Characterization of three naturally occurring lignans, sesamol, sesamolin, and sesamin, as potent inhibitors of human cytochrome P450 46A1: Implications for treating excitatory neurotoxicity

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### Supplementary Tables

#### Table S1 MS/MS conditions for analyzed compounds

| Analyte                      | Transition (m/z) | DP (eV) | CE (eV) | CEP (eV) | EP (eV) | CXP (eV) |
|------------------------------|------------------|---------|---------|----------|---------|----------|
| 16β-hydroxytestosterone     | 305.2→97.2       | 59.0    | 35.0    | 18.65    | 7.0     | 8.0      |
| Carbamazepine               | 370.4→288.1      | 60.0    | 42.0    | 16.40    | 10.0    | 14.0     |

#### Table S2 Primers used for RT-qPCR

| Gene          | Forward 5′-3′         | Reverse 5′-3′         |
|---------------|-----------------------|-----------------------|
| CYP46A1       | AGCATAGGAGGGCTACAACG  | CTGCCATCAAGGACAACT    |
| HMGCR         | CTGCATCGGGCAGCAGTT    | CAGTGCTTGAGCGTAGCC    |
| β-actin       | TATTGGCAACGAGCGGTTC   | ATGCCACAGGATTCCATACCC |

#### Table S3 Molecular docking simulation of compounds with sesamol, sesamin, sesamolin, and soticlestat

| Compounds    | Total Score | Chem Score | CScore | Enzyme-ligand interactions                                                                 |
|--------------|-------------|------------|--------|------------------------------------------------------------------------------------------|
|              |             |            |        | Conventional Hydrogen Bond                                                                 |
|              |             |            |        | Classical Water Hydrogen Bond                                                            |
|              |             |            |        | Pi-Pi stack                                                                                 |
| Sesamol      | 3.17        | -14.745    | 4      | Gly369, Trp368                                                                             |
|              |             |            |        | -                                                                                          |
|              |             |            |        | Trp368                                                                                     |
| Sesamin      | 6.16        | -27.53     | 5      | Gly369, W765 (n=2)                                                                        |
|              |             |            |        | W732 (n=2)                                                                                 |
|              |             |            |        | Phe371                                                                                     |
| Sesamolin    | 6.75        | -24.393    | 5      | Gly369, W765                                                                               |
|              |             |            |        | W765, W770                                                                                 |
|              |             |            |        | Trp368 (n=2)                                                                               |
| Soticlestat  | 6.74        | -38.311    | 2      | Gly369, Trp368                                                                             |
|              |             |            |        | W765                                                                                       |
|              |             |            |        | Trp368 (n=2)                                                                               |

### Supplementary Figure

Fig. S1 Molecule docking simulations of soticlestat with CYP46A1
Fig. S2 Cell viability after treatment with various concentrations sesame lignans