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Biocidal activity of cellulose materials for medical implants

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ABSTRACT: Surface wettability trends, and blood component adhesion of some cellulose acetate phthalate/hydroxypropyl cellulose blend films are analyzed in view of adapting the system to biomedical applications. The results show that intermediate blend compositions of the corresponding films influence the surface tension parameters—controlled by the interactions occurring in the system. Increasing hydrophobicity and, implicitly, decreasing the polar surface tension components, are correlated with the adhesion/cohesion of blood components and plasma proteins. Thus, the work of spreading proteins on the hydrophobic blend surfaces indicated that albumin is not absorbed preferentially, while fibrinogen is characterized by a higher degree of adhesion on the surfaces, and also that selective adsorption of plasma proteins modifies blood compatibility. In addition, the obtained results and the ascertained antimicrobial activity of the studied blends contribute to the development of new applications in the biomedical field. © 2015 Wiley Periodicals, Inc. J. Appl. Polym. Sci. **2015**, *132*, 41932

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INTRODUCTION

Cellulose and its derivatives are of great interest for obtaining new composite materials. In this context, polymer blending is designed to generate materials with optimized structural, morphological, and biological properties.[1–8]

Cellulose acetate phthalate (CAP), a mixed ester of cellulose, is utilized in different medical domains. Its solubility in aqueous media, as well as its resistance to gastric acid and easy solubility in the slightly alkaline environment of the intestine, recommend it as a pharmaceutical excipient and enteric coating for films and pharmaceutical tablets. Recently, the potential of this polymer to inhibit infections caused by several types of herpes virus, such us type 1 Herpes Simplex, and other sexually-transmitted diseases, has been analyzed *in vitro*.[9–12]

At the same time, another cellulose derivative that finds applications in the biomedical field is hydroxypropyl cellulose (HPC).[13] Nowadays, many formulations in pharmaceutical industry are based on HPC. For example, some tablets are now commercially available for aphtha treatment, based on HPC and homo- or copolymers of acrylic acid as major excipients.[14] This kind of tablets demonstrates good oral mucosal adhesion properties and controlled drug release features.

Literature shows that the composite biomaterials from cellulose derivatives can be carefully considered during the design of innovative biomedical scaffolds in biological tissues engineering.[15–18] CAP and HPC, taken individually, are inadequate to meet the diversity of demands in this domain, in contrast to their combinations in different systems, frequently used in the design and construction of medical devices. It has been known for many years that scaffolds based on these complex systems are useful for initial cell attachment and subsequent tissue formation, either *in vitro* as well as *in vivo*. A number of requirements should be met for a proper use of polymer scaffolds, such as biodegradability with controllable degradation rate, structure, porosity, and surface properties; these requirements allow cells to be seeded for a successful differentiation and growth.[19–22]

In our previous articles,[23–25] it has been shown that the solution properties of CAP and HPC are important for a better understanding and control of polymer blending processes, where miscibility is a result of the specific interactions between polymer segments in casting solutions of organic solvents. In addition, some properties related to the morphological and structural-rheological aspects of their mixtures at various compositions and concentrations have been analyzed.

The present article studies the influence of the chemical structures of CAP, HPC, and their corresponding blends on the surface properties, biocompatibility, and antimicrobial activity. In this context, the hydrophobic characteristics of cellulose derivative blends and their interactions with red blood cells, platelets

and sanguine plasma proteins, as well as certain inhibitory effects of cellulose derivative blends on the growth of *E. coli* and *S. aureus* bacteria have been considered. These properties are useful in investigations on specific biomedical applications, including evaluation of bacterial adhesion to the surfaces.

EXPERIMENTAL

Materials

Cellulose acetate with 1.93 substitution degree was used for the synthesis of CAP (Scheme 1). Cellulose acetate was phthaloylated with phthalic anhydride in acetic acid, using anhydrous sodium acetate and triethylamine as basic catalysts.[26] The substitution degrees of CA acetylation (DSac) and CAP phthaloylation (DSph) were 1.73 and 0.7, respectively.

Hydroxypropylcellulose (HPC) (LF, Klucel™) was purchased from Aqualon Company, Hopewell, VA. According to product specifications, HPC LF has a molecular mass of ~100,000 g/mol and "moles of substitution" of 3.4.

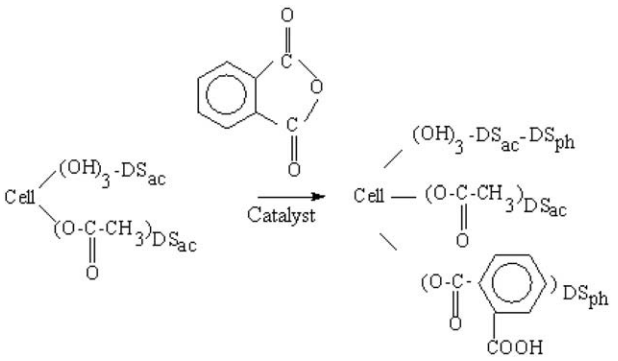
Preparation of CAP/HPC Blend Films

CAP/HPC films with 100/0, 75/25, 50/50, 25/75, 0/100 wt/wt. compositions were prepared from their separated solutions in *N*,*N*-dimethylacetamide (DMAc) at 60 g dL^{-1} concentrations. CAP/HPC films were also obtained from a 40 g dL^{-1} concentrated solution, for antimicrobial activity analysis. The homogeneity of the blend solutions was assured through a magnetic stirring for 7 h, and degassing in the ultrasonic bath. Finally, the CAP/HPC blend solutions were cast on glass plates and solidified by slow drying in saturated atmosphere of the solvent, then under vacuum at 30°C.

Contact Angle Measurements

The static contact angles of different test liquids were measured on surface films using the sessile-drop method. Uniform drops of 2 μL test liquids [double-distilled water (w), methylene iodide (CH_2I_2), and etylene glycol (EG)] were deposited on the film surface and the contact angles were measured after 30 s, with a video-based optical contact angle measuring device,[27] equipped with a Hamilton syringe, in a temperature-controlled environmental chamber. Repeated measurements of a given contact angle were all within an experimental error of ±0.3%.

The acid/base method (LW/AB) [eqs.(1–3)],[28] was utilized for calculating the surface tension parameters of CAP/HPC blend films; the surface tension parameters of test liquids and biological materials[29–34] are presented in Table I, and the contact angles measured between these liquids and the CAP/HPC blend films in Table II:



Scheme 1. Obtaining of CAP from cellulose acetate with 1.93 substitution degree, in the presence of phthalic anhydride.[25,26]

Table I. Surface Tension Parameters (mN m^{-1}) of the Test Liquids Used for Contact Angle Measurements and of the Biological Materials

Material	γ_{lv}^{LW}	γ_{lv}^{AB}	γ_{lv}^{+}	γ_{lv}^{-}	γ_{lv}
Test liquid					
Water[29]	21.80	51.00	25.50	25.50	72.80
Methylene iodide[29]	50.80	0	0.72	0	50.80
Ethylene glycol[29]	44.40	0	0	0	44.40
Biological material					
Red blood cell[30]	35.20	1.36	0.01	46.20	36.56
Platelet[30]	99.14	19.10	12.26	7.44	118.24
Albumin[31,32]	26.80	35.70	6.30	50.60	62.50
Fibrinogen[33]	37.60	3.89	0.10	38.00	41.50
IgG[34]	34.00	17.30	1.50	49.60	51.30

$$1+\cos\theta=\frac{2}{\gamma_{lv}}\left(\sqrt{\gamma_{sv}^{LW}\gamma_{lv}^{LW}}+\sqrt{\gamma_{sv}^{+}\gamma_{lv}^{-}}+\sqrt{\gamma_{sv}^{-}\gamma_{lv}^{+}}\right) \quad (1)$$

$$\gamma_{sv}^{AB}=2\sqrt{\gamma_{sv}^{+}\gamma_{sv}^{-}} \quad (2)$$

$$\gamma_{sv}^{LW/AB}=\gamma_{sv}^{LW}+\gamma_{sv}^{AB} \quad (3)$$

where total surface tension parameter between solid and vapor phases is represented by $\gamma_{sv}^{LW/AB}$, while corresponding polar and disperse parameters are γ_{sv}^{AB} (with electron-donor, γ_{sv}^{-}, and electron-acceptor, γ_{sv}^{+}, components), and γ_{sv}^{LW}, respectively.

Total surface tension parameter between used liquid and vapor phases is represented by γ_{lv}, while corresponding polar and disperse parameters are γ_{lv}^{AB} (with electron-donor, γ_{lv}^{-}, and electron-acceptor, γ_{lv}^{+}, components), and γ_{lv}^{LW}, respectively.

Antimicrobial Activity

The antibacterial properties of CAP/HPC blend films were investigated by the agar diffusion method, their antibacterial efficiency being examined starting from the dimension of the inhibition zone generated in the presence of *Escherichia coli* ATCC 10536 (*E. coli*) and *Staphylococcus aureus* ATCC 6538 *(S. aureus)*. The bacteria were preincubated for 18 h at 37°C. For each bacterial strain, 3 mL of suspension with about 10^7 CFU

Table II. Contact Angles of Different Test Liquids on CAP/HPC Blend Films

CAP/HPC (wt/wt)	Contact angle (°)		
	W	EG	CH_2I_2
100/0	56.00	24.50	38.33
75/25	57.00	55.50	43.00
50/50	64.00	54.00	38.50
75/25	67.00	41.00	39.50
0/100	70.00	52.50	52.00

mL^{-1} were spread onto Petri plates containing Mueller–Hinton agar medium. The excess was removed by aspirating with a pipette (after 10 min),[35] and disinfected steel discs were placed on the agar surface. Circular films, 10 mm in diameter and 100 μm thick, were introduced in the disks. The plates were incubated at 37°C for 24 h. Diameter of the inhibition zone depends both on the polymer present in the disk and on microorganism susceptibility.

RESULTS AND DISCUSSION

Surface Tension Parameters

A previous article,[23] has shown that the specific interactions in a blend, including hydrogen bonding, ion–ion pairing, and electron–donor and electron–acceptor complexation, etc., produce a favorable mixing enthalpy and hence may lead to miscibility among components. The presence of a solvent in the blend system introduces the polymers–solvent interactions as a function of polymers composition, concentration of polymers solution and temperature, and determines different conformations. Interpretation of surface properties results must be performed starting from CAP[36] and HPC[37] structural properties:

(a) the ATR-FTIR spectra of CAP, HPC, and their blends show a remarkably similar aspect for both polymers. Broad transmission bands are distinguished at:

- 3421 cm^{-1} for HPC and 3431 cm^{-1} for CAP-produced by stretching of the —OH groups,
- 723 cm^{-1} for HPC and 1719 cm^{-1} for CAP-produced by stretching of the C═O groups from the ester and carboxylic acid.
- 1252 cm^{-1} for HPC and 1329 cm^{-1} for CAP-produced by stretching of the C—O—C ester bond.

The occurrence of hydrogen bond structures in blends can be evidenced from peaks shape and intensity of the absorption band of the hydrogen stretching vibration.[23] The differences observed among the shape, broadening, and shifting of the mentioned peaks for polymer blends suggest the existence of hydrogen bonding, generated by —OH, C═O, and C—O—C groups. The free and associated groups provide the equilibrium in these polymer blends via hydrogen bonds;

(b) Quantitative measurements of weight loss from TG/DTG plots show that CAP is less thermally stable than the HPC and CAP/HPC blends, as the anhydroglucose units increase the rigidity of the HPC chain.[24]

In this context, one can mention that surface tension parameter results may be raised by means of the aforementioned properties—hydrogen bonding interactions, stability, and rigidity of samples. Table III shows the results for the surface tension component, evaluated by the acid–base method, which involves contact angles errors of ±0.3%. The electron-donor and electron-acceptor parameters obtained by the acid/base method are also presented. It has been observed that both the apolar, γ_{sv}^{LW}, and polar, γ_{sv}^{AB}, surface tension parameters are influenced by the volume fraction of polymer blends from which the films have been prepared. Thus, the γ_{sv}^{LW} values of CAP, HPC, and their blends are higher than the γ_{sv}^{AB} ones, while the polar component of

Table III. Surface Tension Parameters (mN m^{-1}) for CAP/HPC Films at Different Composition of the Blend, According to the Acid/Base Method

CAP/HPC (wt/wt)	Acid–base method				
	γ_{sv}^{LW}	γ_{sv}^{AB}	γ_{sv}^{+}	γ_{sv}^{-}	$\gamma_{sv}^{LW/AB}$
100/0	33.62	11.13	1.41	22.01	44.95
75/25	29.54	0.36	0.00084	37.64	29.95
50/50	31.09	0.53	0.002809	24.70	31.62
25/75	34.86	6.02	0.63	14.47	40.88
0/100	28.23	5.60	0.47	16.72	33.84

CAP (γ_{sv}^{p} = 11.13 $mN\ m^{-1}$) is higher than that for HPC and CAP/HPC blends (γ_{sv}^{p} = 10.36−6.02 $mN\ m^{-1}$), indicating that the surfaces of these last specified samples are slightly hydrophobic, and also that the electron acceptor parameter is lower than the electron donor one.

Yamane *et al.*,[38] attempted to clarify the hydrophilic and hydrophobic nature of cellulose starting from its structural anisotropy. Thus, it may be assumed that hydroxypropyl cellulose, known as possessing hydrophilic characteristics, may produce films with higher wettability—as due the high density of its hydroxyl groups in the equatorial positions of the glucopyranose rings. Conversely, the axial direction of the glucopyranose ring is hydrophobic, because the atoms of the C—H bonds are located on the axial positions of the ring. Reference 38 suggests that the hydrophobic property of cellulose may be created by structural controls, e.g., by reversing the planar orientation. Consequently, any increase in crystallinity determines a decrease of density and an increased hydrophobic character of the polymers.

On the basis of these findings, it is expected that the chain flexibility of HPC and of samples with a higher content of HPC will decrease, due to the voluminous recurrent anhydroglucose units which determine a higher crystallinity.[39] On the other hand, polar components and electron acceptor parameters take lower values, which can be explained by the fact that, in the casting ternary system (CAP/HPC/DMAc) used for obtaining films, besides the polymer/solvent interaction, a polymer/polymer/solvent interaction also occurs.[24] These interactions could affect the rearrangement of macromolecules in solution and, implicitly, the surface tension parameters of CAP/HPC films.

The rheological and morphological investigations made on the CAP/HPC blend and discussed in previous article,[24] led to similar conclusions; the flow activation energy, polarity, and roughness of the corresponding surface at intermediary composition revealed the influence of the hydrogen bonding interactions, rearrangement of macromolecules in solution, accompanied by the occurrence of lyotropic liquid crystal phases.

To highlight the importance of polymer blends in applications as biomaterials and enteric coatings, Chen *et al.*,[40] reviewed some studies on solvent effects, showing that the properties of the solvent used in the casting solution, such as polarity, volatility, and specific interaction with the polymer blend material are critical for surface formation.

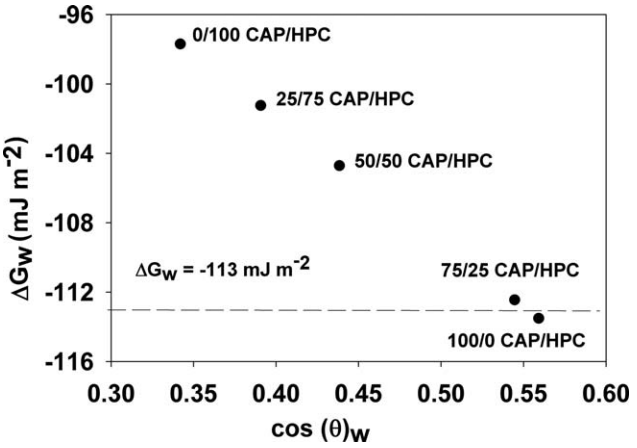


Figure 1. Surface free energy, ΔG_w, versus water contact angle, θ_w, for CAP, HPC, and CAP/HPC blend films.

Surface and Interfacial Properties

The effect of the compositions of CAP/HPC blends on surface properties were analyzed by surface free energy, ΔG_w: expressing the balance between surface hydrophobicity and hydrophilicity [eq. (4)],[29] by the interfacial free energy between two particles of blend films in water phase, ΔG_{sws} [eqs. (5) and (6)], and by the spreading work of water, W_s [eq. (7)].

According to literature,[41,42] which specifies that $\Delta G_w \geq 113$ mJ m^{-2} for more hydrophobic materials, ΔG_w evidences the hydrophobicity of the studied samples, the values increasing when HPC is added into the system (Figure 1). Moreover, the interfacial free energy, ΔG_{sws}, evaluated from solid–liquid interfacial tension, γ_{sl}, using [eq. (5)], has negative values, according to Figure 2.

Therefore, an attraction occurs between the blend surfaces, *s*, immersed in water, *w*, confirming the hydrophobic characteristics of blends:

$$\Delta G_w = -\gamma_{lv}(1+\cos\theta_w) \quad (4)$$

where γ_{lv} and θ_w are given in Tables I and II, respectively.

$$\Delta G_{sws} = -2\gamma_{sl} \quad (5)$$

$$\gamma_{sl} = \left(\sqrt{\gamma_{lv}^{AB}} - \sqrt{\gamma_{sv}^{AB}}\right)^2 + \left(\sqrt{\gamma_{lv}^{LW}} - \sqrt{\gamma_{sv}^{LW}}\right)^2 \quad (6)$$

$$W_s = W_a - W_c = 2\cdot[(\gamma_{sv}^{LW}\times\gamma_{lv}^{LW})^{1/2} + (\gamma_{sv}^{+}\times\gamma_{lv}^{-})^{1/2} + (\gamma_{sv}^{-}\times\gamma_{lv}^{+})^{1/2}] - 2\times\gamma_{lv} \quad (7)$$

At the same time, the hydrophobic character of these polymers was described by the spreading work of water over the surface, W_s, which represents the difference between the work of water adhesion, W_a, and the work of water cohesion, W_c. It was found out that the spreading work of water (Figure 3) takes negative values for CAP, HPC, and CAP/HPC blends, because of the hydrophobic surfaces, whose work of water adhesion is low in comparison with the work of cohesion.

Identification of Compatibility with Blood Components and Antimicrobial Activity

Most tissue-derived cells are anchorage-dependent and require attachment to a solid surface for viability and growth. For this reason, the initial events that occur when a cell approaches a surface are of fundamental interest. In tissue engineering, cell adhesion to a surface is critical because adhesion precedes other events, such as cell spreading, cell migration and, often, differentiated cell functions. Several different techniques for quantifying the extent and strength of cell adhesion have been developed. In fact, quite different techniques are used, so that a comparison among the various studies performed by various researchers is quite difficult. This situation is further complicated by the fact that cell adhesion depends on a larger number of experimental parameters,[43] many of which are difficult to control. The simplest methods for quantifying the extent of cell adhesion on to a surface involve three steps: (1) suspension of cells over a surface; (2) incubation of the sedimented cells in the culture medium for some period of time, and (3) detachment of the loosely adherent cells under controlled conditions. The extent of cell adhesion, which depends on the conditions of the experiment, is determined by quantifying either the number of cells remaining associated with the surface (the "adherent" cell), or the number of cells extracted with repeated washings.[44]

Surface analysis of cellulose blend films was performed for better understanding the interfacial chemistry of adhesion not only with water, but also with the blood components and plasma proteins. The blood-polymer surface interactions depend on blood composition, blood flow, and physicochemical properties of the polymer surface, such as crystallinity, hydrophobicity/hydrophilicity, or on its toxicological and electrical properties.[45–47] On the other hand, bio-incompatible polymers are largely used for blood-contacting devices, under conditions in which blood coagulation is regulated by anticoagulants. In this context, a previous article[48] shows that some polymers, with a suitable macromolecular design, may potentially offer important advantages for bio-microelectronic applications, due to their low dielectric constant values and electrical conductivity, based on energy band-gap representation. Blood compatibility is generated by the modality in which the polymeric surface interacts with blood constituents, such as the red blood cells (rbc) and platelets (p), and also with plasma proteins, such as albumin, immunoglobulin G (IgG), and fibrinogen. In this context, the solid (cellulose blends)—liquid (blood components and plasma

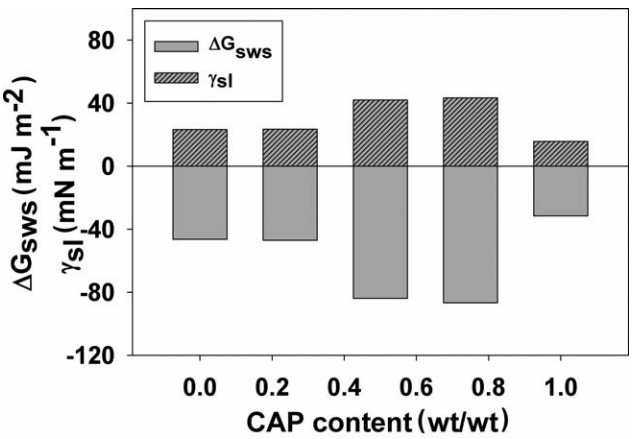


Figure 2. Interfacial free energy, ΔG_{sws}, and solid–liquid interfacial tension, γ_{sl} between two sides of the CAP/HPC blend films in water phase.

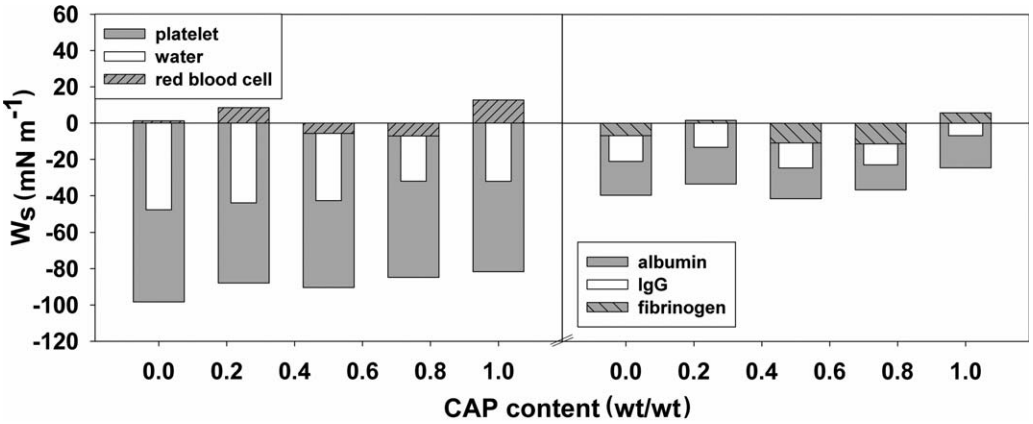


Figure 3. Spreading work, W_s, for water, blood components (red blood cells and platelets) and plasma proteins (albumin, immunoglobulin G, fibrinogen) over the surfaces of CAP/HPC blend films.

proteins) interfacial tensions, γ_{sl}, and the interfacial free energy between two polymer particles in blood phase, ΔG_{sws}, [eqs. (5) and (6)] show that an attraction occurs between the two cellulose surfaces, *s*, immersed in various components found in blood (Figure 3). In addition, the work of spreading of blood components ($W_{s,rbc}$, $W_{s,p}$) and plasma proteins ($W_{s,albumin}$, $W_{s,IgG}$, and $W_{s,fibrinogen}$) over the cellulose surfaces was evaluated with eq. (7), using the surface energy parameters (γ_{lv}, γ_{lv}^{LW}, γ_{lv}^{+}, γ_{lv}^{-}) given in Table I for biological materials.[30–34] Thus, an analysis on the surface tension parameters can be employed to determine the work of adhesion of blood cells onto biomaterials surface (like surfaces of vessel grafts, extracorporeal circuits etc.), where the biomaterial forms the solid substrate, the blood forms the liquid environment, the adhering cell being any of the blood cells. The work of adhesion measures the ease with which cells can adhere, so that determination of the work of adhesion for different cells can help a scientist to predict the manner in which blood cells would react when exposed to a biomaterial.[30] Considering that blood is exposed to a biomaterial surface, cell adhesion decides the life of the implanted biomaterials. Cellular adhesion to biomaterial surfaces can activate coagulation and the immunological cascade, having a direct impact on the thrombogenicity and immunogenicity of a biomaterial, thus influencing its blood compatibility.[47] Consequently, blood compatibility implies prevention of platelet adhesion and deactivation of the intrinsic coagulation system, generated by blood protein adsorption on the polymer surface. In the present article, the work of adhesion of the red blood cells was used as a parameter for characterizing biomaterials versus cell adhesion. The materials which exhibit a lower work of adhesion would have an extent of cell adhesion lower than those with a higher work of adhesion. Figure 3 plots the spreading work for different blood components versus the CAP content. For red blood cell negative values—suggesting that $W_c > W_a$, or slightly positive values—where $W_a > W_c$ appears. Also, for platelets, which are essential in maintaining hemostasis, negative values of the spreading work were recorded, which means a lower work of adhesion, comparatively with the one of cohesion. On the other hand, the results show that, when exposing the platelets to cellulose derivative blend films, an increase of platelets cohesion occurs for hydroxypropyl cellulose and for blends with a higher content of hydroxypropyl cellulose. Figure 3, also representing the spreading work of albumin, fibrinogen, and IgG permits the following observations:

- IgG and albumin exhibit negative values, revealing that cohesion prevails, thus favoring a nonadsorbent behavior at the interface, as required by bio-applications.
- Generally, fibrinogen exhibits negative values, generated by the rejection of fibrinogen off polymeric support.

Blood components are extremely important in deciding the blood compatibility of a material. Moreover, it is known that adhesion of red cells onto a surface, e.g. CAP and their blends with hydroxypropyl cellulose, requires knowledge of the interactions with the vascular components. Thus, endothelial glycocalyx, together with the mucopolysaccharides adsorbed on the endothelial surface of the vascular endothelium, reject the clotting factors and platelets—known as playing a significant role in thrombus formation.[43] The results concerning adhesion or cohesion of biological materials with cellulose compounds can be analyzed in the context of different medical applications. In addition to these assessments, literature[49] describes some methods for determining the degree of adhesion or spreading. Thus, radiolabeled or fluorescently labeled cells permitting measurement of the number of attached cells can be used. Alternatively, the number of attached cells can be determined by direct visualization, by measurement of an intracellular enzyme concentration, or by binding of a dye to an intracellular component, such as DNA. In many cases, the adherent cells are further categorized based on morphological differences (e.g., extent of spreading, formation of actin filament bundles, presence of focal contacts). This technique is simple, rapid, and because it requires simple equipment, it is commonly applied. Unfortunately, it has been found out that control of the force that provides deployment of nonadherent cells is difficult, yielding different laboratory results.

Antimicrobial Activity Assessments

Cellulose derivatives are large-scale commercial products, possessing many useful characteristics, such as hydrophilicity/hydrophobicity, biodegradability, and antibacterial properties.[44,50–53] In this context, the results concerning their

Table IV. Antimicrobial Activity Expressed by the Diameter of the Inhibition Zone (mm) of CAP, HPC, and CAP/HPC Films, Used as a Control Sample Against *S. aureus* and *E. coli*

Concentration (g dL^{-1})	Sample CAP/HPC (wt/wt)	Microorganism	
		S. aureus	*E. coli*
40	100/0	11	10
	75/25	11	10
	50/50	11	10
	25/75	10	8
	0/100	0	0
60	100/0	13	12
	75/25	15	12
	50/50	15	12
	25/75	11	9
	0/100	0	0

interactions with blood components may be applied in the biomedical field, where assessment of bacterial adherence to the polymer surface is required.

The antimicrobial activity of CAP, HPC, and CAP/HPC films—prepared from casting solutions in DMAc at different concentrations—is investigated against *Staphylococcus aureus* (*S. aureus*) and *Escherichia coli* (*E. coli*) bacteria. Table IV and Figures 4 and 5 show that HPC films do not inhibit bacterial growth, and that *Staphylococcus aureus* is more sensitive to the CAP and CAP/HPC films comparatively with *Escherichia coli*.

The differences in the composition of the cell wall of Gram-negative (*E. coli*) and Gram-positive (*S. aureus*) bacteria cause different resistance to killing by antimicrobial agents. As known, the component of Gram-positive bacteria cell walls is peptidoglycan, whereas the major constituents of Gram-negative bacteria cell walls are peptidoglycan, together with other membranes, such as lipopolysaccharides and proteins. These components of the cell walls generate the hydrophilic character of *E. coli* bacteria and the hydrophobic character of *S. aureus*. The studied samples interfere with the bacterial metabolism by electrostatic stacking at the cell surface of bacteria.[54] The results show that the bacterial activity of the tested compounds is dependent on the microorganism nature, composition of cellulose blends and concentration of casting solutions from which the cellulose films were obtained. Thus:

- For slightly hydrophobic samples—CAP and CAP/HPC blends with higher content of CAP—the inhibition areas are higher than those for HPC and also for blends with a higher content of HPC for both microorganisms;

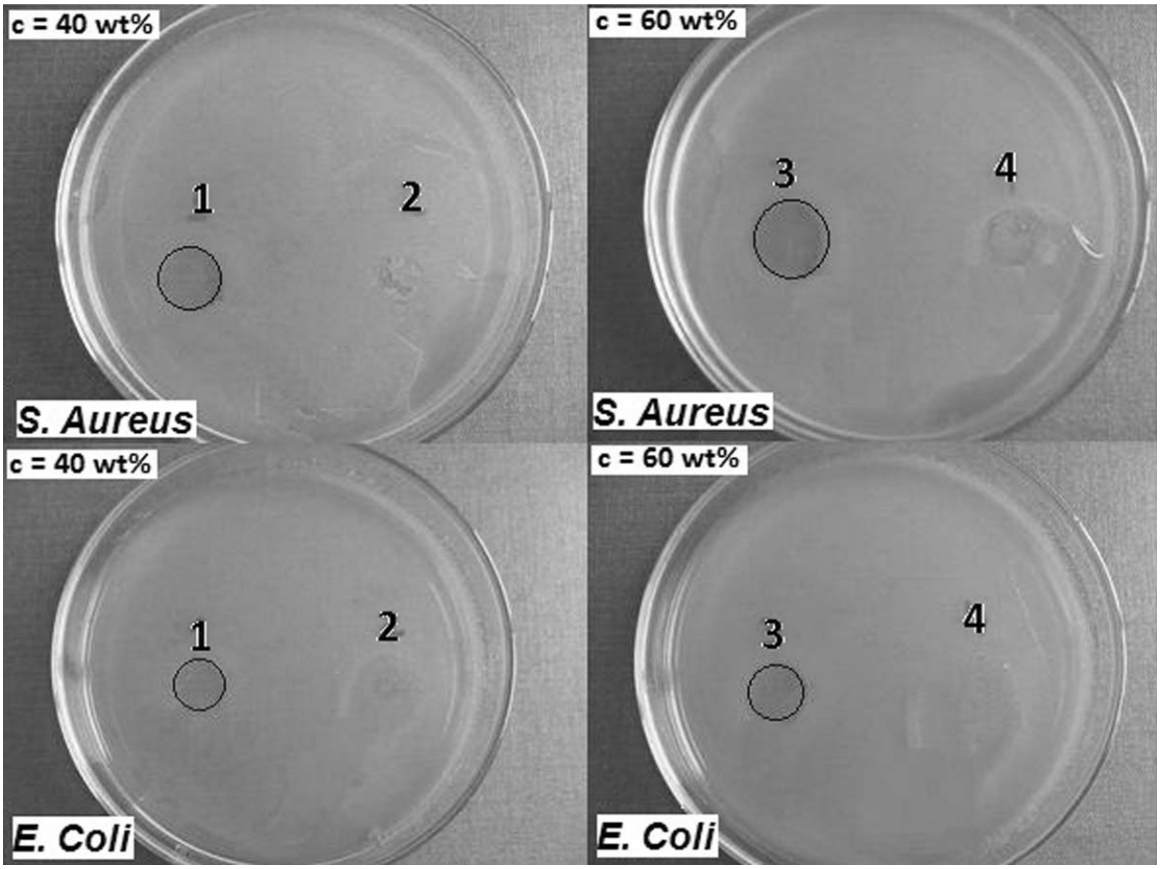


Figure 4. Antimicrobial activity for: (1) and (3) CAP films realized from casting solutions at 40 and 60 g dL^{-1} concentrations, respectively; (2) and (4) HPC films realized from casting solutions at 40 and 60 g dL^{-1} concentrations, respectively, against *S. aureus* and *E. coli*.

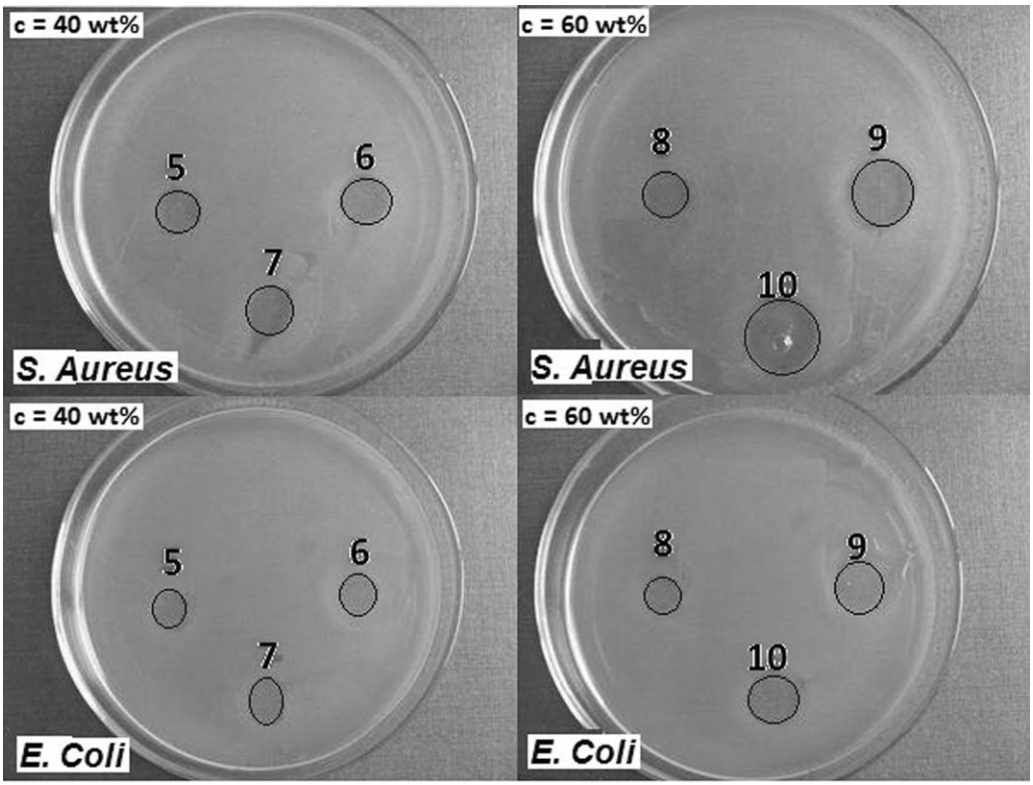


Figure 5. Antimicrobial activity for CAP/HPC films realized from casting solutions of 40 g dL^{-1} concentration and blend compositions of 25/75 (5), 50/50 (6), 75/25 (7), and from casting solutions of 60 g dL^{-1} concentration and blend compositions of 25/75 (8), 50/50 (9), 75/25 (10), against *S. aureus* and *E. coli*.

- CAP inhibits the growth of microorganisms, inhibition becoming stronger with increasing the concentration of the casting solution from which the cellulose films were obtained.
- For the studied compositions of CAP/HPC blends, the differences between the diameters of the inhibition zones are insignificant.

Also, the antimicrobial activity is dependent not only on the chemical structures of the cellulose derivatives, but also on the hydrophilic or hydrophobic character of microorganisms, which generates different interactions with the bacterial cell membrane.

It can be concluded that the exact mechanism of the inhibiting effect of these microorganisms is complex, considering that, besides the cell wall compositions of these bacteria and the surface properties of cellulose derivative blends, other types of interactions also occur, e.g., van der Waals and electrostatic interactions.[55] Thus, the obtained results indicate that adhesion of *E. coli* and *S. aureus* to cellulose film surfaces is mediated mainly by specific interactions, rather than by hydrophobic interactions.

CONCLUSIONS

Films from CAP/hydroxypropyl cellulose prepared from solution in *N*,*N*-dimethylacetamide at different concentrations were obtained and analyzed in terms of their surface tension properties, biocompatibility with various blood components and antimicrobial activity.

According to surface tension data, it can be observed that CAP and blends with a higher content of CAP are more hydrophilic, having more polar component than HPC. In this context, the cellulose derivative blend films-blood components compatibility is dictated by the hydrophobic/hydrophilic character. Generally, it was observed that the spreading work and adhesion work of blood components and plasma proteins for CAP are higher than for HPC and for blends with a higher HPC content. Particularly, the following observations should be made:

- CAP, HPC, and blends with a higher HPC content, more precisely the 25/75 CAP/HPC blend, show positive spreading work values, and consequently, increased adherence of the red blood cells and of fibrinogen to the biomaterial. As to their compatibility with the rest of plasma proteins, namely albumin and immunoglobulin G, it was noticed that all samples exhibited lower values of the spreading work, and therefore smaller material-host interactions. Thus, the proteins spread on the hydrophobic CAP/HPC blend films indicated that albumin is not preferentially absorbed, that fibrinogen is characterized by a higher degree of surfaces adhesion, and also that the selective adsorption of plasma proteins modifies blood compatibility.

Antimicrobial activities, expressed by the diameter of the inhibition zone against *E. coli* and *S. aureus* cells, are determined by the differences in the composition of the cell wall of Gram-negative and Gram-positive bacteria and, implicitly by the type, of interactions, such as van der Waals and/or electrostatic interactions. Specifically, these blends inhibit the growth of

microorganisms, inhibition becoming stronger with the increasing the CAP content and the concentration of the solutions from which the films were obtained, and insignificant for HPC films. Also, *S. aureus* is more sensitive to the CAP and CAP/HPC films comparatively with *E. coli*.

These results will be used in future works focused on biomedical applications, in order to eliminate the implant-induced infections.

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