World Journal of Pharmaceutical Science and Research
www.wjpsronline.com
Review Article
ISSN: 2583-6579
SJIF Impact Factor: 3.454
Year - 2023
Volume: 2; Issue: 2
Page: 11-17

A REVIEW ON MICRO NEEDLE BASED TRANSDERMAL DRUG DELIVERY SYSTEM

Kotha Mounika[1] and Dr. M. Swetha*[1]

[1]Sarojini Naidu Vanita Pharmacy Maha Vidyalaya.

Article Received: 11 February 2023 | | ***Article Revised: 05 March 2023*** | | ***Article Accepted: 25 March 2023***

Corresponding Author: Dr. M. Swetha
Sarojini Naidu Vanita Pharmacy Maha Vidyalaya.

ABSTRACT

Micro needle could be a metric linear unit sized needle its height of 10- 2000µm and also the dimension has 10-50µm, which might penetrate through the cuticle layer to dermal tissue directly while not pain. Microneedles are the wide utilized in the transcutaneous drug delivery system they're painless, efficient, safe, convenient, less invasive, and simple to self-administer with a high drug bioavailability. They're divided in to 4types solid microneedles, coated microneedles, dissolving microneedles, hollow microneedles. Differing kinds of microneedles play totally different roles in numerous analysis fields. Within the recent years, microneedles have oftentimes wont to deliver medication, genes, proteins, RNA & vaccines & have achieved wonderful therapeutic result. In addition, recent biological applications & clinical trials are introduced. Small needles are often improved 3D printing & digital technology contribute to the development of microneedle fabrication technology.

KEYWORDS: Microneedles Transdermal Fabrication techniques.

INTRODUCTION

Microneedles carries with it a plurality of micro-projections, usually starting from 25-2000µm tall, of various shapes, that area unit hooked up to a base support. Application of MN arrays to biological membranes will produce transport pathways of micro meter dimensions.[1] MNs even be used for sampling body fluids, such for measurement the glucose levels in diabetic medical aid transdermic delivery has the advantage of by passing the primary pass impact & permitting sustained unleash of the drug but drug delivery is tough because of the barrier created by the horny layer. Microneedle area unit platform for transdermic drug delivery, it's simple to self-administer, & it exhibits a high drug bioavailability. The dose, delivery rate, & effectuality of the medication will be controlled by the microneedle style & drug formulation.

Types of microneedles

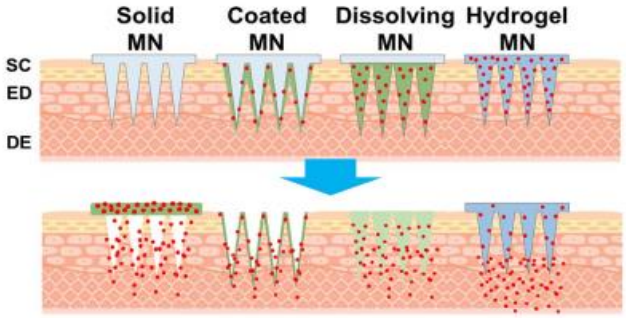

Fig. 1 Schematic illustration of the types of microneedles and their drug delivery methods. *SC* stratum corneum, *ED* epidermis, *DE* dermis, *MN* microneedles

Although the microneedle style varies betting on the delivery technique, form of microneedle, and action of the medication to be delivered, most patches have sure common options. A typical microneedle has the form of a tapered sharp tip with a length of 150–1500 μm, a width of 50–250 μm, and a tip thickness of 1–25 μm.[2] Microneedles area unit sometimes fabricated from metal, silicon, polymer, glass, or ceramic. The drug is mostly placed in or on the microneedle tip, that is fxed to the bottom substrate beneath to create associate degree array. The microneedle array is connected to the patch backing for easy use; this backing includes a skin adhesive to enhance contact with the skin. The microneedles area unit usually classified into four types (Fig. 1). Solid microneedles area unit primarily fabricated from metal and semiconducting material, which give sturdy mechanical properties and don't contain medication. Therefore, once applying the microneedles, it's necessary to any apply the drug to the area. In distinction, once coated microneedles area unit applied on the surface of the skin, the drug is delivered at the same time with the applying. In dissolving microneedles, the drug can be enclosed within the perishable matrix, during which case no sharp waste is created once microneedle application. Hydrogel microneedles enable medication to be delivered slowly because the drug is contained altogether areas like the tip of the microneedle and also the patch backing. Since the characteristics of microneedles vary with the kind, a suitable design ought to be selected for the microneedles according to the drug dose, onset of action, delivery amount, delivery efciency, packaging, sharp waste, and patch-wearing time.

Solid microneedles

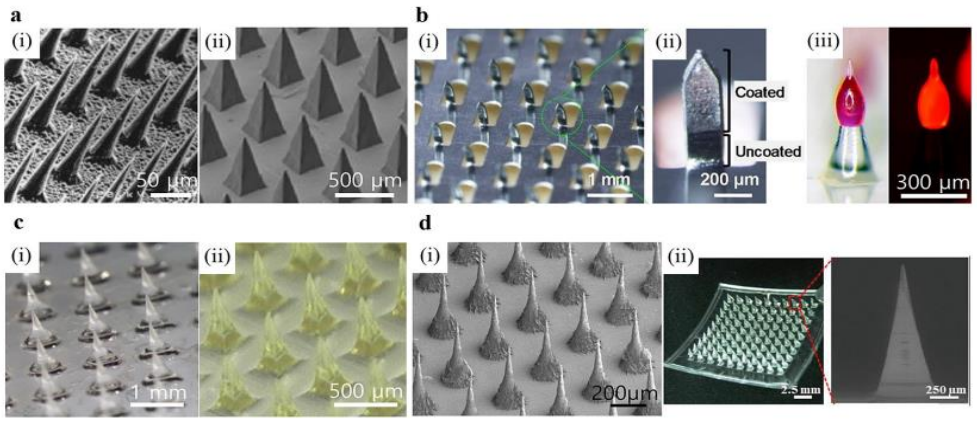

Fig. 2 **a** Silicon solid microneedles (i (Henry et al. 1998) and ii (Park et al. 2010)), **b** coated microneedles (i, ii (Shakya et al. 2017) and iii (Chen et al. 2017)), **c** dissolving microneedles (i (Tas et al. 2017) and ii (Du et al. 2019)*), and **d** hydrogel microneedles (i (Yu et al. 2015) and ii (He et al. 2020). *Reprinted with permission from (Du H et al. (2019) ACS Appl Mater Interfaces 11:43,588–43,598). Copyright (2019) American Chemical Society

Solid microneedles square measure Associate in nursing array containing microscale tapered sharp tips composed of one material while not any medication or excipients, they're inserted into the skin, creating micron-sized pores on the skin surface (Fig. 2a). When the drug is placed on the treated space, the drug passes through the horny layer, the most important barrier of the skin, through these pores; it's simply transferred to the capillaries in the superficial stratum, increasing the bioavailability of the drug.[3] The agent is also developed as a traditional pad or topical skin formulation.[4]

Coated microneedles

Coated microneedles Solid microneedles square measure Associate in Nursing array containing microscale tapered sharp tips composed of one material while not any medicine or excipients, they're inserted into the skin, creating micron-sized pores on the skin surface (Fig. 2a). When the drug is placed on the treated space, the drug passesthrough the stratum, the biggest barrier of the skin, through these pores; it's simply transferred to the capillaries in the superficial derma, increasing the bioavailability of the drug.[5] The agent is also developed as a traditional pad or topical skin formulation.[6] In coated microneedles, the surface of a solid microneedle is coated with a soluble matrix so the drug dissolves apace into the skin when microneedle insertion (Fig. 2b).[7,8] The coating insulation ought to form a film on the surface of the microneedle and maintain adhesion throughout storage and insertion into the skin. To realize this purpose, the coating formulation ought to have adequate viscousness. The placement where the coating formulation is placed ought to be thought-about. Generally, it's economical to position the medicine solely at the tip wherever the microneedle enters the particular skin. In the case of dip coating, the drug-coated space will be controlled via regulation the depth to that the microneedle is unfit into the coating formulation.[8-9] The drug-coated space can be determined by dominant the physical phenomenon of the coating formulation, therefore regulation the spreading of the microneedle. In coated microneedles, the drug will quickly dissolve within the skin, leading to a quick onset of drug action. The thickness of the coating will be exaggerated by repetition the formulation coating; but, it's not appropriate for drug delivery because it needs an oversized dose thanks to dose limitations.[10-11]

Dissolving microneedles[12-18]

Microneedles themselves may be manufactured from soluble or biodegradable materials that contain the medicine and possess sufficient mechanical strength to penetrate the skin (Fig. 2c). Insertion of a dissolving microneedle into the skin doesn't generate sharps waste as a result of it apace dissolves or disintegrates upon contact with the skin fluid. Dissolving microneedles are primarily factory-made using a soluble perishable compound via a solvent casting methodology. Perishable, cellulose-based polymers such as Carboxy Methyl cellulose (CMC) and alkyl cellulose are of times used. Saccharides (e.g. trehalose and sucrose) are enclosed within the microneedles; they promote disintegration of the formulation and stabilize biomolecules. The formulation of the drug-containing tip ought to exhibit compatibility with the drug, give mechanical strength, and have a sufficiently low viscousness for flling the microscale mildew space well while not air bubbles. The bottom substrate containing no drug could have the next viscousness than the tip, may be automatically weak, or could also be a water-insoluble material.

Recently, many studies are conducted for shortening the microneedle patch-wearing time via separating the microneedle tips apace from the bottom substrate without needing the ideas to completely dissolve within the skin. Li et al. according a microneedle patch capable of apace separating once skin insertion by cutting off force. The mechanical strength of the microneedle was controlled by tack a drop on the microneedle additionally, the microneedle

tip was separated at intervals two main from the base substrate that was composed of a foamable material. Jun et al. developed insertion-responsive microneedles for immediate separation of the micro needle after skin application. alittle single wall was designed on the aspect of the microneedle base; the structure enabled speedy mechanical separation of the tip from base. However, like dissolving and coated microneedles, this system is inexpedient for delivering giant doses; studies are being conducted for increasing the number of drug that may be incorporated in these micro needles.[19-22]

Hydrogel micro needles[23-26]

In gel microneedles, the drug is contained all told areas of the microneedle tip, base substrate, and patch backing and is discharged at a slow rate whereas the patch is applied to the skin (Fig. 2d). The micro needle patches are primarily composed of gel, and after they encounter fuids in the skin, they're hydrous however not dissolved. A high quantity of the drug within the gel is delivered to the skin through diffusion. Since the drug may be incorporated within the entire microneedle patch, this system is appropriate for big dose delivery; but, its disadvantage is that the patch-wearing time is long as a result of the drug delivery rate is slow.

Materials for micro needles[27]

Various materials, from metal to compound, square measure utilized in microneedles, looking on the look or parts of the patch. Generally, microneedle materials ought to have sufficient mechanical strength for skin insertion. Non-dissolving microneedles square measure inert, biocompatible, and sufficiently sturdy for skin insertion while not causing Associate in Nursing response. In distinction, the matrices of the coated and dissolving microneedles ought to typically be water-soluble and biocompatible. Additionally, it ought to dissolve or disintegrate within the body while not inducement toxicity. Compatibility between the matrices and medicines is vital throughout the producing method, storage, and transportation of the microneedle patches.

Metal

Metal materials exhibit high mechanical and tensile strength; therefore, they will simply labor under the skin. They are used to manufacture solid, coated, and hollow microneedles. In general, stainless-steel and metallic element (Ti) are typical metal materials utilized in microneedles. Stainless steel is that the most used metal material for microneedle production; but, it exhibits a quicker corrosion rate than Ti alloy. Ti alloys possess stronger mechanical strength than unsullied steel; but, they're costlier.[27-33]

Polymer

The polymers used for microneedle manufacture ought to be water-soluble, biocompatible, and automatically sturdy for skin insertion. The foremost common technique for manufacturing compound microneedle is that the solvent casting method. This technique involves getting Associate in Nursing inverse mildew from the microneedle structure, running a compound formulation on that, drying it, and peeling it from the inverse mildew. Dissolving or colloidal gel microneedles square measure factory-made victimisation the solvent casting technique with numerous varieties of polymers such as hydroxypropyl methylcellulose, hyaluronic acid, CMC, polyvinyl pyrrolidone, and poly(lactic-co-glycolic acid) (PLGA).[34-40]

Glass

Glass microneedles square measure primarily hollow and ready victimization wet etching or micropipette puller. It exhibits sufficient strength for skin insertion, sanctioning simple process of the tapered form. It is easy to sterilize as a result of it's stable at warmth and pressure; the fabric itself is biocompatible. However, it breaks easily; specifically, if the tip of the microneedle is broken and it remains within the skin tissue, it will cause inflammation or granulomas.[41-42]

Ceramic

Since ceramic materials like corundom, orthophosphate, and calcium sulfate exhibit biocompatibility and supply sufficient mechanical strength, studies have explored their use within the preparation of microneedles.[42] (Figure. 3). Microneedle fabrication techniques when planning a microneedle, the target of the microneedle is taken into account first. The drug kind and dose, desirable pharmacokinetics/pharmacodynamics, and targets for use square measure thought of. Next, the foremost optimized microneedle style and materials square measure determined. The producing method for microneedles varies betting on the planning or material. Once specializing in the economic side, a method such as solvent casting, that is simple to line up, is used. In distinction, if the main target is on the accuracy, precision, and reproducibility of needle production, production of metal or semiconducting material microneedles supported MEMS technology may be considered.we'vegotsummarized varied ways reportable till date for microneedle manufacture.

Fabricationtechnology

Microneedle master molds square measure primarily factory-made by deep reactive particle etching for fabricating the tiny microneedle tips, the scale of that ranges over many tens of micrometers with high accuracy and reliability. Because the instrument and maintenance square measure dear, the barrier to enter the feld of microneedle analysis is high, and the technology of production has been restricted to certain firms.

3Dprinting

As the technology for 3D printing advances, microneedle manufacturing has been conducted victimization entry-level 3D printers. As a result of the value and maintenance of 3D printers are cheap, they'll be simply utilised for varied applications. CAD software package allows the planning of novel shapes of microneedles. 3D printing will significantly shorten the product development time thanks to speedy fabrication and modification of the prototypes. However, there's a limit to the materials that may be used, and therefore the low resolution of entry-level 3D printers remains a tangle. Though there square measure high-resolution 3D printers, the instrument value is high. Nevertheless, 3D printing studies have continuing to beat the restrictions. It's expected that the 3D printing technology can alter North Americannation to supply bespoke microneedle patches betting on individual symptoms.

CONCLUSION

Microneedles area unit a stratum drug delivery system that's rapidly growing in analysis because of the benefit of accelerating patient access to medicine through substitution alternative routes of administration. Microneedles may be classified as solid, coating, dissolving, and colloidal gel formulations. They are composed of varied materials like Si, metal, polymer, glass, and ceramic. Varied producing techniques are utilized for transmission distinctive shapes, sizes, and proper - ties. Microneedles still evolve through clinical trials and utilize varied medicine. Most studies have

incontestable favorable results victimization this technique. This system has the potential to produce therapeutic effects in multiple fields.

REFERENCES

1. Waghule T, Singhvi G, Dubey SK, Pandey MM, Gupta G, Singh M, Dua K (2019) Microneedles: a smart approach and increasing potential for transdermal drug delivery system. Biomed Pharmacother, 109: 1249–1258.
2. Henry S, McAllister DV, Allen MG, Prausnitz MR (1998) Microfabricated microneedles: a novel approach to transdermal drug delivery. J Pharm Sci, 87: 922–925.
3. Hoang MT, Ita KB, Bair DA (2015) Solid microneedles for transdermal delivery of amantadine hydrochloride and pramipexole dihydrochloride. Pharmaceutics, 7: 379–396.
4. Haj-Ahmad R, Khan H, Arshad MS, Rasekh M, Hussain A, Walsh S, Li X, Chang MW, Ahmad Z (2015) Microneedle coating techniques for transdermal drug delivery. Pharmaceutics, 7: 486–502.
5. Jiang J, Gill HS, Ghate D, McCarey BE, Patel SR, Edelhauser HF.
6. Prausnitz MR (2007) Coated microneedles for drug delivery to the eye. Invest Ophthalmol Vis Sci, 48: 4038–4043.
7. Gill HS, Prausnitz MR (2007a) Coated microneedles for transdermal delivery. J Control Release, 117: 227–237.
8. Gill HS, Prausnitz MR (2007b) Coating Formulations for Microneedles. Pharm Res, 24: 1369–1380.
9. Shakya AK, Ingrole RSJ, Joshi G, Uddin MJ, Anvari S, Davis CM.
10. Gill HS (2019) Microneedles coated with peanut allergen enable desensitization of peanut sensitized mice. J Control Release, 314: 38–47.
11. Chen Y, Chen BZ, Wang QL, Jin X, Guo XD (2017) Fabrication of coated polymer microneedles for transdermal drug delivery. J Control Release, 265: 14–21.
12. Waghule T, Singhvi G, Dubey SK, Pandey MM, Gupta G, Singh M, Dua K (2019) Microneedles: a smart approach and increasing potential for transdermal drug delivery system. Biomed Pharmacother, 109: 1249–1258.
13. Sullivan S, Koutsonanos D, del Pilar MM, Lee JW, Zarnitsyn V, Choi SO, Murthy N, Compans RW, Skountzou I, Prausnitz MR (2010) Dissolving polymer microneedle patches for infuenza vaccination. Nat Med, 16: 915–920.
14. Hirobe S, Azukizawa H, Hanafusa T, Matsuo K, Quan YS, Kamiyama F, Katayama I, Okada N, Nakagawa S (2015) Clinical study and stability assessment of a novel transcutaneous infuenza vaccination using a dissolving microneedle patch. Biomaterials, 57: 50–58.
15. Edens C, Collins ML, Goodson JL, Rota PA, Prausnitz MR (2015) A microneedle patch containing measles vaccine is immunogenic in non-human primates. Vaccine, 33: 4712–4718.
16. Quinn HL, Bonham L, Hughes CM, Donnelly RF (2015) Design of a dissolving microneedle platform for transdermal delivery of a fixed-dose combination of cardiovascular drugs. J Pharm Sci, 104: 3490–3500.
17. Raphael AP, Crichton ML, Falconer RJ, Meliga S, Chen X, Fernando GJ, Huang H, Kendall MA (2016) Formulations for micro projection/microneedle vaccine delivery: structure, strength and release profiles. J Control Release, 225: 40–52.
18. Mistilis MJ, Bommarius AS, Prausnitz MR (2015) Development of a thermostable microneedle patch for infuenza vaccination. J Pharm Sci, 104: 740–749.
19. Prausnitz MR (2017) Engineering microneedle patches for vaccination and drug delivery to skin. Annu Rev Chem Biomol Eng, 8: 177–200.
20. Prausnitz M, Langer R (2008) Transdermal drug delivery. Nat Biotechnol, 26: 1261–1268.

21. Li W, Terry RN, Tang J, Feng MR, Schwendeman SP, Prausnitz MR (2019a) Rapidly separable microneedle patch for the sustained release of a contraceptive. Nat Biomed Eng, 3: 220–229.
22. Li W, Tang J, Terry RN, Li S, Brunie A, Callahan RL, Noel RK, Rodriguez CA, Schwendeman SP, Prausnitz MR (2019b) Long-acting reversible contraception by efervescent microneedle patch. Science Adv, 5: 1–12.
23. Jun H, Ahn M-H, Choi I-J, Baek S-K, Park J-H, Choi S-O (2018) Immediate separation of microneedle tips from base array during skin insertion for instantaneous drug delivery. RSC Adv, 8: 17786–17796.
24. Al Sulaiman D, Chang JYH, Bennett NR, Topouzi H, Higgins CA, Irvine DJ, Ladame S (2019) Hydrogel-coated microneedle arrays for minimally invasive sampling and sensing of specifc circulating nucleic acids from skin interstitial fuid. ACS Nano, 13: 9620–9628.
25. He R, Niu Y, Li Z, Li A, Yang H, Xu F, Li F (2020) A Hydrogel Microneedle Patch for Point-of-Care Testing Based on Skin Interstitial Fluid. Adv Healthcare Mater, 9: 1901201.
26. Yu J, Zhang Y, Ye Y, DiSanto R, Sun W, Ranson D, Ligler FS, Buse JB, Gu Z (2015) Microneedle-array patches loaded with hypoxiasensitive vesicles provide fast glucose-responsive insulin delivery. Proc Natl Acad Sci USA, 112: 8260–8265.
27. Migdadi EM, Courtenay AJ, Tekko IA, McCrudden MT, Kearney MC, McAlister E, McCarthy HO, Donnelly RF (2018) Hydrogel-forming microneedles enhance transdermal delivery of metformin hydrochloride. J Control Release, 285: 142–151.
28. Courtenay AJ, McAlister E, McCrudden MTC, Vora L, Steiner L, Levin G, Levy-Nissenbaum E, Shterman N, Kearney M-C.
29. McCarthy HO, Donnelly RF (2020) Hydrogel-forming microneedle arrays as a therapeutic option for transdermal esketamine delivery. J Control Release, 322: 177–186.
30. Dharadhar S, Majumdar A, Dhoble S, Patravale V (2019) Microneedles for transdermal drug delivery: a systematic review. Drug Dev Ind Pharm, 45: 188–201.
31. Gupta J, Gill HS, Andrews SN, Prausnitz MR (2011) Kinetics of skin resealing after insertion of microneedles in human subjects. J Control Release, 154: 148–155.
32. Choi HJ, Bondy BJ, Yoo DG, Compans RW, Kang SM, Prausnitz MR (2012) Stability of whole inactivated infuenza virus vaccine during coating onto metal microneedles. J Control Release, 166: 159–171.
33. McCarthy PT, Otto KJ, Rao MP (2011) Robust penetrating microelectrodes for neural interfaces realized by titanium micromachining. Biomed Microdevices, 13: 503–515.
34. Skoog SA, Miller PR, Boehm RD, Sumant AV, Polsky R, Narayan RJ (2015) Nitrogen-incorporated ultrananocrystalline diamond microneedle arrays for electrochemical biosensing. Diam Relat Mater, 54: 39–46.
35. Amalraju D, Dawood AS (2012) Mechanical strength evaluation analysis of stainless steel and titanium locking plate for femur bone fracture. Eng Sci Technol Int J, 2: 2250–3498.