



## 1. Physicochemical Property

| Property         | Value   | Comment  |
|------------------|---------|--|
| Molecular Weight | 346.18  | Contain hydrogen atoms. Optimal:100~600                      |
| Volume           | 353.656 | Van der Waals volume   |
| Density          | 0.979   | Density = MW / Volume  |
| nHA              | 5       | Number of hydrogen bond acceptors. Optimal:0~12              |
| nHD              | 3       | Number of hydrogen bond donors. Optimal:0~7                  |
| nRot             | 2       | Number of rotatable bonds. Optimal:0~11                      |
| nRing            | 4       | Number of rings. Optimal:0~6                                 |
| MaxRing          | 0       | Number of atoms in the biggest ring. Optimal:0~18            |
| nHet             | 5       | Number of heteroatoms. Optimal:1~15                          |
| fChar            | 0       | Formal charge. Optimal:-4 ~4                                 |
| nRig             | 20      | Number of rigid bonds. Optimal:0~30                          |
| Flexibility      | 0.1     | Flexibility = nRot / nRig                                    |
| Stereo Centers   | 4       | Optimal: ≤ 2   |
| TPSA             | 86.99   | Topological Polar Surface Area. Optimal:0~140                |
| logS             | -3.543  | Log of the aqueous solubility. Optimal: -4~0.5 log mol/L     |
| logP             | 3.181   | Log of the octanol/water partition coefficient. Optimal: 0~3 |
| logD             | 2.256   | logP at physiological pH 7.4. Optimal: 1~3                   |

## 2. Medicinal Chemistry

| Property | Value   | Decision | Comment  |
|----------|---------|----------|--|
| QED      | 0.565   | ●        | ■ A measure of drug-likeness based on the concept of desirability;<br>■ Attractive: > 0.67; unattractive: 0.49~0.67; too complex: < 0.34   |
| SAscore  | 5.525   | ●        | ■ Synthetic accessibility score is designed to estimate ease of synthesis of drug-like molecules.<br>■ SAscore ≥ 6, difficult to synthesize; SAscore <6, easy to synthesize          |
| Fsp3     | 0.65    | ●        | ■ The number of sp <sup>3</sup> hybridized carbons / total carbon count, correlating with melting point and solubility.<br>■ Fsp <sup>3</sup> ≥ 0.42 is considered a suitable value. |
| MCE-18   | 121.091 | ●        | ■ MCE-18 stands for medicinal chemistry evolution.<br>■ MCE-18 ≥ 45 is considered a suitable value.  |

|                 |          |   |   |
|-----------------|----------|---|---|
| NPscore         | 2.893    | - | <p>■ Natural product-likeness score.</p> <p>■ This score is typically in the range from -5 to 5. The higher the score is, the higher the probability is that the molecule is a NP.</p>  |
| Lipinski Rule   | Accepted | ● | <p>■ <math>MW \leq 500</math>; <math>\log P \leq 5</math>; <math>Hacc \leq 10</math>; <math>Hdon \leq 5</math></p> <p>■ If two properties are out of range, a poor absorption or permeability is possible, one is acceptable.</p> |
| Pfizer Rule     | Accepted | ● | <p><math>\log P &gt; 3</math>; <math>TPSA &lt; 75</math></p> <p>Compounds with a high log P (&gt;3) and low TPSA (&lt;75) are likely to be toxic.</p>   |
| GSK Rule        | Accepted | ● | <p>■ <math>MW \leq 400</math>; <math>\log P \leq 4</math></p> <p>■ Compounds satisfying the GSK rule may have a more favorable ADMET profile</p>  |
| Golden Triangle | Accepted | ● | <p>■ <math>200 \leq MW \leq 500</math>; <math>-2 \leq \log D \leq 5</math></p> <p>■ Compounds satisfying the Golden Triangle rule may have a more favorable ADMET profile.</p>  |
| PAINS           | 1 alerts | - | Pan Assay Interference Compounds, frequent hitters, Alpha-screen artifacts and reactive compound.   |
| ALARM NMR       | 1 alerts | - | Thiol reactive compounds.   |
| BMS             | 0 alerts | - | Undesirable, reactive compounds.  |
| Chelator Rule   | 1 alerts | - | Chelating compounds.  |

### 3. Absorption

| Property            | Value   | Decision | Comment   |
|---------------------|---------|----------|---|
| Caco-2 Permeability | -4.739  | ●        | Optimal: higher than -5.15 Log unit   |
| MDCK Permeability   | 2.3e-05 | ●        | <p>■ low permeability: <math>&lt; 2 \times 10^{-6}</math> cm/s</p> <p>■ medium permeability: <math>2-20 \times 10^{-6}</math> cm/s</p> <p>■ high passive permeability: <math>&gt; 20 \times 10^{-6}</math> cm/s</p>   |
| Pgp-inhibitor       | 0.097   | ●        | <p>■ Category 1: Inhibitor; Category 0: Non-inhibitor;</p> <p>■ The output value is the probability of being Pgp-inhibitor</p>  |
| Pgp-substrate       | 0.012   | ●        | <p>■ Category 1: substrate; Category 0: Non-substrate;</p> <p>■ The output value is the probability of being Pgp-substrate</p>  |
| HIA                 | 0.009   | ●        | <p>■ Human Intestinal Absorption</p> <p>■ Category 1: HIA+ (HIA &lt; 30%); Category 0: HIA- (HIA &lt; 30%); The output value is the probability of being HIA+</p>   |
| F <sub>20%</sub>    | 0.003   | ●        | <p>■ 20% Bioavailability</p> <p>■ Category 1: F<sub>20%</sub> + (bioavailability &lt; 20%); Category 0: F<sub>20%</sub> - (bioavailability ≥ 20%); The output value is the probability of being F<sub>20%</sub> +</p> |

|            |       |   |  |
|------------|-------|---|--|
| $F_{30\%}$ | 0.003 | ● | ■ 30% Bioavailability<br>■ Category 1: $F_{30\%} +$ (bioavailability < 30%);<br>Category 0: $F_{30\%} -$ (bioavailability $\geq$ 30%); The output value is the probability of being $F_{30\%} +$ |
|------------|-------|---|--|

## 4. Distribution

| Property        | Value  | Decision | Comment  |
|-----------------|--------|----------|--|
| PPB             | 94.78% | ●        | ■ Plasma Protein Binding<br>■ Optimal: < 90%. Drugs with high protein-bound may have a low therapeutic index.                |
| VD              | 1.332  | ●        | ■ Volume Distribution<br>■ Optimal: 0.04-20L/kg  |
| BBB Penetration | 0.789  | ●        | ■ Blood-Brain Barrier Penetration<br>■ Category 1: BBB+; Category 0: BBB-; The output value is the probability of being BBB+ |
| Fu              | 10.43% | ●        | ■ The fraction unbound in plasms<br>■ Low: <5%; Middle: 5~20%; High: > 20%   |

## 5. Metabolism

| Property          | Value | Comment  |
|-------------------|-------|--|
| CYP1A2 inhibitor  | 0.051 | ■ Category 1: Inhibitor; Category 0: Non-inhibitor;<br>■ The output value is the probability of being inhibitor. |
| CYP1A2 substrate  | 0.776 | ■ Category 1: Substrate; Category 0: Non-substrate;<br>■ The output value is the probability of being substrate. |
| CYP2C19 inhibitor | 0.047 | ■ Category 1: Inhibitor; Category 0: Non-inhibitor;<br>■ The output value is the probability of being inhibitor. |
| CYP2C19 substrate | 0.809 | ■ Category 1: Substrate; Category 0: Non-substrate;<br>■ The output value is the probability of being substrate. |
| CYP2C9 inhibitor  | 0.252 | ■ Category 1: Inhibitor; Category 0: Non-inhibitor;<br>■ The output value is the probability of being inhibitor. |
| CYP2C9 substrate  | 0.948 | ■ Category 1: Substrate; Category 0: Non-substrate;<br>■ The output value is the probability of being substrate. |
| CYP2D6 inhibitor  | 0.01  | ■ Category 1: Inhibitor; Category 0: Non-inhibitor;<br>■ The output value is the probability of being inhibitor. |
| CYP2D6 substrate  | 0.419 | ■ Category 1: Substrate; Category 0: Non-substrate;<br>■ The output value is the probability of being substrate. |
| CYP3A4 inhibitor  | 0.302 | ■ Category 1: Inhibitor; Category 0: Non-inhibitor;<br>■ The output value is the probability of being inhibitor. |
| CYP3A4 substrate  | 0.454 | ■ Category 1: Substrate; Category 0: Non-substrate;<br>■ The output value is the probability of being substrate. |

## 6. Excretion

| Property         | Value | Decision | Comment   |
|------------------|-------|----------|---|
| CL               | 11.47 | ●        | <ul style="list-style-type: none"> <li>■ Clearance</li> <li>■ High: &gt;15 mL/min/kg; moderate: 5-15 mL/min/kg; low: &lt;5 mL/min/kg</li> </ul>   |
| T <sub>1/2</sub> | 0.275 | -        | <ul style="list-style-type: none"> <li>■ Category 1: long half-life ; Category 0: short half-life;</li> <li>■ long half-life: &gt;3h; short half-life: &lt;3h</li> <li>■ The output value is the probability of having long half-life.</li> </ul> |

## 7. Toxicity

| Property                | Value | Decision | Comment   |
|-------------------------|-------|----------|---|
| hERG Blockers           | 0.008 | ●        | <ul style="list-style-type: none"> <li>■ Category 1: active; Category 0: inactive;</li> <li>■ The output value is the probability of being active.</li> </ul>   |
| H-HT                    | 0.259 | ●        | <ul style="list-style-type: none"> <li>■ Human Hepatotoxicity</li> <li>■ Category 1: H-HT positive(+); Category 0: H-HT negative(-);</li> <li>■ The output value is the probability of being toxic.</li> </ul>                    |
| DILI                    | 0.196 | ●        | <ul style="list-style-type: none"> <li>■ Drug Induced Liver Injury.</li> <li>■ Category 1: drugs with a high risk of DILI; Category 0: drugs with no risk of DILI. The output value is the probability of being toxic.</li> </ul> |
| AMES Toxicity           | 0.077 | ●        | <ul style="list-style-type: none"> <li>■ Category 1: Ames positive(+); Category 0: Ames negative(-);</li> <li>■ The output value is the probability of being toxic.</li> </ul>  |
| Rat Oral Acute Toxicity | 0.952 | ●        | <ul style="list-style-type: none"> <li>■ Category 0: low-toxicity; Category 1: high-toxicity;</li> <li>■ The output value is the probability of being highly toxic.</li> </ul>  |
| FDAMDD                  | 0.974 | ●        | <ul style="list-style-type: none"> <li>■ Maximum Recommended Daily Dose</li> <li>■ Category 1: FDAMDD (+); Category 0: FDAMDD (-)</li> <li>■ The output value is the probability of being positive.</li> </ul>                    |
| Skin Sensitization      | 0.906 | ●        | <ul style="list-style-type: none"> <li>■ Category 1: Sensitizer; Category 0: Non-sensitizer;</li> <li>■ The output value is the probability of being sensitizer.</li> </ul>   |
| Carcinogenicity         | 0.572 | ●        | <ul style="list-style-type: none"> <li>■ Category 1: carcinogens; Category 0: non-carcinogens;</li> <li>■ The output value is the probability of being toxic.</li> </ul>  |
| Eye Corrosion           | 0.003 | ●        | <ul style="list-style-type: none"> <li>■ Category 1: corrosives ; Category 0: noncorrosives</li> <li>■ The output value is the probability of being corrosives.</li> </ul>  |
| Eye Irritation          | 0.816 | ●        | <ul style="list-style-type: none"> <li>■ Category 1: irritants ; Category 0: nonirritants</li> <li>■ The output value is the probability of being irritants.</li> </ul>   |

|                      |       |   |  |
|----------------------|-------|---|--|
| Respiratory Toxicity | 0.945 | ● | <ul style="list-style-type: none"> <li>■ Category 1: respiratory toxicants; Category 0: respiratory nontoxicants</li> <li>■ The output value is the probability of being toxic.</li> </ul> |
|----------------------|-------|---|--|

## 8. Environmental toxicity

| Property                 | Value | Comment  |
|--------------------------|-------|--|
| Bioconcentration Factors | 1.093 | <ul style="list-style-type: none"> <li>■ Bioconcentration factors are used for considering secondary poisoning potential and assessing risks to human health via the food chain.</li> <li>■ The unit is <math>-\log_{10}[(\text{mg/L})/(1000 \cdot \text{MW})]</math></li> </ul> |
| IGC <sub>50</sub>        | 4.56  | <ul style="list-style-type: none"> <li>■ Tetrahymena pyriformis 50 percent growth inhibition concentration</li> <li>■ The unit is <math>-\log_{10}[(\text{mg/L})/(1000 \cdot \text{MW})]</math></li> </ul>   |
| LC <sub>50</sub> FM      | 6.406 | <ul style="list-style-type: none"> <li>■ 96-hour fathead minnow 50 percent lethal concentration</li> <li>■ The unit is <math>-\log_{10}[(\text{mg/L})/(1000 \cdot \text{MW})]</math></li> </ul>  |
| LC <sub>50</sub> DM      | 6.28  | <ul style="list-style-type: none"> <li>■ 48-hour daphnia magna 50 percent lethal concentration</li> <li>■ The unit is <math>-\log_{10}[(\text{mg/L})/(1000 \cdot \text{MW})]</math></li> </ul>   |

## 9. Tox21 pathway

| Property      | Value | Decision | Comment  |
|---------------|-------|----------|--|
| NR-AR         | 0.097 | ●        | <ul style="list-style-type: none"> <li>■ Androgen receptor</li> <li>■ Category 1: actives ; Category 0: inactives;</li> <li>■ The output value is the probability of being active.</li> </ul>                                |
| NR-AR-LBD     | 0.617 | ●        | <ul style="list-style-type: none"> <li>■ Androgen receptor ligand-binding domain</li> <li>■ Category 1: actives ; Category 0: inactives;</li> <li>■ The output value is the probability of being active.</li> </ul>          |
| NR-AhR        | 0.404 | ●        | <ul style="list-style-type: none"> <li>■ Aryl hydrocarbon receptor</li> <li>■ Category 1: actives ; Category 0: inactives;</li> <li>■ The output value is the probability of being active.</li> </ul>                        |
| NR-Aromatase  | 0.893 | ●        | <ul style="list-style-type: none"> <li>■ Category 1: actives ; Category 0: inactives;</li> <li>■ The output value is the probability of being active.</li> </ul>   |
| NR-ER         | 0.584 | ●        | <ul style="list-style-type: none"> <li>■ Estrogen receptor</li> <li>■ Category 1: actives ; Category 0: inactives;</li> <li>■ The output value is the probability of being active.</li> </ul>                                |
| NR-ER-LBD     | 0.795 | ●        | <ul style="list-style-type: none"> <li>■ Estrogen receptor ligand-binding domain</li> <li>■ Category 1: actives ; Category 0: inactives;</li> <li>■ The output value is the probability of being active.</li> </ul>          |
| NR-PPAR-gamma | 0.971 | ●        | <ul style="list-style-type: none"> <li>■ Peroxisome proliferator-activated receptor gamma</li> <li>■ Category 1: actives ; Category 0: inactives;</li> <li>■ The output value is the probability of being active.</li> </ul> |
| SR-ARE        | 0.818 | ●        | <ul style="list-style-type: none"> <li>■ Antioxidant response element</li> <li>■ Category 1: actives ; Category 0: inactives;</li> <li>■ The output value is the probability of being active.</li> </ul>                     |
| SR-ATAD5      | 0.669 | ●        | <ul style="list-style-type: none"> <li>■ ATPase family AAA domain-containing protein 5</li> <li>■ Category 1: actives ; Category 0: inactives;</li> <li>■ The output value is the probability of being active.</li> </ul>    |

|        |       |   |  |
|--------|-------|---|--|
| SR-HSE | 0.898 | ● | <ul style="list-style-type: none"> <li>■ Heat shock factor response element</li> <li>■ Category 1: actives ; Category 0: inactives;</li> <li>■ The output value is the probability of being active.</li> </ul> |
| SR-MMP | 0.955 | ● | <ul style="list-style-type: none"> <li>■ Mitochondrial membrane potential</li> <li>■ Category 1: actives ; Category 0: inactives;</li> <li>■ The output value is the probability of being active.</li> </ul>   |
| SR-p53 | 0.969 | ● | <ul style="list-style-type: none"> <li>■ Category 1: actives ; Category 0: inactives;</li> <li>■ The output value is the probability of being active.</li> </ul>   |

## 10. Toxicophore Rules

| Property                          | Value    | Comment   |
|-----------------------------------|----------|---|
| Acute Toxicity Rule               | 0 alerts | <ul style="list-style-type: none"> <li>■ 20 substructures</li> <li>■ acute toxicity during oral administration</li> </ul>       |
| Genotoxic Carcinogenicity Rule    | 3 alerts | <ul style="list-style-type: none"> <li>■ 117 substructures</li> <li>■ carcinogenicity or mutagenicity</li> </ul>                |
| NonGenotoxic Carcinogenicity Rule | 1 alerts | <ul style="list-style-type: none"> <li>■ 23 substructures</li> <li>■ carcinogenicity through nongenotoxic mechanisms</li> </ul> |
| Skin Sensitization Rule           | 7 alerts | <ul style="list-style-type: none"> <li>■ 155 substructures</li> <li>■ skin irritation</li> </ul>                                |
| Aquatic Toxicity Rule             | 3 alerts | <ul style="list-style-type: none"> <li>■ 99 substructures</li> <li>■ toxicity to liquid(water)</li> </ul>                       |
| NonBiodegradable Rule             | 1 alerts | <ul style="list-style-type: none"> <li>■ 19 substructures</li> <li>■ non-biodegradable</li> </ul>                               |
| SureChEMBL Rule                   | 1 alerts | <ul style="list-style-type: none"> <li>■ 164 substructures</li> <li>■ MedChem unfriendly status</li> </ul>                      |