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Filtration in Pharmaceutical Industries and Role of Textile
Filtracija v farmacevtski industriji in vloga tekstilij

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Abstract
Filtration is considered the keystone for clarification and control of contamination in pharmaceutical and biopharmaceutical manufacturing. From production to in-process to chemical and research laboratories to the purification of water for sterile and nonsterile products, all of which involve some form of filtration in order to achieve a good manufacturing practice (GMP). Textile materials possess a significant contribution to the pharmaceutical filtration system. Textile material in pharmaceutical filtration is used in the form of filter media or medium. Flexible in nature, large pore distribution and non-metallic properties of textile materials have led to widespread use as filter media for many years. In filtration processes, a proper selection of filter media/membrane material is usually the most critical aspect for ensuring efficient separation. Generally, solid-liquid and solid-gas separation is done by the filter media. This paper emphasises solid-liquid filtration. Moreover, this paper reviews the water requirement, filtration processes and the role of textile in the filtration system of pharmaceutical industries. This paper also offers insight into the current market trend and COVID-19 impact on the pharmaceutical filtration industry. Furthermore, gathered information may be helpful to those studying and working in pharmaceutical engineering, filtration technology, and wastewater treatment and can get knowledge about filtration systems.
Keywords: liquid filtration, textile filter media, water treatment, pharmaceutical filtration, COVID-19 impact

Izvleček
Filtracija velja za temeljni kamen čiščenja in nadzora kontaminacije v farmacevtski in biofarmacevtski proizvodnji. Od proizvodnje do medprocesnih, kemijskih in raziskovalnih laboratorijev čiščenja vode za sterilne in nesterilne izdelke vsi vključujejo določeno obliko filtracije, da dosežejo dobro proizvodno prakso. Tekstilni materiali prispevajo pomemben delež k farmacevtskemu filtracijskemu sistemu. V farmacevtski filtraciji se uporabljajo v obliki filtrnega medija ali medija. Gibka narava, porazdelitev velikih por in nekovinske lastnosti tekstilnega materiala že vrsto let vodijo v široko uporabo filtracije kot filtrnega medija. Pri postopkih filtracije je pravilna izbira filtrnega medija/membranskega materiala po navadi najbolj kritičen vidik zagotavljanja učinkovitega ločevanja. Na splošno se ločevanji trdno-tekoče in trdno-plin izvajata s filtrirnimi mediji. Ta članek obravnava filtracijo trdno-tekoče. Poleg tega obravnava potrebe po vodi, postopke filtracije in vlogo tekstilij v filtrnem sistemu farmacevtske industrije. Daje tudi vpogled v trenutni tržni trend in vpliv COVID-a na filtracijo v farmacevtski industriji. Znanja o filtrnih sistemih so lahko koristna vsem, ki študirajo in delajo na področju farmacevtskega inženirstva, filtracijske tehnologije in čiščenja odpadne vode.
Ključne besede: filtracija tekočin, tekstilni filtrni mediji, priprava vode, farmacevtska filtracija, vpliv covida

1 Introduction

Filtration is the separation of solid particles suspended in a liquid or gas using a porous medium that traps the solids while allowing the fluid to flow through. When the amount of solids in a liquid is reduced, this is called clarification [1]. In the pharmaceutical sector, filtering is a common and well-known activity. Filtration is used to make sterile goods, bulk pharmaceuticals, liquid oral formulations, and wastewater treatment plants (WWTPs) and their effluent receivers [2]. A porous material used to hold particles is known as filter media. There is a variety of materials that may be utilised in the filter medium to satisfy the users' demands. A proper selection of filter media/membrane material in filtering procedures is frequently the most critical aspect for ensuring efficient separation [3]. Cotton, polyester, wool, linen, polypropylene, glass fibre, porous carbon, metals and rayons are some of the materials used to manufacture filter media [4]. New polymeric materials have recently been utilised in filtering processes to purify medications, fluids and wastewaters in the pharma industry, both separately and/or mixed [5]. Surface filtration relies heavily on textile materials and membranes. Textiles such as nonwoven textiles and natural or synthetic fibres may be selected for their ease of installation on the filter tank/module [6]. Apart from the nonwoven structure, metal glands may be installed in the weaving medium in specific situations, cartridge and wax filter can also be incorporated with a woven fabric. The usage of different chemicals (e.g. polymer blends) in the manufacturing of the filter material, as well as the addition of the base material (e.g. nanoparticles, nanotubes) may modify the surface of the existing material and can work as a highly efficient filter [7]. In recent years, textile nanofibers have gained popularity in liquid filtration due to their unique characteristics such as high aspect ratio, cohesiveness, high specific surface area, exclusive physicochemical properties, and the design flexibility for chemical/physical surface functionalisation. They are continually gaining popularity in the pharmaceutical industry as a filter material in liquid and gas filtration [2, 8]. Apart from the general production of drugs, sterile and non-sterile products, the current COVID-19 outbreak impacted the production trend of vaccines, and there has been a sudden rise in demand. Thus, filtration-based technologies are also gaining momentum in vaccine clarification [9].

2 Filtration mechanism used in industry

The pharmaceutical industry needs different filtration methods depending on what sort of chemical solution is being used. Generally, the pharmaceutical industry has three major types of filtration systems (surface, depth and crossflow filtration) [7, 8, 10]. Figure 1 depicts various mechanisms of filtration.

Surface filtration, which operates with direct interception, separates the substance from the medium through which it may travel more readily than other materials in the same environment. The separation is caused by the size of holes in the filter, since the screen enables particles of specific size to pass through but traps molecules which are too big to fit through the pores. The technology is also known as membrane filtration, since it occasionally uses a porous membrane [8, 10, 64]. Deep-bed filters (also known as depth filtration) have been utilised in water and wastewater treatment for over a century. The creation of wells or springs in nature, which are drained from porous media such as rocks and sand, is similar to the principle of deep-bed filtration. Depth filtration holds particle matter further down from the surface than surface filtration [7, 11]. Its primary function is to clarify solutions. Ceramic-filter, sintered filters and nonwoven textile filters are the most frequently used in depth filtering. Recent advances in sintered metal filters include electrostatic precipitators, cyclones and disposable filters that were once highly used in the pharmaceutical industry [12].

Nanofiltration, also known as crossflow filtration, is a recently created device used by pharmaceutical industries seeking a solution of polyvalent cation removal in a low total dissolved solids water (surface or fresh ground water). The term nanofiltration refers to using a filtration membrane with holes that are one nanometre in diameter or smaller. It is comparable to reverse osmosis; however, the trans-membrane pressure required for functioning is much lower. As a result, the procedure is more cost-effective. Nevertheless, nanofiltration has flaws, e.g. the possibility of fouling and scaling on nanofiltration membranes [10, 13].

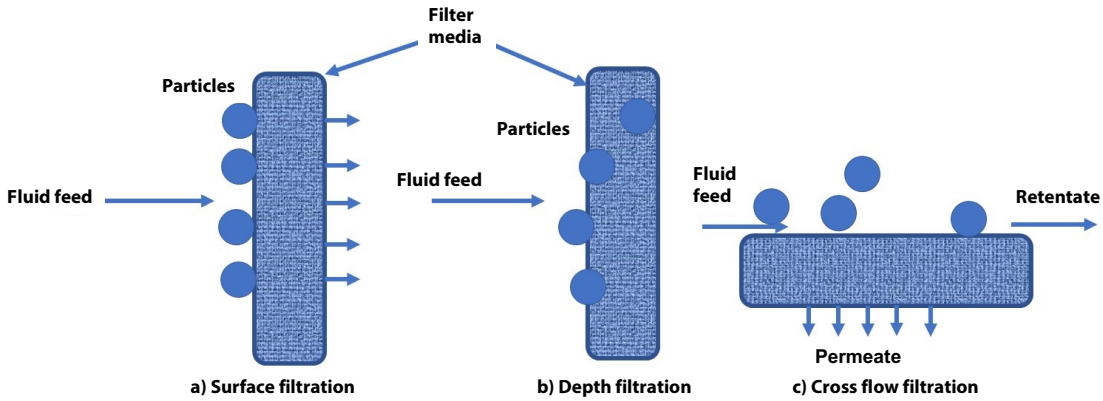

Figure 1: Filtration mechanism [8–13]

3 Water quality and filtration in pharmaceutical industries

Water is an essential component in pharmaceutical and life science processes. Water is utilised as a raw material in the processing, formulation, and production of various pharmaceutical products and active pharmaceutical ingredients (API). Most pharmaceutical industries rely heavily on surface water and groundwater supplies. Water from these sources is contaminated in its natural condition and must be filtered before being used for pharmacological purposes [14]. For pharmaceutical use, water must be treated according to established protocols. Distillation and deionisation are used in this water purification procedure to lower the number of polluted particles, parasites, bacteria, algae, viruses and fungi [15]. Medicinal water systems of varying quality are required depending on the mode of administration of the pharmaceutical medication. Numerous types of water used for medicinal applications are listed below, based on water quality. Water standards are included in pharmacopoeias for both bulk and dosage forms of water [16]. National, regional and worldwide pharmacopoeias specify the pharmacopeial requirements or guidelines for WPU (water for pharmaceutical use), and limits for specific impurities or groups of impurities are either stated or suggested [17]. Companies that want to serve several markets create specifications that match the most stringent criteria of each pharmacopeia [18].

3.1 Drinking water

Potable water is the best way to describe drinking water. Drinking water should be available under constant positive pressure in a plumbing system that is devoid of any flaws that might lead to product contamination. The minimal quality of water should be used to manufacture drugs and other bulk pharmaceutical compounds in drinking water [19]. After assessing the source water's condition, the treatment necessary to make it safe for human consumption is decided. Except for a minor treatment of water drawn from a natural or stored source, drinking water is unaltered [20].

3.2 Bulk purified water (BPW)

In preparing non-parenteral dosages and other pharmaceutical uses, bulk purified water is mainly employed as an excipient. Non-parenteral is most usually used to refer to the route through which oral drugs are taken; consequently, it is critical that the water used in non-parenteral preparations meet the ionic and organic chemical purity criteria [20, 21]. As feedwater for this should be at least a drinking-water source or filtered water which has at least the parameters equalling the drinking water. It must meet the applicable pharmacopeial requirements for chemical and microbiological purity, as well as action and warning limitations. It should also be protected from microbial multiplication and recontamination. A combination of reverse osmosis (RO), RO/electro-deionisation (EDI) and vapour compression can be used to make BPW [22].

3.3 Bulk highly purified water (BHPW)

BHPW is a unique water specification available only in the European Pharmacopoeia. Drinking water should be utilised as an input water source for the preparation of BHPW. This water grade must meet the same quality standards as water for injections (WFI), including endotoxin limits. In combination with other required processes, e.g. ultrafiltration

and deionisation, double-pass RO is one of current manufacturing methods. BHPW can be made in various ways, including RO, ultrafiltration and deionisation. Highly cleansed water needs to be protected from recontamination and microbiological multiplication [18, 19, 23].

3.4 Bulk water for injections (BWFI)

BWFI is a common excipient in the production of parenteral and other pharmaceutical preparations where endotoxin is a concern. BWFI should be prepared with drinking water or filtered water as minimum quality feed water [21].

For pharmaceutical companies, chemical purity in BWFI is a crucial issue. The microbiological quality of the water should be consistent in testing and meet the standards for bacterial endotoxins, which are less than 0.25 IU per ml. Multi-effect distillation is the sole method for obtaining consistent BWFI. It is still the only official way of manufacturing BWFI. BWFI is not sterile water and is not intended to be used as a final dose form. BWFI is an intermediate bulk product that can be used as a component in a recipe. Sterlite water for injection (SWFI) is used for vials. The most outstanding quality of pharmacopeial WPU is BWFI. As a part of the BWFI definition, certain pharmacopoeias set restrictions on the allowed purification processes. Only distillation is permitted as the last purification stage in the International Pharmacopoeia and the European Pharmacopoeia [21–23]. Chemical and microbiological purity (including endotoxin) should be met by BWFI, with appropriate action and warning limits. BWFI should also be safeguarded from microbial multiplication and recontamination [23].

4 Textile materials for pharmaceutical filtration

Pharmaceutical filtration is divided into two-step prefiltration and main filtration. Prefiltration is any filtration procedure that takes place before the final filtration in the manufacturing process [19, 24]. The main goal is to achieve adequate particle removal. The filtration rate and throughput are other factors to consider. Fibre, yarn and fabrics (woven and nonwoven) are the basic textile products. All these textile products are used as filter media for liquid filtration. Textile fibres can be natural or manmade. Table 1 shows the properties of various textile fibres which are frequently used in liquid filtration. The aspect ratio (length and breadth or diameter) of textile fibres made them most suitable for the filter

Table 1: Fibres used in pharmaceutical filtration and characteristics [6, 10, 13]

No.	Fibre category	Fibre name	Maximum service temp (°C)	Principal properties
1	Cellulosic	Cotton, viscose, jute	90	good abrasion and very good alkali resistance, poor acid resistance, inexpensive
2	Polyamide	Nylon	100	excellent abrasion and alkali resistance, poor acid resistance, high strength or flexibility
3	Polyester	Decron, Trevira	150	very good abrasion, good acid resistance, poor alkali resistance, easy cake discharge, long life
4	PTFE (Polytetrafluoroethylene)	Teflon, Rastex	200	fair abrasion, excellent acid resistance, excellent alkali resistance, extreme, excellent cake discharge
5	Polypropylene	Moplefan (trol)	90 (120)	good abrasion, excellent acid resistance, excellent alkali resistance, low moisture absorption
6	Copolymer Acrylic	Dynel, Orlon	120	good abrasion, good acid resistance, and fair alkali resistance
7	Polypeptide	Wool	110	good abrasion, good acid resistance, poor alkali resistance
8	Silicate	Glass fibre	250	poor abrasion, fair acid resistance, poor alkali resistance, suitable for a wide range of chemical solutions

media. Strand in the form of sliver, roving or yarn is also used for the filter media. Fabrics, woven or nonwoven are the largest used textile products as filter materials.

The number of pores, pore size, yarn count and weave type define the fabric filter media. More yarns and a finer yarn count result in smaller pores and a greater number of pores in the woven fabric. Nonwoven filter media is manufactured directly from the fibre and can be used in a variety of liquid filtering systems, including filter presses, horizontal disc filters and rotary drum vacuum filters. Due to the mechanical, chemical and thermal treatments, individual fibres in nonwoven filter media are often interconnected. To preserve the filter media, loose woven materials can be utilised on both sides of the filter [6, 10, 31].

The cellulose textile fibre-based depth filter, which comes in sheet or lenticular cartridge type, is one of the most prevalent prefilters used in biopharmaceutical processes. These prefilters are particularly cost-effective due to comparatively inexpensive raw materials used in their construction, and the thickness and structure of the filter matrix created during the manufacturing process [6]. Cellulose or manufactured textile fibres, inorganic filter aid, fabrics and a polymeric wet-strength resin are the main raw components utilised to make these filters. By refining the fibres, void volume and particle retention capacity of the fibre component of the filter can be adjusted [2–6, 24].

The filter aid is the second most crucial part of the filter sheet. Perlite is volcanic ash with a smooth, glass-like texture and is also used with a mixture of cellulose fibre matrix. The particles of Perlite have a somewhat uniform shape and form thickly within the cellulose fibre matrix. The powder comes in various particle sizes, allowing for a wide range of porosity [3].

Instead of cellulosic prefilters, glass fibres are also used, especially in serum filtrations. These may be borosilicate glass or glass fibres with special coatings such as nitrocellulose polymers. The adsorption of process contaminants, particularly protein-like materials and lipids, is quite successful with these coatings. The adsorptive elimination of pollutants with a nitrated polymer is most likely accomplished through hydrogen bonding. Polypropylene fibres are also a common material for filter media [3, 25]. To limit or eliminate media movement, they can be shaped into fleeces and mats of varying fibre diameters bound together and permanently crosslinked by heat, then bonded by melting. The adhesives and mechanical manipulations of older and less effective sheet creation methods replaced the melt-spinning way of permanently connecting the fibres. Varying the mean fibre size during the fleece formation enables the mat pore size to change progressively [3, 6, 25]. Due to this filtration, the effect will be like a series of prefilters combined into a single prefilter composite. Due to the effectiveness of thinner fibres, the asymmetric morphology provides less resistance to flows, requires lower differential pressures in their operations, can accommodate higher particle loadings and delivers more particle removal. Fibres with mean diameters as tiny as 0.3 μm are capable of retaining particles as small as 1 μm in diameter from a fluid stream. A smaller pore size is created by shrinking fibre diameters rather than tightening mat packing density. This improves filter porosity while allowing for lower operational differential pressures and bigger load capacities [25, 26].

5 Continuous filtration for pharmaceutical industries

Pharmaceutical water system operators strive to create bacteria-free water that meets or exceeds purity standards. To safeguard system components and ensure that the water distributed for use is free of bacteria and most other particle pollutants, water systems employ several filters [27]. Figure 2 depicts a continuous filtration system used in pharmaceutical industries.

Particle filtration and bacterial elimination are the two main filtration products used in pharmaceutical water systems [2]. Before the reverse osmosis (RO) unit, filters are used to reduce or remove particle contaminants, whereas filters after the RO unit are used to decrease or eliminate bacterial contamination. The use of filtration products in pharmaceutical water systems generally falls into two categories, i.e. particle filtration and bacterial removal. Filtration products located before the reverse osmosis (RO) unit reduce or remove particle contaminants, while the filters following the RO unit are intended to reduce or remove bacterial contaminants. Additional filters may be necessary if the water supply includes chemicals that, if not treated, could cause early filter blocking or fouling of RO membranes [2, 25, 28].

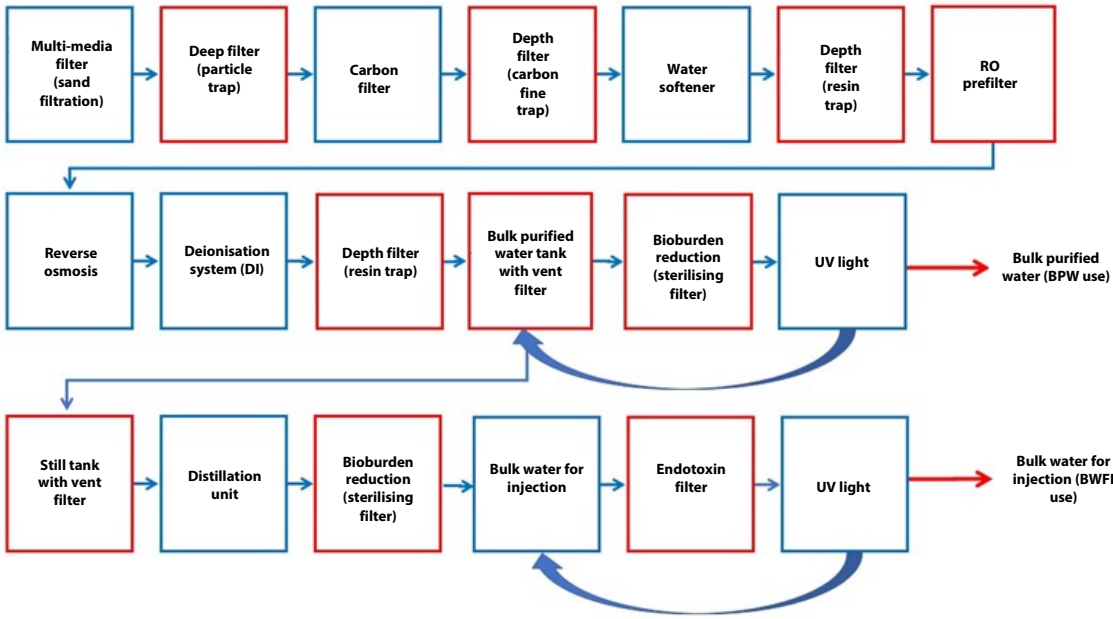

Figure 2: Filtered water system for pharmaceutical use [2, 21, 24, 25, 27, 28]

5.1 Before reverse osmosis (RO) unit

Coarse filtration is commonly used as the first step in water treatment to remove bigger particulates like sediment and silt. Figure 2 depicts a multimedia (sand) filter followed by a depth filter to remove the particles emitted by the multimedia filter. Both filters can be merged into a single particle filter housing in smaller systems [10, 27, 28, 64]. There are two types of depth media for cartridge filters. Self-supporting tubes consist of a polymer, most commonly made of polypropylene or nylon. The melt-blown or nano-spun process is used to create the tube. Pleated flat sheet media, most commonly made of polypropylene or fiberglass, is used in the other type of depth filter [10, 11]. Although polypropylene is the most frequently used material for water and chemical filtration, fiberglass offers a greater filter efficiency. It allows for higher flows and throughput in most applications than polypropylene. Through the thickness of the media, standard depth filters will catch a range of particle sizes. Pleated media filters have a larger surface area than ordinary depth filters and may hold a more significant number of particles on that surface. These items can hold a lot of silt or sediment before they need to be replaced. Yarn wound filters are also used; however, these filters add extractable surfactants to the water when they are installed [3, 6, 25].

Melt-blown and nano-spun polypropylene filters are available in a wide variety of configurations to fit the existing housings. Pleated filtration devices, such as commercial-grade pleated polypropylene (CPF) depth filters, can remove up to three times as much sediment and silt as melt-blown or nano-spun filters. However, pleated filters are more expensive; however, longer life and higher dirt holding capacity and labour savings from less frequent filter changes make pleated filters economically advantageous [2, 6, 29].

The activated carbon filter depicted in the Figure 2 is a granular carbon filter that eliminates chlorine, chloramine and other dissolved organic compounds from the water supply. Cartridges include activated carbon that is immobilised within the filter matrix. It is also possible to employ activated zeta plus carbon. It is made up of activated carbon, cellulose and a positively charged crosslinking polymer, and is designed to deliver the best filtering and purification results for a wide range of fluid issues. This prevents the oxidation of downstream treatment components, particularly RO membranes. Unfortunately, all carbon filters produce carbon fines, and fine carbon particles must be removed with depth/particulate to safeguard downstream equipment. Again, CPF melt-blown or nano-spun polypropylene depth filters and yarn wound filters can be used for carbon fines removal [2, 6, 30]. With

their excellent dirt holding ability, pleated filters could also be used in this situation.

Water softening and deionisation are two resin-based treatment procedures depicted in the system diagram. These resin-based techniques will be used in small and big pharmaceutical water systems. Polishing is the term used to describe this process [30, 31].

These resin beds can be blended or separated. They are highly dependable when it comes to creating USP (US pharmacopeia) grade water; however, they do require regeneration once they are depleted. On-site or off-site regeneration is possible [32]. Before the regeneration, the resin must be separated if utilising a mixed bed. On-site regeneration capabilities are obviously more expensive in terms of capital, but they are cheaper for long-term maintenance. Continuous electro-deionisation is the advanced polishing method. Ion exchange resins in a stack remove cation and anion pollutants from the feedwater, and an electrical current runs through the stack to regenerate the resin continually [33]. The continuous regeneration eliminates the need for traditional ion exchange equipment to be shut down and regenerated regularly, allowing for the production of high-quality water [31–33]. The resin beads used to purify the water in both cases will break down over time and may release resin particles into the water supply. To remove these resin particulates from the water, textile-based depth filters must be fitted once again [34].

5.2 Reverse osmosis unit

The reverse osmosis process is supported by an RO prefilter, as illustrated in Figure 2, which protects the high-pressure RO pump and keeps the membranes from fouling due to particles. Protecting the RO membranes from particles is critical for extending membrane life. To safeguard the RO membranes, CPF offers melt-blown polypropylene, polyester filters, nano-spun polypropylene filters, pleated polypropylene, and nylon filters may be used. Though melt-blown or nano-spun cartridges may cost each less than a pleated cartridge, pleated filters may be desirable due to the lower number of filters and potentially longer filter life [2, 3, 36].

RO systems are the most common method for removing salt and organic material and inorganic and organic pollutants, colloids, microorganisms and endotoxins. Since it effectively removes inorganic/organic impurities (excluding gases), has relatively low operating costs, and is very reliable when pretreatment equipment is appropriately maintained, RO is the primary process for water purification [37].

5.3 After reverse osmosis (RO) unit

Vent filters are utilised at two points in the illustration. These are employed to filter the air directly in touch with the purified water or water for injection storage tanks and protect the water from bacterial and particle contamination. The air inside the tank must be allowed to go out as the tank fills, and when the tank is emptied, air (or a process gas like nitrogen) must be allowed to enter to replace the lost liquid volume [25, 35, 39]. Particle and bacterial contaminants must be eliminated from the tank's air or gas. The filter media must be dry for air to travel freely through it. Almost all vent filters used in biopharmaceutical manufacturing are hydrophobic membranes with pore sizes of 0.22 μm. A hydrophobic membrane such as polypropylene or PTFE is commonly used as such a membrane resists the water vapour [40]. Sterilising grade polypropylene melt-blown media (PPM) or PTM cartridges or capsules is used for ambient temperature storage tanks since most WFI storage tanks are kept at high temperatures [27, 40].

Different particle and bioburden loading are encountered in each biopharmaceutical process. Outside materials can be the path for such particles and organisms into processes. Organisms may be prevalent in the plant atmosphere, like moulds and yeasts, and can enter into the processes during mixing or are introduced through normal handling of ingredients and equipment [41]. Operators may opt to remove the majority of organisms before the sterilising filter or all of them, depending on the nature and amount of organisms. Membrane-based filters handle almost all bioburden reduction filtration [35]. However, high-efficiency pleated depth media filters can remove some big microorganisms, e.g. moulds and yeasts. Using pleated flat sheet media, polypropylene or fiberglass cartridge filters may remove organisms as minor as 1 μm in size. Most moulds and yeasts, as well as spores like Bacillus subtilis, fall into this category. Membrane filters for bioburden reduction come in various materials, with pore sizes ranging from 0.85 μm to 0.22 μm [25]. The filter material and pore size will be determined by the type of fluid being filtered, and the size and number of organisms present. If the fluid

contains a more significant number of bacteria, a sub-micron-rated membrane filter with a pore size of 0.65 μm or 0.45 μm will remove the majority of the bacteria [6, 25]. It is crucial to find out how many and what size organisms there are to remove enough to prevent processes and the sterilising filter from being damaged [42]. The final filtration and point of use filtration WFI systems utilising distillation coupled with storage and distribution systems kept at elevated temperatures need no extra filtration since the water has been sterile and is preserved in a sterile state with heat [38, 43].

Due to the multitude of bacterial entry points into the system, the final filtration utilising "sterilising grade" membrane filters is regularly used as the final bacterial removal process in most ambient temperature pharmaceutical water systems [40]. Sterilising grade filters are typically rated to remove at least 100,000 bacterial colonies per ml without passing through to the product side of the filter. Filters not meeting these removal criteria are considered bioburden reduction filters rather than sterilising grade filters [41, 43]. Typical sterilising grade filters utilised in pharmaceutical water systems are rated to remove particles and bacteria that are 0.22 micron or 0.1 μm or larger in size; however, coarser filters are available as well [38, 42]. In the past, the standard was 0.22 μm. Now, one organism (Acholeplasma laidlawii) has been found to pass through these filters; therefore, manufacturers have developed a finer, 0.1-micron filter to remove this organism [42, 45, 46].

To remove endotoxins (cell fragments), ultrafiltration or charge modified filter media are utilised. Pleated nylon 6,6 membrane and single-layer charge modified nylon 6,6 membrane filter cartridge provides superior microorganism reduction while substantially increasing the life of downstream sterilising grade filters. This filter offers enhanced particle and pyrogenic removal via an electrostatic charge on the membrane [46, 47].

6 Ultrafiltration in pharmaceutical industries

Ultrafiltration (UF) is a pressure-driven membrane transport technology that has been used both in the lab and in the industry. UF is used in industries such as chemical and pharmaceutical manufacturing, food and beverage processing, and wastewater treatment to recycle flow or add value to later products [48]. The capacity of UF to purify, isolate and concentrate target macromolecules in continuous systems is its key selling point. Permeate is the solvent and other dissolved components that flow through the membrane. Retentate components are those that do not pass through [49]. UF is a separation technology that allows labile biopolymer streams (proteins, nucleic acids and carbohydrates) to be processed cost-effectively, even on a large scale, without using high temperatures, solvents or other chemicals. Low shear (e.g. positive displacement) pumps can help reduce shear denaturation. Infusion solvents, serum, vaccines and plasma are just a few of the pharmaceutical industry's products that are manufactured to the highest quality and purity standards [35,50]. UF provides solutions that have been designed to meet the needs of the pharmaceutical and biotechnology industries for a variety of applications [48, 51].

6.1 Wastewater treatment in pharmaceutical industries with ultrafiltration

Ultrafiltration plant for pharmaceutical sector is responsible for water treatment in the pharmaceutical industry [52]. This plant is utilised in the RO prefiltering stage. It helps reverse osmosis membranes by lowering the water's silt density index and removing particles. UF membranes improve RO performance and are widely utilised in desalination systems, pharmaceutical manufacturing and other industries. UF is a multi-skilled system that gives a reliable solution to wastewater problems or clean, reusable water after a complete treatment. The water produced as a result of this treatment can be used for various reasons. This method has water of such high quality that it can also be used for drinking [29].

UF utilises an air-sourced mechanism and provides excellent performance in the elucidation of wastewater. It addresses water scarcity and other water-related issues in enterprises. These systems are meant to eliminate bacteria and other microbiological debris from the water and meet the needs of enterprises across India [29, 53].

6.2 Recent and developing application of ultrafiltration

Ultrafiltration is becoming a potent separating tool for the constantly expanding biotechnology industry. Cell harvesting, depyrogenation of injectable

medicines and enzyme purification are only a few examples. UF has a number of advantages over centrifugation when it comes to bacteria collection. Owing to these advantages, UF membranes are less prone to clogging by cells and debris than microporous filters due to their asymmetric nature. Another possible application of UF is plasma product processing [54]. When human plasma is fractionated using the Cohn process or other novel technologies, there is a requirement to concentrate the essential protein fractions (albumin and globulins) or remove alcohol and salt. UF is a convenient way to accomplish this [24, 55].

7 Selection and options of filter media

The heart of any filtration process is considered the filter media. While the solids to be retained are concentrated on the membrane's feed side, the liquid component is forced to pass through and delivered to the membrane's other side. A filter medium is not uniform by nature, and its dimensions and geometries are derived from irregular pores. The distribution of these pores on the membrane surface may also be uneven. The microfluidic velocity within the holes can produce considerable changes on the filter surface since the flow in the environment only occurs through the pores [56]. This implies that the top layers of the filter cake created on the membrane surface are not uniform and are shaped by the filter medium's composition and qualities. The basic structure of the cake is firmly related to the structure of initial layers since the number of channels in the filter cake is greater than the number in the filter media. This indicates that the filter crayon and the filter material influence one another [57].

In the pharmaceutical sector, various types of filters are employed. When it comes to choosing a suitable filter medium, it is worth considering two things. The first is the fluid's substance, which includes viscosity, the nature of the solids (particle size, shape, size distribution etc.) and the concentration of solids in suspension [42, 44, 46]. The second factor are the equipment and process-related issues, e.g. flow rate, particle size restriction for passing through the filter, sterilisation by heat, radiation or gas, and cost. Solid particles smaller than the narrowest cross-section of the route can be caught by the pores having channels extending along with the filter media. Particle bridging or, in rare situations, physical adsorption is commonly used to explain particle retention. Different filter media are employed depending on the intended use [57–58].

Sand, diatomite, coal, cotton or wool fabrics, fibres, yarn, metal wire cloth, porous quartz plates, chamotte, sintered glass, metal dust and powdered ebonite are some of the most often used filter media [59]. The size and shape of each element from which the filter material is made determine the average pore size and configuration (including tortuosity and connectivity). The average pore size and shape are also influenced by the filter material's manufacturing procedure. Pore characteristics are also influenced by the fibre qualities of the woven fabric or the sintering procedures used for glass and metal powders [26]. In addition, some filter media, particularly fibrous layers, experience substantial compression when exposed to common pressures used in industrial filtration operations. Under the same operating circumstances, other filter materials such as sintered ceramic plates, glass and metal powders are stable. The filtration/separation process also influences pore characteristics. Since the effective pore size decreases as filtering progresses, flow resistance rises. This is due to the particles penetrating the filter media's pores. Filtration is a complicated method for separating solid particles from liquid. The larger pore size in comparison to particle size can also be used. However, the chosen filter medium must be able to adsorb solids and have significant enough cohesive forces between the particles to cause particle aggregation around the pore holes [60]. The utilisation of various water filters and common recommendations are given in Table 2.

In the chemical and pharmaceutical industry, a belt filter is an industrial machine used for solid/liquid separation processes, particularly sludge dewatering. Filtration is accomplished principally by passing the solid for dewatering from a pair of filtering cloths and belts through a roller system.

Filter bags are another option for filtration [8]. Filter bags are composed of felt, which has the advantage of being a three-dimensional filter media that provides both surface and depth filtering. They are available in different sizes and types of filter media with different ratings [25, 40]. Polypropylene filter bags are chemically compatible and can be used in various applications. Polyester filter bags can withstand extreme temperatures and are compatible with acids and petroleum-based fluids. Filter bags

Table 2: Water filter application and recommendation for pharmaceutical industries [2, 6, 21, 28, 48, 61]

No.	Water filter application	Function of filtration	Recommended filter media
1	Particulate Reduction and Trap Filtration	Removal of larger particles and fractured softener or deionisation resin beads before further treatment or use	Polypropylene melt-blown media, nano-spun polypropylene media, polypropylene pleated depth media
2	RO Prefiltration	Protect reverse osmosis membranes from premature fouling by removing particles larger than 1 micron in size	Polypropylene melt-blown media, nano-spun polypropylene media, polypropylene pleated depth media
3	Bioburden Reduction	Used in water distribution systems to remove larger organisms and protect final filters that remove all bacteria	Polyethersulfone (PES) membrane – nylon 6,6 membrane, positively charged nylon 6,6 membrane, high capacity hydrophilic (PVDF) membrane, high capacity polyethersulfone membrane
4	Bacteria Removal, Sterilising Filtration	Protect water quality for the patient, consumer or end use; remove all bacteria; may remove viruses and mycoplasma	Polyethersulfone (PES) membrane – nylon 6,6 membrane, positively charged nylon 6,6 membrane,
5	Ultra-Fine Particle Removal	Prevent sub-micron particles from reaching processes requiring ultra-pure water, such as semiconductor fabrication	Polyethersulfone (PES) membrane – nylon 6,6 membrane, positively charged nylon 6,6 membrane.
6	Tank Vent Filtration	Prevent airborne bacteria and fine particles from contaminating process or product water as it is held in tanks	PTFE membrane, polypropylene membrane, high capacity hydrophobic PVDF membrane

are commonly used to prepare adhesives, syrups, fruit juices, petroleum compounds and fluids with high viscosity [6, 25, 61]. Various filter forms used in the filtration system are shown in Figure 3.

The filters are cleaned using various methods, including manual, mechanical and self-cleaning filter systems. Cleaning is done manually with a water jet. The filters may need to be soaked in chlorine or detergent on occasion. Brushes or knives are used for mechanical cleaning. Disposable trash and labour costs are reduced as a result of automation. Product loss is reduced by using a self-cleaning filter system that requires little user effort. Some examples are magnetically connected industrial filters, self-cleaning filters and tubular backwashing filters, e.g. clearamine and reactogard filters, and piezoelectric ceramic membrane (PCM) [62].

a) b)

Figure 3: Filter forms used in filtration system: a) cartridge of polypropylene and b) carbon filter sheet and cartridge [3, 6, 10, 29, 30]

8 Current market of pharmaceutical filtration and impact of COVID-19

According to the latest market research report "Pharmaceutical Filtration Market" published by Markets™, the global Pharmaceutical Filtration Market is projected to reach 29.7 billion USD by 2027 from 10.9 billion USD in 2022, a CAGR of 17.0% during the forecast period of 2022 to 2027 [63]. This growth can be attributed to the growing biopharmaceutical industry, advanced research, increasing adoption of single-use technologies, increasing the new product, high purity requirements in end-user segments and advances in nanofibre technology [25, 63]. The pharmaceutical filtration market covers filters, systems and other filtration products. The filters used in the current time are membrane filters and depth filters. Polyethersulfone (PES), polyvinylidene difluoride (PVDF), nylon, polytetrafluoroethylene (PTFE), mixed cellulose ester & cellulose acetate (MCE & CA), polycarbonate tracked etched (PCTE), polypropylene (PP), cellulose nitrate (CN), regenerated cellulose (RC) are commonly used membranes [9, 25, 40, 63].

COVID-19, a worldwide epidemic, has affected people and businesses in practically every field. It is an infectious disease caused by a new coronavirus that has only recently been discovered [65]. As the World Health Organisation named the COVID-19 outbreak a pandemic, several prominent pharmaceutical and biopharmaceutical businesses ramped up research and production efforts to create and distribute SARS-CoV-2 viral test kits, vaccines and treatments. The pandemic's economic and social costs have spurred governments worldwide to increase funding for vaccine development and production, resulting in a rise in the use of pharmaceutical filtration products in COVID-19 research and production. Pharmaceutical filtration goods are employed in the production process of vaccines and other therapeutic medications; therefore, demand has increased as government backing, research activities and mass production of vaccines after approvals have increased [9, 64–66]. Removing suspended particles from a fluid medium during vaccine clarification is an important step that affects product recovery and downstream purification. Biopharmaceutical companies are using various filtration techniques and materials to help the downstream process (including filtration and purification) of vaccine production. Merck Millipore has donated USD 0.086 million in research apparatus and supplies to Indonesia's Eijkman Institute for Molecular Biology to speed up vaccine development. Merck has contributed water purification equipment with integrated reverse osmosis membranes for pretreatment and high performance that generate high-quality type-3 clean water. Pall Corporation, a Danaher subsidiary, has provided syringe filters, membrane filters, air filters, and water filters for vaccine and medicine manufacture, and research and development [9, 63].

In addition, the pandemic has provided possibilities for filtration companies to expand their production facilities. In the pharmaceutical filtration industry, the impact of the coronavirus crisis on supply chains, manufacturing and shipments to consumers has been controllable, with positive organic growth. Short- and medium-term predictability is severely limited and has little impact [62, 63, 66].

9 Conclusion

In the pharmaceutical sector, filtration is a crucial process. There is not a single aspect of the pharmaceutical industry that is not touched by filtration. For the pharmaceutical industry, drinking water, purified water and water for injection are required and obtained by different filtration methods. Despite the negative effects of the COVID-19, the market for pharmaceutical filtrations continues to grow. Textile materials in any form play an important role in the pharmaceutical filtration system. The innovative applications of textile filtration fabrics have been widely accepted in the pharmaceutical industry in the process of separation and purification of liquids. Due to their unique characteristics, textile filtration materials help maintain the high level of separation of particles from the fluids. A variety of filters media made from textile products (fibre, yarn, fabric, pleated polypropylene, charged nylon, polyester, nanofibers etc.) is often used in the filtration systems of pharmaceutical industries. In the pharmaceutical industry, the use of novel technology, new polymeric materials, and commercially available patent filters in bag and cartridge forms results in shorter filtration times and higher product quality. Multimedia filter, carbon filter, resin filter, reverse osmosis, distillation and UV lights may be utilised for contamination and particulate removal, and bacteria control.

References

1. SUTHERLAND, K. *Profile of the international filtration & separation industry*. Elsevier Science, 2004, 11–67, doi: 10.1016/b978-185617448-0/50004-x.
2. MAJEKODUNMI, S.O., OLORUNSOLA, E.O. Review of some recent advances on filtration in the pharmaceutical industry. *IOSR Journal of Pharmacy and Biological Sciences*, 2014, **9**(4), 30–38, doi: 10.9790/3008-09443038.
3. JORNIT, M.K. Filter design. In *Filtration and purification in the biopharmaceutical industry*. 3rd ed. Edited by Maik W. Jornitz. Boca Raton : CRC Press, 2019, 41–56, doi: 10.1201/9781315164953.
4. CHAUHAN, V.K., SINGH, J.P., DEBNATH, S. Virgin and recycled polyester filter media: effect of coating, calender roller pressure and roller temperature on dust filtration. *The Journal of The Textile Institute*, 2021, **113**(3), 467–474, doi: 10.1080/00405000.2021.1884361.
5. OSTREICHER, E.A., ARNOLD, T.E., CONWAY, R.S. Charge-modified filter media. In *Filtration and purification in the biopharmaceutical industry*. 3rd ed. Edited by Maik W. Jornitz. Boca Raton : CRC Press, 2019, 1-20.
6. EYVAZ, M., ARSLAN, S., GÜRBULAK, E., YÜKSEL, E. Textile materials in liquid filtration practices: current status and perspectives in water and wastewater treatment. In *Textiles for advanced applications*. Edited by Bipin Kumar and Suman Thakur. London : IntechOpen, 2017, doi: 10.5772/intechopen.69462.
7. MUKHOPADHYAY, A. Pulse-jet filtration: an effective way to control industrial pollution part II: process characterization and evaluation of filter media. *Textile Progress*, 2010, **42**(1), 1–97, doi: 10.1080/00405160903438367.
8. FRANCHI, A., SANTORO, D. Current status of the rotating belt filtration (RBF) technology for municipal wastewater treatment. *Water Practice and Technology*, 2015, **10**(2), 319–327, doi: 10.2166/wpt.2015.038.
9. Global pharmaceutical filtration market research report 2021 - Impact of COVID-19 on the market [online]. Market Growth Reports [accessed 2. 10. 2022]. Available on World Wide Web: <https://www.marketgrowthreports.com/TOC/19614702#TOC accessed on 17/05/2022>.
10. ROY, S. GHOSH, S., BHOWMICK, N. Mechanism of colloidal attachment on textile fibrous media. *Tekstilec*, 2018, **62**(2), 101-109, doi: 10.14502/Tekstilec2019.62.101-109.
11. PERLMUTTER, B.A. *Solid-liquid filtration. Practical guides in chemical engineering*. Elsevier, 2015, 57–77, doi: 10.1016/b978-0-12-803053-0.00005-5.
12. VIGNESWARAN, S., BEN AIM, R. Overview of deep bed filtration: different types and mathematical models. In *Water, wastewater, and sludge filtration*. CRC Press, 2020, 1–16, doi: 10.1201/9781003068655.
13. LI, X., LI, J. Cross-flow filtration. In *Encyclopedia of membranes*. Edited by Drioli E. and Giorno L. Berlin, Heidelberg : Springer, 2016, 1–2, 10.1007/978-3-662-44324-8_2194.
14. STRADE, E. KALNINA, D., KULCZYCKA, J. Water efficiency and safe re-use of different grades of water - topical issues for the pharmaceutical industry. *Water Resources and Industry*, 2020, **24**, 1-16, doi: 10.1016/j.wri.2020.100132.
15. JENKINS, J.O, ORAM, S. Water use attitudes in the UK pharmaceutical industry. *Water and Environment Journal*, 2013, **27**(4), 575–580, doi:10.1111/wej.12000.
16. McCORMICK, K. Water for pharmaceutical uses. *Quality*, 2002, **2**, 193–217, doi: 10.1016/b978-075065113-4/50014-3.
17. ISO 22519:2019. *Purified water and water for injection pretreatment and production systems*. Geneva : International Organization for Standardization, 2019, 35 p.
18. OLAITAN, M.O., MUHAMMAD, B. Assessment of microbiological quality of syrup and water used in pharmaceutical industries in Kano State, Nigeria. *Ife Journal of Science*, 2018, **20**(1), 119–126, doi: 10.4314/ijs.v20i1.12.
19. JORNITZ, M.W. Media and buffer filtration requirements. In *Filtration and purification in the biopharmaceutical industry*. 3rd ed. Edited by Maik W. Jornitz. Boca Raton : CRC Press, 2019, 331–348, doi: 10.1201/9781315164953-14.
20. SPELLMAN, F.R. Drinking water regulations. In *The drinking water handbook*. 3rd ed. Boca Raton : CRC Press, 2017, 25–51, doi: 10.1201/9781315159126-3.
21. SILVERSTEIN, I. Pharmaceutical excipient good manufacturing practices. In *Good manufacturing practices for pharmaceuticals*. 7th ed. Boca Raton : CRC Press, 2018, 227–240, doi: 10.1201/9781315120669-16.
22. SPINKA, H., JACKOWSKI, P. Purified water quality study : technical report (No. ANL-HEP-

TR-00-16). Argonne National Lab., IL (US). United States : N.P., 2000, doi: 10.2172/754234.
23. ABDALLAH, H., SHALABY, M.S., SHABAN, A.M. Design of low energy integrated membranes units for production of highly purified water. *Advanced Energy Conversion Materials*, 2020, **1**(1), 1–14, doi: 10.37256/aecm.112020129.
24. QUIGLEY, George. Prefiltration in pharmaceutical process. In *Filtration and purification in the biopharmaceutical industry.* 3rd ed. Edited by Maik W. Jornitz. Boca Raton : CRC Press, 2019, 1–20, doi:10.1201/9781315164953.
25. Filter Options for Small Molecule Drug Production [online]. Critical Process Filtration, Inc. [accessed 2. 10. 2022]. Available on World Wide Web: <https://www.criticalprocess.com/hubfs/Application%20Summaries%20and%20Selection%20Guides/Sel-Gd_PharmaAPI.pdf>.
26. SHARMA, P.K., MURUGESAN, S., TABORA, J.E. Design of filtration and drying operations. In *Chemical engineering in the pharmaceutical industry: active pharmaceutical ingredients. 2nd ed.* Edited by David J. am Ende and Mary T. am Ende. John Wiley, 2019, 799–831, doi: 10.1002/9781119600800.ch35.
27. VACURA, K. Filtration Industry overview: world pharma and biotechnology market 2008. *Filtration & Separation*, 2008, **45**(8), 22–24, doi: 10.1016/s0015-1882(08)70295-7.
28. PRAGER, Gary. Pharmaceutical water systems. In *Practical Pharmaceutical Engineering.* Wiley, 2018, 53–130, doi: 10.1002/9781119418764.ch2.
29. LEONHAUSER, J., PAWAR, J., BIRKENBEUL, U. Novel technologies for the elimination of pollutants and hazardous substances in the chemical and pharmaceutical industries. In *Industrial wastewater treatment, recycling and reuse*. Elsevier, 2014, 215–234, doi: 10.1016/B978-0-08-099968-5.00005-2.
30. YIGZAW, Y., PIPER, R., TRAN, M., SHUKLA, A. Exploitation of the adsorptive properties of depth filters for host cell protein removal during monoclonal antibody purification. *Biotechnology Progress,* 2008, **22**(1), 288-296, doi: 10.1021/bp050274w.
31. THAKUR, R., DAS, D., DAS, A. Optimization study to improve filtration behaviour of electret filter media. *The Journal of The Textile Institute*, 2016, **107**(11), 1456–1462, doi: 10.1080/00405000.2015.1128207.
32. TRABOCCHI, A. Principles and applications of small molecule peptidomimetics. In *Small molecule drug discovery*. Edited by Andrea Trabocchi and Elena Lenci. Elsevier, 2020, 163–195, doi: 10.1016/b978-0-12-818349-6.00006-6.
33. BARNES, R.G., CHU, C., EMOND, G.T., ROY, A.K. *Charge modified microporous membrane process for charge modifying said membrane, and process for filtration of fluids, U.S. Patent 4473475. 1984-09-25.*
34. LARSON, K.L., HANSEN, C., RITZ, M., CARREÑO, D. Acceptance and impact of point-of-use water filtration systems in rural Guatemala. *Journal of Nursing Scholarship*, 2016, **49**(1), 96–102, doi: 10.1111/jnu.12260.
35. ATKINSON, S. Pharmaceutical plant selects QUA EnviQ ultrafiltration membranes for MBR system. *Membrane Technology*, 2021, **2019**(1), doi: 10.1016/s0958-2118(19)30019-9.
36. CHEN, K.L., SONG, L., ONG S.L., NG, W.J. The development of membrane fouling in full-scale RO processes. *Journal of Membrane Science*, 2004, **232**(1-2), 63–72, doi: 10.1016/j.memsci.2003.11.028.
37. BELKACEM, M., BENSADOK, K., REFES, A., CHARVIER, P.M., NEZZAL, G. Water produce for pharmaceutical industry: role of reverse osmosis stage. *Desalination,* 2008, **221**(1-3), 298–302, doi: 10.1016/j.desal.2007.01.086.
38. PARKINSON, J., BARON, J.L., HALL, B., BOS, H., RACINE, P., WAGENER, M.M., STOUT, J.E. Point-of-use filters for prevention of health care acquired Legionnaires disease: field evaluation of a new filter product and literature review, *American Journal of Infection Control*, 2020, **48**(2), 132–138, doi: 10.1016/j.ajic.2019.09.006.
39. DOSMAR, M., WOLBER, P., BRACHT, K., TRÖGER, H., WAIBEL, P. The water pressure integrity test—A new integrity test for hydrophobic membrane filters. *Journal of Parenteral Science and Technology*, 1992, **46**(4), 102–106.
40. Sterile Tank Vent Filters [online]. Micropure Filtration [accessed 21. 5. 2022]. Available on World Wide Web: <http://www.micropure.com/tankventfilter.htm>.
41. TRABOCCHI, A. Principles and applications of small molecule peptidomimetics. In *Small molecule drug discovery*. Edited by Andrea Trabocchi and Elena Lenci. Elsevier, 2020, 163–195, doi: 10.1016/B978-0-12-818349-6.00006-6.
42. Jornitz, M.W, Membrane pore structure and distribution. In *Filtration and purification in the biopharmaceutical industry.* 3rd ed. Edited by Maik

W. Jornitz. Boca Raton : CRC Press, 2019, 57-67, doi: 10.1201/9781315164953.
43. CARTER, J.R., LEVY, R.V. Microbial retention testing in the validation of sterilizing filtration. In *Filtration in the biopharmaceutical industry*. Edited by T. H. Meltzer and M. W. Jornitz. New York : Marcel Dekker, 1997.
44. Filtration [online]. GMM Pfauder [accessed 12. 5. 2022]. Available on World Wide Web: <https://www.gmmpfaudler.com/lab-and-process-glass/units-processes/filtration>.
45. JOHNSTON, P.R. *Fluid sterilization by filtration*. 3rd edition. Boca Raton : CRC Press, 2004, 15-35.
46. ARANHA, H., MEEKER, J. Microbial retention characteristics of 0.2-microns-rated nylon membrane filters during filtration of high viscosity fluids at high differential pressure and varied temperatures. J*ournal of Pharmaceutical Science and Technology*, 1995, **49**(2), 67–70.
47. GUENEC, O. Sterility testing by filtration in the pharmaceutical industry. In *Filtration and purification in the biopharmaceutical industry*. 3rd ed. Edited by Maik W. Jornitz. Boca Raton : CRC Press, 2019, 571–586, doi: 10.1201/9781315164953-22.
48. ÇELEBIER, M. Ultrafiltration-based sample preparation for pharmaceutical analysis. *Current Pharmaceutical Analysis*, 2021, **17**(8), 951–959, doi: 10.2174/1573412916999200729172653.
49. EBERSOLD, M.F., ZYDNEY, A.L. The effect of membrane properties on the separation of protein charge variants using ultrafiltration. *Journal of Membrane Science*, 2004, **243**(1-2), 379–388, doi: 10.1016/j.memsci.2004.06.043.
50. RAO, S., ZYDNEY, A.L. Controlling protein transport in ultrafiltration using small charged ligands. *Biotechnology and Bioengineering*, 2005, **91**(6), 733–742, doi: 10.1002/bit.20543.
51. ETZEL, M.R., ARUNKUMAR, A. Charged ultrafiltration and microfiltration membranes for antibody purification. In *Process scale purification of antibodies*. 2nd ed. Edited by Uwe Gottschalk. Hoboken : John Wiley & Sons, 2017, 247–268, doi: 10.1002/9781119126942.ch12.
52. CHRISTY, C., RUBIN, D. Selecting the right ultrafiltration membrane for biopharmaceutical applications. *Pharmaceutical Technology Europe*, 2002, **14**(12), 39–45.
53. MAHIRULLAH, M., WIDIASA, I.N. Study on ultrafiltration of hospital wastewater treatment effluent. In *IOP Conference Series: Materials Science and Engineering (Vol. 1053, No. 1, p. 012120)*. IOP Publishing, 2021, doi: 10.1088/1757-899X/1053/1/012120.
54. UROŠEVIĆ, T., POVRENOVIĆ, D., VUKOSAVLJEVIĆ, P., UROŠEVIĆ, I., STEVANOVIĆ, S. Recent developments in microfiltration and ultrafiltration of fruit juices. *Food and Bioproducts Processing*, 2017, **106**, 147–161, doi: 10.1016/j.fbp.2017.09.009.
55. SINGH, V., JAIN, P.K., DAS, C. Performance of spiral wound ultrafiltration membrane module for with and without permeate recycle: experimental and theoretical consideration. *Desalination*, **322**, 94–103, doi: 10.1016/j.desal.2013.05.012.
56. RITSON, J.P. GRAHAM, N.J.D. TEMPLETON, M.R. CLARK, J.M. GOUGH, R. FREEMAN, C. The impact of climate change on the treatability of dissolved organic matter (DOM) in upland water supplies: a UK perspective. *Science of the Total Environment*, 2014, **473-474**, 714–731, doi: 10.1016/j.scitotenv.2013.12.095.
57. CESCON, Anna. JIANG, Jia-Qian. Filtration process and alternative filter media material in water treatment. *Water*, 2020, **12(12)**, 1–20, doi: 10.3390/w12123377.
58. LAVENDER, P. Filter media: treating chemical wastewaters. *Filtration and Separation*, 2008, **45**(4), 16–18, ddoi: 10.1016/S0015-1882(08)70087-9.
59. MORITA, A.K.M., REALI, M.A.P. Fiber filter built with polypropylene fibers applied to water clarification. *Water Supply*, 2019, **19(4)**, 1036–1043, doi: 10.2166/ws.2018.150.
60. LOGSDON, G.S. HORSLEY, M.B. FREEMAN, S.D.N. NEEMANN, J.J., BUDD, G.C. Filtration processes – a distinguished history and a promising future. *Journal of American Water Works Association*, 2006, **98**(3), 150–162, doi: 10.1002/j.1551-8833.2006.tb07613.x.
61. BARBUSIŃSKI, K, FILIPEK, K. Water and wastewater treatment: selected topics. *Clean Technologies*, 2022, **4**(1), 91–96, doi: 10.3390/cleantechnol4010007.
62. MAO, H., FAN, W., CAO, H., CHEN, X., QIU, M., VERWEIJ, H., & FAN, Y. Self-cleaning performance of in-situ ultrasound generated by quartz-based piezoelectric membrane. *Separation and Purification Technology*, 2022, **282**(Part B), 1-10, doi: 10.1016/j.seppur.2021.120031.

63. Pharmaceutical membrane filtration market research report by product (accessories, filters, and systems), material, technique, application, region (Americas, Asia-Pacific, and Europe, Middle East & Africa) - global forecast to 2027 - cumulative impact of covid-19 [online]. Research and Markets [accessed 16. 5. 2022]. Available on World Wide Web: <https://www.researchandmarkets.com/reports/5311221/pharmaceutical-membrane-filtration-market accessed on 16/05/2022>.
64. TYLE, P. Filtration in the pharmaceutical industry. *Journal of Pharmaceutical Sciences*, 1987, **76**(2), 185, doi: 10.1002/jps.2600760223.
65. WHO Director-General's opening remarks at the media briefing on COVID-19 - 11 March 2020 [online]. WHO [accessed 16. 5. 2022]. Available on World Wide Web: <https://www.who.int/director-general/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---11-march-2020>.
66. Pharmaceutical filtration market size, COVID-19. Impact analysis, regional outlook, application development potential, price trends, competitive market share & forecast, 2022 – 2028 [online]. Global Market Insight [accessed 17. 5. 2022]. Available on World Wide Web: <https://www.gminsights.com/industry-analysis/pharmaceutical-filtration-market accessed on 17/05/2022>.