

Formulation and Evaluation of Transdermal Patches of Risperidone USP (Micronized) for Schizophrenia

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Abstract

Risperidone is 3-[2-[4-(6-fluoro-1,2-benzoxazol-3-yl)piperidin-1-yl]ethyl]-2-methyl-6,7,8,9-tetrahydropyrido[1,2-a]pyrimidin-4-one. The primary action of risperidone is to decrease dopaminergic and serotonergic pathway activity in the brain, therefore decreasing symptoms of schizophrenia and mood disorders (Figure 1).

The primary action of Risperidone is to decrease dopaminergic and serotonergic pathway activity in the brain, therefore decreasing symptoms of schizophrenia and mood disorders. Risperidone has a high binding affinity for serotonergic 5-HT_{2A} receptors when compared to dopaminergic D₂ receptors in the brain. The absolute oral bioavailability of risperidone is 70%. The apparent half-life of risperidone is 3 hours (CV=30%) in extensive metabolizers and 20 hours (CV=40%) in poor metabolizers.

The objective of this study is to formulate and evaluate a transdermal patch of Risperidone using a suitable film former. Transdermal patches of Risperidone were prepared by solvent casting method using HPMC K200M and Eudragit RS100. Glycerine and also PEG 400 was used as plasticizer & permeation enhancer. All the formulations were examined for evaluation parameter like physicochemical properties.

The prepared formulation which were evaluated for different physicochemical characteristics like weight of patch, thickness, folding endurance, tensile strength have exhibited satisfactory results.

Based on the evaluation data, the most effective plasticizer was found to be glycerine (F1) as compared to PEG 400 (F2). It was observed that based on the diffusion study that transdermal patch of Risperidone with Glycerine (F1) shows higher release characteristics than the PEG 400 (F2) transdermal patch. Drug content uniformity of F1 (Glycerine) transdermal patch was also higher than the F2 (PEG 400) transdermal patch. It was also observed that the folding endurance was >300 for all the prepared transdermal patches. Based on the studies, it was concluded that the transdermal patch of Risperidone using glycerine (F1) was the best compared to the formulations using PEG 400 (F2).

Keywords: Transdermal; Risperidone; HPMC K200M; Schizophrenia; Glycerine

Introduction

Transdermal drug delivery system

Transdermal drug delivery system is an administration route, where active molecules are administered through the skin in a predetermined and controlled rate. Transdermal delivery represents an attractive alternative to oral delivery of drugs and is poised to provide an alternative to hypodermic injection too. It has a variety of advantages compared with the oral route. In particular, it is used when there is a significant first pass effect of the liver that can prematurely metabolize drugs [1-3].

Transdermal delivery also has advantages over hyper dermic injections which are painful, generate dangerous medical waste and pose the risk of disease transmission by needle re-use. In addition, transdermal systems are non-invasive and can be self-administered. They can provide release for long periods of time up to one week. They also improve patient compliance and the systems are generally inexpensive.

Transdermal delivery system is defined as self-contained, discrete dosage forms known as patches when applied on skin, deliver the drug through skin at a controlled rate to systemic circulation. They can be categorized as undergoing three generations of development from the first generation of systems that produced many of today's patches by

judicious selection of drugs that can cross the skin at therapeutic rates with little or no enhancement. Through the second generation that has yielded additional advances for small molecule delivery by increasing skin permeability and driving forces for transdermal transport. To the third generation that will enable transdermal delivery of small molecule drugs, macromolecules (including proteins and DNA) and virus based and other vaccines through targeted permeabilization of the skin's stratum corneum.

Advantages

- Painless delivery of a therapeutic level of drug [1-3].
- Useful for drugs that have a high first pass effect through

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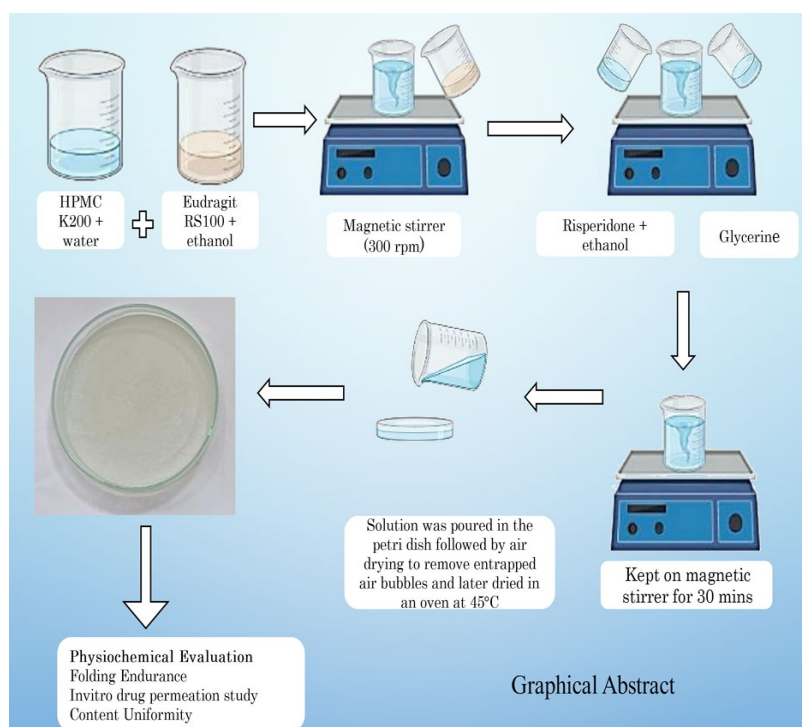


Figure 1: Graphical Abstract.

the liver, have poor oral uptake, need frequent administration, or that interact with stomach acid

- Painless, non-invasive way to deliver substances directly into the body.
- Delivery of drugs that are broken down by stomach acids, not well absorbed from the gut, or extensively degraded by the liver.
- Fewer side effects and easier to use.
- Self-administration.
- Number of doses gets reduced which in turn improves the patient's compliance.
- Useful for patients who are nauseated and unconscious.
- Cost effective.
- Avoidance of GI incompatibility.

Disadvantages:

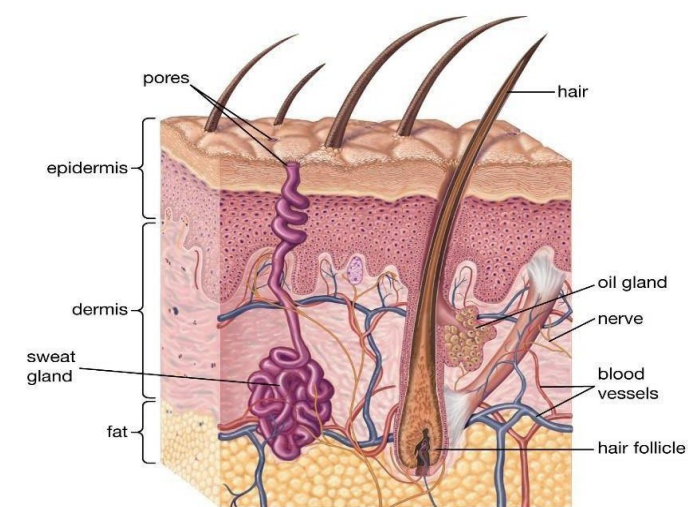
- Transdermal drug system cannot deliver ionic drugs.
- Cannot achieve high drug levels in blood plasma.
- Cannot develop for drugs of large molecular size.
- Cannot deliver drugs in a pulsatile fashion.
- Cannot develop drug or formulation causing irritation to the skin.
- Long-time adherence is difficult.
- May cause allergic reaction.
- The barrier function of the skin changes from one site to another on the same person, from person to person and also with age.

Skin

Skin being the largest organ of the body, with a total area of about 20 square feet along with its derivatives (hair, nails, sweat and oil glands) makeup the integumentary system. (Figure 2) [4]

Skin has three layers:

1. The epidermis, the outermost layer of skin that provides a waterproof barrier and creates our skin tone.
2. The dermis, beneath the epidermis that contains tough connective tissue, hair follicles, and sweat glands.



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Figure 2: Structure of Skin [4].

3. The deeper subcutaneous tissue (hypodermis) is made of fat and connective tissue.

Skin appendages include eccrine sweat glands, apocrine glands, sebaceous glands and hair. The skin's colour is created by special cells called melanocytes, which produce the pigment melanin. Melanocytes are located in the epidermis.

1. Epidermis

It is the uppermost multi-layer of the skin, composed of stratified keratinised squamous epithelium it contains four principle types of cells, such as keratinocytes (90%), melanocytes, Langerhans cells and Merkel cells. The thickness of epidermis varies depending on the cell size and the number of cell layers ranging from about 0.8 mm on the palms and soles down to 0.6mm on the eyelids.

Epidermis is subdivided into 5 layers:

- Stratum corneum (horny layer);
- Stratum lucidum (only found in thick skin – that is, the palms of the hands, the soles of the feet and the digits);
- Stratum granulosum (granular layer);
- Stratum spinosum (prickle cell layer);
- Stratum basale (germinative layer) (Figure 3) [5]

a. The Stratum Corneum

It is the most differentiated top superficial layer of keratinised cells (corneocytes). It consists of 25-30 layers of flattened keratinocytes that contains mostly keratin (tough fibrous protein). The nuclei are absent. Between the cells are lipids from lamellar granules that form major constituent of the water barrier of the skin. These multiple layers act as protective for the deeper layer from injury and microbial abrasion. The thickness of the skin varies over the surface of the body ranges from 1mm to 5 mm, which differs mainly in palms and soles of feet.

b. Stratum Lucidum

It lies immediately below stratum corneum and is considered as a subdivision of stratum corneum. It is thin, more or less transparent, glistening layer. It is present only in the thick

skin of fingertips, palms and soles. This is a highly refractile layer, poorly strained hyaline zone contains eosinophilic cells in the process of keratinization is well advanced.

c. Stratum Granulosum

It is the middle and superficial layer of the non-keratinized portion of the epidermis. These are 1-3 cells thick spindle shaped cells enriched with intensely staining keratohyalin granules which contain cysteine-rich and histidine protein. This keratogenous or transitional zone is a region of intense biochemical activity and morphological changes.

d. Stratum Spinosum

This is the broad layer, where 8-10 layers of many-sided keratinocytes fit closely together. The cells flatten and their nuclei shrink, and look like polygon, thus also called as polygonal cells, prickle cells as they are interconnected by fine prickles which helps in providing strength and flexibility to the skin. Projections of both Langerhans cells and melanocytes also appear in this layer.

e. Stratum Basale

It is the deepest layer of epidermis where basal cells are non-nucleated, columnar and about 6 μm wide with their long axis at right angles to the dermoepidermal junction. It is also called as stratum germinativum due to mitotic active cells which constantly proliferating the skin and renew the epidermis providing constant thickness and healthy balanced skin. The layer contains melanocytes which are responsible for production and distribution of melanin granules to the keratinocytes required for pigmentation, a protective measure against radiations.

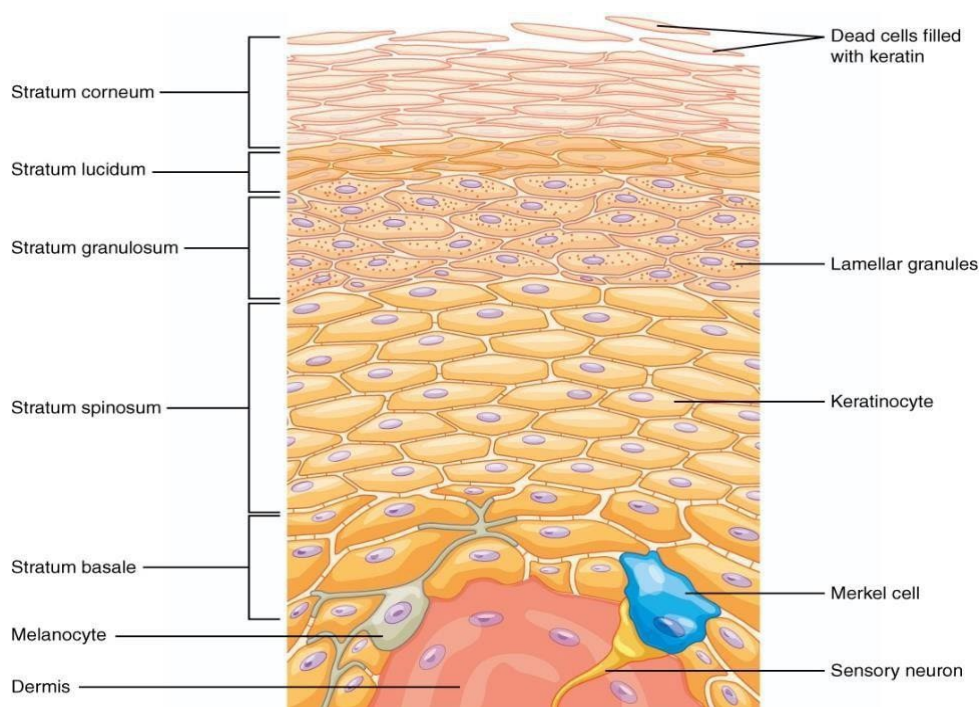


Figure 3: Epidermal layers of skin [5].

2. Dermis

Dermis is the second deeper region lying in between the epidermis and subcutaneous fatty region. It is formed from connective tissues containing collagen and elastin fibres including few cells as fibroblasts, macrophages and adipocytes. Blood vessels, nerve glands and hair follicles are embedded in dermal tissues. The superficial portion of dermis called papillary layer which consists of areolar connective tissues containing fine elastin fibres. The surface area is greatly increased by small finger like projection called dermal papillae which contains papillary loops project into the epidermis. These dermal papillae contain tactile receptors called corpuscles of touch or Meissner corpuscles, nerve endings that are sensitive to touch. The reticular region attached to the subcutaneous layer consists of dense irregular connective tissues containing fibroblast, bundles of collagen and some coarse elastic fibres. These collagen and elastin fibres provide strength, extensibility and elasticity to the skin.

3. Hypodermis

It is a subcutaneous layer which lies deep to the dermis, but not the part of skin. This layer consists of areolar and adipose tissue known as superficial fascia attaching the dermis to the underlying structures. This region also contains nerve endings called lamellate corpuscles that are sensitive to pressure. It serves as the storage depot for fat and contains large blood vessels that supply the skin.

4. Skin appendages

These are also known as skin derivatives which include hair follicles, associated sebaceous glands, sweat glands (Eccrine and apocrine glands) and nails.

a. Hair follicle

It is the product of synthesized protein following cell division at the root of hair pressure. The number of hair per unit area varies at different parts of the body.

b. Sebaceous glands

These are responsible for sebum secretion and constitute of fatty layer over the skin and hair. These are present on face, shoulder, upper chest and scalp but not palms and soles.

c. Eccrine sweat glands

These are salty sweat glands distributed over the surface of the body in order to regulate the body temperature by secreting dilute aqueous solution of salt and some other minor components called salt.

d. Apocrine glands

These are present only on the selected regions of the body such as axillae in anogenital region and around the nipples. Due to emotional stress and sexual stimulation, they secrete milky substance containing protein, lipoprotein, lipids and diverse proteins. These are ten folds larger than the eccrine sweat glands.

e. Nails

Nails are plates of tightly packed, hard, dead, keratinized epidermal cells that form a clear, solid covering over dorsal surface of distal portions of digits.

Functions of the Skin

- Provides a protective barrier against mechanical, thermal and physical injury and hazardous substances [6].

- Prevents loss of moisture.
- Reduces harmful effects of UV radiation.
- Acts as a sensory organ (touch, detects temperature).
- Helps regulate temperature.
- An immune organ to detect infections etc.
- Production of vitamin D

Transdermal Patches

Transdermal Patch is a flexible single-dose preparation intended to be applied to the unbroken skin to obtain a systemic delivery over an extended period of time. Transdermal patches products were first approved in 1981 by FDA [7,8].

Transdermal patches are designed to slowly deliver the active ingredients through the intact skin, resulting in a prolonged and adequately constant systemic absorption rate. The rate limiting step for systemic absorption of the active substance is usually the absorption through skin. Alternatively, the absorption may be limited by incorporating or dissolving the active substance in a [semisolid] reservoir, with a membrane to control the release and diffusion of the active substance from the patch. The transdermal patch can also be formulated combining both drug delivery principles as the means of controlling drug delivery to the surface of the skin.

To ensure the safe and effective use of transdermal patches, the active substance(s) should be delivered through the skin at an adequate rate that is maintained for an appropriate time during patch application and should not irritate or sensitise the skin. The excipients should not have an adverse effect on the skin or exacerbate the adverse effects of the active substance. Skin enhancers should have a reversible impact on the skin barrier. The solvents used should not interact with the components of the patch system.

Transdermal patches usually contain an excess of active substance than that delivered to the patient during use. This excess is necessary to maintain a clinically effective rate of delivery over time and allow the minimum patch surface area. Because the concentration of the active substance can be near to its saturation limit, there is a risk of crystallisation on storage with potential adverse effects on the quality and efficacy of the product. Furthermore, the residual active substance left in the patch after administration can pose a safety risk to the patients, others and the environment. There is also a risk of misuse of discarded transdermal patches e.g., those containing narcotic drugs.

It is acknowledged that transdermal patches can differ in drug content and surface area but still deliver the same amount of drug over the same period of time. It is desirable to minimise the amount of residual active substance in the patch as much as possible.

To deliver the drug transdermally, the patch should have following properties:

- Low molecular weight (<1000Da)
- Low melting point
- Non irritating
- Short half-life
- Affinity for lipophilic and hydrophilic phase

The components of transdermal patch are liner, API, adhesive, backing membrane and matrix filler (Figure 4).

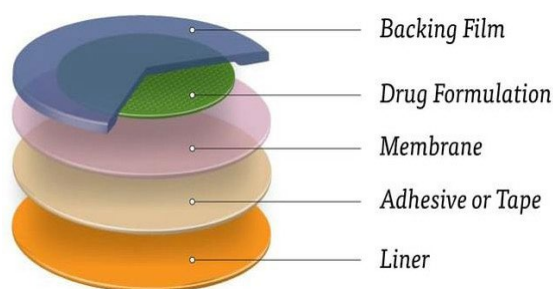


Figure 4: Components of a Transdermal Patch [11].

1. Polymer matrix

Polymer matrix is said to be backbone of TDDS, which control the release of the drug. Polymer should be chemically non-reactive, should not decompose on storage, should be non-toxic, cost should not be high. E.g.: cellulose derivatives, zein, gelatin, shellac, waxes, gums, polybutadiene, hydrin rubber, polyisobutylene, silicon rubber, nitrile, acrylonitrile, neoprene, polyvinyl alcohol, polyvinylchloride, polyethylene, polypropylene, polyacrylate, polyamide, polyurea, polyvinylpyrrolidone, polymethylmethacrylate [8,9].

2. Drug

The transdermal route is an extremely attractive option for the drugs with appropriate pharmacology and physical chemistry. Transdermal patches offer much to drugs which undergo extensive first pass metabolism, drugs with narrow therapeutic window, or drugs with short half-life (fentanyl, nitroglycerine).

3. Pressure Sensitive Adhesives

Adhesive serves to adhere the components of the patch together along with adhering the patch to the skin. The adhesive must possess sufficient adhesion property so that the TDDS should remain in place for a long time. Pressure sensitive adhesives are commonly used

for transdermal patch to hold the skin. Commonly used adhesives are silicone adhesives, polyisobutylenes adhesives, and polyacrylate based adhesives

4. Backing laminates

It has a low modulus or high flexibility (vinyl, polyethylene).

5. Release liner

Protects the patch during storage. The liner is removed prior to use.

6. Other excipients

Various solvents such as Ethanol, Chloroform, and isopropanol is used to prepare drug reservoir. Plasticizers such as dibutylphthalate, PEG are used to provide plasticity to the transdermal patch.

7. Penetration Enhancers

The penetration enhancers are usually used to increase the permeability of skin or substances that reduce the permeability of the skin. The selection of permeation enhancer should be based not only on its efficacy in enhancing the skin permeation but also on its physicochemical and biologic compatibility with the system's other components.

Advantages of Transdermal Patch [10]

- Transdermal patches can avoid gastrointestinal drug absorption difficulties

- Substitute for oral administration of medication when the route is unsuitable

- Avoids the first pass metabolism
- Non-invasive and have patient compliance
- Less greasy and can be easily removed from skin
- Improved bioavailability

Disadvantages of Transdermal Patch

- There is possible local irritation at the site of application.
- Skin's low permeability limits the number of drugs that can be delivered in this manner.

Aim

Formulation and evaluation of Transdermal patches of Risperidone USP (Micronized) using different plasticizers

Objective

1. Selection of appropriate plasticizers
2. Preparation and formulation of Transdermal Patch containing Risperidone
3. Evaluation of Transdermal patch containing Risperidone

Methodology

Preparation of hydrochloric acid (0.1N) solution:

8.33 ml of concentrated HCl was accurately measured and transferred into clean 1000 ml volumetric flask. Dilute it with distilled water and shake vigorously. Make up the volume up to the 1000 ml mark.

Preparation of Risperidone standard solution with (0.1N) HCl solution:

Stock solution:

25 mg of accurately weighed Risperidone was transferred into 25 ml volumetric flask. Ethanol was used as the solvent to dissolve Risperidone, the volume was made up to 25 ml using ethanol to produce stock solution of concentration 1mg/ml. The contents of volumetric flask were shaken well and kept aside.

Working Standard solution:

2ml of this solution was diluted with 100ml ethanol to give a solution of 20µg/ml. Following dilutions were made to obtain readings for calibration curve: (Table 1)

Table 1: Volume of solution for required concentration.

Concentration (µg/ml)	Vol. of Solution (ml)
2	1
4	2
6	3
8	4
10	5
12	6
14	7
16	8
18	9
20	10

Preparation of Calibration curve:

An absorption spectra was obtained using the working standard solution.

λ_{max} observed from the absorption spectra was found to be 283.50nm.

The absorbance of each solution was measured at 283.50nm (λ_{max}) using UV spectrophotometry.

A graph of absorbance v/s concentration was plotted to get R2 (regression factor) (Figure 5)

Observations and Preparation of Transdermal Patches

Materials

Instruments

Transdermal patches were prepared by using solvent casting method. Petri plates of 8 cm diameter were used for casting the patches. A total of four formulations were prepared (Table 2, Table 3, Table 4 and Figure 6).

Table 2: Absorbance of specified concentration.

Concentration (µg/ml)	Vol. of Solution (ml) Absorbance
2	0.088
4	0.201
6	0.334
8	0.375
10	0.522
12	0.606
14	0.616
16	0.671
18	0.827
20	0.894

Table 3: Materials.

Sr. No.	Materials	Use
1	Risperidone	Drug
2	HPMC (K200)	Polymer
3	Eudragit RS 100	Polymer
4	Glycerin	Plasticizer
5	PEG 400	Plasticizer
6	Ethanol	Solvent

Composition of patches containing Risperidone

- HPMC K200M was soaked in water overnight (Table 5).
- Eudragit RS100 was dissolved in the solvent (Ethanol) and added to the soaked HPMC K200M.
- The two polymers were covered with a foil to prevent evaporation of the solvent and stirred on a magnetic stirrer for 30 mins on 300 rpm to prevent air bubbles.
- The drug (Risperidone) dissolved in ethanol was added to the polymer and stirred for additional 15 mins.
- Plasticizer was added to the mixture dropwise and stirred for 5 mins.
- The solution was then poured onto a petri plate.
- The rate of evaporation of solvent was controlled by inverting cap funnel.
- The patch was air dried for 24 hours.
- Each patch was cut into 2×2 cm dimension and physiochemical evaluation was performed (Figure 7).

Result & Discussion

Physiochemical Evaluation

Physical Appearance

Table 4: Instruments.

Sr. No.	Instrument
1	Electronic Balance
2	UV Visible Spectrophotometer
3	Magnetic Stirrer
4	Digital Vernier Calliper
5	Tensile Strength tester

Table 5: Composition of Patches containing Risperidone.

Sr. No.	Ingredients	F1	F2	F3
1	Risperidone (mg)	25	25	25
2	HPMC (K200) (mg)	200	200	200
3	Eudragit (mg)	400	130	130
4	Glycerine (ml)	0.05	-	0.025
5	PEG 400	-	0.05	0.025
6	Ethanol (ml)	10	10	10
7	Purified Water	q.s	q.s	q.s

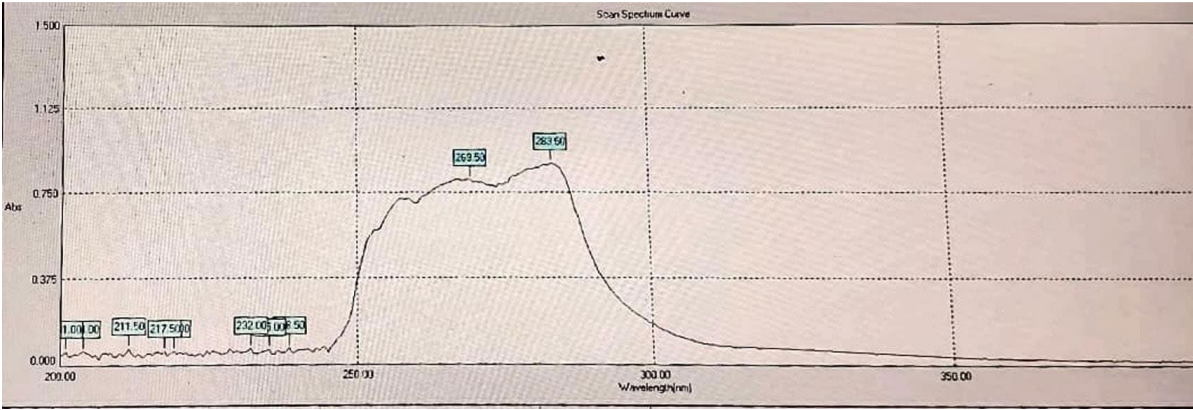


Figure 5: Absorption spectra.

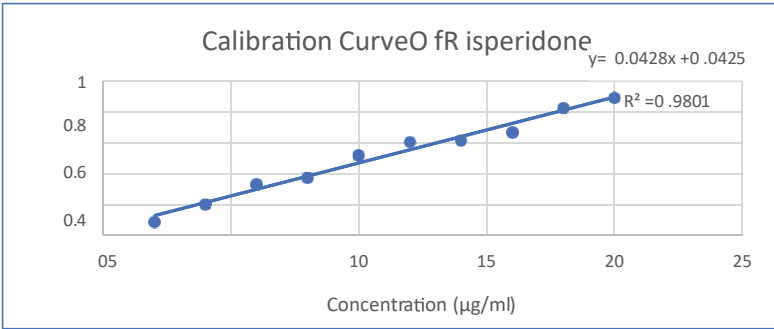


Figure 6: Calibration curve.

Table 6: Physicochemical Evaluations.

Patch	Weight of the patch (g)	Thickness of the patch mm	Folding endurance
F1 (Glycerine)	0.2636	0.04	>300
F2 (PEG 400)	0.3410	0.06	>300
F3 (PEG 400 + Glycerine)	0.3194	0.07	>300

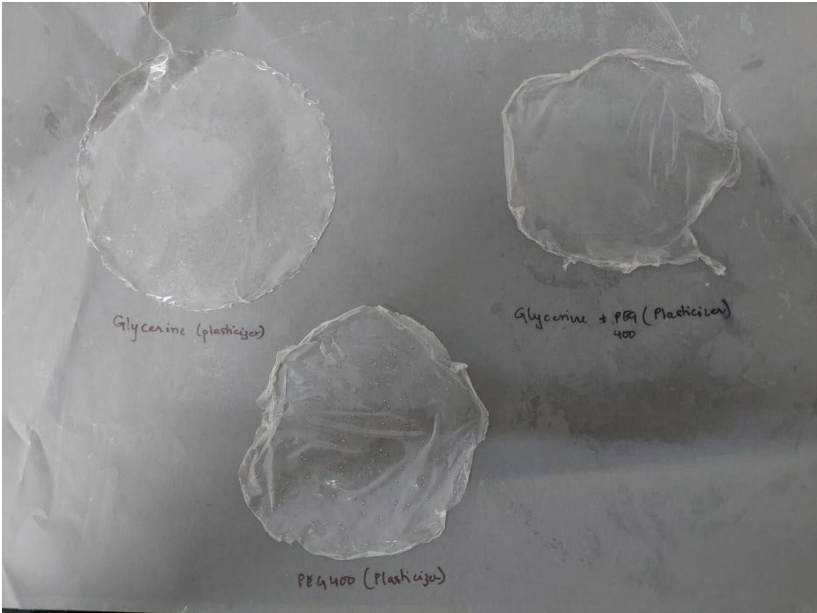


Figure 7: Transdermal Patches of Risperidone.

The prepared transdermal patches were cut in square shape of 2×2cm. They were found to be flexible, transparent.

Weight of the patch

After formulating, the prepared transdermal patches were dried and weighed accurately on a digital balance.

Thickness of the patch

The thickness of the prepared transdermal patches was measured using digital vernier calliper.

Folding Endurance

Folding endurance of the prepared transdermal patches was determined by repeatedly folding one patch at the same place, till it breaks or develops visible cracks on folding number of times manually which was considered satisfactory to reveal good patch properties. Prepared transdermal patches did not show any cracks even after

folding for more than 300 times hence they exhibited good folding endurance.

Observations

In Vitro Drug Permeation Study

In vitro skin permeation studies were performed by using a modified Franz diffusion cell with a receptor compartment capacity of 50 ml. The cellophane membrane was mounted between the donor and receptor compartment of the diffusion cell. The formulated transdermal patches were cut into size of 2 cm² and placed over the drug release membrane and the receptor compartment of the diffusion cell was filled with phosphate buffer pH 7.4. The whole assembly was fixed on a magnetic stirrer, and the solution in the receptor compartment was constantly and continuously stirred using magnetic beads at 100 rpm; the temperature was maintained at 37 ± 0.50 C. The samples of 5 ml were withdrawn at time interval of 1, 2, 3, 4 hrs and analysed for

drug content spectrophotometrically at 283.5 nm against blank. The receptor phase was replenished with an equal volume of phosphate buffer at each time of sample withdrawal. The cumulative amounts of drug permeated per square centimeter of patches were plotted against time (Table 6 and Table 7).

Content Uniformity

The prepared transdermal patches (F1-F3) were tested for the content uniformity. A film of size 1 cm² was cut and placed in a 200ml volumetric flask. 100ml phosphate buffer of pH 7.4 was added. The contents were stirred. After the transdermal patch was dissolved, the absorbance of the solution was measured against the corresponding blank solutions at 283.5nm. The content uniformity was calculated using the formula:

$$\text{Content Uniformity in } \frac{\text{mg}}{\text{ml}} (\%) = \frac{Y1 - 0.0425}{0.0425} \times 100$$

Where, Y1 = Absorbance measured

Observations

Conclusion

Transdermal drug delivery system is an administration route, where active molecules are administered through the skin in a predetermined and controlled rate. In particular, it is used when there is a significant first pass effect of the liver that can prematurely metabolize drugs. The protective function of the skin is, it provides a protective barrier against mechanical, thermal and physical injury and hazardous substances (Table 8).

In the present study, an attempt was made to formulate a transdermal patch of Risperidone. The aim of the study was to prepare a transdermal patch and to investigate the effect of different plasticizers.

The transdermal patches were formulated using HPMC (K200M), Eudragit (RS100), Glycerine, PEG 400 and Ethanol using solvent casting Method. Attempts were made using different grade of HPMC (K100) which did not form ideal patches. Increased concentration of Eudragit resulted in stiff plastic-like patches which were undesirable. When concentration of glycerine was increased, formed patches appeared oily. Use of PEG 400 as a plasticizer yielded patches with precipitated drug. A combination of Glycerine and PEG 400 did not form desired patches.

The prepared patches, each with a different plasticizer were subjected to several evaluation parameters like weight variation, thickness of the patch, drug content, folding endurance and in-vitro drug permeation study. The resultant data of each test was collected and interpreted.

Weight and thickness of all the formulations indicate physical uniformity of the prepared patches. Incorporation of PEG 400 individually and in-combination formed rubber-like patches.

Based on the evaluation data the most effective plasticizer was found to be glycerine (F1) as compared to PEG 400 (F2). It was observed that based on the diffusion study that transdermal patch of Risperidone with Glycerine (F1) shows higher release characteristics than the PEG 400 (F2) transdermal patch. Drug content uniformity of F1 (Glycerine) transdermal patch was also higher than the F2 (PEG 400) transdermal

Table 7: Release studies.

(a) Glycerine						
Time (hrs)	Absorbance (y)	Concentration (x)	Amount (mg/5ml)	Amount (mg/900ml)	CDR	
0	0	0	0	0	0	
1	0.501	10.713	0.054	9.641	9.641	
2	0.283	5.619	0.028	5.057	5.111	
3	0.207	3.843	0.019	3.459	3.541	
4	0.229	4.357	0.022	3.922	4.023	
(b) PEG 400						
Time (hrs)	Absorbance (y)	Concentration (x)	Amount (mg/5ml)	Amount (mg/900ml)	CDR	
0	0	0	0	0	0	
1	0.196	3.586	0.018	3.228	3.228	
2	0.437	9.217	0.046	8.296	8.313	
3	0.208	3.867	0.019	3.480	3.544	
4	0.197	3.610	0.018	3.249	3.332	
(c) Glycerine + PEG 400						
Time (hrs)	Absorbance (y)	Concentration (x)	Amount (mg/5ml)	Amount (mg/900ml)	CDR	%CDR
0	0	0	0	0	0	0
1	0.247	4.778	0.024	4.300	4.300	215.012
2	0.295	5.900	0.029	5.310	5.333	266.673
3	0.309	6.227	0.031	5.604	5.657	282.868
4	0.333	6.787	0.034	6.109	6.193	309.658
Average						268.553

Table 8: Content Uniformity of Risperidone using different plasticizer.

Patch	Absorbance	Content Uniformity (mg/100ml)
F1 (Glycerine)	0.228	4.33
F2 (PEG 400)	0.114	1.70
F3 (PEG 400 + Glycerine)	0.099	1.32

patch. It was also observed that the folding endurance was >300 for all patches. Based on the studies, it was concluded that the transdermal patch of Risperidone using glycerine (F1) was the best compared to the formulations using PEG 400 (F2).

Future Scope

Patient Compliance and Convenience: Focus on the design and development of user- friendly transdermal patches that are comfortable to wear, easy to apply and remove, and do not cause skin irritation. Considering factors like patch size, adhesive properties, and wear time to enhance patient compliance.

Explore the possibility of formulating transdermal patches that contain a combination of risperidone and other medications used for treating schizophrenia. Investigate the synergistic effects, stability, and feasibility of delivering multiple drugs through the transdermal route.

Develop innovative techniques to improve drug delivery efficiency and skin permeation of risperidone.

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