Interaction Between Antifungal Isoxazolo[3,4-*b*]pyridin 3(1h)-one Derivatives and Human Serum Proteins Analyzed with Biomimetic Chromatography and QSAR Approach

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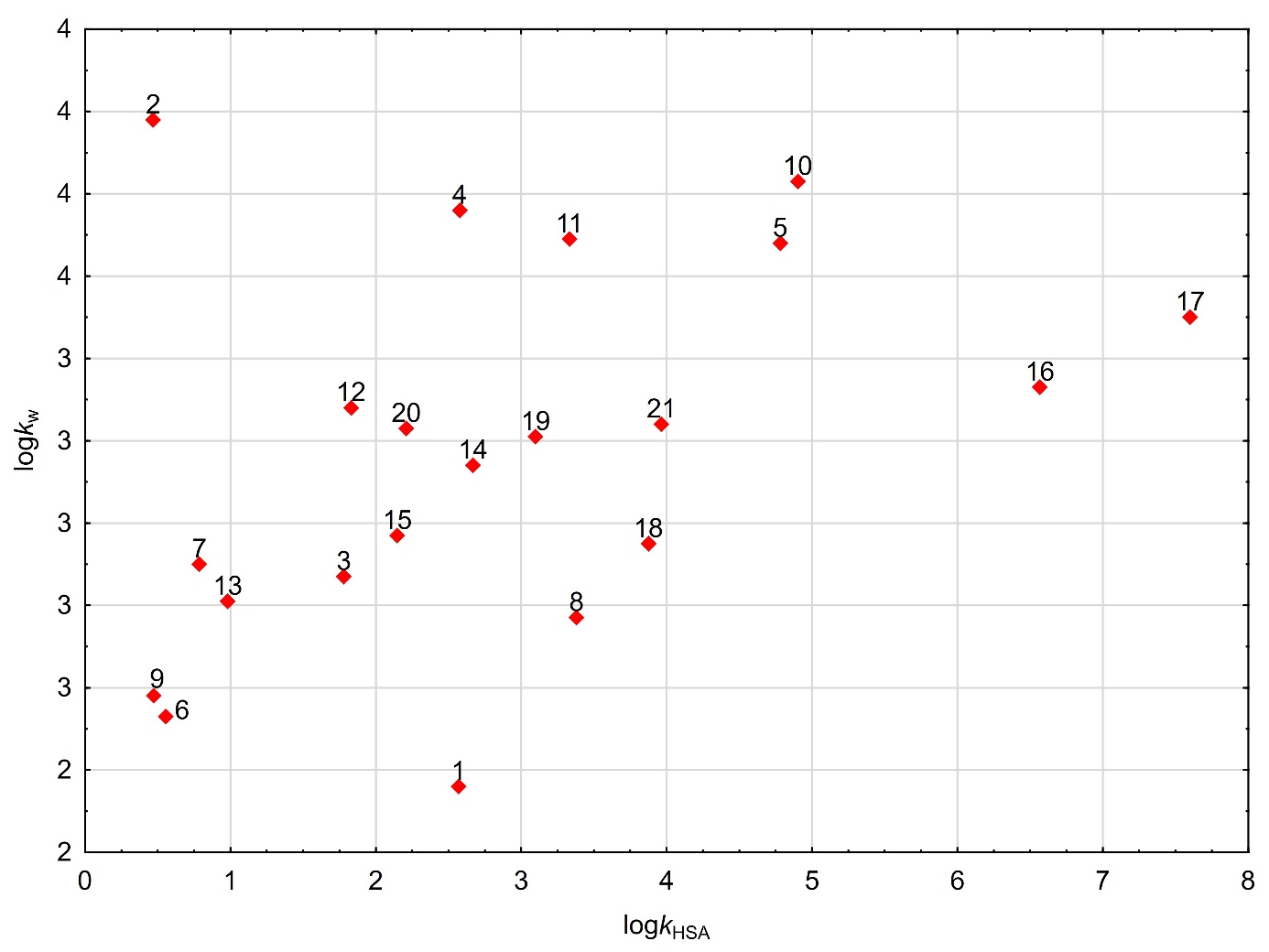
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**Table S1.** Chemical names of pyridino- and quinolino-isoxazolone derivatives.

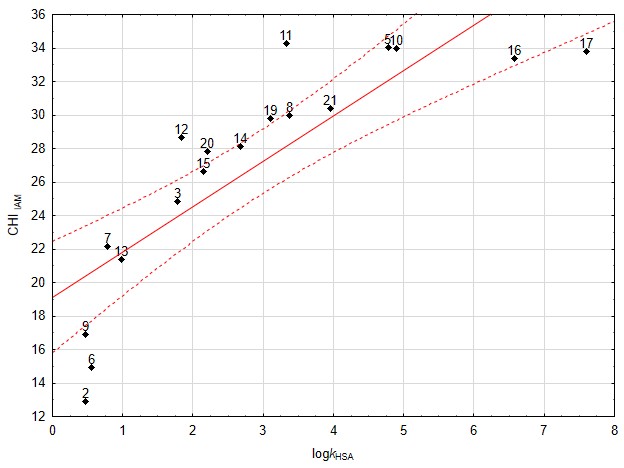
|  |  |
| --- | --- |
| **Compound** | **Chemical Name** |
| 1 | isoxazolo[3,4-*b*]quinolin-3(1*H*)-one |
| 2 | 1-benzylisoxazolo[3,4-*b*]quinolin-3(1*H*)-one |
| 3 | 1-methylisoxazolo[3,4-*b*]quinolin-3(1*H*)-one |
| 4 | 1-benzoylisoxazolo[3,4-*b*]quinolin-3(1*H*)-one |
| 5 | 1-benzyl-4,6-dimethylisoxazolo[3,4-*b*]pyridin-3(1*H*)-one |
| 6 | 1-acetyl-4,6-dimethylisoxazolo[3,4-*b*]pyridin-3(1*H*)-one |
| 7 | 1-ethyl-4,6-dimethylisoxazolo[3,4-*b*]pyridin-3(1*H*)-one |
| 8 | 1-benzoyl-4,6-dimethylisoxazolo[3,4-*b*]pyridin-3(1*H*)-one |
| 9 | 1,4,6-trimethylisoxazolo[3,4-*b*]pyridin-3(1*H*)-one |
| 10 | 1-(3,5-dimethoxybenzyl)-4,6-dimethylisoxazolo[3,4-*b*]pyridin-3(1*H*)-one |
| 11 | 1-butyl-4,6-dimethylisoxazolo[3,4-*b*]pyridin-3(1*H*)-one |
| 12 | 4,6-dimethyl-1-propylisoxazolo[3,4-*b*]pyridin-3(1*H*)-one |
| 13 | 4,6-dimethyl-1-(prop-2-yn-1-yl)isoxazolo[3,4-*b*]pyridin-3(1*H*)-one |
| 14 | 6-methoxy-1-methylisoxazolo[3,4-*b*]quinolin-3(1*H*)-one |
| 15 | 6-fluoro-1-methylisoxazolo[3,4-*b*]quinolin-3(1*H*)-one |
| 16 | 6-chloro-1-methylisoxazolo[3,4-*b*]quinolin-3(1*H*)-one |
| 17 | 1,6,7-trimethylisoxazolo[3,4-*b*]quinolin-3(1*H*)-one |
| 18 | 5,8-dimethoxyisoxazolo[3,4-*b*]quinolin-3(1*H*)-one |
| 19 | 1,7-dimethylisoxazolo[3,4-*b*]quinolin-3(1*H*)-one |
| 20 | 5,8-dimethoxy-1-methylisoxazolo[3,4-*b*]quinolin-3(1*H*)-one |
| 21 | 1,6-dimethylisoxazolo[3,4-*b*]quinolin-3(1*H*)-one |

**Table S2.** Retention times of the studied solutes measured by means of HSA-HPLC chromatography.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **No.** | **TR1** | **TR2** | **TR3** | **mean TR** | **SD** |
| 1 | 4.574 | 4.480 | 4.544 | 4.533 | 0.048 |
| 2 | 1.863 | 1.858 | 1.877 | 1.866 | 0.010 |
| 3 | 3.549 | 3.488 | 3.555 | 3.531 | 0.037 |
| 4 | 4.596 | 4.536 | 4.504 | 4.545 | 0.047 |
| 5 | 7.463 | 7.335 | 7.229 | 7.342 | 0.117 |
| 6 | 1.985 | 1.971 | 1.970 | 1.975 | 0.008 |
| 7 | 2.286 | 2.254 | 2.266 | 2.269 | 0.016 |
| 8 | 5.587 | 5.554 | 5.549 | 5.563 | 0.021 |
| 9 | 1.872 | 1.868 | 1.871 | 1.870 | 0.002 |
| 10 | 7.590 | 7.469 | 7.431 | 7.497 | 0.083 |
| 11 | 5.533 | 5.415 | 5.556 | 5.501 | 0.076 |
| 12 | 3.597 | 3.540 | 3.647 | 3.595 | 0.054 |
| 13 | 2.516 | 2.515 | 2.519 | 2.517 | 0.002 |
| 14 | 4.714 | 4.625 | 4.639 | 4.659 | 0.048 |
| 15 | 4.047 | 3.961 | 3.985 | 3.998 | 0.044 |
| 16 | 9.634 | 9.550 | 9.647 | 9.610 | 0.053 |
| 17 | 10.890 | 10.884 | 10.994 | 10.923 | 0.062 |
| 18 | 6.267 | 6.134 | 6.175 | 6.192 | 0.068 |
| 19 | 5.209 | 5.183 | 5.224 | 5.205 | 0.021 |
| 20 | 4.101 | 4.036 | 4.095 | 4.077 | 0.036 |
| 21 | 6.450 | 6.217 | 6.247 | 6.305 | 0.127 |



**Figure S1.** Comparison of log*k*w and log*k*HSA parameters determined with HPLC methods.



**Figure S2.** Scatterplot comparing CHIIAM and log*k*HSA parameters.

**Table S3.** Statistical parameters of consecutive QSAR models calculated by progressive stepwise regression

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **QSAR Model 1** | | **R** | | **R2** | |
| step 1 | log*k*HSA = 0.257 (±0.042) CHIIAM − 4.041 (±1.176) | 0.834 | 0.695 | |
| step 2 | log*k*HSA = 0.182 (±0.034) CHIIAM + 0.783 (±0.180) CATS3D\_08\_AL – 2.583 (±0.874) | 0.930 | 0.865 | |
| step 3 | log*k*HSA = 0.168 (±0.027) CHIIAM + 0.826(±0.143) CATS3D\_08\_AL + 3.454 (±1.090) MATS6v – 1.780(±0.735) | 0.960 | 0.922 | |

CATS3D\_08\_AL—CATS3D Acceptor-Lipophilic BIN 08 (8.000–9.000 Å)  
MATS6v—Moran autocorrelation of lag 6 weighted by *van der Waals* volume

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **QSAR Model 2** | | R | | R2 |
| step 1 | log*k*HSA = 1.205(±0.244) CATS3D\_08\_AL + 2.138(±0.324) | 0.750 | 0.562 | |
| step 2 | log*k*HSA = 0.988 (±0.202) CATS3D\_08\_AL + 202,322 (±56.960) R8v + 0.374 (±0.558) | 0.862 | 0.743 | |
| step 3 | log*k*HSA = 0.962 (±0.183) CATS3D\_08\_AL + 313.298 (±71.383) R8v+ − 0.620(±0.276) F03[C–N] + 3.482 (±1.474) | 0.895 | 0.821 | |
| step 4 | log*k*HSA = 0.866 (±0.160) CATS3D\_08\_AL + 307.871 (±61.133) R8v+ − 1.084 (±0.293) F03[C–N] – 117.012 (±43.598) JGI5 + 10.890(±3.035) | 0.929 | 0.863 | |

CATS3D\_08\_AL−CATS3D Acceptor-Lipophilic BIN 08 (8.000–9.000 Å)  
R8v+—R maximal autocorrelation of lag 8/weighted by van der Waals volume  
F03[C-N]— Frequency of C–N at topological distance 3   
JGI5—mean topological charge index of order 5