Biological Activity of Chemical Compounds and Their Molecular Structure-Information Approach

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Abstract: A method is proposed for bioscreening chemical compounds. We propose the systemic signs within the framework of an informational approach and the statistical method of compare of molecular qualitative characters. Using the methods of information theory, we offer four classification rules that allow statistically reliably distinguish preparations with high biological action (radioprotection). For the practical use of the rules is sufficient to know only the atomic structure of the molecule. We also use a descriptor that describes the average quasi-valence number of molecules. Quasi-valence number associated with the electrostatic potential of the molecule. It is established that the biological activity of chemical compounds is related with the existence of threshold effects. We have also demonstrated that mathematical informational function is related to the physical properties of molecules (hydrophobicity, electrostatic potential).

Key words: Diversity, information function, radioprotective activity, quasi-valence, sulfur compounds.

1. Introduction

In the article [1], it has been proposed information approach that enables predicting the effective radioprotectors among the series of sulfur compounds. The basis of this approach was the assumption that the effects of radiation on biological objects destroy the information [2]. We assume that each molecule of the radioprotector carries a message to the target molecule. The molecule of radioprotector should contain information on at least two factors: the directional transport and function of performance (recognition and regulation). In this paper, we study the further development of the informational approach which was proposed in the article [1]. We propose another criterion for allotment of effective radioprotective compounds in homologous series of N-substituted S-2-aminoethylthiosulfates (Table 1). These compounds are of interest for modeling biological activity, since, for example, only a replacement substituent at the nitrogen atom of the base molecule leads to a noticeable change of radioprotective efficacy. Here, as an indicator of the effectiveness of chemical radioprotective compound we used therapeutic index $T = \frac{LD_{50}}{ED_{50}}$, and survival ($A$, %).

2. Method and Models

The lack of reliable and comprehensive experimental physical and chemical information about the chemical compounds makes it necessary to develop a methodology for evaluation of the molecular bioactivity, which is based solely on knowledge of the atomic structural formula of the molecule. Coding of specific information that contained in the molecular structure, for a discrete of set elements is realized by using information function of Shannon. It is known that a quantitative measure of the content of information in a multicomponent systems consisting of objects belonging to the same set of elements are determined using Shannon informational function (informational entropy) [2, 3]. For a discrete set of objects the informational function is determined in bits units in the following way:
<table>
<thead>
<tr>
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<tbody>
<tr>
<td>1</td>
<td>(CH$_2$)$_3$CHOH(CH$_2$)$_3$</td>
<td>0.533</td>
<td>0.071</td>
<td>87</td>
<td>7</td>
<td>0.053</td>
</tr>
<tr>
<td>2</td>
<td>(CH$_2$)$_3$CH(OH)CH$_2$</td>
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<td>90</td>
<td>7</td>
<td>0.053</td>
</tr>
<tr>
<td>3</td>
<td>2,4-Ch$_2$C$_6$H$_4$O(CH$_2$)$_4$</td>
<td>0.334</td>
<td>0.043</td>
<td>93</td>
<td>8</td>
<td>0.006</td>
</tr>
<tr>
<td>4</td>
<td>(CH$_2$)$_4$</td>
<td>0.267</td>
<td>0.018</td>
<td>100</td>
<td>15</td>
<td>0.051</td>
</tr>
<tr>
<td>5</td>
<td>4-CH$_2$CH$_2$CH$_2$CH$_2$O(CH$_2$)$_3$</td>
<td>0.376</td>
<td>0.013</td>
<td>100</td>
<td>10</td>
<td>0.031</td>
</tr>
<tr>
<td>6</td>
<td>2-CH$_2$C$_6$H$_4$O(CH$_2$)$_3$</td>
<td>0.471</td>
<td>0.025</td>
<td>78</td>
<td>8</td>
<td>0.036</td>
</tr>
<tr>
<td>7</td>
<td>(CH$_2$)$_3$CH(OH)CH$_2$</td>
<td>0.169</td>
<td>0.017</td>
<td>87</td>
<td>7</td>
<td>0.059</td>
</tr>
<tr>
<td>8</td>
<td>(CH$_2$)$_3$CH(CH$_2$)$_3$CH$_2$</td>
<td>1.017</td>
<td>0.041</td>
<td>80</td>
<td>13</td>
<td>0.059</td>
</tr>
<tr>
<td>9</td>
<td>(CH$_2$)$_3$CH(CH$_2$)$_3$</td>
<td>1.012</td>
<td>0.034</td>
<td>100</td>
<td>25</td>
<td>0.059</td>
</tr>
<tr>
<td>10</td>
<td>(CH$_2$)$_3$CHCH(CH$_2$)$_3$CH$_2$</td>
<td>0.259</td>
<td>0.029</td>
<td>100</td>
<td>9</td>
<td>0.064</td>
</tr>
<tr>
<td>11</td>
<td>(CH$_2$)$_3$CH(OH)CH$_2$</td>
<td>0.538</td>
<td>0.052</td>
<td>93</td>
<td>10</td>
<td>0.053</td>
</tr>
<tr>
<td>12</td>
<td>(CH$_2$)$_3$CHCH(CH$_2$)$_3$CH$_2$</td>
<td>0.485</td>
<td>0.065</td>
<td>66</td>
<td>7</td>
<td>0.064</td>
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<tr>
<td>13</td>
<td>(CH$_2$)$_3$CHCH(CH$_2$)$_3$CH$_2$</td>
<td>0.453</td>
<td>0.065</td>
<td>100</td>
<td>7</td>
<td>0.067</td>
</tr>
<tr>
<td>14</td>
<td>3-CH$_2$[(CH$_2$)$_2$]CHCH(CH$_2$)$_3$CH$_2$</td>
<td>0.550</td>
<td>0.074</td>
<td>93</td>
<td>7</td>
<td>0.067</td>
</tr>
<tr>
<td>15</td>
<td>2,6-(CH$_2$)$_2$C$_6$H$_4$O(CH$_2$)$_3$</td>
<td>0.751</td>
<td>0.060</td>
<td>100</td>
<td>12</td>
<td>0.037</td>
</tr>
<tr>
<td>16</td>
<td>2-CH$_2$C$_6$H$_4$O(CH$_2$)$_3$</td>
<td>0.601</td>
<td>0.045</td>
<td>87</td>
<td>13</td>
<td>0.037</td>
</tr>
<tr>
<td>17</td>
<td>(CH$_2$)$_3$CHCH(CH$_2$)$_3$CH$_2$</td>
<td>0.136</td>
<td>0.016</td>
<td>87</td>
<td>9</td>
<td>0.065</td>
</tr>
<tr>
<td>18</td>
<td>1-CH$_2$[(CH$_2$)$_2$]CH(OH)(CH$_2$)$_3$</td>
<td>0.442</td>
<td>0.059</td>
<td>80</td>
<td>7</td>
<td>0.062</td>
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<tr>
<td>19</td>
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<td>0.737</td>
<td>0.103</td>
<td>80</td>
<td>7</td>
<td>0.058</td>
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<tr>
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<td>0.389</td>
<td>0.040</td>
<td>93</td>
<td>11</td>
<td>0.041</td>
</tr>
<tr>
<td>21</td>
<td>(CH$_2$)$_3$CHCH(CH$_2$)$_3$CH$_2$CH$_3$</td>
<td>0.456</td>
<td>0.055</td>
<td>50-100</td>
<td>8</td>
<td>0.071</td>
</tr>
<tr>
<td>22</td>
<td>CH$_2$CH$_2$CH$_2$</td>
<td>0.465</td>
<td>0.056</td>
<td>50-100</td>
<td>8</td>
<td>0.054</td>
</tr>
<tr>
<td>23</td>
<td>CH$_2$CH$_2$</td>
<td>0.135</td>
<td>0.017</td>
<td>50-100</td>
<td>8</td>
<td>0.073</td>
</tr>
<tr>
<td>24</td>
<td>4-Cl, 2-O(CH$_2$)$_2$C$_6$H$_4$</td>
<td>0.661</td>
<td>0.056</td>
<td>50-100</td>
<td>12</td>
<td>0.023</td>
</tr>
<tr>
<td>25</td>
<td>4,6-Cl$_2$, 2-O(CH$_2$)$_2$C$_6$H$_4$</td>
<td>0.467</td>
<td>0.035</td>
<td>50-100</td>
<td>13</td>
<td>0.023</td>
</tr>
<tr>
<td>26</td>
<td>4-OCH$_2$CH$_2$CH$_2$</td>
<td>0.547</td>
<td>0.078</td>
<td>50-100</td>
<td>7</td>
<td>0.035</td>
</tr>
<tr>
<td>27</td>
<td>(CH$_2$)$_3$CHCH$_2$CH$_2$</td>
<td>0.107</td>
<td>0.085</td>
<td>50-100</td>
<td>12</td>
<td>0.059</td>
</tr>
<tr>
<td>28</td>
<td>(L)(CH$_2$)$_3$CHCH$_2$CH$_2$</td>
<td>0.107</td>
<td>0.061</td>
<td>50-100</td>
<td>18</td>
<td>0.059</td>
</tr>
<tr>
<td>29</td>
<td>3-CH$_2$C$_6$H$_4$O(CH$_2$)$_3$CH$_2$</td>
<td>0.550</td>
<td>0.081</td>
<td>50-100</td>
<td>7</td>
<td>0.054</td>
</tr>
<tr>
<td>30</td>
<td>2-CH$_2$OC$_6$H$_4$(CH$_2$)$_2$</td>
<td>0.538</td>
<td>0.077</td>
<td>50-100</td>
<td>7</td>
<td>0.041</td>
</tr>
<tr>
<td>31</td>
<td>(CH$_2$)$_3$CHCH$_3$CH$_2$</td>
<td>0.259</td>
<td>0.032</td>
<td>50-100</td>
<td>8</td>
<td>0.047</td>
</tr>
<tr>
<td>32</td>
<td>cyclohexanol-(CH$_2$)$_3$</td>
<td>0.256</td>
<td>0.024</td>
<td>50-100</td>
<td>10</td>
<td>0.055</td>
</tr>
<tr>
<td>33</td>
<td>(CH$_2$)$_3$CH</td>
<td>0.732</td>
<td>0.418</td>
<td>0</td>
<td>2</td>
<td>0.029</td>
</tr>
<tr>
<td>34</td>
<td>(CH$_2$)$_3$CHOH(CH$_2$)$_3$</td>
<td>0.505</td>
<td>0.168</td>
<td>0</td>
<td>3</td>
<td>0.041</td>
</tr>
<tr>
<td>35</td>
<td>2-phenethyl-(CH$_2$)$_4$</td>
<td>0.257</td>
<td>0.193</td>
<td>0</td>
<td>1</td>
<td>0.016</td>
</tr>
<tr>
<td>36</td>
<td>4-BrC$_6$H$_4$O(CH$_2$)$_3$</td>
<td>0.391</td>
<td>0.130</td>
<td>0</td>
<td>3</td>
<td>0.025</td>
</tr>
<tr>
<td>37</td>
<td>4-CIC$_6$H$_4$OCH$_2$C$_6$H$_4$</td>
<td>0.354</td>
<td>0.236</td>
<td>0</td>
<td>2</td>
<td>0.025</td>
</tr>
<tr>
<td>38</td>
<td>$[C_6H_4O(CH_2)_2]_2$</td>
<td>2.353</td>
<td>1.882</td>
<td>0</td>
<td>1</td>
<td>0.031</td>
</tr>
<tr>
<td>39</td>
<td>$[C_6H_4O(CH_2)_2O(CH_2)_2]_2$</td>
<td>0.926</td>
<td>0.823</td>
<td>0</td>
<td>1</td>
<td>0.029</td>
</tr>
<tr>
<td>40</td>
<td>CH$_2$-C$_6$H$_4$</td>
<td>1.000</td>
<td>0.444</td>
<td>0</td>
<td>2</td>
<td>0.017</td>
</tr>
<tr>
<td>41</td>
<td>CH$_2$O(CH$_2$)$_3$</td>
<td>1.543</td>
<td>1.029</td>
<td>0</td>
<td>2</td>
<td>0.009</td>
</tr>
<tr>
<td>42</td>
<td>HO(CH$_2$)$_3$</td>
<td>2.029</td>
<td>1.107</td>
<td>0</td>
<td>2</td>
<td>0.032</td>
</tr>
</tbody>
</table>

Table 1: Informational function and radioprotective efficiency of N-substituted S-2-aminoethylthiosulfates (RNHCH$_2$CH$_2$SSO$_3$H).
56  HOCH₂(CH₂)₈CHOHCH₂  1.166  0.729  0  2  0.049
57  HOCH₂CHOH(CH₂)₉   2.093  0.583  0  4  0.049
58  (CH₃)₂CH         1.357  1.256  0  1  -0.007
59  (CH₃)₃CCH₂       2.093  0.881  0  2  0.025
60  (CH₃)₃C          1.173  0.939  0  1  0.011

\[ H = -\sum_{i=1}^{n} p_i \log_2 p_i \]  (1)

under additional conditions: \(0 \leq p_i \leq 1\) and \(\sum_{i=1}^{n} p_i = 1\);

\(n\) is the discrete number of objects (features) of the set, which determine the space of possible values of \(p_i\).

Function \(H\) is an integral index of the multicomponent system. The values of \(p_i\) determine the share of the \(i\)th element in the entire collection of set of elements (e.g., its percentage content carbon atoms in molecule), i.e., \(p_i\) assigns the number of realizations or possible outcomes. Actually, to calculate the values of \(p_i\), we use A. N. Kolmogorov’s combinatorial approach [4] for set of \(n\) elements. Function \(H\) is used for a quantitative determination of the measure of organization or diversity of multicomponent (the number of atoms of different varieties) systems. Measures of information are integral characteristics and characterize the whole set of events. They are associated with the entire set of possible events, and it is in chime with well-known representations on the complex nature of the radioprotective effect of radioprotectors [5]. However, the capacity of the information carrier is not always necessary to use completely, but enough to highlight some of the part of characteristics of the object (the principle of “signatures” [6]). In most cases, not all the total amount of information is used which contains the object but only some part of it characteristics.

There may be significant variations in determining the elements of set and of their method of classification therefore, they will be significantly differ in informational quantity. Each approach gives a certain amount of informational content of the molecule. An important condition for the application of informational theory to objects is the way to distinguish between these objects. In determining of informational function we must to specifically stipulate what attributes or criteria differences are taken into account.

3. Results and Discussion

Search of the linkage of experimental data (Table 1) with molecular structure we shall perform using following particular informational function:

\[ \Delta H_1 = p_H \log_2 p_H - p_C \log_2 p_C. \]  (2)

Here, \(p_H\) and \(p_C\) are the relative proportions of hydrogen and carbon atoms in the chemical structure of the molecule. This descriptor allows us statistically significantly excrete the radioprotective compounds \((ED_{50} \leq 0.07 \text{ mmol/kg})\), which have a high therapeutic index against ineffective chemical compounds even when they used in very high doses.

From Table 1 it follows that if the informational sign of \(\Delta H_1\) is more than the threshold value 0.03 \(bits\), then the chemical compounds posses radioprotective activity and high therapeutic effect. If the informational sign of \(\Delta H_1 < 0.03 \text{ bits}\), then the chemical compounds have no radioprotective activity even when they are used at high doses. Features \(\Delta H_1\) and \(T\) have the alternative variation. Therefore, we can use the statistical method of comparison of dichotomous signs for quantitative confirmation of coupling of the molecular structures with their bioactivity. We divide compounds of Table 1 into two groups. The first group of the chemical compounds (№ 1-32) contains the radioprotectors with a high therapeutic index of \(T \geq 6\) (the number of molecules we denoted by \(q_1\)). The second group of ineffective chemical compounds (№ 33-60) has a low therapeutic index \(T < 6\). The second group contains \(q_2\) chemical compounds. Quantity of the chemical compounds in the first group with a qualitative property of the second group \((\Delta H_1 < 0.03 \text{ bits})\) we will designate as
q_{12} = 3 \text{ (intersection of sets).} \quad \text{Quantity of the chemical compounds of the second group with a qualitative property of the first group } (\Delta H > 0.03 \text{ bits}) \text{ we will designate as } q_{21} = 6. \quad \text{Graphically, the distribution of the chemical compounds we will present in the form of a } 2 \times 2 \text{ table (Fig. 1).}

Quantitative measure of the relationship between dichotomous population signs of \( T \) and \( \Delta H_1 \) we define using the association factor Yule [8]:

\[
\Phi = \frac{q_{11}q_{22} - q_{12}q_{21}}{q_{11}q_{22} + q_{12}q_{21}} = 0.92 \quad (3)
\]

Here \( q_{11} = 29, \quad q_{12} = 3, \quad q_{21} = 8, \quad q_{22} = 20 \) (Fig. 1, Table 2). We will validate the statistical significance of the association factor \( \Phi \) by \( X^2 \) criteria, taking into account the amendments of Yates [8] that leads to the following inequality:

\[
X^2 = \frac{(O_{11}E_{11} - O_{12}E_{12})^2}{E_{11}E_{12}} + \frac{(O_{21}E_{21} - O_{22}E_{22})^2}{E_{21}E_{22}} = 17.6 > \chi^2_{(0.05;1)} = 3.83
\]

The high value of \( X^2 \) and a high statistically significance of the association coefficient \( \Phi = 0.92 \) confirms non-randomness binding of the radioprotective action of the molecules (Table 1) with a qualitative sign of \( \Delta H \). We define the average value of signs for each of the two groups of compounds \#1-32 and \#33-60: \( \Delta H_{1} = 0.051 \text{ bits} \) for the series of chemical compounds in first group (\( N_1 = 32 \)) and \( \Delta H_{2} = 0.011 \text{ bits} \) for the series of chemical compounds of second group (\( N_2 = 28 \)), respectively. We test null hypothesis about equality of variances

\[
S_1^2 = 2.357 \cdot 10^{-4} \quad \text{and} \quad S_2^2 = 9.653 \cdot 10^{-4}
\]

for the two random samples. For this purpose, we use the \( F \) – test of Fisher distribution [9]:

\[
F = \frac{S_2^2}{S_1^2} = 4.078 > F_{27,31;0.95}^{(cr)} = 1.83 \quad (4)
\]

That is the distinction between the two variances can be considered as statistically significant (\( F \)-value is higher than tabulated value of Fisher distribution). Therefore, these two random samples belong to different subsets.

We can get more information about linked events \( T \) and \( \Delta H_1 \), if we draw up table of conjugacy (Table 2) for the normalized ratios (or probabilities) \( p_i \) for bioactive molecules and inactive chemical compounds. We examine whether there is a relationship between events \( \Delta H_1 \) and \( T \).

Obviously, the so-called conditional proportion equal to \( p_{22} = 0.333 \) (from Table 2). At the same time, if the events \( T \) and \( \Delta H_1 \) are absolutely independent, then this ratio must be simple product of proportions \( P_2 \) and \( p_2 \).

That is, from the data of the Table 2 follows that the product of proportions is equal to \( P_2 \cdot p_2 = 0.383 \cdot 0.466 = 0.178 \). The distinction between the proportions of \( p_{22} = 0.333 \) and \( P_2 \cdot p_2 = 0.178 \) is significantly different and therefore these two events are not independent [8]. The linkage between the two events (properties, signs) exists if manifestation of one event depends from manifestation of another event.

Two events are independent if the occurrence of one event does not depend on the occurrence of another event (i.e., \( p_{22} = P_2p_2 \)). We examine the null hypothesis of equality of the average values \( \Delta H_{11} \) and \( \Delta H_{12} \). For this purpose we use the following equation [9]:

\[
I = \frac{v_1f_{21;1-\alpha} + v_2f_{12;1-\alpha}}{\sqrt{v_1 + v_2}}
\]

Here \( v_1 = S_1^2/N_1 \) and \( v_2 = S_2^2/N_2 \), \( \alpha \) is the significance level. From Eq. 5 we obtained average value \( I = 0.013 \) (fractile of \( t \) - distribution). The null hypothesis of equality of mean levels of the two

\[Fig. 1 \quad \text{Distribution of the chemical compounds of series N-substituted S-2-aminoethylthiosulfates in accordance with their dichotomous features.} \]
samples is rejected if \( |\Delta H_{11} - \Delta H_{12}| > t \). In our case \( |\Delta H_{11} - \Delta H_{12}| = 0.04 \), and therefore the distinction between the average values is not random event. That is, these two groups of the chemical compounds of the series N-substituted S-2-aminoethylthio-sulfates are statistically confidently belong to different domains of the partial informational function \( \Delta H_1 \) (first separation principle).

The lack of a simple linear relationship between informational function \( \Delta H_1 \) and a magnitude of the radioprotective effect can be seen as lack of complete "trust" between the carrier of information and decoding receiver. During transmission of information part of the information disappears and the size of the loss itself is a function of the atomic structure of the molecule [3]. Some chemical compounds that belong to the initial a set of data, and for which \( \Delta H_1 > 0.03 \text{bits} \), however, do not possess significant bioactivity.

Apparently, these chemical compounds should be considered only as potentially bioactive. However, for various reasons [1, 10, 11] their bioactivity is not shown one’s worth. For example, the hydrophobic properties of the molecules can limit the bioavailability of the chemical compounds. Only in the presence of well-defined hydrophobic properties of the chemical compounds allows us to get the optimum transport properties of molecules. For radioprotectors this problem is discussed in detail in paper [1].

Further analysis showed that the Eq. 2 correlated with the additive hydrophobicity of the groups CH\(_2\) in molecules. To calculate the hydrophobicity, we used additive model of Leo, Hansch and Elkins [12], which suggests that each atomic group CH\(_2\) makes contribute \( \pi_{CH_2} = 0.52 \) into the total hydrophobicity of the molecule. Fig. 2 shows a positive linear relationship between Eq. 2 and hydrophobicity \( (P) \) of molecules. Hydrophobicity is determined by the contribution only from the CH\(_2\) groups. Statistically significant positive linear association is determined by the following equation:

\[
P = 3.15 + 43.0 \cdot \Delta H_1 \quad (6)
\]

The positive linear correlation coefficient is \( R = 0.88 > R^{(cr)}_{0.05} = 0.25 \). As is known, the correlation coefficient is associated with the random variable \( t \), which is subordinate to the Student distribution: \( t = R(\sqrt{f(1 - R^2)})^{0.5} = 14.11 > t^{(cr)}_{58;0.05} = 1.67 \). Here \( f = N - 1 \) is the number of degrees of freedom. This inequality shows that the interrelation between hydrophobicity and informational function (2) is sufficiently close.

Thus, we found that mathematically abstract definition of the informational function bound up with the physical properties of molecules. Using the Eq. 1 we calculated the informational function \( H \) for molecular structures of Table 1.

We calculated also electronic descriptor \( Z \). To establish the relationship between structure of molecules and bioactivity, we will use Eq. 1 and the average value of quasi-valence of molecule [1, 13, 14]:

\[
Z = \frac{\sum n_j Z_j}{N} \quad (7)
\]

here \( n_j \) is the number of atoms sort of \( j \) each of which have number of valence electrons \( Z_j \) (i.e.,

<table>
<thead>
<tr>
<th>Feature</th>
<th>( \Delta H_1 \geq 0.03, \text{bits} )</th>
<th>( \Delta H_1 &lt; 0.03, \text{bits} )</th>
<th>Sum total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active</td>
<td>( q_{11} = 29 ) ( p_{11} = 0.484 )</td>
<td>( q_{12} = 3 ) ( p_{12} = 0.05 )</td>
<td>( q_1 = 32 ) ( p_1 = 0.534 )</td>
</tr>
<tr>
<td>Inactive</td>
<td>( q_{21} = 8 ) ( p_{21} = 0.133 )</td>
<td>( q_{22} = 20 ) ( p_{22} = 0.333 )</td>
<td>( q_2 = 28 ) ( p_2 = 0.466 )</td>
</tr>
<tr>
<td>Sum total</td>
<td>( Q_1 = 37 ) ( P_1 = 0.617 )</td>
<td>( Q_2 = 23 ) ( P_2 = 0.383 )</td>
<td>( \sum p_i = \sum P_i = 1.00 )</td>
</tr>
</tbody>
</table>
number of electrons on the outer shell of atoms). Summation is carried out over all the atoms in a molecule; \( N \) is the total number of atoms. Within the framework of the pseudopotential theory has been shown [13] that the parameter \( Z \) associates with the pseudopotential of a molecule.

For the series of chemical compounds (Table 1) we found that between complete information function \( H \) and quasi-valence number \( Z \) of molecule exist statistically significant correlated linear linkage (Fig. 3). Again we find the positive linear relationship between the abstract Eq. 1 with the physical parameter of the molecule, i.e., the average quasi-valence number of molecules.

Now we consider the possibility of identifying of the relationship between molecular structure of the chemical compounds and bioactivity of drugs that are not belong to the homologous series. We consider a series of sulfur-containing chemical compounds listed in Table 3. Here we collected drugs that have effective radioprotection at low dose (marked with “+”) and ineffective drugs even when them used at very large doses (marked with “-”). The chemical compounds of each group are listed in ascending order in the number of carbon atoms.

At first we are examining the possibility of differentiation of the chemical compounds by using the parameter \( Z \). As shown by the method of statistical analysis, the parameter \( Z \) separates reliably the chemical compounds having effective radioprotective action of the compounds not having such. To do this we will use the threshold value: \( Z_{\text{front}} = 3.00 \) [1]. Indeed, for the overwhelming majority of chemical compounds having evident anti-radiation effect (50-100% protection) value of the parameter \( Z \) is below the threshold \( Z \leq Z_{\text{front}} = 3.00 \). At the same time, for the chemical compounds having no protective pronounced effect the value of parameter \( Z \) satisfies to inequality \( Z > Z_{\text{front}} \). In this regard, we note that for all purine molecules the parameter \( Z \) also satisfies to the inequality \( Z > Z_{\text{front}} \), wherein the parameter \( Z \) is maximal for guanine \( (Z = 3.5) \). This interrelation has been tested by more than for 150 sulfur-containing chemical compounds, some of which are presented in Table 3. Threshold \( Z_{\text{front}} \) allows us to divide the series of the chemical compounds of Table 3 into two principal groups. The first group includes drugs having anti-radiation effect. The second group consists of the chemical compounds which have no anti-radiation effect or them have weak bioactivity (<50%), even when drugs are used in large dose (second separation principle).

Using Eq. 3 we define the association factor \( \Phi \) between the radioprotective efficacy of the chemical compounds and the value of the parameter \( Z \) (Table 3): \( \Phi = 0.94 \). \( q_{ij} \) is the number of chemical compounds \( i \), which are characterized by the appearance of
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>H₂N(=NH)CH₂SSO₃H</td>
<td>0.15</td>
<td>+</td>
<td></td>
<td>3.60</td>
<td>2.15</td>
</tr>
<tr>
<td>2</td>
<td>H₂N(=NH)CH₃</td>
<td>0.13</td>
<td>+</td>
<td></td>
<td>2.73</td>
<td>1.69</td>
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<td>3</td>
<td>H₂N(=NH)NHCH₂CH₂SPO₃H</td>
<td>0.25</td>
<td>+</td>
<td></td>
<td>3.14</td>
<td>2.06</td>
</tr>
<tr>
<td>4</td>
<td>H₂NCH₃CH₃SSCH₂COOH</td>
<td>0.30</td>
<td>+</td>
<td></td>
<td>3.00</td>
<td>1.92</td>
</tr>
<tr>
<td>5</td>
<td>H₂NCH₃CH₃SSCH₃CONH</td>
<td>0.60</td>
<td>+</td>
<td></td>
<td>2.84</td>
<td>1.88</td>
</tr>
<tr>
<td>6</td>
<td>L-,H₂NCH₂CH₂CH(NH₂)CH₂SPO₃H</td>
<td>0.07</td>
<td>+</td>
<td></td>
<td>2.70</td>
<td>1.76</td>
</tr>
<tr>
<td>7</td>
<td>L-,H₂NCH₂CH₂CH(NH₂)CH₂SPO₃H</td>
<td>0.63</td>
<td>+</td>
<td></td>
<td>2.83</td>
<td>1.96</td>
</tr>
<tr>
<td>8</td>
<td>H₂C(=C(H)₂)CH₂SC(=NH)NH₂</td>
<td>0.31</td>
<td>+</td>
<td></td>
<td>2.56</td>
<td>1.56</td>
</tr>
<tr>
<td>9</td>
<td>H₂NCH₃CH₃CH₃NHCH₂CH₃SH</td>
<td>0.56</td>
<td>+</td>
<td></td>
<td>2.27</td>
<td>1.41</td>
</tr>
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<td>10</td>
<td>H₂NCH₃CH₃CH₃NHCH₂CH₂SPO₃H</td>
<td>0.70</td>
<td>+</td>
<td></td>
<td>2.74</td>
<td>1.90</td>
</tr>
<tr>
<td>11</td>
<td>H₂NCH₃CH₃CH₃NHCH₂CH₂SPO₃H</td>
<td>0.19</td>
<td>+</td>
<td></td>
<td>2.64</td>
<td>1.82</td>
</tr>
<tr>
<td>12</td>
<td>CH₂S(CH₂)₅NH(=NH)CH₂SSO₃H</td>
<td>0.19</td>
<td>+</td>
<td></td>
<td>3.00</td>
<td>1.93</td>
</tr>
<tr>
<td>13</td>
<td>H₂N(CH₃)₂CH(NH₂)CH₂SH</td>
<td>0.34</td>
<td>+</td>
<td></td>
<td>2.24</td>
<td>1.40</td>
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<tr>
<td>14</td>
<td>H₂N(CH₃)₂NHCH₂CH₂CH₂SPO₃H</td>
<td>0.32</td>
<td>+</td>
<td></td>
<td>2.67</td>
<td>1.85</td>
</tr>
<tr>
<td>15</td>
<td>H₂N(CH₃)₂NHCH₂CH(OH)CH₂SPO₃H</td>
<td>0.82</td>
<td>+</td>
<td></td>
<td>2.77</td>
<td>1.89</td>
</tr>
<tr>
<td>16</td>
<td>H₂N(=NH)NH(NH)₂NHCH₂CH₂SPO₃H</td>
<td>0.10</td>
<td>+</td>
<td></td>
<td>2.81</td>
<td>1.95</td>
</tr>
<tr>
<td>17</td>
<td>H₂NCH₃CH₃CH₃NHCH₂CH₂SPO₃H</td>
<td>0.44</td>
<td>+</td>
<td></td>
<td>2.67</td>
<td>1.85</td>
</tr>
<tr>
<td>18</td>
<td>H₂NCH₃CH₃CH(NH₂)NHCH₂CH₂SPO₃H</td>
<td>0.66</td>
<td>+</td>
<td></td>
<td>2.67</td>
<td>1.85</td>
</tr>
<tr>
<td>19</td>
<td>L(+)-H₂N(CH₃)₂CH(NH₂)CH₂SPO₃H</td>
<td>0.14</td>
<td>+</td>
<td></td>
<td>2.67</td>
<td>1.85</td>
</tr>
<tr>
<td>20</td>
<td>(CH₃)₃CNHCSNHCH₂CH₂OH</td>
<td>0.71</td>
<td>+</td>
<td></td>
<td>2.44</td>
<td>1.59</td>
</tr>
<tr>
<td>21</td>
<td>CH₂NH(NH)₂NHCH₂CH₂CH₂SPO₃H</td>
<td>0.31</td>
<td>+</td>
<td></td>
<td>2.61</td>
<td>1.80</td>
</tr>
<tr>
<td>22</td>
<td>H₂N(CH₃)₂NHCH₂CH₂SPO₃H</td>
<td>0.62</td>
<td>+</td>
<td></td>
<td>2.61</td>
<td>1.80</td>
</tr>
<tr>
<td>23</td>
<td>H₂NCH₃CH₃CH₃NHCH₂CH₂SPO₃H</td>
<td>0.62</td>
<td>+</td>
<td></td>
<td>2.61</td>
<td>1.80</td>
</tr>
<tr>
<td>24</td>
<td>H₂N(CH₃)₂NH(NH)₂CH₂SPO₃H</td>
<td>0.21</td>
<td>+</td>
<td></td>
<td>2.61</td>
<td>1.80</td>
</tr>
<tr>
<td>25</td>
<td>H₂N(=NH)NHCH₂CH₃CH₂CH₃NHCH₂CH₂SPO₃H</td>
<td>0.07</td>
<td>+</td>
<td></td>
<td>2.74</td>
<td>1.90</td>
</tr>
<tr>
<td>26</td>
<td>H₂N(=NH)NH(NH)₂CH₂SPO₃H</td>
<td>0.08</td>
<td>+</td>
<td></td>
<td>2.74</td>
<td>1.90</td>
</tr>
<tr>
<td>27</td>
<td>H₂O₃P(CH₃)₂CH₃NH(CH₂)₂NHCH₂CH₂SPO₃H</td>
<td>0.35</td>
<td>+</td>
<td></td>
<td>2.97</td>
<td>1.96</td>
</tr>
<tr>
<td>28</td>
<td>CH₂CONHCH₂CH₃SS(CH₃)₂SO₃H</td>
<td>0.17</td>
<td>+</td>
<td></td>
<td>2.81</td>
<td>1.79</td>
</tr>
<tr>
<td>29</td>
<td>HO₃S(CH₃)₂-SSS-(CH₃)₂SO₃H</td>
<td>0.06</td>
<td>+</td>
<td></td>
<td>2.97</td>
<td>1.72</td>
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<tr>
<td>30</td>
<td>CH₂(CH₃)₂NHCH₂CH₂SSO₃H</td>
<td>0.29</td>
<td>+</td>
<td></td>
<td>2.56</td>
<td>1.63</td>
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<tr>
<td>31</td>
<td>H₂NCH₃CH₂SO₃NH</td>
<td>4.84</td>
<td>+</td>
<td></td>
<td>2.93</td>
<td>1.90</td>
</tr>
<tr>
<td>32</td>
<td>N                                        -</td>
<td>7.69</td>
<td>-</td>
<td></td>
<td>4.20</td>
<td>2.25</td>
</tr>
<tr>
<td>33</td>
<td>CH₂CH(NH₂)COSH</td>
<td>11.4</td>
<td>-</td>
<td></td>
<td>2.77</td>
<td>1.82</td>
</tr>
<tr>
<td>34</td>
<td>H₂NCONHCH₂CH₃SSO₃H</td>
<td>5.00</td>
<td>-</td>
<td></td>
<td>3.47</td>
<td>2.10</td>
</tr>
<tr>
<td>35</td>
<td>H₂NCH₃CH₃SO₃H</td>
<td>5.76</td>
<td>-</td>
<td></td>
<td>2.94</td>
<td>1.85</td>
</tr>
<tr>
<td>36</td>
<td>H₂NCH₃CHOHCH₂SSO₃H</td>
<td>5.35</td>
<td>-</td>
<td></td>
<td>3.26</td>
<td>1.97</td>
</tr>
<tr>
<td>37</td>
<td>H₂NCH₃CH₂(CH₂OH)SSO₃H</td>
<td>4.81</td>
<td>-</td>
<td></td>
<td>3.26</td>
<td>1.97</td>
</tr>
<tr>
<td>38</td>
<td>COOH                                  -</td>
<td>4.60</td>
<td>-</td>
<td></td>
<td>4.46</td>
<td>2.16</td>
</tr>
<tr>
<td>39</td>
<td>(NC)₂C=-(CH)₂</td>
<td>3.94</td>
<td>-</td>
<td></td>
<td>4.00</td>
<td>1.92</td>
</tr>
<tr>
<td>40</td>
<td>H₂NCH₂CH₃SC(=O)CH₂</td>
<td>3.91</td>
<td>-</td>
<td></td>
<td>3.00</td>
<td>2.00</td>
</tr>
<tr>
<td>41</td>
<td>H₂N(=NH)SCH₂CH₂CH₂SO₃H</td>
<td>10.1</td>
<td>-</td>
<td></td>
<td>3.14</td>
<td>2.02</td>
</tr>
<tr>
<td>42</td>
<td>N                                        -</td>
<td>7.87</td>
<td>-</td>
<td></td>
<td>3.23</td>
<td>1.92</td>
</tr>
<tr>
<td>43</td>
<td>N                                        -</td>
<td>10.4</td>
<td>-</td>
<td></td>
<td>2.94</td>
<td>1.88</td>
</tr>
</tbody>
</table>
Biological Activity of Chemical Compounds and Their Molecular Structure-Information Approach

| 44 | CH₂CH₂SC(S)NHCH₂COOH | 5.59 | 3.05 | 1.92 | 0.40 |
| 45 | HOOCCH₂NHCONHCH₂CH₂SH | 5.62 | 3.05 | 1.93 | 0.39 |
| 46 | (CH₃)₂C(SH)CH(NH₂)COOH | 13.4 | 2.70 | 1.75 | 0.57 |
| 47 | CH₂C(=NH)SCH₂CH₂CH₂SSO₃H | 5.08 | 3.08 | 1.89 | 0.43 |
| 48 | CH₂CH₂SC(S)NHCH₂COOH | 4.71 | 3.07 | 1.85 | 0.30 |
| 49 | HOOCCH₂NHCONHCH₂CH₂SH | 5.24 | 3.10 | 1.92 | 0.40 |
| 50 | CH₂CH₂COOH | 5.75 | 2.95 | 1.89 | 0.43 |
| 51 | CH₂NHC(=NH)CH₃SSO₃H | 4.00 | 3.36 | 2.05 | 0.27 |
| 52 | CH₃CH₂OCOCH₂NHCH₂NH₂ | 5.32 | 2.83 | 1.80 | 0.52 |
| 53 | CH₃CH₂OCOCH₂NHCSSCH₂CH₃ | 5.07 | 2.80 | 1.77 | 0.56 |
| 54 | CH₃CH₂OCOCH₂NHCSSCH₂CH₃ | 8.97 | 3.04 | 1.82 | 0.50 |
| 55 | CH₂OCOCH₂CH₂SO₂CH₂CH(NH₂)COOH | 3.18 | 3.14 | 1.83 | 0.49 |
| 56 | CF₃CF₃CH₂OCOCH₂CH₂NHCH₂CH₂S₂O₃H | 3.00 | 3.82 | 2.27 | 0.31 |
| 57 | CH₂SC(S)NHCH₂NHCONHCH₂CH₂SC(S)OCH₃ | 4.42 | 3.41 | 2.09 | 0.23 |
| 58 | CH₂SC(S)NHCH₂NHCONHCH₂CH₂SC(S)OCH₃ | 4.93 | 2.85 | 1.75 | 0.57 |
| 59 | [H₂NC(=NH)NHCH(COOH)CH₂S]⁺ | 3.09 | 3.17 | 2.02 | 0.30 |
| 60 | CH₂SC(S)NHCH₂NHCONHCH₂CH₂SC(S)OCH₃ | 12.3 | 3.06 | 1.96 | 0.37 |

The following inequality: \( \chi^2 = 25.5 > \chi^2_{0.05} = 3.84 \). This inequality confirms the high statistical significance of the association coefficient \( \Phi \). Statistical analysis of the relationship of the electronic parameter \( Z \) and the qualitative characteristic \( j \) \((q_{11} = 28, Z \leq Z_{\text{front}} ; q_{12} = 2, Z > Z_{\text{front}} ; q_{22} = 21, Z \geq Z_{\text{front}} ; q_{21} = 9, Z < Z_{\text{front}} \). Statistical verification of the association coefficient \( \Phi \) by using \( \chi^2 \) statistics gives the
Biological Activity of Chemical Compounds and Their Molecular Structure-Information Approach

Informational function $H$ demonstrated that this interrelation is linear (Fig. 4). Statistics of the positive interconnection will be as follows: the total number of chemical compounds $N = 60$, the linear correlation coefficient of $R = 0.8 > R^{(cr)}_{59,0.05} = 0.25$; Fisher's test is $F = 99.4 > F^{(cr)}_{1,59,0.05}$. Performing last inequality allows us to reject the null hypothesis and accept the presence of a statistically significant of the linear linkage between these factors.

For calculation of the informational function, we use a simple combinatorial approach, and the amount of information is only a function of the number of different kind of atoms of finite set. We note that the angles of slope of the lines in Figs. 3 and 4 are close to each other although the molecular structure of chemical compounds varies considerably. In accordance with the principle of “signatures” [6], we can restrict the realization of informational content if we take into account only some of the object features. These signs characterize the features of biological manifestations of the properties of the chemical compounds. The amount of information contained in a molecule can be defined as the following difference:

$$\Delta H = H_{\text{max}} - H$$

The informational function $H_{\text{max}}$ corresponds to a hypothetical chemical compound for which atoms are uniformly distributed ($p_1 = p_2 = \ldots = p_N$). $N$ is the number of types of atoms in the molecule. A hypothetical molecule has a number of types of atoms as in the real molecule. For example, for the chemical compound № 1 of Table 3 the informational function (1) is equal: $H_{\text{max}} = 2.32$ bits ($N = 5; p_1 = p_2 = \ldots = p_N = 1/5$; C, N, S, O, H). Hypothetical molecule has no real chemical bonds.

For threshold we will take the following value $\Delta H_{\text{front}} = 0.44$ bits (third separation principle). For the chemical compounds (Table 3), which have radioprotective effect and are used at low dose (< 1 mmol/kg), informational function most likely satisfies following inequality: $\Delta H \geq \Delta H_{\text{front}}$. At the same time, for drugs that do not have a high protective effect even at very high doses of preparations (> 3 mmol/kg), most likely outcome: $\Delta H \leq \Delta H_{\text{front}}$. We use the equation (3) to determine the statistical relationship between the factors (Dose of chemicals versus of function $\Delta H$). Table 4 gives values $q_{ij}$ which determine the number of the chemical compounds in the quadrants. Value $q_{11} = 25$ is the number of the compounds for which the dose is less than 1.0 mmol/kg, and at the same time the value of the informational function satisfies to inequality: $\Delta H < \Delta H_{\text{front}}$. $q_{22} = 21$ is the number of compounds for which the dose is much greater than 1.0 mmol/kg (simultaneously the informational function satisfies to inequality: $\Delta H \geq \Delta H_{\text{front}}$). The off-diagonal elements of the Table 4 are equal to $q_{12}$ and $q_{21}$, respectively. Preparations entering in $q_{12} = 5$, applied at a dose of less than 1.0 mmol/kg, and the informational function satisfies the inequality: $\Delta H < \Delta H_{\text{front}}$. Value of $q_{21} = 9$ is the number of compounds that are used in a dose noticeably greater than 1.0 mmol/kg, and at the same time the informational function satisfies the inequality: $\Delta H > \Delta H_{\text{front}}$.

Using data of Table 4, we find from Eq. 3 the coefficient of contingency between dichotomous signs: $\Phi = 0.87$. To verify the accuracy of the statistical

---

**Fig. 4** Field of correlations and scatter chart of electronic $Z$ and information $H$ factors (1) of sulfur compounds. • values of $H$ and $Z$ are taken from Table 3. Line is described by the correlation equation: $H(Z) = 0.450 + 0.465 Z$. $R = 0.80 > R^{(cr)}_{59,0.05} = 0.25$. 

---
Table 4  Mutual conjugacy of classifications.

<table>
<thead>
<tr>
<th>Classes of separation by parameter $\Delta H$</th>
<th>Classes of separation by radioprotective efficacy</th>
<th>Sum total</th>
</tr>
</thead>
<tbody>
<tr>
<td>by Equation (5)</td>
<td>Effective compounds, the dose &lt; 1 mmol/kg</td>
<td></td>
</tr>
<tr>
<td>$\Delta H_2 \geq$</td>
<td>$q_{11} = 25$</td>
<td></td>
</tr>
<tr>
<td>$\Delta H_{2\text{front}}$</td>
<td>$p_{11} = 0.417$</td>
<td></td>
</tr>
<tr>
<td>$\Delta H_2 &lt; $</td>
<td>$q_{21} = 5$</td>
<td></td>
</tr>
<tr>
<td>$\Delta H_{2\text{front}}$</td>
<td>$p_{21} = 0.083$</td>
<td></td>
</tr>
<tr>
<td>Sum total</td>
<td>$Q_1 = 30$</td>
<td></td>
</tr>
<tr>
<td></td>
<td>$P_1 = 0.5$</td>
<td></td>
</tr>
<tr>
<td></td>
<td>$q_{12} = 9$</td>
<td></td>
</tr>
<tr>
<td></td>
<td>$p_{12} = 0.15$</td>
<td></td>
</tr>
<tr>
<td></td>
<td>$q_{22} = 21$</td>
<td></td>
</tr>
<tr>
<td></td>
<td>$p_{22} = 0.35$</td>
<td></td>
</tr>
<tr>
<td></td>
<td>$Q_2 = 30$</td>
<td></td>
</tr>
<tr>
<td></td>
<td>$P_2 = 0.5$</td>
<td></td>
</tr>
<tr>
<td></td>
<td>$q_1 = 34$</td>
<td></td>
</tr>
<tr>
<td></td>
<td>$p_1 = 0.567$</td>
<td></td>
</tr>
<tr>
<td></td>
<td>$q_2 = 26$</td>
<td></td>
</tr>
<tr>
<td></td>
<td>$p_2 = 0.433$</td>
<td></td>
</tr>
</tbody>
</table>

relationship between signs we shall use $\chi^2$ distribution, which we can calculate using the approximate relation [8]:

$$
\chi^2 = N(q_{11}q_{22} - q_{12}q_{21})^2 / q_1q_2Q_1Q_2.
$$

(9)

Here $Q_1 = q_{11} + q_{12}$, $Q_2 = q_{21} + q_{22}$, $Q_1 = q_{11} + q_{21}$, $q_2 = q_{12} + q_{22}$, $N = 60$. From Eq. 9 we obtain the following inequality:

$$
\chi^2 = 18.8 > \chi^2_{1,0.05} = 3.84.
$$

(10)

Consequently, this classification rule really establishes statistically significant relationship between the factors. The chemicals of Table 4 which active at low-dose are grouped around the average values of the informational function $\Delta H_2 = 0.60$ \textit{bits} in the right lower quadrant (Fig. 5). Inactive chemical compounds are grouped in the upper left quadrant around of an average value $\Delta H_2 = 0.14$ \textit{bits}. In fact, the difference between the informational functions $\Delta H_2$ determines the distinction in the molecular states of real molecules and hypothetical molecule with uniform distribution atoms.

The data from Table 4 allow us to find the conditional and unconditional proportions $p_i$ between the dose of the chemicals and informational function. For example, for the unconditional ratio (lower right quadrant of Table 4), we obtain the following value: $p_2 \cdot P_2 = 0.5 \cdot 0.433 = 0.217$. At the same time, we have the following value for conditional proportion: $p_{22} = 0.35$. If the events are independent, then obviously must to be identical the following values: $p_2 \cdot P_2 \equiv p_{22}$. Consequently, a significant distinction between the two values indicates the existence of a link between the dose of the drug and informational function $\Delta H_2$, i.e., atomic structure of molecules.

At the same time on equal terms with classification rule (third separation principle) has a place the classification rule [1, 10], which is set on the knowledge of the complete informational function $H$. Indeed, from the data of Table 3 follows that the average value of complete informational function for effective radioprotectors is equal $H_1 = 1.81$ \textit{bits}, whereas for chemical compounds without radioprotective effect the average value of the complete informational function is equal $H_2 = 1.95$ \textit{bits}. Using the Student's distribution we will examine really whether exist the statistically significant distinction between the average values of $H_1$ and $H_2$. Preliminarily using Fisher's distribution we calculate the distinction between the variances $S_1^2$ and $S_2^2$: $F = S_1^2 / S_2^2 = 1.56 < F_{29,29,0.05}^{(cr)} = 1.8$. Thus, the distinction in variances is not statistically
significant. Hence, to determine statistically significant distinction of the average informational functions $\overline{H}_1$ and $\overline{H}_2$ we can apply approximate inequality:

$$|\overline{H}_1 - \overline{H}_2| = 0.14 > t_{0.05, N} \left( \frac{S_1 + S_2}{\sqrt{N}} \right)$$

where $N = 60$ is the common number of the chemical compounds. The last inequality allows us to reject the null hypothesis concerning equality of averages values. Hence we must recognize that this classification rule establishes the following principle: active chemical compounds (Table 3) are grouped around an average value of $\overline{H}_1$. Inactive chemical compounds are grouped around an average value of $\overline{H}_2$ (fourth separation principle).

4. Conclusion

Thus, the information model allows statistically significantly separate the radioprotectors having a high therapeutic index from of ineffective chemical compounds with a low therapeutic index. The effect of the threshold on the biological action of radioprotective drugs was also demonstrated in the paper [15]. In this paper we analyzed the interrelations of the radio-protective action of sulfur-containing chemical compounds with their quantum-chemical parameters. Threshold effects appear not only in sulfur-containing drugs, but also for radioprotectors of series triptamine analogues [16]. Practical use of the proposed method supposes only knowledge of the atomic structure of the drug molecules and knowledge of the biological response of the body. Information approach allows us to divide the chemical compounds according to their biological activity on the groups both a homologous series and not in homologous series. Identified thresholds of informational function and quasi-valence number of molecules allow us separates biologically active chemical compounds from inactive preparations. Such the simple technique allow for chemists to speed up the process of finding new drugs. This approach does not require knack of to use complicated quantum chemical calculations or method of image identification. It is important we have demonstrated also that informational function is related to the physical properties of molecule (hydrophobicity, electrostatic potential).

In this paper, we use statistical methods to compare qualitative characteristics, which are characterized by dichotomous properties. First, it allows us to look at the phenomenon from a broad perspective, not limited only to the analysis of linear regression models. Second, occurrence of dichotomous properties allow us point out the threshold of drugs action. It is important to note that only part of the information signs of the molecules may determine the biological effects of drugs.

Change of the biological activity of the preparations with change of the parameter $Z$ does not contradict to the mechanism of carcinogenesis [1]. The electrostatic potential of the molecule affects the processes regulating vital functions of biological objects, and thereby may determine a biological action.

References


