

## Indole-3-Carbinol and Breast Cancer

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Breast cancer is the most common cancer in women in the United States, and the second leading cause of cancer-related female deaths in the U.S. Current treatment of breast cancer includes surgery, chemotherapy and radiation, or a combination thereof. Although the majority of patients with metastatic breast cancer will experience initial improvement, long-term survival is only modestly improved with contemporary therapies. As a result, other interventions aimed at preventing this disease and treating it more effectively have been the focus of considerable effort; and emphasis on nutrition and supplementation are most noteworthy in this regard. Most recently, a study revealed that exposure of various human breast cancer cell lines to indole-3-carbinol (I3C)-induced programmed cell death (apoptosis) of these highly malignant cells.<sup>1</sup>

Substantial dietary and epidemiological evidence suggests that fruits and vegetables protect against cancer of the liver, colon, stomach, lung, and breast. These foods are known to contain many phytochemicals, particularly I3C. Cruciferous vegetables (such as broccoli; cauliflower; cabbage; brussels sprouts; and bok choy) are an extremely rich source of this important nutrient. It has been shown that I3C and its metabolites possess anticarcinogenic effects in experimental animals, and inhibit the growth of various human cancer cells.

In terms of breast cancer, I3C has been shown to suppress the growth of both estrogen-dependent and estrogen-independent human breast cancer cell lines, suggesting that in addition to acting as a phytoestrogen (which binds to estrogen receptors on estrogen-dependent breast cancer cells), it also exerts other influences on breast cancer cells that block their ability to replicate. These antiproliferative mechanisms are presently the subject of intensive investigation.

In the aforementioned recent study, I3C not only suppressed the cell division of certain breast cancer cell lines, but induced programmed cell death (apoptosis) of these malignant cells, while producing no such effect on normal breast cells. Simply stated, I3C demonstrates an ability to selectively encourage breast cancer cells to "commit suicide," while allowing normal breast epithelial cells to thrive. This effect may be one of the reasons a high lifetime intake of cruciferous vegetables is associated with a significant reduction in breast cancer, according to epidemiological studies.

Moreover, these findings suggest women with breast cancer may be well-advised to consume cruciferous vegetables, and possibly add I3C supplements to their dietary regimen. In the words of the researchers, "Indole-3-carbinol may have a wide therapeutic application because of its selective apoptosis-inducing activity against cancer cells without inducing apoptosis of non-tumorigenic breast epithelial cells."

As for the mechanism by which I3C produces programmed cell death of breast cancer cells, this recent study demonstrated that I3C induces Bax translocation to the mitochondria and mitochondrial depolarization, resulting in the loss of mitochondrial potential. In turn, this leads to the release of cytochrome c and subsequent cell death in certain breast cancer cell lines, but not in others.

Bax is one of several genes associated with cancer development. Previous studies have shown that during apoptosis, Bax translocates from the cytosol of the cell to the mitochondria. Bax is a 21-kDa pro-apoptotic protein localized in the mitochondria, which regulate programmed cell death. Bax was reported to be a cytosolic protein in healthy living cells; upon induction of apoptosis, it translocates to the mitochondria. This translocation is rapid and occurs at an early stage of translocation.

The discovery that certain natural agents (i.e., isoflavones from soy beans, vitamin E succinate and I3C) can induce apoptosis of various human cancer cell lines has fostered research aimed at the development of cancer drugs that can provide the same kind of selective ability to encourage cancer cells to commit suicide, but even more powerfully. In the meantime, it remains more prudent than ever to recommend daily consumption of I3C sources to your patients, and to consider boosting its consumption in patients with certain cancers as part of the complementary management of such cases.

### *Reference*

1. Rahman KMW, Aranha O, Sarkar FH. Indole-3-carbinol (I3C) induces apoptosis in tumorigenic but not in nontumorigenic breast epithelial cells. *Nutrition and Cancer* 2003;45(1):101-112.

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AUGUST 2003