Supplementary Material

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1. The ADME properties of compound a



| Physicochemi | cal Property | |
|-----------------------|--------------|---|
| Molecular Weight (MW) | 477.100 | 0 |
| Volume | 448.561 | 0 |
| Density | 1.064 | 0 |
| nHA | 5 | 0 |
| nHD | 0 | 0 |
| nRot | 9 | 0 |
| nRing | 3 | 0 |
| MaxRing | 6 | 0 |
| nHet | 9 | 0 |
| fChar | 0 | 0 |
| nRig | 20 | 0 |
| Flexibility | 0.450 | 0 |
| Stereo Centers | 0 | 0 |
| TPSA | 57.650 | 0 |
| logs | -5.954 | 0 |
| logP | 4.818 | 0 |
| logD | 4.316 | 0 |

| Medicinal Chemistry | | | | | Toxicity | | | |
|---------------------|--------------|------------|--------|---|--|---------------|--------|---|
| QED | | 0.232 | • | 0 | hERG Blockers | | • | 0 |
| SAscore | | 2.567 | • | 0 | н-нт | +++ | | 0 |
| Fsp ³ | | 0.167 | • | 0 | DILI | +++ | • | 0 |
| MCE-18 | | 21.000 | • | 0 | AMES Toxicity | | | 0 |
| NPscore | | -0.683 | | 0 | Rat Oral Acute Toxicity | | • | 0 |
| Lipinski Rule | | Accepted | • | 0 | FDAMDD | ++ | | 0 |
| Pfizer Rule | | Rejected | • | 0 | Skin Sensitization | | • | 0 |
| GSK Rule | | Rejected | • | 0 | Carcinogencity | - | • | 0 |
| Golden Triangle | | Accepted | • | 0 | Eye Corrosion | | • | 0 |
| PAINS | | 0 | | 0 | Eye Irritation | | ٠ | 0 |
| | | alert(s) | | | Respiratory Toxicity | | ٠ | 0 |
| ALARM NMR Rule | | 2 alert(s) | DETAIL | 0 | Environmental Toxicity | | | |
| BMS Rule | | 0 | | 0 | Bioconcentration Factors | 2.134 | | 0 |
| Obalatas Bula | | diert(s) | | • | IGC ₅₀ | 5.033 | | 0 |
| Cheidtor Kule | | alert(s) | | 0 | LC ₅₀ FM | 6.536 | | 0 |
| | Absorption | | | | LC ₅₀ DM | 6.776 | | 0 |
| | Absorption | | | | Tox21 Pathway | | | |
| Caco-2 Permeabilit | Y | -4.742 | • | 0 | NR-AR | | • | 0 |
| MDCK Permeability | | 1.4e-05 | ٠ | 0 | NR-AR-LBD | - | • | 0 |
| Pgp-inhibitor | | + | • | 0 | NR-AhR | ++ | | 0 |
| Pgp-substrate | | | ٠ | 0 | NR-Aromatase | +++ | • | 0 |
| HIA | | | • | 0 | NR-ER | ++ | | 0 |
| F _{20%} | | | • | 0 | NR-ER-LBD | + | | 0 |
| F _{30%} | | | • | 0 | NR-PPAR-gamma | | • | 0 |
| | Distribution | | | | SR-ARE | +++ | | 0 |
| | Distribution | | | | SR-ATAD5 | ++ | | 0 |
| PPB | | 99.443% | • | 0 | SR-HSE | | • | 0 |
| VD | | 0.934 | • | 0 | SR-MMP | +++ | | 0 |
| BBB Penetration | | | • | 0 | SR-p53 | +++ | | 0 |
| Fu | | 0.984% | ٠ | 0 | Toxicophore Rules | | | |
| | Metabolism | | | | Acute Toxicity Rule | 0 alert(s) | | 0 |
| OVDIAD inhibite | | | | | Genotoxic Carcinogenicity Rule | 1 alert(s) | DETAIL | 0 |
| CYPIA2 Inhibitor | | + | | 0 | NonGenotoxic Carcinogenicity Rule | 0 alert(s) | | 0 |
| CYPIA2 substrate | | +++ | | 0 | Skin Sensitization Rule | 2 alert(s) | DETAIL | 0 |
| CTP2CI9 Inhibitor | | ++ | | 0 | Aquatic Toxicity Rule | 6 alert(s) | DETAIL | 0 |
| CYP2CI9 substrate | | | | 0 | NonBiodegradable Rule | 4 alert(s) | DETAIL | 0 |
| CTP2C9 Inhibitor | | ++ | | 0 | SureChEMBL Rule | 0 alert(s) | | 0 |
| CTP2C9 substrate | | - | | 0 | FAF-Drugs4 Rule | 1 alert(s) | DETAIL | 0 |
| CYP2D6 Inhibitor | | | | 0 | | | | |
| CYP2D6 substrate | | | | 0 | Tip: For the classification endpoints, the prediction probability values are transformed into six symbols: 0-01() 01-03(- | | | |
| CYP3A4 INNIDITOR | | - | | 0 | -), 0.3-0.5(-), 0.5-0.7(+), 0.7-0.9(++), ar | nd 0.9-1.0(++ | ++). | |
| CTP3A4 SUDStrate | | ++ | | 0 | | | | |
| | Excretion | | | | | | | |
| CL | | 9.008 | • | 0 | | | | |
| Tala | | 0.012 | | 0 | | | | |

Figure S1. The ADME properties of compound a

































































































































Figure S65. Two-dimensional diagram of the interaction between fomesafen and protoporphyrinogen oxidase



Figure S66. Two-dimensional diagram of the interaction between compound **7f** and protop rinogen oxidase