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# The determination of toxicities of sulphonylurea and phenylurea herbicides with quantitative structure-toxicity relationship (QSTR) studies

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#### ABSTRACT

Sulphonylurea and phenylurea herbicides are two groups of herbicides that are most commonly used worldwide. Quantitative structure–toxicity relationship models were derived for estimating the acute oral toxicity of these herbicides to male rats. The 20 chemicals of the training set and the seven compounds of external testing set were described by means of using descriptors for lipophilicity, polarity and molecular geometry, as well as the calculation of quantum chemical descriptors for energy. Model development to predict the toxicity of sulphonylurea and phenylurea herbicides in different matrices was carried out using multiple-linear regression. The model was validated internally and externally. In the present study, QSTR model was used for the first time to understand the inherent relationships between the sulphonyl and phenylurea-type herbicide molecules and their toxic behaviour. Such studies provide mechanistic insight about structure–toxicity relationships and assist in the design of less toxic herbicides.

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#### 1. Introduction

Pesticide compounds are found in significant quantities in the environment and foodstuffs worldwide due to their massive usage (every year an estimated 2.5 million tons of pesticides are applied to agricultural crops worldwide) making their toxicity an unresolved issue (Pimentel, 1995). Sulphonylureas are a family of herbicides which selectively control a range of undesirable plants, such as grasses, which interfere with the growth of foodcrops and vegetables. These herbicides have now been developed and commercialized worldwide for application with all major agronomic crops and for many specialty uses. Sulphonylureas represent a major advance in global crop protection technology and have revolutionized weed control by interfering with a key enzyme required for weed cell growth – acetolactate synthase. Their highly selective and specific mode of action means that these agents are compatible with the global trend toward post emergence weed control and integrated pest management.

Another family of herbicides are phenylurea herbicides. They are used for general weed control in agricultural monagricultural practices, for example, along railroads and industrial areas. Many more derivatives of this class of compounds have been marketed. The herbicidal action of these compounds is based on their ability to inhibit photosynthesis.

Abbreviations: QSTR, quantitative structure–toxicity relationship; LD<sub>50</sub>, lethal dose; QSAR, quantitative structure–activity relationship; HOMO, highest occupied molecular orbital; LUMO, lowest unoccupied molecular orbital; AM1, austin model 1; PRESS, predicted residual sums of squares; SSY, sum of squares of Y.

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E-mail addresses: alperhc@yahoo.com, alperhc58@gmail.com (A. Can). 1382-6689/\$ – see front matter © 2013 Elsevier B.V. All rights reserved. http://dx.doi.org/10.1016/j.etap.2013.02.001

Toxicity has been quantified in terms of  $LD_{50}$ , which is the amount of a material, given all at once, which causes the death of 50% (one half) of a group of test animals. The  $LD_{50}$  is one way to measure the short-term poisoning potential (acute toxicity) of a material in experimental animals and in 1999, 2,607,349 animals on a total of 9,814,171 (Commission of the European Communities, 2003) were used in toxicity studies. The  $LD_{50}$  can be found for any route of entry or administration but dermal (applied to the skin) and oral (given by mouth) administration methods are the most common. The test is expensive, time consuming and ethically questionable and unfortunately alternative methods, such as QSAR models, are not numerous enough or sufficiently investigated to replace many animal tests (Tong et al., 2003).

As experimental determinations of toxicity are costly and time-consuming, it is preferred to develop mathematical equations which can be able to establish the relationships between the toxicity and structure of the toxic compound. The objective of structure–toxicity analyses is to predict toxic activity from information on molecular structure. Quantitative structure–toxicity relationship (QSTR) provides a relevant tool for toxicity evaluation and prediction, and can also give some insight into the mechanism of toxic actions (Schultz et al., 2003; Eriksson et al., 2003).

The aim of this study was to derive a QSTR model allowing us to simulate the acute oral toxicity of phenyl and sulphonylurea herbicides to rats. After calculating numerous molecular descriptors, most effective of them were selected via statistical method. Four descriptors reflecting the main characteristics of the sulphonyl and phenylurea-type herbicide molecules were found in this study. The best QSTR model was established on these four descriptors. The model was tested either internal or external test sets for the validation of the model equation. The test results indicate that the calculated QSTR model can be used with confidence for prediction of toxicity of phenylureatype herbicide molecules.

# 2. Materials and methods

#### 2.1. Toxicity data

The potency was defined as  $\log 1/C$  where C was the molar lethal dose 50 ( $LD_{50}$ ) values of the compounds. Before the calculations in this study,  $LD_{50}$  values (rat, male via oral) and the structural formulas of sulphonyl and phenylurea compounds were obtained from the literatures [1–51]. All this acute toxicity data being reported in mg/kg, for modelling purposes, they were first converted into mmol/kg and then translated to their negative logarithms (see Table 1).

#### 2.2. Molecular descriptors

Before the calculations of molecular descriptors of the compounds, energetically stable molecular structures are needed. For this purpose, all compounds were optimized using MM+ (molecular mechanic) method for generating initial structures at the beginning of the calculations. In order to obtain minimum energy structures, second geometry optimization were performed with AM1 semi-empirical calculations. Geometry optimization calculations employ energy minimization algorithms to locate stable structures. Geometrically optimized structures were used for the calculations of molecular descriptors. Molecular descriptors consist of octanol/water partition coefficient (log P), dipole moment, molar refractivity, polarizability, molar volume, hydration energy, surface area (grid and approximate), molecular mass, HOMO (highest occupied molecular orbital) and LUMO (lowest unoccupied molecular orbital) energies (from AM1 semi-empirical single point calculation). Single-point calculations determine the molecular energy and properties for a given fixed geometry. HyperChem (TM) (Student Edition 8.0, Hypercube, Inc., 1115 NW 4th Street, Gainesville, FL 32,601, USA.) software was used for geometry optimizations and calculations of molecular descriptors except molecular mass.

The HOMO (highest occupied molecular orbital) and LUMO (lowest unoccupied molecular orbital) energies are electronic molecular descriptors.

The steric effects were considered by means of surface areas and molar volume. Surface areas are estimated using a rapid, approximate method due to W.C. Still and co-workers or using a slower grid-based method. Molecular volumes, bounded by Van der Waals or solvent accessible surfaces, are calculated using a grid method (Hasel et al., 1988).

Specifically, the hydration energy and log P were considered as descriptors for hydrophobic effects. Hydration energy (for peptides and similar systems), using a method parameterized by Scheraga (Ooi et al., 1987), is predicted based on the approximate surface area calculation. The log P (the log of the octanol–water partition coefficient), a hydrophobicity indicator, using an atom fragment method developed by Ghose et al. (1988). For a sample of organic molecules, the method yields a correlation coefficient (r) with experimental values of 0.92 and a standard error of 0.36.

As polar descriptors, refractivity, dipole moment and polarizability were calculated. Refractivity is also computed using an atom-based fragment method due to Ghose and Grippen (1987). For a sample of organic molecules, the method yields a correlation coefficient (r) with experimental values of 0.995 and a standard error of 1.1. Polarizability, using an atom-based method due to Miller (1990). For a sample of organic molecules, the method yields a correlation coefficient (r) with experimental values of 0.991 and a standard error of 9.3. Molecular mass is calculated using a straightforward method.

#### 2.3. Statistical analyses

In a first step, attempts were made to relate the  $LD_{50}$  data to the molecular descriptors by means of a linear statistical method. The multiple-linear regression method was selected due to its ability to derive robust model.

# 3. Results

The toxicity of some sulphonylurea and phenylurea herbicides were previously determined experimentally [1–51]. The toxicity data,  $LD_{50}$ , in the literature was converted to log 1/C as described above. Twenty training compounds were used for QSAR study (see Table 2). The quantitative structure–toxicity

Name of compoundD <sub>20</sub> mg/kg [Ref. no.]MW (g/mo)C (mmo/kg)0g/LCAmidoulphuron500 [1355.3400.01181.527Azimsulphuron-methyl500 [3]410.4010.01221.912Chloromuron-methyl500 [3]357.7710.00952.0095Chloromuron-methyl500 [7]414.8200.00952.0095Chloromuron-methyl500 [7]414.8200.00952.0095Cyclosulpharunon500 [7]414.8200.00922.058Dhanetsulphuron-methyl500 [10]395.3900.00222.058Ehassulphuron-methyl500 [10]395.3900.00222.058Flassulphuron-methyl500 [12]454.420.01211.958Habasulphuron-methyl500 [12]454.8110.00211.958Habasulphuron-methyl500 [14]410.870.01211.958Habasulphuron500 [14]410.870.01211.958Habsulphuron-methyl500 [14]410.470.01211.958Habsulphuron-methyl500 [14]410.4640.01221.942Nocsulphuron500 [21]463.3530.01311.854Nocsulphuron500 [21]410.4040.01211.914Nocsulphuron-methyl500 [21]410.4040.01211.914Nocsulphuron-methyl500 [21]410.4040.01211.914Nocsulphuron-methyl500 [21]410.4040.01211.914Nocsulphuron-methyl500 [21]410.4040.0	Table 1 – The LD <sub>50</sub> (mg/kg	), MW (g/mol), C (mmol/kg) and log	g 1/C values of the herbic	ides.	
Amidoughuron         5000 [1]         355.340         0.0141         1.547           Atimsubhuron-methyl         5000 [3]         410.491         0.0132         1.948           Bensubhuron-methyl         100 [3]         357.771         0.0085         2.0089           Chlorsubhuron         103 [3]         357.771         0.0085         2.0089           Chlorsubhuron         100 [7]         421.488         0.0119         1.9258           Ethamestalphuron-methyl         5000 [10]         407.324         0.0122         1.9452           Ethawsubphuron         5000 [10]         407.324         0.0123         1.9110           Foramsubphuron-methyl         5000 [11]         455.442         0.0111         1.9566           Flazsubphuron         5000 [14]         443.811         0.030         2.237           Imacosubphuron         5000 [16]         381.363         0.0131         1.884           Indosubphuron-methyl         5000 [17]         410.404         0.0122         1.916           Obssissubphuron         5000 [16]         381.363         0.0131         1.884           Oxicoubphuron         5000 [17]         410.404         0.0122         1.916           Oxicoubphuron         5000 [18]	Name of compound	LD <sub>50</sub> mg/kg [Ref. no.]	MW (g/mol)	C (mmol/kg)	log 1/C
Azimsulphuron50002424.3940.0181.2928Bensulphuron-methyl5000141.4200.01221.5142Chloraulphuron3033537.7710.08852.0689Chosulphuron500012413.4050.00992.0049Chosulphuron500012412.4280.01191.5258Ethamstalphuron-methyl500010447.3240.01221.9142Ethamstalphuron350010447.3240.01211.9160Fazasulphuron500011445.4610.01071.9588Flazasulphuron-methyl500012463.6610.01071.9588Haloutphuron-methyl500014412.4870.01211.9168Inazosulphuron-methyl500016381.3630.01311.8824Nicosulphuron-methyl500016381.3630.01311.8824Nicosulphuron500017440.4130.01221.9168Inazosulphuron-methyl500012443.4360.01211.9169Nicosulphuron500012443.4360.01211.9169Nicosulphuron500012443.3760.01371.8262Nicosulphuron-methyl500012443.3760.01211.9176Sulfosulphuron-methyl500012443.43760.01211.9176Sulfosulphuron-methyl500012443.43760.01221.9376Sulfosulphuron-methyl500012443	Amidosulphuron	5000 [1]	355.340	0.0141	1.8517
Bensuphuron-methyl         5000 [3]         410.401         0.0122         1.9142           Chlorsmuron-nethyl         3033 [5]         377.771         0.0085         2.0689           Chosuphuron         4102 [6]         413.4850         0.0099         2.0344           Cyclosuphuron         5000 [7]         421.428         0.0119         1.9328           Ethametsuphuron-methyl         5000 [0]         447.428         0.0122         1.9142           Ethamsuphuron         5000 [10]         447.534         0.0123         1.9110           Foramsuphuron         5000 [11]         452.442         0.0111         1.9566           Foramsuphuron-methyl         5000 [12]         463.361         0.0107         1.9668           Halosuphuron-methyl         5000 [12]         463.363         0.0131         1.824           Micsouphuron         5000 [12]         463.431         0.0123         1.9101           Virisouphuron-methyl         5000 [12]         463.436         0.0121         1.9142           Orassuphuron         5000 [12]         463.436         0.0121         1.9142           Orassuphuron         5000 [23]         463.456         0.0101         1.9275           Pravsuphuron-methyl         5000 [2	Azimsulphuron	5000 [2]	424.394	0.0118	1.9288
Chlorauphuron4102 [4]414.8200.00992.0049Chlorauphuron4102 [6]413.4650.00992.034Cyclosuphamuron5000 [7]421.4280.01191.9288Ehamstaulphuron-methyl5000 [8]410.4040.01221.9428Ehamstaulphuron5000 [10]473.540.01331.9110Foramuphuron5000 [11]452.4420.01111.9688Halseulphuron-methyl5000 [12]463.5410.00302.2857Imazosulphuron5000 [14]412.8070.01211.9168Halseulphuron-methyl5000 [14]413.4810.00302.2857Imazosulphuron5000 [14]413.4810.00302.2857Indesulphuron-methyl5000 [14]413.4820.01211.9168Indesulphuron5000 [17]410.4040.01221.942Vicosulphuron5000 [18]449.3730.00171.9716Prirasulphuron-methyl5000 [21]413.4280.01211.9174Yirasulphuron-methyl5000 [21]413.4280.01211.9174Yirasulphuron5000 [23]468.3350.01241.9378Sulforetturon-methyl5000 [24]470.4750.01611.9376Sulforetturon-methyl5000 [24]470.4750.01641.9378Sulforetturon-methyl5000 [24]470.4750.01651.9376Sulforetturon-methyl5000 [24]470.4750.01651.9376Sulforetturon-methyl5000 [24]470.475	Bensulphuron-methyl	5000 [3]	410.401	0.0122	1.9142
Chlosulphuron303 [5]357.710.00852.0689Chosulphuron402 [6]414.4050.00191.0204Cyclosulphuron-methyl500 [7]421.4280.01121.9142Ethanstulphuron3270 [9]398.3500.00022.0858Flazsulphuron5000 [10]407.3240.01131.9110Foramsulphuron-methyl5000 [12]465.3610.01071.9686Flazsulphuron-methyl1287 [13]434.8110.00302.5287Inasculphuron-methyl5000 [14]412.8070.01211.9168Idosulphuron-methyl5000 [16]381.3630.01311.8824Nicssulphuron5000 [17]410.4040.01221.9162Mesulphuron-methyl5000 [18]406.4130.01231.9100System5000 [18]406.4130.01211.9176Pyrazsulphuron-methyl5000 [21]413.4280.01211.9174Pyrazsulphuron-methyl5000 [22]394.3760.01371.8626Pyrazsulphuron-methyl5000 [23]364.3760.01371.8626Sulfosulphuron-methyl5000 [24]470.4750.01061.9786Trissulphuron-methyl5000 [26]387.3850.01241.9191Trissulphuron-methyl5000 [26]387.3850.01261.9894Sulfosulphuron-methyl5000 [26]387.3850.01261.9891Trissulphuron5000 [26]387.3850.01261.9994Trissulphuron5000 [26]387.385 </td <td>Chloromuron-ethyl</td> <td>4102 [4]</td> <td>414.820</td> <td>0.0099</td> <td>2.0049</td>	Chloromuron-ethyl	4102 [4]	414.820	0.0099	2.0049
Cinosulphuron         412 (6)         413.05         0.0099         2.0034           Cyclosulphuron-methyl         500 [8]         410.404         0.012         1.928           Ethamssulphuron         500 [10]         407.324         0.0123         1.9110           Flazasulphuron         500 [11]         453.442         0.0111         1.9566           Flazasulphuron-methyl         500 [12]         463.561         0.0107         1.9688           Halosulphuron-methyl         500 [14]         412.807         0.0121         1.9168           Halosulphuron-methyl         500 [17]         440.444         0.0122         1.9168           Idosulphuron         500 [17]         410.404         0.0121         1.9168           Idosulphuron         500 [17]         410.404         0.0122         1.9168           Vicosulphuron         500 [17]         410.404         0.0121         1.9168           Vicosulphuron         500 [18]         463.316         0.0131         1.8824           Nicosulphuron         500 [21]         413.428         0.0121         1.9168           Vicosulphuron         500 [21]         413.428         0.0121         1.9168           Sulforeturon-methyl         5000 [21]	Chlorsulphuron	3053 [5]	357.771	0.0085	2.0689
Cyclosulphamuron         5000 [7]         421.428         0.0119         19258           Ethamstuphuron         3270 [9]         398.390         0.0082         2.0588           Flazasulphuron         5000 [10]         452.442         0.0111         1.9566           Framsulphuron-methyl         120         453.651         0.01021         1.9568           Halsoulphuron-methyl         2877 [13]         454.811         0.0030         2.5287           Imazosulphuron         5000 [14]         412.807         0.0121         1.9168           Iodosulphuron-methyl         5000 [15]         493.233         0.054         2.2527           Micsoulphuron         5000 [15]         443.433         0.0123         1.9100           Pyrainsulphuron-methyl         5000 [13]         446.433         0.0123         1.9100           Pyrainsulphuron-methyl         5000 [24]         449.475         0.0106         1.9376           Sulfosulphuron-methyl         5000 [24]         440.475         0.0106         1.9376           Sulfosulphuron-methyl         5000 [24]         470.475         0.0106         1.9376           Sulfosulphuron-methyl         5000 [24]         492.429         0.0124         1.9934           Trinsulphuron	Cinosulphuron	4102 [6]	413.405	0.0099	2.0034
Ethansetulphuron-methyl5000 [8]41.04040.01221.9142Ethoxysulphuron5000 [10]407.3240.01231.9110Foramsulphuron-methyl5000 [12]452.4420.01131.9566Haysulphuron-methyl1.287 [13]44.8110.00302.5287Imazosulphuron5000 [14]44.8110.00302.5287Imazosulphuron5000 [15]493.2330.00542.2652Metsulphuron-methyl5000 [16]381.3630.01311.8824Nicsulphuron5000 [17]410.4040.01221.9168Nicsulphuron-methyl5000 [18]468.3360.01071.9716Oxsasulphuron-methyl5000 [21]419.3780.00242.6287Pyrmsulphuron-methyl5000 [22]430.4740.01151.9376Ontor986 [20]493.3730.01241.9374Nilometron-methyl5000 [23]364.3760.01371.8626Sulfoseturon-methyl5000 [26]401.8240.01241.9374Tifensulphuron5000 [26]401.8240.01241.9376Tifensulphuron-methyl5000 [26]401.8240.01241.9376Tifensulphuron-methyl5000 [26]401.8240.01241.9376Tifensulphuron-methyl5000 [26]401.8240.01241.9376Tifensulphuron-Methyl5000 [26]401.8240.01241.9376Tifensulphuron-Methyl5000 [26]401.8240.01241.9376Tifensulphuron-Methyl5000 [2	Cyclosulphamuron	5000 [7]	421.428	0.0119	1.9258
Ethosynuphuron3270 [9]398.3900.00822.0858Flazsaulphuron5000 [1]457.2420.01111.9566Flazsaulphuron-methyl5000 [12]465.3610.01071.9688Halosulphuron-methyl2000 [14]442.8070.01211.9168Iodosulphuron5000 [16]381.3630.01311.8824Nicosulphuron-methyl5000 [16]381.3630.01311.8824Nicosulphuron5000 [17]440.4040.01221.9168Iodosulphuron5000 [18]440.4040.01231.9100Pyrimsulphuron-methyl5000 [19]468.3360.01071.9716Prosulphuron5000 [20]413.4280.01211.9174Pyrimsulphuron-methyl5000 [21]430.4740.01161.9350Sulfonutron-methyl5000 [22]364.3760.01371.8626Sulfosulphuron5000 [23]364.3760.01371.8626Sulfosulphuron-methyl5000 [24]470.4750.01061.9736Tifensulphuron-methyl5000 [25]387.3850.01291.8892Tifosulphuron-methyl5000 [26]49.5260.01061.9766Sulfosulphuron1791 [31]26.7010.00762.1211Tifosulphuron-methyl5000 [29]492.4290.01271.8893Tifosulphuron-methyl5000 [29]493.5300.01361.8727Tifosulphuron-methyl5000 [39]28.3590.01361.2727Tifosulphuron-Ma1700 [36]28	Ethametsulphuron-methyl	5000 [8]	410.404	0.0122	1.9142
Flazasulphuron       500       101       497.324       0.0123       1.9110         Foramsulphuron-methyl       500       112       455.361       0.0107       1.9566         Flupsyulphuron-methyl       1287       133       434.811       0.0030       2.5287         Inazosulphuron       500       144       412.807       0.0121       1.9168         Indosulphuron       678       15       493.233       0.0054       2.2652         Metsulphuron-methyl       500       17       410.404       0.0122       1.9142         Nicosulphuron       500       18       446.413       0.0123       1.9100         Pyramsulphuron-methyl       500       19       468.436       0.0102       1.9174         Rinsulphuron       986       20       419.378       0.0024       2.6287         Pyrazosulphuron-methyl       500       [21       430.474       0.0115       1.9376         Sulforeturon-methyl       500       [24       470.475       0.0106       1.9376         Sulforeturon-methyl       500       [25       387.385       0.0129       1.8824         Thisoulphuron       500       [26       401.824       0.0126       1.8981 <td>Ethoxysulphuron</td> <td>3270 [9]</td> <td>398.390</td> <td>0.0082</td> <td>2.0858</td>	Ethoxysulphuron	3270 [9]	398.390	0.0082	2.0858
Foramsulphuron         500         111         452,442         0.0111         1.9568           Halosulphuron-methyl         1287         13         444,811         0.0030         2.5287           Imazosulphuron         500         14         412,807         0.0121         1.9168           Idosulphuron-methyl         500         16         381,363         0.0131         1.8324           Metsulphuron-methyl         500         16         381,363         0.0122         1.9160           Nicosulphuron         500         18         466,413         0.0122         1.9142           Oxsasulphuron-methyl         500         121         413,428         0.0024         2.6287           Pyrazosulphuron-methyl         500         121         413,428         0.0126         1.9376           Rimsulphuron         500         121         413,428         0.0124         1.9376           Sulforniphuron         500         123         364,376         0.0137         1.8626           Sulfosulphuron-methyl         500         125         387,385         0.0126         1.8981           Trifnesulphuron-methyl         500         126         446,4376         0.0166         1.9766	Flazasulphuron	5000 [10]	407.324	0.0123	1.9110
Flupsuphuron-methyl500[12]465. 3610.01071.9688Halosulphuron-methyl500[14]412.8070.01211.9188Iadsulphuron678[15]433.2330.00542.2552Mazosulphuron500[17]410.4040.01221.9142Oxsasulphuron-methyl500[19]468.3360.01071.9716Oxsasulphuron-methyl500[19]468.3360.01071.9716Prosulphuron986[20]413.3780.00242.6287Pyrazosulphuron-methyl500[21]430.4740.01161.9330Sulfoneturon-methyl500[22]430.4740.01161.9376Sulfoneturon-methyl500[23]364.3760.01271.8824Sulfoneturon-methyl500[24]470.4750.01061.9766Tifensulphuron-methyl500[25]367.3850.01241.9951Tifensulphuron-methyl500[26]443.2560.01061.9766Tifensulphuron-methyl500[29]492.4290.01221.9934Tifensulphuron-methyl500[29]492.4290.01221.9936Tifensulphuron-methyl500[29]492.4290.01241.9951Tifensulphuron-methyl500[29]492.4290.01221.9934Tifensulphuron-methyl500[29]492.4290.01221.9936Tifensulphuron-methyl500[29]2.52550.2151	Foramsulphuron	5000 [11]	452.442	0.0111	1.9566
Halosulphuron1287 [13]434.8110.00302.5287Imazosulphuron5000 [14]412.8070.01211.9168Iodosulphuron5000 [16]381.3630.00542.2652Metsulphuron-methyl5000 [17]410.4040.01221.9142Oxasulphuron5000 [18]466.4130.01231.9100Pyrimsulphuron-methyl5000 [21]413.4280.01071.9716Pyrazosulphuron-methyl5000 [22]430.4740.01161.9376Sulforutpron-ethyl5000 [23]364.3760.01371.8826Sulforutpron-methyl5000 [24]470.4750.01061.9736Tifesulphuron5000 [25]387.3850.01291.8892Tifasulphuron5000 [26]495.3900.01261.8981Tifnsulphuron-methyl5000 [27]395.3900.01261.8981Tifnsulphuron-methyl5000 [28]497.3500.01141.9195Tifnsulphuron-methyl5000 [29]492.2920.01021.9934Tifnsulphuron-methyl5000 [27]395.3900.01261.8981Tifnsulphuron4700 [30]445.2960.01061.9766Chlorbornuron10,000 [33]212.6790.00732.1352Chlorbornuron10,000 [35]268.3590.01361.2971Daimuron5000 [40]22.2050.02151.6669Diffenoxuron10,000 [36]248.390.00362.2514Diuron630 [42]211.2640.00302.2552<	Flupysulphuron-methyl	5000 [12]	465.361	0.0107	1.9688
Imasoulphuron5000 [14]412.8070.01211.9168Iodosulphuron5000 [16]381.3630.00542.2652Metsulphuron-methyl5000 [17]410.4040.01221.9142Nossaulphuron5000 [19]468.3360.01071.9716Pyrimsulphuron-methyl5000 [21]413.4280.00242.6287Pyrazosulphuron-ethyl5000 [22]430.4740.01161.9350Sulforeturon-methyl5000 [23]364.3760.01371.8626Sulforeturon-methyl5000 [24]470.4750.01061.9350Sulforeturon-methyl5000 [26]41.8240.01241.9014Triasulphuron5000 [26]401.8240.01261.8892Triasulphuron5000 [27]395.3900.01261.8981Trifhosysulphuron-methyl5000 [29]492.4290.01021.9344Trifhosysulphuron-methyl5000 [29]492.4290.01021.9345Trifhosysulphuron-methyl5000 [29]492.4290.01021.9345Trifhosysulphuron1215 [32]293.5480.00732.1327Chiorosturon1000 [36]268.3590.04701.3277Chiorosturon5000 [37]366.8090.00362.2514Dimeron1000 [36]266.3300.00352.4569Dimeron1000 [36]268.3590.01251.6662Dimeron1200 [49]164.2070.03901.4929Difenoxuron1384 [41]200.7340.01461.836	Halosulphuron-methyl	1287 [13]	434.811	0.0030	2.5287
Iodosulphuron-methyl2678 [15]493.2330.00542.2652Metsulphuron-methyl5000 [16]381.3630.01311.8824Nicosulphuron5000 [17]41.04040.01221.9100Pyrimsulphuron-methyl5000 [18]466.3130.01231.9100Prosulphuron-methyl5000 [21]413.4280.01211.9176Prosulphuron-methyl5000 [22]43.04740.01161.9350Sulforneturon-methyl5000 [23]364.3760.01371.8626Sulforneturon-methyl5000 [24]367.3850.01291.8892Trifensulphuron5000 [25]387.3850.01291.8892Trifensulphuron-methyl5000 [27]35.3500.01141.9934Trifensulphuron-methyl5000 [28]437.3500.01141.9914Trifusulphuron-methyl5000 [28]437.3500.01141.9934Trifusulphuron-methyl5000 [28]437.3500.01141.9914Trifusulphuron1791 [31]236.7010.00762.1211Chlorotnuron1791 [31]236.7010.00762.1212Chlorotnuron1000 [36]266.3300.00352.4569Diamuron5000 [36]266.3300.00352.4569Diamuron1000 [36]266.3300.00352.4569Diamuron1000 [36]266.3300.00352.4569Diamuron1326 [41]206.2880.00932.257Isporturon1826 [41]206.2880.00302.	Imazosulphuron	5000 [14]	412.807	0.0121	1.9168
Metsulphuron-methyl       500       [1]       381.363       0.0131       1.8824         Nicosulphuron       500       [1]       410.404       0.0122       1.9142         Oxsasulphuron       500       [19]       466.336       0.0107       1.9716         Prinsulphuron-rethyl       500       [21]       413.428       0.0121       1.9174         Rinsulphuron-methyl       5000       [22]       430.474       0.0116       1.9350         Sulforesturon-methyl       5000       [23]       364.376       0.0123       1.8626         Sulforesturon-methyl       5000       [24]       470.475       0.0106       1.9736         Tifensulphuron-methyl       5000       [25]       387.385       0.0129       1.8892         Tifnsulphuron-methyl       5000       [26]       401.824       0.0126       1.8891         Tifnsulphuron-methyl       5000       [29]       492.429       0.0102       1.9394         Tifnsulphuron-methyl       5000       [29]       492.429       0.0102       1.9394         Tifnsulphuron-methyl       5000       [29]       492.429       0.0102       1.9394         Tifnsulphuron-methyl       5000       [29]       492.429	Iodosulphuron	2678 [15]	493.233	0.0054	2.2652
Nicosulphuron         500         17         410.404         0.0122         1.9142           Oxsasulphuron         500         18         406.413         0.0123         1.9100           Primsulphuron-methyl         5000         [2]         419.378         0.0024         2.6287           Prozosulphuron-ethyl         5000         [2]         430.474         0.0116         1.9350           Sulforuphuron-methyl         5000         [2]         430.474         0.0116         1.9350           Sulforuphuron-methyl         5000         [2]         361.376         0.0102         1.9350           Sulfosulphuron-methyl         5000         [2]         387.385         0.0129         1.8892           Triasulphuron-methyl         5000         [2]         395.390         0.0126         1.8891           Triflosulphuron-methyl         5000         [2]         395.390         0.0126         1.8891           Triflosulphuron-methyl         5000         [2]         395.390         0.0126         1.8891           Triflosulphuron-methyl         5000         [2]         395.390         0.0126         1.8919           Triflosulphuron-methyl         5000         [2]         293.548         0.00076 <t< td=""><td>Metsulphuron-methyl</td><td>5000 [16]</td><td>381.363</td><td>0.0131</td><td>1.8824</td></t<>	Metsulphuron-methyl	5000 [16]	381.363	0.0131	1.8824
Cxasaulphuron5000 [18]406.4130.01231.9100Pyrimsulphuron-methyl5000 [19]468.3360.01071.9716Forsulphuron-methyl5000 [21]413.4280.01211.9174Rimsulphuron-ethyl5000 [22]430.4740.01161.9350Sulfoneturon-methyl5000 [23]364.3760.01371.8626Sulfoneturon-methyl5000 [25]487.3850.01291.8892Triasulphuron-methyl5000 [26]401.8240.01241.9051Tribenuron-methyl5000 [27]395.3900.01261.8892Triasulphuron-methyl5000 [29]492.4290.01021.9934Triflosulphuron-methyl5000 [29]492.4290.01021.9934Triflosulphuron-methyl5000 [29]492.4290.01021.9934Triflosulphuron4700 [30]245.6710.00762.1211Chlorbormuron2150 [32]295.5480.00732.1352Chlorotoluron10,000 [35]268.3300.03552.2555Diamuron5000 [40]220.050.25141.6669Dimefuron430 [41]206.2830.00352.2555Linuron146 [43]290.97490.01271.8851Dimefuron5000 [45]22.050.2151.6669Lipuron6400 [39]266.3300.03562.2514Dimefuron146 [43]290.9740.01271.8351Dimefuron146 [43]290.9740.01271.8362Dime	Nicosulphuron	5000 [17]	410.404	0.0122	1.9142
primulphuron-methyl500 [19]468.3360.01071.9716Prosulphuron986 [20]419.3780.00242.6287Prazosulphuron-ethyl5000 [21]430.4740.01161.9350Sulfometuron-methyl5000 [23]364.3760.01371.8626Sulfomulphuron5000 [24]470.4750.01661.9736Tifensulphuron-methyl5000 [25]387.3850.01291.8892Trisulphuron-methyl5000 [26]401.8240.01241.9051Tifensulphuron-methyl5000 [27]95.3900.01261.8891Triflosulphuron-methyl5000 [28]447.3500.01141.9051Triflosulphuron-methyl5000 [29]492.4290.01021.9344Triflosulphuron1791 [31]236.7010.00762.1211Chloromuron1791 [31]236.7010.00762.1211Chlorotluron1790 [33]212.6790.04701.3277Chloroxuron3700 [34]290.7490.01271.8853Daimuron5000 [37]356.8090.00562.2514Difenoxuron1000 [36]266.3300.00352.4569Difenoxuron1306 [42]21.0240.01391.7297Chlorosuron1826 [41]206.2880.00892.0530Jenorun1826 [41]206.2880.00362.2514Difenoxuron1846 [43]249.0970.00462.3372Inuron1826 [41]206.2880.00362.4514Jopoturon	Oxsasulphuron	5000 [18]	406.413	0.0123	1.9100
Prosulphuron         986 [20]         413.728         0.0024         2.6287           Pyrazosulphuron-ethyl         5000 [21]         413.428         0.0121         1.9174           Kimsulphuron         5000 [23]         364.376         0.0137         1.8626           Sulfosulphuron         5000 [24]         470.475         0.0106         1.9736           Tifensulphuron-methyl         5000 [25]         387.385         0.0129         1.8822           Triasulphuron-methyl         5000 [26]         401.824         0.0126         1.8891           Tribenuron-methyl         5000 [26]         493.7350         0.0114         1.9419           Tribunyuphuron-Na         5000 [29]         492.429         0.0102         1.934           Tribusulphuron-methyl         5000 [29]         492.429         0.0102         1.934           Tritosulphuron         700 [30]         445.296         0.0106         1.9766           Buturon         7191 [31]         236.701         0.0076         2.1211           Chlorotouron         1700 [33]         212.679         0.0470         1.3277           Chlorotouron         3700 [34]         290.749         0.0126         2.8514           Diroron         371 [38]	Pyrimsulphuron-methyl	5000 [19]	468.336	0.0107	1.9716
Fyrazosulphuron-ethyl         5000 [21]         413.428         0.0121         1.9174           Rimsulphuron         5000 [22]         430.474         0.0116         1.9350           Sulforenturon-methyl         5000 [24]         470.475         0.0106         1.9736           Sulforenturon-methyl         5000 [25]         387.385         0.0129         1.8826           Sulforenturon-methyl         5000 [26]         387.385         0.0124         1.9051           Triasulphuron         5000 [27]         395.390         0.0126         1.8881           Trifnsulphuron-methyl         5000 [29]         492.429         0.0102         1.9934           Trifnsulphuron-methyl         5000 [29]         492.429         0.0106         1.9766           Buturon         7191 [31]         236.701         0.0076         2.1211           Chlorotoluron         10,000 [33]         212.679         0.0470         1.3277           Chlorotoluron         10,000 [35]         268.359         0.0186         1.7297           Diffenoxuron         3700 [34]         290.749         0.0127         1.8893           Dimeturon         1000 [35]         268.359         0.0186         2.2514           Dimeturon         1000 [36]	Prosulphuron	986 [20]	419.378	0.0024	2.6287
Nimsulphuron5000[2]436.4740.01161.9350Sulfosulphuron-methyl5000[2]366.3760.01371.8626Sulfosulphuron-methyl5000[2]387.3850.01291.8892Trisenuphuron-methyl5000[2]491.8240.01241.9051Tribenuron-methyl5000[2]493.5300.01141.9419Trifloxysulphuron-Na5000[2]492.4290.01021.9841Trifloxysulphuron-methyl5000[2]492.4290.01061.9766Tritosulphuron-methyl5000[2]493.5460.00762.1211Chlorbromuron1791[3]236.7010.00762.1211Chlorbromuron2150[3]226.7910.04701.3277Chlorotoluron10.00[3]212.6790.04701.3277Chlorotoluron10.00[3]233.0970.00152.4514Direnoruron437[3]233.0970.00192.7271Fenorunon6400[3]164.2070.33901.4092Fuometuron500[4]206.2850.00362.555Linuron11861.91641.92640.00302.5255Linuron118641.90070.04662.3372Metoberzuron10.000[4]241.6460.02411.6176Metoberzuron10.000[4]241.6460.02411.6176Metoberzuron10.000[4]241.6520.0083	Pyrazosulphuron-ethyl	5000 [21]	413.428	0.0121	1.9174
Sulfometuron-methyl         5000 [23]         364.376         0.0137         1.8626           Sulfosulphuron         5000 [24]         470.475         0.0106         1.9736           Tifensulphuron-methyl         5000 [25]         387.385         0.0124         1.9051           Triasulphuron-methyl         5000 [27]         395.390         0.0126         1.8892           Triflosyulphuron-methyl         5000 [28]         437.350         0.0102         1.9934           Triflosyulphuron-methyl         5000 [29]         492.429         0.0102         1.9934           Triflosyulphuron-methyl         5000 [29]         492.429         0.0106         1.9766           Buturon         1791 [31]         236.701         0.0076         2.1211           Chlorbornuron         2150 [32]         293.548         0.0073         2.1352           Chlorboluron         10,000 [33]         212.679         0.0470         1.3277           Chlorobluron         10,000 [35]         268.359         0.0126         1.8933           Daimuron         2000 [37]         356.809         0.0035         2.4564           Diaron         2000 [37]         356.809         0.0036         2.2511           Penuron         6400 [39] <td>Rimsulphuron</td> <td>5000 [22]</td> <td>430.474</td> <td>0.0116</td> <td>1.9350</td>	Rimsulphuron	5000 [22]	430.474	0.0116	1.9350
Sulfosulphuron         S000         [24]         470.475         0.0106         1.9736           Trifensulphuron-methyl         S000         [25]         387.385         0.0129         1.8892           Trishulphuron         S000         [27]         395.390         0.0126         1.8981           Trifhoxysulphuron-Na         S000         [28]         437.350         0.0114         1.9934           Trifhoxysulphuron-methyl         S000         [29]         492.429         0.0102         1.9934           Trifusulphuron         M700         [30]         445.296         0.0106         1.9766           Buturon         1791         [31]         236.701         0.0076         2.1211           Chlorothuron         1700         [32]         293.548         0.0073         2.1352           Chlorothuron         10.000         [33]         212.679         0.0447         1.3277           Chloroxuron         3700         [34]         290.749         0.0127         1.8953           Dimeron         10000         [35]         286.330         0.0035         2.2571           Dimeron         2000         [37]         356.809         0.0056         2.2514           Dimeron </td <td>Sulfometuron-methyl</td> <td>5000 [23]</td> <td>364.376</td> <td>0.0137</td> <td>1.8626</td>	Sulfometuron-methyl	5000 [23]	364.376	0.0137	1.8626
Tifensulphuron-methyl500025387.3850.01291.8892Trisoulphuron500026401.8240.01241.9051Tribenuron-methyl500027395.3900.01261.8981Triflusulphuron-Na500029492.4290.01021.9934Triflusulphuron-methyl500029492.4290.01061.9766Buturon1791326.7010.00762.1211Chlorbornuron215032293.5480.00732.1352Chlorbornuron10,00013212.6790.04701.3277Chlorosuron370034290.7490.01271.8953Daimuron500025286.3300.00352.4569Direfuron100036286.3300.00352.4569Direfuron200037356.8090.00192.7271Diruon4373823.0970.00192.7271Fenuron640039164.2070.03301.4092Fluometuron500040232.2050.02151.6669Isoproturon1826141.206.2880.00362.5255Inuron114643249.0970.00462.3327Methyldimron394844270.3740.01461.8356Metobenzuron10,00045259.1030.03861.4135Metobenzuron10,00045259.1030.03861.4135Metobenzuron10,00045 <td< td=""><td>Sulfosulphuron</td><td>5000 [24]</td><td>470.475</td><td>0.0106</td><td>1.9736</td></td<>	Sulfosulphuron	5000 [24]	470.475	0.0106	1.9736
Triasulphuron         5000 [26]         401.824         0.0124         1.9051           Tribenuron-methyl         5000 [27]         395.390         0.0126         1.8981           Trifloxysulphuron-Na         5000 [29]         492.429         0.0102         1.9934           Tritosulphuron         4700 [30]         445.296         0.0106         1.9766           Buturon         1791 [31]         236.701         0.0076         2.1211           Chlorotoluron         10,000 [33]         212.679         0.0470         1.3277           Chloroxuron         3700 [34]         290.749         0.0127         1.8953           Daimuron         5000 [35]         268.359         0.0186         1.7277           Difenoxuron         1000 [36]         263.30         0.0035         2.4569           Dimefuron         2000 [37]         356.809         0.0056         2.2514           Diuron         437 [38]         233.097         0.0019         2.7271           Fenuron         6400 [39]         164.207         0.390         1.4929           Fluometuron         5004 [40]         232.205         0.0215         1.6669           Isoproturon         1826 [41]         206.288         0.0030	Tifensulphuron-methyl	5000 [25]	387.385	0.0129	1.8892
Tribenuron-methyl5000 [27]395.3900.01261.8981Trifboxyulphuron-Na5000 [28]437.3500.01141.9419Trifbusulphuron-Methyl5000 [29]492.4290.01021.9934Tritosulphuron4700 [30]445.2960.01061.9766Buturon1791 [31]236.7010.00762.1211Chlorbromuron2150 [32]293.5480.00732.1352Chlorotoluron10,000 [33]212.6790.04701.3777Chlorotouron3700 [34]290.7490.01271.8953Daimuron5000 [35]268.3590.01861.7297Difenoxuron1000 [36]286.3300.00562.4569Dimefuron2000 [37]356.8090.00562.2571Fenuron6400 [39]164.2070.03901.4092Floometuron5000 [40]232.2050.02151.6669Isoproturon11826 [41]206.2880.00892.5255Linuron1146 [43]249.0970.00462.3372Methyldimron3948 [44]270.3740.01461.8356Metobenzuron10,000 [45]414.5860.02411.6176Metobenzuron10,000 [45]252.1200.08332.0794Monolinuron2100 [48]252.1200.08332.0794Monolinuron1005 [49]138.6520.00401.8541Monolinuron1005 [49]128.6780.01401.8541Monolinuron1005 [49]252.158<	Triasulphuron	5000 [26]	401.824	0.0124	1.9051
Trifloxysulphuron-Na5000[28]437.3500.01141.9419Trifloxylphuron-methyl5000[29]4492.4290.01021.9934Tritosulphuron4700[30]445.2960.01061.9766Buturon1791[31]236.7010.00762.1211Chlorbromuron2150[32]293.5480.00732.1352Chlorothuron10,000[33]212.6790.04701.3277Chloroxuron3700[34]290.7490.01261.7297Difenoxuron5000[35]268.3590.01861.7297Difenoxuron1000[36]286.3300.00352.4569Dimefuron2000[37]356.8090.00562.2514Diruron437[38]233.0970.00192.7271Fenuron6400[39]164.2070.03901.4092Fluometuron5000[40]232.2050.02151.6669Isoproturon1826[41]206.2880.00892.0530Isouron630[42]211.2640.00302.5255Linuron1146[43]249.0970.00462.3372Methyldimron3948[44]270.3740.01461.8356Metobenzuron10,000[45]414.5860.02411.6176Metobenzuron10,000[45]228.6780.01401.8541Monolinuron2100[48]252.1200.00832.0794 <t< td=""><td>Tribenuron-methyl</td><td>5000 [27]</td><td>395.390</td><td>0.0126</td><td>1.8981</td></t<>	Tribenuron-methyl	5000 [27]	395.390	0.0126	1.8981
Trifusulphuron-methyl5000 [29]492.4290.01021.9934Tritosulphuron4700 [30]445.2960.01061.9766Buturon1791 [31]236.7010.00762.1211Chlorbormuron2150 [32]293.5480.00732.1352Chlorotoluron10,000 [33]212.6790.04701.3277Chloroxuron3700 [34]290.7490.01271.8953Daimuron5000 [35]268.3590.01861.7297Difenoxuron1000 [36]286.3300.00352.514Dimefuron2000 [37]356.8090.00562.514Diuron437 [38]233.0970.00192.7271Fenuron6400 [39]164.2070.33901.4092Isoproturon1826 [41]206.2880.00892.5555Linuron630 [42]211.2640.00302.5255Linuron1146 [43]249.0970.00462.3372Methyldimron3948 [44]270.3740.01461.8356Metobenzuron10,000 [45]414.5860.02411.6176Metobenzuron10,000 [45]255.1030.03861.4135Metoksuron3200 [47]228.6780.01401.8541Monuron1005275.7780.04001.8542Monuron10,000 [50]275.7780.04032.7275Neburon11,000 [50]275.780.04031.2375Monuron10,000 [50]25.7570.04032.7275Metory	Trifloxysulphuron-Na	5000 [28]	437.350	0.0114	1.9419
Tritosulphuron4700 [30]445.2960.01061.9766Buturon1791 [31]236.7010.00762.1211Chlorbromuron2150 [32]293.5480.00732.1352Chlorotoluron10.000 [33]212.6790.04701.3277Chloroxuron3700 [34]290.7490.01271.8953Daimuron5000 [35]268.3590.01861.7297Difenoxuron1000 [36]286.3000.00352.4569Dimefuron2000 [37]356.8090.00562.2514Diuron437 [38]233.0970.00192.7271Fenuron6400 [39]164.2070.03301.4092Fluometuron5000 [40]232.2050.02151.6669Isoproturon1826 [41]206.2880.00892.5255Linuron630 [42]211.2640.00302.5255Linuron1146 [43]249.0970.00462.3372Methyldimron3948 [44]270.3740.01461.8356Metoksuron10,000 [45]414.5860.02411.6176Metoksuron3200 [47]228.6780.01401.8541Monlinuron1005 [49]198.6520.00532.2757Neburon11,000 [50]275.1780.04001.8382Siduron7500 [51]232.3260.03231.4910	Triflusulphuron-methyl	5000 [29]	492.429	0.0102	1.9934
Buturon1791 [31]236.7010.00762.1211Chlorbromuron2150 [32]293.5480.00732.1352Chlorotoluron10,000 [3]212.6790.04701.3277Chloroxuron3700 [34]290.7490.01271.8953Daimuron5000 [35]268.3590.01861.7297Difenoxuron1000 [36]286.3300.00352.4569Dimefuron2000 [37]356.8090.00562.2514Dimon437 [38]23.0970.0192.7271Fenuron6400 [39]164.2070.03901.4092Isoproturon1826 [41]206.2880.00892.555Isouron630 [42]211.2640.00302.5255Linuron1146 [43]249.0970.00462.3372Metobromuron10,000 [45]414.5860.02411.6176Metobromuron10,000 [45]259.1030.03861.4135Metoksuron3200 [47]228.6780.01401.8541Monolinuron2100 [48]252.1200.00832.0751Neburon11,000 [50]275.1780.04001.3982Siduron750 [51]232.3260.03231.4910	Tritosulphuron	4700 [30]	445.296	0.0106	1.9766
Chlorbromuron2150 [32]293.5480.00732.1352Chlorotoluron10,000 [33]212.6790.04701.3277Chloroxuron3700 [34]290.7490.01271.8953Daimuron5000 [35]268.3590.01861.7297Difenoxuron1000 [36]286.3300.003524569Dimefuron2000 [37]356.8090.00562.2514Diuron437 [38]233.0970.00192.7271Fenuron6400 [39]164.2070.03901.4092Fluometuron5000 [40]232.2050.02151.6669Isoproturon1826 [41]206.2880.00892.0530Isouron630 [42]211.2640.00302.5255Methyldimron3948 [44]270.3740.01461.8356Metobenzuron10,000 [45]414.5860.02411.6176Metobromuron10,000 [45]259.1030.03861.4135Metoksuron2000 [47]228.6780.01401.8541Monolinuron1000 [46]259.1030.03862.0794Monolinuron1000 [45]198.6520.00532.2757Neburon11,000 [50]275.1780.04001.3982Siduron7500 [51]232.3260.03231.4910	Buturon	1791 [31]	236.701	0.0076	2.1211
Chlorotoluron10,000 [33]212.6790.04701.3277Chloroxuron3700 [34]290.7490.01271.8953Daimuron5000 [35]268.3590.01861.7297Difenoxuron1000 [36]286.3300.00352.4569Dimefuron2000 [37]356.8090.00562.2514Diuron437 [38]233.0970.00192.7271Fenuron6400 [39]164.2070.03901.4092Fluometuron5000 [40]22.2050.02151.6669Isoproturon1826 [41]206.2880.00892.5254Linuron630 [42]211.2640.00302.5255Linuron1146 [43]249.0970.00462.3372Methyldimron3948 [44]270.3740.01461.8356Metobenzuron10,000 [45]414.5860.02411.6176Metobromuron10,000 [45]228.6780.01401.8541Monolinuron2000 [47]228.6780.00832.0794Monuron1053 [49]198.6520.00532.2757Neburon11,000 [50]275.1780.04001.3982Siduron7500 [51]232.3260.03231.4910	Chlorbromuron	2150 [32]	293.548	0.0073	2.1352
Chloroxuron3700 [34]290.7490.01271.8953Daimuron5000 [35]268.3590.01861.7297Difenoxuron1000 [36]286.3300.00352.4569Dimefuron2000 [37]356.8090.00562.2514Diuron437 [38]233.0970.00192.7271Fenuron6400 [39]164.2070.03901.4092Isoproturon5000 [40]232.2050.02151.6669Isoproturon1826 [41]206.2880.00892.5255Linuron630 [42]211.2640.00302.5255Linuron1146 [43]249.0970.00462.3372Methyldimron3948 [44]270.3740.01461.8356Metobenzuron10,000 [45]414.5860.02411.6176Metobromuron10,000 [45]228.6780.01401.8354Metobromuron10,000 [45]228.6780.01401.8354Monolinuron2100 [48]252.1200.00832.0794Monuron1053 [49]198.6520.0532.2757Neburon11,000 [50]275.1780.04001.3982Siduron7500 [51]232.3260.03231.4910	Chlorotoluron	10,000 [33]	212.679	0.0470	1.3277
Daimuron5000 [35]268.3590.01861.7297Difenoxuron1000 [36]286.3300.00352.4569Dimefuron2000 [37]356.8090.00562.2514Diuron437 [38]233.0970.00192.7271Fenuron6400 [39]164.2070.03901.4092Fluometuron5000 [40]232.2050.02151.6669Isoproturon1826 [41]206.2880.00892.5255Linuron630 [42]211.2640.00302.5255Linuron1146 [43]249.0970.00462.3372Methyldimron3948 [44]270.3740.01461.8356Metobenzuron10,000 [45]414.5860.02411.6176Metobenzuron3200 [47]228.6780.01401.8541Monolinuron2100 [48]252.1200.00832.0794Monuron1053 [49]198.6520.00532.2757Neburon11,000 [50]275.1780.04001.3982Siduron7500 [51]232.3260.03231.4910	Chloroxuron	3700 [34]	290.749	0.0127	1.8953
Difenoxuron1000 [36]286.3300.00352.4569Dimefuron2000 [37]356.8090.00562.2514Diuron437 [38]233.0970.00192.7271Fenuron6400 [39]164.2070.03901.4092Fluometuron5000 [40]232.2050.02151.6669Isoproturon1826 [41]206.2880.00892.0530Isouron630 [42]211.2640.00302.5255Linuron1146 [43]249.0970.00462.3372Methyldimron3948 [44]270.3740.01461.8561Metobenzuron10,000 [45]414.5860.02411.6176Metobromuron10,000 [45]259.1030.03861.4135Monolinuron2100 [48]252.1200.00832.0794Monuron1053 [49]198.6520.0532.2757Neburon11,000 [50]275.1780.04001.3982Siduron7500 [51]232.3260.03231.4910	Daimuron	5000 [35]	268.359	0.0186	1.7297
Dimefuron2000 [37]356.8090.00562.2514Diuron437 [38]233.0970.00192.7271Fenuron6400 [39]164.2070.03901.4092Fluometuron5000 [40]232.2050.02151.6669Isoproturon1826 [41]206.2880.00892.0530Isouron630 [42]211.2640.00302.5255Linuron1146 [43]249.0970.00462.3372Methyldimron3948 [44]270.3740.01461.8356Metobenzuron10,000 [45]414.5860.02411.6176Metoksuron3200 [47]228.6780.01401.8541Monolinuron2100 [48]252.1200.00832.0794Monuron1053 [49]198.6520.00532.2757Neburon11,000 [50]275.1780.04001.3982Siduron7500 [51]232.3260.03231.4910	Difenoxuron	1000 [36]	286.330	0.0035	2.4569
Diuron437 [38]233.0970.00192.7271Fenuron6400 [39]164.2070.03901.4092Fluometuron5000 [40]232.2050.02151.6669Isoproturon1826 [41]206.2880.00892.0530Isouron630 [42]211.2640.00302.5255Linuron1146 [43]249.0970.00462.3372Methyldimron3948 [44]270.3740.01461.8356Metobenzuron10,000 [45]414.5860.02411.6176Metoksuron3200 [47]228.6780.01401.8541Monolinuron2100 [48]252.1200.00832.0794Monuron10,53 [49]198.6520.00532.2757Neburon11,000 [50]275.1780.04001.3982Siduron7500 [51]232.3260.03231.4910	Dimefuron	2000 [37]	356.809	0.0056	2.2514
Fenuron6400 [39]164.2070.03901.4092Fluometuron5000 [40]232.2050.02151.6669Isoproturon1826 [41]206.2880.00892.0530Isouron630 [42]211.2640.00302.5255Linuron1146 [43]249.0970.00462.3372Methyldimron3948 [44]270.3740.01461.8356Metobenzuron10,000 [45]414.5860.02411.6176Metobromuron10,000 [46]259.1030.03861.4135Metoksuron3200 [47]228.6780.01401.8541Monolinuron2100 [48]252.1200.00832.0794Monuron1053 [49]198.6520.00532.2757Neburon11,000 [50]275.1780.04001.3982Siduron7500 [51]232.3260.03231.4910	Diuron	437 [38]	233.097	0.0019	2.7271
Fluometuron5000 [40]232.2050.02151.6669Isoproturon1826 [41]206.2880.00892.0530Isouron630 [42]211.2640.00302.5255Linuron1146 [43]249.0970.00462.3372Methyldimron3948 [44]270.3740.01461.8356Metobenzuron10,000 [45]414.5860.02411.6176Metobromuron10,000 [46]259.1030.03861.4135Metoksuron3200 [47]228.6780.01401.8541Monolinuron2100 [48]252.1200.00832.0794Monuron1053 [49]198.6520.00532.2757Neburon11,000 [50]275.1780.04001.3982Siduron7500 [51]232.3260.03231.4910	Fenuron	6400 [39]	164.207	0.0390	1.4092
Isoproturon1826 [41]206.2880.00892.0530Isouron630 [42]211.2640.00302.5255Linuron1146 [43]249.0970.00462.3372Methyldimron3948 [44]270.3740.01461.8356Metobenzuron10,000 [45]414.5860.02411.6176Metobromuron10,000 [46]259.1030.03861.4135Metoksuron3200 [47]228.6780.01401.8541Monolinuron2100 [48]252.1200.00832.0794Monuron1053 [49]198.6520.00532.2757Neburon11,000 [50]275.1780.04001.3982Siduron7500 [51]232.3260.03231.4910	Fluometuron	5000 [40]	232.205	0.0215	1.6669
Isouron630 [42]211.2640.00302.5255Linuron1146 [43]249.0970.00462.3372Methyldimron3948 [44]270.3740.01461.8356Metobenzuron10,000 [45]414.5860.02411.6176Metobromuron10,000 [46]259.1030.03861.4135Metoksuron3200 [47]228.6780.01401.8541Monolinuron2100 [48]252.1200.00832.0794Monuron1053 [49]198.6520.00532.2757Neburon11,000 [50]275.1780.04001.3982Siduron7500 [51]232.3260.03231.4910	Isoproturon	1826 [41]	206.288	0.0089	2.0530
Linuron1146 [43]249.0970.00462.3372Methyldimron3948 [44]270.3740.01461.8356Metobenzuron10,000 [45]414.5860.02411.6176Metobromuron10,000 [46]259.1030.03861.4135Metoksuron3200 [47]228.6780.01401.8541Monolinuron2100 [48]252.1200.00832.0794Monuron1053 [49]198.6520.00532.2757Neburon11,000 [50]275.1780.04001.3982Siduron7500 [51]232.3260.03231.4910	Isouron	630 [42]	211.264	0.0030	2.5255
Methyldimron3948 [44]270.3740.01461.8356Metobenzuron10,000 [45]414.5860.02411.6176Metobromuron10,000 [46]259.1030.03861.4135Metoksuron3200 [47]228.6780.01401.8541Monolinuron2100 [48]252.1200.00832.0794Monuron1053 [49]198.6520.00532.2757Neburon11,000 [50]275.1780.04001.3982Siduron7500 [51]232.3260.03231.4910	Linuron	1146 [43]	249.097	0.0046	2.3372
Metobenzuron10,000 [45]414.5860.02411.6176Metobromuron10,000 [46]259.1030.03861.4135Metoksuron3200 [47]228.6780.01401.8541Monolinuron2100 [48]252.1200.00832.0794Monuron1053 [49]198.6520.00532.2757Neburon11,000 [50]275.1780.04001.3982Siduron7500 [51]232.3260.03231.4910	Methyldimron	3948 [44]	270.374	0.0146	1.8356
Metobromuron10,000 [46]259.1030.03861.4135Metoksuron3200 [47]228.6780.01401.8541Monolinuron2100 [48]252.1200.00832.0794Monuron1053 [49]198.6520.00532.2757Neburon11,000 [50]275.1780.04001.3982Siduron7500 [51]232.3260.03231.4910	Metobenzuron	10,000 [45]	414.586	0.0241	1.6176
Metoksuron3200 [47]228.6780.01401.8541Monolinuron2100 [48]252.1200.00832.0794Monuron1053 [49]198.6520.00532.2757Neburon11,000 [50]275.1780.04001.3982Siduron7500 [51]232.3260.03231.4910	Metobromuron	10,000 [46]	259.103	0.0386	1.4135
Monolinuron2100 [48]252.1200.00832.0794Monuron1053 [49]198.6520.00532.2757Neburon11,000 [50]275.1780.04001.3982Siduron7500 [51]232.3260.03231.4910	Metoksuron	3200 [47]	228.678	0.0140	1.8541
Monuron1053 [49]198.6520.00532.2757Neburon11,000 [50]275.1780.04001.3982Siduron7500 [51]232.3260.03231.4910	Monolinuron	2100 [48]	252.120	0.0083	2.0794
Neburon         11,000 [50]         275.178         0.0400         1.3982           Siduron         7500 [51]         232.326         0.0323         1.4910	Monuron	1053 [49]	198.652	0.0053	2.2757
Siduron         7500 [51]         232.326         0.0323         1.4910	Neburon	11,000 [50]	275.178	0.0400	1.3982
	Siduron	7500 [51]	232.326	0.0323	1.4910

relationship (QSTR) model was calculated using multiplelinear regression method. The variables used as independent descriptors in the QSAR analysis were hydrophobic, electronic, polar, steric, and geometric parameters. Twelve molecular descriptors which are octanol–water partition coefficient (log P), dipole moment, molar refractivity, polarizability, molar volume, hydration energy, surface area (grid and approximate), molecular mass, HOMO and LUMO energies, were calculated for the training compounds (see Table 3).

Stepwise regression analysis was used to select the most effective parameters on the toxicity of the sulphonylurea pesticides. According to stepwise regression, successive regression equations are derived in which parameters will be either added or removed until the  $r^2$  and s values are optimized. The magnitude of the coefficients derived in this manner indicates the relative contribution of the associated parameter to toxicity. Among the twelve molecular descriptors, only four of them were taken placed in the model, as a result of stepwise regression analyses.

Results of QSAR model obtained by the multiple-linear regression analysis of the training set of compounds

Table 2 – Structural formulas and codificati	ion of training compounds.	
Compounds name	Structural formulas	Codification
Amidosulphuron	$CH_{3} \longrightarrow O$ $CH_{3} \longrightarrow O$ $H$	Tr01
Bensulphuron-methyl	$CH_{3} \rightarrow O$ $N \rightarrow N$ $H \rightarrow O$ $CH_{2} \rightarrow O$ $N \rightarrow H$ $H \rightarrow O$ $O = C$ $O $	Tr02
Chlorimuron-ethyl	$ \begin{array}{c} CH_{9} \longrightarrow \\ & & \\$	Tr03
Cinosulphuron	$CH_{3} \longrightarrow O$	Tr04
Ethametsulphuron-methyl	$\begin{array}{c} H \\ CH_{9}-CH_{2}-O \end{array} \xrightarrow{H} \\ CH_{9}-CH_{2}-O \end{array} \xrightarrow{H} \\ H \\$	Tr05
Flazasulphuron	$CH_3 \longrightarrow N$ $H$	Tr06
Metsulphuron-methyl		Tr07
Nicosulphuron	$CH_{3} - O \longrightarrow N \longrightarrow$	Tr08
Oxasulphuron	$H_{3}C$ $N$ $N$ $H_{3}C$ $N$ $H$ $H_{3}C$ $N$ $H$	Tr09

– Table 2 (Continued)		
Compounds name	Structural formulas	Codification
Pyrazosulphuron-ethyl	$CH_{3} \longrightarrow N \longrightarrow C \longrightarrow N \longrightarrow N$	Tr10
Thyfensulphuron-methyl	$H_{3}C$ $N$ $N$ $H_{3}C$ $N$ $H_{1}$ $H_{1}$ $H_{2}$ $H_{3}$ $H_{1}$ $H_{1}$ $H_{2}$ $H_{3}$ $H_{1}$ $H_{2}$ $H_{2}$ $H_{3}$ $H_{2}$ $H_{3}$ $H_{1}$ $H_{2}$ $H_{3}$ $H_{2}$ $H_{3}$ $H_{2}$ $H_{3}$	Tr11
Triasulphuron	$\begin{array}{c} Cl \\ CH_2 \\ CH_2 \\ CH_3 \\ CH_3 \\ O \\ O \\ CH_3 \\ O \\ $	Tr12
Tribenuron-methyl	$\begin{array}{c} H_3C & 0 & 0 \\ N & N & CH_3 & H & 0 \\ CH_3 - 0 & CH_3 & H & 0 \\ \end{array}$	Tr13
Trifloksisulphuron	$\begin{array}{c} F \\ F \\ CH_{2} \\ CH_{3} \\ CH_{3} \\ O \end{array} \xrightarrow{O} \\ N \\ H \\ H \\ H \\ O \end{array} \xrightarrow{O} \\ H \\ H \\ O \\ O \\ O \\ H \\ H \\ O \\ N \\ O \\ O$	Tr14
Triflusulphuron-methyl	$F \xrightarrow{F} CH_{2} \xrightarrow{O} N \xrightarrow{O} CH_{3} \xrightarrow{C} H_{3} \xrightarrow{V} N \xrightarrow{V} H \xrightarrow{V} H \xrightarrow{V} O \xrightarrow{C} O \xrightarrow{C} CH_{3}$	Tr15
Buturon		Tr16



(Tr01–Tr20), demonstrate that the equation (see Table 4), is statistically significant (see Table 5).

The equation is represents the best fitted model among the others which are not shown in this study. As can be deduced from Fig. 1, the goodness-of-fit of the equation is the most significant correlation models possessing a high  $r^2$  (93.07%) and a small s (0.0557) with an overall F test value of 50.34 at the significant level of p < 0.05 (see Table 6).

From a statistical point of view, the equation has a sufficient number of DF (degrees of freedom DF = 15); that can be



Fig. 1 – Plot of observed vs. calculated log 1/C values of the training set compounds obtained by using the equation.

judged significant for overall F and t statistics at the 5% level of probability.

In order to avoid the risk of chance correlation, some circumstances which were pointed out by Kubinyi et al. (1993), have been taken into consideration in the study. Cross-validation was applied to the original data set and the resulting PRESS was calculated. The calculated overall PRESS values for the equation is 0.0486, respectively that are found smaller than the SSY (sum of the squares of the response values of the total observations) values of the observed the equation, which is 0.672 (see Table 6). This proves that the developed model predict better than chance and can be considered statistically significant (Wold, 1991). The ratio PRESS/SSY for the equation, is smaller than 0.4 and it also provides proof that the observed model is valid (Wold, 1991; Rawlings, 1988).

According to correlation matrix Table (see Table 7), there is no intercorrelation between physicochemical parameters. For validity of the model, the correlation constant value should be up to 0.7. In our model equation, the maximum intercorrelation constant value is obtained as 0.6029. It shows that the model does not consist of any chance correlation.

The good predictability of our QSTR model for the phenyl and sulphonylurea pesticides can be understood from the Table 8. The log 1/C value which obtained from model equation is close to experimental value of log 1/C.

Table 3 – QSA	AR study	for training com	pounds.									
Compounds	log 1/C	Dipole moment	НОМО	LUMO	Surface area (approx.)	Surface area (grid)	Volume	Hydration energy	LogP	Refractivity	Polarizability	Mass
Tr01	1.8517	2.91	-9.403	-1.798	513.685	533.849	863.306	-17.354	-0.102	72.599	24.045	355.34
Tr02	1.9142	5.417	-9.507	-1.026	541.664	618.977	1054.545	-13.678	0.704	100.177	35.609	410.401
Tr03	2.0049	5.246	-9.55	-1.179	528.78	603.769	1020.801	-10.533	0.968	99.85	35.065	414.82
Tr04	2.0034	5.262	-9.818	-0.98	535.635	598.429	1047.785	-13.383	0.464	100.579	35.451	413.405
Tr05	1.9142	5.259	-9.657	-1.178	527.099	620.817	1045.538	-11.616	1.064	100.627	35.614	410.404
Tr06	1.911	5.32	-9.53	-1.574	500.67	577.176	957.167	-13.149	1.424	86.284	30.234	407.324
Tr07	1.8824	3.867	-10.281	-1.104	497.673	583.191	967.438	-11.674	0.413	92.305	32.428	381.363
Tr08	1.9142	4.245	-9.355	-1.234	501.698	580.949	1027.253	-10.721	-0.133	98.684	35.614	410.404
Tr09	1.91	5.019	-9.573	-1.306	535.172	644.633	1070.438	-10.766	-0.245	103.512	36.033	406.413
Tr10	1.9174	4.427	-4.899	-0.734	601.847	656.65	1110.766	-13.018	0.476	98.838	36.261	413.428
Tr11	1.8892	5.004	-10.206	-1.386	493.756	569.189	942.694	-12.333	-0.976	89.601	31.95	470.475
Tr12	1.9051	3.89	-10	-0.977	508.187	594.23	999.004	-10.278	0.707	97.255	34.27	387.385
Tr13	1.8981	4.94	-9.972	-1.084	525.037	599.44	1013.729	-9.000	0.66	97.202	34.263	401.824
Tr14	1.9419	7.117	-9.44	-1.3	551.112	628.942	1042.318	-13.693	0.836	92.894	32.706	395.39
Tr15	1.9934	10.82	-9.832	-1.02	582.238	642.732	1141.871	-7.253	2.212	110.906	39.011	437.35
Tr16	2.1211	4.766	-8.7551	0.1163	455.38	444.83	720.131	-2.325	2.322	64.414	25.056	445.296
Tr17	1.3277	4.766	-8.6829	0.1564	427.331	412.517	652.137	-1.624	-0.142	61.418	22.49	212.679
Tr18	1.7297	3.133	-8.8842	0.118	428.602	497.135	836.711	-4.657	1.339	89.612	32.057	268.359
Tr19	1.4092	3.656	-8.6758	0.4626	356.938	367.296	562.334	-3.174	-0.073	52.42	18.727	164.207
Tr20	1.8356	2.243	-8.871	0.3229	434.182	495.971	848.365	-2.601	1.797	89.453	32.249	270.374

Table 4 – Model equation.						
		Equation				
Log 1/C = 1.03492–0.0266253 DM <sup>a</sup> + 0.0806626 log P + 0.00138922 Rf <sup>b</sup> + 0.00206901 mass						
R <sup>2</sup>	Standard error of est.	Mean absolute error	Durbin–Watson statistic			
93.068%	0.056	0.041	1.721			
<sup>a</sup> DM: dipol moi	ment.					
<sup>b</sup> Rf (refractivity	7).					

Table 5 – Multiple regression analyses of model.					
Parameter	Estimate	Standard deviation	T statistic	p-Value	
Constant	1.035	$7.698 \times 10^{-2}$	13.444	0.0000	
Refractivity	$1.389  imes 10^{-3}$	$1.111 \times 10^{-3}$	1.250	0.2303	
Mass	$2.069 \times 10^{-3}$	$2.165  imes 10^{-4}$	9.557	0.0000	
Dipol moment	$-2.662 \times 10^{-2}$	$8.596 \times 10^{-3}$	-3.097	0.0074	
LogP	$8.066\times10^{-2}$	$1.577  imes 10^{-2}$	5.114	0.0001	

Table 6 – Variance analyses of model.						
Source	Sum of squares	Df	Mean square	F rate	p-Value	
Model	0.626	4	0.156	50.34	0.0000	
Residual	0.047	15	0.003			
Total (corr.)	0.672	19				

The model was also tested using with the external test set (see Table 9). Based on the structural diversity of the training set and toxicity data availability, seven different sulphonyl and phenylurea herbicides with their LD<sub>50</sub> values on male rats (oral) were retrieved from literature [1–51] for constituting the external testing set which is useful for testing the predictive power of the quantitative structure–toxicity relationship (QSTR) model. The  $r^2$  value was calculated as 0.682. It shows that the equation has the excellent determining capability of the sulphonylurea and phenylurea toxicity (see Table 10).

# 4. Discussion

As seen from the model, the most effective parameter on the toxicity is  $\log P$  due to this parameter's highest constant value in the equation. Indeed,  $\log P$  increased in a direct relationship with toxicity. This suggests that high lipophilicity is a strong predictor of toxicity with these herbicides. The inverse

Table 7 – Correlation matrix table of model.						
	Constant	Rf	Mass	DM	LogP	
Constant	1.0000					
Rf	-0.6029	1.0000				
Mass	-0.1786	-0.5680	1.0000			
DM	-0.0098	-0.1702	-0.2605	1.0000		
LogP	0.0134	-0.0391	0.0441	-0.2752	1.0000	

proportion between dipole moment and toxicity was predicted from the equation above. The compound which possesses the higher dipole moment, has lower toxicity (log 1/C value). There is a linear correlation between the dipole moment and polarity. The third effective parameter related to toxicity was calculated as mass of the compound. The effect of mass was less than that of dipole moment and log P according to the equation above. As in the effect of log P, the greater the mass of the compound, the toxicity was recorded. In our hands, the least effective parameter which describes toxicity was molar refractivity, which has a linear relationship with the molecular mass. There was a linear relationship between molar refractivity and increasing toxicity.

Table 8 – Observed and calculated log 1/C values with residuals obtained from the equation.					
Compounds	Observed log 1/C	Calculated log 1/C	Residuals		
Tr01	1.85	1.78	0.07		
Tr02	1.91	1.93	-0.02		
Tr19	1.4	1.34	0.06		
Tr05	1.91	1.96	-0.05		
Tr06	1.91	1.97	-0.06		
Tr17	1.32	1.42	-0.1		
Tr16	2.12	2.1	0.02		
Tr07	1.88	1.88	0		
Tr08	1.91	1.89	0.02		
Tr09	1.91	1.86	0.05		
Tr13	1.89	1.92	-0.03		
Tr10	1.91	1.94	-0.03		
Tr11	1.88	1.92	-0.04		
Tr18	1.72	1.73	-0.01		
Tr12	1.9	1.92	-0.02		
Tr14	1.94	1.85	0.09		
Tr15	1.99	1.98	0.01		
Tr04	2	1.92	0.08		
Tr20	1.83	1.8	0.03		
Tr03	2	1.97	0.03		

Table 9 – Structural formulas and codi	fication of setting compounds.	
Compounds Name	Structural formulas	Codification
Azimsulphuron	$CH_{3} \longrightarrow O$ $CH_$	Ts01
Chlorsulphuron	$H_{3}C$ $N$	Ts02
Rimsulphuron	$CH_{3} \longrightarrow N \xrightarrow{(C+)_{3}} N ($	Ts03
Fluometuron		Ts04
Siduron		Ts05
Neburon	$CH_3-CH_2-CH_2-CH_2-H_2-H_3-CH_3-CL$	Ts06
Iodosulphuron	$H_3C$ $N$ $N$ $N$ $H$ $H$ $O$	Ts07

Table 10 – Testing of model with using external test set that not used in modeling.					
Compounds	Literature value of log 1/C	Calculated log 1/C with model equation	Residual		
Ts01	1.92	2.08	0.16		
Ts02	2.06	1.86	-0.2		
Ts03	1.93	1.95	0.02		
Ts04	1.66	1.44	-0.22		
Ts05	1.49	1.66	0.17		
Ts06	1.39	1.59	0.2		
Ts07	2.26	2.18	-0.08		

## 5. Conclusion

It can be concluded from this QSTR study that logP, dipole moment, molar refractivity and molecular mass are the effective parameters which describe sulphonylurea and phenylurea toxicity. For synthesizing less toxic sulphonylurea and phenylurea pesticides, the molecules should be highly polar, water-soluble, and having low molecular mass and refractivity, also. Quantitative structure-activity relationship models for LD<sub>50</sub> value of phenylurea and sulphonylurea herbicides, suggest that if log P values, mass, and molar refractivity increase, herbicide toxicity also increases. However, there is an inverse proportion with toxicity and dipole moment. Researchers may use this model as part of the process of the design of less toxic sulphonylurea and phenylurea pesticides through the estmination of the LD<sub>50</sub> values of new agents. It is hoped that animal usage materials, human labour and time can be saved through the application of this QSAR model.

# **Conflict of interest**

None of the authors has any conflict of interest in this study.

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#### Appendix A. Web references

- http://sitem.herts.ac.uk/aeru/footprint/en/Reports/28. htm (Last accessed date: January 2012).
- [2] http://sitem.herts.ac.uk/aeru/footprint/en/Reports/49. htm (Last accessed date: January 2012).
- [3] http://sitem.herts.ac.uk/aeru/footprint/en/Reports/68. htm (Last accessed date: January 2012).
- [4] http://www.kingtaichem.com/pro\_h\_CHLORIMURON-ETHYL.htm (Last accessed date: January 2012).
- [5] http://pmep.cce.cornell.edu/profiles/herb-growthreg/ cacodylic- cymoxanil/chlorsulfuron/chlsulf\_prf\_0385. html (Last accessed date: January 2012).
- [6] http://www.chinese-pesticide.com/herbicides/ cinosulfuron.htm (Last accessed date: January 2012).
- [7] http://sitem.herts.ac.uk/aeru/footprint/en/Reports/1147. htm (Last accessed date: January 2012).
- [8] http://sitem.herts.ac.uk/aeru/footprint/en/Reports/1146. htm (Last accessed date: January 2012).
- [9] http://sitem.herts.ac.uk/aeru/footprint/en/Reports/281. htm (Last accessed date: January 2012).
- [10] http://sitem.herts.ac.uk/aeru/footprint/en/Reports/319. htm (Last accessed date: January 2012).
- [11] http://sitem.herts.ac.uk/aeru/footprint/en/Reports/357. htm (Last accessed date: January 2012).
- [12] http://sitem.herts.ac.uk/aeru/footprint/en/Reports/341. htm (Last accessed date: January 2012).

- [13] http://sitem.herts.ac.uk/aeru/footprint/en/Reports/1117. htm (Last accessed date: January 2012).
- [14] http://sitem.herts.ac.uk/aeru/footprint/en/Reports/396. htm (Last accessed date: January 2012).
- [15] http://sitem.herts.ac.uk/aeru/footprint/en/Reports/401. htm (Last accessed date: January 2012).
- [16] http://sitem.herts.ac.uk/aeru/footprint/en/Reports/470. htm (Last accessed date: January 2012).
- [17] http://sitem.herts.ac.uk/aeru/footprint/en/Reports/484. htm (Last accessed date: January 2012).
- [18] http://sitem.herts.ac.uk/aeru/footprint/en/Reports/499. htm (Last accessed date: January 2012).
- [19] http://sitem.herts.ac.uk/aeru/footprint/en/Reports/1622. htm (Last accessed date: January 2012).
- [20] http://sitem.herts.ac.uk/aeru/footprint/en/Reports/558. htm (Last accessed date: January 2012).
- [21] http://sitem.herts.ac.uk/aeru/iupac/Reports/1148.htm (Last accessed date: January 2012).
- [22] http://sitem.herts.ac.uk/aeru/footprint/en/Reports/586. htm (Last accessed date: January 2012).
- [23] http://sitem.herts.ac.uk/aeru/iupac/Reports/1149.htm (Last accessed date: January 2012).
- [24] http://sitem.herts.ac.uk/aeru/footprint/en/Reports/603. htm (Last accessed date: January 2012).
- [25] http://sitem.herts.ac.uk/aeru/iupac/Reports/635.htm (Last accessed date: January 2012).
- [26] http://www.kingtaichem.com/pro\_h\_TRIASULFURON. htm (Last accessed date: January 2012).
- [27] http://sitem.herts.ac.uk/aeru/iupac/Reports/655.htm (Last accessed date: January 2012).
- [28] http://sitem.herts.ac.uk/aeru/footprint/en/Reports/1151. htm (Last accessed date: January 2012).
- [29] http://sitem.herts.ac.uk/aeru/iupac/Reports/668.htm (Last accessed date: January 2012).
- [30] http://sitem.herts.ac.uk/aeru/iupac/Reports/674.htm (Last accessed date: January 2012).
- [31] http://sitem.herts.ac.uk/aeru/footprint/en/Reports/1278. htm (Last accessed date: January 2012).
- [32] http://sitem.herts.ac.uk/aeru/footprint/en/Reports/132. htm (Last accessed date: January 2012).
- [33] http://sitem.herts.ac.uk/aeru/footprint/en/Reports/151. htm (Last accessed date: January 2012).
- [34] http://sitem.herts.ac.uk/aeru/footprint/en/Reports/152. htm (Last accessed date: January 2012).
- [35] http://www.who.int/ipcs/publications/pesticides hazard\_rev\_3.pdf (Last accessed date: January 2012).
- [36] http://sitem.herts.ac.uk/aeru/footprint/en/Reports/231. htm (Last accessed date: January 2012).
- [37] http://sitem.herts.ac.uk/aeru/footprint/en/Reports/237. htm (Last accessed date: January 2012).
- [38] http://sitem.herts.ac.uk/aeru/footprint/en/Reports/260. htm (Last accessed date: January 2012).
- [39] http://sitem.herts.ac.uk/aeru/footprint/en/Reports/313. htm (Last accessed date: January 2012).
- [40] http://sitem.herts.ac.uk/aeru/footprint/en/Reports/336. htm (Last accessed date: January 2012).
- [41] http://sitem.herts.ac.uk/aeru/footprint/en/Reports/409. htm (Last accessed date: January 2012).
- [42] http://www.lookchem.com/ISOURON/#TOXICITY (Last accessed date: January 2012).

- [43] http://sitem.herts.ac.uk/aeru/footprint/en/Reports/419. htm (Last accessed date: January 2012).
- [44] http://www.who.int/ipcs/publications/pesticides \_hazard\_rev\_3.pdf (Last accessed date: January 2012).
- [45] JUllmann's Agrochemicals: Plant Growth, Plant and Crop Protection, vol. 2, Wiley-VCH, Weinheim, 2007.
- [46] http://sitem.herts.ac.uk/aeru/footprint/en/Reports/464. htm (Last accessed date: January 2012).
- [47] http://sitem.herts.ac.uk/aeru/footprint/en/Reports/467. htm (Last accessed date: January 2012).
- [48] http://sitem.herts.ac.uk/aeru/footprint/en/Reports/475. htm (Last accessed date: January 2012).
- [49] http://sitem.herts.ac.uk/aeru/footprint/en/Reports/476. htm (Last accessed date: January 2012).
- [50] http://sitem.herts.ac.uk/aeru/footprint/en/Reports/483. htm (Last accessed date: January 2012).
- [51] http://sitem.herts.ac.uk/aeru/iupac/Reports/590.htm (Last accessed date: January 2012).

#### REFERENCES

- Pimentel, D., 1995. Amounts of pesticides reaching target pests: environmental impacts and ethics. J. Agric. Environ. Ethics B 8, 47–84.
- Anonymous, 2003. Third report from the Commission to the Council and the European Parliament on the statistics on the number of animals used for experimental and other scientific purposes in the member states of the European Union. Commission of the European Communities, Brussels.
- Tong, W., Welsh, W.J., Shi, L., Fang, H., Perkins, R., 2003. Structure-activity relationship approaches and applications. Environ. Toxicol. Chem. 22, 1680–1695.

- Schultz, T.W., Cronin, M.T.D., Walker, J.D., Aptula, A.O., 2003. Quantitative structure–activity relationships (QSARs) in toxicology: a historical perspective. J. Mol. Struct. (THEOCHEM) 622 (1), 22.
- Eriksson, L., Jaworska, J., Worth, A.P., Cronin, M.T.D., McDowell, R.M., Gramatica, P., 2003. Methods for reliability and uncertainty assessment and for applicability evaluations of classification- and regression-based QSARs. Environ. Health Perspect. 111, 1361–1375.
- Hasel, W., Hendrickson, T.F., Still, W.C., 1988. A rapid approximation to the solvent accessible surface areas of atoms. Tetrahedron Comput. Meth. 1, 103–116.
- Ooi, T., Oobatake, M.G., Scheraga Nemethy, H., 1987. Accesible surface areas as a measure of the thermodynamic parameters of hydration peptides. Proc. Natl. Acad. Sci. U.S.A. 84 (10), 3086–3090.

Ghose, A.K., Pritchett, A., Grippen, G.M., 1988. Atomic physicochemical parameters for 3-dimensional structure directed quantitative activity relationships.
3. Modelling hydrophopic interactions. J. Comput. Chem. 9, 80–90.

- Ghose, A.K., Grippen, G.M., 1987. Atomic physicochemical parameters for 3-dimensional structure directed quantitative activity relationships 2 modelling dispersive and hydrophobic interactions. J. Chem. Inform. Comput. Sci. 27, 21.
- Miller, K.J., 1990. Additivity methods in molecular polarizability. J. Am. Chem. Soc. 112, 8533–8542.
- Kubinyi, H., Mannhold, R., Krogsgaard-Larsen, P., Timmerman, H. (Eds.), 1993. QSAR: Hansch Analysis and Related Approaches. Wiley-VCH, Weinheim (Ger.).
- Wold, S., 1991. Validation of QSAR's. Quant. Struct.-Act. Relat. 10, 191.
- Rawlings, J.O., 1988. Applied Regression Analysis: A Research Tool. Wadsworth and Brooks/Cole Advanced Books and Software, Pacific Grove, CA, pp. 186–189.