC:PVP 7:3) showed lowest percent moisture absorption than other formulations. This might be because of the low water permeability of ethyl cellulose polymer. The values for the moisture uptake has been given in the Table 11.

3. Tensile strength: The tensile strength was found to be in the range of 0.76 to 0.59. The formulation OND 1 showed the best tensile strength. The values for all the patches is tabulated in the Table 11.

4. % Elongation:

The % elongation was found to be in the range of. The formulation OND 1 showed minimum % elongation among all the other patches 15.25 % to30.5 %.The results obtained for all the formulations is tabulated in the Table 11.

5. Folding Endurance:

The folding endurance was found to be in the range of 71 ± 0.9 to 79 ± 3 The values for all six formulations is given in the Table 11. This data revealed that the patches had good mechanical strength along with flexibility.

6. Weight variation:

The weight variation was to be in the range of 62.50 ± 1.8 to 66.89 ± 1.2. The values for all the formulations is tabulated in the Table 11.

7. Drug content: The drug content was in the range of 92.66 % to 95.9 %. The values are given in the Table 11.

C. Diffusion study:

The rat skin was used to carry out the study. The formulation OND 1 (PVA:PVP; 7:3) showed drug diffusion for 10 hours up to 71.22 %. The % drug diffusion for six formulations is given in the Table 4,5, 6, 7, 8, and 9 along with the Higuchi's plot. The regression for Higuhi's plot for all the formulations is given in table 10. The plot for the diffusion study for all the formulations is given in the Figures 6 and 7 respectively. The Higuchi's plot for the formulations is given in the Figures 8.

4. Conclusion :

The Transdermal Patches were prepared by solvent casting method using combination of HPMC, PVP, PVA and Eudragit in various ratios using Dibutyl phthalate and propylene glycol as plasticizers and oleic acid as a permeation enhancer.As compared to other formulae OND-1 shows best diffusion through the skin. Treatment can be terminated if required which is not possible in oral dosage form. It may be noticed by IR study, there is no incompatibility between drug and polymers.Therefore, it was concluded that our formulae could be very promising transdermal alternative for the treatment of Nausea and Vomiting.

5. Reference

[1]. Rita Wickham. Best Practice Management of CINV in Oncology Patients: II. Antiemetic Guidelines and Rationale for Use. The Journal of Supportive Oncology 2010; 8(1) 10-15.

[2]. Ruff P, Paska W, Goedhals L et al..Ondansetron compared with granisetron in the prophylaxis of cisplatin-induced acute emesis: A multicentre double-blind, randomized, parallel group study. Oncology 1994; 51(1) 113-118.

[3]. Swain K, Pattnaik S, Sahu SC, Mallick S. Feasibility assessment of Ondansetron hydrochloride transdermal systems: physicochemical characterization and in vitro permeation studies. Lat Am J Pharm 2009;28(5):706-714

[4]. Ahmed A, Karki N, Charde R, Charde M, "Transdermal drug delivery systems: an overview" Int J. Bio Adv Res. 2011; 2(1): 38-56.

[5]. Murthy SN, Shobha R, Hiremath, Paranjothy KLK. 'Evaluation of carboxymethyl guar films for the formulation of transdermal therapeutic systems' Int J. Pharm. 2004; (272):11–18.

[6]. Eunsook C, Hyesun G, Inkoo C, "Formulation and evaluation of Ondansetron nasal delivery systems" Int J. Pharm. 2008; (349):101–107.

[7]. Kapoor D, Patel M, Singhal M, "Innovations in Transdermal Drug Delivery System I" Int Pharma sci. Jan-March 2011;1(1): 54-61.

[8]. Chien Y.W. "Novel Drug Delivery Systems",2nd Edition,Drugs And Pharmaceutical Sciences, Volume-50, Marcel Dekker, Inc.

[9]. Finnin B C, Morgan T M, Transdermal penetration. J Pharm Sci. Oct 1999;88 (10):955-958.

[10]. Allen L V, Popovich N G, Ansel H C, Ansel's Pharmaceutical Dosage Forms and Drug Delivery Systems, 8th Edition, Lippincott Williams & Wilkins, 2005:298-315.

[11]. Barry B. Transdermal Drug Delivery. In Ed:

Aulton M E, Pharmaceutics: The Science of Dosage Form Design, Churchill Livingston. 2002:499-533

[12]. Cleary G W, Transdermal controlled release systems. Medical Applications of Controlled Release. 1:203-251.

[13]. Vyas S P, Khar R K, Controlled Drug Delivery: Concepts and Advances, Vallabh Prakashan, 1st Edition. 2002:411-447.

[14]. Barry B W; "Dermatological Formulations: Percutaneous Absorption", Drugs and pharmaceutical sciences, Volume – 18, MARCEL DEKKER, INC. 1983:1-39.

[15]. Patra S, Choudhury A. A, Kar R. K and Barik B. B. Spectrophotometric method Ondansetron HCl. Ind J. Pharm. Sci. 2007; 69(6): 840-1.

[16]. Murthy S N, Sateesh M, Hamsa V, Drug release from terbutaline sulphate transdermal films across human cadaver skin, Indain J Pharm Sci. 59(2);75 76.

[17]. Saxena M, Mutalik S, Reddy MS. Formulation and evaluation of transdermal patches of metoclopramide hydrochloride. Ind drugs. 2006;43(9):740-5.

[18]. Ubaidulla U, Reddy MV, Ruckmani K. Transdermal therapeutic system of Carvedilol : effect of hydrophilic and hydrophobic matrix on in vitro and in Vivo characteristics. AAPS Pharmacy Tech. 2007;8(1):Article 2

[19]. Murthy S N, Shoba Rani, Hiremath R, Formulation and evaluation of controlled release transdermal patches of theophylline-salbutamol sulphate, Drug Dev Ind Pharm, Online published 30/09/2001, 1057-62.

[20]. Evaluation of free films. Indian drugs. 1985; 23(1):45-7.

[21]. www.priory.com/pharmmol/transdermal/pdf

[22]. Prashant M, satturwar S, Fulzele V and Avinash K. dorle evaluation of polymerized rosin for the formulation and development transdermal drug delivery systems. AAPS Pharmscitech. 2005; 6(4):48-53.

[23]. Carmelo Puglia and Francesco Bonina. Effect of Polyunsaturated Fatty Acids and some conventional Penetration Enhancers on Transdermal Delivery of Atenolol. Drug Delivery. 2008; 15: 107–112.

Table 1: Formulation table of Ondansetron HCl Patches

Formulation	Polymer PVP/PVA	Polymer RLPM/RSPM	Polymer HPMC/PVP	Plasticizer	Oleic Acid	solvent
OND-1	7.3	-	-	PG(10%)	10%	WAT.
OND-2	5.5	-	-	PG(10%)	10%	WAT.
OND-3	-	5.5	-	DBP(5%)	10%	ACE.
OND-4	-	7.3	-	DBP(5%)	10%	ACE.
OND-5	-	-	7.3	DBP(5%)	10%	$CHCl_3$
OND-6	-	-	6.4	DBP(5%)	10%	$CHCl_3$

Table 2: Standard Calibration Curve Of Ondansetron HCL

Sr. No.	Concentration (µg/ml)	Absorbance
1	0	0
2	4	0.255
3	6	0.340
4	8	0.452
5	10	0.570
6	12	0.600
7	14	0.819
8	16	0.931

Table-3:SolubilityDataForOndasetronHcl

Solubility medium	Time Duration	Solubility (µg/ml)
Distilled water	24 hours	55.03 ± 4.25
	48 hours	76.94 ± 0.93
Buffer pH 7.4	24 hours	78.5 ± 1.48
	48 hours	93.13 ± 1.8

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Figure 1: Formulated Ondansetron HCl patches

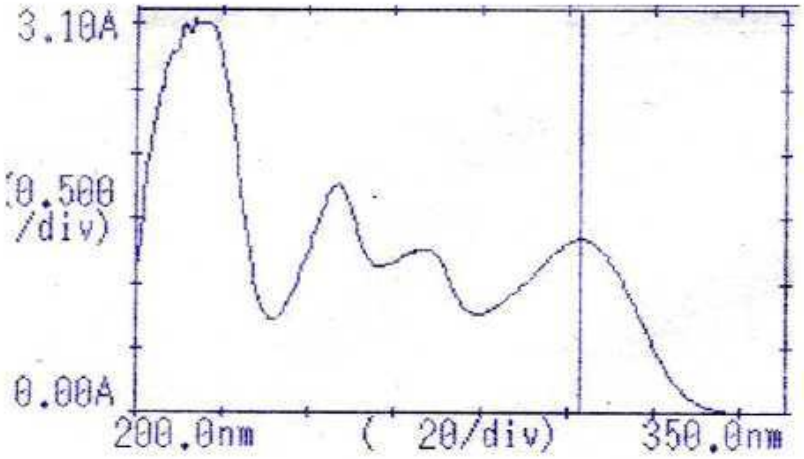

Figure 2: UV spectrum for Ondansetron HCl

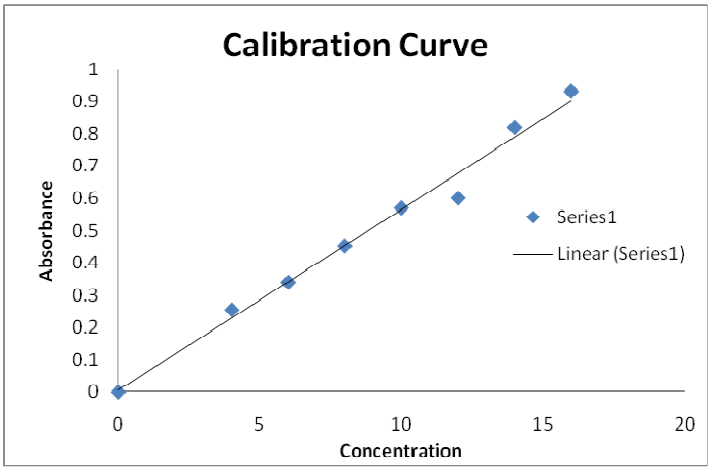

Figure 3: Calibration curve of Ondansetron HCl

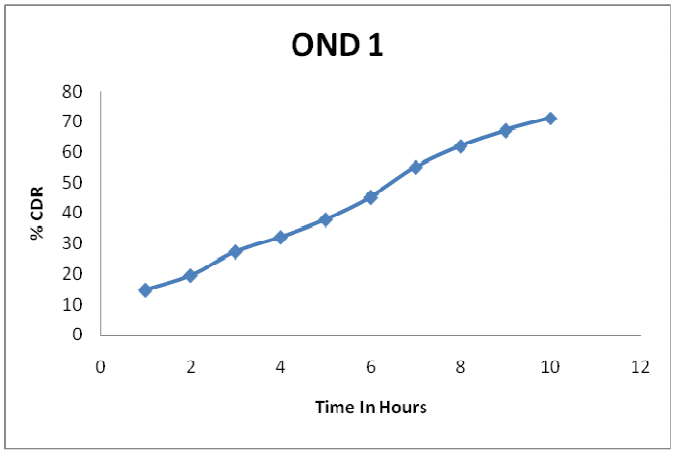

Figure 4: Ex vivo diffusion study of OND F1

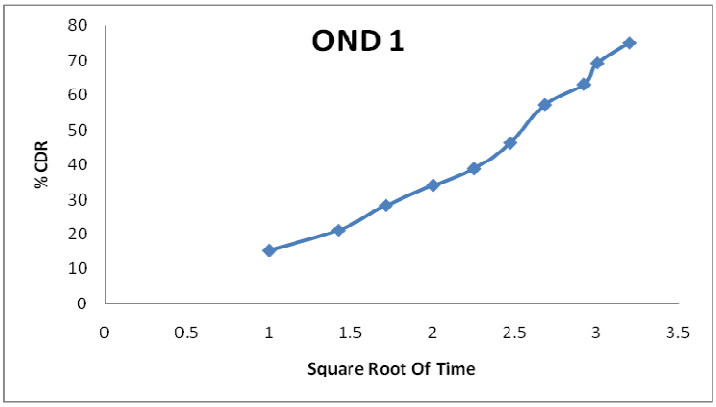

Figure 8: Higuchi's plot for OND

Table 11: Physicochemical evaluation data of Ondansetron HCl Transdermal patches

Formulation code	Thickness (mm) ± SD	Weight Variation (mg) ± SD	% Drug Content ± SD	Folding Endurance ± SD	Tensile Strength	% Elongation	% Moisture Absorption
OND 1	0.036 ± 1.3	66.89 ± 1.2	93.55 ± 0.2	76 ± 1	0.76	15.25 %	4.5 %
OND 2	0.025 ± 1.4	65.05 ± 1.6	93.82 ± 0.4	76 ± 2	0.75	22.89 %	5.07 %
OND 3	0.029 ± 1.5	62.50 ± 1.8	95.08 ± 0.3	79 ± 3	0.67	30.5 %	4.8 %
OND 4	0.033 ± 1.6	66.55 ± 1.6	95.90 ± 0.4	71 ± 0.9	0.71	23.86 %	3.5 %
OND 5	0.045 ± 1.2	63.45 ± 1.9	92.66 ± 0.5	77 ± 1	0.63	29.56 %	5.18 %
OND 6	0.048 ± 1.8	65.24 ± 1.8	95.16 ± 0.6	78 ± 2	0.59	20.54 %	3.9 %