OVERVIEW ON TRANSDERMAL DRUG DELIVERY SYSTEM FOR TREATMENT OF DIABETIS.

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ABSTRACT
Insulin therapy is essential for controlling the blood glucose level for patients with type 1 diabetes and advanced type 2 diabetes. Conventionally, insulin is administered via Subcutaneous route, it may be associated with pain, decreased reduce side effects, and to enhance the pharmaceutical permanence of insulin delivery. Transdermal delivery is an effective, attractive, and non-invasive method. Therefore, the present review was aimed to focus on different transdermal delivery techniques, their respective advantages, limitation, and approaches for transdermal insulin delivery.

Keywords: Diabetes, Transdermal, Insulin, Micro needle.

INTRODUCTION
Diabetes mellitus is a group of metabolic disorders characterized by increased production of glucose by the liver and decreased clearance of glucose into fat and muscle resulting in abnormal accumulation of glucose in the blood. Diabetes is usually caused by the failure of insulin secretion (type 1 diabetes) or defective responsiveness of the body to insulin (type 2 diabetes). Insulin is the first choice to treat type 1 diabetes & insulin can be administered by injections and insulin pump. Individuals with diabetes mellitus may progress to life-threatening problems, including stroke, loss of vision, cardiovascular complication, or even death if the hyperglycemic condition is untreated. Among two types of DM, type 2 diabetes mellitus is more common than type 1 diabetes mellitus, which occurs only in 5-10% of the population. (Pandey M, Choudhury H, 2018) Approximately 425 million adults suffer from diabetes mellitus according to the 2018 report from the International Diabetes Federation. According to the World Health Organization's (WHO) latest statistics, DM had risen from 4.7% in 1980 to 8.5% in 2014 and the WHO projects that DM will be in the seventh place in the palette of the leading causes of death worldwide in 2030 since DM is one of the leading causes of heart and stroke, blindness, kidney failure, and lower limb amputation. Exogenous administration of insulin is essential in the management of both (type and type 2) diabetes. (Zhang Y, Yu J, Kahkoska AR ,2019, Zaric BL, Obradovic M ,2019) What is diabetes?

Diabetes is when your blood glucose*, also called blood sugar, is too high. Blood glucose is the main type of sugar found in your blood and your main source of energy. Glucose comes from the food you eat and is also made in your liver and muscles. Your blood carries glucose to all of your body’s cells to use for energy. Your pancreas—an organ, located between your stomach and spine, that helps with digestion—releases a hormone it makes, called insulin, into your blood. Insulin helps your blood carry glucose to all your body’s cells. Sometimes your body doesn’t make enough insulin or the insulin doesn’t work the way it should. Glucose then stays in your blood and doesn’t reach your cells. Your blood glucose levels get too high and can cause diabetes or prediabetes. Over time, having too much glucose in your blood can cause health problems.

What is prediabetes?
Prediabetes is when the amount of glucose in your blood is above normal yet not high enough to be called diabetes. With prediabetes, your chances of getting type 2 diabetes, heart disease, and stroke are higher. With some weight loss and moderate physical activity, you can delay or prevent type 2 diabetes. You can even return to normal glucose levels, possibly without taking any medicines.
What are the signs and symptoms of diabetes?

The signs and symptoms of diabetes are

- being very thirsty
- urinating often
- feeling very hungry
- feeling very tired
- losing weight without trying
- sores that heal slowly
- dry, itchy skin
- feelings of pins and needles in your feet
- losing feeling in your feet
- blurry eyesight

Some people with diabetes don’t have any of these signs or symptoms. The only way to know if you have diabetes is to have your doctor do a blood test.

**Type 1 Diabetes:**

Type 1 diabetes, which used to be called juvenile diabetes, develops most often in young people; however, type 1 diabetes can also develop in adults. In type 1 diabetes, your body no longer makes insulin or enough insulin because the body’s immune system, which normally protects you from infection by getting rid of bacteria, viruses, and other harmful substances, has attacked and destroyed the cells that make insulin.

Treatment for type 1 diabetes includes

- taking shots, also called injections, of insulin.
- sometimes taking medicines by mouth
- making healthy food choices.
- being physically active.
- controlling your blood pressure levels. Blood pressure is the force of blood flow inside your blood vessels
- controlling your cholesterol levels. Cholesterol is a type of fat in your body’s cells, in your blood, and in many foods.

**Type 2 Diabetes:**

Type 2 diabetes, which used to be called adult-onset diabetes, can affect people at any age, even children. However, type 2 diabetes develops most often in middle aged and older people. People who are overweight and inactive are also more likely to develop type 2 diabetes.

Type 2 diabetes usually begins with insulin resistance a condition that occurs when fat, muscle, and liver cells do not use insulin to carry glucose into the body’s cells to use for energy. As a result, the body needs more insulin to help glucose enter cells. At first, the pancreas keeps up with the added demand by making more insulin. Over time, the pancreas doesn’t make enough insulin when blood sugar levels increase, such as after meals. If your pancreas can no longer make enough insulin, you will need to treat your type 2 diabetes. Treatment for type 2 diabetes includes

- using diabetes medicines
- making healthy food choices
- being physically active
- controlling your blood pressure levels
- controlling your cholesterol level
ANATOMY OF SKIN.

The skin covers a surface area of approximately 2 sq.m. of the human body." (Tanwar H, 2016). It serves as a permeability barrier against the absorption of various chemical and biological agents by transdermally. The human skin consists of mainly three layers. (Jain NK, 1997).

- Epidermis
- Dermis Cita
- Hypodermis

Fig no 1: T.S. of human skin.

Epidermis:

The epidermis is a self-renewing, stratified squamous epithelium covering the entire outer surface of the body. Epidermis mainly composed of two parts: the living or viable cells of the malpighian layer (viable epidermis) and the dead cells of the stratum corneum commonly known as the horny layer. The viable epidermis is divided into four distinct layers such as Stratum lucidum, Stratum granulosum, Stratum spinosum, and Stratum basale. Stratum corneum is the outermost layer of skin also called a horny layer. Stratum corneum is a barrier that restricts the inward and outward movement of chemical substances. (Tanwar H, Sachdeva R, 2016, Robinson JR, Lee VH, 1999)

Dermis:

The dermis is the layer of skin just beneath the epidermis which is 3 to 5 mm thick layer and is composed of connective tissues, which contains blood vessels, lymph vessels, and nerves. (Waugh A, Wilson, 9th Ed., 2001)

Hypodermis:

The hypodermis or subcutaneous tissue supports the dermis and epidermis. It serves as a storage area for fat. Hypodermis layer helps to regulate temperature, provides nutritional support and mechanical protection (Sharma N, Agarwal G, 2011)

TRANSDERMAL DRUG DELIVERY SYSTEM

Transdermal drug delivery systems (TDDS) are also known as “Transdermal patches” or “Skin patches”. These are dosage forms designed to deliver therapeutically exact and effective amount of drug across a patient's skin and in the bloodstream. For effective Transdermal drug delivery systems, the drugs should be easily able to penetrate the skin and easily reach the target site. The transdermal drug delivery system increases patient compliance. A transdermal delivery strategy that transports the insulin across the skin barrier represents the effective and minimally invasive method for insulin delivery. The Altra Therapeutics Pass Port T System was the first product that provides a non-invasive, controllable, and efficient way to deliver insulin via a patch on the skin consists of an applicator and a reservoir. (Sudam KR, Suresh RB, 2016)

Table 1: Ideal characteristics of transdermal drug delivery

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Parameters</th>
<th>Properties</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Molecular weight</td>
<td>&lt;500 Daltons</td>
</tr>
<tr>
<td>2.</td>
<td>Dose</td>
<td>Less than 20 mg/day</td>
</tr>
<tr>
<td>3.</td>
<td>Half-life</td>
<td>10 or less(hr)</td>
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</table>
ADVANTAGES OF TRANSDERMAL DRUG DELIVERY SYSTEM

- The transdermal drug delivery system avoids the first-pass effect.
- Increases bioavailability.
- Reduces dosing frequency.
- Self-administration is possible with the transdermal delivery system.
- The transdermal delivery system does not interfere with gastric and intestinal fluids.
- The transdermal system is an alternative route of administration to accommodate patients who cannot tolerate oral dosage forms.
- The transdermal drug delivery system is suitable for patients who are nauseated or unconscious.
- Drugs with consistent plasma levels are very good candidates for transdermal drug delivery.
- It maintains stable or constant and controlled blood levels for a longer period. (Sudam KR, Suresh RB, 2016)

DISADVANTAGES

- Some patients develop contact dermatitis at the site of application of the patch from one or more of the system components.
- Higher cost compared to the oral formulation.
- Not suitable for the ionic drug.
- It may cause allergic reactions.
- The barrier function of the skin changes from one site to another site of the same person from person to person and with age.
- The molecular weight of less than 500 Da is essential.
- Sufficient lipid and aqueous solubility, a log P (octanol/water) between 1 and 3 are required for permeation through the skin.
- Only potent drugs are suitable candidates for transdermal delivery.
- It cannot deliver the drug from the dosage form in a pulsatile fashion.

Limitations of the transdermal drug delivery system.
1. The difficulty for adhesion of patch to the skin.
2. The drug undergoes degradation in the skin.

Conditions in which Transdermal patches are used A transdermal patch is used when:

When the patient is unable to take oral medicine and has intolerable side effects (including constipation).
1. When patients are nauseated or unconscious.
2. It can be used in combination with other enhancement strategies to produce synergistic effects for treatment.

TYPES OF TRANSDERMAL DRUG DELIVERY SYSTEMS. (V(Sudam KR, Suresh RB, 2016)

1. The single-layer drug in-adhesive patch:
In the single-layer drug in the adhesive patch, there is a single layer of adhesive in the patch. The adhesive layer of this patch also contains the drug. In this type of patch, the adhesive layer not only serves to adhere to the various layer together but is also responsible for the release of the drug from the patch. The adhesive layer is surrounded by a temporary liner and a backing membrane.
The multi-layer drug in the adhesive patch:

The multi-layer drug in the adhesive is similar to the single layer drug in the adhesive system in that both adhesive layers are also responsible for the release of the drug. But it is different however that the other layer of the drug in-adhesive, usually separated by a membrane. This patch also has a permanent backing and release liner.

2. Reservoir patch Reservoir transdermal system:

It has a separate drug layer than the adhesive layer. The drug layer in the reservoir patch is a liquid compartment containing a drug solution or suspension which is separated by the backing layer. In this type of system, the rate of release is zero order kinetic.

1. Matrix patch: The matrix patch containing a drug layer of a semisolid matrix containing a drug solution or suspension. Adhesive layer in the matrix patch surrounds the drug layer partially overlaying it.

2. Vapour patch: In this type of the patch, the adhesive layer not only serves to various layers adhere together but also responsible for releasing vapor from the patch.

COMPOSITION OF TRANSDERMAL PATCH

A transdermal therapeutic system is a multilaminate structure which is composed of the following constituents:

A. Drug = The drug is an active ingredient that is incorporated in the patch

B. Polymer matrix = Polymers are the backbone of the transdermal drug delivery system. Transdermal drug delivery system are fabricated as multi-layered polymeric laminates in which a drug reservoir or a drug-polymer matrix is sandwiched between the two polymeric layers, an outer impervious backing layer that prevents the loss of drug through the backing surface and an inner polymeric layer that functions as an adhesive, or rate controlled membrane.

C. Penetration enhancers = These are the compounds that promote skin permeability by altering the skin structure as a barrier to the flux of the desired penetrate. Different penetration enhancers are used such as:
   - Sulphoxides
   - azones
   - Pyrrolidones
   - Fatty acid
   - Alcohol
   - Surfactants

D. Adhesives = Pressure-sensitive adhesives are used to achieve contact between the skin and transdermal patch. The adhesive should adhere with not more than applied finger pressure, be aggressively and permanently tacky, and exert a strong holding force. Additionally, it should be easily removable from the surface without leaving a residue on the skin.

There are three types of adhesive used mainly.

1. Silicone type adhesive;
2. Poly iso butylene adhesive
3. Poly acrylate based adhesive.

E. Backing membrane = The backing membrane must be impermeable to drug and permeation enhancers. The backing membrane serves as the purpose of holding the entire system together and at the same time, it protects the drug reservoir from exposure to the atmosphere, which could result in the breakage or loss of the drug by volatilization. The backing material used such as polyester, aluminized polyethylene terephthalate and siliconised polyethylene.

F. Release linear = The release liner is a packaging material that prevents the loss of the drug that has migrated into the adhesive layer during storage and protects the finished device against contamination. The material used for release liner is Polyesters foils and other metalized laminates.
NOVEL APPROACHES FOR TRANSDERMAL DRUG DELIVERY SYSTEM.

Microemulsion gel

Microemulsion gel formulation for the transdermal delivery of the Repaglinide for the enhancement of drug penetration and antidiabetic effect. The microemulsion system was prepared by mixing surfactant, co-surfactant, oil (8%), and water. In the micro emulsion, xanthan gum was added to prepare micro emulsion gel while repaglinide was loaded into it under ultra sonication. The rationale behind their study was based on the drug dissolution properties, it avoids the first-pass metabolism, controlled and sustained drug release properties of microemulsion using the transdermal route. This transdermal system demonstrated better glucose reducing property or hypoglycemic effect than other oral formulation. Malakar et al developed a transferosomal gel containing insulin for diabetic treatment. The gel was prepared by reverse-phase evaporation method for the treatment of diabetes mellitus which reduced the blood glucose level.

Transferosomal gel

Transferosomes is a novel, elastic or ultra deformable vesicular drug carrier system composed of phospholipid, surfactant, and water for enhanced transdermal delivery. Presented transferosomal gel system which contains chemical enhancer such as "iodophor" to investigate its use in the permeation of the antidiabetic agent such as insulin into the skin. The transferosomes are prepared by using sodium cholate as a surfactant, soya lecithin as a phospholipid, and insulin as a drug by a conventional rotary evaporation sonication method. This study showed that 78% of insulin was successfully entrapped in the formulation with 2.5 I.U. of the drug and 25% of sodium cholate. The transpersonal gel system with a chemical enhancer iodophor has good potential to disrupt the epidermal layer of the skin to deliver insulin into the skin, thus achieving a higher bioavailability of the drug. Transferosomes are effective as phospholipids vesicles for transdermal drug delivery. Because transferosomes are self-optimized and ultra-flexible membrane properties, they can deliver the drug reproducibly either into or through the skin

Nanoparticle Nanosized colloidal particles such as micelles, solid lipid nanoparticles, niosomes, ethosomes, polymeric and inorganic nano particles have been developed as carriers to enhance the per cutaneous absorption of therapeutic agents. Encapsulation of therapeutic agent into colloidal carrier not only enhances the permeability but also protect the drug from degraded.

Ethosomes = Ethosomes mainly contain phospholipids, alcohol, and water. Compared to the liposomes, ethosomes are characterized by their high concentration of alcohol. Ethosomes are used for transdermal delivery of repaglinide (RPG) in the treatment of type II diabetes mellitus in rats.

Solid lipid nanoparticle=Solid lipid nanoparticle is by nature a special form of nano-emulsions wherein the matrix material is a solid lipid (e.g. highly purified triglycerides, wax, etc.) instead of liquid lipid, i.e. oil. The reports showed decreased blood glucose levels by using transdermal patches loaded with M-SLN when compared with oral administration of Metformin (2mg) in both normal and diabetic rats.

Sweat based electrochemical patch = Lee et al designed and fabricated a disposable wearable multilayer patch that can monitor blood glucose level with a built-in sensor that works on non-invasive sweat based mechanism and also provide the feedback to a transdermal antidiabetic through Micro needles. This wearable patch-based device is claimed to achieve controlled drug release according to patients' sweat glucose levels. The device utilized a silicon patch to collect the sweat from the wearer. This multipoint enzyme-based glucose, temperature, and pH sensors were used in measuring the correlated blood glucose level according to the sweat collected, allowing for more accurate and sensitive glucose measurement.

APPROACHES FOR ENHANCED TRANSDERMAL DRUG DELIVERY SYSTEM

Fig .no 3 Trandermal Drug Delivery Approches
Iontophoresis:
Iontophoresis method involves the application of electromotive force to drive or repel oppositely charged ions through the dermal layers of the skin into the area of the skin to be treated, either into the surrounding tissues for localized treatment or into the circulatory system for systemic treatment. Positively charged ions are driven into skin at the anode side while negatively charged ions are driven into skin at the cathode side. Dependent upon the net charge of the insulin particle, the associated electrical potential has been seemed to fabricate the pace of insulin move across over the skin. Studies have shown increased skin permeation of drugs at anodic /cathodic side of electrodes regardless of predominant molecular ionic charge. Improved drug permeation as a result of iontophoresis technology can be attributed to either one or a combination of the different mechanisms such as electroperturbation (for both charged and uncharged), Electro-repulsion (for charged solutes), electro-osmosis (for uncharged solutes) developed a patch containing insulin formulated in a gel for the iontophoretically driven transdermal delivery of insulin. 232Pillai and Panchagnula investigated transdermal delivery of insulin from poloxamer gel. In this study, gels were considered the most appropriate delivery vehicle for iontophoresis, and insulin was used for diabetic treatment. An insulin gel formulation was prepared using poloxamer 407. Ex vivo and in vivo skin permeation studies were performed with chemical enhancer and/or iontophoresis using rat as the modelanimal.

The poloxamer gel showed physical as well as chemical stability during the storage period. Results of this ex-vivo studies show, using linoleic acid and menthone in combination with iontophoresis showed a synergistic insulin permeation enhancement.

Electroporation:
Electroporation is another attractive technique for the electrically assisted transdermal delivery system). Inelectroporation, a short electric pulse (milliseconds or microseconds) is applied to the skin for the transitory structural perturbation of the lipid bilayer membranes. It is usually known that 0.5 to 1.0 volt of transmembrane potential difference should be required for electroporation. It has been shown that electroporation can also induce the alteration of the stratum corneum lipid domain. The increase in skin permeability is caused by the generation of transientpores during electro-poration. The technology has been successfully used to enhance the skin permeability of molecule s with different size and lipophilicity (i.e. small molecules, Proteins, Peptides, oligonucleotides).(Sudam KR, Suresh RB, 2016)

Sonophoresis:
Ultrasound, especially in the frequencies between 20 to 100 KHz, has shown to significantly increase the permeability of skin which facilitates transdermal drug delivery of the insulin. Ultrasound produces cavitation leads to the formation of localized regions of high permeability. Short application of the ultrasound causes the permeation of the skin before the application of drugs or drug and ultrasound could be applied simultaneously to the skin. Some parameters including frequency, intensity, and application time, can be adjusted to achieve a safe reversible breach in the skin. The R device uses low- frequency ultrasound (55 kHz) for an average duration of 15 s to enhance the skin permeability of the skin. This battery-operated handheld device consists of a control unit, ultrasonic horn with a control panel, a disposable coupling medium cartridge, and a return electrode. The use of other small, lightweight novel ultrasound transducers to enhance the in vitro skin transport of insulin has also been reported by a range of workers.

Laser radiation:
In the laser radiation technique, exposure of the laser to the skin occurred by directly and controlled manner that results in the ablation of stratum corneum without significantly damaging the underlying epidermis. PantecBiosolutions developed Laser skin microporation system. The P.L.E.A.S.E (Painless Laser Epidermal System) device uses a laser that emits light at 294 nm. It was found that laser treatment causes the formation of the cylindrical pore with the diameters ranging from150-200m.
Jet injector:

Jet injector is a velocity-based device, either powder or liquid jet injections, employ a high velocity jet with velocities ranging from 100 to 200 m/s to puncture or penetrate the skin and deliver drugs using a power source (compressed gas or spring). A jet injector is a needle-free device which is capable of delivering electronically controlled doses of medication or insulin which result in improved consistency of delivery and reduced pain for the patient. Instead of solid syringes, the jet injector applies at a high-speed narrow stream containing the insulin to create a tiny hole for insulin transport through the skin. Insulin administration by the jet injector leads to faster onset of action of plasma insulin. It contains compressed air or gas, either by a pressure hose from a large cylinder or a built-in gas cartridge or small cylinder. Although liquid jet injection technology is a needle-free route, the large volume high pressure spray leads to some adverse reactions such as bruising, bleeding, and pain. To minimize the adverse reaction caused by jet injector, Mitragotri and coworkers designed a microjet injection device that only injects solution volumes within the nanolitre range.

Microneedle:

MN devices consisting of the needles of the micron size, which are arranged on a small patch. The micro-scaled needles can disrupt the stratum corneum layer and reach the dermal and epidermal layer of the skin for drug release. The microneedle temporarily created the micro channel for the drug transport but quickly recover after removal of the microneedle to prevent the damage to the skin tissue. Novel and minimally invasive approach, MN is capable of creating superficial pathways across the skin for the transport of small drugs, macro molecules, nanoparticles to achieve enhanced transdermal drug delivery. The sharp tips of micro needle are short enough to limit contact with skin nerves, thus preventing pain sensation and they are narrow enough to induce minimal trauma and reduce the opportunities for infections to develop the following insertion. This method combines the efficacy of conventional injection needles with the convenience of transdermal delivery system formulation such as the patch. Based on the mechanism of action and the type of material used for the microneedle, the MN device is classified into different types. Generally, solid microneedle is designed to pierce the skin to improve the drug transport, hollow microneedles are designed for injection of fluid drug formulation.

Solid microneedle:

Solid microneedles are mostly used for pre-treating the skin by forming the pores. The transdermal delivery by solid MN is also termed as the “poke with patch approach.” Solid Microneedles contains the pointed tips of the needle that penetrate the skin, creates the micron size channel, through which the drug directly enter into the skin layers on the application of the patch, thus increasing penetration. Prausnitz and co-workers demonstrated MN for the hypoglycemic action of insulin in diabetic rats. An array of 105 microneedles was prepared by laser cut from stainless steel sheet, which is then inserted into the diabetic rats after this insulin solution was administered in contact of the skin for 4 hr. This solid metal Microneedles shows increased transdermal delivery of the insulin and decreases BGLs in vivo as much as 80%.
Hollow Microneedle:

Hollow Microneedles have a space inside the microneedle in which the drug solution or dispersion to be filled. Hollow microneedle can be designed to infuse milliliter quantities of fluid into the skin for transdermal delivery. To facilitate the delivery of the drug into the skin by the convection, hollow Microneedles are used to inject insulin or other solution. (Mc Allister DV, Wang PM 2003) Prausnitz and co-workers injected insulin into the diabetic rat's skin through hollow glass microneedle by micro infusion, a 30 min micro infusion of insulin at 10 or 14 psi cause a steady decrease in blood glucose level over a 5 hr period. (Gupta J, Felner EI, 2009)

Dissolving Microneedle:

Dissolving microneedles are formulated with biodegradable polymers by encapsulating the drug into the matrix, and upon insertion into the skin, can fully dissolve and release the drug. The polymer present in the microneedle gets dissolved inside the skin and control the drug release. Chen and coworkers developed a dissolving microneedle patch that contains the starch and gelatin for transdermal insulin delivery. (Ita K, 2015, Ling MH 2013) Some researchers designed fully insertable Microneedles with the supporting structure which provides extended length for counteracting skin compressive deformation during administration. Insulin was first loaded on tips 600 pm tips of high Microneedles which are made up of poly--glutamic-acid, while the next layer of PVA/PVP was filled in Microneedles molds to form the 600 pm high Supporting structure. When these Microneedles are inserted into the skin, both the microneedle and supporting layer dissolved within a 4 min to fully release the drug load.32 Kim et al. developed an alternative technique by applying droplet born air blowing to directly shape the polymer droplets to solidified the Microneedles. A decrease in glucose level in diabetic mice and increasing the bioavailability confirmed the efficacy of insulin delivery. (Dong Y, Ng WK, 2012)

Double layered bullet-shaped microneedle with swellable tips patch:

It developed bullet-shaped, double-layered microneedle with swellable tips that are capable of loading the insulin for interlocking mediated adhesion to the skin tissue which prolonged insulin delivery. The interlocking adhesion was achieved by increasing the volume of swellable tips. Ex vivo tests are carried out, which showed that insulin loaded microneedle was equally distributed throughout the swellable layer. Hence, it is suggested that the double layered bullet-shaped microneedle patches are a potential candidate for the delivery of insulin in diabetes treatment. (Ng LC, Gupta M, 2019, Seong KY, 2017)

Hydrogel-forming microneedle arrays:

It described a new category of MN array which are prepared from hydrogel forming matrices, consisting of cross-linked drug-free polymers. The mechanism of hydrogel-forming MN is by forming the hydrogel from the reservoir type of patch to the capillary circulation under the skin tissue because the skin interstitial fluid can be rapidly taken up by inserted needle tips after application of the MN arrays into the skin. (Donnelly RF, 2012)

Evaluation of transdermal patch

a. In-vitro study
b. In vitro drug release studies
c. Ex-vivo permeation study
d. Stability study
CONCLUSION
The topical administration of therapeutic agents offers many advantages over conventional oral and invasive methods. Here, different technologies for improving the transdermal delivery of insulin for the treatment of diabetes mellitus have been reviewed. Unlike traditional needle injections, transdermal delivery demonstrates a non-invasive and patient friendly method. Transdermal drug delivery systems represent a beneficial innovation for drug delivery, particularly in patients who cannot swallow or remember to take their medications.

REFERENCES