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BIOACTIVE NITROGEN-CONTAINING COMPOUNDS WITH SPATIAL CARBOCYCLIC GROUPS: SYNTHESIS, MODELING OF PHYSICAL PROPERTIES AND USE FOR CREATION OF INORGANIC-ORGANIC HYBRID MATERIALS WITH SPECIFIC PROPERTIES

Keywords: QSRR/QSAR, models, descriptor, calculation, bioactive, bioscreening, antibiocorrosive, tribology, composite.

Quantitative «structure-properties» relationships (QSRR/QSAR) based on experimental data for construction of models of dependences of physical properties of bioactive nitrogen-containing compounds with bioactive spatial carbocyclic groups on molecular structures have been studied. Several sets of molecular descriptors have been used. Presence of the dataset outliers was controlled by using PCA; to ascertain the quality of models cross-validation has been used. Virtual bioscreening and activity towards various microorganisms of the obtained compounds have been established. Inorganic-organic hybrid materials with specific properties based on organic hetero-chain polymers and coordination compounds of some transition metals based on bioactive nitrogen-containing compounds have been obtained and studied. Tribological properties and stability towards various factors (stability towards O_2, CO_2 and moisture complex action); photochemical stability (stability towards ultraviolet and visible light) and isothermal aging of the created composite materials have been studied. By preliminary investigations it was established that the created bioactive composites could be used for prevention of materials from bio-deterioration and non-controlled biodegradation, inhibition of growth and expansion of microorganisms, which are causal factors of infectious diseases and for prophylaxis and treatment of above mentioned diseases.

Ключевые слова: QSRR/QSAR, модели, дескриптор, расчет, биологически активный, биоскрининг, антибиокоррозионный, трибология, композит.

Для построения моделей зависимостей физических свойств биологически активных азотсодержащих соединений с биоактивными пространственными карбоциклическими группами в молекулярной структуре исследованы основанные на экспериментальных данных количественные отношения «структура-свойства» (QSRR/QSAR). Использованы несколько вариантов молекулярных дескрипторов. Их присутствие управлялось при помощи метода PCA; для констатации качества моделей была использована перекрестная проверка. Проведен виртуальный биоскрининг и определена активность полученных соединений по отношению к различным микроорганизмам. Получены и изучены неорганические - органические гибридные материалы со специфическими свойствами на основе органических гетероцепных полимеров и координационных соединений некоторых переходных металлов на основе биологически активных азотсодержащих соединений. Изучены трибологические свойства и устойчивость по отношению к различным факторам (устойчивость к O_2, CO_2 и комплексному воздействию влажности); фотохимическая стабильность (стабильность к ультрафиолету и видимой области света) и изотермическое старение полученных композиционных материалов. В ходе предварительных исследований было установлено, что созданные биоактивные композиты могут быть использованы для защиты материалов от био-разрушения и неконтролируемого биоразложения, ингибирования роста и распространения микроорганизмов, которые являются причиной возникновения инфекционных заболеваний и для профилактики и лечения выше упомянутых заболевания.

Introduction

Biodegradation of synthetic and natural materials by various microorganisms affects a wide range of industries and techniques. In accordance with the existed statistical data more than several hundred kinds of such aggressive microorganisms are known [1-3], which damage especially carbon-containing polymers and materials. The actions of microorganisms on polymers are influenced by two different processes: a) deterioration and degradation of polymers, which serve as a native substance for growth of the microorganisms (direct action); b) influence of metabolic products of the microorganisms (indirect action). Losses caused by destruction of natural and synthetic materials with micromycets reach enormous amounts and constitute annually milliards of dollars [4, 5].

Historical buildings, archeological artifacts (made of metals and their alloys, leather and/or wood), museum exhibits and collections of art work – all of them need protection from influence of various aggressive microorganisms. So together the protection of cultural heritage and various synthetic and natural materials is a global problem and this topic is actually all over the world [6].

One of the ways to protect the synthetic materials from the action of microorganisms is a creation of novel polymer coatings with high bioactivity by modification of various polyfunctional adhesive polymer matrices with biologically active compounds [7]. Therefore, synthesis of compounds for bioactive composites and created antibiocorrosive coatings based on them for various natural, synthetic and artificial materials is extremely significant and requires further developments [8].

For the time being in the various spheres of science and technique is giving scientist’s special attention to asymmetric carbocyclic compounds (such as adamantane and its derivatives). Modification of the various bioactive compounds by immunotropic and membranotropic adamantane group has a great potential because of improvement of their hydrolytic stability and increasing their biological activity [9-12].

Experimental

Nitrogen-containing compounds with spatial (adamantane) carbocyclic groups and adamantane-containing hydrazide coordination compounds of transition metals were synthesised by us earlier [13].

Polyester urethane “PU”:

1) The mixture of 50 g (0.1 mole) polyoxypropylenglycole, 2.6 g (0.05 mole) diethylenglicole and 26.1 g (0.3 mole) toluylendiisocyanate (the mixture of 2,4- and 2,6-isomeres with ratio 65:35 wt. %) was stirred during 1 hrs at 80-90^{0}C until formation of hexamethylendiisocyanate. The monitoring of the reaction were carried out by content of NCO-group (the optimum content of the NCO-group for above mentioned polyester urethane is ~7.6 %).

2) To hexamethylendiisocyanate 0.05 mole hydrazine hydrate (the 1% solution of hydrazine hydrate in dimethyl formamide) with the purpose of chain lengthening was added. The mixture was stirred during 24 hrs. The monitoring of the reaction were carried out by the method of infrared spectroscopy, in particular, by disappearance of the characteristic absorption bands of NCO-group in IR spectra of the research sample (2273 cm^{-1}). It was established that for polyester urethane Mw ≈ 50300.

Sulfur-containing polyester urethane “PUS”: for fuctionalization of hexamethylendiisocyanate was carried its sulphurization with 98 % sulfuric acid (5 % wt. of hexamethylendiisocyanate) out. To the mixture was added drop wise sulfuric acid during 20 minutes until 6.5-6.8 % content of NCO-group. The reaction was carried under stirring condition at 80-90 ^{0}C during 5 hrs out. The degree of the sulphurization of the obtained polyester urethane was contained ~3 % wt. (The degree of the sulphurization was determined by titration of sulpho-groups). It was established that for sulfur-containing polyester urethane Mw ≈ 97400.

Ionomer of sulfur-containing polyester urethane “PUSI”: the sulfurized hexamethylendiisocyanate (Mw ≈ 118000) was cooled on 40-45 ^{0}C and then was carried out the transfer of SO_3H-group from acid to salt form by addition of equimolar (in relation to sulfuric acid) triethylamine. To the obtained iono-containing hexamethylendiisocyanate with the purpose of chain lengthening was added 0.05 mole 1% water-solution of hydrazine hydrate under stirring condition during 24 hrs.

The antibiocorrosive coatings were prepared by the following way: to the cyclohexanone solution of polymeric matrix gradually was added the definite quantity of modifier (3 % wt) and bioactive coordination compound (3-5 % wt) under stirring condition until formation of light color homogenous mass. Later, the obtained composition was laid in the form of thin layer on the surface of the selected various materials (wood, plastic, teflon, etc.) for protection and was delayed on the air during 24-48 hrs at room temperature. After hardening, there was produced homogenous, smooth, mechanically stable protective layer.

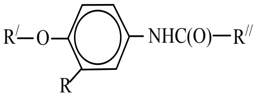
Methods of analysis: Standard methods for obtaining and purify of bioactive compounds were used. Tribological properties of the polymeric matrices have determined using a Spanish Nanovea pin-on-disk Tribometer /Micro Photonics Inc./, Micro-Scratch Tester (MST) /CSM, Neuchatel, Switzerland/ Nicon Eclipse ME 600 Microscope. Standard microbiological methods for study of bactericidal and fungicidal properties of synthesized compounds have used.

Results and discussion

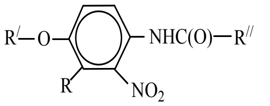
On purpose to establish the correlation between structure of possible bioactive compound and some its fundamental properties we synthesized and studied some anilides and nitroanilides [14] containing spatial carbocyclic groups (adamantane) with various organic radicals in benzene ring (* - Scheme; ** - Ad-Adamantyl).

1. H, CH_3, Ad**(accor. R, R’, R”)
2. H, CH_3, Ad
3. H, C_2H_5, Ad
4. H, Ad, CH_3
5. H, Ad, C_6H_5
6. H, Ad, $CH_2C_6H_5$
7. H, Ad, Ad
8. Cl, 4-ClC_6H_4, Ad
9. H, C_2H_5, Ad
10. H, Ad, CH_3
11. H, Ad, $CH_2C_6H_5$
12. H, Ad, C_6H_5
13. H, Ad, Ad
14. Cl, 4-ClC_6H_4, Ad

In order to select these compounds we considered the availability of their synthesis and possibility of their perspective wide commercialization:



1, 9-14



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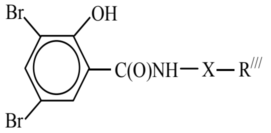


15-16 R$^{////}$=Ad; X = - (15), C_6H_4 (16)

The techniques of quantitative structure-property relationship (QSRR/QSAR) are used for establishing reliable models of biological activities and physical-chemical properties of organic and element-organic molecules. The aforementioned approach is based on representation of molecular structures with numeric quantities. They are calculated via straightforward algorithms and are known as molecular descriptors. Among the latter, considerable attention is granted to the autocorrelation based descriptors [14].

Let us give a brief outline of the approach. Suppose s_1, s_2, …, s_n are variables, which present various molecular substructures. Most often, the paths of the corresponding molecular graphs are considered. As is clear, *n*, i.e., the number of the paths depends on the number of atoms, or, in the graph-theoretical context, on the number of vertices. However, to build statistically reasonable models, one needs to represent molecules with vectors (i.e., series of molecular descriptors) of the same length. Therefore, we introduce a set of the template variables, t_1, t_2, … t_m, where *m* remains constant, i.e., is independent on the size of molecules of the dataset in question. The aforementioned substructures are characterized by special functions. An example is the product of numeric values of a physical property of the atoms of the substructure. That is, if we consider only paths as substructures, we have:

$$f(s_i) = p_i^0 p_i^1$$

Here, p^0 is a physical property of the origin of the ith path and p^1 is that of the terminal vertex (atom) of the path. Examples of the physical property are sigma- and pi-charges, electro negativities, etc. Therefore, we arrive at a vector of the products of the physical properties of the paths, *f*, which has dimensionality equal to *n*.

Autocorrelation vectors are defined as linear transforms of the *f* vectors of the dimensionality *n* to the vectors *a* of the dimensionality *m*. The transform is given by kernel matrices (K):

$$\mathbf{a} = \mathbf{fK},$$

or in the functional form: $a(t) = \int K(t,s) f(s) ds$

The kernel matrix (*K*) has dimensionality (*n,m*). The vector *a* will always be of size *m*, and therefore, independent on the size of the molecule. The kernels are given via various functions. The kernel of 3D-MoRSE descriptor, for example, is given as follows:

$$K(t,s) = \frac{\sin tr(s)}{tr(s)}$$

Here, *r(s)* is the Euclidean distance.

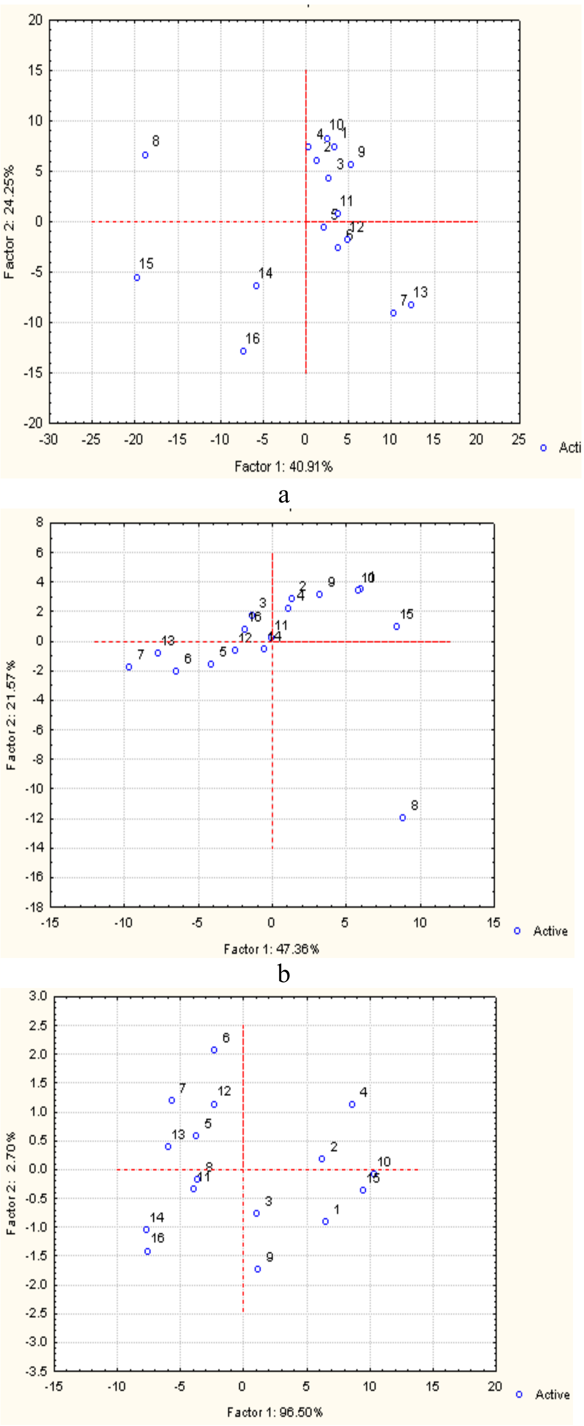
QSPR calculations: We used MDL Isis Draw 2.5.SP4 to build molecular models. Afterwards, we concatenated the models into the dataset by use of EdiSDF 5.02. The textual format of the dataset was SDF. We used VCC-Lab e-Dragon web application for calculation of molecular descriptors. Statistic 6.0 was a tool of our choice for building PCA and PLS models.

Among many available molecular descriptors at our disposal, we selected Radial Distribution Functions (RDF) [15], Crystal Structure Codes (MoRSE) [16], WHIM [17], GETAWAY [18], and traditional topological indices [19]. Our data set [20] contained 16 compounds.

In order to detect outliers i.e., the compounds, which did not belong to the modeling population, we performed PCA [21]. However, unlike to our previous contribution [22], we did not identify any of the investigating compounds as outliers.

As one can see (Fig. 1a), compounds 7, 8, 13-16 12 are situated somehow farther than the main group. This alone does not allow for their removal. For example, the Burden eigenvalues reveal that only compound 8 is an outlier (Fig 1b). When we used the Randič type invariants, none of the com-pounds left the main group (Fig. 1c). Therefore, we decided to keep all of the compounds in the training dataset. It is noteworthy that the Randič type invariants clearly output several clusters of compounds.

Our final step was establishment of relationships between these descriptors and the retentions factors measured experimentally. Our studies show that best model was achieved by employing, again, the GETAWAY descriptors.



a

b

c

Fig. 1 - The outlier detection by means of: PCA: a - The descriptor used is GETAWAY, b - The descriptors used are the Burden eigenvalues, c - The descriptors used are the Randič type invariants

We used PLS [23] as the number of predictors was much higher than that of cases. We used cross-validation to define the optimal number of latent variables. In our study, we used 13 compounds in training set and 3 for the cross-validation tests. Of course, the prediction power was lower in case of cross-validation. We modeled both melting points (mp) and retention factors (Rf) within the same model, which, therefore, had 2 responses.

The results of modeling look impressive as the square of the average correlation coefficient was a high as 0.92. The PRESS was also good enough (Table 1). One can examine the experimental and calculated values (Table 2). A reader should take into account that compounds 4, 13, 16 produced the test (validation) set.

Table 1 - The statistical parameters of the model

Latent Var №	Increase R2 on Y	Average R2 on Y	Increase R2 on X	Average R2 on X
1	0.391833	0.391833	0.286528	0.286528
2	0.286881	0.678714	0.275862	0.562390
3	0.033169	0.711883	0.206076	0.768466
4	0.041860	0.753743	0.109336	0.877802
5	0.121957	0.875700	0.023599	0.901401
6	0.028227	0.903927	0.048229	0.949629
7	0.025273	0.929201	0.030173	0.979802
8	0.023788	0.952989	0.004540	0.984342

Latent Var №	R2 for mp	R2 for Rf	Sc. Press, mp	Sc. Press, Rf	Average Sc. Press
1	0.577891	0.205776	2.254355	1.727976	1.991166
2	0.611797	0.745632	2.094057	1.922039	2.008048
3	0.666069	0.757697	1.780881	1.833227	1.807054
4	0.670454	0.837033	1.763578	1.837925	1.800751
5	0.886302	0.865099	1.268438	1.445234	1.356836
6	0.910597	0.897258	1.211559	1.240578	1.226068
7	0.912324	0.946077	1.198989	1.180627	1.189808
8	0.939416	0.966562	1.389769	1.137673	1.263721

Table 2 - Experimental vs. calculated R/s

Compound	mp, calc	Rf, calc	mp, exp	Rf, exp
1	184.9834	0.518455	178.5	0.60
2	126.5095	0.704182	134.5	0.65
3	142.8738	0.705937	134.5	0.73
4	102.3756	0.591046	121.5	0.42
5	154.5519	0.776873	152	0.80
6	128.6926	0.633454	128.5	0.65
7	171.7885	0.867685	173	0.86
8	167.9010	0.917788	169	0.91
9	193.2231	0.447994	206.5	0.40
10	166.1550	0.486902	166.5	0.50
11	178.3934	0.473237	160	0.41
12	170.2936	0.525245	181.5	0.53
13	198.3374	0.549713	240.5	0.77
14	175.8185	0.426382	176.5	0.45
15	226.3155	0.555867	226.5	0.55
16	183.8285	0.146642	194.5	0.17

Study of bioactive properties of adamantane-containing anilides and nitroanilides

The modeling of the dependence of the structures of used nitrogen-containing adamantane derivatives on their fundamental properties (melting point and R$_f$) allows carrying out the theoretical evaluation of possible bioactivity of same structures. We have carried out the preliminary virtual bioscreening of obtained compounds by using of internet-system program PASS C&T [24]. The estimation of probable bioactivity of chosen compounds was carried out via parameters Pa (active) and Pi (inactive); when Pa>05, the compound also could be shown bioactivity experimentally. Following from above mentioned virtual bioscreening, based on analysis of obtained results, the synthesized compounds with experimentally high probability (Table 3a) (Pa>0.5) possibly will show the following bioactivity: antibacterial, antibacterial activity enhancer, anthelminthic, antiviral (Arbovirus, Influenza, Picornavirus), lipid metabolism regulator, Urologic disorders treatment.

Herewith, in the halogenated nitrogen-containing adamantane (15, 16) derivatives increasing of antiviral (Influenza) activity were observed. The synthesised compounds with experimentally high probability (Table 3b) possibly will show the following bioactivity: antiinfective, dopamine release stimulant, anthelminthic, antiparasitic.

Table 3a - Relative bioactivity of some nitrogen-containing adamantane derivatives (1-14)

Compound	Pa / Pi				
	Lipid metabolism regulator	5 Hydroxytryptamine release inhibitor	Urologic disorders treatment	Antiviral (Influenza)	Antiviral (Picornavirus)
1	–	0.900/ 0.004	0.872/ 0.010	0.791/ 0.004	0.705/ 0.004
2	–	0.834/ 0.004	0.813/ 0.022	0.782/ 0.004	0.673/ 0.013
3	–	0.823/ 0.004	0.797/ 0.027	0.816/ 0.004	0.689/ 0.010
5	–	0.371/ 0.087	–	0.450/ 0.052	0.572/ 0.053
6	0.388/ 0.213	0.256/ 0.179	0.327/ 0.315	0.269/ 0.205	0.509/ 0.097
7	0.344/ 0.241	0.778/ 0.005	0.745/ 0.049	0.638/ 0.011	0.679/ 0.012
8	–	0.746/ 0.005	0.755/ 0.044	0.549/ 0.023	0.724/ 0.005
9	–	0.891/ 0.004	0.855/ 0.013	0.781/ 0.004	–
10	0.973/ 0.003	–	–	–	–
11	0.966/ 0.004	–	–	–	–
12	0.970/ 0.003	–	–	–	–
13	0.971/ 0.003	0.876/ 0.005	0.818/ 0.021	0.775/ 0.005	0.705/ 0.004
14	–	0.843/ 0.005	0.788/ 0.030	0.752/ 0.005	–

	Pa / Pi			
Compound	Antiviral (Arbovirus)	Membrane integrity agonist	Dependence treatment	Antibacterial activity enhancer
1	–	0.703/ 0.101	0.741/ 0.014	–
2	0.869/ 0.003	-	0.545/ 0.056	0.436/ 0.239
3	0.899/ 0.003	0.312/ 0.170	0.389/ 0.174	0.371/ 0.311

End table 3a

5	0.762/ 0.010	0.548/ 0.155	0.350/ 0.218	0.550/ 0.113
6	0.613/ 0.108	-	-	0.663/ 0.022
7	0.803/ 0.005	-	0.404/ 0.160	0.498/ 0.172
8	0.820/ 0.004	0.549/ 0.154	0.543/ 0.057	0.593/ 0.070
9	-	0.752/ 0.083	-	-
10	-	0.770/ 0.075	-	_
11	-	-	-	_
12	-	0.838/ 0.043	-	-
13	-	-	-	-
14	-	0.792/ 0.065	0.720/ 0.017	_

Table 3b - Relative bioactivity of 1-(N-3,5-dibromobenzoyl) aminoadamantane (15) And 4/-(1-adamantyl)-2-hydroxy-3,5-dibromobenzoylanilide (16)

Compound	Pa / Pi			
	Antiviral (Influenza)	Antiviral (Arbovirus)	Antiviral denovirus)	Antiviral (Picornavirus)
15	0.857/ 0.003	-	0.548/ 0.005	-
16	0.903/ 0.002	0. 731/ 0.020	0.617/ 0.004	0.520/ 0.088
Compound	Pa / Pi			
	ntiinfective	Dopamine release stimulant	Anthelmintic (Nematodes)	Antiparasitic
15	0.778/ 0.005	0.848/ 0.009	0.478/ 0.057	0.422/ 0.035
16	0.807/ 0.005	0.749/ 0.029	0.544/ 0.030	0.512/ 0.017

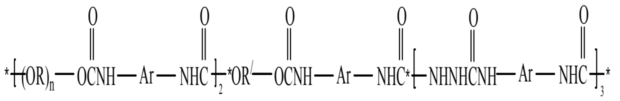
We have tested the bactericidal and fungicidal activity of synthesized compounds according to the method described in [25]. To this target we have applied the test-microorganisms – Pectobacterium aroideae, Fusarium arenaceum, Autinomyces Griseus and Fusarium proliferate. The test results showed that synthesized compounds have revealed selected bactericidal properties and have suppressed the development of research cultures. Microbiological study of the investigated compounds confirmed the evaluated virtual concepts.

Inorganic-organic hybrid materials with specific properties based on synthesised compounds

One of the modern ways to protect the synthetic and natural materials from the action of microorganisms is a creation of novel antibiocorrosive coatings with high bioactivity and multi-vectorial and directional action based on inorganic-organic hybrid composites [8]. Antibiocorrosive coatings mainly contain two components – biologically active compound and polymer matrix, where the bioactive compound dropped. Some polyfunctional hetero-chained organic polymers, such as polyurethane elastomers, polyurethane-acrylates, ionomers, etc., have been successfully used as a matrix for creation of antibiocorrosive coatings. In this regard, special interest provoke in many respects bioactive, including bactericide and fungicide polyurethanes [26, 27].

On the first stage of the research for preparation of "Short-term" action polymeric composites were selected following polyurethanes:

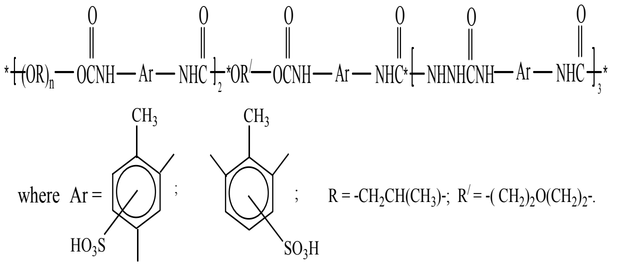
1. Polyester urethane "PU":



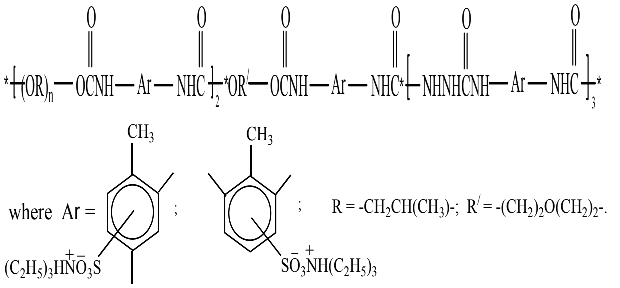
$$*\!\left[(OR)_n-O\overset{\overset{O}{\|}}{C}NH-Ar-NH\overset{\overset{O}{\|}}{C}\right]_2\!*OR'-O\overset{\overset{O}{\|}}{C}NH-Ar-NH\overset{\overset{O}{\|}}{C}*\!\left[-NHNH\overset{\overset{O}{\|}}{C}NH-Ar-NH\overset{\overset{O}{\|}}{C}\right]_3\!*$$

where R = $-CH_2CH(CH_3)-$; R/ = $-(CH_2)_2O(CH_2)_2-$.

2. Sulfur-containing polyester urethane "PUS":



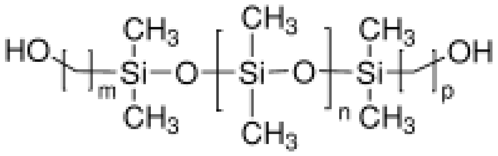
3. Ionomer of sulfur-containing polyester urethane "PUSI":



4. Polyester urethane "BUTYP T-261" based on 4,4-dimethylmethanediisocianate and oligobuthyleneglicoladipinate.

Some adverse effects, in particular, low scratch and wear resistance and environmental degradation have hindered many important applications of polymers [28, 29]. Thus, for physical and/or chemical modification of above-mentioned polyurethanes with the purpose of improving of tribological properties were used silicon-organic oligomers, which will be able to improve several properties of the initial polymer systems including mechanical (elastic, adhesive strength) and thermo physical (frost- and thermal-resistant) and hydrophobicity:

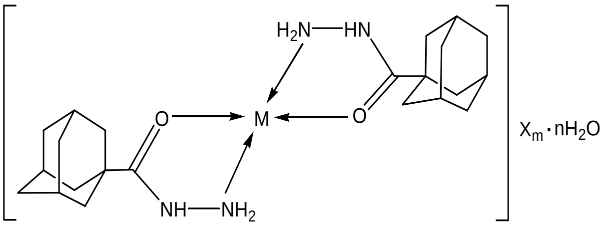
a) Bis(hydroxyalkyl)polydimethylsiloxane:



b) α,ω–dihydroxymethylvinyloligoorganosiloxane: HO{[Si(CH_3)2O] 98.5[Si(CH_3)(CH=CH_2)O] 1.5}XH, where x = 3÷5.

As bioactive compounds for antibiocorrosive coatings we used other nitrogen-containing adamantane derivatives [30,13,31,32] such as transition metals coordination compounds of adamantane-1-carboxylic acid hydrazide synthesised by us [30,13] considering their stability and ability to form dipole-dipole and hydride bonds with the polymeric matrix. It was expected that hydrazide metal complexes will show various applications in the fields such as fungicidal, bactericidal, antiparasitic, antioxidative and cytotoxic studies [31, 32].

The most probable structures of obtained coordination compounds [13] are given bellow:



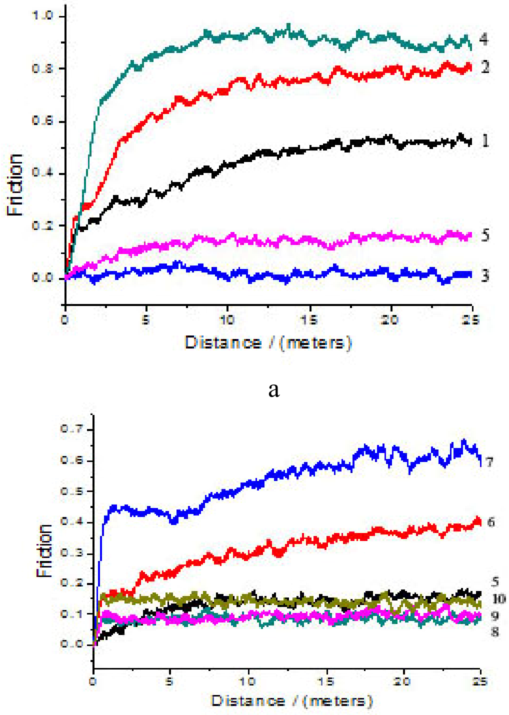
M = Cu, Co, Ni; X = NO_3-, CH_3COO-; m = 1, 2; n = 1, 2.

By using obtained polymeric matrices and coordination compounds (3-5 wt. %) new effective and stable inorganic-organic antibiocorrosive coatings have obtaine.

1 Polyester urethane “PU”
2 Sulfur-containing polyester urethane “PUS”
3 Sulfur-containing polyester urethane “PUS”/ 3% α,ω–dihydroxymethylvinyloligoorganosiloxane
4 Ionomer of sulfur-containing polyester urethane “PUSI”
5 Polyester urethane “BUTYP T-261”
6 Polyester urethane “BUTYP T-261” / 3% coordination compound
7 Polyester urethane “BUTYP T-261” / 5% coordination compound
8 Polyester urethane “BUTYP T-261” / 3% Bis(hydroxyalkyl)polydimethylsiloxane
9 Polyester urethane “BUTYP T-261” / 3% α,ω–dihydroxymethylvinyloligoorganosiloxane
10 Polyester urethane “BUTYP T-261” / 3% α,ω–dihydroxymethylvinyl oligoorganosiloxane / 3% coordination compounds

Tribological properties of the polymeric matrices and antibiocorrosive coatings have studied by using a Nanovea pin-on-disk tribometer from Micro Photonics Inc. The tribometer provides dynamic friction results under rotation conditions 35. 440 steel balls made by Salem Specialty Balls have used with the diameter of 3.2 mm. The tests have performed under the following conditions: temperature 20±2 0C, speed 100 rpm, radius 2.0 mm, loads 5.0 N. The number of revolutions was 3000.

As it was shown by figures 2a and 2b dynamic friction for polyurethane matrices mainly depends on their structure and the structure of modifier.



a

b

Fig. 2 - Dependence of the dynamic friction on distance of sliding for: a) polyurethane matrices and antibiocorrosive coating films based on them (1-5), b) matrix based on polyester urethane (“BUTYP T-261”) and correspond antibiocorrosive coatings (5-10). non-modified and modified with silicon-organic oligomers

By the analysis of curves of dynamic friction variation for non-modifier and modifier polyurethanes and antibiocorrosive coatings based on them (Fig. 2a and b) was established that the value of dynamic friction is high for non-modified polyurethane matrices and coatings based on them. The addition of silicon-organic oligomers (3-5 w. %) to polyuretane matrices leads to decrease of the mentioned above parameter (Fig. 2b).

By doping of bioactive coordination compounds in polyester urethane matrix based on 4,4-dimethylmethanediisocyanate and olygobuthylenglycole adipinate the value the coefficient of dynamic friction is increased. This fact could be explained by influence of their spatial structure. It was shown, that the modification of polyester urethanes by silicon-organic oligomers the dynamical friction was reduced (Fig. 3), what how it appears, is conditioned by high plasticized ability of flexible siloxane oligomers.

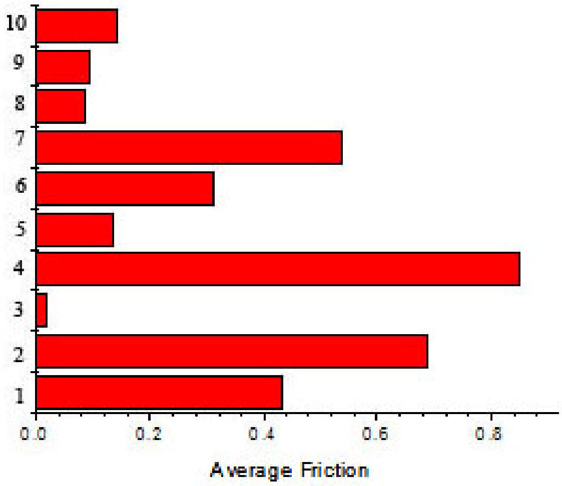


Fig. 3 - The comparison of the values of average dynamic friction for polymer matrices and antibiocorrosive coatings based on them

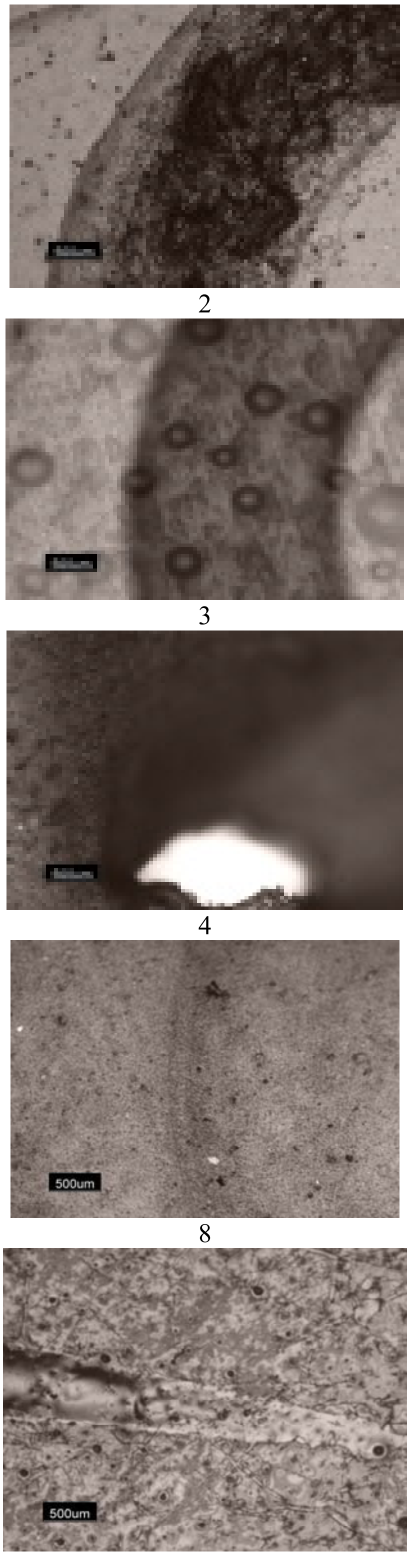
The obtained results were also confirmed by studying of surface morphology (scanning electron microscopy) of the films from modified and non-modified polymeric matrices purpose for creation of antibiocorrosive coatings (Fig. 4). Plastic deformation of corresponding films under the constant load equal to 5N showed that a split behavior of sulfur-containing polyester urethane “PUS”, modified by α,ω–dihydroxymethylvinyloligoorganosiloxane, characterized with less crack nucleation in comparison with non-modifier “PUS”. It must be noted that polyester urethane “BUTYP T-261”, modified by bis(hydroxyalkyl) polydimethylsiloxane, demonstated least crack nucleation among the tested polymeric matrices.

The hydrophobility of obtained antibiocorrosive coatings by gravimetric method was determined. It was established, that during 300 hours their water absorption ability for modified matrices by silicon-organic oligomers not exceeds 0.1%.

The influence of isothermal aging (40 and 600 C), the so-called weather ability (stability towards O_2, CO_2 and moisture complex action) and photochemical stability (stability towards ultraviolet and visible light) was studied. It was shown, that during more than three months (at room temperature) the initial appearance (state), colour, optical transparency and mechanical properties (surface homogeneity without of splits formation) of antibiocorrosive coatings did not worsen.

By preliminary investigations it was established, that the created antibiocorrosive composites could be used for: prevention of materials from biodeterioration and non-controlled biodegradation; inhibition of growth and expansion of microorganisms, which are causal factors of infectious diseases, for prophylaxis and treatment of above mentioned diseases.

The created composites can be also recommended for preparation of protective covers with multivectorial application (film materials and impregnating compositions) stable to biocorrosion; materials with antimycotic properties for prophylaxis and treatment of mycosis; biologically active polymer composite materials for protection of museum exhibits; for human protection during its contact with microorganisms [36].



2

3

4

8

10

Fig. 4 - The surface morphology of the polymeric films for antibiocorrosive coatings based on non-modified and modified polyurethanes

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Conclusions

1. Quantitative «structure-properties» relationships (QSRR/QSAR) based on experimental data for construction of models of dependences of physical properties of biologically active [16] nitrogen-containing com-

pounds with bioactive spatial carbocyclic (adamantane) groups, synthesized by us, on molecular structures have been studied.

2. Several sets of molecular descriptors have been used. Presence of the dataset outliers was controlled by using PCA; to ascertain the quality of models cross-validation has been used.

3. Based on the performed research, one concludes that the best models have been acquired by the use of the GETWAY description of obtained compounds has been carried out.

4. Virtual bioscreening and activity towards various microorganisms of the obtained compounds have been studied. Area of their application has been established. Microbiological study of the investigated compounds confirmed the evaluated virtual concepts.

5. Polyurethanes with various structures as a polymeric matrix for antibiocorrosive coatings were chosen and used. For modification their tribological properties silicon-organic oligomers have used. New effective, photochemical stable and “Short-time” active inorganic-organic antibiocorrosive coatings have been obtained. Tribological properties of the obtained polymeric composites and antibiocorrosive coatings have determined. There was established, that the modification process could used to improve tribological properties of polyurethanes.

References

1. N. Lekishvili, Kh. Barbakadze, D. Zurabishvili, G. Lekishvili, B. Arziani, A. Fainleib, O. Grigorieva, W. Brostow, T. Datashvili. Oxid. Commun. (Intern. J.), 35, 4, 746-761 (2012).
2.Gu Ji-Dong. Int. Biorterior. & Biodegr, 52, 1, 69-91 (2003).
3. M.I. Kurdina, V.E. Malikov, N.E. Zarikova, et. al. Bull. of Dermatol. and Venerol, 5, 49-52 (2002).
4. N. Lekishvili, Kh. Barbakadze, D. Zurabishvili, T. Lobzhanidze, Sh. Samakashvili, Z. Pachulia, Z. Lomtatidze. Antibiocorrosive covers and conservators based on new carbofunctional oligo-siloxanes and biologically active compounds. Oxid. Commun. (Intern. J.), 33, 1, 104-124 (2010).
5. G.T. Howard. Int. Biorterior. & Biodegr. 49, 4, 242-252 (2002).
6. T. Nakaya. Prog. Org. Coat., 27, 173-180 (1996).
7. J. Hazziza-Laskar, et al. Journal of Applied Polymer Science, 58, 1, 77-84 (1995).
8. 41st IUPAC World Chemistry Congress. Chemistry Protection Health, Natural Environment and Cultural Heritage. Programme and abstracts. Turin (Italy), August 5-11. 2007.
9. I.S. Morozov, V.I. Petrov and S.A. Sergeeva, Pharmacology of Adamantanes, Volgograd Medical Academy, Volgograd (2001).
10. N.G. Arcimanovich, T.S. Galushina, T.A. Fadeeva, Adamantanes – medicines of the XXI century. International Journal on Immunorehabilitation. 2, 1, 55-60 (2000).
11. V.Y. Kovtun, V.M. Plakhotnik Using of adamantane carbonilic acids for modification of drugs properties and biologically active compounds. Chem. Pharm. J. 8, 931-940 (1987).
12. Kh. Barbakadze, N. Lekishvili, Z. Pachulia. Adamantane-containing biological active com pounds: synthesis, properties and use. Asian J. Chem., 21, 9, 7012-7024 (2009).
13. N. Lekishvili and Kh. Barbakadze. Asian J. Chem., 24, 6, 2637-2642 (2012).
14. Chemoinformatics, a Textbook. Gasteiger J., Engel Th. Eds. Wiley-VCH, Weinheim, 2003.
15. M.C. Hemmer, V. Steinhauer, J. Gasteiger. Vibrat. Spectr. 19, 151-164 (1999).
16. J. Schuur, Gasteiger. Anal. Chem., 83, 2398-2405 (1997).
17. R. Todeschini, M. Lesagni, E. Marengo. J. Chemom., 8, 263-273 (1994).
18. V. Consonni, R. Todeschini, L. Pavan. J. Chem. Inf. Comput. Sci. 42, 682-692 (2002).
19. R. Todeschini, V. Consonni. Handbook of Molec. descriptors, Wiley-VCH, Weinheim, 2001.
20. L.I. Denisova, V.M. Kosareva, K.E. Lopukhova, I.G. Solonenko. Kh. F. Zh., 9, 18-21 (1975).
21. Otto M. Chemometrics, Wiley-VCH, Weinheim, 1999.
22. G. Lekishvili, L. Asatiani, D. Zurabishvili. Georg. Chem. Journal. 4, 3, 253-256 (2004).
23. P. Geladi, B. R. Kowalski. Anal. Chim. Acta, 185, 1-17 (1986).
24. A.B. Sadim, A.A. Lagunin, D.A. Filiminov, V.V. Poroikov. Internet-System of Prognose of the Spectrum of Bioactivity of Chem. Comp. Chem.-Farm.J, 36, 21-26 (2002).
25. Kh. Barbakadze, D. Zurabishvili, M. Lomidze, I. Sadaterashvili, T. Lobzhanidze and N. Lekishvili. Proceedings of the NAS of Georgia, Chemistry, 34, 45-52 (2008).
26. Yu.V. Savelyev, N.I. Levchenko, A.V. Rudenko et al. Ukraine Patent 63092, (15 Jan., 2004).
27. Yu.V. Savelyev. Handbook of Condensation Thermoplastic Elastomers, edited by S. Fakirov. Willey-VCH Verlag GmbH&Co. KgaA. 2005, pp. 355-380.
28. Y.K. Chen, S.N. Kukureka, C.J. Hooke, M. Rao, J. Mater. Sci., 35, 1269 (2000).
29. Y, Yamamoto and T. Takashima, Wear. 253, 820 (2002).
30. W. Yan, Y.Y. Zheng, D. Bao. Synth. React. Inorg. Met. Org. Nano-Met. Chem. 35, 237 (2005).
31. K. Deepa, K.K. Aravindakshan, Synth. React. Inorg. Met. Org . Nano-Met. Chem. 35, 409 (2005).
32. R.H. Holm, Coord. Chem. Rev. 100, 1990, 183p.
33. S.U. Rehman, M. Mazhar, M. Amin, B. Sadiq, A. Xuequing, S. George, E. Khalid, M.K. Synth. React. Inorg. Met. Org. Nano-Met. Chem. 34, 1379 (2004).
34. I.O. Adeoye, O.O. Adelowo, M.A. Oladipo, O.A. Odunola. Comparison of Bactericidal and Fungicidal Activities of Cu(II) and Ni(II) Complexes of Para-Methoxy and Para-Hydroxy Benzoic Acid Hydrazide, Research Journal of Applied Sciences. 2, 5, 590-594 (2007).
35. W. Brostow, T. Datashvili, B. Huang. Polymer Engineering and Science. 292-296 (2008).
36. Kh. Barbakadze, N. Lekshvili, D. Zurabishvili, Z. Pachulia, Zh. Gurjia, K. Giorgadze, G. Tsintsadze. 2nd International Caucasian Symposium on Polymers and Advanced Materials, Tbilisi, Georgia, 2010, p. 20.

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