Antimicrobial Plastics

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Introduction

Communicable diseases and pathogenic infections are the number one cause of human death worldwide [1]. People contract these infections when they come into physical contact with substances that contain germs - a general term, along with microbes, for bacteria, fungi, and viruses.

Therefore, it continues to be an important task to prevent the spread of germs between people, animals, and inanimate objects. Practicing basic hygiene, like washing ones' hands and regularly cleaning surfaces, has long been a simple way to stay healthy. Nevertheless, these methods are hardly perfect, and people still get sick from infections. Antimicrobial medicines are generally used to treat infection-related illness. However, not all germs succumb to medications; for example, methicillin-resistant *Staphylococcus aureus* (MRSA) is a strain of *S. aureus* that cannot be treated easily in vivo. For these reasons, complementary methods of preventing infections are under development.

One method is to inhibit bacteria before they can enter a biological system and cause infections. This approach has led to the development of antimicrobial materials that cause bacteria to die. These materials either directly kill microbes, a biocidal function, or stop the microbes from reproducing, a biostatic function. Both functions lead to the decline of the overall bacteria population. Figure 1 demonstrates the effectiveness of antimicrobial additives in plastics, in this case a sample of polyethylene gloves [2]. The gloves were infused with quaternary ammonium compounds (an antimicrobial agent) and analyzed over a period of 8 years. Microbiological analyses were performed on the gloves over this time to generate the data for Figure 1.

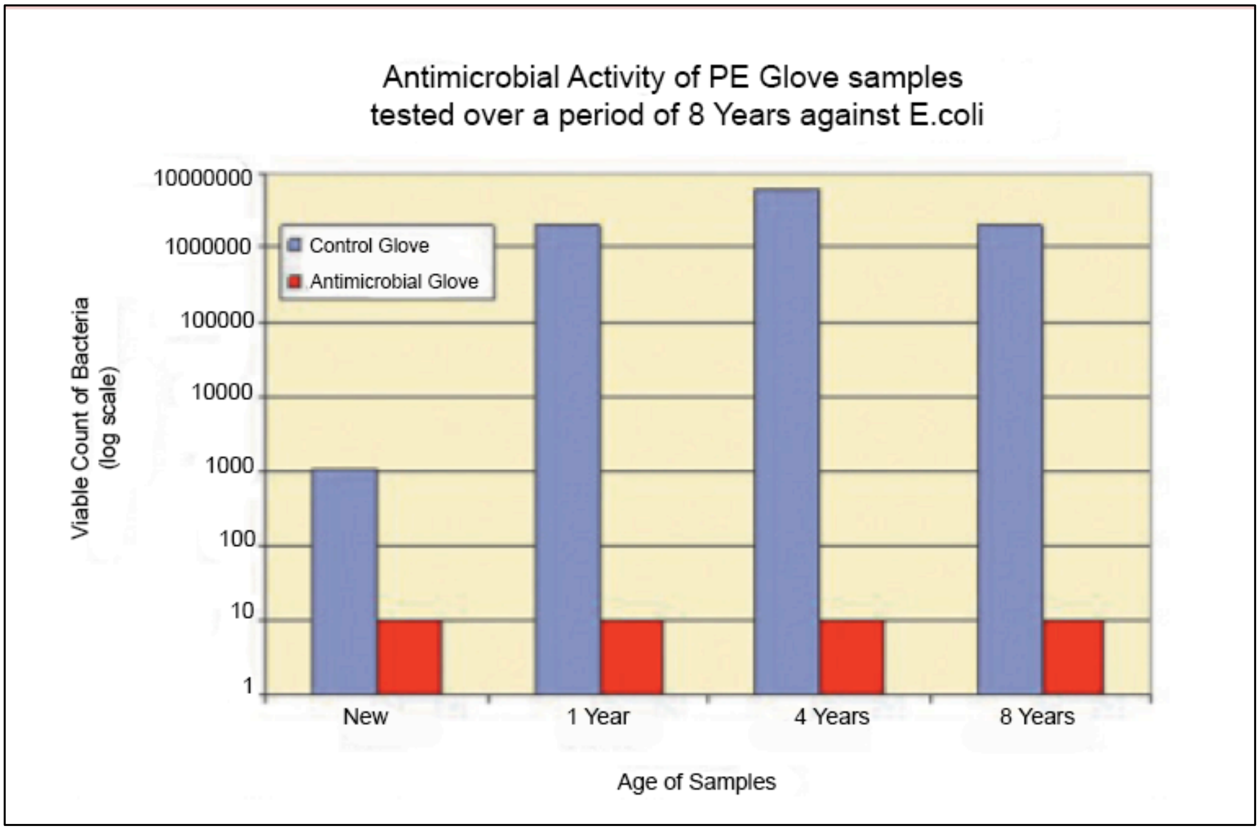

Figure 1: Effectiveness of antimicrobial compounds over an extended period of time

Plastics are one of the most common materials modified with antimicrobial properties because they are heavily used in applications that have a high-risk for germ transfer. For example, medical personnel often use devices composed of plasticized polyvinyl chloride (PVC). Antimicrobial compounds in plastics are intended "to reduce the microbial populations both within in the material and found at the surface" (antimicrobial systems and their uses in plastics).

Antimicrobial additives in consumer plastic products serve either one of two purposes: to preserve the function of a plastic, or to aid in a culture of hygiene. Microorganisms feed on the organic plasticizers used in materials like PVC, which degrades the product over time. The latter purpose is the one more commonly marketed to consumers. Antimicrobial products range from soaps to cutting boards, and are often meant to combat the microorganisms that cause communicable diseases. However, antimicrobial additives are indiscriminate; they inhibit benign and disease-causing bacteria equally. Scientists are concerned that the production of antimicrobial goods has resulted from and is propagating to a culture of extreme cleanliness, in which mysophobia (colloquially "germaphobia") is prevalent. Japan has become a commonly cited example of this phenomenon. The overuse or improper use of antimicrobial agents may cause the selection of bacteria that are resistant to even *in vitro* methods of inhibition, causing an additional health concern.

Antimicrobial Compounds

All antimicrobial compounds are regulated through either the Food and Drug Administration (FDA) or the Environmental Protection Agency (EPA). The FDA controls those additives that are used in products that are intended for use on or in the body, like antimicrobial soaps or food packaging. The EPA manages the products that do not fall under the FDA jurisdiction.

Antimicrobial chemicals used in plastics can be classified as organic or inorganic compounds. Each group of compounds has its own advantages and limitations as to how it can be used in consumer products.

Organic Compounds

Organic-based antimicrobial systems have low molecular weight and may contain a metal ion. They do not chemically interact with the polymer chains, but they diffuse through the plastic material. Equilibrium is achieved between the concentration of the antimicrobial additive at the surface of the material and that within it. As antimicrobial compounds are depleted from the surface and lost to the environment (usually by wiping or washing), the supply within the material moves outward and replenishes the surface's antimicrobial properties. This allows the material to have a very high activity rate and to interact with large numbers of microbes very quickly. On the other hand, the lifetime of the material can be limited. Therefore, these additives are commercially best suited for items that are disposable.

The mobility of organic antimicrobial compounds makes it undesirable for use in products like food packaging, which is regulated by the FDA. Organic compounds are highly soluble in food, and this property would potentially allow antimicrobial agents to enter the biological system through food. This poses various health risks, especially because antimicrobial agents can target the beneficial bacteria in the human body.

Temperature changes can further limit the viable applications of organic additives. At high temperatures, organic-based antimicrobial systems tend to leach additives more easily to the environment. Also, few organic additives can withstand the high temperature used to manufacture most plastics. Therefore, organic antimicrobial additives are best used in materials that do not require heat treatment and are not used at high temperatures. ("choosing antimicrobial additives [2]).

An example of a widely used antimicrobial organic compound is triclosan (2,4,4'-trichloro-2'-hydroxydiphenyl ether). It is one of the main additives in the line of consumer plastics called Microban(R). Its structure is given in Figure 2. Triclosan inhibits bacterial fatty acid synthesis at the enoyl-acyl carrier protein reductase step, which has disruptive effects on cell growth and function ("Mechanism of Triclosan..."[3]). This causes it to have biostatic properties at lower concentrations and biocidal properties at high concentrations. Triclosan is effective against staphylococci, streptococci, mycobacteria, and *Ecsherichia coli*; it is only somewhat effective against MRSA strains. It is used in a 2% solution as a decolonizing agent for patients who have excessive MRSA on their skin ("Triclosan" [4]). Triclosan is one of the few organic additives that can be processed at higher temperatures; it enjoys popularity as an antimicrobial agent ("Polymeric materials..." [5]).

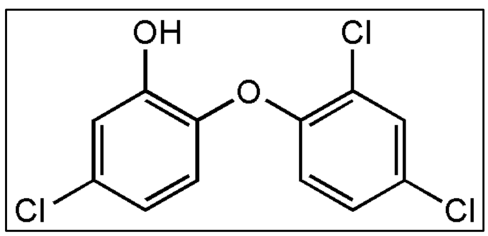

Figure 2: Chemical Structure of Triclosan

Inorganic Compounds

Inorganic antimicrobial agents use metal-ion complexes. The most popular and widely studied metal ion for these purposes is silver (Ag^{+}). Silver nanoparticles are known for their high activity against a broad range of microorganisms: bacteria, fungi, and viruses. Silver is also considerably more toxic towards microbes than towards mammalian cells ("Polymeric materials..."[5]). Silver ions can perform a variety of biostatic functions on a bacterial cell. The primary mechanism is to bind to the cell membrane and disrupt the cell's ability to transport molecules in and out of the cell.

Inorganic antimicrobial additives have some distinct advantages over their organic counterparts. Inorganic compounds have little mobility within a material. They rely on matrix systems like titanium dioxides to undergo ion exchange at the surface of the plastic ("Choosing Antimicrobials..."[2]). As a result, the additives remain within the material for its lifetime, giving it more durable antimicrobial properties. Inorganic systems also have high thermal stability. Inorganic compounds can also cause significant discoloration of a material, which is undesirable if the aesthetics of the material is important. Moreover, some systems that rapidly release silver nanoparticles can cause increased toxicity and excessive discoloration from oxidization by the matrix molecules.

Although silver-ion additives are extremely effective, other inorganic systems are under evaluation. One study compares the efficacy of selenium (Se) nanoparticles in PVC used in biomedical devices to that of silver nanoparticles [6](Tran, Webster). Evaluation of a compound's antimicrobial properties includes qualitative and quantitative analytical methods, conducted generally through zone of inhibition analysis[1] and viable count analysis[2]. MRSA is often the strain of choice for these tests. Tran and Webster found that the presence of selenium decreases the bacterial density on the plastic substrates (polyurethane (PU), PVC, and silicone). Further, their method of coating PVC with Se nanoparticles produced samples that had greater antimicrobial properties than commercially available Ag-coated PVC.

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[1] Zone of inhibition testing is a qualitative analytical method used in microbiology. A circular sample of a substrate coated with antimicrobial substances is placed on an agar media plate evenly covered with microbes and incubated under conditions for optimal microbe growth. A ring of no growth forms around the antimicrobial substrate, and the diameter of this ring is proportional to the log concentration of the antimicrobial compound.

[2] Total viable count is a quantitative analytical method in microbiology. A suspension of microbes is diluted in a solution that neither harms nor promotes the growth of the microbe. The dilution is then plated, and the number of colonies that formed can easily be counted and scaled up to account for the dilution.

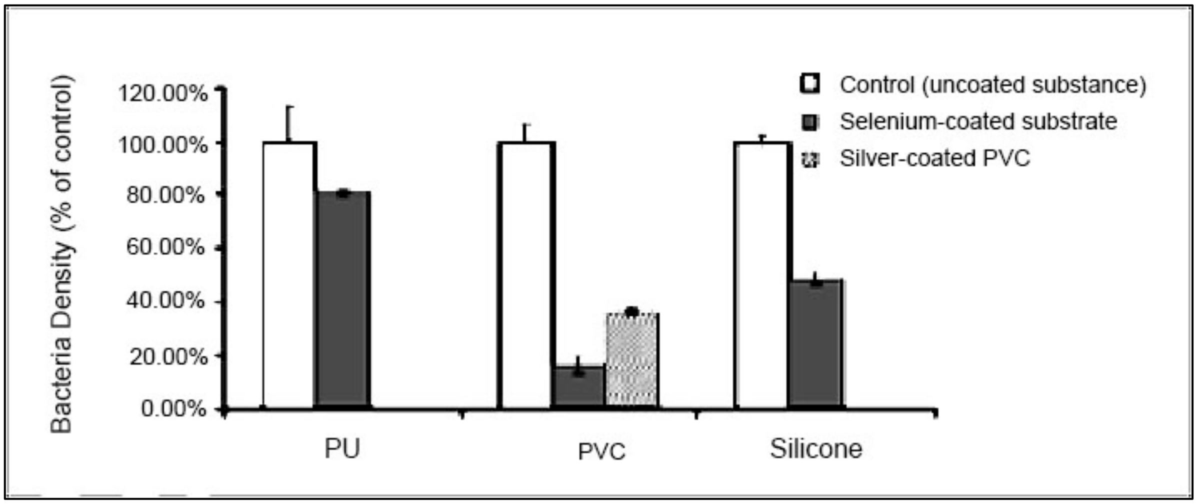

Figure 3: Percent reduction in bacterial density due to Se coating. The Se coating is more effective than Ag coating for the PVC substrate.

Figure 3 shows a bar graph of Tran and Websters' findings. This graph indicates that compared to the control plastic substrate, all samples of plastic that were coated with antimicrobial additives experienced a reduction of bacterial growth, quantified by viable count on the substrate. The varying percentage decreases of bacteria growth for each of the Se-coated plastics were found to have a direct correlation to the Se nanoparticle density on the surface of the plastic; that is, a lower Se nanoparticle density could be associated with a smaller decrease in bacteria growth. Moreover, the variance in percent reduction between Se-coated PVC and Ag-coated PVC indicates that the experimentally created samples had better antimicrobial properties than what was commercially available. The trials for each sample were conducted in triplicate, and 95% error margins were used in composing Figure 3.

Applications

Antimicrobial plastics can be used in a diverse set of widely-used consumer products, as discussed below.

Antimicrobial credit cards and ID cards

A patent was filed in November 2008 with the US Patent Office reporting the invention of "Antimicrobial credit cards, identification cards, membership cards and identification badges and badge holders" by Lisa Holmes [7]. In her patent, Holmes identified that plastic credit cards come into contact with multiple people and surfaces on a daily basis; they are therefore a medium for the transfer of microbes between people and places. Holmes invented a system using antimicrobial additives in the plastics used to form the cards. An alternate method is a transparent coating of PVC or an acrylic polymer that contain antimicrobial compounds. Holmes suggests using either organic or inorganic additives, or a mixture of both, including triclosan and silver zeolite (crystalline aluminosilicate). Holmes' intention is to create cards that not only have strong antimicrobial properties, but also to create a polymer-additive system that benefits the durability and functionality of the plastic card. The inventor now owns the company Antimicrobial Credit Cards and Identification Badges for distributing her products.

Antimicrobial Belts

In February 2013, a patent was filed by Barry Chapman with the US Patent Office reporting the invention of an "Antimicrobial Strap" [8]. Chapman intended the invention to be used in consumer products like shopping cart straps, purse straps, seat belts, and helmet straps, and as functional barriers in public areas like airports and banks. The invention was for antimicrobial agents integrated into the exposed surfaces of a flexible, non-porous plastic strap. One of the possible antimicrobial additives claimed by the patent is an oxidizing agent of a photocatalyst mixture of zinc oxide nano-particles on a matrix of titanium dioxide. This can be recognized as an inorganic antimicrobial system that inhibits the microbes by oxidizing them. Organic compounds like rifamycin and its derivatives were also claimed as possible antimicrobial additives. The additives could be either adsorbed or bonded covalently to the polymer network as a coating over the plastic. A heated plasma spray mechanism was proposed for the coating of the polymer network. A mixture of polymer and antimicrobial additive would be melted and then atomized into an atomized spray to be coated uniformly on the plastic. The inventor is owner of Chapman Medical Products, LLC, which manufactures child restraint belts for shopping carts among other antimicrobial products.

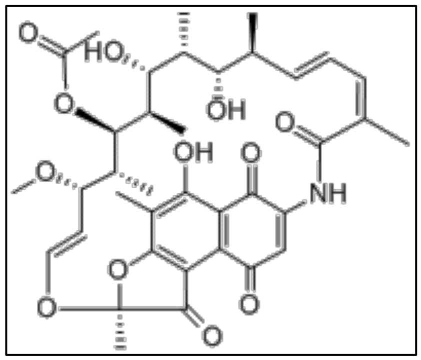

Figure 4: Molecular structure of rifamycin

A Culture of Antimicrobial Products

The use of antimicrobal products has increased significantly in the last ten years. The market for biocides in North America was $73 million in 2001, with an expected market growth rate of 3% through 2006 [9]. In September, a consumer report was published stating that the market for antimicrobial chemicals and disinfectants was expected to grow 6% annually to $1.6 billion by 2017 in the United States alone [10]. The increase in demand of antimicrobial products is partially dependent on the growing economy (in the construction industry, antimicrobial additives can be put in paints as well as plastics), but a strong driving force is a growing public anxiety about pathogenic microorganisms.

Consumers are bombarded with messages about the dangers of germs. News channels often feature stories about "superbugs" in hospitals and food poisoning due to contaminated crops. The natural response is an elevated fear of contracting terrible diseases from everyday activities. In a lecture in 2001, Stephen Levy described the number of antimicrobial products available on the market to increase from a few dozen in the mid-1990s to over 700 in 2001 [11].

Mysophobia is the term for the fear of dirt, germs, and other contaminating agents. Unfortunately there exists no statistics specifically on this psychological condition, since it is often paired with obsessive-compulsive disorder (OCD) tendencies. Therefore, the overall preoccupancy with cleanliness must be analyzed from a cultural standpoint.

For example, Japan - the world's largest consumer of antimicrobial products [12] - has had increasing outbreaks of infection from the Epstein-Barr virus in the past couple generations [13]. Past generations of Japanese people developed the necessary antibodies for the infection in their youth when they shared food with siblings and contracted the virus from transferred saliva. However, as a culture of hygiene has become encouraged, these natural vaccinations no longer occur.

Human and Environmental Impacts of Antimicrobial Compounds

The use of biocides in various industries and in the home has increased over the past decade (Lagaron[14]). Consumers have been encouraged to buy antimicrobial products with biocidal properties to use as a part of daily cleaning practices. This runs the risk of the improper uses of biocides, which can then lead to an increased tolerance to the antimicrobial agents. For example, use of a product below its required concentration, or not using a product in a sustained manner, can cause selectivity of the tolerant bacteria. Genetic selection occurs when environmental factors encourage the survival of certain organisms over others, leading to the evolution of a more tolerant species. In the context of antimicrobial selection, the microbes that have genetic mutations that enable them to survive in an antimicrobial environment will reproduce to form a new species of microbe that is resistant to that antimicrobial mechanism.

Tolerance is characterized by extensive changes in the cellular mechanisms targeted by antimicrobial agents. These changes could be unregulated pumps in the cell wall, or a decrease in cell wall permeability. There are three types of developed tolerance: intrinsic (in which the bacteria develops methods to decrease the concentration of the biocide within the cell), extrinsic (when the bacterial chromosome undergoes extensive mutation), and adaptive (where the bacterial phenotype is changed).

The use of antimicrobial agents can also have environmental impacts. These compounds, when used excessively, can accumulate in the environment, and potentially kill or mutilate organisms, disrupt the food chain, and cause the selection of tolerant microorganisms in certain ecosystems. For example, triclosan is an antimicrobal compound used extensively in Europe - 350 tons annually. Although it can be degraded through several natural mechanisms, studies show that it continues to accumulate in water and soil beyond its predicted no effect concentration (PNEC). The PNEC defines a limit of what a safe concentration is. Although it does not seem to have an effect on certain species (the algae *Scenedesmus sbspicatus,* and rainbow trout), it poses an environmental concern that must be addressed. Elevated levels of antimicrobial agents in the soil could promote increase antimicrobial resistance in the environment [15].

Moreover, studies have been conducted that show that antimicrobial household products may not be as effective as they are marketed to be. In a year-long double-blind trial conducted by Larson et al, households were randomly assigned a cleaning regimen with products that either included antimicrobial agents like triclosan or products without those additives [16]. Microbial cultures were taken from the hands of those members of the household who self-identified as being primary caregivers. The study indicated that there was no difference in the microbial flora at the baseline and the termination of the trial. Thus, there was no evidence to indicate that antimicrobial products decreased the bacteria present in a given household.

Conclusion

Antimicrobial products propagate a culture of extreme cleanliness, however the actual effectiveness of these products in reducing bacteria in a household setting is not proven. Scientists developing antimicrobial products must take into consideration the in vivo usage of the products. However, there are risks associated with antimicrobial agents, namely the selection of microbes that are tolerant to a range of antimicrobial additives.

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