

Toxicity of Silver Nanoparticles and Application of Natural Products on Fabric and Filters as an Alternative

Fatih Karadeniz and Han Seong Kim*

Department of Organic Material Science and Engineering, Pusan National University, Busan 46241, Korea

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There has been increasing attention and research in various nanoparticle applications. Nanoparticles have been used for a variety of purposes in different departments including but not limited to cosmetics, food, machinery, and chemical. A highly sought-after field to use nanoparticles, especially natural or artificial silver nanoparticles (SNPs), is the utilization of their significant antimicrobial properties in daily items such as fabrics, indoor air filters, and, water filtration units where abundant bacterial and fungal growth are inevitable. These applications of SNPs, however, have enabled continuous human exposure and hence paved the way for potential SNP toxicity depending on exposure method and particle size. This potential toxicity has led to researches on safer antimicrobial solutions to be utilized in textile and filtration. In this context, products of natural origin have gained expanding interest due to their eco-friendly, cost-effective, and biologically safe properties along their promising antibacterial and antifungal activities. Natural product-applied fabrics and filters have been shown to be comparable to those that are SNP-treated in terms of ease production, material durability, and antimicrobial efficiency. This article summarizes and assesses the current state of *in vitro* and *in vivo* toxicity of SNPs and discusses the potential of natural products as an alternative.

Key words : Antimicrobial fabric, antimicrobial filter, natural product, silver nanoparticle, toxicity

Background

Fabrics

Fabrics are suitable environments of microbial growth due to moisture retaining, exposure to numerous outdoor environments and large surface. These problems are mainly tried to be solved through different fabric types as well as antimicrobial applications [47]. Development of fabrics coated with antimicrobial agents propose an important treat to commercial products. However, with the discovery and increase of bacterial and fungal strains that are resistant to known antibacterial agents, many studies now turning their attention to develop novel and effective antimicrobial agents. Accordingly, use of nanoparticles as antimicrobial substances has been a major development in numerous fields including various fabric materials with different properties [16, 49]. Silver nanoparticles being the most popular, nanoparticles generally are an effective way of introducing

antimicrobial properties to the surfaces they were applied [32]. Studies promoted nanoparticles to be an important microbial prevention application when bound to desired mediums such as filters and fabric in both industrial and home usage [11, 34, 40]. However, recent studies also pressed on the subject that exhibits potential health risks of nanoparticles [1, 47]. Presence of inorganic nanoparticles is evaluated as a potential risk from an environmental, human health, and safety viewpoints [1].

Air-filters

People in developed countries are reported to spend most of their lives indoors which led the concerns of indoor air quality for healthy individuals [29]. During past decades, studies focused on increased air quality and scientists addressed the crucial relation between indoor air quality and health [5, 9]. There are several reasons to cause indoor air pollution such as human activity, dense population, construction materials of equipment and environmental pollutants [56, 65]. A very efficient and highly used method to regulate and hinder indoor air pollution is air filtering systems that both can be established on ventilation circulators and air conditioning mechanisms [4, 63-65]. This method containing filters made of various materials is considered

*Corresponding author

Tel : +82-51-510-2409, Fax : +82-51-512-8175

E-mail : hanseongkim@pusan.ac.kr

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to filter and prevent airborne pollutants including dust particles and organic debris as well as bacterial and fungal spores [29, 46]. Even though indoor air quality can be significantly raised by air filters applied to ventilation, air conditioner intake, and output holes, it has been suggested that these applications themselves could cause microbial contamination of the air. Possibility of hosting bacterial and fungal spores that have been filtered is suggested to result in contaminated air flow [2, 39, 43].

In consideration of air filters' ability to cause indoor air contamination, new ways to improve the efficiency and usability of air filtering could be of tremendous significance and help in great deal to improvement of the health preservation through indoor air quality. In this context, possibility of antimicrobial agent addition to the air filters is a very efficient way of preventing microbial air contamination. Many researches and industrial manufacturers are concerned about the reduction of bacterial and fungal growth in filtration systems and eager to find an affordable and healthy solution. Similar concerns are present for water filtration systems and antimicrobial introduction to present filters are studied in detail by several studies [27]. Linked attention addressed to adding antimicrobial agents to filters has increased considerably, giving rise to new ideas of antimicrobial agent preparation that can be successfully added to present filters [14]. Antimicrobial agents that can destroy or prevent the growth of several microorganisms have been benefited in several commercial applications up to date. Moreover, microorganisms are evidently showed to accumulate in filter surfaces. In the light of this knowledge, release of organic indoor air pollutants could be directly linked with air filters contaminated by microbial growth [59]. Recent improvements in this context has led to antimicrobial agents being administered to air filters, to regulate the indoor air quality by acting against a wide range of bacterial and fungal contamination which were supposed to be present in the dirty filter. With the discovery and increase of bacterial and fungal strains that are resistant to antibiotics, and the increasing costs that this situation caused, many studies now turning their attention to develop a new and effective antimicrobial resistance, especially in an ecofriendly and cost-effective manner. Such concerns led to use of silver nanoparticles (SNP) being the most popular, nanoparticles generally are an effective way of improving air filtration system

with an antimicrobial touch. Considering the reported drawbacks and potential risks of inorganic nanoparticle use, natural antimicrobial agents are again gaining attention to develop an efficient yet safe solution to indoor air quality regulation.

The toxicity of SNPs

In spite of their prevalent appearance in numerous fields varying from textile to medicine, thorough studies on SNPs' effects on human health is lacking. Very limited information is available on their toxic effect to humans and even less is known about their effect to environment. In addition, risks of constant exposure to SNPs are not systematically identified in regard to environment where SNPs are used. Currently, available reports indicate significant toxicity of silver nanoparticles depending on their different size and shapes (Fig. 1).

Toxicity of SNPs from *in vitro* studies

Several studies reported that SNPs possess toxic properties in cell lines derived from different tissues of mammalian organisms (Table 1). Especially in case of SNPs use in fabrics, contact with SNPs is inevitable and depending on conditions, it is for a prolonged time. A study that used *in vitro* human skin model showed that silver particles were passed to sweat from antibacterial fabrics dependent on fabric quality, pH, and temperature [36]. Paddle-Ledinek et al. [45] stated that skin wound dressings with SNPs were the most toxic among tested on keratinocytes. A study by Samberg et al. [50] also reported the potential cytotoxicity of SNPs exposure for 2 weeks in human keratinocytes. Likewise, Lam et al. [37] dismissed the any potential application of nano-

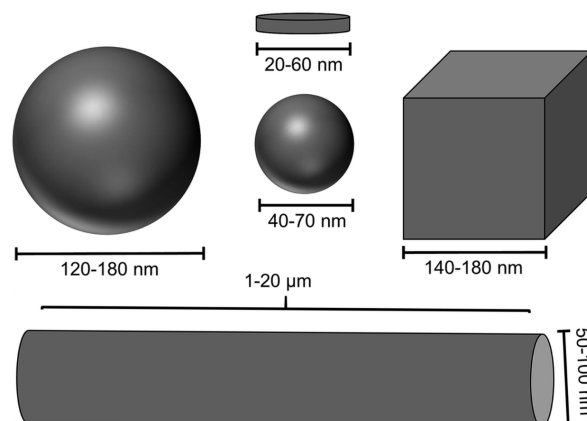


Fig. 1. Approximate shapes and sizes of different silver nanoparticles.

Table 1. Toxicity of silver nanoparticles to mammalian cell lines *in vitro*

Size	Cell line	Dose/Exposure	Result	Ref.
15 nm	Mouse spermatogonial stem cells (C18-4)	5-10 $\mu\text{g}/\text{ml}$ 24 hr	Induced apoptosis and reduced mitochondrial function	[6]
25, 100 nm	Rat liver cells (BRL 3A)	5-50 $\mu\text{g}/\text{ml}$ 24 hr	Elevated oxidative stress and reduced mitochondrial function	[23]
1-100 nm	Mouse fibroblast (NIH3T3)	5-50 $\mu\text{g}/\text{ml}$ 24 hr	Induced apoptotis (via JNK pathway and oxidative stress)	[22]
25 nm	Mouse stem cells and fibroblasts	50 $\mu\text{g}/\text{ml}$ 4-72 hr	Induced apoptosis via DNA damage	[1]
100 nm	Human mesenchymal stem cells	2.5-5.0 $\mu\text{g}/\text{ml}$ 24 hr	Elevated IL-8 expression and chemotaxis	[15]
7-10 nm	Human hepatoma cells (HepG2)	0.1-3.0 $\mu\text{g}/\text{ml}$ 24 hr	Accelerated DNA damage and micronuclei formation	[31]
20-80 nm	Human epidermal keratinocytes	0.34-1.7 $\mu\text{g}/\text{ml}$ 24 hr	Decreased cell viability	[50]

crystalline silver dressings on cultured skin grafts due to its high cytotoxicity to keratinocytes.

On the other hand, air filtering materials that are coated or diffused with SNPs further increases the potential risks through inhalation and digestion. It has been indicated by studies that lung and liver tissues are among the most adversely affected areas for extended exposure to SNPs. In a study with rat liver cell model, depletion of antioxidant defense system molecules and enzymes along with elevated reactive oxygen species (ROS) were observed following introduction of SNPs [23]. Introduction to human liver C3A cells indicated that SNPs exhibited high levels of cytotoxicity. Other studies reported elevated liver biomarkers of aspartate amino transferase, gamma-galactosyl-transferase, and alanine aminotransferase along with inhibited cytochrome P450 enzymes such as SCYP2C, CYP2E1, and CYP1A following to SNPs exposure [8, 35]. The cytotoxicity of SNPs in liver cells is important as it was shown that accumulation of SNPs in liver cells occur not only with digestion but also inhalation. Although different mechanisms were suggested for the liver cytotoxicity of the SNPs, it was predominantly elicited that SNPs induced intensive oxidative stress and caused cell damage.

Lung is an easy to access target for SNPs through inhalation when they were used in air filtration systems. Inhalation of the particles may deliver the particles to the brain by passing nasopharyngeal system. Among limited studies on lung toxicity of SNPs, Soto et al. [55] showed that presence of SNP significantly induced apoptosis in lung epithelial cells. Similar to liver toxicity, oxidative stress, and

cell damage were the main causes for the cytotoxicity in lung cells and alveolar macrophages. In all related series SNP cytotoxicity was size-dependent and the smaller size was always more toxic compared to larger sizes.

There are non-toxic doses of SNPs that were indicated by different sources responsible for regulation of SNPs uses in environments with human interaction. Studies by Kawata et al. [31] and Greulich et al. [15] suggested that these doses may still be toxic in cellular level. In human HepG2 hepatoma cell lines SNP non-toxic doses (<0.5 $\mu\text{g}/\text{ml}$) were observed to induce the expression of pro-apoptotic genes as well as transcription factors linked with cell cycle arrest [31]. Similar doses were also shown to be responsible of cellular damage in human mesenchymal stem cells suggesting that even at designated non-toxic doses of SNPs are unsafe under regular exposure.

In addition to inhalation and digestion through filtration systems, it is now known that human genital system is in contact with SNPs via hygiene and contraceptive products which may facilitate any toxic effect of SNPs. Studies showed that presence of SNPs caused toxicity in mouse spermatogonial C18-4 stem cells, embryonic stem cells and fibroblasts independent of its size and whether it was coated or not [1, 6]. Mouse genital system cells showed reduced mitochondrial function, increased LDH leakage, and apoptosis along DNA damage. Another study by Hsin et al. [22] also reported that SNPs of varying sizes (1-100 nm) without any coating induced elevated ROS production and JNK pathway activation in mouse fibroblasts resulting in mitochondrial pathway apoptosis.

The toxicity of SNPs was also observed in different cell line *in vitro* using cancerous cells. Interestingly, tested SNPs were showed higher toxicity towards cancer cell lines compared to non-cancerous cell lines originated from same tissue. Studies showed that, SNPs induced apoptosis dose-dependently in human HepG2 [13], Huh7 [8] hepatoma, and AML human myeloid leukemia [17] cell lines. It also may be regarded as drug development potential using cancerous cell toxicity of SNPs. Nevertheless, numerous *in vitro* studies clearly suggested that the inhalation and digestion of SNPs caused toxicity dependent on size and dose.

Toxicity of SNPs from *in vitro* studies

Adverse effects of SNP exposure in animal models are recognized recently with increasing studies by time. Although still lacking the detailed mechanisms and decisive clinical trials, studies hinted at toxicity of SNPs in humans through mammalian toxicity studies. Subjection to SNPs used as antimicrobial agents may occur through different ways. Use of SNPs in filtration systems generate exposure through inhalation (air filtration systems), digestion (water filtration systems), and contact (antibacterial fabrics).

A study on rats inhaling 15 nm particles showed that inhaled SNPs rapidly passed into blood circulation and from there to vital organs such as brain, liver, and kidney [58]. Sung et al. [57] examined the effects of SNP inhalation in Sprague-Dawley rats. Rats showed lower tidal volume in lungs along bile duct hyperplasia and liver inflammation following the 6 hr inhalation exposure a day for 90 days, 5 days a week. In another study using C57BL/6 mice, Lee et al. [38] indicated that inhalation exposure to SNPs caused significant changes in brain. A microarray analysis of cerebrum and cerebellum following the exposure showed the

modulation of several genes related to neurodegenerative diseases, brain immune cell function, and motor-neuron disorders. It was suggested that SNPs easily passed the brain-blood barrier and caused what can be called as neurotoxicity. In contrast, another study by Hyun et al. [26] expressed the non-toxic effects of repeated SNP inhalation via the Sprague-Dawley rats. Subjects inhaled the particles through nasal-only way for 28 days, 6 hr a day, 5 times a week to mimic working hours of an average person. Results showed notably higher goblet cells containing neutral mucins than that of with acid mucins in lungs indicating not a toxicity but a susceptibility to infection.

Digestion exposure to SNPs may occur via accidental ingestion of contaminated water through filtration systems or contaminated food products. In rats that were introduced to SNP orally, critical changes in liver tissue were recorded [33]. Dose-dependent but not gender specific changes in alkaline phosphatase activity and cholesterol levels were observed with a minor liver damage. Toxicity of SNP in liver was also reported by Cha et al. [7] in mice following oral exposure for 3 days. Lymphocytic infiltration, and pro-apoptotic and pro-inflammatory gene expression were observed in livers after 3 days. Rahman et al. [48] injected SNPs to male C57BL/6N mice intraperitoneally at the ratios of 100, 500, and 1,000 mg/kg and observed the toxicity in brain. The detected toxicity was suggested to arise from elevated oxidative stress and associated neurotoxicity with deteriorated gene expression.

Results from different studies clearly showed that continuous exposure to high levels of SNPs caused considerable toxicity in vital organs including but not limited to brain, lung, and liver, brain being the most susceptible to toxic effects (Table 2). However, comprehensive and detailed stud-

Table 2. Toxicity of silver nanoparticles to mammalian models *in vitro*

Animal model	Exposure mode/period	Result	Ref.
Sprague-Dawley rat	Inhalation: 6 hr/day, 5 days/week, 90 days	Increased bile duct hyperplasia and induced liver inflammation	[57]
Sprague-Dawley rat	Ingestion; 28 days with daily diet	Critical changes in cholesterol level and alkaline phosphatase activity	[33]
Male C57BL/6N mice	Intraperitoneal injection; 24 hr	Changes in expression of oxidative stress-linked genes in brain	[48]
Sprague-Dawley rat	Inhalation; 6 hr/day, 5 days/week, 28 days	Increased numbers of Neutral mucin containing goblet cells in lungs	[26]
C57BL/6 mice	Inhalation; 6 hr/day, 5 days/week, 14 days	Induced expression of neurodegenerative disease and motor neuron disorder associated genes	[38]

ies are needed for better understanding of SNP toxicity and its capacity body-wide after different modes of exposure. Nevertheless, current data is sufficient to raise awareness to its harmful effects and provide significant information using mammalian models.

Antimicrobial natural products as an alternative

In the light of toxicity risks of SNPs mentioned in this review, natural antimicrobial agents are again gaining attention due to their efficient yet safe utilization for ensuring bacteria-free quality of indoor air, water and fabrics. Therefore, literature consists of several studies that focuses on the possibility of natural-origin antibacterial substances to be applied to filters and fabrics.

Application of natural products to textile products

Although there are recent studies examining the possibility of production of textiles treated with natural antimicrobial agents, use of natural products on fabrics for protection and preservation dates to ancient Egypt where mummies were wrap with herbs and spices to prevent the bacterial and fungal growth. During past decades, textiles that can withstand microbial infection has become an important target to research. For this purpose, several antimicrobial agents were tried and successfully applied to consumer fabrics such as organo-metallics, silver nanoparticles, silicene-based organic materials and phenols. To achieve a favorable product with high efficiency against bacteria and fungi, bio-safety is as important as the inhibitory effect on broad range of bacterial strains and fungi. Due to the this need of safe and effective agents, natural products which can also applied as dyes on fabrics are gaining interest. Active ingredients of natural dyes can inhibit antimicrobial grow without toxicity which give them their popularity in recent researches.

Curcumin is studied for its pharmacological potential as an anti-inflammatory, antifungal and antibacterial activities. It is also a common natural dye that is being used in both textile and food industry. In this context, Han and Yang [21] discussed the possible antimicrobial application of curcumin to wool fabric and suggested that it will also pertain its antimicrobial activity after perpetual laundering and UV light exposure. Singh et al. [54] also explored the possible antimicrobial potential of natural dyes *Acacia catechu*, *Kerria lacca*, *Quercus infectoria*, *Rubia cordifolia* and *Rumex maritimus*. All tested dyes were able show notable inhibitory effect with

minimum inhibitory concentrations varying from 5 to 40 μg , *Quercus infectoria* being the most effective, against commonly present microbial strains *Escherichia coli*, *Bacillus subtilis*, *Klebsiella pneumoniae*, *Proteus vulgaris* and *Pseudomonas aeruginosa*. However, dying process with these natural dyes resulted in dye uptake short of minimum inhibitory concentrations and hence, expressing less antimicrobial activity. Gupta et al. [19] also showed that the antimicrobial activity of natural dyes strictly dependent on the type of fabric they were applied to and their chemical structure. In most of the examined natural dyes, presence of tannins was the main reason behind the relatively higher antimicrobial activity.

Chitosan is a deacetylated derivative of a very abundant natural product chitin from shells of crustaceans and mollusks. Chitosan has been extensively studied and derivatized with promising bioactivities as a result. Among these beneficial properties there are antibacterial, antifungal, antiviral properties make chitosan a lead on producing antimicrobial fabric coating. Chitosan and its derivatives have been the subject of studies focusing on antimicrobial agents use in textile industry. Gupta et al. [18] showed that chitosan can be bound to cotton fabric chemically with the help of cross-linking agents such as glutaric dialdehyde. Shin et al. [52] applied chitosan oligomers on polypropylene nonwoven fabrics as finishing to yield significant antimicrobial activity at 0.01 to 0.05% level against *P. vulgaris*, *S. aureus* and *E. coli*. In a study by Nam et al. [42] a chitosan derivative, N-(2-hydroxyl) propyl-3-trimethylammonium chitosan chloride showed to impart antimicrobial activity when applied to acrylic fiber when added during polyacrylonitrile spinning. Drawbacks of chitosan use in textile industry is the need of high concentration for efficient antimicrobial presence which results in stiff and/or less air permeable fabrics.

Aloe vera is a common ingredient in cosmetics with its rich nutritional constituents. It has been used for ages for skin protection, wound healing and antifungal purposes. Nadiger and Shukla [41] tried to obtain a silk product treated with *A. vera*. Although natural silk contains sericin which is antimicrobial in nature, it is removed during silk pretreatment. Ready to dye silk fabric was treated with *A. vera* via 1,2,3,4-butanetetracarboxylic acid. At the concentration of 15% *A. vera*, this durable *A. vera*-treated silk fabric showed outstanding antimicrobial activity. In another study, Ali et al. [3] finished cotton fabric samples with *A. vera* gel via hydroxyl groups of cotton fabric sing carboxylic acid cross-linking agent. The cotton fabric that contains >3% *A.*

vera gel was able to inhibit the growth of both gram-positive *S. aureus* and gram-negative *E. coli* strains. Cotton fabrics did not lose their strength, crease recovery angle and washing durability after *A. vera* gel finishing and it was suggested that antimicrobial activity of *A. vera* gel treatment was due to the destruction of the bacterial cell wall.

The essential oils are known biocides of plant origin. They are biodegradable, environment friendly and safe to use for human health. Most of the known medicinal plants such as *Mentha piperita*, *Thymus vulgaris*, *Origanum compactum*, *Salvia officinalis* and *Artemisia absinthium* yield extracts and essential oils with antibacterial and antifungal properties. Walentowska and Foksowicz-Flaczyk [60] applied thyme oil to linen-cotton blend and linen fabrics to evaluate its potential in developing antimicrobial fabrics. Linen-cotton blended fabric with 8% thyme essential oil applied showed superior antibacterial and antifungal activity without any loss in fabric quality. Also, examination of the thyme essential oil applied fabrics under Scanning Electron Microscopy indicated that the oil is bound to fabric with good physical and mechanical properties. However, study urges further studies to determine the durability of the fabrics to light exposure and laundering. Sarkar et al. [51] showed that oil extracted from *Syzygium aromaticum* showed exceptional antimicrobial activity (47 mm of zone of inhibition) against *S. aureus* and *Klebsiella pneumonia* when applied to cotton fabrics at the concentration of 01% via dimethylol dihydroxyethylene urea based in-built catalyst. In addition to direct application of essential oils, studies focusing on application of oils via micro-encapsulation also produced promising results. Ozyildiz et al. [44] applied microcapsules containing ozonated red pepper seed oil to nonwoven fabrics and prepared functional fabrics. A complex coacervation method including gelatin and gum arabic was carried out to form red pepper seed oil encapsulation and followed by padding method to apply them on nonwoven fabrics. Results showed that microcapsule-bound functional textile products decreased microbial growth by 5 log in 1 hr. A similar study was also carried out by Javid et al. [28] using chitosan micro-encapsulation of various essential oils. Capsules containing different essential oils with antimicrobial properties were applied to cotton fabric and the fabric quality was examined along antimicrobial effect. It was suggested that antimicrobial activity of the oil-impregnated cotton fabrics increased dependent of essential oil and chitosan concentration. On the other hand, stiffness and wrinkle recovery properties were

in contrast with chitosan concentration although proportional to essential oil levels.

Application of natural products to antimicrobial filtration

Assuring the quality of indoor air and drinking water is vital for human health in today's high paced city dwelling society. Filtration of air and water flow is one of the main steps that control the quality of air and water. However, as a part of their nature, filters used in filtration may lack the ability to dispel all microcontaminants or become the source of bacterial and fungal growth themselves. Therefore, producing filters that has antimicrobial properties is a way to assure the safety of filtration. As mentioned earlier in the review, SNPs are common and efficient way to ensure the antimicrobial efficiency of filtration but comes with several drawbacks such as toxicity to human. In this context, studies focusing on safe antimicrobial filters with natural origin increasingly continue.

Sophora flavescens is an herbal medicine from traditional folk remedies known for its high antimicrobial material content. Jung et al. [30] developed nanoparticles from *S. flavescens* ethanol extract via nebulization-thermal drying process. Spherical nanoparticles ranging sizes from several tens to several hundred nanometers was applied onto filters to remove bioaerosols. Results showed that developed filters were able to deactivate bioaerosols while being more effective for removal of gram-positive than gram-negative airborne bacteria. In a similar attempt, Sim et al. [53] aimed to demonstrate that *S. flavescens* antimicrobial nanoparticles coated active carbon filters were more efficient in air purification, dehumidification, and water purification without any microbial contamination. The coating of *S. flavescens* onto activated carbon filters inactivated *Staphylococcus epidermidis* dependent on the extract concentration. Results were promising for future uses of *S. flavescens* application to control bioaerosol and gaseous pollutants via activated carbon filters. Another study by the same team [25] also used *S. flavescens* nanoparticles to produce hybrid carbon nanotube structures. Antimicrobial hybrid nanoparticles were developed by a twin-head electrospray system using *S. flavescens* nanoparticles and multi-walled carbon nanotubes. Results indicated that air filters were notably superior in terms of antimicrobial and filtration efficiency after the application of natural product nanoparticles. A similar approach was followed to produce natural product antimicrobial nanoparticles from

Euscaphis japonica extract [24]. Natural nanoparticle implemented filters were able to inactivate *S. epidermidis* and *Micrococcus luteus* bioaerosols. Analysis suggested that antimicrobial effect of the nanoparticles was due to containing 1(β)-O-galloyl pedunculagin, quercetin-3-O-glucuronide, and kaempferol-3-O-glucoside which were also shown to exhibit stronger antibacterial effect in some strains and were less toxic compared to inorganic soluble nickel compound.

Similar to their use in fabrics, chitosan and its derivatives are also promising materials for antimicrobial filtration purposes. Wisser et al. [61] suggested the non-toxic, biodegradable chitin-based network from a marine sponge was an efficient support material for metal-organic framework-based gas-separation and air-filtration applications. Results clearly showed that developed composites displayed high potential for filtration of toxic industrial gases. Ferrero et al. [12] used UV curing to coat cotton gauze with chitosan prior to examine their antibacterial activity for water filtration purposes. In continuous water flow, chitosan coated cotton gauze exhibited strong antibacterial activity via rapid reduction of *E. coli*, *S. aureus*, and *K. pneumoniae* bacterial strains.

Han et al. [20] and Woo et al. [62] conducted complementary examinations on antimicrobial air filters deposited with natural products, grapefruit seed extract and propolis. Woo et al. [62] indicated that when deposited in identical level, inactivation rates of grapefruit seed extract and propolis air filters were in the ranges of 92.1-100% of the control filters without any natural product deposition with colony numbers of 10^3 *S. aureus*. Inactivation rates dropped gradually by increasing colony number. Nevertheless, as Han et al. [20] suggested both natural products showed potential to be applied to air filters for inactivation of both gram positive and gram negative bioaerosols, grapefruit seed extract being slightly more effective at same level of deposition compared to propolis air filters.

Conclusion

In conclusion, this compact review was aimed to promote the potential of natural product-origin antimicrobial agents in antimicrobial fabrics and filtrations. Although, both organic and inorganic silver nanoparticles exert very efficient antimicrobial activity when applied to fabrics and filtration units, studies clearly indicated the lack of assessment on their toxic effects. It has been suggested that despite the de-

tailed examinations, current state of the literature shows that silver nanoparticles are not fully safe to use in human environment and bring harmful effects along inactivation of bacteria and fungi. Concordantly, recent studies showed that natural antimicrobial agents derived mainly from plants can be used in production of antimicrobial filtration units and fabrics. Compared to silver nanoparticles natural product antimicrobial agents shows less to none toxicity, a similar efficiency against bacteria and fungi and minimally affect the durability of fabric and filters. Despite the lack of clinical assessment, current data clearly exhibit the very high potential of natural product implemented fabrics and natural product nanoparticle impregnated filters for development of antimicrobial textile and filtration.

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References

1. Ahamed, M., Karns, M., Goodson, M., Rowe, J., Hussain, S. M., Schlager, J. J. and Hong, Y. 2008. DNA damage response to different surface chemistry of silver nanoparticles in mammalian cells. *Toxicol. Appl. Pharmacol.* **233**, 404-410.
2. Ahearn, D. G. 1997. Fungal colonization of air filters and insulation in a multi-story office building: Production of volatile organics. *Curr. Microbiol.* **35**, 305-308.
3. Ali, S. W., Purwar, R., Joshi, M. and Rajendran, S. 2014. Antibacterial properties of *Aloe vera* gel-finished cotton fabric. *Cellulose* **21**, 2063-2072.
4. Ao, C. H. and Lee, S. C. 2005. Indoor air purification by photocatalyst TiO₂ immobilized on an activated carbon filter installed in an air cleaner. *Chem. Eng. Sci.* **60**, 103-109.
5. Bernstein, J. A., Alexis, N., Bacchus, H., Bernstein, I. L., Fritz, P., Horner, E., Li, N., Mason, S., Nel, A., Oullette, J., Reijula, K., Reponen, T., Seltzer, J., Smith, A. and Tarlo, S. M. 2008. The health effects of nonindustrial indoor air pollution. *J. Allergy Clin. Immunol.* **121**, 585-591.
6. Braydich-Stolle, L., Hussain, S., Schlager, J. J. and Hofmann, M. C. 2005. *In vitro* cytotoxicity of nanoparticles in mammalian germline stem cells. *Toxicol. Sci.* **88**, 412-419.
7. Cha, K., Hong, H. W., Choi, Y. G., Lee, M. J., Park, J. H., Chae, H. K., Ryu, G. and Myung, H. 2008. Comparison of acute responses of mice livers to short-term exposure to nano-sized or micro-sized silver particles. *Biotechnol. Lett.* **30**, 1893-1899.
8. Christen, V. and Fent, K. 2012. Silica nanoparticles and silver-doped silica nanoparticles induce endoplasmic reticulum stress response and alter cytochrome P4501A activity. *Chemosphere* **87**, 423-434.

9. Daisey, J. M., Angell, W. J. and Apte, M. G. 2003. Indoor air quality, ventilation and health symptoms in schools: an analysis of existing information. *Indoor Air* **13**, 53-64.
10. Durán, N., Marcató, P. D., De Souza, G. I. H., Alves, O. L. and Esposito, E. 2007. Antibacterial effect of silver nanoparticles produced by fungal process on textile fabrics and their effluent treatment. *J. Biomed. Nanotechnol.* **3**, 203-208.
11. El-Shishtawy, R. M., Asiri, A. M., Abdelwahed, N. A. M. and Al-Otaibi, M. M. 2011. In situ production of silver nanoparticle on cotton fabric and its antimicrobial evaluation. *Cellulose* **18**, 75-82.
12. Ferrero, F., Periolatto, M., Vineis, C. and Varesano, A. 2014. Chitosan coated cotton gauze for antibacterial water filtration. *Carbohydr. Polym.* **103**, 207-212.
13. Filipak Neto, F., Cardoso da Silva, L., Liebel, S., Voigt, C. L. and Oliveira Ribeiro, C. A. 2018. Responses of human hepatoma HepG2 cells to silver nanoparticles and polycyclic aromatic hydrocarbons. *Toxicol. Mech. Methods* **28**, 69-78.
14. Foarde, K. K., Hanley, J. T. and Veeck, A. C. 2000. Efficacy of antimicrobial filter treatments. *ASHRAE J.* **42**, 52-58.
15. Greulich, C., Kittler, S., Epple, M., Muhr, G. and Köller, M. 2009. Studies on the biocompatibility and the interaction of silver nanoparticles with human mesenchymal stem cells (hMSCs). *Langenbeck's Arch. Surg.* **394**, 495-502.
16. Gao, Y. and Cranston, R. 2008. Recent advances in antimicrobial treatments of textiles. *Text. Res. J.* **78**, 60-72.
17. Guo, D., Zhao, Y., Zhang, Y., Wang, Q., Huang, Z., Ding, Q., Guo, Z., Zhou, X., Zhu, L. and Gu, N. 2014. The cellular uptake and cytotoxic effect of silver nanoparticles on chronic myeloid leukemia cells. *J. Biomed. Nanotechnol.* **10**, 669-678.
18. Gupta, D. and Haile, A. 2007. Multifunctional properties of cotton fabric treated with chitosan and carboxymethyl chitosan. *Carbohydr. Polym.* **69**, 164-171.
19. Gupta, D. and Laha, A. 2007. Antimicrobial activity of cotton fabric treated with *Quercus infectoria* extract. *Indian J. Fibre Text. Res.* **32**, 88-92.
20. Han, B. 2015. Investigation of antimicrobial activity of grapefruit seed extract and its application to air filters with comparison to propolis and shiitake. *Aerosol Air Qual. Res.* **2015**, 1035-1044.
21. Han, S. and Yang, Y. 2005. Antimicrobial activity of wool fabric treated with curcumin. *Dye. Pigment.* **64**, 157-161.
22. Hsin, Y. H., Chen, C. F., Huang, S., Shih, T. S., Lai, P. S. and Chueh, P. J. 2008. The apoptotic effect of nanosilver is mediated by a ROS- and JNK-dependent mechanism involving the mitochondrial pathway in NIH3T3 cells. *Toxicol. Lett.* **179**, 130-139.
23. Hussain, S. M., Hess, K. L., Gearhart, J. M., Geiss, K. T. and Schlager, J. J. 2005. *In vitro* toxicity of nanoparticles in BRL 3A rat liver cells. *Toxicol. Vitro.* **19**, 975-983.
24. Hwang, G. B., Heo, K. J., Yun, J. H., Lee, J. E., Lee, H. J., Nho, C. W., Bae, G. N. and Jung, J. H. 2015. Antimicrobial air filters using natural *Euscaphis japonica* nanoparticles. *PLoS One* **10**, e0126481.
25. Hwang, G. B., Sim, K. M., Bae, G. N. and Jung, J. H. 2015. Synthesis of hybrid carbon nanotube structures coated with *Sophora flavescens* nanoparticles and their application to antimicrobial air filtration. *J. Aerosol Sci.* **86**, 44-54.
26. Hyun, J., Lee, B., Ryu, H., Sung, J., Chung, K. and Yu, I. 2008. Effects of repeated silver nanoparticles exposure on the histological structure and mucins of nasal respiratory mucosa in rats. *Toxicol. Lett.* **182**, 24-28.
27. Jain, P. and Pradeep, T. 2005. Potential of silver nanoparticle-coated polyurethane foam as an antibacterial water filter. *Biotechnol. Bioeng.* **90**, 59-63.
28. Javid, A., Raza, Z. A., Hussain, T. and Rehman, A. 2014. Chitosan microencapsulation of various essential oils to enhance the functional properties of cotton fabric. *J. Microencapsul.* **31**, 461-468.
29. Jones, A. P. 1999. Indoor air quality and health. *Atmos. Environ.* **33**, 4535-4564.
30. Jung, J. H., Hwang, G. B., Park, S. Y., Lee, J. E., Nho, C. W., Lee, B. U. and Bae, G. N. 2011. Antimicrobial air filtration using airborne *Sophora Flavescens* natural-product nanoparticles. *Aerosol Sci. Technol.* **45**, 1510-1518.
31. Kawata, K., Osawa, M. and Okabe, S. 2009. *In vitro* toxicity of silver nanoparticles at noncytotoxic doses to HepG2 human hepatoma cells. *Environ. Sci. Technol.* **43**, 6046-6051.
32. Kim, J. S., Kuk, E., Yu, K. N., Kim, J. H., Park, S. J., Lee, H. J., Kim, S. H., Park, Y. K., Park, Y. H., Hwang, C. Y., Kim, Y. K., Lee, Y. S., Jeong, D. H. and Cho, M. H. 2007. Antimicrobial effects of silver nanoparticles. *Nanomed. Nanotechnol. Biol. Med.* **3**, 95-101.
33. Kim, Y. S., Kim, J. S., Cho, H. S., Rha, D. S., Kim, J. M., Park, J. D., Choi, B. S., Lim, R., Chang, H. K., Chung, Y. H., Kwon, I. H., Jeong, J., Han, B. S. and Yu, I. J. 2008. Twenty-eight-day oral toxicity, genotoxicity, and gender-related tissue distribution of silver nanoparticles in Sprague-Dawley rats. *Inhal. Toxicol.* **20**, 575-583.
34. Kokura, S., Handa, O., Takagi, T., Ishikawa, T., Naito, Y. and Yoshikawa, T. 2010. Silver nanoparticles as a safe preservative for use in cosmetics. *Nanomed. Nanotechnol. Biol. Med.* **6**, 570-574.
35. Kulthong, K., Maniratanachote, R., Kobayashi, Y., Fukami, T. and Yokoi, T. 2012. Effects of silver nanoparticles on rat hepatic cytochrome P450 enzyme activity. *Xenobiotica* **42**, 854-862.
36. Kulthong, K., Srisung, S., Boonpavanitchakul, K., Kangwan-supamonkon, W. and Maniratanachote, R. 2010. Determination of silver nanoparticle release from antibacterial fabrics into artificial sweat. *Part. Fibre Toxicol.* **7**, 8.
37. Lam, P. K., Chan, E. S. Y., Ho, W. S. and Liew, C. T. 2004. *In vitro* cytotoxicity testing of a nanocrystalline silver dressing (Acticoat) on cultured keratinocytes. *Br. J. Biomed. Sci.* **61**, 125-127.
38. Lee, H. Y., Choi, Y. J., Jung, E. J., Yin, H. Q., Kwon, J. T., Kim, J. E., Im, H. T., Cho, M. H., Kim, J. H., Kim, H. Y. and Lee, B. H. 2010. Genomics-based screening of differentially expressed genes in the brains of mice exposed to silver nanoparticles via inhalation. *J. Nanoparticle Res.* **12**, 1567-1578.
39. Li, A., Liu, Z., Zhu, X., Liu, Y. and Wang, Q. 2010. The

- effect of air-conditioning parameters and deposition dust on microbial growth in supply air ducts. *Energy Build.* **42**, 449-454.
40. Mpenyana-Monyatsi, L., Mthombeni, N. H., Onyango, M. S. and Momba, M. N. B. 2012. Cost-effective filter materials coated with silver nanoparticles for the removal of pathogenic bacteria in groundwater. *Int. J. Environ. Res. Public Health* **9**, 244-271.
 41. Nadiger, V. G. and Shukla, S. R. 2015. Antimicrobial activity of silk treated with *Aloe vera*. *Fibers Polym.* **16**, 1012-1019.
 42. Nam, C. W., Kim, Y. H. and Ko, S. W. 1999. Modification of polyacrylonitrile (PAN) fiber by blending with N-(2-hydroxy)propyl-3-trimethyl-ammonium chitosan chloride. *J. Appl. Polym. Sci.* **74**, 2258-2265.
 43. Noris, F., Siegel, J. A. and Kinney, K. A. 2011. Evaluation of HVAC filters as a sampling mechanism for indoor microbial communities. *Atmos. Environ.* **45**, 338-346.
 44. Özyıldız, F., Karagönlü, S., Basal, G., Uzel, A. and Bayraktar, O. 2013. Micro-encapsulation of ozonated red pepper seed oil with antimicrobial activity and application to nonwoven fabric. *Lett. Appl. Microbiol.* **56**, 168-179.
 45. Paddle-Ledinek, J. E., Nasa, Z. and Cleland, H. J. 2006. Effect of different wound dressings on cell viability and proliferation. *Plast. Reconstr. Surg.* **117**, 110S-120S.
 46. Pasquarella, C., Sansebastiano, G. E., Ferretti, S., Sacconi, E., Fanti, M., Moscato, U., Giannetti, G., Fornia, S., Cortellini, P., Vitali, P. and Signorelli, C. 2007. A mobile laminar air-flow unit to reduce air bacterial contamination at surgical area in a conventionally ventilated operating theatre. *J. Hosp. Infect.* **66**, 313-319.
 47. Purwar, R. and Joshi, M. 2004. Recent developments in antimicrobial finishing of textiles - A review. *AATCC Rev.* **4**, 22-26.
 48. Rahman, M. F., Wang, J., Patterson, T. A., Saini, U. T., Robinson, B. L., Newport, G. D., Murdock, R. C., Schlager, J. J., Hussain, S. M. and Ali, S. F. 2009. Expression of genes related to oxidative stress in the mouse brain after exposure to silver-25 nanoparticles. *Toxicol. Lett.* **187**, 15-21.
 49. Rai, M., Yadav, A. and Gade, A. 2009. Silver nanoparticles as a new generation of antimicrobials. *Biotechnol. Adv.* **27**, 76-83.
 50. Samberg, M. E., Oldenburg, S. J. and Monteiro-Riviere, N. A. 2010. Evaluation of silver nanoparticle toxicity in skin *in vitro* and keratinocytes *in vitro*. *Environ. Health Perspect.* **118**, 407-413.
 51. Sarkar, R. K., Purushottam, D. and Chauhan, P. D. 2003. Bacteria-resist finish on cotton fabrics using natural herbal extracts. *Indian J. Fibre Text. Res.* **28**, 322-328.
 52. Shin, Y., Yoo, D. I. and Min, K. 1999. Antimicrobial finishing of polypropylene nonwoven fabric by treatment with chitosan oligomer. *J. Appl. Polym. Sci.* **74**, 2911.
 53. Sim, K. M., Kim, K. H., Hwang, G. B., Seo, S., Bae, G. N. and Jung, J. H. 2014. Development and evaluation of antimicrobial activated carbon fiber filters using *Sophora flavescens* nanoparticles. *Sci. Total Environ.* **493**, 291-297.
 54. Singh, R., Jain, A., Panwar, S., Gupta, D. and Khare, S. K. 2005. Antimicrobial activity of some natural dyes. *Dye. Pigment.* **66**, 99-102.
 55. Soto, K., Garza, K. M. and Murr, L. E. 2007. Cytotoxic effects of aggregated nanomaterials. *Acta Biomater.* **3**, 351-358.
 56. Su, W. 1996. Indoor air pollution. *Resour. Conserv. Recycl.* **16**, 77-91.
 57. Sung, J. H., Ji, J. H., Yoon, J. U., Kim, D. S., Song, M. Y., Jeong, J., Han, B. S., Han, J. H., Chung, Y. H., Kim, J., Kim, T. S., Chang, H. K., Lee, E. J., Lee, J. H. and Yu, I. J. 2008. Lung function changes in Sprague-Dawley rats after prolonged inhalation exposure to silver nanoparticles. *Inhal. Toxicol.* **20**, 567-574.
 58. Takenaka, S., Karg, E., Roth, C., Schulz, H., Ziesenis, A., Heinzmann, U., Schramel, P. and Heyder, J. 2001. Pulmonary and systemic distribution of inhaled ultrafine silver particles in rats. *Environ. Health Perspect.* **109**, 547-551.
 59. Verdenelli, M. C., Cecchini, C., Orpianesi, C., Dadea, G. M. and Cresci, A. 2003. Efficacy of antimicrobial filter treatments on microbial colonization of air panel filters. *J. Appl. Microbiol.* **94**, 9-15.
 60. Walentowska, J. and Foksowicz-Flaczyk, J. 2013. Thyme essential oil for antimicrobial protection of natural textiles. *Int. Biodeterior. Biodegradation* **84**, 407-411.
 61. Wisser, D., Wisser, F. M., Raschke, S., Klein, N., Leistner, M., Grothe, J., Brunner, E. and Kaskel, S. 2015. Biological chitin-MOF composites with hierarchical pore systems for air-filtration applications. *Angew. Chemie Int. Ed. Engl.* **54**, 12588-12591.
 62. Woo, C. G., Kang, J. S., Kim, H. J., Kim, Y. J. and Han, B. 2015. Treatment of air filters using the antimicrobial natural products propolis and grapefruit seed extract for deactivation of bioaerosols. *Aerosol Sci. Technol.* **49**, 611-619.
 63. Wu, P. C., Li, Y. Y., Chiang, C. M., Huang, C. Y., Lee, C. C., Li, F. C. and Su, H. J. 2005. Changing microbial concentrations are associated with ventilation performance in Taiwan's air-conditioned office buildings. *Indoor Air* **15**, 19-26.
 64. Xu, Y., Raja, S., Ferro, A. R., Jaques, P. A., Hopke, P. K., Gressani, C. and Wetzel, L. E. 2010. Effectiveness of heating, ventilation and air conditioning system with HEPA filter unit on indoor air quality and asthmatic children's health. *Build. Environ.* **45**, 330-337.
 65. Yu, B. F., Hu, Z. B., Liu, M., Yang, H. L., Kong, Q. X. and Liu, Y. H. 2009. Review of research on air-conditioning systems and indoor air quality control for human health. *Int. J. Refrig.* **32**, 3-20.

초록 : 은나노 입자의 독성 메커니즘 및 천연물을 활용한 은나노 대체 항균 소재 연구

파티 카라데니즈 · 김한성*

(부산대학교 유기소재시스템공학과)

나노 입자는 화장품, 식품, 기계, 화학 산업 등에 다양한 용도로 활용되고 있으며, 그 응용분야가 광범히 하여 나노 입자 사용에 대한 관심과 연구가 지속적으로 증가하고 있는 추세이다. 특히 금속나노 입자 중 하나인 은나노 입자는 항균 및 항진균 효과가 뛰어나 의류, 실내 공기필터, 증류필터 등 다양한 방면에 활용되고 있다. 하지만 은나노 입자의 지속적인 노출 시, 입자 크기와 노출방식에 따라 인체에 독성을 유발하는 것으로 알려져 있어 친환경적이고 생물학적으로 안전한 천연물 유래 소재를 활용한 은나노 입자의 기술개발이 필요하다. 천연물이 적용된 실내필터와 의류는 생산의 용이성, 제품 내구성 및 항균 활성에서 은나노 적용제품과 비교될 수 있는 것으로 나타나고 있다. 본 연구에서는 은나노의 생체 내 미치는 독성 메커니즘에 대해 알아보고 은나노의 대안으로 항균 활성을 지닌 천연물의 항균 활성에 대해 기술하고자 한다.