CODEN [USA]: IAJPBB ISSN : 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES
SJIF Impact Factor: 7.187
https://doi.org/10.5281/zenodo.23887662

Available online at: http://www.iajps.com Research Article

PHARMACOLOGICAL EVALUATION OF "ANTI-DEVELOPMENT AND IN VITRO EVALUATION OF SELEGILINE TRANSDERMAL PATCHES

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Abstract:

The present study was aimed at the formulation and evaluation of Selegiline hydrochloride transdermal patches to provide sustained drug release and improve patient compliance by overcoming the limitations associated with conventional oral therapy. It was freely soluble in methanol and ethanol, soluble in chloroform, and slightly soluble in water and phosphate buffer (pH 7.4). The maximum absorption wavelength (λmax) was found to be 247 nm, and the calibration curve exhibited excellent linearity with an R^2 value of 0.999. FTIR studies confirmed the compatibility of Selegiline hydrochloride with the selected polymers, indicating the absence of significant drug–excipient interactions.Transdermal patches were prepared by the solvent casting method using HPMC and Eudragit RL100 as film-forming polymers, PEG 400 as a plasticizer, and DMSO as a permeation enhancer. The prepared patches were evaluated for physicochemical parameters, including physical appearance, weight variation, thickness, folding endurance, surface pH, moisture loss, moisture absorption, in vitro drug release, and stability.All formulations showed satisfactory physicochemical characteristics with uniform appearance, acceptable thickness, good flexibility, and surface pH values within the normal skin pH range. Among the prepared formulations, F4, containing 50 mg of Eudragit RL100, demonstrated the best overall performance, exhibiting the highest folding endurance and a maximum cumulative drug release of 98.10% over 12 hours. Accelerated stability studies of the optimized formulation carried out according to ICH guidelines showed no significant changes in physical appearance, with only a slight reduction in cumulative drug release (97.82%) after three months, indicating good stability.The findings of this study suggest that the optimized Selegiline hydrochloride transdermal patch is a promising sustained-release drug delivery system with satisfactory physicochemical properties, drug release characteristics, and stability.

Keywords: *Selegiline hydrochloride, Transdermal patch, Solvent casting, Sustained drug release, FTIR, Stability studies.*

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*Please cite this article in press **R. Akhila** et al., **Development And In Vitro Evaluation Of Selegiline Transdermal Patches.,**. Indo Am. J. P. Sci, 2026; 13(11).*

INTRODUCTION:

Transdermal Patch

One method of precisely dosing medication is with a transdermal patch, which is also called a skin adhesive patch. This facilitates the drug's transdermal delivery into the bloodstream. The specific membrane controls how much liquid medicine can travel from the patch reservoir into the bloodstream via the skin. a lot of people have trouble swallowing pills or getting injections, and patches work for longer than pills, so you don't have to take them as often. Pain relief, cardiovascular disease treatment, smoking cessation, motion sickness management, and hormone replacement therapy are just a few of the many therapeutic disciplines that make use of patches.

Components of transdermal patch

Liner It shields the patch while it's in storage. Take the lining off before you use it. As a component of primary packaging, it prevents the medication from escaping the polymer matrix.

Adhesives

To secure the patch to the skin and tie its components together, this component is used. Some common types of adhesives are silicone-based adhesive polymers, polyacrylate, and polyisobutadiene.

The cell membrane

The drug release from reservoirs and multi-layer patches is regulated by the membrane. Composites such as chitosan and poly-2-hydroxyethylmethacrylate are common ingredients. Silicones, EVA copolymers, high-density polyethylene, and polyester polyacrylonitrile are a few examples. Drug The release liner comes into direct touch with the active substance.

Polymer

Polymers used in pharmaceuticals and other additives (e.g., permeation enhancers, plasticizers, adhesives, etc.) must be biocompatible and chemically stable. Shellac, gelatin, chitosan, waxes, cellulose derivatives, and natural rubber are all examples of natural polymers.

2. Polyvinyl pyrrolidone, polyethylene, polyamide, polyurea, and polypropylene are examples of synthetic polymers.

Thirdly, synthetic elastomers such as nitril, hydrin rubber, silicon rubber, polybutadiene, polyisobutylene, and butyl rubber.

The backing shields the patch from the elements, gives it structure, and improves its aesthetics and pliability.

Advantages of TDDS

- A drug can avoid first-pass metabolism by ensuring a continuous and sustained penetration by transdermal delivery over a long period of time.
- Raise the rate of patient adherence.
- The digestive juices from the stomach and intestines are unaffected.
- Maintains steady blood levels, allowing for long-term control.
- Decreased medication concentrations in the blood.
- Use drug candidates with a short half-life and a low therapeutic index; reduce volatility of the medication in plasma levels.
- It is straightforward to eliminate drug administration in the event of toxicity.
- Decrease the frequency of dose and improve patients' compliance.
- Transdermal distribution improves the efficacy of many medications by avoiding problems with the medicine itself, like poor absorption and GI distress.
- The medication schedule has been simplified, which has led to a decrease in drug response variations within and between individuals.

Disadvantages of TDDS

- For the medicine to penetrate the stratum corneum, it needs to have desirable physicochemical characteristics.
- The recommended daily dosage for the medicine is 5 mg; transdermal drug distribution becomes difficult at doses between 10 and 25 mg.
- It's possible for the patch's adhesive, medication, and other ingredients to irritate the skin in certain areas.
- The transdermal administration technique should only be used when there is a well-defined therapeutic need.
- Achieving high drug levels in blood or plasma was not possible.
- The formulation of medications with large molecular sizes is not possible.
- Inflammation at the application site is a possibility.
- It might not be cost-effective.
- The skinbarrier is unique to each person and can even evolve over time in the same individual.

MATERIALS:

Selegiline was procured from Synpharma Research Labs, HPMC K15M and Ethyl cellulose, PEG 400, DMSO, Dichloromethane and Ethanol were obtained from Synpharma Research Labs, Hyderabad. Other chemicals and the reagents used were of analytical grade.

METHODOLOGY:

Formulation design

Preparation of transdermal patches:

The solvent casting evaporation process was used to create transdermal patches containing Selegiline. An appropriate solvent was used to dissolve the medication selegiline. After dissolving the medication Selegiline in methanol, the polymers HPMC and Eudragit RL 100 were added to a boiling tube. As a plasticizer, PEG was added to the mixture and well mixed. Drying of patches was done in a vacuum oven at room temperature after setting aside for 2 hours to remove any trapped air. The mixture was thereafter transferred to a 40 cm2 petri dish that had been previously cleaned. For future analysis, the dried patches were placed in a desiccator and covered with aluminum foil.

Table:1 Formulation of Transdermal patches

F.no	Drug (mg)	HPMC (mg)	Eudragit (mg)	PEG400 (ml)	DMSO (ml)
F1	5	**25**	**-**	**1**	**0.1**
F2	5	**50**	**-**	**1**	**0.1**
F3	5	**-**	**25**	**1**	**0.1**
F4	5	**-**	**50**	**1**	**0.1**

Evaluation of transdermal formulation:

Physical Appearance

Color, transparency, flexibility, and smoothness were all visually assessed for all of the transdermal patches.

Variation in Weight

A computerized weighing scale was used to precisely measure three patches from every batch. We used each person's weight to get their average and standard deviation.

The patch Thickness

Each formulation's average thickness value was determined by measuring the transdermal patches' thickness three times using a screw gauge.

Folding Endurance

In order to find out how much pressure the patches could take before bursting, they were tested for folding endurance. A tiny (2cm × 2cm) section of the patch was folded continually in the same spot without breaking to find the folding endurance value of the patch.

% Moisture Absorb

The patches were carefully measured and put in desiccators with 100 ml of a saturated aluminum chloride solution. We measured the percentage of moisture absorption by comparing the end and initial weights with regard to the beginning weight, and we removed the patches after three days or until their weight remained steady.

$$Percentage\ of\ moisture\ Absorption = Final\ weight - Initial\ weight\ Initial\ weight * 100$$

%Moisture Loss

The patches were weight accurately and kept in a desiccators containing activated silica. The individual patches were weighed repeatedly and the patches were taken out, after 3 days or until a stable weigh of patch was achieved. The percentage of moisture loss was calculated as the difference between initial and final weight with respect to initial weight

$$Percentage\ of\ moisture\ loss = Initial\ weight - Final\ weight\ Initial\ weight * 100$$

In-vitro drug release studies:

Using a modified Franz type glass diffusion cell, the in-vitro research of drug permeability across the Dialysis membrane was conducted. If you want to keep the sink state, you may use the modified cell with a larger capacity (10 ml). Spectrophotometric analysis was performed on the samples to determine the drug content. Refilling the receptor phase with phosphate buffer of the same volume was done with each sample removal.

Stability studies of optimized formulation

The optimized formulation (F4) was subjected to accelerated stability studies according to ICH Q1A(R2) guidelines by storing the patches at 40 ± 2°C and 75 ± 5% relative humidity for three months. The patches were evaluated periodically for physical appearance and in vitro drug release. The formulation showed no significant changes in appearance, and only a slight reduction in cumulative drug release was observed, indicating good stability under accelerated storage conditions.

RESULTS & DISCUSSION:

Evaluation of Transdermal formulation

Table-2: Physicochemical evaluation of Selegiline Transdermal patches

Formulation code	Weight (mg)	Thickness (mm)	Folding endurance	Surface pH	% Moisture loss	% Moisture absorption
F1	206	0.21	246	6.3	2.76	3.37
F2	307	0.32	278	6.5	2.42	3.09
F3	209	0.25	293	6.6	3.59	5.85
F4	314	0.33	342	6.9	4.53	6.38

Physical appearance:
The prepared patches were found to be uniform, smooth, flexible and homogenous.

Weight variation: The weight variation of the formulations ranged from 206 mg to 314 mg. Formulations containing higher polymer concentrations (F2 and F4) exhibited greater weights compared to F1 and F3, which can be attributed to the increased amount of polymer incorporated into the patch matrix. The low variation in weight among patches of the same formulation indicates uniform distribution of drug and excipients throughout the casting film.

Thickness: The thickness of the patches was found to be between 0.21 mm and 0.33 mm. An increase in polymer concentration resulted in a corresponding increase in patch thickness. Formulations F2 and F4, containing 200 mg of polymer, showed higher thickness values than formulations prepared with 100 mg of polymer. Uniform thickness is an important parameter as it contributes to consistent drug loading and release characteristics.

Folding endurance: The folding endurance values ranged from 246 to 342, indicating good flexibility and mechanical strength of all prepared patches. Formulation F4 exhibited the highest folding endurance value (342), followed by F3 (293), suggesting that HPMC-based patches possess superior flexibility compared with ethyl cellulose-based patches. The presence of PEG as a plasticizer may have contributed to improved elasticity and resistance to cracking during repeated folding.

Surface pH: The surface pH of all formulations was found to be within the range of 6.3–6.9, which is close to the normal skin pH. This indicates that the prepared patches are unlikely to cause irritation or discomfort when applied to the skin. The slightly higher pH observed in HPMC-based formulations may be attributed to the hydrophilic nature of the polymer.

Moisture loss: The percentage moisture loss was observed between 2.42% and 4.53%. Ethyl cellulose formulations (F1 and F2) exhibited lower moisture loss values compared to HPMC formulations (F3 and F4). This behavior can be explained by the hydrophobic nature of ethyl cellulose, which restricts water movement and evaporation. Higher moisture loss in HPMC-containing patches is due to the greater affinity of HPMC for water.

Moisture absorption: Similarly, the percentage moisture absorption ranged from 3.09% to 6.38%. HPMC-based formulations showed higher moisture absorption than ethyl cellulose formulations because of the hydrophilic and swelling properties of HPMC. Increased moisture uptake can improve patch hydration and drug diffusion, however, excessive absorption may affect stability.

In vitro release study:

Table-3: In vitro drug release profiles of Selegiline transdermal patch (F1-F4)

Time (hr)	F1	F2	F3	F4
0	0	0	0	0
1	15.86	16.79	17.49	18.10
2	23.40	25.79	26.78	27.84
3	34.49	35.83	36.81	37.49
4	42.10	47.49	48.13	49.53
5	61.23	62.28	63.19	65.43
6	73.58	75.49	73.46	75.10
7	82.63	83.69	85.10	86.92
8	94.15	95.61	96.59	98.10

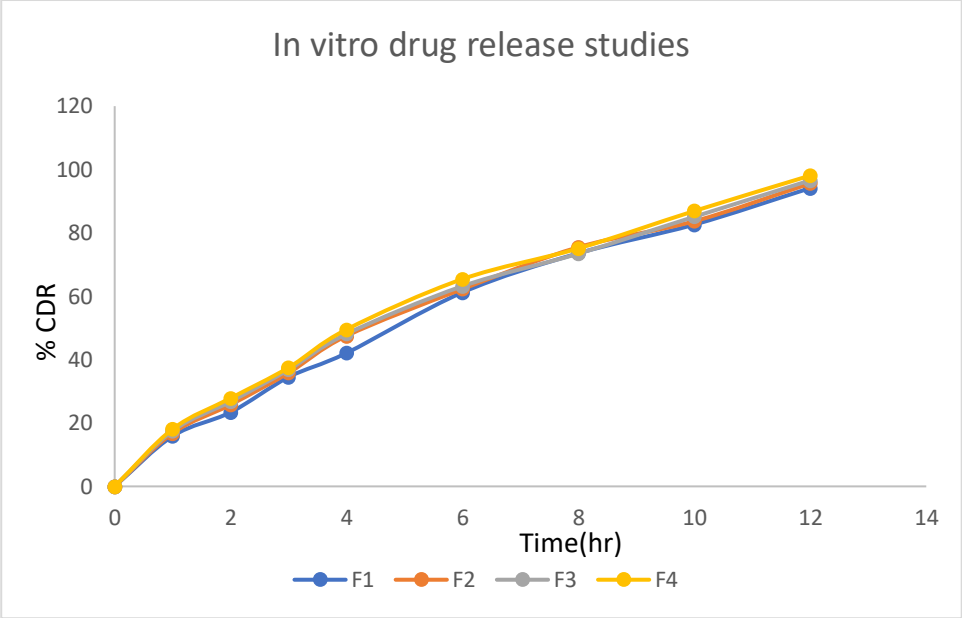


Fig-1: In vitro drug release profiles of Selegiline transdermal patch (F1-F4)

The cumulative drug release increased with time for all formulations. Formulation F4 exhibited the highest cumulative drug release (98.10%) after 8 hours, followed by F3 (96.59%), F2 (95.61%), and F1 (94.15%). The enhanced drug release from F4 may be attributed to the hydrophilic nature of HPMC, which swells upon hydration, creating aqueous channels that facilitate drug diffusion. In contrast, ethyl cellulose-based formulations exhibited comparatively slower drug release because of the hydrophobic nature of the polymer.

marginally from 98.10% to 97.82%, indicating good stability of the formulation under accelerated storage conditions.

Stability studies:

The optimized formulation (F4) was subjected to accelerated stability studies according to ICH guidelines (40 ± 2°C/75 ± 5% RH) for three months. No significant changes were observed in the physical appearance, color, or flexibility of the patches during the study period. The cumulative drug release decreased

Table 4: Stability studies of optimized formulation at 40 ± 2 ^{0}C and 75 ± 5% RH for 3 months

Time in days	Physical appearance	% Cumulative drug release
0	No change in color	98.10
90	Slight yellowish color	97.82

SUMMARY AND CONCLUSION:

The present study successfully formulated and evaluated Selegiline hydrochloride transdermal patches using the solvent casting method with HPMC and Eudragit RL100 as film-forming polymers. Preformulation studies confirmed the suitability of the drug for formulation. Selegiline hydrochloride exhibited acceptable organoleptic properties, a melting point within the reported range, suitable solubility characteristics, and a λmax of 247 nm in phosphate buffer (pH 7.4). The FTIR studies demonstrated the absence of significant drug–polymer interactions, confirming the compatibility of the drug with the selected excipients.All prepared transdermal patches exhibited satisfactory physicochemical properties, including uniform appearance, acceptable weight variation, uniform thickness, good folding endurance, surface pH close to that of the skin, and acceptable moisture loss and moisture absorption values. These findings indicate that the prepared patches possessed suitable mechanical strength, flexibility, and stability for transdermal application.

Among all the formulations, F4, containing 50 mg of Eudragit RL100, showed the best overall performance. It exhibited the highest folding endurance, acceptable physicochemical characteristics, and the maximum cumulative drug release of 98.10**%** over 12 hours, indicating efficient and sustained drug release. The accelerated stability study of the optimized formulation demonstrated no significant changes in physical appearance and only a marginal decrease in drug release after three months, confirming its stability under accelerated storage conditions.

Overall, the study concludes that the optimized Selegiline hydrochloride transdermal patch **(**F4**)** is a promising transdermal drug delivery system capable of providing sustained drug release with satisfactory physicochemical properties and stability. This formulation has the potential to improve patient compliance by reducing dosing frequency and may serve as an effective alternative to conventional oral therapy for the management of conditions requiring Selegiline administration.

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