

# • Characteristics and Applications of Silver-based Inorganic Antimicrobial Agent “NOVARON”

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## 1. Introduction

In recent years, there has been a growing trend toward cleanliness, especially among the younger generation. In addition, serious social problems such as nosocomial infections caused by MRSA, food poisoning caused by pathogenic *E. coli* O-157, and *Legionella pneumophila* causing pneumonia, which became a problem with 24-hour baths, have resulted in an ever-increasing demand for antimicrobial products.

We developed the silver-based inorganic antimicrobial agent “NOVARON” and launched it in 1993. NOVARON comes as uniform, fine particles, and it is used in a wide range of applications because of its superiority in terms of good processability into fibers and resins, and excellent discoloration resistance, etc. This article covers the definition and classification of antimicrobial agents, the antimicrobial mechanisms and applications of NOVARON, and industry initiatives for antimicrobial products.

## 2. What is “antimicrobial”?

There are many different terms related to the antimicrobial field, such as pasteurization, sterilization, microorganism elimination, and antimicrobial activity. Although they are not clearly differentiated in general use, they are defined as shown in Table 1<sup>1)</sup>. In this context, “antimicrobial” is defined as a broad concept that includes pasteurization, sterilization, and disinfection.

Table 1: Definitions of antimicrobial action terms

Term	Definition
Sterilization	To kill or remove all microorganisms from a target object, and the broad definition includes pasteurization and microorganism elimination
Pasteurization	Simply to kill microorganisms in contrast to sterilization meaning killing of all microorganisms
Disinfection	To kill specific microorganisms that are pathogenic to humans and livestock and to prevent infection, but does not mean killing of all microorganisms
Disinfection (Removal of microorganism)	In general, it means the removal of microorganisms from the target object, and includes microorganism elimination by filtration, microorganism elimination by sedimentation, and microorganism elimination by washing. According to the Japanese Pharmacopoeia, complete microorganism elimination by filtration is considered a type of sterilization
Microbiostasis	To inhibit or prevent the proliferation of microorganisms
Preservation	To prevent deterioration of food, pharmaceuticals, cosmetics, and other materials due to harmful microorganisms
Sanitize	Refers to the killing of pathogenic nutrient cells and reduction of other microorganisms in food plants. “Sanitation” may be interpreted as synonymous with food hygiene and environmental hygiene
Antimicrobial and Antifungal	In general, antibacterial refers to the inhibition of proliferation and killing of bacteria, and antifungal refers to the inhibition of proliferation and killing of fungi
Antimicrobial	Refers to all of the following: pasteurization, sterilization, disinfection, microorganism elimination, bacteriostasis, sanitization, etc.

## 3. Classification of antimicrobial agents

Antimicrobial agents can be broadly classified as organic or inorganic. The former has been in use throughout history and their structures vary widely. While we will not describe their antimicrobial activity here, it varies depending on the functional groups they contain. The latter mostly consist of either metals that exhibit antimicrobial activity, or metal ions supported on inorganic carriers. Table 2 shows the antimicrobial actions of the major metal ions<sup>2)</sup>, and it is clear that the majority of inorganic antimicrobial agents use silver,

which is highly active and safe. Although copper and zinc are also used, their antimicrobial activity is 1/10 that of silver or less and they are often used as secondary ingredients.

Table 2: Minimum inhibitory concentration (MIC) (mol/l) of various metal ions against *Salmonella typhi*

Metal ion	Ag <sup>+</sup>	Hg <sup>2+</sup>	Cu <sup>2+</sup>	Cd <sup>2+</sup>	Au <sup>2+</sup>	Co <sup>2+</sup>	Ni <sup>2+</sup>	Pb <sup>2+</sup>
MIC	2.0x10 <sup>-6</sup>	2.0x10 <sup>-6</sup>	1.5x10 <sup>-5</sup>	6.0x10 <sup>-5</sup>	1.2x10 <sup>-4</sup>	1.2x10 <sup>-4</sup>	1.2x10 <sup>-4</sup>	0.005

Metal ion	H <sup>+</sup>	Fe <sup>3+</sup>	Al <sup>3+</sup>	Zn <sup>2+</sup>	Mn <sup>2+</sup>	Ba <sup>2+</sup>	Ca <sup>2+</sup>	Na <sup>+</sup>
MIC	0.001	0.001	0.001	0.001	0.12	0.25	0.5	1.0

Table 3: Major inorganic antimicrobial agents

- Silver-zeolite
- Silver-zirconium phosphate
- Silver-calcium phosphate
- Silver-calcium apatite
- Silver-silica gel
- Silver-calcium silicate
- Silver-magnesium aluminosilicate
- Silver-titanium dioxide
- Silver-potassium titanate
- Silver-silica, alumina
- Silver-soluble glass
- Silver-thiosulfite

We believe the key technical points for inorganic antimicrobial agents to be how we can prepare a carrier that would carry silver, and how we can make good use of secondary components to improve discoloration resistance and lower the cost. Table 3 shows major inorganic antimicrobial agents that have been proposed.

## 4. Characteristics and types of NOVARON

NOVARON is hexagonal zirconium phosphate, an inorganic ion exchanger, loaded with silver ions by ion exchange. Fig. 1 shows its crystal structure. An octahedron of oxygen atoms with zirconium at the center and a tetrahedron of oxygen atoms with phosphorus at the center are three-dimensionally linked by sharing oxygen atoms, and silver ions exist in the cavities inside the skeleton.

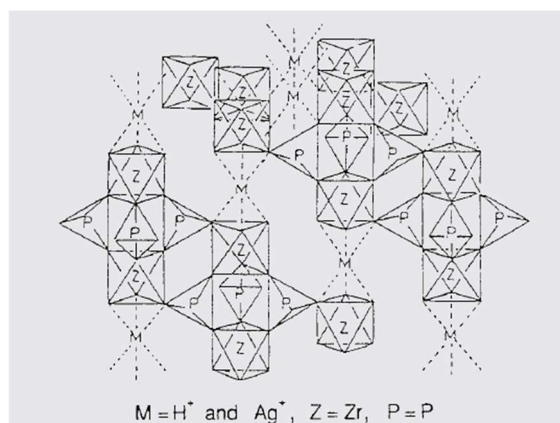


Figure 1: Crystal structure of NOVARON



**Figure 2: Scanning electron microscope photograph of NOVARON AG300**

Fig. 2 shows a scanning electron microscope photograph of NOVARON AG300. Since NOVARON is composed of highly heat-resistant, homogeneous fine particles with low moisture content, it can be used in most applications, including molded plastic products, fibers, paints, and ceramics. The amount of silver ion elution is extremely small, and although discoloration may occur in some cases depending on specific chemicals and conditions, in most cases, the product has excellent resistance to

coloring and discoloration.

At present, we have four standard grades of NOVARON called “AG300,” “AG1100,” “AGZ330,” and “AGT330” (Table 4). We also offer “MZ Series,” masterbatches for polyolefin resins (Table 5).

**Table 4: Grades of NOVARON**

Grade	AG300	AG1100	AGZ330	AGT330
Appearance	White powder	White powder	White powder	White powder
Particle diameter $\mu\text{m}$	0.9	0.9	1.3	0.5
True specific gravity	3	3	4	-
Apparent specific gravity	0.2	0.2	0.3	0.3
Moisture content %	< 1	< 1	< 1	< 1
Main applications	Fibers, films, transparent resins	Fibers, films, transparent resins	Molded resin products (excluding PVC)	Molded PVC products

**Table 5: NOVARON masterbatches**

Grade	MZE1100	MZP6100 7100 7101
Resin	Low-density polyethylene	Polypropylene
MI *1	8	11
Antimicrobial agent	AGZ330	AGZ330
Content %	10	10
Appearance	White pellets	White pellets

\*1: Melt Index

## 5. Antimicrobial effects of NOVARON

NOVARON has been confirmed to have a broad antimicrobial spectrum against various microorganisms. Table 6 shows the minimum inhibitory concentration (MIC) of representative grades AG300 and AGZ330 against various microorganisms. MIC indicates the minimum concentration of chemicals required to prevent the division and proliferation of microorganisms under specific test conditions, and the antimicrobial activity is higher as the value is smaller. Table 7 shows the MIC of NOVARON against methicillin-resistant *Staphylococcus aureus* (MRSA), which is resistant to various antimicrobial agents. This value is equivalent to that against the normal methicillin-sensitive *Staphylococcus aureus* (MSSA), showing that NOVARON is also effective against MRSA.

It should be noted that there is no unified MIC measurement method for insoluble inorganic antimicrobial agents, that the value may vary depending on the method and evaluating conditions, and that MIC and antimicrobial property of antimicrobial-processed products do not sweepingly correlate with each other due to differences in resin types, processing methods, evaluation methods, etc.

Fig. 3 shows the antimicrobial test on NOVARON against *Legionella* bacteria. We added *Legionella* bacteria solution to sterile phosphate buffer solution in which AG300 was suspended, stirred it at 25°C for a predetermined time, and measured the changes in the bacterial count over time. Based on these results, the antimicrobial effect against *Legionella* bacteria is considered to be about the same level as its effect against *Escherichia coli*.

**Table 6: Minimum inhibitory concentration of NOVARON against various microorganisms**

Test microbial strain	AG300	AGZ330
<i>Escherichia coli</i>	125 ppm	125 ppm
<i>Escherichia coli</i> IFO 3301		
<i>Escherichia coli</i> O-157:H7	200	200
<i>Escherichia coli</i> ATCC 043888		
<i>Pseudomonas aeruginosa</i>	125	250
<i>Pseudomonas aeruginosa</i> IID P-1		
Salmonella	250	250
<i>Salmonella typhimurium</i> laboratory isolate		
<i>Staphylococcus aureus</i>	250	250
<i>Staphylococcus aureus</i> IFO 12732		
MRSA Kyoto Microbio Laboratory isolate, methicillin-resistant <i>S. aureus</i>	250	250
<i>Bacillus subtilis</i>	250	250
<i>Bacillus subtilis</i> ATCC 6633		
<i>Candida</i> yeast	500	250
<i>Candida albicans</i> IFO 1594		
<i>Saccharomyces</i> yeast	500	250
<i>Saccharomyces cerevisiae</i> IFO 1950		
<i>Cladosporium</i>	500	500
<i>Cladosporium cladosporioides</i> IFO 6348		
<i>Aspergillus niger</i>	1,000	500
<i>Aspergillus niger</i> IFO 6341		

**Table 7: MIC of NOVARON AG300 against various MRSA**

MRSA strain	MIC
NCTC 10442	125 ppm
64/4176(U.K.)	125
86/9302(U.K.)	125
85/1340(Ugoslavia)	125
85/3566(Holland)	62.5
85/5495(South Africa)	62.5
85/9580(South Africa)	125
85/1774(Italy)	62.5
85/3619(Austria)	62.5
85/4231(Canada)	125
85/4547(Israel)	125
85/2232(USA)	125
85/2235(USA)	125
87/25(Japan)	125
81/108(Japan)	125
(Reference) MSSA 209p	125

(Test method: Liquid culture medium dilution method)

## 7. Safety of NOVARON

As shown in Table 9, NOVARON has been confirmed to be highly safe. Since NOVARON is a fine inorganic powder, it may cause primary physical irritation as a foreign substance when it enters the eyes in a similar fashion to dust and sand, and inhalation into the respiratory system is also undesirable in a similar fashion to general dust. Therefore, depending on the conditions of use of NOVARON, protective equipment such as safety glasses and dust masks, as well as local exhaust ventilation equipment, need to be used.

**Table 9: Results of safety tests on NOVARON**

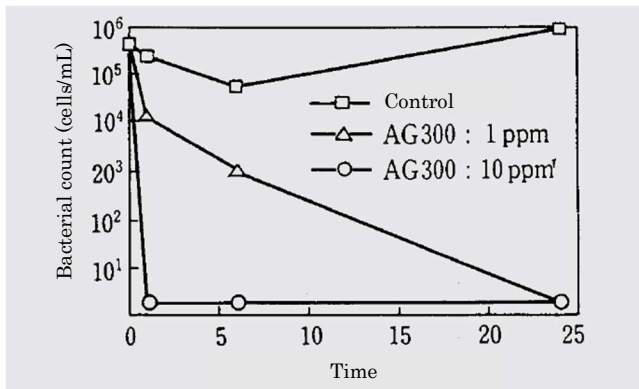
Test item	AG300	AGZ330	
Mutagenicity test	Negative	Negative	
Acute oral toxicity (rat)	LD <sub>50</sub> > 5,000 mg/kg	Untested	
Acute oral toxicity (mouse)	LD <sub>50</sub> > 5,000 mg/kg	LD <sub>50</sub> > 5,000 mg/kg	
Acute dermal toxicity (rat)	2,000 mg/kg or more	Untested	
Primary skin irritation (rabbit)	Weakly irritating PII=0	Weakly irritating PII=0	
Skin sensitization (guinea pig)	Not observed	Untested	
Kawai method skin patch test (human)	Quasi-negative (5% Vaseline dilution)	Untested	
Apparatus and containers/packaging standard test, Ministry of Health and Welfare Notification No. 370	100°C or less	Suitable for PE and ABS with 1% addition	Suitable for PE and PP with 1% addition
	100°C or higher	Untested	Suitable for PE with 1% addition

## 8. Evaluation methods and standards for antimicrobial agents and processed products

### 8.1 Textile processed products

The first antimicrobial product was a pair of socks with antimicrobial processing that was released in 1980. Among antimicrobial products, textile products have a relatively long history, and there have been extensive studies on antimicrobial activity evaluation methods and standards. The Japan Association for the Functional Evaluation of Textiles (formerly known as the Association of Sanitary Processing for Textile Products, abbreviated as SEK), organized by manufacturers of fibers, textiles, and antimicrobial agents, has developed two antimicrobial activity evaluation methods called the "shake flask method" and the "microbial count method," and permits the indication of SEK Mark on textile products that meet the standards for antimicrobial activity and safety. In the shake flask method, 0.75 ± 0.05 g of the sample is placed in 75 ml of a suspension of *Klebsiella pneumoniae* or *Staphylococcus aureus* with the bacterial count adjusted to 1 to 2 × 10<sup>4</sup> cells/ml, and the viable cell count is measured after shaking it for 1 hour at 25 ± 5°C. If the bacterial reduction rate is 26% or higher, the product is considered effective. In the microbial count method, the viable cell count is measured by placing a piece of sample cloth in a 30 ml vial, inoculating 0.2 ml of a suspension of *Klebsiella pneumoniae* or *Staphylococcus aureus* with a bacterial count adjusted to 5 to 30 × 10<sup>5</sup> cells/ml, and leaving the vial at 35 to 37°C for 18 hours. If the difference (logarithm) from the viable cell count of the unprocessed product is 1.6 or more, the product is considered effective.

SEK is also working to develop new antimicrobial activity evaluation methods that improve on the above methods by subdividing antimicrobial properties and safety evaluation methods and standards for different applications, such as



**Figure 3: Antimicrobial activity test on NOVARON AG300 against *Legionella* bacteria**

**Table 8: Resistance acquisition test on NOVARON (MIC)**

Number of cycles	MRSA NS455	<i>Pseudomonas aeruginosa</i> IIDP-1
1	250 ppm	125 ppm
2	250	125
3	250	125
4	250	62.5
5	250	125
6	250	125
7	250	250
8	125	125
9	250	250
10	250	250

Table 8 shows the results of resistance acquisition tests against MRSA and *Pseudomonas aeruginosa* in 10 repeated uses. We observed no change in the MICs of the two bacteria, and there was no emergence of resistant bacteria within the test conditions.

## 6. Antimicrobial mechanism of NOVARON

The antimicrobial mechanism of NOVARON has been examined in detail by Kourai et al.<sup>3,4</sup>. In their examination, they investigated the difference in antimicrobial effect by the presence of light (tungsten lamp) in oxygen and nitrogen atmospheres. As a result, the antimicrobial effect improved in the presence of oxygen and light, even though NOVARON showed antimicrobial actions without oxygen or light. They also studied the effect of changes in illuminance on antimicrobial action, and found that the antimicrobial action increased as illuminance increased. In addition, they studied the generation of active oxygen species in air, oxygen, or nitrogen atmosphere under light or no light, and confirmed that active oxygen was generated only when there was light irradiation in air or oxygen. It has been reported that the coexistence of superoxide dismutase, an enzyme that removes reactive oxygen species, and catalase, a hydrogen peroxide-degrading enzyme, significantly weakens the antimicrobial activity.

Although the elution of silver ions from NOVARON is very small, its solubility has been found to increase with chemicals such as sodium hydroxide and nitric acid. It has also been reported that silver ions elute from NOVARON in the presence of amino acids, proteins, nucleic acids, and alkali-modified *Escherichia coli*<sup>5</sup>.

Based on these facts, it is presumed that the antimicrobial action of NOVARON is delivered by both active oxygen (including hydroxyl radicals) generated by NOVARON itself in the presence of light and water, and silver ions eluted from NOVARON.

Many studies have been conducted on the antimicrobial mechanism of silver ions. Although the details have not been fully elucidated, the prevailing theory is that it acts on the -SH group of cysteine and inhibits the activity of a group of enzymes, mainly in the respiratory chain.

hospital and general use.

In evaluating the antimicrobial activity of antimicrobial products, the following points should be noted. In addition to the above methods, there are various other evaluation methods such as the drop method, sprinkling method, and pressure-adhesion method, and the conditions at the time of testing are not uniform (initial bacterial count, nutrient concentration of the test medium, test temperature, etc.). With the current testing methods, different testing organizations, methods, and conditions may significantly change the test results. Therefore, it is not very meaningful to directly compare data from different testing organizations and methods. It is necessary to carefully select appropriate test methods and conditions for antimicrobial products to make sure that the antimicrobial activity figure alone does not take on a life of its own.

## 8.2 Molded processed products

Because imparting antimicrobial property to molded plastic products is relatively new, and the applications and related industries are so diverse, evaluation standards comparable to those for textile products have hardly been developed.

Although antibacterial and antifungal test methods applicable to plastics, ceramics, and coating films are also defined in JIS standards, these methods should not be applied to inorganic antimicrobial agents, as they are better suited for evaluating conventional organic antimicrobial agents. Since most products processed with inorganic antimicrobial agents are low-elution, contact-type products, an evaluation method from a different viewpoint is needed. The Workshop on Silver and Other Inorganic Antimicrobial Agents, organized by 19 silver antimicrobial agent manufacturers including our company and the Japan Food Research Laboratories, developed the "film adhesion method" as an antimicrobial activity evaluation method, and proposed a standard for confirming antimicrobial activity: under specified test conditions, the viable cell count on the antimicrobial-treated product must be 1% or less of that on the untreated product. Although the test conditions are specified in detail, an overview is given below. In this method, the surface of the test piece is inoculated with 0.5 ml of a suspension of *Escherichia coli* or *Staphylococcus aureus* prepared at  $2 \text{ to } 10 \times 10^5$  cells/ml, covered with a film, and the viable cell count is measured after keeping it under conditions of relative humidity 90% or higher and  $35 \pm 1^\circ\text{C}$  for 24 hours.

For consumers, what is most important is the antimicrobial activity and safety of the actual product, not the antimicrobial activity of the antimicrobial agent itself. Therefore, the Workshop on Silver and Other Inorganic Antimicrobial Agents decided to expand its organization and create an organization that can be widely participated in by antimicrobial products and related industries, and changed its name to the "Society of International sustaining growth for Antimicrobial Articles" in December 1997. This society will actively promote the correct spread of antimicrobial products which ensure better quality and safety, which have less impact on the environment, and which can coexist with microorganisms, in order to contribute to the improvement of the quality of life.

## 9. Applications of NOVARON

As shown in Table 10, NOVARON has been examined for numerous applications. It has already been used in most of these applications. We will show the main applications in the following sections.

### 9.1 Application to fibers

As mentioned above, NOVARON can be kneaded into most fibers because it is a fine particle that contains little moisture. We prepared 6-nylon fiber with addition of 1% NOVARON AG300 by melt-spinning. We evaluated the antimicrobial activity by the shake flask method and found that it exhibited a bacterial reduction rate of 99.9% or more. It maintained the bacterial reduction rate of 99.9% or more even after washing it 100 times according to the method in JIS L0127103, indicating a high durability.

**Table 10: Uses of NOVARON**

Term	Definition
Home appliance products	Dishwashers, refrigerators, washing machines, pots, cooling fans, TVs, telephones, PCs, radio cassette recorders, cameras, video cameras, water purifiers, rice cookers, cutters, cash registers, futon dryers, fax machines, exhaust fans
Kitchenware	Tableware, cutting boards, molds for cutting, trays, chopsticks, tea servers, thermos bottles, kitchen knives, ladles/knife handles, cooking utensils, lunch boxes, rice scoops, bowls, drainage baskets, triangular corners, scrubber receptacles, garbage baskets, drainage bags
Textile products	Shower curtains, futon cotton, air conditioner filters, pantyhose, wigs, zippers, white lab coats, towels, handkerchiefs, hand towels, sheets, futon ticking, pillows, gloves, aprons, curtains, pajamas, diapers, bandages, masks, sportswear
Building materials Housing	Decorative boards, wallpaper floorboards, furniture, tablecloths, window film, handles, mats, carpets, desk mats, artificial marble, handrails, shower nozzles, joints, wax
Toiletries	Toilet seats, tubs, tiles, potties, sanitary waste receptacles, toilet brushes, bath corners, bathtub covers, pumice stones, soap containers, chairs, clothes baskets, shower heads, tubes, washstands
Paper products	Medicine wrapping paper, medicine boxes, sketchbooks, origami, medical records
Leather products	Bags, shoes, watch bands, interior products, upholstery, chairs, gloves, straps, belts
Toys	Dolls, stuffed animals, paper clay, origami, blocks, puzzles
Stationery	Mechanical pencils, ballpoint pens, pencils, erasers, rulers, desk pads, ink erasers, staplers, file folders, magic markers, crayons, writing paper, notebooks, floppy disks, floppy cases
Others	Insoles, cosmetic containers, scrubbers, cosmetic puffs, hearing aids, musical instruments, cigarette filters, adhesive sheets for cleaning, grips for straps, sponges, wet wipes, kitchen towels, cards, microphones, corks, barber shop supplies, vending machines, razor blades, soap, bags, culturing containers, fruit bags, dentures, scales, thermometers, stethoscopes, slippers, clothes cases, toothbrushes, silos, sand, food packaging film, packaging bags, sprays

We carried out melt-spinning of polyester filament (2 denier) with addition of 1% NOVARON AG300 using the 10% masterbatch. Evaluation of its antimicrobial property by the microbial count method confirmed that the fibers retained their antimicrobial properties even after washing and dry cleaning (Table 11).

**Table 11: Evaluation of antimicrobial activity of polyester fibers added with NOVARON**

Sample	Microbial count increase/decrease difference
Product with 1% AG300 addition	3.7
Product with 1% AG300 addition, after 10 washes	2.7
Product with 1% AG300 addition, after 5 dry cleaning processes	3.9

### 9.2 Application to molded plastic products

Table 12 shows the results of preparing polypropylene resin plates containing AGZ300 by injection molding and evaluating the antimicrobial activity by the film adhesion method. It is evident that the antimicrobial effect increases as the amount of antimicrobial agent blended is increased.

The "MZ Series" masterbatches for polyolefin resins contain additives that make it easier for NOVARON to appear on the

surface of molded products. **Table 13** shows the results of investigating the effects of the additive. When the same amount of NOVARON was added to the resin, the viable cell count after antimicrobial activity test was reduced by one to two orders of magnitude with the additive than without the additive.

**Table 12: Antimicrobial property test on polypropylene added with NOVARON**

Bacterial species tested	<i>Escherichia coli</i>		<i>Staphylococcus aureus</i>	
	6 hours	24 hours	6 hours	24 hours
Initial bacterial count	1.6 x 10 <sup>5</sup>		1.4 x 10 <sup>5</sup>	
Control bacterial count	2.4 x 10 <sup>5</sup>	2.6 x 10 <sup>5</sup>	1.3 x 10 <sup>5</sup>	1.0 x 10 <sup>5</sup>
Product without NOVARON addition	2.8 x 10 <sup>5</sup>	4.6 x 10 <sup>5</sup>	1.5 x 10 <sup>5</sup>	2.0 x 10 <sup>5</sup>
Addition of 0.2% NOVARON AG300	3.7 x 10 <sup>3</sup>	4 x 10	4.1 x 10 <sup>5</sup>	7.4 x 10 <sup>2</sup>
Addition of 0.5% NOVARON AG300	1.7 x 10 <sup>2</sup>	<10	4.1 x 10 <sup>3</sup>	<10
Addition of 1.0% NOVARON AG300	<10	<10	1.2 x 10 <sup>2</sup>	<10

Film adhesion method: The sample surface was inoculated with 0.5 ml of a bacterial suspension of *Escherichia coli* or *Staphylococcus aureus* prepared in 1/500 normal bouillon, covered with a 45 mm x 45 mm film, and the viable count was measured after 6 or 24 hours of storage at 35°C.

**Table 13: Effect of additive on antimicrobial polypropylene**

Amount of NOVARON AGZ330 added (%)	Amount of additive added (%)	<i>Escherichia coli</i> viable count
0	-	6.4 x 10 <sup>4</sup>
0.3	-	8.8 x 10 <sup>3</sup>
0.3	0.5	3.0 x 10 <sup>2</sup>
1.0	-	2.8 x 10 <sup>3</sup>
1.0	0.5	<10

Antibacterial activity test method: Film adhesion method

This effect has been observed not only with polypropylene, but also with polyethylene, ABS, etc.

Although NOVARON AGZ330 shows favorable antimicrobial activity when added to molded plastic products, it reduces transparency of transparent resins. While AG300 has high transparency, it may not exhibit sufficient antimicrobial activity depending on the case. Therefore, we developed a new grade that easily imparts antimicrobial activity without causing a loss of transparency. **Table 14** shows the test results when it was added to transparent polystyrene. In addition to this, we have observed similar effects in polycarbonate and AS resins.

**Table 14: Transparency and antimicrobial property tests on NOVARON-added polystyrene resin**

Sample	Transparency HAZE	<i>Escherichia coli</i>			Initial bacterial count		
		Initial bacterial count	Control bacterial count	Test bacterial count	Initial bacterial count	Control bacterial count	Test bacterial count
Product without NOVARON addition	4	4.5x10 <sup>5</sup>	1.8x10 <sup>7</sup>	1.2x10 <sup>7</sup>	3.6x10 <sup>5</sup>	1.0x10 <sup>5</sup>	1.5x10 <sup>5</sup>
Addition of 0.5% transparent grade	11	↑	↑	<10	↑	↑	3x10
Addition of 0.5% NOVARON AGZ330	63	↑	↑	<10	↑	↑	<10

Antibacterial activity test method: Film adhesion method

### 9.3 Application to paints

**Table 15** shows the results of antimicrobial activity tests using test pieces prepared by dispersing 1.0% NOVARON in polyester-based paint, applying it on a wooden board and drying. We carried out the evaluation of antimicrobial activity by inoculating the paint surface with a bacterial solution prepared in normal bouillon diluted to 1/10, covering it with a polyethylene film, and measuring the viable cell count after storage at 25°C for a certain period. The results confirmed the superior antimicrobial effect compared to the product without addition. Furthermore, favorable antimicrobial activity was also exhibited in various paints such as electrodeposition paint for aluminum sashes and powder paint.

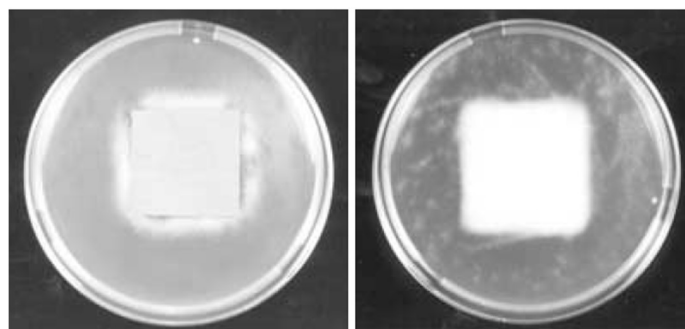
**Table 15: Antimicrobial activity test on NOVARON-added wood paint**

Bacterial species tested	<i>Escherichia coli</i>		<i>Staphylococcus aureus</i>	
	6 hours	12 hours	6 hours	12 hours
Initial bacterial count	1.6 x 10 <sup>5</sup>		1.4 x 10 <sup>5</sup>	
Control bacterial count	2.0 x 10 <sup>7</sup>	3.2 x 10 <sup>9</sup>	9.1 x 10 <sup>5</sup>	2.4 x 10 <sup>6</sup>
Product with no addition	2.8 x 10 <sup>5</sup>	1.9 x 10 <sup>5</sup>	4.1 x 10 <sup>5</sup>	6.2 x 10 <sup>3</sup>
Addition of 1% AG300	3.7 x 10 <sup>4</sup>	3.0 x 10 <sup>2</sup>	4.1 x 10 <sup>4</sup>	<10
Addition of 1% AGZ330	2.1 x 10 <sup>3</sup>	<10	5.2 x 10 <sup>3</sup>	<10

### 9.4 Application to natural leather

We dispersed NOVARON AG300 in acrylic emulsion and applied it to natural leather at 1 wt% by dipping. **Fig. 4** shows a photograph after the antifungal test using *Trichophyton*, which is the causative agent of athlete's foot. While the test piece with no addition showed significant growth of *Trichophyton* on the surface, we observed no proliferation on the test piece added with NOVARON. We carried out this test by placing the test piece on an agar plate medium, spraying it with a conidial suspension of the test strain, and incubating it for 21 days at a temperature of 28 to 30°C and a relative humidity of 85% or higher.

Silver-based inorganic antimicrobial agents generally do not have very high antifungal effects, as can be seen from **Table 6**. However, depending on the type of product, the amount added, the environment in which it is used, etc., they exhibit excellent antifungal effects.



Product with NOVARON addition      Product without NOVARON addition

**Fig. 4: Antifungal test results on natural leather**

### 9.5 Antimicrobial sand for sandbox

Recently, contamination of sandboxes in parks and schools by

microorganisms from dog and cat feces has become a problem, and some parks and schools have taken measures such as fencing off sandboxes or covering them with sheets during the night. Antimicrobial sand has a grain surface coated with an antimicrobial agent by a special treatment.

**Table 16: Field test results of antimicrobial sand with 1% AGZ330 adhesion**

Location	Inspection item	Before test	After 2 months	After 6 months	After 12 months
A	Most probable number of coliform groups	2.4 x 10 <sup>2</sup> MPN/g	3.6	3.6	7.3
	<i>Staphylococcus aureus</i>	3.1 x 10 <sup>5</sup> CFU/g	<10	<10	<10
B	Most probable number of coliform groups	1.1 x 10 <sup>3</sup>	7.3	7.3	28
	<i>Staphylococcus aureus</i>	2.5 x 10 <sup>3</sup>	<10	<10	<10
C	Most probable number of coliform groups	2.4 x 10 <sup>2</sup>	3.6	3.6	3.6
	<i>Staphylococcus aureus</i>	1.1 x 10 <sup>4</sup>	<10	<10	<10
D	Most probable number of coliform groups	1.1 x 10 <sup>4</sup>	6.2	Not measured	Not measured
	<i>Staphylococcus aureus</i>	4 x 10 <sup>3</sup>	<10		

Test was conducted on playgrounds at elementary and junior high schools, etc., with 2% antibacterial sand blended in the surface layer. Evaluation was conducted by a public testing organization

**Table 16** shows the results of a field test in which antimicrobial sand with 1% AGZ330 adhered was mixed with regular sand at the ratio of 2% and placed in the surface layer of a sandbox. Although it varies depending on the conditions of use, the effect has been confirmed to last about one year.

### 10. Points to note in application

In the development of antimicrobial processed products, it is necessary to note the following two points in addition to the imparting of the necessary antimicrobial performance. The first is examination of safety. It is necessary to confirm safety of not only the original substance but also the antimicrobial-treated product, and confirm if there are laws, regulations, voluntary standards, etc. for their intended use, and whether they are compliant. If there are no regulations or standards, the product manufacturer must sufficiently consider safety before carrying out practical application.

The second is confirmation of whether the use of antimicrobial agent deteriorates the original product function. In particular, coloration and discoloration of resins and fibers are the greatest points of concern. Although NOVARON is unlikely to cause coloration or discoloration of resins, etc. because the silver ions are tightly bound and elution is very low, all inorganic antimicrobial agents containing silver inherently have a risk of coloration or discoloration. There are two possible mechanisms. One is caused by the free silver compound itself, and the other is the silver compound acting as a catalyst causing coloration or discoloration of the resin. The risk increases if the resin contains additives or impurities that tend to release silver from the antimicrobial agent or form compounds that undergo covalent or coordination bonding with silver. Previous studies have shown that certain surfactants and mercapto compounds facilitate discoloration. The first method to control coloration and discoloration is to select the appropriate antimicrobial agent, resin, and additives. The second is to combine chemicals that prevent discoloration. Since there are various discoloration mechanisms, different chemicals should be used for different situations. Chemicals that are expected to be effective include heat stabilizers, UV absorbers, metal chelating agents, and ion exchangers.

It is also essential to check for coloration or discoloration in the actual product under conditions that account for the manufacturing process, storage, and actual usage. As an extreme example, discoloration may be caused by the various materials used for packaging.

**Table 17: Thermal discoloration test and antimicrobial property test on polypropylene added with discoloration-resistant grade NOVARON**

Sample	Thermal discoloration test							Antibacterial activity test		
	Straight molded product			Retention-molded product (5 min)			Color difference ΔE	Initial bacterial count	Control bacterial count	Test bacterial count
	L <sub>0</sub>	a <sub>0</sub>	b <sub>0</sub>	L	a	b				
Product without NOVARON addition	49.5	-0.9	-4.6	48.0	-0.6	-4.1	1.6	3.3x10 <sup>5</sup>	1.9x10 <sup>6</sup>	3.2x10 <sup>6</sup>
Addition of 0.5% NOVARON AGZ330	60.0	-1.0	-4.4	55.4	-4.1	9.6	15.1	↑	↑	<10x10 <sup>2</sup>
0.5% addition of discoloration-resistant grade	55.8	-0.5	-5.4	54.5	-1.0	-2.9	2.8	↑	↑	2.0x10 <sup>2</sup>

As we have a rich accumulation of technologies to prevent discoloration caused by silver-based antimicrobial agents, we have developed a new grade with high discoloration resistance. **Table 17** shows the results of tests performed on certain PP resins that undergo thermal discoloration with normal NOVARON grades. It is clear that antimicrobial activity is equivalent to that of the existing grade, and that it suppresses thermal discoloration. In addition to PP, the effect has been confirmed for ABS and polyamide resins, as well as for various types of paints.

### 8. Conclusion

Recently, the antimicrobial boom has grown to a point that seems almost unusual. While antimicrobial products are essential in providing a comfortable living environment for all people, some of the products make us wonder whether they truly need to be antimicrobial. Recognizing that it is the responsibility of antimicrobial agent and processed product manufacturers to create a healthy market for truly necessary antimicrobial products for the 21st century, to develop judgment criteria for antimicrobial performance and safety, and to provide consumers with a correct understanding of antimicrobial agents and their use in an easy-to-understand manner, we are determined to continue to contribute to the development of antimicrobial products.

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