● Novel antiviral processing agent for resins " NOVARON® IV4000 "

Kohei Kumagai, Yoshinao Yamada

Keywords: Antivirus, Resins, Inactivation, Inorganic material, Antibacterial

1. Introduction

COVID-19 has had a profound impact on human health and the economy on a global scale. In 2023, COVID-19 was finally reclassified as Category 5 under the Act on the Prevention of Infectious Diseases and Medical Care for Patients with Infectious Diseases (the same category as seasonal influenza), and economic activity resumed in earnest under the concept of "living with COVID." However, with new variants continuing to be reported in countries around the world, ongoing outbreaks remain a concern. Given this context, there is anticipated to be a steady demand for imparting antiviral effects to plastic and textile products around us. In fact, antibacterial and antiviral treatments have been increasingly applied to public facilities and homes in recent years, and the number of antiviral-treated products with certification marks by the Japan Textile Evaluation Technology Council (SEK) and the Society of International sustaining growth for Antimicrobial Articles (SIAA) is rapidly growing[1]. These certification mark systems grant certification to products that exhibit a certain level of antiviral effect and are safe. Antiviral treatment methods can be roughly classified into two types: coating and resin kneading. The former has the advantage where effects are delivered easily since it can be processed on the surface of the product, while the latter is characterized by low molding and processing costs and high durability. In addition, antiviral agents with high heat resistance and safety are predominantly inorganic materials[2, 3], and silver-based materials in particular (silver-supported metal oxides, silver nanoparticles, etc.) are widely used as antibacterial agents and are seeing growing application[4].

2. Conventional antiviral agents

Tables 1 and **2** show the antiviral activity values of the films coated with our silver-based antiviral agent NOVARON AG1100 and resins in which it is kneaded, respectively. We calculated the antiviral activity value using **Equation 1**.

Table 1: Antiviral activity values of NOVARON AG1100-treated films

Amount added [wt%]	Film thickness [μm]	Coated weight [g/m²]	Antiviral activity value
2	3	0.05	2.3
	7	0.1	3.8
5	8	0.4	4.1
20	2	0.4	4.0

Table 2: Antiviral activity values of NOVARON AG1100-kneaded resins

Resin type	Amount of inorganic filler added to resin		
	2 wt%	3 wt%	4 wt%
PMMA	0.1	1.8	3.9
PP	-	0.4	2.5
ABS	0.2	0.1	0.5

The SIAA certification standard requires an antiviral activity value of 2.0 or higher, and that the antiviral-treated resin reduces the infectious virus count (viral infection titer) of one-hundredth or less of that of the blank resin.

Antiviral activity value: $R = U_t - A_t$ ... (**Equation 1**)

U_t: Average common logarithm of the viral infection titer of 3 specimens after 24 hours of action by blank (untreated) resin

A_t: Average common logarithm of the viral infection titer of 3 specimens after 24 hours of action by the antiviral-treated resin

As shown in **Table 1**, the antiviral activity value of the film with surface treatment by NOVARON AG1100 was higher than 2.0, confirming its high antiviral effect in coating applications. On the other hand, an addition of 4 wt% or more was required to achieve an antiviral activity value of 2.0 or higher in resin kneading applications as shown in **Table 2**. No commercially available agent provides a high antiviral effect at low addition rates in resin kneading treatment, raising concerns about increased costs and degradation of resin properties when large amounts of antiviral agents must be added. In response, we developed NOVARON IV4000, a new antiviral agent for resin kneading that minimizes the amount added to resins while still providing a high antiviral effect.

3. Antiviral agent for resin kneading "NOVARON IV4000"

Since NOVARON IV4000 is composed of only inorganic components and has high heat resistance, it can impart antiviral effects to various resins with addition of 2 wt%. In addition, it is resistant to discoloration as it does not contain silver, and offers cost advantages.

New Products Research Laboratory, General Center of R&D, TOAGOSEI CO., LTD.

3.1 Physical property values of NOVARON IV4000

Since NOVARON IV4000 is white in appearance, it can be incorporated into products without altering their color or appearance (**Fig. 1**). It is a fine powder with an average particle size of approximately 10 μm, has high heat resistance, and a relatively high loose bulk density of 0.8 g/cm^3, making it easy to handle as a powder (**Table 3**).

Figure 1: NOVARON IV4000

Table 3: Typical physical properties of NOVARON IV4000

Item	Physical property
Appearance	White
Average particle diameter	Approx. 10 μm
Heat resistance	300°C or higher
Moisture content	< 1 wt%
Loose bulk density	Approx. 0.8 g/cm^3

3.2 Antiviral property of NOVARON IV4000

First, we evaluated the antiviral property against influenza A virus (H1N1) by using the water dispersion of NOVARON IV4000. We conducted the test according to "Method of antiviral property evaluation of antiviral agents" specified by SIAA (**Fig. 2**). We mixed 100 μL of virus suspension with 900 μL of NOVARON IV4000 water dispersion, which was prepared with sterile purified water to 800 μg/mL, left it standing at 25°C for 24 hours, and measured the infectious virus count (viral infection titer) by the plaque assay technique. Plaque assay is a method of measuring the viral infection titer based on the fact that virus-infected cells undergo degeneration. In this method, we inoculate the monolayer-cultured host cells with a serial-diluted viral solution, culture it by adding agar medium, and count the plaques formed to calculate the plaque formation unit (PFU) by multiplying it by the dilution factor[5]. The control test was conducted using sterile purified water by the same procedure. Although SIAA specifies the action time by the antiviral agent against the virus as 24 hours, we also conducted tests with contact time of 1 minute and 5 minutes to confirm the antiviral property in a short period of time.

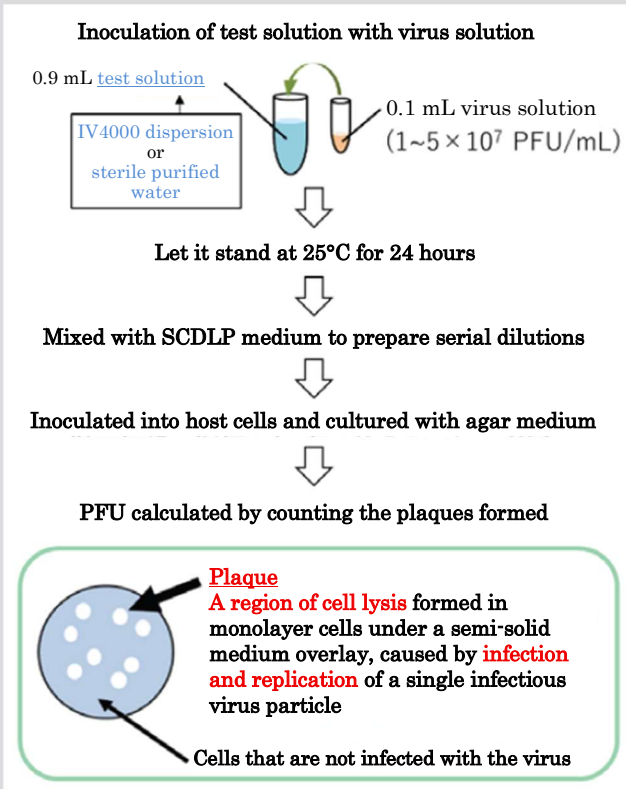

Figure 2: Antiviral property test method (treatment agent)

Fig. 3 shows the results. After 24 hours of contact with the virus solution, a 0.08 wt% water dispersion of NOVARON IV4000 reduced the viral infection titer by 99.99% or more compared to sterile purified water alone without NOVARON IV4000. Furthermore, the viral infection titer was reduced by 99% or more at 1 minute after the contact between the virus and NOVARON IV4000, and reached below the detection limit at 5 minutes. These results show that NOVARON IV4000 delivers its antiviral effect in a very short time. This suggests that NOVARON IV4000 could be effectively applied to products that come into contact with hands and other applications requiring rapid action.

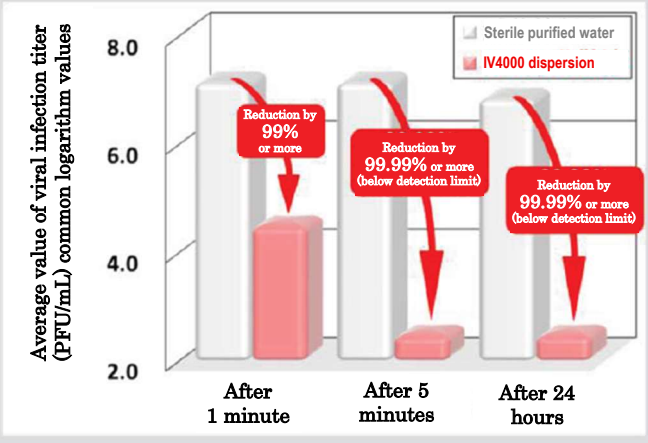

Figure 3: Antiviral property of NOVARON IV4000

3.3 Antiviral property of NOVARON IV4000-kneaded resins

Antiviral-treated resin plates were prepared by adding NOVARON IV4000 to various resin pellets (ABS, PET, and PP) and then injection-molding the mixtures. At the same time, we also prepared blank (untreated) resin plates without the addition of NOVARON IV4000. We carried out antiviral property tests on these resin plates according to ISO 21702: "Measurement of antiviral activity on plastics and other non-porous surfaces." **Fig. 4** shows the test method. We dropped 0.4 mL of influenza A virus (H3N2) solution prepared at 1 to 5×10^7 PFU/mL onto the surface of the antiviral-treated resin or blank resin cut to 5 cm × 5 cm pieces, covered the surface with a 4 cm × 4 cm film, and allowed it to stand at 25°C for 24 hours. We then washed and collected the viral solution dropped onto the resin surface, measured the viral infection titer for each of the collected solutions by plaque assay, and calculated the antiviral activity value using **Equation 1**. The certification standards by SIAA specify an antiviral activity value calculated by **Equation 1** to be 2.0 or higher, which corresponds to the viral infection titer reduction rate of 99% or more.

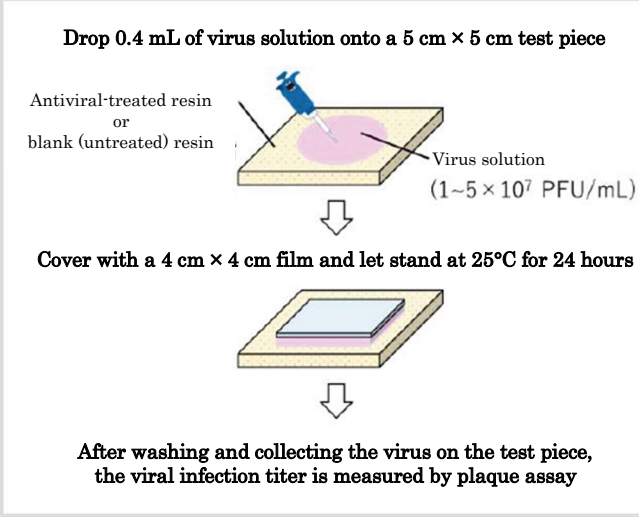

Figure 4: Antiviral property test method (resin molding product, ISO 21702)

Fig. 5 shows the antiviral property test results on ABS resin in which NOVARON IV4000 was kneaded at 2 wt%. While the viral infection titer of the blank ABS resin at 24 hours after contact with the virus suspension was 5.1, it was less than 0.8 for NOVARON IV4000-kneaded ABS resin, indicating that it reduced the viral infection titer by 99.99% or more and that the antiviral activity value was > 4.3. Kneading NOVARON IV4000 into ABS resin at 2 wt% delivers an extremely high antiviral effect against influenza virus.

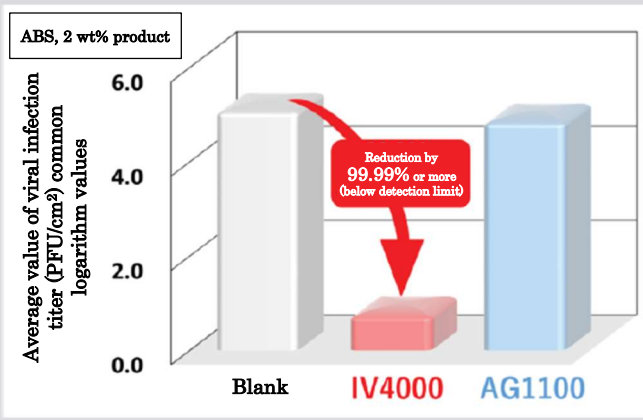

Figure 5: Antiviral property of NOVARON IV4000-kneaded ABS resin

Figs. 6 and **7** show the results of antiviral property test results for test pieces in which 2 wt% and 2.5 wt% of NOVARON IV4000 were kneaded into PET resin and PP resin, respectively, in a similar manner. In both cases, the 24-hour viral infection titer was reduced by more than 99.99% compared to the blank resin, indicating that NOVARON IV4000 can impart a high antiviral effect to a wide range of resins with a low amount of addition.

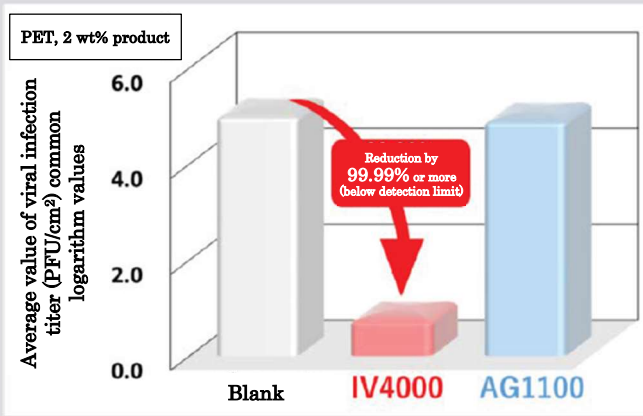

Figure 6: Antiviral property of NOVARON IV4000-kneaded PET resin

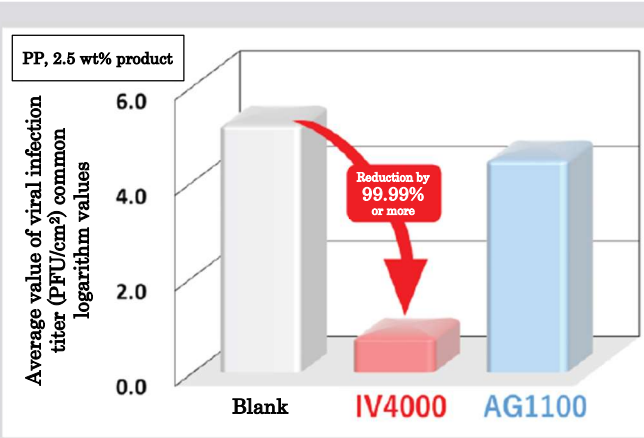

Figure 7: Antiviral property of NOVARON IV4000-kneaded PP resin

3.4 Antibacterial property of NOVARON IV4000-kneaded resins

NOVARON IV4000 exhibits not only antiviral performance, but also a very high antibacterial effect. **Table 4** shows the antimicrobial effect against typical bacteria, *Escherichia coli* and *Staphylococcus aureus*. In a similar fashion to antiviral-treated resins, the antibacterial activity value is 2.0 or higher and the certification standards by SIAA are satisfied when the treated resin reduces the bacterial count to one-hundredth that of a blank resin or less.

The antibacterial activity values of ABS, PET, and PP resins kneaded with 2 wt% NOVARON IV4000 at 24 hours were all 6.3 or higher for *E. coli* and 4.3 or higher for *S. aureus*, indicating extremely high antibacterial activity.

Table 4: Antibacterial property of NOVARON IV4000-kneaded resins

Bacterial species	Characteristics	Antibacterial activity value
Escherichia coli	Indicator bacteria for food and drinking water contamination	> 6.3
Staphylococcus aureus	Pathogens causing suppuration, sepsis, and food poisoning	> 4.3

3.5 Strength of NOVARON IV4000-kneaded resins

To confirm the effect of the addition of NOVARON IV4000 on resin strength, we conducted tensile tests on ABS resin kneaded with 2 wt% NOVARON IV4000 and on blank (untreated) ABS resin. We evaluated the resin strength on type 1BA test specimens of approximately 1 mm thickness, in accordance with JIS K 7161-2, at a test speed of 20 mm/min, a chuck-to-chuck distance of 58 mm, with n = 5 (**Table 5**). The yield stress, nominal yield strain, fracture stress, and nominal fracture strain changed little between the two resins, indicating that the addition of NOVARON IV4000 had little effect on resin strength.

Table 5: Tensile test results of blank ABS resin and ABS resin kneaded with 2 wt% NOVARON IV4000

Sample name	Yield stress [MPa]	Nominal yield strain [%]	Fracture stress [MPa]	Nominal fracture strain [%]
Blank ABS resin	53.2	2.6	40.9	6.8
IV4000-kneaded resin (ABS, 2 wt% kneaded)	49.5	2.7	40.4	7.1

3.6 Light resistance of NOVARON IV4000-kneaded resins

We evaluated the light resistance of antiviral-treated PP resin containing 3 wt% NOVARON IV4000 or silver antibacterial agent NOVARON AG1100, and blank (untreated) PP resin. Using a Sunshine Weather Meter, each resin was exposed to light for 80 hours (equivalent to four weeks outdoors), and the changes in surface color before and after exposure were observed. **Fig. 8** shows photos of each resin before and after the test. When 3 wt% of NOVARON AG1100, a silver-based antibacterial agent, is added to PP resin, light exposure causes yellowing of the resin. On the other hand, PP resin kneaded with silver-free NOVARON IV4000 showed almost no change in color appearance before and after light exposure, as did blank PP resin.

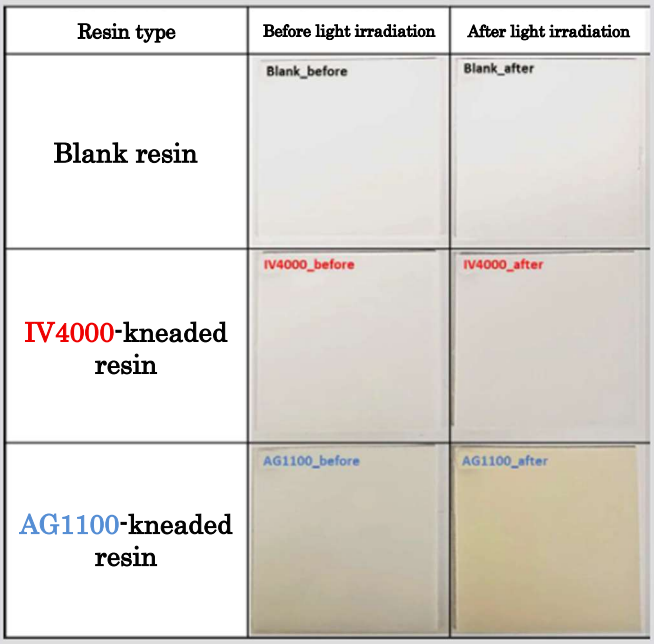

Figure 8: Appearance photographs of blank PP resin and antiviral agent-kneaded PP resin (3 wt% kneaded) before and after light exposure

4. TEM observation of virus that came into contact with NOVARON IV4000

Fig. 9 shows TEM images and conceptual diagrams of influenza A virus (H1N1) before and after contact with NOVARON IV4000. Observations were conducted at Ito Laboratory, Department of Biomedical Sciences, Graduate School of Life and Health Sciences, Chubu University. We confirmed that the influenza virus prior to contact with NOVARON IV4000 had an envelope structure with numerous protruding spikes on its spherical surface. In contrast, 5 minutes after contact with NOVARON IV4000, although the virus retained its spherical envelope structure, the spike projections characteristic of influenza virus particles had changed in shape and decreased in number. In general, infection of a human cell by influenza virus is triggered when a spike of the virus binds to sialic acid, a receptor on the cell surface, and allows the virus to enter the cell[6]. Based on this, the anti-influenza viral mechanism of NOVARON IV4000 is highly likely to involve denaturation of the spike proteins on the viral surface, which play a key role in infection, thereby inhibiting viral infection of cells.

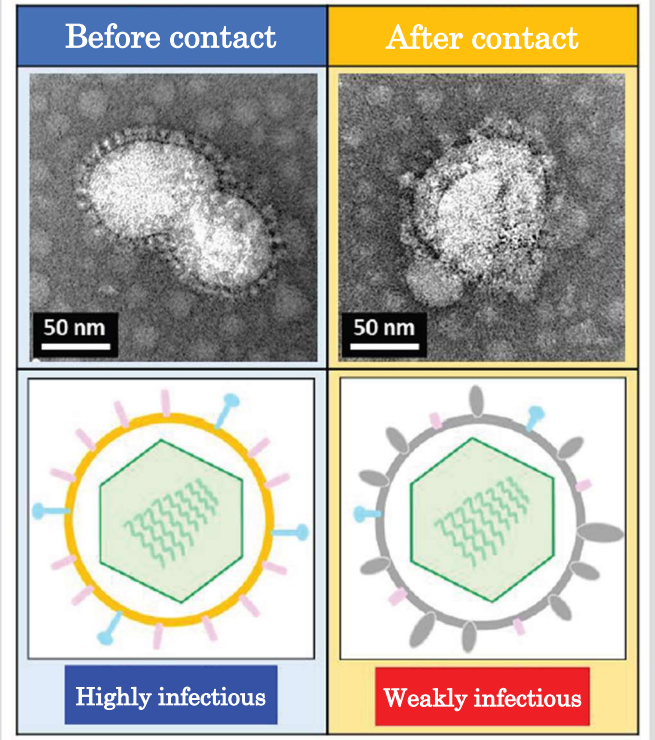

Figure 9: TEM images (top) and conceptual diagrams (bottom) of influenza virus before and after contact with NOVARON IV4000

5. Conclusion

We newly developed NOVARON IV4000, an antiviral agent for resin kneading with a high antiviral effect against influenza virus. This material can impart an extremely high antiviral effect to various resins when kneaded into them at 2 wt%. In addition, it is resistant to discoloration as it does not contain silver, and can be processed at lower costs than the conventional antiviral agents. We expect that antiviral treatment using NOVARON IV4000 will be widely applied to resin kneading applications. We hope to bring our products to more end-users, providing comfortable living spaces for as many people as possible and supporting the new lifestyle of living with COVID.

Reference

1) TORYO HOCHI SHINBUNSHA, "The Coatings Quarterly," vol. 9, No. 3 (2020) pp. 34-35.

2) Y. Yamada, Toagosei Annual Research Report, **22**, 6 (2019)

3) M. Iida and Y. Yamada, Toagosei Annual Research Report, **24**, 24-29 (2021)

4) Y. Matsumura, "Development of Antiviral and Antibacterial Products," (2021) pp. 225-248.

5) Gaush, C. R., Smith, T. F., *Applied Microbiology* **16**, 588-594 (1968).

6) Toray Research Center, Inc, "Antibacterial, Antifungal and Antiviral," (2015) pp. 14-16.