The increase in the frequency and scale of epidemics of infectious diseases gives extreme urgency to the development of new technologies for antiseptic and disinfectant treatment of various media, as well as materials/reagents for their implementation. Antimicrobial polymer materials of various chemical structures, including those containing halogen-active functional groups, are promising in this regard.

This work is devoted to the synthesis and investigation of the properties of granular and fibrous polymer materials with immobilized N-bromosulfonamide groups of different structure. It is shown that copolymers of styrene with divinylbenzene and polypropylene can be used as a carrier polymer. A technique has been developed that allows obtaining polymers with a content of up to 23 % of immobilized active bromine. The compliance of the synthesized materials with the declared structure has been proven by IR spectroscopy and a complex of chemical methods. A decrease in the strength of the obtained polymers compared to the original carriers has been observed, especially in the case of fibers. The stability of the synthesized polymers during storage is lower that of the previously described chlorine-active analogs. For the quantitative determination of active bromine in the target materials, a technique based on its rapid diffusion from the polymer into the taurine solution has been developed. Microbiological research has shown that the synthesized polymers have a pronounced antimicrobial activity, which is higher than that of immobilized N-chlorosulfonamides and is manifested even in the presence of a significant organic load.

The set of investigated characteristics of synthesized polymers with immobilized N-bromosulfonamide groups suggests the prospect of their use as components of antiseptic dressing materials, antimicrobial filters, devices for obtaining antiseptic solutions, and other medical products

Keywords: *antimicrobial polymers, immobilization, N-bromamines, N-bromosulfonamides, active chlorine, N-bromotaurine, zone of microbial growth inhibition*

UDC 691.175.5/.8 +661.463+ 579.61 + 614.446
DOI: 10.15587/1729-4061.2023.278000

NEW MULTIFUNCTIONAL BROMINE-ACTIVE POLYMERS: SYNTHESIS, PROPERTIES, AND ANTIMICROBIAL ACTIVITY

Bohdan Murashevych
PhD, Associate Professor
Department of Biochemistry and Medical Chemistry*
Dmitry Girenko
Doctor of Chemical Sciences, Professor
Department of Physical Chemistry**
Mykola Toropin
Junior Researcher
Research Institute of Electroplating**
Iryna Koshova
PhD, Associate Professor
Department of Microbiology, Virology, Immunology, Epidemiology and Medical and Biological Physics and Informatics*
Vadym Kovalenko
Corresponding author
PhD, Associate Professor
Department of Analytical Chemistry and Chemical Technology of Food Additives and Cosmetics**
E-mail: vadimchem@gmail.com
Oleg Lebed
PhD, Associate Professor
Department of Biotechnology**
Vasyl Chuiko
PhD
Department of Obstetrics and Gynecology*
Valerii Kotok
PhD, Associate Professor
Laboratoire of Charles Coulomb
Université de Montpellier|CNRS
163 rue Auguste Broussonnet, Montpellier, France, 34090
Dmytro Stepanskyi
Doctor of Medical Sciences, Professor
Department of Microbiology, Virology, Immunology, Epidemiology and Medical and Biological Physics and Informatics*
*Dnipro State Medical University
Volodymyra Vernadskoho str., 9, Dnipro, Ukraine, 49044
**Ukrainian State University of Chemical Technology
Gagarina ave., 8, Dnipro, Ukraine, 49005

Received date 03.02.2023
Accepted date 18.04.2023
Published date 28.04.2023

How to Cite: *Murashevych, B., Girenko, D., Toropin, M., Koshova, I., Kovalenko, V., Lebed, O., Chuiko, V., Kotok, V., Stepanskyi, D. (2023). New multifunctional bromine-active polymers: synthesis, properties, and antimicrobial activity. Eastern-European Journal of Enterprise Technologies, 2 (6 (122)), 32–42. doi: https://doi.org/10.15587/1729-4061.2023.278000*

1. Introduction

The events of the past few years related to Covid-19 have clearly revealed the devastating consequences of the pandemic for the modern world [1, 2]. At the same time, new data indicate that the annual probability of new extreme pandemics may increase up to 3 times in the coming decades [3]. This is due to several main factors: climate change [4, 5], an

increase in population density in economic centers [6], intensification of traffic flows [7], a decrease in the immune protection of the population due to aging and negative environmental conditions [8, 9], etc. Obviously, infectious diseases, especially those transmitted by the aerogenic mechanism, pose the biggest threat [10, 11]. Numerous analyzes of the effectiveness of measures to counteract epidemic processes have shown that preventive procedures, primarily disinfection/antiseptic treatment [12, 13] and the use of personal protective equipment [14], are of great importance. Therefore, the creation and implementation of new materials and technologies for disinfection is an important and urgent task.

Halogen-active preparations (hypohaloid acids [15], their salts [16], and various halamines [17]) are the most promising for use as microbiocidal agents. Their attractiveness is due to bactericidal [18], fungicidal [19], virucidal [20], antiprion [21] activities of a wide spectrum, their systemic action [17] (and, as a result, the absence of resistance to them), high speed of achieving the effect, as well as cheapness and availability. Studies stimulated by the pandemic show that, in addition to the classical uses of such drugs (disinfection of various surfaces and water), their medical use as antiseptic [22], wound healing [23], anti-inflammatory agents [24]. Their inhalation use is also promising for the protection and treatment of the respiratory tract [25, 26]. At the same time, the toxicity of these compounds at effective concentrations is low in most cases [27, 28]. The main disadvantage of classical halogen-active preparations is their low stability (especially in solutions) [29], the insufficient purity of industrially produced products based on them [30], as well as the limitation of their final physical forms to solutions and powders. Therefore, in recent decades, the production of functional polymeric materials has been gaining popularity, the variety of forms of which makes it possible to significantly expand the scope of application of halogen-active compounds without reducing microbiocidal activity.

2. Literature review and problem statement

Antimicrobial polymers are currently widespread [31, 32] and are used as components of wound dressings [33], implants [34], catheters [35], elements of medical furniture and equipment [36], personal protective equipment [37], filters of water and air treatment systems [38], etc. Some representatives are even considered as a potential replacement for antibiotics [39]. Such materials differ in the nature of the polymer itself, its manufacturing technology, physical form, physicochemical and mechanical properties. According to the mechanism of microbiocidal action, antimicrobial polymers can be conventionally divided into three groups. The materials of the first group include polymers impregnated with an antimicrobial agent [40], which can be compounds of different chemical nature: surfactants, metal salts, antibiotics, peptides, etc. The polymer itself does not have biocidal properties and serves as a carrier. The basis of the antimicrobial action in this case is the diffusion of the active agent from the polymer into the contaminated medium. The second group includes materials with functional groups covalently bound to the macromolecule and possessing microbiocidal properties. The most common here are polymers with quaternary ammonium and phosphonium groups [41]. Such materials, upon direct contact, disrupt the equilibrium charge of the cell membrane of microorganisms, which leads to their neutralization. In this case, the diffusion of the antimicrobial agent into the treated medium does not occur, and they are mainly used as filters. The synthesis of these polymers is possible by polymerization of the initially active monomer or by functionalization of a suitable polymer carrier; chitosan is the best known of the natural representatives of this group. The third group combines the features of the first two: such polymers contain grafted (immobilized) groups that are capable of releasing an antimicrobial agent into the medium under certain conditions [42]. Thus, these materials have both their own antimicrobial activity and the ability to neutralize pathogens in the medium in which they are placed.

Halogen-active antimicrobial polymers mainly belong to the third group [43, 44]. Polyurethanes, nylons, cellulose, silica gel, etc. can act as carrier polymers. The most common functional group in them is the N-chloroamino group. It is immobilized on a carrier by grafting a cyclic or acyclic amine, amide or imide, followed by "charging" with active chlorine by reacting with a chlorinating agent (more often molecular chlorine or sodium hypochlorite). Chlorine-active polymers in which the N-chlorosulfonamide group is the carrier of active chlorine have also been described [45, 46]. Such materials have powerful microbiocidal properties, can be used as oxidizing agents for various inorganic compounds, and they are shown to be promising as an element of water treatment systems. Bromine-active polymers, which can be synthesized by reacting an analogous polymer with a brominating agent, are described much less. For example, granular bromine-active polymers synthesized by grafting a hydantoin or uracil cycle to chloromethylpolystyrene with subsequent bromination are described in [47]. The resulting materials contain 15–25 % of active bromine, can be recycled and have antimicrobial properties against suspended in water *E. coli* in flow systems. The disadvantage of these materials is the active release of hypobromous acid from them even into distilled water. The synthesis of macroporous styrene-divinylbenzene granular polymers with immobilized N-bromosulfonamide groups in the sodium form from sulfonic acid cation exchangers of the Purolite C-100 type is described in [48]. The content of active bromine in them reaches 33 %. When 1 g of such granules is added to 25 mL of a 0.1 N solution of $FeCl_2$ at room temperature, a complete transition of Fe^{2+} ions to Fe^{3+} is observed after 1 day. The antimicrobial activity of such polymers has also been confirmed: 0.1 g of granules in contact with 1 mL of river water reduces the total microbial count from 35,000 to 48. The disadvantages of the described materials are their existence only in granular form and low stability (the decrease in the concentration of active bromine during storage in a closed container was 10 % within 40 days). Thus, the literature data confirm the possibility of using bromine-active polymers for disinfection, however, they do not always take into account aspects important for their subsequent medical use, and mainly describe granular forms. In addition, purposeful work on studying the properties of bromine-active

materials is rarely carried out, which may be due to the fact that chlorine-active analogs are more attractive for disinfection purposes because of the greater availability of a chlorinating agent (industrial sodium hypochlorite). Obviously, the physicomechanical properties and the economic component of the use of halogen-active polymers depend mainly on the carrier polymer. Grafting or copolymerization technologies for obtaining immobilized traditional organic functional groups with a nitrogen atom are generally quite complex, especially in the case of inert supports such as polypropylene or polyethylene terephthalate [49, 50]. It should be taken into account that for medical materials, such as dressings, the presence of organic fragments, as in the case of [47], is undesirable, since this can cause allergic reactions. Moreover, the presence of complex fragments reduces the stability of such polymers in aggressive environments and under storage, as well as the possibility of their regeneration. Thus, the selection of a suitable carrier polymer and the immobilization of a stable functional group-donor of active bromine on it is a promising task.

Previously, it has been shown that styrene-divinylbenzene copolymers in granular (raw material for the production of cation exchangers of the Purolite C-100 and KU-2-8 type) and fibrous (radiation grafted to a polypropylene thread, raw material for cation exchangers of the FIBAN brand) forms are suitable as a carrier onto which sulfonamide groups can be grafted, which are easily converted into various N-chloro-sulfonamides [51]. Materials functionalized in this way contain a significant (up to 13 %) amount of active chlorine, are extremely stable, chemically resistant, and can be repeatedly regenerated. They have been shown to have antimicrobial [52], virucidal [53], and reparative [54] activity. Also there is the possibility of using them to obtain chlorine-active solutions [55]. The developed methods, the last stage of which consists in "charging" the immobilized sulfamide group with active chlorine, can be used for the synthesis of similar and previously undescribed bromine-active polymers, which, with a high degree of probability, would also have an antimicrobial effect. Thus, previously described procedures should be adapted for obtaining such materials, and the structure, chemical and antimicrobial properties of products obtained should be investigated in order to assess the prospects for their use in the production of medical devices (protective masks, dressings, water and air filters, etc.).

3. The aim and objectives of research

The purpose of the study is the synthesis of granular and fibrous polymers with immobilized N-bromosulfonamide groups and the establishment of their main characteristics. This will allow assessing the prospects for the use of such materials for the production of medical and sanitary-hygienic products. To achieve the goal, it was necessary to solve the following tasks:

– to develop a method for the immobilization of the N-bromosulfonamide group on granular and fibrous styrene-divinylbenzene copolymers, to investigate the physicomechanical properties and stability of the obtained products;

– to study the chemical structure of the obtained polymers and to determine the concentration of immobilized functional groups;

– to reveal the presence of antimicrobial activity of the synthesized materials against different types of microorganisms.

4. Materials and methods of research

4. 1. Object and hypothesis of the study

The object of the study is polymeric materials with immobilized (covalently bonded) N-bromosulfonamide groups, which are considered as potential active components of medical devices with a microbiocidal effect. The subject of research is the synthesis, chemical structure, and antimicrobial properties of such polymers. The main hypothesis is that when such a functional group is immobilized on a neutral carrier polymer, diffusion of active bromine into the external media will be possible. It will begin in the presence of amine compounds in the treated medium, including those of a microbiological origin, due to which the microbiocidal effect will be achieved.

4. 2. Synthesis of polymers with immobilized N-bromosulfonamide groups, their physico-mechanical properties and stability.

Two types of commercially produced polymers have been used as carriers for functionalization, as in [51, 55]: gel styrene-divinylbenzene resin (raw material for the synthesis of sulfonic acid cation exchangers of the Purolite C100 and KU-2-8 types [56]), and a fibrous copolymer of styrene with divinylbenzene on a polypropylene thread (raw material for the production of FIBAN K-1 sulfonic cation exchanger [57]). It was proposed to carry out the immobilization of the N-bromosulfonamide group on the polymer according to a procedure similar to that previously described for the immobilization of the N-chlorosulfonmide group [51, 55], adapting it under the use of a freshly prepared solution of sodium hypobromite as a halogenating agent.

4. 3. Study of the structure and chemical composition of synthesized polymers.

The proof of the structure of the polymers has been carried out using IR spectroscopy on a Spectrum BX II Perkin Elmer IR Fourier spectrometer (USA). The dried polymer samples were ground in an agate mortar with potassium bromide, then pressed into tablets, which were further being analyzed.

The content of immobilized active bromine was being determined by iodometric titration according to two methods. The first technique ("direct titration") is similar to that described earlier for chlorine-active polymers [55]. Weighed sample of 1.0 g of polymeric sodium N-bromosulfonamide or N,N-dibromosulfonamide was being placed in a 250 mL flask, then 100 mL of distilled water, 10 mL of 10 % KI solution and 10 ml of 10 % H_2SO_4 were being added, stirring after adding each reagent. The contents were being heated in a closed flask in a water bath until the release of iodine begins. The released iodine was being titrated with 0.1 N sodium thiosulfate solution. The heating and titration of the analyzed sample were being peri-

odically repeated until the release of iodine into the solution ceases. The content of active bromine in the polymer in mass percent (X) is being calculated by the formula:

$$X = \frac{V \cdot K \cdot 0.00799 \cdot 100}{m},$$

where V – volume of 0.1 N solution of sodium thiosulfate, which was used for titration of the analyzed sample, mL; K – correction factor to normality for the titrant solution; 0.00799 – equivalent mass of active bromine, which corresponds to 1 mL of 0.1 N sodium thiosulfate solution, g/mL; m – the weight of the polymer sample, g.

The second method ("indirect titration after activation with taurine") was specially developed by us and is based on the previously described properties of the studied polymers to release active halogen into aqueous media containing amine activators [55]. After determining the content of active bromine by "direct titration", a weighed sample of 1.0 g of the corresponding polymer was being placed in a flask with 100 mL of distilled water and stirred on a magnetic stirrer for 15–20 minutes to swell. Then, a deliberate excess of taurine (in this case, 0.5 g) was being added to the flask and stirred on a magnetic stirrer for 10 min (in the case of fibrous polymers) or 40 min (in the case of granular polymers). In this case, immobilized active bromine is transferred from the polymer to the taurine molecule, which leads to N-bromotaurine, which is quite stable under the conditions of this experiment [58]. The content of active bromine in the obtained solution of N-bromotaurine (aliquot 1.0 ml) was being determined by standard iodometric titration in acetic acid [59], titrant – 0.002 N solution of sodium thiosulfate. The content of active bromine in the polymer in mass percent (X) is being calculated by the formula:

$$X = \frac{[V \cdot K \cdot C(Na_2S_2O_3)] \cdot M(1/2\,Br_2)}{V_{al}} \cdot \frac{10}{m},$$

where V – volume of 0.002 N sodium thiosulfate solution, which was used for titration of the analyzed sample, mL; K – correction factor to normality for the titrant solution; $C(Na_2S_2O_3)$ – normality of sodium thiosulfate solution, $M(1/2Br_2)$=79.9 – equivalent mass of active bromine, g/mol; V_{al} – aliquot volume, mL; m – weight of the polymer sample, g.

Determination of the content of free –SO_3H groups in polymeric sodium N-bromosulfonamide: immobilized sodium N-bromosulfonamide was being treated with 1.0 N HCI solution to convert it to the H-form, the product was being rinsed with water until the filtrate is neutral, and dried in a desiccator over sulfuric acid to constant weight. Next, a weight sample of 0.3–0.5 g was being placed in 50 mL of distilled water and incubated for 24 h, then titrated potentiometrically with 0.1 N sodium hydroxide solution with a glass electrode to pH 7.0. The content of –SO_3H groups in mg-eq/g is being determined from the titration curve [60].

The content of free –SO_3H groups in polymeric sulfonamide and N,N-dibromosulfonamide was being determined by the exchange capacity of 0.1 N calcium chloride solution [60]. A weight sample of 1.5 g of polymer was being added to 100 mL of calcium chloride solution and kept for 24 hours with occasional stirring. Then 25 mL of the solution was taken and titrated with 0.1 N•NaOH solution in the presence of an indicator – methyl red. The content of –SO_3H-groups (E) in mg-eq/g is being determined by the formula:

$$E = \frac{4 \cdot a \cdot K \cdot N \cdot 100}{g \cdot (100 - W)},$$

where a – the volume of NaOH solution used for titration, mL; N – the normality of the NaOH solution; K – the correction factor for 0.1N NaOH solution; g – the weight of the polymer sample, g; W – the water content in the polymer, %.

4. 4. Study of the antimicrobial activity of the synthesized polymers.

The antimicrobial activity of the obtained materials was being determined by the modified agar well method [61]. The melted and cooled tryptone soy agar was being contaminated with a suspension of test microorganisms. Museum strains of the most common microorganisms *S. aureus*, *C. albicans*, and *E. coli* were used as test cultures. The microbial load was 1×10^7 CFU/mL. The contaminated nutrient medium (20 mL) was being poured into sterile Petri dishes and left to solidify. Then, wells of 8 mm in diameter were being formed in the thickness of the nutrient medium with a sterile puncher. Samples of the test materials were being placed to these wells (0.1 g weighed portions for fibrous materials and weighed granules corresponding to the amount of immobilized active bromine in latter) and 0.1 mL of a sterile isotonic sodium chloride solution was being added to ensure uniform wetting of the sample surface and diffusion of the activator and active bromine. As a control, granular and fibrous samples of polymeric sulfonamide "uncharged" with active bromine and 0.9 % sodium chloride solution were being used. After that, Petri dishes were being incubated for 24–48 hours at 37 °C. All microbiological experiments were being carried out in triplicate. The criterion for the effectiveness of the antimicrobial action of the sample was the diameter of zones of microorganism growth inhibition (average over three repeats).

5. Results of studying the synthesis and properties of polymers with immobilized bromine-active groups

5. 1. Adapted procedure for the synthesis of N-bromosulfonamides immobilized on a polymer, appearance, physico-mechanical properties, and stability of the obtained materials

The developed method is the same for granular and fibrous polymer carriers and is described by the general scheme (Fig. 1).

The sample of 26 g of carrier polymer (I) was being placed in a 3-necked flask with a volume of 1 L, 300 mL of 1,2-dichloroethane were being added, mixed and left for 12 hours (for fiber) and for 24 hours (for granules) to swell. Then, 58.0 g of freshly distilled chlorosulfonic acid were being added from a dropping funnel with vigorous stirring. The reaction mass was being stirred at a temperature of 50–60 °C for 3 hours, then cooled to +20 °C, the polymer were being filtered off on a Schott filter, rinsed several times with 1,2-dichloroethane, unload into a beaker with ice water, mix and filter quickly. The resulting

sulfochloride (II) was being added in portions with stirring to 300 mL of 12 % aqueous ammonia solution cooled to 0 °C, stirred and left for 12 hours. The resulting polymeric sulfamide (III) was being filtered off on a Schott filter, rinsed with water until neutral pH of the wash water and dried first in air and then in a desiccator over sulfuric acid to constant weight. Then 600 mL of 6.0 % sodium hypobromite solution (freshly obtained by dissolving bromine in sodium hydroxide solution) was being placed in a beaker, sulfamide was being added in portions with stirring and left for 12 hours. The resulting N-bromosulfonamide sodium (IV) was being filtered off on a Schott filter, thoroughly rinsed with water until neutral pH of the wash water, dried first in air and then in a desiccator over sulfuric acid to constant weight. To determine the moisture content, the polymers dried in a desiccator were being dried additionally in an oven at 90–95 °C to constant weight. To obtain immobilized N,N-dibromosulfonamide (V), the same procedure was used, only at the stage of bromination, the sodium hypobromite solution is acidified by adding 50 mL of glacial acetic acid.

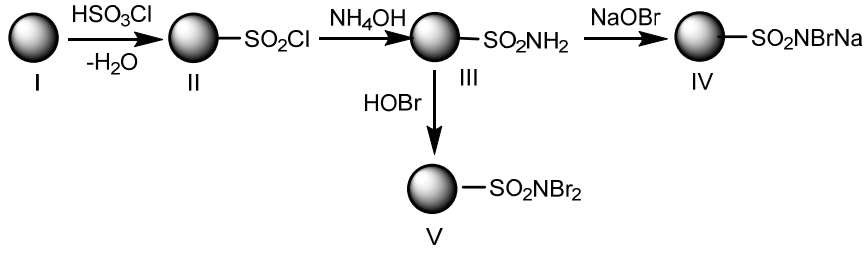
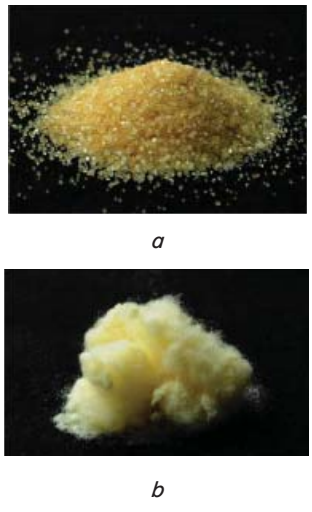


Fig. 1. Scheme for the synthesis of granular and fibrous polymers with immobilized N-bromosulfonamide groups

The functionalized materials obtained by the described method have a more yellow color compared to the initial polymers, the depth of which correlates with the concentration of immobilized bromine (Fig. 2), and, in contrast to chlorine-active analogues, have a more pronounced characteristic odor.



a

b

Fig. 2. Appearance of the synthesized polymers: *a* – granular N-bromosulfonamide sodium; *b* – fibrous N-bromosulfonamide sodium

The moisture content of the polymers after drying in a desiccator over sulfuric acid is 18–20 % for granular and 1.8–2.0 % for fibrous materials. The yields of materials (after drying over sulfuric acid) were: for N-bromosulfonamide sodium in granular and fibrous form – 29.5 g and 26.0 g, respectively; for N,N-dibromosulfonamide in granular and fibrous form – 39.0 g and 32.4 g, respectively.

During the synthesis of granular materials, no noticeable degradation and decrease in the strength characteristics of the polymer carrier was observed, while the resulting fibrous forms have a lower strength than the initial polymers and are more prone to destruction of the fiber structure with the formation of highly dispersed dust.

The storage of polymers for one month in a closed container in the dark showed that the decrease in the concentration of active bromine in them over this period is 4.0–6.0 % for granular forms and 8.0–10.0 % for fibers.

5. 2. Determination of the structure of the synthesized polymers and the content of immobilized functional groups.

The IR spectra of the obtained polymers are similar to the spectra of previously synthesized chlorine-active polymers, are the same for granular and fibrous forms, and confirm the declared structure. Spectra of the initial granular polymeric sulfamide in comparison with the corresponding N-bromochlorosulfonamide sodium and N,N-dibromosulfonamide are shown in Fig. 3, *a–c*, respectively:

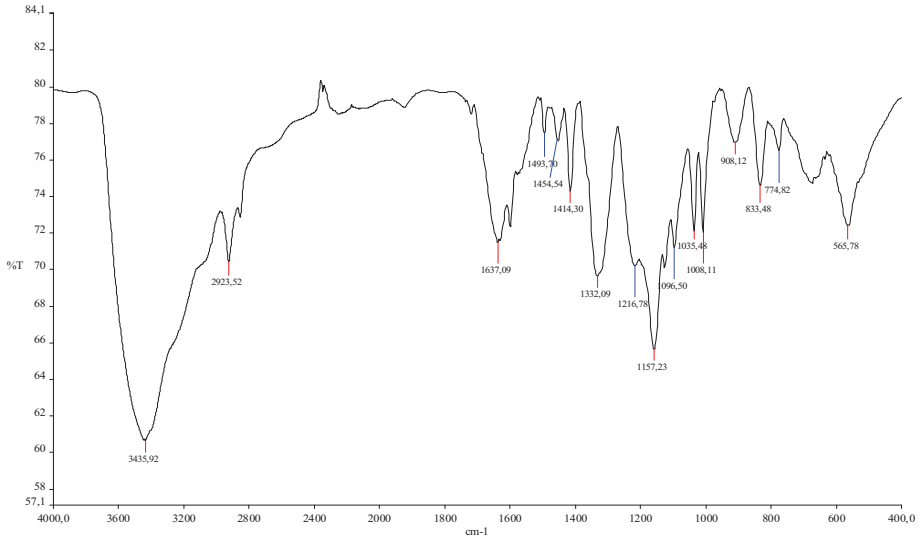
The results of determining the content of immobilized active bromine according to the two described methods are shown in Table 1.

Table 1

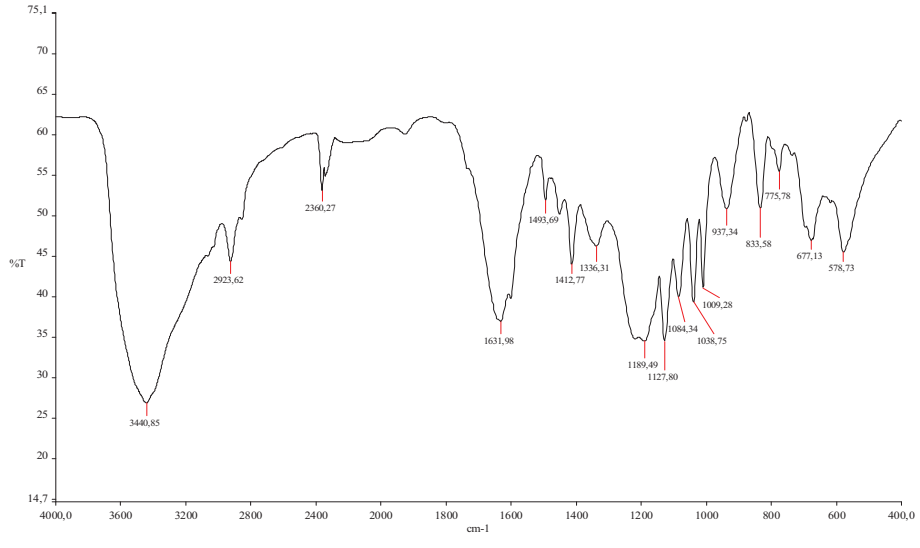
The concentration of immobilized active bromine, determined by two developed methods

Polymer sample	Active bromine concentration (direct titration), % w/w	Active bromine concentration (indirect titration after activation with taurine), % w/w	Divergence of results by different methods, %
Granular N-bromosulfonamide sodium	8.05	7.83	2.73
N-bromosulfonamide sodium	12.85	12.96	0.85
Granular N,N-dibromosulfonamide	14.45	14.38	0.48
Fibrous N,N-dibromosulfonamide	23.37	23.55	0.76

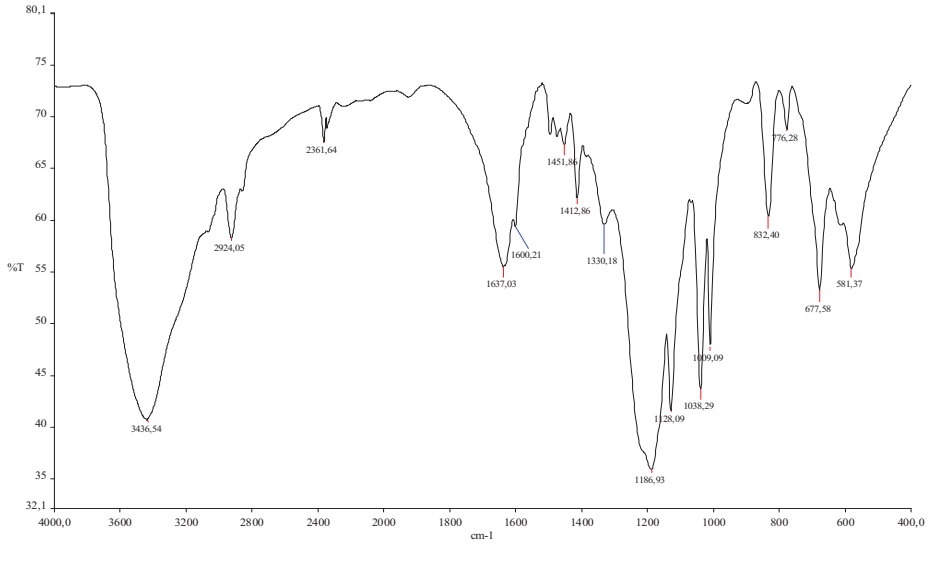
The content of free sulfo groups in the synthesized polymers was 0.30–0.32 mg-eq/g for granular and 0.25–0.27 mg-eq/g for fibrous forms.



a



b



c

Fig. 3. IR spectra of the studied granular polymers: *a* — sulfonamide; *b* — N-bromosulfonamide sodium; *c* — N,N-dibromosulfonamide

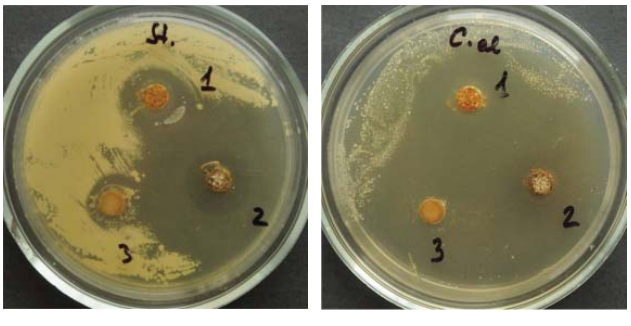
5. 3. Antimicrobial activity of synthesized polymers

Zones of microbial growth inhibition around the studied samples (average of three repetitions) are shown in Table 2; the control did not cause growth retardation in any case. Fig. 4 shows the inhibition zones for *S. aureus* and *C. albicans* caused by specific polymer samples.

Table 2

Zones of microbial growth inhibition around synthesized polymer samples

Polymer sample	Zone of microbial growth inhibition, mm		
	E. coli	*S. aureus*	*C. albicans*
Granular N-bromosulfonamide sodium	25	24	35
Fibrous N-bromosulfonamide sodium	21	18	38
Granular N,N-dibromosulfonamide	35	46	>50
Fibrous N,N-dibromosulfonamide	38	42	>50



a *b*

Fig. 4. Zones of growth inhibition for *S. aureus* (*a*) and *C. albicans* (*b*) around polymer samples: 1 — granular N-bromosulfonamide sodium, 2 — granular N,N-dibromosulfonamide, 3 — fibrous N-bromosulfonamide sodium

Samples which inhibition zones exceeded 50 mm were re-examined one by one in separate Petri dishes.

6. Discussion of the results of synthesis and properties of polymers with immobilized N-bromosulfonamide groups

As can be seen from Fig. 3, the declared structure of the resulting bromine-active polymers is confirmed. The spectra of all compounds contain characteristic absorption bands of the stretching vibrations of the groups $-CH_2-$ at about 2924 cm^{-1}, as well as skeletal stretching vibrations of aromatic fragments –C=C– in the region of 1637 cm^{-1}. The immobilized sulfonamide should have an absorption band of the -NH_2 group in the region of 3420–3430 cm^{-1}, however, the analysis of this signal is complicated by the superposition of the absorption peak of the hydroxyl groups of hydrogen-bonded water molecules adsorbed on the polymer, and signals in this region are present in all samples. The presence of S=O groups in all cases is confirmed by characteristic peaks in the region of 1330–1340 cm^{-1} (asymmetric stretching vibrations), as well as 1200–1220 cm^{-1} and 1150–1190 cm^{-1} (symmetric stretching vibrations), which is consistent with the literature data for polystyrenesulfonamide [62] and bromo-derivatives of benzenesulfonamide [63, 64]. The absorption of the –N–Br bond in the region of 945–932 cm^{-1}, noted by the authors of [63], in this case is not sufficiently informative, because it is situated in the region of "fingerprints". This absorption is small in comparison with the signals of other functional groups, both because of the low specific absorption coefficient and lower concentration on the polymer. Therefore, it is expedient to determine the presence and concentration of immobilized bromine titrimetrically.

The deterioration of the mechanical properties of the synthesized fibrous bromine-active polymers compared to the previously described chlorine-active analogs is probably due to a more intense violation of the macromolecule structure upon immobilization of a bulkier bromine atom. This is indirectly confirmed by a greater tendency of the fibrous N,N-dibromosulfonamide to shedding in comparison with N-bromosulfonamide sodium. At the same time, the initial fibrous sulfamide, "uncharged" with active bromine, did not differ from the corresponding one obtained in the synthesis of immobilized N-chlorosulfonamides. Note that the granular polymers did not show a noticeable decrease in strength. Destruction and subsequent mechanical losses of the fiber also explain the lower yields of such products in comparison with granular ones. The disadvantage of current work at this stage is that the quantitative characteristics of the mechanical properties of the obtained polymers, as well as the structure of their surface, were not studied by us within the framework of this study and should be described separately in the future.

The higher moisture content of granular polymers is obviously due to a less developed surface compared to the fiber, which makes it difficult to dry the material swollen during synthesis. At the same time, all commercially produced polymers of a similar structure also contain a significant amount of bound water (up to 50 % for Purolite C100 cation exchangers and 10–14 % for FIBAN K-1). The increase in the moisture content of bromine-active polymers compared to the starting materials is explained by an increase in hydrophilicity upon the embedding of polar sulfamide groups. Complete drying of such materials via heating is technologically possible, however, we have previously found that this leads to a decrease in strength characteristics, partial decomposition of functional groups, and a slowdown in the diffusion of active halogen into aqueous solutions. Therefore, taking into account the intended purpose of these polymers, it is not advisable.

The stability of the synthesized polymers turned out to be lower that of similar N-chlorosulfonamides – for the latter, the decrease in active chlorine is 2–3 % per year for granules and 5–6 % per year for fibers [51]. These data are consistent with the repeatedly described lower stability of bromine-active compounds compared to chlorine-active ones. This aspect requires further study under different storage conditions.

As can be seen from the results of titrimetric analysis (Table 2), all synthesized materials contain a significant amount of immobilized active bromine. The proof that it is retained on the polymer in the covalently bound (not in adsorbed) form is the fact that no active bromine is detected in distilled water after the sample is soaked in. Taking into account the higher molecular weight of bromine, its concentration in the composition of the functional N-bromosulfon-

amide group generally correlates with that of the previously described chlorine-active polymers. Thus, for immobilized sodium N-chlorosulfonamide, the average molar concentration of active chlorine is 1.1 mmol/g, and for the synthesized sodium N-bromosulfonamides, it is 1.0 mmol/g. It can be concluded that the maximum possible concentration of the active halogen immobilized on such carriers depends on the content of embedded sulfamide groups, and the process of their halogenation using the described synthesis procedure proceeds completely. Note that one of the shortcomings of the study is that we did not determine the concentrations of immobilized sulfamide groups. This is due to the complexity of both chemical (for example, determination of nitrogen by Kjeldahl method or gravimetrical determination of sulfur) and instrumental (derivatography, chromatography) approaches to such analysis due to the peculiarities of the physico-mechanical properties of the carrier polymer and the relatively low concentration of these groups against the background of the macromolecule.

The data of Table 1 indicate a satisfactory convergence of the results of determining the immobilized active bromine concentration by the two developed methods, especially in the case of fibrous polymers. The main disadvantage of "direct titration" is the need to heat the reaction mixture to facilitate the diffusion of reagents, which can lead, on the one hand, to volatilization of the released iodine, and, on the other hand, to additional oxidation of the iodide ion. The method of "indirect titration" seems to be more accurate, but its disadvantage is the time factor, as well as the fact that for the correct choice of the required amount of activator (taurine), it is still necessary to first determine the approximate content of active bromine in the polymer. The possibility of rapid diffusion of bromine from a polymer into the solution of an activator, which we have proven, in addition to being used for analytical purposes, opens up prospects for obtaining antimicrobial bromine solutions in this way. The largest discrepancy between the results, as seen, is observed for granular N-chlorosulfonamide sodium, which is due to the slowest diffusion of active bromine from this polymer into solution and, accordingly, the need to carry out heating for longer when analyzing by the "direct titration" method.

The low content of free sulfo groups proves that the developed procedure makes it possible to avoid the hydrolysis of sulfochloride obtained at the first stage and, accordingly, almost completely convert it into the target sulfonamide for subsequent immobilization of active bromine. At the same time, it is expedient to develop modified polymers that have sulfo groups along with N-bromosulfonamide groups to impart ion-exchange properties to synthesized materials.

As can be seen from Table 3, all studied samples show pronounced antimicrobial properties against all used microorganisms. The growth inhibition zones for these polymers generally exceed those for the previously described for chlorine-active analogs. Thus, in [52], the zones of growth inhibition of *S. aureus* and *C. albicans* around a sample of immobilized fibrous sodium N-chlorosulfonamide with a concentration of 6.8 % active chlorine amounted to about 10.0 mm, which, even taking into account a slightly lower content of the antimicrobial agent, is more than 2 times inferior to the bromine-active fiber studied in this work. More powerful and faster antimicrobial activity of active bromine compounds compared to active chlorine in buffer solutions was described earlier [65]. This activity is due to many factors: higher lipophilicity, higher rate constants of interaction with thiol groups of the most important enzymes of microorganisms, higher content of hypobromous acid in solutions with a pH close to physiological, etc. However, in the same work, a significant decrease in the microbicidal properties of hypochlorous acid and N-bromoamines was declared in the presence of an organic load, the role of which in our case is played by a nutrient medium. Conducted experiment shows that this does not apply to N-bromosulfonamides immobilized on the polymer. Probably the slow diffusion of active bromine from the polymer into the medium does not allow the entire amount of bound active bromine to be immediately neutralized by agar molecules and ensures its gradual effect on microorganisms. This can also explain the smaller inhibition zones around fibrous samples in comparison with granular ones. As can be seen, the polymer samples of N,N-dibromosulfonamides are more powerful microbicides, apparently due to the higher concentration of immobilized active bromine. Among all microorganisms under the experimental conditions, *C. albicans* showed the highest sensitivity. The limiting factor in this microbiological experiment is the inability to avoid the active bromine consumption by the nutrient medium, which leads to an underestimation of the antimicrobial activity. Further suspension tests should evaluate it more accurately. At the same time, this method is demonstrative for comparing the microbicidal properties of the studied samples.

Thus, the results of the research, together with the data obtained earlier for chlorine-active polymers, suggest that the synthesized granular and fibrous styrene-divinylbenzene polymers with immobilized N-bromosulfonamide groups are promising for the manufacture of a wide range of medical products. In particular, for the manufacture of dressings, protective masks, respirators, air and water filters, as well as stable sources of active bromine for the rapid production of antiseptic solutions.

7. Conclusion

1. The method for the laboratory synthesis of granular and fibrous styrene-divinylbenzene bromine-active polymers has been developed. It has been established that their storage stability is 10–12 times lower than that of chlorine-active analogues. For the fibrous forms of the synthesized materials, a loss of strength is noted, which is expressed in shedding of the dried fiber.

2. Using chemical and instrumental methods of analysis, it has been established that the developed methods make it possible to obtain materials with immobilized N-bromosulfonamide groups in the sodium form and in the form of N,N-dibromosulfonamide. The concentration of immobilized active bromine can reach 23 %.

3. It has been shown that the synthesized bromine-active polymers have microbicidal activity against all studied microorganisms. Their antimicrobial properties are more than 2 times higher than those of chlorine-active analogues, and appear even in the presence of a significant organic load.

Conflict of interest

The authors declare no conflicts of interest in relation to this article, as well as the published results of the study, including the financial aspects of conducting the research,

obtaining and using its results, as well as any non-financial personal relationships.

Financing

This study has been conducted with the financial support of the Ministry of Health of Ukraine (within the framework of the state budget scientific project No. 0123U100214 "Complex systems for prevention and therapy of infectious diseases based on innovative forms of active chlorine"), as well as of the Max Planck Society (within the framework of the project "Complex disinfection systems based on high-purity active chlorine/oxygen compounds for the prevention and treatment of infectious diseases" of the grant program "EIRENE Max Planck-Ukraine Cooperation & Mobility Grant").

Data Availability

The manuscript has no associated data. Any additional explanations and materials can be obtained from the corresponding author upon request.

References

1. Shang, Y., Li, H., Zhang, R. (2021). Effects of Pandemic Outbreak on Economies: Evidence From Business History Context. Frontiers in Public Health, 9. doi: https://doi.org/10.3389/fpubh.2021.632043
2. Kaye, A. D., Okeagu, C. N., Pham, A. D., Silva, R. A., Hurley, J. J., Arron, B. L. et al. (2021). Economic impact of COVID-19 pandemic on healthcare facilities and systems: International perspectives. Best Practice & Research Clinical Anaesthesiology, 35 (3), 293–306. doi: https://doi.org/10.1016/j.bpa.2020.11.009
3. Marani, M., Katul, G. G., Pan, W. K., Parolari, A. J. (2021). Intensity and frequency of extreme novel epidemics. Proceedings of the National Academy of Sciences, 118 (35). doi: https://doi.org/10.1073/pnas.2105482118
4. Gupta, S., Rouse, B. T., Sarangi, P. P. (2021). Did Climate Change Influence the Emergence, Transmission, and Expression of the COVID-19 Pandemic? Frontiers in Medicine, 8. doi: https://doi.org/10.3389/fmed.2021.769208
5. Rodó, X., San-José, A., Kirchgatter, K., López, L. (2021). Changing climate and the COVID-19 pandemic: more than just heads or tails. Nature Medicine, 27 (4), 576–579. doi: https://doi.org/10.1038/s41591-021-01303-y
6. Li, R., Richmond, P., Roehner, B. M. (2018). Effect of population density on epidemics. Physica A: Statistical Mechanics and Its Applications, 510, 713–724. doi: https://doi.org/10.1016/j.physa.2018.07.025
7. Hollingsworth, T. D., Ferguson, N. M., Anderson, R. M. (2007). Frequent Travelers and Rate of Spread of Epidemics. Emerging Infectious Diseases, 13 (9), 1288–1294. doi: https://doi.org/10.3201/eid1309.070081
8. Nikolich-Žugich, J. (2017). The twilight of immunity: emerging concepts in aging of the immune system. Nature Immunology, 19 (1), 10–19. doi: https://doi.org/10.1038/s41590-017-0006-x
9. Diani, S., Leonardi, E., Cavezzi, A., Ferrari, S., Iacono, O., Limoli, A. et al. (2022). SARS-CoV-2—The Role of Natural Immunity: A Narrative Review. Journal of Clinical Medicine, 11 (21), 6272. doi: https://doi.org/10.3390/jcm11216272
10. Bloom, D. E., Cadarette, D. (2019). Infectious Disease Threats in the Twenty-First Century: Strengthening the Global Response. Frontiers in Immunology, 10. doi: https://doi.org/10.3389/fimmu.2019.00549
11. Bai, Y., Wang, Q., Liu, M., Bian, L., Liu, J., Gao, F. et al. (2022). The next major emergent infectious disease: reflections on vaccine emergency development strategies. Expert Review of Vaccines, 21 (4), 471–481. doi: https://doi.org/10.1080/14760584.2022.2027240
12. Cozad, A., Jones, R. D. (2003). Disinfection and the prevention of infectious disease. American Journal of Infection Control, 31 (4), 243–254. doi: https://doi.org/10.1067/mic.2003.49
13. Prajapati, P., Desai, H., Chandarana, C. (2022). Hand sanitizers as a preventive measure in COVID-19 pandemic, its characteristics, and harmful effects: a review. Journal of the Egyptian Public Health Association, 97 (1). doi: https://doi.org/10.1186/s42506-021-00094-x
14. Siddiqui, A. A. (2020). The Role of Personal Protective Equipment (PPE) in Prevention of COVID-19 Novel Corona Virus and Fatalities occur due to Non-availability of the PPE. American Journal of Biomedical Science & Research, 9 (6), 490–499. doi: https://doi.org/10.34297/ajbsr.2020.09.001458
15. Block, M. S., Rowan, B. G. (2020). Hypochlorous Acid: A Review. Journal of Oral and Maxillofacial Surgery, 78 (9), 1461–1466. doi: https://doi.org/10.1016/j.joms.2020.06.029
16. Chung, I., Ryu, H., Yoon, S.-Y., Ha, J. C. (2022). Health effects of sodium hypochlorite: review of published case reports. Environmental Analysis Health and Toxicology, 37 (1), e2022006. doi: https://doi.org/10.5620/eaht.2022006
17. Dong, A., Wang, Y.-J., Gao, Y., Gao, T., Gao, G. (2017). Chemical Insights into Antibacterial N-Halamines. Chemical Reviews, 117 (6), 4806–4862. doi: https://doi.org/10.1021/acs.chemrev.6b00687
18. Ashby, L. V., Springer, R., Hampton, M. B., Kettle, A. J., Winterbourn, C. C. (2020). Evaluating the bactericidal action of hypochlorous acid in culture media. Free Radical Biology and Medicine, 159, 119–124. doi: https://doi.org/10.1016/j.freeradbiomed.2020.07.033
19. Bernardi, A. O., Stefanello, A., Garcia, M. V., Parussolo, G., Stefanello, R. F., Moro, C. B., Copetti, M. V. (2018). Efficacy of commercial sanitizers against fungi of concern in the food industry. LWT, 97, 25–30. doi: https://doi.org/10.1016/j.lwt.2018.06.037
20. Miyaoka, Y., Kabir, Md. H., Hasan, Md. A., Yamaguchi, M., Shoham, D., Murakami, H., Takehara, K. (2021). Virucidal activity of slightly acidic hypochlorous acid water toward influenza virus and coronavirus with tests simulating practical usage. Virus Research, 297, 198383. doi: https://doi.org/10.1016/j.virusres.2021.198383

21. Williams, K., Hughson, A. G., Chesebro, B., Race, B. (2019). Inactivation of chronic wasting disease prions using sodium hypochlorite. PLOS ONE, 14(10), e0223659. doi: https://doi.org/10.1371/journal.pone.0223659
22. Gessa Sorroche, M., Relimpio López, I., García-Delpech, S., Benítez del Castillo, J. M. (2022). Hypochlorous acid as an antiseptic in the care of patients with suspected COVID-19 infection. Archivos de La Sociedad Española de Oftalmología (English Edition), 97 (2), 77–80. doi: https://doi.org/10.1016/j.oftale.2021.01.010
23. Kyriakopoulos, A. M., Grapsa, E., Marcinkiewicz, J., Nagl, M. (2019). Swift Cure of a Chronic Wound Infected With Multiresistant Staphylococcus aureus in an Elderly Patient With Stage 5 Renal Disease. The International Journal of Lower Extremity Wounds, 18 (2), 192–196. doi: https://doi.org/10.1177/1534734619834746
24. Dakin, M. H. E. (2014). Pat. No. WO2015063468A1. Anti-inflammatory solution comprising sodium hypochlorite. Available at: https://patents.google.com/patent/WO2015063468A1/en
25. Lackner, M., Rössler, A., Volland, A., Stadtmüller, M. N., Müllauer, B., Banki, Z. et al. (2022). N-chlorotaurine is highly active against respiratory viruses including SARS-CoV-2 (COVID-19) in vitro. Emerging Microbes & Infections, 11 (1), 1293–1307. doi: https://doi.org/10.1080/22221751.2022.2065932
26. Giarratana, N., Rajan, B., Kamala, K., Mendenhall, M., Reiner, G. (2021). A sprayable Acid-Oxidizing solution containing hypochlorous acid (AOS2020) efficiently and safely inactivates SARS-Cov-2: a new potential solution for upper respiratory tract hygiene. European Archives of Oto-Rhino-Laryngology, 278 (8), 3099–3103. doi: https://doi.org/10.1007/s00405-021-06644-5
27. Murashevych, B., Girenko, D., Maslak, H., Stepanskyi, D., Abraimova, O., Netronina, O., Zhminko, P. (2021). Acute inhalation toxicity of aerosolized electrochemically generated solution of sodium hypochlorite. Inhalation Toxicology, 34 (1-2), 1–13. doi: https://doi.org/10.1080/08958378.2021.2013348
28. Slaughter, R. J., Watts, M., Vale, J. A., Grieve, J. R., Schep, L. J. (2019). The clinical toxicology of sodium hypochlorite. Clinical Toxicology, 57 (5), 303–311. doi: https://doi.org/10.1080/15563650.2018.1543889
29. Gow, C. K., Weinhouse, C., Johnson, G. O., Saunders, K. E. (2022). Stability of Free Available Chlorine Levels in Dilute Sodium Hypochlorite Solutions over a 6-Week Period. Journal of the American Association for Laboratory Animal Science, 61 (2), 181–187. doi: https://doi.org/10.30802/aalas-jaalas-21-000080
30. Girenko, D. V., Gyrenko, A. A., Nikolenko, N. V. (2019). Potentiometric Determination of Chlorate Impurities in Hypochlorite Solutions. International Journal of Analytical Chemistry, 2019, 1–7. doi: https://doi.org/10.1155/2019/2360420
31. Bianculli, R. H., Mase, J. D., Schulz, M. D. (2020). Antiviral Polymers: Past Approaches and Future Possibilities. Macromolecules, 53 (21), 9158–9186. doi: https://doi.org/10.1021/acs.macromol.0c01273
32. Kenawy, E.-R., Worley, S. D., Broughton, R. (2007). The Chemistry and Applications of Antimicrobial Polymers: A State-of-the-Art Review. Biomacromolecules, 8 (5), 1359–1384. doi: https://doi.org/10.1021/bm061150q
33. Parham, S., Kharazi, A. Z., Bakhsheshi-Rad, H. R., Kharaziha, M., Ismail, A. F., Sharif, S. et al. (2022). Antimicrobial Synthetic and Natural Polymeric Nanofibers as Wound Dressing: A Review. Advanced Engineering Materials, 24 (6), 2101460. doi: https://doi.org/10.1002/adem.202101460
34. Shahid, A., Aslam, B., Muzammil, S., Aslam, N., Shahid, M., Almatroudi, A. et al. (2021). The prospects of antimicrobial coated medical implants. Journal of Applied Biomaterials & Functional Materials, 19, 228080002110403. doi: https://doi.org/10.1177/22808000211040304
35. Low, J. L., Kao, P. H.-N., Tambyah, P. A., Koh, G. L. E., Ling, H., Kline, K. A., Cheow, W. S., Leong, S. S. J. (2021). Development of a polymer-based antimicrobial coating for efficacious urinary catheter protection. Biotechnology Notes, 2, 1–10. doi: https://doi.org/10.1016/j.biotno.2020.12.001
36. Gulati, R., Sharma, S., Sharma, R. K. (2021). Antimicrobial textile: recent developments and functional perspective. Polymer Bulletin, 79 (8), 5747–5771. doi: https://doi.org/10.1007/s00289-021-03826-3
37. Pullangott, G., Kannan, U., S., G., Kiran, D. V., Maliyekkal, S. M. (2021). A comprehensive review on antimicrobial face masks: an emerging weapon in fighting pandemics. RSC Advances, 11 (12), 6544–6576. doi: https://doi.org/10.1039/d0ra10009a
38. Carmona-Ribeiro, A. M., Araújo, P. M. (2021). Antimicrobial Polymer Based Assemblies: A Review. International Journal of Molecular Sciences, 22 (11), 5424. doi: https://doi.org/10.3390/ijms22115424
39. Kamaruzzaman, N. F., Tan, L. P., Hamdan, R. H., Choong, S. S., Wong, W. K., Gibson, A. J. et al. (2019). Antimicrobial Polymers: The Potential Replacement of Existing Antibiotics? International Journal of Molecular Sciences, 20 (11), 2747. doi: https://doi.org/10.3390/ijms20112747
40. Song, Cvelbar, Strazar, Vossebein, Zille (2019). Chemical, Thermo-Mechanical and Antimicrobial Properties of DBD Plasma Treated Disinfectant-Impregnated Wipes during Storage. Polymers, 11 (11), 1769. doi: https://doi.org/10.3390/polym11111769
41. Nemeş, N. S., Ardean, C., Davidescu, C. M., Negrea, A., Ciopec, M., Duţeanu, N. et al. (2022). Antimicrobial Activity of Cellulose Based Materials. Polymers, 14 (4), 735. doi: https://doi.org/10.3390/polym14040735
42. Santos, M., Fonseca, A., Mendonça, P., Branco, R., Serra, A., Morais, P., Coelho, J. (2016). Recent Developments in Antimicrobial Polymers: A Review. Materials, 9 (7), 599. doi: https://doi.org/10.3390/ma9070599
43. Hui, F., Debiemme-Chouvy, C. (2013). Antimicrobial N-Halamine Polymers and Coatings: A Review of Their Synthesis, Characterization, and Applications. Biomacromolecules, 14 (3), 585–601. doi: https://doi.org/10.1021/bm301980q
44. Liang, J., Wu, R., Wang, J.-W., Barnes, K., Worley, S. D., Cho, U. et al. (2006). N-halamine biocidal coatings. Journal of Industrial Microbiology & Biotechnology, 34 (2), 157–163. doi: https://doi.org/10.1007/s10295-006-0181-5

45. Emerson, D. W. (1990). Polymer-bound active chlorine: disinfection of water in a flow system. Polymer supported reagents. 5. Industrial & Engineering Chemistry Research, 29 (3), 448–450. doi: https://doi.org/10.1021/ie00099a022
46. Bogoczek, R., Kociołek-Balawejder, E. (1989). Studies on a macromolecular dichloroamine — the N,N-dichloro poly(styrene-co-divinylbenzene) sulphonamide. Angewandte Makromolekulare Chemie, 169 (1), 119–135. doi: https://doi.org/10.1002/apmc.1989.051690111
47. Farah, S., Aviv, O., Laout, N., Ratner, S., Domb, A. J. (2015). Antimicrobial N-brominated hydantoin and uracil grafted polystyrene beads. Journal of Controlled Release, 216, 18–29. doi: https://doi.org/10.1016/j.jconrel.2015.07.013
48. Bogoczek, R., Kociołek-Balawejder, E. (1991). N-bromo-poly(styrene-co-divinylbenzene) sulphonamide metal salts. Synthesis and basic properties. Angewandte Makromolekulare Chemie, 188 (1), 85–96. doi: https://doi.org/10.1002/apmc.1991.051880108
49. Li, L., Pu, T., Zhanel, G., Zhao, N., Ens, W., Liu, S. (2012). New Biocide with BothN-Chloramine and Quaternary Ammonium Moieties Exerts Enhanced Bactericidal Activity. Advanced Healthcare Materials, 1 (5), 609–620. doi: https://doi.org/10.1002/adhm.201200018
50. Chen, Y., Han, Q. (2011). Designing N-halamine based antibacterial surface on polymers: Fabrication, characterization, and biocidal functions. Applied Surface Science, 257 (14), 6034–6039. doi: https://doi.org/10.1016/j.apsusc.2011.01.115
51. Toropin, V., Murashevych, B., Stepanskyi, D., Toropin, M., Kremenchutskiy, H., Burmistrov, K. (2019). New forms of immobilized active chlorine and its potential applications in medicine. Journal of the national academy of medical sciences of Ukraine, 25 (3), 340–352. doi: https://doi.org/10.37621/jnamsu-2019-3-340-352
52. Murashevych, B., Koshova, I., Surmasheva, E., Girenko, D., Chuiko, V., Stepanskyi, D. (2022). Broad-purpose antimicrobial chlorine-active polymers: suppression of multidrug-resistant microorganisms and microbial penetration resistance. ScienceRise: Pharmaceutical Science, 5 (39), 64–73. doi: https://doi.org/10.15587/2519-4852.2022.266171
53. Murashevych, B., Stepanskyi, D., Toropin, V., Mironenko, A., Maslak, H., Burmistrov, K., Teteriuk, N. (2022). Virucidal properties of new multifunctional fibrous N-halamine-immobilized styrene-divinylbenzene copolymers. Journal of Bioactive and Compatible Polymers, 37 (6), 453–468. doi: https://doi.org/10.1177/08839115221121852
54. Dronov, S., Mamchur, V., et al. (2019). New wound dressings with prolonged action. Zaporozhye medical journal, 21 (3), 365–373.
55. Murashevych, B., Toropin, V., Stepanskyi, D., Maslak, H., Burmistrov, K., Kotok, V., Kovalenko, V. (2021). Synthesis of new immobilized N-chloro-sulfonamides and release of active chlorine from them. EUREKA: Physics and Engineering, 4, 3–13. doi: https://doi.org/10.21303/2461-4262.2021.001929
56. Abo-Farha, S. A., Abdel-Aal, A. Y., Ashour, I. A., Garamon, S. E. (2009). Removal of some heavy metal cations by synthetic resin purolite C100. Journal of Hazardous Materials, 169 (1-3), 190–194. doi: https://doi.org/10.1016/j.jhazmat.2009.03.086
57. Soldatov, V. S. (2008). Syntheses and the Main Properties of Fiban Fibrous Ion Exchangers. Solvent Extraction and Ion Exchange, 26 (5), 457–513. doi: https://doi.org/10.1080/07366290802301358
58. Walczewska, M., Peruń, A., Białecka, A., Śróttek, M., Jamróz, W., Dorożyński, P. et al. (2017). Comparative Analysis of Microbicidal and Anti-inflammatory Properties of Novel Taurine Bromamine Derivatives and Bromamine T. Taurine 10, 515–534. doi: https://doi.org/10.1007/978-94-024-1079-2_41
59. Williams, W. J. (1979). Handbook of Anion Determination. Butterworth-Heinemann. doi: https://doi.org/10.1016/c2013-0-06303-7
60. Kurisaki, K., Yoshimura, K. (2007). Kinetics of Sulfate Desorption from Strongly Acidic Cation-exchange Resin. Journal of Ion Exchange, 18 (4), 158–161. doi: https://doi.org/10.5182/jaie.18.158
61. Balouiri, M., Sadiki, M., Ibnsouda, S. K. (2016). Methods for in vitro evaluating antimicrobial activity: A review. Journal of Pharmaceutical Analysis, 6 (2), 71–79. doi: https://doi.org/10.1016/j.jpha.2015.11.005
62. Qisheng, R., Wenqiang, H. et. al. (1990). Infrared spectrum feature of the sulfonyl group bound to crosslinked polystyrenes. Acta Polymerica Sinica, 1 (1), 7–12.
63. Gowda, B. T., Usha, K. M. (2003). Infrared and NMR (1H & 13C) Spectra of Sodium Salts of N-Bromo-Mono and Di-Substituted-Benzenesulphonamides. Zeitschrift Für Naturforschung A, 58 (5-6), 351–356. doi: https://doi.org/10.1515/zna-2003-5-618
64. Bogoczek, R., Kociołek-Balawejder, E. (1993). Synthesis and basic characterization of a macromolecular dibromoamine: N,N-dibromo-poly(styrene-co-divinylbenzene)sulfonamide. Polymer, 34 (13), 2883–2888. doi: https://doi.org/10.1016/0032-3861(93)90135-w
65. Gottardi, W., Klotz, S., Nagl, M. (2014). Superior bactericidal activity ofN-bromine compounds compared to theirN-chlorine analogues can be reversed under protein load. Journal of Applied Microbiology, 116 (6), 1427–1437. doi: https://doi.org/10.1111/jam.12474