Journal for Research in Applied Sciences and Biotechnology

www.jrasb.com

ISSN: 2583-4053

Volume-1 Issue-3 || August 2022 || PP. 65-76

https://doi.org/10.55544/jrasb.1.3.9

A Review Article on Transdermal Drug Delivery System Based On-Microneedles

Kanchan Butola

Research Scholar, Department of Pharmaceutical Sciences, Hemwati Nandan Bahuguna Srinagar Garhwal Uttarakhand, INDIA.

Corresponding Author: kanutaro95@gmail.com

www.jrasb.com || Vol. 1 No. 3 (2022): August Issue

Received: 03-07-2022	**Revised:** 24-07-2022	**Accepted:** 03-08-2022

ABSTRACT

Every drug delivery system should work toward preserving the drug's appropriate dose and facilitating its full metabolism within the body. Transdermal delivery of very large ionic and hydrophilic molecules is made possible by the microneedle array. Studies on the effectiveness of microneedles have been conducted extensively. Soon, the market for commercial microneedle-based goods will grow, and they may eventually have a major impact on clinical medicine. This article provides an overview of microneedles, discussing their history, many varieties, current state, potential applications, and recent technological developments.

Keywords- Transdermal, Microneedle, Skin, Patch, Drug delivery.

I. INTRODUCTION

All qualities of the active drug component are important, but the mechanism by which the drug is administered to the body is just as crucial to the medicine's success. As a result, it is essential to look into the best drug delivery strategy taking into account the medicine's properties. Because the patient can take the drug themselves, oral administration is a simple and convenient way of drug delivery. [1]However, applying this strategy to biopharmaceuticals presents unique challenges. Subcutaneous injections have a rapid onset of action and good absorption. However, patient compliance is limited and skilled administration is necessary. That's why it's important for drugs to be easily administered, like by mouth, and to have a high bioavailability, like injection. [2,3]Bypassing the first-pass effect and allowing for continuous release of the medicine are both benefits of transdermal administration. Drug distribution is complicated by the stratum corneum's protective layer. [4,5,6]Transdermal drug delivery using microneedles has the advantages of being simple for self-administration and providing good drug bioavailability. The medicine is able to enter the body straight through the stratum corneum, the skin's outermost layer, and the process is both painless and minimally intrusive. [7]Microneedle design and drug composition allow for precise regulation of dose, delivery rate, and therapeutic effect (Table 1). Micro needles for the delivery of medications and cosmetics have been the subject of numerous studies to date, with each method and substance of production yielding slightly different results. Animal studies and human clinical trials have shown microneedles' effectiveness and safety. [8,9]Here, we take a look back at the various microneedle varieties and materials that went into their creation.

ISSN: 2583-4053

Volume-1 Issue-3 || August 2022 || PP. 65-76

https://doi.org/10.55544/jrasb.1.3.9

Table 1: Advanced Transdermal Drug Delivery Techniques and Available Drugs

Techniques	Manufacturing Companies	Available drugs	Developed drug products
Microporation			
Macroflux®, Microstructured Transdermal System	Zosano Pharma, Inc., 3M	None	Vaccine, Therapeutic Protein, Hydrophilic molecules, Large Molecules
Needleless Injector			
PowderJect®, IntraJect	PowderJect Pharmacuticals, PLC, Weston Medical	None	Insulin, Vaccines, Various Liquid Injectable Medication
Medicated Tatoos			
Med-Tats	Lipper-Man Ltd.	None	Acetaminophen Vitamin C St. John's Wort Echinacea
Heat			
Controlled, Heat Aided Drug Delivery System	Zars, Inc.	None	S-Caine
Iontophoresis			
Phoresor Iontophoretic Drug Delivery System, E-Trans®	Iomed, Alza	Iontocaine, IONSYS™	Other Anaesthetics, Fentanyl
Reverse Iontophoresis			
GlucoWatch®	Cygnus Inc.	GlucoWatch G2 Biographer	None
Phonophoresis			
SonoPrep®	Echo Therapeutics, Inc.	None	Peptide, Other large molecules
Reverse Phonophoresis			
Symphony Diabetese Management System Microparticulate	Echo Therapeutics, Inc	None	Symphony Diabetese Management System
Microparticulate delivery			
SMP	Atrix labs	None	Dapsone, Nucleoside analogs, Anti fungle

Microneedle

Dermatologists have been touting the benefits of microneedling for a variety of skin conditions, including ageing skin, scars (acne, rhytides, surgical), discoloration (dyschromia, melasma), pore size (enlargement), and drug delivery (transdermal). [10]Microneedling may fill a need for patients who want measurable clinical benefits from treatments that require little to no recovery time, as minimally invasive procedures have been reported to expand significantly over the past several years. Microneedles, which range in size from 10 m to 50 m in diameter and 10 m to 2 m in height, are used to safely and painlessly access dermal tissues via the skin's epidermis. In 1971, Gerstel and Place were the first to employ a microneedle to provide medication, paving the path for future transdermal drug delivery systems to use microneedle technology. Microneedles constructed inside a patch can be used for transdermal drug administration. Microneedle patches have been studied for the administration of pharmaceuticals, biopharmaceuticals, and immunizations. A quick reaction is triggered when microneedles penetrate the stratum corneum.[11]

History of microneedles

Since the invention of hollow needles in 1844, hypodermic needles have been used to provide IV drugs to patients. An estimated 16 billion injections will be administered around the world this year, making it one of the most widely used medical devices. After giving birth, the first medical attention that most people will ever receive is an intramuscular vitamin K injection to ward against "haemorrhagic disease of the newborn" (HDN). [12]In addition, a bolus distribution can be used, allowing for accurate titration of medications with a narrow therapeutic index. However, intravenous (IV) administration can be performed even in needle-averse patients. Use of a hypodermic needle has been associated with pain and psychological discomfort. Given these limitations, considerable effort has been made to transform the hypodermic needle into a painless and

ISSN: 2583-4053

Volume-1 Issue-3 || August 2022 || PP. 65-76

https://doi.org/10.55544/jrasb.1.3.9

patient-friendly medication delivery device.[13] Initiatives like this led to the development of a microneedle that may be inserted intradermally or used transdermally. Microneedles, or "cross biomedical micro devices," are a hybrid of hypodermic needles and transdermal patches.[14,15] Mark Prausnitz, a pioneer in the field, has categorised Microneedles as a third-generation TDDS. When absorbed through the skin, these devices create micron-sized pores that can be used to deliver medications.[17] Microneedles are smaller than standard hypodermic needles and have sharper points. When placed under the skin, microneedles can increase the bioavailability of many medicines or high molecular weight compounds by penetrating the stratum corneum. In 1976, Gerstel and Martin of Alza Corporation submitted the first microneedle patent, proposing the use of micron-scale needles for painless transdermal medication delivery. [18-19]However, it wasn't until the 1990s that the microelectronics sector created a set of micro manufacturing tools that were employed in investigations into the usage of microneedles for drug delivery. Drug delivery research with microneedles was pioneered during this time period by three key players using micro manufacturing techniques: Becton Dickinson, Alza Corporation, and the Georgia Institute of Technology. developed a hollow microneedle array in 1995 and published the first work on microneedle arrays. [20]This array was used to inject bacterial plasmid into worms, allowing for their genetic transformation. Microneedle devices for intradermal vaccine delivery for seasonal flu protection have recently been approved by regulatory authorities. Despite progress, microneedle-based drug delivery systems have not had a significant impact in clinical trials due to the fact that most devices only include preclinical and clinical studies. Given the widespread availability of cosmetic microneedle products, it's not unreasonable to expect the introduction of therapeutic microneedle products for the treatment of acute and chronic illnesses in the near future.[21]

Requirements

The medicine is able to reach the dermal tissue beneath the skin because to the pores created by the microneedles. The microneedle has the potential to increase patient compliance because it causes less pain to the patient than traditional hypodermic needles. Improved patient satisfaction, longer-lasting delivery patterns, and dermatological treatment are all possible outcomes. Inadequate permeation across the stratum corneum is TDDS's biggest drawback. Microneedles are one solution to this problem. [22]Therefore, researchers have focused on creating new varieties of microneedles for a wide range of applications, such as injecting or extracting drugs from a tissue, or delivering macromolecules or immunobiologicals. Microneedles and other physical techniques have been developed to enhance transdermal medication delivery. Finally, numerous researchers have tried out novelists' approaches of controlling molecules using microneedles. Several patents have been submitted to halt the invention, which is indicative of the breadth of the microneedle's development as a delivery system for the troublesome macromolecules.[23-24]

II. MICRONEEDLES TYPES

There are four distinct structural types of microneedles, including solid microneedles, coated microneedles, dissolving microneedles, and hollow microneedles.[25-26]

Solid Microneedles

The use of solid microneedles as a skin preparation was first suggested in 1971. In a nutshell, the solid tiny needles are inserted into the skin, creating channels via which the medications can be injected. Solid microneedles have the advantage of being a risk-free method of medication administration. [25]Not contaminated with any harmful substances. When the micro needles are removed, the needles shut. These solid microneedles, which include stainless steel micro needle rollers, metal micro needles, silicon micro needles, and certain polymer microneedles, are produced using laser micromachining, lithography and etching, and micro moulding. Transdermal medication delivery systems may benefit from the use of the solid microneedle to improve their efficacy. [27]

Coated Microneedles

An actual needle is used to puncture the skin, and the medicine is subsequently released through the microneedle tips of the patch. DNA was delivered by microneedles coated in a vaccine with an adjuvant that might remain in the skin for days or weeks after being applied. Memory T-cell production and gene expression were both improved in the DNA vaccine group and immunological responses were elicited more effectively than in the intradermal DNA injection group. [28-29]The results also showed that the coated microneedle patch could lead to long-lasting, powerful antibody responses, suggesting that this method may be useful for delivering vaccinations.

Dissolving Microneedles

In 2005, Miyano et al. were the first to report on dissolving microneedles. There are a number of advantages to using dissolving microneedles, including their simplicity to create, their portability, and their potency as drug carriers. The PVA microneedles dissolved entirely within four minutes of being inserted under the skin. Improved vaccine stability was another benefit of the microneedle patch's increased immune response. When it comes to treating breast cancer, Chen et al. have created a technique that uses microneedles that dissolve after use. Effective, easily administered, and well-tolerated, transdermal medication delivery via microneedle patches is a promising area of research. [30]

Hollow Microneedles

Microneedles, which are hollow and can provide a highly precise dose, measured 1800

ISSN: 2583-4053

Volume-1 Issue-3 || August 2022 || PP. 65-76

https://doi.org/10.55544/jrasb.1.3.9

millimetres in length and 60 millimetres in diameter on the inside. Holes in hollow microneedles can provide quantities of fluids into the skin at various pressure-driven flow rates, allowing for direct drug delivery via the skin. Micro electromechanical system (MEMS) techniques like laser micromachining, integrated lithographic moulding process, microfabrication, and X-ray photolithography are typically used to create these microneedles from a metal or silicon substrate. Therefore, blood analysis systems may be a promising field for the use of hollow microneedles. The transdermal drug delivery system is highlighted by the qualities of hollow microneedles, which include suitable mechanical strength, the distribution of pharmaceuticals in a predetermined quantity at a predetermined flow rate, and the deposition of a substance into the epidermis.

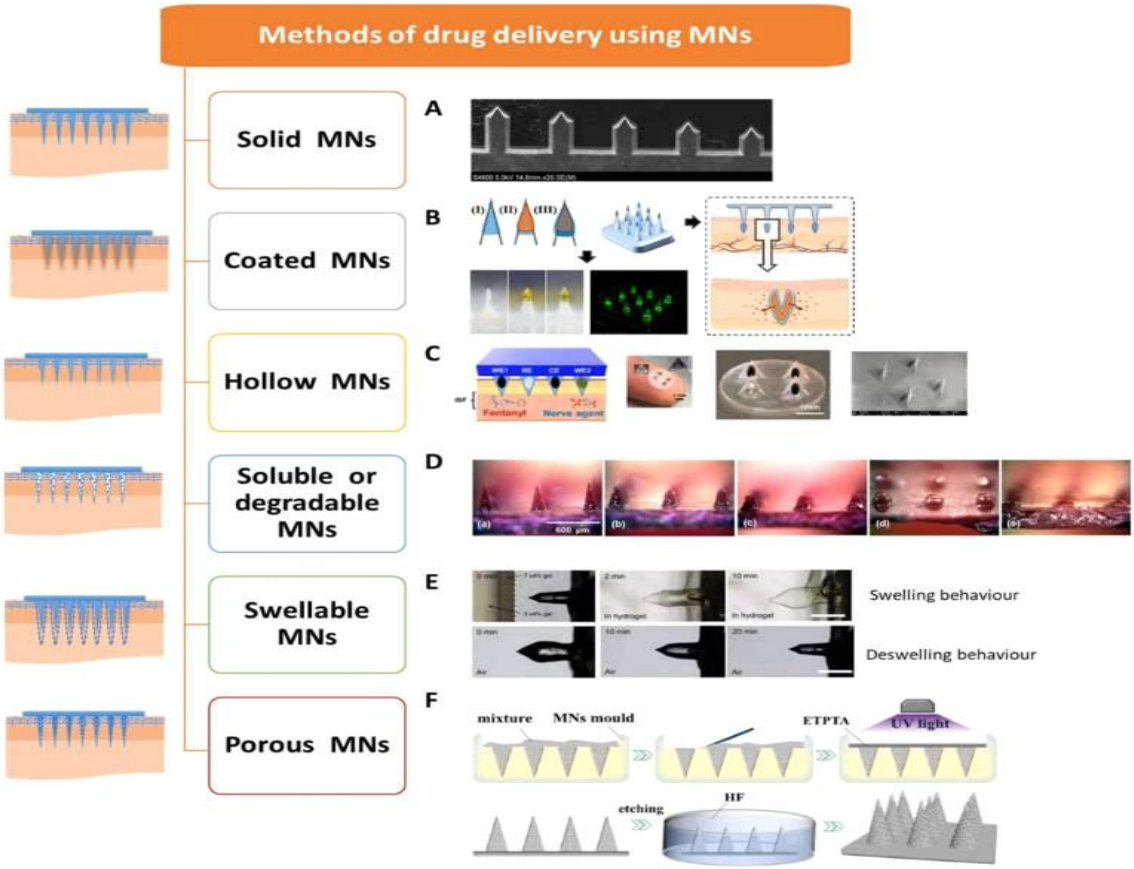

Figure 1: Shows the wide range of MN-based medication delivery strategies currently in use. (A) Sturdy MMs. Use with permission The MNs with the coating, group B. Adapted. Empty MNs (C). Used legally with permission. (D) Soluble or biodegradable MNs inserted into pig cadaver skin (a) before insertion, and (b) 10 seconds, 1 minute, 15 minutes, and 1 hour afterwards. Permission to alter was granted. Expanding MM. Used with the author's approval. Porous MNs (F). Modified with permission.

Table 2: Selected microneedle fabrication techniques

Materials used	Key processing considerations	Improvements over conventional	Reference
Micromilling			
Ceramics, PLGA, PMMA, metals	Micromolding based-multiple cutting tools; prevents geometries as overhanging structures.	Rapid prototyping supports optimization; can use different materials	
Atomized spraying to fill molds			
Affinose, fructose, Trehalose PVA, HPMC PVP, CMC (with glycerol), sodium alginate	Viscosity with 1 and 22 mPa·s and solution of 5% w/v is used; MNs amorphous state is formed; material	No heat required; viscosity-independent; horizontal or layered or laminated MNs	

ISSN: 2583-4053
Volume-1 Issue-3 || August 2022 || PP. 65-76
https://doi.org/10.55544/jrasb.1.3.9

	influenced skin penetration	can be prepared.	
Inkjet printing to fill molds			
PVA, Trehalose, polysorbate 80; trehalose MNs with or without PVA and influenza vaccine	High shear within the nozzle; 1–70 pL droplets; surface tension, and nozzle back pressure affect formation of droplet.	Targeted dispensing reduces material loss; without wetting agents; bilayered MNs can be fabricated	
Droplet-born air blowing			
Insulin-loaded CMC ,HA ,Dye in CMC, or PVP;	Determining of dose is done by concentration and droplet volume; minimal design flexibility	No heat or UV irradiation; free from micromold; ≤ 10 min/patch	
Electro-drawing			
Rhodamine 6G ,PLGA in dimethyl carbonate and Nile red, or rhodamine-labeled human serum albumin MNs on flexible substrate or holder; minimal design flexibility	MNs on flexible substrate or holder; minimal design flexibility	Free from nozzle and micromold; low heat about 20–40 °C; contact free.	
Drawing lithography			
Vitamin C or B3 with maltose,SU-8	Requirement of heat; glass transition determines manufacturing properties; minimal design flexibility processing	Ultrahigh aspect ratio MNs can be prepared which are mold-free.	
3D printing			
A proprietary resin, 3DMCastable	UV irradiation; 50 μm XY resolution; MN width deviated from design; topical application of drug	Solid MN for a patient's finger is produced with rapid prototype.	
Continuous liquid interface production			
TMPTA, PAA, and photopolymerizable derivatives of PEG and PCL; PAA, PCL, and PEG with rhodamine B	UV irradiation; use Bworking curve^ to translate designs to different resins	Oxygen-permeable window eliminates repositioning steps, improves accuracy; ≤ 10 min/patch	
Inkjet printing to coat MN			
Quantum dots coated on PMVE/MA MN; PGA MN coated with PMVE/MA release layer, then itraconazole; SS MN coated with 5-FU, curcumin, or cisplatin in Soluplus; SS MN coated with insulin in gelatin, trehalose, Soluplus, or POX	Formation of drop size (300 pL), duration and frequency of pulse, applied voltage. Contains aqueous colloids, solutions, and some organic solvents.	Uniform, accurate, precise dispensing without agents material loss which is non-contact dispensing; preparation is free of wetting agents.	
Poly-electrolyte multilayers to coat MNs			
Plasmid DNA/poly-1 coated SS	Layer by layer assembly of ultrathin, uniform coatings;	Design films that rapidly deposit	

ISSN: 2583-4053

Volume-1 Issue-3 || August 2022 || PP. 65-76

https://doi.org/10.55544/jrasb.1.3.9

MN; ICMVs/poly-1 with fluorescent ovalbumin coated PLGA MN; PLLA MN coated with release layer, then multilayers including plasmid DNA/poly-1	high weight fractions of therapeutics; tailor release profile with polymer or film structure, i.e., rapid, sustained, or multi-therapeutic release	into skin for sustained release of therapeutics; lipid nanocapsules showed improved protein subunit vaccination	

III. APPLICATION OF MICRONEEDLES[31-35]

The microneedle delivery method has seen widespread usage in cancer therapy, diabetes detection and treatment, and anti-inflammatory and analgesic treatment, among other areas, and has seen rapid development in recent years.

Cancer Therapy

The microneedle delivery method has seen widespread usage in cancer therapy, diabetes detection and treatment, and anti-inflammatory and analgesic treatment, 159-162, among other areas, and has seen rapid development in recent years.

Diagnosis

With the microneedle patch, you can quickly and painlessly remove excess fluid from the skin's interstitium. In order to research the skin interstitial fluid, a microneedle made of MeHA or cross linked by UV exposure was put into the skin, the fluid was retrieved, and then the fluid was separated from the microneedle patch using centrifugation. This research lays out a systematic plan for the future development of diagnostic microneedles. Anti-inflammatory and analgesic medication a treatment for diabetes.

Treatment for diabetes

Insulin delivery in a convenient and aesthetically pleasing carrier: enter the microneedle drug delivery device. For their study, Ling et al. implanted insulin-delivering polymer microneedle patches into diabetic rats. After being inserted beneath the skin for five minutes, the starch and gelatin dissolving microneedle could dissolve entirely and release the insulin. Microneedle patches injected with insulin were stable for at least a month and effectively produced a considerable hypoglycemic impact in diabetic rats. For type 2 diabetic GK/Slc rats, Liu et al. developed a microneedle array with hyaluronic acid-loaded tips to facilitate transdermal delivery of exendin-4. It was concluded that tip-loaded microneedle arrays improved exendin-4 transdermal administration without skin injury and were better to subcutaneous injection in terms of hypoglycemic action.

Anti- inflammatory and analgesic

About 1.5 billion individuals throughout the world experience pain every year. Because of this, evidence supports the use of topical and transdermal medicines for the treatment of both acute and chronic pain. One of the most exciting developments in pain treatment is the use of microneedle patches. [32]Delivered locally, the anti-CGRP peptide developed by Xie et al. can cause selective antihypersensitivity via peripheral antagonism. Calcitonin gene-related peptide receptors (are a type of receptor found in the brain). By use of a microneedle-based treatment for neuropathy. Recently, Chen et al. designed a phototriggerable microneedle system to administer lidocaine via external near-infrared (NIR) light stimulation of the skin. The microneedle patch's PVA/PVP coating layer and PCL-PLA array of supports. Heating generated by light might elicit the release of lidocaine from the microneedle patch, resulting in pain relief when the patch was implanted under the skin and subjected to NIR light stimulation. [34-35]

Development of Microneedles Faces a Number of Obstacles:

Although many potential uses for microneedles have been proposed, so far only a few products have been brought to market. It is important to consider both efficacy and safety while constructing microneedles for the delivery of small or big substances. Traces of metal left under the skin by metallic microneedles can lead to itching, erythema, edoema, discolouration, and other skin reactions. [36]Frequent usage of the microneedle in the same spot can lead to the aforementioned complications. It is important to keep in mind that the thickness of an individual's skin and the frequency with which microneedles are used can affect bioavailability, and that these factors should be taken into account during microneedle manufacture. Research efforts are being focused on improving delivery strategies for compounds that have already been shown to be safe and effective. Many people working in the pharmaceutical industry report this as their top reason for wanting to see microneedles as transdermal drug delivery systems succeed. Challenges abound in the development of diverse microneedles. They are effective, but they can also leave behind biohazardous waste when they are used. [37]The polysaccharide-based microneedles are waste-free since they disintegrate in the skin after usage. Overcoming global disintegration, correct injection into skin, and extensive drug loading at the tip are the most challenging obstacles they face as they develop. Hollow microneedles continue to pique the interest of researchers because of their versatility in handling a wider range of compounds than their solid counterparts. [38]

ISSN: 2583-4053
Volume-1 Issue-3 || August 2022 || PP. 65-76
https://doi.org/10.55544/jrasb.1.3.9

Table 3: Marketed microneedle-based transdermal products (Halder et.al 2020)

BRAND NAME	MANUFACTURER	USES
Metallic microneedle		
Darmaroller®	Derma spark, Canada	For acne and stretch mark treatment
Dissolvable microneedle patch		
MicroHyala®	CosMED Pharmaceutical Co. Ltd., Japan.	Hyaluronic acid present which treat skin wrinkle.
Dissolvable microneedle patch		
VaxMat®	TheraJect Inc., USA	Macromolecules such as vaccines, peptides and proteins delivery.
Microneedle patch		
Micro-Trans®	Valeritas Inc., USA	Deliver the drug to dermis which free from factors as drug size, structure and charge or the nature of the patient's skin.
Dissolvable microneedle patch		
Drugmat®	TheraJect Inc., USA	Able to pass hundreds of microgram of drug rapidly from stratum corneum to epidermal tissue.
Microneedle array-based device		
Nanoject®	Debiotech, Switzerland	Used for intradermal fluid diagnosis, and to deliver drug intra dermally or hypodermically.
Hollow microneedle array		
Soluvia®	Becton Dickinson, USA	It is in form of microinjection system which is accurate for fix intradermal delivery of drugs and vaccine.
Intradermal microneedle injection		
IDflu®/Intanza®	Sanofi Pasteur, Lyon, France	Intradermal delivery of influenza vaccine.
Intradermal microneedle injection		
Micronjet®	NanoPass Inc., Israel	For painless delivery of protein, drugs, and vaccines.
Metallic microneedle array		
Macroflux®	Zosano Pharma Inc., USA	Delivery of peptides and vaccines
Dissolvable peptide microneedle patch		
Microcore®	Corium Int. Inc., USA	To deliver small or large molecules.
Microneedle array-based device		
Dermapen®		For treatment of skin as for acne, hair loss and stretch marks. Also enhance absorption of drug
Hollow microneedle array		
Microstructured transdermal patch	3M Corp., USA	It delivers liquid formulations over a range of viscosities

Recent Patents on Microneedles-

Since microneedle application is a relatively novel approach to transdermal medication delivery, it has inspired a plethora of patent applications. As hollow microneedles can transport more medicine than conventional microneedles, their design and delivery are the primary subject of these patent applications. Because of this primary benefit of being able to deliver a bigger volume than other microneedles, several patents have been focused on technology involving hollow microneedles. [39-40]

ISSN: 2583-4053
Volume-1 Issue-3 || August 2022 || PP. 65-76
https://doi.org/10.55544/jrasb.1.3.9

Table 4: List of Recent patents on microneedle array technologies (Halder et.al 2020)

TITTLE	US PATENT NO.	REMARK	DATE	REFERENCE
Microneedle device	10,945,759	The microneedles device prevents sucction build up between the barrel and patent skin,to reduce the troma and facilates healing to the skin	March 16, 2021	
Operation tool for fluid injector using multi-micro needle device	10,926,072	An instrument for operating a fluid injector that uses a multi-micro device which easily and reliably enables any person to inject in a short time.	February 23, 2021	
Bio/chemical assay devices and methods for simplified steps, small samples, accelerated speed, and ease-of-use	10,948,389	It is investigated to make fast result, easily used, high sensitivity and operated without any professional's skill.	March 16, 2021	
Methods and devices for drug delivery to ocular tissue using microneedle	10,905,586	Formulated microneedle drug delivery to the ocular site.	February 2,2021	
Microneedle device and uses thereof	10,841,115	It is delivered to internal tissues or through a wall of vessels after interaction and it is used for oral and intravenous administration	October 27,2020	
Protective release sheet for microneedle patch	10,821,275	It is easily applied on the skin surface and penetrate through the wall to give better effect	November 3,2020	
Method for manufacturing microneedle by using biocompatible polymer	10,850,083	It solved the degeneration of medicine, insufficient hardness and loss of medicine cost by complicated process	December 1,2020	
Method of manufacturing microneedle and microneedle manufactured thereby	10,786,662	It improve coatability, configuration and active ingredient by endothermic reaction	September 29,2020	
Base composition for microneedle patch and microneedle patch comprising the same	10,793,701	It gives desired softness, flatness, flexibiltity, skin adhesion during use and resist humidity during storage	October 06,2020	
Microneedle patch	10,668,260	The microneedle Patches are useful for therapy and prevention	June 2,2020	
Microneedle beauty device using sound wave vibration	10,786,274	Microneedle provided skin care and capable of adjusting accurate protuding length of microneedle using sound wave vibration	September 29,2020	
Universal vaccine for viral diseases	10,940,196	Investigated relates to a pharmaceutical combination	March 9, 2021	

ISSN: 2583-4053
Volume-1 Issue-3 || August 2022 || PP. 65-76
https://doi.org/10.55544/jrasb.1.3.9

		for one or more immune responses or effectiveness of vaccination in the host and capable of cross-protection against serotypes of virus		
Aptamers for use in inhibition and/or suppression of TLR9 activation	10,947,545	Investigated new aptamer molecules for used in therapy or suppressing the activation of TLR9 in a cell	March 16, 2021	
Inhibitors of Hepatitis C virus polymerase	10,947,210	Provided as medicaments for the treatment of HCV infection	March 16, 2021	

Characterization of Micro needles [41-42]

Loaded pharmaceuticals can be characterised in terms of their particle size, microneedle solution, polydispersity index, viscosity, and zeta potential, among other physicochemical properties. Pretreatment, drug release, and adhesion are all examples of patch processes that benefit from permeation tests. It is possible to measure the size, structure, and crystalline nature of a liposome or nanocarrier using X-ray scattering, transmission electron microscopy, and dynamic light scattering. In vivo-like conditions can be mimicked in a lab to study drug dispersion or microneedle stability at a range of temperatures and pH levels. Additional tests performed on refined microneedles include biocompatibility analysis, in vitro testing, drug content analysis, and solubility analysis.

Test of functional ability

To evaluate the performance of microfluidic lumens, Wang et al. developed a novel fluidic test system. The experiment utilised a syringe pump apparatus that included a syringe filled with a dye, a polymer tube, and a microneedle array. This syringe pump apparatus was used to examine the development of microneedle lumens by directing dye from the syringe to the microneedle orifice. Cracks in the base plate and passage continuity can be examined microscopic during the microfluidic characterisation utilising the microneedle tips.

Insertion studies

During the needle transfer procedure, tissue deflection around the needle, and penetration into human skin, Shawgo et al. utilised a displacement-force test station to quantify the force applied to the needle, needle location, and skin tolerance. Needle insertion was previously detected by measuring the decrease in electrical resistance of the skin, as this was much easier to perceive than the insertion itself. Because the outer layer of skin has a larger electrical resistance than the deep tissue beneath it, the resistance of the skin lowers dramatically when a needle is penetrated.

Safety parameter

Forvi et al. defined the safety parameter as the ratio between the insertion force and the micro needle breakage force. If the ratio is 1, they suggested, microneedle arrays could have potential in biomedical settings. They put silicon microneedles through a battery of computerised safety tests. Compressive failure force was determined using an Enduratec station equipped with microneedles positioned between the punch and the load cell. An appropriate safety margin was determined for the silicon microneedle array samples.

Fracture force calculation

Forvi et al. defined the safety parameter as the ratio between the insertion force and the micro needle breakage force. If the ratio is 1, they suggested, microneedle arrays could have potential in biomedical settings. They put silicon microneedles through a battery of computerised safety tests. Compressive failure force was determined using an Enduratec station equipped with microneedles positioned between the punch and the load cell. An appropriate safety margin was determined for the silicon microneedle array samples.

Dimensional evaluation

Methods exist for evaluating needle geometry and for determining micro needle tip radius, weight, and length. The most common methods are optical or electrical microscopy. With the aid of 3D image analysis, we are able to get a clearer picture of the needle's shape and improve quality assurance. A confocal laser microscope and a scanning electron microscope were used to achieve this. Scanning electron microscopy (SEM) produces an image of a sample by scanning it with a centred beam of electrons that either communicate with the atoms in the sample or generate various indications that reveal surface topography and composition characteristics about the sample. Confocal laser microscopes produce extremely detailed images.

Mechanical properties [44]

Needles can be evaluated geometrically, and the tip radius, weight, and length of micro needles can be measured and calculated. Optical and electrical microscopy are the most often used techniques. Using 3D image analysis, we can acquire a more accurate depiction of the needle's form and tighten up quality control. This was done using a confocal laser microscope and a scanning electron microscope. Scanning electron

ISSN: 2583-4053

Volume-1 Issue-3 || August 2022 || PP. 65-76

https://doi.org/10.55544/jrasb.1.3.9

microscopy (SEM) creates an image by scanning the sample with a centred beam of electrons that interact with the atoms in the sample or generate a variety of indicators that disclose surface topography and composition details about the sample. Detailed images are obtained with confocal laser microscopes.

IV. PENETRATION TEST

In-vitro skin permeation studies

A diffusion cell is an instrument used to measure the amount of drug that passes through the skin. Pig ear skin serves as the primary material used in this experiment, sandwiched in between the receptor and donor areas. [54]Examines the difference between treated and untreated skin with regards to combined permeation profiles using micro needles.

In-vivo animal model studies

Hairless rats will be used in the experiment. In order to put the animal to sleep, it is necessary to apply an appropriate method of anaesthesia. One of the factors taken into account before and after micro needling is trans-epidermal water loss. Delfin Vapometers are used to measure this variable.

V. PERFORMANCE

Studies on skin irritation and recovery

Mild and temporary erythema at the site of administration is the most prevalent adverse effect of microneedle injection. Mild edoema can occur in some patients when HMNs administer fluid infusions through the skin. Possible contributors to this danger include the size of the micro needles, the treatment being provided by microneedles, and the materials utilised to make the needles.

Transepidermal water loss (TEWL) [45]

Two different probes, the DermaLab TEWL and the Tewameter TM 210, were utilised to examine microneedles. employing a diffusion cell and intact animal skin, it may be calculated. Before and after applying the microneedle array, measurements were taken at regular intervals for three minutes while the probes were clamped out of the way above the application site. Results showed that skin permeability was raised when a microneedle was used.

Biological safety test

In a recent study, Wu et al. The ISO 10993-12:2002 standard for "Sample Preparation and Reference Materials" was used to determine the amount of compounds that could be extracted from microneedles. In order to remove chemicals from microneedles, they were submerged in 37°C physiological saline for 72 hours. The extract was then tested for its ability to elicit cutaneous irritation by being applied directly to freshly shaven, uninjured human skin. The microneedles' ability to withstand biological attack was confirmed by the test's negative outcome.

VI. CONCLUSION

Macromolecules can be delivered systemically or locally using transdermal drug delivery methods, a rapidly expanding field. Transdermal drug delivery systems suffer from low permeability across the stratum corneum; however, this problem can be remedied by employing microneedles. In this article, we will examine the several types of microneedles used for drug administration, as well as the most current innovations, evaluation criteria, commercially available drug products, and recently issued patents for microneedle research and development.

REFERENCES

[1] Anissimov YG, Roberts MS. Modelling dermal drug distribution after topical application in human. *Pharm Res.* 2011;28:2119–2129.

[2] Arvanitis ML, Satonik RC. Transdermal fentanyl abuse and misuse. *Am J Emerg Med.* 2002;20:58–59.

[3] acon TH, Hole JG, North M, Burnett I. Analgesic efficacy of sustained release paracetamol in patients with osteoarthritis of the knee. *Br J Clin Pharmacol.* 2002;53:629–636.

[4] Awuchi, C. G., Amagwula, I. O., Priya, P., Kumar, R., Yezdani, U., & Khan, M. G. (2020). Aflatoxins in foods and feeds: A review on health implications, detection, and control. *Bull. Environ. Pharmacol. Life Sci*, *9*, 149-155.

[5] Umama, Y., Venkatajah, G., Shourabh, R., Kumar, R., Verma, A., Kumar, A., & Gayoor, M. K. (2019). Topic-The scenario of pharmaceuticals and development of microwave as; sisted extraction technique. *World J Pharm Pharm Sci*, *8*(7), 1260-1271.

[6] Kumar, R., Saha, P., Lokare, P., Datta, K., Selvakumar, P., & Chourasia, A. (2022). A Systemic Review of Ocimum sanctum (Tulsi): Morphological Characteristics, Phytoconstituents and Therapeutic Applications. *International Journal for Research in Applied Sciences and Biotechnology*, *9*(2), 221-226.

[7] Roshan, K. (2020). Priya damwani, Shivam kumar, Adarsh suman, Suthar Usha. An overview on health benefits and risk factor associated with coffee. *International Journal Research and Analytical Review*, *7*(2), 237-249.

[8] Dubey, A., Yadav, P., Verma, P., & Kumar, R. (2022). Investigation of Proapoptotic Potential of Ipomoea carnea Leaf Extract on Breast Cancer Cell Line. *Journal of Drug Delivery and Therapeutics*, *12*(1), 51-55.

[9] Sahana, S. (2020). Purabi saha, Roshan kumar, Pradipta das, Indranil Chatterjee, Prasit Roy, Sk Abdur Rahamat. *A Review of the 2019 Corona virus (COVID-19) World Journal of Pharmacy and Pharmaceutical science*, *9*(9), 2367-2381

[10] Bind, A., Das, S., Singh, V. D., Kumar, R., Chourasia, A., & Saha, P. Natural Bioactives For The

ISSN: 2583-4053

Volume-1 Issue-3 || August 2022 || PP. 65-76

https://doi.org/10.55544/jrasb.1.3.9

Potential Management Of Gastric Ulceration. *Turkish Journal of Physiotherapy and Rehabilitation*, *32*(3).

[11] Nyarko, R. O., Prakash, A., Kumar, N., Saha, P., & Kumar, R. (2021). Tuberculosis a globalized disease. *Asian Journal of Pharmaceutical Research and Development*, *9*(1), 198-201.

[12] Raj, A., Tyagi, S., Kumar, R., Dubey, A., & Hourasia, A. C. (2021). Effect of isoproterenol and thyroxine in herbal drug used as cardiac hypertrophy. *Journal of Cardiovascular Disease Research*, 204-217

[13] Kumar, R., & Dubey, A. PHYTOCHEMICAL INVESTICATION AND HEPTOPROTECTIVE EVALUTION ACACIA RUBICA EXTRACT ISONIZED AND PARACETAMOL INDUSED ANIMAL TOXICITY. *Turkish Journal of Physiotherapy and Rehabilitation*, *32*(3).

[14] Singh, M. K., Kumar, A., Kumar, R., Kumar, P. S., Selvakumar, P., & Chourasia, A. (2022). Effects of Repeated Deep Frying on Refractive Index and Peroxide Value of Selected Vegetable Oils. *International Journal for Research in Applied Sciences and Biotechnology*, *9*(3), 28-31.

[15] Saha, P., Kumar, R., Nyarko, R. O., Kahwa, I., & Owusu, P. (2021). HERBAL SECONDARY METABOLITE FOR GASTRO-PROTECTIVE ULCER ACTIVITY WITH API STRUCTURES.

[16] Nyarko, R. O., Kumar, R., Sharma, S., Chourasia, A., Roy, A., & Saha, P. (2022). ANTIBACTERIAL ACTIVITY OF HERBAL PLANT-TINOSPORA CORDIFOLIA AND CATHARNTHUS ROSEUS.

[17] Sahana, S., Kumar, R., Nag, S., Paul, R., Chatterjee, I., & Guha, N. (2020). A REVIEW ON ALZHEIMER DISEASE AND FUTURE PROSPECTS

[18] Sahana, S. (2020). Roshan kumar, Sourav nag, Reshmi paul, Nilayan guha, Indranil Chatterjee. A Review on Alzheimer disease and future prospects. *World Journal of Pharmacy and Pharmaceutical science*, *9*(9), 1276-1285.

[19] Nyarko, R. O., Saha, P., Kumar, R., Kahwa, I., Boateng, E. A., Boateng, P. O., ... & Bertram, A. (2021). Role of Cytokines and Vaccines in Break through COVID 19 Infections. *Journal of Pharmaceutical Research International*, *33*, 2544-2549.

[20] PURABISAHA, R. K., RAWAT, S. S. N., & PRAKASH, A. (2021). A REVIEW ON NOVEL DRUG DELIVERY SYSTEM.

[21] Nyarko, R. O., Boateng, E., Kahwa, I., & Boateng, P. O. (2020). A comparison analysis on remdesivir, favipiravir, hydroxychloroquine, chloroquine and azithromycin in the treatment of corona virus disease 2019 (COVID-19)-A Review. *World J. Pharm. Pharm. Sci*, *9*, 121-133.

[22] KUMAR, R., SAHA, P., SARKAR, S., RAWAT, N., & PRAKASH, A. (2021). A REVIEW ON NOVEL DRUG DELIVERY SYSTEM. *IJRAR-International Journal of Research and Analytical Reviews (IJRAR)*, *8*(1), 183-199

[23] Nyarko, R. O., Boateng, E., Kahwa, I., Boateng, P. O., & Asare, B. (2020). The impact on public health and economy using lockdown as a tool against COVID-19 pandemic in Africa: a perspective. *J Epidemiol Public Health Rev*, *5*(3).

[24] Kumar, R., Saha, P., Pathak, P., Mukherjee, R., Kumar, A., & Arya, R. K. EVOLUTION OF TOLBUTAMIDE IN THE TREATMENT OF DIABETES MELLITUS. *Jour. of Med. P'ceutical & Alli. Sci*, *9*.

[25] Kumar, R., Saha, P., Kumar, Y., Sahana, S., Dubey, A., & Prakash, O. (2020). A Review on Diabetes Mellitus: Type1 & Type2. *World Journal of Pharmacy and Pharmaceutical Sciences*, *9*(10), 838-850.

[26] Daharia, A., Jaiswal, V. K., Royal, K. P., Sharma, H., Joginath, A. K., Kumar, R., & Saha, P. (2022). A Comparative review on ginger and garlic with their pharmacological Action. *Asian Journal of Pharmaceutical Research and Development*, *10*(3), 65-69.

[27] Saha, P., Nyarko, R. O., Lokare, P., Kahwa, I., Boateng, P. O., & Asum, C. (2022). Effect of Covid-19 in Management of Lung Cancer Disease: A Review. *Asian Journal of Pharmaceutical Research and Development*, *10*(3), 58-64.

[28] Kumar, R., Jain, A., Tripathi, A. K., & Tyagi, S. (2021, January). Covid-19 outbreak: An epidemic analysis using time series prediction model. In *2021 11th international conference on cloud computing, data science & engineering (Confluence)* (pp. 1090-1094). IEEE

[29] KUMAR, A. (2019). The Scenario of Pharmaceuticals and Development of Microwave Assisted Extraction Techniques.

[30] Kumar, R., & Saha, P. (2022). A Review on Artificial Intelligence and Machine Learning to Improve Cancer Management and Drug Discovery. *International Journal for Research in Applied Sciences and Biotechnology*, *9*(3), 149-156.

[31] Nalimu, F., Oloro, J., Kahwa, I., & Ogwang, P. E. (2021). Review on the phytochemistry and toxicological profiles of Aloe vera and Aloe ferox. *Future Journal of Pharmaceutical Sciences*, *7*(1), 1-21.

[32] Kumar, N., Dubey, A., Mishra, A., & Tiwari, P. (2020). Ethosomes: A Novel Approach in Transdermal Drug Delivery System. *International Journal of Pharmacy & Life Sciences*, *11*(5).

[33] Mukkamala, R., Kumar, R., Banerjee, S. K., & Aidhen, I. S. (2020). Synthesis of Benzyl C-Analogues of Dapagliflozin as Potential SGLT2 Inhibitors. *European Journal of Organic Chemistry*, *2020*(12), 1828-1839.

[34] Bhati, V., Yadav, P. K., & Kumar, R. (2018). Effect of Levels of Inorganic Fertilizers, Organic Manure and Bio-Fertilizers on Plant Growth Attributes of Onion (Allium cepa L.) cv. N-53 under Hot Arid Region of Western Rajasthan, India. *International J. Curr. Micro. Appl. Sci*, *7*, 3593-601.

ISSN: 2583-4053

Volume-1 Issue-3 || August 2022 || PP. 65-76

https://doi.org/10.55544/jrasb.1.3.9

[35] Bugga, P., Alam, M. J., Kumar, R., Pal, S., Chattopadyay, N., & Banerjee, S. K. (2022). Sirt3 ameliorates mitochondrial dysfunction and oxidative stress through regulating mitochondrial biogenesis and dynamics in cardiomyoblast. *Cellular Signalling*, *94*, 110309.

[36] Kumar, S., Yadav, S. P., Chandra, G., Sahu, D. S., Kumar, R., Maurya, P. S., ... & Ranjan, K. (2019). Effect of dietary supplementation of yeast (Saccharomyces cerevisiae) on performance and hemato-biochemical status of broilers.

[37] Dubey, A., Kumar, N., Mishra, A., Singh, Y., & Tiwari, M. (2020). Review on Vinpocetine. *International Journal of Pharmacy & Life Sciences*, *11*(5).

[38] Saha, P., Kumar, A., Bhanja, J., Shaik, R., Kawale, A. L., & Kumar, R. (2022). A Review of Immune Blockade Safety and Antitumor Activity of Dostarlimab Therapy in Endometrial Cancer. *International Journal for Research in Applied Sciences and Biotechnology*, *9*(3), 201-209.

[39] Anubhav, S. P. D., Sanjay, K. D., & Roshan, K. (2022). Evaluation of Enzyme Producing K. Pneumoniae and Their Susceptibility to Other Anti-Biotics. *International Journal of Innovative Science and Research Technology2022*, *7*(5), 351-353.

[40] Kumar, R., Saha, P., Keshamma, E., Sachitanadam, P., & Subramanian, M. (2022). Docking Studies of Some Novel Hetrocyclic Compound as Acat Inhibitors: A Meta Analysis. *Journal for Research in Applied Sciences and Biotechnology*, *1*(3), 33-41.

[41] Pandey, M., Singh, A., Agnihotri, N., Kumar, R., Saha, P., Pandey, R. P., & Kumar, A. (2022). Clinical Pharmacology & Therapeutic uses of Diuretic Agents: A Review. *Journal for Research in Applied Sciences and Biotechnology*, *1*(3), 11-20.

[42] Amle, V. S., Rathod, D. A., Keshamma, E., Kumar, V., Kumar, R., & Saha, P. (2022). Bioactive Herbal Medicine Use for Eye Sight: A Meta Analysis. *Journal for Research in Applied Sciences and Biotechnology*, *1*(3), 42-50.

[43] Kumar, R., Keshamma, E., Paswan, S. K., Saha, P., Trivedi, U., Chourasia, A., & Otia, M. (2022). Alkaloid Based Chemical Constituents of Ocimum santum & Cinchona Bark: A Meta Analysis. *Journal for Research in Applied Sciences and Biotechnology*, *1*(2), 35-42.

[44] Singh, Y., Paswan, S. K., Kumar, R., Otia, M. K., Acharya, S., Kumar, D., & Keshamma, E. (2022). Plant & Its Derivative Shows Therapeutic Activity on Neuroprotective Effect. *Journal for Research in Applied Sciences and Biotechnology*, *1*(2), 10-24

[45] Nyarko, R. O., Roopini, R., Raviteja, V., Awuchi, C. G., Kumar, R., Faller, E. M., ... & Saha, P. (2022). Novel Sars-CoV-2 Variants & Therapeutic Effects. *Journal for Research in Applied Sciences and Biotechnology*, *1*(2), 25-34.