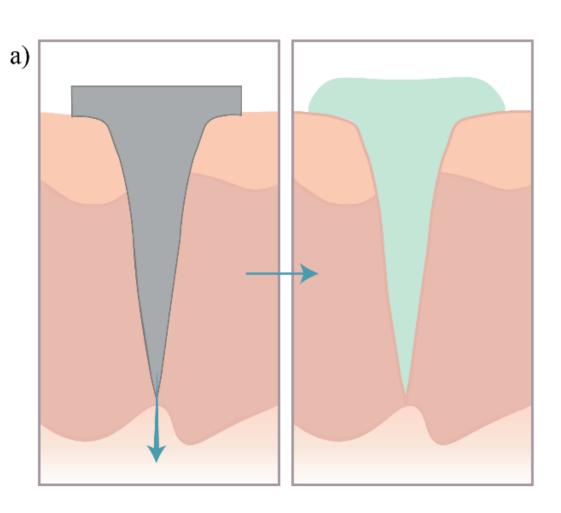


Hollow microneedles: With microflow to therapeutic effects

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1. Introduction



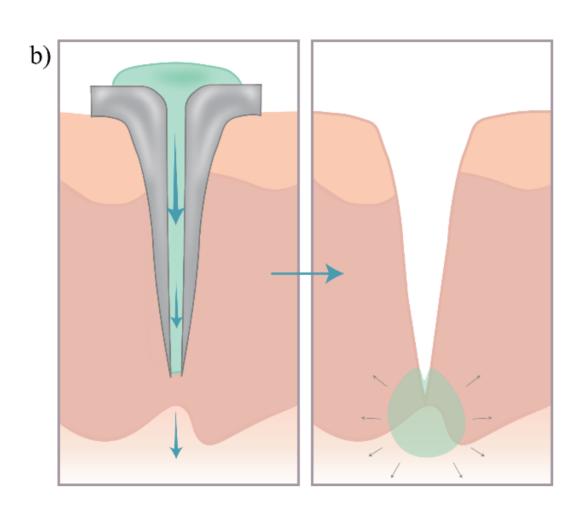


Figure 1. Drug delivery by a) solid microneedles and b) hollow microneedles

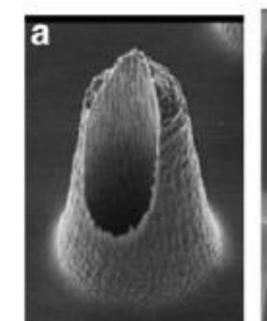
- The microneedles penetrates the SC up to 70-200 μm (length: 50-900 μm , the diameter: < 300 μm) [1].
- Their application will not reach the nerve endings located in the dermis allowing a painless administration
- Microneedles aid the delivery of drugs that are not subject to passive diffusion through the SC and thus, the size of the drug molecule is now not a limiting factor [2].
- Microneedles are categorized as solid and hollow microneedles
- Solid microneedles increase skin permeability to small molecules, proteins and nanoparticles
- For the rapid or controlled release of peptides and vaccines, drug formulations are coated or encapsulated, whereas hollow microneedles deliver API by infusion from the reservoir [3].

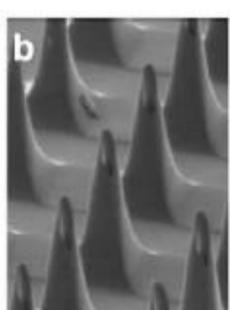
2. Materials and methods

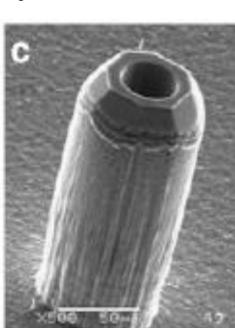
- The research type was descriptive and retrospective
- As information sources, the original articles published in medical journals, as well as Medline and Google Scholar databases, were collected

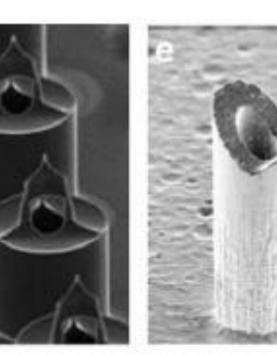
3. Results and discussion

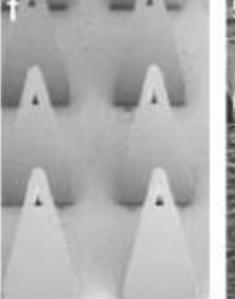
- Drug delivery through the skin is achieved by injecting a liquid formulation via hollow microneedles, which allows continuous delivery of molecules in a minimally invasive manner [4].
- Hollow microneedles transport molecules from a reservoir that contains a drug, gel or solid particles across a membrane, which separate the drug from the skin to achieve controlled release [5]. They can be made from a wide range of materials such as silicone, metal, glass, polymers, ceramics [4] (Figure 2).

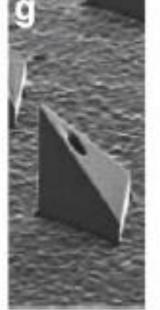


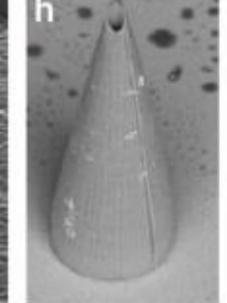














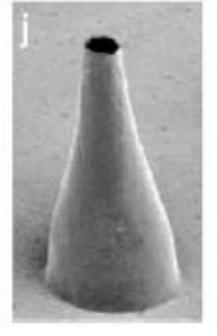




Figure 2. Hollow microneedles made of different materials: silicone (a, b, c, d, e), polymer (f, g, h, i, j) and glass (k)

Drug delivery by hollow microneedles

McAllister et al. produced hollow microneedles to deliver insulin to hairless rats. The results blood sample analysis showed a significant decrease in the concentration of glucose in the blood [6].

Wang et al. applied insulin by hollow microneedles to the skin of a hairless rat *in vivo* and human skin, obtained after *in vitro* autopsy. Fluorescence microscopy and histological staining showed that microneedles delivered insulin at a precise depth, significantly improving drug delivery efficiency [7].

Roxhed et al. designed a hollow microneedle with a drug reservoir patch system for controlled delivery of insulin in diabetic rats. Continuous infusion significantly increased the concentration of insulin in the blood plasma. After three hours of delivery, the concentration of insulin was five times higher than in passive delivery, with an effective decrease in blood glucose levels [8].

Sivamani et al. compared the topical application of hexyl nicotinate by injection with hollow microneedles on the forearm of healthy volunteers, on both intact skin and skin where the upper part of the SC was removed with tape. Microneedles reduced the time to achieve maximum cutaneous blood flow, regardless of whether the SC was removed [9].

Gupta et al. injected lidocaine, into the skin of healthy volunteers, using a single hollow microneedle and compared it to an intradermal injection. Although local anaesthesia effect was the same in both methods, subjects reported significantly less pain sensation when delivering lidocaine using microneedles [10].

5. Conclusion

- With hollow microneedles, the drug is delivered to the systemic circulation quickly, thus avoiding the passage of the drug through the gastrointestinal tract and the first-pass.
- They are especially suitable for use in the pediatric population, but also in other patients who are afraid of needles.
- Pain during application is minimal and higher with microneedles > 1000 μm .

References

[1] Donnelly RF. et al. Optical coherence tomography is a valuable tool in the study of the effects of microneedle geometry on skin penetration characteristicsnd in-skin dissolution. *J Control Release*, 2010;147:333–41

[2] Akhtar N. Microneedles: An innovative approach to transdermal delivery- a review. *Int J Pharm Pharm Sci*, 2014;6:18–25.

[3] Giri Nandagopal MS. et al. Overview of microneedle system: A third generation transdermal drug delivery approach. *Microsyst Technol*, 2014;20:1249–72.

[4] Larrañeta E. et al. Microneedles: A New Frontier in Nanomedicine Delivery. *Pharm Res*, 2016;33:1055–73.

[5] Zorec B. et al. Active enhancement methods for intra- and transdermal drug delivery: A review. *Zdr Vestn*, 2013;82:339–56.

[6] McAllister D V. et al. Microfabricated needles for transdermal delivery of macromolecules and nanoparticles: Fabrication methods and transport studies. *Proc Natl Acad Sci U S A*, 2003;100:13755–60. [7] Wang PM. et al. Minimally invasive extraction of dermal interstitial fluid for glucose monitoring using microneedles. *Diabetes Technol Ther*, 2005;7:131–41.

[8] Roxhed N. et al. Painless drug delivery through microneedle-based transdermal patches featuring active infusion. *IEEE Trans Biomed Eng*, 2008;55:1063–71.

[9] Sivamani RK. et al. Microneedle penetration and injection past the stratum corneum in humans. *J Dermatolog Treat*, 2009;20:156–9.

[10]Gupta J. et al. Rapid local anesthesia in humans using minimally invasive microneedles. *Clin J Pain*, 2012;28:129–35.