

POSTER PRESENTATION

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P01.40. A new approach for quantifying chemosensitizing effects from herb-drug combinations: assessment of Tripterygium Wilfordii-Docetaxel in prostate cancer

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Purpose

Resistance to cancer chemotherapy is a major problem. Herb-drug combinations can offer a new potential to overcome such resistance. To quantitatively assess chemosensitizing effects of herb-drug combinations (HDC), a new approach that takes into account both the chemosensitizing effect (CE) and “safety” considerations of the HDC is proposed and used in describing the cytotoxic activity of Tripterygium wilfordii-docetaxel (TW-Dtx) combination on prostate cancer cell lines.

Methods

The effect of two extracts of TW with Dtx on Dtx resistant PC3 and DU145 cell lines were compared. Cell viability (cytotoxicity) was determined using sulforhodamine B assay after incubation of the cell line. The IC_{50} of herb (H), drug (D) alone and in combination ($IC_{50}H$, $IC_{50}D$, and $IC_{50}CD$ respectively) in resistant cells were obtained. CE and chemosensitizing utility index (CUI) were calculated as: $CE = IC_{50}D / IC_{50}CD$; $CUI = CE (IC_{50}H / Con_H)$ whereas Con_H is the H concentration in the combination.

Results

The values for CE (fold change), CUI (fold change), and $IC_{50}CD$ (nM) from TW extract A-Dtx treatment in resistant PC3 cells were 3.8, 5.8, and 5.8, respectively versus 17.1, 22.0, and 1.5, respectively from TW extract B-Dtx treatment when low Con_H relative to $IC_{50}H$ was

used. The corresponding values from extract A versus B-Dtx treatment in resistant DU145 cells were >1.3, >4.5 and 75.3 versus >27.6, >55.2 and 3.63, respectively. However, CE values can dramatically increase with higher Con_H .

Conclusion

Based on the above CE, CUI or ICCD values, TW extract B-Dtx appeared to be consistently superior to extract A-Dtx combination. However, assessment based on CE value alone may be misleading since it can change dramatically with Con_H used. CUI together with $IC_{50}CD$ are preferred and may prove to be a useful practical tool for assessing chemosensitizing effect of other HDCs.

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