

Protandim, a fundamentally new antioxidant approach in chemoprevention using mouse two-stage skin carcinogenesis as a model.

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Abstract

Oxidative stress is an important contributor to cancer development. Consistent with that, antioxidant enzymes have been demonstrated to suppress tumorigenesis when being elevated both *in vitro* and *in vivo*, making induction of these enzymes a more potent approach for cancer prevention. **Protandim**, a well-defined combination of widely studied medicinal plants, has been shown to induce superoxide dismutase (SOD) and catalase activities and reduce superoxide generation and lipid peroxidation in healthy human subjects. To investigate whether **Protandim** can suppress tumor formation by a dietary approach, a two-stage mouse skin carcinogenesis study was performed. At the end of the study, the mice on a **Protandim**-containing basal diet had similar body weight compared with those on the basal diet, which indicated no overt toxicity by **Protandim**. After three weeks on the diets, there was a significant increase in the expression levels of SOD and catalase, in addition to the increases in SOD activities. Importantly, at the end of the carcinogenesis study, both skin tumor incidence and multiplicity were reduced in the mice on the **Protandim** diet by 33% and 57% respectively, compared with those on basal diet. Biochemical and histological studies revealed that the **Protandim** diet suppressed tumor promoter-induced oxidative stress (evidenced by reduction of protein carbonyl levels), cell proliferation (evidenced by reduction of skin hyperplasia and suppression of PKC/JNK/Jun pathway), and inflammation (evidenced by reduction of ICAM-1/VCAM-1 expression, NF- κ B binding activity, and nuclear p65/p50 levels). Overall, induction of antioxidant enzymes by **Protandim** may serve as a practical and potent approach for cancer prevention.

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