Coriolus versicolor extracts: relevance in cancer management

*M. Szeto BSc RD**

ABSTRACT

Cancer patients are increasingly seeking options in complementary and alternative medicine. Natural health products have by far become the most popular modality. Mainstream health care professionals need to engage in an open dialogue with their patients as cancer care becomes more multifaceted.

KEY WORDS

CAM, natural health products, mushroom extracts, PSK, PSP

1. INTRODUCTION

Pappas and Perlman quoted Lerner's definition of complementary and alternative medicine (CAM) as "those approaches to the diagnosis, treatment, and care of a disease that fall outside conventional treatments" [1]. The rise in the popular use of CAM in cancer patients is a global phenomenon [2]. Some studies indicate that the prevalence of CAM use in industrialized societies reaches 31.4% [3]. In the United States, it rises to as high as 42%–69% [2].

One of the most popular CAM modalities is natural health products (NHPS), also called dietary supplements [2–4]. A national survey conducted by Health Canada in 2005 indicated that 71% of Canadians use NHPS, the term officially coined to include vitamins and minerals, herbal products, traditional Chinese medicines (TCMS), homeopathic medicines, probiotics, and products such as amino acids and essential fatty acids [5]. Among cancer patients, the percentage using these products is as high as 45%–60% [6]. In fact, a survey by the British Columbia Cancer Agency found that almost 90% of their patients had used NHPS [6]. A Canadian survey discovered that cancer patients use CAM primarily to (in descending order) "increase quality of life, prevent recurrence of cancer, provide a feeling of control over life, aid conventional medical treatment, treat breast cancer, treat side effects of conventional treatments, attempt to stabilize current condition and compensate for failed conventional medical treatments" [4]. However, the most common reason listed was to boost the immune system [4].

For at least five millennia, mushrooms have been harvested for their nutritional and medicinal value and diversity of bioactive compounds [7,8]. Since about the end of the 1970s, mushroom research has focused largely on cancer. Substances isolated from more than 50 species of mushrooms have been touted as "immunoceuticals." Immunoceuticals are substances that, when taken orally, produce immunotherapeutic effects. They have the potential to enhance the body's natural immune defence against abnormal tissue growth.

Immunoceuticals isolated from more than 30 mushroom species have demonstrated anticancer properties in animals, but many fewer have been involved in human cancer research. Of those that are studied in human cancer, all are classified chemically as β-D-glucans (linear polymers of D-glucose with monosaccharides attached) bound to proteins. Collectively they are known as "proteoglycans." Polysaccharide K (PSK) and polysaccharide peptide (PSP) are the only two proteoglycans that have been systematically investigated in human cancer [7]. They are chemically related constituents extracted from the mushroom *Coriolus versicolor.*

The mushroom *C. versicolor* comes from the polypore family and belongs to the Hymenomycetes class [9]. Scientifically, it is known as *Trametes versicolor* or *Polyporus versicolor* [10]. Common names include "turkey tail" mushroom, Yun-zhi, PSP, PSK, cloud mushroom, Krestin (Kureha Chemical Industry Co., Tokyo, Japan) [9–12], and in Japan, kawaratake, which means "mushroom by the river bank" [13].

The *Compendium of Materia Medica* written by Li Shi Zhen during the Ming Dynasty in China described *C. versicolor* as a medicine that rejuvenates and extends life with chronic use [8]. It is classified as

Stephen M. Sagar, BSc(Hons) MB BS MRCP FRCR FRCPC DABR, Associate Professor of Oncology and Medicine, McMaster University, Hamilton, Ontario, Canada, Section Editor.

zhi in TCM [9]. Because of high *in vivo* antitumour activity, low risk of toxicity, and stability during serial cultivation, PSP and PSK have claimed more spotlight than other immunoceuticals [14]. More research attention overall has been gained by PSK because it was discovered long before PSP. A chemical engineer first stumbled upon its anticancer properties in 1965 when his neighbour recovered sufficiently from his life-threatening cancer to return to work after taking a hot-water extract of a mushroom [7,15]. This incident led to the discovery of PSK in Japan. The Chinese isolated PSP in 1983 [7].

In TCM, *C. versicolor* was originally used to dispel heat, remove toxins, strengthen the body, increase energy and spirit, and enhance the host's immune function [13]. In the clinical practice of TCM, *C. versicolor* is prescribed for various types of cancers, chronic hepatitis, and infections of the upper respiratory, urinary, and digestive tracts [13]. Although not widely available, *C. versicolor* extracts have nonetheless been commercialized and are marketed for healthy people and cancer patients. Claims are made that *C. versicolor* extracts enhance the immune system of healthy individuals; in cancer patients, they are reputed to mitigate the side effects of conventional cancer treatments, to reduce cancer recurrence and metastasis, and to improve overall quality of life (Supreme Health Foods) [9].

Extracts of *C. versicolor* are popular as a NHP in East Asia. Japan has used them as an adjunctive therapy to conventional cancer treatment [10]. Despite their fame in East Asia, they are almost unheard of in Western countries, except in Asian communities. Cancer patients of Asian background are using *C. versicolor* extracts—some without their physician's knowledge.

The purpose of the present article is to provide an overview of *C. versicolor* extracts, to examine the purported benefits of those extracts, and to discuss the evidence behind the existing claims for their use in cancer patients. It is not the intention of this article to summarize existing research, a task that has already been undertaken in a comprehensive manner by Kidd [7].

2. DISCUSSION

2.1 *C. versicolor* Extracts

Hot water is used to extract the proteoglycans PSK and PSP from *C. versicolor*'s cultured mycelium (thread-like extensions) [16]. The polypeptide component has an abundance of acidic amino acids, glutamic and aspartic acids, and neutral amino acids such as valine and leucine, but minimal amounts of basic amino acids such as lysine and arginine.

Glucose is the primary monosaccharide that forms the polysaccharide component [14]. Essentially, PSK and PSP are similar except for the presence of other monosaccharides—namely fucose in PSK and rhamnose and arabinose in PSP [8]. More precisely, PSK and PSP are not pure compounds. Their structure is complex.

In PSK, at least 4 different subfractions may have important actions of their own. The immunotherapeutic activities ascribed to PSK have been associated with the highest molecular weight subfraction. More research is needed to delineate the subfractions and their separate functions [17].

Similarly, only a few key structural components of PSP have so far been identified. Aqueous extracts of *C. versicolor* often contain PSP of various molecular weights. The high molecular weight PSPs (>10 kDa) are considered to be immunologically active [13].

2.2 Pharmacokinetics and Mechanism of Action

Animal studies indicate that *C. versicolor* extracts are biologically active. In mice, the full molecular spectrum of radiolabelled PSK is absorbed within 24 hours following oral administration. Radiolabelled PSK or its by-products are found in the digestive tract, bone marrow, salivary glands, thymus, adrenal gland, brain, liver, spleen, pancreas, and tumour tissue in sarcoma-bearing mice. Liver and bone marrow have the highest and longest duration of activity. About 70% of radiolabelled PSK is eliminated by expired air, 20% in feces, 10% in urine, and 0.8% in bile. Almost 86% is eliminated within 24 hours [11].

Numerous *in vitro* and *in vivo* immunologic studies using *C. versicolor* extracts have been conducted. *In vitro* studies show that *C. versicolor* extracts promote the action of T lymphocytes, B lymphocytes, monocytes, macrophages, bone marrow cells, natural killer cells, and lymphocyte-activated killer cells. They also enhance the proliferation of antibodies and various cytokines such as interleukins 1, 2, 6, and 8, interferons, and tumour necrosis factor [13].

Among other immune-enhancing effects, cytokines have the ability to trigger a series of reactions that stimulate cytotoxic T cells against tumour growth. The hypothesis is that PSK induces T cells in an antigen-specific manner [13,14]. Studies found that PSP suppressed growth in various human cancer cell lines and increased immunoglobulin G (IgG) and C3 complement protein in immunodeficient mice [14]. *In vivo* studies also revealed that *C. versicolor* extracts have the ability to restore immunologic responsiveness to a normal level after it is reduced by tumour burden or chemotherapy. The extracts also stimulate the production of complement proteins, interferon, and interleukins *in vivo* [13].

Besides immunostimulatory effects, PSK has been reported to possibly have anti-metastatic effects [18]. The metastasis of cancer cells involves multiple stages. Interference with cancer metastasis by PSK occurs not just at any one stage, but at various stages.

Migration of tumour cells depends on detachment of the cells from the primary lesion. Evidence suggests that PSK suppresses the motility of tumour cells *in vitro* and *in vivo* [18]. It inhibits tumour invasion, adhesion, and production of extracellular matrix degradation enzymes *in vitro*. These enzymes are produced by the tumour cells to destroy the basement membrane, a specialized layer of extracellular matrix that divides the epithelial tissue from the underlying connective tissue. To migrate and form metastases, cancer cells need to break this barrier. Furthermore, PSK suppresses tumour progression by inhibiting angiogenesis *in vivo* [14,18].

Another mechanism for the anticancer function of PSK and PSP is their role as antioxidants and free radical scavengers [14]. Free radicals are associated with DNA damage and carcinogenesis. Superoxides and hydroxyl radicals—the end products of cellular metabolism—are the most aggressive cellular reactive oxygen species generated by the mitochondria. Superoxides are changed to the less potent hydrogen peroxide by the enzyme superoxide dismutase. However, when hydrogen peroxide is exposed to a metallic ion (iron or copper), it is converted into highly reactive hydroxyl radicals [19]. The activity of superoxide dismutase has been shown to be mimicked by PSK, which thereby provides some oxidative stress reduction. In addition, PSP has been shown to be a good scavenger of superoxides and hydroxyl radicals [14,18].

2.3 Drug Interactions and Safety

No reports of drug interactions with *C. versicolor* extracts are currently known [11]. Given that PSK does not involve the hepatic drug-metabolizing enzymes, it does not appear to affect the pharmacology of other drugs, including most of the chemotherapy agents [17]. But because of the immunostimulating effects of *C. versicolor* extracts, cautions have been raised about their concurrent use with any immunosuppressant. Use of the extracts in autoimmune disease or in transplant patients may be contraindicated [13].

The use of *C. versicolor* extracts has not been associated with any serious adverse reactions [7]. Subacute and chronic toxicity tests with PSK have been undertaken. No toxicity has been observed. No serious adverse effects have been reported in clinical trials of PSP to date. Doses of *C. versicolor* extracts up to 15 g daily over a long period have not been linked with any side effects [7]. Rare cases of nausea, vomiting, loss of appetite, and diarrhea have occurred [10]. Passage of dark-coloured stools (not a result of occult blood), darkening of fingernails, and low-grade hematologic and gastrointestinal toxicities have been reported when the extracts were used in conjunction with chemotherapy agents. These effects were thought possibly to be caused by the chemotherapy agents themselves [11]. However, the safety of the extracts has not yet been established in young children, pregnant or nursing women, and people with severe liver or kidney disease.

2.4 Clinical Evidence

Current evidence does not suggest that the raw mushroom is itself an effective anticancer agent [10]. Interestingly, despite the known immunostimulatory benefits in the tumour burden host, *C. versicolor* extracts do not appear to have any immune effect in the normal host [14].

The core clinical evidence on PSK was garnered primarily from extensive research in Japan. Japanese researchers have conducted large-scale clinical trials using PSK as a biologic response modifier (BRM) in cancer patients since 1970. Since the 1970s, BRMs have been used by the larger medical community as adjuvant immunotherapy for cancer. The idea has been to enhance the "host versus tumour response" by increasing the host's ability to defend against tumour progression without antigen specificity [17] in the hopes of reducing morbidity and extending survival. Although BRMs such as interferons, interleukins, and bacille Calmette–Guerin abound, they have not been found helpful in some types of cancers—lung cancer, for example. The search for an effective lung cancer immunotherapy agent continues, but thus far, the answer remains elusive [20]. In Japan, PSK research involves primarily cancers of the stomach, colon and rectum, esophagus, nasopharynx, and lung [non-small-cell (NSCLC) types] and the human leukocyte antigen B40-positive breast cancer subset [7].

2.4.1 Polysaccharide K

In 1977, PSK became commercially available on the Japanese market as Krestin [15]. Japan approves the use of PSK as an immunotherapeutic agent for gastric, colorectal, and lung cancers [18]. In essence, PSK has been shown to extend survival to 5 years or more [7], with several studies appearing to support recognition of PSK's benefits and providing an impetus towards ongoing clinical use in Japan.

During 1978–1980, for example, 579 patients in 97 hospitals who underwent gastrectomy for gastric cancer were included in a randomized controlled trial with 3 arms. All groups received an induction dose of the chemotherapy agent mitomycin C (MMC) on the day of gastrectomy and the following day. The first group was then given PSK orally, 3 g daily, for a year starting 1–2 weeks after surgery. Instead of PSK, the second group received another chemotherapy agent, futraful (FT), in the same manner. The third group received FT and PSK in combination. Although the 5-year survival rate for the third group (MMC+FT+PSK) was the best, followed by that for the first group (MMC+PSK), the difference in the rate between these two groups was statistically nonsignificant. Similarly, the difference between the first group (MMC+PSK) and

the second group (MMC+FT) was nonsignificant. However, the 5-year survival rate was significantly better ($p < 0.01$) in the third group (MMC+FT+PSK) than in the second group (MMC+FT) [21]. These results imply that, for maximum survival benefit, the use of PSK as a BRM has to be carefully combined with appropriate chemotherapeutic agents.

A large-scale randomized controlled trial aimed at determining the immunotherapeutic effects of PSK in the survival of patients who underwent curative resection for colorectal cancer was conducted in Japan with a follow-up time of more than a median of 4 years. During 1985–1987, 462 patients from 35 health institutions were selected, and 448 who met the eligibility criteria were entered into the trial. Patients were randomly assigned to either the treatment or the control group. Patients in the control group received chemotherapy (intravenous MMC) the day of, and the day after, surgery, followed by another chemotherapy agent (oral 5-fluorouracil) for up to 6 months or until tumour recurrence. Patients in the treatment group received PSK orally (3 g daily) for a period of 3 years in addition to the same chemotherapy regimen as in the control group. The two groups were well balanced except for the size of the rectal tumours, which was significantly larger in the PSK group ($p < 0.05$). The study found that the 3-year disease-free survival and the overall survival in the PSK group (colon and rectal cancers combined) were significantly better than were those in the control group ($p = 0.0134$ and $p = 0.0130$ respectively). The 3-year disease-free survival and overall survival for the rectal cancer patients alone were both also better for the PSK group, but neither value reached statistical significance [15]. These results are quite remarkable, because colorectal cancer recurrence is highest within 1–2 years of resection [15]. One caveat is that these results can be interpreted only in the context of colorectal cancer that is curatively resectable.

During 1976–1985, 185 patients at a university hospital in Japan were treated with definitive radiotherapy for stages I–III NSCLC. In 62 patients who had relatively good prognostic factors after radiotherapy, plus satisfactory regression of tumours and performance status, PSK 3 g daily was administered orally in a "2-weeks on, 2-weeks off" cycle. The patients were then evaluated for 5-year survival rate. The 5-year survival rate was found to be significantly higher in patients who were administered PSK—39% for stage I and II patients ($p = 0.005$) and 22% for stage III patients ($p = 0.004$) respectively, as compared with 16% and 5% in patients not receiving PSK.

The authors of this clinical trial acknowledged a gross bias because of better prognostic factors and an anticipation of treatment benefit in the patients given PSK. They strongly felt that patients with high curative probability should be chosen for immunotherapy, because PSK in this case will eliminate the few tumour cells remaining after irradiation, maintain post-irradiation stromal reactions, enhance the reactivity of tumours to radiation, and preserve the dominance of host in the host–tumour relationship. They also felt that, despite anticipation, the benefits of PSK could not be ignored, because the survival rate for patients with stage III disease who received PSK was better than that of patients with stage I or II disease who did not receive PSK. Also, for patients more than 70 years of age, this study found significantly higher 5-year survival in the PSK group than in the non-PSK group ($p = 0.007$) [22]. That finding is encouraging because lung cancer affects mostly older individuals. The authors felt that age-related immunodeficiency contributes to a less than desirable outcome of radiation therapy and that the use of PSK as an adjunctive BRM can potentially improve survival outcomes in these older radiation therapy patients [22]. Results may not apply to lung cancer patients with poor radiation outcomes.

2.4.2 Polysaccharide Peptide

Since the 1990s, PSP research has taken place mostly in China. Compared with PSK, PSP is still in its infancy. To date, 8 phase II and phase III double-blind trials have indicated that PSP has benefits against stomach and esophageal cancers and NSCLC. One multicentre double-blind phase III trial involving 189 cancer patients demonstrated that PSP significantly reduces fatigue, loss of appetite, anorexia, vomiting, dryness of mouth or throat, sweating, and pain ($p < 0.01$) [7,23]. The authors of this trial also found that the Karnofsky performance status of patients taking PSP was significantly improved as compared with that in control patients ($p < 0.05$) [7].

A more recent phase II double-blind controlled trial was conducted in Hong Kong, China. Based on inclusion and exclusion criteria, the study recruited 34 patients with similar demographic and clinical characteristics at baseline from a university-based tertiary centre. These patients, who had completed conventional treatment for advanced NSCLC, were randomly assigned to a PSP and a control group. The treatment group received 3 capsules of PSP (from purified Yun-zhi) 3 times daily; the control group received an identical placebo (crystallized sucrose). At the end of 28 days, the PSP group showed a significant increase in serum leukocyte and neutrophil counts ($p < 0.05$) and the control group showed a significant decrease ($p < 0.05$). In the PSP group, serum IgG and IgM increased significantly ($p = 0.02$ and $p = 0.04$ respectively) as well. This finding has clinical value because lung cancer patients with lower IgG and IgM have a higher incidence of pulmonary infection and a poorer prognosis [23].

As compared with placebo, PSP did not improve associated cancer symptoms (for example, nausea, lack of appetite, fatigue, and so on). However, the proportion of patients who withdrew from the study because of disease progression was significantly lower in the PSP group than in the control group (5.9%

and 23.5% respectively, $p = 0.04$). The authors concluded that PSP treatment appears to be associated with slower deterioration of advanced NSCLC [23].

Research thus far shows that PSP has promise in ameliorating symptoms and possibly extending survival in stomach and esophageal cancers and in NSCLC [23]. More randomized controlled trials are required to delineate efficacy.

2.5 Practice Implications

Cancer is the leading cause of premature death in Canada [24]. It is estimated that, every week on average, 2944 Canadians will be diagnosed with cancer and 1354 Canadians will die of the disease. The leading cause of death in North America is NSCLC, which comprises 80% of all primary lung cancer [23,24]. Long-term survival in certain high-prevalence cancers, even in the early stages of the disease, continues to be poor because of metastasis. In some cases, the cancer is much advanced at the time of diagnosis, further limiting treatment options and effectiveness [20,23].

The prolonged clinical use of PSK in Japan, with the survival benefits observed, and the existing research and evidence on PSP deserve proper attention from a wider medical audience. Although currently inconclusive, the studies suggesting that PSP has the ability to palliate cancer symptoms are particularly encouraging. Individuals with cancer are often plagued by a loss of appetite and anorexia attributable to cancer progression and the compounding effects of cancer treatment. Symptomatic improvement may contribute to enhanced quality of life and reduced anxiety and stress levels, possibly conferring additional benefits with regard to immune response [25].

Evidence suggests a benefit for PSK as a CAM in stomach, colorectal, and lung cancers—especially when the underlying prognosis is reasonable. Integrating PSK as an adjunct to conventional therapy in the West may need more investigation, because the chemotherapeutic agents commonly used in Japanese may not be the same as those used in Western medicine. The evidence to date suggests the utility of conducting larger prospective double-blind controlled trials to study PSP as adjunctive therapy in cancers of the stomach and esophagus and in NSCLC. With known minimal toxicity and side effects, and no known drug interactions, *C. versicolor* extracts appear even more favourable.

Integration of CAM into mainstream cancer care continues as various unconventional therapies are proved safe and effective [26]. Barriers nonetheless remain. The spectrum of CAM modalities involves tremendous variation in degree of benefit, risk, standardization, and clinical evidence. Some products have been shown to improve quality of life at minimal risk; some require judicious use because of potentially harmful effects; and still others remain of questionable value [3,27]. Because of these disparities, mainstream medicine is often reluctant to accept and invest the necessary resources into CAM research [28].

One study showed that 72% of cancer patients use more than one CAM approach and that 15% use seven or more approaches. This phenomenon presents huge challenges for researchers who want to investigate a single modality [2]. At the same time, 60%–80% of cancer patients use CAM concurrently with conventional treatment, chemotherapy, radiotherapy, and surgery [2]. Evaluating the effectiveness of conventional therapy is as pivotal to the advancement of cancer care as is discerning the effects of CAM on conventional therapy.

Despite rampant use of CAM, estimates suggest that 70% or more of cancer patients do not discuss CAM use with their physicians [4,29]. This number may vary greatly depending on the particular group of cancer patients. An Ontario study showed that almost 47% of breast cancer patients reported the use of CAM to their physicians [4].

The most common reason given by patients for not disclosing information about CAM use is that their physician never raised the issue. Other patients feel that CAM use is not important for physicians to know [3]. Some patients may fear dismissal of their choice of CAM. For example, oncologists have been known to discourage most patients from the use of dietary supplements when such use is brought to their attention [3]. At the same time, cancer patients increasingly want information on CAM, and some believe that equal access to CAM should be part of standard cancer care [2,28].

As cancer rates and patient survival time continue to increase, it is predictable that the use of CAM will also increase [2]. Especially when patients are dealing with advanced cancer, the use of CAM is a rational choice [30]. When faced with such a calamity, cancer patients often opt to try "something else" so as to maintain hope and, likely, to reduce the sense of despair [2,30]. Many studies aimed at identifying reasons for the use of CAM in cancer patients have urged an open and non-judgmental dialogue between patients and clinicians [1–4,30,31].

Regardless of whether health care professionals want to acknowledge CAM, use of CAM is on the rise, the largest increase being in NHPS or dietary supplements [32]. Clinicians need to be more sensitive about patient values and beliefs and should not view patients who use CAM as "unrealistic, gullible, and ungrateful" [1]. Clinicians need to be unbiased and knowledgeable—and prepared to give advice about CAM using existing evidence. In light of the invisible use of CAM, it is important to take the initiative to help cancer patients obtain unambiguous, valid, and reliable information and avoid unnecessary harm.

Although physicians should have the primary responsibility in addressing CAM issues, other health care professionals—nurses, dietitians, pharmacists—should play a collaborative role [4,31] and utilize one

other's expertise. Frenkel and Borkan devised a suggested decision tree to help primary care physicians select and integrate appropriate CAM modalities [33]. A group of pharmacists in British Columbia developed a structured approach on how to advise patients on NHPs [6]. The American Dietetic Association developed a practice paper on dietary supplements [34] that provides a framework to position and assist dietitians in becoming more adept at amalgamating CAM knowledge into practice.

Guidelines for counselling cancer patients about NHPs also exist. The patient-centred model from Stewart *et al.* proposed asking non-judgmental questions such as "Have you ever used or thought about using anything else to treat (symptoms or condition) such as herbal medicine, vitamins, or other nutritional supplements?" [31]. Smith and Boon [31] suggested using Dr. David Eisenberg's step-by-step approach in counselling patients who use CAM:

1. Have the patient identify the specific symptom or symptoms that he or she wishes to alleviate.
2. Ask the patient to maintain a symptom diary.
3. Discuss the patient's preferences and expectations with respect to CAM options.
4. Review the safety and efficacy of the options.
5. Help the patient identify a suitable CAM provider if necessary (preferably licensed).
6. Help the patient identify key questions to ask the selected CAM medicine provider.
7. Schedule a follow-up visit to review the patient's progress.
8. Follow up and review the patient's response to treatment.
9. Document the process.

Although resources are available, it is unclear how often various professionals engage in discussions about CAM. A national survey undertaken in Canada found that information about NHPs comes mostly from family, friends, and the Internet [5]. Yet the same survey found that the most trusted sources of information are physicians, pharmacists, the health department, and dietitians [5]. Despite the thirst for CAM information, a uniform, interdisciplinary, and systematic approach to dealing with such issues in the cancer setting is lacking [6]. Because CAM is a vast topic, a collaborative approach will enable information sharing, create a more efficient process, and provide a paramount approach to optimizing and enhancing cancer care.

3. CONCLUSIONS

The existing evidence on *C. versicolor* extracts is positive. The role of PSK as a BRM in cancer therapy is well established in Japan, and preliminary research on PSP is promising. Communities in North America are becoming more globally diverse and multicultural. The prevalent use of *C. versicolor* extracts in certain ethnic communities despite geographic boundaries should give this topic a definite place in the universal search for better adjunctive cancer therapy.

Cancer patients are actively seeking information on CAM. They are self-treating with CAM for a variety of reasons. Health care professionals should respond appropriately by becoming more knowledgeable. Clinicians should exercise due diligence in initiating communication with patients. The use of CAM will continue to increase, especially in the area of NHPs. Continued research to separate products that are safe and beneficial from those that may cause harm is imperative.

Use of CAM in cancer patients is an important reality to which health care professionals need to awake and respond.

4. REFERENCES

1. Pappas S, Perlman A. Complementary and alternative medicine. The importance of doctor–patient communication. *Med Clin North Am* 2002;86:1–10.
2. Richardson MA, Sanders T, Palmer JL, Greisinger A, Singletary SE. Complementary/alternative medicine use in a comprehensive cancer center and the implications for oncology. *J Clin Oncol* 2000;18:2505–14.
3. Swarup AB, Barrett W, Jazieh AR. The use of complementary and alternative medicine by cancer patients undergoing radiation therapy. *Am J Clin Oncol* 2006;29:468–73.
4. Boon H, Stewart M, Kennard MA, et al. Use of complementary/alternative medicine by breast cancer survivors in Ontario: prevalence and perceptions. *J Clin Oncol* 2000;18: 2515–21.
5. Canada, Health Canada. Drugs & health products; advisories, warnings & recalls—natural health products [Web resource]. Ottawa: Health Canada; February 2, 2006. [Available at: www.hc-sc.gc.ca/dhp-mps/advisories-avis/natur/index_e.html; cited November 24, 2006]
6. de Lemos ML, John L, Nakashima L, O'Brien RK, Taylor SC. Advising cancer patients on natural health products—a structured approach. *Ann Pharmacother* 2004;38:1406–11.
7. Kidd PM. The use of mushroom glucans and proteoglycans in cancer treatment. *Altern Med Rev* 2000;5:4–27.
8. Ng TB. A review of research on the protein-bound polysaccharide (polysaccharopeptide, PSP) from the mushroom *Coriolus versicolor* (Basidiomycetes: Polyporaceae). *Gen Pharmacol* 1998;30:1–4.
9. Supreme Health Foods. Health food supplements: the difference between yunzhi and reishi [Web page]. Richmond Hill, ON: Supreme Health Foods; n.d. [Available at: www.supremehealthfoods.com/corpweb/yunzhi-reishi.html; cited October 10, 2006]
10. American Cancer Society. Making treatment decisions, *Coriolus versicolor* [Web page]. Atlanta: American Cancer Society; June 1, 2005. [Available at: www.cancer.org/docroot/ETO/content/ETO_5_3X_Coriolous_Versicolor.asp; cited October 3, 2006]
11. Memorial Sloan–Kettering Cancer Center. Cancer information:

integrative medicine: about herbs, botanicals & other products: *Coriolus versicolor* [Web page]. New York: Memorial Sloan–Kettering Cancer Center; October 3, 2006. [Available at: www.mskcc.org/mskcc/html/69194.cfm; cited October 3, 2006]

12. Natural Medicines Comprehensive Database. *Coriolus* mushroom [Web page]. Stockton, CA: Therapeutic Research Faculty; December 1, 2006. [Available at: www.naturaldatabase.com (subscription required); cited December 1, 2006]
13. Chu KK, Ho SS, Chow AH. *Coriolus versicolor*: a medicinal mushroom with promising immunotherapeutic values. *J Clin Pharmacol* 2002;42:976–84.
14. Ooi VE, Liu F. Immunomodulation and anti-cancer activity of polysaccharide–protein complexes. *Curr Med Chem* 2000;7: 715–29.
15. Mitomi T, Tsuchiya S, Iijima N, *et al.* Randomized, controlled study on adjuvant immunochemotherapy with PSK in curatively resected colorectal cancer. The Cooperative Study Group of Surgical Adjuvant Immunochemotherapy for Cancer of Colon and Rectum (Kanagawa). *Dis Colon Rectum* 1992;35: 123–30.
16. University of Texas M.D. Anderson Cancer Center. Complementary/integrative medicine: herbal/plant therapies: *Coriolus versicolor*: detailed scientific review [Web page]. Houston, TX: University of Texas M.D. Anderson Cancer Center; n.d. [Available at: www.mdanderson.org/departments/CIMER/display.cfm?id=BF40CDD9-ED6B-11D4-810200508B603A14&method=displayFull&pn=6EB86A59-EBD9-11D4-810100508B603A14; cited: October 3, 2006]
17. Fisher M, Yang LX. Anticancer effects and mechanisms of polysaccharide-K (PSK): implications of cancer immunotherapy. *Anticancer Res* 2002;22:1737–54.
18. Kobayashi H, Matsunaga K, Oguchi Y. Antimetastatic effects of PSK (Krestin), a protein-bound polysaccharide obtained from Basidiomycetes: an overview. *Cancer Epidemiol Biomarkers Prev* 1995;4:275–81.
19. Salganik R. The benefits and hazards of antioxidants: controlling apoptosis and other protective mechanisms in cancer patients and the human population. *J Am Coll Nutr* 2001;20: 464S–75S.
20. Raez LE, Fein S, Podack ER. Lung cancer immunotherapy. *Clin Med Res* 2005;3:221–8.
21. Niimoto M, Hattori T, Tamada R, Sugimachi K, Inokuchi K, Ogawa N. Postoperative adjuvant immunochemotherapy with mitomycin C, futraful and PSK for gastric cancer. An analysis of data on 579 patients followed for five years. *Jpn J Surg* 1988;18:681–6.
22. Hayakawa K, Mitsuhashi N, Saito Y, *et al.* Effect of Krestin (PSK) as adjuvant treatment on the prognosis after radical radiotherapy in patients with non-small cell lung cancer. *Anticancer Res* 1993;13:1815–20.
23. Tsang KW, Lam CL, Yan C, *et al. Coriolus versicolor* polysaccharide peptide slows progression of advanced non-small cell lung cancer. *Respir Med* 2003;97:618–24.
24. Canadian Cancer Society. About cancer; cancer statistics; lung cancer stats [Web page; Canada-wide statistics]. Toronto: Canadian Cancer Society; April 2006. [Available at: www.cancer.ca/ccs/internet/standard/0,2283,3172_14459__langId-en,00.html; cited: November 10, 2006]
25. Hernandez–Reif M, Ironson G, Field T, *et al.* Breast cancer patients have improved immune and neuroendocrine functions following massage therapy. *J Psychosom Res* 2004;57:45–52.
26. Cassileth BR, Deng G. Complementary and alternative therapies for cancer. *Oncologist* 2004;9:80–9.
27. Grunberg SM. Stage shift and complementary/alternative medicine. *J Clin Oncol* 2000;18:3455–6.
28. Richardson MA, White JD. Complementary/alternative medicine and cancer research: a national initiative. *Cancer Pract* 2000;8:45–8.
29. Lippert MC, McClain *r*, Boyd JC, Theodorescu D. Alternative medicine use in patients with localized prostate carcinoma treated with curative intent. *Cancer* 1999;86:2642–8.
30. Correa–Velez I, Clavarino A, Eastwood H. Surviving, relieving, repairing, and boosting up: reasons for using complementary/alternative medicine among patients with advanced cancer: a thematic analysis. *J Palliat Med* 2005;8:953–61.
31. Smith M, Boon H. Counseling cancer patients about herbal medicine. *Patient Educ Couns* 1999;38:109–20.
32. Eisenberg DM, Davis RB, Ettner SL, *et al.* Trends in alternative medicine use in the United States, 1990–1997. *JAMA* 1998; 280:1569–75.
33. Frenkel MA, Borkan JM. An approach for integrating complementary–alternative medicine into primary care. *Family Prac*t 2003;20:324–32.
34. American Dietetic Association (ADA). Advocacy & the profession; ADA practice papers; dietary supplements [Web page]. Chicago: ADA; 2005. [Available at: www.eatright.org/cps/rde/xchg/ada/hs.xsl/advocacy_922_ENU_HTML.htm; cited: September 14, 2006]

Correspondence to: Maria Szeto, 222 Kingsdale Avenue, Toronto, Ontario M2N 3X2 Canada.
E-mail: mszeto@primus.ca

* Graduate student, Master of Science in Clinical Nutrition, University of Medicine and Dentistry of New Jersey, School of Health Related Professions, Newark, New Jersey, U.S.A.