CREATION OF SMART WEARABLE TEXTILE-BASED DRUG DELIVERY SYSTEM WITH THE USE OF HOLLOW FIBERS FOR HEALTHCARE AND MEDICATION

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Creation of Smart Wearable Textile-based Drug Delivery System with the Use of Hollow Fibers for Healthcare and Medication

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A thesis submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy

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CERTIFICATE OF ORIGINALITY

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ABSTRACT

Fiber technology has played an essential role in the textile industry for making life easier and more convenient. Numerous textile problems can hence be solved and different functions can be promoted. However, overcapacity of the industrial fibers has become a controversial issue due to the vigorous development of textiles and technology. Thus, the combination of traditional textile knowledge and innovated technology would be an upward trend for research and development. This is believed to solve the problems of overcapacity and to supplement creativity into industrialization in the meanwhile.

This research is crucial to develop a wearable textile-based drug delivery system for the ease of life and healthcare, in terms of hollow fibers. With the hybridization of medicine and textile technology, a long-term wearable, applicable and transdermal drug delivery system with the advantages of precise and controllable rate is being developed. The system is implemented through loading compound drugs (either chemical or herbal medicines) into the hollow fibers which could be made for different types of fabrications such as by weaving, knitting, felting, laminating and embroidery. Subsequently, the release rate of drugs from the hollows would be further controlled or catalyzed with the application of the thermal-stimuli textile-based drug delivery system. As a result, healthcare and medication could be offered by this transdermal system after a series of instrumental and pre-clinical experiments.

Hollow fiber is acknowledged to be a remarkable drug carrier for the system. It was found that the industrial hollow fibers and their fabrications had positive achievements towards drug loading and release. In accordance with the research findings, compound

drugs, either in form of liquid or crystal solid, could be loaded inside the hollows of fibers by vacuum under negative pressure. Significant medical performances, which were the anti-bacteria and anti-breast cancer abilities, were achieved by the drug delivery approach from the antibiotic-loaded and anticancer drugs-loaded hollow fibers respectively. Different heating geometric distributions were observed by capturing the infra-red thermography of the combination of thermal e-fabric and drug delivery layers. The highest thermal energy level were given at the central spot while the heat energy decreased gradually at the quadrilateral and the peripheral areas. Higher significance in promoting the release of encapsulated drugs or liquid at higher temperature was resulted from both biological cell test and physical test of visible absorbance. No obvious burst release of liquid was found at the beginning stage of delivery. A self-care textile wearable for breast cancer post-surgical care and therapy (i.e. a bra for females and a sweatshirt / pullover for males) was designed. Staple hollow fibers – yarns with different twist levels and the woven fabrics with different constructions were prototyped. Hollow fibers were extracted from the yarns for further observation. Successful liquid loading and transportation was resulted from the extracted hollow fibers.

This research has given a new way of thinking towards the excavation of novel ideas from traditional textile materials. It is believed to be a meaningful breakthrough of developing an environmentally-friendly, convenient, repeatable and wearable textile-based drug delivery system by using industrial hollow fibers. Public convenience for medication could be unfolded and the wastage resulted from over production could also be minimized by giving the traditional fibers a ‘second life’ with new medical function.

PUBLICATIONS

Refereed Journal Publications

1. **Cheung, T. W.**, Luo, X. and Li, L*.

   'Functional design of traditional hollow fibers: opening up a second life of being a medical drug delivery carrier', Textile Research Journal. DOI: 10.1177/0040517517723023. (First Published July 28, 2017).

2. **Cheung, T. W.** and Li, L*.

   'A review of hollow fibers in application-based learning: from textiles to medical', Textile Research Journal. DOI: 10.1177/0040517517741164. (First Published November 21, 2017).

3. **Cheung, T. W.**, Yang, C. and Li, L*.

   'An Integrated Design of Self-care Textile Wearables: Exploration of Thermal-stimuli Effects and Drug Delivery Function', Textile Research Journal. DOI: 10.1177/0040517518797339. (First Published September 3, 2018).

Refereed Conferences

1. **Cheung, T. W.** and Li, L*.

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CHAPTER 1

INTRODUCTION

1.1 Background of Study

In the era of rapid technological development, advanced textile technology has been placed in a focal position in various areas. Fiber technology was found to solve a great deal amount of existing difficulties in the modern society. Numerous research studies have been done towards the textile and material technology in the applications of medical domain. Hollow fibers, which are provided with superior structural and morphological benefits, have become one of the most promising fibers in the medical and healthcare applications.

Hollow fibers have been extensively utilized as an essential component in making medical devices such as for kidney and liver dialysis, cell culturing and drug screening. Because of their exceptional characteristics like high loading capacity of inner channel and high surface-area-to-volume ratio, hollow fibers had been investigated as significant drug carriers for medical therapies such as treating vaginal bacteria and periodontal disease with the corresponding antimicrobial agent-loaded hollow fibers. Many scaffolds and wound dressings had also been made of the drug releasing hollow fibers for wound healing and relieving.

It was considered that the drug delivery system by utilizing hollow fibers consists of two major processes, drug loading into the inner hollow and drug releasing from the hollow to the target site of action through human's skin or inside the body. Drugs can be loaded into the hollow of fibers through the two ends by injection or vacuum suction

at which the drugs can flow along the fibers through capillary action. Drugs can also be loaded by dissolving in the liquid polymer during electrospinning. For the drug releasing process, it is thought to be released from the interior channel of the fibers to the outside area by diffusion.

Nevertheless, there are still some challenges of the conventional hollow fiber - drug delivery system. Some of the medical apparatus with the utilization of drug releasing hollow fibers may require sophisticated production and chemical processes. For examples, forming the encapsulated drug-loaded particles or dissolving drugs with the electrospinning liquid solvent were needed. Moreover, repeated drug loading within the system and loading compound drugs may not be guaranteed as well. Regarding to the vitalization of textile industry, overcapacity of industrial fibers is an important factor of causing surplus and wastage. It is considered to bring about some new approaches of giving the over-produced fibers a ‘brand new life’ in order to be in line with globalization on sustainable development.

By the reasons of the promising features of hollow fibers, the challenges of former drug delivery system and the overcapacity of industrial fibers, it is essential to develop an environmentally-friendly, convenient, repeatable and wearable hollow fiber - drug delivery medical system for sustainable development by reassigning a new medical function (i.e. drug delivery) of the ready-made hollow fibers. The implementation of this system is believed to bring considerable advantages to both textile science and medical care industries. Convenient public use of the system could be conserved and the matter of wastage from over production could also be minimized.

The proposed project was mainly divided into three parts, 1) a pilot study of textile-based drug delivery system by using industrial hollow fibers with anti-bacterial and anti-cancer applications; 2) an advanced study of wearable hollow fiber - drug delivery system with thermal stimulation technology; 3) an integrated design approach of the self-care textile wearable with thermal-stimuli drug delivery function by using hollow fibers.

In this project, a pilot study was firstly conducted for opening up an advanced drug loading and releasing function of the industrial , ready-made hollow fibers so as to give them a 'second life'. The drug loading capability of these hollow fibers was investigated with the use of woven fabrics (i.e. half of the yarns were made of the hollow fibers) via the process of drug loading under negative pressure (i.e. vacuum). The effectiveness of the drug delivery system were examined through the antibacterial performance of the drug-loaded fabrics and the drug release kinetics of the hollow fibers. Another pilot study was performed by investigating the ability of suppressing the growth and proliferation of breast cancer cells with the application of hollow fibers and its fabricated nonwovens. After performing the pilot study, an advanced study on the significance of controlling or catalyzing the rate of drug release by the system with the combination of thermal stimulation technology was conducted. Two layers, which are the drug delivery layer (i.e. non-woven fabric) and the thermal conductive e-fabric layer (i.e. it is embroidered with silver-coated conductive yarns), were made for studying the thermal distribution influenced by different levels of temperature. Hereafter, an integrated self-care textile wearable with thermal-stimuli drug delivery function was designed. Prototype investigation of staple hollow fibers – yarns and the woven fabrics were conducted. Subsequent biological trials will be conducted in the future.

The proposed system is believed to offer significant benefits to patients and to provide a fundamental basis of an enduring development of wearable smart textiles in different medical aspects for a variety of therapeutic applications. Thereupon, the market demand of having a simple, convenient, repeatable and wearable textile drug delivery system for treating different kinds of illnesses or bacterial infections could be satisfied. It is also forecasted that functional smart textiles would keep on develop constantly and vigorously from now onwards.

1.2 Research Objectives

This project aims to focus on developing a wearable textile-based drug delivery system by using hollow fibers, investigating the feasibility of the drug delivery performance of the industrial hollow fibers and also the possibility of the system by combining with thermal stimulation technology for healthcare and medication.

(a) To study the physical properties, structure, morphology, characteristics and the general medical and healthcare applications of hollow fibers.
(b) To study and optimize the methods of loading drugs into the channels of hollow fibers and the mechanisms of drug loading and releasing.
(c) To study the drug loading performance via physical experimentation of the project-aimed hollow fibers.
(d) To study the drug release performance and the functional medical performance via biological experimentation of the project-aimed hollow fibers.
(e) To study the thermal sensitive and self-heating feasibilities of the project-aimed hollow fibers with the combination of thermal-stimuli technology.

1.3 Methodology

The methodology approach was begun with literature review and background study on the properties, the hollow structures and the characteristics of hollow fibers. Then, the current medical applications with the uses of textiles and hollow fibers were also discussed. Then, physical testing and characterization of the project-aimed hollow fibers were conducted. Drug loading methods were investigated and the suitable one was chosen for subsequent studies. Hollow fibers were fabricated in order to excavate the possibilities of the wearable textile-based drug delivery system. Evaluation of the functional medical performance and design was performed with biological experimentations. The effectiveness of the textile-based drug delivery system with controllable dose or at a catalyzed rate was investigated with the integration of thermal stimulation technology. An integrated self-care textile wearable with thermal-stimuli drug delivery function was designed. Staple hollow fibers – yarns and the nonwovens made of these yarns were prototyped. After the successfulness of the pilot and advanced studies, prototype development and a collection of the wearable textile-based drug delivery apparel system would be done in the future. The route of the methodological approach was shown in Figure 1-1.

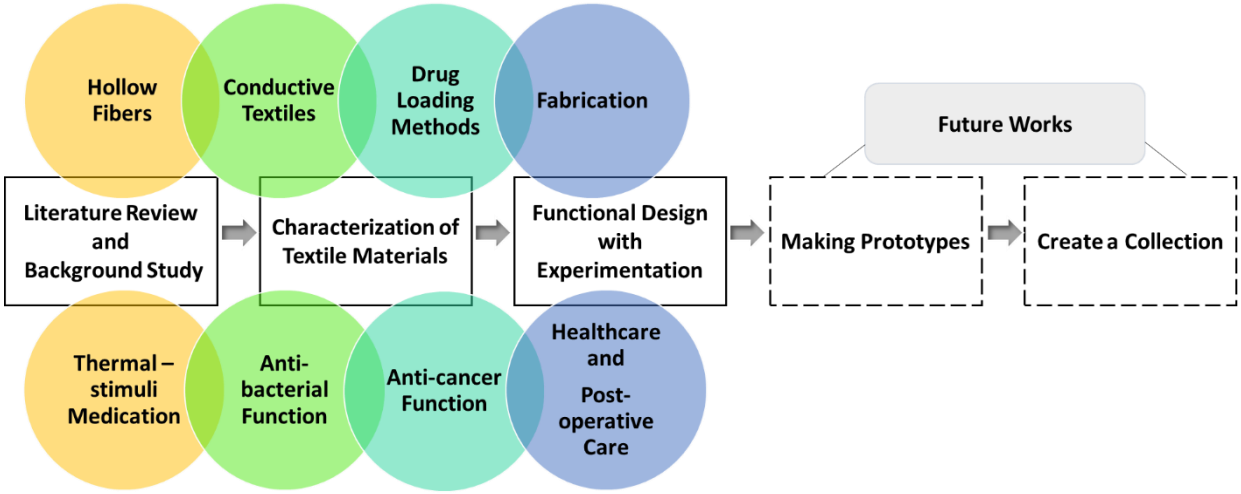


Figure 1-1 Systematic Approach of the Research Methodology.

1.4 Outline of Thesis

In chapter 1, the overview of background, objectives, scope of study and research significance and values for implementing the functional, thermal-stimuli, therapeutic and textile-based drug delivery system by using industrial, ready-made hollow fibers were introduced.

In chapter 2, literature review on the contents of the development of hollow fibers, the significance of hollow fibers in the medical and healthcare field, the mechanisms of drug delivery of hollow fibers and the applications of hollow fibers in medical devices, were studied. The importance and positive impacts for applying the hollow fiber drug delivery system in this project were also demonstrated in this chapter via reviewing corresponding literatures.

In chapter 3, the systematic approach of methodology throughout the research, division of experimentation (i.e. primary, secondary and tertiary levels of study), experimental details and the procedures, summary of thesis and limitations of research were

presented.

In chapter 4, the experimental details and the procedures of the pilot study of textile-based drug delivery system by using hollow fibers were outlined. Results and the corresponding discussions of the physical and biological investigations were also made in this chapter.

In chapter 5, the experimental details and the procedures of the pilot study of hollow fiber - drug delivery system with anti-cancer function were outlined. Results and the corresponding discussions of the physical and biological investigations were also made in this chapter.

In chapter 6, the experimental details and the procedures of the advanced study of hollow fiber - smart textiles with thermal-stimuli drug delivery function were outlined. Results and the corresponding discussions of the physical and biological investigations were also made in this chapter.

In chapter 7, the integrated design approach of the self-care textile wearable with thermal-stimuli drug delivery function and the prototype investigation of staple hollow fibers - yarns were illustrated.

In chapter 8, conclusion, limitations and future works of the hollow fiber - drug delivery system and the innovation of functional smart textiles in the medical and healthcare industry were illustrated.

1.5 Research Significance and Values

In spite of the fact that a number of research studies have been done on the utilization of hollow fibers in medical devices, the production processes were complicated and the concept of textile-based drug release system have not been put in practice. This project would very possibly lead to significant contribution and continuation in medical and healthcare development, smart textile industry and functional innovation of fashion.

This research study could bring the innovation of hollow fiber - drug delivery system forward. Besides, the conceptual idea of wearable textile-based drug delivery system for external medical applications could be potentially realized. Mass production and industrialization of the wearable medical devices for convenient public use could be happened once the system is successfully conducted. High values could be added into the research study which include 1) replacement of one-time delivery by repeatable drug loading and releasing; 2) loading complex compositions or compound drugs which include chemical-based and herbal-based medicine; 3) using common materials available in the current textile market; 4) precise control of drug release rate and dose by hollow structure and thermal therapy and 5) drug release might be independent of the environmental changes.

Generally, the research project could generate a potential novel way of medical treatment by integrating multidisciplinary collaborations of textiles, physics, chemistry and biology. It could provide impressive benefits and alternatives to patients who need long-term care and therapy by wearing an aesthetic and multifunctional medical apparels.

CHAPTER 2

LITERTURE REVIEW

2.1 Introduction

Hollow fibers are highly valued in the textile industry. Their physical properties and other superior characteristics make them a crucial material for innovations in textiles in the medical field, where they could provide solutions to therapeutic challenges. The inner lumen of hollow fibers has potential for use in medical and healthcare devices. For example, hollow fibers could be used to delivering drugs to target sites of organs, enhancing blood purification and dialysis, promoting cell culture system, and enabling effective drug screening. The use of hollow fibers could have beneficial effects on medical and therapeutic performance; a market for hollow fiber based medical clothing is anticipated for conducing to an efficient, long-term and convenient commercial medical therapy. This review discusses the development of medical textiles and describes the use of hollow fibers in different medical contexts as well as the benefits of their medical and healthcare applications.

2.2 Study of Medical Textiles

The development of medical textiles and the outstanding features of using textiles in medical areas were outlined in chapter 2.2.

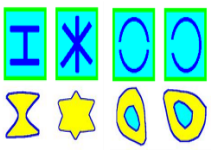
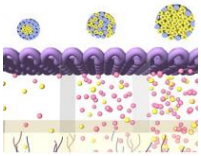
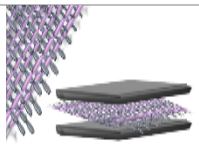
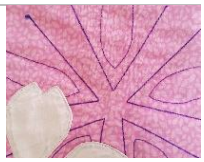
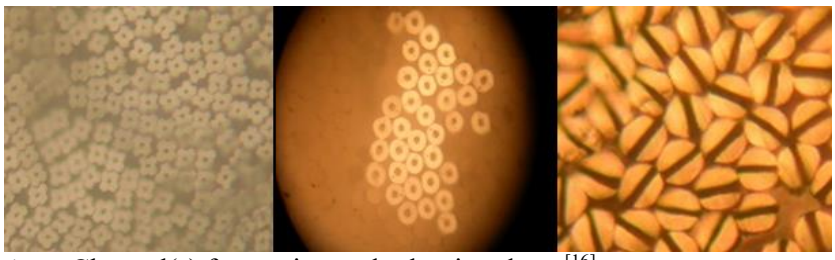
2.2.1 Development of Medical Textiles

Natural fibrous materials were first used in wound closures, wound dressings and surgical sutures started from 5000 BC.[1] From 1952 onwards, textiles, such as woven polyvinylchloride tubes and polyester, have been used in vascular implants due to the

property of high strength, stability and bio-durable qualities.[2,3,4] Textiles are indispensable in various medical and healthcare applications. Sutures, which consist of monofilament, multifilament, braided or twisted textile, are used in the repair of injured tissues and wound closure due to their absorbency, capillarity, elasticity, specific tensile strength and stress tolerance.[5] There is extensive interest in advanced medical textiles with hygienic and antimicrobial functionalities. For examples, several functional fibers such as chitin fibers, calcium alginate fibers and dextran fibers have been used in wound dressings and medical bandages.[2,6] Bio-artificial organs such as the artificial liver, prosthetic grafts, valve sewing grafts and vascular implants can also be manufactured using fibrous membranes and textile-based substrates and benefit from their elasticity, strength, stiffness and permeability.[3,7-9] Furthermore, artificial bioactive scaffolds could also use hollow fibers for drug delivery.[12,13] Such a system would allow drugs to be released to the target site through the skin or tissues.[10,11] It was proposed that the porous hollow fiber membrane could be incorporated into a three-dimensional scaffold for enhancing the delivery of nutrient and culture media (Table 2-1).[14]

Table 2-1 Advantages of Textiles in Medical Applications.

Sustainable Usage： Can be laundered and ironed;
Cover： Basic functions of textiles, protection, aesthetics and individual expression;
Comfort： Soft and light, can be used in moisture management, breathable and flexible;
Physical and Mechanical Properties: Stiff, strong, fluid-permeable;

Methods of Textile Synthesis	**Fiber**	**Yarn**	**Fabric**	**Finishing**
				
	Material Advance[15]	Structural Capacities	Layering System	Highlighted Technology
General Medical Applications of Textiles	**Medical Devices**		**Applications**	
	1. Sutures; 2. Wound dressings and medical bandages; 3. Bio-artificial organs, prosthetic grafts, valve sewing grafts and vascular implants;		1. Repairing and securing the injured tissues and wound; 2. Haemostatic compression, protection from pathogenic infection and promotion of wound healing; 3. Duplicating and restoring the normal functions of organs and for life support;	
Advantages	**Hollow Fibers**			
				
	1. Channel(s) for storing and releasing drugs[16]; 2. High surface-area-to-volume ratio; 3. High loading capability; 4. Local delivery;			
Application of Hollow Fibers	**Medical Devices**		**Applications**	
	1. Artificial bioactive scaffolds;		1. Release of drugs to the target site through the skin or tissues; 2. Therapeutic treatment.	

The skin is the largest organ of the human body, and its functions include protection, thermoregulation, and thermal and mechanical sensing. Clothing, “the second skin”, covers most parts of body. It provides an additional shielding barrier against pathogens and allergens[17-19] and provides a portable microclimate. In Nocker’s view, comfort in terms of texture and thermal properties is an essential factor in designing medical clothing.[20]

2.3 Study of Hollow Fibers

The development and production methods of hollow fibers, types of hollow fibers with different cross-sectional hollow structures and their superior structural characteristics were outlined in chapter 2.3.

2.3.1 Development of Hollow Fibers

Hollow fiber is a filament with one or several axial empty cores (Figure 2-1). Specifications such as the diameter of synthetic hollow fibers can be easily controlled. Hollow fiber has been the focus of commercial interests due to its lightness and softness. Theoretically, hollow fiber can be derived from any conventional textile, such as polyester and polyamide. Hollow fibers with porous structures are widely used for desalting and purification in water-treatment systems, concentration and clarification in the food industry, and blood treatments in medicine. In apparel and household applications, hollow fiber is widely used as a filler in pillows, quilts and winter coats because it is able to retain still air and therefore offers outstanding warmth retention properties.[21] Additionally, hollow fiber is up to 20 percent lighter than normal fiber per unit volume. It is also softer and exhibits hygroscopic properties. For these reasons, it is preferred by the intimate apparel industry. Overall, hollow fiber has a sound industrial base and promising potential for many applications.[22]

Asymmetric hollow polyamide fibers were initially invented by DuPont for antifouling and desalination of seawater in 1965.[23] In the 1970s, three-dimensional, curly, eccentric fibers came into use.[24] Toyobo began to promote asymmetric hollow fibers constructed from cellulose triacetate.[23] In the 1990s, multi-channel hollow fibers such as a ‘four-hole’ fiber were fabricated, and the manufacturing methods were improved

(Figure 2-2).[24]

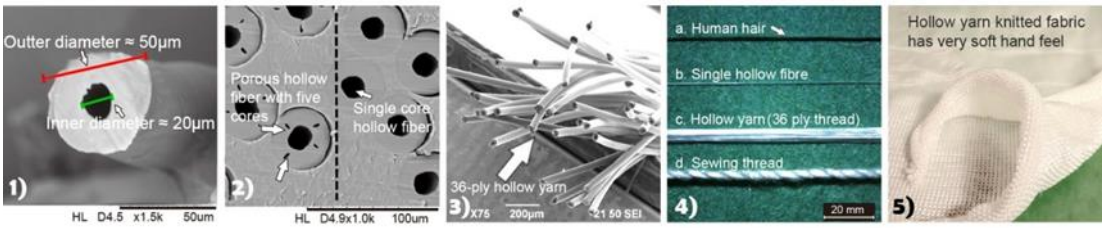


Figure 2-1 Characteristics of Hollow Fibers. 1) Cross-section of hollow fiber under SEM; 2) Two types of hollow fibers; 3) Bundles of hollow fibers (plied yarn); 4) Hollow fibers and yarns in comparison to hair and sewing thread; 5) Photo of fabric knitted with hollow yarns.

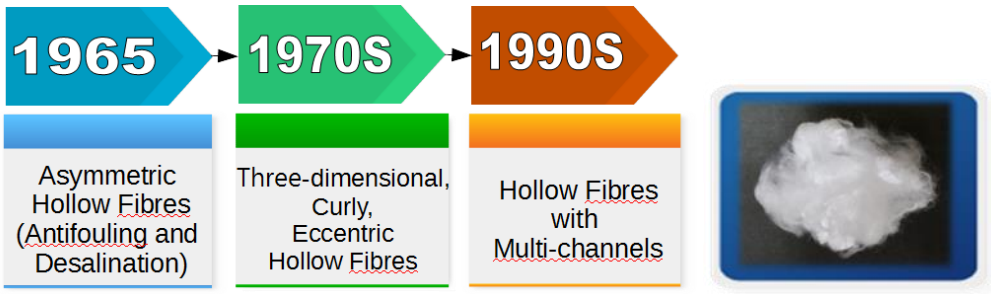


Figure 2-2 History of Hollow Fibers. The asymmetric hollow fibers were invented by DuPont in 1965 for antifouling and desalination of seawater. Three-dimensional hollow fibers were created in the 1970s.[24] Multi-channel hollow fibers with internal structure were manufactured in the 1990s (left).[24] A sample of hollow staple fibers (right).

Numerous researchers have investigated the characteristics of hollow fibers, which include the high surface-area-to-volume ratio, superior drug loading capability, high surface reactivity and the ability to maintain a controlled rate of drug release. Because of these characteristics, hollow fibers are generally believed to have potential in the production of medical textiles.

2.3.2 Production of Hollow Fibers

Hollow fibers can be made using a spinneret containing an outer concentric capillary and a central concentric capillary.[25] The spinneret may consist of one or multiple

bores.[26] The individual fibers or filaments are extruded by forcing the melting polymer or the spinning solution through an orifice. The extruded fibers are solidified by coagulation or cooling.[27,28] Various hollow shapes can be created using orifices of different shapes. Plug-in-orifice spinnerets, tube-in-orifice spinnerets and segment-arc spinnerets (i.e., spinnerets with C-shaped orifices) are examples of different kinds of spinnerets used in the production of hollow fibers.[28] Different spinning methods also exist, such as melt spinning, wet spinning, dry spinning, 'dry-wet' coagulation spinning and electro-spinning (Figure 2-3).

Melt spinning is commonly used in manufacturing fibers, as it is cost-effective and practical for industrial purposes. The polymer is melted to a certain melt viscosity[29] at which point the heat applied should be greater than the polymer's melting point. The melted polymer is then extruded via the outer concentric capillary of the spinneret, and the polymer is immediately solidified by cooling, which maintains the structural uniformity of the hollow fibers.[25,30] Kim and colleagues[31] noted that the polymer melt viscosity and the structure of hollow fibers are governed by the spinning temperature, while the number of micro-pores can be increased by the melt-draw ratio. Fine hollow fibers with small diameters can be obtained by the melt spinning method.[25]

Wet spinning is a type of solution spinning system similar to melt spinning. As reported by Li and colleagues,[30] hollow fibers used in the production of membranes have been mainly generated by wet spinning. Wet-spun hollow fibers have been extensively used in producing membranes for dialysis and ultrafiltration.[25] Dry spinning is another method for producing very thin fibers for hollow fiber membranes; a volatile solvent is used to dissolve the polymer, and the liquid polymer is heated and solidified by

evaporation.[26]

As described by Wienk and colleagues,[32] dry-wet spinning was successfully used to prepare hollow fibers for ultrafiltration membranes with a mixture of two polymers, poly (ether sulfone) (PES) and poly (vinyl pyrrolidone) (PVP). The liquid polymer was extruded via a tube-in orifice spinneret. The three phases of the induced-phase separation are vapour penetration of non-solvent at the outer surface, immersion precipitation at the outer surface and immersion precipitation at the inside surface.[32] Polyvinylidene fluoride (PVDF) hollow fiber membranes manufactured by the dry-wet spinning method have large cavities and small macro-voids at the inner and outer walls, respectively. The permeation stream of the membranes is enhanced when alcohol is used as an internal coagulant.[33] Spinning hollow fibers from the polymer dope of poly-L-lactic acid were also investigated by applying the dry-wet coagulation spinning method. Schakenraad and colleagues,[34] found that a porous matrix and dense non-porous skin can be created on both sides of hollow fibers.

In addition to the manufacture of hollow fiber membranes, phase separation (e.g., non-solvent induced phase separation (NIPS)) has been used to obtain a porous membrane.[35] In NIPS, the polymeric solution is prepared by dissolving the polymers and additives together under particular conditions, i.e., rate of stirring, temperature and duration. Hollow fibers are extruded via the spinneret and then poured into a non-solvent coagulation solution. Water, which acts as an internal coagulation medium, is used to create the inner pores of the hollow fibers. Hollow fiber membranes can thus be manufactured by solidification during induced phase separation.[36]

A high surface-area-to-volume ratio and porosity of fibers can be obtained by electro-

spinning. The larger the magnitude of the electric field, the smaller the external and internal diameters of the hollow fibers.[13] Fibers produced by a strong electrostatic force can be extremely long and fine, with diameters from nanometers to micrometers. Electro-spinning technology had been applied to tissue engineering for scaffold fabrication[13] and the production of nanocrystalline HAp-assembled hollow fibers (NHAHF).[37] Immiscible solutions such as polyvinylpyrrolidone (PVP) polymer and Ti(OiPr)4 can help to produce hollow fibers with a smooth inner structure.[13] Hollow fibers with very small diameters can be produced by coaxial electro-spinning. The spinneret consists of a needle that can delimit the bore, and the liquid polymer is connected to the needle. An orbicular aperture is located between the needle of the spinneret and the capillary, which features an end adjacent to the second liquid and an end situated away from the needle bore. The liquid polymer is fed via the needle, and the second liquid is fed via the capillary. A high-voltage electrical field is applied to create a jet to produce the hollow nanofibers.[38] Hollow nanofibers such as anatase TiO2 hollow fibers can be used as a channel for the transportation of nanofluid.[39]

2.3.3 Types of Hollow Fibers

Although circular-shaped bores are the common configuration used in hollow fibers, shapes of various cross section have been produced using customized spinnerets. The Teijin Group created a functional polyester hollow fiber termed ‘WELLKEY’, which was the first sweat-absorbent and quick-drying fiber. It has a unique cross section with many pores. A hollow polyester fiber with an octagonal cross section was also invented by the Teijin Group; this fiber is both sweat absorbent and useful for heat shielding and insulation.[40-42] Pentagonal hollow fibers have been used in carpet production because of their soil- and dirt-resistant features.[43,44] DuPont developed a certification mark

('Quallofll') for the production of hollow fibers with four channels, which performed well in thermal insulation applications[21] (Figure 2-3).

Apart from the variety of hollow shapes, hollow fibers with different wall thicknesses have been developed. Various fiber wall thicknesses can be created by altering the core fluid pin of the spinneret. The thickness of the fibers can therefore be changed easily by adjusting the pin size.[27]

2.3.4 Outstanding Characteristics of Hollow Fibers

Khoddami and colleagues[45] conducted an experiment based on the mechanical properties of hollow polyester fibers and solid polyester fibers. The thickness and stiffness of the hollow fiber based fabrics were higher than those of fabrics made from solid fibers.[45] Further comparing with solid fibers, the channels of the hollow fibers can help to trap more air, providing better thermal insulation.[46-47] Sweat can be absorbed by microporous hollow fibers through capillary action as well,[48] enabling more comfortable textiles (Figure 2-3).

Numerous studies have reported the characteristics of hollow fibers that make them useful for medical purposes. Hollow fibers have an intrinsically high surface-area-to-volume ratio and a high loading capacity.[49] Hollow fibers can have a surface-area-to-volume ratio of nearly 10,000 m2m-3.[50] The high surface-area-to-volume ratio can enhance the pore surface area. The higher the void surface area, the greater the surface reactivity.[51] As a result, the drug-loading flexibility and the rate at which drug molecules disperse can be increased.[52] Additionally, membranes employing these features of hollow fibers can provide superior selectivity and permeability for

ultrafiltration and fluid flow (figure 2-3). Fiber with honeycomb cross-sectional structure had also been produced and further carbonized into carbon hollow fibers.[53]

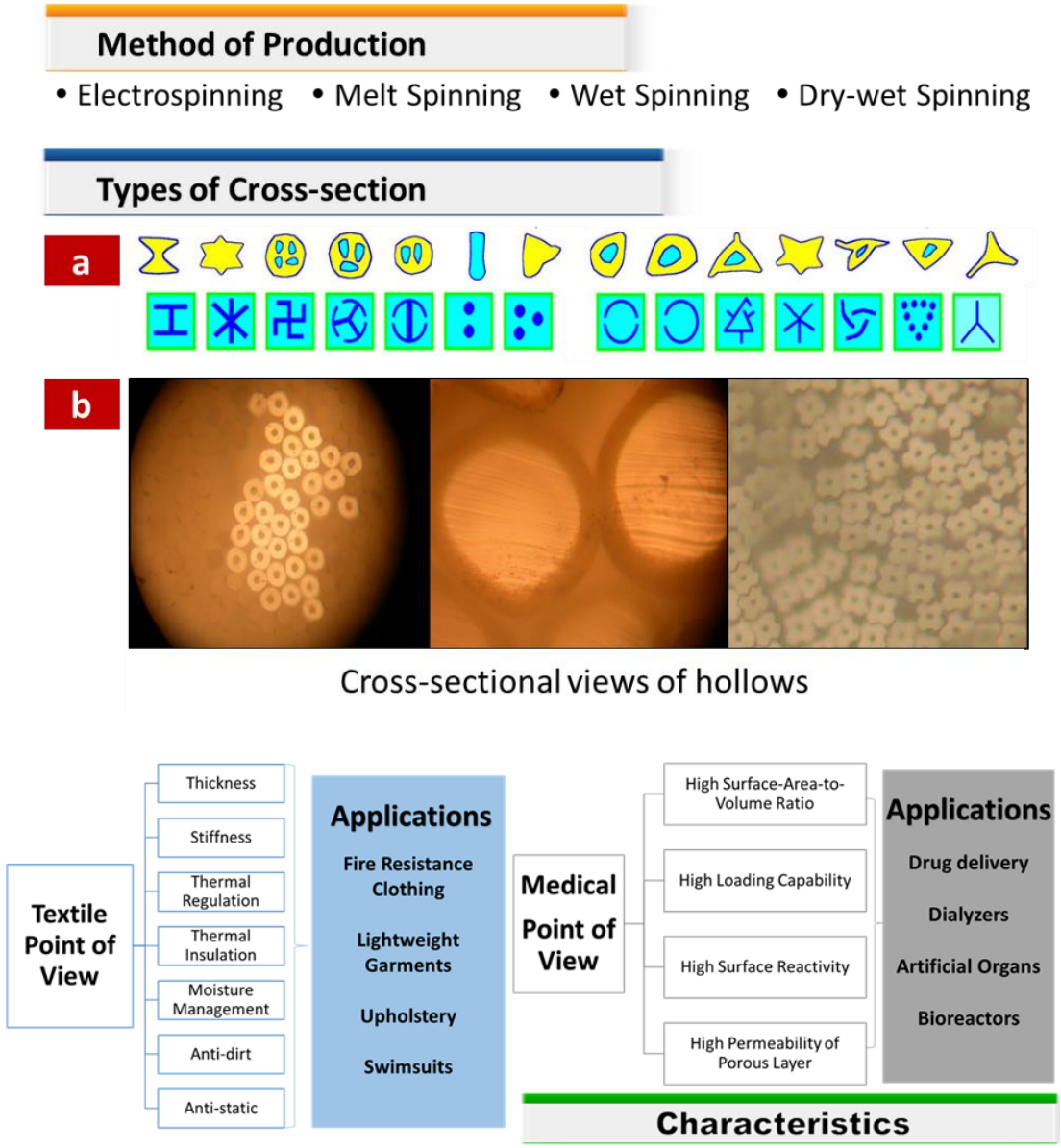


Figure 2-3 Schematic Summary of Hollow Fibers. Production can be categorized into electrospinning, melt spinning, wet spinning, and dry–wet coagulation spinning.[25-39] (a) Various types of cross-sections can be made by using different spinnerets.[16] (b) Microscopic images of different types of industrial hollow fibers.[16] Both textile and medical properties of hollow fibers contribute to the usefulness of medical textiles.

2.4 Hollow Fibers for Drug Delivery

The idea of combining the general properties of textiles and the specific characteristics of hollow fibers for medical applications has been explored for decades and demonstrates their high potential for use in as drug delivery systems and fluid permeability.

Drug delivery involves the release of medicine inside the body or through the skin of patients. Targeted drug delivery at a slow, controlled rate is highly desirable.[54] Drug loading and drug release are the constituents of drug delivery. Several factors are believed to influence drug loading and release, including the solubility and the state of drugs, the distribution of drugs inside the carrier, release kinetics and the chemical composition of the fibers.[55] Pharmacokinetics and pharmacodynamics play significant roles in drug delivery. Pharmacokinetics is defined as the way that the human body responds to the type of drug,[56] the concentration of drug in the blood and the capability of the body to remove drugs from the blood.[57] The word is also used to denote the study of the absorption, metabolism and excretion of drugs across time. Consequently, the interrelationship between the appropriate amount of drugs and the corresponding response can be deduced. The chemical toxicity of drugs can be eliminated through the control of pharmacokinetics.[58]

Another principle, pharmacodynamics, is defined as how the drugs influence the human body.[56] It involves the relationship between the concentration of drugs at the site of reaction and the therapeutic responses across time. The effective dose is determined by the drug concentration at the relevant receptors. The medical responses and side effects can be monitored based on the above two principles, the capability of patients to

metabolize and remove drugs and the interaction between body and drugs (Figure 2-4).[58]

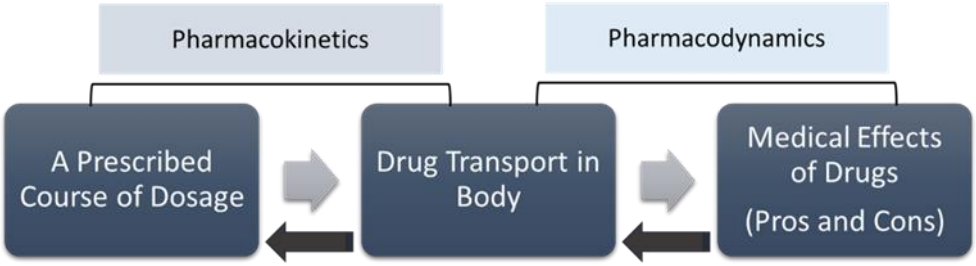


Figure 2-4 Principles of Drug Delivery. Pharmacokinetics and pharmacodynamics are the two main principles for executing the drug delivery system.[57-58]

Controlled release technology (CRT) using drug carriers has the potential to overcome the problems caused by conventional drug administration.[59] CRT enables drugs to be directed exclusively to the site of action, to prevent early drug metabolism and to continue administration over long periods.[60] Protein drugs can be protected from destruction by enzymes through encapsulation with controlled release.[59] Zero-order delivery and local drug delivery are two important elements of controlled release.

Zero-order delivery aims to provide a constant rate of drug administration to the blood independent of drug concentration. The drug delivery system should ensure release of a certain dose, diminishing the risks of overdosing or under-dosing. As a result, a constant effect can be maintained. Drugs can also be released gradually after an initial burst of release. Additionally, the period of drug release can be lengthened, and the drugs can be kept at a lower concentration to reduce the chance of overdose. Direct local drug delivery is also possible. Therefore, adverse or toxic effects associated with overdose and the distribution of drugs to non-target organs or tissues can be prevented. Some drugs readily pass through the skin due to its large surface area. They can then be

absorbed in the blood capillaries after reaching the epidermis and dermis.[60]

Hollow fibers are believed to be effective drug carriers because of the intrinsic high surface-area-to-volume ratio and a high loading capacity.[49,61] Fluid flow through micro- or nano-sized channels may also be important.[62] As the shell wall thickness and hollow cavity diameter can be modified in correspondence with the diffusion coefficient, the uniformity of diffusion and a pre-determined rate of release can also be monitored.[63] Some hollow fibers may also contain a selectively permeable porous layer that can further control the rate of drug flow and release. Additionally, the encapsulated drug can be protected inside the pore to maintain stability.

Pharmacokinetics can be enhanced for better delivery of drugs to the site of interest.[64] Moreover, as drugs can be released at a low rate over a long time, frequent injections may not be required.[65] Drugs can be delivered directly to the target organs via hollow fibers; thus, the risks of overdosing, under-dosing and chemical toxicity can be eliminated (Figure 2-5).[66]

The drugs are loaded into the bore, which runs along the whole length of the hollow fibers, through the tips of the fibers when they are dipped into the solution, or through injection or vacuum suction. Drugs can also be dissolved in the liquid polymer by electrospinning.[67] A drug-loaded core granulate can be formed by blending the drugs with the polymer solution.[65] There are three drug-loading mechanisms: physical adhesion of drugs onto fiber surfaces, chemical attraction between drugs and fibers by covalent bonds and physical encapsulation of drugs inside the lumen of the fibers (Figure 2-6).[67] An amount of the drug solution is released from the inner core of the

fibers to the exterior area by liquid flow, liquid leakage, diffusion or capillary action. Zero-order delivery and extended drug release are aims of development.[68] The fluid dynamics of the hollow fiber - drug delivery system are based primarily on diffusion, capillary action, inter-fiber liquid transport and intra-fiber liquid transport. Hollow fibers are a type of reservoir drug-loaded systems; drugs are added into the core by binding of the polymeric shell. Drugs diffuse via the polymeric shell from the interior core at limited rates in a diffusion-controlled system.[69] Diffusion is a net movement of liquid from an area of higher concentration to an area of lower concentration. The fluid moves down the concentration gradient until dynamic equilibrium is reached. No energy is needed in the process; thus, diffusion is a form of passive transport.

Cellulosic hollow fibers manufactured by the dry-wet inversion spinning method have been used as a successful drug carrier. Two different types of drugs were loaded into separate sets of hollow fibers via capillary forces. Needle-punched non-woven wound-healing textiles could be constructed from the fibers with the support of polyester needle webs. Various phases of wound healing and sustainable drug release were shown.[70] In addition, a 'multiple' drug delivery system was developed using biodegradable nanoparticles containing hollow micro-fibers. This system was intended to allow the release of different drugs from the nanoparticles and the fiber walls to the target sites through two-step diffusion either in sequence or simultaneously. The hollow micro-fibers maintained the nanoparticles in a set location. Wound healing or other antimicrobial treatments could be used along with this drug delivery system. Nevertheless, surgical implantation was required.[71]

Hollow fiber drug delivery systems have been used to treat vaginal bacteria and

periodontal disease. An intra-uterine device (IUD) is a long-term reversible contraceptive that stimulates a cytotoxic inflammatory reaction to decrease sperm mobility and thus prevent fertilization and the fusion of gametes. However, the inter-uterine environment becomes hostile to implantation, and although an IUD is one of the most effective methods of contraception,[72] insertion can introduce vaginal bacteria into the uterus. The bacteria then enter the uterus, fallopian tubes and ovaries and cause pelvic and uterine infections. The infection may also spread to the rest of the body. Therefore, the IUD was modified using hollow fibers to reduce the risk of pelvic inflammation. Nylon 6 hollow fibers have been used to produce chlorhexidine-releasing IUDs. Chlorhexidine diacetate, an antibacterial agent that destroys the cytoplasmic membrane of gram-positive bacteria, can be released through the nylon 6 hollow fibers at a rate of 114μg day-1 to reduce the occurrence of vaginal bacterial infection within 24 hours.[73,74] Aside from side effects such as uterine bleeding, devices that release levonorgestrel or norethisterone through hollow nylon monofilaments were inserted easily into the uterus via the post-menopausal cervix; these devices avoid the risks that arise from administering the progestogens systematically.[75] Poly (L-lactide) (PLLA)-based hollow fibers have also been investigated for loading and releasing hormones. Synthetic steroid hormones were inserted into silicon-cemented hollow fibers using a syringe. Zero-order release of levonorgestrel was achieved in vivo and in vitro. This technology could contribute to the development of a contraceptive device.[34,76] For the treatment of periodontal disease, tetracycline-loaded hollow fibers were placed in the gingival sulcus.[77]

Hollow fiber catheters can enhance drug distribution into the central nervous system and increase the surface area of the brain tissue. Homogenous drug delivery and greater

volumetric flow of drugs can be achieved with the larger surface area of hollow fibers. As there are abundant nano-pores on the catheter walls, encumbrance mismatch can be eliminated due to the similarity of the hollow fiber porosity to that of the brain tissue.[78]

During drug delivery via hollow fibers in the small intestine, the potential transit time of the gastrointestinal tract (GIT) was reduced, and a controlled rate of drug release can be obtained.[79]

Dry-wet spinning had been used to manufacture hollow fibers constructed from poly (L-lactide) (PLLA) with high crystallinity and porosity. Hollow fibers can act as a rate-controlling device in drug delivery systems during application onto the barrier membrane. A considerable amount of drugs can be released at the original stage, and then, successively smaller amounts of drugs can further released gradually over the final stage of half-life. Nevertheless, a number of factors can influence the rate of release. These include the number of fibers in a bunch, internal diameter of a bunch of fibers, composition of fibers, mass capability and the ratio of fiber weight to material weight.[80] The hollow fiber membranes, which were constructed from PLLA-dioxane-water using the liquid-liquid demixing process, were found to have a porous layer. The membranes formed by the PLLA-(chloroform/toluene)-methanol system were found to exhibit complete microporous formation. The loaded drugs were released when the crystal carriers dissolved; the drugs could then diffuse through the membranes. Long-term and short-term zero-order release of drugs was shown.[35] Another example of the production of PLLA-based hollow fibers by the dry-wet spinning method was their use to manufacture a bioactive scaffold. The mechanism was similar to that used in the hollow fiber membrane system. Drugs were loaded into the micro-particles, and the rate

of drug release was lower when the drug-loaded micro-particles were trapped in the hollow fibers due to the large resistance of drug diffusion through the walls of the fibers.[12] Eenink et al. (as cited in Ranade and Cannon, 2011) discovered that biodegradable hollow fibers could be manufactured using poly-L-lactic acid to allow subcutaneous delivery.[49]

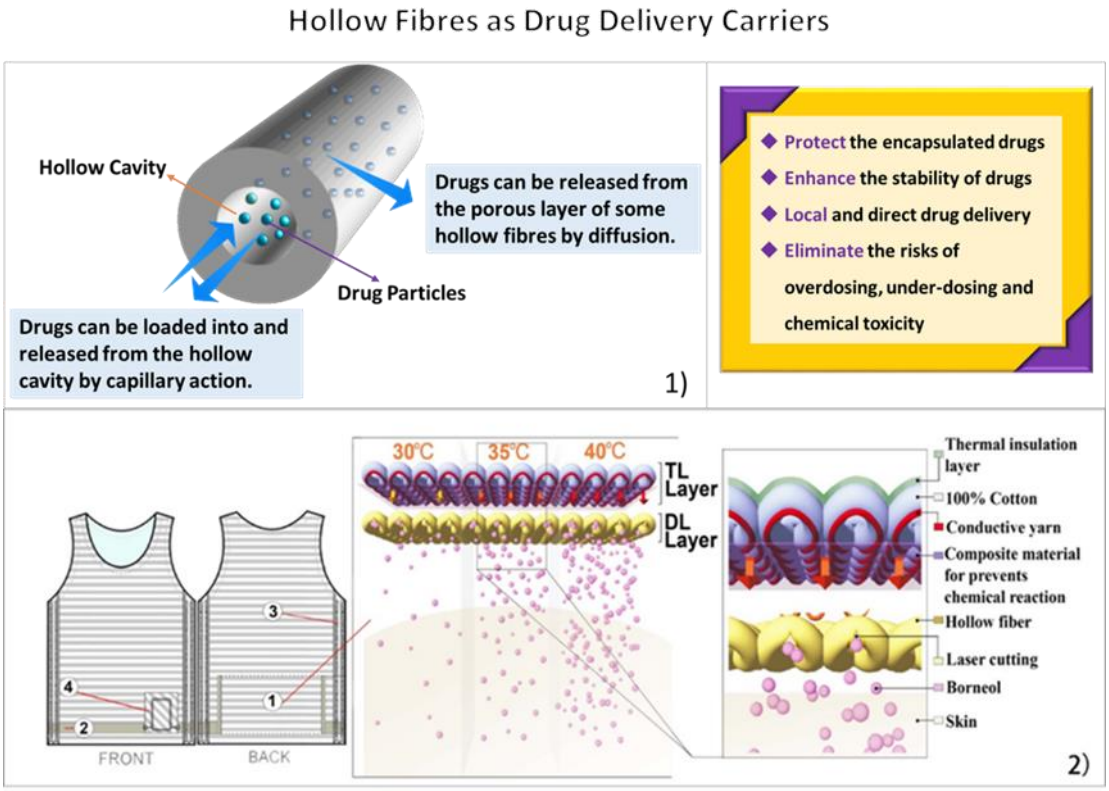


Figure 2-5 Applications of Hollow Fibers in Medicine. The medical applications of hollow fibers can be generally divided into six major areas: drug delivery, dialysis (e.g., artificial organs), gas exchange (hollow-fiber bioreactors), cell culture, liquid-phase micro-extraction and drug screening (hollow-fiber assays) hollow-fiber biotechnology. 1) Hollow fibers can be used in drug delivery because of the effectiveness of drug loading and release.[49,61-66] 2) From the future point of view, a functional textile-based thermal-stimuli drug delivery apparel system would be a potential innovation for producing multi-functional skin-protective clothing.

Electrospun bioactive hollow glass fibers were fabricated into a non-woven structure. Drugs were infused using a vacuum pump with compression and decompression at the

two joints of fibers, respectively. It was discovered that a greater amount of loaded drugs resulted with an increased fiber length. In contrast, shorter fibers would decrease the drug-loading capacity but enhance the rate of drug release.[81] Hong et al. (as cited in Zeng et al.[61]) also invented mesoporous bioactive glass hollow fibers (MBGHFs). These fibers with a hollow core were found to hold far more drug than did the solid fibers.[61] The drug-loading capability of the hollow fibers was greater than that of solid fibers.

To investigate the drug-loading capability of hollow fibers, dexamethasone and methotrexane were used as the bioactive agents. Hollow fibers are a popular nano-carrier for localized drug delivery at a predetermined rate.[15]

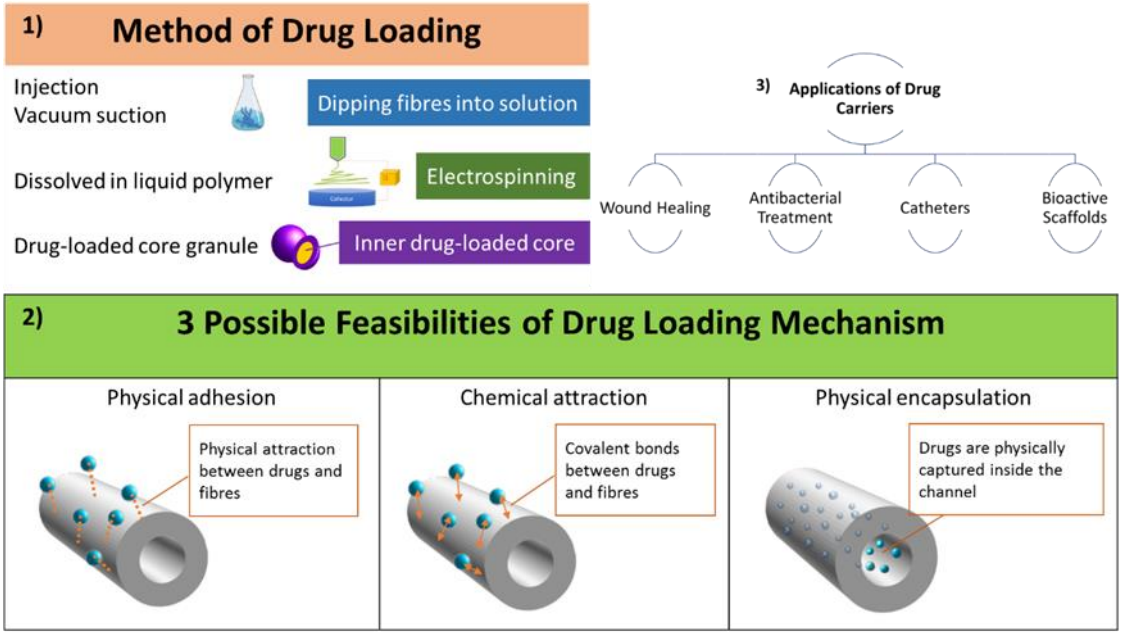


Figure 2-6 Drug Loading Methods and Mechanism. Drugs can be loaded into and released from the cavity of hollow fibers by capillary action. Drugs can also be released through diffusion. Local delivery can be guaranteed, and drugs can be protected by encapsulation inside the cavity. Risks of overdosing, under-dosing and chemical toxicity can be diminished or eliminated. 1) Method of drug loading; 2) three possible drug-loading mechanisms [65,67]; 3) applications of drug carriers.

2.5 Hollow Fibers for Other Medical Purposes

Regarding to the promising features of hollow fibers such as higher loading capability and high permeability, implementation of biomedical textiles by utilizing the fibers has been launched.

Hollow fiber membranes are vital components of drug delivery and dialysis systems. The membranes are semipermeable which enables controlled delivery of materials and chemical mobilization of the fiber walls.[82] Hollow fiber dialyzers are created using a bundle of hollow fibers, abridged and secured at both ends using potting material, polyurethane, inside the sheet of the tube, which acts as a selectively permeable membrane. Dialysis could be performed because of the selectively permeable membranes, and the fluid could flow effectively inside the channels of the hollow fibers. Efficient and prompt clearing of metabolic waste was reported by using hollow fibers with various densities.[83-86] The micro-porous membrane of a mechanical lung is generally constructed from hollow polypropylene fibers.[87] It is highly permeable to gases because of the small diameter of the fibers. Respiratory exchange can be successfully such that carbon dioxide is removed from the blood, and oxygen is provided as cells flow through the lumen of the hollow fibers.[83,88-92] Hollow fiber bioreactors were first introduced for the in vitro testing of antibiotics in the 1980s. Hollow fibers are positioned in parallel inside the cartridge, and the cells attach and grow outside the fibers in the extracapillary spaces (ECS). Since the fibers are cylindrical and small in diameter; as a result, specific nutrients and wastes can flow and exchange across the hollow fiber walls out of or into the cell-culture medium. The rate of filtration can also be enhanced. A large number of cells can attach and grow in a small volume due to the large surface-area-to-volume ratio.[93-98] Hollow fiber liquid-

phase microextraction (HFLPME) consists of a membrane constructed from a hydrophobic polymer such as polypropylene in a hollow fiber. In the three-phase system, the pores of the hollow fibers are filled by soaking in the organic solvent via capillary action. The aqueous acceptor can load into the lumen of fibers with one sealed end. Analyte can diffuse through the pores of the fibers from the region of aqueous sample to the organic region. The analyte is extracted into the acceptor solution for analysis.[99] A hollow fiber assay (HFA) was developed as a substitute for conventional anticancer drug screening. Tumour cells were loaded into the hollow fibers, and the fibers were implanted into the bodies of mice at subcutaneous (s.c.) or intraperitoneal (i.p.) positions. Anticancer drugs were administered to the mice for a specific period of time (Figure 2-7).[100-103]

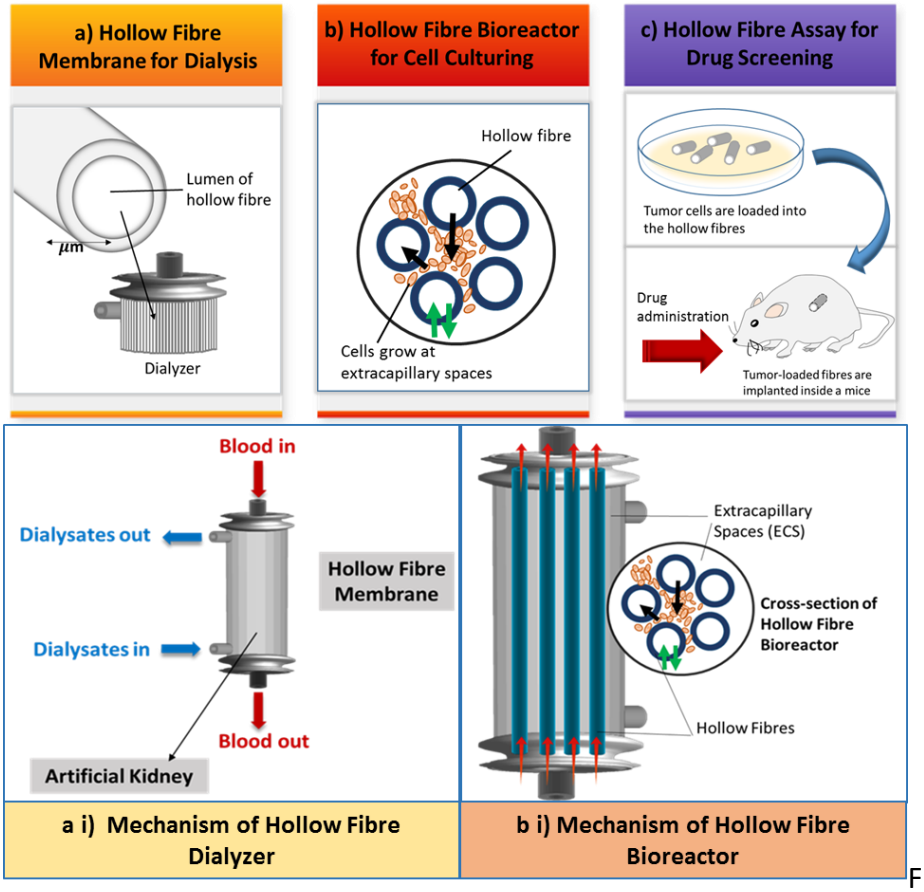


Figure 2-7 Microscopic Images of Hollow Fiber Medical Devices. a) Hollow fiber membrane of a dialyzer[83-86]; b) osteosarcoma cells were cultured in an artificial culture medium in a hollow fiber bioreactor[93-98]; c) development of blood vessels around hollow fibers that were implanted inside NMRI mice.[100-103]

2.5 Summary and Limitations of Hollow Fibers in Medical Applications

In this chapter, the utilization of hollow fibers in medical and therapeutic areas was comprehensively explored. Hollow fibers have been typically associated with the invention of medical textiles. These biomedical textiles have been extensively developed in recent decades. The characteristics of hollow fibers have been used to produce improved medical devices. A drug delivery system using hollow fibers could be used to develop various medical textiles with wound-healing and antibacterial functions. The use of hollow fibers has also been extended to other medical devices such as dialyzers, bioreactors and drug-screening assays. Although the performance of hollow fibers in medical areas is remarkable, some limitations remain. For examples, hollow fibers are mainly used in internal medical systems and surgical implants, as in artificial organs and dialyzers. As a number of factors may influence the fluid dynamics, loading capability and permeability of hollow fibers, such as the composition, internal diameter and the ratio of fiber weight to material weight, it may be difficult to control all these parameters when manufacturing hollow fibers and associated devices.

CHAPTER 3

RESEARCH METHODOLOGY OF WEARABLE TEXTILE-BASED DRUG DELIVERY SYSTEM BY USING HOLLOW FIBERS

3.1 Introduction

This chapter illustrates the methodology for developing the wearable textile-based drug delivery system with the use of industrial hollow fibers. The experimental procedures include 1) physical characterization of hollow fibers; 2) physical analysis of the drug delivery ability with hollow fibers' unique structure; 3) pilot study of the hollow fiber based drug delivery system with anti-bacterial function; 4) pilot study of the hollow fiber based drug delivery system with anti-breast cancer function; 5) advanced study of hollow fiber based smart textiles with thermal-stimuli drug delivery function; 6) integration of fashion and smart intelligent function in medical application. The outline of the approaches is as follows:

i) Selection process of the commercial, ready-made hollow fibers based on the requirements and literature review.

ii) Analysis of the drug delivery capability of the fibers by physical characterization.

iii) Pilot study of the hollow fiber based drug delivery system with theoretical concepts and functional textile design in medical field.

iv) Advanced study of the wearable hollow fiber based drug delivery system with the hybridization of thermal therapy for controlling or catalysing the rate of drug release.

v) Integrated design of the self-care textile wearable with thermal-stimuli drug delivery function and prototype development of staple hollow fibers - yarns.

3.2 Research Methodology

This research project will be investigated according to the 'Product Development Pyramid' shown in Figure 3-1. It aims to reach the top of the pyramid for the creation of a collection of self-care medical textile wearable. The pyramid is divided into three major levels with a bottom-up approach which are 1) literature review, physical characterization and physical analysis; 2) functional design of the hollow fiber based medical textiles and clothing; 3) creation of prototypes and a collection of medical textile wearable in the future. For physical analysis, characterization with microscopic analysis was conducted; for functional design, drug delivery function with the integration of thermal-stimulating system was investigated through physiochemical and biological experiments; for the future works of the thesis and the on-going progress, creations of prototypes and a collection will be made based on the fundamental design concepts and functional ideas.

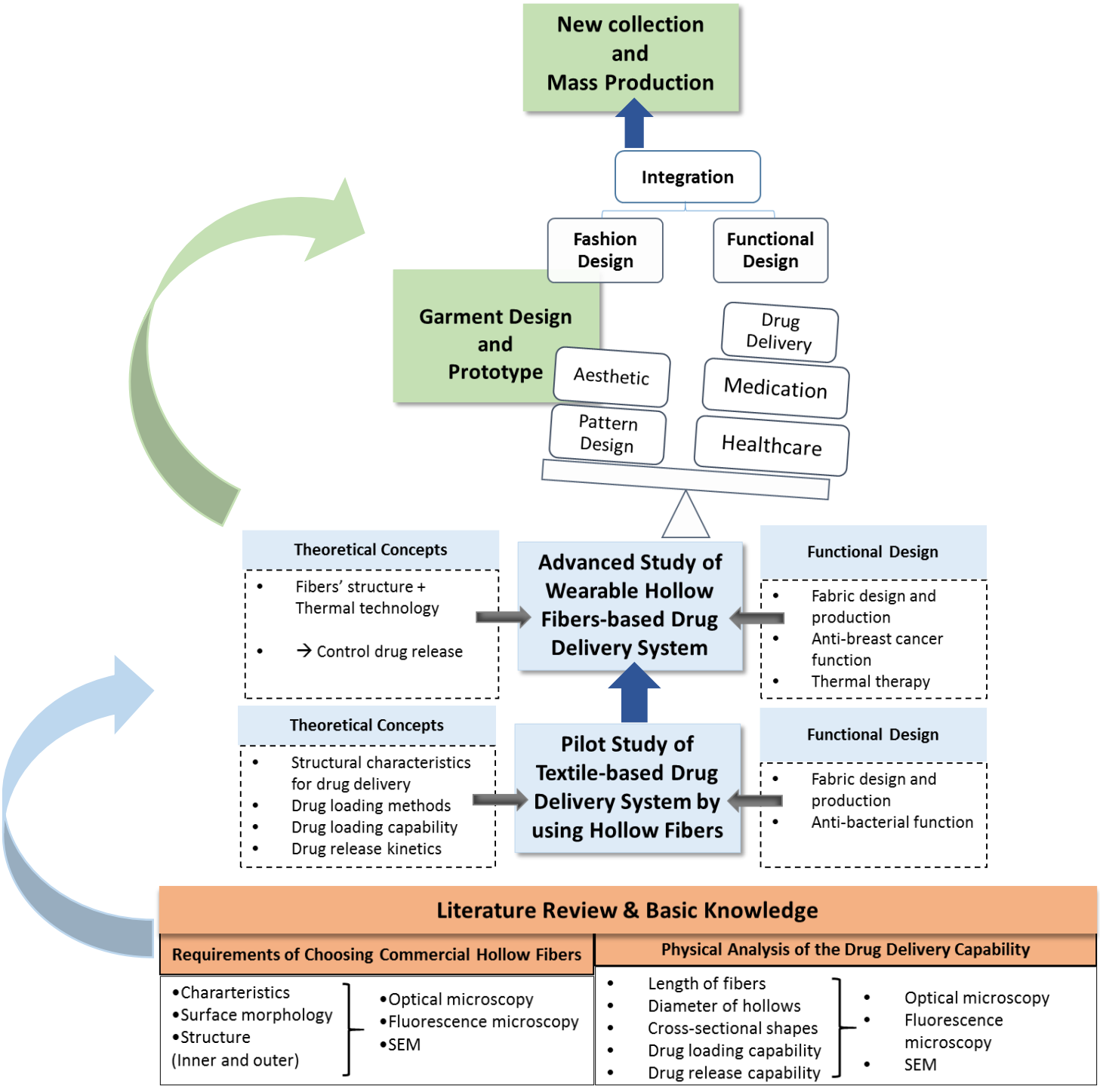


Figure 3-1 Product Development Pyramid of Textile-based Drug Delivery System.

3.2.1 Division of Research Experimentation

Research experimentation is divided into four main stages, which are 1) compartmentalization of experimental components; 2) primary research; 3) secondary research and 4) tertiary research. For the initial stage of experimentation, compartmentalization of different components was conducted so as to divide them into appropriate categories (i.e. textile materials for research, functional design of the system, physical and biological analysis) with an organized manner. Later on, three levels of research approaches were performed which are the primary research via literature review and background study, secondary research via physical characterization and tertiary research via biological experiment.

1) Compartmentalization of Experimental Components

A) Textile Materials

i) Commercial hollow fibers

ii) Silver-coated conductive yarns

iii) Fabrics made of hollow fibers (i.e. woven and non-woven fabrics)

iv) Staple hollow fibers - yarns

B) Functional Design

i) Repeatable drug loading with compound drugs

ii) Drug delivery function within the structure of hollow fibers

iii) Controlled or catalysed rate of drug release with the thermal-stimuli technology

C) Physical Analysis

i) Optical microscopic analysis

ii) Fluorescence microscopic analysis

iii) Scanning electron microscopic analysis

iv) Drug release kinetic analysis

v) Infra-red thermographic analysis

vi) Thermal-stimulated drug release and liquid release analysis

D) Biological Analysis

i) Anti-bacterial analysis

ii) Anti-cancer analysis

2) Primary Research

The concepts and basic knowledge for this research were obtained by reading journals, patents, books, online resources from internet and attending seminars. The possibilities of applying hollow fibers in medical devices and the methods of drug loading were reviewed.

i) Literature Review of Medical Textiles

The advantages of using textiles in medical applications instead of using other materials and the development of medical textiles with their excellent biological features were studied.

ii) Literature Review of Hollow Fibers

The historical development and the production of hollow fibers were firstly reviewed.

Different production methods which include melt spinning, wet spinning, dry spinning, dry-wet coagulation spinning, electro-spinning and with the use of specific spinnerets were introduced. Various types of hollow fibers with unique cross-sectional shapes and characteristics such as high surface area and high loading capacity were also illustrated. Secondly, the current applications of hollow fibers in medical contexts, especially for using in drug delivery devices and other systems that need the transportations of materials through the hollows (e.g. dialysis and cell culturing) were specified. The benefits of using hollow fibers with their superior structural characteristics in medical devices were also reported.

The potential industrial application of hollow fibers in manufacturing medical textiles and clothing were also brainstormed and reported.

3) Secondary Research

Continuous experiments (i.e. physical and biological examinations) were conducted to investigate the possible outcomes between the structure of hollow fibers and the performance of drug delivery all-arounds. Besides, the interconnection of thermal therapy and the structure features of hollow fibers for a controlled or catalysed rate of drug release was also examined.

i) Characterization of Hollow Fibers

Two types commercial hollow fibers, which are nylon 6 (PA 6) hollow fibers and nylon-polyester (PA-PET) staple crimped hollow fibers, were utilized in pilot and advanced studies respectively. The outer structure, inner feature of hollows and the surface morphology of hollow fibers were observed through optical microscopy, fluorescence

microscopy and scanning electron microscopy. The hollow fibers in yarn structure had also been examined.

ii) Physical Analysis of Drug Delivery Performance

The relationship among the length of fibers, the diameter of hollows and the drug loading and release performance was also investigated through optical microscopy, fluorescence microscopy and scanning electron microscopy.

4) Tertiary Research

The drug loading methods and performances in loading compound drugs were verified by microscopic analysis. The drug delivery capability of hollow fibers were further verified by the successive biological experiments and drug release kinetics analysis. Functional design with therapeutic performances (i.e. anti-bacteria and anti-breast cancer) were also examined continuously. Controlled or catalysed release of drugs through the channels of hollow fibers was subsequently investigated with an extra technological function of thermal-stimuli therapy.

3.2.2 Standard

The referred standards for biological experiments are as follows:

1) AATCC 147:2004. Antibacterial activity assessment of textile materials: parallel streak method.
2) ATCC Cell Culture Standard

3.2.3 Sample Preparation

Nylon 6 (PA 6) hollow fibers, woven fabrics made of PA 6 hollow fibers, nylon-

polyester (PA-PET) staple crimped hollow fibers, non-woven fabrics made of PA-PET hollow fibers, and yarns made of hollow fibers were the materials used for specimen preparation. The thermal distribution effect had been investigated by combining with the thermal conductive e-fabric layer (i.e. with silver-coated conductive yarns).

3.2.4 Applications and Technology

Drug loading mechanism, drug release kinetics, anti-bacterial application, anti-breast cancer application and thermal-stimuli technology were the main areas of the research thesis.

3.2.5 Procedures

Pilot Study of Textile-based Drug Delivery System by Using Hollow Fibers

For the procedures of drug loading, vacuum at negative pressure was principally applied. During the process, drug solution was believed to be simply driven into the lumens of hollow fibers (i.e. either in the structure of textile fibers or fabrics) within 20 minutes. The drug-loaded specimens were flushed by deionized water (D. I. water) in order to remove the surface-attached drugs and were then cured in air at the final stage.

For the procedures of physical testing, the liquid-driven drug release kinetics of hollow fibers was studied. The drug releasing conjunction between the length of the hollow fibers (i.e. short and long fibers) and the hollow structure was investigated by using a precise quantitative balance weighting method. The drug releasing speed over time was measured.

For the procedures of biological testing, an antibacterial analysis which was based on

the principle of AATCC 147 method was utilized. The drug releasing capability from the channels of hollow fibers of the antibiotic Penicilin-Streptomycin-loaded woven fabrics (i.e. half of the yarns were made of the hollow fibers) was investigated. The bacteriostatic activity in accordance with the narrowing of streaks and the size of inhibition zone was qualitatively determined which was corresponding to the drug releasing capability.

Pilot Study of Hollow Fiber - Drug Delivery System with Anti-cancer Function

For the procedures of drug loading, two different loading methods, which are the simple direct infiltration with magnetic stirring and vacuum at negative pressure, were utilized. In the process of simple direct infiltration, drug solution was attempted to be loaded along the hollow fibers (i.e. either in the structure of textile fibers or fabrics) with the rotating magnetic field. For the method of vacuum, drug solution was loaded into the lumens of hollow fibers under negative pressure. The drug-loaded specimens were flushed by deionized water (D. I. water) in order to remove the surface-attached drugs and were then dried in air.

For the procedures of physical testing, the influence of fluid viscosity on the loading efficiency of hollow fibers was also investigated by using loading contents with different viscosities respectively. The loading efficiency was calculated by measuring the original weight of hollow fibers before loading, the original weight of drugs given and the weight of loaded drugs.

For the procedures of biological testing, the anticancer activity of the 5-Fluorouracil (5-FU) loaded hollow fibers and hollow fiber based non-woven fabrics (i.e. drug loading

layer) were studied with the use of MDA-MB-231 breast cancer cells. The drug releasing capability of hollow fibers was examined by the quantitative analysis of cytotoxic and cell growth inhibition effects.

Advanced Study of Hollow Fiber - Smart Textiles with Thermal-stimuli Drug Delivery Function

For the procedures of drug loading, two different loading methods, which are the simple direct infiltration with magnetic stirring and vacuum at negative pressure, were utilized. In the process of simple direct infiltration, drug solution was attempted to be loaded along the hollow fibers (i.e. either in the structure of textile fibers or fabrics) with the rotating magnetic field. For the method of vacuum, drug solution was loaded into the lumens of hollow fibers under negative pressure. The drug-loaded specimens were flushed by deionized water (D. I. water) in order to remove the surface-attached drugs and were then dried in air.

For the procedures of physical testing, thermal distribution of the thermal conductive e-fabric layer with the application of silver-coated conductive yarns was examined. Different levels of heating temperatures were achieved under different levels of electric power supply. The heating geometric allocations of the fabric layer was observed through capturing the infra-red thermography of the different heating levels. The stability of electrical conductivity was studied and the thermal distribution at particular temperature intervals was measured. The liquid release with thermal stimulation was investigated by heating dye-loaded specimens in a heat block at a specific temperature and at regular time intervals. Visible absorbance was measured using a microplate reader.

For the procedures of biological testing, the relationship between temperature and the drug releasing ability from the heated non-woven fabrics (i.e. drug loading layer) was investigated by the anti-breast cancer analysis. Each of the drug-loaded non-woven fabrics was placed inside a tube of cell culture medium. Each tube was heated at specific temperature (i.e. 37 ℃ and 42 ℃). After 1 hour, the solution was centrifuged under 8000 rpm for 2 minutes. The supernatant was collected from each tube and was then placed into a well of breast cancer cells.

Integrated Design Approach of the Self-care Textile Wearable with Thermal-stimuli Drug Delivery Function

For the design approach, a special made textile wearable for breast cancer post-surgical care and therapy (i.e. a bra for females and a sweatshirt / pullover for males) was chosen. The textile wearable consists of three layers which include the inner drug delivery layer (DL), the middle thermal conductive e-fabric layer (TL) and an outer layer.

For the prototype development approach, staple hollow fibers - yarns with different twist amounts had been prototyped for realizing the concept of making medical textile wearables. Structural characteristic of the yarns and their drug loading ability had been examined with the use of optical microscopy. Besides, woven fabrics with the utilization of the staple hollow fibers - yarns had also been prototyped. Fabrics with different bulkiness and weave patterns had been made.

3.2.6 Limitations of Research

1) Variations in textile structures by different methods of fabrication (e.g. weaving,

knitting and felting).

2) Integration of thermal therapy into entire textile wearable.

3) Multidisciplinary conflicts among different areas.

3.2.7 Summary of Thesis

Since hollow fibers are known as one of the promising fibers for being significant drug carriers in respect to different medical therapeutics, thus, the drug loading and releasing functions of hollow fibers and hollow fiber based fabrics were analyzed through the physical and biological experimentations. In advance of the implementation of the hollow fibers drug delivery system, the effectiveness of the system with precise dose of drug release at a controllable or catalyzed rate was further investigated by integrating with thermal-sensitive technology. The performance of a functional, convenient, comfortable and self-care medical wearable with the drug delivery system was examined.

CHAPTER 4

PILOT STUDY OF TEXTILE-BASED DRUG DELIVERY SYSTEM BY USING HOLLOW FIBERS

4.1 Introduction of the Pilot Study

Progress with time, fiber technology keeps moving forward along with the optimization of both materials and structures. The textile industry has dominated a large portion with its important role in the modern society. Nevertheless, increasing amount of wastage due to the overcapacity of industrial fibers has been resulted with the growth of textile and fiber industry. As the industrial fibers have been produced more than that demanded, as a result, it is essential to explore the new uses of the over-produced fibers.

This pilot study aims to excavate the new functions of the traditional, industrial and ready-made hollow fibers with overcapacity and so as to give the fibers a brand new second life with various applications. An environmentally-friendly, convenient and repeatable drug delivery medical system can be hence unearthed with the application of hollow fibers. The problem of wastage of the over-produced hollow fibers could also be eliminated. It is believed that this textile-based drug releasing system could moderate the current medical problems and suffices the incompleteness of recent drug delivery apparatus as some of them may not allow repeated drug loading and some might require sophisticated preparation processes with the use of chemical methods. The implementation and acknowledgement of textile-based drug delivery system for industrial production and public use can therefore be preserved. Moreover, it is also considered that the delivery function of hollow fibers is not only limited to drugs but other matters for a variety of purposes. In general, the hollow fiber - drug delivery

system of this project could help to solve the problems of traditional drug delivery systems which include: 1) replacement of one-time delivery by repeatable drug loading and releasing; 2) loading chemical-based and herbal-based medicine; 3) using common materials available in the current textile market.

4.2 Experimentation and Development

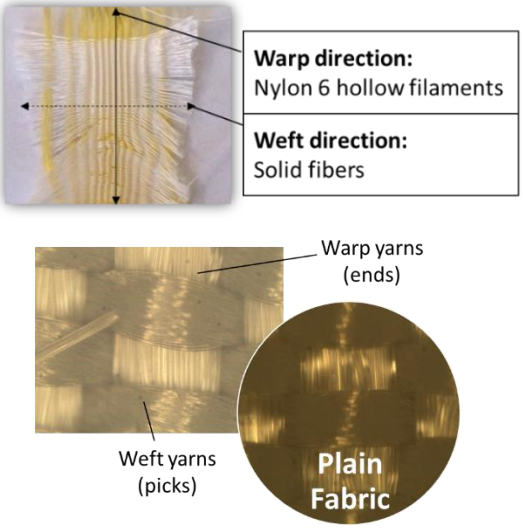
In chapter 4.2, preparation of hollow fiber and fabric specimens, structural and morphological study by scanning electron microscopy, experimental procedures of the drug loading methods, in vitro antibacterial experimentation and drug release kinetics analysis were demonstrated.

4.2.1 Preparation of Fiber and Fabric Samples

Nylon 6 or Polyamide 6 (PA 6) hollow fiber, which is a popular industrial fiber type in the textile market, belongs to the domain of polyamide. This study focuses on finding the new medical drug delivery function of this conventional, commercial and ready-made fiber in the medical-textile industry.

Nylon 6 hollow fibers were cut into 3 cm and 20 cm respectively for the comparison of the drug loading and releasing capability. Plain woven fabric samples with an area of 1 cm x 1 cm each, which the warp yarns were made of the nylon 6 hollow fibers while the weft yarns were made of solid fibers, were used for the antibacterial analysis. Through the determination of the number of yarns per unit length of the woven fabric, there were 20 ends per cm for the warp density while 23 picks per cm for the weft density approximately. The physical properties (i.e. breaking tenacity and elongation) of hollow fibers had no obvious change before and after drug loading (Table 4-1).

Table 4-1 Hollow Fiber and Fabric Samples.

	Hollow Fiber	Fabric
Name of Textiles	Nylon 6 / PA 6 (Polyamide) Hollow Fibers 	Woven Fabric made of PA 6 Hollow Fibers and Solid Fibers 
Description of Textiles	Continuous Hollow Filaments	Weave Structure: plain fabric Warp Density: ~ 20 ends per cm Weft Density: ~ 23 picks per cm

Physical Properties of Hollow Fibers		
	Before Loading:	**After Loading:**
Breaking Tenacity	3.18 cN/dtex	3.35 cN/dtex
Breaking Tenacity (CV%)	3.93%	2.9%
Breaking Elongation	76.8%	71.4%

4.2.2 Structural and Morphological Study by Scanning Electron Microscopy

The general structure, cross-sectional shape and the surface morphology of the nylon 6 hollow fibers were analyzed by applying the scanning electron microscopy. 10 cm of the fiber was cut for observation. There were total five lumens found in the cross-sectional area, one large lumen with approximately 15 μm internal diameter and four small channels in the peripheral of the core. The general diameter of the hollow fibers was approximately 40 μm. Smooth surface of fibers could be seen in Figure 4-1.

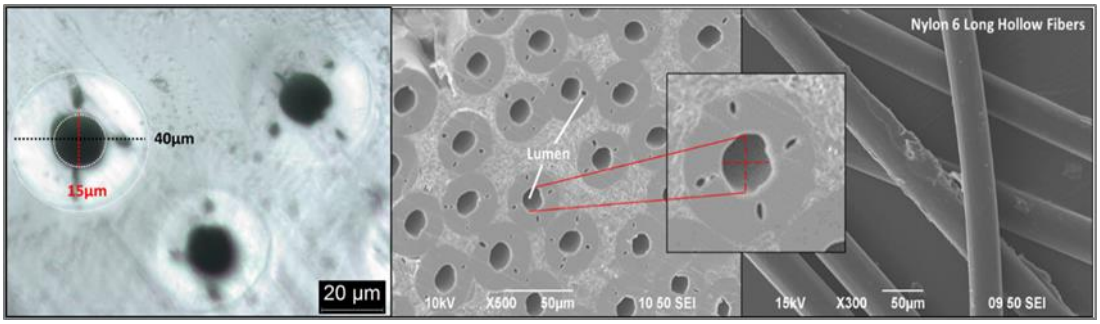


Figure 4-1 Scanning Electron Microscopy Micrographs of Nylon 6 Long Hollow Fibers. One large lumen with 15 µm internal diameter surrounded by 4 small channels could be observed per fiber. Smooth surface could also be seen.

4.2.3 Experimental Procedures of the Drug Loading Methods

Vacuum under negative pressure was the main drug loading method applied with the samples of long hollow fibers and woven fabrics respectively. For the method of loading drug solution into a long hollow fiber, a 10 cm specimen was cut. One end of the fiber was connected with the pump while another end was submerged into the drug solution. Negative pressure of 0.5 atm (i.e. vacuum) was subjected to the pump for 45 minutes in order to drive the drug solution into the lumens of the hollow fiber (Figure 4-2 a). For the method of loading drug solution into fabric or short fiber samples, the specimens were firstly submerged into a vacuum flask of a specific drug solution. The vacuum flask with the samples and the drug solution was sealed and swung slowly and thoroughly by hand until the big bubbles inside were removed. A negative pressure of no more than 0.5 atm was applied and subjected to the beaker for 15 to 30 minutes. The drug-loaded samples were then flushed by deionized water (D. I. water) for 3 times and were finally cured in air (Figures 4-2 b and 4-6 ai).

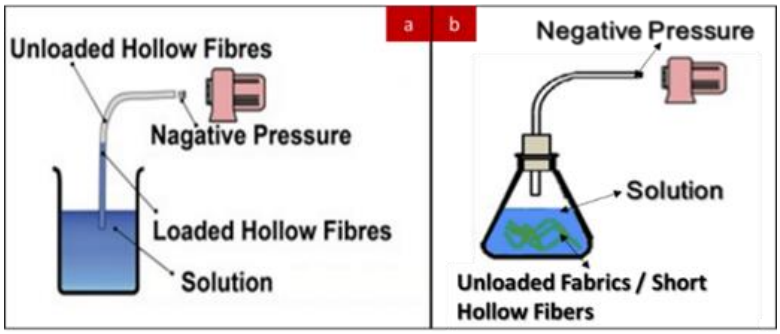


Figure 4-2 Schematic Figures of Drug Loading Methods. a) The schematic figure of the method of loading drugs into long hollow fibers. The drug solution was pumped into one end of the fiber by negative pressure. b) The schematic figure of the method of loading drugs into fabrics or short hollow fibers. The hollow fibers were submerged into the drug solution and the vacuum flask was sealed. The drug solution was driven into the lumen of fibers by negative pressure.

4.2.4 Experimental Procedures of In Vitro Antibacterial Analysis

This study aimed to focus on the in vitro antibacterial experimentation for investigating the effectiveness and efficiency of drug release from hollow fibers fundamentally. Further implementation of the textile-based drug delivery system is believed to be supported based on this investigation. The objective of the antibacterial analysis was referred to the principle of AATCC 147 method[104] with some amendments on the requirements of analysis. Four pieces of hollow fiber based fabric samples with an area of 1 cm x 1 cm each were cut. Three of the four pieces were loaded with antibiotic Penicilin-Streptomycin solution by the method of vacuum shown in Figure 4-2 b and one of them as the control specimen. After the drug loading process, the surface of the drug-loaded fabrics were washed with deionized water (D. I. water) to remove the drug attached on the surface of fabrics. The drug-loaded fabrics were then cured in air. The control and the drug-loaded specimens were placed onto an agar plate. Each of the specimens was lay across the parallel bacterial inoculum steaks which were spaced 0.5 cm apart. The bacteriostatic activity of the drug-loaded fabrics was determined

qualitatively based on the narrowing of streaks and the size of inhibition zone (Figure 4-6 aii).

4.2.5 Experimental Procedures of Drug Release Kinetics Analysis

The drug release kinetics, which is based on the liquid-driven drug delivery system of the hollow fibers, was studied. Polyethylene glycol (PEG) solution, deionized water (D. I. water) and ethanol were used as the loading agents for studying the relationship between the drug release kinetics of the lumen and the length of the hollow fibers. 3 cm and 20 cm of the hollow fibers were cut for comparing the differences in drug release kinetics between the short and long length of fibers. The liquid release from the lumens of the specimens was evaluated by a precise balance weighting. In order to eliminate the releasing of liquid out of the inner channel of the fibers, the completed fiber specimens were positioned as 'U' shape. The two opposite ends of the long fibers were positioned in parallel alignment.

4.3 Results and Discussion

In chapter 4.3, the drug loading and releasing performances of the nylon 6 hollow fibers were studied through the characterization and experimentations. Both bio-medical and physical practices were accomplished with the capillarity of the fibers.

4.3.1 Characterization of Hollow Fiber and the Drug Loading Capability

The industrial, ready-made nylon 6 hollow fibers were the main components of this pilot study. Fourier Transform Infrared Spectroscopy (FTIR) analysis had been performed for characterizing the structure of molecules of the nylon 6 hollow fibers by the spectrum of transmittance and the infrared absorption wavenumbers. The chemical

formula of polyamide 6 (PA 6) is known as $(C_6H_{11}NO)n$.[105] Several absorption regions could be identified as the fingerprint of PA 6 which include C=C stretch at 1610 – 1680 cm^{-1}, C=O stretch at 1680 – 1750 cm^{-1}, C-H stretch at 2840 – 3095 cm^{-1} and N-H stretch (primary amines) at around 3350 cm^{-1} (Figure 4-3 a)[106].

The drug loading capability of the hollow fibers was analyzed by the utilization of Optical Microscopic Characterization. It was observed that drugs were loaded into the channel of the hollow fibers in liquid phase, oil phase and suspended solid phase respectively. The drug loading method under negative pressure (vacuum), which was known for assisting in pulling water upward inside the lumens based on the capillary action[107], was verified. Various types of therapeutic drugs which include argyi oil, antibiotics and anti-cancer agents could be loaded successfully into the lumens of hollow fibers which are believed to be feasible in contributing to the applications of biomedical smart textile and clothing with drug delivery capability[108] (Figures 4-3 c to 4-3 e).

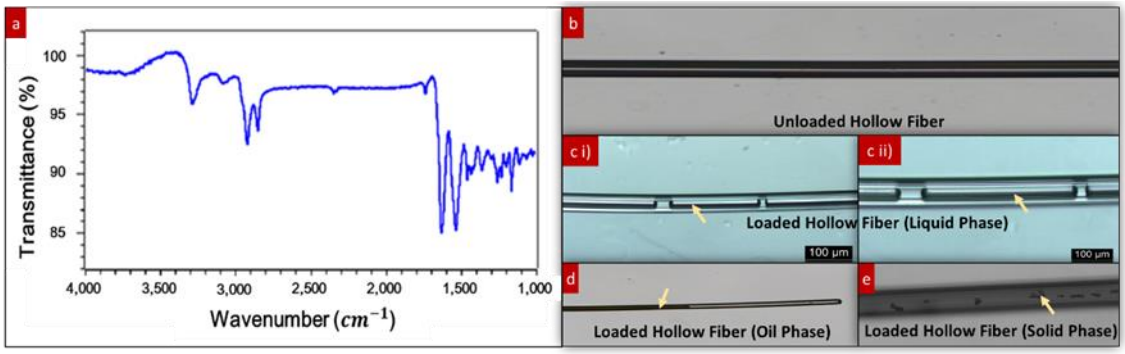


Figure 4-3 Fourier Transform Infrared Spectroscopy (FTIR) and Optical Microscopy Analysis. a) Fourier Transform Infrared Spectroscopy (FTIR) analysis of nylon 6 hollow fiber. Optical Microscopy analysis of b) unloaded and c – e) loaded hollow fibers. b) Unloaded hollow fiber; ci - cii) loaded hollow fibers in liquid phase; d) in oil phase and e) in solid phase.

The micro-channels of hollow fibers could be observed by the cross-sectional view

(Figure 4-4 a). The capillary of the hollow fibers could also be clearly identified with the use of fluorescence microscopy (Figure 4-4 c). To further examine the drug loading capability of the hollow fibers, loading dyes into the channels of fibers was performed. Methyl orange dye solution was loaded into the hollow fibers through pumping into one end of the fiber by negative pressure. Two woven fabrics were made for the dye-loading analysis, one consisted of nylon 6 hollow fibers as the warp yarns and another with the hollow fibers as the weft yarns. Although hollow fibers were woven into two directions (i.e. lengthwise and widthwise) respectively, there was no difference between the two fabrics as they had the same interlacement of the weave structure. It was observed that dyes were favorably loaded into the hollow fibers, either in warp or weft direction of the woven fabrics (Figure 4-4 b). It was thought that the drugs could be loaded into the channels of the fibers via the capillary action and the alteration of pressure. Fibers with lumens could facilitate the capillary action of fluid.[109] Fluid could rise inside the capillary of hollow fibers with an aid of surface-tension effect and the capillary action which was induced by the molecular forces between the fluid molecules and the wall of the capillary channel.[110]

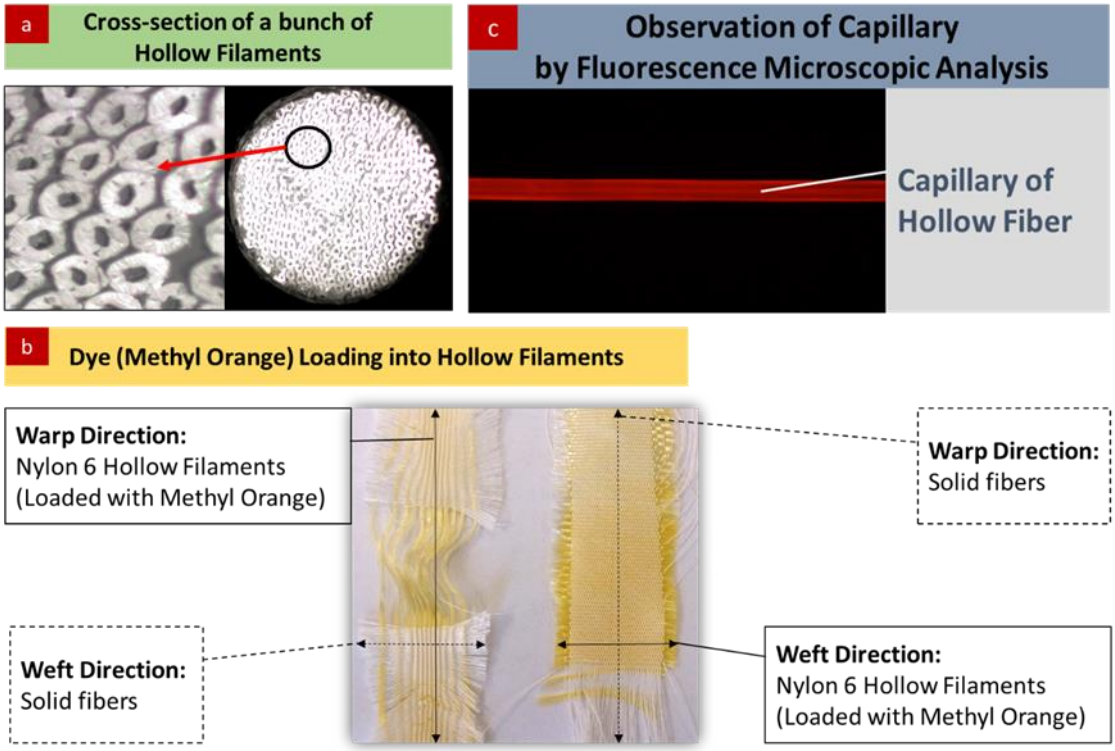


Figure 4-4 Cross-sectional Analysis, Methyl Orange Loading Analysis and Fluorescence Microscopic Analysis. a) Cross-section of a bunch of hollow fibers; b) loading of methyl orange dye solution; c) fluorescence microscopic analysis of fiber's capillary.

4.3.2 Drug Release Kinetics Analysis

For the drug release kinetics analysis, 3 cm and 20 cm length of hollow fibers were cut and loaded with 3 kinds of liquids (i.e. ethanol, D.I. water and PEG4000 solution) respectively. The hollow fibers were cut with an intact surface for drug release-length study as the surface morphology and the integrity could affect the efficiency of drug loading. The liquid releasing speed from the channels of hollow fibers was presented by the measurement of the weight ratio (W_r / W_0) where W_0 was the original weight of hollow fibers and W_r was the weight of hollow fibers after a duration of drug release. Specimens of both ethanol and PEG4000 solution were found to release relatively faster from the lumens of the shorter fiber (i.e. 3 cm) than that from the longer fiber (i.e. 20 cm) while the releasing speed of water from the shorter and the longer fiber was

believed to be similar at the initial stage of duration. Constant releasing speed of the three types of fluids could be identified when equilibrium was reached after a period of time (Figures 4-5 a to 4-5 c). Ethanol was found to have the fastest releasing or evaporating speed among the 3 liquid samples while PEG4000 solution was found to have the lowest speed at a specific duration (Figures 4-5 di and 4-5 dii). It was implied that PEG could help to decrease the escaping velocity of water molecules and that could assist the slow releasing of drugs with the use of hollow fibers in the textile-drug delivery system. The higher the viscosity of the fluid, the greater is the fluid friction induced between layers that resists the motion of flow. Internal friction between fluid molecules and external friction of how the viscous fluid interacts with the fibers are the two main factors. In contrast, the flowing velocity of a non-viscous fluid should be the same all along the channel based on the Poiseuille's law. Moreover, the fluid flow is defined as the volume of fluid transports a medium per unit time. The speed of fluid flow can increase when the cross-sectional area is smaller. The change of the fiber length and size was generally believed to influence the drug releasing speed as reducing the length of fibers (i.e. shorter fibers) would diminish the amount of drug loading and promote the rate of drug release.[94] The speed of flow would be inversely proportional to the length of fibers. Consequently, the results indicated that the change of size of hollow fibers had significant influence in controlling the rate of drug release from the capillary for different medical purposes. The risks of overdosing and chemical toxicity of drugs at the initial stages were believed to be prevented with the control and slower rate of drug delivery[71,79] by applying longer fibers in order to lengthen the distance of delivery and to reduce the diffusion velocity consequently.

4.3.3 In Vitro Antibacterial Analysis

To further examine the significance of the hollow fibers on the primary function of drug delivery, bio-medical analysis was conducted in respect with treating bacteria by using antibiotic-loaded hollow fiber based woven fabrics. Before performing the antibacterial experiment, the percentage of liquid loading of fabric by the method of vacuum was calculated. A formula of $[(W_2 - W_1) / W_1] \times 100\%$ was used for the calculation where W_1 was the dry weight of fabric and W_2 was the wet weight of fabric with the removal of surface liquid after vacuum loading. It was observed that the percentage of liquid loading could up to 68%.

For the antibacterial analysis of the drug-loaded hollow fiber based woven fabrics, a qualitative estimate of bacteriostatic activity of the antibiotic Penicillin-Streptomycin loaded hollow fiber based textile samples was resulted (Figure 4-6 b). It was indicated by the growth of the bacteria decreased from one end of the streak to another. The narrower the bacterial inoculum streaks, the thicker was the clear zone of inhibition, the stronger was the bacterial growth inhibition. It was observed that narrowing of streaks and a clear bacteria inhibition zone were successfully formed by the drug-loaded fabrics (i.e. II, III and IV) while there was no obvious change by the control specimen (i.e. I). The bacterial growth inhibition was believed to be significant for the drug-loaded hollow fiber based fabrics through the method of vacuum. Since the drug-loaded fabric samples had been washed for three times before the antibacterial testing, it was therefore believed that the drugs adhered on the surface of the fabrics had been washed away and the bacteriostatic effect would be induced by the delivery of drugs from the channels of the hollow fibers to the target site of action by diffusion.

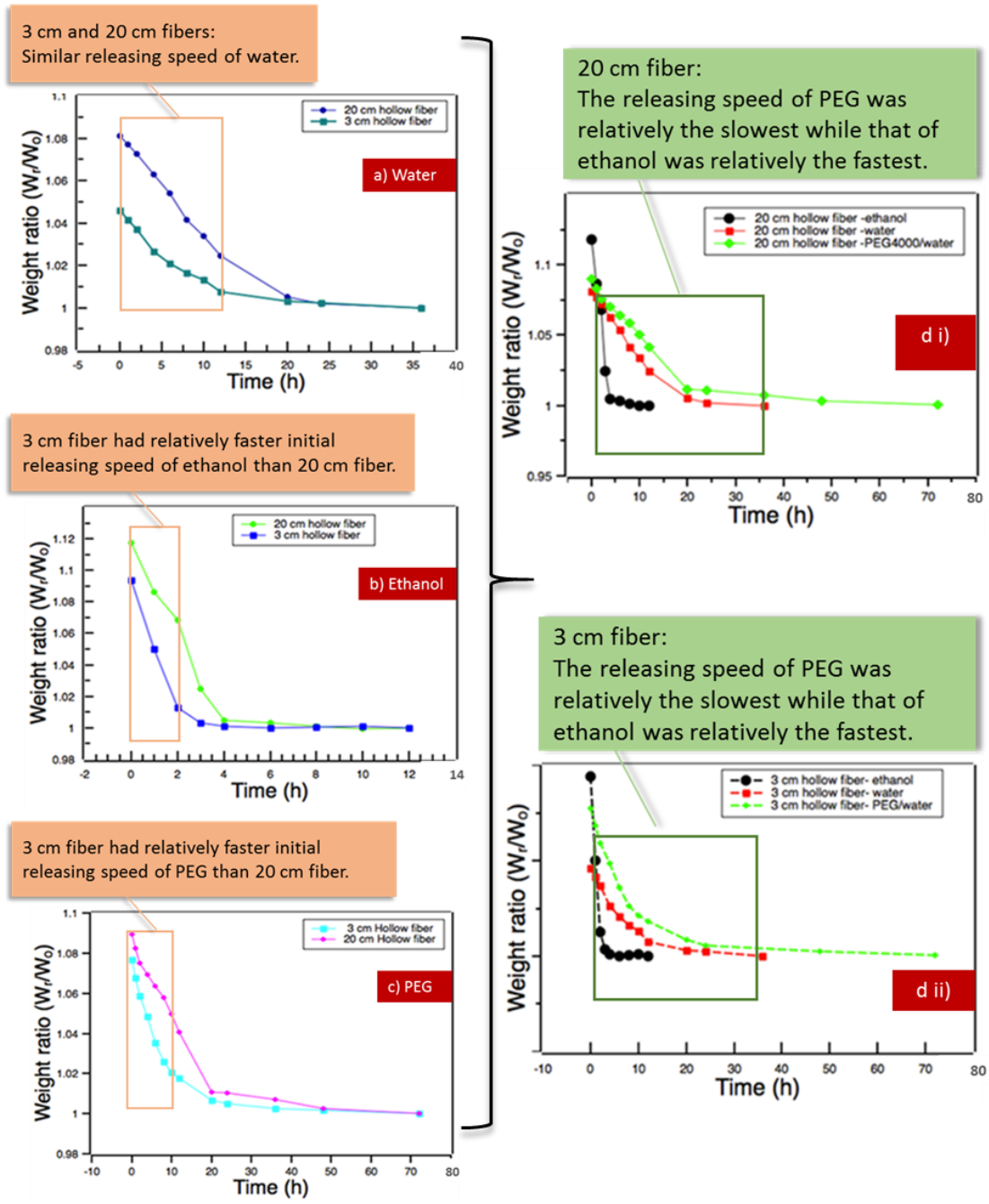


Figure 4-5 Releasing Kinetic Analysis. a) Water, b) ethanol, and c) PEG4000 solution were released from 3 cm and 20 cm hollow fibers respectively. a) Similar releasing speed of water was observed from both the shorter and longer hollow fibers at the initial stage. b, c) Ethanol and PEG4000 solution were found to had relatively faster releasing speed from the lumens of the shorter hollow fiber (i.e. 3 cm) than that from the longer one (i.e. 20 cm) initially. di, dii) Ethanol was found to have the fastest releasing or evaporating speed among the 3 liquid samples while PEG4000 solution was found to have the lowest speed.

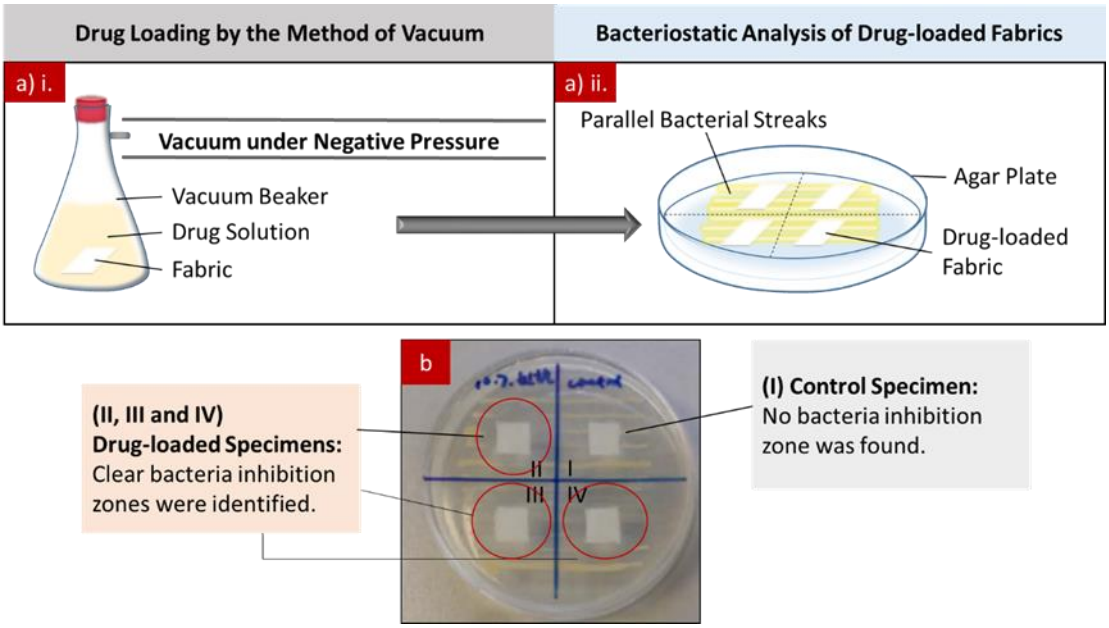


Figure 4-6 Schematic Diagram of Drug Loading Methods and the Results of Anti-bacterial Analysis. a) Schematic diagram of drug loading process by vacuum (i) and the antibacterial analysis of the drug-loaded fabrics (ii). b) Specimens II, III and IV were the Antibiotic Penicillin-Streptomycin drug-loaded samples while I was the control specimen. Narrowing of streaks and a clear bacteria inhibition zone were formed for the drug-loaded fabric samples II, III and IV respectively.

4.4 Summary of the Pilot Study

In this pilot study, the drug loading and releasing functionality from the interior channels of the hollow fibers were examined and verified so as to form a basis for the future works with the two textile dimensions, fibers and fabrics. Accordingly, the subsequent experimental procedures can be further refined and clarified. The first hand primary data can help to specify an appropriate direction of hollow fibers' usages. Through the direct purchase of the ready-made hollow fibers, the idea of 'new uses for old things' had been successfully proved. Matters in phase of liquid, oil or solid were favorably loaded into the channels of the hollow fibers and the release of antibiotic Penicillin-Streptomycin could also be affirmed. The sustainable use of hollow fibers with the drug loading and releasing functions can also be exhibited.

CHAPTER 5

PILOT STUDY OF HOLLOW FIBER – DRUG DELIVERY SYSTEM WITH ANTI-CANCER FUNCTION

5.1 Introduction of the Pilot Study

According to the pilot study on the usage of commercial hollow fibers for drug delivery, the concept of opening up new uses of traditional textile fibers had been realized by the primary exhibition of the textile drug delivery system with the ready-made hollow fibers physically and biologically.

Breast cancer is one of the most common cancer diseases. It ranks as the number one killer among women cancer in Hong Kong and the number three killer in the world.[111] It was found that breast cancer has accounted for 25.1% of the total number of new cases of cancer in Hong Kong.[112] Besides, it was also discovered that there is a tendency of more females begin to suffer from breast cancer at a younger age nowadays.[111]

Postoperative breast reconstruction operation, either breast reconstruction from one's own tissue (i.e. mastectomy) or prosthesis (i.e. wearable or implanted artificial breast), is a very common way for postoperative remediation. However, possible cancer remnants, local cancer recurrence and metastasis would still be a concern when these are discovered after the surgery. Various attempts have been made to treat the possible cancer remnants and to diminish the opportunity of cancer recurrence, examples like radiotherapy, chemotherapy, targeted therapy and hormone therapy by tablet or injection[113,114] (Figure 5-1). Nevertheless, the effect of some of the conventional

treatments is not prolonged or significant. Some of these treatment even cause side effects, such as swelling and thickness of the breast, blistering of skin tissues, feeling fatigue, weakening of immune system and getting muscle aches and headaches[111,112]. Meanwhile, the risk of recurrence may not be eliminated thoroughly.[113] Postoperative care is a considerable issue and it is crucial to produce a smart textile with drug delivery function for a long duration of treatment.

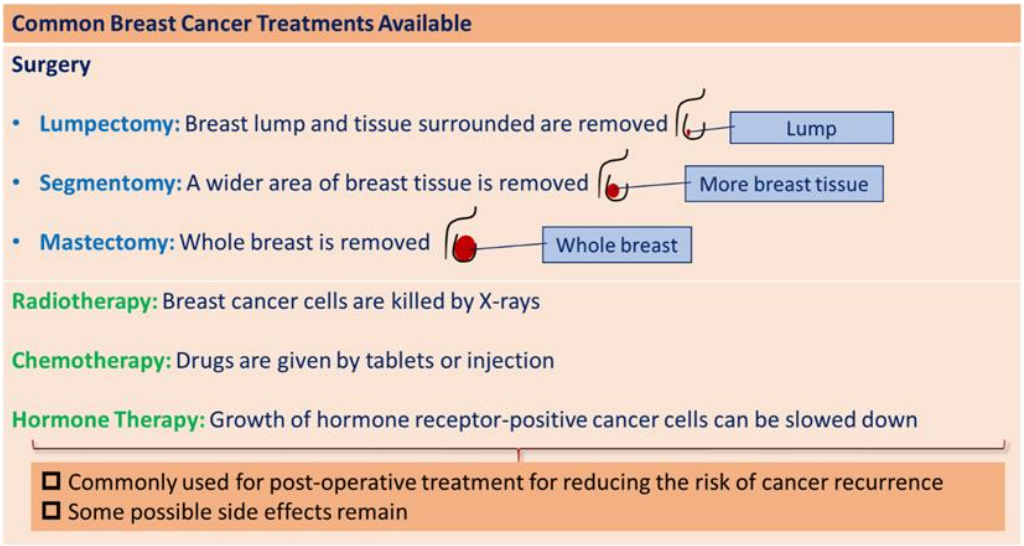


Figure 5-1 Common Current Breast Cancer Treatments.

Nevertheless, some limitations of the current transdermal textile technology still exist. The major concerns are that a) the technology may be far from industrialization as it might not be sufficiently mature for real practice and commercialization; b) drugs may not able to be reloaded; c) the preparation process might be complicated, as the materials are typically prepared via chemical methods that might not be suitable for loading complex compositions or compound drugs; and d) some of the technology are probably not scalable in terms of safety and size. These drawbacks have hindered the development and acceptance of textile-based drug release systems between the industry and general public.

Therefore, this study aims to develop the hollow fiber - smart textiles to treat breast cancer by the drug delivery ability. Unlike those existing textile-based drug release systems, this system is believed to 1) offer repeatable drug loading and releasing; 2) be suitable for loading compound drugs; 3) give convenience and comfort to breast cancer patients without influenced by the external factors easily; 4) be commercialized and industrialized. This is a versatile and simple method for 5- Fluorouracil (5-FU, C4H3FN2O2, 130.08g/mol, Sigma-aldrich) drugs to be carried in the core of hollow staple fibers of non-woven fabrics, while maximizing convenience and comfort level for patients with breast cancer. The burdens on medication could be greatly reduced and thus the quality of life could be improved.

5.2 Experimentation and Development

The experimental design of the research project was categorized into several parts, which includes 1) characterization of hollow fibers; 2) drug loading methods; 3) drug loading and releasing investigation through physical analysis; 4) drug loading and releasing investigation through biological analysis.

5.2.1 Preparation of Fiber Materials and Specimens

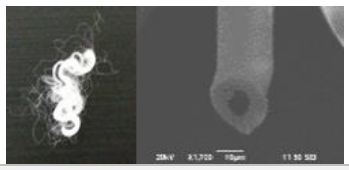
This project focused on the utilization of nylon-polyester (PA-PET) staple crimped hollow fibers. Non-woven fabrics, which were made of the PA-PET hollow fibers, would be the specimens of the drug loading layer for the experiments in this study. The drug loading and releasing functionality of the synthetic staple crimped hollow fibers were exhibited with the consolidation of the anti-breast cancer drugs, textile fibers and fabrics.

Nylon-polyester staple crimped hollow fibers had been selected for being a drug carrier due to the high surface area to volume ratio and drug loading capability of the lumen. The waviness of the crimped fibers is thought to contribute to an efficient yarn spinning and fabric production. Fibers can be assembled easily in non-woven fabrics. Dimensional stability and bulkiness of fabrics can be preserved as well (Table 5-1).[115] The staple crimped hollow fibers were produced by melt spinning. During the spinning process, the melted polymeric spinning solution was extruded from the spinneret with a specific hollow shape. The stream of polymer was then cooled and solidified. The structural configuration of the hollow fibers could be kept uniform. Crimps were added and maintained via the relaxation process.

5.2.2 Preparation of Fabric Samples

For the preparation of the non-woven fabric specimens (i.e. drug loading layer), the hollow fibers were utilized in making the prototype of non-woven fabrics by using the needle-punching method. A spun-bonded web was made by mechanically orienting and interlocking the fibers with an aid of the barbed felting needles. The interlocked web with certain thickness and density was created and the needle-punched non-woven fabric was made (Table 5-1).

Table 5-1 Experimental Elements of the Drug Loading Layer.

Name of Elements	**Nylon-polyester staple crimped hollow fibers**	**Non-woven fabrics made of hollow fibers**	**Fluorouracil (5-FU)**
			
Specification of Hollow Fiber	Fiber Fineness: 1.5D Fiber Length: 38 mm Internal Diameter of Hollow: ~ 8 - 10μm Overall Diameter of Fiber: ~ 20μm		

5.2.3 Experimental Procedures of the Drug Loading Methods

Two different drug loading approaches had been investigated and compared with one another. The first drug loading method was started with simple direct infiltration. A bunch of staple crimped hollow fibers were submerged inside a glass container with the drug solution. The soaked fibers were then stirred up along with the rotating magnetic field of a magnetic stirrer at 280 rpm. Applying the mechanism of vacuum loading under negative pressure was the second method for examination. A bunch of staple crimped hollow fiber samples were firstly submerged into a tube of drug solution. The tube together with the samples and the drug solution was sealed inside a Büchner flask. The flask was then subjected to a vacuum machine with a water circulating vacuum pump and the drug solution was loaded into the fibers under the pressure of 0.05 – 0.06 mPa for 20 minutes.[116] The samples were exported and dried in air. The drug loading method would be optimized and the most suitable method would be chosen between the above two for the investigation of the non-woven fabrics (i.e. drug loading layer) (Figure 5-2).

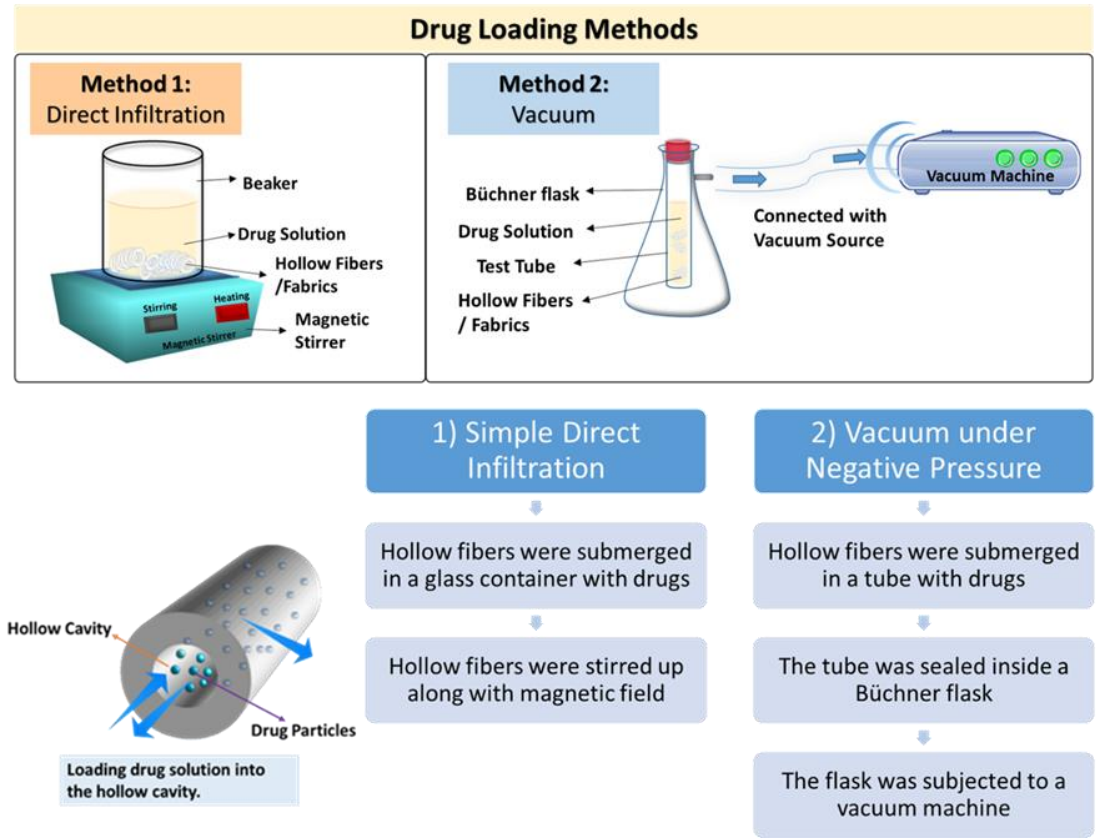


Figure 5-2 Schematic Representation of the Drug Loading Methods. (a) Schematic representation of the simple direct infiltration. (b) Schematic diagram of the vacuum loading. Hollow fibers or fabrics were submerged into a tube of drug solution.

5.2.4 Experimental Procedures of Physical Characterization of Drug Loading Efficiency

The influence of fluid viscosity on the loading efficiency of hollow fibers was initially investigated by using two different types of loading content, water and polyethylene glycol (PEG) solution. The loading efficiency was calculated by measuring the original weight of hollow fibers before loading, the original weight of drugs given and the weight of loaded drugs. The loading efficiency of the non-woven fabrics with the two loading methods (i.e. direct infiltration and vacuum) was also examined to provide a primary data for the subsequent biological analysis.

5.2.5 In Vitro Primary Study of Anti-breast Cancer by the Hollow Fiber - Drug Delivery System

The anti-breast cancer activity of the 5-FU (anticancer drugs)-loaded hollow fibers was first studied by utilizing MDA-MB-231 breast cancer cells. The breast cancer cells were cultivated and passaged prior to the anticancer experiment. 0.025 g of hollow fibers were placed onto an upper transwell with a selectively permeable membrane. Breast cancer cells with a concentration of 1×10^6 / ml were placed at the lower layer of each well of a plate. The plate was then incubated at 37 ℃ for 24 hours which could ensure the cells were completely attached at the bottom of the well. Migration of the drugs from the lumens of the hollow fibers to the target site of cells could also be guaranteed by the permeable filtering of the transwells. After the investigation of the hollow fibers, non-woven fabrics which were made of hollow fibers with a size of 0.8 cm × 0.8 cm each, were loaded with 5-FU drugs and undergone the same anticancer experimental procedures. The viability and the cell growth inhibition of the breast cancer cells were recorded by calculating the percentage of viability and the cell count respectively (Figure 5-3).

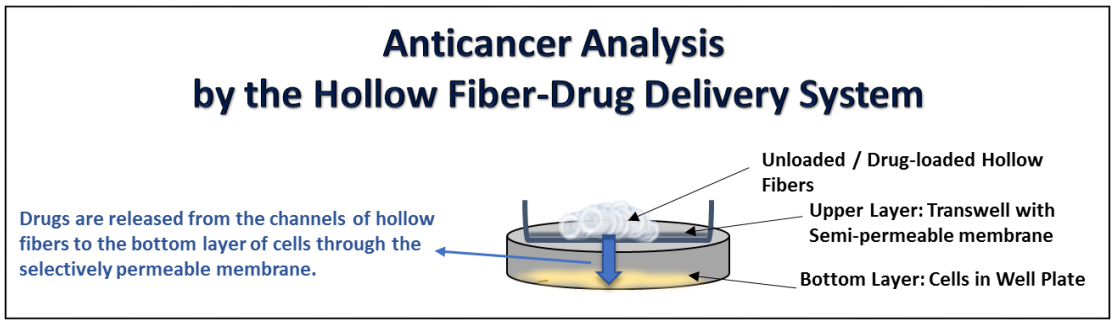


Figure 5-3 Schematic Representation of Anti-breast Cancer Analysis for the Primary Study of the Hollow Fiber - Drug Delivery System. The cancer cells were cultivated and passaged prior to the anticancer experiment. Hollow fibers or fabrics were placed onto an upper transwell with a selectively permeable membrane. Breast cancer cells were placed at the lower layer of each well of a plate. Migration of the drugs from the lumen of the hollow fibers to the target site of cells could also be guaranteed by the permeable filtering of the transwells.

5.3 Results and Discussions

This section has been divided into two main parts, 1) physical characterization of hollow fibers and the drug loading capability; 2) biological analysis of hollow fiber - drug delivery system in related to the medical function of anti-breast cancer.

5.3.1 Characterization of Hollow Fibers and the Drug Loading Capability

The structure and morphology of hollow fibers were studied by using scanning electron microscopy while the drug loading capability through the channels of hollow fibers was analyzed by both optical and fluorescence microscopies.

5.3.1.1 Structural and Morphological Study by Scanning Electron Microscopy

The cross-sectional structure of hollows and the surface morphology of the nylon-polyester staple crimped hollow fibers were analyzed by the scanning electron microscopic investigation. There was only one single lumen observed in the cross-sectional view with an internal diameter of approximately 8 – 10μm. The general diameter of the hollow fibers was approximately 20μm. Smooth surface could be seen in Figure 5-4.

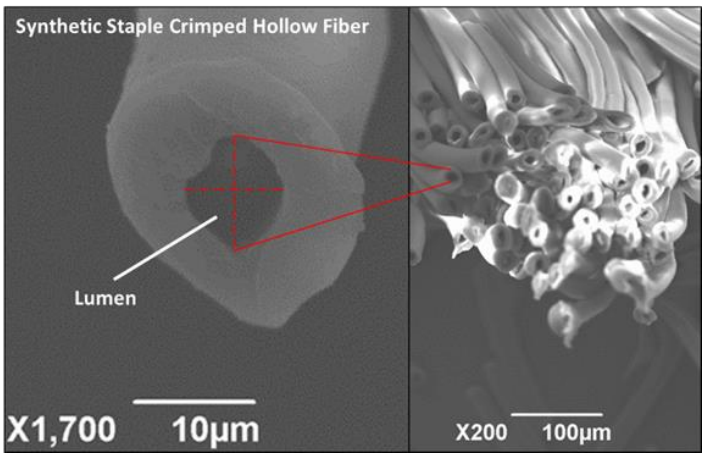


Figure 5-4 Scanning Electron Microscopy Micrographs of Nylon-polyester Staple Crimped Hollow Fibers. One single lumen with an internal diameter of approximately 8 – 10 μm was observed per fiber. Smooth surface morphology was seen.

5.3.1.2 Microscopic Analysis of the Drug Loading Capability

The drug loading capability of the hollow fibers was firstly observed by optical microscopy shown in Figure 5-5. It was observed that drugs in either liquid phase (with the use of anti-cancer medicine like 5-FU) or crystal solid phase (with the use of Chinese medicinal herbs called Borneol or Bing Pian) could be successfully loaded into the channels of the hollow fibers. The drug loading method under negative pressure (vacuum), which was known for assisting in pulling water upward inside the lumens based on the capillary action,[107] was verified. For the application of vacuum suction, an appropriate suction flow rate could be generated so as to extract the air out of the internal lumens of the hollow fibers. The air pressure inside the hollow fibers would be hence diminished to a certain value which would be smaller than the atmospheric pressure outside the fibers. As a result, drugs could flow into the lumens of fibers. Significant loading of therapeutic drugs such as the 5-FU anti-breast cancer drug solution into the channels of the hollow fibers was also verified. It is believed to be an essential evidence for the production of medical smart textiles and wearables for transdermal therapy. Additionally, gas bubbles were found inside the lumens of hollow fibers from the optical and fluorescence microscopic images (Figure 5-6). It may indicate that the inner pressure of hollow fibers is small enough to drag in the drug solution inside the fibers' channels as gas bubbles remained and did not burst.

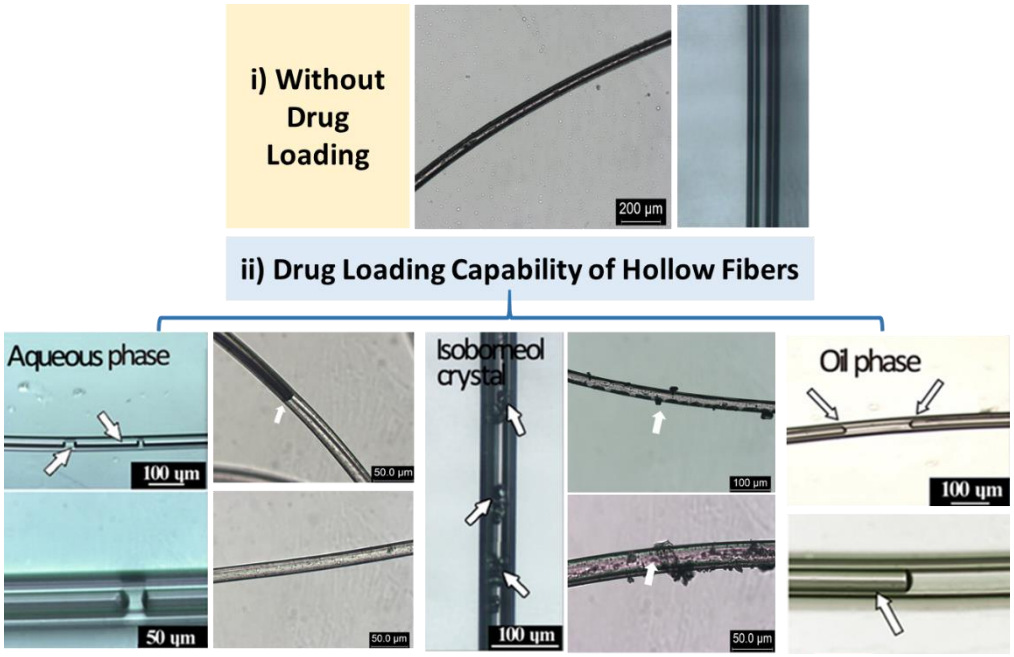


Figure 5-5 Optical Microscopic Analysis of Drug Loading Capability. It was observed that drugs in liquid phase and crystal solid phase could be successfully loaded into the channels of the hollow fibers respectively.

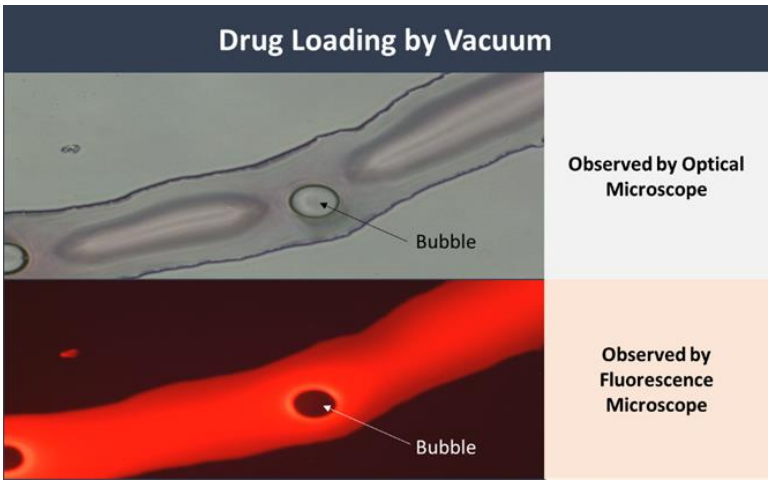


Figure 5-6 Optical and Fluorescence Microscopic Analysis of the Vacuum-drugs-loaded Hollow Fiber. Bubbles were found inside the lumens of hollow fibers.

5.3.2 Physical Characterization of Drug Loading Efficiency

The influence of fluid viscosity on the loading efficiency of hollow fibers was firstly examined by loading water and polyethylene glycol (PEG) solution respectively. By using the same loading method of vacuum, the drug loading efficiency of water was 18.4% higher than that of PEG. It is generally believed that the higher the viscosity, the

higher the resistance of a fluid to flow through the channels of hollow fibers. As the viscosity of PEG is relatively higher than water, there would be stronger intermolecular forces between molecules that may hinder the rate of flow.[117,118] The drug loading efficiency of PEG was thus lower. By measuring the weight of fluid-loaded fibers on consecutive day intervals, it was discovered that the rate of weight loss of water-loaded fibers was similar with that of PEG-loaded fibers. It may imply that the release rate of fluid with higher or lower viscosity within the hollow fibers was similar (Figure 5-7 a).

The drug loading efficiency of the non-woven fabrics by using different loading methods, direct infiltration and vacuum was also investigated so as to provide preliminary data for the anti-cancer analysis. Therefore, fabrics were placed in an open ventilated condition on day 2 for simulating the air-dry process after drug loading. On days 3 and 4, fabrics were placed back to a container in order to simulate the situation when being inside the cell plate. The drug loading efficiency of the hollow fibers by vacuum was 19.4% higher than that of direct infiltration. It was thought that the method of vacuum could allow higher rate of flow and loading ability. By measuring the weight of drug-loaded fabrics on consecutive day intervals, it was found that the rate of weight loss on day 2 was much higher than that on days 3 and 4 for both methods. The rate of weight loss became constant where the ventilation of air was diminished on days 3 and 4. It was also discovered that the weight of infiltration-drugs-loaded fabric on day 2 had already decreased to that on day 0 which was the original weight of the fabric without loaded-drug. In contrast, the weight of vacuum-drugs-loaded fabric on days 2, 3 and 4 was still higher than that on day 0. It may further indicate that the loading ability of the method of vacuum was more significant (Figure 5-7 b).

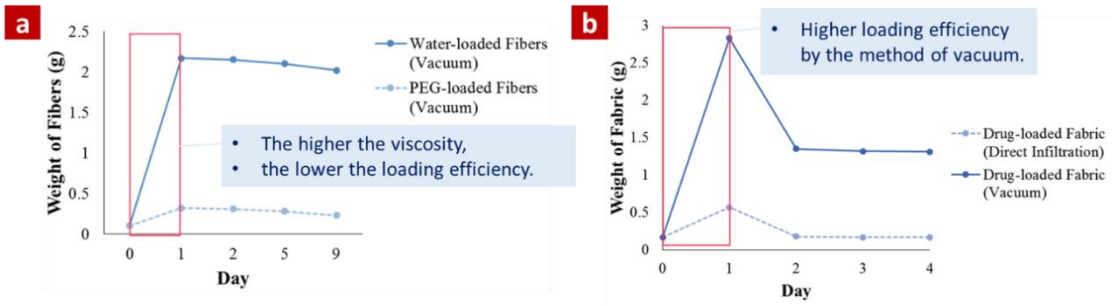


Figure 5-7 Physical Characterization of Drug Loading Efficiency. (a) The higher the viscosity, the higher the resistance of a fluid to flow through the channels of hollow fibers. (b) The drug loading efficiency of the method of vacuum was higher than that of the method of direct infiltration which could allow higher rate of flow and loading ability.

5.3.3 In Vitro Anti-breast Cancer Analysis by the Hollow Fibers - Drug Delivery Layer

The effectiveness of drug release from hollow fibers and that of non-woven fabrics (i.e. drug delivery layer) was illustrated by the in vitro anti-breast cancer investigation. Meanwhile, the anticancer effect was represented by the cancer cell count and cellular viability with the use of trypan blue dye exclusion. The total number of cells and the percentage of cellular viability were calculated with the formulae as shown below:[119]

1) The total number of cells = cell count / ml × volume of cell suspension
2) The percentage of cellular viability = (total number of viable cells / total number of viable and dead cells) × 100%

To investigate and compare the drug delivery performance of the staple crimped hollow fibers and the effectiveness of delivering drugs from the fibers to the target sites of breast malignant cells, MDA-MB-231 breast cancer cell line was chosen and grown. 5-FU anticancer drug was chosen to be the loading agent. At the beginning, the anticancer drug was loaded into hollow fibers by two different methods, direct infiltration (i.e. immersion) for 10 seconds and vacuum under negative pressure for 20 minutes as a

preliminary examination. The time for drug loading was varied for the two methods. It was because the drugs might not be given enough time for infiltrating into the lumens of hollow fibers within 10 seconds whereas much of the solution might only be adhered on the surface of fibers. Due to this prediction, an anti-breast cancer analysis by observing the cell count was performed. It was found that much fewer breast cancer cells in the culture plate could grow and survive when drugs were delivered from the vacuum-drugs-loaded hollow fibers than that from the infiltration-drugs-loaded hollow fibers for 2-Day, 4-Day and 6-Day delivery respectively. The results suggest that more drugs were carried by the vacuum-drugs-loaded hollow fibers as drug loading into the lumens was significantly higher with sufficient loading time. Thus, more drugs could be released to the cultured cancer cells and inhibited their growth. Significant breast cancer cell growth and proliferation inhibition was shown by the vacuum-drugs-loaded hollow fibers. Additionally, the rate of drug delivery was the fastest in the initial stage while became slower for a duration of drug delivery. It may due to the reason that the concentration gradient of encapsulated drugs was the highest in the initial phase. Therefore, faster release profile could be obtained at the beginning. Nevertheless, reduction of concentration gradient occurred after a period of time which diminishing the rate of drug diffusion. The rate of drug delivery would become slower and sustained. (Figure 5-8).

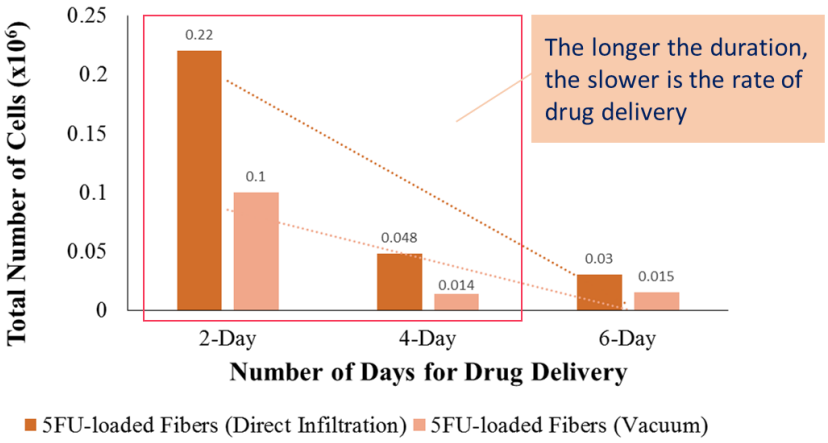


Figure 5-8 The Cancer Cell Count after 2-Day, 4-Day and 6-Day Drug Delivery by Drug-loaded Hollow Fibers. Fewer breast cancer cells could grow and survive when drugs were delivered from the vacuum-drugs-loaded hollow fibers to the culture plate than that from the infiltration-drugs-loaded hollow fibers for 2-Day, 4-Day and 6-Day delivery respectively. Significant breast cancer cell growth inhibition was shown by the vacuum-drugs-loaded hollow fiber. The rate of drug delivery was the fastest in the initial stage while became slower for a duration of drug delivery.

To proceed the investigation of the drug release performances by the vacuum-drugs-loaded and the infiltration-drugs-loaded hollow fibers, both the total number of cancer cells and the percentage of cellular viability were counted during 2-Day drug delivery. Before the test, drugs were loaded into the hollow fibers by two different methods, direct infiltration with magnetic stirring for 20 minutes and vacuum under negative pressure for 20 minutes. The drug loading duration was the same for both methods because this factor should be kept constant this time for finding out which method would induce higher loading ability into the hollows. Besides, magnetic stirring was applied in the method of direct infiltration for examining whether the prompted magnetic current would have the same loading effect as vacuum. According to the result, it was shown that the average percentage of cell viability was 92.1% for the untreated cancer cells which are grown under normal conditions. The percentage of cell viability was reduced to 60.4% and 74.1% when the vacuum-drugs-loaded hollow fibers and the

infiltration-drugs-loaded hollow fibers were placed respectively for 2-Day drug delivery. Cytotoxic effect was successfully shown by using both drug loading approaches. Furthermore, higher portion of cancer cells became unviable or dead when vacuum-drugs-loaded hollow fibers were placed as its percentage of cell viability was lower than that of infiltration-drugs-loaded hollow fibers (Figure 5-9 a). In regard to the cancer cell count, a significant decrease in the total number of cells from 2.42×10^6 cells to 0.43×10^6 cells and 0.76×10^6 cells when the vacuum-drugs-loaded hollow fibers and the infiltration-drugs-loaded hollow fibers were placed respectively for 2-Day drug delivery. Much fewer breast cancer cells could grow with the application of drug-loaded hollow fibers. It indicated that the drug solution was successfully released from the hollows for both loading methods and effective inhibition of cell proliferation was shown. Additionally, higher significance of inhibition effect was found for the method of vacuum. This could be because more drug solution had been loaded into and stored inside the hollows by the method of vacuum under negative pressure. Thus, more effective release of drugs to the target site of cancer cells accordingly (Figure 5-9 b).

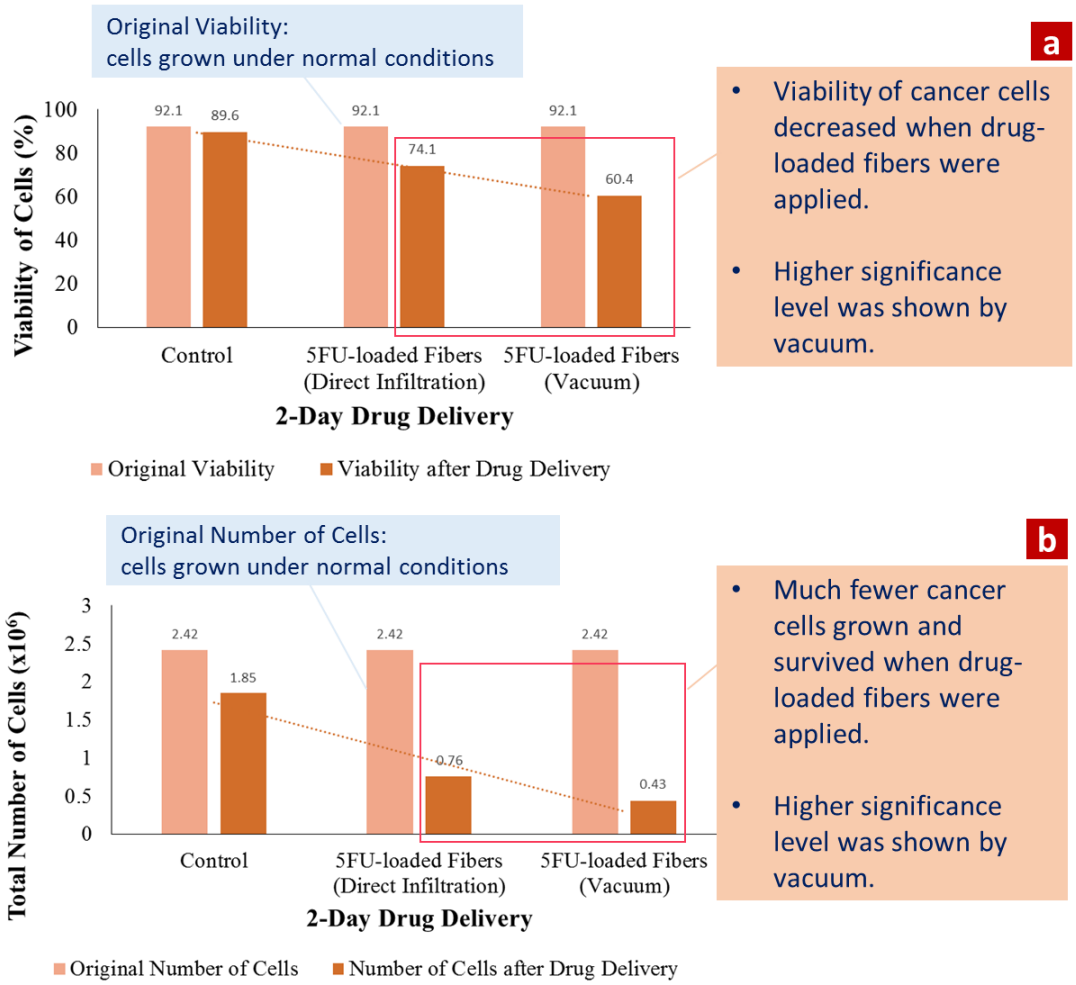


Figure 5-9 Cellular Viability and Cell Count after 2-Day Drug Delivery by Drug-loaded Hollow Fibers. (a) Cytotoxic effect was successfully shown when drug-loaded fibers were applied. Higher portion of cancer cells became unviable or dead when vacuum-drugs-loaded hollow fibers were placed. (b) A significant inhibition of cell proliferation when drug-loaded fibers were applied. Higher significance of inhibition effect was found for the method of vacuum.

By observing the microscopic imaging of cancer cell distribution in the bottom layer of transwells in Figure 5-10, a) no hollow fiber was placed on the upper layer; b) hollow fibers without loaded drugs were placed on the upper layer; c) infiltration-drugs-loaded hollow fibers were placed on the upper layer and d) vacuum-drugs-loaded hollow fibers were placed on the upper layer. In accordance with the observation, cancer cells grew rapidly under the normal condition (Figure 5-10 a). Although the morphological appearance of cancer cells in Figure 5-10 c iii was similar with that in Figure 5-10 a iii,

a reduction of cell proliferation and an alteration of cell appearance were shown in Figure 5-10 c i when being compared with Figure 5-10 a i. It may due to the situation that only some portions of the cell growth had been suppressed by applying infiltration-drugs-loaded fibers. According to the image of cancer cells with released drugs from vacuum-drugs-loaded hollow fibers (Figure 5-10 d), it was found that the morphological structure of cells was very varied from the normal cells and a large reduction of viable cells could be seen when compared with the others.

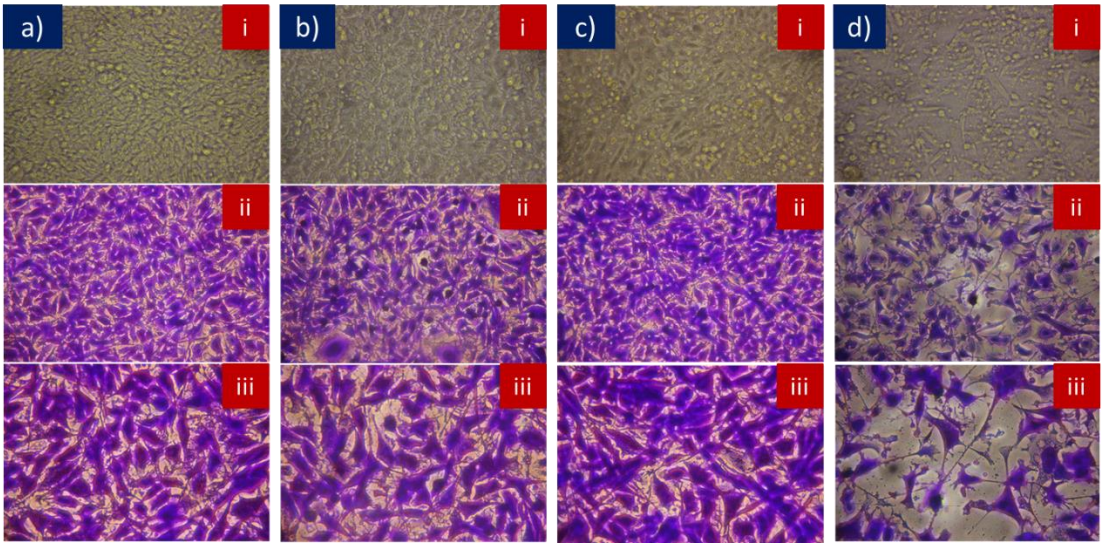


Figure 5-10 Microscopy of Breast Cancer Cell Distribution with 2-Day Drug Delivery. The morphology of cancer cells in (c) and (d), which were treated with released drugs from hollow fibers, was different from the normal cancer cells. The morphology of cells was very different from the normal cells and fewer viable cells could be seen in (d).

In addition to the textile-based drug delivery system, fabrication of non-woven fabrics was made for further examining the effectiveness of drug loading and release functions of hollow fibers when they were in different textile structure, orientation and geometrical arrangement. Similar as the previous investigation, both the total number of cancer cells and the percentage of cellular viability were counted during 2-Day drug delivery. Based on the result, it was shown that the percentage of cell viability was originally 93.8% for the untreated cancer cells which were grown under normal

conditions. The percentage of cell viability was reduced to 53.6% and 60.3% when the vacuum-drugs-loaded fabrics and the infiltration-drugs-loaded fabrics were placed respectively for 2-Day drug delivery. Cytotoxic effect towards breast cancer cells was successfully induced by utilizing the two approaches. Moreover, more unviable and dead cancer cells were found with the released drugs from vacuum-drugs-loaded fabric as its percentage of cell viability was lower than that of infiltration-drugs-loaded fabric (Figure 5-11 a).

Regarding to the total number of cancer cells, a significant decrease in the total number from 0.54×10^6 cells to 0.26×10^6 cells and 0.35×10^6 cells when the vacuum-drugs-loaded fabric and the infiltration-drugs-loaded fabric were placed respectively for 2-Day drug delivery. It was believed that the drug solution was also successfully released from the hollow fibers even they were fabricated and interlocked in a random structure. Significant cell growth inhibition was identified by the two methods. Furthermore, more promising inhibition effect was found for the method of vacuum. It was estimated that more drug solution had been loaded into and stored inside the hollows by the method of vacuum under negative pressure. Thus, more effective release of drugs from different directions of the fibers to the target site of cancer cells was resulted (Figure 5-11 b).

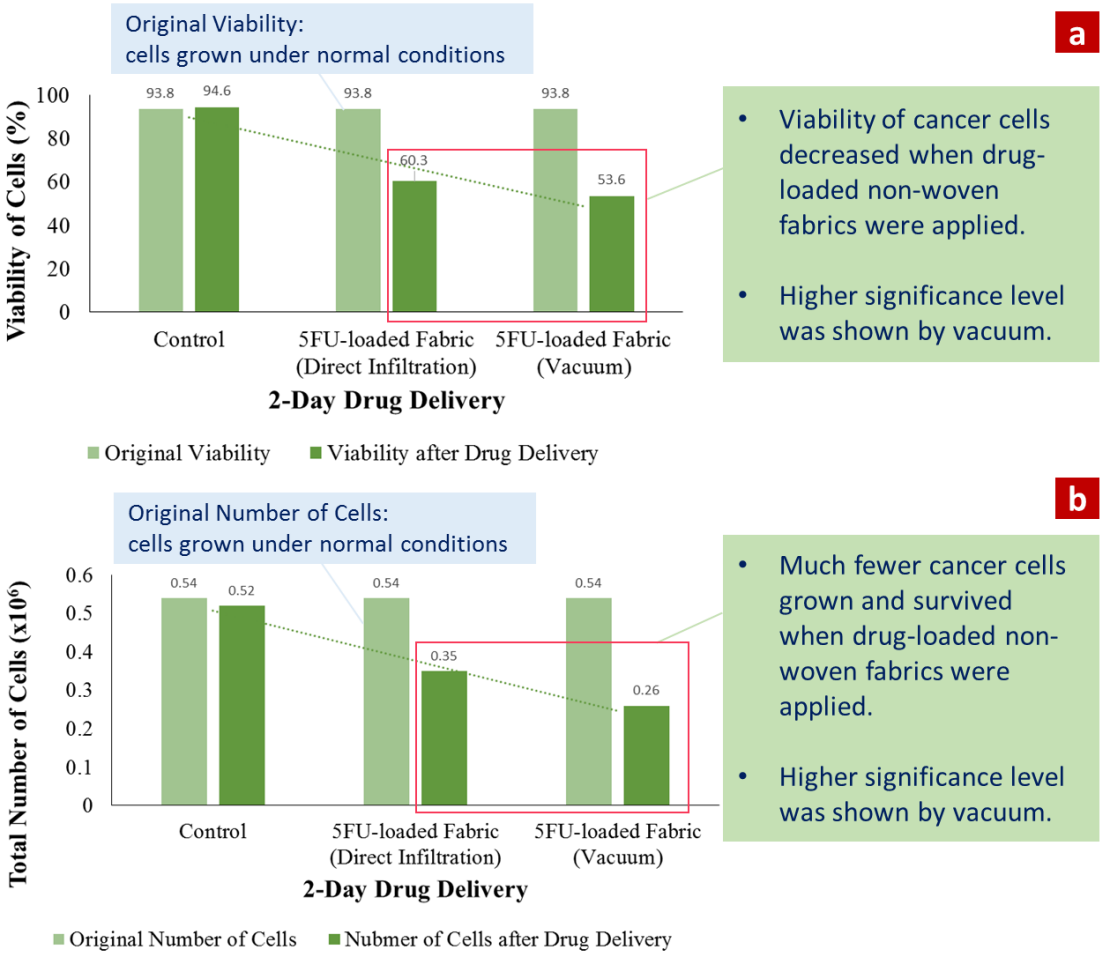


Figure 5-11 Cellular Viability and Cell Count after 2-Day Drug Delivery by Drug-loaded Non-woven Fabrics. (a) Cytotoxic effect was successfully shown when drug-loaded fabrics were applied. Higher percentage of cancer cells became unviable or dead when vacuum-drugs-loaded fabric was placed. (b) A significant inhibition of cell proliferation when drug-loaded fabrics were applied. Higher significance of inhibition effect was found for the method of vacuum.

According to the results of the biological analysis, it was found that significant anti-breast cancer performance could be resulted from both infiltration-drugs-loaded hollow fibers and vacuum-drugs-loaded hollow fibers. Nevertheless, more effective result could be seen from the drug loading of vacuum under negative pressure. A possible explanation for the reason is that more drug solution was transported and has flown through the hollows for filling the voids due to differential pressure inside the suction system.[120,121] Besides, the adhesion between the walls of hollows and the drug fluid

was perhaps greater than the cohesion between drug molecules, thus, capillary forces might also be attributed to pull the drug solution to fill in the hollows.[122] By contrast, the anti-breast cancer performance was less significant resulted from the loading method of direct infiltration with magnetic stirring. Although rotating magnetic field was caused by the motor-driven magnet.[123] the turbulence induced was not sufficient for loading the same amount of drug solution as that by vacuum-driven approach.

5.4 Summary

To confirm the feasibility of the proposed idea, we used a "5-Fluorouracil (5-FU)" which is known as an anti-breast cancer (i.e. antimetabolite and antineoplastic) drug, approach to be loaded into nylon-polyester staple crimped hollow fibers for treating the breast cancer cells (i.e. MDA-MB-231 breast cancer cells) during the process of drug release. Trypsin-EDTA solution, Dulbecco's modified eagle medium (DMEM) and fetal bovine serum (FBS) were used for cell culture and passage. Borneol (Bing Pian), which is a kind of Chinese medicinal herbs, was utilized to observe the isoborneol crystals loading capability (i.e solid phase) of the hollow fibers. Pure water and 5-FU drugs were utilized to observe the loading capability of aqueous phase respectively.

The proposed study will have potentially significant positive ramifications for medical development, innovation in both chemical-based and herbal-based medicine, and care possibilities for patients. Furthermore, this research will serve as a basis for future research, thereby drawing considerable attention, and related works may be performed to pursue other potential applications. Moreover, the proposed system will integrate advanced technologies in various fields, such as textiles, medicine, chemistry, physics, and biology. By creating a new form of medical treatment, this study will offer

considerable benefits to patients who seek long-term medical treatment and to the apparel industry by creating aesthetic, multifunctional, and high-value-added commercial apparel products. It is expected that the developed garment will span multidisciplinary gaps and create an innovative form of medical therapy. The potential of creating the brasseries or tops which can help to mitigate the progression of breast cancer is believed to be realized with the advancement of the transdermal thermal hollow fiber – drug delivery system.

CHAPTER 6

ADVANCED STUDY OF HOLLOW FIBER – SMART TEXTILES WITH THERMAL-STIMULI DRUG DELIVERY FUNCTION

6.1 Introduction of the Advanced Study

Thermal stimulation involves the supply of heat energy by utilizing heat-releasing objects with designated thermal conductivity. In the process of implementing the thermal-stimuli drug delivery function, two different layers of the smart textile wearables, which are the thermal conductive e-fabric layer (TL) and the drug delivery layer (DL), were studied. For realizing the concept, both layers were attached together. Different electric-heating temperatures could be obtained by the thermal conductive e-fabric layer when connecting to different levels of electric power supply. Hereafter, a designated level of heat energy could be transferred to the drug delivery level through conduction, convection and radiation for a specific medical requirement of drug release. It is believed that an efficient delivery of drugs to the human body under optimum conditions could be achieved by the self-heating system in a precise and controllable manner with defined delivery strategies (Figure 6-1).

This advanced study had been categorized into the following approaches which include i) infra-red thermographic study of thermal distribution; ii) biological study of drug release with thermal stimulation; iii) physical study of liquid release with thermal stimulation. The study would be an important milestone for comprehending the utilization of different heating temperature and geometric allocations with respect to different heating geometric position of ergonomics such as limbs, joints, abdomen and head. Besides, thermal stimulation could also play a crucial role in optimizing the drug

releasing speed, releasing profile and its therapeutic performances (Figure 6-1).

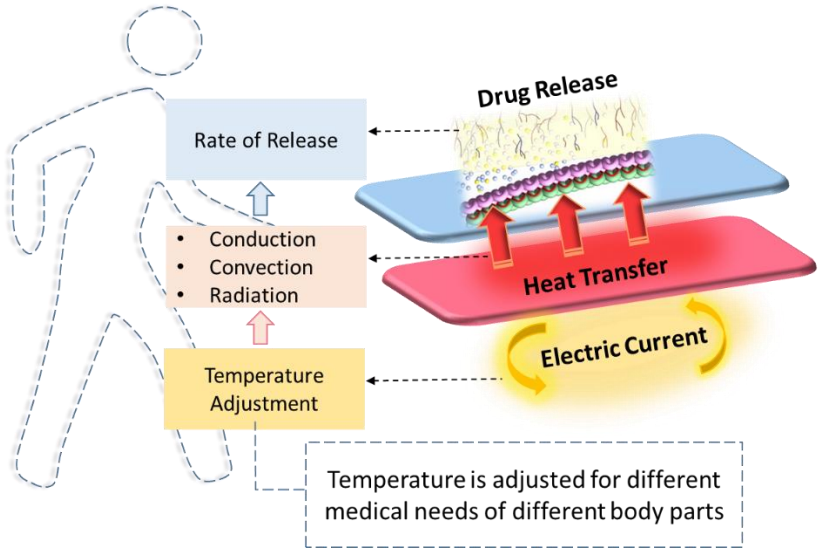


Figure 6-1 Schematic Diagram of Thermal-Stimuli Drug Delivery System. Temperature can be adjusted for different medical purposes of different body parts. A designated level of heat energy can be transferred to the drug delivery layer for a specific medical requirement of drug release.

6.2 Experimentation and Development

6.2.1 Preparation of Materials and Specimens

- Drug Delivery layer

The nylon-polyester (PA-PET) staple crimped hollow fibers, which had been the specimens for the experimentation in chapter 5, were also used for making the needle-punched non-woven fabrics (i.e. drug delivery layer) for this advanced study.

- Thermal Conductive E-fabric Layer

When preparing the thermal conductive e-fabric layer for infra-red thermographic investigation, the electrical-conductive thermal components were made by parallel three lines of silver-coated (Ag-coated) nylon conductive yarns (47tex, linear electric resistance: 1.0 Ω/cm) embroidered through the proposed non-woven fabrics made of hollow fibers. Self-heating function would be performed. During a real situation of

thermal stimulation, direct current electric power supply with specific voltage (v) would be provided at the two electrodes. After a specific duration, the heating temperature can maintain at a constant level. Silver-coated yarns had been chosen for the thermal-stimuli drug delivery system because of their outstanding chemical, mechanical and physical properties such as high mechanical stability and flexibility, good spinning ability and light in weight. Besides, as silver can be uniformly coated onto the surface of non-conductive nylon fibers, thus, reliable resistance towards laundry and corrosion can be functioned which provides significant performance in conducting electric current. (Figures 6-2 and 6-3).[124]

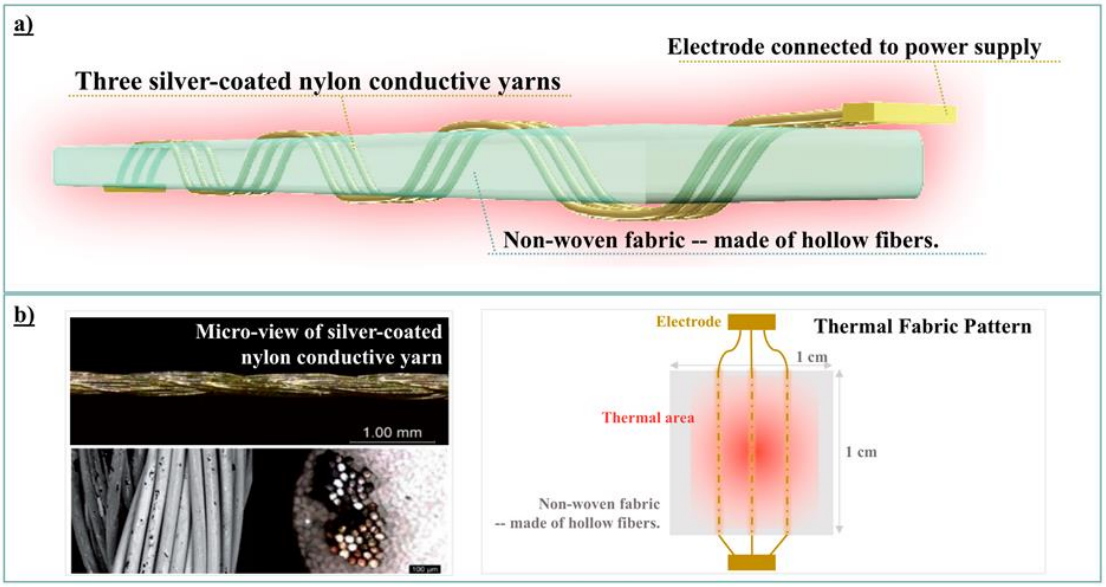


Figure 6-2 Smart Textile Fabric with Thermal-stimuli Drug Delivery Function. Electrical-conductive thermal fabrics made by silver-coated conductive yarns embroidered through the proposed non-woven fabrics made of hollow fibers: a) the 3D view of the fabric structure; b) the micro-view of silver-coated nylon conductive yarn & the thermal fabric pattern drawing.

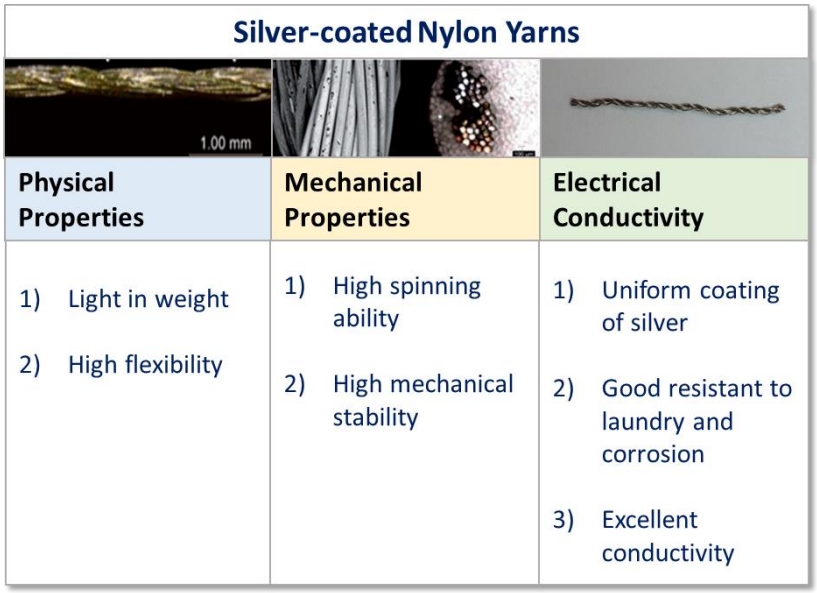


Figure 6-3 Outstanding Properties of Silver-coated Nylon Yarns.

6.2.2 Experimental Procedures of Drug Loading Method

Vacuum loading was chosen for the advanced study based on the significant results in chapter 4 and chapter 5. The drug delivery layers (non-woven fabrics) were submerged into a flask of drug solution and then subjected to a vacuum machine under the pressure of 0.05 – 0.06 mPa for 20 minutes. The exported drug delivery layers were dried in air (Figure 6-4).

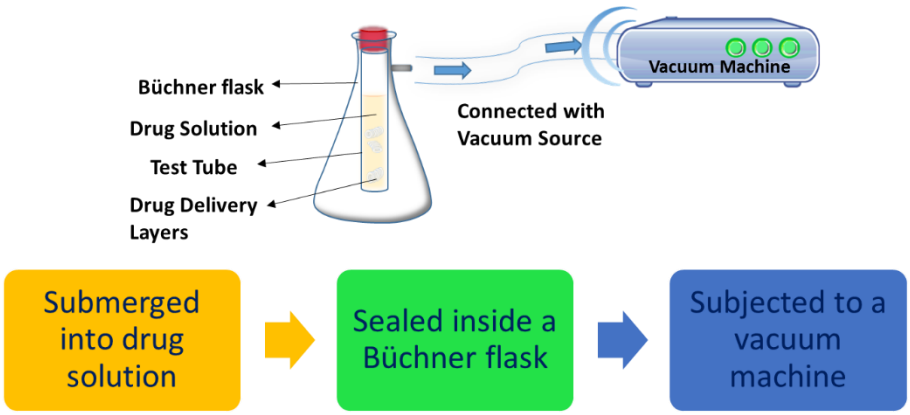


Figure 6-4 Schematic Representation of the Drug Loading Method by Vacuum.

6.2.3 Experimental Procedures of Infra-red Thermography

For investigating the thermal distribution of the thermal conductive e-fabric layer, silver-coated conductive yarns exhibited different levels of sheer resistances through different yarn embedding arrangements. Under different levels of electric power supply and following the Joule's law, different levels of heating temperatures could be achieved. The heating geometric allocations of the fabric layer was observed through capturing the infra-red thermography of the different heating levels. Besides, the stability of electrical conductivity was studied and the thermal distribution at particular temperature intervals was measured.

6.2.4 Experimentation Procedures of Drug Release with Thermal Stimulation under Biological Investigation

To further study the implementation of the hollow fiber - drug delivery system with thermal stimulation, the drug delivery layers (i.e. non-woven fabrics), which were under thermal heating with the use of digital block heater, were investigated. Each of them was placed inside a tube of cell culture medium. Each tube was heated at specific temperature (i.e. 37℃ and 42℃). After 1 hour, the solution was centrifuged under 8000 rpm for 2 minutes. The supernatant was collected from each tube and was then placed into a well of breast cancer cells (Figure 6-5). The effect of thermal heating towards the drug release function from the crimped hollow fiber structure and the relationship between temperature and the effects of drug release kinetics from the non-woven fabrics were examined.

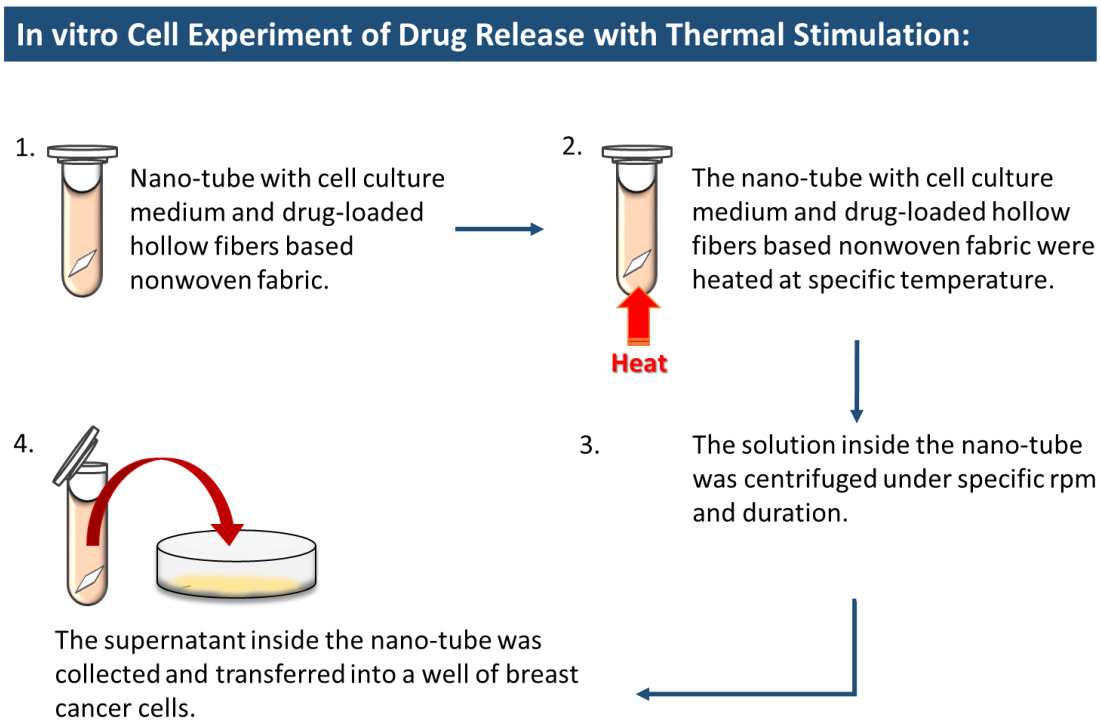


Figure 6-5 Flow Chart of In Vitro Cell Experiment of Drug Release with Thermal Stimulation. The drug-loaded hollow fiber based non-woven fabric with the medium were heated at specific temperature. The supernatant collected was then transported into a well of breast cancer cells for further investigation.

6.2.5 Experimental Procedures of Liquid Release with Thermal Stimulation under Physical Investigation

Loading agent, 1% blue acid dye, was diluted to specific concentrations (1:5, 1:25 and 1:125) respectively for calibration and comparison. The dye-loaded specimens (i.e. non-woven fabrics) were placed in a sealed centrifuge tubes containing 1 ml deionized water. The specimens were then placed in a digital heat block at a specific temperature (25 ℃, 37 ℃, 40 ℃, 43 ℃). At regular time intervals (1 hour, 2 hours, 3 hours), 0.3 ml of solution was taken from a centrifuge tube. Visible absorbance was measured using a microplate reader at a specific wavelength (Table 6-1 and Figure 6-6).

Table 6-1 Experimental Elements of Liquid Release with Thermal Stimulation.

	Fluid Delivery Layer	Instruments for Thermal Stimulation
Name of Elements	a) Nonwovens made of Hollow Fibers 	a) Digital Block Heater 

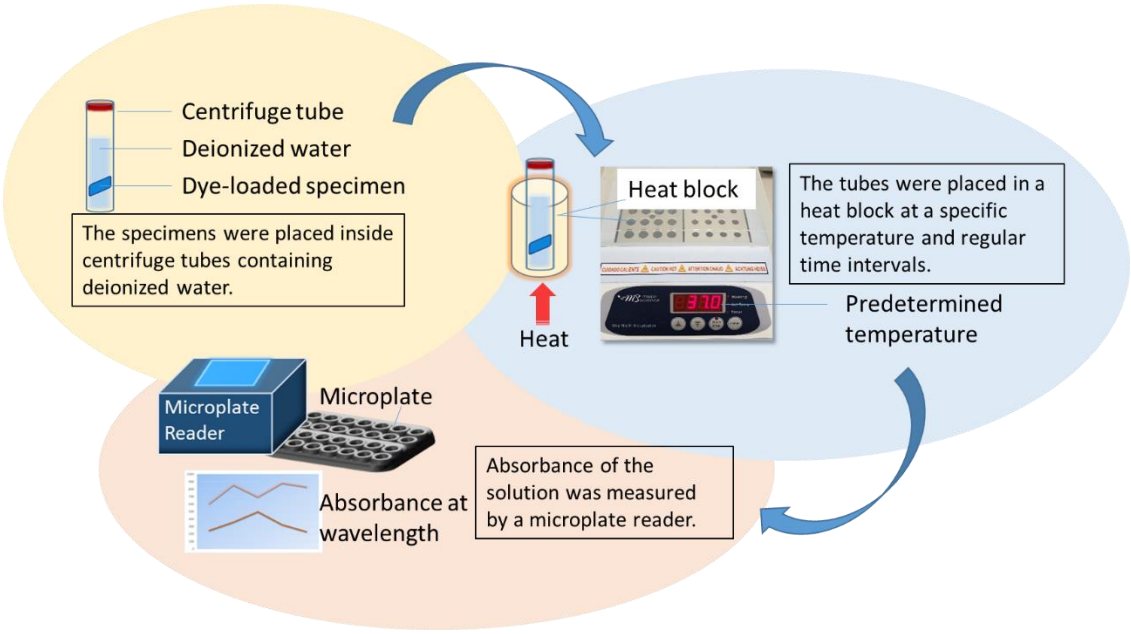


Figure 6-6 Schematic Diagram of Liquid Release with Thermal Stimulation under Physical Investigation. The dye-loaded specimens (i.e. non-woven fabrics) were placed in a sealed centrifuge tubes containing 1 ml deionized water. The specimens were then placed in a digital heat block at a specific temperature. At regular time intervals, specific amount of solution was taken from a centrifuge tube. Absorbance was measured using a microplate reader at a specific wavelength.

6.3 Results and Discussion

6.3.1 Thermal Distribution of Thermal Conductive E-fabric Layer

The drug delivery or releasing textile wearable is a topical transdermal system. Therefore, in this wearable itself, it is composed of two layers for thermal-stimuli drug delivery function: the first layer is the electric-heating and high thermal conductive e-fabric layer (TL), with silver-coated conductive yarns embedded through and the second layer is the drug contained/delivery layer (DL). In the thermal conductive e-fabric layer, silver-coated conductive yarns exhibited different levels of sheer resistances through different yarn embedding arrangements. Under different levels of electric power supply and following the Joule's law, different levels of heating temperatures could be achieved.

Herein, in this research, an analysis of the heating effects by integrating both thermal and drug delivery layers was conducted (Figure 6-7). The different heating levels (ranged from 25 ℃ to 42 ℃) were achieved by different levels of power supply, while various allocations of heating effects were achieved by embedding silver-coated conductive yarns in different parts of the TL, as shown in Figure 6-8. Infra-red thermography of the different heating levels was captured as shown in Figure 6-9. In general, three different heating geometric allocations, which include the central spot, quadrilateral area and peripheral area, were shown. Highest temperature was indicated at the central spot (i.e. in color white to red), whereas temperature decreased gradually from the center to the nearby quadrilateral area (i.e. in color yellow) and the temperature became the lowest at the peripheral area (i.e. in color blue). It is believed that the variation in heating geometric allocations and thermal distribution could influence the drug releasing mechanism with respect to the medical needs of different parts of body

such as limbs, joints, abdomen and head. Therefore, silver-coated conductive yarns would have different arrangements embedded into the proposed TL to generate various amount of heat energy for designated therapeutic effects.

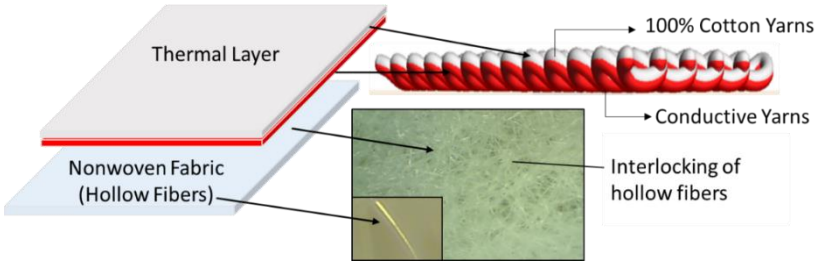


Figure 6-7 Combination of Thermal-stimuli and Drug Delivery Layers. It was made by embroidering the thermal conductive e-fabric layer with silver-coated conductive yarns through the non-woven fabric made of hollow fibers (drug delivery layer).

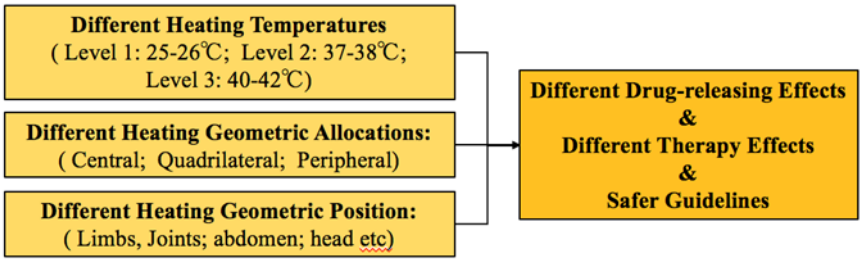


Figure 6-8 The Three Basic Influencing Factors towards Drug Delivery.

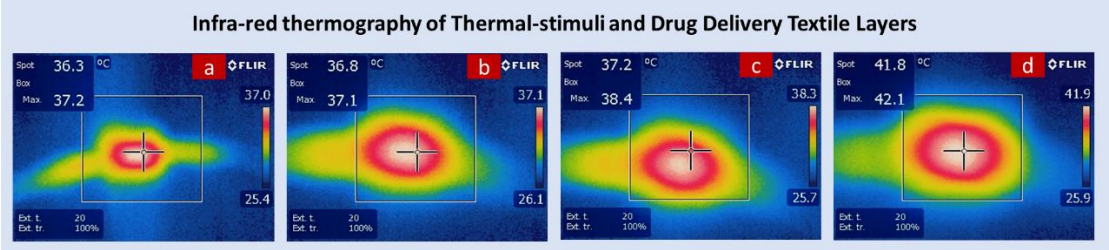


Figure 6-9Infra-red Thermography of Thermal-stimuli and Drug Delivery Textile Layers. a) to d) Different heating levels (ranged from 25 ℃ to 42 ℃) were achieved by different levels of power supply, while the various geometric allocations of heating effects were observed.

6.3.2 Drug Release with Thermal Stimulation under Biological Investigation

After the primary investigation of the textile-based drug delivery system by using hollow fibers, thermal-stimuli therapeutic technology was integrated in order to promote the effectiveness of drug release. The drug delivery layer, which was the non-

woven fabric made of PA-PET staple crimped hollow fibers, was initially investigated with thermal stimulation in order to examine the effect of thermal heating towards the drug release kinetics from and within the crimped hollow structure of fibers. Temperatures of 25 ℃ (i.e. room temperature as control), 37 ℃ (i.e. body temperature) and 42 ℃ (mild heating temperature) were the target range of thermal stimulation given to the 5-FU-loaded non-woven fabric specimens (Table 6-2). The effectiveness of drug release at a particular heating temperature and heating duration was examined by calculating the viability of breast cancer cells after the released drugs were collected from the heated specimens and transferred to the plates with breast cancer cells.

Table 6-2 Indications of Drug-loaded Specimens.

	Status	***Room Temperature***	***Thermal Stimulation***
Specimen 1	Control	25 ℃	/
Specimen 2	Heated	/	37 ℃
Specimen 3	Heated	/	42 ℃

According to the results shown in Figure 6-10 a, 5-FU-loaded non-woven fabrics were being placed at 25 ℃ as the control and heated at 37 ℃ for 60 minutes respectively. It was observed that a decrease of cancer cell viability from 93.25 % (i.e. cancer cells grown under normal condition) to 86.50 % (i.e. treated with drug released from 25 ℃ - control specimens) and 85.80 % (i.e. treated with drug released from 37 ℃ - heated specimens) respectively. Additionally, fewer cancer cells grew and survived for the heated specimens when comparing with the control one. For the results of Figure 6-10 b, 5-FU-loaded non-woven fabrics were heated at 37 ℃ and 42 ℃ for 60 minutes respectively. It could also be seen that a decrease of cancer cell viability from 92.05% (i.e. cancer cells grown under normal condition) to 87.00 % (i.e. treated with drug released from 37 ℃ - heated specimens) and 86.15 % (i.e. treated with drug released

from 42 ℃ - heated specimens) respectively. Fewer cancer cells grew and survived for the 42 ℃ - heated specimens comparatively.

To summarize the above results, more cancer cells became unviable and dead after being treated with the drugs released from the heated-specimens at higher temperature. Cytotoxic effect was slightly more prominent when providing mild heating temperature than that by applying body temperature. Similarly, body temperature could contribute to better cytotoxic performance when comparing with room temperature. It may due to the reason that as the encapsulated drugs inside the channels were heated up with thermal stimulation, the drug molecules would be excited to move. The surface tension of drug fluid would be reduced by the energy of molecular movement. The drug fluid would become less viscous with increasing temperature. The rate of drug flow through the channels to the target site of cancer cells would thus be enhanced with decreasing resistance.[125,126] Furthermore, only a slight reduction in the percentage of viability was observed for the treated cancer cells. It was probably because the drug released from the specimens for one hour only possessed a little portion of the encapsulated drugs which might not outweigh the growth of cancer cells entirely. No apparent burst effect was shown for the first hour upon the placement of the drug-loaded fabrics at the cell plates. Rate limiting effect of drugs could be encouraged with the use of staple crimped hollow fibers.

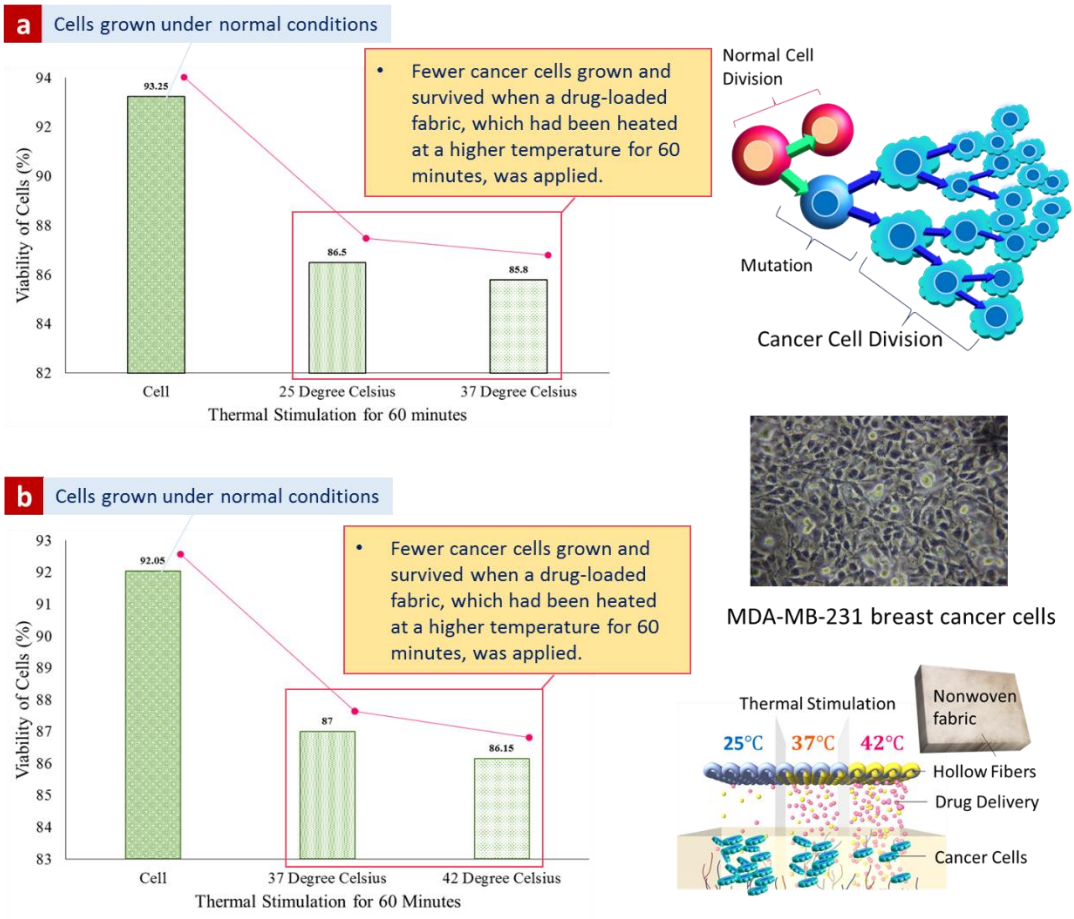


Figure 6-10 Viability of Cells by treating with Thermal-stimulated Drug Delivery Specimens. a) 5-FU-loaded non-woven fabrics were being placed at 25 ℃ as the control and heated at 37 ℃ for 60 minutes respectively. b) 5-FU-loaded non-woven fabrics were heated at 37 ℃ and 42 ℃ for 60 minutes respectively.

6.3.3 Liquid Release with Thermal Stimulation under Physical Investigation

6.3.3.1 Results

Regarding to the biological analysis of drug delivery, physical investigation of liquid release was also performed in order to make a comprehensive study together with both biological and physical perspectives. For measuring the visible absorbance (i.e. optical density) of the liquid dye released from the heated specimens, wavelength of maximum dye absorption at 595 nm was chosen. Based on the results of Figure 6-11 a i) and a ii), linear relationship between optical density (O.D.) and concentration of released dye was observed. The measurement of O.D. at wavelength with maximum absorbance

increased with increasing concentration of dye solution and vice versa.

To compare and contrast the result of visible absorbance for different durations, a summary was outlined as followings. After the first 1-hour release, the measurement of O.D. of specimen 1 (control, 25 ℃) was the lowest, the O.D. of specimen 3 (heated, 40 ℃) was a little higher than that of specimen 2 (heated, 37 ℃) and the O.D. of specimen 4 (heated, 43 ℃) was the highest. The higher the temperature given for thermal stimulation, the higher was the concentration of dye released (Table 6-3 and Figure 6-11 b).

During the second 1-hour release, the order of O.D. of the specimens became slightly different. It was observed that the rate of dye released from specimen 1 was markedly higher when being compared with those specimens with thermal stimulation. Gradual increase of O.D. was identified from specimen 2 while slight increase of O.D. was shown for specimen 3 and specimen 4 respectively (Figure 6-11 b).

After the third 1-hour duration, only the O.D. of specimen 1 kept increasing but was slower in rate whereas the O.D. of the other specimens with thermal stimulation decreased or unchanged. For specimen 2, the rate of dye release became nearly constant from 2-hour to 3- hour thermal stimulation. For specimen 3, the O.D was found to descent after 3-hour thermal stimulation and the value was even lower than that after 1-hour heat stimulation. For specimen 4, the measurement of O.D. decreased after 3-hour heat stimulation which was found to be the same as that after 1-hour heat stimulation (Figure 6-11 b).

Table 6-3 Indications of Dye-loaded Specimens.

	Status	*Room Temperature*	*Thermal Stimulation*
Specimen 1	Control	25 ℃	/
Specimen 2	Heated	/	37 ℃
Specimen 3	Heated	/	40 ℃
Specimen 4	Heated	/	43 ℃
Thermal Stimulation (Duration)			
1-hour : First 1-hour	2-hour : Second 1-hour	3-hour: Third 1-hour	

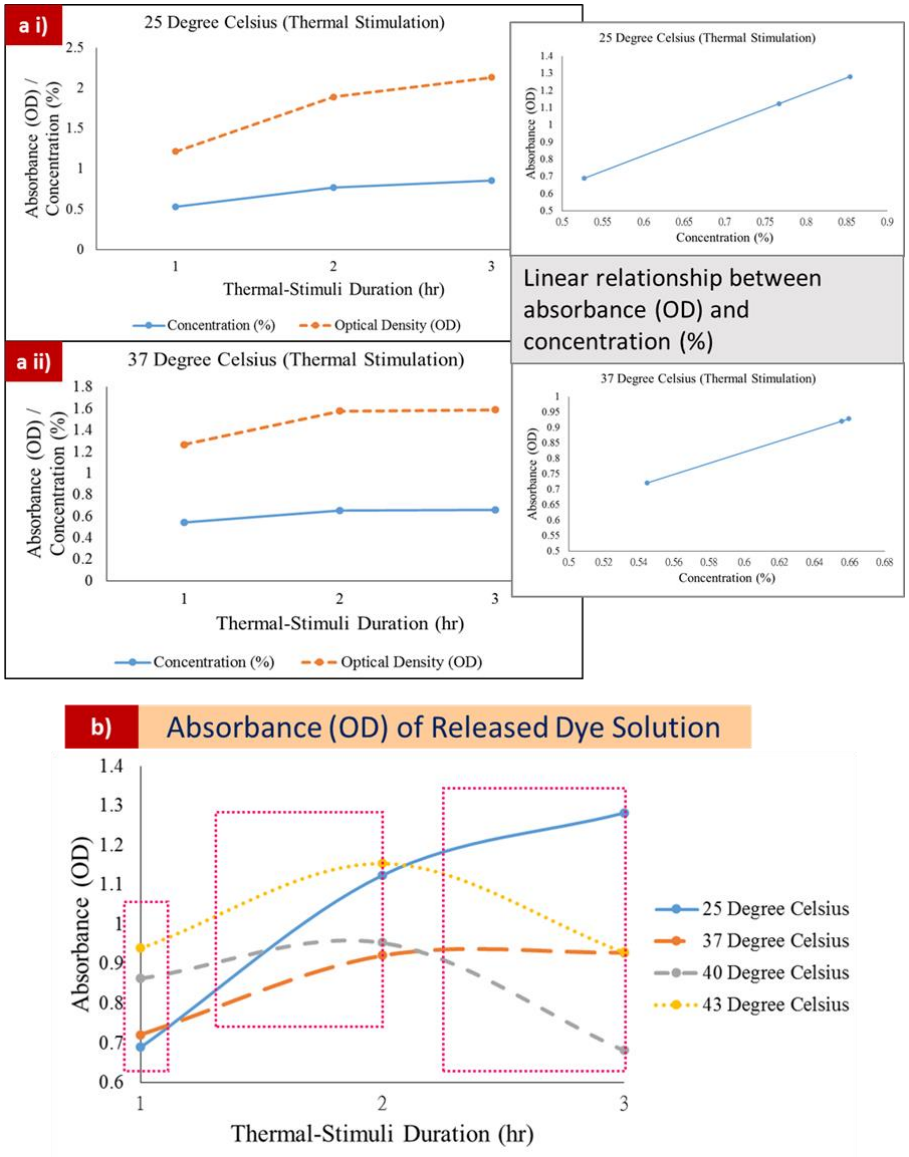


Figure 6-11 Visible Absorbance of Released Dye. a) i) and ii) Linear relationship between absorbance (O.D.) and concentration of released dye. b) Visible absorbance of released dye in related to thermal stimulation at 25℃, 37℃, 40℃ and 43℃ respectively at different durations.

6.3.3.2 Discussion and Inferences on the Basis of the Results

For 1-hour thermal stimulation, it was shown that the higher the temperature given, the higher was the concentration of dye released. It was found that the O.D. of all specimens had increased after 2-hour duration. However, the rate of dye release from the specimen at room temperature (i.e. specimen 1) was relatively the highest. Especially when being compared with specimen 2 which had been heated at 37℃, both of them had similar values of O.D. after one hour. However, the rate of dye release was distinctly slower for specimen 2. Besides, only the O.D. of the specimen 1 remained increasing after 3 hours.

The following inferences and hypothesis had been made on the basis of the results. i) It may due to the reason that the given thermal energy had accelerated the rate of dye released from specimens 2, 3 and 4 respectively at the initial stage, thus, higher amount of encapsulated dyes had released during the first 1-hour for the specimens with thermal stimulation. Due to the similar interpretation of the result of cell test, the dye molecules could be excited and move more vigorously from the lumens of hollow fibers when being heated up. The higher the temperature was given, the less viscous was the dye solution, the faster was the releasing movement of dye solution. As a result, higher concentration of released dye was obtained with increasing temperature via thermal stimulation.[125,126] This may essential for rapid onset of medication. ii) The synthetic hollow fibers are considered as thermoplastics in nature, it was also thought that thermal energy may influence the original crimped structure of hollow fibers and also the construction of fabric internally and externally. Consequently, the fluid flow inside the crimped lumens may be restricted by the structural alteration due to the effect of heat. However, as the given heat is below the glass transition temperature (Tg) of the

thermoplastic components, the fibers would not be melted or totally deformed (Figure 6-12).[127]

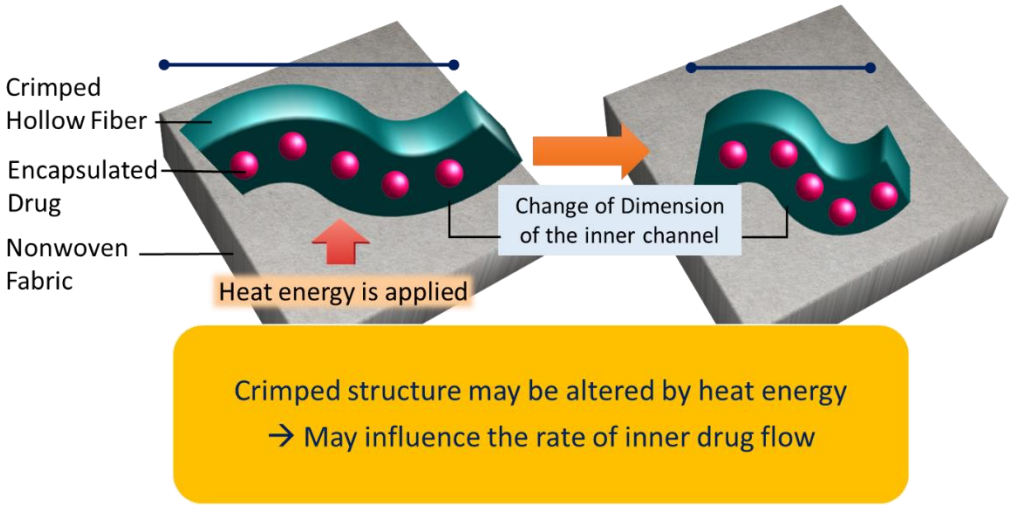


Figure 6-12 Influence of Hollow Fibers' Structure by Thermal Energy.

A forecast for further development of the system had also been made based on the results and the knowledge of textile dyeing. It is known that the anionic acid dyes (with SO_3^-) could fix to polyamide (PA) fibers which with cationic sites through hydrogen bonds, ionic linkages and Van der Waals forces. This would make a significant paradigm and inference for controlling drug release with affinity-based drug delivery mechanism such as binding anionic drugs to cationic sites of hollow fibers which are made of polyamides. It was reported that the pharmacophore of a drug which consisted of a negatively-charged sulphonate functional group ($R\text{-}SO_3^-$) may be attracted towards the ammonium cations of the receptor.[128] Therefore, it was believed that controllable release of drugs can be retained via the electrostatic attraction between the anionic drugs and cationic receptors of fibers for this proposed investigation. Thermal stimulation is believed to trigger the release or diffusion of the therapeutic drugs from hollow fibers (at internal lumens and outside membranes) through breaking the ionic attraction. Release of drugs could be monitored more effectively. Drug molecules inside hollow

fibers could be stabilized via thermodynamics (Figure 6-13).[129,130]

According to Figure 6-11 b, as the rate of dye release for specimen 2 (heated, 37 °C) was moderate and steady, therefore, it would be an ideal approach for controlling the release of drugs by regulating humans' body temperature within a definite margin. The e-fabric layer with 'self-thermoregulation' ability would be useful for maintaining the thermal balance, stability of heat distribution and homeostasis of human body within the boundaries of body temperature. A stable and consistent thermal stimulation would be maintained within the wearable for regulating the constant drug release at body temperature regardless of environmental changes.

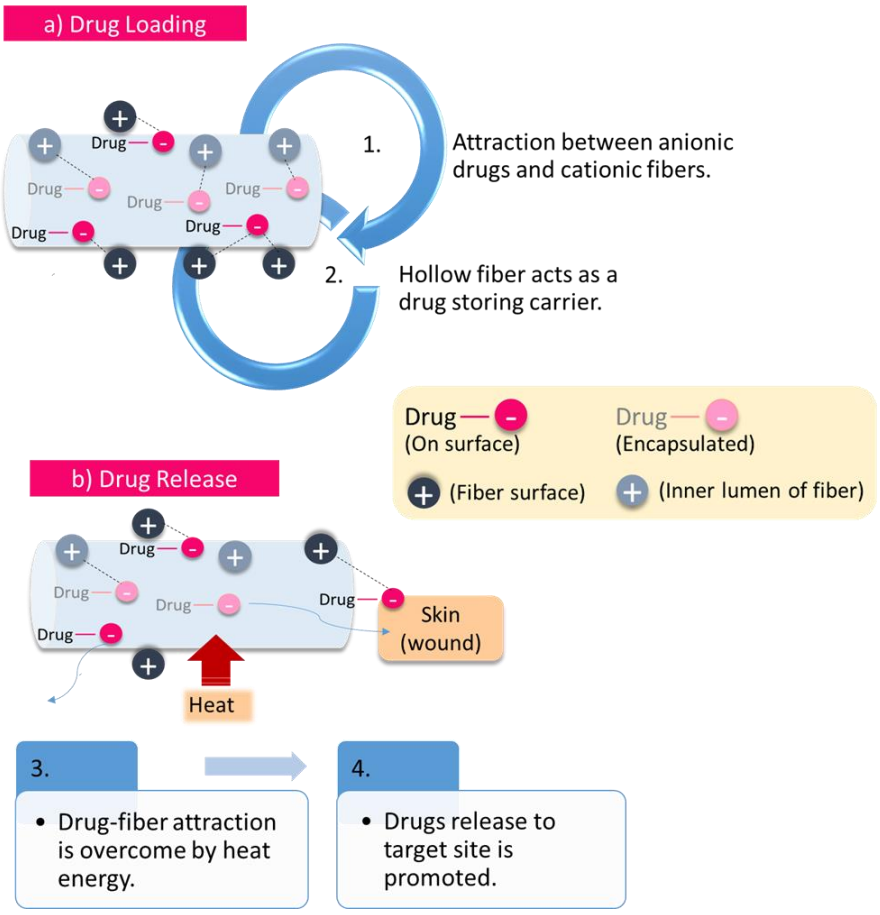


Figure 6-13 Affinity-based Drug Delivery Mechanism by using Hollow Fibers.

6.4 Summary

To develop a smart textile wearable with thermal-stimuli drug delivery function, the drug delivery layer (DL) with the use of hollow fibers and the thermal conductive e-fabric layer (TL) by using silver-coated conductive yarns had been combined for subsequent studies.

Infra-red thermographic study had been performed for observing the heating geometric allocations of the combined DL-TL fabrics at different levels of electric power supply. It was observed that the central spot exhibited the highest thermal energy and the energy became lower at the quadrilateral area, while the peripheral area exhibited the lowest. For investigating the influence of thermal stimulation on drug delivery performance within hollow fibers, biological cell analysis had been performed. It was shown that lower cell viability (i.e. higher cytotoxic effect) could be induced with the drugs delivery through the heated-specimens with higher thermal stimulated energy (i.e. higher temperature). Burst effect had not apparently shown for the first hour delivery. Furthermore, physical investigation had also been done by analyzing the visible absorbance of liquid release under influence of thermal stimulation. Linear relationship was indicated between optical density and the concentration of released dye. During the first hour delivery, the concentration of released dyes increased with higher temperature provided. For succeeding hours, the rate of dye released became slower for those with thermal stimulation while that for the control kept increasing. It was resulted that thermal energy could accelerate the release rate of drugs at the beginning for rapid onset of therapeutic action. Changes of structure and dimension of synthetic hollow fibers would be induced by thermal stimulation. Fluid flow through the crimped lumens would

thus be restricted. Besides, the rate of liquid delivery at 37 ℃ was found to be stable and moderate. It was believed that a stable and consistent drug release could be controlled by 'self-regulating' body temperature with the use of thermal conductive e-fabric layer and also the structural changes of synthetic hollow fibers by thermal energy. Under the hypothesis of the attraction between anionic pharmacophore of drugs to cationic receptors of hollow fibers, controlling drug release with affinity-based drug delivery mechanism was believed to be significant for future development.

CHAPTER 7

INTEGRATED DESIGN OF SELF-CARE TEXTILE WEARABLE WITH THERMAL-STIMULI DRUG DELIVERY FUNCTION

7.1 Integrated Design Approach of the Self-care Textile Wearable with Thermal-stimuli Drug Delivery Function

To implement the self-care textile wearable with thermal-stimuli drug delivery function, a special made textile wearable for breast cancer post-surgical care and therapy (i.e. a bra for females and a sweatshirt / pullover for males) was designed. The textile wearable consists of three layers which include the inner drug delivery layer (DL), the middle thermal conductive e-fabric layer (TL) and an outer layer.

For the inner drug delivery layer, specimens of staple crimped hollow fibers and the non-woven fabrics made of hollow fibers were initially prepared for physical and biological investigations in chapter 5 and chapter 6. The drug loading function of the hollow fibers in both liquid and crystal solid phases was examined. 5-Fluorouracil, which is known as an anticancer drug, was loaded into the staple crimped hollow fibers for treating the MDA-MB-231 breast cancer cells during the process of drug release. For the future implementation, other fabric constructions like woven and knitted structures can also be made of drug-loaded staple hollow fibers - yarns. The drug delivery layer can be detached for cleaning and re-loaded with drugs. The drug delivery function is not only for one-time treatment but repeatable (Figure 7-1).

For the middle thermal conductive e-fabric layer, silver-coated conductive yarns were

embroidered through a cotton fabric and then embedded with the drug delivery layer. Different heating temperature levels was exhibited by applying different levels of electric power supply (Figure 7-2 and Figure 7-3).

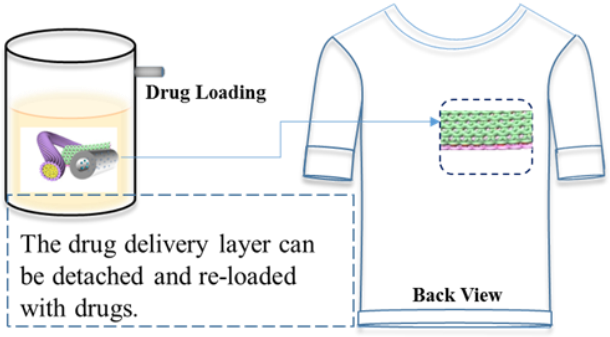


Figure 7-1 The Self-care Textile Wearable with Repeatable Drug Delivery Function. The drug delivery layer can be detached for cleaning and re-loaded with drugs. The drug delivery function is not only for one-time treatment but repeatable.

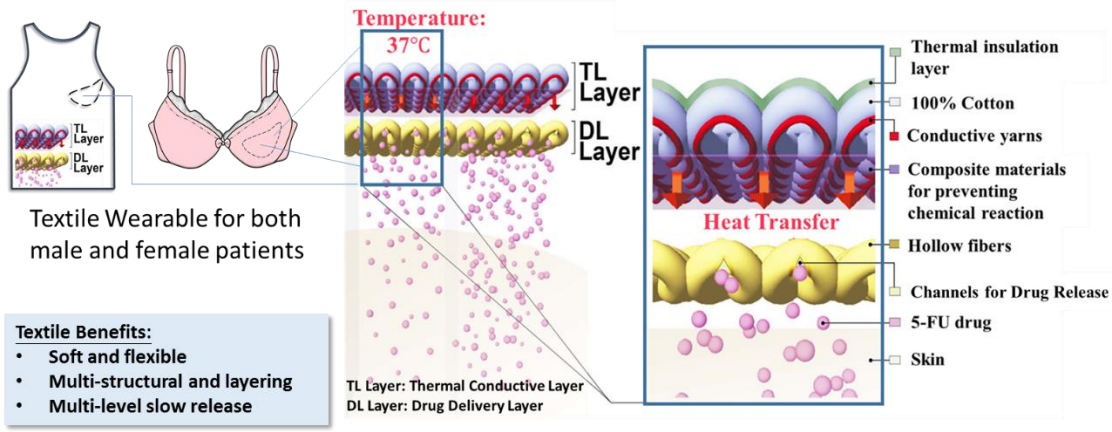


Figure 7-2 Thermal-stimuli Drug Delivery Self-care Textile Wearable. The textile wearable, which consists of the thermal conductive e-fabric layer and the drug delivery layer, provides a convenient and comfortable medication for breast cancer patients.

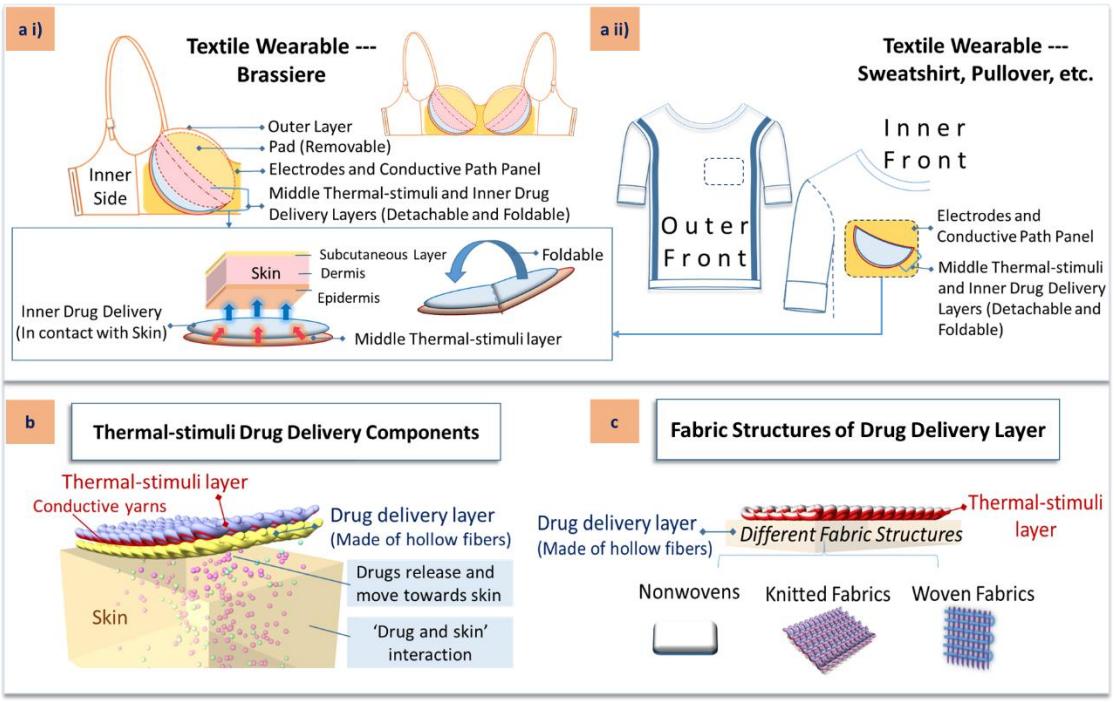


Figure 7-3 An Integrated Approach of the Self-care Textile Wearable. a) i) and ii) A textile wearable for breast cancer post-surgical care and therapy (i.e. a bra for females and a sweatshirt / pullover for males) is designed as a pilot study. This textile wearable is generally divided into three layers which are the inner drug delivery layer, the middle thermal conductive e-fabric layer and an outer layer; b) thermal-stimuli drug delivery components; c) possible fabric structures of making the drug delivery layer.

7.2 Pilot Prototype Investigation of Staple Hollow Fibers - Yarns

It has been previously mentioned that other fabric constructions such as woven and knitted structures could be made as the drug delivery layer. Staple hollow fibers, which had been initially manufactured with the use of a specific spinneret, were directly utilized as the main components for yarn spinning through the conventional processes of carding, drafting, opening and twisting. Staple hollow fibers - yarns with various twist amounts had been hence produced for making the prototypes of woven fabrics.

Physical analysis of the structural characteristic of the staple hollow fibers - yarns (Figure 7-4 a) had been performed with the use of optical microscope. A cavity was

observed from the segmented hollow fiber which was extracted from the staple hollow fibers - yarn (Figure 7-4 b). Lumens of hollow fibers were apparently observed from the cross-section of yarns (Figure 7-4 c).

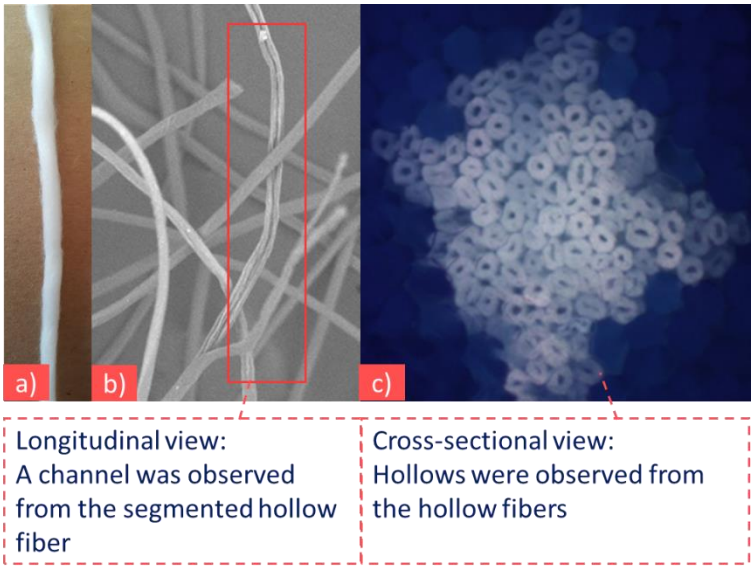


Figure 7-4 Prototype of Staple Hollow Fibers - Yarns. a) Yarns made of hollow fibers. b) Longitudinal view: a channel was observed from the segmented hollow fiber which was extracted from the yarns. c) Cross-sectional view: hollows were observed from the hollow fibers of the yarns.

Drug loading ability of staple hollow fibers - yarns had also been examined through optical microscopic analysis. The staple hollow fibers - yarn specimens were submerged into liquid and then together subjected to vacuum loading under the pressure of 0.05 – 0.06 mPa for 20 minutes (i.e. method 2 of drug loading, which has been mentioned in chapter 5 and 6, had been chosen). Then, single fibers were separated and extracted from the yarn specimens for observation. A clear hollow cavity was identified from the control specimen without loading (Figure 7-5 a i) whereas a liquid column was observed from the liquid-loaded specimen (Figure 7-5 a ii). Based on Figure 7-5 c, liquid movement along the path of hollow cavity could been seen from images 1 - 3. It was shown that liquid could be encapsulated inside the hollow fibers even the fibers had been undergone the yarn spinning process such carding, combing, twisting, drawing

and roving. It could form an important foundation for realizing the concept of manufacturing different types of drug-loaded fabrics and textile wearables. Moreover, twisted areas were observed from the hollow fibers that were extracted from the yarns (Figure 7-5 b).

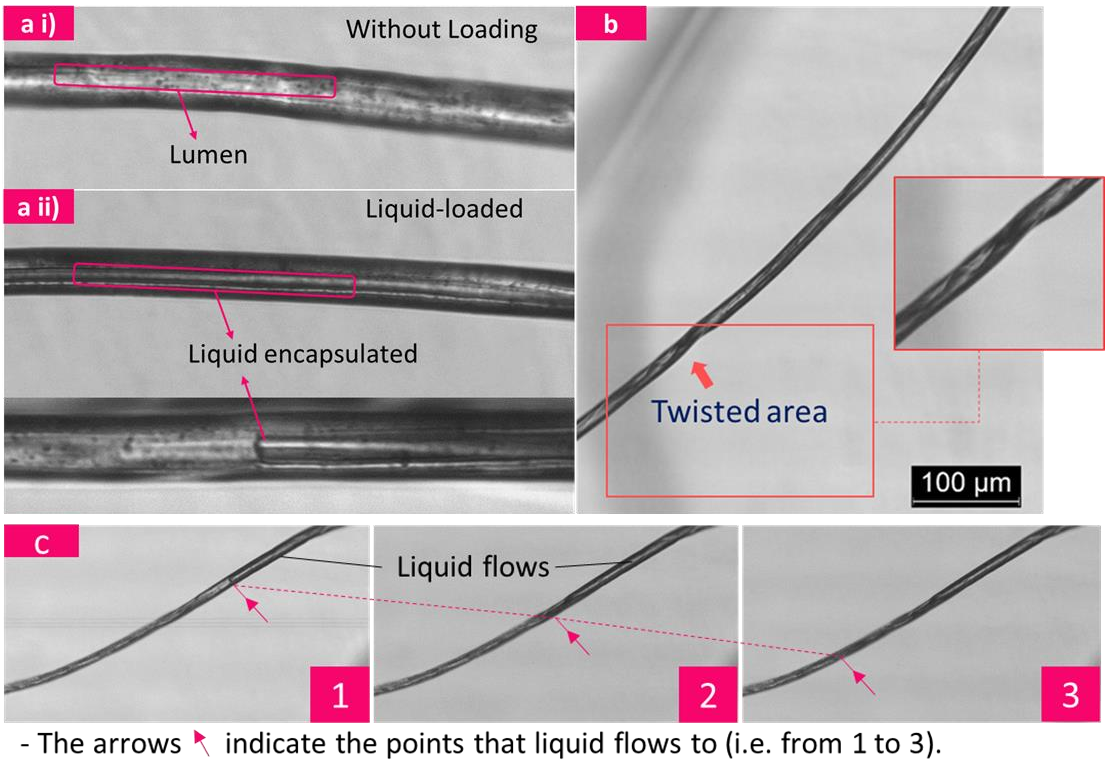


Figure 7-5 Structural Morphology and Drug Loading Ability of Staple Hollow Fibers - Yarns. a) i) A hollow cavity was observed from the control specimen without loading and ii) a column of liquid was observed from the liquid-loaded specimen. b) Twisted area was observed from the extracted hollow fibers. c) Liquid movement was observed along the hollow fiber.

At present, yarns with different open porous structure had been developed for enhancing the properties of moisture transmission, water absorption and textile comfort. In the past years, hollow yarns or air-rich yarns had been produced by using polyvinyl alcohol (PVA) fibers as the core and other fiber types such as cotton as the sheath. It was reported that a hollow air space or voids could be made along the yarn axis by dissolving the core PVA fibers at particular temperature. The performances of absorbing

water, hydrophilicity and water vapor transportation were greatly improved. Besides, the fabrics which were made of the hollow yarns could give a bulkier structure, higher compressibility and softer hand feel (Figure 7-6 b).[131,132]

The proposed staple hollow fibers - yarns are directly made of staple hollow fibers (Figure 7-6 c). According to the results previously mentioned, pores throughout cross-section of the yarns were observed. Successful loading and movement of fluid inside the lumens of hollow fibers were also identified. This would be an important first stage for manufacturing textile garments and apparels with drug delivery function. Moreover, the staple hollow fibers - yarns are believed to enhance the physiological-comfort due to the bulky structure and softness. It would be significant for reducing the risk of causing allergy and irritated skin dermatitis because of the coarse texture of medical textiles. The water vapor transmission of the synthetic fibers could also be improved with the formation of pores which could further enhance the physiological-comfort and exudate management at the same time (Figure 7-7). Besides, the yarns are highly compressible, these could make resilient fabrics or bandages for providing cushioning effect and distributing pressure evenly. These are essential for making medical garments for patients with pressure ulcer. Furthermore, it would be a more eco-friendly way for manufacturing yarns with hollow structure. It is because subsequent stages of using water and heat energy for dissolution of fibers are not required. The staple hollow fibers, which were facing the situation of overcapacity, had been given a ‘second life’ for converting into functional ‘staple hollow fibers - yarns’. The problems of surplus and wastage can be avoided that conforms to our goal of implementing an environmentally-friendly medical textile wearables.

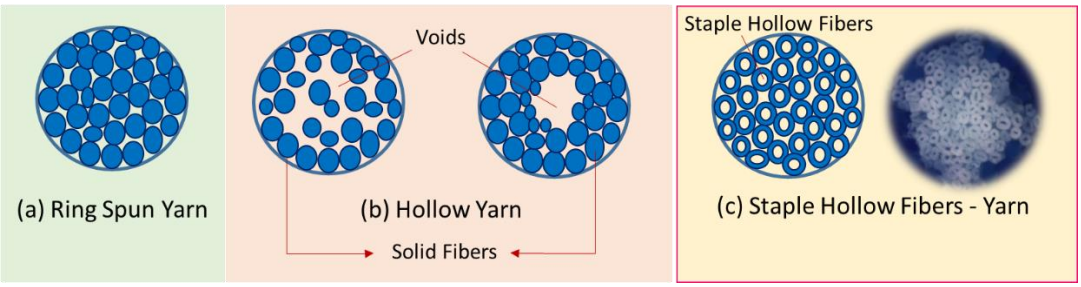


Figure 7-6 Cross-section of Yarns. a) Ring spun yarn. b) Hollow yarn. c) The proposed staple hollow fibers - yarn.

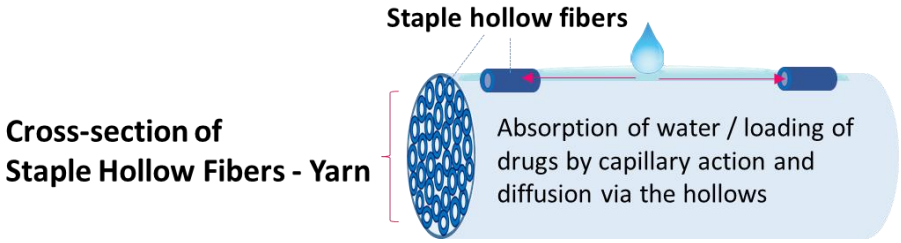


Figure 7-7 Absorption of Water and Loading of Drugs through the Staple Hollow Fibers -Yarns.

7.3 Pilot Prototype Investigation of Woven Fabrics by using Staple Hollow Fibers - Yarns

Two sets of yarns (i.e. warp yarns are the solid yarns and weft yarns are the staple hollow fibers - yarns) were interlaced at right angles to form a woven fabric. The three primary motions, which are the processes of shedding, picking and beating-up, were involved. Woven fabrics with different bulkiness could be made by using staple hollow fibers - yarns with different twist amounts and different weaving patterns. Staple hollow fibers - yarns with higher twist level (i.e. 25 T/M) were used to produce woven fabrics with more compact interlacement while yarns with lower twist level (i.e. 10 T/M) were used to make looser and bulkier fabric. Twill weave structure could help to increase the weft density (i.e. staple hollow fibers - yarns). It was thought that bulky structure and higher yarn density could increase the fabric's surface area which could facilitate the drug-skin permeation (Figure 7-8).

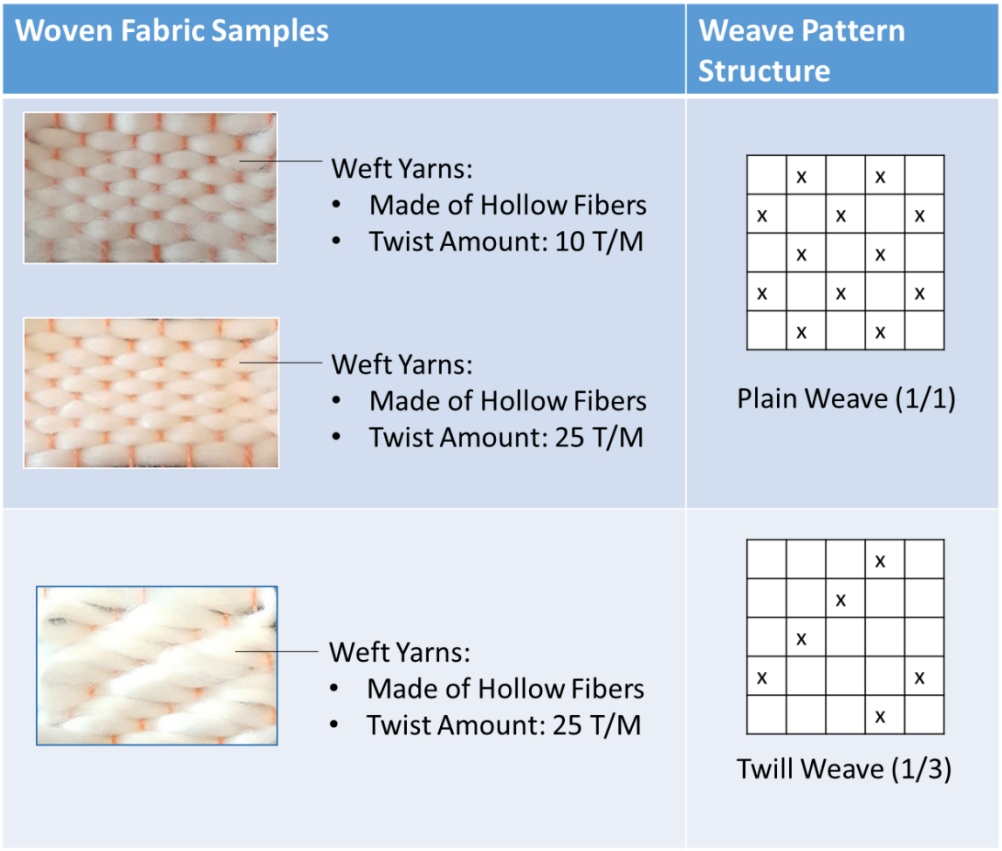


Figure 7-8 Prototype of Woven Fabrics by using Staple Hollow Fibers - Yarns.

7.4 Future Study of a Self-care Textile Wearable with Thermal-stimuli Drug Delivery Function

After the investigation of the drug delivery capability of hollow fibers and the thermal distribution of the thermal conductive e-fabric layer, subsequent studies, which include producing the drug delivery layer in form of woven and knitted structures and optimizing the loading process such as duration and negative pressure given, will be performed. The effectiveness in controlling or catalyzing the release of drug with the use of thermal stimulation will be further studied in the future. It is generally considered that with the integration of the thermal conductive e-fabric layer, heat transfer towards the drug delivery layer would become more effective and hence the performance of controlled and precise drug release could be enhanced. Further in the future research, it is proposed to develop a slim, light, washable, controllable and intelligent electric-

heating and drug releasing system.

As aforementioned, the three factors, which include different levels of heating temperature, various thermal allocations and different heating periods, may exhibit different effects on the drug release amount and therapeutic performances. Additionally, the thermal conductivity and heat loss to the peripheral environment may also influence the stability of heating temperature of the thermal fabric layer itself. Besides, the thermal stimulation may help to increase the drug diffusivity through the topical transdermal system and hence leads to high-effective therapeutic performance over a definite period of time. A stable and long-lasting drug-release effect could be improved as well. Through this model establishment, the thermal textile wearable could therefore be well-designed so as to give an appropriate drug dose over a given time at a target heating temperature.

For the product development, the conceptual idea of the textile wearable with thermal-stimuli drug delivery ability for external medical applications will be extensively realized for prototype making, i) spinning of hollow fibers into various yarn structures; ii) loading compound drugs into the hollow fibers or yarns for different therapeutic functions; iii) producing various fabrications (i.e. woven, knitted and nonwovens) with the use of the drug-loaded hollow fibers or yarns; and iv) manufacturing aesthetic and multifunctional medical textile wearables such as bras, sweatshirts, pullovers, fashion accessories and other possibilities (Figures 7-9, 7-10 and 7-11). Through the product development process, more medical functions of drug-loaded hollow fibers can be originated. Modification can be made time by time so as to improve and maintain the quality of the textile wearable and to satisfy the market demands.

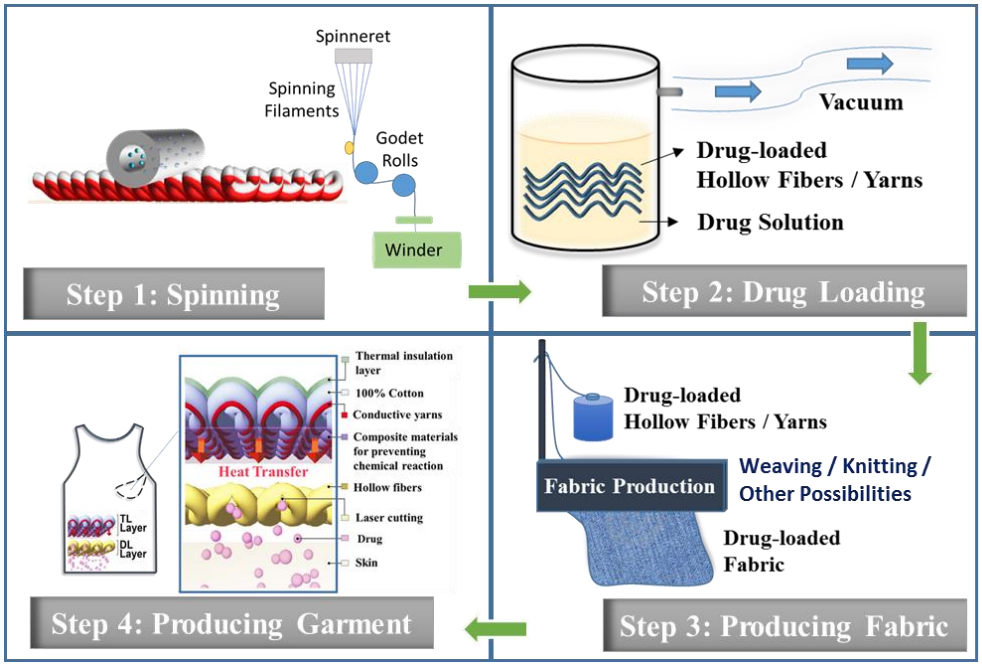


Figure 7-9 Product Development of the Textile Wearable with Thermal-stimuli Drug Delivery Ability.

Figure 7-10 Production Chain from Hollow Fibers to Self-care Textile Wearables.

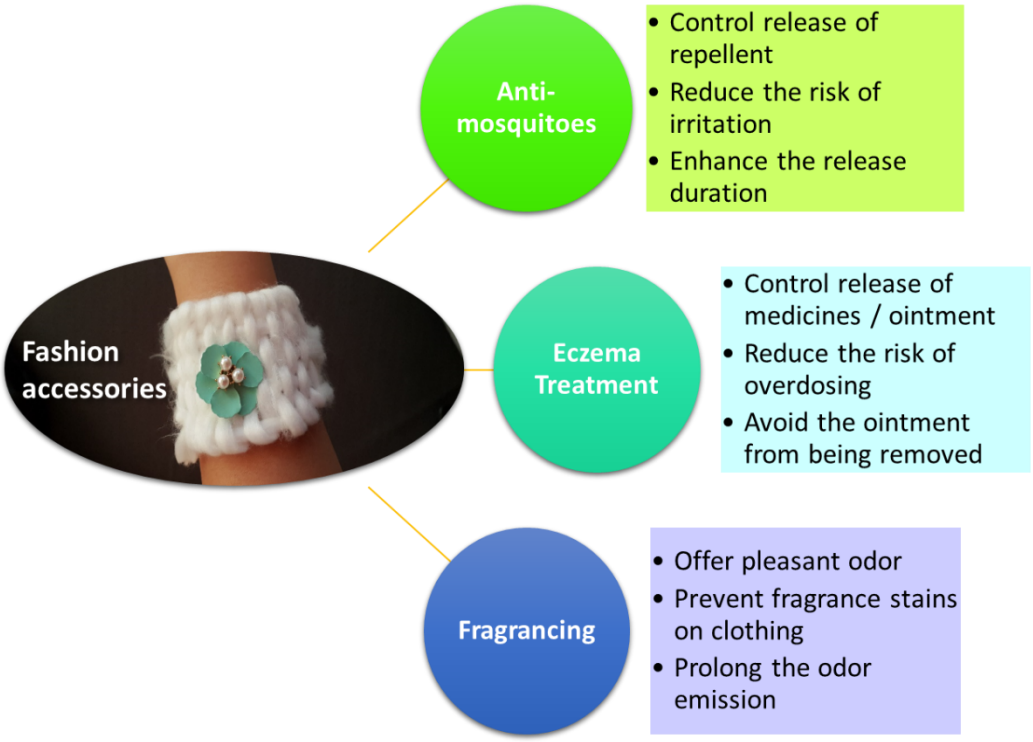


Figure 7-11 Applications of Fashion Accessories with Loading and Releasing Functions.

7.5 Summary

After the fundamental analysis of the drug delivery performance via thermodynamics, an integrated design of a self-care textile wearable and prototype investigation of staple hollow fibers - yarns and woven fabrics was outlined.

For the integrated design approach on the basis of the fundamental results of drug delivery, the self-care textile wearable for post-surgical care and therapy had been designed. It is generally divided into three layers which are the inner drug delivery layer, the middle thermal conductive e-fabric layer and an outer layer. Staple hollow fibers - yarns with different twist amounts had prototyped. Lumens of hollow fibers could be clearly seen from cutting the cross-section of yarns. Drug loading ability could be exhibited from the extracted hollow fibers from the yarns. Besides, woven fabrics with different construction and bulkiness had also been prototyped by using the staple hollow

fibers - yarns. Future study of the product development was illustrated.

CHAPTER 8

CONCLUSION, LIMITATIONS AND FUTURE WORKS

8.1 Overall Conclusion

In this research thesis, a textile-based drug delivery system was developed by using commercial hollow fibers and thermal-stimuli technology in advanced level. This proposed functional, medical and protective textile system combines four smart technologies which are 1) design and manufacture of functional textile and apparel products, 2) modelling of textile and drug delivery system, 3) biological evaluation of the system's effectiveness and efficiency and 4) thermal stimulation of the drug delivery – textile system. Significant drug loading capability was shown through the physical microscopic analysis. Effective function of drug release towards the anti-bacterial medication and anti-breast cancer therapy was found. Thermal geometric distribution of the TL-DL layers and the liquid delivery with thermal stimulation were examined.

From chapters 1 to 3, the general introduction, literature review and the methodology used for the proposed study were introduced. From chapters 4 to 7, the experimental findings of the research study were introduced and elaborated.

In chapter 4, significant loading and releasing of drugs, either in the phase of liquid, solid or oil, via the inner lumens of hollow fibers were verified. Effective anti-bacterial function was performed with the use of antibiotic-loaded hollow fiber based woven fabrics.

In chapter 5, loading chemical-based and herb-based drugs into hollow fibers were

further affirmed with the utilization of 5-FU drugs and Chinese medicinal herbs (Borneol) respectively. Significant suppression of breast cancer cell growth was induced with the use of 5-FU loaded hollow fibers and fabric specimens.

In chapter 6, the heating geometric distribution on the DL-TL fabrics at different levels of thermal energy given was observed. The highest thermal energy level was indicated at the central spot whereas the lowest heating level was exhibited at the peripheral area. For the influence of thermal stimulation on drug delivery function towards cell growth, higher cytotoxic effect was caused by the drugs released from the heated-specimens at higher temperature. Through the visible absorbance investigation of liquid release under thermal stimulation, it was found that thermal energy triggered higher amount and higher rate of dye release at the beginning. No apparent burst release was found for the initial stage of delivery. The rate of liquid delivery was moderate and stable at 37℃.

In chapter 7, the integrated design of the self-care textile wearable for post-surgical care and therapy was illustrated. Prototype making of staple hollow fibers - yarns and the woven fabrics was performed. Successful liquid loading was observed from the extracted hollow fibers of the yarns.

The proposed hollow fiber based drug delivery system is made to offer a convenient, comfortable and soft apparatus that can be applied for 24-hour periods and function continuously. It may also help to improve the quality of life of patients, to reduce production costs and to promote efficiency. If it is successfully developed, the proposed system will represent a great technological achievement that will advance cross-disciplinary and multidisciplinary knowledge.

8.2 Limitations and Future Implementation

The research findings are believed to give impetus to advanced development of a new therapeutic method and wearable medical equipment for external uses of medication. Being a functional and wearable textile equipment, the proposed innovation of the drug delivery system can be used as a substitute for medical plasters and ointment. Different types of medicines (including both chemical-based and herbal-based medicines) can also be carried by hollow fibers so as to offer a wide range of medical and healthcare applications such as making bandages, bedclothes, garments or other textile accessories and clothing for patients from all ages.

Pre-clinical trials will be further conducted to evaluate the pharmacology and the significance of the transdermal drug delivery from the textile-based system. Once a series of trials and experiments are successful, it is planned to have a prototyping model of the wearable hollow fiber based drug delivery system (i.e. self-care wearables) preliminarily (Figure 8-1). Thus, the characteristics of the final product can be approximated within this scale-down approach. Modification and optimization of the system will be conducted so as to achieve the most significant result for a large-scale commercialization. After the successfulness of the prototyping development model, a collection of wearable hollow fiber based medical devices or clothing which consists of both fashion and function (i.e. compressing the growth of malignant cells or eliminating bacteria at the therapeutic sites) will be designed and then potentially manufactured with the application of hollow fibers.

However, some deficiencies and limitations have not been comprehended completely in the project such as the variation of textile fabrications with the use of the staple

hollow fibers - yarns, the integration of thermal therapy into the system for an entire self-care wearable and the way to arrange the defined releasing point inside the lumen of the hollow fibers with different cross-sections. Therefore, the future implementation would also focus deeply on i) the hydrodynamic characterization between the fiber wall and the viscosity of loaded drugs; ii) the fluid encapsulating and releasing effect with respect to yarns of different twist amounts; iii) the relationships among the internal structure of lumens, thermal conductivity and drug delivery of the textile materials made of hollow fibers; iv) the examination of the affinity-based drug delivery system; v) the maintenance of steady and moderate drug release by 'self-regulating' of body temperature with the use of thermal conductive e-fabric as well as vi) the proper way of optimizing the releasing area and speed via the structures of yarns and fabrics for catalyzed or controlled therapeutic action.

Figure 8-1 A Collection of Wearable Hollow Fiber based Medical clothing. It consists of both fashion and medical function and could be potentially manufactured for mass production.

PROJECT TIMETABLE

Total Years of Study = 4 Years (48 Months)								
Months	1 – 6	7 – 12	13 – 18	19 – 24	25 – 30	31 – 36	37 – 42	43 - 48
Literature Review	x x	x x	x x	x x	x x	x x	x x	
Characterization of Hollow Fibers	x							
Physical Analysis of Drug Delivery System	x	x x	x					
Biological Analysis of Drug Delivery System		x	x x	x x				
Integration of Thermal Therapy			x x	x x	x x	x x	x	
Physical Analysis of Thermal-stimuli Drug Delivery System				x x	x x	x x	x	
Biological Analysis of Thermal-stimuli Drug Delivery System				x x	x x	x x	x	
Prototype Development				x x	x x	x x	x x	
Integrated Design of Self-care Textile Wearable							x x	
Data Analysis	x	x x	x x	x x	x x	x x	x x	x
Thesis Writing							x x	x x

APPENDIX

LIST OF ACRONYMS AND TECHNICAL TERMINOLOGY

5-FU	Fluorouracil
Ag	Silver
CRT	Controlled release technology
D. I. water	Deionized water
DL	Drug delivery layer
DMEM	Dulbecco's modified eagle medium
ECS	Extracapillary spaces
FBS	Fetal bovine serum
FTIR	Fourier Transform Infrared Spectroscopy
GIT	Gastrointestinal tract
HFA	Hollow fiber assay
HFB	Hollow fiber membrane bioreactor
HFIM	Hollow fiber infection model
HFLPME	Hollow fiber liquid-phase microextraction
IAHLD	Integrated artificial heart – lung device
i.p.	Intraperitoneal
IUD	Intra-uterine device
MBGHFs	Mesoporous bioactive glass hollow fibers
NHAHF	Nanocrystalline HAp-assembled hollow fibers
NIPS	Non-solvent induced phase separation
O.D.	Optical density
PA 6	Nylon 6

PA-PET	Nylon-polyester
PEG	Polyethylene glycol
PES	Poly (ether sulfone)
PLLA	Poly (L-lactide)
PVA	Polyvinyl alcohol
PVDF	Polyvinylidene fluoride
PVP	Poly (vinyl pyrrolidone)
s.c.	Subcutaneous
Tg	Glass transition temperature
TL	Thermal conductive e-fabric layer
v	Voltage

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