TEST Engineering & Management

May – June 2020
ISSN: 0193-4120 Page No. 6098-6101

A Comparative Analysis of Microneedle Design for Transdermal Drug Delivery in Biomedical Applications

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Article Info
Volume 83
Page Number: 6098 - 6101
Publication Issue:
May - June 2020

Article History
Article Received: *19 November 2019*
Revised: *27 January 2020*
Accepted: *24 February 2020*
Publication: *17 May 2020*

Abstract

Transdermal drug delivery using micro-electromechanical systems is one of the promising areas in the field of biomedical applications. Among various TDD systems, drug delivery through microneedles is a novel and promising alternative to oral medications and transdermal patches. In this paper, microneedle structures and their interaction with human skin have been analyzed theoretically and through simulation using COMSOL MULTIPHYSICS version 4.2.

Keywords: *TDD, Microneedles, COMSOL Multiphysics. MEMS*

I. INTRODUCTION

Medications taken orally through pills or tablets are limited to poor absorption and gastrointestinal effects. Hypodermic needles or injections are the alternative to oral administration but has certain limitations that include pain, possible infection, and expertise required for delivery.

he tissue damage and infection during a needle insertion and needle breakage are the major issues related to hypodermic needles.Transdermal drug delivery has been developed to administer the drug delivery in a controlled and painless manner. Many studies have been done in methods like chemical enhancers, electric fields, ultrasound, and thermal methods, but hardly have made any impressiveimpact on medical practiceto date. Transdermal drug delivery is one of the major current research areas and among all systems drug deliveryby using **MICRONEEDLES** is the most promising alternative in the domain.

II. LITERATURE REVIEW

In the recent review of various researches, silicon based microneedles for Transdermal drug delivery has been widely used. These include hollow out-of-plane solid microneedles, with cylindrical or pyramidal shapes and of various micrometer dimensions. Fabrication processes that have been used extensively are ICP etching, DRIE, thin film deposition, surface micromachining, laser micromachining etc. Few researches have been done on SiO2 stainless steel and other metal microneedles. Among all different materials, polymer microneedles are less expensive and show better safety record. The important devices for TDD are fluid jet injectors,powder jet injectors, transdermal patches, and microneedles. As reported, thesedevices are fabricated using surface micromachining and etching techniques for dermal diphtheria and influenza vaccination.

III. STRUCTURE AND GEOMETRY

In this thesis, a unique analysis has been carried out for a specific structure of microneedle in which the microneedle conical tip is sharpened and the bottom portion is a cylindrical hollow shape with outlet at the side-walls of the microneedle conical shape. Theoretical analysis has been done to find the strength and deformation of the microneedle under stress in order to determine an optimized dimension for the design.

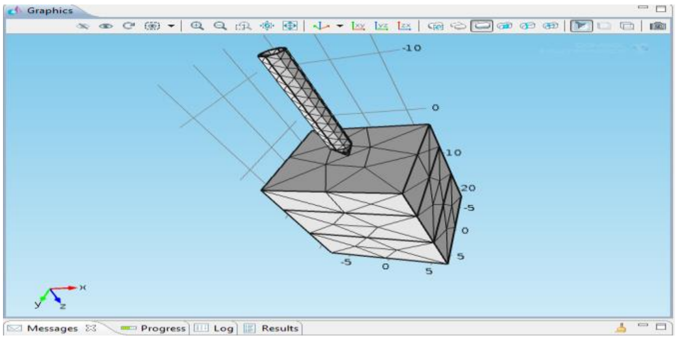

Fig 1: Tetrahedral structure of microneedle interacting with human skin

During skin insertion, there may be mechanical failure in microneedles due to bending or buckling. Mechanical failure occurs when load is greater than yield strength of the material. The geometry of the needle determines the critical loading.

$$F_{maxcompressive} = \sigma_y A$$

Where A=Area of Microneedle tip= π $(RL+rl+R^2-r^2)$

R=Outer radius of the tip, r=Inner radius if the tip

L=Outer slant height of the tip, l=Inner slant height of the tip

$$F_{skin} = P_{piercing}A\text{, where A= Area of insertion}$$

Assumptions and calculated values:-

R=2 µm, r=1 µm, L=5 µm, l=4 µm, A=53.38 µm^2

Material	Yield Strength(σ_y)	$F_{maxcompressive}$
Si	7GPa	373.66mN
SiO_2	8.4GPa	448.39mN
Si_3N_4	360MPa	19.21mN
Glass	3.6GPa	192.17mN
PMMA	120MPa	6.405mN
PLGA	46.1MPa	2.46mN

TABLE (1): Calculation of maximum compressive force

Material	Yield Strength(σ_y)	$F_{maxfreebend}$
Si	7GPa	1.7mN
SiO_2	8.4GPa	2.142mN
Si_3N_4	360MPa	0.918µN
Glass	3.6GPa	91.8 mN
PMMA	120MPa	0.0306 mN
PLGA	46.1MPa	0.117 µN

TABLE (2): Calculation of maximum free bending force

Maximum bending force experienced by the Microneedle:-

$$F_{maxfreebend} = \sigma_y (I_1 + I_2)/cL$$

Where;

$I_1 = (\pi/64)(D^4 - d^4)$, $I2=Dy^3/396$

D=outer diameter, d=inner diameter

y=length of conical section, L=length of the Microneedle

Assumptions and calculated values:-

D=50µm, d=40µm, y=103.07µm, I_1=1.81x10^{-19}m, I_2=1.38x10^{-19}m

$$F_{insertion} = F_{bending} + F_{stiffness} + F_{buckling} + F_{friction} + F_{cutting}$$

SKIN LAYER	THICKNESS(mm)	DENSITY (kg/m^3)
Stratum Corneum	0.02	1300
Epidermis	0.05	1200
Dermis	0.05	1200

TABLE (3): Mechanical properties of human skin

IV. RESULTS

Finite element analysis has been done using COMSOL Multiphysics to analyze the stress and mechanical failure due to insertion in skin.

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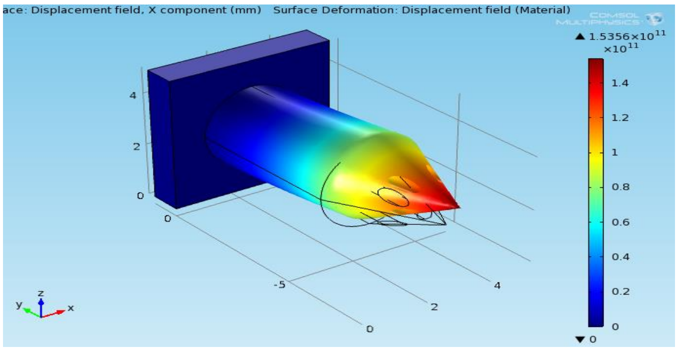

Fig 2:- Stress-displacement simulation for a single microneedle.

Force applied at the tip of the microneedle is 1N. The simulation result shows deformation of microneedle structure Von Mises effective stress has a maximum value of 153 GPa.

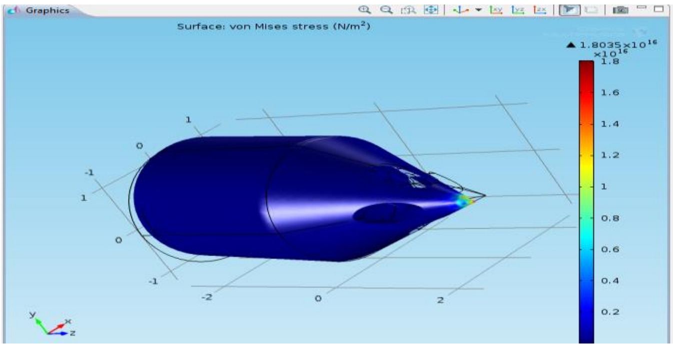

Fig 2: - Stress analysis of a single microneedle

It has been observed that the stress on the side wall is reduced.

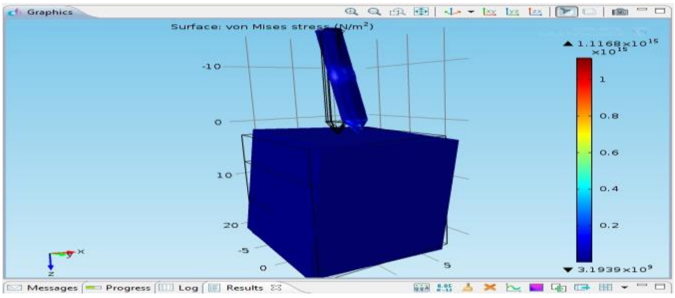

Fig 3: - Microneedle interaction with skin having Young's modulus 4.2x 10^5 N/m^2

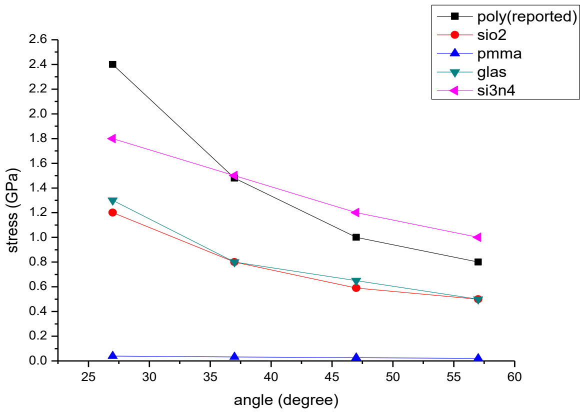

Fig 4: - Stress versus Wedge angle

From the above comparison graph it can be concluded that in every material stress decreases with increase in wedge angle. And among all the material stress is minimum in the case of polymer (PMMA).

V. DISCUSSION

A pressure of 3.183 x 10^6 Pa is axially applied at the needle tip, required to pierce the skin.After applying the theoretically calculated bending force of 1N at the tip of the microneedle, the finite element method simulation showed the maximum stress at the tip portion, which exceeded the yield strength of the material. The average stress at the bottom of the microneedle section is below 1GPa which is below the yield strength of the material.Optimized dimensions of microneedle provide sufficient mechanical strength to pierce the human skin and with minimal pain and less deformation.

VI. CONCLUSION

Microneedles that penetrate the skin barrier have the potential to deliver drugs across skin in a painless way.Controlled injection through microneedles has remained a challenge. Again biodegradable polymers may be explored as the ideal material for the design of microneedles due to its safety and low cost mass production.

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Dr. Sushanta Kumar Kamilla is a Professor in the Department of Physics, Institute of Technical Education and Research, Siksha 'O' Anusandhan (Deemed to be University), Bhubaneswar (Odisha), India. Dr. Kamilla did his Ph.D. in Materials Science & Engineering from I.I.T. Kharagpur with specialization in growth and characterizations of compound semiconductor materials. With nearly 25 years of teaching experience in both B.Tech and M.Tech level, Dr. Kamilla's research area of interest includes III-V and II-VI Magnetic Semiconductor Materials and Devices, Thin film and VLSI Fabrication Technology, Nanoscience and Nanotechnology, MEMS and Biosensor. He has been guiding several M.Tech (25 nos) and Ph.D. (12 nos) research scholars in Physics, Electronics, VLSI and Microelectronics Engineering. He has published more than 50 research papers in peer reviewed international journals of repute. He is guest editor of Advanced Science Letter (American Science Publication) and International Journal of Nano and Biomaterials (Inderscience Publication). Dr. Kamilla and his research group has filed and published 19 nos. of Indian Patents which have been indexed in Thomson and Reuter data based. Now Dr. Kamilla is taking responsibility of IPR Cell of SOA University.