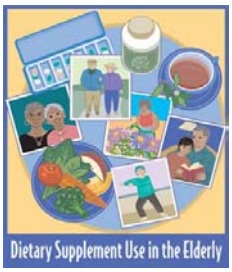

Application of Computers, Bioinformatics, and Modeling To Predict Effectiveness and Safety of Dietary Supplements

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Computational methods (bioinformatics/data mining/structure-activity relationships [SAR]) are finding increased use and acceptance in the development and recognition of therapeutics as well as in the identification of unwanted toxicities.

SAR approaches are useful in the discovery and design of new chemopreventative agents. They are, however, dependent upon the availability of reliable efficacy data derived from experiments with 100-400 chemicals. Such data are available for SAR modeling of dietary supplements that are potential cancer preventative agents or antioxidants. However, there are insufficient data to develop SAR models of other cellular targets possibly responding to dietary supplements.

Unlike standard therapeutics, which possess quantifiable beneficial effects and dietary supplements, at this time, are not characterized by such information. Accordingly, the usual risk versus benefit assessment paradigms are not applicable as we require absolute safety of candidate dietary supplements. Validated SAR models of toxicological phenomena, of which there is a substantial number, are very useful in identifying and even eliminating such potential hazards. Such models also are useful in providing mechanistic information and in identifying possible drug-drug interactions.

SAR modeling, in conjunction with data mining techniques, are promising tools to generate "virtual" biological or toxicological profiles that can identify structurally dissimilar agents that act by common mechanisms and thereby allow the recognition of new chemopreventative agents.

Future applications of SAR methodologies to identify and assess the action of dietary supplements depend upon the identification of additional chemopreventative targets and experimental data regarding their susceptibility to inhibition and/or modulation. Additionally, early feasibility studies have indicated that toxicogenomic data obtained with DNA microarrays are perfect substrates for SAR analyses of the effects of chemicals on the activities of specific genes. Application of these approaches to "nutrition-genomics" may be the most profitable strategy to identify molecular targets and to study the effect of dietary supplements. This, in turn, may lead to the identification and/or synthesis of safe and effective chemopreventative dietary supplements.

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