Synopsis

Name of the candidate: **Vinaya Kumar K B**

S.R.No.: 01-02-00-10-12-11-1-08811

Degree registered: **Ph.D**

Thesis title: **Design, Development and Performance Study of Microneedle and Micropump-based Transdermal Drug Delivery System**

Research Supervisors: **Prof. K. Rajanna and Prof. N. S. Dinesh**

Transdermal drug delivery is the most preferred drug delivery method, due to its high efficiency and less side effects. In conventional transdermal drug delivery, the delivery of macromolecular drugs (ex: Insulin, vaccines etc.) is limited by skin barrier. Several possible approaches have been proposed to overcome this limitation (chemical, electrical, ultrasound, microneedle etc.). Among these, the microneedle approach is considered as one of the best method to improve the effective delivery of drug. These microneedles penetrate into the outermost skin layers namely stratum corneum and epidermis. The thickness of the above mentioned skin layers will impose the constraints on the design of microneedle for the successful delivery of drug. On the other hand, along with the microneedle, the micropump is one more important functional module essential for a continuous drug delivery application such as insulin delivery for diabetic patients.

The aim of the present work is to improve the transdermal drug delivery using microneedle and micropump technology. Details on the fabrication, evaluation of both solid and hollow microneedle structures have been presented. Issues such as penetration reliability, liquid delivery into the skin and microneedle packaging are also discussed. Peristaltic micropump was developed to achieve a controlled flow of drug through the microneedle array. The developed micropump was successfully characterized to meet the typical drug delivery pump requirements such as: fail-safe mechanisms, adequate delivery of drug against blood pressure, ease of tubing and flow control over wide range. The micropump was integrated with necessary electronics and characterized for the complete drug delivery operation. Finally, the microneedle and micropump

-based system was tested and studied *in vivo* for insulin delivery. Results obtained were compared with the standard subcutaneous delivery with the same dose rate and found that they are in good agreement. The thesis is divided into seven chapters.

Chapter 1

The present chapter discusses a general brief introduction along with literature survey about microneedle and micropump for drug delivery applications. Information on fabrication of the microneedle array using different methods and their characterization to improve the transdermal drug delivery has been discussed. It also includes the information on the usage of micropump in drug delivery application.

Chapter 2

This chapter discusses the design, fabrication and characterization of cup shaped solid silicon microneedle array for leak proof drug delivery application. The mechanical stability of the fabricated microneedle to insert into the skin has been studied. The drug filled cup shaped microneedles were inserted into mice skin and drug dissolution was confirmed using fluorescence imaging technique.

Chapter 3

In this chapter, details on the fabrication of out-of-plane Si microneedle array using both isotropic and anisotropic etching processes has been presented. The fabricated microneedles were coated with Ti by sputtering and Au by electroplating method to make it suitable for implantable bio-devices. The mechanical failure mechanism of the microneedles was experimented using the in-house developed experimental setup. Fluid flow through the microneedle array was studied for different inlet pressures.

Chapter 4

Development of a tapered hollow stainless steel microneedle array using femto second laser machining process has been presented in this chapter. The mechanical stability of the fabricated microneedle array was studied for axial and transverse loading. The skin histology was carried out to study the microneedle penetration into the rat skin. Fluid flow through the

microneedle array was studied for different inlet pressures. Information on the packaging of the microneedle array to protect the microneedle bore blockage from dust and other atmospheric contamination has also been included.

Chapter 5

This chapter reports on the design, development, testing and precision flow controlling of the peristaltic pump. A geared DC-motor was used to drive the fluid filled silicone tube to achieve the squeezing action. Variation of the flow rate due to different back pressures has been studied. The fail-safe property of the developed pump showed a low leak rate of ~ 0.14 % for a maximum inlet pressure of 140 kPa. Finally, the precision flow controlling was achieved by close-loop controlling of the DC motor driven peristaltic pump.

Chapter 6

This chapter discusses the integration of important sub-systems (microneedle, micropump and necessary electronics) for the minimally invasive, continuous and precision insulin delivery system. Using this microneedle and micropump-based system, successfully delivered insulin into a diabetic rat. The results obtained were comparable with the subcutaneous delivery of insulin with the same dose rate.

Chapter 7

In this chapter, the first section summarizes the salient features of the work presented in this thesis. The last section reports a scope for carrying out further work.