A Letter to the Editors of the
Townsend Letter for Doctors and Patients

Dear Sirs:

A pseudo controversy concerning Indole-3-Carbinol (I3C) and Diindolylmethane (DIM) is being promoted by the Life Extension Foundation in response to an article comparing I3C to DIM in the Sept/Oct 2001 Townsend Letter (1).

As one of the original investigators of the role of I3C in hormonally-related cancers, I am disturbed by the distortions made by Life Extension in their January 2002 magazine. There is no evidence that I3C is active in its own right, while there is abundant evidence that I3C is a "pro-nutritional" which is converted by stomach acid to DIM, ICZ, LTR, CTR, ASB and other polymers in varying amounts. The exact mix depends upon the acidity of the stomach. This unpredictable process is modulated by achlorhydria, and consumption of proton-pump inhibitors or antacids. The higher the pH, the greater the relative formation of DIM.

Contrary to the claims made in the Life Extension article, the trimers (triple molecules from I3C) and ICZ (dioxin-like double molecule from I3C), in addition to any beneficial effects that they may induce, also induce a series of undesirable side effects, including induction of estrogen receptor activity, inhibition of apoptosis, etc.

In addition, ascorbigen (ASB) induces 4-hydroxylation to yield the known carcinogenic 4-hydroxyestrogens, as noted by Sepkovic et al. almost 10 years ago (2). Any compound, capable of inducing 4-hydroxylation is hardly desirable, as incorrectly implied in the article.

It should also be noted that all of the responses to I3C in cell culture studies, actually reflect the actions of DIM, since I3C is almost quantitatively converted to DIM in cell culture media at 37 C in about 24 hours.

Most importantly, the implication made by Life Extension that DIM promotes breast cancer is inaccurate and misleading. In fact, DIM has been recently been shown by leading investigators to inhibit the growth and potential spread of breast cancer in vivo (3).

(more)

In comparison to I3C, DIM is a more stable compound which exhibits beneficial effects at lower doses, and without the undesirable side effects of I3C. DIM's stability and potency at lower doses are evidence of its greater benefits, in contrast to the undesirable responses observed with I3C products.

In view of the demonstrated safety benefits of DIM versus I3C, it is clear that DIM is the compound of choice.

Sincerely yours,

H. Leon Bradlow, PhD.

References:

1. Zeligs MA. *"The Cruciferous Choice: DIM or I3C?"* Townsend Letter for Doctors and Patients; August/September 2001; 217:47-53.

2. Sepkovic DW, Bradlow HL, Michnovicz J, Murtezani S, Levy I, Osborne MP. *"Catechol estrogen production in rat microsomes after treatment with indole-3-carbinol, ascorbigen, or beta-naphthaflavone: a comparison of stable isotope dilution gas chromatography-mass spectrometry and radiometric methods."* Steroids. 1994 May;59(5):318-23.

3. Janet Tou, Chibo Hong and Leonard F. Bjeldanes. *"The Influence of 3'3-Diindolylmethane on Breast Tumor Growth, Invasion and Metastasis."* Experimental Biology 2001, March 31-April 4, 2001, Orlando, Florida.

- - - - - - - -

(more)

Michael A. Zeligs, M.D.
Boulder Community Hospital
Boulder, CO 80302

Dear Dr. Zeligs,

Indole-3-carbinol (I3C) and one of its proximal products, Diindolylmethane, are supplements that show real promise for treatment of certain conditions such as pre-cancerous lesions of the cervix.

Until recently, most in vitro, animal and clinical studies only used I3C. However, in the stomach I3C is converted into a variety of compounds, including Diindolylmethane, and it is clear that I3C itself is not one of the active compounds.

Many experiments, including clinical studies, suggest that Diindolylmethane is significantly more active than I3C for the desired effects. At a minimum, the use of Diindolylmethane avoids problems associated with I3C, such as the production of unknown, poorly-characterized and potentially harmful products.

Since undesirable effects of I3C have been reported, such as promotion of liver cancer in fish, I believe that the effects of I3C products need to be evaluated and compared for their individual and combined actions.

From my researcher's perspective, the ideal indole compound would promote beneficial effects, be stable, inexpensive, and not have any adverse effects. Based on the data, absorbable Diindolylmethane is the only I3C-derived indole currently being marketed that comes close to meeting the requirements for such a "designer indole."

Sincerely,

Karen J. Auborn, Ph.D.

# # #

For more information on Diindolylmethane, please visit http://www.DIMFAQ.com