| | Lidocaine | | | | | |
|---|---|---|---|---|---|---|
| | 0 mM | 1 mM | 2 mM | 3 mM | 4 mM | 5 mM |
| | 1.4376 | 1.2829 | 1.0469 | 0.8076 | 0.5031 | 0.0729 |
| | 1.4489 | 1.2855 | 1.0556 | 0.8314 | 0.5474 | 0.0762 |
| | 1.46 | 1.2634 | 1.0484 | 0.8679 | 0.51 | 0.0763 |
| Average | 1.4488333 | 1.2772667 | 1.0503 | 0.8356333 | 0.5201667 | 0.0751333 |
| Avedev | 0.0074889 | 0.0092444 | 0.0035333 | 0.0215111 | 0.0181556 | 0.0014889 |
| Ratio | 100 | 88.15829 | 72.492812 | 57.676293 | 35.902451 | 5.1857818 |
| | 0.516891 | 0.6380613 | 0.2438744 | 1.4847195 | 1.2531156 | 0.1027647 |

| | Lidocaine | | | | | |
|---|---|---|---|---|---|---|
| dose | 0 | 1 | 2 | 3 | 4 | 5 |
| Average | 100 | 88.15829 | 72.492812 | 57.676293 | 35.902451 | 5.1857818 |
| Avedev | 0.516891 | 0.6380613 | 0.2438744 | 1.4847195 | 1.2531156 | 0.1027647 |

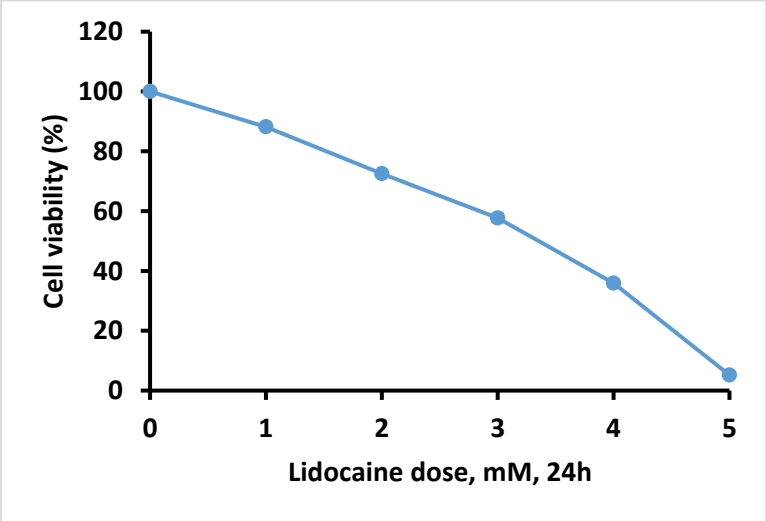


**Figure S1A. Effects of lidocaine on cell viability in HepG2 cells.** HepG2 cells were treated with the specified concentrations of lidocaine for 24 hours.

| | Cisplatin | | | | | |
|---|---|---|---|---|---|---|
| | 0 uM | 5 uM | 10 uM | 20 uM | 50 uM | 80 uM |
| | 1.4479 | 1.3537 | 1.2098 | 0.7398 | 0.7366 | 0.6525 |
| | 1.4326 | 1.3311 | 1.2007 | 0.7867 | 0.6906 | 0.6185 |
| | 1.3902 | 1.3719 | 1.1822 | 0.7955 | 0.6722 | 0.58 |
| Average | 1.4235667 | 1.3522333 | 1.1975667 | 0.774 | 0.6998 | 0.617 |
| Avedev | 0.0222444 | 0.0140889 | 0.0102444 | 0.0228 | 0.0245333 | 0.0246667 |
| Ratio | 100.00000 | 94.98911 | 84.12438 | 54.37048 | 49.15822 | 43.34184 |
| | 1.56259 | 0.98969 | 0.71963 | 1.60161 | 1.72337 | 1.73274 |

| | Cisplatin | | | | | |
|---|---|---|---|---|---|---|
| dose | 0 | 5 | 10 | 20 | 50 | 80 |
| Average | 100.0 | 95.0 | 84.1 | 54.4 | 49.2 | 43.3 |
| Avedev | 1.56259 | 0.98969 | 0.71963 | 1.60161 | 1.72337 | 1.73274 |

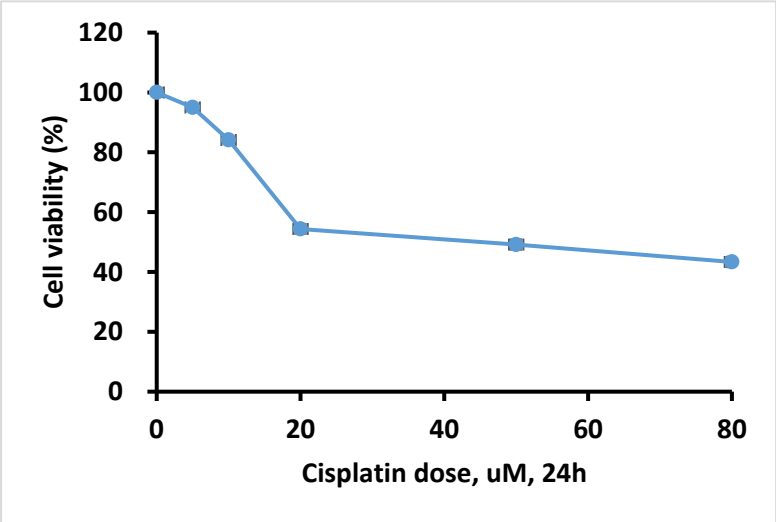


**Figure S1B. Effects of cisplatin on cell viability in HepG2 cells.** HepG2 cells were treated with the specified concentrations of cisplatin for 24 hours.

| | 5-FU | | | | | |
|---|---|---|---|---|---|---|
| | 0 uM | 10 uM | 20 uM | 50 uM | 100 uM | 200 uM |
| | 1.3653 | 1.1278 | 1.3215 | 1.3293 | 1.2923 | 1.1379 |
| | 1.4473 | 1.1125 | 1.3288 | 1.2978 | 1.3288 | 1.102 |
| | 1.3875 | 1.0669 | 1.3225 | 1.3414 | 1.3691 | 1.113 |
| Average | 1.4000333 | 1.1024 | 1.3242667 | 1.3228333 | 1.3300667 | 1.1176333 |
| Avedev | 0.0315111 | 0.0236667 | 0.0030222 | 0.0166889 | 0.0260222 | 0.0135111 |
| Ratio | 100 | 78.740984 | 94.588226 | 94.485848 | 95.002502 | 79.829054 |
| | 2.2507401 | 1.690436 | 0.2158679 | 1.1920351 | 1.8586859 | 0.9650564 |

| | 5-FU | | | | | |
|---|---|---|---|---|---|---|
| dose | 0 | 10 | 20 | 50 | 100 | 200 |
| Average | 100 | 78.740984 | 94.588226 | 94.485848 | 95.002502 | 79.829054 |
| Avedev | 2.2507401 | 1.690436 | 0.2158679 | 1.1920351 | 1.8586859 | 0.9650564 |

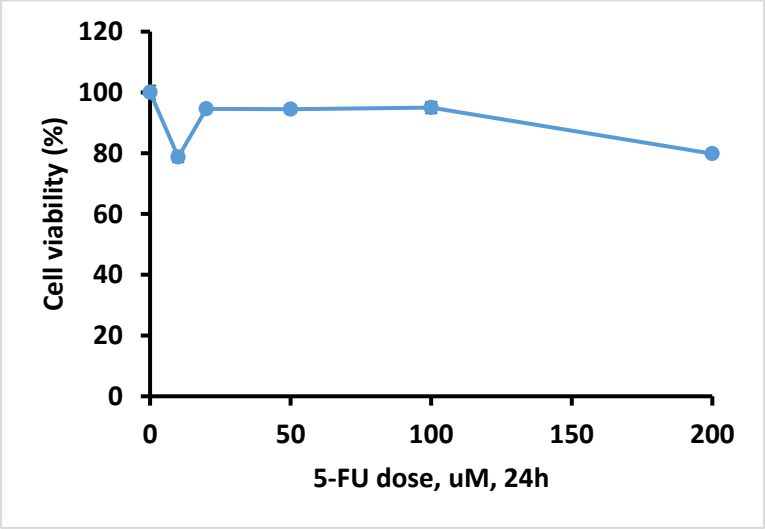


**Figure S1C. Effects of 5-FU on cell viability in HepG2 cells.** HepG2 cells were treated with the specified concentrations of 5-FU for 24 hours.

| | Lidocaine | | | | | |
|---|---|---|---|---|---|---|
| | 0 mM | 1 mM | 2 mM | 3 mM | 4 mM | 5 mM |
| | 2.1556 | 1.9458 | 2.0276 | 1.7924 | 1.5339 | 1.1329 |
| | 2.0169 | 1.758 | 1.7449 | 1.7749 | 1.5319 | 1.0425 |
| | 2.0576 | 1.9071 | 1.7001 | 1.6796 | 1.5893 | 1.1411 |
| Average | 2.0767 | 1.8703 | 1.8242 | 1.7489667 | 1.5517 | 1.1055 |
| Avedev | 0.0526 | 0.0748667 | 0.1356 | 0.0462444 | 0.0250667 | 0.042 |
| Ratio | 100 | 90.061155 | 87.841287 | 84.218552 | 74.719507 | 53.233495 |
| | 2.5328646 | 3.6050786 | 6.5295902 | 2.2268235 | 1.2070432 | 2.0224394 |

| | Lidocaine | | | | | |
|---|---|---|---|---|---|---|
| dose | 0 | 1 | 2 | 3 | 4 | 5 |
| Average | 100 | 90.061155 | 87.841287 | 84.218552 | 74.719507 | 53.233495 |
| Avedev | 2.5328646 | 3.6050786 | 6.5295902 | 2.2268235 | 1.2070432 | 2.0224394 |

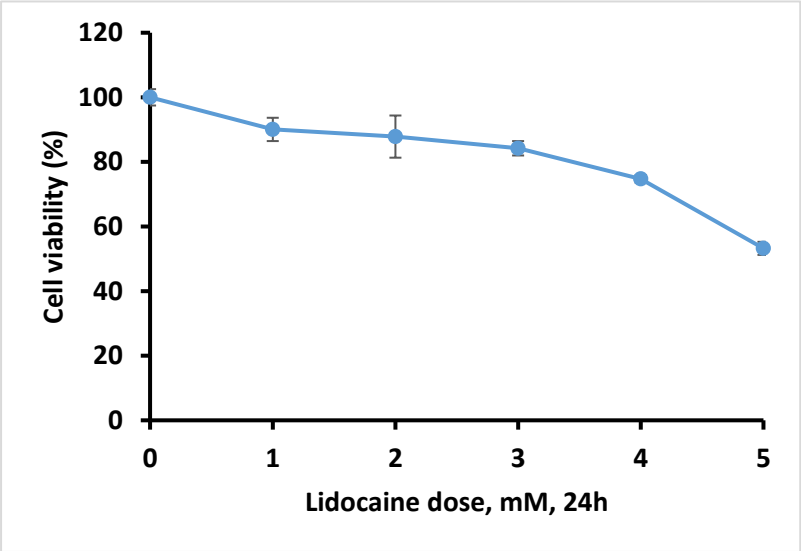


**Figure S2A. Effects of lidocaine on cell viability in Hep3B cells.** Hep3B cells were treated with the specified concentrations of lidocaine for 24 hours.

| | Cisplatin | | | | | |
|---|---|---|---|---|---|---|
| | 0 uM | 5 uM | 10 uM | 20 uM | 50 uM | 80 uM |
| | 1.9222 | 1.7888 | 1.7393 | 1.3251 | 1.0001 | 0.5127 |
| | 1.9884 | 1.8728 | 1.7417 | 1.3522 | 0.9325 | 0.5304 |
| | 2.1256 | 1.9025 | 1.7414 | 1.3475 | 0.943 | 0.5032 |
| Average | 2.0120667 | 1.8547 | 1.7408 | 1.3416 | 0.9585333 | 0.5154333 |
| Avedev | 0.0756889 | 0.0439333 | 0.001 | 0.011 | 0.0277111 | 0.0099778 |
| Ratio | 100.0000 | 92.1789 | 86.5180 | 66.6777 | 47.6392 | 25.6171 |
| | 3.7617 | 2.1835 | 0.0497 | 0.5467 | 1.3772 | 0.4959 |

| | Cisplatin | | | | | |
|---|---|---|---|---|---|---|
| dose | 0 | 5 | 10 | 20 | 50 | 80 |
| Average | 100.0000 | 92.1789 | 86.5180 | 66.6777 | 47.6392 | 25.6171 |
| Avedev | 3.7617 | 2.1835 | 0.0497 | 0.5467 | 1.3772 | 0.4959 |

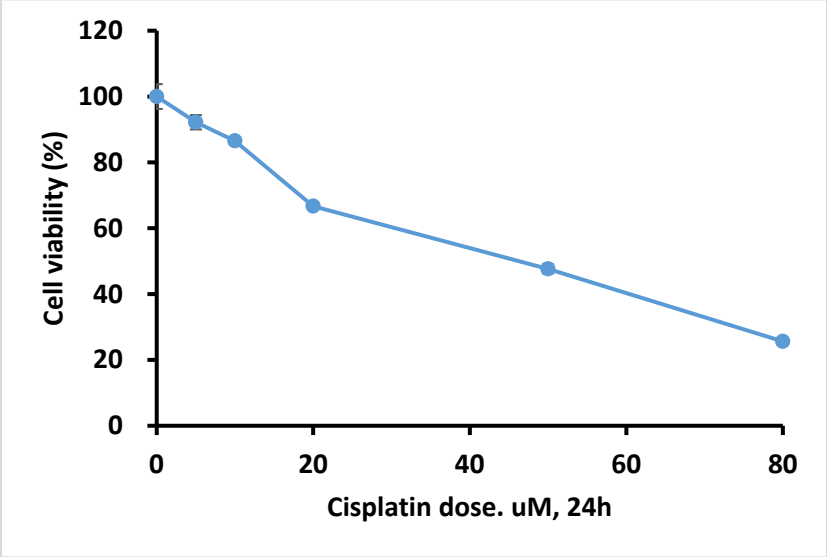


**Figure S2B. Effects of cisplatin on cell viability in Hep3B cells.** Hep3B cells were treated with the specified concentrations ofcisplatin for 24 hours.

| 5-FU |
|---|

| | 0 uM | 10 uM | 20 uM | 50 uM | 100 uM | 200 uM |
|---|---|---|---|---|---|---|
| | 1.9339 | 1.7707 | 1.7047 | 1.7802 | 1.7222 | 1.5475 |
| | 1.9189 | 1.8946 | 1.7652 | 1.7459 | 1.7645 | 1.6735 |
| | 1.986 | 1.7957 | 1.7922 | 1.7799 | 1.7943 | 1.64 |
| Average | 1.9462667 | 1.8203333 | 1.7540333 | 1.7686667 | 1.7603333 | 1.6203333 |
| Avedev | 0.0264889 | 0.0495111 | 0.0328889 | 0.0151778 | 0.0254222 | 0.0485556 |
| Ratio | 100.0000 | 93.5295 | 90.1230 | 90.8748 | 90.4467 | 83.2534 |
| | 1.3610 | 2.5439 | 1.6898 | 0.7798 | 1.3062 | 2.4948 |

| | 5-FU | | | | | |
|---|---|---|---|---|---|---|
| dose | 0 | 10 | 20 | 50 | 100 | 200 |
| Average | 100.000 | 93.529 | 90.123 | 90.875 | 90.447 | 83.253 |
| Avedev | 1.361 | 2.544 | 1.690 | 0.780 | 1.306 | 2.495 |

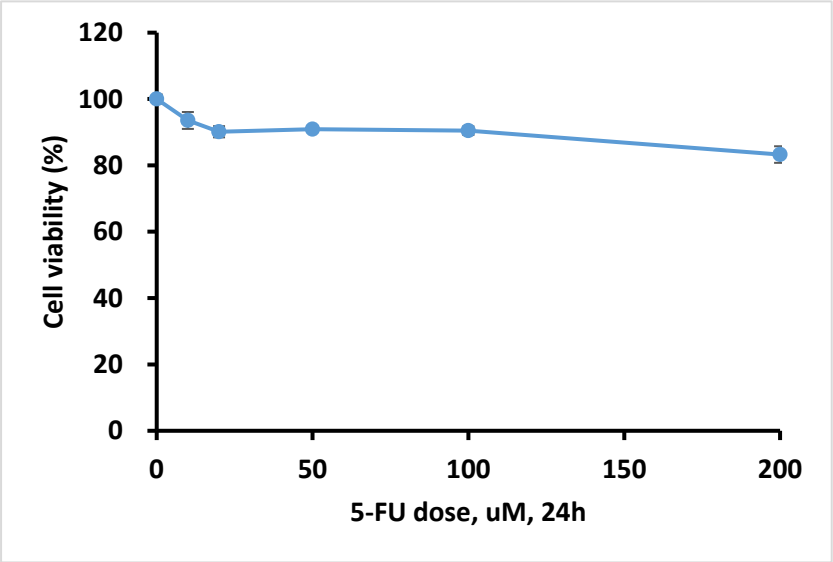


**Figure S2C. Effects of 5-FU on cell viability in Hep3B cells.** Hep3B cells were treated with the specified concentrations of 5-FU for 24 hours.

| | Cisplatin dose, 24h | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| 570 nm- 650 nm | 0 uM | 0.156 uM | 0.3125 uM | 0.625 uM | 1.25 uM | 2.5 uM | 5 uM | 10 uM | 20 uM | 40 uM |
| Lidocaine c | 0 mM | 1.1946 | 1.1607 | 1.1119 | 1.1865 | 1.1082 | 1.0455 | 1.0615 | 0.8613 | 0.6701 | 0.6538 |
| | 1 mM | 1.0282 | 1.0391 | 1.0154 | 1.0055 | 1.005 | 0.9644 | 1.0041 | 0.8557 | 0.7105 | 0.516 |
| | 2 mM | 0.9063 | 0.915 | 0.9073 | 0.8387 | 0.8506 | 0.8215 | 0.8577 | 0.7385 | 0.6078 | 0.1811 |
| | 3 mM | 0.6686 | 0.6655 | 0.68 | 0.7128 | 0.6094 | 0.6731 | 0.6616 | 0.5455 | 0.3021 | 0.1853 |
| | 4 mM | 0.5705 | 0.4978 | 0.4983 | 0.4787 | 0.5 | 0.4868 | 0.4742 | 0.3842 | 0.167 | 0.4117 |
| | 5 mM | 0.5337 | 0.5612 | 0.4885 | 0.5341 | 0.4606 | 0.4574 | 0.4873 | 0.3994 | 0.393 | 0.2288 |
| | 6 mM | 0.0825 | 0.109 | 0.115 | 0.1109 | 0.0985 | 0.1155 | 0.08 | 0.0922 | 0.0419 | 0.0288 |
| | 7 mM | 0.0157 | 0.0166 | 0.0173 | 0.0177 | 0.0174 | 0.0168 | 0.0155 | 0.0152 | 0.0152 | 0.013 |

Drug: lido

Data points entered:

| lido | Fraction affected |
|---|---|
| 1 | 0.1409 |
| 2 | 0.1004 |
| 2 | 0.244 |
| 3 | 0.1407 |
| 3 | 0.4452 |
| 4 | 0.2641 |
| 4 | 0.5282 |
| 5 | 0.6037 |
| 5 | 0.5594 |
| 6 | 0.8339 |
| 6 | 0.9412 |
| 7 | 0.9985 |
| 7 | 0.9977 |

Median-effect parameters:

| | lido |
|---|---|
| Dm: | 3.05051 |
| lower 95%: | 2.27E+00 |
| upper 95% | 4.09306 |
| m: | 3.73695 +/- 0.949416 |
| y-int: | -1.8101 +/- 0.587507 |
| r: | 0.76471 |
| CCSI: | -0.92049 |

Drug: cisplatin

Data points entered:

| cisplatin | Fraction affected |
|---|---|
| 0.156 | 0.0288 |
| 0.3125 | 7.01E-02 |
| 0.625 | 0.0069 |
| 1.25 | 0.0732 |
| 2.5 | 0.1263 |
| 5 | 0.1127 |
| 10 | 0.2821 |
| 20 | 0.4439 |
| 40 | 0.4577 |

Median-effect parameters:

| | cisplatin |
|---|---|
| Dm: | 51.00931 |
| lower 95%: | 10.41621 |
| upper 95% | 19:09 |
| m: | 0.69761 +/- 0.161227 |
| y-int: | -1.1913 +/- 0.140795 |
| r: | 0.85315 |
| CCSI: | -0.4556 |

Drug: MAX:MAX

Combinatic lido cisplatin

Ratio: 40:00.0

Data points entered:

| lido | cisplatin | Fraction affected |
|---|---|---|
| () | () | |
| 1 | 5.71429 | 0.1601 |
| 2 | 11.4286 | 0.2912 |
| 3 | 17.1429 | 0.4414 |
| 4 | 22.8571 | 0.6097 |
| 5 | 28.5714 | 0.673 |
| 6 | 34.2857 | 0.9755 |
| 7 | 40 | 1 |

Median-effect parameters:

| | lido | cisplatin |
|---|---|---|
| | () | () |
| Dm: | 2.24369 | 12.82108 |
| lower 95%: | 1.17E+00 | 6.68512 |
| upper 95% | 4.30307 | 24.58897 |
| m: | 4.79408 +/- 2.109970 | |
| y-int: | -1.6825 +/- 1.258173 | |
| r: | 0.71274 | |
| CCSI: | -0.887 | |

CI Simulations

| Fa | CI | Est. s.d. | lido | cisplatin |
|---|---|---|---|---|
| | | | () | () |
| 0.02 | 30.475 | 30.4211 | 0.99633 | 5.69332 |
| 0.05 | 1.01E+01 | 7.41E+00 | 1.21402 | 6.93727 |
| 0.1 | 4.55E+00 | 2.74E+00 | 1.41878 | 8.10734 |
| 0.15 | 2.919 | 1.63E+00 | 1.56252 | 8.92869 |
| 0.2 | 2.171 | 1.162 | 1.68027 | 9.60153 |
| 0.25 | 1.75 | 0.9039 | 1.78418 | 10.19534 |
| 0.3 | 1.483 | 0.7394 | 1.88021 | 10.74405 |
| 0.35 | 1.299 | 0.6243 | 1.9719 | 11.26798 |
| 0.4 | 1.166 | 0.5386 | 2.06173 | 11.78131 |
| 0.45 | 1.066 | 0.472 | 2.15171 | 12.29549 |
| 0.5 | 0.987 | 0.4186 | 2.24369 | 12.82108 |
| 0.55 | 0.923 | 0.3748 | 2.3396 | 13.36914 |
| 0.6 | 0.871 | 0.3383 | 2.44171 | 13.95262 |
| 0.65 | 0.827 | 0.3076 | 2.55294 | 14.58826 |
| 0.7 | 0.789 | 0.2817 | 2.67744 | 15.29964 |
| 0.75 | 0.755 | 0.26 | 2.82154 | 16.12307 |
| 0.8 | 0.724 | 0.2424 | 2.99604 | 17.1202 |
| 0.85 | 0.694 | 0.2291 | 3.22181 | 18.41034 |
| 0.9 | 0.663 | 0.2219 | 3.54821 | 20.27547 |
| 0.95 | 0.625 | 0.2267 | 4.14667 | 23.69523 |
| 0.99 | 5.62E-01 | 0.2717 | 5.85105 | 33.43457 |

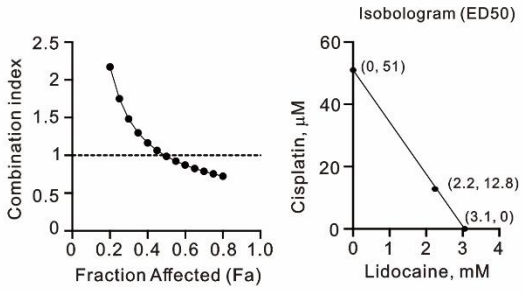





Figure S3A Combination index of lidocaine with cisplatin in HepG2 cells. The combination index for lidocaine in conjunction with cisplatin was calculated. Additionally, Isobolograms ($ED_{50}$) for the combinations of lidocaine with cisplatin or 5-FU were determined using CalcuSyn software.

| | 5-FU dose, 24h | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| 570 nm- 650 nm | 0 uM | 5 uM | 10 uM | 20 uM | 50 uM | 100 uM | 200 uM | 250 uM | 350 uM | 500 uM |
| Lidocaine c 0 mM | 1.1281 | 1.0427 | 1.0702 | 1.0828 | 1.0606 | 0.9362 | 1.0532 | 0.9926 | 0.8941 | 0.7622 |
| 1 mM | 1.1341 | 1.0386 | 1.0471 | 1.0396 | 1.0036 | 0.995 | 1.0621 | 1.0731 | 1.0394 | 0.9526 |
| 2 mM | 1.0215 | 1.0328 | 1.0208 | 1.0876 | 0.9456 | 0.9884 | 0.9294 | 1.0363 | 1.0044 | 0.9631 |
| 3 mM | 0.9762 | 0.9426 | 0.9864 | 0.9682 | 0.9562 | 0.8667 | 0.8045 | 0.9387 | 0.9623 | 0.8536 |
| 4 mM | 0.8377 | 0.7933 | 0.7767 | 0.8463 | 0.7601 | 0.8416 | 0.7275 | 0.77 | 0.7138 | 0.5962 |
| 5 mM | 0.4565 | 0.5153 | 0.5112 | 0.553 | 0.4389 | 0.4819 | 0.4512 | 0.441 | 0.4119 | 0.3218 |
| 6 mM | 0.198 | 0.2139 | 0.1898 | 0.2034 | 0.1796 | 0.1954 | 0.1599 | 0.1508 | 0.1387 | 0.127 |
| 7 mM | 0.0133 | 0.0135 | 0.015 | 0.0158 | 0.0138 | 0.015 | 0.0132 | 0.0131 | 0.0118 | 0.0116 |

Drug: lido

Data points entered:

| lido | Fraction affected |
|---|---|
| 1 | 0.1409 |
| 2 | 0.1004 |
| 2 | 0.244 |
| 3 | 0.1407 |
| 3 | 0.4452 |
| 4 | 0.2641 |
| 4 | 0.5282 |
| 5 | 0.6037 |
| 5 | 0.5594 |
| 6 | 0.8339 |
| 6 | 0.9412 |
| 7 | 0.9985 |
| 7 | 0.9977 |

Median-effect parameters:

| | lido |
|---|---|
| Dm: | 3.05051 |
| lower 95%: | 2.27E+00 |
| upper 95% | 4.09306 |
| m: | 3.73695 +/- 0.949416 |
| y-int: | -1.8101 +/- 0.587507 |
| r: | 0.76471 |
| CCSI: | -0.92049 |

Drug: 5-FU

Data points entered:

| 5-FU | Fraction affected |
|---|---|
| 200 | 0.0721 |
| 250 | 1.26E-01 |
| 350 | 0.2139 |
| 500 | 0.3314 |

Median-effect parameters:

| | 5-FU |
|---|---|
| Dm: | 692.8752 |
| lower 95%: | 608.1357 |
| upper 95% | 789.4226 |
| m: | 1.98516 +/- 0.148752 |
| y-int: | -5.6392 +/- 0.370400 |
| r: | 0.99443 |
| CCSI: | ######## |

Drug: MAX:MAX

Combinatic lido 5-FU

Ratio: 01:20

Data points entered:

| lido () | 5-FU () | Fraction affected |
|---|---|---|
| 1 | 00:00.0 | 0.0843 |
| 2 | 40 | 0.168 |
| 3 | 60 | 0.2383 |
| 4 | 80 | 0.3623 |
| 5 | 100 | 0.6175 |
| 6 | 120 | 0.8868 |
| 7 | 140 | 1 |

Median-effect parameters:

| | lido () | 5-FU () |
|---|---|---|
| Dm: | 2.63394 | 52.67876 |
| lower 95%: | 1.40253 | 28.05059 |
| upper 95% | 4.94651 | 98.93024 |
| m: | 4.84146 +/- 2.284853 | |
| y-int: | -2.0363 +/- 1.362456 | |
| r: | 6.88E-01 | |
| CCSI: | -0.887 | |

CI Simulations

| Fa | CI | Est. s.d. | lido () | 5-FU () |
|---|---|---|---|---|
| 0.02 | 1.337 | 9.06E-01 | 1.18E+00 | 23.57909 |
| 0.05 | 1.216 | 0.7056 | 1.43E+00 | 28.67545 |
| 0.1 | 1.133 | 0.5775 | 1.67305 | 33.4609 |
| 0.15 | 1.087 | 5.10E-01 | 1.8408 | 36.81598 |
| 0.2 | 1.054 | 0.4648 | 1.97811 | 39.56222 |
| 0.25 | 1.029 | 0.4312 | 2.09921 | 41.98427 |
| 0.3 | 1.01E+00 | 4.05E-01 | 2.21106 | 44.22117 |
| 0.35 | 9.88E-01 | 3.83E-01 | 2.3178 | 46.35598 |
| 0.4 | 0.971 | 3.64E-01 | 2.42233 | 48.44668 |
| 0.45 | 0.955 | 0.3478 | 2.527 | 50.53994 |
| 0.5 | 0.939 | 0.3337 | 2.63394 | 52.67876 |
| 0.55 | 0.925 | 0.3213 | 2.7454 | 54.90809 |
| 0.6 | 0.91 | 0.3105 | 2.86403 | 57.28053 |
| 0.65 | 0.895 | 0.301 | 2.9932 | 59.86394 |
| 0.7 | 0.879 | 0.2931 | 3.1377 | 62.75391 |
| 0.75 | 0.862 | 0.2868 | 3.30487 | 66.09742 |
| 0.8 | 0.844 | 0.2826 | 3.5072 | 70.14399 |
| 0.85 | 0.822 | 0.2815 | 3.76881 | 75.37627 |
| 0.9 | 0.795 | 0.2859 | 4.14671 | 82.93415 |
| 0.95 | 0.753 | 0.3037 | 4.83872 | 96.77449 |
| 0.99 | 0.672 | 0.367 | 6.80459 | 136.0918 |

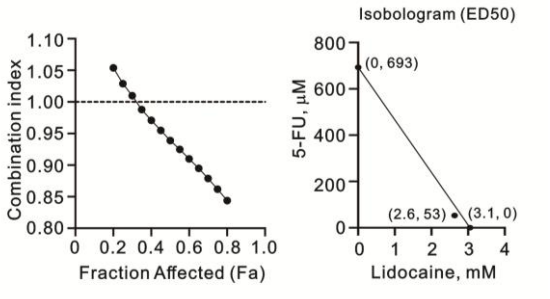


Figure S3B Combination index of lidocaine with 5-FU in HepG2 cells. The combination index for lidocaine in conjunction with 5-FU was calculated. Additionally, Isobolograms ($ED_{50}$) for the combinations of lidocaine with cisplatin or 5-FU were determined using CalcuSyn software.

| | Cisplatin dose, 24h | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| 570 nm- 650 nm | 0 uM | 0.156 uM | 0.3125 uM | 0.625 uM | 1.25 uM | 2.5 uM | 5 uM | 10 uM | 20 uM | 40 uM |
| Lidocaine c | 0 mM | 1.1986 | 1.16 | 1.2004 | 1.2054 | 1.1836 | 1.1041 | 1.0705 | 0.9538 | 0.7231 | 0.4789 |
| | 1 mM | 1.1614 | 1.1231 | 1.1821 | 1.113 | 1.0871 | 1.0505 | 1.0199 | 1.0002 | 0.6525 | 0.3882 |
| | 2 mM | 1.0638 | 1.0704 | 1.0728 | 1.1005 | 1.0302 | 0.9984 | 0.938 | 0.7539 | 0.5157 | 0.2239 |
| | 3 mM | 0.9654 | 1.0111 | 1.0124 | 1.1233 | 0.9988 | 0.9063 | 0.7877 | 0.6112 | 0.3685 | 0.1295 |
| | 4 mM | 0.9151 | 0.9447 | 0.9225 | 0.9742 | 0.8692 | 0.8088 | 0.5967 | 0.3933 | 0.2224 | 0.0758 |
| | 5 mM | 0.6156 | 0.6379 | 0.5894 | 0.6051 | 0.5354 | 0.4945 | 0.2881 | 0.1839 | 0.1359 | 0.0454 |
| | 6 mM | 0.2252 | 0.2621 | 0.2565 | 0.229 | 0.2044 | 0.1717 | 0.1185 | 0.0918 | 0.0643 | 0.0295 |
| | 7 mM | 0.0179 | 0.0205 | 0.0218 | 0.0192 | 0.0199 | 0.016782 | 0.0178 | 0.0142 | 0.0138 | 0.0118 |

Drug: Lido

Data points entered:

| Lido | Fraction affected |
|---|---|
| 4 | 0.2641 |
| 4 | 0.2433 |
| 5 | 0.6037 |
| 5 | 0.4942 |
| 6 | 0.8339 |
| 6 | 0.8212 |
| 7 | 0.9985 |
| 7 | 0.9949 |

Median-effect parameters:

| | Lido |
|---|---|
| Dm: | 4.67204 |
| lower 95%: | 4.27693 |
| upper 95% | 5.10364 |
| m: | 11.57942 +/- 2.068408 |
| y-int: | -7.7525 +/- 1.523740 |
| r: | 9.16E-01 |
| CCSI: | -0.99239 |

Drug: cisplatin

Data points entered:

| cisplatin | Fraction affected |
|---|---|
| 0.156 | 0.0381 |
| 0.3125 | 0.0043 |
| 0.625 | 7.54E-05 |
| 1.25 | 0.0183 |
| 2.5 | 0.0849 |
| 5 | 0.1131 |
| 10 | 2.11E-01 |
| 20 | 0.4041 |
| 40 | 0.6087 |

Median-effect parameters:

| | cisplatin |
|---|---|
| Dm: | 36.26585 |
| lower 95%: | 3.96881 |
| upper 95% | 331.3867 |
| m: | 1.15723 +/- 0.405865 |
| y-int: | -1.8047 +/- 0.354432 |
| r: | 0.73303 |
| CCSI: | ######## |

Drug: MAX:MAX

Combinatic Lido cisplatin

Ratio: 01:00.6

Data points entered:

| Lido | cisplatin | Fraction affected |
|---|---|---|
| () | () | |
| 1 | 00:00.0 | 0.0775 |
| 2 | 1.25 | 0.1468 |
| 3 | 1.875 | 0.2506 |
| 4 | 2.5 | 0.51 |
| 5 | 3.125 | 0.8558 |
| 6 | 3.75 | 0.956 |
| 7 | 4.375 | 1 |

Median-effect parameters:

| | Lido | cisplatin |
|---|---|---|
| | () | () |
| Dm: | 2.50235 | 1.56397 |
| lower 95%: | 1.46433 | 0.9152 |
| upper 95% | 4.27621 | 2.67263 |
| m: | 5.34938 +/- 2.084173 | |
| y-int: | -2.1309 +/- 1.242791 | |
| r: | 7.54E-01 | |
| CCSI: | -0.887 | |

CI Simulations

| Fa | CI | Est. s.d. | Lido | cisplatin |
|---|---|---|---|---|
| | | | () | () |
| 0.02 | 0.964 | 6.42E-01 | 1.21E+00 | 0.75556 |
| 0.05 | 0.715 | 0.3726 | 1.44E+00 | 0.90195 |
| 0.1 | 0.62 | 0.2763 | 1.65945 | 1.03716 |
| 0.15 | 0.589 | 2.40E-01 | 1.80935 | 1.13084 |
| 0.2 | 0.576 | 0.2194 | 1.93108 | 1.20693 |
| 0.25 | 0.57 | 0.2058 | 2.03778 | 1.27361 |
| 0.3 | 5.68E-01 | 1.96E-01 | 2.13579 | 1.33487 |
| 0.35 | 5.69E-01 | 1.88E-01 | 2.2289 | 1.39306 |
| 0.4 | 0.571 | 1.82E-01 | 2.31969 | 1.44981 |
| 0.45 | 0.574 | 0.1768 | 2.41022 | 1.50639 |
| 0.5 | 0.579 | 0.1727 | 2.50235 | 1.56397 |
| 0.55 | 0.584 | 0.1692 | 2.598 | 1.62375 |
| 0.6 | 0.591 | 0.1665 | 2.69939 | 1.68712 |
| 0.65 | 0.598 | 0.1644 | 2.80935 | 1.75584 |
| 0.7 | 0.608 | 0.1631 | 2.93182 | 1.83239 |
| 0.75 | 0.619 | 0.1628 | 3.07284 | 1.92053 |
| 0.8 | 0.633 | 0.1638 | 3.24262 | 2.02664 |
| 0.85 | 0.651 | 0.1673 | 3.46078 | 2.16299 |
| 0.9 | 0.678 | 0.1756 | 3.77339 | 2.35837 |
| 0.95 | 0.726 | 0.1984 | 4.33906 | 2.71191 |
| 0.99 | 0.852 | 0.2902 | 5.90755 | 3.69222 |

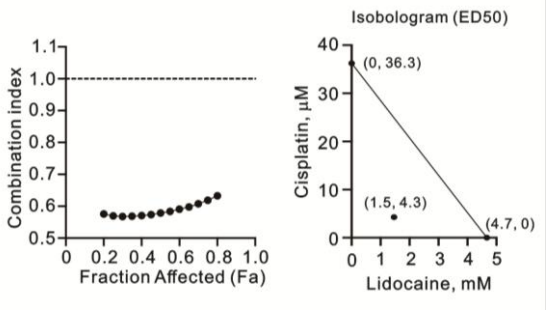


Figure S3C Combination index of lidocaine with cisplatin in Hep3B cells. The combination index for lidocaine in conjunction with cisplatin was calculated. Additionally, Isobolograms ($ED_{50}$) for the combinations of lidocaine with cisplatin or 5-FU were determined using CalcuSyn software.

| | 5-FU dose, 24h | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| 570 nm- 650 nm | 0 uM | 5 uM | 10 uM | 20 uM | 50 uM | 100 uM | 200 uM | 250 uM | 350 uM | 500 uM |
| Lidocaine ( 0 mM | 1.1281 | 1.0427 | 1.0702 | 1.0828 | 1.0606 | 0.9362 | 1.0532 | 0.9926 | 0.8941 | 0.7622 |
| 1 mM | 1.1341 | 1.0386 | 1.0471 | 1.0396 | 1.0036 | 0.995 | 1.0621 | 1.0731 | 1.0394 | 0.9526 |
| 2 mM | 1.0215 | 1.0328 | 1.0208 | 1.0876 | 0.9456 | 0.9884 | 0.9294 | 1.0363 | 1.0044 | 0.9631 |
| 3 mM | 0.9762 | 0.9426 | 0.9864 | 0.9682 | 0.9562 | 0.8667 | 0.8045 | 0.9387 | 0.9623 | 0.8536 |
| 4 mM | 0.8377 | 0.7933 | 0.7767 | 0.8463 | 0.7601 | 0.8416 | 0.7275 | 0.77 | 0.7138 | 0.5962 |
| 5 mM | 0.4565 | 0.5153 | 0.5112 | 0.553 | 0.4389 | 0.4819 | 0.4512 | 0.441 | 0.4119 | 0.3218 |
| 6 mM | 0.198 | 0.2139 | 0.1898 | 0.2034 | 0.1796 | 0.1954 | 0.1599 | 0.1508 | 0.1387 | 0.127 |
| 7 mM | 0.0133 | 0.0135 | 0.015 | 0.0158 | 0.0138 | 0.015 | 0.0132 | 0.0131 | 0.0118 | 0.0116 |

Title:
Date:
Investigator:
Filename: CalcuSyn2

Drug: Lido

Data points entered:

| Lido | Fraction affected |
|---|---|
| 4 | 0.2641 |
| 4 | 0.2433 |
| 5 | 0.6037 |
| 5 | 0.4942 |
| 6 | 0.8339 |
| 6 | 0.8212 |
| 7 | 0.9985 |
| 7 | 0.9949 |

Median-effect parameters:

| | Lido |
|---|---|
| Dm: | 4.67204 |
| lower 95%: | 4.27693 |
| upper 95% | 5.10364 |
| m: | 11.57942 +/- 2.068408 |
| y-int: | -7.7525 +/- 1.523740 |
| r: | 9.16E-01 |
| CCSI: | -0.99239 |

Drug: 5-FU

Data points entered:

| 5-FU | Fraction affected |
|---|---|
| 10 | 0.057 |
| 20 | 0.0458 |
| 50 | 0.0656 |
| 100 | 0.1764 |
| 350 | 0.2139 |
| 500 | 0.3314 |

Median-effect parameters:

| | 5-FU |
|---|---|
| Dm: | 2435.429 |
| lower 95%: | 624.6309 |
| upper 95% | 9495.712 |
| m: | 0.57634 +/- 0.106418 |
| y-int: | -1.9518 +/- 0.209870 |
| r: | 0.93808 |
| CCSI: | -0.95016 |

0
Drug: MAX:MAX
Combinatio Lido 5-FU
Ratio: 01:20

Data points entered:

| Lido | 5-FU | Fraction affected |
|---|---|---|
| () | () | |
| 1 | 20 | 0.0843 |
| 2 | 960:00:00 | 0.168 |
| 3 | 60 | 0.2383 |
| 4 | 00:00.0 | 0.3623 |
| 5 | 100 | 0.6175 |
| 6 | 120 | 0.8868 |
| 7 | 140 | 1 |

Median-effect parameters:

| | Lido | 5-FU |
|---|---|---|
| | () | () |
| Dm: | 2.63394 | 52.67876 |
| lower 95%: | 1.40253 | 28.05059 |
| upper 95%: | 4.94651 | 98.93024 |
| m: | 4.84146 +/- 2.284853 | |
| y-int: | -2.0363 +/- 1.362456 | |
| r: | 0.68784 | |
| CCSI: | -0.887 | |

CI Simulations

| Fa | CI | Est. s.d. | Lido () | 5-FU () |
|---|---|---|---|---|
| 0.02 | 8.644 | 7.8987 | 1.18E+00 | 23.57909 |
| 0.05 | 2.344 | 1.4658 | 1.43E+00 | 28.67545 |
| 0.1 | 1.055 | 5.17E-01 | 1.67E+00 | 33.4609 |
| 0.15 | 0.764 | 3.38E-01 | 1.84E+00 | 36.81598 |
| 0.2 | 0.657 | 0.2724 | 1.98E+00 | 39.56222 |
| 0.25 | 0.61 | 0.2399 | 2.09921 | 41.98427 |
| 0.3 | 0.588 | 2.21E-01 | 2.21106 | 44.22117 |
| 0.35 | 0.579 | 0.2096 | 2.3178 | 46.35598 |
| 0.4 | 0.577 | 0.202 | 2.42233 | 48.44668 |
| 0.45 | 5.80E-01 | 1.97E-01 | 2.527 | 50.53994 |
| 0.5 | 5.85E-01 | 1.94E-01 | 2.63394 | 52.67876 |
| 0.55 | 0.593 | 1.92E-01 | 2.7454 | 54.90809 |
| 0.6 | 0.604 | 0.1916 | 2.86403 | 57.28053 |
| 0.65 | 0.616 | 0.1923 | 2.9932 | 59.86394 |
| 0.7 | 0.63 | 0.1944 | 3.1377 | 62.75391 |
| 0.75 | 0.647 | 0.1983 | 3.30487 | 66.09742 |
| 0.8 | 0.669 | 0.205 | 3.5072 | 70.14399 |
| 0.85 | 0.696 | 0.2161 | 3.76881 | 75.37627 |
| 0.9 | 0.735 | 0.2365 | 4.14671 | 82.93415 |
| 0.95 | 0.803 | 0.2837 | 4.83872 | 96.77449 |
| 0.99 | 0.979 | 0.4547 | 6.80459 | 136.0918 |

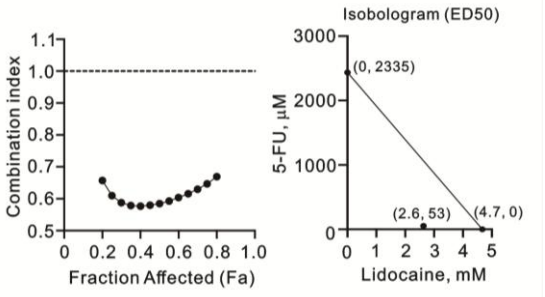





Figure S3D Combination index of lidocaine with 5-FU in Hep3B cells. The combination index for lidocaine in conjunction with 5-FU was calculated. Additionally, Isobolograms ($ED_{50}$) for the combinations of lidocaine with cisplatin or 5-FU were determined using CalcuSyn software.