Lipofilnost salicilamida

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Lipophilicity study of salicylamide

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Molecular lipophilicity was studied using salicylamide as a model drug. Log *P* value for the target compound was experimentally determined by the »shake-flask« method and calculated using nine different computer programs based on atom/fragment contributions, structural parameters, atom-type electrotopological-state indices and neural network modeling, or topological structure descriptors. Our analysis demonstrates good agreement between the experimentally observed log *P* value of salicylamide and the value calculated by the CSLogP program, based on topological structure descriptors and electrotopological indices.

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Since lipophilicity has been recognized for its importance in QSPR (**Q**uantitative **S**tructure-**P**roperty **R**elationship) studies, efforts have been made to determine the log *P* (logarithm of partition coefficient in *n*-octanol/water) values of a number of compounds. Log *P* is closely related to the transport properties of drugs and their interaction with receptors. This parameter can be either determined experimentally or calculated. Because experimental measurements are time consuming and difficult, computational methods are very valuble tools for calculation of log *P*'s for large sets of compounds in QSAR studies, particulary at the screening stage. A number of different computer programs for prediction of lipophilicity have been recently developed. In our work, nine computer programs based on different theoretical approaches for predicting log *P* have been compared with experimental data. Many methods for calculating log *P* values are reported in the literature. The most common ones are classified as »atom-type«, »fragmental« and »E-state indices« methods (1–3).

Salicylamide was used as a model drug for investigations of molecular lipophilicity. It is a salicylic acid derivate mostly used in combinations with other analgesics or antipyretics. It is readily absorbed from the gastrointestinal tract and distributed to most body tissues. Although salicylamide is not as effective as acetilsalicylic acid or paracetamol, it is still used in Asia, North and South America in combined medicines for symptoms associated with cold and influenza (4).

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The aim of our work was to correlate the experimentally determined and calculated log *P* values for salicylamide using nine different computer programs.

EXPERIMENTAL

»Shake-flask« method

Partition coefficient (*P*) for salicylamide between *n*-octanol and phosphate buffer was determined at 25 °C by the »shake-flask« method. Before the partitioning of salicylamide, the buffer (0.15 mol L^{-1}, pH = 7.4) and *n*-octanol (99%, Sigma, USA) were saturated with each other (5, 6). Salicylamide was dissolved in ethanol (96%, Kemika, Croatia) at a concentration of 2 mg mL^{-1} to give the stock solution. Calibration was done in exactly the same manner as the partitioning, except that *n*-octanol was not used. The amounts of the sample were chosen so that absorbance (λ = 236 nm) of 0.1 to 0.8 was measured. Partitioning experiments were performed in the systems *n*-octanol/phosphate buffer 1:20, 1:30, 1:70 and 1:80 (*V*/*V*). All solutions were pipetted into glass vials; the *n*-octanol and stock solution were added with a microliter syringe. The phases were shaken together on a mechanical shaker (Viggo, Sweden) for 30 minutes, centrifuged (Rotofix 32, Switzerland) at 2500 rpm for 20 min to afford complete phase separation, and the *n*-octanol phase was removed. Absorbance of the buffer phase was measured using Shimadzu UV/VIS spectrophotometer (Japan) at 236 nm. The instrument was zeroed by the blank solution. The concentration was then calculated from a calibration graph of salicylamide. Calculation of log *P* values was performed as follows:

$$\log P = \log \left(\frac{y - x}{x} \frac{V_{buff}}{V_{oct}} \right) \qquad (1)$$

where: *P* – partition coefficient, *y* – total mass of salicylamide (mg), *x* – mass of salicylamide in the buffer phase after partitioning (mg), V_{buff} – volume of phosphate buffer (mL), V_{oct} – volume of *n*-octanol (mL).

Calculation methods

HyperChem 7.0. – The computer program HyperChem 7.0 predicts log *P* values using the atom-additive method according to Ghose, Prichett and Crippen (7). Their approach avoids correction factors and calculates lipophilicity on an individual atom basis by employing a large number of atom types. The following equation is used to calculate the *n*-octanol-water partition coefficient:

$$\log P = \sum_{i}^{n} n_i a_i \qquad (2)$$

where n_i is the number of atoms of type *i*, and a_i is the contribution of the corresponding atom type. The program lists atom contributions for each atom type and calculates the log *P* value by summing up all atom contributions.

XLOGP 2.0. – XLOGP 2.0* is a computer program based on additive atomic contributions, which calculates log *P* values according to Wang, Fu and Lai (8). The program classifies atoms by their hybridization states and their neighboring atoms. The program also includes correction factors to account for some intramolecular interactions. Log *P* calculation is described as shown in equation:

$$\log P = \sum_{i}^{n} a_i A_i + \sum_{i}^{n} b_j B_j \qquad (3)$$

where a_i and b_j are regression coefficients, A_i is the number of occurrences of the *i*th atom type, and B_j is the number of occurrences of the *j*th correction factor identified by the program. The program listed each non-hydrogen atom in the salicylamide molecule. The first column is the number of a certain atom, the second column is the ID number of atom type, the third column indicates the atom type symbol and the last column indicates its contribution to the log *P* value. The program includes the correction factors for the intramolecular H-bond. In the last row, contributions are summarized and the log *P* value of the target compound is given.

KowWin. – The KowWin** program calculates log *P* values of organic compounds using the atom/fragment contribution (AFC) method developed by the Syracuse Research Corporation (SRC). SMILES (Simplified Molecular Input Line Entry System) notation created by the structure-drawing program CambridgeSoft's (ChemDrawPro) is used as the chemical structure input (9). The log *P* value of salicylamide is calculated by summing up all atom/fragment contribution values, multiplied by the frequency of its occurrence in the molecule, the correction factor for the steric interaction between the hydroxy and carbonyl function and the linear equation constant. The advantage of this program is the SRC Database, which includes the CAS Registry Number and the experimentally determined log *P* value of the target compound (10).

MLOGP. – The MLOGP program is included in the DRAGON 3.0 program (3), the software for the calculation of a large number of molecular descriptors. A method for predicting log *P* values was developed by Moriguchi *et al*. (11). The disadvantage of this program is that the calculation procedure is not shown to the user, but only the log *P* value of the target compound.

CLOGP. – The CLOGP*** program is based on the fragmental method developed by Leo and Hansch (12, 13) and has become the standard in the field of rational drug design. The calculation result is accompanied by a picture of the chemical structure as generated by the DEPICT algorithm. Aromaticity of the benzene ring is indicated by circle inside ring. The result of log *P* value calculation by the CLOGP program is displayed in the »Map Box«. The first line in the »Map Box« is SMILES notation of salicylamide. The

* The method is available on-line at http://cheminfo.pku.edu.cn/calculator/xlogp

** The method is available on-line at http://esc.syrres.com/interkow/logkow.html

*** The method is available on-line at http://www.biobyte.com/bb/prod/clogp40.html

second line indicates the numbers of non-hydrogen atoms, the third Isolating Carbons (A – aliphatic, a – aromatic), the fourth numbers of the polar fragments, and the fifth the location of hydrogen atoms. The last lines indicate the location of atoms in rings. All fragments and a variety of different types of correction factors, accounting for the way in which different fragments influence one another, are listed at the end of »Map Box«. After fragment constants were assigned to all fundamental fragments and all corrections were accounted for, the summation was done by the equation:

$$\log P = \sum_{i}^{n} a_i f_i + \sum_{j=1}^{m} c_j \qquad (4)$$

where f_i is the fragment constant of the ith fragment, a_i is the number of occurrences of the ith fragment, and c_j is the jth correction factor. The estimated log P value is the output (14).

miLogP 1.2. – The miLogP 1.2* program calculates log P values as a sum of group contributions and correction factors. The group contributions were obtained by fitting calculated log P values with experimental log P values for a training set of several thousands of drug-like molecules (15, 16). The disadvantage of this program is that again the calculation procedure is not shown to the user, but only the log P value of the target compound.

ALOGPS 2.1. – The ALOGPS 2.1** package includes programes to predict lipophilicity and aqueous solubility of chemical compounds. A method for predicting log P values based on atom-type electrotopological-state (E-state) indices and associative neural network modeling was developed by Tetko *et al*. (17–20). This method combines electronic and topological characters to predict lipophilicity of the analyzed molecules. After E-state indices are assigned to each atom type according to the neighboring atoms, the estimatated log P value of the target compound is obtained.

IAlogP. – This is another calculation program*** that predicts lipophilicity of chemical compounds using neural network algorithms and Molconn-Z indices, including E-state indices for atom types.

CSLogP. – This package**** includes programs to predict log P, log $D_{(pH=2)}$, log $D_{(pH=5)}$, and log $D_{(pH=7.4)}$. Log D is the logarithm of distribution coefficient at a particular pH. It is not constant and will vary according to the protogenic nature of the molecule. The partition coefficient applies to neutral species, whereas the distribution coefficient applies to ionizable species. The program is based on topological structure descriptors and E-state indices (21).

Statistical analysis of the results was performed using the StatSoft 6.0 program.

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* The method is available on-line at http://www.molinspiration.com

** The method is available on-line at http://146.107.217.178/lab/alogps/start.html

*** The method is available on-line at http://www.logp.com

****Demo version of the method is available on-line at http://www.chemsilico.com

RESULTS AND DISCUSSION

The experimental results are summarized in Table I; each value is the average of five determinations. Calculations of the log P value for each computer program are shown in Figs. 1 and 2 (HyperChem 7.0, XLOGP 2.0), and Tables II–IV (KowWin, CLOGP, ALOGPS 2.1). The aim of this work was to determine the lipophilicity of salicylamide and to correlate it with log P values predicted by nine theoretical methods (Table V).

All computer programs showed to be relatively simple and applicable to QSPR studies. Fig. 3 shows that all programs except CSLogP underestimate the log *P* value of

Table I. Log P *value for salicylamide by the »shake-flask« method*[a]

n-octanol/ buffer *(V/V)*	c_1	$\overline{A}_2 \pm$ SD (n = 5)	c_2	log *P*	log *P* ± SD
1:20	1×10^{-3}	0.351 ± 0.002	3.05×10^{-5}	1.12	1.15 ± 0.02
	1.25×10^{-3}	0.423 ± 0.003	3.65×10^{-5}	1.17	
	1.5×10^{-3}	0.508 ± 0.002	4.5×10^{-5}	1.14	
	1.75×10^{-3}	0.585 ± 0.003	5.2×10^{-3}	1.15	
	2×10^{-3}	0.668 ± 0.002	5.9×10^{-3}	1.16	
1:30	1×10^{-3}	0.239 ± 0.012	2×10^{-5}	1.31	1.35 ± 0.02
	2×10^{-3}	0.429 ± 0.005	3.8×10^{-5}	1.36	
	2.5×10^{-3}	0.532 ± 0.008	4.7×10^{-5}	1.37	
	3.5×10^{-3}	0.755 ± 0.002	6.7×10^{-5}	1.35	
	4×10^{-3}	0.879 ± 0.003	7.8×10^{-5}	1.34	
1:70	3×10^{-3}	0.288 ± 0.007	2.45×10^{-5}	1.73	1.65 ± 0.07
	4×10^{-3}	0.380 ± 0.003	3.3×10^{-5}	1.72	
	5×10^{-3}	0.515 ± 0.007	4.58×10^{-5}	1.60	
	6×10^{-3}	0.627 ± 0.005	5.5×10^{-5}	1.61	
	8×10^{-3}	0.819 ± 0.003	7.35×10^{-5}	1.59	
1:80	3×10^{-3}	0.324 ± 0.001	2.75×10^{-5}	1.44	1.38 ± 0.04
	4×10^{-3}	0.431 ± 0.002	3.8×10^{-5}	1.41	
	6×10^{-3}	0.650 ± 0.001	5.85×10^{-5}	1.36	
	7×10^{-3}	0.776 ± 0.006	6.85×10^{-5}	1.35	
	8×10^{-3}	0.881 ± 0.003	7.75×10^{-5}	1.36	
Grand mean log *P* value ± SD					1.38 ± 0.19

[a] For calculation see Eq. *(1)*.

c_1 – concentration of stock solution in *n*-octanol before partitioning (mol L^{-1})
$\overline{A}_2$ – mean absorbance in buffer solution after partitioning (λ = 236 nm)
c_2 – concentration of salicylamide in buffer solution after partitioning (mol L^{-1})
log *P* – logarithm of the partition coefficient

Atomic contributions:	
Atom 1 (C):	0.007
Atom 2 (C):	0.007
Atom 3 (C):	0.007
Atom 4 (C):	0.007
Atom 5 (C):	–0.103
Atom 6 (C):	0.160
Atom 7 (C):	0.071
Atom 8 (O):	0.486
Atom 9 (O):	–0.351
Atom 10 (N):	–0.053
Atom 11 (H):	–0.326
Atom 12 (H):	–0.326
Atom 13 (H):	0.334
Atom 14 (H):	0.334
Atom 15 (H):	0.334
Atom 16 (H):	0.334
Atom 17 (H):	–0.326
Log *P* of salycilamide = 0.596	

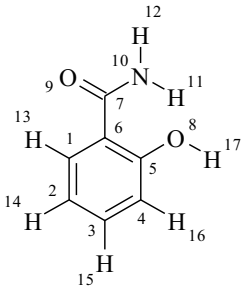

Fig. 1. Calculation of the log *P* value for salicylamide by the computer program HyperChem 7.0.

No.	type	symbol	contribution
1	54	N.am.h2	–0.646
2	29	C.2.x (pi>0)	–0.027
3	34	C.ar	0.296
4	32	C.ar.h	0.337
5	32	C.ar.h	0.337
6	32	C.ar.h	0.337
7	32	C.ar.h	0.337
8	35	C.ar.x	–0.151
9	70	O.3.h (pi=1)	0.296
10	75	O.2	–0.184
Internal H-bond			0.429

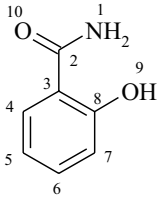

Fig. 2. Calculation of the log *P* value for salicylamide by the computer program XLOGP 2.0.

Table II. Calculation of the log P *value for salicylamide by the computer program KowWin (LogKow)*

SMILES: NC(=O)(c(cccc1)c1O)
MOL FOR: C7 H7 N1 O2
MOL WT: 137.14

TYPE	NUM	LOGKOW v1.66 FRAGMENT DESCRIPTION	COEFF	VALUE
Frag	1	-NH_2 [aliphatic attach]	–1.4148	–1.4148
Frag	6	Aromatic Carbon	0.2940	1.7640
Frag	1	-OH [hydroxy, aromatic attach]	–0.4802	–0.4802
Frag	1	-C(=O)N [aromatic attach]	0.1599	0.1599
Factor	1	Ortho-Hydroxy to misc. -C(=O)- correction	0.7770	0.7770
Const		Equation Constant		0.2290

Log Kow = 1.0349

Experimental Database Structure Match:
Name: o-Hydroxybenzamide
CAS Registry Number: 000065-45-2
Experimental Log Kow: 1.28
Experim. Reference: Hansch, C *et al.* (1995)

Table III. Calculation of the log P *value for salicylamide by the computer program CLOGP*

SMILES: NC(=O)c1ccccc1O
ATOM #: 12..3.4.56789.0
ISOC-ID:.....a.aaaaa..
FRAG-ID: 11..1.....2
H-COUNT: 2.....1111..1
RING 1:.....a.aaaaa..

Class	Type	Log(P) Contribution Description	Comment	Value
Fragment	# 1	NH2-Amide [a]	Measured	–1.260
Fragment	# 2	Alcohol or Hydroxy [a]	Measured	–0.440
Carbon	Hydrog	6 aromatic isolating carbons		0.780
ExFragment	SigRho	4 hydrogens on isolating carbons		0.908
Electronic		1 potential interaction; 1.00 used	WithinRing	0.339
H-bnd/sigI	Ring 1	Frag-pair: 1 & 2		0.950
RESULT	4/22+	All fragments measured	CLOGP	1.277

Table IV. Calculation of the log P *value for salicylamide by the computer program ALOGPS 2.1*

Name:	Salicylamide
CAS RN:	65-45-2
Formula:	C7H7NO2
Weight:	137.14
SMILES:	NC(c(cccc1)c1O)=O
logP:	0.74
logS:	–1.22
E-state indices:	
SaaCH	6.1521
SaasC	0.0810
SdO	10.4840
SdssC	–0.6129
SsNH2	4.9156
SsOH	8.9801
SdO(amide)	10.4840
SsNH2(oth)	4.9156
SsOH(phen)	8.9801
Se1C3C3ad	0.3287
Se1C3N1d	3.1095
Se1C3O1a	5.8021
Se2C3O1s	6.4691
SeaC2C2aa	5.4631
SeaC2C3aa	2.3229
SeaC3C3aa	0.5046
logP knn=96	sigma=0.99
logS knn=26	sigma=0.64 similar molecules:
–1.76 the_same	NC(c(cccc1)c1O)=O
–0.40r*r=0.60	OC(c1ccc(N)cc1)=O
–1.52r*r=0.55	OC(c1ccccc1N)=O
–1.59r*r=0.40	O=C(c1ccc(N)cc1)OC
–2.32r*r=0.35	Nc1ccc(C(OCC)=O)cc1
–2.92r*r=0.30	NC(c(cccc1)c1C(N)=O)=O
–2.63r*r=0.28	O=C(c1ccc(N)cc1)CC
–0.72r*r=0.27	Nc(cccc1)c1O

Table V. Comparison of the experimentally obtained log P *and predicted log* P *values*

	log P	$\Delta_{(logPexp–logPcal)}$
»Shake-flask«	1.382	–
HyperChem 7.0	0.596	0.786
XLOGP 2.0	0.93	0.452
LogKow	1.0349	0.3471
MLOGP	0.683	0.699
CLOGP	1.277	0.105
miLogP	0.4	0.982
ALOGPS 2.1	0.74	0.642
IA logP	1.01	0.372
CSLogP	1.45	–0.068

salicylamide. The lowest log *P* value was obtained by the miLogP program. The differences between experimental (log P_{exp}) and calculated (log P_{cal}) log *P* values were first compared according to the Mannhold and Dross (1) criteria: differences between experimental and calculated values lower than ± 0.5 were evaluated as acceptable, differences

higher than ± 0.5 as unacceptable. According to these criteria, the calculations done by programs XLOGP, LogKow, CLOGP, IA logP and CSLogP might be considered acceptable. The best correlation between the experimentally determined and calculated log *P* values was found for the CSLogP program. However, our own proposal for the criteria to evaluate the differences between experimental and calculated log *P* values is as follows: differences lower than 5% might speak for high accuracy, differences between 5 and 10% for acceptable accuracy and differences higher than 10% for unacceptable accuracy of calculation methods. According to our criteria, the best correlation between experimental and calculated values was found again for the CSLogP program with the lower than 5% (4.9%), followed by the CLOGP program (7.5%). Errors for all another programs were significantly higher (more than 25%). We are inclined to beleive that the latter criteria are more realistic and particularly suited for analyzing the predictive power of different computer programs.

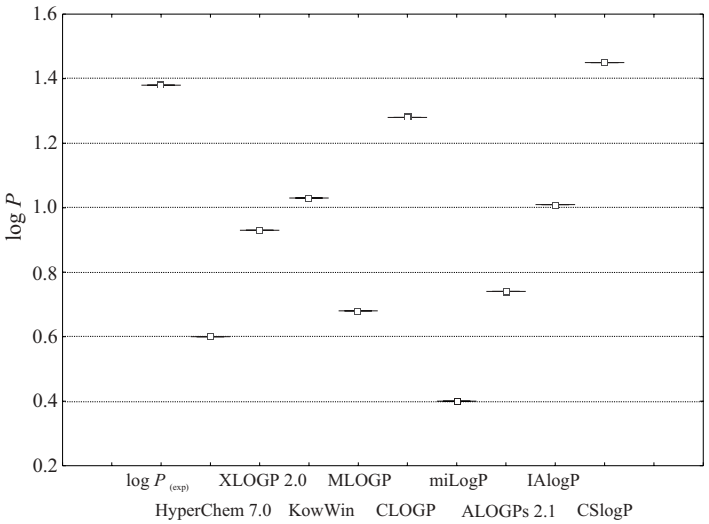

Fig 3. Box & Whisker Plot for the experimentally determined and calculated log *P* values for salicylamide.

CONCLUSIONS

The widespread application of lipophilicity to QSPR studies easily explains the need for quick procedures to predict molecular lipophilicity. Routine application of computer programs demands a continuous check of their validity by comparison with experimental data. We studied nine commonly used calculation methods, based on different theoretical approaches, and correlated the calculated log *P* values with experimentally determinated log *P* values. Our analysis demonstrates the best agreement between the experimentally observed log *P* value of salicylamide and the value calculated by the

CSLogP program. Topological descriptors encode relevant information about a molecule and their combination with e-state indices seems to offer a promising alternative for a more consistent log *P* value. To get a reliable picture on the applicability of calculation methods in lipophilicity studies, numerous substances of varying lipophilicity should be studied.

REFERENCES

1. R. Mannhold and K. Dross, Calculation procedures for molecular lipophilicity: a comparative study, *Quant. Struct.-Act. Relat.* **15** (1996) 403–409.
2. V. Pliska, R. Mannhold, H. van de Waterbeemd and H. Kubinyi, *Lipophilicity in Drug Action and Toxicology*, VCH, Weinheim 1996.
3. R. Todeschini and V. Consonni, *Handbook of Molecular Descriptors*, Wiley-VCH, Weinheim 2000.
4. *Goodman and Gilman's, The Pharmacological Basis of Therapeutics* (J. G. Hardman and L. E. Limbird, Eds.), 10th ed., Mc Graw Hill, New York 2001.
5. C. D. P. Klein, G. F. Tabeteh, A. V. Laguna, U. Holzgrabe and K. Mohr, Lipophilicity and membrane interactions of cationic-amphiphilic compounds: syntheses and structure-property relationships, *Eur. J. Pharm. Sci.* **14** (2001) 167–175.
6. O. Wong and R. H. McKeown, Substituent effects on partition coefficients of barbituric acids, *J. Pharm. Sci.* **77** (1988) 926–932.
7. A. K. Ghose, A. Pritchett and G. M. Crippen, Atomic physicochemical parameters for three dimensional structure directed quantitative structure-activity relationships III: Modeling hydrophobic interactions, *J. Comput. Chem.* **9** (1988) 80–90.
8. R. Wang, Y. Fu and L. Lai, A new atom-additive method for calculating partition coefficients, *J. Chem. Inf. Comput. Sci.* **37** (1997) 615–621.
9. D. Weininger, SMILES a chemical language and information system. 1. Introduction to methodology and encoding rules, *J. Chem. Inf. Comput. Sci.* **28** (1988) 31–36.
10. W. M. Meylan and P. H. Howard, Atom/fragment contribution method for estimating octanol-water partition coefficients, *J. Pharm. Sci.* **84** (1995) 83–92.
11. I. Moriguchi, S. Hirono, I. Nakagome and H. Hirano, Comparison of reliabity of log *P* values for drugs calculated by several methods, *Chem. Pharm. Bull.* **42** (1994) 976–978.
12. C. Hansch, A. Leo and D. H. Hoekman, *Exploring QSAR: Fundamentals and Application in Chemistry and Biology*, American Chemical Society, Washington DC 1995.
13. C. Hansch, A. Leo and D. H. Hoekman, *Exploring QSAR: Hydrophobic, Electronic, and Steric Constants*, American Chemical Society, Washington DC 1995.
14. J. T. Chou and P. C. Jurs, Computer-assisted computation of partition coefficients from molecular structures using fragment constants, *J. Chem. Inf. Comput. Sci.* **19** (1979) 172–178.
15. P. Ertl, B. Rohde and P. Selzer, Fast calculation of molecular polar surface area as a sum of fragment-based contributions and its application to the prediction of drug transport properties, *J. Med. Chem.* **43** (2000) 3714–3717.
16. C. A. Lipinski, F. Lombardo, B. W. Dominy and P. J. Feeney, Experimental and computational approaches to estimate solubility and permeability in drug discovery and development settings, *Adv. Drug Del. Rev.* **23** (1997) 3–25.
17. J. J. Huuskonen, D. J. Livingstone and I. V. Tetko, Neural network modeling for estimation of partition coefficient based on atom-type electrotopological state indices, *J. Chem. Inf. Comput. Sci.* **40** (2000) 947–955.

18. I. V. Tetko, V. Y. Tanchuk, T. N. Kasheva and A. E. P. Villa, Internet software for the calculation of the lipophilicity and aqueous solubility of chemical compounds, *J. Chem. Inf. Comput. Sci.* **41** (2001) 246–252.
19. I. V. Tetko, Neural network studies. 4. Introduction to associative neural networks, *J. Chem. Inf. Comput. Sci.* **42** (2002) 717–728.
20. I. V. Tetko and V. Y. Tanchuk, Application of associative neural networks for prediction of lipophilicity in ALOGPS 2.1 program, *J. Chem. Inf. Comput. Sci.* **42** (2002) 1136–1145.
21. L. B. Kier and L. H. Hall, The E-state as an extended free valence, *J. Chem. Inf. Comput. Sci.* **37** (1997) 548–552.

S A Ž E T A K

Lipofilnost salicilamida

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U radu je dan pregled istraživanja molekularne lipofilnosti na primjeru salicilamida. Log *P* vrijednost određena je eksperimentalnom (»shake-flask«) metodom i izračunata je pomoću devet različitih računalnih programa koji se temelje na atom/fragmentarnoj metodi, strukturnim parametrima, atom elektrotopologijskim indeksima uz modeliranje putem neuronskih mreža i topologijskim deskriptorima. Statistička obrada dobivenih rezultata pokazala je najbolju korelaciju eksperimentalno dobivene vrijednosti s log *P* vrijednošću dobivenom računalnim programom CSlogP, koji se temelji na topologijskim deskriptorima i elektrotopologijskim indeksima.

Ključne riječi: lipofilnost, salicilamid, log *P*, računalno modeliranje

Farmaceutsko-biokemijski fakultet, Sveučilište u Zagrebu, Zagreb