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Design and invitro evaluation of selegiline patches for transdermal drug delivery system

L.Rajini*, Dr.Arjun goje, J.Shashank, A.Sirisha, B.Shirisha, J.Shivani, S.Sowjanya.

Department of pharmaceutics, Teegala Ram Reddy College of Pharmacy, Telangana, India

Corresponding author: L. Rajini

ABSTRACT

Selegiline, also known as L-deprenyl is a medication which is used in the treatment of Parkinson's disease and major depressive disorder. It is provided in the form of a capsule or tablet taken by mouth for Parkinson's disease and as a patch applied to skin for depression. In present study transdermal drug delivery of Selegiline was developed to overcome the first pass metabolism and to reduce frequency of dosing compared to oral route.

Keywords: Selegiline, Transdermal patches, Methocel K4M

INTRODUCTION

Controlled drug delivery

Treatments of acute and chronic diseases have been accomplished by delivery of drugs to patients using various pharmaceutical dosage forms. These dosage forms are known to provide a prompt release of drug. The difference between sustained release and controlled release is shown by fig.1.

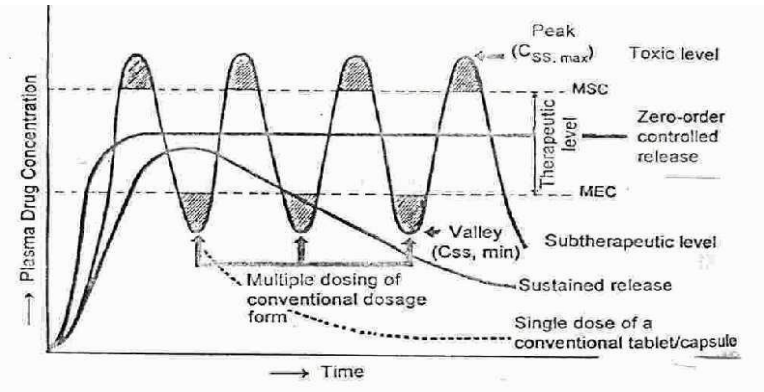

Fig 1: Comparative graphs of conventional, sustained- and controlled release delivery systems.

Structure of skin

An average adult skin has a surface area of approximately 2 square meters and receives about one third of the blood circulating through the body. It is one of the most readily accessible organs of the human body with a thickness of only a few millimeters (2.97+/-0.28 mm). Its major roles are to regulate body temperature, protect tissues from infection, prevent fluid loss.

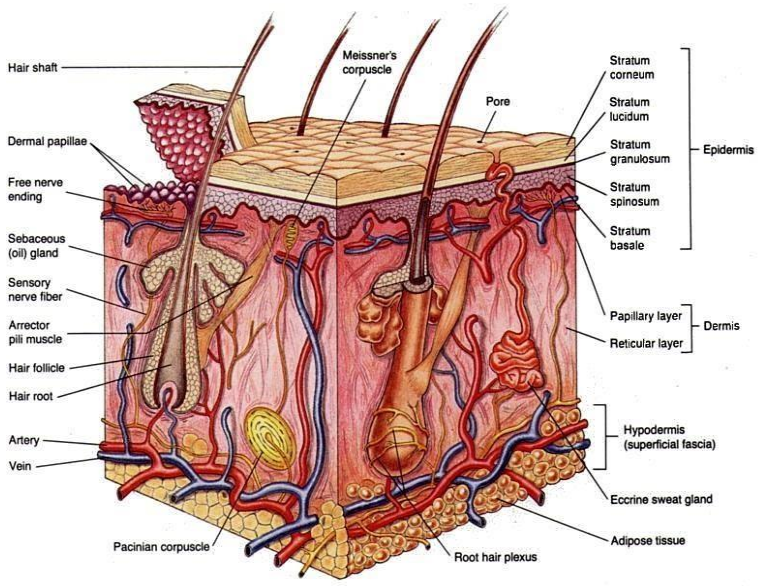

Fig 2: Structure of skin

Aim and Objectives

The aim of the work is Development and optimization of Matrix Transdermal patches of Selegiline. To prepare Transdermal patches containing Selegiline drug with different polymers, Evaluation of prepared Transdermal patches for different parameters like. Folding endurance, Thickness of the patches, Percentage elongation, Weight variation, Drug content

MATERIALS AND METHODS

Table 1: List of Materials Used

Name of the material	Source
Selegiline	NATCO LABS
Methocel K4M	Merck Specialities Pvt Ltd, Mumbai, India
Methocel K15M	SD fine chemicals, Mumbai, India
Methocel K100M	SD fine chemicals, Mumbai, India
Methanol	Merck Specialities Pvt Ltd, Mumbai, India
Dichloromethane	Merck Specialities Pvt Ltd, Mumbai, India
Propylene glycol	Merck Specialities Pvt Ltd Mumbai, India
Tween-80	Merck Specialities Pvt Ltd Mumbai, India

Table 2: List of Equipment's used

S.No.	Instruments	Manufacturer
1.	Digital weighing balance	Wensar
2.	ter, cyber pH- 14L	Lab India
3.	Franz diffusion cell	Borosil
4.	Glassware	Borosil, Mumbai, India.
5.	UV-Spectrophotometer	Lab India

METHODOLOGY

Preformulation study

Preformulation studies were primarily done to investigate the physicochemical properties of drug and to establish its compatibility with other excipients.

Selection of drug and other ingredients

Selegiline was selected as model drug based on its physico-chemical and biological properties and also based on its suitability for Transdermal drug delivery system. Methocel K4M, Methocel K15M, Methocel K100M were selected as matrix forming polymers.

Preparation of Phosphate Buffer pH 6.8

Accurately measured 250 ml of 0.2 M potassium dihydrogen phosphate in a 1000 ml of volumetric flask and added 195.5 ml of

Formulation
Development of Transdermal patches

Transdermal drug delivery patches were prepared by solvent casting method.

Solvent casting method

Transdermal patches were prepared according to the formula shown in Table 7.1. Methocel K4M, Methocel K15M, Methocel K100M were weighed in requisite ratios and they were then dissolved in dimethyl formamide and ethanol as solvent using magnetic stirrer. Selegiline (40 mg) with a magnetic stirrer.

Table 3: Formulations of SelegilineTransdermal Patch

S.No	Ingre dients	F1	F2	F3	F4	F5	F6	F7	F8	F9
1	Drug(mg)	100	100	100	100	100	100	100	100	100
2	Metho cel K4M(mg)	100	200	300	-	-	-	-	-	-
3	Metho cel K15M(mg)	-	-	-	100	200	300	-	-	-
4	Metho cel K100M(mg)	-	-	-	-	-	-	100	200	300
5	Dimet hyl forma mide(ml)	10	10	10	10	10	10	10	10	10
6	Ethan ol(ml)	5	5	5	5	5	5	5	5	5
7	Propyl ene glycol (Drops)	5	5	5	5	5	5	5	5	5

Evaluation of Transdermal patch by physical methods

Physical appearance: All the Transdermal patches were visually inspected for color, clarity, flexibility & smoothness.

Thickness: This thickness of the patches was assessed at 3 different points using screw gauze. For each formulation, three randomly selected patches were used.

Weight variation: The three disks of 2x2 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.

Moisture uptake: The percent moisture absorption test was carried out to check the physical stability and integrity of the patch at high humid conditions. In the present study the moisture absorption capacities of the patch were determined in the following manner.

$$\text{Percentage moisture absorbed} = \frac{\text{Final weight} - \text{Initial weight}}{\text{Initial weight}} \text{ X } 100$$

Evaluation of Transdermal patch by permeation studies

Diffusion cell: Permeation studies were carried out on Franz diffusion cells. The Franz diffusion cell contains two compartments, the donor and receptor compartment. The receptor compartment is mm and holds a volume of 15 ml.

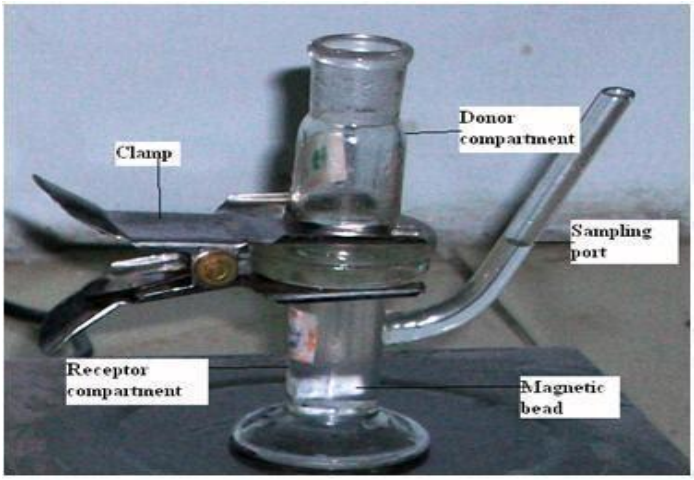

Fig 3: Franz diffusion cell

In vitro permeation studies using dialysis membrane

In vitro permeation of Selegiline from Transdermal patches through dialysis membrane (Hi-Media) with molecular weight cut off of 12000 was studied

Kinetic modeling of drug release

Mechanism of drug release

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.

Zero order release model

To study the zero–order release kinetics the release rate data are fitted to the following equation.

$$Q = K_0 t$$

Where, Q= amount of drug released at time t

K_0=zero order release rate constant

First order release model

The release rate data are fitted to the following equation

$$\ln (100-Q) = \ln 100 - k_1 t$$

Where, Q= percent drug release at time,
K_1= first order release rate constant
The plot of log % drug release versus time is linear.

Higuchi's Release Model

To study the Higuchi release kinetics, the release rate data were fitted to the following equation

$$Q = K_H t^{1/2}$$

Where, Q= percent drug release at time t
K_H= Higuchi's (diffusion) rate constant

In Higuchi's model, a plot of % drug release versus square root of time is linear.

RESULTS AND DISCUSSION

Table 4: Standard graph of Selegiline

Concentration (µg/ml)	Absorbance
0	0
0.5	0.152
1	0.291
1.5	0.412
2	0.561
2.5	0.732

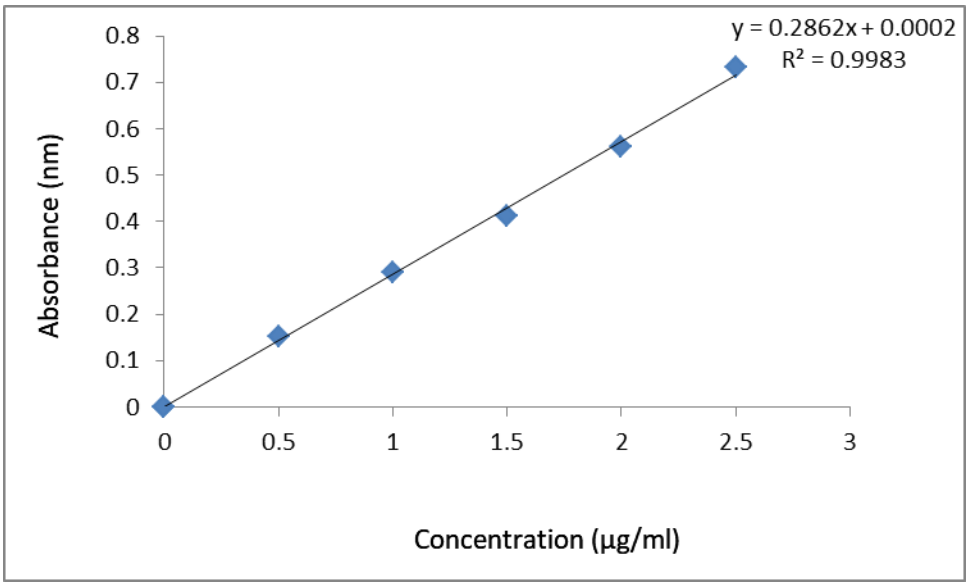

Fig 4: Standard curve of Selegiline

Evaluation of Selegiline Transdermal patches

Physical appearance: All the Transdermal patches were visually inspected for colour, clarity, flexibility.

Table 5: Evaluation of Selegiline Transdermal patch by physical methods

·mula tion	Weight variatio n (mg)	Thickne ss (mm)	Folding enduran ce	Drug content (%)	Moisture uptake (%)	Moistur e content (%)
F1	215	0.118	210	99.16	1.89	2.15
F2	318	0.121	199	97.53	1.91	1.86
F3	420	0.119	183	98.61	2.05	2.13
F4	217	0.115	195	97.06	1.76	1.92
F5	316	0.122	218	98.43	1.85	2.86
F6	415	0.119	182	99.24	2.06	2.16
F7	218	0.117	193	98.47	2.12	2.23
F8	319	0.115	214	97.64	2.07	1.89
F9	419	0.116	209	97.73	2.11	2.17

Table 6: Evaluation of Selegiline Transdermal patch by In-vitro permeation studies using dialysis membrane

Time	% Drug release								
(Hrs)	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
0.5	7.65	5.46	6.93	8.41	8.19	8.61	7.03	8.32	7.32
1	15.83	10.63	11.55	15.63	14.52	16.83	13.16	15.76	13.45
2	24.53	18.51	19.67	24.76	22.76	25.02	19.05	19.08	22.96
3	29.76	27.81	27.31	33.61	31.15	31.07	26.46	25.31	30.42
4	35.91	36.91	35.52	40.86	39.73	39.21	34.72	32.67	38.17
5	44.05	41.06	42.65	46.76	48.76	46.76	40.16	39.04	46.58
6	48.16	50.73	50.61	51.62	55.72	52.43	46.79	45.36	52.16
7	52.73	57.86	57.47	59.76	60.08	59.17	52.46	52.14	59.14
8	58.91	66.48	66.08	63.91	66.25	64.39	58.07	58.76	64.08
9	64.16	74.91	73.43	70.43	70.91	69.47	66.34	64.91	71.95
10	68.91	81.43	82.16	76.05	78.06	74.91	72.16	69.02	77.16
11	74.51	86.61	89.16	81.73	82.14	79.85	76.01	73.43	82.66

12	79.05	89.05	98.03	86.17	86.03	83.06	80.32	77.52	88.17

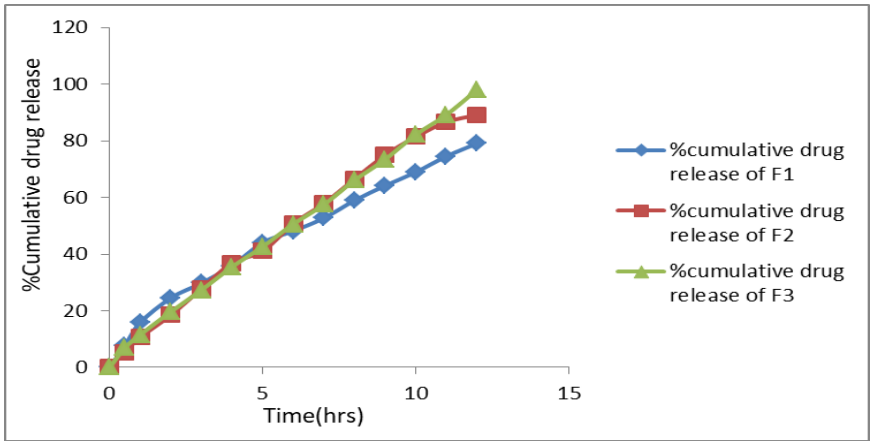

Fig 5: % drug release of F1, F2, F3

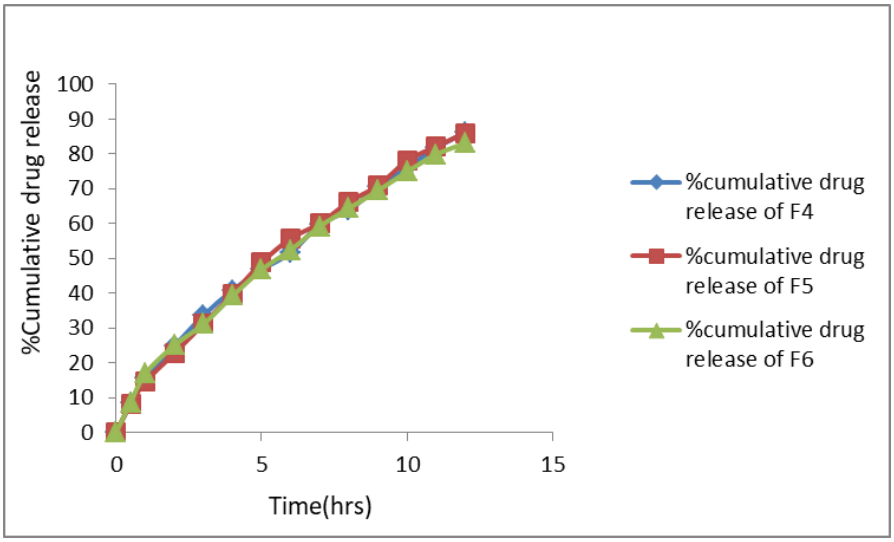

Fig 6: %ge drug release of F4, F5, F6

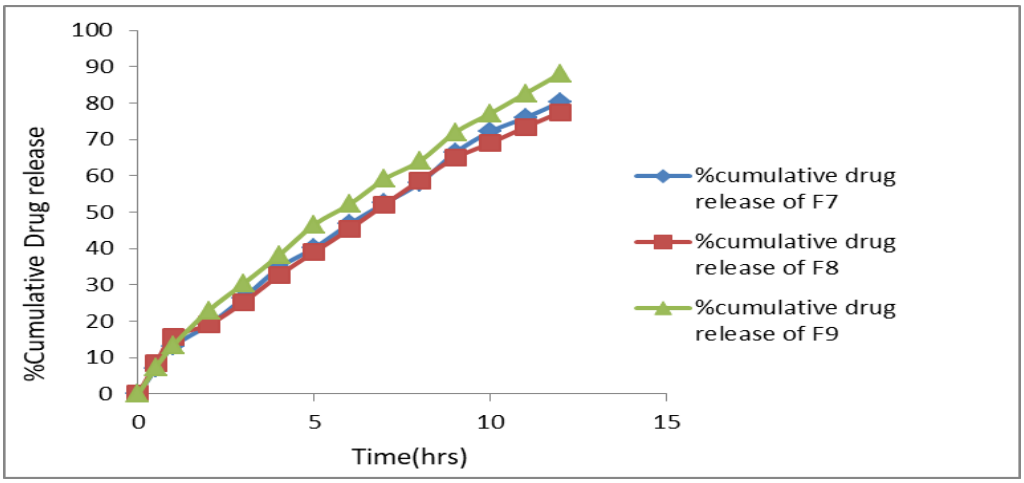

Fig 7: %ge drug release of F7, F8, F9

The prepared Selegiline Transdermal patches were evaluated for In-vitro permeation studies using dialysis membrane, among all the 9 formulations F2 formulation was shown 97.16% cumulativedrugreleasewithin12hours.

Table 7: Kinetics of In-vitro permeation studies of optimized formulation

CUMULATIVE (%) RELEASE Q	TIME (T)	ROOT (T)	LOG (%) RELEASE	LOG (T)	LOG (%) REMAIN	RELEASE RATE (CUMULATIVE % RELEASE/t)	1/CUM% RELEASE	PEPPAS log Q/100	% Drug Remaining	Q01/3	Qt1/3	Q01/3-Qt1/3
0	0	0			2.000				100	4.642	4.642	0.000
6.93	0.5	0.707	0.841	-0.301	1.969	13.860	0.1443	-1.159	93.07	4.642	4.532	0.110
11.55	1	1.000	1.063	0.000	1.947	11.550	0.0866	-0.937	88.45	4.642	4.456	0.186
19.67	2	1.414	1.294	0.301	1.905	9.835	0.0508	-0.706	80.33	4.642	4.315	0.327
27.31	3	1.732	1.436	0.477	1.861	9.103	0.0366	-0.564	72.69	4.642	4.173	0.468
35.52	4	2.000	1.550	0.602	1.809	8.880	0.0282	-0.450	64.48	4.642	4.010	0.632
42.65	5	2.236	1.630	0.699	1.759	8.530	0.0234	-0.370	57.35	4.642	3.856	0.785
50.61	6	2.449	1.704	0.778	1.694	8.435	0.0198	-0.296	49.39	4.642	3.669	0.973
57.47	7	2.646	1.759	0.845	1.629	8.210	0.0174	-0.241	42.53	4.642	3.491	1.151
66.08	8	2.828	1.820	0.903	1.530	8.260	0.0151	-0.180	33.92	4.642	3.237	1.405
73.43	9	3.000	1.866	0.954	1.424	8.159	0.0136	-0.134	26.57	4.642	2.984	1.658
82.16	10	3.162	1.915	1.000	1.251	8.216	0.0122	-0.085	17.84	4.642	2.613	2.029
89.16	11	3.317	1.950	1.041	1.035	8.105	0.0112	-0.050	10.84	4.642	2.213	2.428
98.03	12	3.464	1.991	1.079	0.294	8.169	0.0102	-0.009	1.97	4.642	1.254	3.388

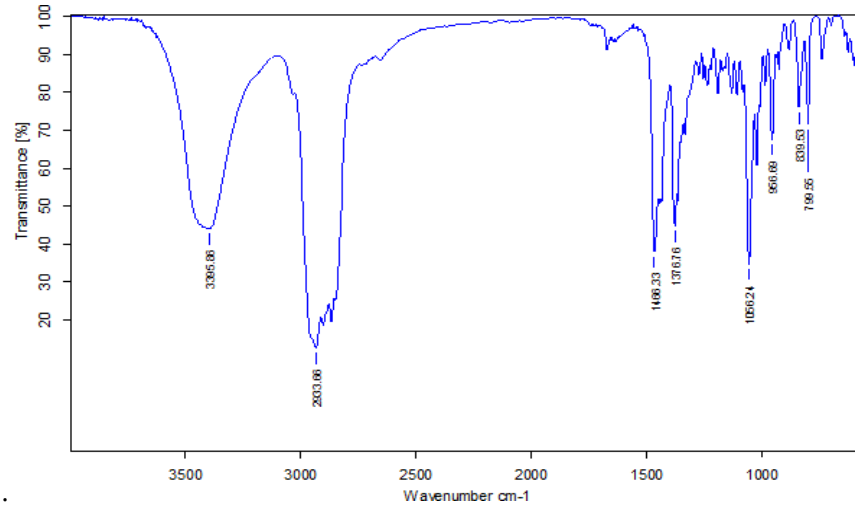

Fig 8: FTIR of pure drug

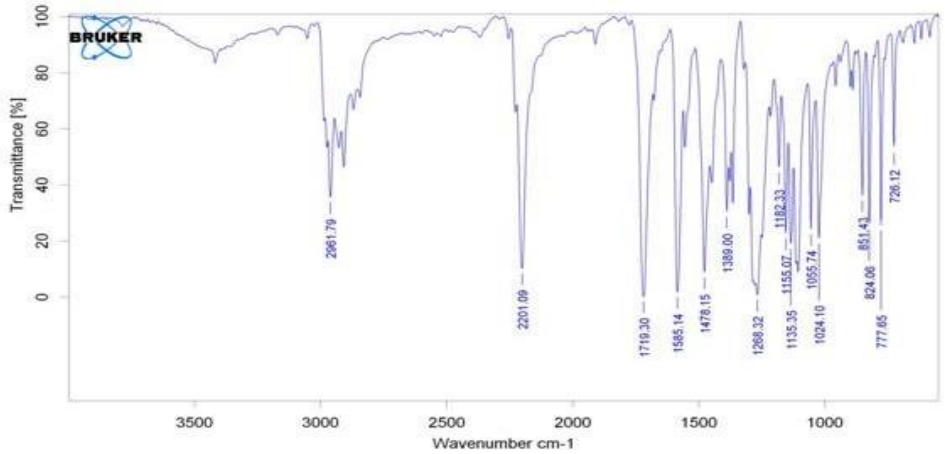

Fig 9: FTIR of optimized formulation

CONCLUSION

In present study transdermal drug delivery of Selegiline was developed to overcome the first pass metabolism and to reduce frequency of dosing compared to oral route. Oral drug delivery system has various drawbacks like poor bioavailability due to hepatic metabolism (first pass) and the tendency to produce rapid blood level spikes (both high and low), leading to a need for high and/or frequent dosing, which can be both cost prohibitive and inconvenience.

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