FUNCTIONAL MEDICINE UPDATE
May 2008
ISSN 1092-1761
Vol. 28, No. 5

Pharmaceuticals in Surface Waters

It is now recognized that pharmaceutical compounds reach the environment and can be considered as environmental contaminants. A wide range of drugs including antibiotics anti-convulsants, and hormones have been found in the effluents and surface waters of several countries. During the course of a five-month inquiry, an investigation by the Associated Press discovered that drugs have been detected in the drinking water supplies of 24 major metropolitan areas in the United States. The concentrations of these pharmaceuticals are tiny, measured in quantities of parts per billion or trillion. Utility companies insist their water is safe. But the presence of so many prescription drugs and over-the-counter medicines in drinking water is heightening worries among scientists of long-term consequences to human health.
REF #1-2

Adaptogens and Phytochemicals that Influence Human Health

In Chinese medicine, ginseng (Panax ginseng C.A. Meyer) has long been used as an adaptogen to promote longevity and enhance bodily functions. Many pharmacological actions of ginseng are attributed to one type of its constituents: ginsenosides. There have been recent advances in the study of ginsenosides on angiogenesis, which is related to many pathological conditions including tumor progression and cardiovascular dysfunctions. Angiogenesis in the human body is regulated by two sets of counteracting factors: angiogenic stimulators and inhibitors. The anti-tumor and anti-angiogenic effects of ginsenosides have been demonstrated in various models of tumor and endothelial cells, indicating that ginsenosides with opposing activities are present in ginseng. The lines of evidence uncovered by recent work support that the interaction between ginsenosides and various nuclear steroid hormone receptors may explain the diverse pharmacological activities of ginseng. REF #3

Earlier this year, the *Journal of Agricultural and Food Chemistry* published a report on four wild berry species, all integral to the traditional subsistence diet of Native American tribal communities. Biological activity was screened using a range of bioassays that assessed the potential of these berries to affect diabetic microvascular complications, hyperglycemia, pro-inflammatory gene expression, and metabolic syndrome symptoms. Berry samples showed the ability to modulate lipid metabolism and energy expenditure in a manner consistent with improving metabolic syndrome. The overall results demonstrate that these berries traditionally consumed by tribal cultures contain a rich array of phytochemicals that have the capacity to promote health and protect against chronic diseases. REF #4

Because of its 5000-year-old tradition, Traditional Chinese medicine (TCM) has held, and still holds, an important position in primary health care in China, both in rural and well-developed areas. The Chinese government has undertaken enormous efforts to

modernize TCM by investing capital in scientific research in TCM. *Vinca* alkaloids, taxanes, and camptothecins are natural products used in cancer chemotherapy. Controlled clinical studies have shown that homoharringtonine and arsenic trioxide can exert profound activity against leukemia. Increased knowledge of the molecular mechanisms of TCM-derived drugs and recent developments in their applications demonstrate that the combination of TCM with modern cutting-edge technologies provides an attractive strategy for the development of novel and improved cancer therapeutics. REF #5

"Inflammaging:"A Proposed Name for a Chronic Condition among the Elderly
"Inflammaging" is a term proposed and described by Dr. Claudio Franceschi in a recent article in *Nutrition Reviews*. Inflammation is necessary to cope with damaging agents and is necessary for survival, particularly to cope with acute inflammation during the reproductive years. But chronic exposure to a variety of antigens, especially to some viruses such as cytomegalovirus, for a period much longer than that predicted by evolution, induces a chronic low-grade inflammatory status that contributes to age-associated morbidity and mortality. Centenarians are unique in that, despite high levels of pro-inflammatory markers, they also exhibit anti-inflammatory markers that may delay disease onset. REF #6

Inflammation is a process related with the onset of several neurodegenerative disorders, including Alzheimer's disease (AD). A set of discoveries has strengthened the idea that altered patterns of in the glia-neuron interactions constitute early molecular events within the cascade of cellular signals that lead to neurodegeneration in AD. In effect, neuroinflammation is responsible for an abnormal secretion of proinflammatory cytokines that trigger signaling pathways that activate brain tau hyperphosphorylation in residues that are not modified under normal physiological conditions. Elucidation of the events that control the transitions from neuroprotection to neurodegeneration should be a critical point toward elucidation of AD pathogenesis. REF #7

Dietary Influences on Inflammation and Aging
Genistein and resveratrol individually inhibit adipogenesis in 3T3-L1 adipocytes and induce apoptosis in cancer cells. A research group at the University of Georgia recently investigated whether the combination of genistein and resveratrol resulted in enhanced effects on adipogenesis, lipolysis, and apoptosis in 3T3-L1 cells by treating preadipocytes and mature adipocytes with genistein and resveratrol individually at 50 and 100 micromol/L and in combination. The results indicate that genistein and resveratrol in combination produce enhanced effects on inhibiting adipogenesis, inducing apoptosis, and promoting lipolysis in 3T3-L1 adipocytes. REF #8

In the 1990s, it was suggested that the intake of fish might protect the elderly from developing cognitive impairment or dementia. Researchers at Oxford University designed a study with the objective of examining the cross-sectional relation between intake of different amounts of various seafood (fish and fish products) and cognitive performance. The subjects of this study were 2031 individuals, aged 70-74 years, recruited from the general population of Western Norway. The researchers found that most cognitive functions were influenced by fish intake. The associations between total intake of seafood

and cognition were strongly dose-dependent, and the effect was more pronounced for nonprocessed lean fish and fatty fish. REF #9

Immunity, Inflammation, and Allergy in the Gut

The gut immune system has the challenge of responding to pathogens while remaining relatively unresponsive to food antigens and the commensal microflora. In the developed world, this ability appears to be breaking down, with chronic inflammatory diseases of the gut commonplace in the apparent absence of overt infections. Whether food intake can modify the course of rheumatoid arthritis (RA) is an issue of continued scientific and public interest. There have been reports that a significant improvement can be obtained in RA patients by fasting followed by an individually adjusted vegetarian diet. REF #10-12

That probiotics and prebiotics can have an impact on intestinal targets is well-established. Documentation of their influence in sites beyond the intestinal tract is growing. Effects on the microecology and pathology of the oral cavity, stomach, and vaginal tract have been observed, likely mediated through immune influences. REF #13

Bacterial endotoxin is a potentially inflammatory antigen that is abundant in the human gut. Endotoxin circulates at low concentrations in the blood of all healthy individuals, although elevated concentrations are associated with an increased risk of atherosclerosis. British and Scottish researchers sought to determine whether a high-fat meal or smoking increases plasma endotoxin concentrations and whether such concentrations are of physiologic relevance. The results of their study indicated that low-grade endotoxemia may contribute to the post-prandial inflammatory state and could represent a novel potential contributor to endothelial activation and the development of atherosclerosis. REF #14

Clinician/Researcher of the Month

Hasan Mukhtar, PhD
Helfaer Professor of Cancer Research
Director and Vice Chair for Research
Department of Dermatology
University of Wisconsin
Medical Science Center, Room B-25
1300 University Avenue
Madison, WI 53706

Dr. Hasan Mukhtar is a Helfaer Professor of Cancer Research and the Director and Vice Chair for Research in the Department of Dermatology, School of Medicine and Public Health, at the University of Wisconsin, Madison. He is also the co-leader of the Cancer Chemoprevention Program at the Paul P. Carbone Comprehensive Cancer Center.

Dr. Mukhtar has made major contributions in identifying novel diet-based agents and in defining molecular targets for cancer chemoprevention. He is the author of 384+ original, peer-reviewed publications, many of which have appeared in high-impact journals. Dr.

Mukhtar serves as an Editorial Board member/Associate Editor of 22 scientific journals in diversified fields of cancer, pharmacology, toxicology, biochemistry, dermatology, and photobiology. He serves on grant review committees of the National Institutes of Health, the American Cancer Society, the Department of Veterans Affairs, the Department of Defense, and many private organizations.

Dr. Bland and Dr. Mukhtar have a discussion about Dr. Mukhtar's research, with a particular focus on his discoveries related to the green tea constituent epigallocatechin-3-gallate (EGCG) and the induction of apoptosis and cell cycle arrest in human carcinoma cells. Dr. Mukhtar advocates and emphasizes the importance of targeting multiple signaling pathways when researching agents with chemopreventive and therapeutic potential. REF #15-19

In Closing: Triumphs and Trials in the Application of Traditional Medicines

Traditional medicines must pass along a pathway of discovery, isolation, and mechanistic studies before eventual deployment in the clinic. Dr. Bland closes this issue with a discussion of an article focusing on research into the compounds artemisinin, triptolide, celastrol, capsaicin, and curcumin. REF #20

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