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FORMULATION AND EVALUATION OF ONDANSETRON HCL TRANSDERMAL PATCHES

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ABSTRACT

The skin can be used as the site for drug administration for continuous transdermal drug infusion into the systemic circulation. For the continuous diffusion penetration of the drugs through the intact skin surface membrane-moderated systems, matrix dispersion type systems, adhesive diffusion controlled systems and micro reservoir systems have been developed. Various penetration enhancers are used for the drug diffusion through skin. In matrix dispersion type systems, the drug is dispersed in the solvent along with the polymers and solvent allowed to evaporate forming a homogeneous drug-polymer matrix.

Matrix type systems were developed in the present study. In the present work, an attempt has been made to develop a matrix-type transdermal therapeutic system comprising of Ondansetron HCL with different concentration of various polymers alone using solvent evaporation technique. The physicochemical compatibility of the drug and the polymers was studied by infrared spectroscopy. The results obtained showed no physical-chemical incompatibility between the drug and the polymers. F5 formulation has been selected as the best formulation among all the other formulations. The in vitro drug diffusion studies from the formulation were found to be sustained release. All the evaluation parameters obtained from the best formulation were found to be satisfactory. The data obtained from the in vitro release studies were fitted to various kinetic models like zero order, first order,

Higuchi model and peppas model. From the kinetic data it was found that drug release follows peppas model release by diffusion technique from the polymer.

Keywords: Transdermal drug delivery, Ondansetron HCL, Eudragit-L100, Eudragit-S100

INTRODUCTION

Transdermal drug delivery The idea of delivering drugs through skin is old, as the use is reported back in 16th century B.C. Today the transdermal drug delivery is well accepted for delivering drug to systemic circulation. Until recently, the use of transdermal patches for pharmaceuticals has been limited because only a few drugs have proven effective delivered through the skin typically cardiac drugs such as nitroglycerin and hormones such as estrogen.

DEFINITION

Transdermal therapeutic systems are defined as self contained discrete dosage forms which, when applied to the intact skin, deliver the drug(s), through the skin, at controlled rate to the systemic circulation. The first Transdermal drug delivery (TDD) system, Transdermal-Scop developed in 1980, contained the drug Scopolamine for treatment of motion sickness. The Transdermal device is a membrane-moderated system. The membrane in this system is a microporous polypropylene film. The drug reservoir is a solution of the drug in a mixture of mineral oil and polyisobutylene. This study release is maintained over a one-day period.

Non-medicated patch markets include thermal and cold patches, nutrient patches, skin care patches (a category that consists of two major sub-categories — therapeutic and cosmetic), aroma patches, and weight loss patches, and patches that measure sunlight exposure. Transdermal drug delivery has many advantages over conventional drug delivery and can be discussed as follows.

MATERIALS AND METHOD MATERIALS

Ondansetron Hydrochloride, Eudragit-L100, Eudragit-S100, Dichloromethane, Dibutyl phthalate Methanol was provided by Centre of pharmaceutical sciences JNTU, Hyderabad.

METHODOLOGY

Table 1: Formulation of Ondesarton hydrochloride Patches

INGREDIENTS	FORMULATION CODE											
	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
Eudragit-L100 (%)	0.5	1.0	1.5	2.0	2.5	3.0	-	-	-	-	-	-
Eudragit-S100 (%)	-	-	-	-	-	-	0.5	1.0	1.5	2.0	2.5	3.0
Dichloromethane (%)	8	8	8	8	8	8	8	8	8	8	8	8
Methanol (%)	12	12	12	12	12	12	12	12	12	12	12	12
Dibutyl phthalate(mL)	25	25	25	25	25	25	25	25	25	25	25	25

RESULTS AND DISCUSSION

Initially the drug was tested by UV to know their significant absorption maximum which can be used for the diffusion study of the drug.

Analysis of drug

UV scans

The lambda max of Ondansetron HCL was found to be 305 nm.

B. construction of calibration curve:

Table 2: Standard graph of Ondansetron HCL

Concentration(µg/ml)	Absorbance (at 305 nm)
0	0
5	0.121
10	0.225
15	0.334
20	0.439
25	0.546

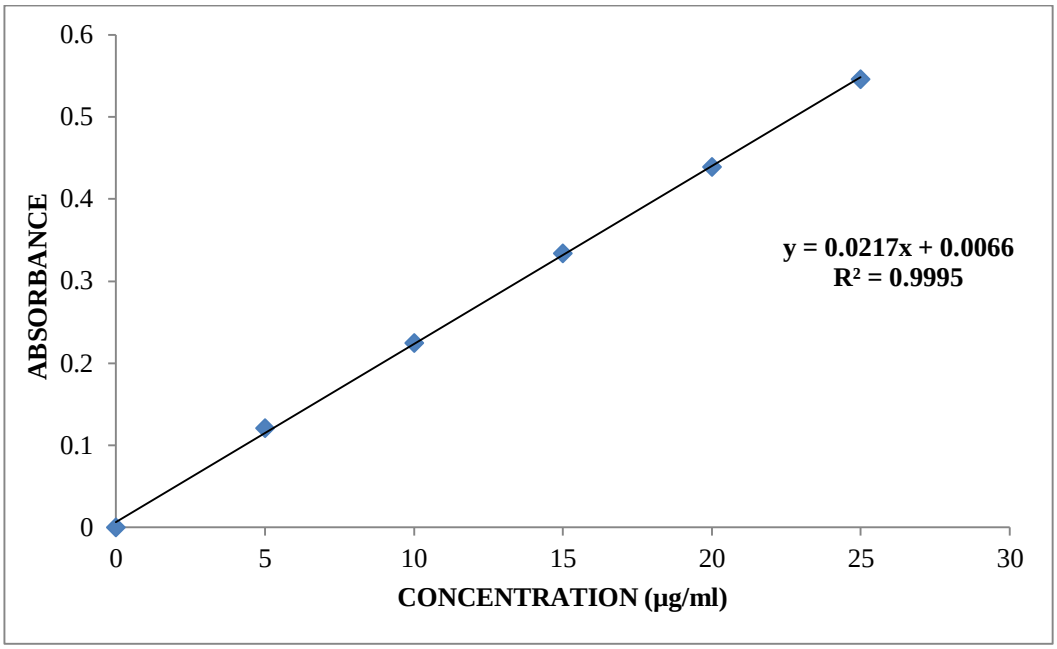

Figure 1: Standard calibration curve of Ondansetron HCL

Preformulation study

Totally, twelve formulation trials were done with the aim to achieve the successful matrix type Ondansetron HCL transdermal patches. The blend trials prepared for the drug was evaluated for various physical parameters and content uniformity of drug by UV.

A. Colour, odour, taste and appearance

Table 3: Results of identification tests of drug

Parameter	Ondansetron HCL
Color	White
Odor	Odorless
Taste	Bitter
Appearance	A whity powder

B. Melting point determination:

Table 4: Results of melting point determination tests of drug

Drug	Reported melting point
Ondansetron HCL	178.5 0c to 179.5 0c

C. Determination of solubility:

Table 5: Solubility Determination

Solvent	Drug solubility(mg/ml)
Distilled water	54.26
pH 7.4 phosphate buffer	77.23

Evaluation of Patch

The formulations F1 to F12 were varying in thickness when compared to other formulations which is due to the variation in the polymer concentration. Which shows the increase in polymer concentration increases the thickness of patch. For all other formulations it was found to be in between 0.041±0.007 to 0.051±0.004 mm.

All formulations from F1 to F 12 shows weight variation in between 70 ±9.58 to 79 ±6.85 mg.

Folding endurance from formulations F1 to F12 was found to be in between 81 ± 0.15 to 89 ± 2.15 which can withstand the foldings of the skin.

All formulations showed % drug content from 95.1 ± 2.61 to 99.74 ± 1.57.

Table 6: Evaluation of patches

Formulation Code	Average weight(mg)	Thickness (mm)	Folding endurance	Flatness (%)	Appearance	% Drug Content
F1	75±1.05	0.046 ± 0.003	81 ± 0.15	100	Transparent	97.11 ± 2.10
F2	78 ±5.36	0.049±0.008	86 ± 1.39	99	Transparent	98.28 ± 0.45
F3	71 ±2.84	0.051±0.004	85 ± 2.26	100	Transparent	97.69 ± 2.21
F4	75 ±5.41	0.041±0.009	80 ± 1.84	100	Transparent	95.10 ± 2.61
F5	77 ±9.18	0.049±0.004	82 ± 3.10	100	Transparent	99.95 ± 3.87
F6	79 ±4.69	0.041±0.007	89 ± 2.15	100	Transparent	98.35 ± 0.59
F7	70 ±9.58	0.047±0.001	84 ± 2.36	99	Transparent	99.11 ± 2.34
F8	76 ±3.86	0.045±0.009	87 ± 2.04	100	Transparent	99.74 ± 1.57

F9	74 ±7.29	0.048±0.006	82 ± 2.96	100	Transparent	98.48 ± 0.44
F10	79 ±6.85	0.043±0.001	88 ± 4.64	99	Transparent	97.10 ± 2.91
F11	76 ±8.94	0.049±0.006	83 ± 1.72	100	Transparent	98.87 ± 2.48
F12	78 ±8.49	0.047±0.005	87 ± 2.68	100	Transparent	99.45 ± 2.61

In vitro diffusion study:

All the formulation in vitro diffusion study was carried out by using Franz type diffusion cell under specific condition such as temp maintained at 32 ± 0.5 oC. The diffusion was carried out for 12 h and 5 ml sample was withdrawn at an interval of 1 h.

Table 7: In vitro drug permeation of Ondansetron HCL containing different concentrations of Eudragit-L100

Time (hr)	F1	F2	F3	F4	F5	F6
0	0	0	0	0	0	0
1	4.22	7.04	2.81	3.68	4.56	2.17

2	13.57	14.07	10.37	7.29	10.32	9.74
3	16.78	22.00	15.20	13.04	16.44	16.54
4	20.09	28.75	23.03	20.61	21.80	22.20
5	28.77	30.42	30.43	24.68	29.08	29.44
6	36.28	39.25	38.17	29.30	35.44	35.87
7	54.93	48.77	43.39	36.94	51.36	42.76
8	66.75	56.42	46.45	45.22	67.97	50.62
9	73.37	60.38	54.91	57.35	76.35	58.26
10	79.12	76.86	60.38	74.73	82.15	62.79
11	83.69	86.19	64.99	89.11	95.64	72.08
12	97.29	89.22	69.51	92.89	99.12	81.32

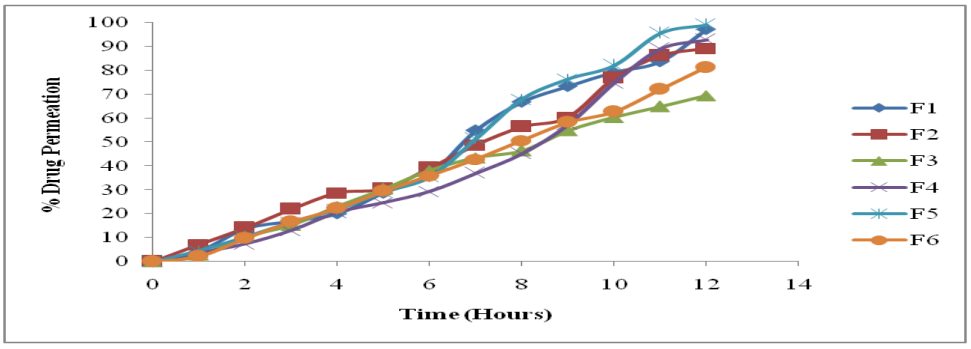

Figure 2: Cumulative % drug permeation of Ondansetron HCL patch (F1, F2, F3, F4, F5 and F6)

The formulations F1 to F6 were prepared by different concentrations of Eudragit-L100 (0.5, 1.0, 1.5, 2.0, 2.5, 3.0 %) in 2*2 cm2patch, the drug release or drug permeation from the patch was dependence on the concentration of polymer in the matrix. At low polymer concentration the drug permeation is more within 12 hours it was total amount of drug was permeated. The 2.5% concentration of polymer was showed maximum drug released at 12 hours 99.12%. Hence in that 6 formulation F5 formulations showed total drug release at desired time period.

Table 8: In vitro drug permeation of Ondansetron HCL containing different concentrations of Eudragit-S100

Time	F7	F8	F9	F10	F11	F12
0	0	0	0	0	0	0
1	5.14	7.29	4.98	6.26	5.11	7.45
2	8.66	11.63	9.35	9.95	10.65	13.56
3	12.73	16.13	12.70	15.46	19.27	22.72
4	17.65	23.80	17.74	21.10	25.49	34.94
5	23.22	29.10	22.88	28.10	33.63	47.88
6	30.49	35.54	29.18	34.02	41.60	53.46
7	36.73	40.81	33.99	39.85	49.35	62.87
8	44.30	48.21	41.40	47.21	53.61	69.01
9	53.10	67.06	47.78	57.23	63.49	79.70
10	66.08	78.10	54.20	64.04	70.45	85.64
11	79.99	82.64	60.21	69.71	79.33	90.31
12	82.33	86.78	65.52	76.69	83.80	94.75

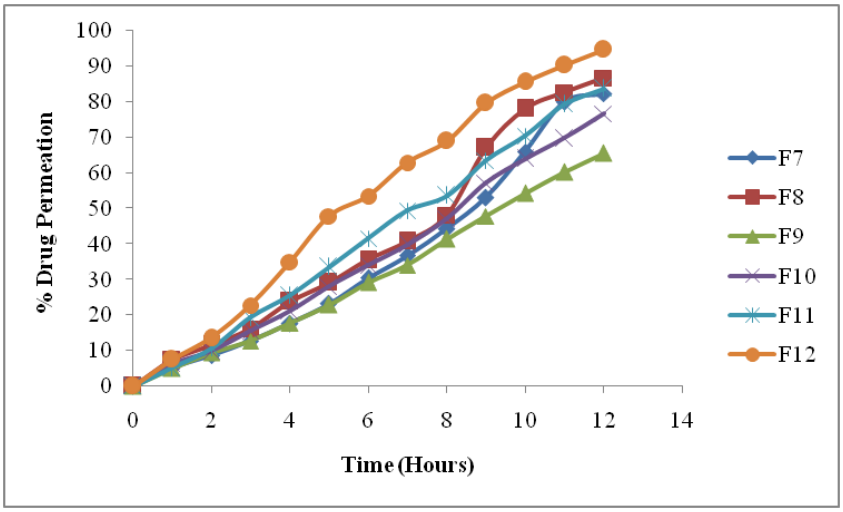

Figure 3: Cumulative % drug permeation of Ondansetron HCL patch (F7, F8, F9, F10, F11 and F12)

The formulations F7 to F12 were prepared by different concentrations of Eudragit-S100 (0.5, 1.0, 1.5, 2.0, 2.5, 3.0%) in 2*2 cm2 patch the drug release or drug permeation from the patch was dependence on the concentration of polymer in the matrix. The 0.5% (F7) concentration of polymer was showed maximum drug release 79.99 within 11 hours. The 1.0% (F8) concentration of polymer was showed maximum drug released at 12 hours 86.78%. The 1.5% (F9) concentration of polymer was showed less drug release 62.15 at 12 h. The 2.0% (F10) concentration of polymer was showed maximum drug released at 12 hours 76.69%. The 2.5% (F11) concentration of polymer was showed maximum drug released at 12 hours 83.80%. The 3.0% (F12) concentration of polymer was showed maximum drug released at 12 hours 94.75%.

Hence in that 6 formulations F12 formulations showed total drug release at desired time period.

Among all 12 formulations F5 formulation showed good drug permeation from the patch.

Among all in vitro evaluation parameters F5 formulation passed all evaluation parameters.

Kinetic models for Ondansetron HCL

Various models were tested for explaining the kinetics of drug release. To analyze the mechanism of the drug release rate kinetics of the dosage form, the obtained data were fitted into zero-order, first order, Higuchi, and Korsmeyer-Peppas release model.

Table 9: Kinetics data of F5 Ondansetron HCL patch

CUMULATIVE (%) RELEASE Q	TIME (T)	ROOT (T)	LOG(%) RELEASE	LOG (T)	LOG (%) REMAIN	RELEASE RATE (CUMULATIVE % RELEASE / t)	1/C RE
0	0	0			2.000		
18.6	1	4.560	1.270	0.000	1.911	18.600	0.0
27.1	2	10.320	1.433	0.301	1.863	13.550	0.0
34.3	3	16.440	1.535	0.477	1.818	11.433	0.0
46.6	4	21.800	1.668	0.602	1.728	11.650	0.0
51.6	5	29.080	1.713	0.699	1.685	10.320	0.0
59.8	6	35.440	1.777	0.778	1.604	9.967	0.0
66.4	7	51.360	1.822	0.845	1.526	9.486	0.0
72.8	8	67.970	1.862	0.903	1.435	9.100	0.0

79.9	9	76.350	1.903	0.954	1.303	8.878	0.0
85.3	10	82.150	1.931	1.000	1.167	8.530	0.0
92.6	11	95.640	1.967	1.041	0.869	8.418	0.0
95.9	12	99.120	1.982	1.079	0.613	7.992	0.0

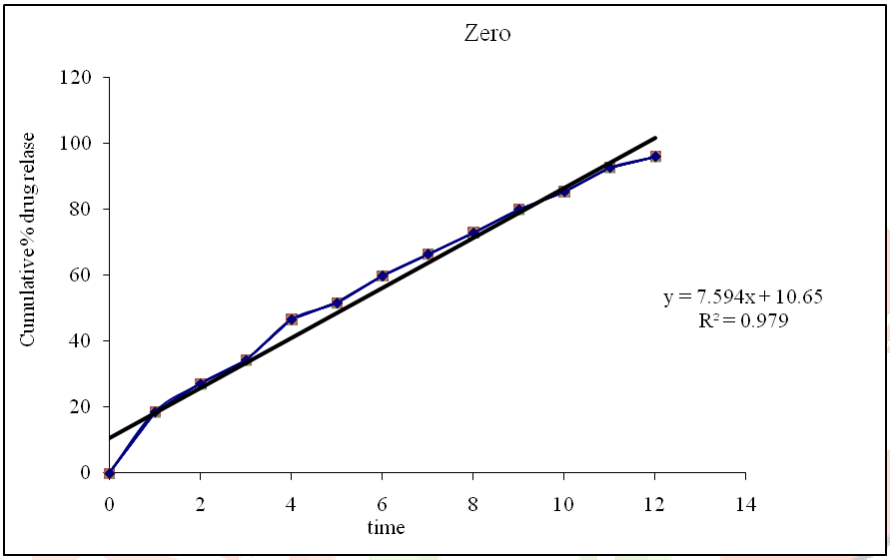

Figure 4 : Graph of Zero order kinetics

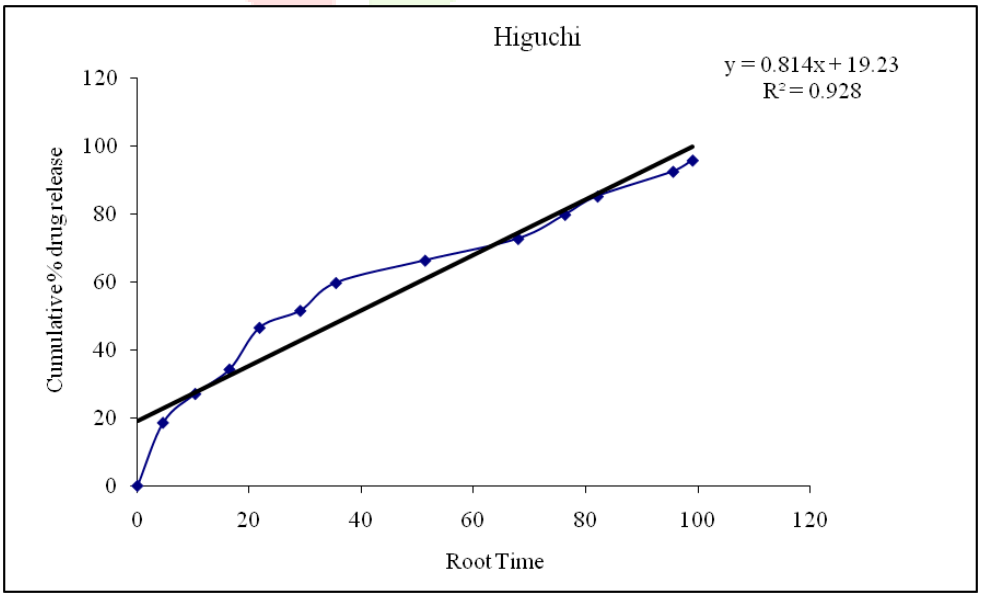

Figure 5 : Graph of Higuchi release kinetics

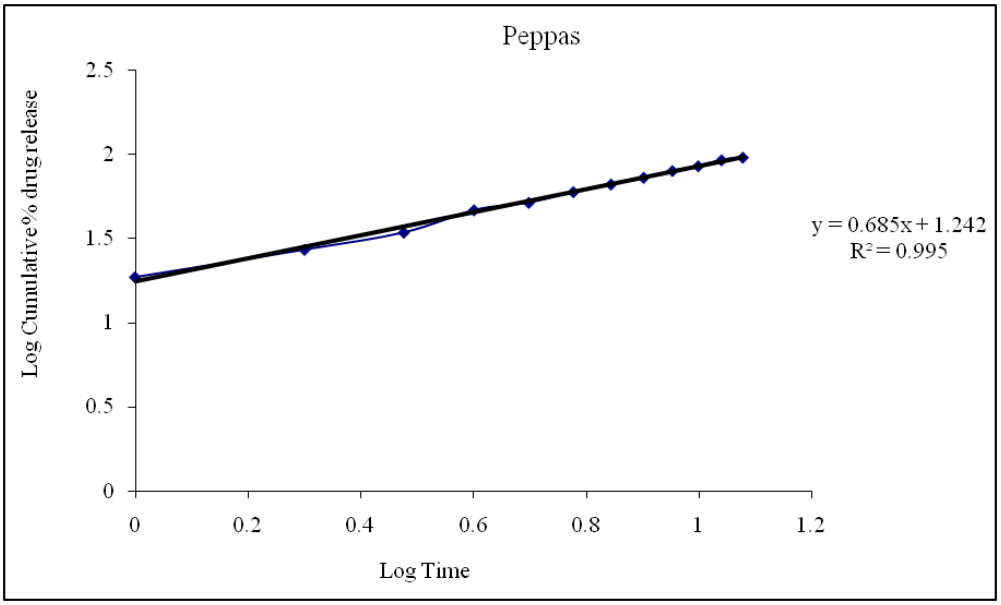

Figure 6 : Graph of peppas release kinetics

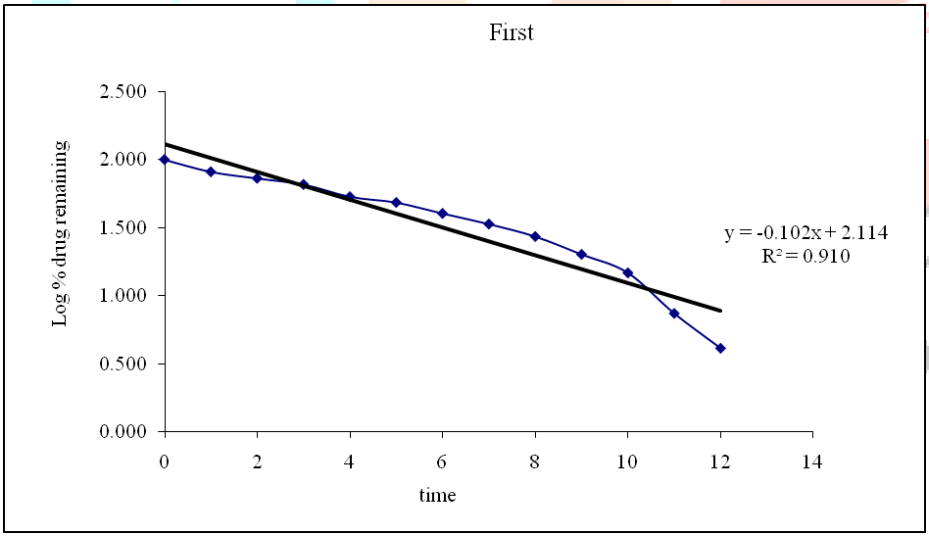

Figure 7 : Graph of First order release kinetics

From the above data the optimized formulation followed peppas model rule.

Compatibility studies:

IR SPECTROSCOPY:

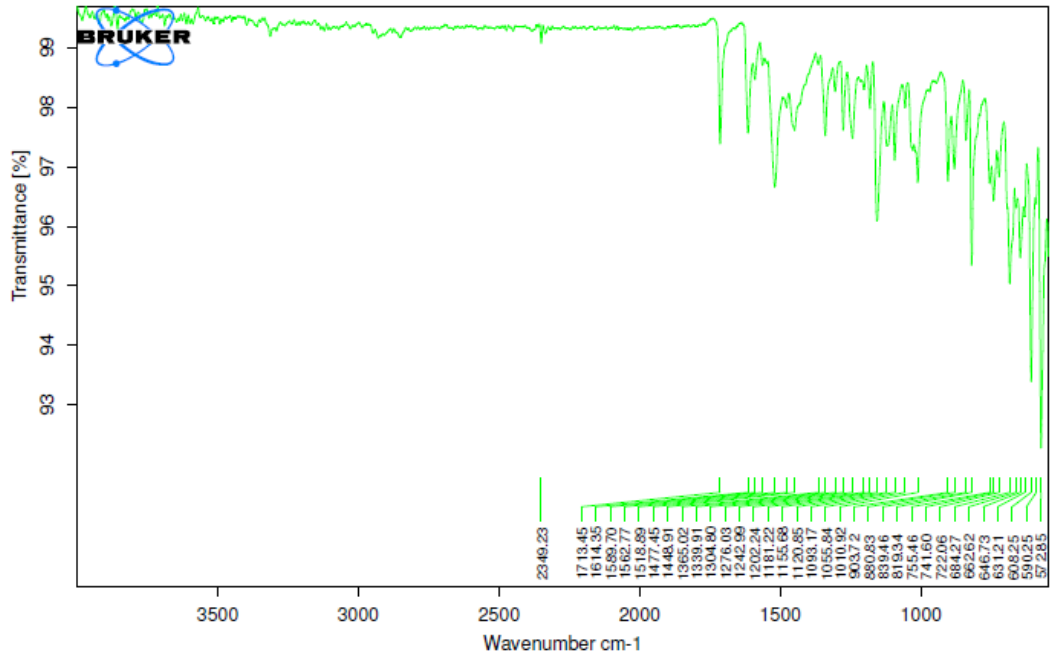

Figure 8: FTIR Spectrum of pure Ondansetron HCL drug

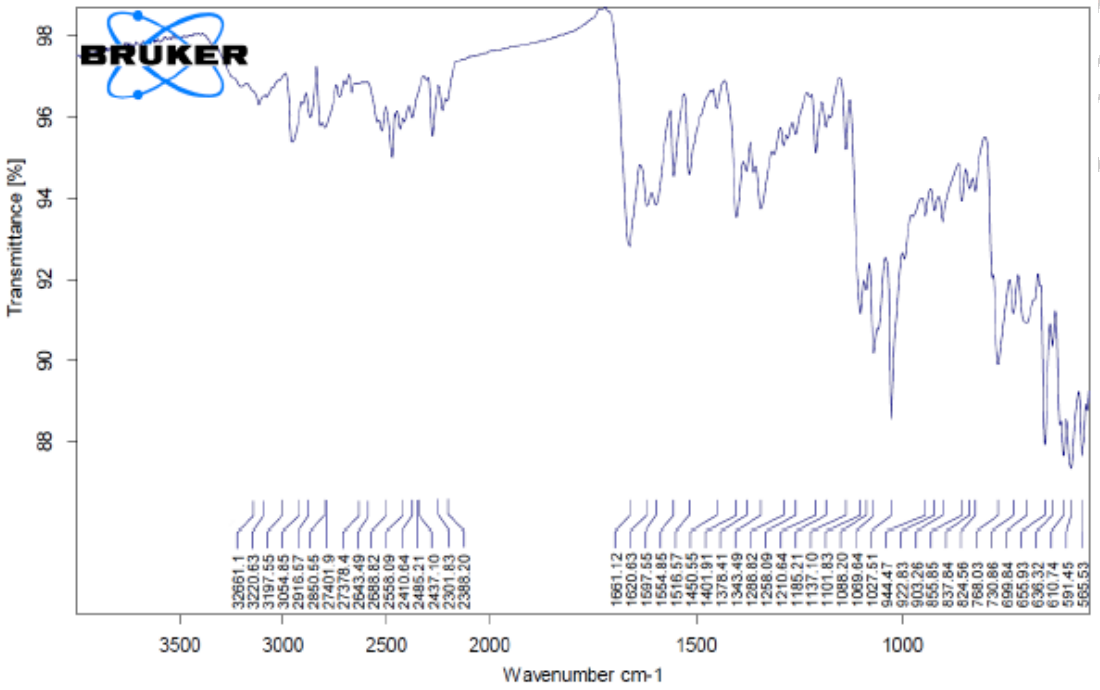

Figure 9: FTIR of Optimized formulation

The compatibility studies of the drug with excipients indicate no characteristic visual changes and no additional peaks were observed during FT-IR studies.

Conclusion

In the present investigation an attempt has been made to design and develop the formulation of Ondansetron hydrochloride patches using different types of polymers by solvent evaporation technique and mercury substrate method. The drug used is the best studied for therapy in treating hypertension.

Ondansetron hydrochloride was successfully formulated as controlled release transdermal patches, which prevents the frequency of administration and gives good patient compliance.

From the experimental results obtained, F5 formulation has been selected as the best formulation among all the other formulations. The in vitro drug diffusion studies from the formulation were found to be sustained release. All the evaluation parameters obtained from the best formulation were found to be satisfactory.

The data obtained from the in vitro release studies were fitted to various kinetic models like zero order, first order, Higuchi model and peppas model.

From the kinetic data it was found that drug release follows peppas order release by diffusion technique from the polymer.

Based on the observations, it can be concluded that the attempt of formulation and evaluation of the Ondansetron hydrochloride patches was found to be successful in the release of the drug for an extended period of 12 hrs.

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