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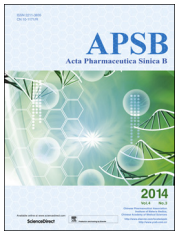

REVIEW

Nutraceuticals as potential therapeutic agents for colon cancer: a review

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Abstract Colon cancer is a world-wide health problem and the second-most dangerous type of cancer, affecting both men and women. The modern diet and lifestyles, with high meat consumption and excessive alcohol use, along with limited physical activity has led to an increasing mortality rate for colon cancer worldwide. As a result, there is a need to develop novel and environmentally benign drug therapies for colon cancer. Currently, nutraceuticals play an increasingly important role in the treatment of various chronic diseases such as colon cancer, diabetes and Alzheimer's disease. Nutraceuticals are derived from various natural sources such as medicinal plants, marine organisms, vegetables and fruits. Nutraceuticals have shown the potential to reduce the risk of colon cancer and slow its progression. These dietary substances target different molecular aspects of colon cancer development. Accordingly, this review

Abbreviations: ACC, acetyl CoA carboxylase; ACF, aberrant crypt foci; ACL, ATP-citrate lyase; ASTX, astaxanthin; COX-2, cyclooxygenase 2; DHA, decahexaenoic acid; DMH, 1,2-dimethylhydrazine; DR, death receptor; EGCG, epigallocatechingallate; EPA, eicosapentaenoic acid; FAS, fatty acid synthase; 5-FU, 5-fluorouracil; GADD, growth arrest and DNA damage; HMG-CoA, 3-hydroxy-3-methyl-glutaryl CoA; HUVEC, human umbilical vein endothelial cell; IGF, insulin-like growth factor; IL, interleukin; LDH, lactate dehydrogenase; MMP, matrix metallo-proteins; NF-κB, nuclear factor-kappa B; PRAP, prolactin receptor associated protein; TCA, tricarboxylic acid cycle; TNF, tumor necrosis factor; TRAIL, tumor necrosis factor-related apoptosis-induced ligand; VEGF, vascular endothelial growth factor

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briefly discusses the medicinal importance of nutraceuticals and their ability to reduce the risk of colorectal carcinogenesis.

1. Introduction

Colon cancer is one of the most dangerous forms of cancer, with potential to spread to distinct parts of the body including liver, lung, ovaries and other gastrointestinal organs. So far, 5-fluorouracil (5-FU) is the first choice for colon cancer treatment, acting as an inhibitor of DNA synthesis[1,2]. However, while synthetic chemical anticancer drugs prolong survival, they often have adverse effects and off-target actions. Based on this, nutraceuticals and phytochemicals have been investigated for colon cancer therapeutics[3]. Nutraceutical is a term derived from nutrition and pharmaceutical, and are sometimes termed "functional foods"[4]. Nutritional phytochemicals have a strong historical background and significant applications in modern medicine. These compounds are used in medicinal and commercial industries for cosmetics, food aids and additives[5].

Nutraceuticals have the ability to control the DNA damaging factors in cancer cells and regulate DNA transcription in tumors. They possess numerous therapeutic benefits such as antiobesity effects, cardiovascular effects, antidiabetic effects, immune enhancement, natural antioxidant activity, and anti-inflammatory effects[6,7]. Fig. 1 shows different classes of nutraceuticals and their uses. The different stages of colon cancer warrant various treatment options such as chemotherapy, surgery, radiation and phytotherapy. All other forms of cancer therapeutics have significant adverse effects. Plant-derived nutraceuticals are advantageous for the treatment of colon cancer with additional benefit of improving overall health[8]. These nutritional compounds have provided better treatment and showed fewer adverse effects[9]. The incidence and mortality rates for colon cancer have been increasing in most of the countries, particularly US, European and part of Asian countries. This increasing incidence of colon cancer appears due to changing dietary constituents, physical activity patterns, as well as genetic influences[10]. Fig. 2 shows the mortality and incidence rate of colon cancer in 2005–2012.

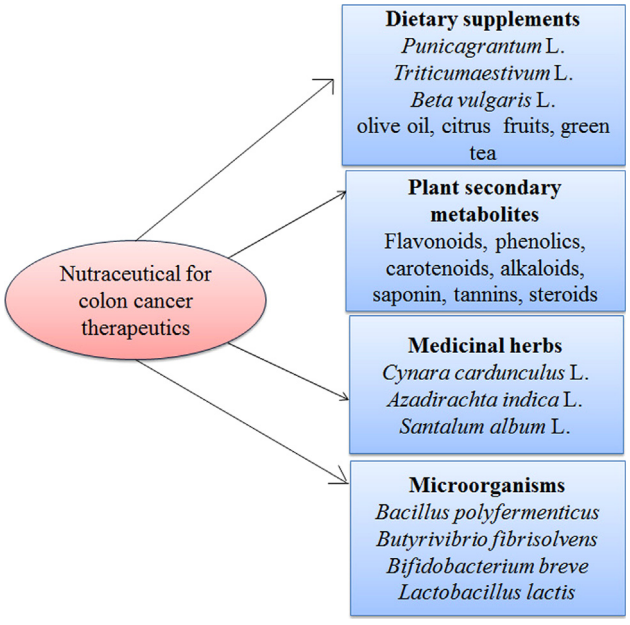

Figure 1 Different classes of nutraceuticals and their uses.

Reactive oxygen species can cause problems in normal cells. Free radicals such as O_2^- and OH^- may increase normal human colonocyte activity and result in the formation colon polyps. Natural antioxidants such as quercetin are derived from fruits and plant resources and can limit the oxidative damage in colon cells. Quercetin belongs to a family of plant-derived flavonoid phytochemicals and is effective for inducing apoptosis in colon cancer cells. Likewise, dietary uses of onion might be able to suppress the proliferation of normal cells. Onion contains high levels of quercetin, which inhibits the effects of colon cancer proliferation in both *in vitro* and *in vivo* studies[11]. Lentinan naturally occurs in the edible mushroom *Lentinus edodes*. The lentinan compound is known as β-1,3-glucan. It is one of the important drugs used as anticancer agents and is used clinically for colon cancer treatment. Lentinan significantly reduces the formation of colon tumors in an animal model.

Selenium is an important dietary mineral found in broccoli extract, red wine, dietary fiber, pepper, soya, cloves, fenugreek, ginger, apple and other vegetables. Selenium is associated with up to a 50% decrease in the risk for colon cancer[12,13]. Yellow mustard oil is synthesized by the brassica family of plants and has been examined for its potential anticancer properties. Mustard contains a complex mixture of long-chain polysaccharides that may play a protective role in colon cancer formation[14]. Essential oils such as eicosapentanoic acid (EPA), docosahexaenoic acid (DHA) and omega-3 fatty acids are also used to treat and prevent cancer and cardiac diseases. Particularly, the consumption of fish and fish products reduces the risk of colon cancer progression[15]. Recently developed live micro-organisms such

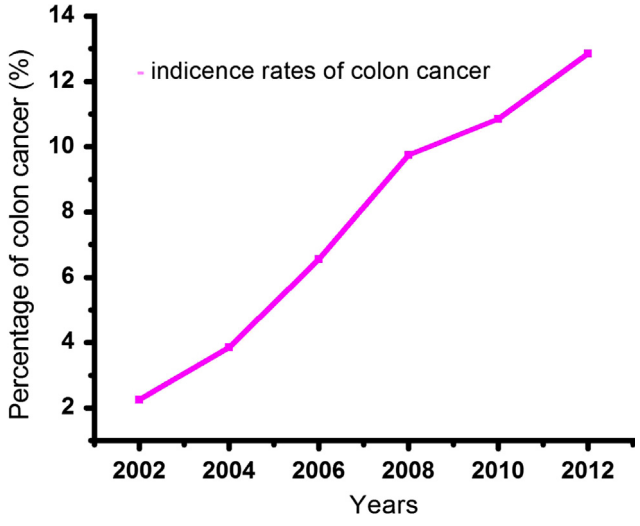

Figure 2 The mortality and incidence rate of colon cancer in the years 2002–2012.