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Development of Transdermal Drug Delivery for Antiemetic Drug

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ABSTRACT:
The aim of the present study was to develop and evaluate Hydrogel based transdermal delivery of Ondansetron hydrochloride. The different hydrophilic polymer HPMC K4 M and Citric acid as cross linking agent were used for the formulation of hydrogel. The prepared transdermal hydrogel were evaluated for different physicochemical evaluation, *invitro* drug release and characterization. All the hydrogels showed maximum release at 12h, the % Cumulative Drug Release was found between 75.47 % - 91.12%. Formulation F10 was selected as best formulation among F1-F17 formulations with 91.12% of drug release at 12h. The optimized formulation for formulation design was found to be F18 having the combination of drug (Ondansetron hydrochloride) and polymer (HPMC K4 M) & crosslinking agent (Citric acid) as which showed 82.33% of Drug Release at 12h, whereas iontophoretic optimized formulation F18I with a current density of 1.555mA showed 57.69% of *invitro* Drug release at 12h. The optimized formulation hydrogel were subjected to accelerated stability studies and were found stable at 40ºC/75% RH for 30 days according to ICH guidelines.

KEYWORDS: Ondansetron hydrochloride, Transdermal, HPMC K4 M, *in-vitro* permeation.

I. INTRODUCTION:

The development of a novel delivery system for existing drug molecules not only improves the drug"s performance in terms of efficacy and safety but also improves patient compliance and overall therapeutic benefit to a significant extent(1).Transdermal Drug Delivery System (TDDS) are self-contained, discrete dosage forms which when applied to the intact skin, deliver the drug at a controlled rate to the systemic circulation with minimal inter and intra patient variation. Hence bypasses first pass metabolism, enhancement of Therapeutic efficacy and maintenance of steady plasma level of drug(1). In general, the drug delivery potential of chemical modalities is limited. Therefore, physical permeation enhancement techniques gained a lot of focus in the recent past. The physical penetration enhancement techniques used to enhance permeation include iontophoresis, electroporation and sonophoresis(2). Delivery via the transdermal route is an interesting option because transdermal route is convenient and safe it Avoid of first pass metabolism, gastro-intestinal and Minimizing undesirable side effects(3). Skin is the most intensive and readily accessible organ of the body as only a fraction of millimeter of tissue separates its surface from the underlying capillary network. The release of a therapeutic agent from a formulation applied to the skin surface and Transdermal permeation is based on passive diffusion(4–6). Routes of Skin Penetration are appendageal route, transcellular route, and intercellular route(7–9). Hydrogel-based formulations are being looked at for transdermal iontophoresis to obtain enhancedpermeation of drug and other products like hormones and nicotine(10,11). Iontophoresis is the process of enhancing the permeation of topically applied therapeutic agents through the skin by the application of electric current. It involves the physiologically acceptable electrical currents (0.1–1.0 mA/cm2) to drive charged permeants into the skin through electrostatic effects and make ionic drugs pass through the skin into the body by its potential gradient(12). Types of iontophoresis are reverse iontophpresis, pulsatile or switching iontophoresis, iontophoresis and electrophoresis combination(13–15).

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II. MATERIALS AND METHODS:

Ondonsetron, HPMC K4 M, Potassium di-hydrogen orthophosphate, hydrochloric acid was received from yarrow chem products and citric acid from merk specialities pvt limited and sodium hydroxide from SD Fine-chem ltd.

FORMULATIONS OF ONDANSETRON TRANSDERMAL HYDROGEL

Preparation of transdermal Hydrogel

Transdermal Hydrogel containing Ondansetron were prepared by Chemical crosslinking method, using different ratios of HPMC K4 M and Citric acid. The Polymer(HPMC K4 M) in different ratios were dissolved in solvent(distilled water) and drug (ondansetron) dissolved in (0.1N Sodium hydroxide) then drug solution is added to the polymer solution,The Citric acid (crosslinking agent) solution is added to the drug-polymer solution under constant stirring,then it is homoginized for 20 minutes.solution were poured in to petridish allow to dry at 40±2^{0}C for 24hr to remove water, then samples kept at 80±2^{0}C for crosslinking reaction to obtain Hydrogel(16,17).

Formulation

Table. No 1: Percentage composition of Ondansetron formulations

Formulation code	Ondansetron (Drug) Polymer Ratio %	Citric acid Conc. %	Mixing Time min
F1	2	3	30
F2	1	6	30
F3	1.5	6	20
F4	1.5	3	40
F5	1.5	4.5	40
F6	1.5	4.5	30
F7	1	3	30
F8	1.5	4.5	30
F9	1.5	4.5	30
F10	2	6	30
F11	2	4.5	40
F12	1	4.5	40
F13	2	4.5	20
F14	1	4.5	20
F15	1.5	3	20
F16	1.5	6	40
F17	1.5	4.5	30

Iontophoretic system(18–20)

The Anode electrode was placed in the formulation in the donor compartment about 2mm above the cellulose acetate membrane. The cathode was inserted into the receptor compartment.

The combination of electric source (current), ionic permeant in reservoir system (therapeutic agent), the receiver compartment makes it an ideal iontophoretic system.

When the active and indifferent reservoir systems are placed on the skin, the current sources supply electronic current, which gets converted to ionic current when passed into the drug solution. The ionic current flows from the active reservoir, through and across the skin approaching the reservoir, and back through the skin into the reservoir. At the reservoir, it is transformed back into electronic current completing the circuit.

Evaluation(21,22)**:**

1. Physical apperance:

The physical appearance (i.e. color, clarity, and smoothness) and homogeneity of the prepared

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transdermal hydrogel tested by visual observations(21).

2. pH of determination

Hydrogel pH was measured by directly dipping pH meter rod into hydrogel.

Readings were taken in triplicate manner(21,23).

3. Determination of viscosity:

The viscosity of the Hydrogel formulations was determined using Brookfield viscometer with spindle no. 6 at 10 rpm at the temperature of 25^0C(24).

4. Spredability test

Spredability (gcm/sec) is expressed in terms of time taken in seconds by two slides to slip off from the hydrogel placed between them, under certain load. The standardized weight tied on the upper plate was 20 g and length of the glass slide was 7.5 cm. Spreadability was calculated by using the following formula(25):

$$\text{Spreadability} = \frac{\text{Weight} \times \text{Length}}{\text{Time}}$$

5. Drug content uniformity

Phosphate buffer of pH 7.4 was used to dissolve 1 ml of hydrogel and volume was made up to 10 ml. Drug content was deduced using UV-visible spectrophotometer at wavelength 310 nm after suitable dilution(26).

6. Swelling index

In order to measure swelling index of hydrogel, gravimetric method was used. Hydrogel with cross linker was dipped in buffer of pH 7.4. The swollen hydrogels were removed from medium and weighed at specific time interval of 0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4, 4.5 hours until the weight of swelled hydrogel became constant. Extra water was separated from hydrogel surface by slight tapping of surface with filter paper. Percentage swelling was measured using formula given below(27).

$$\text{Swelling\%} = \frac{w2 - w1}{w1} * 100$$

Where

W1= Initial weight of hydrogel

W2= weight after each sample

7. In-vitro Drug Diffusion Studies with and without iontophoresis:

In-vitro diffusion studies were performed by using a Franz diffusion cell with a receptor compartment capacity of 25 ml. The dialysis membrane was mounted between the donor and receptor compartment of the diffusion cell. The receptor compartment of the diffusion cell was filled with phosphate buffer pH 7.4 for Invitro diffusion study and for iontophoresis, the receptor compartment is filled with phosphate buffer pH7.4 and 75mM NaCl. The whole assembly was fixed on a hot plate magnetic stirrer, and solution in the receptor compartment was constantly and continuously stirred using magnetic beads and the temperature was maintained at 37 ± 0.5°C. The samples were withdrawn at different time intervals and analyzed for drug content spectrophotometrically. The receptor phase was replenished with an equal volume of phosphate buffer at each sample withdrawal(20,28).

8. Release kinetics

To analyse the mechanism of the drug release rate kinetics of the dosage form, the data obtained were plotted as:

a) Cumulative percentage drug released Vs time (In-Vitro drug release plots)

b) Cumulative percentage drug released Vs Square root of time (Higuchi‟s plots)

c) Log cumulative percentage drug remaining Vs Time (First order plots)

d) Log percentage drug released Vs log time (Peppas plots)

9. Stability studies of hydrogel

The purpose of stability testing is to provide evidence on how the quality of a drug substance or drug product varies with time under the influence of a variety of environmental factors such as temperature, humidity and light and to establish a retest period for the drug substance or a shelf life for the drug product and recommended storage conditions. To assess the drug and formulation stability, stability studies were done according to ICH guidelines.

Accelerated stability studies of hydrogel were carried out at temperature of 40^0C±2^0Cand relative humidity of 75% ± 5% for a period of 1 month (15 and 30 days). Hydrogel was evaluated for physicochemical properties(29).

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III. Results:

Evaluation of Transdermal Hydrogel:

Physical Appearance, pH and spredability of hydrogels.

Table No. 2: Physicochemical parameters of prepared formulations F1-F17

Formulation code	Appearence	Clarity	Homoginicity	pH	Spreadability (g.cm/sec)
F1	Colour less	Clear	Excellent	6.83	18.6
F2	Colour less	Clear	Excellent	6.98	19.5
F3	Colour less	Clear	Excellent	6.33	11.8
F4	Colour less	Clear	Excellent	6.47	15.3
F5	Colour less	Clear	Excellent	6.42	14.9
F6	Colour less	Clear	Excellent	6.85	17.5
F7	Colour less	Clear	Excellent	6.82	18.5
F8	Colour less	Clear	Excellent	6.36	10.9
F9	Colour less	Clear	Excellent	6.34	11.4
F10	Colour less	Clear	Excellent	6.47	14.7
F11	Colour less	Clear	Excellent	6.32	12
F12	Colour less	Clear	Excellent	6.74	15.3
F13	Colour less	Clear	Excellent	6.76	15.6
F14	Colour less	Clear	Excellent	6.37	16.7
F15	Colour less	Clear	Excellent	6.54	14.3
F16	Colour less	Clear	Excellent	6.89	18.4
F17	Colour less	Clear	Excellent	6.75	14.9

Table No. 3: Physicochemical parameters of prepared formulations F1-F17

Formulation Code	Viscosity	Swelling index	Drug diffusion	Drug content
F1	93.12	93.12	93.12	93.12
F2	89.21	89.21	89.21	89.21
F3	91.46	91.46	91.46	91.46
F4	89.98	89.98	89.98	89.98
F5	90.89	90.89	90.89	90.89
F6	90.87	90.87	90.87	90.87
F7	86.84	86.84	86.84	86.84
F8	90.88	90.88	90.88	90.88
F9	90.9	90.9	90.9	90.9
F10	95.94	95.94	95.94	95.94
F11	94.86	94.86	94.86	94.86
F12	88.42	88.42	88.42	88.42
F13	93.98	93.98	93.98	93.98
F14	87.72	87.72	87.72	87.72

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F15	89.09	89.09	89.09	89.09
F16	92.32	92.32	92.32	92.32
F17	90.85	90.85	90.85	90.85

7.4. In-Vtro Diffusion Study:

In vitro diffusion studies of Ondansetron transdermal hydrogel were carried out by using dialysis membrane and diffusion cell in PBS pH 7.4 solution.. The release data are given in the Table 3 for formulation F1 to F17.

Table No. 4: Comparative data of percentage drug release from the formulation of F1 to F9

Time(hr)	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
0	0	0	0	0	0	0	0	0	0
2	18.52	14.45	14.90	13.66	13.44	14.57	17.39	14.23	13.44
4	29.81	29.81	28.12	28.68	27.32	23.03	29.81	24.73	22.70
6	47.88	42.56	42.98	42.14	41.72	38.36	39.76	38.22	38.92
8	58.95	58.95	58.95	60.77	55.17	50.69	49.57	49.57	50.97
10	75.75	75.75	74.49	72.95	70.15	66.37	64.83	69.73	69.73
12	88.19	87.70	84.63	81.31	83.03	83.03	76.03	83.03	83.03

Table No. 5: Comparative data of percentage drug release from the formulation of F10 to F17

Time(hr)	**F10**	**F11**	**F12**	**F13**	**F14**	**F15**	**F16**	**F17**
0	0	0	0	0	0	0	0	0
2	14.57	16.60	13.66	15.47	14.57	14.57	15.47	14.45
4	24.95	25.74	20.78	28.68	24.73	22.70	23.37	28.68
6	38.36	40.18	40.18	39.76	35.98	37.38	37.38	42.98
8	59.93	53.77	49.57	55.73	49.57	51.39	49.57	53.77
10	81.77	74.77	59.65	72.95	64.97	63.57	63.57	68.47
12	91.14	89.30	75.42	87.70	77.63	79.72	76.40	83.03

Kinetics of drug release:

Table No.6 Comparison of zero order of in vitro drug release F1-F9

Time(hr)	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2	18.52	14.45	14.90	13.66	13.44	14.57	17.39	14.23	13.44

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4	29.81	29.81	28.12	28.68	27.32	23.03	29.81	24.73	22.70
6	47.88	42.56	42.98	42.14	41.72	38.36	39.76	38.22	38.92
8	58.95	58.95	58.95	60.77	55.17	50.69	49.57	49.57	50.97
10	75.75	75.75	74.49	72.95	70.15	66.37	64.83	69.73	69.73
12	88.19	87.70	84.63	81.31	83.03	83.03	76.03	83.03	83.03

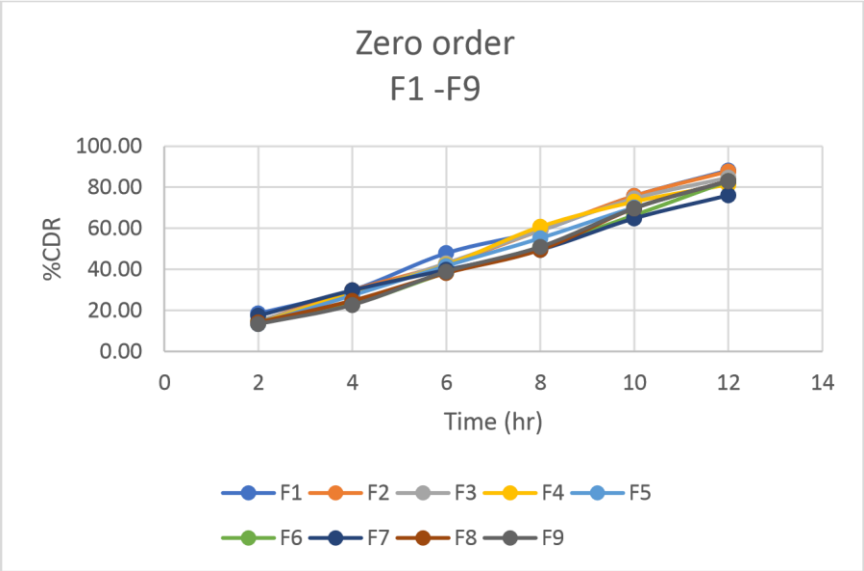

Fig.No. 1: Comparison of zero order of in vitro drug release of formulation F1-F9

Table No.7: Comparison of zero order of in vitro drug release F10-F17

Time(hr)	F10	F11	F12	F13	F14	F15	F16	F17
0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2	14.57	16.60	13.66	15.47	14.57	14.57	15.47	14.45
4	24.95	25.74	20.78	28.68	24.73	22.70	23.37	28.68
6	38.36	40.18	40.18	39.76	35.98	37.38	37.38	42.98
8	59.93	53.77	49.57	55.73	49.57	51.39	49.57	53.77
10	81.77	74.77	59.65	72.95	64.97	63.57	63.57	68.47
12	91.14	89.30	75.42	87.70	77.63	79.72	76.40	83.03

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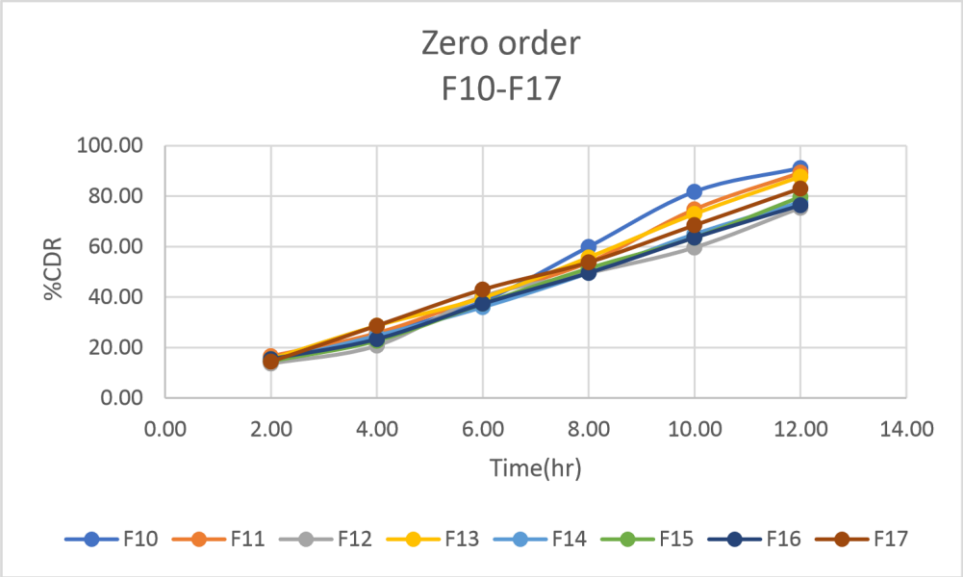

Fig.No.2: Comparison of zero order of in vitro drug release F10-F17

Table No.8: Comparison of First order of in vitro drug release F1-F9

Time(hr)	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2	1.91	1.93	1.93	1.94	1.94	1.93	1.92	1.93	1.94
4	1.85	1.85	1.86	1.85	1.86	1.89	1.85	1.88	1.89
6	1.72	1.76	1.76	1.76	1.77	1.79	1.78	1.79	1.79
8	1.61	1.61	1.61	1.59	1.65	1.69	1.70	1.70	1.69
10	1.38	1.38	1.41	1.43	1.47	1.53	1.55	1.48	1.48
12	1.07	1.09	1.19	1.27	1.23	1.23	1.38	1.23	1.23

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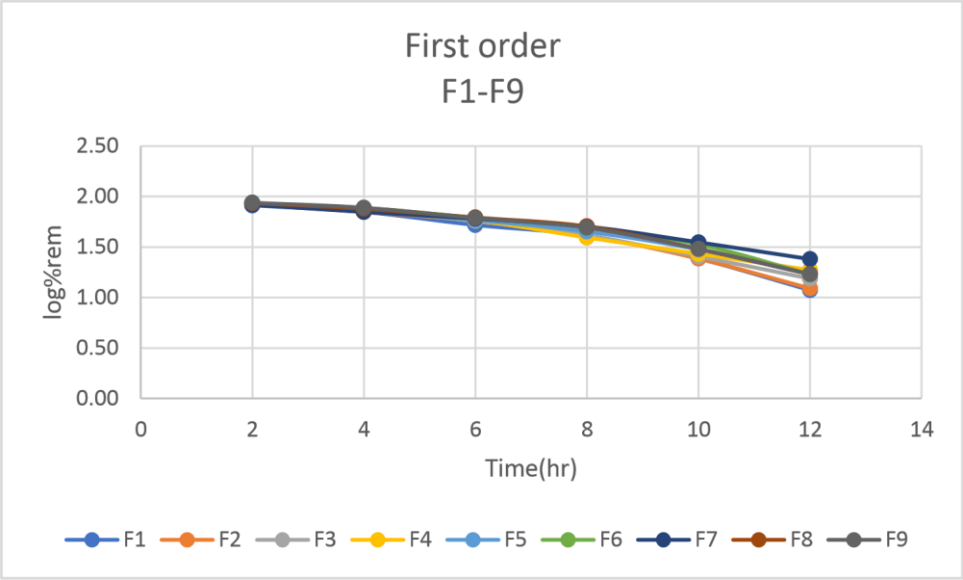

Fig.No.3: Comparison of First order of in vitro drug release F1-F9

Table No.9: Comparison of First order of in vitro drug release F10-F17

Time(hr)	F10	F11	F12	F13	F14	F15	F16	F17
0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2	1.93	1.92	1.94	1.93	1.93	1.93	1.93	1.93
4	1.88	1.87	1.90	1.85	1.88	1.89	1.88	1.85
6	1.79	1.78	1.78	1.78	1.81	1.80	1.80	1.76
8	1.60	1.66	1.70	1.65	1.70	1.69	1.70	1.66
10	1.26	1.40	1.61	1.43	1.54	1.56	1.56	1.50
12	0.95	1.03	1.39	1.09	1.35	1.31	1.37	1.23

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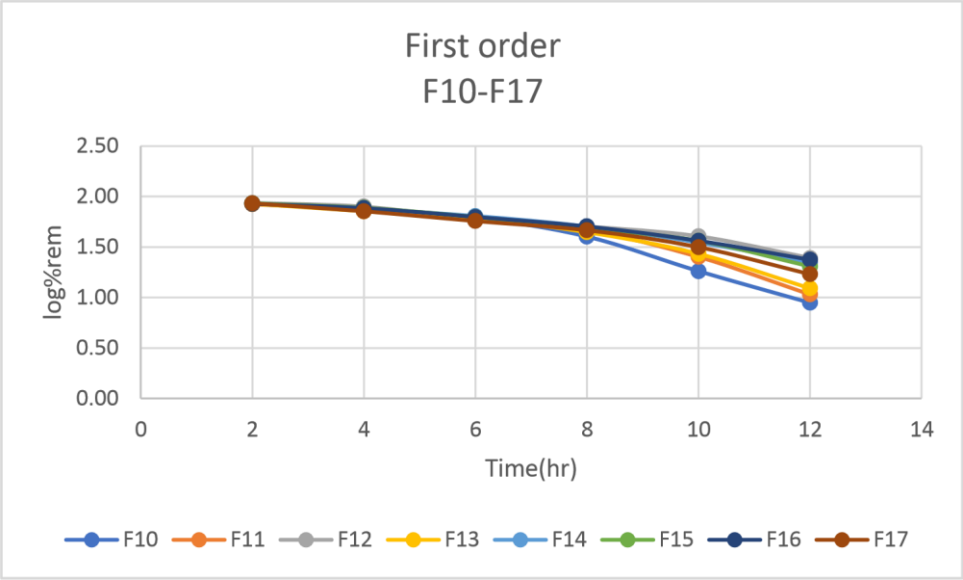

Fig.No.4: Comparison of First order of in vitro drug release F10-F17

Table No.10: Comparison of Higuchi model of in vitro drug release F1-F9

SQRT	F1	F2	F3	F4	F5	F6	F7	F8	F9
0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
1.41	18.52	14.45	14.90	13.66	13.44	14.57	17.39	14.23	13.44
2.00	29.81	29.81	28.12	28.68	27.32	23.03	29.81	24.73	22.70
2.45	47.88	42.56	42.98	42.14	41.72	38.36	39.76	38.22	38.92
2.83	58.95	58.95	58.95	60.77	55.17	50.69	49.57	49.57	50.97
3.16	75.75	75.75	74.49	72.95	70.15	66.37	64.83	69.73	69.73
3.46	88.19	87.70	84.63	81.31	83.03	83.03	76.03	83.03	83.03

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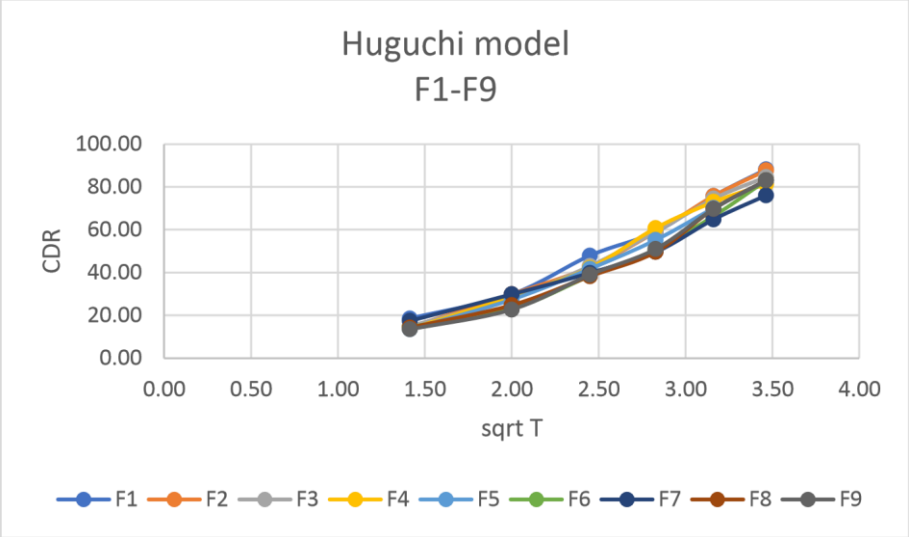

Fig.No.5: Comparison of Higuchi model of in vitro drug release F1-F9

Table No.11: Comparison of Higuchi model of in vitro drug release F10-F17

SQRT	F10	F11	F12	F13	F14	F15	F16	F17
0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
1.41	14.57	16.60	13.66	15.47	14.57	14.57	15.47	14.45
2.00	24.95	25.74	20.78	28.68	24.73	22.70	23.37	28.68
2.45	38.36	40.18	40.18	39.76	35.98	37.38	37.38	42.98
2.83	59.93	53.77	49.57	55.73	49.57	51.39	49.57	53.77
3.16	81.77	74.77	59.65	72.95	64.97	63.57	63.57	68.47
3.46	91.14	89.30	75.42	87.70	77.63	79.72	76.40	83.03

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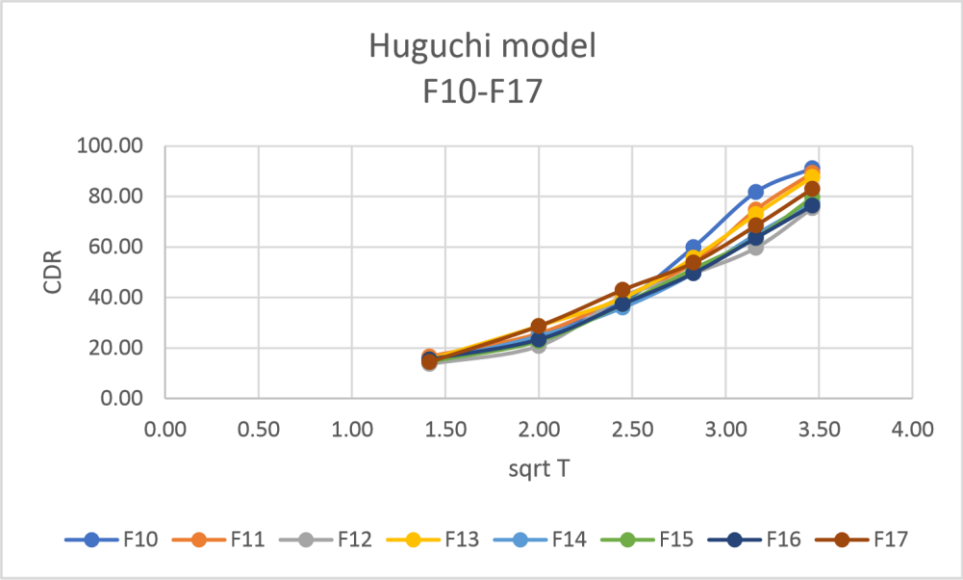

Fig.No.6: Comparison of Higuchi model of in vitro drug release F10-F17

Table No.12 Comparison of Korsmeyers-peppas equation of in vitro drug release F1- F9

logT	F1	F2	F3	F4	F5	F6	F7	F8	F9
0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
0.30	1.27	1.16	1.17	1.14	1.13	1.16	1.24	1.15	1.13
0.60	1.47	1.47	1.45	1.46	1.44	1.36	1.47	1.39	1.36
0.78	1.68	1.63	1.63	1.62	1.62	1.58	1.60	1.58	1.59
0.90	1.77	1.77	1.77	1.78	1.74	1.70	1.70	1.70	1.71
1.00	1.88	1.88	1.87	1.86	1.85	1.82	1.81	1.84	1.84
1.08	1.95	1.94	1.93	1.91	1.92	1.92	1.88	1.92	1.92

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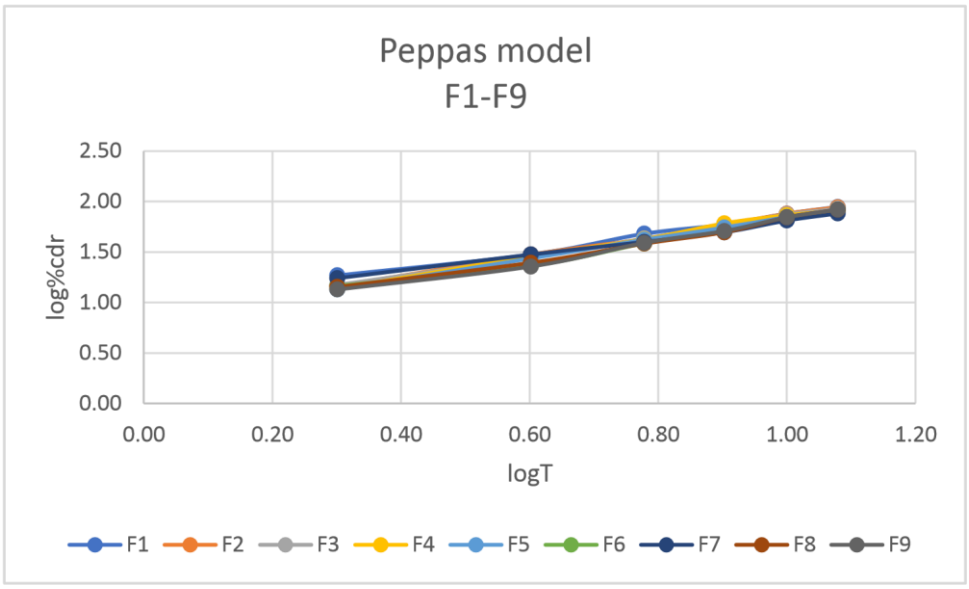

Fig.No.7: Comparison of Korsmeyers-peppas equation of in vitro drug release F1- F9

Table No.13: Comparison of Korsmeyers-peppas equation of in vitro drug release F10- F17

logT	F10	F11	F12	F13	F14	F15	F16	F17
0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
0.30	1.16	1.22	1.14	1.19	1.16	1.16	1.19	1.16
0.60	1.40	1.41	1.32	1.46	1.39	1.36	1.37	1.46
0.78	1.58	1.60	1.60	1.60	1.56	1.57	1.57	1.63
0.90	1.78	1.73	1.70	1.75	1.70	1.71	1.70	1.73
1.00	1.91	1.87	1.78	1.86	1.81	1.80	1.80	1.84
1.08	1.96	1.95	1.88	1.94	1.89	1.90	1.88	1.92

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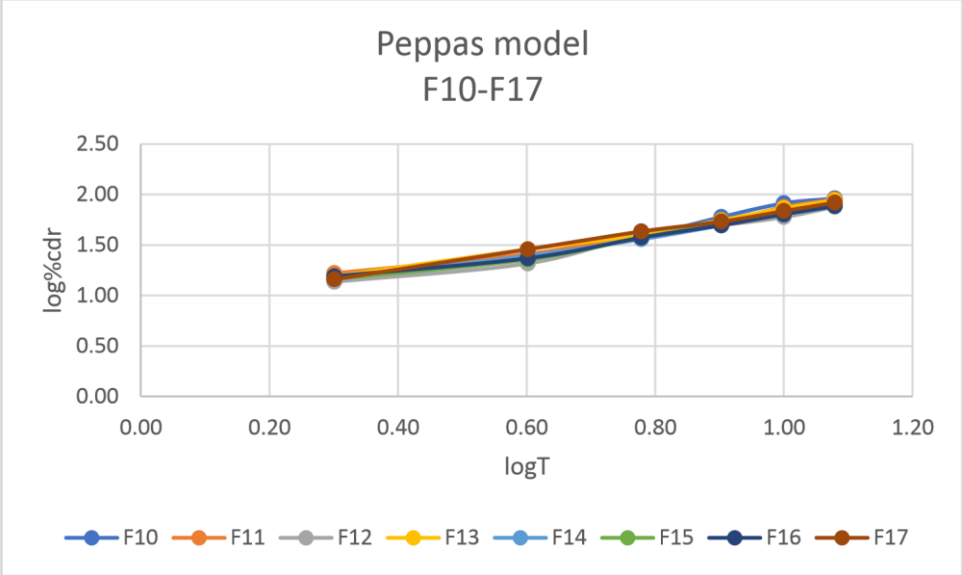

Fig.No.8: Comparison of Korsmeyers-peppas equation of in vitro drug release F10- F17

Table No. 14: Comparison of orders of in vitro release from the formulation F1 to F17

Formulation code	Zero Order	First Order	Higuchi	Peppas
F1	0.9969	0.9307	0.9797	0.9942
F2	0.9988	0.9365	0.9823	0.9969
F3	0.998	0.96	0.9847	0.9971
F4	0.9938	0.9811	0.9892	0.9904
F5	0.9998	0.9508	0.9853	0.9997
F6	0.9943	0.9108	0.9571	0.9983
F7	0.994	0.9542	0.9739	0.9895
F8	0.9933	0.9186	0.9568	0.9947
F9	0.9943	0.9289	0.9631	0.9964
F10	0.9865	0.9125	0.9529	0.9901
F11	0.9917	0.8861	0.9492	0.9969
F12	0.9924	0.95	0.9685	0.9737
F13	0.9969	0.9064	0.9659	0.9932
F14	0.997	0.9451	0.9648	0.9975
F15	0.996	0.9321	0.9631	0.9983
F16	0.997	0.951	0.9657	0.9992
F17	0.9989	0.938	0.9832	0.9976

IV. DISCUSSION:

The pure drug Ondansetron which was bought from Yarrow chem products, Mumbai, was used in the present investigation. In the present study, an attempt has been made to formulate Ondansetron loaded Transdermal hydrogel where HPMC K4 M was used as polymer base, citric acid as crosslinking agent. The prepared Ondansetron loaded Transdermal hydrogel were systematically subjected to physicochemical evaluation, *invitro* drug release and characterization.

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The observed melting point was found to be within range of the standard melting point of Ondansetron, therefore this indicates the purity of the drug sample. Transdermal hydrogel of Ondansetron were prepared successfully by chemical crosslinking method using HPMC K4M and citric acid as polymer and crosslinking agent respectively in different combinations and proportions.

The pH of the formulations F1 to F17 ranged from 6.32 to 6.98.The result results was found to be satisfactory and in the range **o**f 6-7.4.It can be concluded that the prepared hydrogels fulfilled the requirement of gel-based formulations for dermatological use.

Viscosity of the developed formulations F1 to F17 varied from753.16 to 844 cps and was found to be uniform. The viscosity increased with increase in (polymer) HPMC K4 M concentration.

spreadability of Ondansetron hydrogels decreased by increasing the Polymer (HPMC K4 M) concentration and the formulation F1 to F17 values were in the range of 10.9 to 19.5 gmcm/sec and The formulation F2 shows the maximum spredability compared to others due to low concentration of polymer(HPMC K4 M) and crosslinking agent (citric acid) ,F8 has low spredability due to high concentration of drug polymer ratio and citric acid concentration**.** It can be concluded that the prepared hydrogels fulfilled the requirement of gel-based formulations for dermatological use which should have several favorable properties such as greaseless and ease of spreadability.

The drug content was observed good uniformity in all transdermal Hydrogel Form the formulations F1 to F17 drug content is ranged from 86.84 to 95.94%. Swelling rages of hydrogel formulation F10 shows maximum swelling 85.68% and F7 shows minimum swelling 61.57%.

Formulation F1 to F17 exhibits drug release value in the range between 75.47% to 91.12%. it was observed that the formulation F1 and F17 has got maximum of drug release, this is because

of concentration of drug and HPMC K4 M, hydrophilic nature of HPMC K4 M which causes swelling due to the presence of large amount of water which is the main property of hydrogel, helps in the penetration drug and F10 formulation shows better drug release compared to others because of concentration of drug and HPMC K4 M, hydrophilic nature of HPMC K4 M which causes swelling.

The drug release data was fitted into the different models like zero order, first order, Korsmeyer Peppas and Higuchi equation for each formulations. It suggests that the release of drug from the formulations may follow any one of these models. F1 was found to follow zero order and higuchi equation.

V. Conclusion:

The present investigation was focused on formulation, evaluation and optimization of Ondansetron transdermal hydrogel by the application of Iontophoretic permeation enhancement technique and to increase the bioavailability of the drug and its half-life.

Preformulation studies for drug-polymer and drug cosslinking agent compatibility by FTIR gave confirmation about their purity and showed no interaction between the drug and selected polymer and crosslinking agent.

Various formulations of trandermal hydrogel were developed by using release rate controlling polymer like HPMC K4M and crosslinking agent like citric acid by chemical crosslinkig method. The used materials and method were found to be compatible and suitable for the study.

The formulations conducted for physicochemical parameters such as drug content uniformity, swellinking index, pH, viscosity, spredability were found to be within the limit of pharmacopoeial standards. Among F1-F18 formulations, F10 shows the good physicochemical parameters.

BIBILOGRAPHY:

[1]. Tanwar H, Sachdeva R. Transdermal Drug Delivery System: A Review.International Journal Of Pharmaceutical Science, 2016;7(6):2274-90.

[2]. Charoo NA, Rahman Z, Repka MA, Murthy SN. Electroporation: an avenue for transdermal drug delivery. Curr Drug Deliv. 2010 Apr;7(2):125–36.

[3]. Kaur T. Transdermal drug delivery system: Innovations in skin permeation. 2017;5.

[4]. Aulton ME. Pharmaceutics: The Science of Dosage Form Design. Churchill Livingstone; 1988. 734 p.

[5]. Chien YW. Novel drug delivery systems [Internet]. New York : M. Dekker; 1992 [cited 2024 Feb 1]. 826 p. Available from: http://archive.org/details/noveldrugdeliver50chie

[6]. Choudhary N, Singh A. Transdermal drug delivery system: A review. Indian J Pharm Pharmacol. 2021 Apr 28;8:5–9.
[7]. Naik A, Kalia YN, Guy RH. Transdermal drug delivery: overcoming the skin's barrier function. Pharm Sci Technol Today. 2000 Sep 1;3(9):318–26.
[8]. Rastogi V, Yadav P. Transdermal drug delivery system: An overview. Asian J Pharm. 2012 Jul 1;6:161.
[9]. Patel R, Baria AH. Formulation and evaluation considerations of transdermal drug delivery system. Int J Pharm Res. 2011 Jan 1;3:1–9.
[10]. Mohite PB, Adhav S. A hydrogels: Methods of preparation and applications. Int J Adv Pharm. 2017 Mar 27;6(3):79–85.
[11]. Ahsan A, Tian WX, Farooq MA, Khan DH. An overview of hydrogels and their role in transdermal drug delivery. Int J Polym Mater Polym Biomater. 2021 May 25;70(8):574–84.
[12]. Puranik P, Panzade P. IONTOPHORESIS: A FUNCTIONAL APPROACH FOR ENHANCEMENT OF TRANSDERMAL DRUG DELIVERY. Int J Pharm Biol Sci Arch [Internet]. 2021 Jun 4 [cited 2024 Feb 2];9(3). Available from: http://ijpba.in/index.php/ijpba/article/view/190
[13]. Dhote V, Bhatnagar P, Mishra PK, Mahajan SC, Mishra DK. Iontophoresis: a potential emergence of a transdermal drug delivery system. Sci Pharm. 2012;80(1):1–28.
[14]. Potts RO, Tamada JA, Tierney MJ. Glucose monitoring by reverse iontophoresis. Diabetes Metab Res Rev. 2002;18 Suppl 1:S49-53.
[15]. Banga AK, Bose S, Ghosh TK. Iontophoresis and electroporation: comparisons and contrasts. Int J Pharm. 1999 Mar 1;179(1):1–19.
[16]. Carvalho SM, Mansur AAP, Capanema NSV, Carvalho IC, Chagas P, de Oliveira LCA, et al. Synthesis and in vitro assessment of anticancer hydrogels composed by carboxymethylcellulose-doxorubicin as potential transdermal delivery systems for treatment of skin cancer. J Mol Liq. 2018 Sep 15;266:425–40.
[17]. Tavera-Quiroz MJ, Díaz JJF, Pinotti A. Characterization of Methylcellulose Based Hydrogels by Using Citric Acid as a Crosslinking Agent. 2018;13(17).
[18]. Barry BW. Novel mechanisms and devices to enable successful transdermal drug delivery. Eur J Pharm Sci Off J Eur Fed Pharm Sci. 2001 Sep;14(2):101–14.
[19]. Kalia YN, Naik A, Garrison J, Guy RH. Iontophoretic drug delivery. Adv Drug Deliv Rev. 2004 Mar 27;56(5):619–58.
[20]. Vemulapalli V, Banga AK, Friden PM. Optimization of iontophoretic parameters for the transdermal delivery of methotrexate. Drug Deliv. 2008 Sep;15(7):437–42.
[21]. Singh V, Chaubey N. Design and Evaluation of Topical Hydrogel Formulation of Aceclofenac for Improved Therapy. J Drug Deliv Ther. 2019 Sep 15;9:118–22.
[22]. Mankotia P, Choudhary S, Sharma K, Kumar V, Kaur Bhatia J, Parmar A, et al. Neem gum based pH responsive hydrogel matrix: A new pharmaceutical excipient for the sustained release of anticancer drug. Int J Biol Macromol. 2020 Jan 1;142:742–55.
[23]. Smith AA, Muthu AK, Rao WBP, Manavalan R. Formulation Development and Evaluation of Ondansetron Hydrochloride sustained release Matrix tablets. J Pharm Sci. 2009;
[24]. Ibrahim MM, Hafez SA, Mahdy MM. Organogels, hydrogels and bigels as transdermal delivery systems for diltiazem hydrochloride. Asian J Pharm Sci. 2013 Feb 1;8(1):48–57.
[25]. Newly Developed Topical Cefotaxime Sodium Hydrogels: Antibacterial Activity and In Vivo Evaluation - PubMed [Internet]. [cited 2024 Feb 9]. Available from: https://pubmed.ncbi.nlm.nih.gov/27314033/
[26]. Injectable in situ gel of methotrexate for rheumatoid arthritis: Development, in vitro and in vivo evaluation. J Appl Pharm Sci. 2019 May;9(5):40–8.
[27]. Qindeel M, Ahmed N, Sabir F, Khan S, Ur-Rehman A. Development of novel pH-sensitive nanoparticles loaded hydrogel for transdermal drug delivery. Drug Dev Ind Pharm. 2019 Apr;45(4):629–41.
[28]. Ammar HO, Mohamed MI, Tadros MI, Fouly AA. Transdermal Delivery of Ondansetron Hydrochloride via Bilosomal Systems: In Vitro, Ex Vivo, and In Vivo Characterization Studies. AAPS PharmSciTech. 2018 Jul;19(5):2276–87.
[29]. Injectable in situ gel of methotrexate for rheumatoid arthritis: Development, in vitro

and in vivo evaluation. J Appl Pharm Sci. 2019 May;9(5):40–8.