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Breast cancer prevention and treatment with oleanane triterpenoids

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Breast cancer is one of the most frequently diagnosed malignancies and main causes of death in women worldwide. Current treatment options, including surgery, radiotherapy, adjuvant chemotherapy and hormone therapy, may not be adequate to significantly reduce the current morbidity and mortality of breast cancer. The value of natural products and dietary phytochemicals, including triterpenoids, in the prevention and treatment of breast cancer has been established. Oleanolic acid, an oleanane-type pentacyclic triterpenoid, is present in various dietary and medicinal plants. Emerging studies indicate that oleanolic acid and other oleanane triterpenoids modulate multiple intracellular signaling pathways and exhibit chemopreventive and antitumor properties in various cancer models. Several oleanane triterpenoids have been prepared by chemical modification of oleanolic acid moiety, and some of these compounds are considered to be the most potent anti-inflammatory and anticarcinogenic triterpenoids known to mankind. This lecture will critically examine the potential role of oleanane triterpenoids in chemoprevention and treatment of mammary cancer. The available preclinical studies using these agents and underlying molecular mechanisms will be presented. Our laboratory has undertaken an extensive research program to investigate mechanism-based chemopreventive effect of a novel oleanane triterpenoid, namely methyl amooranin (AMR-Me), employing dimethylbenz(*a*)anthracene (DMBA)-induced rat mammary tumorigenesis, a classical animal model that resembles human breast cancer. This lecture will present our results on the effects of AMR-Me on mammary tumor incidence, tumor burden, and tumor histopathological indices during DMBA-induced rat mammary carcinogenesis. Mechanistic results demonstrating the regulatory influence of AMR-Me on cell proliferation, apoptosis, proapoptotic protein Bax, antiapoptotic protein Bcl-2, estrogen receptors, Wnt/ β -catenin signaling, and nuclear factor-kappaB-mediated inflammatory cascade during experimental mammary tumorigenesis will be analyzed. Several challenges and future directions of research to translate already available impressive preclinical evidence on oleanane triterpenoids to clinical practice of breast cancer prevention and therapy will also be discussed.

Biography

Anupam Bishayee has 25 years of combined experience in pharmaceutical and biomedical research, teaching, administration and service. His research focuses on elucidation of the cancer preventive and therapeutic effects of medicinal plants, natural products, dietary, and synthetic agents using several pre-clinical models of cancer. His various other projects are funded by the National Institutes of Health as well as private pharmaceutical/biotechnological companies. He has published more than 102 original research papers and authoritative review articles in high-impact, peer-reviewed journals, 10 book chapters, and presented nearly 40 papers at various national and international scientific events.

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