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Phycocyanin in Triple Negative Breast Cancer

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Triple-negative breast cancer includes tumors that lack the oestrogen receptor (ER), progesterone receptor (PR) and HER-2 genes, and represent significant clinical challenges as these cancers are highly aggressive and are resistant to conventional endocrine therapy and suffer a lack of targeted therapies.

Existing therapeutic strategies for triple-negative breast cancer include anthracycline/taxane combinations, platinum agents, and other DNA damaging agents and EGFR therapy.

Phycocyanin is an important food supplement and molecule extracted from the algae Arthrospira platensis. It is a natural, water-soluble and non-toxic molecule with potent anti-cancer, anti-oxidant and anti-inflammatory properties. Particularly, it is shown to have anti-cancer activity against colon, hepatocellular, cervical and leukemic cell lines.

A study revealed the antineoplastic mechanism of phycocyanin in triple-negative breast cancer. It was found that:

PC inhibits proliferation and colony formation ability of breast cancer cells in a dose-dependent manner: The triple negative MDA MB 231 cells were found to be most sensitive to PC with an IC50 of 5.98 µM in as early as 24 h.

PC inhibits wound healing and migration of MDA MB 231 breast cancer cells: Classic wound healing assay results showed that PC treated cells showed decreased wound healing in comparison to control. The result of the clonogenic assay showed that PC treated cells showed a significant reduction in colony formation when compared to controls, indicative of potent inhibition of cell growth and reproductive integrity. PC could inhibit cell migration via cytoskeleton disruption and also confer adhesiveness to cells, thereby playing an important role in suppressing invasion.

PC induces G0/G1 cell cycle arrest of MDA MB 231 breast cancer cells

PC induced significant G0/G1 cell cycle arrest. In comparison to untreated controls, there is an increase in the percentage of cells in the G0/G1 phase (62.1 ± 1.1 % Vs 73.2 ± 0.2 %) with a concomitant decrease in the percentage of cells in S (18.4 ± 1.1 % Vs 14.3 ± 0.04 %) and G2-M phases (17.7 ± 3.5 % Vs 10.7 ± 0.4 %) of the cell cycle. With PC treatment, there is an increase of about 1.17 fold in the number of cells in G0/G1 phase as compared to untreated controls, suggesting the role of PC in inhibiting entry into the S-phase

PC induces apoptosis of MDA MB 231 breast cancer cells

In a study to determine the extent of apoptosis in MDA MB 231 cells by Annexin V PE and 7AAD staining, results showed that PC treated MDA MB 231 cells demonstrated a high induction of apoptosis in comparison to untreated controls. The percentage of apoptotic cells increased gradually from 2.69 % in untreated controls to 14.99 % and 21.43 % in IC25 and IC50 treated cells with a fold increase of 5.57 and 7.96 respectively.

PC targets MAPK signaling in MDA MB 231 breast cancer cells

In a study to determine the specific signaling pathway targeted by PC to induce apoptosis in MDA MB 231 breast cancer cells, PC treatment did not alter the phosphorylation levels of both AKT and NFkB-p65 whereas a significant decrease in the phosphorylation of ERK1/2 was observed as early as 30 min following treatment with a maximal decrease at 90 min.

PC inhibits COX-2 expression in breast cancer cells

The levels of COX-2 protein and mRNA were determined by Western blot and qPCR, respectively. Results showed that PC-treated cell showed a decrease in COX-2 protein and mRNA levels. There was a decrease in PGE2 production (a downstream product of COX-2) in arachidonic acid-stimulated MDA-

MB-231 cells upon treatment with PC. The basal level of PGE2 released in MDA MB 231 cells was 29.7 pg/ml. Upon stimulation with 10 µM arachidonic acid for 18 h and followed by treatment to PC for 24 h, there was a decrease in the level of PGE2 from 114.6 pg/ml to 70.7 pg/ml.

PC inhibits channel formation of breast cancer cells

High COX-2 expression in TNBCs promotes increased angiogenesis which is in turn mediated by key regulators like VEGFR2 and MMP-9. Based on this, the kinetics of vascular channel formation in MDA MB 231 cells upon treatment with PC were determined by vasculogenic mimicry assay. Results showed that a 3 µM dose of PC significantly inhibited the number of vascular channels formed as compared with untreated control cells. qPCR analysis showed a significant decrease in the mRNA levels of VEGFR2 and MMP-9 by 1.17 and 5.55 fold, respectively. Therefore failure of cells to form patterned networks on matrigel and decrease in transcription of genes involved in regulating angiogenesis endorses the antiangiogenic potential of PC.

PC is non-toxic to blood cells

In a study to determine PC's compatibility to RBC's and platelet aggregation inhibitory effect by in vitro hemolytic assay and aggregation assay, results showed no aberrant morphological changes to RBC's and showed an inability to cause platelet aggregation upon treatment with PC- indicating that PC is safe to use for therapy.

Conclusion

In conclusion, this study demonstrated that PC in TNBC cells (i) inhibits the proliferation (ii) promotes change in the Bcl-2/Bax ratio (iii) inhibits metastasis via actin cytoskeleton disruption (iv) suppresses angiogenesis and (v) down-regulates MAPK signaling pathways to elicit cell death. This study proposes that PC could be used as a promising anti-cancer therapeutic agent in TNBCs without toxicity to normal cells.

References

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