Apoptosis 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 ß-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 ß-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 significantly (>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 Maital mushroom, Grifron® Pro fraction®, GD, demonstrates cytotoxic effect via oxidative stre on prostatic cancer cells *in vitr* leading to apoptosis. Potentiation GD with vitamin C ar chemosensitizing effect of GD carmustine may also ha implications in clinical utilit Therefore, this unique mushroo extract may have a great potenti for alternative therapeut modalities of prostate cancer.

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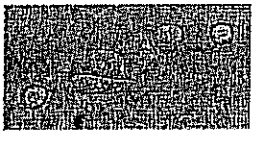
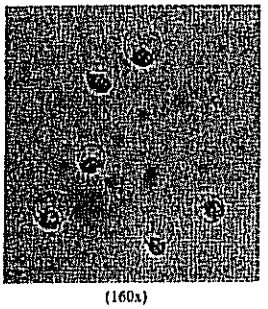
Cell Morphology

A) Control (untreated)



(160x)

B) GD-treated (cell blebbing)



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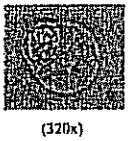
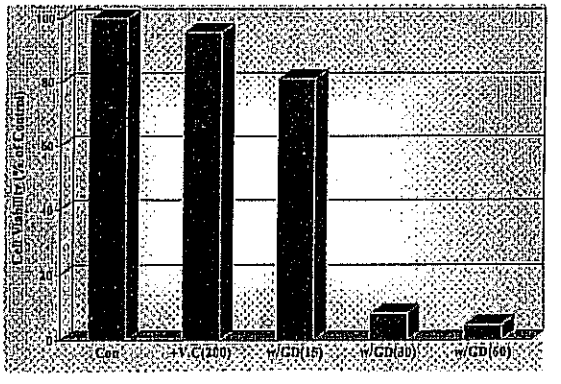


(320x)

Cell morphology change with GD (cell blebbing). Effect of GD (480 µg/ml) on cell morphology at 6h was examined under a microscope. Control (A) with normal morphology and GD-exposed (B) cells with "cell blebbing" are shown.

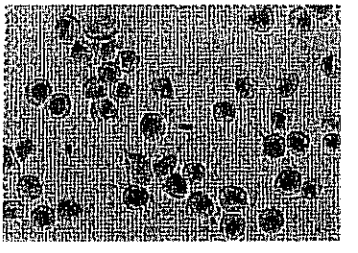
Effects of GD/Vit.C Combinations on Cell Viability



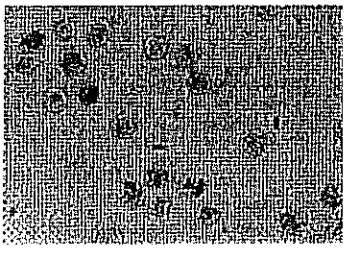
Effects of GD/Vit.C combinations on cell viability. Cells were treated with 200 µM Vit.C alone or combined with 15, 30, and 60 µg/ml GD for 24h and cell viability was evaluated. The data are mean of three independent experiments.

In Situ Hybridization (ISH)

A) Control cells



B) GD-treated cells



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