Bibliography
General Conclusion of the Study

The salient features of the present dissertation reveals that diallyl sulfide (DAS), a organosulfide from garlic, as a potential cancer chemopreventive agent as well as to meet out the challenge of one of the most perplexing problem in cancer chemotherapy i.e. multiple drug resistance. DAS supplementation retarded the growth; onset, multiplicity and malignancy of DMBA induced mouse skin tumors. DAS was found capable of inducing apoptosis in the skin tumors, thus suggesting induction of apoptosis as one of the key mechanism of its chemopreventive efficacy. DAS was also found to modulate the cell cycle regulatory genes viz. tumor suppressor p53 and p21/waf1 thus checking the growth of neoplastic cells. DAS was found to shift the balance between the wild type and mutant p53 towards tumor suppressor function of p53. The induction of wild type p53 by DAS caused the transcriptional activation of p21/waf1, which may lead to the pathway to apoptosis. Thus it could be suggested that the anticancer mechanism of DAS involves induction of p53 dependent apoptosis in tumor cells mediated through p21/waf1 induction. Since chemoprevention aims to kill or eliminate cancerous cells at an early stage, the ability of DAS to modulate the levels of p21/ras as early as after the 24hrs of single application of initiating dose of DMBA indicates its chemopreventive potential at early stages of tumor development. Moreover, the modulatory effect of DAS on p21/ras in DMBA induced skin tumors suggest that DAS can suppress the growth of tumors harboring ras mutations. The DAS administration was also able to reverse the MDR in drug resistant human K562 leukemic cells and in mouse liver, further contributing to its beneficial health effects.

The study thus demonstrates a causal link between nutrition and improved cancer chemotherapy suggesting that DAS can act as a nontoxic anticancer agent of dietary origin. Furthermore, its ability to modulate MDR would find its usefulness in the improvement of the conventional chemotherapy by cytotoxic drugs. The characterization of the chemopreventive activity of food constituents and related compounds along with their mechanism of action will ultimately help formulate dietary advice for the general population and/or prophylactic drug strategies for individuals at particular risk of developing cancer. Such research has the potential to improve, in a fundamental way in reducing the global cancer burden.


Bibliography


Bibliography


114


Bibliography


effects of garlic constituents on DNA adduct formation in human lymphocytes in

Hainaut, P. and Vahakangas, K. (1997). p53 as a sensor of carcinogenic exposures:
mechanisms of p53 protein induction and lessons from p53 gene mutations.
*Path. Biol. 45*: 833-844.

in two human sarcoma cell lines as a new member of the ras gene family

agents on the metabolic activation of the carcinogenic arylamines PhIP and 4-

22*: 712-722.


Cip1 is a potent inhibitor of G1-cyclin-dependent kinases. *Cell, 75*: 805-816.


Harvey, J. J. (1964). An unidentified virus which causes the rapid production of

carcinogen-induced tumorigenesis in p53-deficient mice. *Nature Genet. 5*: 225-
229.

Hayes, J. D. and Pulford, D. J. (1995). The glutathione S-transferase supergene family: regulation of GST and the contribution of the isoenzymes to cancer
600

Hecker, E. (1978). Structure activity relationships in diterpenes esters irritant and
cocarcinogenic to mouse skin. *In: Carcinogenesis, Vol 2: Mechanism of tumor
promotion and cocarcinogenesis* (Slaga, T. J., Sevak, T. J. and Boutwell, R. K.
edn.) Rav. Press. NY, pp 11-42.


Leishmania donovani is conferred by amplification of a gene homologous to


Mercer, W.E., Shields, M.T., Lin, D., et al. (1991). Growth suppression induced by wild-type p53 protein is accompanied by selective down-regulation of...


Bibliography


Bibliography


Bibliography


