Aptosis in Prostatic Cancer Cells with Maitake D-fraction Extract: Potential Alternative Therapy
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Objectives: To explore more effective treatment for hormone-refractory prostate cancer due to the failure of conventional therapies, we investigated the proposed antitumor effect of β-glucan compound called Grifron extracted from Maitake mushroom, on prostatic cancer cells in vitro.

Methods: Human prostatic cancer PC-3 cells were treated with varying concentrations of the highly purified β-glucan preparation (Grifron® Pro D-fraction®, GD) and cell viability was determined at 24h. Lipid peroxidation (LPO) assay and in situ hybridization (ISH) were performed to unravel the antitumor mechanisms of GD.

Results: Dose-response study showed that almost complete cell death (>95%) was attained with GD>480 μg/ml in 24h. Combinations of merely 30-60 μg/ml of GD with 200 μM vitamin C were also as effective as 480 μg/ml GD alone, inducing >90% cytotoxic cell death. Its chemosensitizing effect on various anticancer drugs showed little potentiation of their efficacy with GD except for ~90% reduction in cell viability with the carmustine/GD combination. The significance (>50%) elevated LPO level with ISH positive staining on GD- treated cells indicated oxidative membrane damage, resulting in apoptotic cell death.

Conclusions: A bioactive glucan, an extract from Maitake mushroom, Grifron® Pro D-fraction®, GD, demonstrates cytotoxic effect via oxidative stress on prostatic cancer cells in vitro leading to apoptosis. Potentiating GD with vitamin C or chemosensitizing effect of GD with carmustine may also have implications in clinical utility. Therefore, this unique mushroom extract may have a great potential for alternative therapeutic modalities of prostate cancer.

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Cell Morphology
A) Control (untreated)

B) GD-treated (cell blebbing)

(HI)

Cell morphology change with GD (cell blebbing). Effect of GD (480 μg/ml) on cell morphology at 24h was examined under a microscope. Control (A) with normal morphology and GD-exposed (B) cells with "cell blebbing" are shown.

Effects of GD/Vit.C Combinations on Cell Viability

Effects of GD/Vit.C combinations on cell viability. Cells were treated with 200 μM Vit.C alone or combined with 15, 30, and 60 μg/ml GD for 24h and cell viability was evaluated. The data are mean of three independent experiments.

In Situ Hybridization (ISH)
A) Control cells

B) GD-treated cells

In situ hybridization (ISH). Control and GD (50 μg/ml)-treated cells at 12h were evaluated apoptotic by the ISH assay. A greater than 3 (92/100) of GD-treated cells were positively stained (B), while <10% (8/100) of controls showed specific staining (A). (magnification: 200x)