

Supp1. The list of 57 global descriptors

2D van der Waals surface area

2D van der Waals volume

2D van der Waals surface area of H-bond acceptor atoms

2D van der Waals surface area of H-bond donor atoms

2D van der Waals surface area of all H-bond atoms

2D van der Waals hydrophobic surface area

2D van der Waals surface area of negative chargable group

2D van der Waals surface area of positive chargable group

2D van der Waals surface area of polar group

Calculated logP

Calculated molecular refractivity

Calculated buffer solubility

Charge_polarization

Formal_charge

Fraction of 2D van der Waals surface area of chargable groups

Fraction of 2D van der Waals surface area of H-bond acceptor groups

Fraction of 2D van der Waals surface area of H-bond donor groups

Fraction of 2D van der Waals hydrophobic surface area

Fraction of 2D van der Waals surface area of negative chargable groups

Fraction of 2D van der Waals surface area of polar groups

Fraction of 2D van der Waals surface area of positive chargable groups

Fraction of aromatic atoms

Fraction of hetero atoms

Fraction of rotatable bonds

Hydrophobic surface area (The sum of van der Waals surface area with absolute values of MPEOE charges less than 0.2)

Local dipole index (the average of the charge differences over all bonded atom pairs)

Molecular weight

Negative charged polar surface area (The sum of van der Waals surface area with values of MPEOE charges less than 0.2)

Number of aromatic bonds

Number of aromatic rings

Number of H-bond acceptors

Number of H-bond donors

Number of N

Number of negative chargable groups
Number of negative charged groups
Number of O
Number of P
Number of positive chargable groups
Number of positive charged groups
Number of rigid bonds
Number of rings
Number of rotatable bonds
Polarity parameter
Polarizability (by Miller method)
Positive charged polar surface area (The sum of van der Waals surface area with values of MPEOE charges greater than 0.2)
Pure water solubility
Maximum negative charge
Maximum positive charge
Ratio donors to acceptor (The number of hydrogen bond donors / The number of hydrogen bond acceptors)
Relative negative charge (The partial charge of the most negative atom divided by the total negative charge)
Relative positive charge (The partial charge of the most positive atom divided by the total negative charge)
Calculated boiling point
Calculated melting point
Solvation free energy
Total absolute atomic charge
Total negative charge
Total positive charge

Supp2. List of tested promiscuous drugs.

Drug Name	Pharmacological action from MeSH ¹
ZD6474 ^{2,3}	Not annotated
SU6668 ²	Not annotated
EKB569 ³	Not annotated

Imatinib ³⁻⁶	Antineoplastic Agents (Protein Kinase Inhibitors)
Sutent ^{3,5}	Antineoplastic Agents (Angiogenesis Inhibitors)
Sorafenib ^{3,5}	Antineoplastic Agents (Protein Kinase Inhibitors)
AG-013736 ³	Not annotated
Staurosporine ³	Enzyme Inhibitors
Aspirin ^{6,7}	Anti-Inflammatory Agents, Fibrinolytic Agents, Platelet Aggregation Inhibitors (Cyclooxygenase Inhibitors)
Clozapine ⁷⁻¹⁰	Antipsychotic Agents (Serotonin Antagonists, GABA Antagonists)
Aripiprazole ⁸	Antipsychotic Agents
Ziprasidone ⁸	Antipsychotic Agents (Serotonin Antagonists, Dopamine Antagonists)
Zotepine ⁸	Antipsychotic Agents
Quetiapine ⁸	Antipsychotic Agents
Olanzapine ⁸	Antiemetics, Antipsychotic Agents (Serotonin Uptake Inhibitors)
Risperidone ⁸	Antipsychotic Agents (Serotonin Antagonists, Dopamine Antagonists)
Haloperidol ⁸	Antiemetics, Antipsychotic Agents (Dopamine Antagonists), Anti-Dyskinesia Agents
Chlorpromazine ⁸	Antiemetics, Antipsychotic Agents (Dopamine Antagonists)
Imipramine ⁸	Antidepressive Agents (Tricyclic Adrenergic Uptake Inhibitors)
Agomelatine ⁸	Hypnotics and Sedatives
Clotrimazole ¹¹	Anti-Infective Agents, Local Antifungal Agents
Benzyl Benzoate ¹¹	Insecticides
Nicardipine ¹¹	Antihypertensive Agents (Calcium Channel Blockers), Vasodilator Agents
Delavirdine ¹¹	Anti-HIV Agents (Reverse Transcriptase Inhibitors)

Chlorambucil ¹¹	Antineoplastic Agents (Alkylating)
Sulfinpyrazone ¹¹	Uricosuric Agents
Indomethacin ¹¹	Anti-Inflammatory Agents, Cardiovascular Agents, Gout Suppressants, Tocolytic Agents (Cyclooxygenase Inhibitors)
Tacrine ¹¹	Cholinesterase Inhibitors, Parasympathomimetics Nootropic Agents
Phenazopyridine ¹¹	Local Anesthetics
SP600125 ³	Not annotated

Supp3. List of tested H1-antihistaminergic drugs.

Generation	Drugs
1st generation	<ul style="list-style-type: none"> * Ethylenediamine class: Diphenhydramine, Carbinoxamine, Doxylamine, Clemastine, Dimenhydrinate * Alkylamine class: Chlorphenamine, Brompheniramine * Piperazine class: Cyclizine, Hydrixyzine, Meclizine * Tricyclics and Tetracyclics class: Promethazine, Alimemazine, Cyprohepatadine, Azatadine, Ketotifen
2nd generation	Acrivastine, Cetirizine, Loratadine, Terfenadine, Azelastine, Levocabastine
3rd generation	Desloratadine, Fexofenadine

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