scientific reports

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Bergenin inhibits growth of human cervical cancer cells by decreasing Galectin-3 and MMP-9 expression

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Cervical cancer is still the leading cause of cancer mortality worldwide even after introduction of vaccine against Human papillomavirus (HPV), due to low vaccine coverage, especially in the developing world. Cervical cancer is primarily treated by Chemo/Radiotherapy, depending on the disease stage, with Carboplatin/Cisplatin-based drug regime. These drugs being non-specific, target rapidly dividing cells, including normal cells, so safer options are needed for lower off-target toxicity. Natural products offer an attractive option compared to synthetic drugs due to their well-established safety profile and capacity to target multiple oncogenic hallmarks of cancer like inflammation, angiogenesis, etc. In the current study, we investigated the effect of Bergenin (C-glycoside of 4-O-methylgallic acid), a natural polyphenol compound that is isolated from medicinal plants such as Bergenia crassifolia, Caesalpinia digyna, and Flueggea leucopyrus. Bergenin has been shown to have anti-inflammatory, anti-ulcerogenic, and wound healing properties but its anticancer potential has been realized only recently. We performed a proteomic analysis of cervical carcinoma cells treated with bergenin and found it to influence multiple hallmarks of cancers, including apoptosis, angiogenesis, and tumor suppressor proteins. It was also involved in many different cellular processes unrelated to cancer, as shown by our proteomic analysis. Further analysis showed bergenin to be a potent-angiogenic agent by reducing key angiogenic proteins like Galectin 3 and MMP-9 (Matrix Metalloprotease 9) in cervical carcinoma cells. Further understanding of this interaction was carried out using molecular docking analysis, which indicated MMP-9 has more affinity for bergenin as compared to Galectin-3. Cumulatively, our data provide novel insight into the anti-angiogenic mechanism of bergenin in cervical carcinoma cells by modulation of multiple angiogenic proteins like Galectin-3 and MMP-9 which warrant its further development as an anticancer agent in cervical cancer.

Keywords Bergenin, Cervical cancer, HPV, Galectin 3, Matrix metallo protease 9

Cervical cancer poses a significant threat to the health of women and is leading cause of mortality in womens worldwide. Cervical cancer is primarily associated with high-risk human papillomavirus (HPV) infection, among other risk factors¹. According to the Globacon 2020 cancer facts, 6,04,127 new cervical cancer cases and 3,41,831 deaths were reported among all age groups worldwide. Furthermore, cervical cancer is the fourth most common malignancy among females, with a 13.3% incidence rate and a 7.3% mortality rate. The risk factors besides infection with HPV for cervical cancer include early sexual maturity, polygamy, early pregnancy, multiple pregnancies,

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