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Innovations in transdermal delivery: Exploring nicotine patches, microneedles and glucose monitoring technologies

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Abstract

Transdermal devices for delivering drugs have been invented in response to obstacles caused by oral administration of medications. An adhesive patch comprising medication that is applied topically for transferring a preset proportion of treatment through the skin and into the bloodstream is called a transdermal patch. The method of manufacturing for various transdermal application types, including matrix patches, is described in this review article. Addiction to cigarettes affects millions different people throughout. One example of a nicotine replacement treatment that is currently widely accessible and utilized is transdermal nicotine patches. Nicotine substitution therapy is an assortment of products that provide nicotine and are authorized for use as a smoking cessation aid for the treatment of withdrawal. An increasing number of participants have been impacted by the global rise in diabetes in the past few years are experiencing discomfort and infections because of the intrusive design of most commercial glucose meters. Non-invasive blood glucose monitoring technology is now a hot issue for research worldwide and a novel approach that has the potential to help a lot of patients.

Keywords: Transdermal Patches; Nicotine patches; Nicotine replacement therapy; Transdermal Glucose Monitoring

1. Introduction

A different approach of delivering medications via the skin layer is transdermal drug administration. The medication penetrates the bloodstream through the skin and travels throughout the body's systems before reaching at the intended location [1]. The method of distributing medication through the skin and enabling it to penetrate the bloodstream to trigger systemic effects is commonly referred to as transdermal medication delivery [2]. This is the drug delivery technique that releases the medication into the body more successfully. In the pharmaceutical sector, the system is increasingly becoming more prevalent. It gives the body an extended course that is highly effective [3]. Another way of delivering medication is offered by a transdermal drug delivery device, which comes both as active and passive models. Pharmaceuticals are now able to pass across the skin barrier owing to these devices [4]. Transdermal management offers a significant advantage over oral and injectable methods owing to its capability to avoid first pass metabolism and improve patient compliance, respectively [5]. There are multiple types of administration modalities depending on the delivery route, comprising intravenous injection, lung inhalation, mucous administration, transdermal administration, and oral medication [6]. A non-invasive device that identifies the patient's drug requirement and thereafter administers the appropriate amount of the active agent at a suitable rate is the goal of drug treatment [7]. When contrasting transdermal delivery to the oral route, there are several advantages. It is specifically utilized in situations when the liver has a strong first-pass effect that may cause pharmaceuticals to be metabolized too soon [8]. The skin serves as the body's greatest interface with the outside world, protecting the body from microbes and external stresses while also retaining nutrients like water [9]. The outermost layer of the skin, referred to as the stratum corneum, keeps medicines and other chemicals from rapidly entering the systemic circulation [10]. Drugs are delivered transdermally, if they are absorbed into the bloodstream through the skin. Both passive as well as active transdermal products can transfer the medicine;

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whilst active technologies disrupt the stratum corneum to enhance delivery, passive devices do not. This area of the pharmaceutical industry is quite humble because passive transdermal drug delivery requires very specialized physicochemical characteristics [11]. By using specially designed medicated adhesive patches to the skin, transdermal drug delivery provides several benefits to overcome complications related to oral delivery and hypodermic injected [12]. Additionally, several medicine types, including hydrophilic and hydrophobic chemicals, have been transported with this technology [13]. People have been applying different chemicals to their skin to promote healing since the beginning of time. Different theme strategies have been developed in more recent periods to treat acute symptoms. An American solution that could deliver scopolamine to the body for three days at a time was approved by the FDA in 1979. The intended use of this solution was to treat stroke. Ten years later, nicotine patches were released as the initial [14]. Transdermal administering drugs offers the following main benefits: fewer adverse effects, longer period of action leading to a decrease in dose frequency, increased being absorbed, and more consistent plasma levels [15]. Drug is dependent on the drug's concentration at the site of action, which is reliant on the dosage form and the degree of drug absorption at the point of action. The conventional methods of administering medication have been by injection and tablet [6]. TDDS offer benefits such as reduced pain, bruising, bleeding, improved patient acceptance, compliance, and elimination of needle-associated risks and medical waste [16]. The even distribution of numerous therapeutic substances has been greatly affected by TDDS, especially among the areas of pain management, hormone therapy, and the treatment of problems affecting the central nervous system and cardiovascular circulation [17].

2. Advantages

- The treatment concentration in plasma stabilizes [15].
- When the oral route in health care administration is inappropriate, such as in cases of vomiting or diarrhoea because they may be used as an alternative [18].
- Prevents the first-pass metabolism of liver and keeps blood levels stable for a longer period of duration [19].
- Allows rapid termination of drug therapy by removing the skin application [16].
- The treatment is painless, and patient compliance is increased [3].
- Steer clear of providing doses frequently [20].
- Liposomal formulations can be applied topically to deliver drugs through the skin.
- They offer controlled release and can avoid the first-pass metabolism in the liver [21].
- Penetration can be enhanced through the skin using niosomes as drug carriers in transdermal drug delivery [22].

3. Disadvantages

- Some medications, like the transdermal scopolamine patch, are painful when applied behind the ear [23].
- Expensive; steer clear of ionic drugs [24].
- A therapeutic level cannot be reached by a high chemical drug level [15].
- Due to the skin's inherent resistance to drug entrance, only strong medications are suitable prospects for transdermal patches [18].
- A few individuals develop an allergic reaction at the application site for one or more system components, that prompts for stopping the treatment [24].
- The circulation does not contain substances with very high or very low partition coefficients. Drugs having a high melting point can be administered this way since they don't require refrigeration and have a low solubility in fat and water [14].
- Suitable only for drugs with a molecular weight below 500 daltons [16].
- Long time adhere is difficult [18].

4. Skin's Structure: [20,24,25]

The skin's thickness has played an essential part when establishing the transdermal medication delivery's restrictions. The skin, the most significant organ in the human body, provides a not uncomfortable and attentive interface for the systemic administration of drugs.

- Epidermis: The epidermis is traversed by compounds that enter the blood system from the layers of skin. The topmost layer of the epidermal is made up of the hydrophobic SC. This layer is made up of 10–20 multiple layers of cornea-cite and typically has a thickness of 15 nm.

- Dermis: The dermis comprises nerve endings, vessels for blood, and lymphatic vesicles. For treatments absorbed into the epidermis, the dermis vast microvasculature network serves as the starting point of resorption.
- Hypodermis: the outermost layer of skin or subcutaneous fat tissue, encourages the dermis and epidermis. It's designated as the region of fat accumulation. This layer offers spontaneous protection, nutritional support, and temperature regulation assistance. It conveys the main blood vessels, nerves, and occasionally sensory pressure organs to the skin. Drugs administered subcutaneously must pass through all three layers and enter the circulatory system.

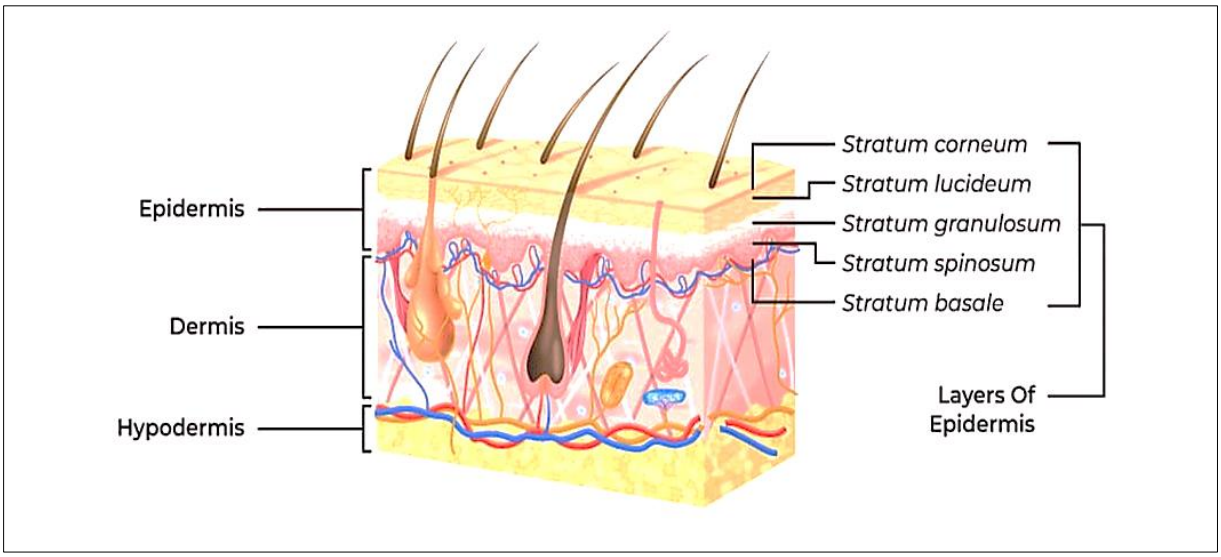

Figure 1 Skin Anatomy and Physiology [20]

5. Function of Skin: [26]

The skin has three main functions:

- Protection
- Thermoregulation
- Sensation

6. Basic component of TDDS

- **polymer matrix:** The medication is manufactured by dispersing it in an artificial chemical compound base, either in liquid or solid condition. It should be pharmacological and biodegradable with the medicine as well as other components of the system, such as penetration enhancers. They additionally must distribute a medication regularly and successfully for the duration of the product's intended usage and may be in a safe state [27].
- **Drug:** Identifying an appropriate pharmaceutical is important for constructing an operational transdermal drug delivery system. Some of the desired characteristics of a medication for transdermal distribution are as follows [28].
- **Enhancers of Permeation:** These substances change the skin's ability to act as a barrier to the flow of a desired penetrant, increasing skin permeability [29].
- **Pressure-sensitive adhesive:** This serves to both stick the patch to the skin and maintain the individual components together. For the TDDS to stay in place for a prolonged amount of time, its adhesive needed for it to possess enough adhesion properties. Often, pressure-sensitive adhesives have been used to hold the skin in place for transdermal patches. Adhesives having silicone, polyisobutylenes, and poly-Acrylates bases are commonly utilized [30].
- **Backing laminate:** The following requirements for the backing laminate layer must be
    - It must be chemically resistant.
    - It ought to be adaptable
    - Its tensile strength is good.
    - It must not cause inflammation [15].

- **Release liner:** The protective liner encapsulating the patch during storage must be removed off and let out right before the patch gets stuck to the skin. As consequently, it is thought of as a component of the main packaging material as opposed to the drug's dose form [31].
- **Additional excipients:** Up until now, pressure-sensitive adhesive has been used to adhere epidermal devices to the skin. The device's face or back, alongside the pressure-sensitive adhesive extending peripherally, are two possible arrangements for the adhesive [28].

7. Formulation approaches utilized in the development of TDDS: [30,31,32]

- **Adhesives:** Transdermal patches require to adhere adequately in order to deliver drugs through the skin repeatedly and constantly. Transdermal systems frequently utilize a variety of adhesives, such as silicone and Polyimide butylenes.
- **Membrane permeation:** This kind that technology offers encapsulates the drug reservoir in a shallow compartment made of a rate-controlling polymeric membrane, which may be micro porous or non-porous, and a drug-impermeable metallurgical plastic laminate.
- **Matrix Dispersion:** In this kind, the medication has an even distribution within a matrix of hydrophilic or lipophilic macro-molecules. This drug-containing polymer the disc is installed in a compartment constituted of a drug-impermeable backing layer, connected to an occlusive base plate.
- **Micro Reservoir:** The medicine distribution technique integrates reservoir and matrix-dispersion methods. The medicinal product is initially suspended in aqueous solutions of a polymer that dissolves in water, and the solution is then evenly distributed in a lipophilic polymer to generate thousands of unbreakable, microscopic starts ringing of drug reservoirs.

8. Factor affecting drug penetration: [3]

Drug penetration can be affected by two different types of ingredients, comprising physiochemical and biological components. Those components are mentioned below.

8.1. Biological factors

- Skin age
- Skin condition
- Species difference
- Blood supply
- Skin metabolism
- Regional skin site.

8.2. Physiochemical factors

- Temperature and pH
- Skin hydration
- Diffusion coefficient
- Drug content
- Molecular size and shape
- Partition coefficient.

9. Transdermal Patches

A transdermal patch is used to enter the skin and enter the bloodstream to conduct the specified dosage. The US Food and Drug Administration approved transdermal patch products for for the inaugural time in 1981. Drugs with short biological half-lives can be repeatedly injected via transdermal delivery, which also prevents pulsed entrance into the systemic circulation and allows for controlled, continuous drug oversight [33]. The first the transdermal route patch to be commercially available for the prevention of motion sickness was the compound Scopolamine patch. Subsequently, transdermal patches containing clonidine, Oestradiol and fentanyl have been made available for use in addressing chronic pain, hypertension, and hormone replacement treatment, respectively [34]. The goal of all pharmaceutical researchers and the industry is to develop a medication delivery system that is both safe and effective. Drug administration via the transdermal method can have both systemic and local therapeutic effects. Because transdermal medication delivery avoids first pass metabolism and gastrointestinal side effects, it is a desirable alternative to oral

drug administration [35]. Through the skin, the medication enters the systemic circulation without being lost in transit to its intended location. It enhances the prolonged drug release, minimizes unwanted side effects, and promotes physiological and pharmacological response [36]. The limitations of infusion settings have fuelled the development of patch pumps. These pumps are designed to stick to the skin using an adhesive, be small and light, and not require infusion sets. The cost and extent of insurance coverage are other factors to consider [37]. A defined dose of treatment can be provided by directly delivering pharmaceuticals via the skin into the bloodstream through through the application of a transdermal patch, and this is a transdermal carrier system. The patch may decrease systemic side effects and increase a treatment's therapeutic efficacy because it may control the medication's release [38]. Constant blood levels are achieved by transdermal patches, they also prevent dose dumping, first pass metabolism, and improve patient compliance. Transdermal drug delivery systems are characterized as discrete, self-contained dosage forms that, when applied to undamaged skin, allow the medication to enter the systemic circulation at a controlled rate through the skin [39]. Transdermal patches function incrementally. The treatment is given in a reasonably high dose inside the patches, which are to be worn on the skin for a longer duration of time, and through the diffusion process, it directly enters the bloodstream through the skin [40].

9.1. Fundamental Transdermal Patch Component

Transdermal patches typically consist of up of many layers with the intention of delivering the medication into the bloodstream through the skin. Depending on the medication being held and the intended rate of drug release, the patch's precise shape and composition may change. The patches outermost layer, known as the backing layer, guards the inner layers from the elements. A flexible, waterproof substances like polyethylene or polypropylene is used to create this layer. The adhesive layer's goal is to adhere the patch to the skin while maintaining it intact. In general, it is made up of a powerful, hypoallergenic adhesive that is appropriate for skin. Drugs that undergo absorption through the skin have been identified in the drug layer. It was developed to release the medication progressively and at an ongoing rate. The rate at which the medicines that are released from the patch is managed by the rate-controlling membrane. On average, semi-permeable materials have been employed for manufacturing membranes, allowing enable regulated medication transport through the membrane. Once the patch has been applied to the skin's surface, it must be removed [1].

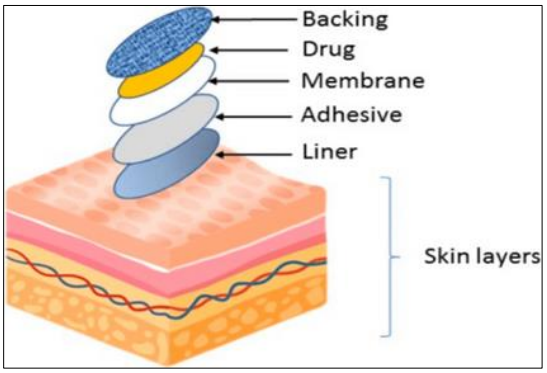

Figure 2 Basic component of a transdermal medical patch [1]

9.2. Types of Transdermal Patches

9.2.1. Single-layer Drug-in-Adhesive

The medication is contained in this system's sticky layer. The adhesive layer in this kind of patch releases medications in the process of holding the system as a whole and its individual layers to the skin together. There is a backing and a temporary liner covering the adhesive layer [30,41]

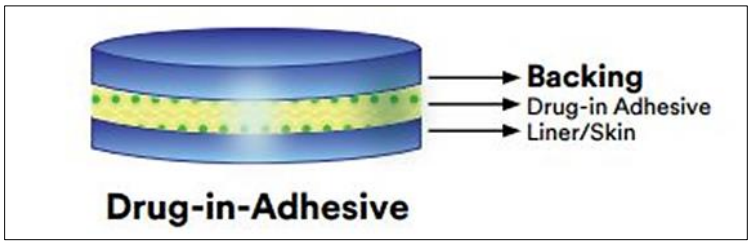

Figure 3 Single Layer Drug in Adhesive [20]

9.2.2. Multi-layer drug-in-adhesive patches

Transdermal patches with a number of layers are composed of an adhesive layer that modulates medication release and a drug reservoir layer. Multi-layer systems consist of a permanent backing laminate and a transient protective layer. Painkillers, smoking cessation medications, and hormone therapy are all delivered by multi-layer patches; the amount of time of drug delivery is at least seven days [35].

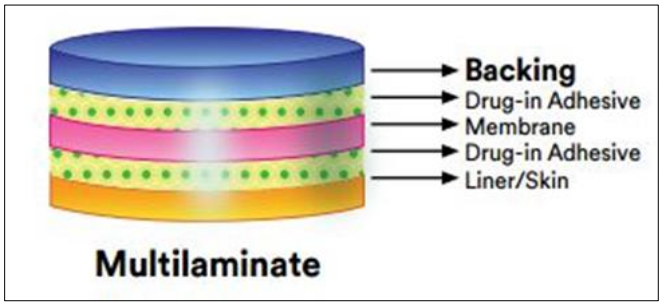

Figure 4 Multi-Layer Drug in Adhesive [20]

9.2.3. Drug Reservoir-In-Adhesive

A distinct drug layer is present in the drug reservoir-in-adhesive system, in contrast to the single-layer and multi-layer drug-in adhesive systems. The drug layer and drug solution or suspension have been separated by the sticky layer, therefore acts as a barrier. This patch also includes a backing layer. This kind of system follows zero order kinetics [42].

9.2.4. Vapor transdermal patches

The vapour patch serves essentially two purposes: it attaches the several layers together and releases vapour. Since they have the capacity to release essential oils for up to six hours, they are mostly utilized for de-congestion. There are also controller vapour patches accessible via the market that improve sleep quality. Vapour patches, which are necessary to cut back on the number of cigarettes, are also available on the market place [42].

9.2.5. Matrix

One of the components of this system is a semisolid matrix medicament layer that is in direct contact with the liner and includes a medication in the form of a solution or suspension. Before covering the entire device, the sticky coating partially obscures the drug layers inside. Patients with mild to severe Alzheimer's disease may benefit from this therapeutic approach [14].

9.2.6. Matrix-dispersion system

In this kind, the medicine is uniformly distributed within a hydrophilic or lipophilic polymer matrix. This medication-containing polymer disc is installed in a compartment made of a drug-impermeable backing layer, fixed to an occlusive base plate. The glue is dispersed around the outermost portion to create an adhesive rim strip rather than being placed on the front of the drug reservoir [5].

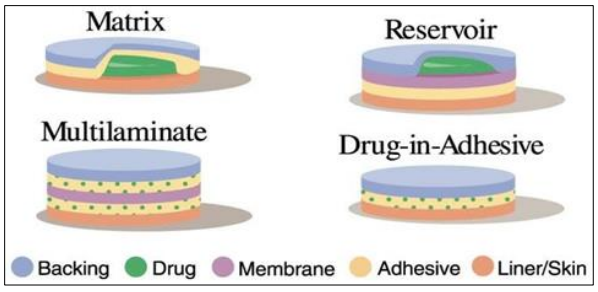

Figure 5 Schematic diagram of various types of transdermal patches [35]

9.3. Un-favourable circumstances for using a transdermal patch: [42]

- When a person is experiencing severe discomfort.

- When a rapid titration of the dose is required.
- When the dosage requirement is 30 mg or less per 24 hours or less.

9.4. Factors Affecting on Transdermal Patches: [40]

The following are some of the many variables influencing the effectiveness of transdermal patches:

- Biochemical Elements
- Elements of Formulation
- Elements of Physicochemistry

9.4.1. Biochemical Elements

- The skin's pH
- Skin hydration status
- Application site
- Race and gender
- Candidate age
- Skin pathological condition
- Lipid layers on the epidermis

9.4.2. Elements of Formulation

- Enhancers of penetration
- Patch or drug release characteristics
- Vehicle pH

9.4.3. Elements of Physicochemistry

- Drug molecules' molecular size and shape
- Partition coefficient
- Stability and half-life of the patch or drug within the patch
- Concentration of Drugs [37].

9.5. Techniques applied in the creation of transdermal patches: [43]

- Systems with membrane moderation
- Diffusion-controlled adhesive system
- Dispersion matrix system
- System of micro-reservoirs

9.6. Recent Advances in the field of transdermal patches: [43]

- Patch technology for protein delivery
- Pain-free diabetic monitoring using transdermal patches
- Transdermal testosterone patch gadget for young female patients undergoing unexpected premature ovarian failure.
- Oxybutynin transdermal patch for overactive bladder
- Pain relief
- Molecular absorption enhancement technology.

9.7. Transdermal Model

Following the application of a patch, there was some time during which concentrations surged and peaked approximately 10 hours later. Following this, concentrations declined through the remaining time of the treatment period. Concentrations declined with greater speed once the patch was removed, usually 16 hours after application. The trough exposure rose when the patch was worn for 24 hours, but the peak exposure was not significantly different. Although the Invisipatch and the Nicorette patch are identical in other ways, there appeared to be a minor delay in digestion [44].

9.8. Mechanism of Action of Trasdermal Patches

The great majority of transdermal patches are made to fixate dynamically at a rate of zero application over a period of time that can be anywhere from seven hours to many different days after the patch is put to the skin. This is a very useful preventative drug for a variety of illnesses. Measurable amounts of the drug in the patient's blood, detectable levels of the drug and its metabolites in the patient's urine, the patient's clinical response to treatment with controlled medications, and the patient's blood levels of the drug are all indicators of percutaneous drug retention [14].

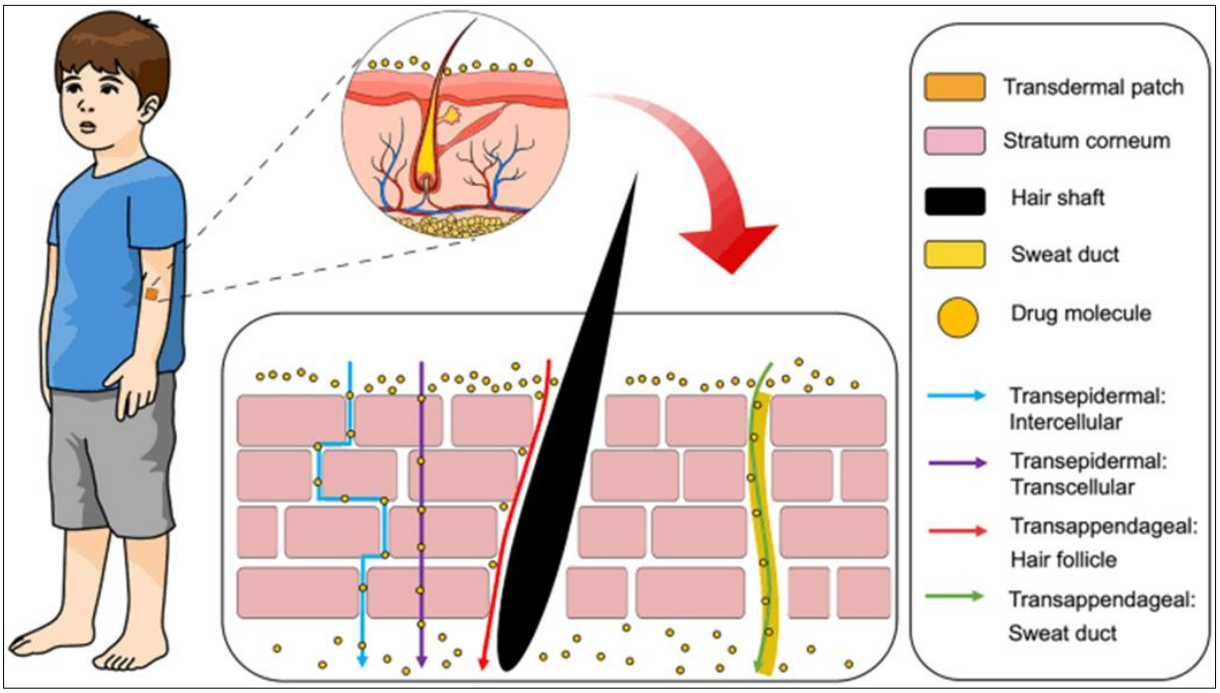

Figure 6 Schematic representations of transdermal drug delivery mechanism [14]

10. Nicotine Replacement Therapy

To address nicotine dependence, replacement therapy using nicotine is used. It can be purchased in a variety of dose forms, such as inhalers, gums, fast-acting lozenges, nasal sprays, and transdermal delivery systems. Because transdermal distribution avoids hepatic first-pass metabolism, eliminates frequent dosage, eliminates plasma level peaks and valleys, improves patient compliance, and all of these benefits make it an attractive way of administering nicotine [45]. Research has been done on the neuroprotective properties of nicotine as well as its use in treating the symptoms of Parkinson's disease (PD). The receptors for n (nAChRs) are the site of nicotine's protective action, as demonstrated by multiple experiments [46]. The World Health Organization claims that smoking causes up to half of tobacco users' deaths, which directly contributes to more than 5 million deaths worldwide. Even though 74% of smokers, according to a recent Gallup poll, would wish to stop, smoking is extremely addicting due to its quick delivery of nicotine to the brain and ease of dosage titration [47]. To address brain physiology in smoking cessation treatment, nicotine replacement therapy (NRT) uses nicotine gum for dosing spikes during craving events and transdermal patches for steady background levels to reduce withdrawal symptoms and relapse [36]. NRT has a limited success rate of 18–24% after a year and an overall long-term failure rate of 90% [48].

The effects of nicotine on cognition are still debatable in humans, however they might be helpful for conditions like memory loss. When a medication is removed, any neuroadaptations (homeostatic corrective mechanisms) to chronic nicotine become visible, making it easier to study the effects of nicotine on learning and memory [49]. With a 1.7% global prevalence, conventional tobacco use during pregnancy continues to be a public health concern. There are significant variations among the nations; Ireland (38.4%), Uruguay (29.7%), and Bulgaria (29.4%) have the greatest percentages, while Tanzania (0.2%), Burundi (0.3%), and Sri Lanka (0.3%) have the lowest rates. Compared to America (5.9%), Europe has a greater estimated prevalence (8.1%), but it is lower than Asia (25%) [50].

Millions of Americans attempt to stop smoking each year with the help of nicotine replacement therapy, or NRT. Pharmacological treatment treatments, such as NRT, have the potential to reduce up to $1,450 in costs each life year.

The goal of nicotine replacement therapy is to progressively and carefully diminish a person's exposure to nicotine, ideally until the person no longer has a physical reliance on nicotine. Using a nicotine transdermal patch equipment is one of the most successful ways of accomplishing this [51]. Nicotine is the active component found in pharmaceutical medicines used in nicotine replacement rehabilitation. When these products are used to help smokers quit smoking, millions of people are exposed to nicotine each and every day. Pharmaceutical NRTs are products meant to help people quit smoking that are administered like medication or drugs [52]. Products containing nicotine replacement treatment have an authorization to ease withdrawal symptoms and help people stop smoking. The reasoning behind this is that NRT offers a different source of nicotine, which lessens the emotional state of withdrawal. There are the two stages in the quitting process. In order to overcome the loss of the behaviour aspect of the habit, the smoker initially continues at a lower dose and speed of nicotine availability [53].

10.1. Limitations of nicotine replacement therapy

The potential of creating a confusing plot line due to the variety of the technique and findings found in the current literature may be the restriction of a systematic review, contemplating the novelty of this research line. In order to create an distinct narrative line, we therefore chose the items that were most pertinent. Compared to NRTs, whose studies have been established over past experiences century, the volume of extant literature on ENDS is varied and considerably smaller due to the young nature of this field. It is unattainable to conduct RCTs on humans that compare tobacco use to NRT and/or ENDS in pregnant women due to ethical concerns. It ought to become noted that most of the studies cited are based on animal models, which have drawbacks when it comes to generalizing findings to people [50].

10.2. Future Scope

- The development of transdermal delivery systems necessitates achieving a balance between cost and patient safety/comfort while allowing for deeper transdermal transport. Enhancement strategies are required since unharmed.skin is insufficiently permeable to most medication [54].
- Liposomes, niosomes, and micro-emulsion are examples of innovative formulation techniques and technologies of the future. This approach aims to enhance the governance of medication that is essentially less soluble in the majority of common formulation excipients [30,55].
- A large variety of possible delivery medications, including methotrexate, steroids, interferon, anti fungal, and antibacterial agents, are developed. Transdermal patch sales are expected to rise in the future and have grown at a pace of 25% annually in recent years [56].

11. Microneedle designs

Designs of microneedles Although there are many different designs of microneedles, there are two main types: in-plane and out-of-plane. Microneedles that are formed in-plane align with the needle parallel to the fabrication surface, whereas those that are formed out-of-plane align there with the needle perpendicular to the fabrication surface. Out-of-plane microneedles that can be additionally classified into two categories: solid and hollow. The two differ in that the hollow microneedles comprise a conduit inside of them that permits fluid passage, whilst the solid microneedles do not. An analysis of in-plane compared out-of-plane microneedles. An in-depth analysis of the methods of manufacturing utilized to create in-plane and out-of-plane microneedles [57]. Comparing microneedles to more conventional parenteral administrations like intravenous, intramuscular, and subcutaneous injections, their unique qualities such as enhanced patient compliance and self-administration have garnered significant attention recently for their potential as novel transdermal drug delivery systems. The industrialization and clinical applications of microneedles and patches, particularly in personalized health care, have been inhibited by the significant challenges encountered with their exact production on a micro scale. Many studies have recently been released on the use of 3D printing to create transdermal drug delivery systems. These research efforts not only use a variety of printing techniques but also various formulation strategies to create advanced bio-inspired microneedles and artificial cargo delivery systems [58].

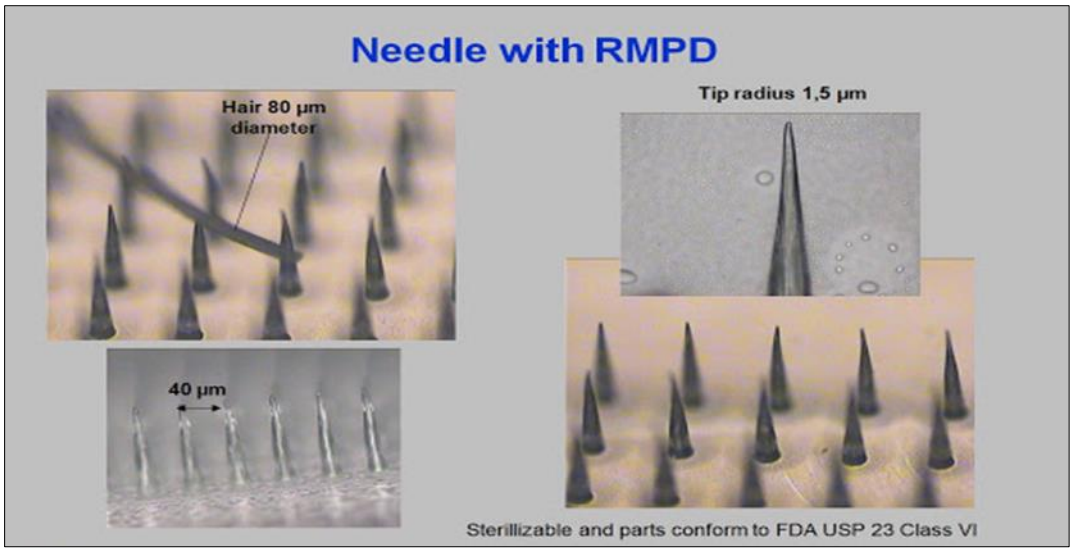

Figure 7 Polymer tapered-cone microneedles made of poly-lactide-co-glycolide and encapsulating calcine within their tips [57]

11.1. Assessment of in-brain drug delivery by microneedles

In order to examine how well the gold encapsulation performed in regulating drug release from the MN, we precisely produced two groups of MN that were loaded with 25 weight percent melatonin. In order to provide a meaningful comparison, the second batch of MNs (Au-Mel-MNs) contains 200 nm of gold coated on the MN surface, whereas the first batch (Mel-MNs) does not have a gold encapsulating layer [59].

11.2. Future Perspective of Microneedles

The many materials used in MN formulations and fabrication processes, as well as the methods of manufacture themselves, are represented in this overview. Considerable work has been done to demonstrate TDD with MNs that's effective well. According to their individual documents, a very wide range of materials have been used in the manufacture of MNs. From 2010 to 2017, a large number of patents were filed. This highlights the enormous potential of MNs in a variety of fields, including diagnostics, biomedical engineering, cosmetics, and pharmaceutical. MNs should be optimized for safety and health concerns in the near future so that they can be used as a therapy option to treat different illnesses. Given that so many MNs are undergoing clinical trials, MNs have a bright future. Their potential for administering drugs to children is likewise rather high. An attempt was made to summarize the types of MNs, materials, and processes used in MN manufacturing facilities in this review [60].

12. Transdermal Glucose Monitoring

Associated blood glucose levels with interstitial fluid glucose levels are extremely important, and using an iontophoretic method to extract interstitial fluid for glucose sampling has been investigated it. Reverse iontophoresis, skin microporation, patch management of permeation enhancers, ultrasound to boost transdermal flux, and glucose fluorescence tagging are some of the methods. The technique used by the GlucoWatch Biographer to transfer glucose from interstitial fluid to the sensor interface is called reverse iontophoresis; this method enables consistent glucose measurements. This method has been known to cause widespread skin irritation; also, it is not possible to employ this device when perspiring profusely [61].

those suffering from type 1 diabetes (T1D), continuous glucose monitoring (CGM) lowers HbA1c and lowers the frequency of episodes of hypoglycemia, increasing glycaemic management. CGM is especially useful for virtual consultations since it can send data to the cloud, where it may be saved, shared, and accessed by both the patient and the health-care provider. Using shared CGM data, remote virtual consultations have improved patient outcomes during the COVID-19 epidemic by enabling patients to remotely plan their goals and make thorough revisions to their glycaemiccontrol. CGM is still not as widely used as it could be, particularly among teenagers. Moreover, CGM systems are frequently utilized sporadically. Misuse may be linked to issues with payment, pain on a physical, issues with the insertion and retention of sensors on the skin, worries regarding data accuracy, disruption of sports and daily activities, and skin reactions [62].

Blood glucose meters, which are based on minimally invasive finger stick tests and have an important customer segment worth US $6.1 billion, are the most often used glucose monitoring devices. Roche Diagnostics, Bayer, Abbott, Medtronic, and Life Scan have the majority of this market share. Non-invasive glucose monitoring, or NGM, have grown increasingly popular recently though, as it helps diabetics who must pierce their skin more than four times a day to verify the information their blood sugar levels. While many distinct NGM techniques have been proven, Raman spectroscopy and absorbance spectroscopy are the most commonly utilized technologies. Although NGM eliminates the need for a strip, which greatly reduces the costs of repeated assessments, it is not quite as precise and specific as blood glucose meters [63].

12.1. Benefits of Using CGM In Daily Diabetes Care

- A substantial amount of investigation demonstrates how using CGM can enhance a diabetic's quality of life and health outcomes. In actuality, this constitutes a paradigm shift in the way that diabetes patients are treated—from reactive measures to proactive measures to prevent high and low blood sugar levels.
- The use of CGM devices has been linked to a decrease HbA1c in people with type 2 diabetes mellitus (T2DM) treated with insulin or a non-insulin therapy, as well as in children and adults with type 1 diabetes mellitus (T1DM), when compared with SMBG.
- The use of CGM has a connection to a lower risk of hypoglycemia in patients with T1DM and T2DM. These glycaemic positive aspects have usually been shown in prospective trials over time frames of up to 12 months; however, as the COMISAIR prospective study showed. An ongoing effect of individuals with T1DM using the Dexcom G4 real-time CGM instrument for a period of three years [64].

12.2. Methods of Monitoring Blood Glucose Concentration

- **Invasive Blood Glucose Monitoring:** Since invasive blood glucose detection technology is currently widely used, practical, and convenient, blood glucose measurement is currently measured by both hospitals and home glucometer using the procedure of first drawing blood and then analyzing it in vitro. In hospitals, an automated biochemical analysis measures the blood glucose concentration precisely after taking a subject's blood in the morning while they are fasting. Although the results are correct, this method's high venous blood extraction volume, lengthy detection time, and labour-intensive approach make it unsuitable for continuous monitoring of diabetics and can serve as a valuable foundation for diabetes diagnosis. Self-monitoring of blood glucose (SMBG) is the process of measuring blood glucose levels at a given moment employing an electronic glucose meter that is often kept at home [65].
- **Non-Invasive Blood Glucose Monitoring:** The most recent advancements in glucose monitoring include non-invasive approaches that mostly use optical techniques and minimally invasive methods which utilize fluids from the body other than blood, such as perspiration, saliva, and interstitial fluid (ISF), which compromise the skin barrier without puncturing blood vessels. Continuous glucose monitoring systems are minimally invasive devices that automatically and continuously check blood sugar levels. These devices are currently on the market. The goal of non-invasive technology is to improve this subject by offering a way to measure blood sugar levels without puncturing the skin [66].

13. Conclusion

TDDS technology prevents first-pass metabolism and other sensitivities linked to different alternative drug administration routes, it is the preferred drug injection modality for transdermal delivery across skin types. This is because it is commonly recognized as the creation of a mass delivery mechanism. Drugs can be infused into the systemic circulation through the skin using a variety of devices using TDDS. Until they reach the target tissue, drugs are generally safely and reliably given using TDDS and remain stable and safe from biochemical changes. However, an increasing number of novel pharmaceutical items are being created for transdermal distribution as a result of our growing knowledge of the structure and functions of the skin, as well as how to change these aspects. The qualities of the transdermal device and the properties of the medication. When employed in drug therapy, TDDS reduces negative effects, improves bioavailability, uniforms plasma levels, and maintains product quality while reducing absorption. The essential components of a patch cooperate to release the drug via the skin. The controlled therapeutic application of TDDS would be the main focus of its future prospects.

The idea behind nicotine-assisted reduction therapy (NRT) is that by increasing nicotine levels, the smoker will find it easier to cut back on cigarettes and reduce their likelihood of experiencing compensation, which should result in a reduction in the number of pollutants they inhale. Since nicotine replacement therapy has a well-established safety profile, it is always safer to use it to help someone quit smoking than to keep smoking. This conclusion is supported by

the current data. The study on microneedles has been positive, with an emphasis on assessing safety risks to clarify possible uses in medicine and pharmacy.

Compliance with ethical standards

Disclosure of conflict of interest

The authors disclose that no direct or indirect conflicts of interest.

References

[1] Wong WF, Ang KP, Sethi G, Looi CY. Recent Advancement of Medical Patch for Transdermal Drug Delivery. Medicina, 2023; 59(4): 778 1-20.

[2] Kubde JA, Dr. Sarode S. A comprehensive study on topiramate transdermal drug delivery systems. International Journal of Pharmaceutical and Clinical Research, 2024; 6(1): 01-06.

[3] Jayaprakash R, Hameed J, Anupriya. An Overview of Transdermal Delivery System. Asian J Pharm Clinical Research, 2017; 10(10): 36-40.

[4] Yadav V. Transdermal Drug Delivery System: Review. IJPSR, 2012; 3(2): 376-382.

[5] Kumar AJ, Pullakandam N, Prabhu LS, Gopal V. Transdermal Drug Delivery System: An Overview. International Journal of Pharmaceutical Sciences Review and Research, 2010; 3(2): 49-54.

[6] Jeong WY, Kwon M, Choi HE, Kim KS. Recent Advances in Transdermal Drug Delivery Systems: a Review. Biomaterials Research, 2021; 25(24): 1-15.

[7] Guy RH. Transdermal Drug Delivery. Drug Delivery System, 2007; 22: 442–449.

[8] Prausnitz MR, Langer R. Transdermal Drug Delivery. Nature Biotechnolog, 2008; 26(11): 1261-1268.

[9] Manikkath J, Sumathy TK, Manikkath A, Mutalik S. Delving Deeper into Dermal and Transdermal Drug Delivery: Factors and Mechanisms Associated with Nanocarrier-Mediated Strategies. Current Pharmaceutical Design, 2018; 24(27): 3210-3222.

[10] Ita K. Dissolving Microneedles for Transdermal Drug Delivery: Advances and Challenges. Biomedicine & Pharmacotherapy, 2017; 93: 1116–1127.

[11] Watkinson AC, Kearney MC, Quinn HL, Courtenay AJ, Donnelly RF. Future of the Transdermal Drug Delivery Market Have We Barely Touched the Surface? Expert Opinion on Drug Delivery, 2015; 17(59): 1-35.

[12] Seah BC, Teo BM. Recent Advances in Ultrasound-Based Transdermal Drug Delivery. International Journal of Nanomedicine, 2018; 13: 7749–7763.

[13] Ramadon D, McCrudden MTC, Courtenay AJ, Donnelly RF. Enhancement strategies for transdermal drug delivery systems: current trends and applications. Drug Deliv Transl Res. 2022; 12(4): 758-791.

[14] Jain RG, Mittal M, Dr Kundal SS. Recent Advancements in Transdermal Drug Delivery System: A Review: Pharmaceutical Science-Pharmaceutics. International Journal of Life Science and Pharma Research. 2023; 13(3): 24-39.

[15] Choudhary N, Singh AP, Singh AP. Transdermal Drug Delivery System: A Review. Indian Journal of Pharmacy and Pharmacology, 2021; 8(1): 5–9.

[16] Deulkar DA, Kubde JA, Hatwar PR, Bakal RL. A review on transdermal drug delivery system. GSC Advanced Research and Reviews, 2024; 18(02): 347–361.

[17] Motwani AN, Hatwar PR, Bakal RL, Deulkar DA, Gupta AA. Sustained Release Drug Delivery System – An Overview. World Journal of Pharmacy and Pharmaceutical Sciences, 2024; 13(2): 510-521.

[18] Sandhu P, Bilandi A, Kataria S, Middha A. Transdermal Drug Delivery System (Patches), Applications Present Scenario. International Journal of Research in Pharmacy and Chemestry, 2011; 1(4): 1139-1151.

[19] Ramteke KH, Dhole SN, Patil SV. Transdermal Drug Delivery System: A Review. Journal of Advanced Scientific Research, 2012; 3(1): 22-35.

[20] Shinde N, Manikpuriya S, Dr. Sanap G. Review of Transdermal Drug Delivery System. World Journal of Pharmaceutical Sciences, 2023; 13(1): 835-857.

[21] Shaikh MSH, Hatwar PR, Bakal RL and Kohale NB. A comprehensive review on Liposomes: As a novel drug delivery system. GSC Biological and Phamaceutical Sciences, 2024; 27(01): 199-210.

[22] Deulkar DA, Kubde JA, Hatwar PR, Bakal RL and Motwani AN. Niosomes: A promising approach for targeted drug delivery. GSC Biological and Pharmaceutical Sciences, 2024; 29(01): 179–195.

[23] Yeole KG, Kitukale SR, Dr. Bakal RL, Hatwar PR, Chakare SY. Transdermal Drug Delivery System. International Journal of Research and Analytical Review. 2023; 10(2), 275-279.

[24] Upadhyay G, Verma S, Parvez N, Sharma PK. Recent Trends In Transdermal Drug Delivery System - A Review. Advances In Biological Research, 2014; 8(3): 131-138.

[25] Rabiei M, Kashanian S, Samavati SS, Jamasb S, McInnes SJP. Nanomaterial And Advanced Technologies in Transdermal Drug Delivery. Journal Of Drug Targeting, 2019; 28(4): 356-367.

[26] Lawton S. Skin 1: the structure and functions of the skin. Nursing Times [online], 2019; 115(12): 30-33.

[27] Shukla MK, Shukla K, Srivastava H. A Review on Transdermal Patches. World Journal Pharmacy and Pharmaceutical Sciences, 2023; 12(9): 1250-1261.

[28] Prabhakar D, Sreekanth J, Jayaveera KN. Transdermal Drug Delivery Patches: A Review. Journal of Drug Delivery & Therapeutics, 2013; 3(4): 213-221.

[29] Kumar P, raza R, Mittal A, Alam S, Surya P, Chauhan N. Approaches and Evaluation of Transdermal Drug Delivery System. International Journal of Drug Development & Research, 2015; 7(1): 222-233.

[30] Sharma N, Agarwal G, Rana A C, Bhat Z A, Kumar D. A Review: Transdermal Drug Delivery System: A Tool for Novel Drug Delivery System. International Journal of Drug Development & Research, 2011; 3(3): 70-84.

[31] Patel D M, Kavitha K. Formulation and Evaluation Aspects of Transdermal Drug Delivery System. International Journal of Pharmaceutical Sciences Review and Research, 2011; 6(2): 83-90.

[32] Bathe R, Kapoor R. Transdermal drug delivery system: formulation, development and evaluation-An overview. International Journal of Biomedical and Advance Research, 2015; 6(01): 1-10.

[33] Sonia D, Thakur G And Ashish K. Transdermal Patches: A Recent Approach to New Drug Delivery System. International Journal of Pharmacy and Pharmaceutical Sciences, 2019; 3(5): 26-34.

[34] Amjadi M, Sheykhansari S, Nelson BJ, Sitti M. Recent Advances in Wearable Transdermal Delivery Systems. Adv Mater, 2018; 30(7): 1-19.

[35] Al Hanbali OA, Khan HMS, Sarfraz M, Arafat M, Ijaz S, Hameed A. Transdermal patches: Design and current approaches to painless drug delivery. Acta Pharm, 2019; 69(2): 197-215.

[36] Japairaia KA, Mahmooda S, Almurisic SH, Venugopald JR, RebhiHillese A, Azmanaa M, Ramana S. Current Trends in Polymer Microneedle for Transdermal Drug Delivery. International Journal of Pharmaceutics, 2020; 587: 119673

[37] Dafe VN, Hatwar PR, Bakal RL, Kubde JA, Jumde KS. Transdermal insulin delivery via microneedle technology, patches, and pumps offers a promising alternative to traditional subcutaneous injections for diabetes management. GSC Biological and Pharmaceutical Sciences, 2024; 29(01): 233–242.

[38] Mahdiyyaha AA, Diyaha NW, Hendrad E. Transdermal Patches: A Review of a New Drug Delivery System Approach. International Journal of Medical Reviews and Case Reports, 2022; 6(9): 25-31.

[39] Reddy MD, Kumar VV, Kumar PK, Harshini P, Lahari P, Sunitha C. Formulation Evaluation Nicotine Transdermal Patches by The Using of Hydrophilic and Hydrophobic Polymers. World Journal of Pharmaceutical Research, 2018; 7(16): 1101-1115.

[40] Maske A, Shelke S, Ajgunde RR, Bavge S. A Review Article on Transdermal Patches. International Journal of Research Publication and Reviews, 2023; 4(6): 456-462.

[41] Rotake SB, Hatwar PR, Bakal RL and Kohale NB, Transdermal drug delivery system recent advancements: A comprehensive review, GSC Biological and Pharmaceutical Sciences, 2024, 28(02), 059–072.

[42] Ravi S, Sharma PK, Bansal M. A Review: Trasdermal Drug Delivery of Nicotine. International Journal of Drug Development & Research, 2011; 3(2):1-8.

[43] Prasantha A, Remya S B, Prasobh G R, Chandran Subhash M P. A Review on Transdermal Patches. Human Journals, 2022; 23(4): 283-298.

[44] Olsson Gisleskog PO, Perez Ruixo JJ, Westin A, Hansson AC, Soons PA. Nicotine Population Pharmacokinetics in Healthy Smokers After Intravenous, Oral, Buccal and Transdermal Administration. Clinical Pharmacokinetics, 2021; 60(4): 541–561.

[45] Abdallah IA, Hammell DC, Stinchcomb AL, Hassan HE. A Fully Validated LC–MS/MS Method For Simultaneous Determination of Nicotine and Its Metabolite Cotinine in Human Serum and Its Application to A Pharmacokinetic Study After Using Nicotine Transdermal Delivery Systems with Standard Heat Application in Adult Smokers. Journal Of Chromatography, 2016; 1020: 67–77.

[46] Kyaw WT, Nagai M, Kaneta M, Kubo M, Nishikawa N, Tsujii T, Iwaki H, Nomoto M. Effect of Nicotine on The Pharmacokinetics of Levodopa. Clinical Neuropharmacology, 2013; 36(2): 46-51.

[47] Rasmussen S, Horkan KH, Kotler M. Pharmacokinetic Evaluation of Two Nicotine Patches in Smokers. Clin Pharmacol Drug Dev.2018; 7(5): 506-512.

[48] Gulati GK, Chen T, Hinds BJ. Programmable carbon nanotube membrane-based transdermal nicotine delivery with microdialysis validation assay. Nanomedicine. 2017; 13(1): 1-9.

[49] Lester RA. Cognitive Mechanisms Underlying Relapse to Nicotine. Rev. Neurosci., 2011; 22(4): 467–470.

[50] 46)Sebastian S, Giorgia S, Vicente Andreu-Férnández, Oscar García-Algar. Impact of Nicotine Replacement and Electronic Nicotine Delivery Systems on Fetal Brain Development. Int. J. Environ. Res. Public Health, 2019; 16(24): 5113.

[51] Linakis MW, Rower JE, Roberts JK, Miller EI, Wilkins DG, Sherwin CMT. Population pharmacokinetic model of transdermal nicotine delivered from a matrix-type patch. Br J Clin Pharmacol. 2017; 83(12): 2709-2717.

[52] Lee PN, Fariss MW. A Systematic Review of Possible Serious Adverse Health Effects of Nicotine Replacement Therapy. ArchToxicol, 2017; 91: 1565–1594.

[53] McNeill A, Foulds J, Bates C. Regulation of nicotine replacement therapies (NRT): a critique of current practice. Addiction. 2001; 96(12): 1757-68.

[54] Prausnitz MR, Mitragotri S, Langer R. Current status and future potential of transdermal drug delivery. Nat Rev Drug Discov. 2004; 3(2): 115-24.

[55] Bagmar NA, Hatwar PR and Bakal RL. A Review on targeted drug delivery system. World Journal of Pharmaceutical Research. 2023; 12(19), 288-298.

[56] Sharma N. A Brief Review on Transdermal Patches. Organic And Medicinal Chemistry IJ, 2018; 7(2): 58-62.

[57] Sivamani RK, Liepmann D, Maibach HI. Microneedles and transdermal applications. Expert Opin Drug Deliv, 2007; 4(1): 19-25.

[58] Yang Q, Zhong W, Xu L, Li H, Yan Q, She Y, Yang G. Recent progress of 3D-printed microneedles for transdermal drug delivery. Int J Pharm, 2021; 593: 120106.

[59] Wang Y, Chen Z, Davis B, Lipman W, Xing S, Zhang L, Wang T, Hafiz P, Xie W, Yan Z, Huang Z, Song J, Bai W. Digital automation of transdermal drug delivery with high spatiotemporal resolution. Nat Commun. 2024; 15(1): 511.

[60] Ali R, Mehta P, Arshad MS, Kucuk I, Chang MW, Ahmad Z. Transdermal Microneedles-A Materials Perspective. AAPS PharmSciTech. 2019; 21(1): 12.

[61] Pandey PC, Shukla S, Skoog SA, Boehm RD, Narayan RJ. Current Advancements in Transdermal Biosensing and Targeted Drug Delivery. Sensors (Basel), 2019; 19(5): 1028.

[62] Boscari F, Vettoretti M, Cavallin F, Amato AML, Uliana A, Vallone V, Avogaro A, Facchinetti A, Bruttomesso D. Implantable and transcutaneous continuous glucose monitoring system: a randomized cross over trial comparing accuracy, efficacy and acceptance. J Endocrinol Invest. 2022; 45(1): 115-124.

[63] Vashist SK. Continuous Glucose Monitoring Systems: A Review. Diagnostics. 2013; 3(4): 385-412.

[64] Klupa T, Czupryniak L, Dzida G, Fichna P, Jarosz-Chobot P, Gumprecht J, Mysliwiec M, Szadkowska A, Bomba-Opon D, Czajkowski K, Malecki MT, Zozulinska-Ziolkiewicz DA. Expanding the Role of Continuous Glucose Monitoring in Modern Diabetes Care Beyond Type 1 Disease. Diabetes Ther. 2023; 14(8): 1241-1266.

[65] Tang L, Chang SJ, Chen CJ, Liu JT. Non-Invasive Blood Glucose Monitoring Technology: A Review. Sensors (Basel), 2020; 20(23): 6925.

[66] Lin T, Gal A, Mayzel Y, Horman K, Bahartan K. Non-invasive glucose monitoring: a review of challenges and recent advances. Curr. Trends Biomed. Eng. Biosci, 2017; 6(5): 1-8.