

Turmeric and Chinese goldthread synergistically inhibit prostate cancer cell proliferation and NF- κ B signaling

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ABSTRACT:

Background: Pre-clinical studies using bioactive compounds from botanicals appear to offer some protection against cancer. Research using single bioactives contributes greatly to our understanding of their mechanism of action, but *in vitro* studies demand concentrations that are higher than achievable in humans (μ M). However, maintaining these bioactives in the presence of other compounds originally derived from the food or extract of origin may synergistically lower the bioactive dose so translatability becomes feasible. The objective of this study was to determine if bio-efficacy of phytonutrients can be enhanced when used in combination even at doses that are ineffective for any compound when used in isolation.

Methods: The anti-proliferative and molecular effects of herbs (turmeric and Chinese goldthread) and their bioactives (curcumin and *ar*-turmerone, berberine and coptisine, respectively) were determined in isolation and in combination. Using CWR22Rv1 and HEK293 cells, cell proliferation (as assessed by the MTT assay) and NF- κ B promoter activity (using a luciferase reporter construct) were evaluated and synergy of action was assessed by the Chou-Talalay method utilizing CompuSyn[®] software.

Results: Turmeric and Chinese goldthread act synergistically (combination index < 1) when inhibiting cell proliferation with all cell lines tested. The synergy of action of combinations of companion bioactives from the same herb (i.e., curcumin/*ar*-turmerone and berberine/coptisine) and bioactives from different herbs (i.e., curcumin/berberine) help to explain why turmeric and Chinese goldthread are more effective than their major bioactives in isolation. At the molecule level, curcumin+*ar*-turmerone and curcumin+coptisine synergistically attenuated TNF α -stimulated NF- κ B promoter activity. Even compounds with poor efficacy become more biologically active in the presence of companion compounds. Importantly, the effects of

combining any two bioactives or herbal extracts were highly synergistic at concentrations approaching physiological significance (nanomolar).

Conclusions: These results suggest that bioactives in combination (as plant extracts or isolated compounds) are highly synergistic at the cellular and molecular level at physiologically relevant concentrations. These data help to explain why complex mixtures of botanicals may be more efficacious than their bioactives in isolation.

Keywords: Synergy; Chou-Talalay; turmeric; Chinese goldthread; curcumin; berberine; *ar-turmerone*; coptisine; prostate cancer; NF- κ B