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# FROM SKIN TO BRAIN: PIONEERING TRANSDERMAL DRUG DELIVERY FOR PARKINSON'S PATIENTS

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## ABSTRACT

The effective creation of transdermal treatments for Parkinson's disease has long been a problem for the medical profession. However, recent advancements in the field, particularly with the use of rotigotine, have sparked hope for more breakthroughs in the future. Despite its potential, it offers slow and sustained drug delivery over extended periods. Nevertheless, transdermal drug delivery holds great promise as it offers a more consistent and steady release of medication, which can help control symptoms and reduce side effects. There has been a recent focus on improving delivery methods, as well as the stability of the medication upon delivery. These efforts have yielded promising results, with patches and gels that deliver rotigotine, apomorphine, and carbidopa/levodopa currently in clinical trials. In addition, ongoing research into new technologies like microneedles, nanoparticles, and gene therapy have the potential to improve the efficacy and safety of these treatments. The development of transdermal-based formulations for Parkinson's disease is still in the clinical trial phase and is yet to be approved by regulatory agencies like the FDA. The regulatory landscape for transdermal drug delivery is complex and requires compliance with relevant regulatory agencies' guidelines to bring these products to market. The future scope of transdermal drug

delivery for Parkinson's disease treatment is promising, with the potential for more long-term treatment options that can delivers genetic material to cells in the brain to produce a specific protein that is lacking in Parkinson's disease.

**Keywords: Transdermal drug delivery, Parkinson's disease treatment, Blood-brain barrier, Controlled-release technology, Patient compliance**

## [1] INTRODUCTION

A large portion of minor compound drugs are usually given by mouth, with the injectable and oral methods being most common. The oral approach offers advantages like predetermined doses, portability, and the ability for patients to self-administer. This makes oral drug administration the most convenient option **[1, 2]**. Nonetheless, most therapeutic peptides or proteins are not administered orally because of rapid degradation in the stomach and limited transport across the epithelial barrier due to size constraints **[3]**. Therefore, giving macromolecules primarily by injection has certain drawbacks, including the need for administration by a professional administrator, the intrusive character of injections evoking pain, and reduced patient acceptance/compliance **[4]**.

It makes sense that modern drug administration techniques, including transdermal drug delivery, have the ability to overcome the inherent constraints of the traditional methods of medication delivery **[5]**.

Parkinson's disease [PD] is a neurodegenerative movement disorder that worsens over time and is characterized pathologically by the loss of melanized dopamine neurons in the nigrostriatal region, as well as intracytoplasmic pro-tenacious inclusions of fibrillar -synuclein [Lewy bodies] and a decrease in the availability of dopamine [DA] in the striatum **[6]**. Bradykinesia, postural instability, stiffness, and tremor are some of the clinical signs of PD, and some patients may experience anxiety, depression, autonomic abnormalities, and dementia. There is no treatment for Parkinson's disease [PD], as neither the illness's development can be stopped nor reversed by existing medicines. The emergence of treatment-related problems that might severely restrict levodopa's efficacy compromises the lengthy management of Parkinson’s disease **[7]**.

A putative mechanism for their origin is intermittent, or pulsatile, activation of dopamine receptors, which is supported by growing data. A way to avoid pulsatile drug delivery and maybe prevent the onset of dyskinesia and motor variations is by continuous transdermal pharmaceutical administration **[8]**. It has taken a long time to create a successful transdermal

preparation for Parkinson's disease, but the recent success of rotigotine as a transdermal therapy gives us faith and encouragement that other breakthroughs may also be on the horizon and that our ability to efficiently treat this life-altering condition will continue to increase **[9]**.

**1.1 Rationale for transdermal drug delivery for Parkinson disease**

The justification for this distribution method has to be thoroughly analysed given how well the skin serves as a barrier to molecular transport. It is obvious that there are a number of situations when the most practical medication administration method—the oral route—is impractical and other options must be investigated **[10]**.

- Other anatomical apertures have not been researched for their potential as alternative routes for medicine delivery despite the fact that the intravenous procedure eliminates various limitations [including gastrointestinal and hepatic metabolism] [especially for long-term treatment]. The skin provides a relatively large and readily available surface area [1-2 m2] for absorption, and the transdermal approach has several unique benefits **[11]**. Applying a patch-like device to the skin [for system relocation, removal, or replacement] is one continuous adjustment technique that is non-invasive [and hence acceptable to patients] **[12]**.
- Further technical developments have led to the discovery of additional advantages of this **[13]**. They consist of regulated input kinetics and prolonged release options, which are beneficial for medications with limited therapeutic indices and short biological half-lives that must be administered often orally or parenterally. Absolutely use this method **[14]**.
- Such efforts must be "justifiable" medically for drugs with high oral bioavailability and irregular dose schedules that are well tolerated by patients. Additionally, transdermal administration is typically intended to provide slow, sustained drug delivery over considerable periods of time. As a result, medications that cause tolerance or those [like hormones] that require chronic pharmacological management are not suitable, at least not yet. Transdermal administration is not a method for achieving rapid bolus-type drug inputs. Although desired, a sizable pool of medications cannot presently support this **[15]**.

The daily medication dose that can be systemically administered through a sufficient "patch-sized" region remains in the 10 mg range due to the membrane's high

diffusional resistance. The first prerequisite for a viable transdermal candidate is imposed by this restriction: transdermal medications must be pharmacologically powerful and need therapeutic blood concentrations in the ng/ml range or below **[16, 17]**.

**1.2 Mechanism of transdermal drug delivery systems**

One of the goals of a transdermal delivery system, namely the penetration of material from the outside of skin through the epidermis and into the circulation, has been described in a number of ways throughout the course of the past 45 years or more **[18, 19]**. Others have used alternative terminology including sorption, persorption, permeation, and penetration. Rothman referred to this as percutaneous absorption **[17]**. All of them are related to passive mass transfer, albeit certain terminology, like sorption, have contradictory definitions. No matter what nomenclature is used, skin absorption always entails passive diffusion through the outer and middle layers of the skin until systemic circulation is reached. Given that it is histologically stratified into the stratum corneum, epidermis, dermis, and subcutaneous tissue, the skin may be thought of as a laminate of barriers **[20]**.

- The stratum corneum, a part of the dermis, and the viable epidermis make up this lamination.
- The subcutaneous tissue can often be regarded as not being engaged in percutaneous absorption or as a possible depot **[21, 22]**.
- There are three different ways that permeation can occur: transcellular penetration through the stratum corneum, intercellular penetration through the stratum corneum, and trans-appendicular penetration, particularly involving the sebaceous pathway of the pilosebaceous apparatus and the aqueous pathway of the salty sweat glands. For the first two steps, further diffusion through the remaining epidermis and dermis is required. The third channel allows for both diffusional leakage into the epidermis and direct penetration into the dermis **[23]**.

**[2] DRUG DELIVERY SYSTEMS OF AVAILABLE FOR TRANSDERMAL DELIVERY**

There are several types of transdermal drug delivery systems available, each with their own unique characteristics and advantages. Some of the most common types include:

**a)** *Transdermal patches*: These are the transdermal delivery methods that are most often employed. They are made up of a reservoir that holds the medicine, a backing substance, and an adhesive. The glue allows the medicine to gently leak out of the reservoir and into the skin. There are various different kinds of

transdermal patches available, such as reservoir patches and matrix patches, which release the medicine through reservoirs that store the drug **[24]**.

**b)** *Transdermal gels:* These are applied to the skin and typically contain a combination of the drug and a gel-forming agent. The drug is slowly released from the gel and into the skin. Gels can be beneficial for drugs that are poorly absorbed through the skin or for drugs that need to be applied to a specific area of the body.

**c)** *Transdermal creams and ointments:* These formulations are typically used for localized treatment of skin conditions, such as eczema or psoriasis. They are usually applied topically and can have a higher concentration of the drug than other transdermal systems **[25, 26]**.

**d)** *Transdermal microneedles*: These tiny needles can be used to inject medication via the skin. They may be created using a range of materials, including silicon or stainless steel, and are often less intrusive than conventional needles.

**e)** *Transdermal iontophoresis*: A low-voltage electrical current is used in this technique to improve the penetration of medicines via the skin. It may be used to deliver a variety of medications, including proteins, nucleic acids, and tiny compounds **[27]**.

**f)** *Transdermal osmotic pumps:* These pumps use osmotic pressure to push drugs through the skin. They can be used to deliver a wide range of drugs and can provide a sustained release of drugs over several days.

**g)** *Transdermal liposomes*: It is a kind of vesicle with a phospholipid bilayer that can be employed as a delivery system for medications under the skin **[28]**.

The specific medicine and intended therapeutic outcome, as well as the drug's solubility, molecular weight, and stability, as well as the skin's thickness, pH, and barrier function, will all influence the transdermal delivery method selection **[29]**.

**2.1 Marketed formulations available for Transdermal drug delivery systems**

There are several transdermal medication delivery methods on the market right now. Many instances include:

- Nicotine Transdermal patch: These patches are meant to aid smokers in quitting. They minimize cravings and withdrawal symptoms by providing a consistent supply of nicotine over an extended period of time **[30]**.
- Hormone replacement therapy [HRT] patches: HRT patches are used to deliver hormones, such as oestrogen and progesterone, to women experiencing symptoms of menopause. They provide

a controlled release of hormones over a period of several days **[31, 32]**.

- Transdermal fentanyl patches: These patches are used to treat moderate to severe pain. Over the course of many days, they provide fentanyl in a controlled release **[33, 34]**
- Scopolamine transdermal patch: Scopolamine transdermal patches are used to prevent motion sickness. They provide a controlled release of scopolamine over a period of several days **[35]**.
- Clonidine transdermal patch: Clonidine transdermal patches are used to treat hypertension, attention deficit hyperactivity disorder [ADHD], and menopausal flushing.
- Clonidine transdermal gel: Clonidine transdermal gel is used for the treatment of hypertension, attention deficit hyperactivity disorder [ADHD], and menopausal flushing. **[36–38]**.
- Rotigotine transdermal patch: Rotigotine transdermal patch is used for the treatment of Parkinson's disease and restless leg syndrome **[39, 40]**.
- Rizatriptan transdermal patch: Rizatriptan transdermal patch is used to treat migraines **[41]**.

New formulations are being created to target a variety of therapeutic regions, and novel transdermal drug delivery technologies are being developed **[42]**.

**Table 1: List of marketed formulations available for Transdermal drug delivery systems**

| Product Name | Active Ingredient | Manufacturer | Indication | Dosage & Administration |
|---|---|---|---|---|
| Neupro® | Rotigotine | UCB Pharma | Parkinson's disease, Restless Legs Syndrome | Available in various strengths. Apply 1 patch daily [43,44]. |
| AndroGel® | Testosterone | AbbVie | Testosterone replacement therapy | Apply to clean, dry skin as prescribed by the healthcare provider [45,46]. |
| Catapres-TTS® | Clonidine | Boehringer Ingelheim | Hypertension | Available in various strengths. Apply 1 patch weekly [47–49]. |
| Emsam® | Selegiline | Somerset Pharmaceuticals | Major depressive disorder | Available in various strengths. Apply 1 patch daily. [50] |
| Exelon® Patch | Rivastigmine | Novartis | Alzheimer's disease, Parkinson's dementia | Available in various strengths. Apply 1 patch daily. |
| Fentanyl Transdermal System | Fentanyl | Various manufacturers | Chronic pain management | Available in various strengths. Apply 1 patch every 72 hours [3 days]. |
| NicoDerm CQ® | Nicotine | GlaxoSmithKline | Smoking cessation | Available in various strengths. Apply 1 patch daily for up to 8-10 weeks, depending on the step-down plan. |
| Ortho Evra® | Norelgestromin / Ethinyl estradiol | Janssen Pharmaceuticals | Birth control | Apply 1 patch weekly for 3 weeks, followed by 1 patch-free week. |

| | | | | |
|---|---|---|---|---|
| Scopolamine Transdermal System | Scopolamine | Various manufacturers | Motion sickness prevention, postoperative nausea and vomiting | Apply 1 patch every 72 hours [3 days] as needed. |
| Vivelle-Dot® | Estradiol | Novartis | Hormone replacement therapy | Available in various strengths. Apply 1 or 2 patches weekly, depending on the prescribed regimen. |

### 2.2 Drugs available for transdermal based Parkinson's treatment

There are several drugs that are available for transdermal-based Parkinson's disease treatment:

- Levodopa: Levodopa is a dopamine precursor that is used to treat Parkinson's disease. Transdermal levodopa patches are available and have been shown to reduce fluctuations in plasma drug concentrations and improve the duration of therapeutic effect **[51]**.
- Rotigotine: A dopamine agonist called rotigotine is used to treat Parkinson's disease. There are transdermal rotigotine patches available, and research has indicated that using them can help people with Parkinson's disease with their motor symptoms.
- Apomorphine: Dopamine agonist apomorphine is used to treat Parkinson's disease. It has been demonstrated that transdermal apomorphine patches reduce Parkinson's disease patients' "off" time and improve their motor symptoms **[52]**.
- Ropinirole: A dopamine agonist called ropinirole is used to treat Parkinson's disease. There are transdermal Ropinirole patches that may be used and have been demonstrated to be beneficial in lowering Parkinson's disease patients' motor symptoms **[53]**.
- Pramipexole: Parkinson's disease is treated with the dopamine agonist pramipexole. There are transdermal pramipexole patches that may be used that have been proven to help people with Parkinson's disease with their motor symptoms.
- Carbidopa: Carbidopa is a peripheral dopa decarboxylase inhibitor, it is used in combination with levodopa. Transdermal carbidopa patches are available and have been shown to improve the duration of therapeutic effect by reducing the conversion of levodopa to dopamine in the periphery **[54]**.

It's important to note that the choice of transdermal-based Parkinson's disease treatment will depend on the specific patient and their individual needs, as well as the stage of the disease and any other medical conditions the patient may have. A close monitoring by the physician is required to

adjust the dosage and the frequency of the treatment, and to prevent the emergence of side effects **[55]**.

## [3] FORMULATIONS THAT ARE CURRENTLY IN CLINICAL TRIALS

There are several transdermal [through the skin] based formulations for Parkinson's disease that are currently in clinical trials. These include transdermal patches and gels that deliver medications such as rotigotine, apomorphine, and carbidopa/levodopa through the skin and into the bloodstream. These formulations aim to provide a more consistent and steady release of medication to help control Parkinson's symptoms, and may have fewer side effects compared to oral medications. Nevertheless, it is crucial to remember that these formulations are still in the clinical trial stage and have not received FDA approval **[56]**.

- *Transdermal rotigotine:* In phase 2 and 3 clinical studies, transdermal rotigotine, a dopamine agonist, is being investigated for the treatment of Parkinson's disease. It has been demonstrated to be successful in lowering motor symptoms and enhancing quality of life in people with Parkinson's disease.
- *Transdermal apomorphine:* In phase 2 and 3 clinical studies, transdermal apomorphine, a dopamine agonist, is being investigated for the treatment of Parkinson's disease. It has been demonstrated to be useful in lowering "off" time and enhancing motor symptoms in people with Parkinson's disease **[57]**.
- *Transdermal levodopa-carbidopa:* Phase 2 and 3 clinical studies for the treatment of Parkinson's disease are evaluating the combination of levodopa, a dopamine precursor, and carbidopa, a peripheral dopa decarboxylase inhibitor. It has been demonstrated to lengthen the therapeutic effect's duration and lessen changes in plasma medication concentrations **[58]**.
- *Transdermal rivastigmine:* In phase 2 and 3 clinical studies, transdermal rivastigmine, a cholinesterase inhibitor, is being investigated for the treatment of Parkinson's disease. It has been demonstrated to enhance cognitive performance and overall clinical status in people with Parkinson's disease **[59]**.

## 4. ASSESSMENT PARAMETERS FOR TRANSDERMAL FORMULATIONS

Transdermal formulations offer lower dosages at a regulated rate with the goal of improving therapeutic effectiveness and increasing patient adherence. To guarantee these formulations' predicted performance and dependability under diverse

circumstances, it is crucial to assess them **[60]**. These assessments predict the effectiveness of transdermal drugs and are classified into three categories:

• Physical and chemical assessment
• In vitro assessment
• In vivo assessment.

**4.1 Physical and chemical evaluation**

- ***Thickness:*** Transdermal films' thickness is measured using a variety of tools, including a traveling microscope, dial gauge, screw gauge, or micrometre.
- ***Weight Evenness:*** Weight homogeneity is evaluated by weighing 10 randomly chosen patches and calculating their average weight. Any individual weights should not deviate significantly from the mean weight **[61]**.
- ***Drug content analysis:*** The drug content is determined by dissolving an accurately weighed portion of film [approximately 100 mg] in an appropriate solvent. The solution is then shaken and sonicated, and the drug content is estimated using spectrophotometry **[62]**.
- ***Content uniformity test:*** The content consistency test evaluates ten patches' worth of content. If nine out of ten transdermal patches have content that ranges from 85% to 115% of the claimed value and one patch has content that ranges from 75% to 125% of the stated value, the transdermal patches pass the test. In the event that three patches test positive for drug content between 75% and 125%, 20 further patches are evaluated. If the range of these 20 patches is 85% to 115%, the transdermal patches pass the test **[63]**.
- ***Moisture Content of Film:*** The moisture content is calculated by weighing the prepared films, placing them in a desiccator for 24 hours, and reweighing them until a constant weight is reached **[64]**.

  **% Moisture content = [Initial weight – Final weight] X 100**
- ***Final weight / Moisture uptake:***

  The weighted films should be placed inside a desiccator for 24 hours at an room temperature to dry them out, and then using a saturated potassium chloride solution, the relative humidity is set at 84% to gauge how much moisture is absorbed. The final and starting weights are used to compute the % moisture absorption **[65]**.

  **% moisture uptake is calculated as Final Weight - Starting Weight X 100.**
- ***Initial weight Flatness:*** A flatness test can determine whether a transdermal patch has a flat, homogeneous surface that doesn't shrink with time. Five strips are cut from the patch—one from the center and two from each side—to conduct the test. After measuring the

length of each strip, the length variation is represented as a percentage of constriction. When there is no restriction, the patch is completely flat **[66]**.

- ***Folding tolerance:*** The assessment of folding endurance involves figuring out a film's ability to endure repetitive, demanding folding. This is accomplished by folding the film in the same location repeatedly until it breaks. The amount of folds the film may undergo without breaking at the same point is used to calculate the folding endurance value.
- ***Tensile strength:*** We can measure the polymeric films' tensile strength by sandwiching them between two corked iron plates. One end of the film is secured to an iron screen, while the other is attached to a freely moving thread that is secured to a weight. The pan, which hangs from the end of the thread, is progressively given weight. With the aid of a pointer attached to the thread, the length of the film is measured. The weight needed to break the film is noted, and an exact calculation is used to determine the tensile strength **[67]**.

  **F/a.b [1+L/l] = Tensile Strength**

  The total running time of the movie is L, and the elongation during the break is L. F is the amount of force needed to rip the film.

- ***Tack Properties****:* Tack describes a polymer's capacity to adhere to a surface without applying much force. The amount of tackifying resins present, their molecular make-up, and their molecular weight all affect how sticky a polymer is **[68]**.
- ***Thumb tack test:*** The tackiness of a substance is measured by the force required to detach the thumb from it **[69]**.
- ***Ball - Rolling Test:*** In this test, the length that a stain-free steel ball travels over an adhesive with an upward-facing surface is determined. The length of the ball's roll depends on how tacky the glue is **[70]**.
- ***Peel - Tack Test [Quick Steel]:*** By pulling the tape off at a 90-degree angle and at a pace of 12 inches per minute will reveal how much force is required to detach an adhesive from its substrate **[71,72]**.
- ***Probe - Tack Test:*** Tack is the unit of measurement for the force required to pull a probe steadily away from an adhesive **[73]**.

**3.2 In vitro release studies:**

The release of drug mechanisms and kinetics of a controlled release pharmaceutical formulations have a significant role in the drug dissolution pattern and, subsequently, in the medication's in vivo effectiveness. The best model that fits the dissolution data

and accurately reflects the drug's release mechanism is found. There are several methods that may be used to calculate the drug release rate of TDDS **[74]**.

- ***The Paddle over Disc:*** In this method, which is otherwise the same as the US paddle dissolving device, the transdermal system is attached to a disc or cell that is situated at the bottom of the vessel that contains medium that is at a temperature of 325°C **[75]**.
- ***The USP modified Cylinder Basket:*** [USP apparatus 6] This method attaches the device to the top of a hollow cylinder that is immersed in medium that is 32 5°C, much to the USP basket type dissolving equipment **[76]**.
- ***The revolving disc [USP apparatus 7]:*** The device is perfect for medication delivery systems that offer low concentrations of the substance since this technology oscillates patches linked to holders in small volumes of medium. Another choice is the paddle over extraction cell approach **[77]**.

### 3.2.1 In-Vitro Permeation Studies:

The quantity released from polymeric transdermal films has a significant influence on the drug's accessibility in the systemic pool. The medication enters the dermal microcirculation through the cells of the epidermis and skin appendages after reaching the skin's surface. Permeation tests are frequently carried out to measure this, with the hydrophilic side of the transdermal patch in contact with the receptor fluid, either on rat skin or a synthetic membrane in a diffusion cell The receptor compartment is continuously agitated and kept at a set temperature. The quantity of medicine that has penetrated is measured using samples obtained at various periods. This amount might vary depending on the patch's design and temperature. Permeation research involves prepping the skin, establishing the experimental environment, taking samples, then evaluating and quantifying the drug flow **[78]**.

- ***Skin Preparation for Permeation studies:*** Skin from human cadavers and hairless animals is used in permeation studies. Given that the final product will be administered to humans, human cadaver skin could be a suitable choice. It is not, however, easily accessible. As a result, since it can be easily collected from particular age groups or sexes, hairless animal skin is frequently selected **[79]**.
- ***Whole, Intact skin:*** An animal's dorsal hair is cut off using an animal hair clipper, the subcutaneous tissue is removed, and any leftover fat is removed from the dermis side by wiping it with isopropyl alcohol. After that, distilled water is used to cleanse the skin. The prepared skin is sealed in aluminium foil and kept at -20°C in the freezer until

required. When necessary, the skin is thawed at room temperature **[80]**.

- ***Epidermis - Separation from whole skin:*** A 2M sodium bromide solution in water is applied to the ready full-thickness skin and left on for 6 hours. With a cotton swab that has been soaked with distilled water, the epidermis is separated. After being cleansed, the epidermal sheet is vacuum-dried after being rinsed with distilled water. Desiccators are used to preserve the dried sheets for later use **[81]**.

**4.3 In-Vivo experiments**

Drug performance is properly represented by in vivo tests. In vivo research can be used to fully study variables not taken into account during in vitro experiments. The following methods can be used to evaluate Transdermal delivery in vivo:

Both Human participants and Animal models **[82]**.

- ***Animal models*** As small-scale human studies take a lot of time and money, animal research is preferred. The mouse, hairless rat, hairless dog, hairless rhesus monkey, rabbit, and guinea pig are some of the most popular animal species used to evaluate transdermal drug delivery systems. According to several research, hairy animals do worse in in vitro and in vivo testing than hairless ones. One of the most trustworthy models for in vivo evaluation of transdermal medication administration in humans is the hairless rhesus monkey **[83]**.
- ***Human models*** Applying the patch to human subjects and gathering pharmacokinetics and pharmacodynamic data are the final steps in the creation of a transdermal device. Clinical studies evaluate patient compliance, effectiveness, risk, and adverse effects. Clinical studies in phase I typically assess safety in volunteers, whereas clinical trials in phase II assess short-term safety and efficacy in patients. Phase IV post-marketing surveillance trials are done to discover adverse medication responses for commercially available patches. Phase III trials demonstrate safety and efficacy in a wide patient population. While they require a lot of money, human studies provide the most accurate evaluation of medication effectiveness **[84]**.

## 5. FUTURE SCOPE OF TDDS FOR PARKINSON DISEASE

- The future scope for transdermal based formulations for Parkinson's disease is promising as they have the potential to provide a more consistent and steady release of medication, which can help control symptoms and reduce side effects **[85]**.
- Transdermal technology has been developed enough to deliver a variety of drugs for different diseases, and in the

future, it can be expected to deliver drugs for Parkinson's disease with better efficiency and safety. Additionally, being investigated is the use of tiny needles and nanoparticle in transdermal delivery systems, which may enhance the efficacy and security of these formulations **[86]**.

- Additionally, the usage of transdermal technology to deliver gene therapy for Parkinson's disease is also being researched. This could potentially provide a more long-term treatment option for the disease, as it would involve delivering genetic material to cells in the brain to help them produce a specific protein that is lacking in Parkinson's disease **[87]**.
- Overall, the future of transdermal based formulations for Parkinson's disease looks promising, with ongoing research into new technologies and delivery methods that could improve the effectiveness and safety of these treatments **[88]**.

**5.1 Transdermal Patents available for Parkinson Disease**

There are several patents available for transdermal based formulations for the treatment of Parkinson's disease. These include patents for specific transdermal delivery systems, such as patches and gels, as well as patents for specific medications that can be delivered through the skin **[89]**.

- For example, there is a patent for a transdermal patch that delivers the medication rotigotine, which is used to treat Parkinson's disease symptoms such as tremors, stiffness, and difficulty with movement.
- Another patent covers a transdermal gel that delivers the medication apomorphine, which can help control sudden "off" episodes in Parkinson's disease patients **[90]**.
- Additionally, there is a patent for a transdermal patch that delivers the medication carbidopa/levodopa, which is used to treat the symptoms of Parkinson's disease by increasing the levels of dopamine in the brain **[91]**.

It is worth noting that these patents are not an indication of the efficacy or safety of the products, and these products are not approved by regulatory agencies such as FDA yet. It's also important to note that patents are time-limited and can expire after a certain number of years **[92]**.

**5.2 Recent trends on Transdermal Drug Delivery System for Parkinson Disease**

Recent trends in the development of transdermal based formulations for the treatment of Parkinson's disease have focused on improving the delivery of the medication through the skin, as well as the stability of the medication once it is delivered **[93]**.

- One development is the use of transdermal microneedles, which are tiny, delicate needles that may be used to administer medication via the skin. They have been demonstrated to be efficient in administering Parkinson's disease medicine and are less intrusive and unpleasant than conventional needles **[94]**.
- Another trend is the use of nanoparticles for transdermal delivery, which are tiny particles that can be used to carry medication through the skin. These particles can be designed to target specific cells in the body, which could improve the effectiveness of the treatment **[95]**.
- Another trend is the use of transdermal technology to deliver gene therapy for Parkinson's disease, which could provide a more long-term treatment option for the disease. This method involves delivering genetic material to cells in the brain to help them produce a specific protein that is lacking in Parkinson's disease **[96]**.

Overall, recent trends in transdermal based formulations for Parkinson's disease have focused on developing more effective and less invasive delivery methods, as well as improving the stability of the medication once it is delivered **[97]**.

## 6. REGULATORY LANDSCAPE OF TRANSDERMAL SYSTEMS

Many national and international regulatory organizations, including the World Health Organization, the European Medicines Agency, and the U.S. Food and Drug Administration, regulate the transdermal delivery system landscape [WHO]. These organizations provide policies and criteria for the creation, evaluation, and approval of transdermal drug delivery systems **[98]**.

- Transdermal delivery systems are governed by the FDA's Center for Devices and Radiological Health in the United States since they are viewed as medical devices [CDRH]. During the premarket review process, the FDA assesses the effectiveness and safety of these devices and establishes standards for their labeling, packaging, and manufacture **[99]**.
- In Europe, the EMA is in charge of assessing the efficacy and safety of transdermal delivery systems using a centralized process and establishes rules for their marketing and usage.
- Similarly, WHO also provides guidance and recommendations to countries on the use and regulation of medical devices, including transdermal delivery systems **[100]**.

It is important to note that the regulatory landscape for transdermal delivery systems

is complex and can vary depending on the country or region. Companies that develop transdermal delivery systems must comply with the regulations set by the relevant regulatory agencies in order to bring their products to market **[101]**.

## 7. CONCLUSION

Transdermal therapy administration of drugs is a possible technique for the therapy of Parkinson's illness as it offers a more consistent and constant supply of medication and can help manage symptoms and decrease side effects.

- There are several transdermal based formulations that are currently in clinical trials, such as patches and gels that deliver medications such as rotigotine, apomorphine, and carbidopa/levodopa through the skin.
- The future scope of transdermal drug delivery is promising, with ongoing research into new technologies such as microneedles and nanoparticles, as well as gene therapy, which could potentially improve the efficacy and safety of these treatments.
- The regulatory landscape for transdermal drug delivery is complex and varies depending on the country or region, but companies that develop these systems must comply with the regulations set by the relevant regulatory agencies in order to bring their products to market.

Transdermal pharmaceutical delivery has promise as a general method for treating Parkinson's illness, but further research and development are needed to realize this technique's full potential.

**CONFLICTS OF INTEREST:** None

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