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## *Welcoming a New Initiative— Natural Products Canada*

*Peter Jones, PhD*

Consumer demand for products derived from natural sources based on their health and environmental benefits is steadily increasing. Canada's natural-products sector has greater potential to become a major player in the global market. Hence, an initiative directed towards bringing a diverse group of private and public-sector organizations together for building and maintaining a role for Canadian innovators and producers in the global market is highly essential. Natural Products Canada (NPC) is a Centre of Excellence for Commercialization and Research of natural products. It enables companies adopt validated natural products and technologies to market faster, cheaper, and more efficiently.

NPC links companies, researchers, subject matter experts, investors, and others to foster a thriving ecosystem of natural-product commercialization. Working hard to avoid duplication, NPC is based on collaboration and connectivity, making sure that the best ideas, products, and companies are well-supported as they face hurdles such as regulatory issues, intellectual property, and market growth.

The nationwide network of nodes brings together Ag-WestBio Inc. (NPC-West), the Ontario Bioscience Innovation Organization (NPC-ON), the Institute of Nutrition and Functional Foods, Université Laval (NPC-Québec) and the PEI BioAlliance (NPC-Atlantic). Affiliated entities include the Richardson Centre for Functional Foods and Nutraceuticals.

With a vision to see Canada thrive as the Silicon Valley of natural products, NPC has four main pillars of operation:

1. Connect—Help companies and researchers find the technical, business, and financial resources they need to advance along the commercialization continuum.
2. Evaluate—Provide professional assessment of product or technology with the goal of helping the proponent reach their full potential.
3. Accelerate—Advise and guide companies on the key initiatives and best resources to speed up their path to market.
4. Invest—With partners, provide strategic investment to opportunities that show high potential to benefit Canada.

A key differentiator of this new organization is its national mandate and regional operations—NPC delivers its services via regional directors hosted at strategic nodes across the country. Currently, four regional nodes exist, with regional directors in each providing on-the-ground support, with plans to add

more in the near future.

NPC's definition of natural products is broad, encompassing personal health products such as nutraceuticals, cosmeceuticals, functional foods, and functional ingredients, as well as agricultural feeds, biopesticides, and green replacements for traditional chemicals.

Still in its first year of operations, NPC is currently developing its investment process as well as creating a database of the technologies, platforms, service providers, investors, and expertise essential to the successful commercialization of natural products.

To learn more about how their program can help you, visit www.naturalproductscanada.com

## *Psychobiotics: A Novel and Promising Clinical Indication for Probiotics*

*David Lescheid, PhD*

A recent worldwide guideline suggests probiotics are only clinically useful for diseases associated with the gastrointestinal tract (GIT) and possibly the skin.[1] However, increasing evidence indicates this proposed clinical use of probiotics is too restrictive and should include other diseases as well as central nervous system (CNS) disorders.[2] Indeed, a new term, "psychobiotics," was coined in 2013 to define "a live organism that, when ingested in adequate amounts, produces a health benefit in patients suffering from psychiatric illness."[3]

Commonly known functions of probiotics include restoring stable and diverse populations of commensal microbes in the gut, supporting repair of hyperpermeable epithelial barriers, preventing infection by potentially pathogenic microorganisms, and affecting metabolism through the production of numerous bioactive metabolites.[4] Probiotics are consumed orally and, therefore, colonization is limited to the GIT. However, their effects can extend systemically to multiple organs, including those of the CNS, via three important pathways:

1. endocrine pathways, via production of bioactive metabolites (e.g. neurotransmitters, short-chain fatty acids [SCFAs, such as butyrate, propionate, and acetate], and indole derivatives) that enter circulation;[5]
2. inflammatory pathways, via modulation of various mediators of inflammation (e.g. Toll-like receptors, cytokines, chemokines),[6] as well as by restoring and maintaining epithelial barriers;[7]

3. neural pathways (e.g. metabolites influence activity of the vagus nerve and enteric nervous system).[8]

Emerging evidence also supports host-microbiota interactions as important regulators of the epigenome,[9] providing another pathway whereby probiotics could have a widespread effect.

Important neurotransmitters such as dopamine, norepinephrine, γ-amino butyric acid (GABA), serotonin, and tryptophan are produced by probiotics through a number of different mechanisms.[10] Moreover, SCFAs (produced when bacteria ferment certain fibres) also trigger release of serotonin from enterochromaffin cells in the GIT,[10] providing another way probiotics influence neurotransmitter biology.

Altering neurotransmitter levels via probiotics results in behavioural changes in animal models, including reduction of stress-induced corticosterone, anxiety, and depression-related behaviours compared to controls,[10] and reduction of anxiety and despair in various rodent models of stress.[11] In some studies, the effect of probiotics on these behaviors was noninferior to the common anxiolytic diazepam (i.e. Valium) [12] and the antidepressant citalopram (i.e. Celexa),[13] suggesting meaningful clinical effects in humans could be achieved. The benefits of probiotics were negated by vagotomy in some animal models,[10] identifying the vagus nerve as an important pathway relaying probiotic-derived signals from the gut to the brain.

The suggestion that mental health could be affected by the influence of probiotics on an altered microbiome is novel and therefore, few clinical studies exist. Nevertheless, most clinical trials are promising, including significant improvement in mood scores,[14] reduction of anxiety and stress responses,[12] improvement in a number of different scores of anxiety and depression,[15] decreased anxiety symptoms,[16] and reduction of negative thoughts associated with sad mood.[17] Moreover, functional magnetic resonance imaging (fMRI) showed ingestion of probiotics by healthy adults for four weeks could alter different regions of the brain associated with the control of central processing of emotion and sensation.[18]

We are entering a new era of understanding how the microbiome influences health and disease. Although more clinical trials are needed,[19] the increasing evidence base indicating probiotics do influence the CNS suggests probiotics should be considered by clinicians as an adjunct to other treatments for their patients with mental health disorders.

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# *Antioxidant Polyphenols and Carotenoids in the Prevention and Management of Osteoporosis*


*Venkateshwar Rao, PhD, and Leticia Rao, PhD*


## Introduction

Osteoporosis is a skeletal disease characterized by bone loss and structural deterioration of the bone tissue, leading to an increase in bone fragility and susceptibility to fractures, most frequently in the hip, wrist, and spine.[1] Bone loss is associated with factors such as age, menopause in women, smoking, alcohol excess, calcium and vitamin D deficiency, low weight and muscle mass, and anticonvulsant and corticosteroid use, as well as certain comorbid conditions such as rheumatoid arthritis.[1, 2] Worldwide, it has been estimated that fractures caused by osteoporosis account for approximately one in three among women, and approximately one in five among men over the age of 50.[1, 3] Although the mechanisms underlying osteoporosis are not fully understood, there is evidence to indicate that oxidative stress, a condition that can be characterized by an imbalance of prooxidants and antioxidants—with the scale being tipped towards an excess of prooxidants, creating abnormally high concentrations of reactive oxygen species (ROS)—could contribute to the development of osteoporosis.[2, 3, 4, 5] ROS are a family of highly reactive, oxygen-containing molecules that interact readily with cellular constituents, bringing about changes in the structure and function

of the cells. The dynamic nature of bone formation and resorption are dependent upon the activity of osteoblast and osteoclast cells.[2] Several recent studies reported the impact of oxidative stress on the osteoclast differentiation as well as on its function resulting in an increase in bone resorption.[6]

Furthermore, recent in vitro studies have also shown the important detrimental role of ROS on osteoblast activity. In addition to in vitro and animal models, there is also increasing clinical evidence to suggest that oxidative stress might be involved in the pathogenesis of osteoporosis.[2, 3, 5]

Some of the common drugs and hormones used for the prevention and management of osteoporosis include Zoledronate, Ibandronate, Raloxifene, Strontium Renalate, Calcitonin, and PTH.[2, 3] Although effective in the prevention of further loss of bone cells, many of these drugs do not induce new bone formation. Further, there are some undesirable side effects that are associated with their administration. As alternative or complementary strategies, there is increased interest in the use of antioxidants in the prevention, management, and possibly treatment of osteoporosis. Antioxidants are known to mitigate the damaging effects of oxidative stress on cells. Epidemiological evidence has indicated a link between dietary intake of antioxidants and bone health.[4, 7] Fruits and vegetables are important sources of antioxidant phytochemicals that have been shown to play an important role in bone metabolism. Higher consumption of fruits and vegetables has been correlated with a reduction in the risk for the development of osteoporosis.[8] Plant foods contain—in addition to the well-know water-soluble and fat-soluble antioxidant vitamins such as A, E, K, and C—other constituents that are also potent antioxidants. Included in this group are the polyphenols (water-soluble) and the carotenoids (lipid-soluble) phytochemicals. They have been studied extensively as beneficial compounds in the prevention and management of osteoporosis.

**Polyphenols and Carotenoids**

Polyphenols are a group of water-soluble compounds that include both flavonoid and nonflavonoid constituents such as ellagic acid, stilbenes, anthocyanins, catechins, flavones, flavonols, and isoflavones.[9] The antioxidant properties of polyphenols have been widely studied and reported in the literature. Numerous studies have shown the health-promoting properties of polyphenols, providing additional mechanisms through which they promote skeletal health by reducing resorption of bone caused by high oxidative stress.[2, 3, 9, 10] These studies strongly support the role of polyphenols in the delayed onset or reduction in the progression of osteoporosis. The protective effects of polyphenols against diseases, including osteoporosis,

have generated new expectations for improvements in health.

Carotenoids, similar to polyphenols, are a group of fat-soluble compounds having strong antioxidant properties.[7, 8] Main dietary sources of carotenoids are fruits and vegetables. One of the carotenoid studied extensively for its beneficial properties against several chronic diseases including osteoporosis is lycopene.[2, 3] Tomatoes and tomato products are the major source of lycopene in human diet.[6, 8] In vitro studies in our laboratory have shown that lycopene is effective in promoting osteoblast activity and inhibiting the activity of osteoclast. In a recently completed clinical study with postmenopausal women at high risk for osteoporosis, bone turnover biomarkers were measured before and after the ingestion of lycopene. Results showed higher levels of lycopene in the serum, lower levels of oxidative stress, lower osteoclast activity, and higher osteoblast activity.[6] These results led us to conclude that carotenoids such as lycopene can play an important role in the prevention and management of osteoporosis.

**Conclusion**

Osteoporosis is one of the major human health disorders prevalent globally. Although postmenopausal women are at a higher risk, men are also prone to osteoporosis. Although the mechanisms of osteoporosis are not fully understood, there is evidence to suggest that oxidative stress plays an important role in its causation. Traditionally drugs are used for the treatment of osteoporosis; however, there is a great deal of interest in using alternate and complementary strategies in the prevention and management of osteoporosis. In this context, antioxidants are being studied extensively and in particular naturally present antioxidant phytochemicals such as polyphenols and carotenoids. Based on encouraging results from in vitro studies, clinical and human intervention studies are now being conducted. Undoubtedly, more long-term studies measuring bone turnover markers, as well as clinical endpoints such as bone mass density (BMD), need to be done. However, current published literature provides convincing evidence that polyphenols and carotenoids do provide beneficial role in the prevention and management of osteoporosis. At present, there are no dose guidelines for the ingestion of these compounds. Certainly it is not the intention of the authors to suggest that the use of medication in the treatment of osteoporosis be stopped. However, it seems prudent to include dietary and/or supplementary sources of these antioxidant phytochemicals for maintaining bone health.

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**Content Director:**
Peter Jones, PhD

**Editors:**
Leah Gillingham, PhD
Peter A.S. Alphonse, PhD

**Distribution Manager**
Krystle Lussier

**NFH**
3405 F.-X.-Tessier
Vaudreuil-Dorion (Québec)
J7V 5V5
1 866 510-3123
info@nfh.ca
www.nfh.ca