

6TH WORLD FORUM ON BREAST AND CERVICAL CANCER



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Pre-clinical evaluation of kaempferide, a flavonoid from *Chromolaena odorata*, as a potential drug candidate against cervical cancer

Despite the advancement in HPV prevention strategies, cervical cancer is still a leading cause of cancer death. We isolated and identified kaempferide in our lab from *Chromolaena odorata*, commonly known as Siam weed. Among the cancer cell lines of various origins, the cervical cancer cell line, HeLa was the most sensitive to kaempferide. Cytotoxic potential of kaempferide was assessed against the cervical cancer cell lines, HeLa and SiHa, which possess HPV-18 and -16 integrated genome respectively. Kaempferide led to a strong induction of apoptosis in HeLa and SiHa cells while being non-toxic to the rapidly dividing normal human fibroblasts. Acute and chronic toxicity studies conducted in vivo proved that the compound is pharmacologically safe. Anti-proliferative and anti-migratory effects were assessed through colony formation and wound healing assays. Gene and protein expression changes were measured using qRT-PCR and Western blotting. Human cervical cancer xenograft model was raised in NOD-SCID mice using HeLa cells. The mouse xenograft tissues were subjected to histopathological analysis, immunohistochemistry and TUNEL assay to confirm apoptotic mode of cell death.

Our study reveals the antioncogenic potential of kaempferide, which down-regulates expression of the E6 and E7 oncoproteins of HPV-18 and HPV-16 and up-regulates the tumor suppressors, p53 and pRb, leading to significant tumor growth reduction. This is the first report depicting kaempferide as an inhibitor of HPV oncoproteins, positioning it as a potential drug candidate for cervical cancer. The present study confirms the therapeutic efficacy of kaempferide against cervical cancer using in vivo models and explores its mechanism of action.

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Keywords

Kaempferide, *Chromolaena odorata*, cervical cancer, HPV oncoproteins, E6, E7.

Biography

Dr. Ruby John Anto took her PhD from Amala Cancer Research Centre, Thrissur and did her post-doctoral studies at Rajiv Gandhi Centre for Biotechnology (RGCB), Thiruvananthapuram. She started her career as Scientist C at RGCB and later served as a visiting scientist at M.D. Anderson Cancer Center, Houston, USA. After joining back, she was part of the Cancer Research Program of RGCB till her retirement from RGCB as Scientist G in April, 2023. Currently Dr. Anto is serving as the Chief Scientist at the Centre of Excellence in Nutraceuticals, KSCSTE, Government of Kerala, and as an Honorary Scientist at the Institute of Advanced Virology, Thonakkal, Thiruvananthapuram. Her research focuses on bioprospecting for natural products having therapeutic potential against cancer, inflammatory disorders and other lifestyle diseases. Currently she is also investigating the viral etiology of different cancers and evaluating the efficacy of natural products in regulating viral carcinogenesis. She is a recipient of National Woman Bio-Scientist Award, from Department of Biotechnology, Govt. of India and Keystone Symposia Global Health award by Bill & Melinda Gates Foundation. Dr. Anto is a Fellow of National Academy of Sciences, India and Kerala academy of Sciences. She is an editorial board member in several scientific journals and possesses National as well as International research collaborations. She is a reviewer of several reputed International journals and National funding agencies. Her work has been published in several reputed peer-reviewed journals. She also holds National and International patents to her credit. Dr. Ruby has more than 7500 citations and has an H-index of 41 from around 70 International peer-reviewed research publications, in high impact factor journals. Her team has isolated Uttroside B, a compound having exceptional efficacy against liver cancer. Her invention on the therapeutic efficacy of uttroside B, which received 'Orphan drug' designation against liver cancer by the US FDA, has been granted patents from the US, Canada, Europe, South Korea and Japan and the technology has been transferred to the multinational company, Q Biomed.