BG-4, a bioactive peptide from *Momordica charantia,* promotes apoptosis in ovarian cancer cells

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Introduction

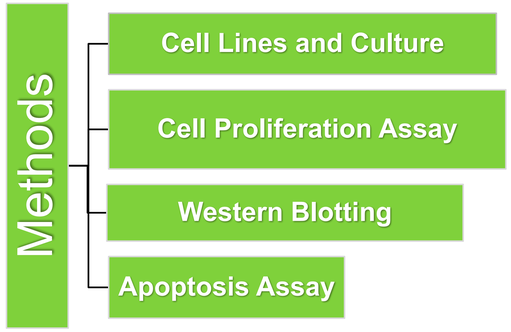
- **OVCA is the most deadly form of gynecological cancers[1]**
- **High rate of OVCA is correlated to the absence of screening which leads to diagnosis of disease at advanced stages[2]**
- **High fatality rate of OVCA is due to late presentation of disease, cancer persistence, and chemotherapy resistance[3]**
- **A key approach to combatting cancer is through activation of the apoptosis pathway[4]**
- ***Momordica charantia*, commonly known as the bitter melon, comes from the family Cucurbitacae[5]**
- ***Momordica charantia* is reported to have anti-oxidant, anti-inflammatory, anti-cancer, anti-diabetic, anti-bacterial, anti-obesity, and immunomodulatory activities [5]**
- **Previous studies have shown these anti-cancer properties on various forms of cancer[4]**
- **Specifically, BG-4, a specific peptide found in *Momordica charantia* was shown to inhibit proliferation in colon cancer cells by promoting apoptosis through down-regulation of anti-apoptotic proteins, up-regulation of pro-apoptotic proteins, and modification of cell cycle proteins[4]**

Objectives

The objective of this research is to determine the ability of BG-4 to cause cytotoxicity to ovarian cancer cells (A27801AP and COV318) and determine the mechanism involved by measuring proteins associated with apoptosis. Specifically,

- **Effect of BG-4 on Bcl-2 and XIAP (anti-apoptotic proteins)**
- **Effect of BG-4 on BAX and capsase-3 (pro-apoptotic proteins)**
- **Effect of BG-4 on p21 and CDK2 (cell cycle proteins)**

Experimental Design



Results

Effect of BG-4 on OVCA cell proliferation

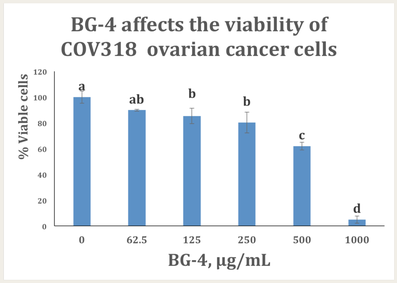


Figure 1. BG-4 purified from *Momordica chrantia* caused dose-dependent cytotoxicity in COV318 OVCA cells. BG-4 treatment led to a decrease in viable cell count by 19.8% at 250 µg/mL. Mean values represented as bars with different letter(s) are statistically different from each other (P<0.05, n=2).

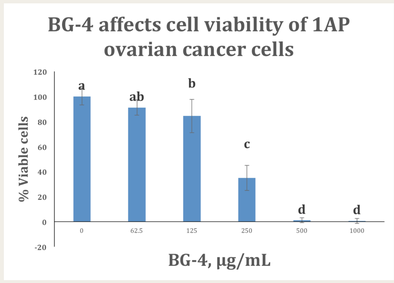


Figure 2. BG-4 purified from *Momordica chrantia* caused dose-dependent cytotoxicity in 1AP (A27801AP) OVCA cells. BG-4 treatment led to a decrease in viable cell count by 65.1% at 250 µg/mL. Mean values represented as bars with different letter(s) are statistically different from each other (P<0.05, n=2).

Effect of BG-4 on apoptotic markers

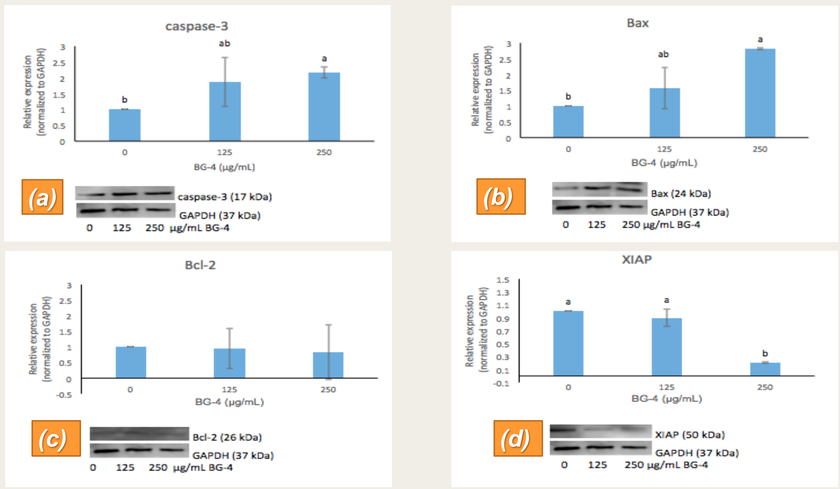


Figure 3. BG_4 modified expression of apoptotic proteins. (a) BG-4 promoted apoptosis by increasing caspase-3 (a) and BAX (b) leading to a reduced expression of XIAP (c) and no change in expression of Bcl-2 (d). Mean values represented as bars with different letter(s) are statistically different from each other (P<0.05, n=2).

Cell cycle markers

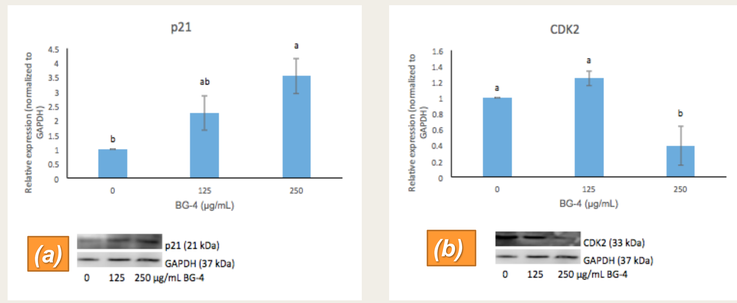
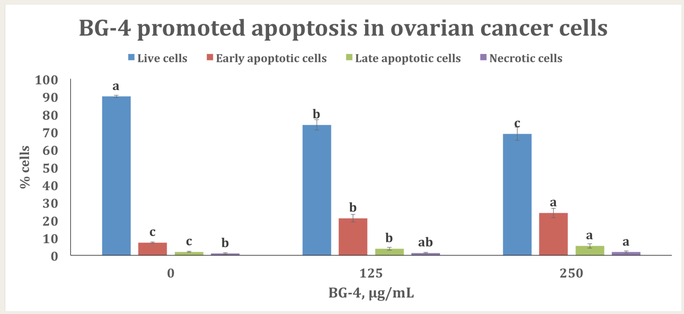


Figure 4. BG-4 modified expressions of cell cycle proteins in 1AP OVCA cell line). BG-4 increased the expression of p21 (a) leading to a reduction in expression of CDK2 (b). All analyses were done in at least two independent replicates. Mean values represented as bars with different letter(s) are statistically different from each other (P<0.05, n=2)



BG-4 induces apoptosis in OVCA 1AP cells as measured by flow cytommetry. Quantification of OVCA cells undergoing apoptosis as a result of BG-4 treatment. The live cells were from 89.955% (untreated) to 73.92% and 68.83% for 125 µg/mL and 250 µg/mL treatment, respectively. Early apoptotic cells were from 7.10% (untreated) to 20.99% and 23.95% for 125 µg/mL and 250 µg/mL treatment, respectively. Late apoptotic cells were from 1.965% (untreated) to 3.72% and 5.37% for 125 µg/mL and 250 µg/mL treatment, respectively. Necrotic cells were from 0.98% (untreated) to 1.36% and 1.81% for 125 µg/mL and 250 µg/mL treatment, respectively. Mean values represented as bars with different letter(s) are statistically different from each other (P<0.05, n=2).

Conclusions

- **BG-4 from *Momordica charantia* possesses anti-cancer properties**
- **BG-4 has the capability of activating apoptosis in human ovarian cancer cells**
- **The findings support the idea for potential use of BG-4 as an ovarian cancer therapeutic agent and should be further studied using *in vivo* models of ovarian carcinogenesis**

References

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