



A “REVIEW ON MICRONEEDLE AS TRANSDERMAL PATCHES”

Punam S. Kharole*, Reema jagnit

Bachelor of pharmacy
Gondia college of pharmacy, Gondia, Maharashtra

Abstract: Microneedles have shown to be safe and easy-to-use for drug administration, a nouvelle alternative to hypodermic needle injections, and an array in which drugs can be included to attain a controlled release as to achieve a higher drug delivery. Several works have demonstrated that such devices dramatically increase transdermal delivery of large molecules, thus nowadays microneedles have been regarded as a potential technology approach to be employed alone or with other enhancing methods such as electroporation and iontophoresis, as well as with different drug carriers. Hence, this review is mainly focused on presenting the results obtained when combining microneedles with a variety of strategies to ease drug diffusion through skin, including physical enhancers and drug carrier systems.

Keywords: *Tansdermal drug delivery system, trandermal patches, skin, mechanism of absorption, microneedle transdermal patches.*

INTRODUCTION

Transdermal drug delivery system (TDDS):

Definition: TDDS delivers the drug beyond human skin effectively. Transdermal drug delivery is controlled rate method which delivers drug to the systemic circulation. The drug molecule penetrates the different layers of skin and give therapeutic effect. Transdermal drug delivery is limited by outer layer of skin i.e., stratum corneum. Transdermal drug delivery has number of applications it includes pain management, smoking cessation, hormone replacement therapy.

TRANSDERMAL PATCHES

Definition: Transdermal patch is the adhesive medicated patch which delivers a specific dose of medication into the bloodstream through the skin by placing it over the skin. Transdermal patches provide a controlled released drug delivery system. Small drug molecules enough to penetrate the skin can only delivered through this method. To overcome restriction of the transdermal patches to the skin microneedle transdermal patch developed.

MICRONEEDLE TRANSDERMAL PATCHES

Definition:

Microneedle transdermal patches are the micro sized needle micro-patch that consist drug required for specific effect which penetrates the stratum corneum barrier layer of skin and delivered the drug into the systemic circulation for their therapeutic effect of drug.

To overcome drawbacks & significant limitation Transdermal drug delivery system adopted as safe and easily accessible, more efficient & patient friendly.

SKIN

Skin is the largest body organ of humans. It consists 4 layers that are SC and outer layer of non-viable epidermis which forms the main barrier for transdermal patches. The optimal pH range of skin is between 4.7 to 5.75. Skin is composed by flattened keratin-rich cells the corneocytes. These dense cells surrounded by complex mixture of intracellular lipids.

The main function of the skin is protecting the skin from environment, regulates the body temperature & sensing. Skin is potential site for systemic delivery of drug. TDDS used to avoid possibility & problems of stomach emptying, pH effects, first-pass metabolism and enable to input control. The main aim is to delivered drug to the targeted site on the skin by transdermal drug delivery system and advantages of transdermal route are limited metabolic activity & for some drug required continuous delivery.

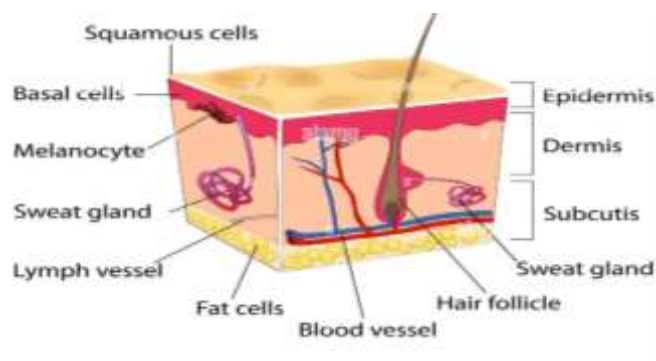


fig: 1 anatomy of skin

MECHANISM OF DRUG ABSORPTION THROUGH SKIN

The drug can absorb through different pathways which is depending upon the physiochemical property of skin.

TANSFOLLICULAR ROUTE: (TRANSAPPDAGEAL PATHWAY)

It is the shorter pathway that drug diffused via sweat glands, oil glands, hair follicles and pores of outer surface. (opening via ducts) Trans follicular route provides larger area for diffusion of drugs.

TRANSCELLULAR ROUTE: (TRANSEPIDERMAL PATHWAY)

It is a hydrophilic pathway in which the drug delivery through the corneocytes having highly hydrated keratin. Transcellular route passes the drug through cytoplasm of cell. The drug passes by corneocytes of stratum corneum. A number of partition and diffusion steps required to pass drug through cell of cytoplasm (matrix) due to aqueous pathway to the hydrophilic drug.

INTRACELLULAR ROUTE:

In intracellular route diffusion of drug through the continuous lipid matrix present in the cell. It is suitable for lipophilic drugs that water travel 50 times more by this pathway. The barrier of this route formed by corneocytes the drug pass through alternating lipid and diffuse to the inner side by partitioned into lipid bilayer.

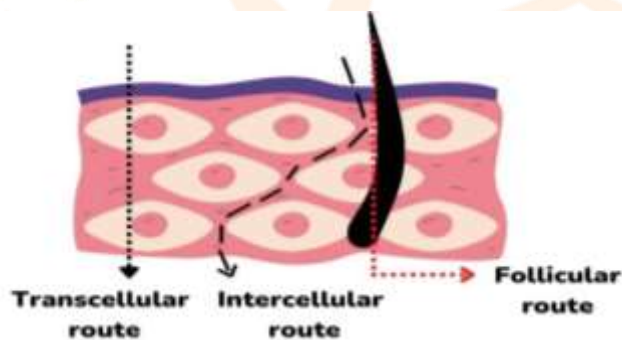


Fig: 2 (a) mechanism of drug absorption through the skin
(b) routes of drug permeation through the skin.

MICRONEEDLE (MNs) TRANSDERMAL PATCHES

MNs are advanced drug delivery systems that of a micro patch consisting with very tiny microneedles which designed to painless penetration to the outer layer of the skin (i.e. stratum corneum). Quick response observed due to disruption of stratum corneum by microneedle patches. Although microneedles were first proposed in 1976.

Microneedle patches are combine & convenience with the efficiency of an injection. Microneedles have 3dimensional microstructure with length <1000. It can pierce the barrier layer of skin stratum corneum and generate transient microchannel which drug molecule can diffuse into the skin. That are typically used for painless, minimally invasive, and self-administered treatments.

The Microneedle Transdermal Patches categorized are as follows:

- 1) Solid microneedles
- 2) Drug-coated microneedle (polymer microneedle)
- 3) Dissolving microneedle
- 4) Hollow microneedle

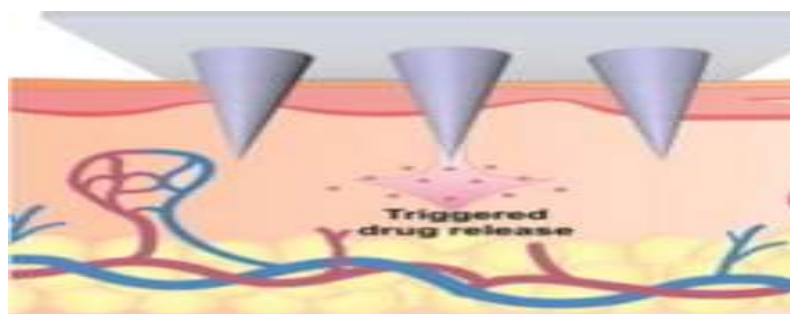


fig: 3 microneedle transdermal patches

TYPES OF MICRONEEDLES

1) SOLID MICRONEEDLE

Solid microneedles fabricated from polymer, silicon & metal by using micro-molding technique. It is patterned into a sharp geometry which pierce to the skin layer (stratum corneum) that creates microchannel drug usually loaded (microneedle array). The solid microneedle penetrates the skin & drug uptakes in systemic circulation for their therapeutic effect of drug.

2) COATED/POLYMER MICRONEEDLE

Coated microneedle prepared with drug-containing dispersion polymer by using polymerization method. For smart coated microneedle preparation electrodynamic atomization principle reported. Polymer microneedle had 3D structures the fabrication inclined by UV exposure, deep x-ray exposure. These microneedles fabricated by LIGA techniques (lithography, electroplating & molding). It is used for better drug targeting.

3) DISSOLVING MICRONEEDLE

Dissolving microneedle designed by water soluble material i.e. sugar, chondroitin CMC (carboxymethylcellulose) It is fabricated by micro-molds by using polymer filled in specified structure after solidification mold microneedle inserted in mold cavities with drug content. It is the multilayered microneedles adding air bubble in by particle base molding method. It is designed to deliver adequate amount of drug for required therapeutic effect.

4) HYDROGEL MICRONEEDLES

The hydrogel-forming microneedles is "super swelling" polymeric composition. It is rate controlling membrane by hydrophilic materials that swell by inserted into the skin which coated with polymeric material.

5) HOLLOW MICRONEEDLE

Hollow microneedles are same as conventional dosage form of hypodermic needle but the hollow patch smaller in size & pressure applied to modulates the drug flow rate which inserted into the hollow cavity. It is designed to deliver liquid formulation in quick delivery. These are expensive to fabricate the micro patch LIGA technique used to form hollow microneedle.

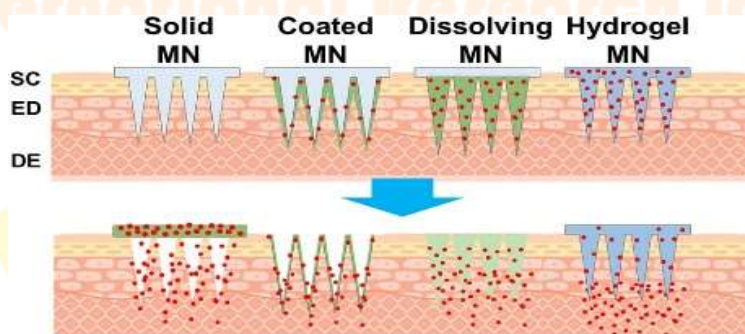


Fig: 4 types of microneedle patches

Examples of microneedle transdermal patches:

sr no.	product name	indications
1)	smart patch	insulin delivery for diabetes.
2)	micron pen	vaccine delivery (e.g., flu vaccine)
3)	microneedle patch	hormone replacement therapy (e.g., estradiol for menopause)
4)	derma roller	skin rejuvenation and anti-aging treatments.
5)	hydrogel-microneedle patch	localized pain management (e.g., for arthritis or back pain)
6)	vaccine micro patch	delivery of vaccine antigens (e.g., covid-19 vaccines)

ADVANTAGES:

Microneedle patches may reduce the risk of pain during insertion and tissue trauma (injury) and infection.

- 1) No Frequent dosage required for the delivery of drug in microneedle patches.
- 2) Improved patient compliance by avoidance of first pass hepatic metabolism
- 3) Enhances bioavailability of drug as well as high concentration of drug delivered.
- 4) Various types of fabricated needles can be use depending upon the need and duration of action i.e. solid and hollow
- 5) MNs reduces the adverse effect regards with the overdose of drug (withdrawal of drug can possible by removing the patches) reduces the chances of toxicity is convenient route and simple dosing of drug.
- 6) Small microneedles provide highly targeted drug administration.
- 7) Suitable for drug with very short half life
- 8) Like other transdermal drug delivery system that avoid degradation of drug, gastrointestinal irritation, enzymatic deactivation and liver metabolism.
- 9) Longer duration of action
- 10) Bolus and Control released of drug substance.

DISADVANTAGES:

- 1) Microneedles patch difficult to apply on the skin.
- 2) Microneedle patches cause skin irritation due to allergy and sensitive skin.
- 3) The microneedles are small and thinner than diameter of hair, it left under the skin if the tip is broken.
- 4) If the amount of drug higher under the skin it may cause local inflammation.
- 5) If the drug having hydrophilic structure, it does not achieve therapeutic level due to lower permeation to the skin.

CONDITIONS IN WHICH THE MICRONEEDLE TRANSDERMAL PATCHES ARE USED:

Microneedles are used in variety of conditions primarily focusing on various diseases and therapies. Microneedle patches offer the painless traditional hypodermic injection.

- **CHRONIC PAIN:** Microneedle patches deliver the drug directly to the skin which offers painless and effective delivery.
- **DIABETES:** microneedle patches used to deliver insulin and potentially for glucose monitoring.
- **HORMONE REPLACEMENT THERAPY:** Microneedle patches used to deliver the hormones i.e. estrogen
- **CANCER TREATMENT:** Microneedle patches deliver the anticancer drugs, vaccines and gene therapy in cancer treatment
- **COSMETIC TREATMENTS:** This used in cosmetic purpose improving skin texture and anti-aging.
- **VACCISNE DELIVERY:**

i.e. hepatitis B

CONDITIONS IN WHICH MICRONEEDLE PATCHES ARE NOT USED:

- **SKIN CONDITION**
(Inflammatory skin lesion, active acne and open wounds.)
- **WART TREATMENT**
- **JOINTS** (knee, elbows, hands) Due to movement and friction it may cause irritation.

EVALUATION PARAMETERS OF MICRONEEDLE PATCHES**1. MECHANICAL PROPERTIES****INSERTION FORCE & SKIN PENETRATION**

Microneedle patches exert sufficient force to penetrate the barrier layer of skin. (stratum corneum) without causing any of the fracture and excess of bending. The insertion force influenced by the geometry of microneedle, properties of material, and skin characteristics.

COMPRESSION & BENDING STRENGTH:

The mechanical strength of microneedle under compression and bending should ensures that the patch can withstand application forces without deformation.

2. DRUG RELEASE AND PERMEATION**RELEASE KINETICS:**

The rate and extent of drug release of Microneedle patches are influenced by factors needle material, coating, and drug formulation.

PERMEATION ENHANCEMENT:

MN patches enhance permeability of skin by creating microchannels which facilitating the delivery of larger or hydrophilic drug molecules.

BIORELEVANT TESTING:

In vitro models that show the same effect of human skin conditions (e.g., using gelatin sheets) it helps to predict the in vivo performance of microneedle patches.

3. BIOCOMPATIBILITY AND SAFETY**CYTOTOXIC EFFECT:**

Evaluate the cytotoxic effects of microneedle materials that ensures they are safe in use of clinical setting.

SKIN IRRITATION:

Clinical studies determinate the potential of MN patches scases the skin irritation or allergic reactions, it ensuring their safety for repeatedly use.

HISTOLOGICAL ANALYSIS:

Post-application of MNs tissue examination helps to identify any adverse effects on skin integrity and healing.

4. STRUCTURAL AND MORPHOLOGICAL CHARACTERISTICS**NEEDLE GEOMETRY:**

The shape (e.g., conical, pyramid, cylindrical) and dimensions (height, base width) of MNs affect their insertion efficiency and drug delivery capacity.

SURFACE MORPHOLOGY:

Microscopic examination (e.g., SEM) of MN arrays provides insights into their uniformity, sharpness, and potential defects.

COATING INTEGRITY:

For coated MNs, assessing the uniformity and adherence of the coating ensures consistent drug delivery.

5. SKIN INTERACTION AND HEALING**TRANSEPIDERMAL WATER LOSS (TEWL):**

Monitoring TEWL before and after Microneedle patch application which helps to assess the extent of skin barrier disruption and recovery time.

SKIN RESEALING TIME:

Evaluates that how quickly the skin heals by post-application is crucial for determining the safety and comfort of Microneedle patches.

MATERIAL OF MICRONEEDLE PATCHES**DISSOLVING POLYMER**

A dissolving polymer used in microneedle patches which fabricates & designed to painless and safely insertion into the skin to penetrates the barriers and exerts their therapeutic outcomes.

It gives gentle insertion & dissolution of MNP, Antigen stability, Humoral immune response, protection against viral changes.

POLYVINYLPIRROLIDONE (PVP)

MNP designed to presented as a proof of concepts, vivo experiments were not performed.

POLYVINYL ALCOHOL (PVA)

These MNP reduces the blood glucose level (hypoglycemic)

POLY LACTIC CO-GLYCOLIC ACID (PLGA)

WAT browning, reduces inflammation, better glucose homeostasis, increase of energy expenditure, decreases body weight.

METALS

The metallic MNP are commonly used due to their biocompatibility and the mechanical strength. These MNs have superior mechanical properties, including high strength, hardness, and toughness, which allow the better precise insertion capability. Due to these features, they can penetrate the skin without being fractured or buckled & even in the case of the higher porosity. Metallic materials are well suited for manufacturing MNP.

Eg Stainless steel, Titanium, Nickel and nickel-based alloys, Silicon and Ceramics Silicon, Glass and ceramic composites.

SUGARS AND SACCHARIDES

Maltose, trehalose, sucrose

HYDROGEL-FORMING MATERIALS

Methacrylate hyaluronic acid (MeHA)

polyethylene glycol diacrylate (PEGDA)

FUTURE ASPECTS**1. Personalized Medicine**

Microneedle patches deliver to patient-specific & suitable combinations of drugs based on genetic profiles or disease states of personal.

2. Vaccine Delivery

Microneedle patches are alternatives to traditional needles for vaccine delivery. Painless application of MN patches for self-administration makes them suitable for mass immunization & in pandemic scenarios.

3. Biomarker Monitoring and Diagnostic purpose.

In Microneedle systems may incorporate biosensors for real-time monitoring of biomarkers in intestinal fluid & other glucose, lactate, enabling diagnostic and therapeutic feedback loops.

4. Smart MN Patches

Integration with wearable electronics may allow MNs to provide on-demand drug release triggered by physiological signals pushing forward the field of closed-loop systems.

5. Expanded Drug and Biologic Delivery

Microneedle systems are developed to deliver biologics and small molecules that are hard to deliver orally or via conventional patches.

6. Global Health and Accessibility

Due to their ease of use, low cost, and reduced need for cold-chain storage, Microneedle patches could revolutionize healthcare in low-resource settings.

7. Regulatory and Commercial Expansion

As regulatory bodies develop guidelines specific to MN technologies, more products are expected to reach the market.

CONCLUSION

Microneedle patches are rapidly growing in its range of applications. Microneedles are 3D microstructures with microscale length of usually <1000 µm. The microneedle patches can penetrate the stratum corneum and generate transient microchannels through which external molecules can passively diffuse into the skin. Microneedle-based transdermal delivery approach will offer a self-management, patient-friendly, and efficient administration route for drug delivery. MNTP's can eliminate the limitations of conventional drug delivery systems. Microneedle patches are patient friendly, easily accessible, more efficient in use & self-administration can possible.

REFERENCE

1. Valsa Remony Manoj*, Hima Manoj, REVIEW ON TRANSDERMAL MICRONEEDLE-BASED DRUG DELIVERY **ASIAN JOURNAL OF PHARMACEUTICAL AND CLINICAL RESEARCH** 2018 Vol 12, issue1 2019 (19-29)
2. Shital H. Bariya, Mukesh C. Gohel, Tejal A. Mehta and Om Prakash Sharma MICRONEEDLES: an emerging transdermal drug delivery system **JOURNAL OF PHARMACY AND PHARMACOLOGY**, 64, PP. (11-29)
3. Tao Han, Dignata Bhusan Das POTENTIAL OF COMBINED ULTRASOUND AND MICRONEEDLE FOR ENHANCED TRANSDERMAL DRUG PERMEATION: A REVIEW **EUROPEAN JOURNAL OF PHARMACEUTICS AND BIOPHARMACEUTICS** (2015) (312-328)
4. Mei-Chin Chen, et.al CHITOSAN MICRONEEDLE PATCHES FOR SUSTAINED TRANSDERMAL DELIVERY OF MACROMOLECULES **AMERICAN CHEMICAL SOCIETY PUBLICATION** (2012) (4022-4031)
5. Rigved Nagarkar, Mahima Singh, Hiep X. Nguyen, Sriramakamal jonnalagadda A REVIEW OF RECENT ADVANCES IN MICRONEEDLE TECHNOLOGY FOR TRANSDERMAL DRUG DELIVERY **JOURNAL PRE-PROOF** (2020) (1-18)
6. Jaspreet Singh Kochhar, Wan Xuan Selina Lim, Shui Zou, Wei Yan Foo, Jing Pan and Lifeng Kang MICRONEEDLE INTEGRATED TRANSDERMAL PATCH FOR ONSET AND SUSTAINED DELIVERY OF LIDOCAINE **AMERICAN CHEMICAL SOCIETY** (2013) (4272-4280)
7. Joke A. Bouwsta*, P. Loan Honeywell-Nguyen, Gert S. Gooris, Maria Ponc STRUCTURE OF SKIN BARRIER AND ITS MODULATION BY VESICULAR FORMULATION **PROGRESS IN LIPID RESEARCH** 42 (2003) (1-36)
8. Vikas Chander Jhawar, Vipin Saini, Sunil Kamboj, Nancy Maggon TRANSDERMAL DRUG DELIVERY SYSTEM: APPROACHES AND ADVANCEMENT IN DRUG ABSORPTION THROUGH SKIN **INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES REVIEW AND RESEARCH** (2013) (47-56)
9. Zhisun Yuan, Hongzhao Zhang, Wentao Hu, Xiao Yu, Si qin, Chengyong Wang and Fenglin Zhang STATE-OF-THE-ART REVIEW OF METALLIC MICRONEEDLES: STRUCTURE, FABRICATION AND APPLICATION **CHINESE JOURNAL OF MECHANICAL ENGINEERING** (2025) (38-21)
10. Sean P. Sullivan, Dimitrios G. Koutsonanos, Maria del Pilar Martin, Jeong-woo lee, Vladimie Zaentsyn, Niren Murthy, Richard w. Cmpans, Loanna Skountzou and Mark R. prausnitz DISSOLVING POLYMER MICRONEEDLE PATCHES FOR INFLUENZA VACCINATION **HHS PUBLIC ACCESS** (2010) (915-920)
11. Zhang, Y, et.al., 3D PRINTING OF MICRONEEDLES FOR TRANSDERMAL DRUG DELIVERY: RECENT PROGRESS AND FUTURE PERSPECTIVES. **DRUG DELIVERY AND TRANSLATIONAL RESEARCH**, (2020) (527-538)
12. Kim, Y. C., Park, J. H., & Prausnitz, M. R. MICRONEEDLES FOR DRUG AND VACCINE DELIVERY. **ADVANCED DRUG DELIVERY REVIEWS**, (2012) (1547-1568)
13. Takeuchi, K., et al. MICRONEEDLES FOR BIOSENSING APPLICATIONS: A REVIEW. **BIOSENSORS AND BIOELECTRONICS**, (2022) 201, 113937.
14. Yu, J., et al., MICRONEEDLE-ARRAY PATCHES LOADED WITH HYPOXIA-SENSITIVE VESICLES PROVIDE FAST GLUCOSE-RESPONSIVE INSULIN DELIVERY. **PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES**, (2015) 112(27), 8260-8265.
15. Arya, J., et al. TOLERABILITY, USABILITY AND ACCEPTABILITY OF DISSOLVING MICRONEEDLE PATCH ADMINISTRATION IN HUMAN SUBJECTS. **BIOMATERIALS**, (2017) 128, 1-7
16. PRAUSNITZ MR, ET AL. "MICRONEEDLES FOR TRANSDERMAL DRUG DELIVERY." **ADV DRUG DELIV REV**. 2004;56(5):581-587.
17. HENRY S, ET AL. "MICROFABRICATED MICRONEEDLES: A NOVEL APPROACH TO TRANSDERMAL DRUG DELIVERY." **J PHARM SCI**. 1998;87(8):922-925.
18. PRAUSNITZ, M. R., & LANGER, R. (2008). TRANSDERMAL DRUG DELIVERY. **NATURE BIOTECHNOLOGY**, (2008). 26(11), 1261-1268.
19. DONNELLY, R. F., SINGH, T. R. R., & WOOLFSON, A. D. (2010). MICRONEEDLE-BASED DRUG DELIVERY SYSTEMS: MICROFABRICATION, DRUG DELIVERY, AND SAFETY. **DRUG DELIVERY**, 17(4), 187-207.