BIOEFFECTICITY, ANTIOXIDATIVE AND CHEMOPREVENTIVE PROPERTIES OF NOVEL PLANT-BASED PHYTOCHEMICALS- A CASE FOR EPIVERNODALOL AND KOLAVIRON

Ebenezer O. Farnombi and Olatunde Owoeye

Drug Metabolism and Toxicology Research Laboratories, Department of Biochemistry and Department of Anatomy, College of Medicine, University of Ibadan, Nigeria

Abstract: Convincing and compelling evidences arising from both pre-clinical and clinical investigations indicate that plant-based diets rich in a wide variety of phytochemicals with potent antioxidant properties are effective in preventing or reversing chronic degenerative diseases. Antioxidants are considered to bring about their effects by attenuating oxidative events that contribute to the pathophysiology of these diseases. There is now good evidence linking high intake of phytochemicals in fresh fruits and vegetables with low incidence of certain cancer. These compounds contain a number of functional groups such as phenolic hydroxyl groups attached to ring structures bestowing the antioxidant activity. They are multifunctional and can act as reducing agents, hydrogen donating antioxidants, metal chelators and singlet oxygen quenchers. The implication of reactive oxygen species (ROS) in chronic degenerative diseases including diabetes, cancer, arthritis, cardiovascular diseases and neuronal disorders continues to underpin the search for novel non-toxic antioxidant indications from plant extracts. Extracts from Vernonia amygdalina (bitter leaf) exhibited significant antioxidant properties in various model systems and induced phase 2 antioxidant enzymes. Employing bioassay-guided fractionation, we characterized Epivernodalol from Vernonia amygdalina using spectroscopic methods including 1H-NMR, 13C-NMR, MS, UV and IR spectra. Our data showed that Epivernodalol was active against skin cancer as demonstrated by its efficacy in HT-144 skin melanoma cell line. Kolaviron, a natural antioxidant biflavonoid isolated from the seeds of Garcinia kola (Guttiferae) elicited striking inhibitory effects on diverse biochemical and cellular events associated with the multistage process of carcinogenesis. Specifically, kolaviron elicited marked antioxidant, metal chelating and free radical scavenging activities in a series of assays involving ROS, modulated redox status and liver dysfunction induced by known liver carcinogens, up-regulated antioxidant defense capacity, modulated gene expression and signal transduction mechanisms and reduced in vivo markers of oxidative stress. In addition, kolaviron ex-vivo and in vitro protected against oxygen-derived radical-induced DNA damage and oxidative stress in human lymphocytes and rat liver cells using the comet assay. Furthermore, kolaviron suppressed Dimethylnitrosamine-induced oxidative damage and expression of cyclooxygenase-2 (COX-2) and inducible nitric oxide synthase (iNOS) by inhibiting nuclear factor kappa B (NF-kB) and activator protein-1 (AP-1) in rat liver. These antioxidants could be developed into novel therapeutic agents capable of protecting against direct injurious effects of ROS and can fundamentally alter the molecular signaling cascades which play an important role in the pathogenesis of chronic degenerative diseases.

Key words: Kolaviron, Epivernodalol, Garcinia Kola, Vernonia amygdalina, chemoprevention, protein expression