



Faculty of Engineering

Micro-Needle Integrated with Micro-Pump for Drug and Blood Deliveries in Polygonal Inner Structures of Micro-Channels

Yana Shaheera binti Yunos

**Master of Engineering
2020**

Micro-Needle Integrated with Micro-Pump for Drug and Blood Deliveries in
Polygonal Inner Structures of Micro-Channels

Yana Shaheera binti Yunos

A thesis submitted

In fulfillment of the requirements for the degree of Master of Engineering

(Mechanical Engineering)

Faculty of Engineering
UNIVERSITI MALAYSIA SARAWAK

2020

DECLARATION

I, Yana Shaheera binti Yunos (15020312), Faculty of Engineering hereby declare that the work entitled Micro-Needle Integrated with Micro-Pump for Drug and Blood Deliveries in Polygonal Inner Structures of Micro-Channels is my original work. I have not copied from any other students' work or from any other sources except where due reference or acknowledgement is made explicitly in the text, nor has any part been written for me by another person. The thesis has not been accepted for any degree and is not concurrently submitted in candidate of any other degree.



.....
Signature

Name: Yana Shaheera binti Yunos

Matric No.: 15020312

Faculty of Engineering

Universiti Malaysia Sarawak

Date : 15 June 2020

DEDICATION

Specially dedicated to

My beloved parents, Yunus bin Aili and Suriany binti Mohd Yusof, and the only sibling I have, Yazeed Shazeril who have encouraged and keep supporting me through the journey in master's education.

ACKNOWLEDGEMENT

First and foremost, I thank Allah and both of my parents, Mr. Yunus bin Aili and Mrs. Lily Suriyani binti Mohd. Yusof for continuously giving me strength and supports to finish up my thesis and undergo my Master of Engineering. Not to be forgotten, I would like to take this opportunity to express my deep gratitude to my supervisor, Ir. Dr. Mohd Danial Bin Dato' Dr. Haji Ibrahim, for his patience, advices, supervision, guidance and continuous support throughout my research project.

I would also like to thank to my exchange programme supervisor, Assoc. Prof. Dr. Nobuo Watanabe, who were involved in the experimental validation of this research project and Mr. Miyagi, who helped me for the construction of the experimental setup during my stay at Shibaura Institute of Technology, Japan. Without his supervision and passionate participation, the validation research work could not have been successfully conducted. I would also like to thank to my co-supervisor Prof. Ir. Dr. Andrew Ragai Henry Rigit for his advice and support throughout the research.

Special thanks to Siti Nur Azizah binti Amran for helping me together in conducting the experiment, Norliza binti Marusman to stay all night long at laboratory to accompany me, labmates, Mohd Rahmat bin A Rahman, Wong Lee Kwang and Muhammad Zaidi bin Mohtar and friends including juniors of the lab members. Finally, I would like to thanks to those who have contributed to the completion of my project directly or indirectly.

ABSTRACT

Blood is a complex suspension that demonstrates non-Newtonian rheological characteristics. The study of hemorheology has been of great interest in the fields of biomedical engineering and medical researches for many years. Micro-channel such as micro-needle has been an expanding medical technology in recent years due to their ability to penetrate tissue and deliver therapy with minimal invasiveness and patient discomfort. Micro-channel geometries have been used to study the inertial insertion focusing on behaviour of particles suspended as variations in design. The studies have enhanced fluid delivery in biomedical field. This research presents a comparison on dynamic characteristics of flow velocity and pressure losses in micro-needle using numerical and experimental analysis. The advancement of research is also conducted by integrating the micro-needles with micro-pump to improve their functions during fluid deliveries. The micro-needles with channel inner design of circle, square, hexagon and dodecagon came with various design parameters. These geometry studies had improved the flow performance and the efficiencies in delivering drug and blood using polygonal structured micro-needles.

Keywords: Micro-needle, micro-pump, polygonal, fluid delivery

Jarum Mikro Bersepadu dengan Pam Mikro untuk Penghantaran Dadah dan Darah dalam Saluran Mikro Berstrukturkan Poligon

ABSTRAK

Darah adalah satu unsur yang kompleks untuk menunjukkan karakter-karakter bukan Newtonian. Pembelajaran tentang reologi darah telah memberi impak yang besar dalam kejuruteraan bioperubatan bertahun lamanya. Salah satu contoh saluran mikro yang telah lama berkembang dalam bidang teknologi perubatan adalah jarum mikro yang faktor utamanya adalah mampu menembusi tisu-tisu dan menghantar terapi dengan kesakitan yang minimum dan mengurangkan ketidakselesaan pesakit. Geometri saluran mikro telah lama digunakan untuk mengkaji perilaku dalaman zarah yang mengalir dalam variasi rekabentuk. Pembelajaran ini telah meningkatkan penghantaran cecair dalam bidang bioperubatan. Penyelidikan ini mengemukakan perbandingan di antara ciri-ciri dinamik terhadap halaju pengaliran dan kehilangan tekanan dalam saluran mikro menggunakan analisis berangka dan eksperimen. Kemajuan di dalam penyelidikan ini juga dikendalikan dengan menyepadukan jarum mikro dengan pam mikro untuk meningkatkan lagi fungsi semasa penghantaran cecair. Jarum mikro dengan saluran dalaman berbentuk bulat, empat segi, heksagon dan dodekagon, didatangkan dengan reka bentuk parameter yang lain. Pembelajaran geometri ini telah meningkatkan prestasi halaju dan keberkesanan dalam penghantaran ubat cecair dan darah dengan menggunakan jarum mikro dengan berstrukturkan poligon.

Kata kunci: Jarum mikro, pam mikro, poligon, penghantaran cecair

TABLE OF CONTENTS

	Page
DECLARATION	i
DEDICATION	ii
ACKNOWLEDGEMENT	iii
ABSTRACT	iv
<i>ABSTRAK</i>	v
TABLE OF CONTENTS	vi
LIST OF TABLES	x
LIST OF FIGURES	xiv
LIST OF ABBREVIATIONS	xviii
CHAPTER 1: INTRODUCTION / LITERATURE REVIEW	1
1.1 Background of Research	1
1.2 Problem Statement	1
1.3 Aims of Research	2
1.4 Objectives	2
1.5 Scope of Research	3
1.6 Micro-needle Developments	3
1.6.1 Anatomy of Mosquito's Fascicle	3
1.6.2 Stratum Corneum of Human Skin	5
1.6.3 Micro-needle Application in Drug Delivery	7
1.7 Expansions of Micro-pump	8
1.7.1 Introduction to Micro-pump	8
1.7.2 Application of Piezoelectric Micro-pump in Medical Field	10
1.8 Integration of Micro-pump with Micro-needle	10

1.8.1	Application in Medical Field	10
1.9	Fundamentals of Microfluidic	11
1.10	Blood Rheology	13
1.10.1	Viscosity of Blood	13
1.11	Fluid-Wall Interaction	14
CHAPTER 2: MATERIALS AND METHODS		16
2.1	Research Methodology	16
2.2	Numerical Study	17
2.2.1	Micro-needle Designs	17
2.2.2	Micro-pump Design	18
2.2.3	Material Selections & Design Parameters	20
2.3	Setup of Simulation Study	23
2.3.1	Modelling in ANSYS®	23
2.3.1.1	Geometry	24
2.3.1.2	Mesh	25
2.3.1.3	Fluent	27
2.3.1.4	Results	29
2.4	Experimental Study	30
2.4.1	Experimental Apparatus Setup	31
2.4.2	Design of Experiments	36
2.4.2.1	Vertical Micro-channel Design of Experiment	37
2.4.2.2	Horizontal Micro-channel Design of Experiment	38
CHAPTER 3: RESULTS		40
3.1	Numerical Simulations on Micro-pump	40

3.1.1	Diaphragm Movement at 0.04m/s	40
3.1.2	Diaphragm Movement at 0.08 m/s	45
3.2	Numerical Simulations on Micro-needles	49
3.2.1	Velocity Profiles	49
3.2.1.1	Drug Flow Results	49
3.2.1.2	Blood Flow Results	59
3.2.2	Pressure Differences	69
3.2.2.1	Drug Flow Results	69
3.2.2.2	Blood Flow Results	79
3.3	Experimental Results	89
3.3.1	Drug Flow Results-30ml/min	89
3.3.2	Glycerin-based Solution as Blood Flow Results-30ml/min	91
3.3.3	Glycerin-based Solution as Blood Flow Results-35ml/min	93
CHAPTER 4: DISCUSSION		96
4.1	Numerical Simulations on Micro-needles	96
4.1.1	Summary on Drug Flow Results	96
4.1.2	Summary on Blood Flow Results	99
4.1.3	Discussions on Flow Results	102
4.1.4	Analysis of Drug Delivery Flow	104
4.1.5	Analysis of Blood Delivery Flow	107
4.1.6	Discussions on Results Analysis	109
4.2	Numerical Simulations on Micro-needle Integrated with Micro-pump	113
4.2.1	Drug Flow Results	113
4.2.1.1	Diaphragm Movement at 0.04m/s	113
4.2.1.2	Diaphragm Movement at 0.08m/s	114

4.2.2	Blood Flow Results	116
4.2.2.1	Diaphragm Movement at 0.04m/s	116
4.2.2.2	Diaphragm Movement at 0.08m/s	117
4.2.3	Discussions on Result Analysis	118
4.3	Experimental Validation Results	119
4.3.1	Pressure Losses for Drug Delivery	119
4.3.2	Pressure Losses for Glycerin-based Solution as Blood Delivery	120
4.4	Comparison on Simulation and Experimental Data	121
4.4.1	Drug Delivery	121
4.4.2	Blood Delivery	122
CHAPTER 5: CONCLUSION AND RECOMMENDATION		124
5.1	Conclusion	124
5.2	Recommendation	125
REFERENCES		126
APPENDICES		133

LIST OF TABLES

	Page	
Table 2.1	Properties of materials	20
Table 2.2	Initial values of calculations for inlet of micro-pump	20
Table 2.3	Parameters of fluids used in numerical simulation	23
Table 2.4	Meshing size	25
Table 2.5	Simulation meshed domain	26
Table 2.6	Materials used in simulation	28
Table 2.7	Experiment's parameters	31
Table 3.1	Drug flow results pumped at 0.04 m/s	42
Table 3.2	Blood flow results pumped at 0.04 m/s	43
Table 3.3	Blood flow results pumped at 0.04 m/s	44
Table 3.4	Drug flow results pumped at 0.08 m/s	46
Table 3.5	Blood flow results pumped at 0.08 m/s	47
Table 3.6	Blood flow results pumped at 0.08 m/s	48
Table 3.7	Drug flow results for circular design using polysilicon	51
Table 3.8	Drug flow results for circular design using titanium	52
Table 3.9	Drug flow results for square design using polysilicon	53
Table 3.10	Drug flow results for square design using titanium	54
Table 3.11	Drug flow results for hexagon design using polysilicon	55
Table 3.12	Drug flow results for hexagon design using titanium	56
Table 3.13	Drug flow results for dodecagon design using polysilicon	57
Table 3.14	Drug flow results for dodecagon using titanium	58
Table 3.15	Blood flow results for circular design using polysilicon	61

Table 3.16	Blood flow results for circular design using titanium	62
Table 3.17	Blood flow results for square design using polysilicon	63
Table 3.18	Blood flow results for square design using titanium	64
Table 3.19	Blood flow results for hexagon design using polysilicon	65
Table 3.20	Blood flow results for hexagon design using titanium	66
Table 3.21	Blood flow results for dodecagon design using polysilicon	67
Table 3.22	Blood flow results for dodecagon design using titanium	68
Table 3.23	Drug pressure differences results for circular design using polysilicon	71
Table 3.24	Drug pressure differences results for circular design using titanium	72
Table 3.25	Drug pressure differences results for square design using polysilicon	73
Table 3.26	Drug pressure differences results for square design using titanium	74
Table 3.27	Drug pressure differences results for hexagon design using polysilicon	75
Table 3.28	Drug pressure differences results for hexagon design using titanium	76
Table 3.29	Drug pressure differences results for dodecagon design using polysilicon	77
Table 3.30	Drug pressure differences results for dodecagon design using titanium	78
Table 3.31	Blood pressure differences results for circular design using polysilicon	81
Table 3.32	Blood pressure differences results for circular design using titanium	82
Table 3.33	Blood pressure differences results for square design using polysilicon	83

Table 3.34	Blood pressure differences results for square design using titanium	84
Table 3.35	Blood pressure differences results for hexagon design using polysilicon	85
Table 3.36	Blood pressure differences results for hexagon design using titanium	86
Table 3.37	Blood pressure differences results for dodecagon design using polysilicon	87
Table 3.38	Blood pressure differences results for dodecagon design using titanium	88
Table 3.39	Pressure losses reading for circle micro-channel	90
Table 3.40	Pressure losses reading for square micro-channel	90
Table 3.41	Pressure losses reading for hexagon micro-channel	91
Table 3.42	Pressure losses reading for dodecagon micro-channel	91
Table 3.43	Pressure losses reading for circle micro-channel	92
Table 3.44	Pressure losses reading for square micro-channel	92
Table 3.45	Pressure losses reading for hexagon micro-channel	93
Table 3.46	Pressure losses reading for dodecagon micro-channel	93
Table 3.47	Pressure losses reading for circle micro-channel	94
Table 3.48	Pressure losses reading for square micro-channel	94
Table 3.49	Pressure losses reading for hexagon micro-channel	94
Table 3.50	Pressure losses reading for dodecagon micro-channel	95
Table 4.1	Results for circle design of micro-needle	96
Table 4.2	Results for square design of micro-needle	96
Table 4.3	Results for hexagon design of micro-needle	97

Table 4.4	Results for dodecagon design of micro-needle	97
Table 4.5	Summary results of micro-needle design	98
Table 4.6	Results for circle design of micro-needle	99
Table 4.7	Results for square design of micro-needle	99
Table 4.8	Results for hexagon design of micro-needle	100
Table 4.9	Results for dodecagon design of micro-needle	100
Table 4.10	Summary results of micro-needle design	101
Table 4.11	Summary of drug flow analysis of 0.1 mm micro-needle	104
Table 4.12	Summary of drug flow analysis of 0.15 mm micro-needle	105
Table 4.13	Summary of blood flow analysis of 0.1 mm micro-needle	107
Table 4.14	Summary of blood flow analysis of 0.15 mm micro-needle	108
Table 4.15	Drug flow results when pumped at 0.04 m/s	113
Table 4.16	Analysis on performance for drug flow results when pumped at 0.04 m/s	114
Table 4.17	Drug flow results when pumped at 0.08 m/s	115
Table 4.18	Analysis on performance for drug flow results when pumped at 0.08 m/s	115
Table 4.19	Blood flow results when pumped at 0.04 m/s	116
Table 4.20	Analysis on performance for blood flow results when pumped at 0.04 m/s	117
Table 4.21	Blood flow results when pumped at 0.08 m/s	117
Table 4.22	Analysis on performance for blood flow results when pumped at 0.08 m/s	118

LIST OF FIGURES

		Page
Figure 1.1	Mosquito's proboscis	4
Figure 1.2	Mosquito's fascicle tip	5
Figure 1.3	Thickness of human skin	6
Figure 1.4	Micro-pump chip	9
Figure 1.5	Piezoelectric working chamber	9
Figure 1.6	Viscosity of blood	14
Figure 2.1	Quadrupletip micro-needles	18
Figure 2.2	Polygonal inner micro-channels	18
Figure 2.3	TCS Micropump Ltd. micro-pump design	19
Figure 2.4	Micro-pump designs	19
Figure 2.5	Summary of model build up	24
Figure 2.6	Dimension setting	25
Figure 2.7	Drawing in design modeler	25
Figure 2.8	Meshed models	26
Figure 2.9	Number of elements in meshed models	27
Figure 2.10	Fluent launcher	27
Figure 2.11	Simulation setting	28
Figure 2.12	Material of diaphragm of micro-pump	28
Figure 2.13	Setting for diaphragm of micro-pump	29
Figure 2.14	Value of inlet	29
Figure 2.15	Value of outlet	29
Figure 2.16	Number of iterations applied in simulations	29

Figure 2.17	Result vectors	30
Figure 2.18	Simulations for one setting parameters	30
Figure 2.19	Circular rod	32
Figure 2.20	Hexagon rod	32
Figure 2.21	Dodecagon rod	32
Figure 2.22	NC machine	32
Figure 2.23	Square rod	32
Figure 2.24	L-shaped wall	33
Figure 2.25	Acrylic wall	33
Figure 2.26	Silicone used in experimental setup	34
Figure 2.27	Hardener used in experimental setup	34
Figure 2.28	Chamber connected to suction pump	34
Figure 2.29	Silicon molds	34
Figure 2.30	Bending of glass tube during manometer setup	35
Figure 2.31	Attaching manometer	35
Figure 2.32	Mercury used in experimental setup	35
Figure 2.33	Manometer set up	35
Figure 2.34	User manual of twin syringe pumps	36
Figure 2.35	Setting of twin syringe pumps	36
Figure 2.36	Vertical micro-channel design concepts	37
Figure 2.37	Trial designs of experiment	38
Figure 2.38	Location of manometer	38
Figure 2.39	Horizontal micro-channel design concepts	38
Figure 2.40	Final designs of experiment	39

Figure 3.1	Example of experimental results reading	89
Figure 4.1	Summary results of 0.1 mm diameter micro-needle	97
Figure 4.2	Summary results of 0.15 mm diameter micro-needle	98
Figure 4.3	Results comparison between 0.1 mm and 0.15 mm diameter micro-needle	98
Figure 4.4	Summary results of 0.1 mm diameter micro-needle	100
Figure 4.5	Summary results of 0.15 mm diameter micro-needle	101
Figure 4.6	Results comparison between 0.1 mm and 0.15 mm diameter micro-needle	101
Figure 4.7	Velocity versus energy losses analysis of 0.1 mm diameter micro-needle	104
Figure 4.8	Per unit area analysis of 0.1 mm diameter micro-needle	105
Figure 4.9	Velocity versus energy losses analysis of 0.15 mm diameter micro-needle	106
Figure 4.10	Per unit area analysis of 0.15 mm diameter micro-needle	106
Figure 4.11	Velocity versus energy losses analysis of 0.1 mm diameter micro-needle	107
Figure 4.12	Per unit area analysis of 0.1 mm diameter micro-needle	108
Figure 4.13	Velocity versus energy losses analysis of 0.15 mm diameter micro-needle	109
Figure 4.14	Per unit area analysis of 0.15 mm diameter micro-needle	109
Figure 4.15	Relationship of tube diameter on the relative viscosity of flowing blood	112
Figure 4.16	Relative apparent viscosity of whole blood in varying	113

	diameter	
Figure 4.17	Drug flow comparison pumped at 0.04 m/s	114
Figure 4.18	Drug flow comparison pumped at 0.08 m/s	115
Figure 4.19	Blood flow comparison pumped at 0.04 m/s	116
Figure 4.20	Blood flow comparison pumped at 0.08 m/s	117
Figure 4.21	Average pressure losses of water as drug delivery in designated micro-channel for flow rate 30 ml/min	120
Figure 4.22	Comparison on different flow rate of glycerin-based solution as blood delivery	121
Figure 4.23	Comparison on simulation and experimental results for drug delivery at 30 ml/min	122
Figure 4.24	Comparison on simulation and experimental results for blood delivery at 30 ml/min	123
Figure 4.25	Comparison on simulation and experimental results for blood delivery at 35 ml/min	123

LIST OF ABBREVIATIONS

AC	Alternate Current
cm	Centimeter
CAD	Computer-Aided Design
CFD	Computational Fluid Dynamics
E_L	Energy Losses in Micro-needle
g	Gravitational force
$k-\varepsilon$	k-epsilon
MEMS	Micro-Electro Mechanical System
mm	Millimeter
NC	Numerical Control
Pro-E	Pro-Engineering
ρ	Density of Fluid
SEM	Scanning Electron Microscope
v	Velocity of Fluid Delivery
wt %	Weightage Percentage
y	Elevation of fluid flow
μm	Micrometer
η	Dynamic Viscosity of Blood
\emptyset	Diameter of Micro-needle

CHAPTER 1

INTRODUCTION / LITERATURE REVIEW

1.1 Background of Research

Injecting drug and blood withdrawing techniques are obtained either from arteries or veins. Using hypodermic needle to penetrate human skin until it reaches the arteries or veins is surely uncomfortable and painful. From the beginning of the realization of painless needle from mosquito's mechanism of blood withdrawal, lots of research has been conducted to improve the efficiency of the micro-needles for drug delivery and blood withdrawal from various sizes of needle and designs. From hypodermic needles to the current conventional micro-needle, the advancement of the researches leads to the technologies of micro-needles. This technology is aimed at improving the flow and performance while completing the task of penetrating the human outermost skin to withdraw blood or injecting drugs into the living organisms' vessels (Khumpuang et al., 2007).

1.2 Problem Statement

The manufacturing of micro-needle is recognized in medical field for diabetic patients, but because of their limitations to deliver large amount of liquid, their usage is restricted to infuse insulin only. Micro-needle patches are bound for small volume of insulin delivery into human skin and are convenient for patients as they must take regularly the insulin.

Due to the limitations of volume delivered, the micro-needle needs to be improved in length and diameter, so it can be attached to the syringe and deliver certain volume of drug and blood straight into the blood stream. Conventional micro-needle only passes the human skin barrier, stratum corneum for the drug to be diffused into human body. This is also the reason why the micro-needle needs to increase the length so that blood and other drug which contains more molecules inserted into the vessels, while keeping the velocity constant during the delivery.

Increasing the length of micro-needle is a better option to deliver it direct to vessel and attaching micro-pump can increase velocity of the fluid. Thus, a larger volume of fluid can be delivered while keeping micro-needle in micron size.

1.3 Aims of Research

This research would be able to assist the practicing engineer to increase and improve the design of micro-needle integrated to a micro-pump to achieve better flow performance in drug and blood delivery into human body effectively and efficiently. Thus, by doing so, our medical industry on designing and manufacturing medical appliances can be improved.

1.4 Objectives

The objectives of the study are:

- i. to evaluate and predict average velocity in micro-needle when micro-pump is attached

- ii. to investigate and compare the flow pattern in both numerical and experimental results
- iii. to improve flow dynamic and static characteristics of drug and blood delivery
- iv. to evaluate the energy losses in micro-channels during delivery
- v. to investigate and compare the inverse area dynamic profiles in micro needles during delivery

1.5 Scope of Research

To comply with the objectives, there are several considerations and constraints that need to be considered. They are:

- i. using human blood is prohibited in experiments
- ii. velocity inlet for drug delivery is based on calculation using the Bernoulli's equation
- iii. velocity inlet for blood delivery is based on laminar inflow of blood flow
- iv. micro-pump's diaphragm movement is converted from the specification of lowest and highest micro-pump flow rate value.

1.6 Micro-needle Developments

1.6.1 Anatomy of Mosquito's Fascicle

Only female mosquitos feed on human blood to obtain the protein needed for their eggs production. They feed via a tubular component of their mouth which is called proboscis. The proboscis itself consists of labium and fascicle. Labium acts as protective sheath while

the fascicle, which is mandibles (thin tube), maxilla with tooth of saw tips and flat hypopharynx with a central salivary duct, provides a primary path that channels the blood flow (Jones, 1978). The fascicle of *Aedes Aegypti* is commonly 1.8 mm long and 11 μm in internal radius (Daniel et al., 1983). The itching effect produced after biting human skin is due to the allergic reaction of the mosquito's saliva as they secrete during the blood sucking process to prevent the platelet to aggregate (Ribeiro et al., 1984). Figure 1.1 shows a SEM (Scanning Electron Microscope) picture of mosquito's proboscis (Swaminathan, 2006).

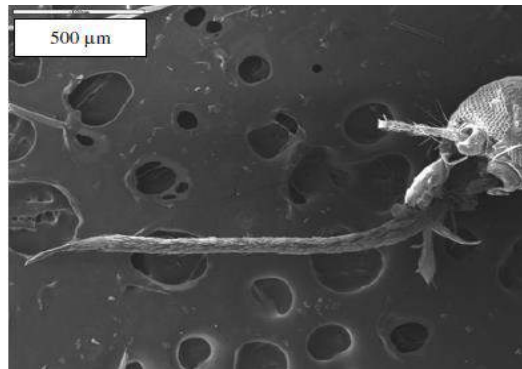


Figure 1.1: Mosquito's proboscis (Swaminathan, 2006)

Once mosquito landed on its host, they start thrusting their proboscis onto the human skin. To find suitable spot so that the proboscis can penetrate the skin without bending, they probe other spot as the fascicle tip anchors down the outermost layer of skin (Ramasubramaniam et al., 2008). The tip of the fascicle is very sharp that it is claimed to taper from 10 μm to less than 1 μm over the last 50 μm of the fascicle and the v-shaped of the tip ridged near the tip almost to 50 μm in length (Wick et al., 1984).

The basic of developing and designing a painless needle will be based on the typical hypodermic needle's tip used and mosquito's fascicle tip shape. The mosquito