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Natural compounds, chemotherapeutic drugs may become partners in cancer therapy

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Research in the Linus Pauling Institute at Oregon State University suggests that some natural food compounds, which previously have been studied for their ability to prevent cancer, may be able to play a more significant role in treating it - working side-by-side with the conventional drugs that are now used in chemotherapy.

A new study just published in the *International Journal of* Cancer examined the activity of chlorophyllin and found that, on a dose-by-dose basis, it was 10 times more potent at causing death of colon cancer cells than hydroxyurea, a chemotherapeutic drug commonly used in cancer treatment.

Beyond that, chlorophyllin kills cancer cells by blocking the same phase of cellular division that hydroxyurea does, but by a different mechanism. This suggests that it - and possibly other "cocktails" of natural products - might be developed to have a synergistic effect with conventional cancer drugs, helping them to work better or require less toxic dosages, researchers said.

"We conclude that chlorophyllin has the potential to be effective in the clinical setting, when used alone or in combination with currently available cancer therapeutic agents," the researchers wrote in their study.

The concept of combining conventional or new cancer drugs with natural compounds that have been shown to have anti-cancer properties is very promising, said Rod Dashwood, professor and director of the Cancer

Chemoprotection Program in the Linus Pauling Institute.

"Most chemotherapeutic approaches to cancer try to target cancer cells specifically and do something that slows or stops their cell growth process," Dashwood said. "We're now identifying such mechanisms of action for natural compounds, including dietary agents. With further research we may be able to make the two approaches work together to enhance the effectiveness of cancer therapies."

Chlorophyllin is a water-soluble derivative of chlorophyll - the green pigment found in most plants and many food products that makes possible the process of photosynthesis and plant growth from the sun's energy. Chlorophyllin is inexpensive, and animal studies plus human clinical data suggest that it can be ingested at relatively high levels without toxicity.

In the new study, researchers found that pharmacologic doses of chlorophyllin caused colon cancer cells to spend more time than normal in their "synthesis phase" in which DNA is duplicated. Timing is critical to the various phases of cell growth, researchers said, and this disruption started a process that ultimately led to cell death, the study found.

In particular, the presence of high levels of chlorophyllin caused a major reduction in the level of ribonucleotide reductase, an enzyme critical to DNA synthesis, researchers found. This is also the mechanism of action of hydroxyurea, one drug already being used for cancer chemotherapy.

"In cancer research right now there's interest in approaches that can reduce ribonucleotide reductase," Dashwood said. "At the doses used in our experiments, chlorophyllin almost completely stops the activity of this enzyme."

Further research is needed both in laboratory and animal studies, with

combinations of chlorophyllin and existing cancer drugs, before it would be appropriate for human trials, Dashwood said. Chlorophyllin, in general, is poorly absorbed from the human gastrointestinal tract, so it's unclear what levels might be needed for therapeutic purposes or how well they would work.

Other dietary agents also might have similar potential. Work just published by LPI researchers in the journals Carcinogenesis and Cancer Prevention Research explored the role of organic selenium compounds in killing human prostate and colon cancer cells. Colorectal and prostate cancers are consistently among the leading causes of cancer mortality in the United States, and will account respectively for 18 percent and 9 percent of all cancer deaths in 2009, according to estimates from the American Cancer Society.

In the recent studies, a form of organic selenium found naturally in garlic and Brazil nuts was converted in cancer cells to metabolites that acted as "HDAC inhibitors" - a promising field of research in which silenced tumor suppressor genes are re-activated, triggering cancer cell death.

"Whether it's HDAC inhibition leading to one manner of cancer cell growth arrest, or loss of ribonucleotide reductase activity leading to another, as seen with chlorophyllin, there's significant promise in the use of natural products for combined cancer therapies," Dashwood said. "These are areas that merit continued research."

Source: Oregon State University (news : web)

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