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Extended Abstract

Food Summit: Berries for cancer prevention- Gary D Stoner - Medical College of Wisconsin

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Abstract

A considerable amount of research has been conducted in the past two decades to evaluate the cancer preventative potential of berries. Wild berries are a neighbourhood of the human diet for several centuries. Their major use is for nutrition, although some varieties are used for medicinal purposes. The utmost important marketable sorts of berries include members of the Vaccinium genus (blueberry, lingonberry, cranberry, bilberry), Rubus genus (blackberry, red rasp-berry, blackcap, cloudberry), Fragaria genus (strawberry), and the Sambucusgenus (elderberry, red elderberry). These berries contain a vast array of phytochemicals, many of which are of potential importance for human health. Phytochemicals are non-nutritive compounds, produced mainly by secondary metabolism, that protect the plant from UV light, predators, and parasites, regulate chemical pathways, and supply flavor and color to the berry. Perhaps the most interesting phytochemicals in berries are the polyphenols, which impart to berries much of their antioxidant potential. The polyphenols can be divided into phenolic acids, which consist of an aromatic ring structure with at least one hydroxyl group, and the flavonoids, which are more complex molecules. The phenolic acids represent about 30% of the daily intake of polyphenols in humans and the flavonoids about 70%. There are numerous collections of flavonoids that include the anthocyanidins, flavanols, flavonols, isoflavones, flavones, and flavonones. These groups differ in the number and distribution of hydroxyl groups on the basic chemical structure. More complete descriptions of the classes of phytochemicals in berries, including the flavonoids, are found in recent reviews by Seeram and from laboratory.

Maximum studies have used black raspberries, though, other berry types such as strawberries, blackberries, blueberries, red raspberries, acai and others are also accomplished of preventing cancer. Initially, a series of berry extracts were shown to decrease the production rate of cancer cells in vitro and/or to stimulate apoptosis. The inhibitory potential of these extracts was frequently attributed to their content of ellagitannins or anthocyanins. Preclinical studies confirmed that freezedried berry powders were effective in avoiding chemical carcinogen-induced cancer in the rodent oral cavity, esophagus, and colon, and an anthocyanin-rich extract inhibited UV-induced skin cancer in mice. Mechanistic studies showed that the berries prevented the conversion of premalignant lesions in rodent tissues to malignancy by reducing cell proliferation, inflammation, and angiogenesis and by stimulating apoptosis and cell differentiation. Multiple genes associated with all of these cellular functions are protectively modulated by berries. For example, berries down-regulate the expression levels of genes in the P13K/Akt, MAPK, ERK ½, AP-1 and mTOR signaling pathways (proliferation), COX-2, iNOS, NF-κB, IL-1β and IL-12 (inflammation), VEGF and HIF-1α (angiogenesis), and up regulate caspase 3/7 and Bax (apoptosis), and both keratin and mucus-associated genes for squamous and glandular differentiation, respectively. Bio-fractionation studies indicate that the most active inhibitory compounds in berries are the anthocyanins and ellagitannins. The fiber fraction of berries is also active in preventing cancer in rodents and study is needed to recognise the active polysaccharides in this fraction. Human clinical trials indicate that freeze-dried berry formulations elicit little or no toxicity in humans when administered in the diet at concentrations as high as 60g/day for as long as nine months. The endorsement of berry anthocyanins and ellagic acid into blood is rapid but minimal; i.e., less than 1% of the controlled dosage. Almost 70% of the ordered anthocyanins are metabolized by the enteric bacteria into protocatechuic acid (PCA) that has substantial cancer preventative activity. Black raspberry formulations have exposed to cause histologic regression of oral leukoplakic lesions in the oral cavity, dysplastic lesions in the esophagus, and polyps in the rectum of patients with familial adenomatous polyposis. These results are very promising and the mechanisms for these effects will be discussed.

Strawberry, blackberry, and blueberry powders are also tested for their capability to inhibit NMBA tumorigenesis in the rat esophagus when added at 5 and 10% of the diet. Strawberries and blackberries were approximately as active in preventing tumors as BRB. However, blueberries were inactive. Both straw-berries and blackberries reduced the formation of NMBA induced O -MeGua adducts in esophageal DNA; whereas blueberries had no effect on adduct formation. The reason(s) for the inactivity of blueberries is unknown. Apart from the other three berry types, there are too low levels of

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ellagitannins in blueberries. In addition, blueberry anthocyanins have a delphinid in skeleton whereas the anthocyanins in BRB and blackberries have a cyanidin skeleton and those in strawberries have both pelaro-gonidin and cyanidin skeletons. These alterations in chemical arrangement may be responsible for the different biological activities of the berry types. A second bioassay using blueberries is now being utilized to confirm the previous results and further determines the basis for the inactivity of blueberries.

Effects of Freeze-Dried Strawberries, Blackberries, and Blueberries on NMBA-Induced Rat Esophageal Tumorigenesis when Administered in the Diet Before, During, and 712 Part IV / Other Bioactive Food Components in Cancer Prevention and/or Treatmentusing blueberries is currently being utilized to confirm the previous results and furtherdetermine the basis for the inactivity of blueberries.

Chemoprevention of lung cancer has proven to be difficult, both in rodents and in humans. Thus, it is perhaps not surprising that a diet containing 10% freeze-dried strawberries was ineffective in reducing lung tumors in mice that were induced either by 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK) or benzo(a)pyrene (B(a)P).In this study, strain A/J mice were administered the strawberry diet beginning one week before initial carcinogen treatment and throughout the study. NNK and B(a)P were administered i.p. over a 2-week period beginning at week 2 of the bioassay. At 24 weeks, there were no differences in lung tumor incidence or multiplicity in any of the groups. Successes in reducing carcinogen-induced cancers in the oral cavity, esophagus, and colon, where berry components come into direct contact with the tissues, and the failure to inhibit lung tumors in mice suggest that the active components in berries fail to reach the lung in sufficient amounts to elicit protection. This inference is sustained by studies detailing that the anthocyanins and ellagitannins from berry juices are poorly absorbed in rodents and their plasma levels decline rapidly. However, the shielding effects of dietary BRB powder against estrogen-mediated mammary cancer in rats suggest that adequate amounts of protective compounds reach the mammary gland through systemic delivery. Thus, the protecting effects of dietary berry powders seem to be organ and site dependent. In addition, the gains and encounters to the clinical application of utilizing berries for cancer prevention will be discussed and suggestions made for future trials.

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