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ARTICLE REVIEWED

The impracticality of cancer incidence reduction by conventional therapeutic and surgical approaches is a major challenge in designing chemoprevention efficacy trials via non toxic natural products. Chemoprevention of cancer is an intervention in the carcinogenic process by chemical agents that block or reverse the malignant transformation of cells. Many natural products have shown cancer chemopreventive potential in a variety of bioassays systems and animal models. An effective and acceptable chemopreventive agent should have (a) no toxic effects in normal cells (b) high efficiency against multiple sites (c) capable of oral consumption (d) known mechanism of action (e) low cost and (f) acceptance by human population. In this review the chemopreventive effects of individual natural products such as ashwagandha, tulsi, carotenoids, vitamin C & E, soy, ω-3 fatty acids, green tea resveratrol and anthocyanins have been discussed. Other important natural chemopreventive agents not discussed are curcumin, vitamin D, calcium, selenium, retinoids, folic acid and protease inhibitors. The difficulties involved in the development and characterisation of an ideal chemopreventive agent, their adverse effects and their mechanism of action have been highlighted.

More than 1000 agents have been selected and evaluated in preclinical studies for chemopreventive activity, ranging from in vitro mechanistic and cell-based transformation assays to carcinogen induced & transgenic, knock out animal models. >40 promising agents and their combinations are currently being evaluated clinically as chemopreventive agents for major cancer targets. Many food derived agents are extracts containing multiple compounds or class of compounds. Hence, co-development and characterization of a single active substance of a few putative active compounds is important as they can provide the mechanistic and pharmacological data to ensure reproducibility. Characterization of efficacy and safety and suitable cohorts for clinical intervention are critical to progress in chemopreventive agents against molecular targets, another approach is to evaluate efficacy at the cellular and tissue levels for antiprogression/ antiproliferation, antimutagenesis, detoxifying carcinogens, inhibition of oncogene activity, induction of terminal differentiation, restoring immune response, induction of apoptosis, inhibition of angiogenesis and DNA synthesis. An important component of clinical and preclinical studies in chemoprevention is identification of earlier intermediate biomarkers in intraepithelial neoplasia that reflect carcinogenesis/ chemopreventive mechanism i.e. proliferation (eg. proliferating cell nuclear antigen, MIB-I), differentiation signals (eg. apoptosis, DNA methylation, oncogene or tumour suppressor expression). Thus various molecular evidence of

chemoprevention need to be investigated as well as their structure-activity relationships. An advantage of natural products in cancer prevention is that they also have apparent benefit in other chronic diseases such as heart disease, etc. The potential of single chemopreventive is limited by potency and toxicity at efficacious doses. Simultaneous or sequential administration of multiple agents can increase efficacy and reduce toxicity. I believe that continued efforts are needed especially well designed preclinical studies using models that closely mimic/represent human disease. This should be followed by human clinical trials in suitable high risk population. Thus future progress basic and translational research in chemoprevention with natural products will help our understanding of carcinogenesis on the basis of new findings in cancer-related functional genomics and proteomics which will contribute to the characterization of molecular and genomic cancer biomarkers that can be used to evaluate cancer risk in prospective cohorts as well as surrogate end points in clinical studies.

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