

## Novel Route for Insulin Administration: Transdermal Route

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### ABSTRACT:

Diabetes is a chronic disease that occurs when your blood glucose, also called blood sugar is too high. Diabetes complications include macro vascular and micro vascular disease. Diabetes mellitus is the chronic pathogenic condition which is primarily due to inadequate insulin secretion and is responsible for major health care problems worldwide cost billions of dollars annually. Insulin is delivered by subcutaneous route. Mainly because it is most safe and effective route of administration. This review examines some of recent proposals for insulin transdermal drug delivery system along with particular attention to its latest invention of novel drug delivery system. This delivery system includes the insulin patches. An insulin patch works by being placed on the skin and agents within the patch help insulin to pass through the skin and then into blood stream. It contains set dose of insulin that is absorbed over a number of hours. Transdermal drug delivery system is a field worth exploring due to its significant advantages over oral route in administration of antidiabetic drug and biosensing of blood glucose level to ensure better clinical outcomes in diabetes management. Insulin delivered via transdermal system is able to avoid the chemical and enzymatic degradation in digestive tract and this approach can also provide sustained release to maintain therapeutic concentration for prolonged time, contributing to better patient compliance.

**KEYWORDS:** Portal system, nano particles, biodegradable polymer, Innovation, Medication theory Management (MTM).

### I. INTRODUCTION:

Diabetes is a condition that arises from elevated blood glucose, commonly referred to as blood sugar. It is a chronic illness in which the body either cannot use the insulin it generates efficiently or does not make enough of it.

Your pancreas naturally produces insulin, a hormone that aids in controlling blood glucose levels. This hormone may work in tandem with glucagon to regulate blood glucose levels; glucagon

has catabolic effects, whilst insulin acts through anabolic pathways.

### SYMPTOMS:

Diabetes symptoms can strike without warning. The signs of type 2 diabetes might be subtle and take years to manifest.

Diabetes symptoms include: \* extreme thirst; \* increased frequency of urination; \* blurred vision; \* fatigue; \* inadvertent weight loss.

Diabetes can harm blood vessels in the kidneys, heart, eyes, and nerves over time. Diabetes increases a person's risk of heart attack, stroke, and renal failure, among other illnesses. Diabetes can harm the blood vessels in the eyes, resulting in permanent vision loss.

Because diabetes damages nerves and reduces blood flow, many patients with the disease experience foot difficulties. This may result in amputation and foot ulcers.

#### a) **Type 1 diabetes:**

Also referred to as insulin-dependent, juvenile, or childhood-onset diabetes, type 1 diabetes is characterized by insufficient insulin production and necessitates the daily prescription of insulin. Nine million persons worldwide have type 1 diabetes in 2017, with high-income nations housing the bulk of this population. Its etiology and prevention strategies are unknown.

#### b) **Type 2 diabetes:**

This condition alters the way your body uses glucose, or sugar, as fuel. If left untreated, it prevents the body from utilizing insulin as it should, which can result in elevated blood sugar levels. Type 2 diabetes has the potential to seriously harm the body over time, particularly the blood vessels and nerves.

Early detection is crucial to preventing type 2 diabetes's worst effects.

Type 2 diabetes can have modest symptoms. It can take a few years for others to see them. Although they are frequently milder, the symptoms can resemble those of type 1 diabetes.

As a result, the illness may not be discovered for several years after symptoms start to appear and after complications have developed.

Type 2 diabetes affects more than 95% of those who have the disease. Before, type 2 diabetes was referred to as adult onset or non-insulin dependent. This kind of diabetes was only diagnosed in adults until recently, but it is now increasingly occurring in youngsters as well.

➤ **Gestational diabetes**

Hyperglycemia, or blood glucose levels above normal but below the diagnostic range for diabetes, is referred to as gestational diabetes. Pregnancy is the time when gestational diabetes happens.

Obstetrical and delivery complications are more likely to arise in women with gestational diabetes. Future type 2 diabetes is also more likely to affect these women and maybe their offspring. Rather than relying on patient reports of symptoms, parental screening is used to diagnose gestational diabetes.

➤ **INTRODUCTION OF TRANSDERMAL PATCHES:**

Currently, research on insulin patches, an experimental method of delivering insulin, is in its early stages.

An insulin patch works similarly to transdermal patches like those for nicotine or muscle soreness, in that it tries to deliver insulin through the skin without causing pain.

If insulin patches are effectively created, individuals undergoing insulin therapy will have the opportunity to take their medication without the need for needles or catheters—a thin tube that the body uses to receive insulin from insulin.

• **HOW DOES AN INSULIN PATCH OPERATE?**

When an insulin patch is applied to the skin, substances within the patch facilitate insulin's passage through the skin and into the bloodstream.

A predetermined amount of insulin is contained in an insulin patch, and it is absorbed over several hours.

Insulin patches have been developed in two different ways: bolus insulin patches, which release insulin more quickly to counteract blood sugar spikes after meals, and basal insulin patches, which release insulin more gradually throughout the day to counteract the liver's gradual release of glucose.

• **The difficulties in creating insulin patches**

Although insulin is a large molecule and is typically not absorbed by the skin, creating an effective insulin patch has proven difficult. Insulin patches may seem like an obvious form of delivery. To avoid blood glucose levels that are too high or too low, insulin patches need agents to help the insulin pass through the skin in a controlled and consistent manner.

Insulin patches for boluses

Researchers at the University of KwaZulu-Natal are currently working on developing a bolus insulin patch.

Pectin-containing dermal patches are used in bolus insulin patches to deliver the insulin.

The bolus insulin patch has only been tested on rats thus far, but the findings suggest that the patch may prove to be an effective treatment option in the future.

• **Basal insulin patch:**

A US company named Prometheon is presently working on the TruePatch, a basal insulin patch.

The dermoadhesive gel used in the patch serves as a reservoir for insulin, which is progressively adsorbed into the bloodstream.

Animal clinical trials have demonstrated that the patch consistently lowers blood pressure.

➤ **DELIVERY OF TRANSDERMAL INSULIN:**

Protecting the body from illness and infection is one of the skin's main functions. Because of how strong this barrier is, many pharmaceutical substances are kept out of the bloodstream. Both passive and active drug transport across the skin (transdermal barrier) are being developed to get around this defense.

A drug can act locally by diffusing through the skin or systemically by penetrating the capillaries through passive transdermal delivery. The most common forms of passive delivery are patches, creams, and sprays. Aspirin and nicotine are the only small molecule medications that can be administered via passive transdermal delivery. Because of its size, insulin cannot pass through the skin passively.

In contrast, active transdermal delivery entails rupturing the skin barrier through chemical or mechanical means. Active transdermal systems have the ability to deliver proteins and other large

molecule formulations through the skin and into the bloodstream by means of an applied force, such as ultrasound or an electrical current.

Companies are creating a variety of active transdermal delivery technologies to get around the skin's formidable barrier. It is hoped that this will allow products that were previously thought to be undeliverable via this route to be delivered via the transdermal market.

- **U-Strips from Dermisonics (No Longer Active)**

The U-Strips skin pad from Dermisonics combines ultrasonic science and microelectronics. In order to sufficiently widen pores to allow big molecules like insulin to pass through the skin and eventually enter the bloodstream, it uses alternating ultrasonic waveforms. The Medi-Cap, Ultrasonic, Applicator, and Dose Controller are the four components of the system. Together, they generate ultrasonic transmissions that dilate pores and permit large molecule drugs to enter the bloodstream. It records the dose administered, varies the rate and frequency of delivery, and stores the information for sixty days. To enable personalized dose monitoring and management, this information can be downloaded via modem and sent to your doctor as a dose report.

- **LidoSite Vyteris:**

The Vyteris transdermal drug delivery system uses low-level electrical energy to deliver drugs through the skin in a comfortable manner using iontophoretic delivery technology. It is stated that this technology enables accurate dosing, allowing for control over the dosage, rate, and pattern of drug delivery. Compared to current drug administration techniques, this may provide therapeutic, financial, and lifestyle benefits. Insulin delivery is just the beginning for each of these technologies; there are many more potential uses. All of these businesses want to be able to use these techniques to help treat a range of illnesses.

➤ **ADVANTAGES OF TRANSDERMAL ROUTE OF DRUG ADMINISTRATION:-**

Transdermal route of drug administration is becoming increasingly popular due to following advantages.

1. Provides smooth plasma concentration of a drug without fluctuations, for a long period.
2. Drug reaches systemic circulation which avoiding first pass hepatic metabolism.

3. The simplified medication regimen leads to improve patient compliance and reduce side effect as well as inter and intra-patient variability.

4. Equivalent therapeutic effect can be elicited with less amount of dose if given as transdermal patch as compared to dose of same drug if given orally.

5. Can be route of drug administration of choice in patients who are unconscious.

➤ **DISADVANTAGES OF TRANSDERMAL ROUTE OF DRUG ADMINISTRATION:-**

1. The drug, the adhesive, or excipients in patch formulation may cause rashes, local irritation, erythema, or contact dermatitis.

2. Drugs with hydrophilic structure will not be able to reach systemic circulation unless modified to some suitable form.

3. Doses of only 5 mg or less can be administered in a day.

4. Only potent drugs are suitable candidates for transdermal patch because of the natural limits of drug entry imposed by skins impermeability.

5. The barrier function of the skin changes from one site to another on the same person, from person to person, and with age.

## II. LITERATURE SURVEY :-

[1] **A review literature on science of diabetes mellitus :-**

**By Rajeev Kumar Varma**

**Abstract :-**

Diabetes is a pancreatic disease or disorder that prevents the pancreas from secreting insulin into the bloodstream. Without insulin, glucose cannot enter cells, which is why insulin is necessary for glucose to enter cells and give energy to all of the body's cells. Diabetes type 1 is caused by defects in the parts of the body that aid in the secretion of insulin. Ten percent of cases of diabetes mellitus are of the type. type-1 diabetes, which primarily affects young people. The incidence of type-2 diabetes mellitus is approximately 90%. It mostly happens after the age of forty. In this instance, insulin is secreted, but in small amounts, and it is linked to aspects of our lifestyle like binge eating and exercise, etc.

The following symptoms, such as increased thirst, hunger, and urination, are linked to diabetes. Patients classified as pre-diabetic are those who fall between the normal and diabetic range. Numerous interventions and therapies are available to help treat diabetes, such as portion

control, exercise, and water consumption. In the treatment of diabetes, metformin is essential because it lowers the level of glucose production. The United States leads the world in diabetes incidence, with China, India, and Brazil coming in second.

**[2] Transdermal insulin delivery using choline-based ionic liquids (CAGE):-**

**By - Eden E L Tanner, Kelly N Ibsen, Samir Mitragotr**

**Abstract :**

The use of deep eutectic solvents (DES) like choline and geranic acid (CAGE) for transdermal drug delivery showcases the importance of ion ratio modulation in influencing characteristics such as viscosity, diffusivity, and conductivity. By varying the choline to geranic acid ratio, unique compositions of CAGE were created, each with distinct physicochemical properties. These variations impacted skin permeability differently, with compositions containing excess geranic acid demonstrating higher insulin delivery into the dermis. This underscores the importance of exploring ion ratios in optimizing drug delivery systems.

**[3] Novel routes of insulin delivery for diabetes treatment :-By - Suchita Panda, Dr Falguni Patra and Dr Beduin Mahanti**

**Abstract :**

Since the 1920s, subcutaneous insulin has been used to treat diabetes; however, despite the availability of several formulations, intensive insulin therapy involving several daily injections has not been widely accepted in the medical community. In the years since the 1920s, a number of non-enteral delivery methods for insulin have been tried and tested, including ocular, buccal, rectal, vaginal, oral, nasal, and uterine. Many researchers held the opinion until recently that noninvasive insulin delivery was associated with a bioavailability that was too low to provide a practical clinical approach. But an increasing amount of data points to inhaled insulin as a reliable, well-tolerated, and noninvasive substitute for regular subcutaneous insulin injections. Crucially, compared to conventional insulin, inhaled insulin exhibits a more physiological insulin profile. Additional research is required to verify long-term effectiveness and pulmonary safety, to compare the various strategies, and to more fully characterize their respective roles in practice. Inhaled insulin may play a bigger role in

diabetes management as the significance of stricter glycaemic control becomes more apparent and as the number of patients with type 2 diabetes receiving insulin rises. Insulin is necessary for all patients with type 1 diabetes and many with advanced type 2 diabetes mellitus (T2DM) in order to maintain blood glucose levels within the desired range. Subcutaneous insulin injections are the method of administering insulin that is most frequently used. Insulin can be administered subcutaneously using a variety of tools, including insulin pens, insulin pumps, and vials and syringes. Despite being the most common method of administering insulin, subcutaneous delivery is linked to injection pain, needle phobia, lipodystrophy, noncompliance, and peripheral hyperinsulinemia. Consequently, there is a need to deliver insulin as physiologically as possible with minimally invasive or non-invasive methods. The first non-invasive and alternative method of administering insulin that was approved was inhaled insulin, however it has since been taken off the market. Technologies are being investigated to enable the delivery of insulin without invasive procedures. Investigations are being conducted on oral, buccal, nasal, peritoneal, and transdermal insulin delivery methods. The history, current state, and future of different insulin delivery methods are the main topics of this review article. The various insulin delivery routes have been the main topic of this article.

**[4] An overview of transdermal patches:-BY:**

**Ajit Kumar Vishwakarma**

**Navneet Kumar Verma**

**Abstract:**

Transdermal drug delivery allows for a consistent blood level profile, controlled drug release into the patient, a decrease in systemic side effects, and occasionally even increased efficacy over other dosage forms. One benefit of administering medications transdermally is that it is generally painless. Because of its large surface area, systemic access via underlying lymphatic and circulatory networks, ease of access, and non-invasive drug delivery, the skin is a popular choice for drug delivery. The primary goal of the transdermal patch system is to minimally alter medication delivery between and within patients while delivering medication through the skin at a predetermined rate.



#### [5] A Review On Transdermal Patches:-

By : Pawan Jalwal

##### Abstract:

One benefit of administering medications transdermally is that it is generally painless. Because of its large surface area, systemic access via underlying lymphatic and circulatory networks, ease of access, and non-invasive drug delivery, the skin is a popular choice for drug delivery. Transdermal delivery, the process of delivering medication through the skin for a systemic effect, was first used in 1981 when Ciba-Geigy introduced Transdermal V (now known as Transdermal Scope) to treat motion sickness-related nausea and vomiting. Transdermal drug delivery allows for a consistent blood level profile, controlled drug release into the patient, a decrease in systemic side effects, and occasionally even increased efficacy over other dosage forms. The primary goal of transdermal drug delivery systems is to minimally vary between and within patients while delivering medications into the systemic circulation through the skin at a predetermined rate.

#### [6] Formulation and In- vitro Evaluation of Baclofen Transdermal Patches:-

By: Muaadh A. Mohamed Ali

A.M Sabati

Bassam Abduh Ali

##### Abstract:

This study aims to formulate and evaluate transdermal patches containing baclofen using various plasticizers, penetration enhancers, and polymers. A compatibility study was conducted on a drug that contained different film-forming polymers. Furthermore, research was done on in-vitro permeation through animal skin to determine the optimal formulation. Supplies and Procedures: Following research on the incompatibility between baclofen and other polymers, transdermal patches containing 16 percent pure baclofen were developed. Subsequently, the physicochemical characteristics of the prepared patches were assessed in order to identify the ideal formulation for in-vitro release analysis. Findings and Discussion: There was no interaction between baclofen and the polymers utilized in the drug excipient compatibility study. With the exception of formulation, all physicochemical studies of formulated patches were satisfactory. The formula F13, which included propylene glycol as a plasticizer, dimethyl sulfoxide as a penetration enhancer, and polyvinyl alcohol as a film-forming and bioadhesive polymer, was the best one to

choose. The study's conclusion is that baclofen can be made into transdermal patches with a suitable 24-hour drug release and an acceptable appearance.

### III. CONCLUSION:-

In conclusion, transdermal for insulin delivery represent promising avenue in diabetes treatment. Developing a successful non penetrative insulin drug delivery system has continuously been consider as drawback for the pharmaceutical researchers due to presence of various biological barriers be it anatomical or physiological. The existence of these barriers limits the entry of insulin. From the last few decades the researchers aimed to find various non-invasive insulin administration routes which is not only safe, effective and convenient to the patients but also cost-efficient. From all of the available routes and technologies which possesses a great potential for the delivery of insulin. Among them these transdermal patches offer a convenient and non-invasive method of administering insulin appears to be most therapeutically viable approach till date, potentially improve in patient compliance and quality of life while they are not yet widely available, ongoing research and development in this area hold great potential for the future of diabetes management. However its essential to note that further studies and clinical trials are necessary to validate there long term safety and efficacy before widespread adoption in diabetes treatment so that in the future the diabetic patients can able to take the insulin by more conveniently and hassle free manner in diabetic treatment.

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