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Review article

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# The impact of bioactive textiles on human skin microbiota

## Short title: Bioactive textiles and the skin microbiota

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## Graphical abstract

## Highlights (max 85 characters including spaces/each)

- Bioactive textiles can provide many benefits for a healthy and safe lifestyle.
- The demand for bioactive textiles with antimicrobial activity has increased.
- Antimicrobial textiles can influence the skin microbiota of the wearer.
- The impact of antimicrobial textiles on human skin, requires intensive investigation.
- According to its impact, antimicrobial textiles may find different applications.

## Abstract

In order to support the elevated market demand for the development of textiles with specific benefits for a healthy and safe lifestyle, several bioactive textiles with defined properties, including antimicrobial, antioxidant, anti-inflammatory, anti-odor, and anti-repellent, anti-ultraviolet (UV) radiation, have been proposed. Antimicrobial textiles, particularly, have received special interest considering the search for smart, protective textiles that also impact health and well-being. Although the incorporation of antimicrobials into textile material has been well succeeded, the addition of such components in textile clothing can influence the balance of the skin microbiota of the wearer. While most antimicrobial textiles have demonstrated good biocompatibility and antimicrobial performance against bacteria, fungi, and viruses, some problems such as textile biodegradation, odor, and dissemination of unwanted microorganisms might arise. However, little is known about the impact of such antimicrobial textile-products on human skin microbiota. To address this issue, the present review, for the

first time, gives an overview about the main effects of antimicrobial textiles, *i.e.*, antibacterial, antifungal, and antiviral, on skin microbiota while driving future investigation to elucidate their putative clinical relevance and possible applications according to their impact on skin microbiota. This knowledge may open doors for the development of more microbiota friendly textiles or antimicrobial textile-products able to target specific populations of the skin microbiota aiming to alleviate skin disorders, malodor, and allergies by avoiding the growth and spread of pathogenic microorganisms.

## 1. Introduction

The skin is the main interface of the human body with the environment while housing millions of commensal microorganisms, the so-called skin microbiota [1]. A healthy skin is dependent of the balance between the resident members of skin microbiota, particularly bacteria, fungi, and viruses, in an intricated network which varies in density, composition, and function [2]. However, when such balance is disturbed, dysbiosis leads to alterations in the skin microbial members, often with the defeat of commensal microbes by pathogens competing for space and nutrients, resulting in the occurrence of many dermatological pathologies [3].
Taking into consideration its significant diversity, size, and composition, the skin microbiota can vary according to *intrinsic or individual factors,* namely age, gender, body area, health conditions, genetics, hygiene habits, and the use of cosmetics and medication [2, 4]. Although usually resistant to colonization from most transient microorganisms, acting as a barrier against infection, it can also be influenced and/or modulated by several *extrinsic factors*, such as temperature, humidity, ultraviolet (UV) radiation, climate, and geographical localization [4]. In addition to the aforementioned factors, it is now recognized that textile materials can also have a recognizable impact in the microorganisms found in the skin [5, 6].

In fact, the close contact between textile materials, more specifically clothing, and skin provides an ideal basis for the attachment of microorganisms transferred from human skin to textile and vice-versa [5]. Microbial growth on textiles can be responsible for its biological degradation, loss of strength and elongation, discoloration, and unpleased odor [7, 8]. On the other hand, clothing textiles can spread microorganisms with elevated potential to cause cross infection, transfer of disease, allergic reactions, and odor among humans [4, 9]. To overcome such problems caused by microbial growth on textiles, the search for new bioactive molecules with antimicrobial properties has become a top priority for the textile industry.

To date, an elevated demand for a productive and healthier lifestyle has generated a specific market for textiles and clothing with the ability to promote the ‘well-being’ of consumers. In this sense, bioactive textiles, particularly antimicrobial textiles, are a real necessity, for example, in hospitals and health care institutes that are prone to microbial contamination and where the transmission of pathogens via clothing and bedding is a major concern [9, 10]. Therefore, to minimize microorganism growth and its possible dissemination caused by textiles in a hospital environment, a range of antimicrobial textiles containing antibacterial, antifungal, and/or antiviral activities have been developed [11-13]. Besides, there is also another demand for antimicrobial textiles to be used as dermato- therapeutic strategy for

cutaneous disorders caused by skin microbial dysbiosis. In this case, the main target is the modulation of specific members of the skin microbiota to ameliorate the symptoms of certain dermatological conditions through the usage of antimicrobial textiles [14, 15]. At this point, antimicrobial-based textiles could act as a "complementary treatment" in many cases of microbiota skin dysregulation while decreasing the intake of oral medication and of antimicrobial resistance.

Despite intensive investigation being endorsed in the last decade for the development of several antimicrobial textiles, most of them focus on the antibacterial activity as main strategy to minimize microbial growth on textiles [11, 13]. While much consideration has been given to avoid microbial colonization, and the problems that arise from it, namely textile biodegradation, odor, and microorganisms' dissemination, the impact of such antimicrobial textile materials on the human skin microbiota has been poorly investigated.

To overcome such limitation, the following review tackles the intrinsic relationship between textile clothing and human skin microbiota while highlighting the foremost effects of antimicrobial-based textiles, particularly antibacterial, antifungal, and antiviral, on skin microbiota. This review also emphasizes the importance of intensive investigation in such field to give the possibility of antimicrobial textile-products finding specific applications, including biomedical and personalized usages according to their impact on skin microbiota. This knowledge may open doors for the development of more microbiota friendly textiles or antimicrobial textile-products able to target specific populations of the skin microbiota aiming to alleviate skin disorders, while could also avoiding microorganism growth, spreading, malodor, and allergies.

## 2. The human skin and its microbiota

The main function of the human skin is to maintain body temperature and to protect the body from infections and toxic substances. Therefore, the skin acts as a physical, chemical, immunological, radiation and free radical barrier [16]. Structurally, it is composed of *i*) two distinct layers, namely epidermis and dermis, *ii*) sweat glands, and *iii*) sebaceous glands (Figure 1). The epidermis is mainly composed by keratinocytes (~80%) and its structure provides support and fortifies the skin barrier [1]. It also sustains the microorganisms on the skin and helps counter pathogens through modulation of the innate immune system [17]. The dermis contains connective tissue, nerves, vascular structures, and a variety of skin appendages, including hair follicles, sweat glands, and sebaceous glands. Immune cells, namely macrophages and dendritic cells are also found and help initiate innate immune response within the skin [17]. Sweat glands are responsible for the thermoregulation of the body through the evaporation of water and acidification of the skin. Additionally, they also contain antimicrobial molecules, i.e., free fatty acids and antimicrobial peptides which inhibit microbial colonization. Sebaceous glands secrete lipid-rich sebum that prevents the skin from desiccation and supplies the resident microbiota with nutrients [1]. Skin thickness, folds, and the distribution/density of hair follicles and glands along the body have been useful to characterize different types of skin microenvironments with specific pH, moisture, sebum content, temperature, and topography [8, 18]. These skin microenvironments are then subdivided into:

*i)* *Dry*: this type of skin is usually present in the forearms, hands, buttocks, and legs, and has no moisture.

*ii)* *Moist:* the increased moisture of this zone is due to the production of sweat. This type of skin is found namely at the axilla, antecubital fossa, navel, groin, popliteal fossa, and soles.

*iii)* *Oily*: these areas have an oily environment due to the elevated number of sebaceous glands which produce sebum. Oily skin can be found on the forehead, alar creases, retroauricular creases, and the back.

The environment of these anatomical areas is significantly influenced by the abundance and activity of skin glands which influence the pH, temperature, and moisture of the skin. In this sense, different skin areas affect the distribution of microorganisms and provide an important barrier against the colonization of potentially pathogenic microorganisms and against overgrowth of the already present opportunistic microorganisms [19]. Moreover, the characterization of microbiota per skin type has been extremely valuable for elucidating the etiology of common skin disorders and has also supported the development of several therapies for different cutaneous conditions [20-22].

The human skin microbiota is composed by a community of microorganisms which inhabits the skin together with its associated microbial structural elements, namely proteins, lipids, polysaccharides, and nucleic acids [2, 17]. Overall, the skin microbiota contains between 100 and $10^7$ bacterial cells per $cm^2$, including bacteria, fungi, viruses, and archaea members [18]. The skin microbiota can be directly and indirectly influenced by *intrinsic factors* (skin zone, and personal variability, such as gender, age, lifestyle, genetics, hygiene routine, the use of cosmetics, medication, and health conditions) and *extrinsic factors* (geographical location, climate, and seasonality) [1, 20, 23, 24]. However, the microbial diversity that colonizes healthy individuals appears to be similar [3, 25].

In healthy adults, the bacterial microbiota or bacteriome is mainly represented by four phyla (> 90%): Actinobacteria (36-51%), Firmicutes (24-34%), Proteobacteria (11-16%), and Bacteroidetes (6-9%) [1, 26]. In general, the more representative species are *Staphylococcus epidermidis*, *Cutibacterium (formerly Propionibacterium*) *acnes*, *Corynebacterium* spp., *Micrococcus* spp., *Streptococcus* spp., and *Actinobacter* spp. [17, 24, 27]. Dry areas of the skin present a more heterogenous bacterial community distributed along the four phyla previously mentioned [25, 28]. Moist sites are predominated by members of the phyla *Firmicutes* and *Actinobacteria,* represented by *Staphylococcus* and *Corynebacterium* species, respectively [1, 17, 20]. This suggests the preference of these bacteria for areas with high humidity (Figure 1). In addition, oily sites where sebaceous glands are dense and active, are mostly dominated by *Actinobacteria* members, namely lipophilic *Corynebacterium* and *Cutibacterium* species [1, 20]. Sebaceous glands are relatively anoxic and support the growth of facultative anaerobes bacteria, namely *Cutibacterium acnes* which hydrolyzes the triglycerides into sebum-releasing free fatty acids onto the skin. These free fatty acids also contribute to the acidic pH (∼5) of the skin surface which helps to create unfavourable growth conditions for many pathogenic microorganisms [25]. On the other hand, this low pH found in the skin surface favors the growth of commensal bacteria such as *Staphylococcus* spp. and *Corynebacterium* spp. These bacteria usually aid in preventing the growth of pathogenic microorganisms [18, 29].

Compared to bacteriome, the mycobiome, also known as fungal microbiota, is relatively found in smaller proportion in the human skin [30]. For instance, species of *Malassezia* are predominant in dry (~83%), moist (~80%) and oily areas (~99%) [3, 24]. Species of *Cryptococcus*, *Rhodotorula*, *Aspergillus*, *Candida*, and *Epicoccum* are also present, but in less density [2, 22, 24]. While *Malassezia* species predominate on all core-body and arm sites, foot sites display high fungal diversity, including members of *Malassezia* (50-80%), *Aspergillus*, *Cryptococcus*, *Rhodotorula*, and *Epicoccum* genera [21, 22].

On the contrary, the virome has been less detected and characterized because they include both the host´s endogenous retro-viruses, viruses that infect host cells (persistently or occasionally), and viruses that infect other components of the microbiome [30, 31]. While eukaryotic DNA viruses found in the human skin are unique to the individual rather than site specific, other DNA viruses, more specifically human papillomaviruses, Merkel cell polyomavirus, and Molluscum contagiosum virus, which are associated with dermatological lesions, were detected in about half of the subjects using shotgun metagenomic sequencing [32]. Apart from bacteriophages, namely those associated with species of *Cutibacterium* and *Staphylococcus,* no core of DNA virome has been found to be conserved across individuals [1].

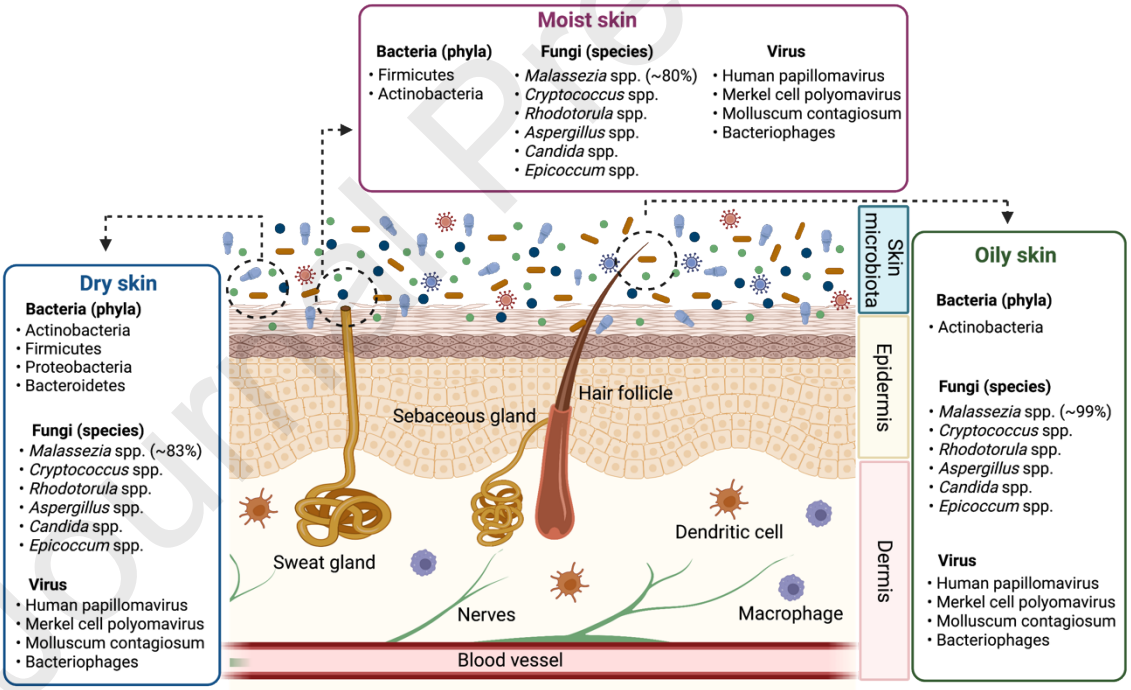


**Figure 1: The human skin: composition and microbiota distribution per skin microenvironment**. The image highlights the structure of skin, its composition, and the main members of the microbiota according to the skin microenvironments, herein represented by dry, moist, and oily skin.

Although there is microbial heterogeneity between the different skin microenvironments, its composition in such sites is highly consistent in healthy humans [3]. Nevertheless, there is a shift in skin microbiota composition in many dermatological disorders,

such as acne vulgaris, psoriasis, and atopic dermatitis (AD), where a proliferation of specific members is reported [2, 3]. For instance, the development of high-throughput molecular methods to characterize and identify microorganisms, including amplicon sequencing and whole-genome sequencing (shotgun metagenomic sequencing), has provided unprecedented insights into the microbiota of the skin both in healthy humans and in case of skin disorders [28]. Currently, the emergent cosmetics and textile industry has now created the necessity to explore how such products impact the human skin microenvironment and consequently, the microbiota.

## 3. Clothing textiles and Skin microorganisms: an intrinsic relationship

The large surface area of clothing textiles, its prolonged contact with human skin, friction, and humidity, favors the transfer of microorganisms from human skin to textiles and from textiles to skin [8, 33]. The presence and activity of microbial colonization and onto clothing textiles has been intensively investigated by several reasons, including alterations in its physico-chemical characteristics such as, textile biodegradation, discoloration, loss of strength and elongation, unpleasant odor, biofilm formation, among others [7, 8].

The interaction between the wearer and clothing is an opportunity for skin microorganisms to attach and colonize the textile surface, which can lead to the growth of certain strains and damage to the fibers [8, 34]. During this process, the absorption of sweat, sebum and metabolites from microorganisms to clothing can also contribute to the outgrowth of several microorganisms, including non-pathogenic and pathogenic strains [33]. As consequence, textiles, in particular clothing, have high potential to spread microorganisms which can cause cross infection, transfer of diseases, allergic reactions, and unpleased odors in humans [4, 9].

Currently, the growth of non-pathogenic, pathogenic, or odor-causing strains on textiles is dependent not only on the nature or composition of the textile, but also by individual habits of the wearer [8, 23]. Taking into consideration the potential of microorganisms to survive and colonize different types of textile fibers [35], it is not surprising that bacteria and fungi have been associated with discoloration and degradation of various type of fibers, including wool, silk, cotton, flax, and polyester [29, 36]. However, different textile fibers present distinct surface properties and functional groups which together impact not only adsorption and retention of sweat, but also microbial attachment, growth, colonization, and spreading [5].

In this sense, some studies have shown a selective attachment of microorganisms onto different fiber types. For example, while *Staphylococcus* spp. showed a significant anchorage in almost all textile fibers [5, 34], *Staphylococcus hominis* had an elevated affinity for cotton and did not growth in viscose and fleece [34]. Like cotton, wool promoted growth of many bacteria members, including *Staphylococcus epidermidis, Enhydrobacter* spp., *Cutibacterium* spp., and *Micrococcus* spp. [34]. Whereas polyester provided greatest growth for *Cutibacterium spp.*, *Enhydrobacter spp.*, and *Micrococcus* spp. [5, 34], cellulose-based fibers, namely viscose or Tencel$^{TM}$ showed low microbial growth rate for most axillary bacteria, except for *Staphylococcus* spp. [5, 34]. On the other hand, *Corynebacterium* spp., was not able to strive on cotton, acrylic, wool, viscose, nylon, fleece, and polyester, which explains that only low numbers of *Corynebacterium* spp. could be isolated from worn clothes [5, 34].

Intriguingly, Sterndorff *et al*. showed that unworn cotton T-shirts had a native microbiome dominated by *Acinetobacter* species, whereas unworn polyester had no detectable bacterial microbiota. In addition, compared to worn polyester T-shirts, worn cotton T-shirts demonstrated an elevated bacterial genera diversity, like those found in human skin microbiota [23]. These findings demonstrate that, in fact, the properties of the textile fibers can directly affect microbial attachment, growth, and colonization. Synthetic fibres are often resistant to microbial colonization due to their hydrophobic nature and poor adsorbing capacity [29]. By contrast, natural fibres are more susceptible to microbial colonization because they have high moisture retention properties and their polymer linkages can be more readily accessed by microbial enzymes, especially after fabric processing in which their protective layers are removed. Additionally, natural fibres can provide nutrients and energy sources for microorganisms in the form of carbohydrates or proteins which support microbial growth and colonization [43].

Whereas the association of microorganisms to textiles has been well documented, the impact of textiles, on cutaneous microbiota remains poorly documented. Nevertheless, the effects of clothing textiles on skin microbiota have been mainly correlated with: *i*) no adverse effects on the ecological balance of healthy skin microbiota [19], *ii*) alterations in skin homeostasis, sweat production, and unpleased odor [37], *iii*) specific changes in the composition of skin microbiota [6], and *iv*) modulation of the virulence of skin microbiota members [27].

Although some natural fibers, such as cotton and flax, have been used since antiquity for their positive influence on skin, their direct impact on cutaneous skin microbiota, namely bacteria, has received special interest. For instance, in comparison to cotton, flax textiles demonstrate strong inhibitory effects on *S. aureus* and *S. epidermidis* while exerting cytotoxicity on keratinocytes [27]. In addition, whilst wool and synthetic fabrics with harsh textile fibers may exacerbate atopic dermatitis (AD), cotton and silk have been traditionally recommended for patients with AD due to their ability to alleviate the symptoms [38]. Remarkably, the relationship between clothing and skin has emerged as a new field to explore how textiles can be used to treat or alleviate skin disorders through the modulation of skin microbiota members [38, 39].

Given its broad applications, including dermatological, the improvement of textiles with functions of breathability, waterproofing, the addition of quick-dry, increased comfort (compared to cotton and silk), and antimicrobial properties, have emerged as a key tools for the textile industry [33, 40]. However, to give the possibility of these new textiles to find biomedical and more personalized applications, a deeper understanding of how they affect the human skin microbiota needs to be addressed and clarified. This knowledge may open doors for future design and development of more microbiota friendly textiles or specific antimicrobial textile-products able to alleviate skin disorders, while avoid microorganism growth, colonization, spreading, malodor, and allergies.

## 4. Bioactive textiles: a real market necessity

Functional textiles, also called bioactive textiles, aim to take care of the health and hygiene of the consumer while contributing to his/her well-being. For that, novel functional properties have been added to textiles, including antioxidant, anti-inflammatory, water-repellent, mosquito-repellent, flame-retardant, UV protection, and antimicrobial activity [12]. This functionalization can be achieved through several techniques, including electrospinning, nanotechnologies, plasma treatment, polymerization, micro/nanoencapsulation, layer-by-layer, and sol–gel techniques by which beneficial elements are incorporated with or without sustained release [12, 41, 42]. Of note, vitamins, probiotics, antimicrobial agents, enzymes, fragrances, oils, chemicals, and others are common examples of components found in bioactive textiles [12, 14, 41].

Currently, bioactive textiles, particularly antimicrobial textiles, are a real necessity, for example, in hospitals and health care facilities, where the clothes of patients, healthcare workers, and doctors can easily become the vehicle for microbial spreading from one person to another facilitating the well-known nosocomial infections [9, 10]. In this regard, it is known that such infections are frequently caused by *Acinetobacter baumannii, Enterococcus* spp*., Escherichia coli*, *Klebsiella pneumonia*, *Pseudomonas aeruginosa,* and *Staphylococcus* spp. [43]. Of note, it was demonstrated that staphylococci and enterococci can survive for several months in commonly used hospital fabrics [44]. Therefore, to minimize microbial growth and its possible dissemination caused by textiles in a hospital environment, for example, a range of medical textiles with antimicrobial activities have been developed [11-13]. Besides, there is also another demand for antimicrobial textiles to be used as dermato- therapeutic strategy for cutaneous disorders caused by skin microbial dysbiosis. In this case, the main target is the modulation of specific members of the skin microbiota to ameliorate the symptoms of certain dermatological conditions through the usage of antimicrobial textiles [14, 15].

In general, these bioactive textiles are based on their specificity against microorganisms, *i.e*., antibacterial, antifungal, and antiviral textiles. Depending on the treatment and the concentration of antimicrobial compound used and retained in the fabric, antimicrobial textiles may be biocide or biostatic [9]. Whereas biocide kills the microorganism, biostatic ones inhibit their growth. Interestingly, these properties may find different market applications. For example, whilst antimicrobial textiles with biocide properties could be more useful in hospitals and health care institutions as a strategy to avoid the dissemination of microorganisms, clothing textiles with biostatic mechanism may be suitable for specific dermatological purposes.

Though many antimicrobial textiles have been designed, minimum requirements are needed before introduction into the market for human use. These include: being non-toxic to the consumer, not causing irritation or any allergic reaction, efficient against specific microorganisms, suitable for textile processing and manufacturing, having a durable effect even after laundering, not impacting the quality or appearance of textile, causing no odor in both the textile and in the person and should be recycled without any negative impact for the environment.

Despite intensive investigation being endorsed in the last decade for the development of antimicrobial textiles, most of them focus on the antibacterial activity to minimize microbial growth and consequently avoiding textile biodegradation, odor, and microbial spreading. However, little is known about the impact of such textile-products on human skin microbiota.

To overcome this, the next topics give an overview of the foremost effects of antimicrobial textiles, *i.e*., antibacterial, antifungal, and antiviral, on skin microbiota while driving the need for future investigations. This could elucidate the real impact of antimicrobial textiles on skin microbiota and clarify their putative clinical relevance toward possible applications.

### *4.1 Antibacterial textiles*

The development of antibacterial textiles has been introduced as an emergent necessity for various purposes, including the inhibition of microbial growth, biodegradation, unpleased odor development, biofilm formation, reduction of microbial propagation in medical and health care environments, and as an alternative approach for dermato-therapies. In practice, there are two main strategies to obtain antibacterial textiles: i) by the incorporation of antibacterial components into textile fibers during the spinning process or ii) through the application of specific antibacterial agents during the finishing stage.

Usually, antibacterial textiles contain active elements, namely *synthetic components* which include metals (silver, copper, zinc, cobalt, and titanium), quaternary ammonium compounds, and triclosan [15, 19, 33, 45, 46], and *natural components* such as bamboo, chitosan, alginate, vitamins, and oils [14, 42], or the combination of synthetic and natural components [47]. The chemical properties and structure of the components determine the possible modes of the antibacterial action, which are referred to the different ways of killing the microorganisms. Examples of such modes of action include damage to the cell wall or cell membrane, or either inhibition of the synthesis of these structures, leading to cell leakage, and cell death [33]. In addition, inhibition of DNA/RNA, protein synthesis or the inhibition of specific metabolic processes within the cell are other possibilities [43].

The incorporation of such components has been applied in diverse textile fibers, including cotton, silk, flax, wool, and polyester [46, 48]. Their antibacterial properties have been well evaluated through several *in vitro* assays [42, 49]. Regarding *in vivo* evaluation, antibacterial textiles have been tested in two main types of volunteers, namely healthy participants, or patients with specific type of skin dysbiosis. In this sense, the next sections highlight the most important impact of the available antibacterial textiles in these specific groups of volunteers.

#### *4.1.1 Evaluation of antibacterial clothing in healthy individuals*

As mentioned before, the human skin microenvironment contains a broad bacterial diversity. This is an important feature of a healthy skin since the ecological balance of bacteria acts as a natural barrier and protects from the overgrowth of pathogens [50]. Protection from pathogens is given by resident microbiota which creates non-favourable conditions for the growth of pathogens, which are kept from colonizing the skin by competition with the resident members [28]. Subsequently, skin bacteria are rarely pathogenic to the host while benefiting the host by enhancing the skin barrier [50]. Conversely, the use of antimicrobials in textile

clothing can accidently alter the skin physiology which may lead to an overgrowth of transient organisms and a disruption in the microbiome balance of the skin.

Thereupon, *in vivo* studies are a necessary and important tool to understand the interactions between antimicrobial-treated fabric with the skin microenvironment of the wearer. As well, several antibacterial textiles have been tested in healthy volunteers with the aim of evaluating their potential impact on human skin microbiota [46]. For example, three antimicrobial-treated fabrics (*i.e*., fabric 1: triclosan; fabric 2: zinc pyrithione derivative; and fabric 3: silver chloride and titanium dioxide) were placed on the forearm of 19 healthy participants [46]. After 24 hours, fabric 1 had a minor effect on reducing general bacterial populations on the skin. In this case, the triclosan-treated fabric was effective in reducing *Staphylococcus* populations on the fabric itself but not for overall aerobic bacterial counts. Fabric 2 was clearly the most potent antibacterial agent with a significant reduction of bacterial populations in comparison to the fabric control (untreated). Fabric 3 treated with the silver chloride-titanium dioxide did not show any antimicrobial activity *in vivo,* compared to control fabrics. Curiously, these results emphasize the importance of *in vivo* evaluation of different antimicrobial-based textiles in contact with the human skin. However, a limitation of the study was that only one place of the body (forearm, considered as a dry skin region) was evaluated. An evaluation of different skin microenvironments along time could provide important insights about the real impact of these different antibacterial textiles in the human skin microbiota.

Within metals, silver is one of the most used antibacterial agents in the textile industry due to its broad-spectrum of antibacterial properties against both Gram-positive and -negative bacteria [51]. To evaluate its impact on the human skin microbiota, a placebo-controlled side-to-side study was performed in 60 healthy volunteers [19]. For that, each participant received T-shirts constructed in 2 halves: an antibacterial half comprising silver-finishes or silver-loaded fibres and a non-antibacterial control side. For that, the microbiota of the scapular skin was analyzed weekly over six weeks. In comparison to the control, the antibacterial halves did not disturb the skin microbiota in number or composition. According to the authors, despite the antibacterial effect of silver, the silver-based antimicrobial clothes did not show any adverse effects on the ecological balance of the healthy skin microbiota. Another study evaluated the impact of polyester textiles treated with different concentrations of silver chloride (SC) in reducing axillary odor and evaluated the bacterial populations before and after multiple washes [49]. Treated fabrics were matched with an untreated control fabric and worn against the axillae of 8 healthy males. Results showed that the SC-treated fabrics did not lower odour intensity compared with the untreated fabrics after two days. In addition, bacterial populations extracted from the SC-treated fabrics were also not significantly lower, despite there being evidence of antimicrobial activity in *in vitro* testing. However, a limitation of the study was the small size of sample and the short time of evaluation. Another study that monitored 12 volunteers for twelve weeks, demonstrated that the changes induced by antibacterial clothing were specific for individuals, but more defined by gender and body site [52]. Compared to non-silver t-shirts, silver-threaded t-shirts increased the skin's microbial biomass in most of the volunteers. Although the most abundant taxa remained unaffected, silver t-shirts caused an increase in diversity and richness of low-abundant bacteria and a decrease in chemical diversity of skin. Both effects were mainly observed in women participants. These findings suggest a notable

impact of the silver threaded clothing on the skin microbiota and chemistry when analyzed along time and according to the gender.

Although synthetic chemicals and metal-based antimicrobial textiles have been successful developed and tested both *in vitro* and *in vivo*, they seem to be a threat towards damaging the environment as there is still limited information available about their exact impact. Therefore, intensive investigation has given priority to explore the functionalization of textiles with natural compounds. This approach could provide antibacterial textiles with an elevated biological safety, particularly for the skin microbiota while showing outstanding antimicrobial performance against external pathogenic bacteria.

Among natural components, chitosan is presently one of the most attractive and sustainable biopolymers in use due to its availability and remarkable intrinsic properties, including biocompatibility, biodegradability, water-biding capacity, antimicrobial and immunomodulatory properties [53]. These features make chitosan an attractive substitute for synthetic and chemical components in different application fields, including cosmetics and in the textile industry [54, 55]. In fact, its polycationic nature allows it to be combined with anionic dyes or to form strong ionic bonds with fabric materials [56]. Despite the well demonstrated *in vitro* antimicrobial properties of chitosan against several pathogenic bacteria, such as *Staphylococcus* spp., *Acinetobacter baumanni*, *Pseudomonas aeruginosa, and Cutibacterium acnes* [42, 57], the direct impact of chitosan-based textiles in the skin microbiota of healthy humans has been poorly investigated. In an attempt to overcome such limitation, cotton fabric impregnated with different concentrations of chitosan were used to evaluate their effect in specific bacterial members isolated from the skin of 14 healthy individuals [55]. Herein, the susceptibility of *Staphylococcus* species to chitosan was correlated with specific virulence factors and with the concentration of chitosan. The most efficient combination was the molecular weight at the higher concentration, where half of the isolates underwent a reduction on their viable numbers to negligible levels within 24 h of contact, while at lower concentrations, the reduction was always lower than 50%. In comparison to *S. epidermidis*, the antibacterial effect of chitosan in *S. aureus* was much more pronounced in terms of viable numbers reduction. This suggest that chitosan acts selectively upon the different bacterial strains. Although the exact mechanism of the antimicrobial activity of chitosan has not been elucidated, the authors correlated the effect of chitosan with its capacity to change cell membrane permeability due to the interactions between polycationic chitosan and electronegative charges on the cell surfaces, interaction of diffused hydrolysis products with microbial DNA, and chelation of metals and essential nutrients. In fact, these results emphasize that chitosan can be potentially useful as a skin microbiome-modulating compound when incorporated into human textiles. In addition, these results also explain why chitosan-based textiles are mostly tested in individuals with specific skin dysbiosis.

Altogether, these findings suggest that despite most antibacterial textiles developed not inducing significant impact on the skin microbiota, the existence of key differences between the distinct antibacterial-based textiles used, was demonstrated. This variation could, however, be correlated with specifications of the different study designs performed without the existence of any standardization protocol yet. To clarify this, intensive investigation needs to be addressed using a combination of individual parameters (i.e., age, gender, genetics, healthy conditions of the wearer, body site, skin type, use of cosmetics and medication) with the

textile's properties (i.e., nature/composition of textile fiber and antibacterial agent, process to add/functionalize the textile) and correlate them. This evaluation is a fundamental prerequisite to assess the real impact of antibacterial-treated fabric in the human skin microbiota while clarifying their clinical relevance.

### *4.1.2 Evaluation of antibacterial clothing in skin disorders*

As mentioned previously, skin diseases such as atopic and seborrheic dermatitis, acne, alopecia, and psoriasis usually result from microbial dysbiosis [20, 22]. In this scope, the use of antimicrobial textiles with the capacity to induce specific changes in the microbial communities of the skin has emerged as therapeutic strategy to treat, control, or alleviate the symptoms of such conditions [39, 45, 48, 58, 59].

Atopic dermatitis (AD) has been one of the most promising candidates for the treatment with antibacterial textile clothing [14, 45, 48, 59]. AD is a chronic, relapsing inflammatory skin disease characterized by the impairment of the skin-barrier function, increased oxidative cellular stress, and elevated colonization of *S. aureus* [60]. Reduction of the over infection caused by *S. aureus* decreases skin inflammation and improves the flares, so the target has been to locally reduce the colonization by *S. aureus* in the skin. In this sense, zinc-oxide (ZnO) functionalized textile demonstrated both *in vitro* and *in vivo* good rates of biocompatibility and antibacterial activity [45]. The patients with AD who wore ZnO textile overnight during 3 consecutive days presented a rapid improvement of AD severity, pruritus, and sleep quality. These results were correlated with the oxidative capacity of the ZnO textile combined with its strong antibacterial activity, namely against *S. aureus* and *K. pneumoniae.* These findings suggest that the incorporation of ZnO to textile clothing may be an alternative to reduce the colonization of *S. aureus*, while contributing to the improvement of AD severity. In a similar way, 15 patients with AD had the flexures of the elbows covered with silver-coated textiles on one arm and untreated cotton on the other, for 7 days [48]. In this case, the clinical improvement was correlated with a significant low numbers of *S. aureus* on the silver-coated cotton site in comparison to untreated cotton. In fact, the incorporation of metals, namely silver, to cotton has shown a potent antibacterial activity *in vivo*, while reducing the clinical symptoms of AD with the wearing comfort characteristic of cotton [59].

Another approach, used a *S. aureus*-infected skin model to measure the antibacterial potential [15]. For that, 5 commercial clothes with documented clinical benefits in treating AD were used: Sample #1 (Lyo-Zinc which consisted of 74% lyocell, 19% SmartCell sensitive fibre, and 7% spandex); Sample #2 (Silk-Aegis, a pure form of silk consisting exclusively of fibroin and containing a finish of AEGIS AEM 5772/5, an insoluble colorless, odorless ammonium as antibacterial agent; Sample #3 (Padycare, a micromesh material of 82% polyamide, 18% lycra with woven silver filaments with a silver content of 20% in total (130 $g/m^2$ ); Sample #4 (Smart-Zinc, Smartcel sensitive consisting of 70% Supima cotton, 18% lyocell, and 12% elasthane); and Sample #5 (Modal-Silver, Binamed made of 79% modal, 14% silver yarn, and 7% lycra). In the real-life setup simulating a dry skin microenvironment, all samples failed to reduce *S. aureus.* Silver and zinc-fabrics showed a slight activity only under

unrealistic moist conditions. When using standard suspension tests, samples differed considerably in their antibacterial effectiveness, where silver and zinc containing fibres outperformed AEGIS endowed silk fabrics. Besides, under practical (dry) wear conditions, garments were unable to modify skin colonization of *S. aureus*, although effectiveness could be triggered by wetting the garments. These findings reveal interesting differences in the antibacterial effectiveness of conventional AD clothes as well as the ideal condition to achieve better modulation of *S. aureus* colonization.

Another interesting study evaluated the percutaneous penetration of silver and its inflammatory effect on the skin [61]. For that, 15 healthy individuals and 15 patients with AD, wearing a garment containing 13% silver for 8 hours along five days were tested. Urinary excretion of the silver revealed that the dermal absorption of silver after five days is low and did not cause any systemic effects. Furthermore, dermal exposure to silver from the investigated fabric did not alter the levels of interleukin-1 in the skin, indicating the absence of a local pro-inflammatory effect. According to the authors, the dermal absorption of silver after wearing a silver-containing garment not exceeding the current reference dose, did not significantly differ between healthy volunteers and patients with AD, and did not lead to increased levels of pro-inflammatory signals in the stratum corneum. In the same line, other study evaluated the effectiveness of a silk fabric (MICROAIR DermaSilk®) coated with alkoxysilane quaternary ammonium in 16 children affected by AD [58]. After 7 days, the children who wore tubular arm covers made of this antibacterial fabric had a significant improvement in the mean value of the 'local SCORAD' index. Although this special silk fabric seems to be able to improve skin lesions in AD, it was not possible to demonstrate a specific antibacterial activity against *S. aureus in vivo*, as shown *in vitro*.

Chitosan has also been tested for the same purpose. As mentioned before, chitosan-based textiles can be potentially useful as a modulator of the skin microbiota. To test this hypothesis, 78 volunteers with AD were used to verify the effect of chitosan-coated or uncoated cotton pyjamas for 8 weeks [14]. In comparison to uncoated, the chitosan-coated pyjamas showed be well tolerated, presenting a trend of disease severity improvement. According to the authors, these data were correlated with the fact that chitosan may exert a specific inhibitory effect upon *S. aureus*, while allowing the proliferation of other staphylococcal species. Considering the positive effects of antibacterial textiles on the modulation of skin microbiota, particularly in patients with AD, some clinical trials are in progress, namely, to evaluate the therapeutic potential of antibacterial therapeutic clothing based on silver or chitosan with moderate to severe AD [62]. In this case, all therapeutic clothing is to be worn at night during the 12-month intervention period while usual care is continued. The primary objective of such trial is to assess the effectiveness of antibacterial clothing (silver and chitosan group) and compare to the control. The main outcomes are correlated with the eczema area and severity index observed between the different groups, *S. aureus* skin colonization, and safety. This kind of approach can provide us with key clarifications about the clinical efficiency of antibacterial clothing in patients with moderate and severe AD. Despite AD, further studies have demonstrated that antibacterial-based textiles and clothes can also find additional biomedical applications, such as in hospitalized chronic ventilator-dependent patients to reduce health care-associated infection (HAI) indicators [63], in wounds as antimicrobial wound dressings [64, 65], to decrease contamination in hospital scrubs [66], and to fight skin cancer cells [67].

In this sense, a double-blind controlled trial demonstrated that replacing hospital textiles by copper oxide impregnated textiles reduced the antibiotic treatment initiation events, fever days, and antibiotic usage in hospitalized chronic ventilator-dependent patients [63], thus suggesting that impregnated biocidal textiles may be an important measure aimed at reducing HAIs in long-term care medical settings. In addition, antimicrobial wound dressings could cover the wound bed, acting as a barrier to prevent bacteria from invading the wound while stimulating skin regeneration in immunocompromised patients [64]. Moreover, antimicrobial textiles can also be designed to control skin-related infections while targeting skin cancer cells [67]. However, to corroborate these specific biomedical applications, more investigation and clinical trials are necessary to evaluate the real impact of such products in the human skin microbiota, as well as their functionalities and clinical relevance.

### *4.2 Antifungal textiles*

Fungal infections represent a huge global problem resulting in over 1.7 million of deaths every year [68]. The main hosts for fungi proliferation are food crops, animal species and textiles. Focusing in the last one, textiles are excellent substrates for fungi attachment and proliferation because they provide appropriate moisture, nutrients, and temperature. Taking this into consideration, contaminated textile materials significantly contribute to the spread of several fungi, namely in a hospital environment, where such materials easily infect professionals and patients [9]. Despite this complex scenario, global warming and accompanying climate changes have resulted in an increased incidence of many fungal diseases [69]. In this context, new strategies to prevent and treat fungal diseases is mandatory. Notably, the development of antifungal textiles has emerged as an attractive alternative for numerous applications [70-73].

In this sense, the incorporation of antifungal components into textile fibers has received special attention to avoid the dissemination of fungi. For example, cotton fabric coated with guanazole, silver and zinc exhibited a broad range of antimicrobial properties against bacterial as well as fungal pathogens, *i.e*., *Aspergillus niger*, *Fusarium chlamydosporum and Penicillium* sp. [74]. Cellulose fibers containing fungal synthesized zinc oxide (ZnO) nanoparticles (NPs) using *Phanerochaete chrysosporium* demonstrated antifungal activity against opportunistic pathogenic *Aspergillus. niger*, *Geotrichum candidum* and *Phanerochaete chrysosporium* [75]. ZnO NPs–cellulose also demonstrated antibacterial activity against *S. aureus* and *E. coli*. Although these approaches exemplify the successful development of more eco-friendly antifungal textiles *in vitro*, most of them have not been tested in humans, yet. Remarkably, the lack of information about how antifungal textiles impact the human skin microbiota continues the most important limitation regarding their clinical use.

Pathogens that cause fungal infections, such as *Candida albicans and non-C. albicans*, are widespread and may cause various clinical manifestations ranging from localized, superficial mucocutaneous disorders to invasive diseases that involve multiple organ systems and are life-threatening [76]. Globally, it is estimated that nearly a billion humans have cutaneous fungal infections, many dozens of millions have mucosal candidiasis, and more than 150 million patients suffer from serious fungal diseases, among which candidiasis being the most prevalent [77]. Besides that, azole derivatives, namely fluconazole and ketoconazole,

recommended for the treatment of candidiasis, are correlated with several side-effects, including hepatotoxicity, endocrine disturbances, and liver injury [77]. In addition, the significant increase of azole-resistant fungal strains has supported the development of new antifungal therapies or combined therapies carried out with at least two different antifungal agents or strategies. Curiously, antifungal textiles have emerged as a promising alternative for the treatment of superficial fungal infections alone or in combination with the current therapy as a strategy to decrease the intake of oral antifungals.

In fact, high expectations arise for topical cutaneous applications in wound dressings, *i.e*., bandages, gauzes, and strips [70]. In this scope, cotton wound dressings containing ketoconazole and β-cyclodextrin demonstrated a controlled and slow release of these antifungal compounds with a fungicide activity against skin fungus, namely *C. albicans* and *A. niger* [71]. However, contrary to antibacterial textiles, the effect of antifungal textiles has been mostly tested in animal models. For example, pharmaceutical textiles imprinted with lipid microparticles of Econazole nitrate (ECN) demonstrated *in vitro* antifungal activity against a broad range of *Candida* species [72]. Translating to *in vivo* model, ECN textiles preserved its antifungal efficacy in mice with cutaneous candidiasis. Interestingly, percutaneous absorption studies demonstrated that ECN released from pharmaceutical textiles concentrated more in the upper skin layers, where superficial fungal infections develop in the skin. Considering the broad biocidal properties of copper, it was hypothesized that introducing copper into a wound dressing would not only reduce the risk of wound and dressing contamination but would also stimulate wound repair [73]. To test this hypothesis, non-stick dressings composed of a highly absorbent internal mesh fabric and an external non-woven fabric were made, and each was impregnated with copper oxide particles [73]. The application to wounds inflicted in genetically engineered diabetic mice resulted in increased gene and *in-situ* upregulation of proangiogenic factors, increased blood vessel formation, and enhanced wound closure. The present study reports both the potent broad spectrum antifungal properties of these wound dressings and the lack of adverse reactions as determined in rabbits and porcine wound models. Another similar approach explored the borneol-modified chitosan (BMC) as a novel antimicrobial material with potential applications in multifunctional textiles, healthcare, and flexible skin electronics [57]. This material showed *in vitro* and *in vivo* adhesive properties and antimicrobial activities against *E. coli*, *Bacillus subtilis*, and *A. niger*. When in contact with guinea pig skin, the material successfully defended against pathogens while protecting the skin microbiota. Altogether, these results reinforce the idea that such technology may be a promising strategy to develop pharmaceutical garments for the treatment of superficial fungal infections.

In fact, the development of antifungal textiles for the prevention and treatment of superficial fungal infections, namely dermatophytosis, can be a next reality. Nowadays, dermatophytosis are a widespread problem worldwide which usually affect the keratinized tissue, including skin, hair, and nails [78]. Taxonomically, the dermatophytes belong to three genera, *i.e*., *Trichophyton*, *Microsporum*, and *Epidermophyton*. The clinical manifestations of dermatophyte infections are generally termed "*tinea*" with the indication of the anatomical area affected. Therefore, infections of hair on the scalp or beard are termed "*tinea capitis*" and "*tinea barbae*", respectively, those of nails "*tinea unguium*" and those of glabrous skin "*tinea corporis*" or "*tinea pedis*" and "*tinea manuum*," in case of foot or hand involvement,

respectively. In these cases, patients spread the pathogens through the propagation of skin units from infected areas directly or via commodities, implying that textiles with direct contact to the affected skin areas, are the major pathogen carriers. Thus, whereas textiles in contact with infected skin can serve as a carrier for fungus propagation, antifungal textiles could contribute to control dermatophytosis by disrupting the chain of infection and transmission. Therefore, testing of antimicrobial fabrics for their antifungal activities and potential impact on human skin microbiota are fundamental prerequisites to assess their putative clinical relevance for prevention and treatment of dermatophytosis.

Fabrics finished with either didecyldimethylammonium chloride (DDAC), poly-hexamethylenbiguanide, copper and two silver chloride concentrations were tested for their antifungal activity against *Trichophyton rubrum*, *Trichophyton mentagrophytes*, and *C. albicans* [79]. While all samples showed a clear inhibition of *C. albicans*, activity against *Trichophyton sp*. varied significantly; for example, DDAC completely inhibited *T. rubrum* growth, whereas *T. mentagrophytes* growth remained unaffected even in direct contact with the fibres. These results show the importance of adding *T. mentagrophytes* as a test organism in textile dermatophyte efficacy tests. In addition, innovative keratin-based carriers encapsulating terbinafine were designed to overcome the drawbacks related to the use of this drug. Therapeutic textiles functionalized with keratin-based particles (100% keratin; 80% keratin/20% keratin-PEG) encapsulating terbinafine were developed to evaluate the controlled release of terbinafine from the functionalized textiles as well as its antifungal activity against *Trichophyton rubrum* [80]. Textiles functionalized with 80% keratin/20% keratin-PEG encapsulating terbinafine showed a 2-fold inhibition halo compared with the textiles containing 100% keratin-encapsulating terbinafine. However, no activity was observed for the textiles functionalized with keratin-based particles without terbinafine. Although these strategies present therapeutic potential towards dermatophytosis, most studies are still limited to *in vitro* approaches. As consequence, there is no knowledge about how most antifungal textiles impacts the human skin microbiota. Unfortunately, this lack of information limits the potential biomedical applications of antifungal textiles as well as its clinical translation.

In the same line of dermatophytosis, another possible approach for antifungal textiles, could be the use of antifungal socks for the prevention and treatment of *tinea pedis*. Tinea pedis is a preventable skin disease common in elderly or diabetic patients. Daily foot washing is effective for prevention, but can be difficult for many patients. Additionally, conventional methods cannot eliminate fungi within the stratum corneum, a common site for fungal invasion. Trying to find an alternative for this, an interesting study investigated the antifungal effects, cytotoxicity, permeability, and efficacy of non-woven textiles containing polyhexamethylene biguanide (PHMB) mixed with sophorolipid [81]. Clinically-isolated *Trichophyton* were applied to the feet of four healthy volunteers and then immediately treated with the following methods: washing with soap, no washing, a non-woven textile with PHMB, and a textile without PHMB. Sophorolipid with various concentrations significantly facilitated PHMB penetration into the stratum corneum. Significant antifungal effects were achieved after 30 min, with low cytotoxicity. Textiles containing PHMB significantly reduced CFU of fungi in healthy volunteers to levels comparable to soap washing. These results indicate the utility of PHMB textiles for *tinea pedis* prevention in clinical settings. For instance, these findings accentuate the importance for more *in vivo* studies to evaluate and clarify the effects of antifungal textiles

on human skin microbiota members, as well as their role in the prevention and treatment of dermatophytosis.

Overall, the findings presented here reinforce the idea that antifungal textiles could have a key role in the prevention and treatment of several superficial fungal infections while avoiding pathogenic fungal dissemination. However, a deeper understanding of the real impact of such products in the human skin microbiota is necessary to drive its biomedical and/or personalized applications.

### *4.3 Antiviral textiles*

The main proposal for the development of antiviral textiles is the possibility of reducing the propagation and transmission of several viral infections, including those mainly caused by herpes, influenza, and coronaviruses [82-86]. It is known that textile materials, particularly clothing, play a significant role in the spread and transmission of infectious diseases because of their vulnerability to microbial attack. Even though discoloration, biodegradation, and odor are usually correlated to microbial colonization on textiles, particularly by bacteria and fungi, these signals are not observed by the presence of virus on textiles [87]. Different from those, viruses are not considered to be 'alive' due to reliance on a host-cell to reproduce and survive. Therefore, viruses cannot replicate or grow on textile surface, but they can remain as infectious viral particles for several hours or days in many textile materials [87]. As a consequence, textiles are an important vehicle for the spread and transmission of virus either by direct or indirect contact [10].

In fact, the presence of viable particles of virus in textile materials has been investigated in the last years, particularly with the emergent necessity to avoid the spread of respiratory viruses [86]. For instance, some works have shown that the lifespan, survival, and stability of infectious virus vary according to the nature and composition of textile fabrics [88]. In this scope, it was demonstrated that polio and vaccinia virus were recovered up to 20 and 14 weeks, respectively, from wool fabrics previously exposed to the virus, but they persisted for shorter periods of time on the cotton fabrics [89]. By contrast, human coronaviruses remain viable less than 24 hours in cotton [88, 90], ≥72 h in polyester, and ≥6 in polycotton [90]. These findings highlight the potential of textiles to act as fomites for several viruses, including human coronaviruses.

In this line, it is consensual that the COVID-19 pandemic has created a necessity for critical public healthcare measures, including physical distancing, ventilation, medical protective clothing, and face masks to limit the spread of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Consequently, for personal protective equipment (PPE), the measures generated two main approaches of strategies mainly subdivided into: *i*) the management of contaminated textiles, clothing, masks, gloves, etc, [91] and *ii*) the development of protective textiles with effective antiviral activity [85]. In fact, several works have demonstrated different stratagems to remove viruses or inactivate them from contaminated textiles, which include diverse wash cycles, temperature, drying and UV exposition [90, 91]. Despite some promising results in this field, it is still difficult to measure an efficient decontamination for textile reuse by typical domestic and commercial procedures

in a day-to-day routine, for example. On the other hand, the huge losses that resulted from the COVID-19 pandemic [92] has positively influenced the research and development of antiviral textiles as a potential tool to reduce the spread of viruses through the utilization of protective clothing, medical-surgical masks, and N95 masks [84, 87]. Hereupon, antivirus textiles can significantly reduce the spread of viruses while decreasing the risk of cross-infection and re-infection, protecting people's health and safety.

With this purpose, a range of antiviral agents such as organic compounds (quaternary ammonium compounds, triclosan, polyhexamethylene biguanide and *N*-halamines), synthetic or natural polymers (polypyrrole, chitosan, and natural dyes), graphene materials, metal-based materials (copper, silver, zinc, and their oxides and salts), hybrid peptides, and even soap have been incorporated into different textile materials [82, 84-86, 93-95]. Although many of these exert both bactericidal and virucidal properties, there have distinct key responses dictated by the differences between bacterial and viral structures and behaviors which still need to be addressed [87].

Of note, several *in vitro* assays have demonstrated a good rate of biocompatibility and antiviral performance, as well as the capacity of antiviral textiles to disrupt the viability of viruses while preventing their spread through effective mechanisms to kill, inactivate, and reduce their attachment in such materials [85, 86, 93, 94, 96]. On the contrary, the translation for *in vivo* models, particularly to evaluate how such materials impact the human skin microbiome, little has been explored and documented. Whereas there is a lack of information in this field, most studies have predominantly focused on the interactions between protective face masks impregnated with antimicrobial agents, including antiviral components, and the skin microenvironment.

To date, various types of protective face masks with different levels of protection, comfort, and antiviral activity to support the market demands have been developed [95, 97, 98]. Whilst much attention has been given to design face masks able to limit the spread of viruses from both inside and outside the mask, and their effectiveness after decontamination procedures, the microenvironment created by mask-wearing, particularly the mask-skin microbiome, should also be considered as a key aspect for intensive investigation. In general, the most important effects linked to the mask microenvironment include skin irritation and discomfort, and local microbiota dysbiosis correlated with various other dermatological conditions, namely acne, rosacea, eczema, and seborrheic dermatitis [99, 100].

Succinctly, prolonged face mask usage can cause facial heat, moisture, and sebum accumulation in the skin microenvironment [33, 101]. These physiological alterations create a new microclimate underneath the mask which is presently linked to changes in the skin microbiota and significant increase in acne flare-ups [33, 40]. The so-called "*maskne*" is a new form of mechanical acne resulting from continuous textile-skin adherence and friction which refers both to new diagnoses and to aggravation of pre-existing acneiform eruption [101]. In this case, the overproduction of sebum correlated to the prolonged use of face masks can disrupt the skin microbiota balance causing considerable dysbiosis. This effect facilitates the growth and colonization of selected species, namely *Cutibacterium acnes*, the most prevalent resident of sebaceous zones and a key member linked to acne and other skin pathologies [101]. Despite maskne, the occurrence of other dermatological conditions caused by a dysbiotic microbiota can also occur, such as flare-ups of eczema linked to the colonization of *S. aureus,* seborrheic

dermatitis related to Fusobacteria, *S. aureus* and *Streptococcus*, and rosacea correlated to *Demodex follicolorum* [2].

Despite some studies pointing out to the impact of protective face masks on the skin microenvironment, particularly in the skin microbiota, systematic and clinically controlled studies are needed to characterize and quantify specific microbial alterations along the underside of the face mask, as well as the the pathophysiologic mechanisms and chronology for the development of a dysbiotic microbiota. Overall, intensive investigation in such field should be a top priority and an intrinsic correlation, for example, between the following three parameters should be performed (Figure 2):

i) *Textile properties*: nature, composition, number of layers, air permeability, breathability, stickiness, type of antimicrobial agent, and preparation method.
ii) *Human parameters*: age, gender, genetics, healthy conditions, hygiene habits, cosmetic and medication use.
iii) *Environmental factors*: moisture, temperature, geographical location, climate.

This knowledge is of major importance to determine the local consequences of normal and prolonged mask wear, and its real impact on skin microbiota. This unravels the need for more dynamic investigation since it is necessary to consider not only the direct interaction skin-mask textile, but also individual parameters and environmental factors for a more comprehensive evaluation. Besides face masks, the combination of these parameters could also be translated to assess the effect of other antiviral/antimicrobial textiles on skin microbiota.

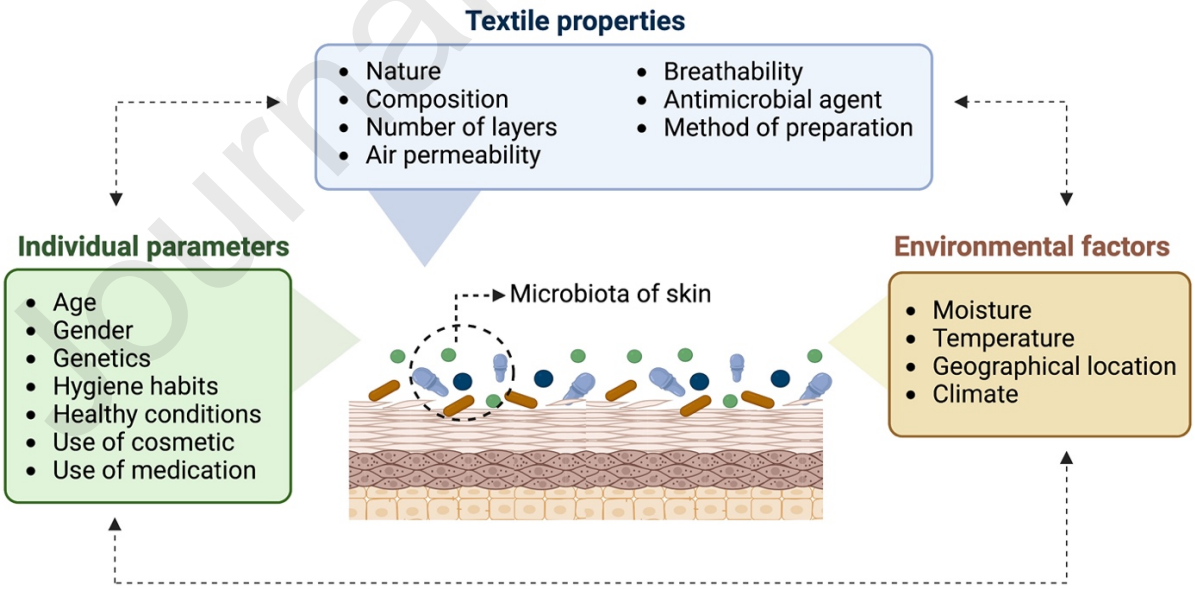


**Figure 2: Parameters intrinsically correlated with the human skin microbiota.** The skin microbiota can be influenced or modulated not only by the direct interaction between skin-mask textiles, but by a combination of the properties of the textile material, individual parameters, and environmental factors.

## 5. Key points & Final remarks

Bioactive textiles are one of the most dynamic fields of research and one that needs to be on the lookout for innovative technologies and products considering their wide-ranging applications. Regarding antimicrobial textiles and clothing, they can find valuable purposes according to their main effects on textile material and on the human skin microbiota (Figure 3). In general, antimicrobial textiles can be used to:

- Decrease textile attack and colonization.
- Decrease biological textile degradation and discoloration.
- Avoid unpleased odor, both in the textile material and human.
- Decrease propagation and transmission of several infectious diseases.
- Prevent, control, and treat several cases of skin microbiota dysregulation, including bacterial dysbiosis and superficial fungal infections, e.g., using antimicrobial clothing, pyjamas, gloves, and socks.
- Act as a barrier to prevent microbial invasion and colonization while stimulating skin regeneration in case of wounds, for example, as antimicrobial wound dressings.
- Target the superficial skin cancer microenvironment, acting as regulator of the skin microbiota while fighting skin cancer cells.

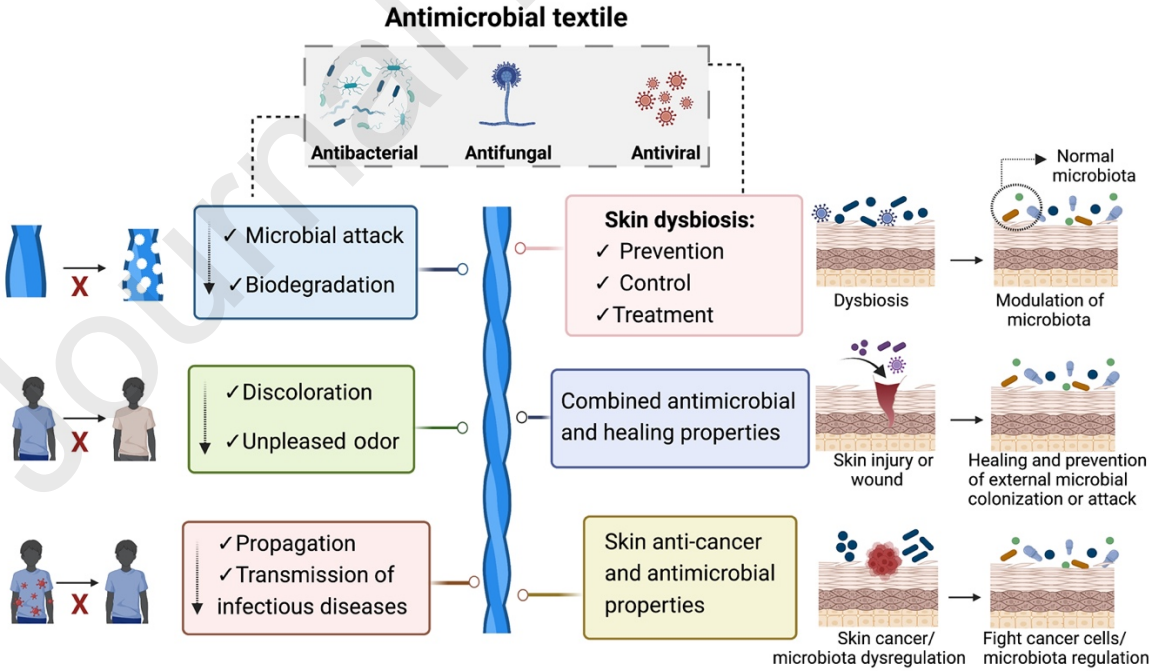


**Figure 3: Schematic representation of the antimicrobial textile's applications according to their main effects on textiles and on the human skin microbiota.** Different antimicrobial textiles can provide protection against textile attack and colonization by microorganisms, biological degradation, discoloration, and unpleased

odor both in the textile material and in humans. Such products can also be used to significantly decrease the propagation and consequently the transmission of several infectious diseases. According to their direct effects on the human skin microbiota, antimicrobial textiles can also find many biomedical applications, including 1) the prevention, control, and treatment of numerous cases of microbiota skin dysregulation (e.g. bacterial dysbiosis and superficial fungal infections; 2) antimicrobial wound dressings, where they can act as a barrier to prevent microbial invasion and colonization while at the same time stimulate skin regeneration; and 3) target the skin cancer microenvironment, acting as regulator of the skin microbiota while fight skin cancer cells.

To date, there is still very limited information available about the exact impact of antimicrobial textiles in the environment. In this sense, there must be a well-planned and managed system for the disposal and treatment of such antimicrobial-based textiles to avoid a problem like plastic management, chemical disposal or adaptative resistant microorganisms. Consequently, it is essential to think about technologies and natural components to create antimicrobial textiles products with key properties and benefits, which include green, safe, with high-efficiency and performance, whereas meeting industrial parameters for the manufacturing process. In such challenging field, the cooperation of different expertises of research, such as biotechnology, textile materials science, microbiology, cellular biology, medicine, chemistry, and pharmacology will be necessary and crucial to satisfy the present demand for safe antimicrobial textiles products.

## Declarations

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***Author contributions***

CSO contributed with conceptualization, literature investigation, writing-original draft, writing-review & editing. FKT contributed with writing-review & editing and validation. All authors read and approved the submitted version.

***Conflict of interest***

The authors declare that they have no conflicts of interest.

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