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Patents for Antibacterial Metallic Coating and Its Future Trend in Japan

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ABSTRACT : *This paper was a review for antibacterial metallic coating patents in Japan mainly. Antibacterial matters are divided into three groups: organic materials, photocatalyst such as titanium oxides and metals. Each category has its own functional mechanism. In this paper, we focused on metallic elements. Generally, they bind with proteins existing at outer membranes leading to various enzyme inhibitions. And most of the patents available for practical applications have been concentrated on silver, copper and their compounds. We summarized the trend of antibacterial metallic coatings in Japan including our research activities and discussed about the future scope in this paper.*

I. INTRODUCTION

The 21th century in Japan is the modern age where we seek for comforts in various ways more and more. We need antibacterial effect for materials not only in sanitary areas such as restrooms, sewage disposal, bathrooms etc, but also food-related, clothing, dwelling place, offices and whatever we human beings would be related and wherever we would be active. It accelerates the trend of high functionalization for materials on one hand, while aging of population, an unique characteristics particularly in Japan, also makes it pronounced on the other hand.

In 1990's of Japan, antibacterial effect started a huge boom. Since some bad quality goods having no scientific grounds were mixed into so called antibacterial commodities, the accelerated boom seems to have stopped and be stagnant. However, the technology related to antibacterial materials still forms a huge market shown in Fig.1[1] . Totally, antibacterial matters form the huge market corresponding to the size of three hundred millions US dollars in Japan at the turn of the century and is still growing incorporating lots of applications into it, being estimated as 8 billion US dollars finally.

In Japan, the antibacterial matters are classified further into 6 categories according to Japan Patent Office, i.e. Photocatalyst, Silver, Heterocyclic compound, Copper, Vegetable matter, Amine & quaternized ammonium salts[1]. And their applications are divided into 7 groups, i.e. water treatment, domestic houseware, basic goods (fibers, leather, paper, encasement, container, clothes etc.), Machinery & Appliances, Construction & Paint, Separation and others. The characteristics of antibacterial materials market in Japan can be described as follows, from the viewpoint of patent application. #1: Photocatalyst and silver have been the most often applied as patent in recent years. being followed by heterocyclic compounds and copper in this order. #2: The patent application of photo catalyst is very remarkable particularly in water treatment and separation. #3: The application of vegetable matters increases in domestic houseware related to foods. #4: Heterocyclic compounds and silver are applied to the basic goods e.g. clothes remarkably. #5: In machinery & appliances, silver and photocatalyst are applied very often. #6: In construction and paints field, silver, photocatalyst and heterocyclic matters tend to be mixed each other for their uses.

In this paper, metallic materials are the most important issue. From the viewpoint, silver and copper are selected for the following discussion. The antibacterial matters are usually used as bulk material. However, it should be an excellent idea to put the antibacterial matters as film, i.e. surface coating. Coating technology for antibacterial purpose has been mainly painting. However, some applications of coating processes to the purpose would be possible, if the antibacterial matters would be metallic matters. In this paper, the authors focus on metallic materials, introduce some representative patent applications, classified and summarized them from the viewpoint of surface coating technology. And the future scope will be proposed finally.

II. MECHANISM OF ANTIBACTERIAL EFFECTS

From the viewpoint of antibacterial matters, the antibacterial effects are classified into three groups, the effects by metallic materials, photocatalyst and organic compounds. Fig.2 shows the effect schematically[2]. From the mechanistic viewpoint, the antibacterial materials can be classified into three main groups - Organic matters, photocatalyst and metals. The overwhelming organic antibacterial could damage the cytoplasm covered with peptidoglycan layer. It would be caused mainly by the fluidity change of membranous double layers and/or their local destruction.

On the other hand, photocatalyst such as titanium oxide etc. has other mechanism for antibacterial effect. When photocatalyst such as titanium oxide (anatase) gets light in certain wavelength width, the valency band forms positive holes by excitation of electrons up to the conduction band. The positive hole formed as a result of the process tends to get electrons strongly from hydroxide ions around it, which leads to the formation of radical anion such as OH^-. The strong oxidation power of these radicals would express the antibacterial effect.

The antibacterial effect by metallic materials is quite different. There are still arguments about the mechanism and any fixed idea about it has not been still established. However, the ion dissolution mechanism has dominated others so far. According to the hypothesis, metallic ion would bind to the proteins on the cell membrane, which deteriorate or inhibit the metabolic functions such as enzyme actions. There may be quite a few metals who could show such an inhibition effect against the biological enzyme actions. Actually, researchers have found the phenomena for many metals so far[3-10]. However, the application possibility would be restricted to a few metals from the viewpoint of patents. For they must be easy to be provided commercially and also safe for human beings. The restrictions have forced us to focus only on two metals, copper and silver, for the purpose inevitably.

Those two metals have been used for antibacterial effects since ancient times. Both metals are easy to get and use commercially, since they are widely available in significant quantities. From the functional viewpoints, they work well for antibacterial effects in relatively small quantities. Actually, silver could show the effect in several ppm, while copper in several tens of ppm under a certain condition[11]. However, they are never harmful for human beings. Fig.3 shows the number of patent applications for antibacterial effects by the two metals according to Japan Patent Office (JPO)[1]. It suggests that the patents have been concentrated on silver and copper in these several decades. Fig.4 shows the application fields for both metals.

III. ANTIBACTERIAL MATERIALS AND ITS REPRESENTATIVE EXAMPLES PROPOSED IN JAPAN

Those antibacterial metallic materials, silver and copper, described in the previous section could be used not only as bulk materials, but also as surface coating. Since the dissolved metal ion would play an important role to reveal antibacterial effects, surface modification should be the most important part of constituents. Surface coating applicable for the purpose could be devised in various ways, since there are many treatment processes. For example, electroplating[12-13], non-electroplating[14-15] etc. have been representative methods from aqueous solutions. On the other hand, physical vapor deposition (PVD: vacuum deposition, sputtering method etc.)[16-19], chemical vapor deposition (CVD)[20-23], and other coating methods from vapor phases could be also mentioned as possible alternatives. However, dominant patent applications have been concentrated on supported metal by various carriers such as zeolite, silica gels etc., rather on metals themselves. Therefore, a great abundance of patents have issued those supported silver and silver compounds by various carriers and they would be used as embrocation, films etc.

The utilization of carriers has been significant particularly for silver, since silver compounds are generally weak to sunlight and chloride ion. To improve the chemical instability of silver and silver compounds, the patent applications have been related mostly to supporting techniques for silver and silver compounds since 1985 in Japan. And the application fields range from films and other moldings to sanitary ceramics and metals at this point. As supporting carriers for silver, silicate, e.g. zeolite[24-26], silica gel etc[27-28]. can be mentioned firstly, from the viewpoint of application numbers. Zeolite can contain silver ion in a stable condition, which would control the reactivity of silver ion as a result. And the silica gel supporting Thiosulfato Silver Complex has been also utilized for versatile applications[29]. Secondary, phosphoric compounds follow to silicate from the viewpoint of application versatility[30-31]. Silver ion can be supported in the network structure of inorganic phosphoric compounds such as zirconium phosphate[32-33]. The structure would control the dissolution of silver and the change in color which has been always industrial problems in practical application cases. Borosilicate glasses can also support silver and silver compounds.

The dissolution of glass could control the production of silver ion[34-35]. Activated carbon and its fibers are also utilized as carrier for silver and its compounds[36-37]. Being compared with other carriers, the initial amount of silver dissolution is relatively high for activated carbon. Even though there are few cases without carriers supporting silver and silver compounds. N-stearyl-L-gultaminic acid can be mentioned as an example[38-39]. The silver compound has the antibacterial effect for the dissolution of silver and the water repellency appears due to the effect by the stearyl group. This is a typical example that the compound itself controls the silver dissolution.

Also for copper for antibacterial effects, carriers supporting copper and its compounds have been utilized. Zeolite[40-41], silica gel[42-43] and phosphates[44-45] support antibacterial copper. However, copper is used in more versatile forms, being compared with silver, since it does not deteriorate nor convert due to the existences of light and chloride ion. As for the utilization of supporting carriers, almost the same materials can be mentioned as concrete example. As for that without carriers, copper naphthenate[46], copper-amine complex[47], copper carbonate[48], copper oxide[49] etc.

IV. THE ANTIBACTERIAL COATING IN JAPAN

From the general tendencies for silver and copper antibacterial compounds or their simple substances, the patents for metallic coatings in Japan can be re-summarized properly. Using the three keywords, 'silver (or copper)', 'antibacterial effect' and 'coating", publicized patents relating to the antibacterial coating by silver and/or copper or their compounds could be detected on the JPO web. As for silver and its compounds, 177 cases could be cited from 1993 to 2013. On the other hand, 167 cases were cited in the same period. Fig.5 and Fig.6 show how the number of applications changed in the period for silver/silver compounds and copper/copper compounds, respectively. Each number contains domestic application (colorless bar: Published Japanese patent application) and those from foreign countries (color bar: Japanese translation of PCT international application). Both figures have bimodal peaks for application numbers for published Japanese patent application. One of them appeared at the end of last century and the other at around 2006. The concept for antibacterial effect appeared clearly in 90's and a lot of patents were submitted. However, the number decreased since the beginning of the new century. It could be attributed to that some goods of inferior quality were mixed among the patent applications in the first peaks. However, the number increased again and reached another peak around 2006. A large number of patent applications at the second peak belong to photocatalytic antibacterial compounds. Photocatalytic antibacterial compounds are generally based on titanium oxide. Therefore, it means silver and/or copper are mixed into the original compounds. The application number seems to decrease again since the second peak. However, we expect that it will increase once again due to the countermeasure against influenza.

The both figures reveal the tendency for the application from foreign countries. The increase of those applications which targeted Japan got delayed and the peaks were shifted from the first peaks of domestic applications. The tendency was true for silver and copper. It suggests the two points. One of them is that Japan has lead the antibacterial effects by metals, particularly silver and copper, in the world. The other one is Japanese are generally sensitive to hygiene. From the viewpoint, Japan has had the ability to create new antibacterial markets originally.When we come to think about coating processes, we can see very easily how very much the embrocation method has been dominated, being compared with other surface treatments such as electroplating, sputtering, vacuum coating etc. It suggests that silver and copper would be used not as simple body, but as compound supported by carriers also on material surfaces. When the keywords, antibacterial + X, were input into the JPO database, the list as a result is varied from process to process. Fig.7 shows how the number of lists from the database depends on the keywords. As X, four representative coating techniques, application, sputtering, vacuum deposition and plating, were used. The figure shows very clearly how many patents belong to the embrocation category.

Here some representative patent applications for embrocation methods are mentioned as examples. First of all, we have to mention Zeolite-silver coating from the viewpoint of broad utilization possibility. The JP10-265959A[50] claims silver-zeolite coating solution and coating method. Their devised solution is basically composed of aluminum alkoxide, alkoxysilane, alkoxided of alkali metal or alkoline-earth metal, amines, amino-base organoalkoxysilane and is mixed with a polar solvent. In the latter solvent, a silver salt is added and dissolved to form the solution. The solution, is applied on the surface of a metal by dip coating and spraying and calcined at 200-800°C to form a zeolite coating film carrying silver. The JP 07-065339A[51] claimed the stacked layers composed of n-type semiconductor oxide and silver compounds.

N-type semiconductor oxide plays the role for photocatalytic function, while silver compounds work as source of antibacterial silver ion. The stacked layers are formed by embrocation basically. The JP 02-019308A[52] claims the laminated silicate carrying silver, copper and zinc which could be coated by spray coating, dipping brushing etc. The JP03-007201A[53] claims dissolutive glass containing ion of metal such as silver or copper. The metals gradually dissolve as ion to express antibacterial effects. The dissolutive glass with antibacterial metals are crushed to ≤300μm, preferably 5-50μm particle diameter and they are supposed to attach on clothing surfaces for the antibacterial effect. The JP 06-065012A[54] claims the antibacterial and antifungal ceramics and their production. But basically, their objective antibacterial and antifungal ceramics are obtained by coating the base or the base previously coated with an electrically conductive layer and the electrically conductive base with a titanium oxide layer containing at least one metallic ion selected from silver, copper, zinc and platinum or further coating the product with a titanium oxide layer or a platinum layer. Therefore, the antibacterial effect appears with the combination of photo-catalytic characteristics and antibacterial silver ion. The mixed solution would be applied to various material surfaces and then heat-treated.

On the other hand, some metallic coating processes by plating, sputtering, vacuum coating etc. have been proposed. JP 2010-247450A[55] claimed an antibacterial film composed of silver, copper and/or their alloys made by vapor deposition process. JP 2000-288108A[56] claimed an antibacterial metal sputtering mask. In this patent, silver, zinc, copper, titanium oxide and zinc oxide are stuck to the mask. Sputtering is generally better than vacum coating as described above. The former is more flexible for different base materials and shapes. And in addition, sputtering could provide stronger adhesion than vacuum coating.

As for plating method, the authors' patents could be mentioned. JP 2006-342418A[57] claimed the tin-copper alloy film by heating stacked layers composed of tin and copper. Some intermetallic compounds such as Cu_6Sn_5, Cu_3Sn would be the source to produce copper ion leading to antimicrobial effects. JP 2008-050695A[58] claimed tin-silver alloy film by heating stacked layers composed of tin and silver. In this case, intermetallic compounds between silver and tin show antibacterial effects. In both cases, the process to produce stacked single layers is mainly plating. However, other any coating processes or their complex combinations could be utilized. Fig.8 shows the concept to produce alloy films in this patent. The process is called HSSL Process[59-64]. In this process, the plural stacked phases should be prepared at the first stage. One of the stacked phases is always a low melting-point metal such as tin, zinc etc. When the surface layer is heated just below or above the melting temperature, the low melting-point metal layer is molten or semi-molten. Then the foreign atom from the higher melting-point phase in solid state is accelerated to diffuse into the lower melting-point layer. The diffusion occurs simultaneously when the solid phase is melted. And the alloy layer produced by diffusion increases the melting temperature and as a result, it is solidified at once. Since the intermetallic compound is the key component for antibacterial effects, the production condition generally depends on heating temperature and heating time. Fig.9(58) shows the experimental conditions for the production of antibacterial tin-silver compounds.

The substrate was a carbon steel (JIS SS400). Tin layer of 5 micrometers was formed at the first stage by electroplating from tin sulfate bath at the current density of $1A/dm^2$. Then silver film was produced on the tin plated steel specimen by a radio-frequency magnetron sputtering apparatus. The thickness of silver film was 1 micrometer. For the sputtering process, a silver target whose diameter was four inches. The system was evacuated and filled with argon gas of 0.5Pa. The specimen was heated to the various temperatures. The atmosphere in the furnace was not regulated and the heat treatment process was carried out completely in ambient atmosphere. The formed alloy film was basically composed of intermetallic compounds between tin and silver. The main phase was Ag_3Sn. The white circle plots correspond to the case where a large amount of the original tin and silver were remained without reactions. On the other hand, the black circle plot corresponds to the case where the sound Ag_3Sn phase was formed dominantly. In the patent, the boundary between the two cases was formulated mathematically.

$$Y=64\exp[-X/46] + 1681\exp[-X/1.4]+185 \qquad (1)$$

All of these specimens with intermetallic compounds were confirmed to show antibacterial effects. Even though the precise mechanism on how to reveal antibacterial effects, the patent attributed it to the ionic dissolution of the intermetallic compound. And the assumption has been supported by many scientific papers. The intermetallic compound is relatively stable and the dissolution of silver could be controlled properly. It would help to prevent the deterioration of the material itself, while it would continue to show antibacterial effects. Our patent applications have utilized a standardized evaluation method for antibacterial effects[58,65]. It is now formulated by ISO22196.

The test is usually called the Film Covering Method and it provides us the useful information needed for practical applications. The specimens were put in a plastic Petri dish, while the bacterial solutions was prepared according to a certain procedure.

The bacteria were incubated in 10mL of a nutrient broth for 24 hours at 35 degrees Celsius, and then diluted two-thousand fold with sterilized water and established as a bacterial solution. The diluted bacterial solution was applied to the specimen (16 micro litter per centimeter) and then a polymer film was laid over the solution. The sample was kept in an incubator for 24 hours at 35 degrees Celsius. After the incubation, a solution of 10mL of sterilized water containing 200 micro litter of Tween 80 (a nonionic surfactant and emulsifier) was introduced into the plastic Petri dish and the bacteria attached to the specimen and polyethylene film were washed into the aqueous solution. To determine the number of viable cells, serial decimal dilutions of the cell suspension were made, a 0.1mL portion of which was uniformly spread on an agar medium. The plate was incubated at 35 degrees Celsius for 24 hours and the colonies formed were counted. The viable cell count was represented as colony forming unit per milliliter (CFU/mL). The final colony formation number was measured to evaluate the antibacterial properties. This evaluation method is very suitable to concrete antibacterial goods. And the effort, achievements and versatile applicability to realize a reproducible and practical evaluation process to a standard should be estimated very highly. However, it is still doubtful for the method that one could apply to biofilm phenomena, the broader concept. Bacterial in practical environments never work as an unit, but as a group in biofilm.

Both types of bacterial have much different properties. Therefore, the countermeasures should be different according to the changes of properties. The important perspective is still lacking also in the patent applications. The unavailability, the lack of antibacterial continuousness etc, might lead to that of biofilm related concepts.

V. FUTURE SCOPE

In this paper, various patent applications for antibacterial effects and the tendency in Japan were introduced, focusing particularly on antibacterial metals (Cu and Ag) and their surface coating processes. The application of the antibacterial metals to the surface was devised in various ways. However, the embrocation has been dominant, while there are few cases for plating, sputtering, vacuum deposition etc. It means how very important the combination of the antibacterial metals and other materials as carrier. These supporting materials could control the dissolution of the antibacterial metals and change of properties for practical application. From the viewpoint, the genuine surface coating of metals themselves might be low efficient and it might be not so easy for the patents to be put into practical uses. And the importance of biofilm should be too good to be missed. As described above, antibacterial countermeasures have been investigated based on the bacterial action against planktonic bacteria which behave in free spaces as a single body. However, they originally work as team or group in biofilm. Sadly, the bacterial properties, shape etc. are changed in biofilms. It leads to the serious fact that the conventional antibacterial agents and countermeasures don’t work at all.

The knowledge and information about biofilms began to appear in 80’s and they have been accumulated since then gradually. They are still on the cradle stage and new findings still continue to emerge at this point. However, the patents have been not considered from the viewpoint enough. As for the patents in the next decades, the perspective should be taken into account, so that the larger market will be formed not only in Japan, but also in entire world.

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REFERENCES

[1] JPO. Antibacterial compounds shown by patents and their application. Guidebook for patent map in various technology fields 2013; Available from: http://www.jpo.go.jp/shiryou/s_sonota/map/kagaku24/0/c-01.htm.

[2] Kanematsu, H., Antibacterial Materials for Safety, Security and Reliability, ed. H. Kanematsu. 2010, Chiba, Japan: Yoneda Shuppan Co,. 154.

[3] Gristina, A.G., et al., An in vitro study of bacterial response to inert and reactive metals and to methyl methacrylate. J Biomed Mater Res, 1976. **10**(2): p. 273-81.

[4] Colmano, G., S.S. Edwards, and S.D. Barranco, Activation of antibacterial silver coatings on surgical implants by direct current: preliminary studies in rabbits. Am J Vet Res, 1980. **41**(6): p. 964-6.

[5] Valenti, P., et al., The effect of saturation with Zn2+ and other metal ions on the antibacterial activity of ovotransferrin. Med Microbiol Immunol, 1987. **176**(3): p. 123-30.

[6] Pelova, R., et al., Antibacterial and antitumor activity of platinum complexes of hydrazinopyrimidines and amidrazones. Pharmazie, 1987. **42**(4): p. 251-2.

[7] Baena, M.I., et al., Bactericidal activity of copper and niobium-alloyed austenitic stainless steel. Curr Microbiol, 2006. **53**(6): p. 491-5.

[8] Moricz, A.M., et al., Opposite effect of Cu(II) and Se(IV) ions on the antibacterial-toxic action of mycotoxins. Acta Biol Hung, 2007. **58**(3): p. 301-10.

[9] Jing, H., Z. Yu, and L. Li, Antibacterial properties and corrosion resistance of Cu and Ag/Cu porous materials. J Biomed Mater Res A, 2008. **87**(1): p. 33-7.

[10] Ma, S., et al., Assessment of bactericidal effects of quaternary ammonium-based antibacterial monomers in combination with colloidal platinum nanoparticles. Dent Mater J, 2012. **31**(1): p. 150-6.

[11] Yotaro Murakami, Current Situation for Antibacterial Materials, in MMC News 2005. p. 7.

[12] Amano, R. and F. Ishiguro (1997). Antibacterial Nickel-Chromium Plating Film and Plating Method. JPO. Japan. **JP,10-068100,A(1997)**.

[13] Kobayashi, H. (2006). Silver-Plated Fibrous Material. JPO. Japan. **JP, 2008-031507,A**.

[14] Sugiura, Y. and Y. Sugiura (1996). Antibacterial Plating Layer. JPO. Japan. **JP, 09-157860,A(1997)**.

[15] Kaneshiro, Y. and K. Mizuno (2007). Conductive Pile. JPO. Japan. **JP, 2007-321312,A**.

[16] Ichimura, H. (1999). Antimicrobial Raw material Sheet. JPO. **JP,11-081129,A(1999)**.

[17] Nakamura, K. and K. Nakamura (1998). Antibacterial Inorganic Porous Composition and Use Thereof. JPO. Japan. **JP,2000-154340,A**.

[18] Nakamura, H., et al. (1999). AG-Based Antimicrobial Agent, Its Production and Antimicrobial Resin Composition. JPO. Japan. **JP,11-228306, A(1999)**.

[19[Yamamoto, T. (2007). Antibacterial Material and Method for Producing the Same. JPO. Japan. **JP,2009-143841,A**.

[20] Takamatsu, K., et al. (1996). Silicon Fiber. JPO. Japan. **JP,09-296366,A(1997)**.

[21] Imai, O. and K. Ogata (1996). Coating Material for Medical Use. JPO. Japan. **JP, 10-110257,A(1998)**.

[22] Ketayama, M., et al. (1999). Anti-Fogging Mirror for Bathroom. JPO. Japan. **JP, 2000,321411,A**.

[23] Fujimoto, H., et al. (1999). Flowing Droplet Type Antifog Mirror for Bathroom. JPO. Japan. **JP,2001-046198,A**.

[24] Hirano, M., et al. (2005). Dentifrice Composition and Method for Preventing Discoloration of Dentifrice Composition. JPO. Japan. **JP,2007-008843,A**.

[25] Taniguchi, A., et al. (2005). Antibacterial Zeolite and Antibacterial Resin Composition. JPO. Japan. **JP,2007-091501,A**.

[26] Kurihara, Y., et al. (2006). Antibacterial Zeolite Particle and Antibacterial Resin Composition. JPO. Japan. **JP,2008-001557,A**.

[27] Uchino, T., et al. (1994). Antinicrobial Coating Composition, Method for Coating the Same and Product Therefrom. JPO. Japan. **JP,08-027404,A(1996)**.

[28] Tomioka, T., et al. (1995). Antimicrobial Composite Material and Its Production. JPO. Japan. **JP,07-233018,A(1995)**.

[29] Tomioka, T., et al. (2004). Antibacterial Composite resin, Antibacterial composite resin Composition and Method for Producing the Same. JPO. Japan. **JP,2004-107675,A**.

[30] Oku, T., et al. (1991). Antibacterial/Antifungal Pottery Product. JPO. Japan. **JP, 2000-233984,A**.

[31] Tanase, M. and N. Yamamoto (2000). Antibacterial Resin Composition. JPO. Japan. **JP,2002-053756,A**.

[32] Koma, H., et al. (1993). Production of Silver based Inorganic Antimicrobial Thin Film and Silver Based Antimicrobial Agent. JPO. Japan. **JP,06-330285,A(1994)**.

[33] Koma, H. and F. Shima (1994). Dental Material Composition. JPO. Japan. **JP, 07-330532,A(1995)**.

[34] Kuroki, J. and K. Ito (1991). Material for Building Having Antibacterial Property and Antifungal Property. JPO. Japan. **JP,05-105492,A(1993)**.

[35] Kamiya, Y. and K. Tanaka (1995). Antimicrobial Composite Glass Particle. JPO. Japan. **JP,08-245240,A(1996)**.

[36] Nakajima, H., et al. (1996). Microbicidal Activated Carbon Fiber and Its Production. JPO. Japan. **JP,09-296328,A(1997)**.

[37] Mizutori, S., et al. (1996). Production of Silver-Dispersed Carbon Material. JPO. Japan. **JP,2000-02687,A**.

[38] 3M Innovative Company (2008). Silver Coating and its Production Method. JPO. Japan. **JP,2008-537986,A**.

[39] Tomioka, T., et al. (1992). Germicidal Composition. JPO. Japan. **JP, 06-087712,A(1994)**.

[40] Echigo, Y., et al. (2007). Antibacterial Granule and its Production Method. JPO. Japan. **JP, 2007-161498,A**.

[41] Yasuda, H. (2008). Deodorizing, Antibacterial, and Antifungal Resin Sheet and Its Installation Method. JPO. Japan. **JP,2009-172272,A**.

[42] Hagiawara, Z. (1995). Antimicrobial Composition. JPO. Japan. **JP, 09-030915,A(1997)**.

[43] Ogawa, T., et al. (1997). Antibacterial and Antifungal Agent and Its Production. JPO. Japan. **JP,11-029426,A(1999)**.

[44] Murata, T., et al. (2006). Medical Brain Tube and Production Method Thereof. JPO. Japan. **JP,2008-023071, A**.

[45] Shimoyama, Y., et al. (2010). Compound Base Material and Manufacturing Method of the Same. JPO. Japan. **JP,2012-095969,A**.

[46] Yamada, Y., et al. (1997). Preservative for Timber. JPO. Japan. **JP, 10-235612,A(1998)**.

[47] Hasegawa, Y., et al. (2007). Antimicrobial Composition, Coating Material, and Electrodeposition Coating Material. JPO. Japan. **JP,2008-285509,A**.

[48] Nishisaka, M. (1996). Production of Patina for Antibacterial and Antimycotic Usage. JPO. Japan. **JP,09-194901,A(1997)**.

[49] Fukushima, Y. (1996). Plant Picture Designing Device. JPO. Japan. **JP, 08-115351,A(1996)**.

[50] Koura, S. and K. Sakado (1997). Silver-Zeolite Coating Solution and Coating Method. JPO. Japan. **JP,10-265959,A(1998)**.

[51] Miyasaka, A., et al. (1997). Metallic Material Excellent in Antibacterial Property. JPO. Japan. **JP,09-195061,A(1997)**.

[52] Otani, A., et al. (1988). Antimicrobial Silicate Having Film-Forming Property. JPO. Japan. **JP,02-019308,A(1990)**.

[53] Hirose, K., et al. (1989). Antifungal and Deodorant Agent. JPO. Japan. **JP, 03-007201,A**.

[54] Taoda, H. (1992). Antibacterial and Antifungal Ceramics and Their Production. JPO. Japan. **JP,06-065012,A(1994)**.

[55] Mase, H., et al. (2009). Antibacterial Film. JPO. Japan. **JP,2010-247450,A**.

[56] Miyauchi, T. (1999). Antibacterial Metal Sputering Mask. JPO. Japan. **JP,2000-288108,A**.

[57] Kanematsu, H., et al. (2005). Sn-Cu Alloy Thin Film Having Antibacterial Property, Sn-Cu Alloy Thin film-Formed Article Having Antibacterial Property, and Method for Producing Sn-Cu Alloy Thin Film-Formed article Having antibacterial Property. JPO. Japan. **JP,2006-342418,A**.

[58] Yoshitake, M., et al. (2007). Antibacterial Article and Method of Producing Antibacterial Thin Film. JPO. Japan. **JP,2008-050695,A**.
[59] Kanematsu, H., et al. (2002). "Tin-Nickel Alloy Films Produced from Stacked Single Layers by Heating and Their Characteristics." AESF Sur/Fin 2002, Annual International Technical Conference: 685-694.
[60] Kanematsu, H., et al. (2003). "Corrosion Characteristics of Alloy Films Produced by HSSL Process." AESF SUR/FIN 2003: 673-682.
[61] Kanematsu, H. and T. Oki (2004). "Heat Treatment-Alloying, Plating Process." Journal of High Temperature Society of Japan **30**(4): 191-196.
[62] Ikigai, H., et al. (2005). "Antibacterial Activity by Alloying of Tin & Copper Plating." SFIC Sur/Fin 2005: 497-503.
[63] Kanematsu, H., et al. (2006). "Various Properties of Tin-Copper Alloy Filim Produced by Heat Treatment." SFIC Sur/Fin 2006: 864-870.
[64] Kanematsu, H., et al. (2006). "Alloying of Stacked Nickel/Zinc Films Through Heat Treatment." SFIC Proceedings Sur/Fin 2006: 360-369.
[65] Kanematsu, H., et al. (2009). "Evaluation of Various Metallic Coatings on Steel to Mitigate Biofilm Formation." International Journal of Molecular Science **10**(2): 559-571.

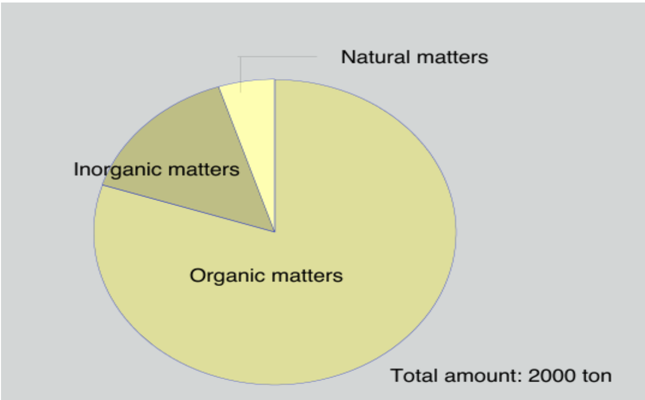

Fig.1 The breakdown of antibacterial materials in Japan

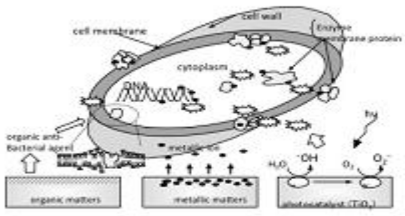

Fig.2 Mechanism of antibacterial effects for various materials.

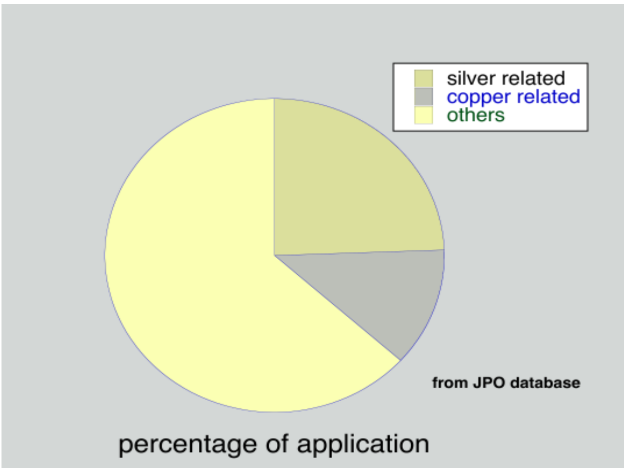

Fig.3 Application percentages of various matters searched from the database of JPO.

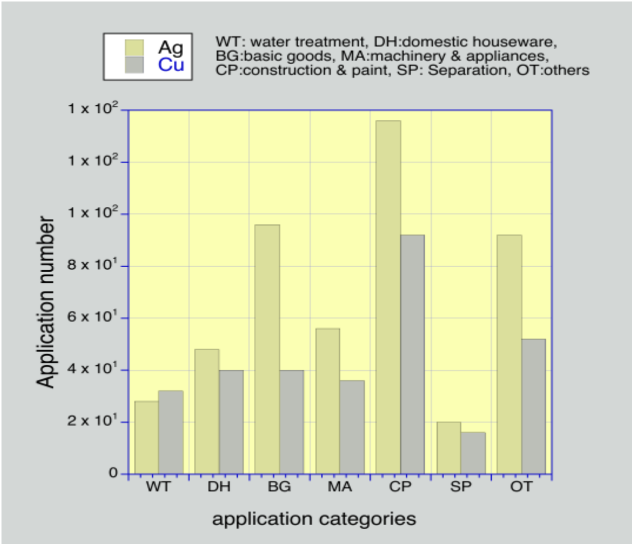

Fig.4 Patents applications for antibacterial silver and copper.

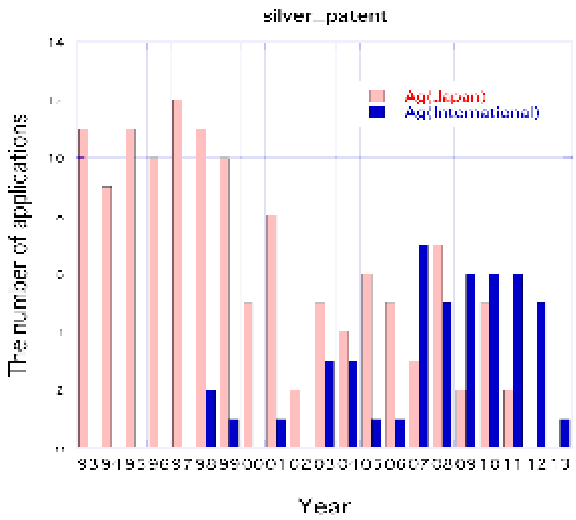

Fig.5 Change of application tendency for silver related antibacterial patents.

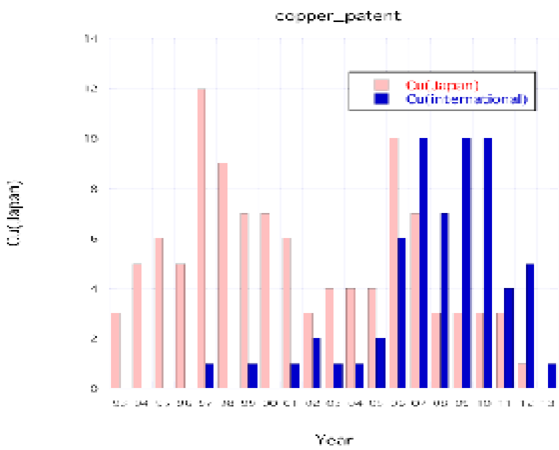

Fig.6 Change of application tendency for silver related antibacterial patents.

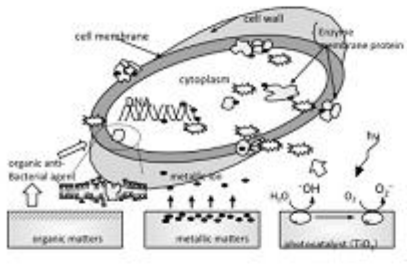

Fig.2 Mechanism of antibacterial effects for various materials.

Fig.7 Additional keywords and the retrieval numbers from the database of JPO.

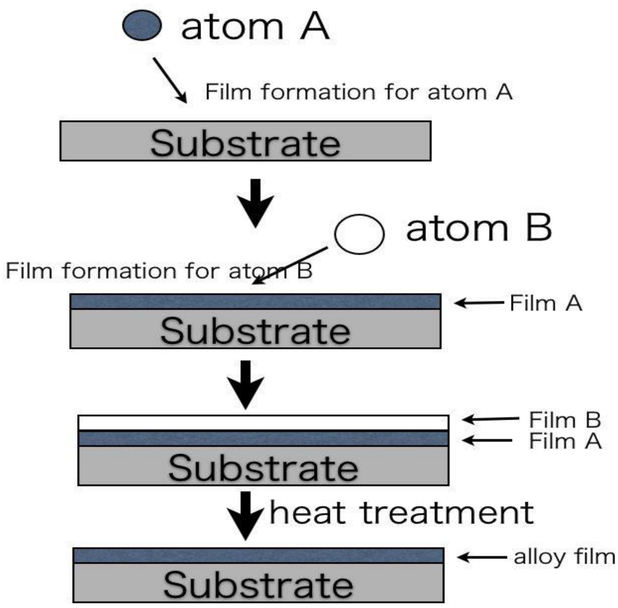

Fig.8 Concept for Heating Stacked Single Layers Process

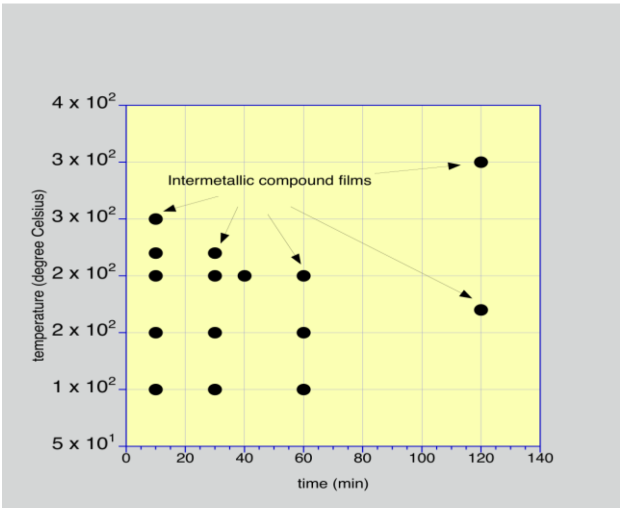

Fig.9 Heat Treatment Conditions and Produced Film