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Data Mining on Structure-Activity/Property Relationships Models

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Abstract: Molecular descriptors family on structure-activity/property relationships studies were carried out in order to identify the link between compounds structure and their activity/property. A number of fifty-five classes of properties or activities of different compounds sets were investigated. Single and multi-varied linear regression models using molecular descriptors as variables were identified. The models with estimation and prediction abilities and associated characteristics were stored into a database. A data mining analysis using classification and clustering were applied on the obtained database for searching and extracting useful information. The methodology applied in searching and extracting for information and the obtained results are presented.

Key words: Knowledge-Discovery in Database (KDD) % cluster analysis % Structure-Activity/Property Relationships (SAR/SPR) % Molecular Descriptors Family (MDF)

INTRODUCTION

Data mining (DM), also called Knowledge-Discovery in Databases (KDD) or Knowledge-Discovery and Data Mining, is the process of automatically searching large volumes of data for patterns using tools such as classification, association rule mining and/or clustering. The term has been defined as the nontrivial extraction of implicit, previously unknown and potentially useful information from data [1], being considered as the science of extracting useful information from large data sets or databases [2].

Data mining techniques are use in search of consistent patterns and/or systematic relationships between variables in business [3], evaluation of web-based educational programs [4], computer science [5], chemistry [6], engineering [7], medicine [8] and in all domains where a large amount of date must be analyzed.

A new method of quantitative structure-activity/property relationships abbreviated as MDF SAR/SPR (molecular descriptors family on the structure-activity/property relationships) has been introduced by Jäntschi in 2004 [9] and reviewed in 2005 [10]. Since then, samples of compounds with different properties or activities have been investigated and analyzed. Some results on different properties (retention chromatography index [9], relative response factor [11], molar refraction [12], octanol/water partition coefficient [13-15] or activities (insecticidal activity [16], herbicidal activity [17], antioxidant efficacy [18], inhibition activity [19-21], toxicity [22, 23], antituberculotic activity [24] and antimalarial activity [25]) have been reported. In addition, the overall results from the use of molecular descriptors family on structure property/activity relationships has also been published [26].

The best performing models in terms of correlation coefficients and cross-validation scores were collected into a database. On this amount of information, data mining techniques have been applied in order to identify consistent patterns and/or relationships between variables of MDF SAR/SPR models.

MATERIAL

A number of fifty-five sets of compounds were included into analysis. The set abbreviation, activity or property of interest and class of compounds are presented in Table 1.

Univariate and multivariate models were obtained by applying the MDF SAR/SPR methodology on the samples of compounds; the models were stored into a database. The molecular descriptors are the variables used by the models.

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Table 1: Characteristics of the sets included into analysis

No.	Abbreviation	Activity /Property	Compounds
1	DevMTOp00	LC_{50}/EC_{50}-fertilization of sea urchin	ordnance compounds
2	DevMTOp01	LC_{50}/EC_{50}-embryological development of sea urchin	
3	DevMTOp02	LC_{50}/EC_{50}-germination of sea urchin	
4	DevMTOp03	LC_{50}/EC_{50}-zoospore germination of green macroalgae	
5	DevMTOp04	LC_{50}/EC_{50}-germling length of green macroalgae	
6	DevMTOp05	LC_{50}/EC_{50}-germling cell number of green macroalgae	
7	DevMTOp06	LC_{50}/EC_{50}-survival and reproductive success of polychaete	
8	DevMTOp07	LC_{50}/EC_{50}-redfish larvae survival	
9	DevMTOp08	LC_{50}/EC_{50}-juveniles survival of opossum shrimp	
10	DevMTOp09	NOEC-fertilization of sea urchin	
11	DevMTOp10	NOEC-embryological development of sea urchin	
12	DevMTOp11	NOEC-germination of sea urchin	
13	DevMTOp12	NOEC-germling length and cell number of green macroalgae	
14	DevMTOp14	NOEC-survival and reproductive success of green macroalgae	
15	DevMTOp15	NOEC-survival and reproductive success of polychaete	
16	DevMTOp16	NOEC-redfish larvae survival	
17	DevMTOp17	NOEC-juveniles survival of opossum shrimp	
18	DevMTOp18	LOEC-fertilization of sea urchin	
19	DevMTOp19	LOEC-embryological development of sea urchin	
20	DevMTOp20	LOEC-germination of sea urchin	
21	DevMTOp21	LOEC-germling length and cell number of green macroalgae	
22	DevMTOp22	LOEC-survival and reproductive success of green macroalgae	
23	DevMTOp23	LOEC-survival and reproductive success of polychaete	
24	DevMTOp24	LOEC-redfish larvae survival	
25	DevMTOp25	LOEC-juveniles survival of opossum shrimp	
26	DHFR	Inhibition activity	2, 4-diamino-5-(substituted-benzyl) pyrimides
27	Dipeptides	inhibition activity	dipeptides
28	RRC433_lbr	toxicity	para substituted phenols
29	RRC433_pka	relative toxicity	
30	Ta395	cytotoxicity	quinolines
31	Tox395	mutagenicity	
32	19654	antiallergic activity	substituted N 4-methoxyphenyl benzamides
33	22583	anti-HIV-1 potencies	HEPTA and TIBO derivatives
34	26449	antituberculotic activity	polyhydroxyxanthones
35	3300	growth inhibition activity	taxoids
36	41521	insecticidal activity	neonicotinoids
37	52344	antioxidant efficacy	3-indolyl derivates
38	52730	toxicity	alkyl metal compounds
39	23110	toxicity	benzene derivates
40	23158	toxicity	mono-substituted nitrobenzenes
41	23167	toxicity	polychlorinated organic compounds
42	40846_1	inhibition activity on carbonic anhydrase I	substituted 1,3,4-thiadiazole-and 1,3,4-thiadiazoline-disulfonamides
43	40846_2	inhibition activity on carbonic anhydrase II	
44	40846_4	inhibition activity on carbonic anhydrase IV	
45	Triazines	herbicidal activity	substituted triazines
46	23159e	octanol/water partition coefficients	polychlorinated biphenyls
47	33504	boiling point	alkanes
48	36638	water activated carbon adsorption	organic compounds
49	IChr_10	retention chromatography index	organophosphorus herbicides
50	MR_10	molar refraction	cyclic organophosphorus
51	PCB_rrf	relative response factor	polychlorinated biphenyls
52	PCB_lkow	octanol/water partition coefficient	
53	PCB_rrt	relative retention time	
54	RRC433_lkow	octanol/water partition coefficient	para substituted phenols
55	31572	octanol-water partition coefficient	volatile organic compound

LC_{50} = Lethal concentration to 50% of the test organisms

EC_{50} = Effective concentration to 50% of the test organisms

NOEC = No observed effect concentration

LOEC = Lowest observed effect concentration

Table 2: Characters in molecular descriptors name

Letter	Characters
First	I-i-A-a-L-l
Second	m-M-n-N-S-P-s-A-a-B-b-G-g-F-f-H-h-I-i
Third	m-M-D-P
Fourth	R-r-M-m-D-d
Fifth	D-d-O-o-P-p-Q-q-J-j-K-k-L-l-V-E-W-w-F-f-S-s-T-t
Sixth	C-H-M-E-G-Q
Seventh	g-t

The characters used on molecular descriptors name are presented in Table 2.

The name of each descriptor had seven letters that defined the modality of construction [11]:

- Compound characteristic relative to its geometry or topology-the 7th letter;
- Atomic property (cardinality, number of directly bonded hydrogen's, atomic relative mass, atomic electronegativity, group electronegativity and partial charge, semi-empirical Extended Hückel model, Single Point approach)-the 6th letter;
- Atomic interaction descriptor-the 5th letter;
- Overlapping interaction model-the 4th letter;
- Fragmentation criterion (minimal fragments, maximal fragments, Szeged fragments criterion and Cluj fragments criterion (P) [27, 28]-the 3rd letter;
- Cumulative method of fragmentation properties (smallest fragmental descriptor value from the array, highest value, smallest absolute value and highest absolute value; *average group*: sum of descriptor values, average mean for valid fragments, average mean for all fragments, average mean by atom, average mean by bond; *geometric group*: multiplication of descriptor values, geometric mean for valid fragments, geometric mean for all fragments, geometric mean by atom and geometric mean by bond; *harmonic group*: harmonic sum of values, harmonic mean for valid fragments, harmonic mean for all fragments, harmonic mean by atom and harmonic mean by bond)-the 2nd letter;
- Linearization procedure applied in molecular descriptor generation (identity, inverse, absolute, an inverse of absolute, natural logarithm of absolute value and simple natural logarithm)-1st letter.

METHOD

The MDF SAR/SPR database was interrogated and the interest information was obtained by using a series of PHP programs. The SPSS software was used for data summarizing and analyzing. The 95% confidence intervals were computed by using dedicated software based on binomial distribution hypothesis [29].

Two steps cluster analysis and hierarchical cluster analysis were used as methods in searching the patterns where was appropriate. The two-step cluster analysis was used on searching patterns overall models. This technique was choused because has specific feature: automatic selection of the best number of clusters and ability to create cluster models simultaneously based on categorical and continuing variables. The hierarchical cluster method has been used for identification of similarities on the best performing MDF SAR/SPR models and was been choused because it is an easy to implement well-documented method and provides as result dendrograms, tree-like structures that illustrate the relationships between the entries.

RESULTS

Fifty-five sets were included into analysis, cumulating an amount of one-hundred and ninety-five models. One hundred fifty-six models were for activities estimation and prediction (95% CI [144-166]) and thirty-eight models for properties estimation and prediction (95% CI [28-50]).

Seventy-three models reported estimation and prediction of activity (95% CI [64-80]) and nineteen models (95% CI [12-27]) estimation and prediction ability of property. The number of MDF SAR models varied from two to eleven (for the set no. 40, Table 1) and for MDF SPR models varied from two to eight (for the set no. 48, Table 1). The statistical characteristics of all models and of the best performing models (in terms of closest squared correlation coefficient and cross-validation score to one) are presented in Table 3.

The MDF SAR/SPR models stored into database used two hundred and eighty-four molecular descriptors. Almost sixty-nine percent of them were used just by one model (one hundred and ninety-six descriptors, 95% CI [180-211]). The distribution of the descriptors used by MDF SAR/SPR models was:

- Two descriptors were used by six models (imDrkQt and lPMDVQg)
- Four descriptors were used by five models (ASPrVQg, IiMMWHt, IMPrkQg and iSMMWHg)

Table 3: Statistical characteristics of the MDF SAR/SPR models

Act/Prop	Param	n_v	Mean [95%CI]	Median	Min	Max	StDev
All models							
Activity	r^2	156	0.9023 [0.8783-0.9263]	0.9489	0.0122	1.0000	0.1514
	v		2 [2-2]	2	1	5	1.1003
	n_{sample}		28 [24-31]	23	5	69	21.4680
Property	r^2	38	0.8698 [0.8077-0.9319]	0.9772	0.1208	1.0000	0.1889
	v		4 [2-6]	2	1	24	6.0663
	n_{sample}		77 [48-105]	24	10	209	86.2200
Best performing models							
Activity	r^2	45	0.9807 [0.9714-0.9900]	0.9992	0.9037	1.0000	0.0310
	v		3 [2-3]	2	2	5	1.0288
	n_{sample}		19 [13-24]	8	5	69	17.9450
Property	r^2	10	0.9572 [0.8993-1.0000]	0.9883	0.7368	1.0000	0.0808
	v		3 [2-4]	2.5	2	6	1.3703
	n_{sample}		80 [16-144]	27	10	209	90.1200

r^2 = squared correlation coefficient; v = number of descriptors used in models;

n_{sample} = sample size; n_v = number of valid samples; 95% CI = 95% confidence interval;

Min= minimum; Max = maximum, StDev = standard deviation

Table 4: Descriptors in all models versus best performing models

Descriptors	Descriptors	
-all models-	-best models-	
(Absolute frequency)	(Absolute frequency)	Total
1	1	89
1 Total		89
2	1	24
	2	2
	3	1
2 Total		27
3	1	11
	3	1
3 Total		12
4	1	9
	2	4
4 Total		13
5	1	3
	2	1
5 Total		4
6	1	2
6 Total		2
Total		147

- Sixteen descriptors were used by four models (AHMMVQg, aHPMwQt, aIDmjQg, iAMrVQg, iBMmwHg, iHDdFHg, iHMMtHg, IiDrQHg, iIPmWHt, ImmRDCg, imMrFHt, inDmwHg, INPRJQg, inPRlQg, isMdTHg, iSMmEQt)
- Twenty one descriptors were used by three models (ABDmtQg, ASMmVQt, AsPmVQt, aSPRtQg, IADRSHg, IBPMWQt, iGPrfHt, iIMdLGg, iIMdTMg, iImrKHt, InMdTHg, isDRTCg, isDRtHg, ismRSEg, iSPRtQg, lfDdOQg, LHDmjQg, lIDrFEg, lIMdLGg, liMDWHg, LsDMpQg)
- Forty-five descriptors were used by two models (ABmrtQg, AHDmEQg, aHMmjQt, AiMrKQt, AIPmVQt, AiPmVQt, aIPMwQt andRJQt, aSMMjQg, iAPmEQg, ibDMFHt, IbMmjHg, IBMrkGg, IBMRQCg, IbPdPHg, iFmRFMt, iFPMECg, IHDRKEg, iHMMTQt, IIDDKGg, IiMMSGg, imDdSCg, ImDmEEt, IMDMtQt, ImDrFEt, iMMMjQg, IMmrKQg, imMrtCg, inMRkQt, InPdJQg, inPRjQt, isDDkGg, IsMRKQg, ISPdlMg, IsPdOQg, lFDMwEt, lfDMWHt, lFMMKQg, LHDROQg, LIDmjQg, lImrKHt, lmMrsGg, lNPmfQt, LSPmEQg, LsPrDQt).

One hundred and forty-seven descriptors have been used in the best performing models. The correspondences between using the descriptors in all models and in best performing models are presented in Table 4.

The partial squared correlation coefficient (the squared correlation coefficient between each descriptor from the model and property or activity of interest) varied for the all models from 0.0001 to 0.9995 with an average of 0.3645. For the best performing models, the values of the partial squared correlation coefficients varied from 0.0001 to 0.9794 with an average of 0.2959. The average values of partial squared correlation coefficients for all models and for the best performing models according with the activity or property of interest are summarized in Table 5. The descriptors that obtained greater value of partial squared correlation coefficients are not found in the best performing model.

Table 5: The average contribution of the descriptors to the model

Set abb.	Avg$_{r2\text{-}best}$	Avg$_{r2\text{-}all}$
MDF SARs		
DevMTOp00	0.8673	0.9113
DevMTOp01	0.6632	0.7753
DevMTOp02	0.4144	0.5866
DevMTOp03	0.0398	0.3232
DevMTOp04	0.2221	0.4454
DevMTOp05	0.1355	0.3823
DevMTOp06	0.3040	0.5251
DevMTOp07	0.4579	0.6160
DevMTOp08	0.3384	0.5284
DevMTOp09	0.4035	0.5883
DevMTOp10	0.4169	0.5941
DevMTOp11	0.1692	0.4368
DevMTOp12	0.0214	0.3060
DevMTOp14	0.1092	0.3786
DevMTOp15	0.1100	0.3905
DevMTOp16	0.2451	0.4669
DevMTOp17	0.1447	0.3694
DevMTOp18	0.5083	0.6717
DevMTOp19	0.2888	0.5032
DevMTOp20	0.1391	0.3846
DevMTOp21	0.0721	0.3492
DevMTOp22	0.1946	0.4475
DevMTOp23	0.1430	0.4033
DevMTOp24	0.4997	0.6464
DevMTOp25	0.0441	0.3559
DHFR	0.1482	0.1680
Dipeptides	0.5145	0.4603
RRC433_lbr	0.1612	0.2329
RRC433_pka	0.2623	0.2144
Ta395	0.1027	0.1002
Tox395	0.2053	0.2712
19654	0.1360	0.3286
22583	0.2288	0.1908
26449	0.3874	0.5332
3300	0.2408	0.2761
41521	0.2407	0.4365
52344	0.5083	0.4243
52730	0.5806	0.7092
23110	0.1298	0.2106
23158	0.3011	0.2719
23167	0.3546	0.3636
40846_1	0.3264	0.4271
40846_2	0.1319	0.2170
40846_4	0.2529	0.2621
Triazines	0.4323	0.4613
Min	0.0214	0.1002
Max	0.8673	0.9113
Average	0.2800	0.4210
Set abb.	Avg$_{r2\text{-}best}$	Avg$_{r2\text{-}all}$
MDF SPRs		
23159	0.0089	0.1685
31572	0.2274	0.2581
33504	0.5297	0.6416
36638	0.2880	0.3051
IChr10	0.5998	0.4005
MR10	0.8971	0.9075
PCB_lkow	0.2268	0.3327
PCB_rrf	0.2712	0.2843
PCB_rrt	0.4687	0.7021
RRC433_lkow	0.2308	0.3011
Min	0.0089	0.1685
Max	0.8971	0.9075
Average	0.3748	0.4302

Avg$_{r2\text{-}best}$ = the average of the partial squared correlation coefficient on best performing models;

Avg$_{r2\text{-}allt}$ = the average of the partial squared correlation coefficient on all models

Table 6: Two steps cluster analysis: results

		All models			
		---			Best
Letter	Ch	Cluster 1 (41)	Cluster 2 (14)	Total	model
1st	I	25	13	38	31
	i	30	14‡	44	38
	A	7	4	11	7
	a	10	3	13	5
	L	13	4	17	8
	l	28	10	38	31
2nd	m	10	7	17	9
	M	3	4	7	7
	n	12	7	19	13
	N	7	1	8	5
	S	11	8	19	12
	P	5	1	6	5
	s	19	7	26	18
	A	14	5	19	13
	B	6	7‡	13	9
	b	2	6‡	8	6
	G	7	2	9	8
	F	3	7‡	10	4
	f	2	1	3	2
	H	14	9	23	16
	I	17	8	25	11
	i	3	7‡	10	4
3rd	m	13	8	21	10
	M	29	14‡	43	36
	D	31	13	44	34
	P	31	11	42	34
4th	R	22	10	32	23
	r	26	13	39	32
	M	11‡	14‡	25	20
	m	28	13	41	25
	D	12	8	20	15
	d	10	10‡	20	14
5th	D	7	2	9	4
	d	4	2	6	3
	O	6	0	6	5
	o	3	2	5	2
	P	3	3	6	4
	p	5	2	7q	4
	Q	1	3‡	4	3
	q	6	1	7	6
	J	7	6	13	6
	j	9	5	14	6
	K	3	7‡	10	5
	k	10	8‡	18	13
	L	7	2	9	6
	l	4	2	6	5
	V	8	6	14	10
	E	5‡	9‡	14	9
	W	1	4‡	5	5
	w	9	7	16	8
	F	4‡	10‡	14	7
	f	9	2	11	5
	S	7	5	12	8
	s	6	6	12	5
	T	6	6	12	9
	t	10	7	17	8
6th	C	10	7	17	6
	H	9‡	14‡	23	20
	M	17	7	24	16
	E	10	5	15	12
	G	12	8	20	11
	Q	40	14	54	44
7th	g	40	14	54	41
	t	31	13	44	51

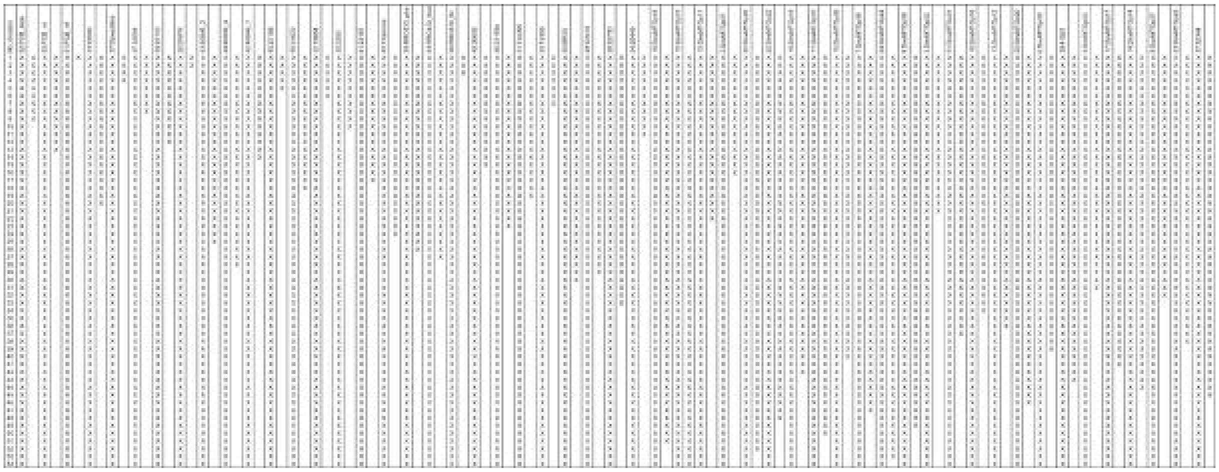

Fig. 1: Best performing MDF SAR/SPR models analysis: Icile plot

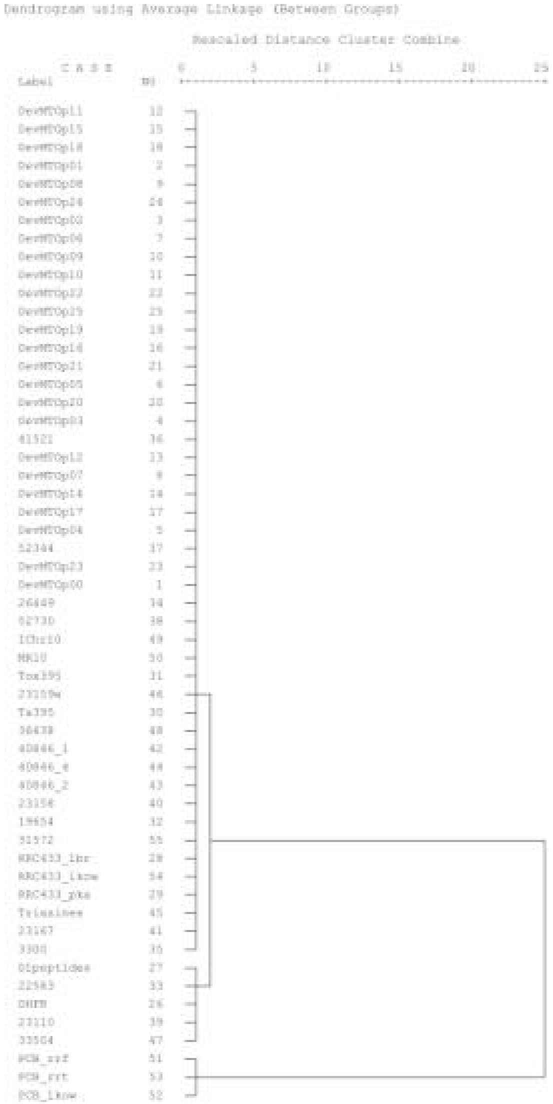

Fig. 2: Best performing MDF SAR/SPR models analysis: Dendrogram

Summarizing the characters that were included into the descriptors name it can be observed that, with a single exception, all characters for first, third, fourth, fifth, sixth and seven descriptor name letters appear in the descriptors names if all MDF SAR/SPR models. The same observation is valid for analysis of the best performing ones. There were identified that three characters out of nineteen from the second descriptor letter (the letters a, g and h, Table 2) did not appear in any model. In order to applied cluster analysis techniques the frequency of the characters into the models according with the set name were transformed as qualitative variables (yes/no).

The summaries of the results obtained by performing the two-steps cluster analysis on all models as well as on the best performing models are presented in Table 6 (Letter = the letter in the descriptor name, Ch = character, Best model = the model that obtained a squared correlation coefficient and cross-validation leave-one-out score as close to one as possible). There were included into the Table 6 the absolute frequency of appearance of the character into the name of descriptors and the attribute importance into the cluster (‡ = significant importance in cluster at a significance level of 5%).

The hierarchical cluster technique was applied in order to analyze the best performing models. The Icile plot is presented in Fig. 1 and the associated dendrogram in Fig. 2.

DISCUSSION

Searching the information regarding the MDF SAR/SPR models for patterns revealed important information for activity/property characterization of compounds classes by applying the molecular descriptors family methodology.

As it can be observed from Table 3, the average of the correlation coefficient obtained by MDF SARs is greater comparing with the value obtained by the MDF SPRs, while the number of variables is less for MDF SARs than for MDF SPRs when all models are considered. When the best performing models are analyzed it can be observed that the squared correlation coefficient average obtained by the MDF SAR models is very closed to the squared correlation coefficient average obtained by MDF SPR models and the average of the descriptors is the same.

Just forty-five percent of the molecular descriptors that were used in one model on completely sample of models could be found in the best performing models (Table 4). Sixty percent of the molecular descriptors used by two models on whole samples were found again on the best performing models (Table 4). Fifty-seven percent of the molecular descriptors used by three models on whole samples were found again on the best performing models; almost eighty-one percent of the molecular descriptors used by four models on whole samples were found again on the best performing models. All molecular descriptors used by five and respectively six models on whole samples were found as being used on the best performing models too (Table 4). These observations sustained the stability and consistency of the MDF SAR/SPR method in identification of the molecular descriptors that are able to identify the strongest relationships between compounds structure and associated activity or property.

Analyzing the data presented in Table 4 it can be observed that the average, minimum and maximum values of average contribution of descriptors are smaller values for the best performing models than the values obtained on all models. This observation leads to the conclusion that the best performing models are obtained by combination of descriptors and the molecular descriptors that had a value of the partial correlation coefficient closest to one are not always found in the best performing model.

Two clusters were obtained by applying the two-steps cluster technique on the all models, showing that there exist some similarities between MDF SARs/SPRs models. One cluster used forty-one sets of compounds while the second cluster used fourteen compounds. Four characters had significant importance into the first cluster obtained by analyzing all models (Table 6):

C The character *M* (the overlapping descriptors interaction on the maximal fragments) as fourth position on descriptors name

C The characters *E* (interaction descriptor of the second atom property divided to the distance between the atoms) and *F* (interaction descriptor of the square first atom property divided to the square distance between atoms) as fifth position on descriptors name

C The character *H* (number of directly bonded hydrogen's as atomic property) as sixth position on descriptors name.

In the second cluster, the one that comprise fourteen sets of compounds, fourteen characters revealed to have significant importance in clustering:

- The character *i* (the inverse linearization procedure applied in global molecular descriptor generation) as first position on descriptors name
- The characters *B* (as average mean by atom), *b* (average mean by bond), *F* (geometric mean by atom), *i* (harmonic mean by bond) as second position on descriptors name (the cumulative method of fragmentation properties)
- The character *M* (the maximal fragments criteria) as third position on descriptors name
- The characters *M* (the overlapping descriptors interaction on the maximal fragments) and *d* (the overlapping descriptors interaction on threat descriptors as Cartesian vectors) as fourth position on descriptors name
- The characters *Q* (the squared product between first and second atoms properties), *K* (the product between the first and second atoms properties and the distance between them), *k* (the inverse of K), *E* (interaction descriptor of the second atom property divided to the distance between the atoms) and *W* (the square of the first atom property divided to the distance between two atoms) as fifth position on descriptors name
- The character *H* (number of directly bonded hydrogen's as atomic property) as sixth position on descriptors name.

On the sample of best performing MDF SAR/SPR models, the two-step cluster analysis was able to identify two clusters. This could be explained by the absence of similarities of descriptors characters used by the best performing models. The most frequently met characters on the descriptors name on the best performing models were:

- The *i* character-the first position on descriptors name (the inverse linearization procedure applied in global molecular descriptor generation)
- The *s* character-the second position on descriptors name (the product between the first and second atoms properties divided to the distance rice to power three)
- The *M* character-the third position on descriptors name (the maximal fragments criteria)
- The *r* character-the fourth position on descriptors name (the overlapping descriptors interaction obtained by treating descriptors as scalars and computing resultant relative to conventional origin)
- The *k* character-the fifth position on descriptors name (the inverse of the product between the first and second atoms properties and the distance between them)
- The *Q* character-the sixth position on descriptors name (semi-empirical Extended Hückel model, Single Point approach as atomic property)
- The *t* character-the first position on descriptors name (molecular topology).

Taking into account the above information, it can be concluding that there could not be identify similarities or patterns on the MDF SAR/SPR models even if the results of the analysis of all models say something else. Note that in the analysis of the all MDF SAR/SPR models were included for each set of compounds the univariate models that in most of the cases obtained weak performances in terms of estimation and prediction abilities.

The quantitative variables similarities of the best performing models were analyzed with hierarchical cluster technique. Looking at the icile plot (Fig. 1) it can be analyzed what happen at each clusterization step. At the start step (the one that is not represented on icicle plot, Fig. 1), each set of compounds was a cluster unto itself (the number of clusters at the start point being equal with fifty-five). Starting with the first step, the sets were ordered in the icicle plot according with their combination into clusters. The 15:DevMTOp15 set is linked first with 12:DevMTOp11 set, being follow by the 24:DevMTOp24 set and so on until all the clusters are formed. From the dendrogram (Fig. 2) it can be observed that at a small distances three clusters are formed: one that comprised forty-seven sets and other two that comprised five and respectively three sets. The differences between the obtained three clusters are at the level of sample size and number of descriptors used by model. On the cluster that comprised forty-seven sets the sample sizes varied from five to forty and the number of molecular descriptors from two to three. On the cluster that comprised five sets the sample seizes varied from fifty-seven to seventy-three and the number of descriptors from two to five, while on the cluster that comprised three sets the number of compounds were of two hundred and nine and the number of variables from two to six. At a short distance, two clusters are linked together (the one that comprised forty-seven and the other that comprised five sets). All the clusters are linked together at the maximum distance as possible.

The research reached its goal of searching the patterns on MDF SAR/SPR models. The results shown that on the studied sets of compounds the MDF SAR/SPR method identified models that are unique for each set do to the complex information obtained from compounds structure. Based on the obtained results the MDF SAR/SPR method will be updated by analyzing of the usefulness of the three characters from the second position descriptor name that were not identified in any model. The development of the MDF SAR/SPR database by analyzing and including of more compounds sets will be done in the future. Data mining techniques applied on larger sets of compounds could revealing important information for characterization of activities or properties of compound based on information obtained from the structure.

CONCLUSIONS

The data mining techniques applied on MDF SAR/SPR models revealed that is not possible any classification of characters used on descriptors name and thus on their construction. This result sustains the ability of MDF SAR/SPR method on identification of those structure characteristics of compounds that are linked with the activity or property of interest.

The hierarchical cluster analysis is a useful technique in identification of similarities of MDF SAR/SPR models regarding the quantitative variables, in our case the squared correlation coefficient, the number of descriptors used by models and the sample sizes.

Data mining techniques applied on larger sets of compounds analyzed with MDF SAR/SPR method could reveal important information for characterization of activities or properties of compound based on information obtained from the structure.

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