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Inhibition of cisplatin resistant ovarian cancer cell growth both *in vitro* and in mouse xenograft tumor via autophagy activation, angiogenesis inhibition and targeting HIF-1α and SNAIL1

Objectives: Ovarian cancer (OC) is the most lethal gynecologic malignancy. Patients with OC are treated with surgery, chemotherapy and/or radiation therapy, however, OC becomes resistant to these treatment strategies. We have demonstrated that *Emblica officinalis* (Amla) extract (AE) have anti-neoplastic effect on OC cells *in vitro* and *in vivo*. In this study, we determined the effects of AE on chemotherapy resistant OC cells both *in vitro* and in mouse xenograft tumor.

Methods: Cisplatin resistant OC cells A2780cis were used. Anti-proliferative effects of AE on A2780cis cells *in vitro* were studied using MTT assay. Effect of AE on expression of autophagy markers – LC3B and beclin 1 was studied in A2780cis cells both *in vitro* and in A2780cis cells derived mouse xenograft tumors using immunocytochemistry and Western blot. The expression of proangiogenic receptor IGF1R and angiogenic marker CD31 were determined. Expression of angiogenesis regulatory transcription factor HIF-1α, metastasis-associated transcription factor - SNAIL1 and adhesion protein - E-cadherin in OC cells and A2780cis cells derived tumor after AE treatment was studied.

Results: AE dose and time dependently inhibited A2780cis cell proliferation. AE significantly increased the expression of the autophagic proteins beclin1 and LC3B-II under *in vitro* conditions and in mouse xenograft tumor. AE also significantly reduced the expression of HIF-1α and IG1R expression in mouse xenograft tumors. AE reduced endothelial cell antigen-CD31 positive blood vessels, Ki67 expression in mouse xenograft tumor. Additionally, AE reduced expression of EMT associated transcription factor - SNAIL1 and induced expression of E-cadherin under *in vitro* condition and in A2780cis cells derived mouse xenograft tumor.

Conclusion: AE inhibits cisplatin resistant OC cell growth both *in vitro* and in mouse xenograft tumor possibly via activation of autophagy, inhibition of angiogenesis, targeting HIF-1α and SNAIL1.

Biography

Alok De has received his PhD from University of Calcutta. He is a Research Biologist at Kansas City VA Medical Center. His research focuses on to use the extract of *Emblica officinalis* as an alternative or adjunct therapeutic agent in helping to fight ovarian cancer. He has published more than 45 papers in reputed journals. He has been serving as reviewers of many journals and as an Editorial Board Member of Cancer Cell and Micro environment.

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