# Prediction of Melting Point for Drug-like Compounds Using Principal Component-Genetic Algorithm-Artificial Neural Network

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Principal component-genetic algorithm-multiparameter linear regression (PC-GA-MLR) and principal component-genetic algorithm-artificial neural network (PC-GA-ANN) models were applied for prediction of melting point for 323 drug-like compounds. A large number of theoretical descriptors were calculated for each compound. The first 234 principal components (PC's) were found to explain more than 99.9% of variances in the original data matrix. From the pool of these PC's, the genetic algorithm was employed for selection of the best set of extracted PC's for PC-MLR and PC-ANN models. The models were generated using fifteen PC's as variables. For evaluation of the predictive power of the models, melting points of 64 compounds in the prediction set were calculated. Root-mean square errors (RMSE) for PC-GA-MLR and PC-GA-ANN models are 48.18 and 12.77 °C, respectively. Comparison of the results obtained by the models reveals superiority of the PC-GA-ANN relative to the PC-GA-MLR and the recently proposed models (RMSE = 40.7 °C). The improvements are due to the fact that the melting point of the compounds demonstrates non-linear correlations with the principal components.

Key Words : Quantitative structure-property relationship. Melting point. Drug-like compounds. Genetic algorithm. Artificial neural network

# Introduction

Melting point is a fundamental physical property of organic compounds, which has found wide use in chemical identification, as a criterion of purity and for the calculation of other important physicochemical properties such as vapor pressure and aqueous solubility.<sup>1,2</sup> The solubility of a compound in water is strongly correlated with its melting point. An estimate of the water-solubility of a compound before it is synthesized, or available in sufficient purity for analytical measurements, would be most useful.<sup>3</sup> Adequate aqueous solubility is necessary for a compound to be transported to the active site within an organism. As noted above, melting point affects solubility, and solubility controls toxicity in that, if a compound is only poorly soluble, its concentration in the aqueous environment may be too low for it to exert a toxic effect.<sup>4,5</sup> Thus, it would be helpful to be able to estimate the melting point of a compound from its chemical structure.<sup>6,7</sup> Prediction methods for melting point. mainly can be categorized as property-property relationship (PPR), group contribution, and quantitative structure-property relationship (QSPR).<sup>89</sup> Comprehensive reviews of the subject reveal that many studies involved hydrocarbons and homologous compounds.<sup>10-12</sup> This is because of the difficulty of melting point prediction for various organic compounds, since the numerous factors that control it are not easy to quantify.

The prediction of physicochemical and biological properties/ activities of organic molecules are the main objective of quantitative structure-property/activity relationships (QSPRs/ QSARs). The QSPR/QSAR models now correlate chemical

structure to a wide variety of physical, chemical, biological (including biomedical, toxicological, ecotoxicological) and technological properties.13-17 QSPR/QSAR models are obtained on the basis of the correlation between the experimental values of the property/activity and descriptors reflecting the molecular structure of the compounds. To obtain a significant correlation, it is crucial that appropriate descriptors be employed. A wide variety of molecular descriptors has been reported for using in QSPR/QSAR models.<sup>18</sup> However, as the number of descriptors (variables) increases, the model becomes complicated, and its interpretation is difficult if many variables are used in modeling. Therefore, the application of these techniques usually requires variable selection for building well-fitted models. A better predictive model can be obtained by ortogonalization of the variables by means of principal component analysis (PCA).<sup>19,20</sup> The principal component analysis was used to compress the descriptor groups into principal components (PC's). In order to reduce the dimensionality of the independent variable space, a limited number of PC's are used.<sup>21</sup> Hence, selecting the significant and informative PC's is the main problem in all of the PCA-based calibration methods.<sup>22-25</sup> Different methods have been addressed to select the significant PC's for calibration purposes. The simplest and most common one is a top-down variable selection where the PC's are ranked in the order of decreasing eigenvalues and the PC's with highest eigenvalue is considered as the most significant one and, subsequently, the PC's are introduced into the calibration model. However, the magnitude of an eigenvalue is not necessarily a measure of its significance for the calibration.<sup>25</sup> In the other method,

which is called correlation ranking, the PC's are ranked by their correlation coefficient with the property and selected by the procedure discussed for eigenvalue ranking.<sup>22,23</sup> Better results are often achieved by this method. Recently, genetic algorithm (GA) has been applied for the selection of the most relevant PC's instead of the older methods. Comparison of the results obtained using GA principal component selection with the two above-mentioned methods shows that GA gives a better result and close to the correlation ranking.<sup>26-28</sup> GA is a stochastic method to solve optimization problems applying evolution hypothesis of Darwin and different genetic functions. *i.e.*, cross-over and mutation.<sup>29,30</sup> Genetic algorithm is robust, global and generally more straightforward to apply in situations where there is little or no a *priori* knowledge about the process to be controlled.<sup>29</sup>

Artificial neural networks (ANNs) have become popular in QSPR/QSAR models due to their success where complex non-linear relationships exist amongst data.<sup>31,32</sup> An ANN is formed from artificial neuron, connected with coefficients (weights), which constitute the neural structure and are organized in layers. The layers of neurons between the input and output layers are called hidden layers. Neural networks do not need explicit formulation of the mathematical or physical relationships of the handled problem. These give ANNs an advantage over traditional fitting methods for some chemical applications. For these reasons in recent years. ANNs have been applied to a wide variety of chemical problems.<sup>33,42</sup>

Very recently, QSPR models have been applied for prediction of the melting point of 323 set of drug-like compounds.<sup>43</sup> Ability of these models for prediction of the melting point is poor (for example, root-mean square error of the models is approximately 40.7 °C). In order to predict accurately melting point of the same compounds. in the present work, principal component-genetic algorithm-multiparameter linear regression (PC-GA-MLR) and principal component-genetic algorithm-artificial neural network (PC-GA-ANN) models were employed to generate QSPR models between the principal components and melting point of the compounds and the results were compared with each other, the previous work and the experimental values.

#### **Data and Methodology**

**Data set and theoretical descriptors.** Melting points were taken from the recently published paper.<sup>43</sup> The data are mostly for the compounds that are solid at room temperature but also include some liquids and gaseous compounds. The melting points are spread between -118 and 345 °C. The z-matrices (molecular models) were constructed with Hyper-Chem 7.0 and molecular structures were optimized using AM1 algorithm.<sup>44</sup> In order to calculate the theoretical descriptors, *Dragon* package version 2.1 was used.<sup>45</sup> For this propose the output of the HyperChem software for each compound fed into the *Dragon* program and the descriptors were calculated. As a result, a total of 1481 theoretical

descriptors were calculated for each compound in data sets (323 compounds).

**Data pretreatment.** The theoretical descriptors were reduced by the following procedure: 1) descriptors that are constant have been eliminated (292 descriptors). 2) in addition, to decrease the redundancy existing in the descriptors data matrix, the correlation of descriptors with each other and with melting point of the molecules are examined. and collinear descriptors (R > 0.9) are detected. Those of the descriptors which have the pair wise correlation coefficient above 0.9 and having the lower correlation with melting point values are removed from the data matrix (758 descriptors). 3) before statistical analysis, the descriptors are scaled to zero mean and unit variance (autoscaling procedure). The data matrix (431 descriptors) is subjected to principal component analysis using Matlab software package.<sup>46</sup> Multiparameter linear regression was obtained using spss software.<sup>47</sup>

Genetic algorithm (GA). To select the most relevant principal components, evolution of population was simulated.48.52 Each individual of the population defined by a chromosome of binary values represented a subset of principal components. The number of genes at each chromosome was equal to the number of principal components. The population of the first generation was selected randomly. A gene took a value of 1 if its corresponding principal component was included in the subset: otherwise, it took a value of zero. The number of genes with a value of 1 was kept relatively low to have a small subset of principal components.52 that is, the probability of generating 0 for a gene was set greater (at least 60%) than the value of 1. The operators used here were crossover and mutation. The probability of the application of these operators was varied linearly with generation renewal (0-0.1% for mutation and 60-90% for crossover). The population size was varied between 50 and 250 for different GA runs. For a typical run, the evolution of the generation was stopped when 90% of the generations took the same fitness. The GA program was written in Matlab 6.5.53

Artificial neural network (ANN). A feed forward artificial neural network with a back-propagation of error algorithm was used to process the non-linear relationship between the selected principal components and the melting point. The number of input nodes in the ANN was equal to the number of PC's. The ANN models confined to a single hidden layer, because the network with more than one hidden layer would be harder to train. A three-layer network with a sigmoid transfer function was designed. The initial weights were randomly selected between 0 and 1. Optimization of the weights and biases was carried out according to the resilient back-propagation algorithm. The data set was randomly divided into three groups: a training set, a validation set and a prediction set consisting of 195, 64 and 64 molecules, respectively. The training and validation sets were used for the model generation and the prediction set was used for evaluation of the generated model. The performances of training, validation and prediction of models are

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evaluated by the mean percentage deviation (MPD) and root mean square error (RMSE), which are defined as follows:

$$MPD = \frac{100}{N} \sum_{i=1}^{N} \left| \frac{P_i^{exp} - P_i^{cal}}{P_i^{exp}} \right|$$
(1)

$$RMSE = \sqrt{\sum_{i=1}^{N} \frac{(P_i^{exp} - P_i^{cal})^2}{N}}$$
(2)

where  $P_i^{exp}$  and  $P_i^{cal}$  are experimental and calculated values of melting point with the models and N denote the number of data points. Individual percent deviation (IPD) is defined as follows:

$$IPD = 100 \times \left(\frac{P_i^{cal} - P_i^{exp}}{P_i^{exp}}\right)$$
(3)

The processing of the data was carried using Matlab 6.5.<sup>46</sup> The neural networks were implemented using Neural Network Toolbox Ver. 4.0 for Matlab.<sup>54</sup>

#### **Results and Discussion**

**Principal component analysis.** After the elimination of the constant and one of the collinear ones. 431 descriptors remained from 1481 theoretical descriptors calculated for the compounds. The results of application of PCA on the descriptors data matrix were shown that 99.9% of the variances in the descriptors data matrix are explained by 234 first PC's. Therefore, we focused our analysis on these PC's, and the reminders, which are noisy factors, were not considered.

Principal component-genetic algorithm-multiparameter linear regression. Obtaining the number of significant principal components is the main problem in the PCA-based methods. The first 234 principal components (PC's) were found to explain more than 99.9% of variances in the original data matrix. As noted previously, not all of the PC's is informative for QSAR/QSPR modeling.25-27 Then, we used GA for the selection of the most relevant PC's instead of the older methods. The selected PC's are PC1, PC2, PC3, PC4, PC5, PC6, PC7, PC9, PC15, PC32, PC33, PC36, PC37, PC39 and PC86. As can be seen, the selected principal components are not based on their eigenvalue. For example, PC9 and PC15 are selected and PC8 is not considered in the model. This is due to the fact the information contents of some extracted PC's may not be in the same direction of the activity data. Multiparameter linear correlation of melting point values for 195 compounds in training set was obtained using the fifteen principal components. The calculated values of melting point for the compounds in training, validation and prediction sets using the PC-GA-MLR model have been plotted versus the experimental values of it (Figure 1).

Principal component-genetic algorithm-artificial neural network. To process the non-linear relationships exists bet-



**Figure 1**. Plot of calculated values of the melting point using the PC-GA-MLR model *versus* the experimental values of it for training, validation and prediction sets.

ween the melting point and the PC's, the ANN modeling method combined with PCA for dimension reduction and GA for feature selection was employed. A principal component-genetic algorithm-artificial neural network (PC-GA-ANN) model, which combines the PC's with ANN, is another PC-based calibration technique for non-linear modeling between the PC's and dependent variables.25-28 The input vectors were the set of PC's, which were selected by GA, and therefore, the number of nodes in the input layer was dependent on the number of selected PC's. In the PC-GA-MLR model it is assumed that the PC's are independent of each other and truly additive relevant to the property under study. ANNs are particularly well-suited for QSAR/QSPR models because of their ability to extract non-linear information present in the data matrix. For this reason the next step in this work was generation of the ANN model. There are no rigorous theoretical principles for choosing the proper network topology; so different structures were tested in order to obtain the optimal hidden neurons and training cycles.34-42 Before training the network, the number of nodes in the hidden layer was optimized. In order to optimize the number of nodes in the hidden laver, several training sessions were conducted with different numbers of hidden nodes (from one to thirty two). The root mean square error of training (RMSET) and validation (RMSEV) sets were obtained at various iterations for different number of neurons at the hidden layer and the minimum value of RMSEV was recorded as the optimum value. Plot of RMSET and RMSEV versus the number of nodes in the hidden layer has been shown in Figure 2. It is clear that the twenty nine nodes in hidden layer is the optimum value.

This network consists of fifteen inputs (including PC1, PC2, PC3, PC4, PC5, PC6, PC7, PC9, PC15, PC32, PC33, PC36, PC37, PC39 and PC86), the same PC's in the PC-GA-MLR model, and one output for melting point. Then an ANN with architecture 15-29-1 was generated. It is note-worthy that training of the network was stopped when the RMSEV started to increases *i.e.* when overtraining begins.



Figure 2. Plot of RMSE for training and validation sets *versus* the number of nodes in hidden layer.



Figure 3. Plot of RMSE for training and validation sets *versus* the number of iterations.

The overtraining causes the ANN to loose its prediction power.<sup>31</sup> Therefore, during training of the network, it is desirable that iterations are stopped when overtraining begins. To control the overtraining of the network during the training procedure, the values of RMSET and RMSEV were calculated and recorded to monitor the extent of the learning in various iterations. Results showed that overfitting did not see in the optimum architecture (Figure 3).

The generated ANN was then trained using the training and validation sets for the optimization of the weights and biases. For the evaluation of the predictive power of the generated ANN, an optimized network was applied for prediction of the melting point values in the prediction set, which were not used in the modeling procedure (Table 1). The calculated values of melting point for the compounds in training, validation and prediction sets using the ANN model have been plotted *versus* the experimental values of it in Figure 4.

It is clear that the calculated values of melting point are in good agreement with those of the experimental values. The



**Figure 4**. Plot of calculated values of the melting point using the PC-GA-ANN model *versus* the experimental values of it for training, validation and prediction sets.



**Figure 5**. Plot of the residual for calculated values of the melting point using the PC-GA-ANN model *versus* the experimental values of it.

correlation equation for all of the calculated values of melting point (Mp) from the ANN model and the experimental values is as follows:

$$Mp(cal) = 0.969 Mp(exp) + 4.381$$
(4)

(R = 0.9850; MPD = 9.326; RMSE = 12.623; F = 10445.99)

Similarly, correlation of Mp(cal) *versus* Mp(exp) values in the prediction set gives equation (5):

$$Mp(cal) = 0.972 Mp(exp) + 5.623$$
 (5)

Plot of the residual for melting point values in the training, validation and prediction sets *versus* the experimental values of it has been illustrated in Figure 5. It is clear that the propagation of errors in both sides of zero is random. Then there is not systematic error in the model.

As a result, it was found that properly selected and trained neural network could fairly represent dependence of melting point for the drug-like compounds on the PC's. Then the

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Experimental

Cal

Res.

Table 1. Continued

No. Compound

Table 1. Experimental and calculated values of melting point for the drug-like compounds in training, validation and prediction sets using PC-GA-MLR and PC-GA-ANN models along with the residual for the calculated values by PC-GA-ANN model

			Cal	-	51	Meprobamate
No.	Compound	Experimental	(PC-GA-ANN)	Res.	52	Gentamicin
	Turining		, , , , , , , , , , , , , , , , , , , ,		53	Physotigmine
,	Traning	110	110.2	0.3	54	Bupivacaine
1	Halounane	-118	-118.5	0.5	55	Amidopyrine
2	Diethyl ether	-116.3	-120.2	3.9	56	Acecarbromal
5	Ethylene oxide	-111.3	-112.0	0.7	57	Celiprolol
4	Chloroform	-63.7	-62.3	-1.4	58	Tolnaftate
5	Methoxyflurane	-35	-35.9	0.9	59	Amphotalide
6	Benzyl alcohol	-15.3	-14.9	-0.4	60	Valnoctamide
7	Nicotinyl alcohol	-7.7	5.1	-12.8	61	Ifenprodil
8	Amphetamine	11.3	31.8	-20.5	62	Baminine
9	Glyceryl trinitrate	13.5	10.5	3.0	63	Alverine
10	Propofol	19	2.2	16.8	64	Pericyazine
11	Nikethamide	25	32.1	-7.1	65	Attonine
12	Ephedrine	36	24.7	11.3	66	Morphazinamide
13	Methyl nicotinate	39	36.7	2.3	67	Chlophadianol
14	Trimipramine	45	55.0	-10.0	20	C mopriculation D=4imal
15	Phencarbamide	48	39.7	8.3	60	Traductor a
16	Hvoseine	59	43.4	15.6	09	Terbutalme
17	Prometazine	60	57.5	2.5	70	Capobenic acid
18	Gemfibrozil	61	92.0	-31.0	71	Propizepine
10	Proceine	61	65.5	-4.5	72	Nadolol
20	Dichlorabhenazone	65.5	67.1	-1.6	73	Bamethan
20	Etomidata	67	80.3	_13.3	74	Nimodipine
21	Lionaccino	67 5	<b>7</b> 0.0	-13.3	75	Mecloqualone
22	Daghotalit	67.5	79.9	-12.4	76	Febantel
23	Pendutoioi	08	78.3	-10.5	77	Clonidine
24	Marthanala	71	80.4 47.0	-15.4	78	Xylometazoline
25	Mephenesin	71.5	37.3	14.2	79	Diazepam
20	Phenadoxone	75	/1.1	3.9	80	Thozalinone
27	Ibuproten	/6	110.7	-54.7	81	Aminorex
28	Mebutamate	77	71.4	5.6	82	Praziquantel
29	Oxprenolol	77.5	56.5	21.0	83	Simvastatin
30	Methadone	78	61.1	16.9	84	Butalbital
31	Allylestrenol	80	80.0	0.0	85	Phenazopyridine
32	Bamifylline	80	106.1	-26.1	86	Erythrocentaurin
33	Nabumetone	80	67.0	13.0	87	Carbaryl
34	Anileridine	83	83.3	-0.3	88	Fexofenadine
35	Fentanyl	83	67.2	15.8	89	Letosteine
36	Amphetaminil	85	84.2	0.8	90	Acetylsalicylic acid
37	Methdilazine	87	91.1	-4.1	91	Tetrazepam
38	Noxythiolin	88	90.1	-2.1	92	Felodivin
39	Vinylbital	90	83.4	6.6	93	Metoclopramide
40	Phenindamine	91	<b>92</b> .9	-1.9	94	Atenolol
41	Carisoprodol	92	87.6	4.4	95	clotrimazole
42	Beclamide	92.5	99.1	-6.6	96	Salacetamide
43	Perphenazine	94	110.8	-16.8	97	Morazone
44	Thenalidine	95	75.2	19.8	98	Astemizole
45	Tropicamide	96.5	96.6	-0.1	00	Acemetacin
46	Aldicarb	99	97.6	1.4	100	Mafenide
47	Acetylpheneturide	100	96.2	3.8	100	Haloneridal
48	Phenocoll	100.5	1177	-17.2	101	Glumidino
49	Piperidione	100.0	106.1	-4 1	102	A zotodina
50	Isoxsuorine	102 5	94.8	77	103	Azatadine
	тоохоцине	1.02.0	74.0		104	restosterone

N0.	Compound	Experimental	(PC-GA-ANN)	Res.
51	Meprobamate	104	104.1	-0.1
52	Gentamicin	105	104.9	0.1
53	Physotigmine	105.5	88.2	17.3
54	Bupivacaine	107	89.2	17.8
55	Amidopyrine	108	136.4	-28.4
56	Acecarbromal	109	105.4	3.6
57	Celiprolol	110	107.8	2.2
58	Tolnaftate	111	121.1	-10.1
59	Amphotalide	113	119.7	-6.7
60	Valnoctamide	113.5	111.1	2.4
61	Ifenprodil	114	115.5	-1.5
62	Bamipine	115	104.8	10.2
63	Alverine	116	128.1	-12.1
64	Pericyazine	116	116.1	-0.1
65	Atropine	118	114.8	3.2
66	Morphazinamide	118.5	91.8	26.7
67	Chlophedianol	120	125.4	-5.4
68	Pridinol	120	99.3	20.7
69	Terbutaline	120.5	130.8	-10.3
70	Capobenic acid	121	124.6	-3.6
71	Propizepine	122	150.0	-28.0
72	Nadolol	124	117.9	6.1
73	Bamethan	125	114.0	11.0
74	Nimodipine	125	126.3	-1.3
75	Mecloqualone	126	153.3	-27.3
76	Febantel	129	128.3	0.7
77	Clonidine	130	136.1	-6.1
78	Xylometazoline	131	124.8	6.2
79	Diazepam	133	127.3	5.7
80	Thozalinone	133	133.5	-0.5
81	Aminorex	136	145.7	-9.7
82	Praziquantel	136	128.2	7.8
83	Simvastatin	136.5	142.4	-5.9
84	Butalbital	138	138.8	-0.8
85	Phenazopyridine	139	147.9	-8.9
86	Erythrocentaurin	140	161.0	-21.0
87	Carbaryl	142	144.1	-2.1
88	Fexofenadine	142	141.0	1.0
89	Letosteine	142	149.8	-7.8
90	Acetylsalicylic acid	l 14 <b>2</b> .4	172.9	-30.5
91	Tetrazepam	144	126.4	17.6

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152

153

153

151.5

149.1

146.5

140.9

153.7

152.7

144.6

157.1

146.7

162.3

134.2

140.9

148.2

152.4

148.1

180.9

4.1 -7.2

-5.7

2.4 -9.1

2.3

-13.2

15.8

10.13.3

-0.4 4.9

-27.9

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Table 1. Continued

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Tabl	e I. Commueu				1401	e I. Commueu	
No.	Compound	Experimental	Cal (PC-GA-ANN)	Res.	No.	Compound	Exper
105	Taurolidine	154	152.8	1.2	158	Glipizide	20
106	Colchicane	156	160.7	-4.7	159	Oxazepam	20
107	moricizine	156	157.3	-1.3	160	Lonidamine	20
108	Omeprazole	156	150.3	5.7	161	Amodiaquine	20
109	Urapidil	156	137.3	18.7	16 <b>2</b>	Indoramin	20
110	Salicylic acid	157	163.0	-6.0	163	Vigabatrin	20
111	Succisulfone	157	152.0	5.0	164	Methetion	2
112	Lidoflazine	159	153.8	5.2	165	Pimozide	2
113	Azacyclonol	160	158.1	1.9	166	Oxycodone	2
114	Benzydamine	160	164.0	-4.0	167	Hydroxyprogesterone	2
115	Didanosine	160	156.1	3.9	168	Hydrocortisone	22
116	Ketorolac	160.5	178.2	-17.7	169	Apazone	22
117	Oxaprozin	160.5	161.7	-1.2	170	Acitretin	22
118	Aldosterone	164	176.3	-12.3	171	Nalidixic acid	22
119	Pizotifen	164	169.8	-5.8	172	Salinazid	23
120	Tolrestat	164	175.0	-11.0	173	Diaveridine	23
121	Lorazepam	166	184.1	-18.1	1 <b>7</b> 4	Phenopyrazone	23
122	Sulfamethoxazole	167	161.7	5.3	175	Pvrimethamine	2.
123	Chlortetracycline	168.5	168.3	0.2	176	Nicotinic acid	23
124	Glyburide	169	170.0	-1.0	177	Caffiene	23
125	Benperidol	170	161.2	8.8	178	Prednisolone	24
126	Metopimazine	170	160.5	9.5	179	Cromolyn	24
127	Tolazamide	170	183.7	-13.7	180	Clometacin	24
128	Isoniazid	172	188.2	-16.2	181	Domperidone	24
129	Hvdralazine	172.5	166.3	6.2	182	Metolazone	2
130	Nifedipine	173	179.0	-6.0	183	Finasteride	2
131	Lovastatin	174.5	159.5	15.0	184	Nifenazone	2
132	Amisometradine	175	167.6	7.4	185	Pemoline	2
133	Acifran	176	179.3	-3.3	186	Dexamethasone	20
134	Melphalan	177	170.2	6.8	187	Ciprofloxacin	20
135	Propallylonal	177	179.7	-2.7	188	Hydroflumethiazide	2
136	Sulpiride	178	184.0	-6.0	189	Acefvlline	_
137	Zomenirac	178	177.0	1.0	190	Dantrolene	2'
138	Nomifensine	179	165.8	13.2	191	Fluorouracil	- 28
139	Sulthiame	180	174.8	5.2	192	Prazosin	23
140	Acepromazine	182.5	174.7	78	193	Enoxolone	29
141	Amphenidone	182.5	173.2	03	194	Diazoxide	3
142	Sulfacetamide	182.0	179.4	3.6	195	Orotic acid	3
143	Bazofibrata	185	196.8	-0.8		Validation	c.
140	Aestehavemide	160	160.6	-0.6	196	Trichlorethylene	_5
144	Receiverside	169	1/9.0	9.4 11.0	197	Methyl salicylate	_
145	Clamination	107	1945	-11.8	198	Benzyl benzoate	
140	Compranine	189.5	184.5	5.0	199	Prilocaine	
147	Carbamazepine	190	181.0	9.0	200	Ethopropazine	
148	Embutramide	190.5	181.4	9.1	200	Isosorbide	
149	Apronal	194	197.3	-3.3	201	Fluanisone	Ň
150	Clebopride	194	141.2	52.8	203	Disulfiram	
151	Methotrexate	195	196.4	-1.4	203	Ethylecterol	
152	Aceglutamide	197	189.8	7.2	204	Moxaverine	
153	Aceneocoumarol	197	208.6	-11.6	200	Pentifylline	<
154	Furonazide	199	209.9	-10.9	200	Piprozolin	· · · · · ·
155	Polythiazide	202.5	205.2	-2.7	207	Alclofense	( (
156	Ampicillin	203	237.0	-34.0	200	Ketonrofen	: t
157	Picrotoxin	203	199.1	3.9	209	Recoptoten	

Table 1	Continued

No.	Compound	Experimental	Cal (PC-GA-ANN)	Res.
158	Glipizide	205	218.5	-13.5
159	Oxazepam	205.5	179.5	26.0
160	Lonidamine	207	206.8	0.2
161	Amodiaquine	208	206.3	1.7
162	Indoramin	208	217.2	-9.2
163	Vigabatrin	209	201.8	7.2
164	Methetion	210	198.8	11.2
165	Pimozide	216	211.9	4.1
166	Oxycodone	219	208.3	10.7
167	Hydroxyprogesterone	222.5	213.5	9.0
168	Hydrocortisone	223	235.9	-12.9
169	Apazone	228	212.5	15.5
170	Acitretin	229	215.0	14.0
171	Nalidixic acid	229.5	219.1	10.4
172	Salinazid	232.5	235.6	-3.1
173	Diaveridine	233	227.8	5.2
174	Phenopyrazone	233	217.5	15.5
175	Pyrimethamine	233.5	230.3	3.2
176	Nicotinic acid	235.5	215.7	19.8
177	Caffiene	232.5	213.3	74.7
178	Prednisolone	240.5	231.7	8.8
170	Cromolyn	240.0	238.6	0.0 2 J
180	Clometacin	241	235.0	161
181	Domperidone	242 5	220.9	_6.8
187	Matolszone	242.5	249.5	-0.0 16.6
192	Finastarida	252	235.4	71
100	T masterioe Niferezone	203	243.9	19.6
104	Domolino	253	204.4	10.0
102	Perionne Davou athagan a	259	215.5	43.2
100	Dexamemasone	200	202.7	-2.7
187	Cipronoxacin Under flerer additional dat	200	259.9	0.1
188	Hydroffumethiazide	270.5	202.8	7.7
189	Aceryline	271	278.1	-7.1
190	Dantrolene	279.5	283.8	-4,3
191	Fluorouracil	283	281.2	1.8
192	Prazosin	285	274.5	10.5
193	Enoxolone	296	284.7	11.3
194	Diazoxide	330.5	334.5	-4.0
195	Violidation	345	347.6	-2.6
196	Trichlorethylene	-86	-85.7	-0.3
197	Methyl salicylate	-8	-7.5	-0.5
198	Benzyl benzoate	18	31.4	-13.4
199	Prilocaine	37	63.9	-26.9
200	Ethopropazine	53	39.9	13.1
201	Isosorbide	61	66.4	-5.4
202	Fluanisone	67.5	70.6	-3.1
203	Disulfiram	71	67.8	3.2
204	Ethylesterol	77	69.4	7.6
205	Moxaverine	78	81.0	-3.0
206	Pentifylline	82	70.8	11.2
207	Piprozolin	86	83.4	2.6
208	Alclofenac	91	120.5	-29.5
209	Ketoprofen	94	90.4	3.6
	record of the second se	27	2 M - T	0.0

Melting Point for Drug-like Compounds

Table 1. Continued

Res.

-1.2

4.7 3.9

12.5

-1.0

7.4

-40.4

-6.2

-6.0 -14.6

-1.3

11.1

4.6 -27.8

8.0

-7.7

23.4

-16.9

-7.2 4.5

-20.4

-0.2

-7.9

12.5

8.2

11.0

-5.5

-20.3

-2.4

-12.4

-3.9

-5.3 -7.5

-13.1

-1.8

-7.1

-24.9

-2.5

-5.3

1.4

2.6

14.8

-14.6

44.5 -7.7

-4,5

2.0

6.8

5.6

1.4

5.2

-2.0

1.0

0.2

1.6

20.2

8.6

-21.9

Table 1. Continued	
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	No.	Compound	Experimental	Cal (PC-GA-ANN)	Res.	No.	Compound	Experimental	Cal (PC-GA-ANN)
211       Hycanthone       100.6       124.4       -23.8       227       Ramindine       69       90.9         213       Bearony pherovide       105       103       103       268       Proprophenes       75       70.3         214       Functiporfen       110       991       10.9       270       Guaphenesin       80       67.5         215       Acctantilide       114       119.3       -5.3       271       Metroconte       80       83.6         216       Dibenzepin       116       109.3       6.7       272       Bearconte       90       83.6         217       Attacoline       120       105.2       14.8       273       Megrothine       92       103.1         216       Derizonote       124.3       15.8       -3.8       277       Pjobronan       106       107.3         221       Beary Inophine       132       135.8       -3.8       279       Pjorboptiad ine       113       148.4         223       Attacyntek       109       7.7.2       -18.2       Tonal bearonine       113       148.4         224       Cubrontine       144       145.6       -1.6       281       Meyorone	210	Cocaine	98	109.3	-11.3	266	Chlorambucil	66	67.2
212       Berazoy peroxide       105       103.7       1.3       208       Propovplene       75       70.1         213       Metarminol       107.5       92.5       15.0       209       Eliszold       78       74.1         214       Planchychin       110       90.1       10.9       270       Guiphensein       80       67.5         215       Acatanihde       114       119.3       -5.3       271       Merrofinate       92       132.4         216       Acatanihde       120       105.2       14.8       273       Magnothine       92       132.4         218       Acabrolol       121       13.4       -13.4       274       Tamoxifan       90       106.0       100.3       101.2         216       Tobutanide       128.5       11.3       14.7       270       Diptrino       101.3       143.8         221       Berzy Imorphine       136       15.1       -18.2       279       Cyproheptal ine       113       104.3       13.8       271       Proincial       113       103.7       124.2       204.2       204.2       204.2       204.2       204.2       204.2       204.2       204.2       204.2 <td< td=""><td>211</td><td>Hycanthone</td><td>100.6</td><td>124.4</td><td>-23.8</td><td>267</td><td>Ranitidine</td><td>69</td><td>90.9</td></td<>	211	Hycanthone	100.6	124.4	-23.8	267	Ranitidine	69	90.9
213       Metaraminol       107,5       92,5       15.0       269       Eisazol       78       74.1         214       Flubiporfon       110       19,1       -5.3       271       Metrofonate       83       84.0         216       Diberzepin       116       109,3       6.7       272       Encocatine       90       82.6         217       Antacoline       120       105.2       14.8       273       Magnotine       92       103.2         218       Acaburolo       121       134.4       -13.4       274       Tamoxifen       96       102.2         219       Berazionophine       132       135.8       -3.8       277       Piporbana       106       107.3         223       Alzapride       139       157.2       -18.2       279       Cyrobeptad ine       113       108.4         224       Carbatamide       144       145.6       -16.2       281       Moprone       118       110.0         225       Carbatamide       144       145.7       7.3       284       Lorisidine       122.4       99.0         224       Combatine       151       143.7       7.3       284       Lorisidine	212	Benzoyl peroxide	105	103.7	1.3	268	Propoxyphene	75	70.3
214       Fluchiprofen       110       99.1       10.9       270       Guaiphenesin       80       67.5         215       Accistinide       114       119.3       -5.3       271       Metrioticate       83       84.0         216       Accistinide       120       105.2       14.8       273       Maynothine       92       132.4         218       Accistinide       121       134.4       -134.4       274       Tumoxifen       92       132.4         218       Benzytmore       124.3       150.9       -26.6       275       Metaprotenol       100       100.5       181.1         221       Benzytmore       132       135.8       -3.8       277       Pipobroman       106       107.3         223       Mephytotini       136       157.0       -18.2       279       Cyrobeptadine       113       108.4         224       Camatinite       142       133.5       8.5       285       Elyptritine       115       142.8         223       Carbutanide       144.145.6       -1.6       281       Moperone       118       116.0         224       Chinating       7.3       284       Lofescadne       124	213	Metaraminol	107.5	92.5	15.0	269	Etisazol	78	74.1
215       Acetanihide       114       119.3       -5.3       271       Metrifonate       83       84.0         216       Debrazynin       116       109.3       6.7       272       Benzocnine       90       82.6         218       Acebutolo       121       134.4       -13.4       274       Tamovafan       96       102.2         128       Acebutolo       121       134.4       -13.4       274       Tamovafan       96       102.2         129       Benzynenphine       123       135.8       -3.8       277       Probroman       106       107.3         221       Matzgride       139       157.2       -18.0       278       Acevleysteine       105.5       98.4         224       Cambutamide       144       145.6       -16       281       Moperone       118       110.0         225       Cambutamide       144       146.6       -16       281       Moperone       118       112.0       127.4         225       Cambutamide       148       148.2       -0.2       284       Encisionine       131       132.0       130.3       130.0       130.5       130.0       130.0       142.0       142.0 <td>214</td> <td>Flurbiprofen</td> <td>110</td> <td>99.1</td> <td>10.9</td> <td>270</td> <td>Guaiphenesin</td> <td>80</td> <td>67.5</td>	214	Flurbiprofen	110	99.1	10.9	270	Guaiphenesin	80	67.5
216       Dibetazepin       116       109.3       6.7       272       Benzocaine       90       82.6         217       Antazoline       120       105.2       14.8       273       Maprotiline       92       132.4         218       Acabutolol       121       134.4       -13.4       274       Tamovářen       96       102.2         219       Benzarone       124.3       150.9       -26.6       275       Metaproternol       100       106.0         217       Difandanize       132.5       135.8       -38.8       277       Pipobronat       100       107.3         224       Cimetidme       142       133.5       85.2       280       Piprituline       115       142.8         224       Cimetidme       142       135.8       235       283       Benzora and       120       127.7         224       Tinilabrottal       148       145.2       -0.2       238       Benzora and       120       127.7         225       Bučavanac       133       138.0       15.0       285       Bitosanate       131       132.2         235       Metonidazole       157       173.3       -21.2       285 <td< td=""><td>215</td><td>Acetanilide</td><td>114</td><td>119.3</td><td>-5.3</td><td>271</td><td>Metrifonate</td><td>83</td><td>84.0</td></td<>	215	Acetanilide	114	119.3	-5.3	271	Metrifonate	83	84.0
217     Antzoline     120     105.2     14.8     273     Maprotiline     92     132.4       218     Acebulolo     121     134.4     -14.3     274     Manoxifen     96     102.2       219     Beazarone     124.3     150.9     -26.6     275     Metaprotermol     100     105.0       220     Tolbutanizle     128.5     113.8     1-4.7     276     Difenidol     103.5     118.1       218     Accylarytskine     105.5     98.4     145.5     278     Accylarytskine     105.5     98.4       224     Cametidine     142     133.5     8.5     280     Flupitrine     113     188.4       224     Cametidine     144     145.6     -1.6     281     Moperone     118     110.0       225     Carbutanide     144     145.6     -7.4     282     Temazepan     120     127.4       226     Faiobennidone     150     147.7     7.3     284     Lofexidine     131     138.2       228     Salbutanol     151     143.7     7.3     284     Lofexidine     141     142.9       228     Batexanae     133     138.0     150.9     287     Suffinymzone     136.	216	Dibenzepin	116	109.3	6.7	272	Benzocaine	90	82.6
218         Acebitolol         121         134.4         -13.4         274         Tamoxifen         96         102.2           219         Benzyarore         124.3         150.9         -26.6         225         Metaproternol         100         106.0           220         Tolbutamide         128.5         138.8         14.7         270         Diferidol         103.5         118.1           221         Benzyhnophine         132         135.8         -38         277         Pipobroman         106.5         107.3           224         Cimetidine         142         135.5         8.5         280         Fujpitine         113         164.5           225         Carbutamide         144         145.6         -1.6         281         Mojerone         118         110.0           226         Pyrinoine         146.5         153.9         -7.4         282         Enoisama         131         132.0           228         Salibutamoi         151         143.7         7.3         284         Edorikitore         141         141.2         142.9           228         Balexama         153         138.0         150.0         285         Sulibutamot         131.1	217	Antazoline	120	105.2	14.8	273	Maprotiline	92	132.4
219       Benzarone       124.3       150.9       -26.6       275       Metaprotecnol       100       106.6         220       Tolbutamide       128.5       113.8       14.7       276       Difensióol       103.5       118.1         212       Benzylmorphine       132       135.8       -3.8       277       Pipofroman       106       107.3         223       Alizagride       139       157.2       -18.2       279       Cyproheptad ine       113       108.4         224       Cimetidine       142       135.5       8.5       280       Fluptrine       115       142.2.8         225       Carbutamide       144       145.6       -1.6       281       Moprone       118       110.0         226       Parinoline       146.5       153.9       -7.4       282       Entoscinate       131       132.2         228       Sulfutanol       151       143.7       7.3       284       Lofexidine       126       142.9       92.9         228       Burkanol       150       153       136.0       136.5       136.5       136.5       136.5       136.5       136.5       136.5       136.5       136.5       136.5	218	Acebutolol	121	134.4	-13.4	274	Tamoxifen	96	102.2
220         Tolbutamide         125.3         113.8         14.7         276         Diffended         103.5         118.1           221         Beax, incomphine         132         135.8         -3.8         277         Pipobroman         106         107.3           224         Cimentaine         136         154.0         -18.0         278         Acetylexitene         109.5         98.4           224         Cimentaine         142         135.5         85.5         280         Flippirtine         115         143.5           225         Carbutamide         144         145.6         -1.6         281         Emazepan         120         127.7           227         Thialbarbital         146.5         153.9         -7.4         282         Emazepan         120         124.4         99.0           228         Buitswaraa         153         138.0         15.0         285         Bitoscanate         131         138.2           230         Ketobemidone         156         167.4         -11.4         280         Proglumide         142         149.9           231         Dity dynomphine         157         178.3         -21.3         287         Sulfinynzazee	219	Benzarone	124.3	150.9	-26.6	275	Metaproterenol	100	106.0
221       Beaxtmorphine       132       135.8       -3.8       277       Pipotroman       106       107.3         222       Maghenytoin       136       154.0       -18.0       278       Acerolaysteine       109.5       98.4         224       Alizupride       139       157.2       -18.2       270       Cyproheptad ine       113       108.4         224       Cunstitumide       144       143.5       8.1       6.1       281       Moperone       118       110.0         225       Carbutamide       148       148.2       -0.2       283       Betrazic acid       122.4       99.0         228       Sulfatunol       151       143.7       7.3       284       Loftscäine       131       138.2         230       Kotobemidane       156       157.4       -1.4       287       Sulfaturol       134.5       130.0         231       Ditydomorphine       157       178.3       -2.1.3       287       Sulfaturyazone       136.5       156.9         233       Metholital       160       158.4       2.29       Proglumide       142       149.9         234       Habazepan       164       160.9       3.1	220	Tolbutamide	128.5	113.8	14.7	276	Difenidol	103.5	118.1
222       Mephenytoin       136       154.0 $-18.0$ 278       Acerly/systeme       109.5       98.4         223       Alizarjohe       139       157.2 $-18.2$ 270       Cyprohepati line       113       108.4         224       Cimeticline       142       133.5       8.5       280       Fluptritine       115       142.8         225       Curbutamide       144       145.6 $-1.6$ 281       Meperone       118       110.0         226       Pyrinolne       146.5       153.9 $-7.4$ 282       Temazepan       120       127.7         227       Thialberbini       148       148.2 $-0.2$ 283       Betroscie acid       131       138.2         230       Ketobernidone       156       157.4 $-11.4$ 287       Suffinyrazone       136.5       156.9         231       Dily dyronophine       157       178.3 $-21.3$ 287       Nethoridazole       141       141.2       149.9         234       Halazepan       164       169.9       31       290       Ketobernidine       145       153.5       133.5         235       Clobazan	221	Benzylmorphine	132	135.8	-3.8	277	Pipobroman	106	107.3
223       Alizapride       139       157.2 $-18.2$ 279       Cyproheptical ine       115       142.8         224       Cimetidine       142       133.5       8.5       280       Fluptimine       115       142.8         225       Carbutamide       144       145.6 $-1.6$ 281       Moperone       118       110.0         226       Psimoline       146.5       153.9 $-7.4$ 282       Temizapam       120       127.7         715ialberbinl       148       143.7 $7.3$ 284       Lofexidine       122.4       99.0         228       Salbutamol       151       143.7 $7.3$ 284       Lofexidine       126       142.9         210       Retrobindene       156       158.9       10.8       288       Aprobarbitane       141       141.2         223       Methonidzole       159       148.2       10.8       288       Aprobarbitane       146       133.5         234       Halazepam       164       160.9       3.1       291       Chorizoronen       147.5       139.3         235       Clobazem       167       19.3       7.7       292       Fe	222	Mephenytoin	136	154.0	-18.0	278	Acetylcysteine	109.5	98.4
224         Cimeticine         142         133.5         8.5         280         Fluptime         115         1428           225         Carbutamide         144         145.6         -1.6         281         Moperone         118         1100           226         Pyrinoline         146.5         153.9         -7.4         283         Benzoic acid         122.4         99.0           228         Sublixamol         151         143.7         7.3         284         Lofexidine         12.6         142.9           229         Bufexamac         153         138.0         15.0         285         Bitoscanate         131.01         134.5         130.00           230         Ketobemidene         156         167.4         -11.4         287         Sulfinpyrazone         136.5         156.9           232         Methallanl         160         158.4         1.6         299         Proglumide         142         149.9           234         Methaltanl         160         158.4         1.6         290         Keitoconazole         146         133.5           235         Clobazam         167         159.3         7.7         291         Cloraconen         147.5	223	Alizapride	139	157.2	-18.2	279	Cyproheptad ine	113	108.4
225       Carbatamide       144       145.6 $-1.6$ 281       Mogerone       118       110.0         226       Pyrinoline       146.5       153.9 $-7.4$ 283       Benzoic acid       122.4       99.0         227       Taiaberbinl       151       143.7 $7.3$ 284       Lofexidine       126       142.9         220       Bučevamac       153       133.0       150       285       Bioscanate       131       138.2         230       Ketobemidone       156       167.4 $-11.4$ 285       Bioscanate       131       138.2         230       Metonorphine       157       178.3 $-21.3$ 288       Aprobarbitone       141       141.2         234       Halazepam       164       160.9       31       290       Ketooazale       146       133.5         235       Clobazam       167       159.3       7.7       291       Choircomen       147.5       139.3         236       Sumatrptan       169       161.2       7.8       293       Naproxen       152       157.5         238       Heptabarbital       174       158.1       159       294	224	Cimetidine	142	133.5	8.5	280	Flupirtine	115	142.8
226Pyrinoline146.5153.9-7.4282lemazepan120127.7227Thialberbinl148148.2-0.2283Benzoica acid122.499.0228Salbutamol151143.77.3284Lofexidine126142.9229Butexemae153138.015.0285Bitoscanate131138.2230Ketobemidone156157178.3-21.3287Suffinyruzone136.5156.9231Dihydromorphine157178.3-21.3288Aprobarbione141141.2233Methallatal160158.41.6290Ketoconazole146133.5235Clobazam167159.37.7292Felbamate151140.0236Sumatriptan164160.93.1290Ketoconazole146133.5235Clobazam167159.37.7292Felbamate151140.0236Sumatriptan164169.9294Amobarbial156176.3237Hydroquinine172181.5-9.5293Maproxen152157.5238Heptabarbial174158.115.9295Phenallymal156176.3241Androstanolone181164.116.9206Warain157148.4240Ximoprofen178183.7-57297Bucetin164 <td>225</td> <td>Carbutamide</td> <td>144</td> <td>145.6</td> <td>-1.6</td> <td>281</td> <td>Moperone</td> <td>118</td> <td>110.0</td>	225	Carbutamide	144	145.6	-1.6	281	Moperone	118	110.0
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	226	Pyrinoline	146.5	153.9	-7.4	282	Temazepam	120	127.7
228Salbutamol15114.3.77.32.84Lofexutine1.20142.9229Bulexamac153138.015.0285Bitoscanate131138.2230Ketobemidone156167.4-11.4286Phenscetin134.5130.0231Dify dromophine157178.3-21.3288Aprobatione141141.2233Methallanal160158.41.6289Proglumide142149.9234Halazepam164160.93.1290Ketoconazole146133.5235Clobazam167159.37.7291Cloricromen147.5139.3236Sumatriptan169161.27.8292Felbamate151140.0237Hydroptinine172181.5-9.5294Amobarbital156158.4240Ximoprofen178183.7-5.7297Bucetin160172.4241Androstanolone181164.16.9298Faratrin164169.3243Verazide189186.030300Acetaminophen169176.5244Acdiastanolone189186.0302Tetracycline172.5174.3245Probenecid195190.446302Tetracycline172.5174.3244Vardolone203205.5-2.5303Amoxapine178.118	227	Thialbarbital	148	148.2	-0.2	283	Benzoic acid	122.4	99.0
229Bufexamac153138.0150285Bitoscanate151138.2230Ketobemidone156167.4 $-11.4$ 287Suffinyyrazone136.5156.9231Dilty dromorphine157178.3 $-21.3$ 287Suffinyyrazone136.5156.9232Methonidazole159148.210.8288Aprobarbione141141.2233Methallatal160158.41.6299Nepdunide142149.9234Halazepam167159.37.7291Cloricromen147.5139.3235Clobazam167159.37.7291Cloricromen147.5139.3236Sumatriptan169161.27.8293Naproxen152157.5238Heptabarbital174158.11.5.9295Phenalymal156176.3239Mephobarbital176181.6-5.6296Warfarin157148.4241Androstanolone181164.116.9298Famotidine163166.9242Zox azolamine184183.80.22.99Tyramine164169.3243Verazide189186.03.0300Acctaminophen169172.4244Acadasulfone194210.4-16.4301Risperdone170183.1245Probenecid194210.4-16.4301	228	Salbutamol	151	143.7	7.3	284	Lotexidine	126	142.9
230       Ketobernidone       156 $167.4$ $-11.4$ 285       Picificity arzone       136.5       156.9         231       Duby dromorphine       157       178.3 $-21.3$ 288       Aprobarbitone       141       141.2         233       Methallatal       160       158.4       1.6       289       Proglumide       142       149.9         234       Halazepam       164       160.9       3.1       291       Cloricromen       147.5       139.3         235       Clobazam       167       159.3       7.7       292       Felbanate       151       140.0         237       Hydroquinine       172       181.5 $-9.5$ 294       Amobarbital       156       176.3         238       Heptabarbital       176       181.6 $-5.6$ 295       Phenalymal       156       158.4         240       Amobarbital       176       181.6 $-5.6$ 295       Phenalymal       156       158.4         240       Ximoprofen       178       183.8       0.2       299       Tyramine       164       169.3       166.9         241       Androbarbolone       184       183.8 <td>229</td> <td>Bufexamac</td> <td>153</td> <td>138.0</td> <td>15.0</td> <td>285</td> <td>Bitoscanate</td> <td>131</td> <td>138.2</td>	229	Bufexamac	153	138.0	15.0	285	Bitoscanate	131	138.2
231Dihydromorphine157178.3 $-21.3$ 287Suffinity argume136.5156.9232Metronidazole159148.210.8288Aprobarbione141141.2233Methallatal160158.41.6289Proglumide142149.9234Halazepam164160.93.1290Ketoconazole146133.5235Clobazam167159.37.7291Cloricromen147.5139.3236Sumatriptan167159.37.7292Felbamate151140.0237Hydroquinine172181.5 $-9.5$ 293Naprosen152157.5238Heptabarbital174158.115.9295Phenallymal156158.4240Ximoprofen178183.7 $-5.7$ 297Bueetin160172.4241Androstanolone181164.116.9298Famotidine163166.9242Zox zolamine184183.80.2299Tyramine164169.3244Acediasulfone194210.4-16.4301Rieperdone170183.1245Probenecid194210.4-2.4305Dextromoramide180182.5247Otsoliol203205.5-2.5304Oxymetholone172.5174.3246Alphadolone200192.08.0303Amoxa	230	Ketobemidone	156	167.4	-11.4	280	Phenacetin	134.5	130.0
222Metronidazole159148.210.8288Approachinge141141.2233Methallatal160158.41.6289Proglumide142149.9234Halazepam164160.93.1290Ketoconazole146133.5235Clobazam167159.37.7291Cloricromen147.5139.3236Sumatriptan169161.27.8293Naproxen152157.5238Heptabarbital174158.115.9294Annotarbital156176.3239Meptobarbital176181.6-5.6296Warfarin157148.4240Ximoprofen178183.7-5.7297Bucetin160172.4241Androstanolone181164.116.9297Bucetin163166.9242Zox azolamine184183.80.2299Tyramine164169.3243Verazide189186.03.0300Acetaminophen169176.5244Acediasulfone194210.4-16.4301Risperdone170183.1245Probenecid195190.44.6302Tetracycline172.5174.3246Alphadolone200192.08.0303Amoxapine175.5182.6247Ursodiol203205.5-2.5304Oxymetholone178<	231	Dihydromorphine	157	178.3	-21.3	287	Sullinpyrazone	130.5	156.9
233Methallatal160158.41.6239Progumber142149.9234Halazepenn164160.93.1290Ketoconazole146133.5235Clobazam167159.37.7291Cloricromen147.5139.3236Sumatriptan169161.27.8293Naproven152157.5237Hydroquinine172181.5-9.5294Amobarbital156158.4238Heptobarbital174158.115.9295Phenallynnal156158.4240Ximoprofen178183.7-5.7297Bucetin160172.4241Androstanolone181164.116.9298Famotiline163166.9242Zox azolamine184183.80.2299Tyramine164169.3243Verazide189186.03.0300Acetaminophen169176.5244Acediasulfone194210.4-16.4301Risperdone170183.1246Alphadolone200192.08.0303Amovapine175.5182.6247Ursodiol203205.5-2.5304Oxymetholone178202.9248Sotalol207209.4-2.4305Destromoramide180182.5254Acadissulfone210184.625.4306Clozapine183<	232	Metronidazole	159	148.2	10.8	288	Aprobarbitone	141	141.2
234Halazepam164160.93.1290Reflection 2012140153.3235Clobazam167159.37.7291Clobaromen147.5139.3236Sumatriptan169161.27.8292Felbamate151140.0237Hydroquinine172181.5 $-9.5$ 294Antobarbital156176.3238Heptabarbital176181.6 $-5.6$ 295Phenallymal156158.4239Mephobarbital176181.6 $-5.6$ 296Warfarin157148.4241Antrostanolone181164.116.9298Famotidine163166.9242Zox azolamine184183.80.2299Tyramine164169.3243Verazide189186.03.0300Acetaminophen169176.5244Acediasulfone194210.4 $-16.4$ 302Tetracycline170183.1245Probenecid195190.44.6302Tetracycline175.5182.6247Ursodiol203205.5 $-2.5$ 303Amoxapine175.5182.6249Acecanide210184.625.4306Clozapine189187.6251Azapropazone228232.9 $-4.9$ 309Spiperone190187.4262Chlorazamil233247.6 $-14.6$ 309Spiper	233	Methallatal	160	158.4	1.6	289	Proglumide Kataanaa 1	142	149.9
235Clobazam167159.37.7291Clothen147.3139.3236Sumatriptan169161.27.8293Naproxen151140.0237Hydroquinine172181.5 $-9.5$ 293Naproxen152157.5238Heptabarbital174158.115.9295Phenallymal156158.4240Ximoprofen178183.7 $-5.7$ 296Warfarin157148.4241Androstanolone181164.116.9298Famoilane160172.4243Verazide189186.03.0300Acetaminophen169176.5244Acediaulfone194210.4 $-16.4$ 301Risperdone170183.1245Probenecid195190.44.6302Tetracycline172.5174.3246Alphadolone200192.08.0303Amoxapine175.5182.6247Ursodiol203205.5 $-2.5$ 304Oxymetholone178202.9248Sotalol207209.4 $-2.4$ 305Destromoramide189187.4251Azagropazone228232.9 $-4.9$ 307Glisoxepid189187.4251Azagropazone228232.9 $-4.9$ 308Spiperone190187.4252Chlorazanil233247.6 $-14.6$ 308Spiperone<	234	Halazepam	164	160.9	3.1	290	Clasismum	140	133.2
226Sumatriptan169161.27.8292Perturbation1511400237Hydroquinine172181.5 $-9.5$ 293Naproxen152157.5238Heptabarbital174158.115.9294Amobarbital156176.3239Mephobarbital176181.6 $-5.6$ 295Phenallymal156158.4240Ximoprofen178183.7 $-5.7$ 296Warfarin157148.4241Androstanolone181164.116.9298Famotidine163166.9242Zox azolamine184183.80.2299Tyramine164169.3244Acediasulfone194210.4 $-16.4$ 300Acetaminophen169176.5244Acediasulfone195190.44.6302Tetracycline172.5174.3246Alphadolene200192.08.0304Moxapine175.5182.6247Ursodiol203205.5 $-2.5$ 303Moxapine175.5182.6249Acecainide210184.625.4305Destromoramide189187.6250Propy Hibiouracil219218.10.9307Gisoxepid189187.6251Azapropazone228232.9 $-4.9$ 309Hymecromone194179.2253Sulfamerazine234243.9 $-9.9$ 310<	235	Clobazam	167	159.3	7.7	291	Cioncromen	147.5	139.3
237Hydroquinine172181.5 $-9.5$ 295Homolarbital132137.5238Heptabarbital174158.115.9295Phenallymal156158.4239Mephobarbital176181.6 $-5.6$ 296Phenallymal156158.4240Ximoprofen178183.7 $-5.7$ 296Warrainin160172.4241Androstanolone181164.116.9297Bucetin160172.4242Zox azolamine184183.80.2299Tyramine164169.3244Acediasulfone194210.4 $-16.4$ 300Acectaminophen169176.5244Acediasulfone195190.44.6302Tetracycline172.5174.3245Frobenecid195190.44.6302Tetracycline175.5182.6247Ursodiol203205.5 $-2.5$ 304Oxymetholone178202.9248Sotalol207209.4 $-2.4$ 306Clozapine183188.3250Propythiouracil219218.10.9307Glosxoptid189187.6251Azapropazone228232.9 $-4.9$ 308Spiperone190187.4252Chlorazmil233247.6 $-14.6$ 308Spiperone190187.4253Sulfamerzine234241244.4 $-3.4$ </td <td>236</td> <td>Sumatriptan</td> <td>169</td> <td>161.2</td> <td>7.8</td> <td>292</td> <td>Nerrouon</td> <td>151</td> <td>140.0</td>	236	Sumatriptan	169	161.2	7.8	292	Nerrouon	151	140.0
238Heptabarbital174158.115.9295Phenallynal150170.3239Mephobarbital176181.6 $-5.6$ 296Warfarin157148.4240Ximoprofen178183.7 $-5.7$ 297Bucetin160172.4241Androstanolome181164.116.9298Famotdine163166.9242Zox azolamine184183.80.2299Tyramine164169.3243Verazide189186.03.0300Acetaminophen169176.5244Acediasulfone194210.4 $-16.4$ 301Risperdone170183.1245Probenecid195190.44.6302Tetracycline172.5174.3246Alphadolone200192.08.0303Amoxapine175.5182.6247Ursodiol203205.5 $-2.5$ 304Oxymetholone178202.9248Sotalol207209.4 $-2.4$ 305Destromoramide180182.5249Acecainide210184.625.4306Clozapine183188.3250Proylthiouracil219218.10.9307Glisoxepid189187.6251Azarpopazone228232.9 $-4.9$ 308Spiperone190187.4252Chlorazanil233247.6 $-14.6$ 309Hymecromo	237	Hydroquinine	172	181.5	-9.5	293	Amobarbital	154	176.2
239Mephobarbital176181.6 $-5.6$ 299Warfarin150150.7240Ximoprofen178183.7 $-5.7$ 297Bucetin160172.4241Androstanolone181164.116.9298Famotidine163166.9242Zox azolamine184183.80.2299Tyramine164169.3243Verazide189186.03.0300Acetaminophen169176.5244Acediasulfone194210.4 $-16.4$ 300Acetaminophen169176.5244Acediasulfone200192.08.0303Amovapine175.5182.6247Ursodiol203205.5 $-2.5$ 304Oxymetholone178202.9248Sotalol207209.4 $-2.4$ 305Dextromoramide180182.5249Acecarinide210184.625.4306Clozapine183188.3250Propythiouracil219218.10.9307Glisosepid189187.4251Azapropazone228232.9 $-4.9$ 308Spiperone190187.4252Chlorazanil233247.6 $-14.6$ 309Hymecromone194179.2253Sulfamerazine234243.9 $-9.9$ 310Piroxicam198212.6254Amiloride241244.4 $-3.4$ 311Car	238	Heptabarbital	174	158.1	15.9	224	Phenallymal	156	170.5
240Ximoprofen178183.7 $-5.7$ 2.97Buckin167172.4241Androstanolone181164.116.9298Famotidine163166.9242Zox azolamine184183.80.2299Tyramine164169.3243Verazide189186.03.0300Acetaminophen169176.5244Acediasulfone194210.4 $-16.4$ 301Risperdone170183.1245Probenecid195190.44.6302Tetracycline172.5174.3246Alphadolone200192.08.0303Amoxapine175.5182.6247Ursodiol203205.5 $-2.5$ 304Oxymetholone178202.9248Sotalol207209.4 $-2.4$ 306Clozapine180182.5249Acecainide210184.625.4306Clozapine183188.3250Propythiouracil219218.10.9307Glisoxepid189187.6252Chlorazanil233247.6 $-14.6$ 308Spiperone190187.4252Chlorazanil233247.6 $-14.6$ 309Hymecromone194179.2253Sulfamerazine234243.9 $-9.9$ 310Piroxicam198212.6254Amiloride241244.4 $-3.4$ 311Caroxazone <td>239</td> <td>Mephobarbital</td> <td>176</td> <td>181.6</td> <td>-5.6</td> <td>295</td> <td>Warfarin</td> <td>150</td> <td>138.4</td>	239	Mephobarbital	176	181.6	-5.6	295	Warfarin	150	138.4
241Androstanolone181164.116.9298Famotidine163166.9242Zox azolamine184183.80.2299Tyramine164169.3243Verazide189186.03.0300Acetaminophen169176.5244Acediasulfone194210.4 $-16.4$ 301Risperdone170183.1245Probenecid195190.44.6302Tetracycline172.5174.3246Alphadolone200192.08.0303Amosapine175.5182.6247Ursodiol203205.5 $-2.5$ 304Oxymetholone178202.9248Sotalol207209.4 $-2.4$ 305Dextromoramide180182.5249Acecainide210184.625.4306Clozapine183188.3250Propylthiouracil219218.10.9307Glisoxepid189187.4252Chlorazanil233247.6 $-14.6$ 309Hymecromone194179.2253Sulfamerazine234243.9 $-9.9$ 310Piroxicam198212.6254Amiloride241244.4 $-3.4$ 311Caroazone203158.5257Fofosal268266.91.1314Griseofulvin219217.0258Moxestrol280241.8382315Thioacetazone </td <td>240</td> <td>Ximoprofen</td> <td>178</td> <td>183.7</td> <td>-5.7</td> <td>290</td> <td>Bucetin</td> <td>160</td> <td>172.4</td>	240	Ximoprofen	178	183.7	-5.7	290	Bucetin	160	172.4
242Zox azolamine184183.80.2299Tyramine164169.3243Verazide189186.03.0300Acetaminophen169176.5244Acediasulfone194210.4-16.4301Risperdone170183.1245Probenecid195190.44.6302Tetracycline172.5174.3246Alphadolone200192.08.0303Amoxapine175.5182.6247Ursodiol203205.5-2.5304Oxymetholone178202.9248Sotalol207209.4-2.4305Dextromoramide180182.5249Acecainide210184.62.5.4306Clozapine183188.3250Propylthiouracil219218.10.9308Spiperone190187.4251Azapropazone228232.9-4.9308Spiperone190187.4252Chlorazanil233247.6-14.6309Hymecromone194179.2253Sulfamerazine234243.9-9.9310Piroxicam198212.6254Amiloride241244.4-3.4311Caroxazone203158.5255Azathioprine243.5240.33.2212Baclofen207214.7256Morphine255234.720.3313Bupereorphine209<	241	Androstanolone	181	164.1	16.9	298	Eamotidine	163	166.9
243Verazide189186.03.0300Acctaminophen169176.5244Accdiasulfone194210.4 $-16.4$ 301Risperdone170183.1245Probenecid195190.44.6302Tetracycline172.5174.3246Alphadolone200192.08.0303Amoxapine175.5182.6247Ursodiol203205.5 $-2.5$ 304Oxymetholone178202.9248Sotalol207209.4 $-2.4$ 305Dextromoramide180182.5249Acccainide210184.625.4306Clozapine183188.3250Propythiouracil219218.10.9307Glisoxepid189187.6251Azapropazone228229 $-4.9$ 308Spiperone190187.4252Chlorazanil233247.6 $-14.6$ 309Hymecromone194179.2253Sulfamerazine234243.9 $-9.9$ 310Piroxicam198212.6254Amiloride241244.4 $-3.4$ 311Caroxazone203188.5255Azathioprine243.5240.33.2312Baclofen207214.7256Morphine255234.720.3313Buprenorphine209213.5257Fosfosal268266.91.1314Griscofulvin <td>242</td> <td>Zox azolamine</td> <td>184</td> <td>183.8</td> <td>0.2</td> <td>290</td> <td>Tyramine</td> <td>164</td> <td>169.3</td>	242	Zox azolamine	184	183.8	0.2	290	Tyramine	164	169.3
244Acediasulfone194210.4 $-16.4$ 303Risperdone103103245Probenecid195190.44.6302Tetracycline172.5174.3246Alphadolone200192.08.0303Amoxapine175.5182.6247Ursodiol203205.5 $-2.5$ 304Oxymetholone178202.9248Sotalol207209.4 $-2.4$ 305Dextromoramide180182.5249Acceainide210184.625.4306Clozapine183188.3250Propylthiouracil219218.10.9307Glisoxepid189187.6251Azapropazone228232.9 $-4.9$ 308Spiperone190187.4252Chlorazanil233247.6 $-14.6$ 309Hymecromone194179.2253Sulfamerazine234243.9 $-9.9$ 310Piroxicam198212.6254Amiloride241244.4 $-3.4$ 311Caroxazone203158.5255Azahioprine243.5240.33.2312Balfofen207214.7256Morphine255244.720.3313Buprenorphine209213.5257Fosfosal268266.91.1314Griscofulvin219217.0258Moxestrol280241.838.2315Thioacetazone<	243	Verazide	189	186.0	3.0	300	Acetaminophen	169	176.5
245Probenecid195190.44.6307Tetracycline175.5174.3246Alphadolone200192.08.0303Amoxapine175.5182.6247Ursodiol203205.5 $-2.5$ 304Oxymetholone178202.9248Sotalol207209.4 $-2.4$ 305Dextromoramide180182.5249Acecainide210184.625.4306Clozapine183188.3250Propylthiouracil219218.10.9307Glisoxepid189187.6251Azapropazone228232.9 $-4.9$ 308Spiperone190187.4252Chlorazanil233247.6 $-14.6$ 309Hymecromone194179.2253Sulfamerazine234243.9 $-9.9$ 310Piroxicam198212.6254Amiloride241244.4 $-3.4$ 311Caroxazone203158.5255Azathioprine243.5240.33.2312Baclofen207214.7256Morphine255234.720.3313Buprenophine209213.5257Fosfosal268266.91.1314Griscofulvin219217.0258Moxestrol280241.838.2315Thioacetazone227.5220.7259Flucytosine296294.21.8316Oxibendazole<	244	Acediasulfone	194	210.4	-16.4	301	Risperdone	170	183.1
246Alphadolone200192.08.0303Amoxapine175.5182.6247Ursodiol203205.5 $-2.5$ 304Oxymetholone178202.9248Sotalol207209.4 $-2.4$ 305Dextromoramide180182.5249Acecainide210184.625.4306Clozapine183188.3250Propythiouracil219218.10.9307Glisoxepid189187.6251Azapropazone228232.9 $-4.9$ 308Spiperone190187.4252Chlorazanil233247.6 $-14.6$ 309Hymecromone194179.2253Sulfamerazine234243.9 $-9.9$ 310Piroxicam198212.6254Amiloride241244.4 $-3.4$ 311Caroxazone203158.5255Azathioprine243.5240.33.2312Baclofen207214.7256Morphine255234.720.3313Buprenorphine209213.5257Fosfosal268266.91.1314Griseofulvin219217.0258Moxestrol280241.838.2315Thioacetazone227.5220.7259Flucvtosine296294.21.8316Oxibendazole230224.4 <i>Prediction</i>	245	Probenecid	195	190.4	4.6	302	Tetracycline	172.5	174.3
247Ursodiol203205.5-2.5304Oxymetholone178202.9248Sotalol207209.4-2.4305Dextromoramide180182.5249Acecaninide210184.625.4306Clozapine183188.3250Propylthiouracil219218.10.9307Glisoxepid189187.6251Azapropazone228232.9-4.9308Spiperone190187.4252Chlorazanil233247.6-14.6309Hymecromone194179.2253Sulfamerazine234243.9-9.9310Piroxicam198212.6254Amiloride241244.4-3.4311Caroxazone203158.5255Azathioprine243.5240.33.2312Baclofen207214.7256Morphine255234.720.3313Buprenorphine209213.5257Fosfosal268266.91.1314Griseofulvin219217.0258Moxestrol280241.838.2315Thioacetazone227.5220.7259Flucytosine296294.21.8316Oxibendazole230224.4Prediction-116.70.7318Lotifen238232.8261Tetrachloroethylene-22.3-24.11.8319Zolimidine242244.0<	246	Alphadolone	200	19 <b>2</b> .0	8.0	303	Amoxapine	175.5	182.6
248Sotalol207209.4-2.4305Dextromoramide180182.5249Acecainide210184.625.4306Clozapine183188.3250Propylthiouracil219218.10.9307Glisoxepid189187.6251Azapropazone228232.9-4.9308Spiperone190187.4252Chlorazanil233247.6-14.6309Hymecromone194179.2253Sulfamerazine234243.9-9.9310Piroxicam198212.6254Amiloride241244.4-3.4311Caroxazone203158.5255Azathioprine243.5240.33.2312Baclofen207214.7256Morphine255234.720.3313Buprenorphine209213.5257Fosfosal268266.91.1314Griseofulvin219217.0258Moxestrol280241.838.2315Thioacetazone227.5220.7259Flucytosine296294.21.8316Oxibendazole230224.4Prediction317Ubenimex233231.6232.8231.6260Sevoflurane-116.70.7318Lotrifen238232.8261Tetrachloroethylene-22.3-24.11.8319Zolimidine242244.0	247	Ursodiol	203	205.5	-2.5	304	Oxymetholone	178	202.9
249Acecainide210184.625.4306Clozapine183188.3250Propylthiouracil219218.10.9307Glisoxepid189187.6251Azapropazone228232.9-4.9308Spiperone190187.4252Chlorazanil233247.6-14.6309Hymecromone194179.2253Sulfamerazine234243.9-9.9310Piroxicam198212.6254Amiloride241244.4-3.4311Caroxazone203158.5255Azathioprine243.5240.33.2312Baclofen207214.7256Morphine255234.720.3313Buprenorphine209213.5257Fosfosal268266.91.1314Griscofulvin219217.0258Moxestrol280241.838.2315Thioacetazone227.5220.7259Flucytosine296294.21.8316Oxibendazole230224.4Prediction317Ubenimex233231.6231.6232.8232.8260Sevoflurane-116-116.70.7318Lotrifen238232.8261Tetrachloroethylene-22.3-24.11.8319Zolimidine242244.0262Paraldehyde12.628.9-16.3320Flumequine253 <td>248</td> <td>Sotalol</td> <td>207</td> <td>209.4</td> <td>-2.4</td> <td>305</td> <td>Dextromoramide</td> <td>180</td> <td>182.5</td>	248	Sotalol	207	209.4	-2.4	305	Dextromoramide	180	182.5
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	249	Acecainide	210	184.6	25.4	306	Clozapine	183	188.3
251Azapropazone228232.9 $-4.9$ 308Spiperone190187.4252Chlorazanil233247.6 $-14.6$ 309Hymecromone194179.2253Sulfamerazine234243.9 $-9.9$ 310Piroxicam198212.6254Amiloride241244.4 $-3.4$ 311Caroxazone203158.5255Azathioprine243.5240.33.2312Baclofen207214.7256Morphine255234.720.3313Buprenorphine209213.5257Fosfosal268266.91.1314Griseofulvin219217.0258Moxestrol280241.838.2315Thioacetazone227.5220.7259Flucytosine296294.21.8316Oxibendazole230224.4Prediction317Ubenimex233231.6260Sevoflurane $-116$ $-116.7$ $0.7$ 318Lotrifen238232.8261Tetrachloroethylene $-22.3$ $-24.1$ 1.8319Zolimidine242244.0262Paraldehyde12.628.9 $-16.3$ 320Flumequine253252.0263Tranylcypromine2821.07.0321Reserpine264.5264.3264Ifosfamide4851.7 $-3.7$ 322Hydrochlorthiazide274272.4	250	Propylthiouracil	219	218.1	0.9	307	Glisoxepid	189	187.6
252Chlorazanil233247.6 $-14.6$ 309Hymecromone194179.2253Sulfamerazine234243.9 $-9.9$ 310Piroxicam198212.6254Amiloride241244.4 $-3.4$ 311Caroxazone203158.5255Azathioprine243.5240.33.2312Baclofen207214.7256Morphine255234.720.3313Buprenorphine209213.5257Fosfosal268266.91.1314Griseofulvin219217.0258Moxestrol280241.838.2315Thioacetazone227.5220.7259Flucytosine296294.21.8316Oxibendazole230224.4 <i>Prediction</i> -116-116.70.7318Lotrifen238232.8261Tetrachloroethylene-22.3-24.11.8319Zolimidine242244.0262Paraldehyde12.628.9-16.3320Flumequine253252.0263Tranylcypromine2821.07.0321Reserpine264.5264.3264Ifosfamide4851.7-3.7322Hydrochlorthiazide274272.4265Triprolidine6059.30.7323Acedapsone289268.8	251	Azapropazone	228	232.9	-4.9	308	Spiperone	190	187.4
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	252	Chlorazanil	233	247.6	-14.6	309	Hymecromone	194	179.2
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	253	Sulfamerazine	234	243.9	-9.9	310	Piroxicam	198	212.6
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	254	Amiloride	241	244.4	-3.4	311	Caroxazone	203	158.5
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	255	Azathioprine	243.5	240.3	3.2	312	Baclofen	207	214.7
257       Fosfosal       268       266.9       1.1       314       Griseofulvin       219       217.0         258       Moxestrol       280       241.8       38.2       315       Thioacetazone       227.5       220.7         259       Flucytosine       296       294.2       1.8       316       Oxibendazole       230       224.4         Prediction       317       Ubenimex       233       231.6         260       Sevoflurane       -116       -116.7       0.7       318       Lotrifen       238       232.8         261       Tetrachloroethylene       -22.3       -24.1       1.8       319       Zolimidine       242       244.0         262       Paraldehyde       12.6       28.9       -16.3       320       Flumequine       253       252.0         263       Tranylcypromine       28       21.0       7.0       321       Reserpine       264.5       264.3         264       Hosfamide       48       51.7       -3.7       322       Hydrochlorthiazide       274       272.4         265       Triprolidine       60       59.3       0.7       323       Acedapsone       289       268.8	256	Morphine	255	234.7	20.3	313	Buprenorphine	209	213.5
258       Moxestrol       280       241.8       38.2       315       Thioacetazone       227.5       220.7         259       Flucytosine       296       294.2       1.8       316       Oxibendazole       230       224.4         Prediction       317       Ubenimex       233       231.6         260       Sevoflurane       -116       -116.7       0.7       318       Lotrifen       238       232.8         261       Tetrachloroethylene       -22.3       -24.1       1.8       319       Zolimidine       242       244.0         262       Paraldehyde       12.6       28.9       -16.3       320       Flumequine       253       252.0         263       Tranylcypromine       28       21.0       7.0       321       Reserpine       264.5       264.3         264       Hosfamide       48       51.7       -3.7       322       Hydrochlorthiazide       274       272.4         265       Triprolidine       60       59.3       0.7       323       Acedapsone       289       268.8	257	Fosfosal	268	266.9	1. <b>1</b>	314	Griseofulvin	219	217.0
259       Flucytosine       296       294.2       1.8       316       Oxibendazole       230       224.4         Prediction       317       Ubenimex       233       231.6         260       Sevoflurane       -116       -116.7       0.7       318       Lotrifen       238       232.8         261       Tetrachloroethylene       -22.3       -24.1       1.8       319       Zolimidine       242       244.0         262       Paraldehyde       12.6       28.9       -16.3       320       Flumequine       253       252.0         263       Tranylcypromine       28       21.0       7.0       321       Reserpine       264.5       264.3         264       Ifosfamide       48       51.7       -3.7       322       Hydrochlorthiazide       274       272.4         265       Triprolidine       60       59.3       0.7       323       Acedapsone       289       268.8	258	Moxestrol	280	241.8	38.2	315	Thioacetazone	227.5	220.7
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	259	Flucytosine	<b>2</b> 96	294.2	1.8	316	Oxibendazole	230	224.4
260Sevoflurane-116-116.70.7318Lotrifen238232.8261Tetrachloroethylene-22.3-24.11.8319Zolimidine242244.0262Paraldehyde12.628.9-16.3320Flumequine253252.0263Tranyleypromine2821.07.0321Reserpine264.5264.3264Ifosfamide4851.7-3.7322Hydrochlorthiazide274272.4265Triprolidine6059.30.7323Acedapsone289268.8		Prediction				317	Ubenimex	233	231.6
261Tetrachloroethylene-22.3-24.11.8319Zolimidine242244.0262Paraldehyde12.628.9-16.3320Flumequine253252.0263Tranyleypromine2821.07.0321Reserpine264.5264.3264Ifosfamide4851.7-3.7322Hydrochlorthiazide274272.4265Triprolidine6059.30.7323Acedapsone289268.8	260	Sevoflurane	-116	-116.7	0.7	318	Lotrifen	238	232.8
262Paraldehyde12.628.9-16.3320Flumequine253252.0263Tranylcypromine2821.07.0321Reserpine264.5264.3264Ifosfamide4851.7-3.7322Hydrochlorthiazide274272.4265Triprolidine6059.30.7323Acedapsone289268.8	261	Tetrachloroethylene	-22.3	-24.1	1.8	319	Zolimidine	242	244.0
263         Tranylcypromine         28         21.0         7.0         321         Reserptine         264.5         264.3           264         Ifosfamide         48         51.7         -3.7         322         Hydrochlorthiazide         274         272.4           265         Triprolidine         60         59.3         0.7         323         Acedapsone         289         268.8	262	Paraldehyde	12.6	28.9	-16.3	320	Flumequine	253	252.0
264         Ifosfamide         48         51.7         -3.7         322         Hydrochlorthiazide         274         272.4           265         Triprolidine         60         59.3         0.7         323         Acedapsone         289         268.8	263	Tranylevpromine	28	21.0	7.0	321	Reserpine	264.5	264.3
265         Triprolidine         60         59.3         0.7         323         Acedapsone         289         268.8	264	Ifosfamide	48	51.7	-3.7	322	Hydrochlorthiazide	274	272.4
	265	Triprolidine	60	59.3	0.7	323	Acedapsone	289	268.8

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optimized neural network could simulate the complicated nonlinear relationship between melting point values and the PC's. The RMSE of 48.176 for the prediction set by the PC-GA-MLR model should be compared with the value of 12.77 for the PC-GA-ANN model. As can be seen, ability of the proposed model to predict the melting point is very higher than the QSPR models proposed in recently published paper (RMSE of 12.767 should be compared with 40.7 °C). It can be seen that although parameters appearing in the PC-GA-MLR model are used as inputs for the generated PC-GA-ANN model, the statistics has shown a large improvement. These improvements are due to the fact that melting point of the compounds shows non-linear correlations with the principal components.

The melting point of a compound is governed by the intermolecular hydrogen-bonding ability of the molecules. the molecular packing in crystals (effects from molecular shape, size, and symmetry), and other intermolecular interactions such as charge transfer and dipole-dipole interactions in the solid phase.<sup>6</sup> The solubility of a compound can be regarded as a partitioning of the compound between its crystal lattice and the solvent. If the forces holding the molecule in the crystal are high, then the solubility will be low. For the same reason the melting point will be high. since melting point is a measure of the energy required to disrupt the crystal lattice. The molar aqueous solubility can be calculated using melting point of compounds by the general solubility equation.<sup>2</sup> Then melting points affect solubility, and solubility controls toxicity in that; if a compound is only poorly soluble, its concentration in the aqueous environment may be too low for it to exert a toxic effect.<sup>5</sup> As a result prediction of melting point of the compounds using the proposed non-linear model is a valuable method in designing new drugs within a specified range of melting point and solubility.

### Conclusions

Quantitative-structure property relationships have been applied for prediction of melting point for 323 drug-like compounds by using the principal component-genetic algorithm-multi parameter linear regression (PC-GA-MLR) and principal component-genetic algorithm-artificial neural network (PC-GA-ANN) methods. Comparison of the statistical parameters obtained for training, validation and prediction sets by the PC-GA-MLR and PC-GA-ANN models demonstrate superiority of the PC-GA-ANN model over the PC-GA-MLR model. Root-mean square error of 48.18 for the prediction set by the PC-GA-MLR model should be compared with the value of 12.77 °C for the PC-GA-ANN model. Since the improvement of the results obtained using non-linear model (PC-GA-ANN) is considerable, it can be concluded that the non-linear characteristics of the principal components on melting point of the compounds is serious.

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