**Table 1**: IC50 values of the tested compounds in µM against the studied cancer and normal cells.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Cpd. No. | HepG-2 | MDA-MB-231 | A549 | OEC |
| 19 | 0.339 ± 0.026 | 0.329 ± 0.003 | 0.293 ± 0.013 | 1.622 ± 0.015 |
| 20 | 0.400 ± 0.033 | 0.318 ± 0.017 | 0.308 ± 0.021 | 1.255 ± 0.036 |
| 21 | 0.446 ± 0.038 | 0.628 ± 0.034 | 0.305 ± 0.024 | 1.658 ± 0.022 |
| 22 | **0.268 ± 0.016** | **0.284 ± 0.006** | **0.199 ± 0.009** | **1.465 ± 0.025** |
| 23 | 0.454 ± 0.015 | 0.718 ± 0.038 | 0.368 ± 0.037 | 1.648 ± 0.007 |
| 24 | 0.855 ± 0.026 | 1.062 ± 0.027 | 0.477 ± 0.044 | 1.394 ± 0.021 |
| 25 | **0.254 ± 0.013** | **0.304 ± 0.003** | **0.267 ± 0.004** | **1.330 ± 0.015** |
| 26 | 0.283 ± 0.014 | 0.708 ± 0.051 | 0.209 ± 0.007 | 1.075 ± 0.027 |
| 27 | 0.250 ± 0.011 | 0.430 ± 0.008 | 0.220 ± 0.038 | 1.396 ± 0.004 |
| 28 | 0.458 ± 0.017 | 0.597 ± 0.029 | 0.413 ± 0.012 | 1.246 ± 0.022 |
| 29 | 0.801 ± 0.02 | 0.852 ± 0.039 | 0.586 ± 0.031 | 1.677 ± 0.019 |
| 30 | **0.201 ± 0.047** | **0.208 ± 0.041** | **0.226 ± 0.023** | **1.471 ± 0.013** |
| 5-FU | 0.617 ± 0.06 | 0.674 ± 0.022 | 0.637 ± 0.057 | 4.079 ± 0.028 |
| Meth.\* | 0.145 ± 0.007 | 0.148 ± 0.011 | 0.125 ± 0.013 | 1.124 ± 0.031 |

\* Meth. = Methotrexate

**Table 2:** Selectivity indices (in descending order) of new compounds and reference anticancer agents.

|  |  |  |  |
| --- | --- | --- | --- |
| Cop. No. | SI HepG-2 | SI MDA-MB-231 | SI A549 |
| 19 | 4.785 | 4.930 | 5.536 |
| 20 | 3.138 | 3.947 | 4.075 |
| 21 | 3.717 | 2.640 | 5.436 |
| 22 | 5.466 | 5.158 | **7.362** |
| 23 | 3.630 | 2.295 | 4.478 |
| 24 | 1.630 | 1.313 | 2.922 |
| 25 | 5.236 | 4.375 | 4.981 |
| 26 | 3.799 | 1.518 | 5.144 |
| 27 | 5.584 | 3.247 | 6.345 |
| 28 | 2.721 | 2.087 | 3.017 |
| 29 | 2.094 | 1.968 | 2.862 |
| 30 | 7.318 | 7.072 | 6.509 |
| 5-FU | 6.611 | 6.052 | 6.403 |
| Meth.\* | 7.752 | 7.595 | 8.992 |

\* Meth. = Methotrexate

**Table 3**: Apoptotic gene levels in A549 cells treated with **22.**

|  |  |  |  |
| --- | --- | --- | --- |
| Comp. Code | Apoptotic Markers | | BAX/Bcl2 Ratio |
| **Bax** | **Bcl2** |  |
| 22 | 8.01 | 0.28 | 28.60 |
| 5-FU | 5.91 | 0.34 | 17.38 |
| Control | 1.00 | 1.00 | 1.00 |

**Table 4**: Calculated parameters for Lipinski's rule of five.

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Comp. ID | M. wt. g/mol | Log P | HBA | HBD | nVs | Rot. bonds | TPSA Å2 | %ABS |
| Lipinski a | ≤ 500 | ≤ 5 | ≤ 10 | ≤ 5 | ≤ 1 | - | - | - |
| Veber b | - | - | - | - | 0 | ≤ 10 | ≤ 140 | - |
| 19 | 305.31 | 0.91 | 4 | 2 | 0 | 3 | 154.08 | 55.84 |
| 22 | 337.17 | 1.93 | 3 | 2 | 0 | 3 | 93.24 | 76.832 |
| 25 | 372.38 | 1.13 | 6 | 0 | 0 | 6 | 117.78 | 68.366 |
| 28 | 386.41 | 1.57 | 6 | 0 | 0 | 7 | 117.78 | 68.366 |
| 5-Fluorouracil | 112.09 | -0.27 | 2 | 2 | 0 | 0 | 65.72 | 86.327 |
| Methotrexate | 454.44 | -0.34 | 9 | 5 | 1 (TPSA > 140) | 10 | 210.54 | 36.364 |