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ELECTRO-OPTICAL AND MORPHOLOGICAL CHARACTERIZATION OF PVA FOILS WITH SULFATHIAZOLE

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Sulfathiazole is a short-acting drug used as oral and topical antimicrobial. The main physical-chemical characteristics of sulfathiazole were calculated by using the molecular modelling software. The biological activity was estimated from the difference between HOMO and LUMO levels. Thin foils from pure poly(vinyl alcohol) (PVA) gel and for PVA gel containing Sulfathiazole were obtained. They were studied from the birefringence and from the surface properties points of view. The birefringence induced by stretching was measured using a Babinet Compensator both for pure and for PVA with Sulfathiazole. The birefringence of the pure and containing Sulfathiazole PVA foils increases by increasing the degree of stretching. The higher birefringence of the Sulfathiazole PVA foils demonstrates that the sulfathiazole increases the alignment availability of the polymer chains. The morphology of PVA foils was studied by AFM methodology which relieved the surface quality of the pure and containing sulfathiazole PVA foils.

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1. Introduction

Sulfathiazole or 4-amino-*N*-(1,3-thiazol-2-yl) benzene-sulphonamide, from sulfonamides class, was synthesized in the beginning of 1930's and used as drug from 1935 for infections treatment until the penicillin was discovered. The first who establish the sulphonamide antibacterial effects was the German pathologist and bacteriologist Gerhard Domagk [1]. Sulfathiazole is a short-acting drug used as oral and topical antimicrobial. In combination with sulfabenzamide and sulfacetamide it is used, sometimes, in aquariums. Poly(vinyl alcohol), PVA, is an important material used in biomedical purposes, as biosensors, electrochemical sensors, or as membranes with selective permeability [2,3]. The PVA foils are frequently used as polymer transparent matrices for the visible range [4-7]. The guest molecules as sulfathiazole can be ordered in polymer host matrices by mechanical procedures (flow, stretching). PVA foils cast from water solutions are transparent, have high tensile and tear resistance and also are of low costs [5]. The polymer foils can be birefringent due to the macromolecules intrinsic optical anisotropy. By stretching process a supplementary induced birefringence is added to the initial one. Consequently, in the stretching process the optical characteristics of the films are changed. PVA foils are usually uniax materials [4] with their optical axis parallel to the stretching direction. The purpose of this paper is to establish the Sulfathiazole influence on the stretched PVA foils and to characterize by AFM the surfaces of the pure and containing Sulfathiazole PVA foils.

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2. Experimental

2.1. PVA foils preparation

Polymer foils were obtained from PVA of molecular weight 65000-85000, 20% solution in distilled and deionised water (Loba Feinchemis-Austria). A viscous and transparent solution of PVA has been obtained after the mixture was stirred for 6h at a temperature of about 80-90^{0}C. A part of the obtained gel was mixed by stirring at room temperature (293K) for 4h with sulfathiazole (in a concentration of 10^{-3}mol/l) Two kind of gels – PVA pure and mixed with sulfathiazole were cast on glasses by means of a doctor blade with a slit of 0.6mm. The foils were dried by water evaporation at low pressure 1-2mmHg for 48h [4-7].The dried foils were stretched under heating to become anisotropic.

2.2. HyperChem calculations

Some physical-chemical properties of the sulfathiazole molecule were established by using one of the most complete molecular modeling software – HyperChem. The semi-empirical method used here was AM1 which is generally the most accurate computational method included in HyperChem [8-11] and considered the best for collecting quantitative information [12].
The ionization potential I along with the electron affinity A, is related with the chemical hardness η and electronegativity χ of the molecule through the next equations [13]:

$$\eta = \frac{I - A}{2} \tag{1}$$

$$\chi = \frac{I + A}{2} \tag{2}$$

From the Koopmans theorem [14] one can consider:

$$I \approx -\varepsilon_{HOMO} \tag{3}$$

and

$$A \approx -\varepsilon_{LUMO} \tag{4}$$

The chemical behavior can be also correlated with the visible-UV spectra. A small energy gap means that absorption bands are shifted toward the visible. Generally, the spectroscopic excitation energy is about the chemical hardness (one half of *I – A)*.

2.3. Birefringence determination

The birefringence was determined by using a Babinet Compensator [15, 16] standardized at λ = 589.3 nm for different degrees of stretching. The stretching degree was evaluated by the ratio of the semi axes of an ellipse in which a circle (initially drawn on the PVA foil) degenerates by stretching.

2.4. Atomic force microscopy measurements

The surface morphology of the polymer films, obtained by the procedure as described above, was observed by AFM methodology with a Scanning Probe Microscope Solver PRO-M (NT-MDT, Russia) setup, at room temperature (23°C). The height images were recorded using AFM taping mode, wherein the cantilever force was controlled to be large enough to explore the surface features, yet small enough to avoid the sample damage. The film surfaces were scanned by a rectangular silicon cantilever NSG10 (NT-MDT, Russia) having a spring constant of 11.8 N/m and a resonance frequency of 234 kHz in a tapping mode. The scan area and speed were 5x5 μm^2 and 10 μm/s, respectively. The foil surfaces were compared in terms of roughness parameters such as: peak to valley height, root mean square roughness, surface area ratio, texture aspect ratio, material volume of the surface, core void volume of the surface and valley void volume of the surface.

The *peak to valley height*, *St*, is defined as the sum of the largest peak height value and the largest valley depth from the mean plane within the sampling area.

The *root mean square roughness* parameter, *Sq*, is the root mean square of the surface departures from the mean plane within the sampling area. The digital equation that represents this algorithm is displayed below:

$$Sq = \sqrt{\frac{1}{MN}\sum_{j=1}^{M}\sum_{i=1}^{N} z^2\left(x_i, y_j\right)} \tag{5}$$

where M is the number of columns in the surface and N is the number of rows in the surface.

The *surface area ratio*, *Sdr*, is the ratio of the increment of the interfacial area of a surface over the sampling area. This parameter is often used to describe the "complexity" of the surface. It is the ratio of the area of the surface including the z height data to the nominal area of the surface. A perfectly flat surface would have a Sdr of 0%. The mathematical formula for this parameter is as follows:

$$Sdr = \frac{\sum_{j=1}^{N-1}\sum_{i=1}^{M-1} A_{ij} - (M-1)(N-1)\times\Delta x\times\Delta y}{(M-1)(N-1)\times\Delta x\times\Delta y}\times 100\% \tag{6}$$

where,

$$A_{ij} = \frac{1}{4}\left(\sqrt{\Delta y^2 + \left(z\left(x_i, y_j\right) - z\left(x_i, y_{j+1}\right)\right)^2} + \sqrt{\Delta y^2 + \left(z\left(x_{i+1}, y_{j+1}\right) - z\left(x_{i+1}, y_j\right)\right)^2}\right)\times \left(\sqrt{\Delta x^2 + \left(z\left(x_i, y_j\right) - z\left(x_{i+1}, y_j\right)\right)^2} + \sqrt{\Delta x^2 + \left(z\left(x_i, y_{j+1}\right) - z\left(x_{i+1}, y_{j+1}\right)\right)^2}\right) \tag{7}$$

The *texture aspect ratio*, *Str*, is used to identify the uniformity of the texture of the surface (isotropy vs. anisotropy) and it is computed from the autocorrelation function (τ_x, τ_y) as follows:

$$Str = \frac{\min\left(\left(\sqrt{\tau_x^2 + \tau_y^2}\right)\right)}{\max\left(\left(\sqrt{\tau_x^2 + \tau_y^2}\right)\right)}, 0 < Str \le 1 \tag{8}$$

Larger values of the Str ratio (Str > 0.5) indicates stronger isotropy, whereas smaller values of the Str ratio (Str < 0.3) indicate stronger anisotropy.

The *material volume of the surface*, *Sm*, is defined as the material portion enclosed in the 10% bearing area and normalized to unity.

$$Sm = \frac{V_m\left(h_{0.10}\right)}{(M-1)(N-1)\cdot\Delta x\cdot\Delta y} \tag{9}$$

Functionally, the material volume reflects the resistance against wear and friction.

A *core void volume of the surface*, *Sc*, is enclosed from 10% to 80% of surface bearing area and normalized to the unit sampling area.

$$Sc = \frac{V_v\left(h_{0.10}\right) - V_v\left(h_{0.80}\right)}{(M-1)(N-1)\cdot\Delta x\cdot\Delta y} \tag{10}$$

The *valley void volume of the surface*, *Sv*, is defined as a void volume at the valley zone from 80% to 100% surface bearing area.

$$Sv = \frac{V_v\left(h_{0.80}\right) - V_v\left(h_{1.00}\right)}{(M-1)(N-1)\cdot\Delta x\cdot\Delta y} \tag{11}$$

Functionally, the void volumes reflect the fluid retention property.

3. Results and discussions

3.1. Calculation results

By using the molecular modelling software, the main physical-chemical characteristics of sulfathiazole were calculated. The biological activity was estimated from the difference between HOMO and LUMO levels.

The characteristic energies emphasizing the stability of sulfathiazole molecule are listed in Table 1.

Table 1. Characteristic energies of sulfathiazole

Total energy (kcal/mol)	- 67443,925
Binding energy (kcal/mol)	- 2578,037
Heat of formation (kcal/mol)	19.808
Electronic energy (kcal/mol)	- 377649,330
Nuclear energy (kcal/mol)	310205,405

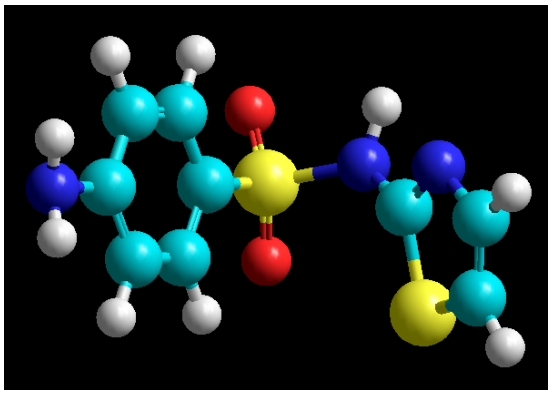


Fig.1 Optimized geometry of Sulfathiazole molecule (green-carbon, blue- nitrogen, red-oxygen, yellow-sulfur and white-hydrogen)

The molecular dipole moment, polarizability, hydration energy, molecular refractivity and LogP for this molecule were calculated.

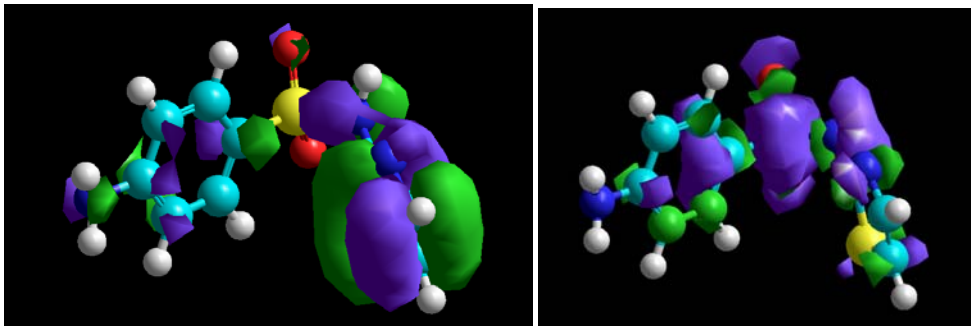
Hydration energy is defined as the energy absorbed when a substance is dissolved in water. LogP (the octanol/water partition coefficient) and molar refractivity are considered molecular descriptors [17] that can be used related to one structure for observing its chemical behavior. LogP plays an important role for biochemical interactions [18] and it is related to the hydrophobic character of the molecule.

From Table 2 it results that Sulfathiazole is a polar, polarizable and less hydrophobic molecule characterized by high hydration energy.

Table 2. Electro-optic characteristics of Sulfathiazole molecule

Dipole moment (D)	6.51
Polarizability ($Å^3$)	22.75
Refractivity ($Å^3$)	68.63
Hydration energy (kcal/mol)	- 15.18
Log P	- 1.50

The difference between the highest occupied molecular orbital (HOMO) and the lowest unoccupied molecular orbital (LUMO), called the HOMO – LUMO gap (Fig.2), gives a measure of the biological activity (Table3).



(a) *(b)*

Fig.2 HOMO orbital (a) and LUMO orbital (b) of Sulfathiazole plotted by HyperChem

The value of this gap may be used to estimate the computed ionization potential and the molecular electronegativity by taking into account the relations (1-4). A small gap is characteristic for soft molecules and it means small excitation energies, consequently these molecules will be more polarizable than the molecules with large gap (hard molecules).
In the case of sulfathiazole the following values have been obtained:

Table 3. Energetic parameters of sulfathiazole

HOMO (eV)	- 9.28	*I* (eV)	9.28
LUMO (eV)	1.36	A(eV)	-1.36
Chemical hardness (eV)	5.37	Electronegativity χ (eV)	3.96

3.2. Birefringence characterization

The birefringence of the PVA films was determined by using a Babinet compensator and its values demonstrate that the ordering degree increases with the degree of stretching of the films. From Fig.3 it results that the birefringence of the pure PVA foils is smaller than that of the films containing sulfathiazole. Thus, sulfathiazole increases the degree of order in PVA films, probably by dipolar interactions with the side chains of polymer [19].

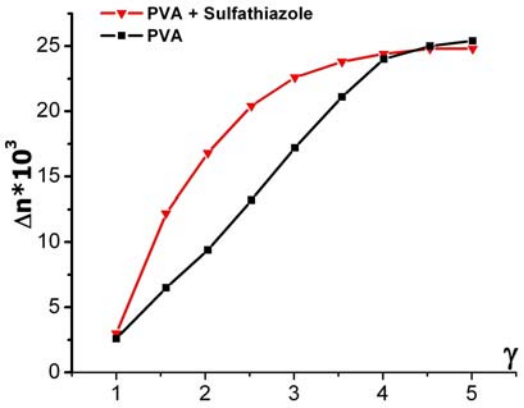


Fig.3 Birefringence vs. degree of stretching for a) pure PVA and b) PVA+ sulfathiazole films

3.3. AFM characterization

The data obtained by HyperChem calculations and the experiments using the poly (vinyl alcohol) films obtained from pure PVA gel and from gel with sulfathiazole show that dipolar molecule of sulfathiazole facilitates the ordering of the polymer chains in the films, homogenizing their surface.

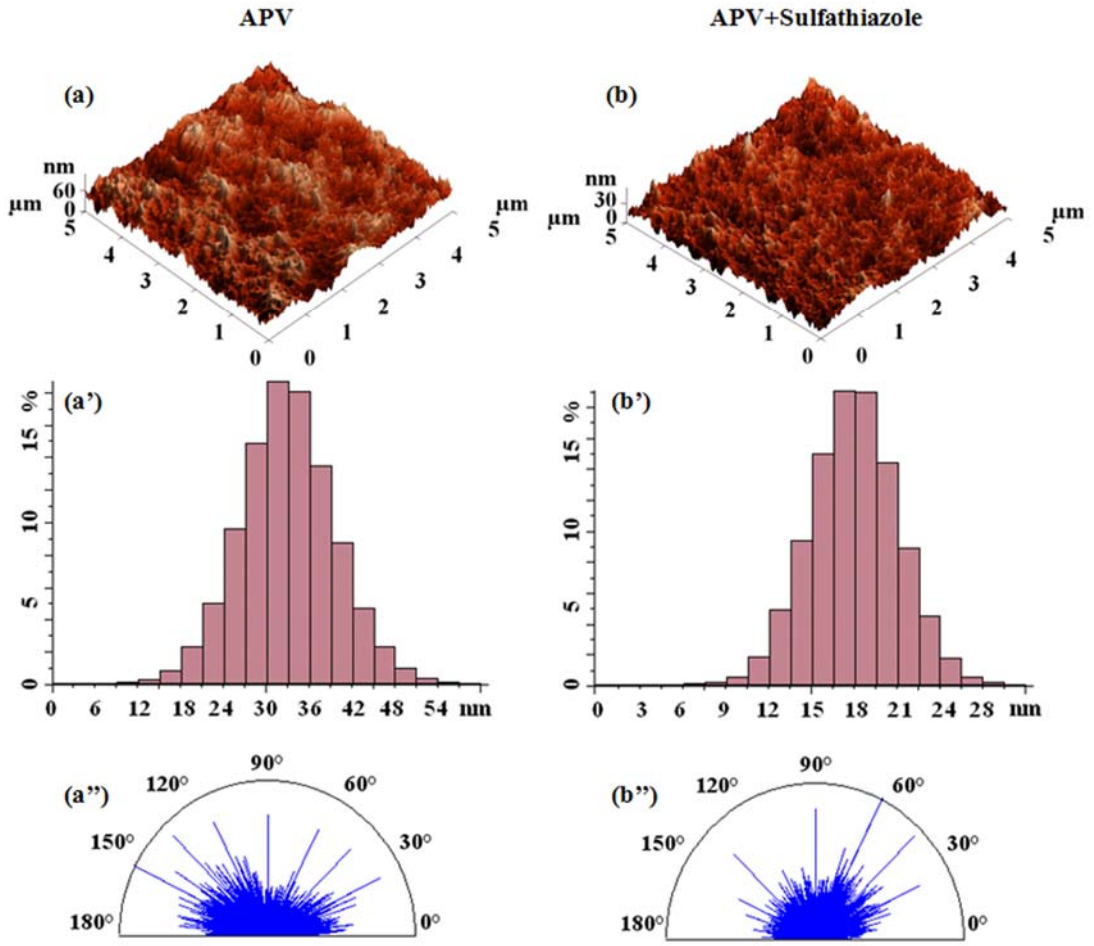


Fig.4 Three-dimensional tapping mode AFM height images (a, b), height histograms (a', b') and angular spectra (a'', b'') for APV and APV + sulfathiazole samples

Table 4. Roughness parameters calculated from 1 x 1 µm² AFM images of pure APV and APV + sulfathiazole films

Sample	Roughness parameters						
	Sz (nm)	Sq (nm)	Sdr (%)	Str	Sm (ml/m^2)	Sc (ml/m^2)	Sv (ml/m^2)
Pure APV	62.1	6.8	2.19	0.500	$3.2 \cdot 10^{-4}$	$8.0 \cdot 10^{-3}$	$8.1 \cdot 10^{-4}$
APV + sulfathiazole	32.6	3.3	0.58	0.682	$1.5 \cdot 10^{-4}$	$4.1 \cdot 10^{-3}$	$3.7 \cdot 10^{-4}$

As expected the roughness parameters such as: peak to valley height (St), root mean square roughness (Sq) and surface area ratio (Sdr) calculated from surface topography images (Fig.4a and b) using the relations (5) and (6), were smaller in the presence of sulfathiazole compared to the pure PVA films (Table 4) indicating the formation of a smooth surface topography.

The height histogram (Fig.4a', b') is also an important analytical tool that provides information about the height distribution and is the best indicator for the flatness of the surface. A

flat surface such as that of sample APV + sulfathiazole is characterized by high and narrow histogram peaks (Fig.4 b').

The material volume (calculated using equation 9) is not only a geometrical descriptor of the surface, but also has significant functional implications. Thus functionally, the material volume reflects the resistance against wear and friction. For a flat-topped surface, such as of APV + sulfathiazole sample, the material volume ratio may increase quickly, showing good running-in properties whereas for a spiked surface, such as of APV sample, the function shows a slow increase with the truncation level, indicating that the top part of the material is easily worn (Table 4).

The void volumes (core void volume of the surface (calculated using equation 10) and valley void volume of the surface (calculated using equation 11)) are proposed here to provide useful information, such as fluid retention ability of a surface, for potential applications of these compounds in biomedicine. For APV + sulfathiazole film surface, the calculated values for Sc and Sv were lower than those obtained for APV film surface (table 4), indicating a weaker fluid retention capacity. This implies the possibility of using the sample with sulfathiazole for applications where is not required a high fluid retention capacity, such as external applications in treatment of skin diseases.

The angular spectrum was shown in a polar plot for an easy evaluation of the isotropic surface property for each sample (Fig.4a'', b''). As it can be see, both films show surface isotropy. The larger value of the texture aspect ratio (formula 8) obtained for APV + sulfathiazole sample compared with pure APV (Table 4) indicates stronger surface isotropy induced by the presence of sulfathiazole in PVA film.

4. Conclusions

The PVA foils containing sulfathiazole are currently used in antimicrobial purposes in external treatments. Having into view this biomedical application, the surface properties and the birefringence of the PVA foils containing Sulfathiazole were established by specific means. Sulfathiazole, as a dipolar molecule influences the qualities of the studied PVA films. The films are more anisotropic, their birefringence (determined by a Babinet compensatory) increases by stretching the polymer foils under gentile heating. The roughness parameters of the foils' surface determined by AFM are smaller in the presence of Sulfathiazole compared with that of the pure PVA foils. Additionally, the functional parameters indicating a weaker fluid retention capacity, imply the possibility of using the sample with sulfathiazole for external applications in treatment of skin diseases.

Acknowledgements

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