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Evaluating the efficacy of transdermal patches of ciprofloxacin hydrochloride after their formulation and administration

Neha Mishra
Department of Pharmacy, IIMT College of Pharmacy, Greater Noida, India.
Corresponding author email: mishraneha179506@gmail.com

Dr. Pushpendra Jain
Department of Pharmacy, IIMT College of Pharmacy, Greater Noida, India.

***Abstract*---**Aim: To formulate and evaluate of transdermal patches of ciprofloxacin hydrochloride. Materials and Methods: To maximise bioavailability by avoiding pre-systemic hepatic metabolism, an effort was made to design a transdermal treatment system for Ciprofloxacin hydrochloride employing polymers such as HPMC, EC, and ERS100. Physical and chemical characteristics, in vitro drug release investigations and stability experiments were carried out on the prepared patches. Results: T1, T8, and T15 formulations were chosen for stability experiments at room temperature and 40 °C for a period of 45 days, respectively. The findings of the stability experiments indicated that the prepared patches may be stored for up to 45 days. The T8 formulation has shown promising results, thus the correct method should be used for commercial and scale manufacturing. Conclusion: The effectiveness of these patches will need to be studied over the course of many years in pharmacokinetic and pharmacodynamic investigations.

***Keywords*---**Ciprofloxacin hydrochloride, *in-vitro* drug release studies, stability, transdermal patches

Introduction

The pharmaceutical sciences, in particular drug delivery technologies, have seen some dramatic advancements in this century [1]. Modern drug delivery methods are gaining popularity as people become more aware of the dangers of traditional methods of administering and applying drug [2]. This means that multidose drug formulations, such as oral liquids and tablets that are delivered in many doses, tend to create substantial fluctuations in drug concentration in the bloodstream [3].

Aside from therapeutic efficacy, the driving force for the development of innovative drug delivery methods is cost [4]. Developing a new drug typically costs $250 million (about Rs. 900 crores) and takes 1215 years from start to finish [5]. Developing a novel drug delivery system from an existing drug molecule can be done in half the time and at a 20% lower cost than developing a new drug [6].

Materials and Methods

Materials

Ciprofloxacin hydrochloride was given gift sample from Fourrts India Pvt, Ltd. Hydroxy Propyl Methyl Cellulose, Ethyl Cellulose, Eudragit were provided by reputed labs. Analytical-grade materials were used for everything else.

General method of preparation of transdermal patches:

Molding methods were used to create Ciprofloxacin hydrochloride transdermal patches of the matrix type in this investigation [7]. This project required the use of a circular glass mould with a diameter of 4.5 cm and a height of 1 cm, which resulted in a total surface area of 15.91cm^2 being made.

A) preparation of casting solutions:

A 1:1 combination of chloroform and methanol was used to dissolve weighed amounts of polymers in the casting solutions [8]. In order to create a homogeneous mixture of the different polymer solutions, the medication, plasticizer, and permeation enhancers were separately added and well combined [9]. It was set aside to enable the trapped air to bubble to the surface.

B) preparation of transdermal patches:

Each of the circular glass moulds is filled with 3 cc of casting solution, which will be poured over the mercury surface after the moulds have been set. After being allowed to cure for 24 hours at room temperature, the glass moulds holding the casting solutions were baked for 30 minutes at 40-45 degrees Celsius to eliminate any remaining solvents [10]. Following the removal of the patches from the clothes, discs with a diameter of 4.4cm were cut from them (15.21cm^2 surface area). They were placed in a desiccator in preparation for future research.

Evaluation of Transdermal Patches

The generated patches' physicochemical properties, in vitro diffusion experiments, skin irritation, and stability studies were all evaluated in depth 11.

Physico- Chemical Parameters: [12]

Evaluations were made based on the following variables.

Film thickness:

In order to get an average thickness, six measurements were made using an Electronic Digital Micrometer (AEROSPACE- CHINA).

Determination of average weight and weight variation:

Using an electronic scale, researchers weighed six patches in order to see whether there were any changes in drug content or in-vitro behaviour between the patches that were made. The patch's average weight and standard deviation were determined using the following calculations.

Average weight of each patches = Total weight of 5 patches/5

$$\text{Standard deviation} : \sigma = \sqrt{\frac{\sum(x_i - \mu)^2}{N}}$$

Where x = Weight of individual patch; X = average weight; n = number of patches

Determination of tensile strength:
To evaluate tensile strength, we employed an apparatus developed in our laboratory. A clip fastened the static end of the strip to the moveable rod of a railing and the moving end to the static end of the strip. In order to enhance the pulling power, the weights were progressively added to the pan. The elongation was calculated at the same time by making a note on the graph paper of the distance travelled by the pointer before the film broke. As a result of this measurement, the film's break force was recorded.

Determination of hardness:
A wooden platform with a top surface of 16 × 16 cm and a height of 11 cm was built in our lab to measure the strips' hardness. On one end of the iron rod, a tiny pan was placed horizontally while the other end was reduced to a sharp point. A 0.2 cm-diameter hole was drilled onto the top of the wooden stand to hold the pan rod. A 3-volt battery was used to create an electric circuit that only works when the metal plate and the pointy end of the rod come into contact. The film was sandwiched between a metal plate and the pointed end of the metal rod." Weaker weights were introduced progressively, every 10 seconds for a few seconds, until a light bulb appeared. As a measure of hardness, the final weight was taken into account.

Determination of percentage moisture content:
A patch's mechanical strength and drug release behaviour may be affected by its moisture content, hence the moisture content of the designed patch was evaluated in this work by placing the patch under vacuum desiccation and weighing it repeatedly until consistent weights were achieved. The following calculation was used to determine the patch's moisture content.
Percentage moisture content = Initial weight - Final weight / Initial weight

Determination of percentage moisture uptake:
Excess moisture in a desiccator (a saturated solution of sodium chloride) was added to the desiccator to keep the film at a consistent weight for 24 hours before it was removed and subjected to 75 percent relative humidity (a saturated solution of sodium chloride) in the desiccator.
Percentage moisture uptake = final weight- initial weight / final weight

Determination of drug content:
Small sections of a 15.21cm^2 patch were cut and placed in a graduated glass stoppered flask, which was kept at 45-50°C with a 1:1 combination of chloroform and methanol. For 24 hours, it was placed in a shaker and rapidly shaken. Shimadzu UV-1700 at 241 nm was used to quantify the quantity of medication in the filtrate. A fake patch was also used to produce blank solution. It was necessary to do the test twice in order to ascertain the concentration of the

medication. To find out how much medication was in each vial, the researchers performed the steps listed below twice.

Procedure for *in-vitro* drug release studies:

Franz diffusion cells were used to conduct in vitro permeation investigations. Both the donor and the receptor compartments are included. A cellulose membrane separated the diffusion cell's donor and receptor sections. The custom-made patches protected the membrane from damage. The receptor compartment of the diffusion cell was filled with phosphate buffer pH 7.4. At 50 rpm, magnetic beads were used to constantly mix the solution in the receptor compartment while the whole system was positioned on a magnetic stirrer. A temperature of 371 °C was maintained throughout the experiment. The drug content was determined by taking samples at various times and analysing them. Each time a sample was taken, the phosphate buffer in the receptor phase was refilled with an equivalent amount. Time was plotted against the cumulative proportion of medication released per patch area.

Stability Studies

Drug dosage forms must be designed and evaluated with the active ingredient's stability in mind. The appearance, colour, flavour, taste, or texture of a medication formulation may vary over time as a result of the drug's stability. When chemical changes aren't immediately apparent, they may be discovered by chemical analysis. Data collected by scientists on a formulation's stability allows the proposed product's shelf life to be accurately predicted and, where required, dosage forms may be reformulated.

Therefore, the chosen films were stored at room temperature and at 40 °C for 45 days in order to evaluate their long-term stability. Physical and chemical characteristics, as well as *in-vitro* diffusion experiments, were assessed in patches on days 15^{th}, 30^{th}, and 45^{th}.

Results and Discussion

General method of preparation of transdermal patches:

Molding methods were used to create Ciprofloxacin hydrochloride transdermal patches of the matrix type in this investigation. For this project, a flat circular glass mould with diameter 4.5 cm and a height of 1 cm was produced with a total surface area of 15.91cm^2.

Table 1: Ciprofloxacin hydrochloride transdermal patches compositions

"Ingredients	T_1	T_2	T_3	T_4	T_5	T_6	T_7	T_8	T_9	T_{10}
Ciprofloxacin hydrochloride in (mg)	10	10	10	10	10	10	10	10	10	10
Hydroxyl Propyl Methyl Cellulose in Parts								45	4.0	3.5

Ethyl Cellulose in Parts	4.5	4.0	3.5	3.0	2.5	2.0	1.0	0.5	1.0	1.5
Eudragit Rs.100 in Parts	0.5	1.0	1.5	2.0	2.5	3.0	4.0			
Glycerol in % w/w	30	30	30	30	30	30	30	30	30	30
DMSO in w/w	20	20	20	20	20	20	20	20	20	20"

"Ingredients	T_{11}	T_{12}	T_{13}	T_{14}	T_{15}	T_{16}	T_{17}	T_{18}	T_{19}	T_{20}	T_{21}
Ciprofloxacin hydrochloride in (mg)	10	10	10	10	10	10	10	10	10	10	10
Hydroxyl Propyl Methyl Cellulose in Parts	3.0	2.5	2.0	1.0	4.5	4.0	3.5	3.0	2.5	2.0	1.0
Ethyl Cellulose in Parts	2.0	2.5	3.0	4.0							
Eudragit Rs.100 in Parts					0.5	1.0	1.5	2.0	2.5	3.0	2.0
Glycerol in % w/w	30	30	30	30	30	30	30	30	30	30	30
DMSO in w/w	20	20	20	20	20	20	20	20	20	20	20"

T_1-T_7: "10%w/w of EC: ERS100; T_8-T_{14}: 5%w/w of HPMC: EC; T_{15}-T_{21}: 10%w/w of HPMC: ERS100"

Physico- Chemical parameters

Molded patches of ciprofloxacin hydrochloride loaded with various ratios of HPMC, EC, and ERS100 were created. The physicochemical and *in-vitro* drug release properties of the produced patches were examined.

The average weight of a patch with a surface area of 15.21cm^2 was found to vary significantly amongst patches made with various polymer ratios. According to the data, the average weight of patches 1-21 is 6-8. T1-T7 had the highest average weight among the 21 patches, whereas T15-T21 had the lowest. Using 10% w/w polymers instead of 5% w/w polymers in other formulations has resulted in the increased weight of T1-T7 patches.

The thickness of the patches (T1-T21) did not vary much, as measured by an aerospace digital electronic micrometre (table 9). This shows that the patches might be made in the same way over and over again.

The moisture content of the coded transdermal patches (T8-T14) differed significantly (table 2-4). In T8-T21, the HPMC polymer, which is hydrophilic, was shown to have a higher moisture content and water absorption than other patches. Using both hydrophobic polymers, the patches T1 through T7 exhibited decreased moisture content and absorption.

Table 2-4 shows that the tensile strength of patches T8-T15 is greater than that of other patches, whereas table 5 shows that the hardness of patches T8-T15 is lower than that of other patches.

Using a SHIMADZU UV-1700 spectrophotometer, the drug content of all patches was verified to be the same (table: 2-4).

Table 2: Physico-chemical characteristics of Ciprofloxacin hydrochloride transdermal patch formulations (T1-T7)

Formulation Code	Polymer Ratio EC: ERS100	Physical Appearance	Weight Variation (grams)	Thickness (mm)	Tensile Strength (kg/cm^2)	Moisture Content (%)	Moisture Uptake (%)	Drug Content (mg/cm^2)
T1	4.5:0.5	"Translucent, Flexible, Smooth.	0.592 ±0.028	0.175 ±0.009	0.946	3.31 ±0.18	5.43 ±0.01	0.5969
T2	4:1	Translucent, Flexible, Smooth.	0.566 ±0.017	0.184 ±0.013	0.927	2.77 ±0.16	4.97 ±0.004	0.547
T3	3.5:1.5	Translucent, Flexible, Smooth.	0.474 ±0.019	0.147 ±0.003	0.945	2.59 ±0.43	4.05 ±0.001	0.6449
T4	3:2	Translucent, Flexible, Smooth.	0.500 ±0.009	0.152 ±0.008	0.943	2.48 ±0.90	3.77 ±0.009	0.5437
T5	2.5:2.5	Translucent, Flexible, Smooth.	0.497 ±0.01	0.167 ±0.006	0.895	2.43 ±0.66	3.15 ±0.01	0.6219
T6	2:3	Translucent, Flexible, Smooth.	0.502 ±0.008	0.195 ±0.018	0.839	2.09 ±0.49	2.64 ±0.02	0.6002
T7	1:4	Translucent, Flexible, Smooth"	0.525 ±0.001	0.056 ±0.043	0.890	1.24 ±0.57	1.99 ±0.025	0.5739

Table 3: Physico-chemical characteristics of Ciprofloxacin hydrochloride transdermal patch formulations (T8-T14)

Formulation Code	Polymer Ratio EC: ERS100	Physical Appearance	Weight Variation (grams)	Thickness (mm)	Tensile Strength (kg/cm^2)	Moisture Content (%)	Moisture Uptake (%)	Drug Content (mg/cm^2)
T8	4.5:0.5	"Transparent, Flexible, Smooth	0.322 ±0.006	0.157 ±0.015	1.755	8.75 ±0.015	10.12 ±0.006	0.5634
T9	4:1	Transparent, Flexible, Smooth	0.322 ±0.006	0.120 ±0.07	1.645	7.55 ±0.007	9.88 ±0.009	0.5456
T10	3.5:1.5	Transparent, Flexible, Smooth	0.327 ±0.008	0.119 ±0.001	1.599	7.09 ±0.017	8.98 ±0.013	0.5391
T11	3:2	Transparent, Flexible, Smooth	0.304 ±0.005	0.102 ±0.008	1.555	6.63 ±0.002	8.17 ±0.016	0.5128
T12	2.5:2.5	Transparent, Flexible, Smooth	0.284 ±0.008	0.084 ±0.016	1.60	5.88 ±0.01	7.76 ±0.035	0.5542
T13	2:3	Transparent, Flexible, Smooth	0.293 ±0.005	0.134 ±0.005	1.504	5.14 ±0.03	6.85 ±0.048	0.6101
T14	1:4	Transparent, Flexible, Smooth"	0.286 ±0.008	0.135 ±0.006	1.551	4.36 ±0.009	5.67 ±0.009	0.6239

Table 4: Physico-chemical characteristics of Ciprofloxacin hydrochloride transdermal patch formulations (T15-T21)

Formulation Code	Polymer Ratio EC: ERS100	Physical Appearance	Weight Variation (grams)	Thickness (mm)	Tensile Strength (kg/cm^2)	Moisture Content (%)	Moisture Uptake (%)	Drug Content (mg/cm^2)
T15	4.5:0.5	"Transparent, Flexible, Smooth	0.283 ±0.01	0.152 ±0.009	1.360	6.09 ±0.24	7.51 ±0.017	0.6134
T16	4:1	Transparent, Flexible, Smooth	0.318 ±0.001	0.150 ±0.008	1.247	5.77 ±0.009	6.93 ±0.083	0.5654
T17	3.5:1.5	Transparent, Flexible, Smooth	0.310 ±0.001	0.112 ±0.017	.389	4.98 ±0.017	6.22 ±0.037	0.5456
T18	3:2	Transparent, Flexible, Smooth	0.304 ±0.004	0.167 ±0.006	1.338	4.08 ±0.038	5.95 ±0.009	0.6173
T19	2.5:2.5	Transparent, Flexible, Smooth	0.337 ±0.009	0.188 ±0.016	1.287	3.56 ±0.061	5.28 ±0.044	0.5765
T20	2:3	Transparent, Flexible, Smooth	0.289 ±0.01	0.150 ±0.008	1.241	2.83 ±0.17	4.53 ±0.006	0.5351
T21	1:4	Transparent, Flexible, Smooth"	0.361 ±0.02	0.144 ±0.003	1.124	2.14 ±0.19	3.45 ±0.002	0.6213

Table 5: Formulated patches are characterised by their hardness (T1-T21)

"Formulation code	Hardness (grams)	Formulation code	Hardness (grams)	Formulation code	Hardness (grams)
T_1	175	T_8	12.76	T15	44
T_2	172	T_9	16.59	T16	49
T_3	170	T10	19.33	T17	54
T_4	169	T11	20.33	T18	47
T_5	155	T12	21.20	T19	51
T_6	134	T13	19.32	T20	54
T_7	110	T14	18.02	T21	60"

In vitro drug release studies

Polymers have an effect on drug release, according to research done in vitro. Table 7-12 and graph 2-4 describe the 24-hour cumulative drug release (mg/cm^2) and cumulative percentage release of T1-T21 patches. Due to the hydrophilic nature of both the polymers EC and ERS100 used, the HPMC concentration of the T8 patch was increased, resulting in an increase in drug release from the patch. Because of the hydrophobic polymer ERS100, Patch T15 had a lower release rate than Patch T8.

Stability studies

T1, T8, and T15 patches showed no change in physico-chemical and in vitro drug release investigations as a result of stability studies (table 13-15 & graph: 5).

Table 6: Ciprofloxacin hydrochloride calibration graph

S. No.	Concentration mcg/ml	Absorbance @ 276 nm
"1.	0	0.000
2.	2	0.193
3.	4	0.421
4.	6	0.613
5.	8	0.800
6	10"	0.985

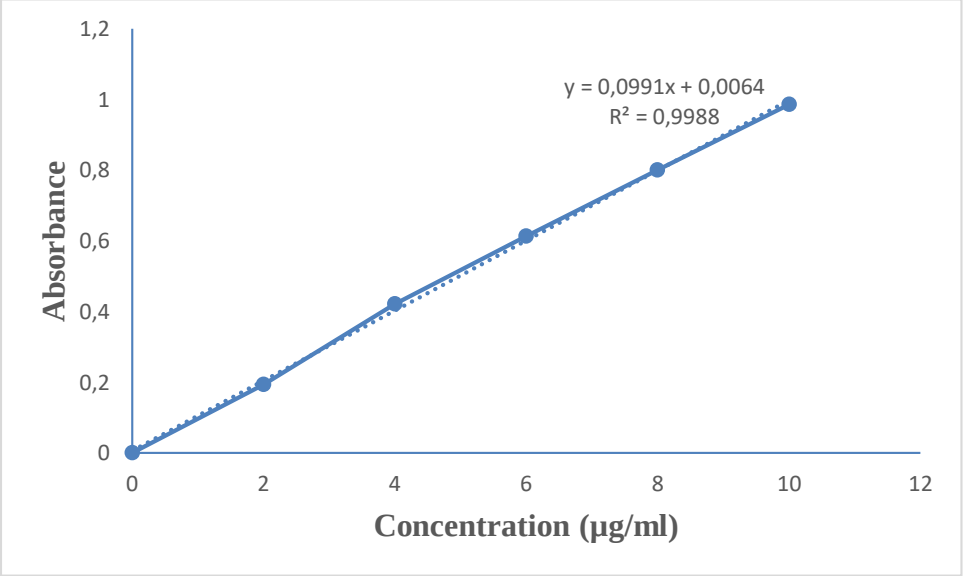

Figure 1: Ciprofloxacin hydrochloride calibration graph in 0.1 N HCl

Table 7: Polymers like EC & ERS100 are used to create Ciprofloxacin hydrochloride transdermal patches, which release a cumulative quantity of the drug over time: (T1-T7)

"Polymer ratio EC:ERS 100	Cumulative amount release (mg/cm^2) of drug at										
	1 h	2 h	3 h	4 h	5 h	6 h	7 h	8 h	9 h	10 h	24 h
4.5:0.5	0.1062	0.0165	0.0197	0.0234	0.0275	0.0450	0.0505	0.0556	0.0616	0.0666	0.1550
4:1	0.0091	0.0114	0.0146	0.0183	0.0229	0.0257	0.0298	0.0358	0.0395	0.0469	0.1302
3.5:1.5	0.0096	0.0123	0.0137	0.0165	0.0198	0.0234	0.0280	0.0330	0.0372	0.0413	0.1163
3:2	0.0063	0.0114	0.0123	0.0174	0.0220	0.0247	0.0280	0.0326	0.0358	0.0390	0.1081
2.5:2.5	0.0027	0.0059	0.0082	0.0119	0.0156	0.0192	0.0229	0.0270	0.0312	0.0339	0.1026
2:3	0.0017	0.0040	0.0091	0.0128	0.0160	0.0197	0.0234	0.0266	0.0298	0.0330	0.0915
1:4"	0.0009	0.0027	0.0063	0.0096	0.0123	0.0165	0.0197	0.0238	0.0266	0.0303	0.0694

Table 8: Ciprofloxacin hydrochloride transdermal patches made with polymers like EC and ERS 100: cumulative percentage release (T1-T7)

"Polymer ratio EC:ERS 100	Cumulative percentage release (mg/cm^2) of drug at										
	1 h	2 h	3 h	4 h	5 h	6 h	7 h	8 h	9 h	10 h	24 h
4.5:0.5	1.79	2.71	3.25	3.87	4.57	7.49	8.42	9.27	10.27	11.12	25.92
4:1	1.61	2.03	2.62	3.30	4.14	4.64	5.40	6.49	7.17	8.51	23.74
3.5:1.5	1.44	1.87	2.08	2.51	3.08	3.58	4.30	5.08	5.72	6.37	17.99
3:2	1.12	2.05	2.22	3.15	3.99	4.50	5.09	5.94	6.53	7.13	19.82
2.5:2.5	0.39	0.90	1.27	1.86	2.46	3.05	3.64	4.31	4.97	5.42	16.44
2:3	0.25	0.63	1.47	2.09	2.62	3.31	3.85	4.39	4.92	5.46	15.20
1:4"	0.10	0.42	1.06	1.70	2.10	2.82	3.46	4.10	4.59	5.23	12.04

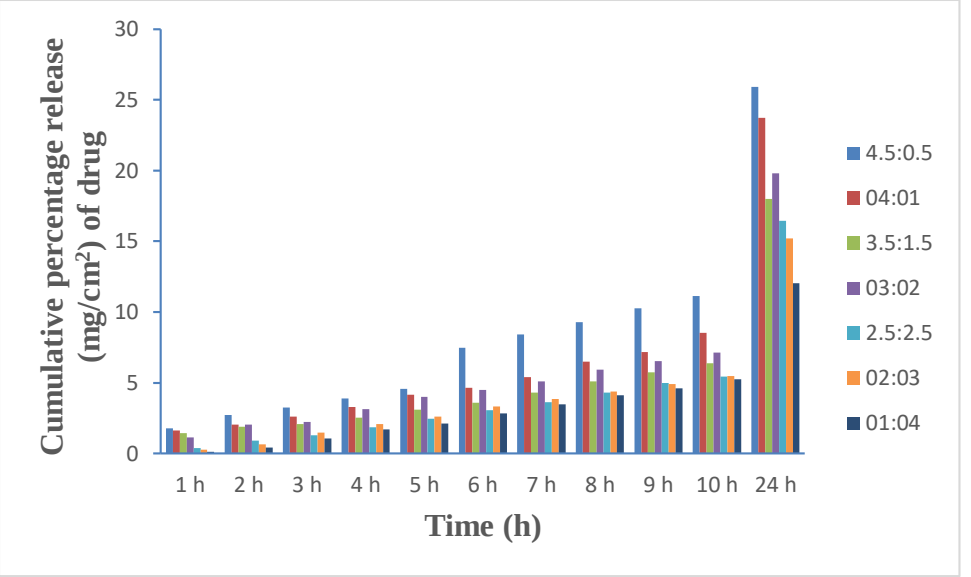

Figure 2: *In-vitro* release profile of patches (T1-T7)

Table 9: Ciprofloxacin hydrochloride transdermal patches made with polymers like HPMC and EC: cumulative amount release (T8-T14)

"Polymer ratio HPMC:EC	Cumulative amount release (mg/cm²) of drug at										
	1 h	2 h	3 h	4 h	5 h	6 h	7 h	8 h	9 h	10 h	24 h
4.5:0.5	0.0266	0.0353	0.0583	0.0689	0.0818	0.0906	0.1035	0.1384	0.1596	0.1743	0.4836
4:1	0.0215	0.0330	0.0468	0.0629	0.0790	0.0841	0.0988	0.1094	0.1495	0.1706	0.4560
3.5:1.5	0.0123	0.0335	0.0464	0.0524	0.0643	0.0740	0.0832	0.0906	0.1044	0.1191	0.4090
3:2	0.0142	0.0312	0.0418	0.0515	0.0602	0.0666	0.0749	0.0855	0.1007	0.1113	0.3839
2.5:2.5	0.0096	0.0146	0.0312	0.0408	0.0496	0.0616	0.0717	0.0772	0.0938	0.0956	0.3560
2:3	0.0059	0.0114	0.0142	0.0344	0.0444	0.0551	0.0602	0.0827	0.0860	0.0947	0.3480
1:4"	0.0022	0.0031	0.0220	0.0316	0.0381	0.0482	0.0560	0.0652	0.0744	0.0864	0.3289

Table 10: Release of Ciprofloxacin hydrochloride transdermal patches made with polymers like HPMC & EC: cumulative percentage release (%): (T8-T14)

"Polymer ratio HPMC:EC	Cumulative percentage release (mg/cm²) of drug at										
	1 h	2 h	3 h	4 h	5 h	6 h	7 h	8 h	9 h	10 h	24 h
4.5:0.5	4.67	6.22	10.31	12.19	14.47	16.03	18.31	24.52	28.28	30.89	85.79
4:1	3.90	5.99	8.53	11.49	14.44	15.37	18.07	19.99	27.34	31.23	83.58

3.5:1.5	2.23	6.16	8.55	9.66	11.10	13.67	15.38	16.75	19.31	22.04	75.82
3:2	2.71	6.03	8.09	9.98	11.68	12.94	14.56	16.62	19.58	21.64	74.80
2.5:2.5	1.68	2.59	5.58	7.32	8.90	11.66	12.89	13.88	16.87	17.21	64.29
2:3	0.97	1.83	2.28	5.60	7.26	8.99	9.85	13.52	14.05	15.48	57.04
1:4"	0.31	0.46	3.48	5.03	6.06	7.69	8.94	10.42	11.89	13.81	52.68

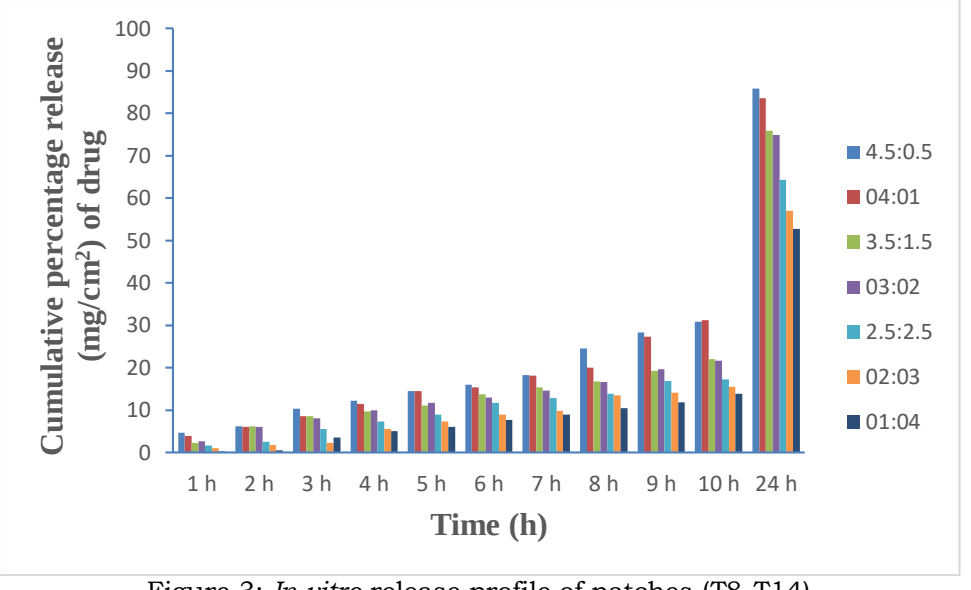

Figure 3: *In-vitro* release profile of patches (T8-T14)

Table 11: Transdermal patches containing Ciprofloxacin hydrochloride manufactured with polymers such as HPMC and ERS100: (T15-T21)

"Polymer ratio HPMC:ERS 100	Cumulative amount release (mg/cm²) of drug at										
	1 h	2 h	3 h	4 h	5 h	6 h	7 h	8 h	9 h	10 h	24 h
4.5:0.5	0.0192	0.0298	0.0468	0.0574	0.0671	0.0744	0.0832	0.0924	0.1007	0.1186	0.2931
4:1	0.0123	0.0257	0.0358	0.0413	0.0515	0.0666	0.0740	0.0828	0.0892	0.0961	0.2710
3.5:1.5	0.0156	0.0234	0.0264	0.0363	0.0496	0.0616	0.0712	0.0763	0.0864	0.0952	0.2627
3:2	0.0096	0.0160	0.0252	0.0363	0.0413	0.0574	0.0643	0.0712	0.0772	0.0846	0.2406
2.5:2.5	0.0073	0.0105	0.0131	0.0229	0.0293	0.0372	0.0478	0.0524	0.0611	0.0736	0.2240
2:3	0.0045	0.0074	0.0119	0.0144	0.0243	0.0312	0.0386	0.0469	0.0574	0.0671	0.1799

1:4"	0.0022	0.0056	0.0105	0.0132	0.0192	0.0252	0.0349	0.0432	0.0570	0.0593	0.1623

Table 12: Release of Ciprofloxacin hydrochloride transdermal patches made with polymers like HPMC and ERS100: cumulative percentage release (T15-T21)

"Polymer ratio HPMC:ERS 100	Cumulative percentage release (mg/cm^2) of drug at										
	1 h	2 h	3 h	4 h	5 h	6 h	7 h	8 h	9 h	10 h	24 h
4.5:0.5	3.09	4.82	7.59	9.32	10.90	12.09	13.52	15.02	16.37	19.30	47.72
4:1	2.13	4.49	6.28	7.26	9.05	11.74	13.04	14.59	15.73	16.95	47.88
3.5:1.5	2.80	4.23	4.82	6.59	9.04	11.23	12.99	13.97	15.79	17.39	48.10
3:2	1.58	2.55	4.04	5.83	6.65	9.26	10.38	11.50	12.47	13.66	38.94
2.5:2.5	1.21	1.77	2.25	3.96	5.05	6.40	8.24	9.04	10.56	12.71	38.81
2:3	0.79	1.39	2.17	2.68	4.49	5.99	7.16	8.70	10.68	12.49	33.56
1:4"	0.31	0.83	1.64	2.09	3.05	4.02	5.57	6.90	8.17	9.50	26.24

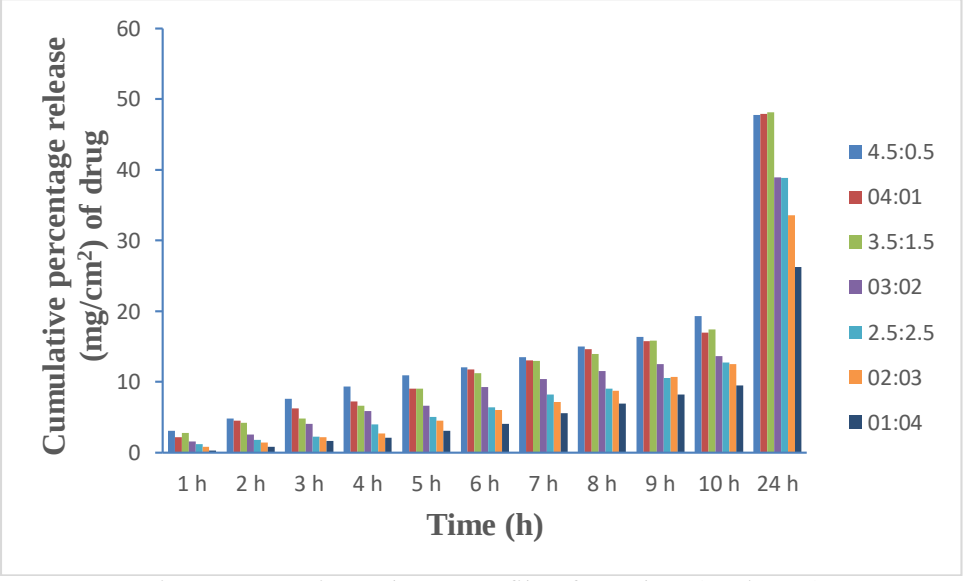

Figure 4: *In-vitro* release profile of patches (T15-T21)

Table 13: Testing the stability of Ciprofloxacin hydrochloride's newly designed transdermal patch (T1) at a temperature of 40 degrees Celsius

Time in days	Physical Appearance	Weight Variation (grams)	Thickness (mm)	Moisture Content (%)	Moisture Uptake (%)	Drug Content (mg/cm^2)	Cumulative amount release (mg/cm^2) at 24 h	Cumulative percentage release at 24 h
“0	Translucent, Flexible, Smooth	0.595 ±0.014	0.184 ±0.007	3.11 ±0.011	5.35 ±0.027	0.5870	0.1552	26.42
15	No change	0.592 ±0.016	0.186 ±0.009	3.18 ±0.017	5.81 ±0.021	0.5868	0.1559	26.55
20	No change	0.596 ±0.011	0.187 ±0.007	3.23 ±0.012	5.99 ±0.015	0.5866	0.1545	26.32
45	No change”	0.598 ±0.013	0.190 ±0.011	3.27 ±0.013	6.07 ±0.030	0.5971	0.1531	25.62

Table 14: Testing the stability of Ciprofloxacin hydrochloride's newly designed transdermal patch (T8) at a temperature of 40 degrees Celsius

Time in days	Physical Appearance	Weight Variation (grams)	Thickness (mm)	Moisture Content (%)	Moisture Uptake (%)	Drug Content (mg/cm^2)	Cumulative amount release (mg/cm^2) at 24 h	Cumulative percentage release at 24 h
“0	Translucent, Flexible, Smooth	0.328 ±0.008	0.163 ±0.017	8.81 ±0.017	10.18 ±0.008	0.564	0.4838	85.83
15	No change	0.333 ±0.017	0.164 ±0.011	8.87 ±0.007	10.47 ±0.020	0.5643	0.4841	85.83
20	No change	0.336 ±0.012	0.167 ±0.006	9.03 ±0.05	10.77 ±0.025	0.5634	0.4834	85.84
45	No change”	0.389 ±0.020	0.171 ±0.004	9.41 ±0.029	11.30 ±0.027	0.5625	0.4824	85.80

Table 15: Testing the stability of Ciprofloxacin hydrochloride's newly designed transdermal patch (T15) at a temperature of 40 degrees Celsius

Time in days	Physical Appearance	Weight Variation (grams)	Thickness (mm)	Moisture Content (%)	Moisture Uptake (%)	Drug Content (mg/cm^2)	Cumulative amount release (mg/cm^2) at 24 h	Cumulative percentage release at 24 h
"0	Translucent, Flexible, Smooth	0.289 ±0.017	0.458 ±0.011	6.15 ±0.26	7.57 ±0.019	0.6140	0.2933	47.77
15	No change	0.297 ±0.025	0.160 ±0.018	60.4 ±0.006	7.77 ±0.14	0.5990	0.2909	48.58
20	No change	0.305 ±0.019	0.153 ±0.33	6.31 ±0.011	8.04 ±0.16	0.6127	0.2881	47.02
45	No change"	0.309 ±0.030	0.21 ±0.044	6.98 ±0.19	8.38 ±0.27	0.6110	0.2827	46.27

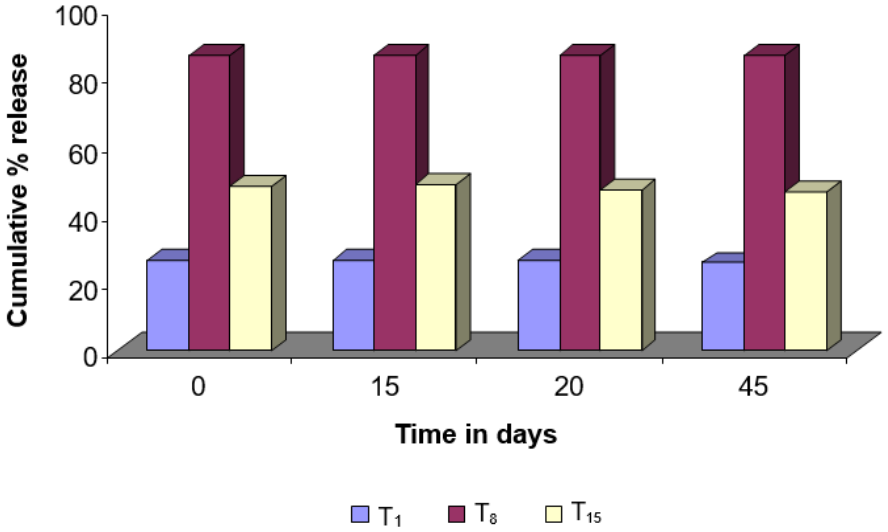

Figure 5: Stability experiments at 40°C compared the cumulative % release of transdermal patches T1, T8, and T15

Conclusion

To maximise bioavailability by avoiding pre-systemic hepatic metabolism, an effort was made to design a transdermal treatment system for Ciprofloxacin hydrochloride employing polymers such as HPMC, EC, and ERS100. Physical and chemical characteristics, *in vitro* drug release investigations and stability experiments were carried out on the prepared patches.

The average weight of the patches varied significantly, which may be attributable to the different quantities of polymers utilised in their construction. All twenty-one patches had the same thickness, with no obvious changes. When compared to patches made with HPMC:ERS100 and EC:ERS100, the HPMC:EC patches had higher % moisture content and percentage moisture absorption. A possible explanation for this is that HPMC and EC have a larger percentage of hydrophilic polymer HPMC, while patches with HPMC:ERS100 combination have a lower percentage of hydrophobic polymer ERS100.

Patches made from HPMC:EC had higher tensile strength, but lower hardness than other patches, which may have something to do with the polymer composition. The drug content of all the patches was the same. The in vitro drug release profiles of the formulations T8-T14 were superior to those of the other formulations. Polymer properties, plasticizers, and/or permeability enhancers all have a role.

T1, T8, and T15 formulations were chosen for stability experiments at room temperature and 40 °C for a period of 45 days, respectively. The findings of the stability experiments indicated that the prepared patches may be stored for up to 45 days. The T8 formulation has shown promising results, thus the correct method should be used for commercial and scale manufacturing. The effectiveness of these patches will need to be studied over the course of many years in pharmacokinetic and pharmacodynamic investigations.

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