Antioxidant found in many foods and red wine is potent and selective killer of leukemia cells

April 23 2007

A naturally occurring compound found in many fruits and vegetables as well as red wine, selectively kills leukemia cells in culture while showing no discernible toxicity against healthy cells, according to a study by researchers at the University of Pittsburgh School of Medicine. These findings, which were published online March 20 in the *Journal of Biological Chemistry* and will be in press on May 4, offer hope for a more selective, less toxic therapy for leukemia.

“Current treatments for leukemia, such as chemotherapy and radiation, often damage healthy cells and tissues and can produce unwanted side effects for many years afterward. So, there is an intensive search for more targeted therapies for leukemia worldwide,” said corresponding author Xiao-Ming Yin, M.D., Ph.D., associate professor of pathology, University of Pittsburgh School of Medicine.

Leukemia is not a single disease but a number of related cancers that start in the blood-forming cells of the bone marrow. Meaning literally “white blood” in Greek, leukemia occurs when there is an excess of abnormal white blood cells. There are both acute and chronic forms of leukemia, each with many subtypes that vary in their response to treatment. According to the National Cancer Institute, about 44,000 new leukemia cases will be diagnosed in the United States in 2007, and there will be about 22,000 leukemia-related deaths.

Based on previous reports that anthocyanidins, a group of naturally occurring compounds widely available in fruits and vegetables as well as red wine, have chemopreventive properties, Dr. Yin and his collaborators studied the effects and the mechanisms of the most common type of a naturally modified anthocyanidin, known as cyanidin-3-rutinoside, or C-3-R, which was extracted and purified from black raspberries, in several leukemia and lymphoma cell lines.

They found that C-3-R caused about 50 percent of a human leukemia cell line known as HL-60 to undergo programmed cell death, or apoptosis, within about 18 hours of treatment at low doses. When they more than doubled the concentration of C-3-R, virtually all of the leukemia cells became apoptotic and died. C-3-R also induced apoptosis in other human leukemia and lymphoma cell lines.

When the investigators studied the mechanism of cell death in the leukemia cells, they found that C-3-R induced the accumulation of peroxides, a highly reactive form of oxygen, which, in turn, activated a mitochondria-mediated apoptotic pathway. Mitochondria are specialized structures located within all cells in the body that contain enzymes needed by the cell to metabolize foodstuffs into energy sources. In contrast, when the researchers treated normal human blood cells with C-3-R, they did not find any increased accumulation of reactive oxygen species and there were no apparent toxic effects on these cells.

Previous studies have shown that C-3-R possesses strong antioxidant activities, a characteristic shared by other polyphenols, such as those found in green tea, which could be responsible for their chemoprevention effects. Dr. Yin's work suggests that although C-3-R demonstrates antioxidant effects in the normal cells, it paradoxically induces an oxidative "stress" in the tumor cells. It is possible that this differential effect of C-3-R may account for its selective toxicity in the tumor cells.

According to Dr. Yin, these results indicate that C-3-R has the promising potential to be used in leukemia therapy with the advantages of being highly selective against cancer cells. “Because this compound is widely available in foods, it is very likely that it is not toxic even in purified form. Therefore, if we can reproduce these anti-cancer effects in animal studies, this will present a very promising approach for treating a variety of human leukemias and, perhaps, lymphomas as well.”

Source: University of Pittsburgh