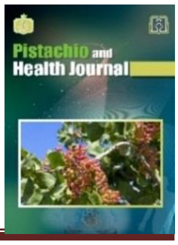

A Review of Applied Disinfection Methods in Foods Industry and Pistachio Processing

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Abstract

The most common method of dealing with the pathogens is applying disinfectants. Thus far, a wide range of disinfectants and antiseptics has been introduced to the food industry and different centers. Latest studies highlight the application of nanoparticles and other novel compounds. The present work is a review article on applying new chemical disinfectants in the food industry. It reviews the papers published indifferent scientific databases. To conduct the present study, the keywords, such as disinfectant, antiseptic, bactericide, bacteriostatic, antibacterials, microbicides, and biocides, are searched at different databases, including Web of Science, SCOPUS, PubMed, Science Direct, and Google Scholar. Totally, 600 articles on new materials and their disinfectant application are selected from 2009-2018.Among the selected papers, 477 were about applying compounds such as silver/its nanoparticles, complexes, zinc oxide/its nanoparticles, titanium dioxide, and electrolyzed water (EOW).Reviewing different articles on the new disinfectants, it is concluded that the recent studies mainly focus on the application of nanoparticles, complexes, and innovative physiochemical methods, including electrolysis in producing applied disinfectants in the food industry (e.g., pistachio industry). Among the above items, the EOW disinfectant, more commonly used in the food industry, seems to have the least complications for the environment and people's health. However, given this disinfectant novelty, it is required to conduct more studies on its toxicity.

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1. Introduction

Pathogenic microorganisms are the agents of threatening infections of different types of organisms [1]. They can be found indifferent environments, particularly susceptible environments, such as waste [2], wastewater [3], food [4], and even air [5]. Thus far, different methods have been applied for limiting the growth of these microorganisms in the mentioned environments, especially waste and wastewater [6]. The new technologies are also used to identify environmental pollution [7].

Disinfectants are materials applied for destroying the organisms present in environments and inanimate objects. They are used for cleaning tools, objects, clothes, surfaces, tiles, toilets, and bathrooms. These materials, being commonly chemical, affect the bacteria, viruses, fungi, and other organisms by either destroying them or preventing their growth [8].

The first comprehensive explanation for using disinfectants in surgical operations was published in 1867 by the English surgeon Joseph Lister as an article entitled “the Antiseptic Principle of the Practice of Surgery”. This article has adopted the theory of pathogenic microbes first discussed by Louis Pasteur. According to this study, materials such as phenol can kill most microbes and disinfect the surgical site [9]. Some similar disinfection methods have been applied in the past by several scientists, such as Hippocrates and Galen, as well as the ancient Sumerians. Joseph Smith used materials such as alcohol for the first time for disinfecting wounds and injuries. The initial use of disinfectants can be traced back to ancient times for embalming the corpses. Nowadays, the solution of water and phenol, with specific and constant strength, is applied for the effectiveness and strength of disinfectants [10].

Long before discovering penicillin, the human had already learned (via experiments) to apply certain raw materials as antimicrobials. Since 600-500 BC, the Chinese use moldy juice of salty bean for treating infections. The term Antibiosis was first used by Vuillemin in 1889 to describe the competitive nature of biological communities in which only the strongest and most competent beings survive. A few years later, the term was used for the antagonism of the microorganisms. The first antibiotic was discovered in 1928 by Alexander Fleming. He accidentally noticed the antibacterial effect of the substance secreted by a fungus *penicillium notatum*. Howard Florey purified the substance and prescribed it to treat infections systemically. Later, the scientists detected some other natural substances, including tetracycline, streptomycin, and cephalosporins, to be used as antibiotics. When the chemists identified the structure of these substances, various types of industrial antibiotics were produced by changing them. Thus, the new antibiotics were obtained with higher effectiveness and chemical stability [11].

Thus far, different types of chemical materials have been used as disinfectants or antiseptics, including phenol derivatives, alcohols, aldehydes, halogens (hypochlorites and chloramines), detergents (quaternary *ammonium compounds), heavy metal compounds, and* gas sterilizers (ethylene oxides and propiolactones). At present, these materials or their compounds are widely used as disinfectant or antiseptic with bactericidal or sporicidal effects [12, 13]. Their short life and instability in the environment, besides their toxicity, limit their application [14] since, in addition to evaporation, they react with the compounds and become inactive. Therefore, it is of high significance to obtain chemicals with minimal toxicity for human cells that not only maintain sufficient moisture for conducting the chemical reactions but also remain in the environment for some time [15].This study aims to review the published articles on the application of modern chemical disinfectants in the food industry. The articles investigated have been published in scientific databases since 2009. Moreover, it is attempted to present the characteristics of the disinfectants investigated in the present work.

2. Materials and Methods

The present study explored the articles published on Web of Science, SCOPUS, PubMed, Science Direct, and Google Scholar about new chemical disinfectants. For this purpose, first, the disinfection-related keywords, including disinfectant, antiseptic, bactericide, bacteriostatic, antibacterials, microbicides, and biocides, were searched. Altogether, 600 articles on new materials and their disinfectants were selected from 2009-2018. Among the selected articles, 477 were about the application of compounds such as silver and its nanoparticles (12 articles), different ligands and complexes, especially metal complexes (146 articles), zinc oxide and its nanoparticles (109 articles), titanium dioxide (98 articles), and electrolyzed water (EOW) (12 articles) (Fig. 1). The articles in the last 4 years, leading up to 2018, have the highest number (Fig. 2).

Then, articles published on Science Direct on the toxicity of these compounds were reviewed. A total of 117 articles were on the toxicity of silver and its nanoparticles, 31 were on the toxicity of zinc oxide, and 7 were on the toxicity of complexes, all published in Science Direct. Some of these studies were investigated in this article.

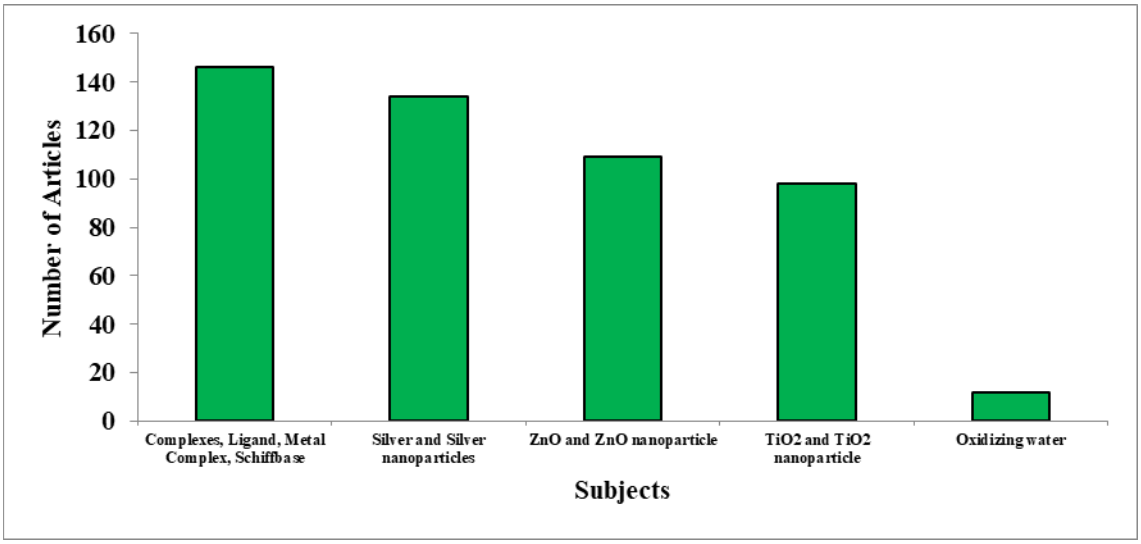

Fig. 1- The number of articles on the application of different compounds as disinfectants since 2009

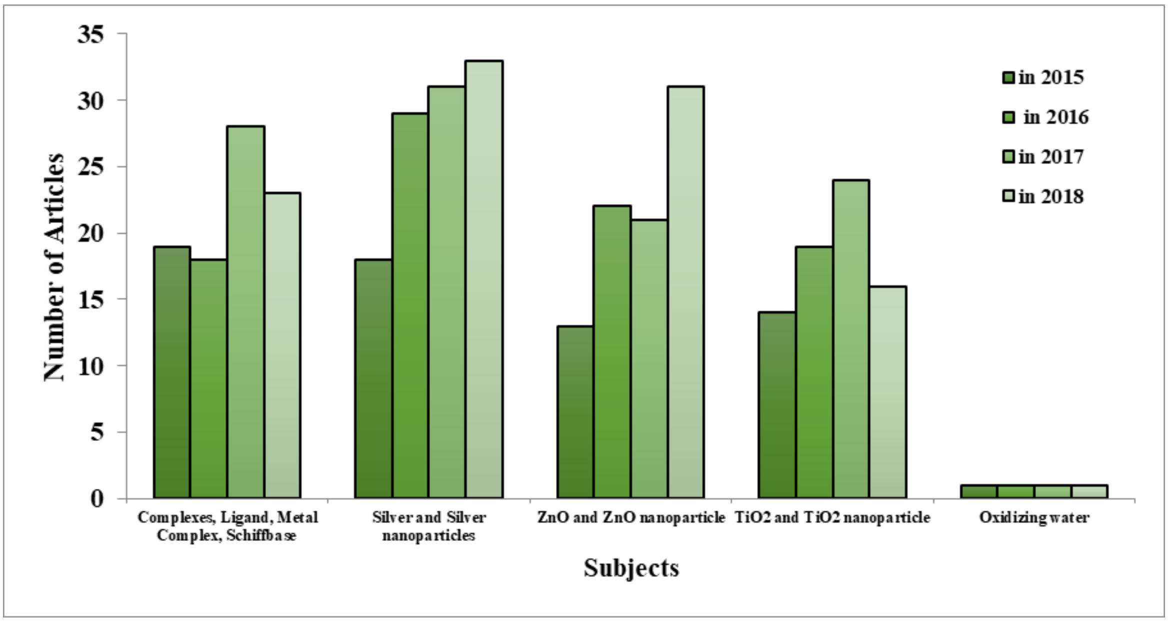

Fig. 2- The number of articles on the application of different compounds as disinfectants in the last four years, leading up to 2018

4. Discussion

In the following sections, some articles on the toxicity of silver compounds and the its nanoparticles, zinc oxide, titanium dioxide, and complexes are reviewed and investigated.

Silver and its nanoparticles

Silver is among the elements known to have antimicrobial properties since ancient Rome. Silver and its nanoparticles have antimicrobial properties against several gram-negative bacteria, including Escherichia, Acinetobacter, Pseudomonas, Salmonella, and Vibrio, and some gram-positive bacteria, including Bacillus, Clostridium, Enterococcus, Listeria, Staphylococcus, and Streptococcus [16]. Some studies indicate different fungi types, including *Aspergillus niger*, *Candida albicans*, and *Saccharomyces cerevisiae*, to be sensitive to compounds containing silver [17]. Moreover, some other studies show the antimicrobial properties of silver nanoparticles against hepatitis B [18], AIDS [19], and syncytial virus [20], as well as murine norovirus [21]. Thus, in recent decades, the application of compounds containing silver and its nanoparticles has been increased. The excessive use of nanoparticles has raised concerns about their accumulation and uncontrollable toxicity. One of such concerns is related to the threat of water resources and organisms within aquatic ecosystems, investigated in various studies [22, 23]. In these studies, the effect of silver and its nanoparticles on specific organisms in these ecosystems are investigated. For example, in a study about the toxicity of silver (Ag), gold (Au), and gold-silver (Au-Ag) nanoparticles on marine microalgae, it is indicated that the toxicity of metal nanoparticles on aquatic organisms, such as microalgae, depends on the physical and chemical characteristics of such compounds, including solubility, affinity, and aggregability. Accordingly, it is concluded that given the antibacterial nature of silver, the toxicity of such nanoparticles is high for microalgae [22]. In another study, it is attempted to investigate the toxicity of silver ions and polymers covered with silver nanoparticles on the early development stages of sea urchin embryo. In this study, the embryo of a specific type of sea urchin called *Strongylocentrotus droebachiensis* is separately exposed to silver ions (Ag^+) and silver nanoparticles (AgNPs). The results indicate that, in the embryonic stage, various cells, including Archentron elongation, primary and secondary mesenchymal, and Spiculogenic, are affected by silver ions and silver nanoparticles during their developmental period. The results also show that silver ions affect cells in the early stages of the embryo, while in its late stages, the cells are not affected by silver ions. Increasing the concentration of Ag+ and AgNPs causes more destruction during fetal growth [23]. In an additional work, the toxicity mechanisms of silver nanoparticles on Hela (Hela cells are a collection of human epithelial cells prepared in 1951 from a person named Henrietta Lacks and stored; they are reproduced on culture medium and used in studies, especially virological studies) and A549 cells are investigated. A special fluorescent probe is applied to study the dissemination status of silver nanoparticles in living cells. Activation of the Methallothioneins protein in response to silver nanoparticles, acting as a chelating agent in the cell, explains the relationship between the presence of ions and cell mortality. It is also likely that silver nanoparticles enter the cell via endocytosis process, and the produced lysosome releases Ag^+; this can ultimately cause cell damage [22].

Titanium dioxide

Titanium dioxide (TiO_2) is a nanoparticle with numerous applications. In several studies, TiO_2 has been used as a photocatalyst and disinfectant either alone or in combination with other materials and visible and ultraviolet light [24]. Further, many studies have been conducted on the toxicity of titanium dioxide nanoparticles. One of these studies is about the vascular toxicity of TiO_2 nanoparticles and carbon nanotubes in vitro and in vivo. The mentioned study investigates the effect of TiO_2NPs nanoparticles on endothelial cells in vitro and in the zebrafish embryo. In vitro results indicate that TiO_2 nanoparticles have no cytotoxic and oxidative properties; however, they have genotoxic effects and bring about abnormalities in the form of pericardial edema [25]. In another study entitled "TiO2 photocatalysis of 2-isopropyl-3-methoxy pyrazine taste and odor compound in aqueous phase: Kinetics, degradation pathways and toxicity evaluation," this substance is produced from actinomyces and causes taste and odor in water resources. TiO2 photocatalyst destroys 95% of this substance in 20 minutes. Toxicity evaluation indicates that TiO_2photocatalyst has low toxicity [26]. A study also aims to investigate the toxicity of TiO_2 nanoparticles on algae and the oxygen production process. In this study, two species of algae, i.e., *Karenia Brevis* and *Skeletonema costatum*, are exposed to TiO_2 nanoparticles with an average size of 5-10 nm; the results show the growth of both algal species to be limited by TiO_2 nanoparticles.

X-ray spectroscopy indicates that the epithelial cells of K. Brevis have been destroyed, and their organelles are exposed to unrecognizable TiO_2 nanoparticles. The content of Malondialdehyde (it is an intracellular organic substance with the formula of CH_2 $(CH)_2$ known as a biomarker for oxidative stress) of these two species increases significantly compared to the control ($P<0.05$). This study shows that TiO_2 nanoparticles can stop the growth of algae; this is owing to the oxidative stress arising from Reactive Oxygen Species (ROS) production in the cell. In these algae, antioxidant levels change, altering the balance between oxidants and antioxidants. Thus, due to the accumulation of ROS, algal cells oxidate lipids and stop cell growth. The stopping of the electron transfer chain indicates that the production and accumulation site of ROS is chloroplast [27]. In another research, the toxicity of silver nanoparticles on zebrafish embryo is investigated under different contact conditions. In this study, zebrafish embryonic cells are exposed to TiO_2under natural light (visible) and ultraviolet light conditions; then, toxicity parameters, such as abnormality, viability, and biochemical biomarkers, are evaluated. The results indicate that, under UV irradiation, the mortality of larvae increases [24]. Moreover, a different study evaluates the toxicity of TiO_2, ZrO_2, Fe, Fe_2O_3, and Mn_2O_3 nanoparticles on s*accharomyces* yeast. According to its results, Mn_2O_3 nanoparticles result in the highest cell wall destruction, while TiO_2 and other nanoparticles do not cause any [28].

Complexes

Complexes consist of an organic compound called a ligand and a metal. They have various applications; it is worth noting that metal complexes have many applications as therapeutic or diagnostic agents. The most famous metal-based drug is cisplatin, being highly effective in treating cancer. The compounds of gold, gallium, and bismuth are effective in treating arthritis and rheumatism. Moreover, complexes have an antimicrobial role; if the related ligand forms a complex with a metal having antimicrobial properties, it can be used as an antimicrobial agent. Thus, due to the antimicrobial properties of the complexes, numerous applications are considered for them. For example, Theodore Rosu et al. (2006) have synthesized a complex consisting of Schiff-base ligand and copper, and its antimicrobial properties are considered using some bacteria, including *Escherichia coli, Klebsiella pneumonia*, *Acinetobacter*, *Pseudomonas aeruginosa*, and *Staphylococcus aureus*. The results of comparing the antimicrobial properties of Schiff-base ligand with complex obtained from Schiff-base ligand and metal indicate that the antibacterial power of the latter is by far higher than that of the former. According to this study, *Escherichia coli, Acinetobacter*, *Pseudomonas aeruginosa*, and *Staphylococcus aureus* are more sensitive to the complex [29]. Thus far, few studies have been performed on the toxicity of complexes; in total, only 7 articles have been published on this issue on the Science Direct database, some of which express its antimicrobial properties rather than its toxicity to human cells. Some studies have been conducted about the toxicity of chlortetracycline (CTC) ligand and its metal complex on wastewater microorganisms. The metal complexes include calcium, magnesium, copper, and chromium complexes. The sustainability trend of the aforementioned metal complexes in the environment are as follows: Mg-CTC>Ca-CTC>Cu-CTC>Cr-CTC. To evaluate the toxicity, two bacteria are applied, i.e., one gram-positive bacterium called *Bacillus thuringiensis* (Bt) and one gram-negative bacterium called *Enterobacter aerogenes* (*EA*). CTC metal complex has a higher toxicity than CTC alone for Bt; however, as for Ea, CTC and its metal complex are equally toxic. In natural wastewater, unlike synthetic wastewater, CTC and its metal complex are not toxic to bacteria. Hence, the results indicate that CTC is toxic to bacteria if biologically available; however, in the natural wastewater, since CTC is absorbed by suspended materials and solids in wastewater, it is thus not biologically available for the bacteria and has no toxic effect [30]. A study conducted in 2015aims to determine the antifungal and antibacterial effect of iron, copper, and silver complexes (by the microdilution method) on standard fungal isolates (*Aspergillus niger* and *Candida albicans*) and bacteria (*Escherichia coli*, *Staphylococcus aureus*, and *Pseudomonas*); further, the minimum inhibitory concentration (MIC) is calculated for the complexes. Also, for evaluating the toxicity of two synthesized complexes, the cellular life method (mouse skin cells) is adopted using the MTT test. The antimicrobial test results show that the iron complex has fewer antimicrobial properties than the related ligand; however, in terms of toxicity for mouse skin cells, it has the same toxicity as the ligand. The silver complex has much more antimicrobial properties than the related ligand alone; however, as regards toxicity, it is not significantly different from the related ligand [15].

Electrolyzed water

One of the new compounds recently introduced as an antimicrobial agent is Electrolyzed Oxidized Water. It is obtained by passing the saltwater solution through cathode and anode electrodes [31]. These two electrodes are usually separated from each other using membranes permeable to some ions (for ionic communication and electrolysis).O_2 and Cl_2gases,as well as Hypochlorous acid, are produced in the anode; the content of the solution produced by electrolysis has a redox potential of +700 to +800 mV with a pH of 4,providingthis solution with a high oxidizing ability [32]. In the antimicrobial process, this solution can damage the cell wall and disrupt he cellular metabolic process. Although EOW is a strong acid, unlike hydrochloric and sulfuric acid, it is not corrosive to skin, mucus, or organic compounds. Itis known as an antimicrobial solution with minimal toxic and environmental effects mainly used in the food industry [31]. EOW was first used in Japan in 1980, being introduced immediately as a safe antimicrobial agent to the food industry. The solution was used to kill bacteria of raw fish without reducing its quality.

Moreover, the Hazard analysis and critical control points (HACCP) system suggested this solution to control critical points in various food industries [33]. EOW has been reported to have strong antimicrobial properties against a variety of pathogenic bacteria, including *Escherichia coli* O157:H7 [34], *Listeria monocytogenes* [35], *Bacillus cereus*[36], and *Salmonella typhimurium* [37]. Besides, it has antiviral properties against Hepatitis-B and immunodeficiency virus [38]. It also has the antifungal ability to remove fungi from various seeds [36]. EOW can be used for washing fruits, vegetables, and some washable foods to increase their durability [39, 40]. Using EOW for disinfecting the meat board reduces *Escherichia coli* O157:H7 by 5 Log CFU/100cm2.Furthermore, this solution decreases Log10 CFU/g 9-10 in the pure culture of *Enterobacter aerogenes* and *Staphylococcus aureus* after 30 seconds of contact. Generally, its use seems to be much more economical than other disinfectants [41]. Another study has confirmed these results for *Escherichia coli* O157: H7 and *Listeria monocytogenes* [42]. No study on EOW toxicity has yet been registered in scientific databases, probably due to the novelty of the field. However, since this substance is mainly accepted as an antimicrobial agent in the food industry, and it has been approved by systems such as HACCP, its low toxicity is almost agreed by everyone.

5. Conclusion

By reviewing various articles on new disinfectants, it is concluded that the focus of recent research is on using nanoparticles, complexes, and novel physicochemical methods, including electrolysis, in producing disinfectants. Meanwhile, it seems that the EOW disinfectant, mostly used in the food industry, has the least negative effect on the environment and human health. In certain food industries, such as pistachio processing, related to pathogenic microorganisms, the application of the EOW disinfectant is economically reasonable; it is effective on a wide range of microorganisms. However, further studies on its toxicity are required to investigate and evaluate its effectiveness in other industries and centers.

Conflict of interest

The authors of present research declare that there is no conflict of interest.

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