Green tea polyphenols in prostate cancer therapy

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Abstract: Adenocarcinoma of the prostate is a significant cause of mortality in adult males in North America. Several epidemiological studies, showing a reduced risk of prostate cancer incidence in men in Asian countries compared with men in the USA, suggest that dietary and/or environmental choices have a significant impact on prostate cancer development and progression. Oral consumption of green tea polyphenols has shown much promise in the treatment and prevention of prostate cancer. This paper will review some of the known direct anticarcinogenic actions of green tea polyphenols like antioxidant action, selective inhibition of angiogenesis, modulation of prostate cell growth signals and selective apoptosis of prostate cancer tumour cells. We suggest that the inclusion of green tea polyphenols in the treatment protocol for patients with prostate cancer would provide an additional therapeutic benefit.

Keywords: prostate cancer, green tea polyphenols, antioxidants, apoptosis, review

Introduction

Adenocarcinoma of the prostate is the second leading cause of death in men over fifty in the USA (Rhim and Kung 1997; Amir et al 1999; Morris and Scher 2000). The actual incidence of prostate carcinoma might even be higher since autopsy findings show that only about one-third of actual cases clinically manifest (Sagalowsky and Wilson 1998).

The incidence of prostate cancer in the USA is 12% higher than prostate cancer incidence in Japan. However, Japanese men who immigrated to the United States have a similar incidence of prostate cancer as Caucasian men in the USA (Sagalowsky and Wilson 1998; Gupta, Ahmad, Muktar 1999; Chhabra and Yang 2001). This evidence, demonstrating similar prostate cancer risk in these two separate ethnic groups only after the adoption of an American lifestyle and diet, suggests that environmental or dietary causes significantly contribute to the aetiology of prostate cancer.

There are few reports of the concurrent use of antioxidants in the treatment of prostate cancer. However, we suggest, based on the strength of the evidence in breast cancer studies, that antioxidant supplementation during prostate cancer treatment would have a beneficial effect. These benefits might include not only preventing or diminishing side effects of radiotherapy and chemotherapy (Weijl et al 1997) but, more importantly, a selective destruction of androgen-independent cell types causing a more complete remission of prostate cancer. In particular, the selective triggering of apoptosis in prostate cancer cells (Gupta, Ahmad, Mohan et al 1999; Rice-Evans 1999; Schmitt and Lowe 1999) by certain antioxidants would have a beneficial effect in halting the growth of the androgen-independent cell population.

There are conflicting reports of the benefits, or risks, involved with the concurrent use of antioxidants in cancer management (Labriola and Livingston 1999; Lamson and Brignall 1999; Kong et al 2000; Webb 2000). It is important to design antioxidant protocols that are based on the prior identification of a patient’s current oxidative stress, as well as on the knowledge of the unique and synergistic effects of different combinations of antioxidants (Gupta, Ahmad, Muktar 1999; Halliwal 1999; Shklar and Oh 2000; Zhou et al 2003). There are a variety of antioxidants that have been proposed as effective for cancer management, this paper will focus on the use of green tea polyphenols in prostate cancer prevention and therapy.

Complementary care practitioners have recognised the importance of diet and supplements in decreasing the risk of the possible initiation and progression of cancerous cells by maintaining optimal immunity, detoxification and cellular repair. It is important to have a good understanding

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of the aetiology, cellular biology, epidemiology and conventional treatment for prostate cancer. A more thorough understanding of the mechanisms of antioxidant action would aid in designing therapy protocols that, by specifically targeting critical pathways in carcinogenesis, would have maximal therapeutic value. Most of the current antioxidant and cancer therapy research has been done on animal models and prostatic carcinoma cells in vitro. However, an increased understanding of multiple antioxidant action in conjunction with chemotherapy and radiation would provide the foundation for further research like clinical trials. Complementary medical treatment of patients with prostate cancer is the most effective and curative approach.

Green tea polyphenols and cancer prevention
There is currently much evidence supporting the value of regular consumption of certain foods, minerals and vitamins in the prevention and treatment of cancer. Daily consumption of certain liquids, like tea (Camilla sinensis), might also be beneficial in cancer prevention. Green tea in particular has many of the qualities of an ideal chemopreventive agent. For example, green tea beverages are relatively inexpensive, have low or no reported toxicity, are widely accepted (they are second only to water as the most consumed beverage in the world, with a daily average of 120 mL consumed per person), can be orally consumed and are highly efficacious. Plausible mechanisms for their therapeutic action also have been reported (Yang 1997; Ahmad and Muktar 1999; Ahmad et al 2000; Muktar and Ahmad 2000; Yang et al 2002; Adhami et al 2003; Gupta et al 2003; Hastak et al 2003). Significant advances in our understanding of the mechanism and therapeutic value of green tea extracts in the prevention and treatment of prostate cancer are continuously being made.

The traditional name for substances from vegetable extracts that help convert animal skin to leather was tannins. These tannins (commonly referred to as tannic acid) exist as water-soluble polyphenols in tea extracts as well as in many other plant foods and herbs. The main polyphenols in green tea are the flavon-3-ols, which are commonly known as catechins (Chung et al 1998). These include epicatechin, epicatechin 3-gallate, epigallocatechin (EGC) and epigallocatechin-3-gallate (EGCG). These components make up at least 30% of the dry weight of green tea. Green tea also contains a certain amount of caffeine (3%–6% dry weight), theanine (a major and specific amino acid in green tea, 1%–2% of dry weight) and other flavonoids like quercetin. Other significant components in green tea include protein (15%), lignan (6.5%), organic acids (1.5%) and chlorophyll (0.5%) (Medical Economics Staff and Gruenwald 2000).

Major mechanisms of action
Green tea extracts have been shown to exhibit a variety of actions in vitro in human and animal cells and cell lines. Some of the more promising mechanisms that are more directly involved in the prevention or treatment of cancer include the ability to: (1) act as powerful antioxidants; (2) selectively inhibit tumour cell growth; and (3) specifically augment tumour cell death. There are also several indirect actions of green tea extracts that might be anticarcinogenic. These include: (1) optimisation of the liver function, to reduce the toxicity of metabolic and xenobiotic by-products; (2) promotion of the growth of beneficial intestinal bacteria, to enhance immune surveillance and repair damage done to intestinal cells following chemotherapy or radiation therapy; and (3) stimulation of weight loss to reduce the obesity associated risk of chronic degenerative diseases like cancer (Dulloo et al 1999, 2000; Anonymous 2000; Kao et al 2000). This paper will only discuss the direct effects of green tea polyphenol supplementation on cancer cells.

Direct anticarcinogenic effects
Antioxidant action
The uncontrolled propagation of free radicals like reactive oxygen species (ROS) or reactive nitrogen species (RNS) is suggested to play a major role in the initiation and progression of cancer. Antioxidant supplementation, in particular as an adjuvant therapy to conventional treatment (Weijl et al 1997; Labriola and Livingston 1999; Lamson and Brignall 1999) has been shown to protect against free radical damage induced spontaneously during cellular oxidative respiration or through medical interventions like chemotherapy and/or radiation therapy.

Tea polyphenols have been shown to effectively scavenge ROS and RNS. The antioxidant activity of green or black tea polyphenols specifically inhibits the formation of 8-hydroxy-2′-deoxyguanosine, a major indicator of oxidative damage to DNA (Moyad et al 1999; Weisburger 1999). Green tea polyphenols also inhibit the ability of RNS to help form potentially DNA damaging nitrosamine and modified