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A review of hollow fibers in application-based learning: from textiles to medical

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Abstract

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 deliver drugs to a target site, enhance blood purification, promote cell cultures, and enable drug screening. The use of hollow fibers could have beneficial effects for medical and therapeutic performance; a market for hollow fiber-based medical clothing is anticipated for promotion of 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 use and their potential industrial applications in medical textiles and clothing.

Keywords: capabilities and limitations, future trends of textiles, hollow fibers, medical textiles, potential applications, production, therapeutic and healthcare functions

Rapid technological development has created advanced technology for many fields, and a large amount of research has focused on exploring textile technologies in the medical area, in particular medical devices, in which hollow fibers are among one of the promising developments. This paper summarizes selected major applications of hollow fibers in medical and healthcare settings, including drug carriers, dialyzers, artificial organs, bioreactors, drug delivery, blood purification, cell cultures, and drug screening. Some of the limitations of using hollow fibers and rising trends are also addressed. The interconnection between hollow fibers and textile-medical therapy is the principal focus, and the corresponding research findings are examined together. It is predicted that hollow fibers' structure and characteristics could make a tremendous contribution to the medical field.

Development of medical textiles

Natural fibrous materials were first used in wound closures, wound dressings, and surgical sutures from 5000 BC.¹ The biological features of different textiles were further investigated in the 1950s.² From 1952 onwards, textiles have been used in vascular implants. The first textile-made vascular graft was created by Voorhees and colleagues, who replaced the infected aortic vessels of a dog with woven polyvinylchloride tubes.³ Further advances in vascular grafts and heart valve cuffs used polyester because of its

high strength, stability and bio-durable qualities.^{2,4}

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 Hygiene is essential to wound management because of the danger of infection, and thus there is extensive interest in advanced medical textiles with hygienic and antimicrobial functionalities. For example, several functional fibers such as chitin fibers, calcium alginate fibers, and dextran fibers have been used in wound dressings and medical bandages.² Hemostatic and compressive functions, as well as comfort, breathability, flexibility, and moisture management are important factors.⁶ For implants, 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} The use of biomedical textiles with drug delivery functions based on hollow fibers has also been investigated. Such a system would allow drugs to be released to the target site through the skin or tissues.^{10,11} Artificial bioactive scaffolds could also use hollow fibers for drug delivery,^{12,13} and it was proposed that the porous hollow fiber membrane could be incorporated into a threedimensional scaffold for enhancing the delivery of nutrient and culture media (Table 1).¹⁴ Moreover, further implementation of biomedical textiles by utilizing hollow fibers has also been launched for increasing the effectiveness of dialysis,^{15–17,18} for examining antibiotic drugs via hollow fiber cell-culture cartridges,¹⁹⁻²⁴ and for screening anticancer drugs through cell-loaded hollow fiber implantation in mammals.²⁵⁻²⁸ Although recent work done with the use of hollow fibers in the medical area is not as great as other materials, they are still the significant constituents for contributing to the value-added commercial medical textile system.

Table 1. Advantages of textiles in medical applications



Textile and medical devices

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 the body. It provides an additional shielding barrier against pathogens and allergens^{30–32} 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.³³

The development of hollow fiber

Hollow fiber is a filament with one or several axial empty cores (Figure 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 nylon, 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.³⁴ Additionally, hollow fiber is up to 20% 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.³⁵



Figure 1. Characteristics of hollow fibers: (a) cross-section of hollow fiber under SEM; (b) Two types of hollow fibers; (c) group of hollow fibers (plied yarn); (d) hollow fiber and yarn in comparison to hair and sewing thread; (e) photo of fabric knitted with hollow yarn.

Asymmetric hollow polyamide fibers were initially invented by DuPont for antifouling and desalination of seawater in 1965.³⁶ In the 1970s, three-dimensional, curly, eccentric fibers came into use.³⁷ Toyobo began to promote asymmetric hollow fibers constructed from cellulose triacetate.³⁶ In the 1990s, multi-channel hollow fibers such as a "four-hole" fiber were fabricated, and the manufacturing methods were improved (Figure 2).³⁷



Figure 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.37 Multi-channel hollow fibers with internal structure were manufactured in the 1990s (left).37 A sample of hollow staple fibers (right).

Numerous researchers have investigated the characteristics of hollow fibers, which

include 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.

Production of hollow fibers

Hollow fibers can be made using a spinneret containing an outer concentric capillary and a central concentric capillary.³⁸ The spinneret may consist of one or multiple bores.³⁹ 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.^{40,41} Various hollow shapes can be created using orifices of different shapes. Plug-in-orifice spinnerets, tubein-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.⁴¹ Different spinning methods also exist, such as melt spinning, wet spinning, dry spinning, "dry–wet" coagulation spinning and electrospinning (Figure 3).



Figure 3. Schematic summary of hollow fibers. Production can be categorized into

electrospinning, melt spinning, wet spinning, and dry–wet coagulation spinning.38–52 (a) Various types of cross-sections can be made by using different spinnerets.29 (b) Microscopic images of different types of industrial hollow fibers.29 Both textile and medical properties of hollow fibers contribute to the usefulness of medical textiles.

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,⁴² 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.^{38,43} Kim and colleagues⁴⁴ noted that the polymer melt viscosity and the structure of hollow fibers are governed by the spinning temperature, while the number of micropores can be increased by the melt–draw ratio. Fine hollow fibers with small diameters can be obtained by the melt spinning method.³⁸

Wet spinning is a type of solution spinning system similar to melt spinning. As reported by Li and colleagues,⁴³ 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.³⁸ 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.³⁹

As described by Wienk and colleagues,⁴⁵ 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 vapor penetration of nonsolvent at the outer surface, immersion precipitation at the outer surface, and immersion precipitation at the inside surface.⁴⁵ Polyvinylidene Fuoride (PVDF) hollow fiber membranes manufactured by the dry–wet spinning method have large cavities and small macrovoids at the inner and outer walls, respectively. The permeation stream of the membranes is enhanced when alcohol is used as an internal coagulant.⁴⁶ 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 colleagues⁴⁷ 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., nonsolvent induced phase separation (NIPS)] has been used to obtain a porous membrane.⁴⁸ 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.⁴⁹

A high surface-area-to-volume ratio and porosity of fibers can be obtained by electrospinning. 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. Electrospinning technology had been applied to tissue engineering for scaffold fabrication¹³ and the production of nanocrystalline HAp-assembled hollow fibers.⁵⁰ Immiscible solutions such as 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 electrospinning. 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 highvoltage electrical field is applied to create a jet to produce the hollow nanofibers.⁵¹ Hollow nanofibers such as anatase TiO₂ can be used as a channel for the transportation of nanofluid.52

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 (Figure 3). 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.^{53–55} Pentagonal hollow fibers have been used in carpet production because of their soil- and dirt-resistant features.^{56,57} DuPont developed a certification mark ("Quallofil") for the production of hollow fibers with four channels, which performed relatively well in thermal insulation applications.³⁴

ameliorated by combining microfibers and hollow fibers together.58

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.⁴⁰ Due to the maturity of textile technology, hollow fibers with different cross-sectional shapes and dimensions can be manufactured at reasonable production cost for a wide range of functions.

Outstanding characteristics of hollow fibers

Khoddami and colleagues⁵⁹ conducted an experiment based on the mechanical properties of hollow polyester fibers and solid polyester fibers. It was reported that the thickness and stiffness of the hollow fiber-based fabrics were higher than those of fabrics made from solid fibers.⁵⁹ Further comparing with solid fibers, the channels of the hollow fibers can help to trap more air, providing better thermal insulation.^{58,60} Sweat can be absorbed by microporous hollow fibers through capillary action as well,⁶¹ enabling more comfortable textiles (Figure 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.⁶² Hollow fibers can have a surface-area-to-volume ratio of nearly 10,000m²/m³.⁶³ The high surface-area-to-volume ratio can enhance pore surface area. The higher the void surface area, the greater the surface reactivity.⁶⁴ As a result, the drug-loading flexibility and the rate at which drug molecules disperse can be increased.⁶⁵ Additionally, membranes employing these features of hollow fibers can provide superior selectivity and permeability for ultrafiltration and fluid flow (Figure 3). Fiber with honeycomb cross-sectional structure had also been produced and further carbonized into carbon hollow fibers.66

The application of hollow fibers in the medical field

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 drug delivery systems, fluid permeability, and ultrafiltration. Hollow fibers have been used in extracorporeal medical devices, percutaneous medical devices, and implanted bio-artificial organs. The current medical applications of using hollow fibers, which include drug carriers, dialyzers, artificial organs, bioreactors, drug delivery, blood purification, cell culture, and drug screening, will be summarized (Figure 4).



Figure 4. Medical applications of hollow fibers. The medical applications of hollow fibers can be generally divided into six major areas, which include drug delivery, dialysis, gas exchange, cell culture, liquid-phase micro-extraction, and drug screening. Drug delivery systems, artificial organs, hollow fiber bioreactors, and hollow fiber assays are examples of these six areas.

Drug delivery

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.⁶⁷ 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.⁶⁸ 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,⁶⁹ the concentration of drugs in the blood, and the capability of the body to remove drugs from the blood.⁷⁰ 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 pharmacokinetics⁷¹

Another principle, pharmacodynamics, is defined as how the drugs influence the human body.⁶⁹ 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 5).⁷¹

Controlled release technology (CRT) using drug carriers has the potential to overcome the problems caused by conventional drug administration.⁷² CRT enables drugs to be directed exclusively to the site of action, to prevent early drug metabolism and to continue administration over long periods.⁷³ Protein drugs can be protected from destruction by enzymes through encapsulation with controlled release.⁷² Zero-order delivery and local drug delivery are two important elements of controlled release.



Figure 5. Principles of drug delivery. Pharmacokinetics and pharmacodynamics are the two main principles for executing the drug delivery system.^{70–71}

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 over- or under-dosing. As a result, a constant effect can be maintained. Drugs can also be released gradually after an initial burst 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.⁷³

Hollow fibers are believed to be effective drug carriers because of the intrinsic high surface-area-to-volume ratio and a high loading capacity.^{62,74} Fluid flow through microor nano-sized channels may also be important.⁷⁵ As the shell wall thickness and hollow cavity diameter can be modified in correspondence with the diffusion coefficient, the uniformity of diffusion and a predetermined rate of release can also be monitored.⁷⁶ 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.⁷⁷ Moreover, as drugs can be released at a low rate over a long time, frequent injections may not be required.⁷⁸ Drugs can be delivered directly to the target organs via hollow fibers; thus, the risks of over-dosing, under-dosing, and chemical toxicity can be eliminated (Figure 6).⁷⁹



Figure 6. 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. (a) Hollow fibers can be used in drug delivery because of the effectiveness of drug loading and release.^{62,74–79} (b) From the future point of view, a functional textile-based thermal-stimulus drug delivery apparel system would be a potential innovation for producing multi-functional skin-protective clothing. (This is our recent and ongoing project supported by GRF funding.) The loaded drugs would be transported from the clothing to skin and diffuse through the skin layers. Thus, skin-protective treatment would be provided.

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.⁸⁰ A drug-loaded core granulate can be formed by blending the drugs with the polymer solution.78 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 7).⁸⁰ 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.⁸¹ 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 system; 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.⁸² 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.



Figure 7. 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 over-dosing, under-dosing, and chemical toxicity can be diminished or eliminated. (a) Method of drug loading; (b) applications of drug carriers; (c) three possible drug-loading mechanisms.^{78,80}

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 woundhealing 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.⁸³ In addition, a "multiple" drug delivery system was developed using biodegradable nanoparticles containing hollow microfibers. 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 microfibers 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.⁸⁴

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 interuterine environment becomes hostile to implantation, and although an IUD is one of the most effective methods of contraception,⁸⁵ 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 chlorhexidinereleasing 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 $114 \,\mu\text{g/d}$ to reduce the occurrence of vaginal bacterial infection within 24 h.^{86,87} 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.⁸⁸ 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.47,89 For the treatment of periodontal disease, tetracycline-loaded hollow fibers were placed in the gingival sulcus.90

Hollow fiber catheters can enhance drug distribution into the central nervous system and increase the surface area of the brain tissue. Homogeneous 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 brain tissue.⁹¹

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.⁹²

Dry-wet spinning has been used to manufacture hollow fibers constructed from 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 initial stage, and then successively smaller amounts of drugs can be further released gradually over the final stage of the 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.⁹³ The hollow fiber membranes, which were constructed from PLLA-dioxane-water using the liquidliquid 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 shortterm zero-order release of drugs was shown.⁴⁸ 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 microparticles, and the rate of drug release was lower when the drug-loaded microparticles were trapped in the hollow fibers due to the large resistance of drug diffusion through the walls of the fibers.¹² Eenink and colleagues (as cited by Ranade and Cannon) discovered that biodegradable hollow fibers could be manufactured using poly-L-lactic acid to allow subcutaneous delivery.⁶²

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 in an increased fiber length. In contrast, shorter fibers would decrease the drug-loading capacity but enhance the rate of drug release.⁹⁴ Hong and colleagues (as cited by Zeng and colleagues⁷⁴) also invented mesoporous bioactive glass hollow fibers (MBGHFs). These fibers with a hollow core were found to hold far more drug than the solid fibers.⁷⁴ 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 nanocarrier for localized drug delivery at a predetermined rate.⁹⁵

Dialysis by artificial kidney and liver

Hollow fiber membranes are vital components of drug delivery and dialysis systems. A considerable number of extracorporeal and intracorporeal medical devices are equipped with hollow fiber membranes, including dialyzers, bioreactors, and hollow fiber assays. The hollow fiber membranes were invented and used in the 1960s. The membranes were semipermeable and had a roughly cylindrical structure with an internal diameter of less than 25 mm and an external diameter of less than 1 mm. Reverse osmosis and transposition of materials took place by selective crossing of the walls of the bundle of fibers. Controlled delivery of materials and chemical mobilization of the fiber walls were possible.¹⁵ Dialysis could be performed using hollow fibers because of the selectively permeable hollow fiber 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.⁹⁶ A dialyzer, which is a type of extracorporeal device, acts as an artificial organ to control solute and water transfer across a semipermeable membrane by diffusion and convection. The stream of blood and dialysate can be separated along the membrane. 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. An artificial kidney is one example of an implantable dialyzer. Polyester and viscose rayon are the two common types of textile used in mechanical kidneys.⁹⁷ The main function of the artificial kidneys is to purify the blood of patients by countercurrent flow of blood and dialysates via the bundles of hollow fibers.¹⁶ The ultrathin inner surface of the polysulfone hollow fibers provides low resistance for efficient permeation of solutes through the hollow fiber membrane.¹⁷ An artificial liver is another type of implantable dialyzer. Hollow viscose fibers are the major components of artificial livers.⁹⁷ The mechanism of artificial livers is similar to that of artificial kidneys; the blood plasma of a patient is purified by supplying fresh blood plasma and discarding the patient's original plasma. The freshly supplied plasma and the patient's plasma are separated inside the dialyzers (Figure 8).¹⁶



Figure 8. Schematic diagram of dialyzers using hollow fibers. Hollow fibers are one of the major components of dialyzers.^{16,18} The countercurrent flow of blood and dialysates can be maintained by the use of these artificial organs.

Gas exchange by a mechanical lung and artificial heart - lung device

The microporous membrane of a mechanical lung is generally constructed from hollow polypropylene fibers.⁹⁷ The membrane is selectively permeable to different states of matter; it is minimally permeable to liquids but highly permeable to gases because of the small diameter of the fibers. Researchers have also coated the hollow fibers with polymethylpentene.⁹⁸ Respiratory exchange can be successfully performed by the mechanical lung such that carbon dioxide is removed from the blood, and oxygen is provided as cells flow through the lumen of the hollow fibers.^{16,98} The respiratory system can be used to prevent acute and chronic lung disease.⁹⁹ These hollow fiber oxygenators are widely substituted for conventional oxygenators made of silicone because of the lower volume for perfusion and lower resistance to blood flow. Less plasma protein and platelets are thus consumed.⁹⁸ The micropores of the hollow fiber membrane can be filled with gas continually, and the rate of transmural gas diffusion through the fiber wall can be increased. As the fibers are mainly hydrophobic, water invasion into the hollow fiber wall can be prevented, and the life span of the membrane can be prolonged. Thinned asymmetric and composite symmetric microporous hollow fibers have been used as plasma resistance materials to prevent plasma leakage when the pores are filled with blood plasma.⁹⁹ It was also found that the hollow fiber membranes could be fabricated with a thickness of 0.8–0.9 mm using the triple orifice spinneret to selectively separate and pervaporate the gas.⁴³ Accompanying the invention of mechanical lung, an integrated artificial heart-lung device (IAHLD) has been developed using a hollow fiber membrane. Hollow fibers are aligned in grids for

channeling blood and efficient gaseous exchange.¹⁰⁰ Effective gaseous exchange can also be created by transverse mixing as the blood flows past the hollow fiber fabric while the gas flows inside the pores.¹⁰¹ Blood–gas contact can be avoided if the micropores of the hollow fiber membrane are closed at the end toward the blood-contact surface and an ultrathin layer of high density is formed.¹⁰²

Cell culture by hollow fiber bioreactor

Hollow fiber bioreactors and hollow fiber cell-culture cartridges were first introduced for the in vitro testing of antibiotics and anti-HIV drugs in the 1980s and 1990s, respectively. Hollow fiber bioreactors are an in vivo-like device, as the capacity of bacteria within the body can be derived from the number of bacteria grown within the bioreactors.¹⁹ The hollow fibers are positioned in parallel inside the cartridge, and the cells attach and grow outside the fibers in the extracapillary spaces (ECS). The cellculture medium is pumped along the interior of the hollow fibers from the end ports of the cartridge, which can be maintained and circulated constantly for a certain period of time. The nutrients and the dissolved oxygen of the cell medium can therefore diffuse from the interior of the hollow fibers to reach the cells at the ECS by crossing through the walls of fibers, and the waste can diffuse out of the cells to the hollow fibers.²⁰⁻²² Hollow fibers are cylindrical and small in diameter; as a result, large molecules that may either restrict or enhance the growth of cells can be overcome by the selectively permeable nature of the fibers and the size of the pores. 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 of the bioreactor 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.²² The hollow fiber bioreactor has been used in many applications, including the production of recombinant proteins and antibodies, the growth of HIV virus, and the testing of the antibiotic effect of different bacteria.^{19,22}

A liver model is an example of a hollow fiber membrane bioreactor. Liver-tissue engineering has been used to replace animal-derived tissue. The mass transfer of nutrients and metabolites can be controlled when the cell-culture medium flows through the lumen of the hollow fibers and across the fiber walls. The biochemical and the physical conditions of liver function can also be replicated.²³ The hollow fiber infection model is another example of a bioreactor used for in vivo-like generation of antibodies, genetically engineered proteins, viruses and vaccines, and cell culture. The contagious or contaminating substance cannot diffuse through the hollow fibers into the cell-culture medium because of the porous support of hollow fibers to secure the biosafety of the medium. In conjunction with the porous nature of hollow fibers, the high surface-

area-to-volume ratio of hollow fibers could provide a satisfactory support for culture cells at a high density. Additionally, fast exchange between the areas of growing cells and the central reservoir is possible. Equilibrium of the nutrients, metabolites, and drugs across the hollow fibers can be reached quickly.²⁴ The temporal variation of drug concentration in vivo can also be modeled in this way (Figure 9).¹⁹



Figure 9. Schematic diagram of bioreactors using hollow fibers. Hollow fibers are enclosed in parallel inside the cartridge. The cells can grow in the extracapillary spaces outside of the fibers. Nutrients, wastes, and drugs can diffuse and exchange across the hollow fibers. Control of the mass transfer of nutrients and metabolites can be achieved when the media flows through the channels of the hollow fibers and across the walls of the fibers.^{19–24,103}

Hollow fiber liquid-phase micro-extraction

Liquid-phase micro-extraction has been used for drug analysis and environmental monitoring. Hollow fiber liquid-phase micro-extraction (HFLPME) consists of a membrane constructed from a hydrophobic polymer such as polypropylene in a hollow fiber. HFLPME can be classified into two different configurations: the two-phase system and the three-phase system. 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 hollow fibers from the region of aqueous sample to the organic

region. The analyte is extracted into the acceptor solution inside the lumen of the hollow fibers, and the sample is then analyzed.¹⁰⁴

Drug screening by hollow fiber assay

A hollow fiber assay (HFA) was developed as a substitute for conventional anticancer drug screening. This advanced in vivo screening method was designed by the National Cancer Institute in 1995 because of the opportunity of growing at least 50 tumor cell lines inside the hollow fibers. Tumor 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.²⁵ Anticancer drugs were administered to the mice for a specific period of time. From the investigation by Phillips and colleagues,²⁶ angiogenesis could be induced in mice by tumor-cell-loaded hollow fibers. Short-term in vivo pharmacodynamic endpoints and microtubule disruption was demonstrated using the HFA.²⁵ New blood vessels for nutrient and oxygen supply to cells developed around the HFA, as the loaded tumor cells secreted growth factor, which diffused out of the hollow fibers to the tissues nearby.²⁷ Encapsulation of mammal cells in the hollow fibers could be used either as an extravascular device for encapsulating insulin-secreting cells or an intravascular device inside the abdominal space (Figure 10).²⁸



Figure 10. Microscopic images of hollow fiber medical devices. (a) Hollow fiber membrane of a dialyzer;18 (b) osteosarcoma cells were cultured in an artificial culture medium in a hollow fiber bioreactor;19–24,103 (c) development of blood vessels around hollow fibers that were implanted inside NMRI mice.²⁶

Conclusion and perspectives

Capabilities and limitations of hollow fibers in medical applications

Hollow fibers have been typically associated with the invention and use 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 example, 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.

Future trends and breakthrough of using hollow fibers in medical textiles

The drug delivery capacity of hollow fibers is likely to remain a focal point of medical textiles. Multifunctional protective textiles and clothing have great potential. It is believed that this clothing can be constructed by using the fabrics (i.e., woven, knitted, or non-woven) made of drug-loaded hollow fibers. The loaded drugs can then be transported onto the skin and diffuse into the inner layers. Consequently, growth of bacterial pathogens on the skin can be prevented or halted. A convenient and comfortable skin-protective treatment can be given to wearers and even for continuous medical function. This would be a future substitution for curing skin or other illnesses instead of by using the conventional methods of medical plasters and ointment. Beyond their use in drug delivery and ultrafiltration, the mechanical properties of hollow fibers, such as thermal insulation and moisture wicking, could also be useful in medical textiles and clothing. The combination of medical functionality and textile comfort may be part of an emerging industry. Internal implantation of medical devices is a substantial concern of patients, as it is accompanied by tremendous risks and adverse consequences to health. For example, internal devices may require regular replacement by surgery, or the organ may by rejected. Therefore, the ability to use external medical devices with the same functions as implanted devices will be transformative. Medical textile and clothing systems using hollow fibers are thought to be a potential system for external use.

Evolution of material science and future textile development

Material science has greatly expanded in recent years. New material applications can be provided by the advanced material technology that can enhance the efficiency and timeliness of the systems in which they are used. It is imperative to integrate the "upstream" and "downstream" aspects of the textile industry. In developed economies, such as Japan and Germany, the market for textile industrial application in the medical field is relatively larger than that in the areas of traditional uses and home remedies. As the fundamental uses of advanced chemical fibers are transformed into commercial purposes, chemical fibers are increasingly exploited. To manage the problems of today and the future, interdisciplinary collaborations are essential to the exploration of technology. New technologies and the consolidation of new industries will result. The use of hollow fibers in the medical area is one important example.

In consonance with the textile market, the production cost of natural fibers is relatively higher than that of many synthetic fibers as they are limited in resources. The price of hollow fibers is approximately 40% lower than that of cotton fibers. The technological production of hollow fibers is originally derived from the integration of material science and the comprehensive improvement of textile machinery. It is known that synthetic hollow fibers are generally similar to natural cotton fibers due to having a hollow canal that runs through the length of the fibers. This morphological structure has brought about some exceptional advantages such as being light and soft, and having good moisture absorbency and heat insulation. Application is usually the next stage to be explored once the technology is mature enough and the associated market has developed. The main difference between traditional textile and industrial textile products depends on the needs of downstream technology, as well as the re-integration and innovation of the upstream technology. Challenges and opportunities often coexist. For example, there are some difficulties in spraying and extruding the central square lumen of hollow fibers by existing textile technologies. The future development of hollow fiber technology will be investigated via the route of various industrial applications. Therefore, limitless prospects could be unearthed with mature industrial technology and the exceptional advantages of hollow fibers for a wide range of medical applications such as ultrafiltration and drug delivery through the hollows. Through a few decades of textile spinning development, the basic textile and clothing uses have already reached a very high standard, and hollow fibers are one of the products made with mature textile technologies. Optimization of both textile material and yarn structure has been successfully achieved through a layering system. Furthermore, due to the advantages of being soft, light, and flexible, textiles have been widely recognized and appreciated by various industries. A great potential of the textile industry has also been gradually realized.

In this review paper, the development of medical textiles and the medical applications

of hollow fibers, such as drug delivery and dialysis, and their advantages have been illustrated. The future aspect of using hollow fibers in multi-functional medical textiles and the progression of material science have also been mentioned. This paper provides a comprehensive and systematic exploration of hollow fibers in medical and therapeutic areas.

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