

Chapter 10

Recommendations

Research recommendations

Research done to date suggests that cruciferous vegetables contain constituents that reduce cancer risk. Governments, voluntary organizations and the private sector should continue to invest in research to elucidate the roles of these foods and their constituents in cancer risk reduction. Research is needed in particular in the following areas.

- 1. Improve our understanding of the basic metabolism in both animals and humans of the compounds contained in cruciferous vegetables. In particular, there is a need to:**
 - better understand the pharmacokinetics, pharmacodynamics and pharmacogenetics of isothiocyanates and indoles. This information is needed to relate knowledge of effects in vitro and in animals to those in humans.
 - develop methods to quantify the levels of specific isothiocyanates, their conjugates and indoles in plasma. This information is needed to aid understanding of their cancer preventive potential and to relate their function in humans to that in animals and in vitro.
 - better understand the interactions between isothiocyanates, indoles and other nutrients contained in cruciferous vegetables, especially in animal models, in which the compounds have typically been studied alone.
- 2. Improve estimates of intake of cruciferous vegetables and their constituents in epidemiological studies. In particular, there is a need to:**
 - better understand the influence of the ingestion of intact glucosinolates on the delivery of isothiocyanates and indoles to the lower gastrointestinal tract;
 - better understand the influence of intestinal bacterial flora on the metabolism of compounds contained in cruciferous vegetables;
 - better understand the biological significance of the effects of cruciferous vegetables and compounds therein on changes in cell growth, apoptosis and proliferation in vitro, in animals and in humans;
 - better understand the role of polymorphisms of glutathione *S*-transferases and other metabolizing enzymes in the metabolism of isothiocyanates and other compounds in cruciferous vegetables;
 - conduct short-term dietary interventions in humans to assess the impact of glutathione *S*-transferase polymorphisms on isothiocyanate metabolism and excretion;
 - create additional transgenic animals to elucidate the roles of specific genes in metabolizing compounds in cruciferous vegetables.
- 3. Conduct short-term interventions to assess the effect of cruciferous vegetable intake on validated intermediate markers of effect, such as precancerous tissue changes, alteration of gene expression, DNA damage, or other markers known to lie in the causal pathway to cancer.**
- 4. Conduct phase 2 trials in humans to begin to evaluate the agents derived from cruciferous vegetables that have been shown to be chemopreventive in animal systems.**
 - improve dietary assessment methods for cruciferous vegetables to include information on storage, processing and cooking methods, which can substantially modify their nutrient content;
 - develop and validate better biomarkers of intake of cruciferous vegetables and of supplements of compounds present in cruciferous vegetables. As these biomarkers might well include isothiocyanate or indole excretion products, proper interpretation will require careful attention to effects on the timing of excretion of factors such as metabolizing gene polymorphisms or other cancer risk factors.
 - use an optimized method to assess glucosinolate intake in large-scale epidemiological studies with stratification for genetic polymorphisms for relevant metabolic and response genes.

5. **Conduct studies to better understand the possible benefits of cruciferous vegetables or the compounds they contain on infectious agents important to human cancer risk, including human papillomavirus and *Helicobacter pylori*.**
6. **Conduct studies to better understand the potential toxicity of compounds contained in or derived from cruciferous vegetables, including nitriles, which are formed during the degradation of glucosinolates, and compounds formed during the metabolism of isothiocyanates and indoles.**
- Better describe the functional importance of modulation of phase I and phase II enzymes in terms of risk and prevention of cancers at various sites. This information is needed to understand the general risks and benefits of compounds contained in foods but is also

important for understanding the potential adverse interactions of high doses of foods or derived compounds delivered in supplements in the metabolism of prescription drugs.

- Develop better methods to determine risk:benefit ratios for compounds such as indole-3-carbinol that potentially have both beneficial and adverse effects. Such methods are needed for the proper design of human clinical trials.
- Better understand the potential long-term effects of the goitrogenic compounds contained in cruciferous vegetables on thyroxin biosynthesis in humans.

Public health recommendations

We recommend that governments and nongovernmental organizations promote and support the intake of crucif-

erous vegetables as part of a diet containing a variety of fruits and vegetables for cancer risk reduction and health promotion. We further recommend that:

1. Cruciferous vegetables should not be promoted in preference to other vegetables, in either public education messages or in agricultural policies.
2. On the basis of concern about toxicity and uncertain benefits, it is inadvisable to consume nutritional supplements containing high levels of compounds derived from cruciferous vegetables or analogous synthetic compounds. Similar caution should be exercised in the consumption of modified cruciferous vegetables designed to contain substantially increased concentrations of such compounds.