Optimal chemotherapeutic combination of 9 natural compounds in treating PC-3 prostate cancer cells

Background:
- Prostate cancer accounts for 9.9% of all new cancer cases in the United States annually.
- Despite a high 5-yr survival rates (~98%), prostate cancer is still the second leading cause of cancer deaths for men in the United States.
- Frequency coupled with eventual hormone & drug resistance are attribute to prostate cancers lethality.
- Natural compounds are often used and studied for their potential chemotherapeutic effects or their sensitizing effects which increases the cancer cells susceptibility to treatment.

Introduction:
- Cell viability assays to determine the concentration at which half the PC-3 cells died (IC50)
- Mixture design Surface methodology (MDRSM) with cell viability to determine most effective combination

Table 1:

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Methods: PC-3, human prostate carcinoma cells incubated at 37°C and 5% CO2. Cell viability assays to determine the concentration at which half the PC-3 cells died (IC50) or mixture of compounds (MDRSM tests). MDRSM tests used individual compound IC50 values according to Table 1. All tests were normalized DMSO vehicle control, repeated in biological triplicate, and viability was assessed via alamarBlue cell viability protocol.

Results:
- The most potent compounds did not contribute equally in combination (Fig. 3 A)
- Every combination relied solely on 1 or 2 compounds with 0% of the 3rd compound
- Cell viability was significantly reduced in each combination except for 100% Shikonin (Fig. 4 A).
- EGCG and Beta-Elemene's IC50 values were ~170 to 200µM higher than all other compounds
- Emodin, Silybin and EGCG appear to act as cell cycle inhibitors (Fig. 6A, C and Fig. 7C)

Conclusion:
- The natural compounds effectively reduced PC-3 cell viability
- The effect of each compound was unique to each combination indicating possible interference/overlap of the compounds

Figure 1: Graphical Abstract:

Figure 2: More red = more dead

Figure 3: These compounds had the lowest IC50s.

Figure 4: Fig. 4 represents each individual point from Fig. 3 A & B. All were statically significant less than the initial treatment value other than Fig. 4A column 2.

Figure 5: MDRSM plots of 3 groups, A: BB, Em, Sy; B: Cur, Em, Ttd; C: Cur, BB, Wo. These plots represent preliminary data from the initial run, more tests are necessary.

Figure 6: The use of EGCG & Beta-el was discontinued due to in the MDRSM plots according to Table 1.

Figure 7: IC50 values of BB, Cur, Em, Shk, Ttd & Wo used in the MDRSM plots according to Table 1.

References:

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