



On the Occasion of World Cancer Day 2015; the Possibility of Cancer Prevention or Treatment with Antioxidants: The Ongoing Cancer Prevention Researches

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ABSTRACT

On February, 2014 World Cancer Day (WCD) was established to raise alertness of cancer and to encourage its prevention, detection, and treatment. In fact, WCD is celebrated every year on the 4th of February all over the world to commemorate all the accomplishments of the WHO. In this paper, we aimed to present the scientific evidence for the role of antioxidants in cancer. Damage to cells by reactive oxygen species, especially the damage to DNA, has been found to play a crucial role in the development of cancer. Exogenous antioxidants can prevent free radical damage associated with cancer development. However, whether or not taking dietary antioxidants can prevent or reduce the risk of developing cancer in humans is not clear. Some researchers have suggested that antioxidants counteract with drugs or toxins, which induce oxidative stress and hence prevent damage to cells or body organs.

Keywords: Antioxidant, cancer, herbs

INTRODUCTION

On February, 2014 World Cancer Day (WCD) was founded to raise alertness of cancer and to encourage its prevention, detection, and treatment.^[1,2] In fact, WCD is celebrated worldwide every year on the 4th of February to commemorate the cancer-related accomplishments of the WHO.^[3-5] The first WCD celebration was planned in Geneva, Switzerland in 1933 under the direction of Union for International Cancer Control with the support

of various other well-known cancer societies, treatment centers, research institutes, and patient groups.^[3,4] The WCD event was founded to help find the resources needed to fight and control this deadly disease.^[4-6] Moreover, the WCD is celebrated to help inform the public about cancer risk factors preventive measures, the benefits of early detection. In this review, we present the scientific evidence for the preventive role of antioxidants on cancer.^[7,8]

Free radicals and in particular reactive oxygen species (ROS) are formed naturally in the body when an atom or a molecule either loses or gains an electron. Free radicals play an important role in many normal cellular processes.^[9,10] However, at high concentrations, they can damage all major components of cells including proteins, DNA, and cell membranes. These damages to cells, especially the damage to DNA, can play a crucial role in the development of cancer.^[11] Moreover, some

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environmental toxins like cigarette smoke, may contain large amounts of free radicals or stimulate the body's cells to produce more free radicals.^[11]

The body makes some antioxidants, which are called endogenous antioxidants. However, the body also relies on exogenous sources of antioxidants for the rest of its protection against ROS and free radicals.^[12-14] If free radicals and ROS can cause cancer, antioxidants, therefore, should be able to prevent or inhibit this process.^[14,15]

Exogenous antioxidants can prevent free radical induced damage associated with cancer development.^[16-19] However, whether or not taking dietary antioxidants can prevent or reduce the risk of developing cancer in humans is not clear.^[20,21] It has been suggested that antioxidants counteract with drugs^[22,23] or toxins,^[20-23] which induce oxidative stress and hence prevent damage to cells or body organs.^[22-25]

In laboratory and preclinical studies in cancer prevention^[26,27] or immune system stimulation^[28] through medicinal plants with antioxidant activity, promising results have been achieved. However, the cohort and case-control studies, which have investigated the use of dietary antioxidants in the risk of cancer in humans have achieved mixed results.

Due to inadequate control for biases, which might influence the results, observational studies must be viewed with much caution. Randomized controlled clinical trials are considered to provide more reliable evidence of the harm or benefit of a health-related intervention. The results of the most important trials are summarized below.

THE LINXIAN GENERAL POPULATION NUTRITION INTERVENTION TRIALS

Effect of synthetic alpha-tocopherol

The first trial was a large-scale randomized trial investigating the effect of synthetic alpha-tocopherol on cancer risk in healthy Chinese people at increased risk of developing gastric and esophageal cancers.^[29] The subjects were randomly assigned to take a combination of 50 µg selenium, 15 mg beta-carotene, and 30 mg synthetic alpha-tocopherol, per day for 5 years or no supplement. The results of the study demonstrated that the risk of developing gastric cancer and/or esophageal cancer was not affected by antioxidant supplementation. However, people who took antioxidants had lower death due to gastric cancer but not for to esophageal cancer.^[29] In this study, 10 years after antioxidants supplementation ended, the reduced risk of gastric cancer death was no longer

found for those who took antioxidants, in comparison to those who did not.^[30]

Effect of alpha-tocopherol and beta-carotene

In the second trial, which was conducted in Finland, 5–8 years consumption of synthetic alpha-tocopherol and/or beta-carotene could reduce the incidence of different cancers in some middle-aged male smokers. The initial results of the study showed an increase in the incidence of lung cancer in the subjects who took 20 mg per day beta-carotene supplementation.^[31] There were no effects of alpha-tocopherol or beta-carotene supplementation on the incidence of renal pelvis, bladder, ureter, pancreas, colorectal, kidney, pharyngeal, laryngeal or esophageal cancers.^[32]

Effects of beta-carotene and Vitamin A on lung cancer

In a trial in the United States, daily supplementation with beta-carotene and Vitamin A on people who were at high risk of lung cancer due to having a history of smoking or exposure to asbestos showed that daily supplementation with both 25,000 IU retinol and 15 mg beta-carotene was associated with increased lung cancer and increased death from all-cause mortality.^[33] A later report in 2004 showed that the adverse effects persisted up to 6 years after the consumption of these supplements ended. However, the enhanced risks of all-cause mortality and lung cancer were no longer statistically significant.^[34]

In another study in 1996, 50 mg beta-carotene administration every other day for 12 years had no effect on cancer mortality, cancer incidence, and all-cause mortality among US male subjects.^[35]

Every other day administration of 50 mg beta-carotene, 600 IU Vitamin E, and 100 mg aspirin has also had no benefit or the incidence of cancer and cardiovascular diseases in US women of over 45 years.^[36] In 2005, similar results were published for Vitamin E consumption.^[37]

Effects of selenium and alpha-tocopherol on cancer in a trial published in 2004, daily supplementation with 100 µg selenium, 20 mg zinc, 6 mg beta-carotene, 30 mg synthetic Vitamin E, and 120 mg Vitamin C for a median of 7.5 years had no effect on the incidence of cardiovascular or cancer diseases or all-cause mortality, too.^[38]

In an international trial reported in 2005, no effect of daily supplementation with 400 IU synthetic alpha-tocopherol which was administered for 7 years was seen in the incidence of major cardiovascular events such as stroke, heart attack or death from heart disease, cancer incidence or death from cancer in people diagnosed with cardiovascular disease or diabetes.^[39]

The next trial was conducted in US, began in 2001 and was stopped in 2008. The trial investigated whether daily supplementation with 200 µg selenium, 400 IU synthetic Vitamin E or both would reduce the incidence of prostate cancer in men over 50 years. The results showed that the use of these supplements for a period of about 5.5 years did not affect the incidence of prostate or other cancers.^[39,40] Updated findings, reported in 2011, demonstrated that, following 1.5 years off supplements, the cases of prostate cancer among men taking Vitamin E alone were 17% more compared to placebo group.^[41] No increase in prostate risk was observed for men assigned to take Vitamin E plus selenium or selenium alone compared with men assigned to take a placebo.^[39]

In a trial which was conducted in 2009 the use of 500 mg Vitamin C, 400 IU Vitamin E or combination of the two, every other day for a median of 7.6 years did not reduce the incidence of prostate cancer or other cancers including leukemia, melanoma, lymphoma, and cancers of the bladder, pancreas, lung, colon, and rectum.^[42]

The above-randomized controlled clinical trials did not show that dietary antioxidant supplements are always beneficial in primary cancer prevention. However, it is possible that the lack of benefit in most of the clinical studies can be related to the effects of the tested antioxidants on cancer. They all were consumed as purified chemicals and their effects might be different when they are consumed as natural foods, which contain complex mixtures of minerals, vitamins, and various antioxidants. This acquires a more complete understanding of the antioxidant content of individual foods, how the various antioxidants interact with each other, and the factors that influence the uptake and distribution of food-derived antioxidants in the body. These are all active areas of ongoing cancer prevention research.^[42-45]

Another question, which might be raised is that whether or not people already diagnosed with cancer should take antioxidant supplements? Recent studies reported that antioxidant supplements during cancer treatment might alter the effectiveness or reduce the toxicity of specific therapies.^[46-53] Other trials have reported mixed results; some of them found that people who took antioxidants during cancer therapy had worse outcomes, especially if they were smokers.^[54-74]

Additional large randomized controlled studies are necessary to provide clear evidence about the benefits or harms of taking antioxidant supplements during cancer treatment.

CONCLUSIONS

In sum, a lot of *in vitro* studies have shown that exogenous antioxidants are able to help prevent the

free radical damage associated with the development of cancer. However, researches in humans have not demonstrated convincingly that taking antioxidant can reduce the risk of developing cancer, and some studies have even shown an increased risk for some cancers, particularly, in smokers.

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