**Symmetry between Structure–Antibacterial Effect of Polymers Functionalized with Phosphonium Salts**

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**Abstract:** In actual context, when the terms of biomass and bioenergy are extensively used, it becomes clear that the comparative study of some biopolymers, such as cellulose and chitosan, can offer a large usage range, based on the scientific progress obtained in the biomaterials field. Starting from the structural similarity of these two polymers, we synthesized composite materials by grafting on their surface biocide substances (phosphonium salts). After testing the biocidal effect, we can conclude that the antibacterial effect depends on the ratio of support to phosphonium salt, influenced by the interaction between the cationic component of the biocides and by the anionic component of the bacterial cellular membrane. It was also observed that for the materials obtained by cellulose functionalization with tri-n-butyl-hexadecyl phosphonium bromide, the bacterial effect on *E. coli* strain was much better when chitosan was used as the support material.

**Keywords:** chitosan; cellulose; phosphonium salts; symmetry; antibacterial effect; functionalized materials

1. **Introduction**

Cellulose and chitosan are the most abundant natural polymers [1–4], being of animal or vegetal origin [3–7], non-toxic and biodegradable [3]. Both of these polymers present, grafted onto their structure, different functional groups that confer them with good biocompatibility and superior properties to natural precursors [3,8–10]. The studied biopolymers (chitosan and cellulose) present a structural symmetry [2,11,12], being formed from the same basic structural units, linked by the same β-glycosidic bonds. The main difference between these compounds is the presence of amino groups grafted at C2 in the case of chitosan and the presence of hydroxyl groups in the case of cellulose (Figure 1).

![Figure 1. Chitosan (Ch) and cellulose (Cel) symmetrical structures. (* suggest that in picture are represented only the basic structural units)](null)

**Figure 1.** Chitosan (Ch) and cellulose (Cel) symmetrical structures. (* suggest that in picture are represented only the basic structural units)
In the native state, both biopolymers present a limited number of applications compared to the higher number of applications of modified biopolymers. By chemical modification, the most important native properties of these polymers are improved, or new properties are induced, including the substantial antimicrobial effect of modified polymers. It is well known that chitosan molecules present intrinsic antimicrobial activity due to the presence of an amino group [13], but through chitosan modification, new products are obtained with remarkable antimicrobial effects. From such products, the following can be noted: chitosan derivatives obtained by functionalization with ammonium quaternary salts [13–15], or derivatives containing phosphonium salts [15–18]. From the point of view of cellulose, the antimicrobial potential can be evidenced only for its derivatives [3,13,19,20], with the native product presenting only an insignificant antimicrobial effect. Based on these observations, it is justified the preparation of such advanced materials, especially due to their effective antibacterial activity against pathogen microorganisms. Experimental data proved that chitosan and its derivatives present a large antibacterial spectrum, having a higher destruction rate against Gram-positive and Gram-negative bacteria, [3,13,16,18,21,22].

Chitosan antibacterial activity depends on several factors, such as the chitosan deacetylation degree, molecular weight, medium pH, hydrophilic/hydrophobic characteristic, chelating capacity, solubility, and temperature [14,23]. An important role is played by the amino group from the chitosan structure [3,14,23,24], which can alter the bacteria surface morphology due to the modification of the bacterial membrane permeability [3,14,25,26]. The particularity of cellulose is represented by the presence of the three hydroxyl groups on the structure (one for each monomer unit); in this way, they are able to form strong intra- and inter-molecular hydrogen bonds [8].

The presence of the amino group on the chitosan molecule impresses a strong nucleophilic character [9], allowing further functionalization with a large number of pendant/active groups in order to modulate its structure for different specific applications. This structural versatility leads to a large number of applications: in the food industry, due to the formation of protective films used for product preservation [10,27–29]; in medicine and pharmacy as an antibacterial and antifungal agent [17,21,30]; in tissue engineering [9,31,32] and wound healing [9,33,34]; in the pharmaceutical industry [9,28,35]; in the textile industry [28,36]; in wastewater treatment technology [28,37,38], etc. The abundance of the hydroxyl groups on the cellulose surface allow its further modification with different chemical groups, leading specific properties. Such a modified material presents a large number of specific applications: high performance bio-degradable materials [39], biomedical engineered materials [5,39,40], antimicrobial agent [13,19,20,41], catalyst [42], textile industry [43], flocculant in wastewater treatment plants [37,44–46], and so on.

It is well known that the microbial infections represent a real challenge in many areas of modern life, determining an increased interest for the development of biocompatible materials with bacteriostatic and bactericidal activity [11,16,47,48]. The obtained experimental data demonstrate that by the functionalization of natural polymers (Cel and Ch) with active groups (containing N and P atoms), their antimicrobial activity is improved [47,48]. In this contest, we aim to prepare, characterize and compare the antimicrobial activity of materials prepared by the functionalization of two natural polymers with phosphonium salts. In present paper, we compare the antimicrobial behaviors of materials obtained by the functionalization of cellulose and chitosan with dodecyl-triphenyl phosphonium bromide (DDTPPPBr) and tri-n-butyl-hexadecyl phosphonium bromide (HDTBPBr)—the structures are depicted in Figure 2.
1.0 g L\(^{-1}\)) after preparation, all the obtained materials were characterized by using Fourier transform infrared spectroscopy (FT-IR, Bruker, Billerica, MA, U.S.A.).

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The method used for further functionalization of the used supports was the dry solvent impregnation method (SIR) [49–52]. Accordingly, with the SIR method, materials used for Cel and Ch functionalization (DDTPPBr HDTBPBr) were dissolved in distilled water. Further, the obtained solutions were mixed with solid support and kept in contact for 24 h at 298 K. After that, all samples are filtered, washed with DI water, and the obtained material was dried for 24 h at 323 K [47,48,50,51]. In this way, different materials were prepared by varying the ratio between the support and antimicrobial compound (ratios of support to antimicrobial material = 1:0.012, 1:0.025, 1:0.050, 1:0.075, 1:0.1, 1:0.2, 1:0.3, 1:0.4, 1:0.5). After preparation, all the obtained materials were characterized by using Fourier transform infrared spectroscopy (FT-IR, Bruker, Billerica, MA, U.S.A.).

2. Materials and Methods

In the present work, the modified biopolymers were obtained by functionalization through impregnation by using two compounds with good antimicrobial activity. This preparation method was used in order to prevent the appearance of unwanted reaction products.

2.1. Materials Preparation and Characterization

To prepare the materials used in present study, two different support materials were used: chitosan (Ch, having a deacetylation degree of 90%, and a molecular weight of 1–3 \(\times\) \(10^5\), purchased from Acros Organics, Janssen Pharmaceutical, Geel Belgium) and cellulose powder (Cel-powder, having the commercial name of Avicel PH-101, purchased from Sigma-Aldrich, Merck, KGaA, Darmstadt, Germany). As compounds with antimicrobial activity, two phosphonium salts were used: dodecyl-triphenyl phosphonium bromide (98% purity, purchased from Thermo Fisher, Kandel, Germany) and tri-n-butyl-hexadecyl phosphonium bromide (98% purity, purchased from ThermoFischer, Kandel, Germany). The method used for further functionalization of the used supports was the dry solvent impregnation method (SIR) [49–52]. Accordingly, with the SIR method, materials used for Cel and Ch functionalization (DDTPPBr HDTBPBr) were dissolved in distilled water. Further, the obtained solutions were mixed with solid support and kept in contact for 24 h at 298 K. After that, all samples are filtered, washed with DI water, and the obtained material was dried for 24 h at 323 K [47,48,50,51]. In this way, different materials were prepared by varying the ratio between the support and antimicrobial compound (ratios of support to antimicrobial material = 1:0.012, 1:0.025, 1:0.050, 1:0.075, 1:0.1, 1:0.2, 1:0.3, 1:0.4, 1:0.5). After preparation, all the obtained materials were characterized by using Fourier transform infrared spectroscopy (FT-IR, Bruker, Billerica, MA, U.S.A.).

2.2. Preparation of Bacterial Cultures Used during Antibacterial Tests

During antibacterial tests, we studied the dependence between exhibited antibacterial efficiency and the ratio of the support to the antimicrobial agent. After preparation, each material was transferred into the Petri dish, where the microbial culture was further added. During each test, we used a bacterial suspension with an initial concentration of \(1 \times 10^8\) colony-forming units (CFU). In order to highlight the antimicrobial activity against Gram-negative bacteria, Escherichia coli ATCC 25,922 and Pseudomonas aeruginosa ATCC 27,853 were used as the inocula. Antimicrobial activity against Gram-positive bacteria was determined by using the Staphylococcus aureus ATCC 25,923 strain. All tests were performed in triplicate.

Bacterial cultures were obtained by the inoculation of a solid non-selective nutritive media with 1 \(\mu\)L (approximately \(1 \times 10^8\) CFU) bacterial suspension. This media was cast in Petri plates and incorporated with 0.2 g from the material to be tested. For all seeding processes, complete dehydrated culture media were used—Plate Count Agar purchased from Merck (peptone from casein 5.0 g L\(^{-1}\), yeast extract 2.5 g L\(^{-1}\), D (+) glucose 1.0 g L\(^{-1}\), agar 14.0 g L\(^{-1}\)). For each set of experiments, a Petri plate was inoculated with a blank sample (M0—control sample), consisting only of culture media and 1 \(\mu\)L of the bacterial inoculum. We simultaneously inoculated two different Petri plates containing culture media, the bacterial inoculum and un-functionalized support material (M1—Ch, and, respectively, M2—Cel). All Petri plates were incubated for 48 h at 310 K, after which

![Figure 2. DDTPPBr and HDTBPBr antimicrobial agents’ structures.](image-url)
inoculum. We simultaneously inoculated two different Petri plates containing culture me-

From the data depicted in Figure 3, we can observe that the Ch-specific bands are 
attenuated, which can be associated with the surface functionalization with DDTPPBr or

The efficiency of the functionalized chitosan and cellulose against the reference strain was expressed as the 
bacterial inhibition rate [19,21,30], expressed as the ratio between colony formation units 
counted on the functionalized material over the number of colony formation units, as can 
be seen in Equation (1):

\[
R.I. = \left[ 1 - \frac{CFU_{\text{test}}}{CFU_{\text{control}}} \right] \times 100
\]  

\(CFU_{\text{control}}\) = number of colony formation units on the control plate 
\(CFU_{\text{test}}\) = number of colony formation units on the test plate.

3. Results and Discussions
3.1. Characterization of Prepared Material by FT-IR

The obtained materials were characterized by Fourier transform infrared spectroscopy 
highlight the presence of pendant groups associated with the presence of DDTPPBr and 
HDTBPBr, concomitant with the presence of Ch- and Cel-specific groups. Obtained spectra 
are depicted in Figure 3 (spectra recorded for Ch-DDTPPBr and Ch-HDTBPBr) and Figure 4 
(spectra recorded for Cel-DDTPPBr and Cel-HDTBPBr).

![Figure 3. FT-IR spectra recorded for (a) Ch-DDTPPBr and (b) Ch-HDTBPBr materials.](image)

![Figure 4. FT-IR spectrum for (a) Cel-DDTPPBr and (b) Cel-HDTBPBr materials.](image)
From the data depicted in Figure 3, we can observe that the Ch-specific bands are attenuated, which can be associated with the surface functionalization with DDTPPBr or HDTBPBr [47]. From Figure 3a, we can observe the presence of the P–O–Ar-specific vibrations located at wave numbers between 1240 and 1190 cm\(^{-1}\). We can also observe the presence of a specific peak for C–O from the DDTPPBr phenyl group located at 1200 cm\(^{-1}\). From the spectrum recorded for Ch-HDTBPBr (Figure 3b), we can observe the presence of the vibrations specific to the alkyl phosphate groups, located at 1180–1150 and 1080 cm\(^{-1}\).

Based on the spectra depicted in Figure 4, we can observe that cellulose specific bands are attenuated, which can be associated with the support functionalization with DDTPPBr or HDTBPBr [48]. In both spectra, we can observe the presence of P–O–Ar specific vibrations located between 1240 and 1190 cm\(^{-1}\). The peak located at 1200 cm\(^{-1}\) is specific for the elongation vibrations of the C–O bond from the DDTPPBr phenyl group [53]. Specific bands for Ch and Cel were explained in detail in previous published papers [47,54] and are briefly presented in Table 1.

### Table 1. Ch- and Cel-specific FT-IR specific vibrations bands.

| Group         | FT-IR Bands (cm\(^{-1}\)) | Observations                                      |
|---------------|----------------------------|---------------------------------------------------|
| Chitosan      |                            |                                                   |
| CH\(_3\)-OH   | 1380–1420                  |                                                   |
| N–H           | 1570                       |                                                   |
| C=O           | 1660                       |                                                   |
| C–H           | 2870; 2924                 |                                                   |
| O–H           | 3430                       |                                                   |
| Cellulose (Cel) |                            |                                                   |
| O–H           | 3660 Large band            |                                                   |
| C–H           | 2893 Small plateau; stretching vibrations in polysaccharides | |
| CH\(_2\)      | 1428; 1367                 | Vibrations specific to the crystalline structure of cellulose |
| C–O           | 1334; 1158                 |                                                   |
| O–C–O         | 1104; 1027; 897 Amorphous region in cellulose | |
| OH\(_2\)      | 1600–900; 1633 Water molecules vibrations | |

By comparing the FT-IR spectra recorded for functionalized Ch with the control spectrum (and corroborating them with the data depicted in Table 1), we can observe a small displacement of the vibrations associated with the stretching of the chitosan hydroxilic groups. Such behavior is associated with the formation of physical intermolecular bonds (hydrogen bonds) between compounds used for functionalization and chitosan. A similar behavior is observed in the case of functionalized Cel, when the small displacements of the hydroxilic groups vibrations were associated with the formation of hydrogen bonds between the support and used antimicrobial agent. Based on this observation, we can conclude that the two used polymers were successfully functionalized with DDTPPBr and HDTBPBr.

### 3.2. Antimicrobial Effect of Prepared Materials

#### 3.2.1. Case of a Heterotrophic Inoculum

Phosphonium salts used for cellulose and chitosan functionalization differ both in the length of the alkyl chain (dodecyl and hexadecyl) grafted on the chitosan or cellulose base structure, as well as through the quaternizing substituent (triphenyl or tributyl).

Regardless of the phosphonium salt used for the support functionalization, we can conclude that the antimicrobial activity of the obtained materials is directly proportional to the increase in the functionalization ratio (as can be observed from Figure 5).
Figure 5. Inhibitory effects of chitosan (M1), cellulose (M2). Chitosan:extractants derivatives and cellulose:antimicrobial agent derivatives on growth of heterotrophic inoculum.

From the data depicted in Figure 5, we can observe a different behavior in the case of the Ch-DDTPPBr material, when the highest inhibition rate was obtained, even at the lowest functionalization ratio, meaning that is not necessary to further increase the functionalization ratio. Such behavior can be explained if we consider that in the heterotroph inoculum used during experiments, Gram-negative bacteria are predominant because such microorganisms present a higher sensibility at the antimicrobial agent’s action. The different behavior of Cel-HDTBPBr against the E.coli strain can be explained if we consider that the physical bonds established during cellulose functionalization are not so strong. So, the antimicrobial agent can be easily attached to the cellular wall, affecting the membrane permeability, leading to cell death. As well, the behavior observed in the case of Cel-HDTBPBr against the heterotroph inoculum is associated with the cumulative antibacterial effect of cellulose and the used phosphonium salt.

3.2.2. Case of Reference Strains
Antimicrobial Effect of Ch-DDTPPBr and Cel-DDTPPBr

From the data presented in Figure 6, we can observe an inhibition effect of 100% when Ch-DDTPPBr and Cel-DDTPPBr plates were inoculated with S. aureus ATCC 25,923 and E. coli ATCC 25,922 strains, regardless of the functionalization ratio. Likewise, we can observe a limited antimicrobial activity (maximum 46.6%) in the case of the P. aeruginosa ATCC 27,853 strain, regardless of the functionalization ratio.

Figure 6. The antimicrobial effect observed in the case of Ch, cell, Ch-DDTPPBr and Cel-DDTPPBr materials.
In the case of Cel-DDTPBr plates inoculated with the *P. aeruginosa* strain, we observed an insignificant increase in antimicrobial activity (from 32% to 39.8%) by increasing ten-fold the functionalization ratio. By contrast, in the case of Ch-DDTPBr, a ten-fold functionalization rate increase led to an increase in antimicrobial activity from 31% to 46.6%. A possible explanation of such behavior is represented by the lower permeability of the *P. aeruginosa* cell wall [55] being correlated with its great adaptability to the antimicrobial agent action, which confers a greater resistance [56]. The DDTPBr antibacterial agent used for functionalization, despite its strong hydrophobic character, was not able to penetrate the cellular wall of *P. aeruginosa*, explaining in this way the lower antimicrobial activity. Based on the data presented in Figure 5, we can observe that the best antimicrobial activity was exhibited by the materials obtained from chitosan functionalization. Such behavior can be explained only if we take into account the intrinsic antimicrobial activity of chitosan [13]. A significant number of researchers proved that the adsorption and interaction with the bacterial cellular membrane, followed by perturbation of the membrane selectivity and further by cell death, is favored by the presence of a positive charge on the biocide surface [3,16,18,57].

**Antimicrobial Effect of Ch-HDTBPBr and Cel-HDTBPBr**

In Figure 7 are presented the data regarding the antimicrobial effect of Ch-HDTBPBr and Cel-HDTBPBr against *S. aureus*, *E. coli*, and *P. aeruginosa* strains. Based on the obtained data, we can observe that the antimicrobial effect of Ch-based materials against *S. aureus* is complete, regardless of the functionalization ratio.

![Figure 7](image-url)

**Figure 7.** The antimicrobial effect of Ch-HDTBPBr and C-HDTBPBr materials.

Gram-positive bacteria present a thick peptidoglycanic wall, enabling a strong interaction between the cationic phosphonium salt (HDTBPBr) and anionic component from the bacterial membrane [57,58]. Such interactions are possible due to the presence of teichoic acids in the cellular membrane of Gram-positive bacteria [58–60].

Regarding the antimicrobial activity of new produced materials against Gram-positive bacteria, based on the data presented in Figure 7, we can observe that in the case of Ch-HDTBPBr, the antibacterial activity is proportional to the functionalization ratio. However, it was not possible to reach an inhibition degree of 100%. In this case, we can say that the tested material only has a bacteriostatic effect [13,28]. It is possible that the material affected the permeability of the cellular membrane but was unable to obtain the equilibrium needed to destroy the cellular membrane and to cause bacterial death [61–63]. When the cellulose was functionalized with HDTBPBr, it was observed that the inhibition rate is proportional with the functionalization ratio. Total bactericidal effect was obtained against the *S. aureus* strain for a functionalization ratio Cel:HDTBPBr = 1:0.3. By performing the antibacterial
tests against Gram-negative bacteria, it was not possible to obtain a total bactericidal effect. When the prepared cellulosic materials were tested against the \textit{P. aeruginosa} strain, it was observed that the inhibition effect increased from 6\% to 21.6\% when the functionalization ratio increased from 1:0.01 to 1:0.1. Further, by increasing the functionalization ratio from 1:0.1 to 1:0.5, we observed an increase in the antimicrobial inhibition rate from 21.6\% to 42.6\%. A similar behavior was observed against the \textit{E. coli} strain; when the functionalization ratio increased from 0.01 to 0.5, the inhibition rate increased from 42.7\% to 89.1\%. The different behavior of Cel-HDTBPBr, against the \textit{E. coli} strain, can be explained if we consider that the physical bonds established during cellulose functionalization are not so strong, so the antimicrobial agent can easily attach to the cellular wall, affecting the membrane permeability. Additionally, this significant antibacterial effect can be associated with the cumulative antibacterial effect of cellulose and the used phosphonium salt.

Among the studied agents with antimicrobial activity, DDTPPBr presents the highest hydrophobicity, due to the presence of the phenyl substituent, which has a higher hydrophobicity compared with the butyl substituent from HDTBPBr. Additionally, the shortest alkyl segment (dodecyl) is equivalent to a lower distance between the support surface and the pendant group, which can lead to a considerable increase in the antimicrobial effect of the prepared materials. All these observations are consistent with the literature, which emphasizes the role of the hydrophilic–hydrophobic equilibrium against the bacteria cellular wall, and the strong relationship between the hydrophobicity of an antibacterial agent and the bactericidal effect [57, 64–66]. In addition, an important role regarding the antimicrobial activity of different materials is played by the electrostatic attractions exerted between DDTPPBr, HDTBPBr and the bacterial cell membrane. Strong electrostatic attractions between the antimicrobial agents and bacterial cell membrane lipids lead to bacteria cells death [66, 67]. Starting from this, it is possible to better understand the bactericide effect of materials obtained by cellulose functionalized with HDTBPBr against the \textit{E. coli} strain. This material can achieve strong electrostatic attractions [68, 69], strong intra- and intermolecular hydrogen bonds [3, 5, 43], which finally lead to a higher bacterial inhibition rate.

4. Conclusions

Cellulose and chitosan are two biopolymers with a higher biocompatibility, being non-toxic compounds with a large number of applications into the biomedical field. These polymers present similar structures, formed by the same type of \(\beta\)-glycosidic bonds between monomeric units. Regarding the chemical behavior of these polymers, cellulose is a neutral or anionic polysaccharide, while chitosan is a neutral or cationic polysaccharide. Such a difference can lead to different behavior against bacteria.

Materials obtained by the functionalization of studied polymers with DDTPPBr exhibited a total bactericidal effect against Gram-positive bacteria and against the \textit{E. coli} strain. Similarly, materials obtained by the functionalization of studied natural polymers with HDTBPBr exhibited a maximal bactericidal effect only against Gram-positive bacteria. The interaction of cationic components from the polymer structures with the negatively charged components from the bacterial citoplasmatic membranes represents an important step in terms of antibacterial effect.

Based on the hydrophobicity aspect, we proved that by increasing the hydrophobicity of cationic biocides, the possibility that they interact with the citoplasmatic membrane is increased. This observation is in concordance with the experimental data from the present study, in which the best antimicrobial effects were observed in the case of materials obtained by functionalization with DDTPPBr, which present the highest hydrophobicity.

Due to the environmental regulation, and lack of by-products, the functionalization technique is the preferred one for the preparation of new materials with improved properties and large applicability, starting from synthetic or natural polymers.
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