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CHEMISTRY

Metal Complex Bactericides with Detergent Properties

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Abstract—This communication describes the possibility of developing new metal complex bactericides with detergent properties that have no analogues. They irreversibly suppress bacteriophages, intestinal bacteria, virions, cocci, salmonella, trichomonas, and *Becreus* spores in fat-containing contaminants on the surfaces of various materials, in combination with washout of contaminants. In doses lethal to pathogens, the bactericide is safe for microflora, animals, and humans. The results seem to be relevant to the case of COVID-19 and possible worsening of the epidemiological situation.

Keywords: bactericides, detergents, metal complexes, disinfection

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Currently, there are known bactericidal complexes $[Cu(AC)NH_3]X$ and $Cu(Ida)NH_3$, where AC^- are amino acid anions and Ida^{2-} is the anion of C-substituted iminodiacetic acids (products made of hydrolysates of protein-containing wastes), $X = Cl^-$, $1/2SO_4^{2-}$ [1]. Products based on these compounds are used to treat deposits from waste treatment plants or waste repositories, in sanitary engineering, and household chemical goods instead of chlorine oxidants. The action of the complexes is based on the reactions

$$Cu(AC)NH_3 + HY \rightarrow NH_4[Cu(AC)Y]$$

or

$$Cu(Ida)NH_3 + HY \rightarrow NH_4[Cu(Ida)Y],$$

where Y is a group composed of radicals with amino groups $->C-NH_3^+$ and carboxyl groups $-COO^-$ of substituents of amino acid residues in protein polypeptide chains, DNA and RNA. The inclusion of $Cu(AC)^+$ or Cu(Ida) into native structures terminates nutrition, respiration, and excretion of microorganisms, leads to cell membrane charge neutralization and cell collapse, precludes excystation and viral replication, and inactivates enzymes [1]. In the biologically hazardous objects such as deposits of waste treatment facilities, the lethal dose (based on copper) of the complexes is 50–60 mg/kg of the medium (on a dry basis) for bacteriophages and microbes and 80–85 mg/kg for helminth eggs and tick larvae, which is lower than the maximum allowable concentrations for these objects. The use of such doses does not prevent the vital activity of aquatic flora and soil microflora. In terms of toxic action, these bactericidal complexes refer to hazard category four [1]. However, their applicability for special treatment during COVID-19 pandemic proved to be limited. The complexes do not behave as detergents; they do not diffuse into human-made contaminants containing fats and oils, which act as the media for the development of pathogens and deposition of bacteriophages, in particular COVID-19. We developed a detergent based on iminodiacetate derivatives of polymucosaccharides and iminodiacetate derivatives of fatty acid triglycerides, which were called "polycomplexones" and are produced from hydrolysates of protein-containing wastes [2, 3]. It is clear that the coordination moieties $CuLNH_3$, where L is the iminodiacetate radical, in the compounds of polycomplexones with copper amine complexes are analogous to $Cu(Ida)NH_3$. We assumed that polymucosaccharide and triglyceride derivatives with these coordination moieties would also act as wetting agents and biphilic molecules. In this case, compounds formed by polycomplexones with copper amine complexes would behave as metal complex bactericides with detergent properties. Below these compounds are designated as BDs.

RESULTS AND DISCUSSION

The synthesis was carried out using polycomplexones produced in Russia, which contained 47.6% of iminodiacetate derivatives of polymucosaccharides (mainly hyaluronic and sialic acids) and 52.4% of imi-

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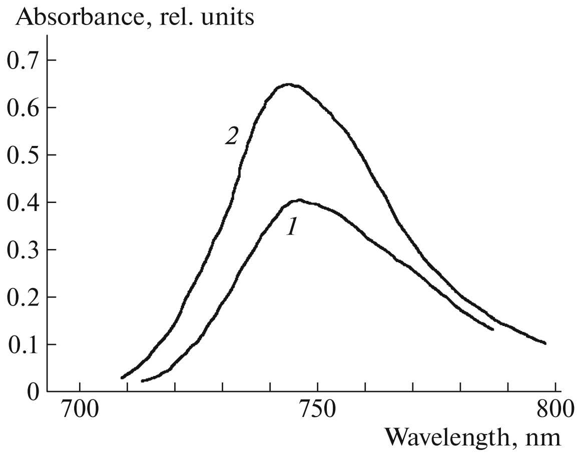

Fig. 1. Absorption spectra of a BD solution and a $Cu(Ida)NH_3$ solution.

nodiacetate derivatives of fatty acid triglycerides, with the total content of iminodiacetate groups of 2.67 mmol/g (on a dry basis) [2].

BDs were synthesized by treating polycomplexones with a solution of copper chloride ammonia complex with a concentration of 2 mol/L, equal to the content of L in the polycomplexone. Figure 1 presents the absorption spectra of a BD solution and a $Cu(Ida)NH_3$ solution. The spectra exhibit an absorption band at 745 nm, corresponding to the $T_{2g} \rightarrow E_g$ transition of copper atoms. The wavenumber of this transition depends on the composition of the coordination sphere and the shape of the coordination polyhedron. Hence, the structures of the coordination spheres in the BD and $Cu(Ida)NH_3$ are similar.

The standard toxicological and hygienic testing of BDs was carried out on laboratory animals (rats, mice, rabbits). It was found that BD corresponds to hazard category four (low-hazardous substance). The half-lethal dose LD_{50} is 12.5 g/kg; the compound does not irritate mucous membranes, respiratory tract, or skin and does not have a general toxicity.

The infected media were prepared using a mixture of sediments from the silt retention ponds of municipal and pig farm waste treatment facilities. The mixture had a strong fecal odor. The bacterial composition was established by standard bacteriological testing protocols for environmental objects by inoculation of the mixture on the blood medium and the Endo agar [3] and by phase contrast microscopy using the Goryaev chamber (Russia). The medium was found to contain bacteriophases (enveloped and non-enveloped viruses), E. coli, streptococcus, micrococcus, diplococcus, staphylococcus, enterococcus, intestinal ameba, salmonella, trichomonas, spores, and clostridium. The total content was approximately 1×10^{14} units/μL. The mixture, together with cooking fat (GOST 28414-89), was dispersed into a beef extract broth with brewed starch [4]. The media had a putrid fecal odor. The total content of lipids in the media determined by the extraction method is given in Table 1. The media as approximately 3 mm-thick layers were deposited on glass, plastic, nickel, steel, ceramic tile, and concrete plates (1 × 1 cm), incubated at 35°C for an hour, and kept in air until a dense coating formed. The contaminants had a pungent odor and were not washed out with hot water. Their surface was hydrophobic. A solution of BD containing 0.5 mol/L of $Cu(Ida)NH_3$ was applied onto the contaminants in portions with a dosing device. The BD solution was absorbed by the contaminant. During the treatment, the intensity of release of volatile components with a pungent odor decreased. The treatment was continued until the fecal odor disappeared, which indicated that microbial respiration stopped. The treated contaminant was washed away with water and the microbe content was measured. The washout was found to contain no living microorganisms. Hence, the doses at which the microbial respiration stopped corresponded to lethal doses, and disappearance of the odor can serve as a reliable rapid test of treatment efficiency. The lethal doses of copper present in BD depending on the content of lipids are summarized in Table 1.

It can be seen from Table 1 that the doses correlate with the content of lipids. The doses are lower for nonporous surfaces such as glass, metal, and plastic than for porous surfaces such as ceramic tiles or concrete.

The efficiency of surface decreasing upon bactericidal treatment was estimated by IR spectroscopy in relation to a nickel plate, which is most difficult to degrease. Figure 1 presents the IR spectrum of the nickel plate irrigated with the solution and the spectrum of this plate after washout.

The spectrum of the contaminated plate surface exhibits bands at 3400–3200 cm^{-1} corresponding to molecular group vibrations in cellulose and starch,

Table 1. Lethal BD doses in the washout of contaminants with different lipid contents

Lipids, % (on a dry basis)	BD dose, mg/kg				
	glass	plastic	steel	ceramic tiles	concrete
10	0.75–0.77	0.76–0.78	0.74–0.75	0.78–0.80	0.82–0.85
20	0.83–0.86	0.84–0.86	0.79–0.83	0.98–1.06	1.15–1.18
30	0.92–0.97	0.94–0.99	1.22–1.27	1.30–1.33	1.40–1.53

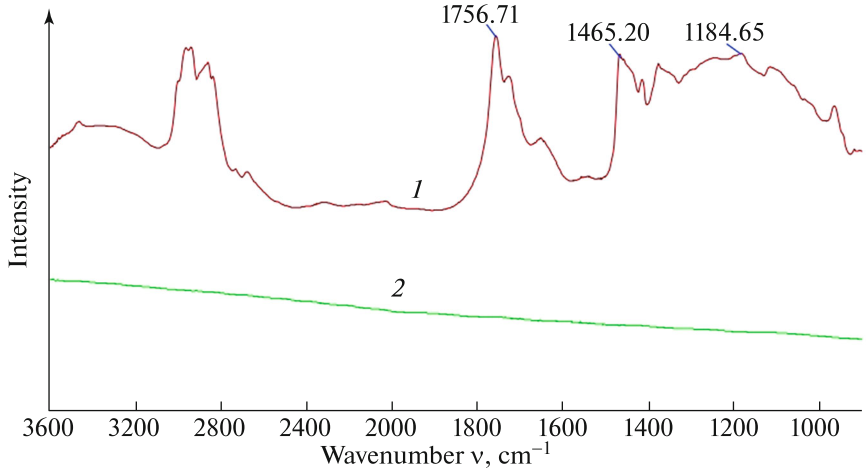

Fig. 2. IR spectra of (*1*) a contaminated nickel plate surface and (*2*) a nickel plate surface after washout of the contaminant.

bands at 1760 and 1184 cm^{-1} for vibrations of lipid molecules, and a band at 1463 cm^{-1} for protein molecules present in contaminants. After the washout, these bands are no longer present in the IR spectrum, that is, the contaminant is removed from the plate.

The studies showed that BD is simultaneously a bactericidal agent and a detergent. As noted above, on treatment of a contaminated surface a BD solution is absorbed by the contaminant. Figure 3 shows the micrography of the surface of disinfected contaminant with a lipid content of 35% on a nickel plate before washout. It can be seen that the surface is non-uniform and has visible particles. Apparently on treatment with a BD solution, triglyceride derivatives as biphilic molecules are inserted into fat particles. This provides for the diffusion of polymucosaccharide derivatives into the contaminants, resulting in their destruction and degradation into particles. Probably, polymucosaccharide chains, in particular hyaluronic acid derivatives with molecular weights of 5–15 million Da, form hydrophilic shells around the particles. This results in separation of the contaminant from the surface. During diffusion, the $CuLNH_3$ complexes contact with bacterial colonies and bind the protein structures of viruses, toxins, and proteases. In this case, the consumption of BD will increase in proportion with the content of lipids.

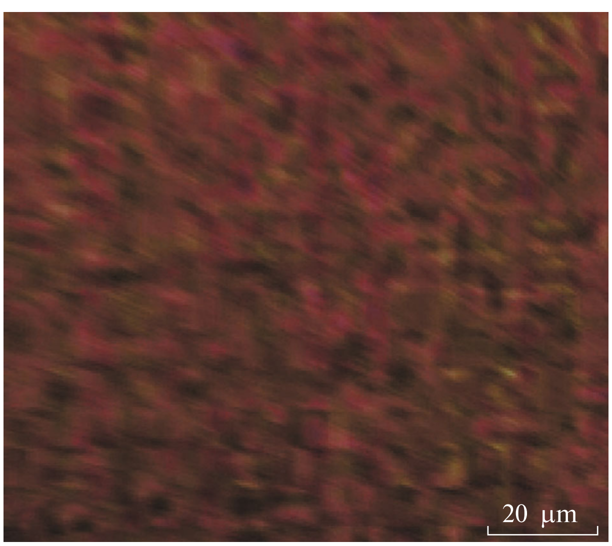

Fig. 3. Micrograph of the surface of disinfected contaminant.

Currently, during the pandemic, the use of chlorine-containing disinfectants significantly increased [4, 5]. Chlorinated lime, sodium hypochlorite, chlorhexidine, and the like are used most often [6, 7]. For increasing their efficiency, they are combined with hard surfactants [8]. The use of these agents on a large scale would obviously lead to excessive contents of toxic compounds, including dioxins [9], both in items that directly contact with people and in municipal waste sewage. In this respect, BD may be promising as a readily available base for health safe agents for special industrial sanitizing of items that can accommodate viruses and pathogens and also for the development of a line of antibacterial household products for house cleaning, cleaning of sanitary and kitchen devices, and dishwashing. Currently, the authors, together with potential manufacturers, have developed documentation for the production of BD and BD-based formulations.

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