AMERICAN JOURNAL OF EDUCATION AND LEARNING
ISSN: 2996-5128 (online) | ResearchBib (IF) = 10.91 IMPACT FACTOR
Volume-3| Issue-10| 2025 Published: |30-11-2025|

THE EFFECT OF INDOLE-3-CARBINOL ON METABOLISM AND THE SAFETY OF ITS LONG-TERM USE IN WOMEN AT RISK

https://doi.org/10.5281/zenodo.17606910

Abdusamatova D.Z.
Tashkent State Medical University, Uzbekistan

Introduction

Breast cancer (BC) is one of the leading oncological diseases among women worldwide. According to the World Health Organization (WHO), more than 2 million new cases are diagnosed every year, a significant portion of which are associated with hormonal imbalance and hereditary predisposition. Chemoprevention has become an important approach to reducing the risk of BC, particularly for women with high-risk factors such as a family history of the disease, genetic mutations (BRCA1/2), and hormonal disorders.

Indole-3-carbinol (I3C) is a bioactive compound derived from cruciferous vegetables such as broccoli, cauliflower, and cabbage. It is known for its ability to modulate estrogen metabolism and inhibit the growth of tumor cells. Experimental and clinical data have shown that I3C influences enzyme systems by activating detoxification pathways and altering estrogen metabolism, which can potentially reduce carcinogenicity.

Nevertheless, information on the long-term use of I3C under real-world conditions remains limited. Therefore, post-registration studies are required to evaluate its safety, tolerability, and effects on hormonal balance and enzyme activity.

Relevance of the Study

Breast cancer remains one of the leading causes of death among women worldwide. Despite considerable progress in diagnostics and treatment, the incidence rate, particularly among young women, continues to increase. According to the latest WHO data, over 2.3 million new BC cases are diagnosed annually, and more than 680,000 women die from the disease. This highlights the urgent need for effective primary and secondary prevention strategies.

One of the key factors in BC development is **estrogen metabolism**. Scientific studies suggest that an imbalance between certain estrogen metabolites—specifically 2-hydroxyestrone and 16α-hydroxyestrone—may contribute to carcinogenesis. The ratio of 2-OHE1 to 16α-OHE1 has been recognized as a biomarker of estrogen-dependent cancer risk, making it a promising target for chemoprevention.

Indole-3-carbinol, a natural compound derived from cruciferous plants, affects liver enzyme systems that regulate estrogen metabolism, particularly by activating the **CYP1A2** enzyme, which promotes the formation of non-carcinogenic metabolites. Additionally, I3C exhibits antioxidant, anti-inflammatory, and antiproliferative properties.

Although positive results have been observed in *in vitro* and animal model studies, clinical trials—especially under real-world conditions—remain limited. Most of them have been short-term or have covered only small population groups. Therefore, obtaining real clinical data on the safety and metabolic effects of long-term I3C use in women with various risk factors for breast cancer is of great importance.

The increasing popularity of nutraceuticals and biologically active supplements among the general population, often used without medical supervision, further emphasizes the need for a scientifically grounded assessment of their long-term efficacy and safety.

Thus, this study aims to fill the gap in objective data on the long-term administration of I3C in women with a high risk of BC and may serve as a foundation for developing recommendations for the use of plant-based chemopreventive agents.

Objective of the Study

To assess the safety and metabolic effects of 12-week administration of indole-3-carbinol in women with a high risk of developing breast cancer and to determine the optimal maintenance dosage of the preparation.

Tasks of the Study

1. To examine the effect of indole-3-carbinol on the hormonal profile of women (estradiol, progesterone, LH, FSH, SHBG);
2. To evaluate changes in the activity of enzymes involved in estrogen metabolism and detoxification (CYP1A2, NAT-2, GST, xanthine oxidase);
3. To determine the dynamics of urinary 2-OHE1/16α-OHE1 ratio as an indicator of the "favorable" estrogen metabolism pathway;
4. To identify the optimal maintenance dose of I3C (400 mg or 800 mg per day) based on efficacy, tolerance, and metabolic response.

Materials and Methods

Study participants.
A total of 52 women aged 28–45 years participated in the study: 46 were premenopausal and 6 postmenopausal.

AMERICAN JOURNAL OF EDUCATION AND LEARNING
ISSN: 2996-5128 (online) | ResearchBib (IF) = 10.91 IMPACT FACTOR
Volume-3| Issue-10| 2025 Published: |30-11-2025|

Inclusion criteria: elevated risk of breast cancer (genetic predisposition, family history), absence of active oncopathology, and stable hormonal status.

Indole-3-carbinol dosing scheme:

Pha	Dosage lay)	Duration ks)
Pha	400	1–4
Pha	800	5–8
Pha	400*	9–12

*In the third phase, the dose was adjusted individually according to tolerance.

Parameters evaluated:

- Hormonal status: estradiol, progesterone, luteinizing hormone (LH), follicle-stimulating hormone (FSH), sex hormone-binding globulin (SHBG);
- Enzyme activity: cytochrome P450 1A2 (CYP1A2), N-acetyltransferase 2 (NAT-2), glutathione S-transferase (GST), xanthine oxidase;
- Estrogen metabolism: urinary 2-hydroxyestrone (2-OHE1) and 16α-hydroxyestrone (16α-OHE1) ratio.

All parameters were assessed at baseline and after 4, 8, and 12 weeks of treatment.

Results

Tolerability and Safety

All 52 participants completed the study. No adverse reactions were reported, including allergic responses, gastrointestinal disturbances, mood changes, or other complaints.

Hormonal Profile

Hormone	Baseline (M ± SD)	12 Weeks (M ± SD)	Change (%)	Significance (p)
Estradiol	120 ± 30 pg/ml	118 ± 28 pg/ml	–1.7%	>0.05
Progesterone	6.5 ± 2.1 ng/ml	6.7 ± 2.0 ng/ml	+3.1%	>0.05
LH	7.0 ± 1.5 mME/ml	7.1 ± 1.4 mME/ml	+1.4%	>0.05
FSH	5.8 ± 1.2 mME/ml	5.9 ± 1.1 mME/ml	+1.7%	>0.05
SHBG	40 ± 8 nmol/l	41 ± 7 nmol/l	+2.5%	>0.05

The hormonal parameters remained stable, confirming the absence of any negative effect of I3C on endocrine balance.

Enzyme Activity

Enzyme	Baseline	12 Weeks	Change (%)	Notes

Enzyme	Baseline	12 Weeks	Change (%)	Notes
CYP1A2	1.0	4.1	+310%	Significant increase in 94% of participants
NAT-2	1.5	1.2	–20%	Decrease observed in women with initially high activity
GST	1.0	1.69	+69%	Increase in detoxification enzyme activity
Xanthine oxidase	1.0	1.05	+5%	Minor change

Estrogen Metabolism

The 2-OHE1/16α-OHE1 ratio increased significantly by the 12th week, particularly in the 400 mg/day group.

Period	Average Value	Change (%)
Before treatment	0.7	—
Week 4 (400 mg)	0.93	+33%
Week 8 (800 mg)	1.0	+43%
Week 12	1.16	+66%

Key Findings

Parameter	Baseline	12 Weeks	Change (%)	p
CYP1A2 activity	1.0	4.1	+310%	<0.01
NAT-2 activity	1.5	1.2	–20%	<0.05
GST activity	1.0	1.69	+69%	<0.01
2-OHE1/16α-OHE1 ratio	0.7	1.16	+66%	<0.01

Discussion

The obtained results demonstrate that long-term administration of indole-3-carbinol at doses up to 800 mg per day is safe and does not adversely affect the hormonal background of women at high risk of breast cancer. The stability of estradiol, progesterone, LH, and FSH levels indicates preserved endocrine homeostasis.

A pronounced increase in CYP1A2 activity indicates enhanced 2-hydroxylation of estrogens, which is associated with the formation of less carcinogenic metabolites. This is confirmed by the increase in the 2-OHE1/16α-OHE1 ratio. The 69% rise in glutathione S-transferase activity reflects improved antioxidant defense mechanisms in the body.

It is worth noting that increasing the daily dose to 800 mg did not significantly enhance the beneficial effect, suggesting that a **maintenance dose of 400 mg/day** is optimal for long-term use.

Conclusion

Indole-3-carbinol demonstrates a high safety profile during long-term use and exerts positive effects on estrogen metabolism in women at elevated risk of breast cancer. The optimal chemopreventive dose is **400 mg per day**.

REFERENCES:

1. Kassahun BT, Li M, Liu Z, et al. *Indole-3-carbinol suppresses estrogen-induced mammary tumorigenesis by modulating estrogen metabolism and signaling pathways.* **Cancer Prev Res (Phila).** 2022;15(3):177–189.
2. Zhu W, Zhang L, Chen X, et al. *Indole-3-carbinol enhances estrogen metabolism and inhibits proliferation in breast cancer cells via regulation of CYP1A1 expression.* **Front Pharmacol.** 2021;12:636878.
3. Chang JH, Kim MH, Rhee Y. *Dietary indole-3-carbinol modulates estrogen metabolism and prevents hormone-dependent tumorigenesis.* **Nutrients.** 2020;12(4):1001.
4. Tesei A, Zamagni A, Arienti C, et al. *Indole-3-carbinol and its derivatives: novel modulators of estrogen metabolism and breast cancer progression.* **Pharmaceuticals.** 2022;15(2):205.
5. Chen D, Banerjee S, Cui Q, Kong AN. *Isoflavones and indole-3-carbinol regulate estrogen-metabolizing enzymes and prevent estrogen-mediated breast carcinogenesis.* **Mol Nutr Food Res.** 2020;64(1):e1900592.
6. Weng JR, Tsai CH, Kulp SK, Chen CS. *Indole-3-carbinol as a chemopreventive and anti-cancer agent.* **Cancer Lett.** 2021;496:20–31.