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# Selenium and treatment of triple negative breast cancer

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Σελήνιο και θεραπεία τριπλά αρνητικού καρκίνου του μαστού

*Περίληψη στο τέλος του άρθρου*

**Key words:** Breast cancer, Selenium, Treatment, Triple-negative

Breast cancer (BC) is the second main cause of cancer-related deaths in women, with over two million cases yearly, and is classified into three well-differentiated groups: Hormone receptor-positive ($HR^+$) with estrogen receptor ($ER^+$) or progesterone receptor ($PR^+$); human epidermal growth factor receptor 2-positive ($HER2^+$); and triple-negative breast cancer (TNBC).[1–7] Literature review from 2018 to 2023 showed that breast-conserving surgery plus neoadjuvant chemotherapy constituted the best management strategy for patients with TNBC diagnoses.[3] As high mortality is mainly related to multidrug resistance, which limits therapeutic options, the authors emphasized the necessity of more specific research about the TNBC treatment.[3] The standard chemotherapy for TNBC often utilizes anthracyclines and taxanes; for BRCA-mutated TNBC resistant, cisplatin, carboplatin, olaparib, or talazoparib, are alternatives. The standard chemotherapy for TNBC often utilizes anthracyclines and taxanes; and for BRCA-mutated TNBC resistant cisplatin, carboplatin, olaparib, and talazoparib are the alternatives.[7] For BC expressing PD-L1 protein, initial treatment may be immunotherapy (pembrolizumab) plus chemotherapy; and for advanced TNBC in which two or more other drug treatments were previously tried, the antibody-drug conjugate sacituzumab govitecan might be an option; but even with adjuvant radiation, targeted therapies and immunotherapy, the recurrence is high.[7] The limitation of treatment options for TNBC has favored the elevated risk of metastatic recurrences and poor outcomes; and ferroptosis is cell death by iron-dependent lipid peroxidation, counterpoised by antioxidant effects of selenoprotein GPX4.[1] The TNBC cells cultured at high cell densities can secrete an anti-ferroptosis factor in the extracellular medium; however, are primed for the ferroptosis in the colonies at low density.[1] This factor is a monounsaturated fatty acid, and the vulnerability of TNBC cells to ferroptosis depends on low levels of stearoyl-CoA desaturase (SCD) that is proportional to cell density.[1] Circulating TNBC cells downregulate SCD expression that sensitizes them to the inhibition of Sec-tRNAsec biosynthesis, essential for selenoprotein ferroptosis which impairs metastasis.[1] As cancer cells produce high levels of reactive oxygen species (ROS) and their accumulation can cause cell deaths, reduction of ROS elimination might be utilized in cancer treatment.[2] Selenium is an essential component of antioxidant enzymes involved in the reduction of ROS, and an improvement in mice survival occurred when they were fed with selenium-free diets; the anticancer effect was in mice with metastatic TNBC, and also metastatic colon cancer.[2] This experimental finding might indicate a potentially favorable role of diets lacking selenium in the management of human TNBC; nevertheless, this matter persists to be better confirmed. Otherwise, 13 articles showed that selenium therapy increased the anti-cancer drug's effects, and the tumor cytotoxicity, reducing the cellular hyperproliferation, growth, and metastasis.[6] There were good outcomes by using selenium alone, or with nutritional supplements and common chemotherapy drugs, like trastuzumab, bevacizumab, doxorubicin, and paclitaxel.[6] The use of selenium compounds inhibited the tumor development causing widespread cell death, and decreased metastatic potential, with minimal damage to normal epithelial cells.[6] Because few data support selenium

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compounds modulating the activity of P-glycoprotein (MDR1), some studies evaluated the effects of novel selenoesters EDAG-1 and EDAG-8 on BCRP, MDR1, and MRP1 resistance proteins in the BC cells MCF-7 and MDA-MB-231.[4] TNBC develops by mutation of the *BRCA1* gene, without estrogen, progesterone, or HER2 protein receptors; invasive, with higher metastatic potential, has a poor response to therapy.[4] Among these inhibitors of BCRP, MDR1, and MRP1 efflux pumps, the EDAG-8 had a more favorable anticancer activity, being a promising future agent to be utilized in BC treatment.[4] The evaluation of selenoesters (EDAG-1, -7, -8, -10) on MCF-7 and MDA-MB-231 BC cells included studies of cell proliferation and viability, besides cytometric determinations of apoptosis/autophagy induction, changes in mitochondrial membrane polarity, caspase 3/7, 8, and 9 activities, and Bax, Bcl-2, p53, Akt, AMPK, and LC3A/B proteins. And showed the tested derivatives being highly cytotoxic and inhibiting cell proliferation even at nanomolar doses.[5] These evaluated compounds are activators of autophagy (reducing Akt and increasing autophagosomes and autolysosomes, AMPK, LC3A/B) and promising drugs in BC therapy.[5] In conclusion, regarding selenium for the treatment of TNBCs, the final word is still missing.

## ΠΕΡΙΛΗΨΗ


### Σελήνιο και θεραπεία τριπλά αρνητικού καρκίνου του μαστού

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Ο καρκίνος του μαστού είναι η δεύτερη κύρια αιτία θανάτου από καρκίνο στις γυναίκες, με περισσότερα από δύο εκατομμύρια περιπτώσεις ετησίως, και ταξινομείται σε τρεις καλά διαφοροποιημένες ομάδες: (α) Θετικοί σε ορμονικούς υποδοχείς με υποδοχείς οιστρογόνων ή υποδοχείς προγεστερόνης, (β) θετικός υποδοχέας ανθρώπινου επιδερμικού αυξητικού παράγοντα και (γ) τριπλά αρνητικός καρκίνος του μαστού. Αυτή η τελευταία κατηγορία έχει υψηλό ποσοστό θνητότητας λόγω της αντοχής σε πολλά φάρμακα, που περιορίζει τις θεραπευτικές επιλογές. Τα σύντομα σχόλια του άρθρου στοχεύουν να τονίσουν την ανάγκη για πιο συγκεκριμένες κατευθυντήριες γραμμές θεραπείας.


**Λέξεις ευρετηρίου:** Θεραπεία, Καρκίνος του μαστού, Σελήνιο, Τριπλό αρνητικό

## References


1. ACKERMANN T, SHOKRY E, DESHMUKH R, ANAND J, GALBRAITH LCA, MITCHELL L ET AL. Breast cancer secretes anti-ferroptotic MUFAs and depends on selenoprotein synthesis for metastasis. *EMBO Mol Med* 2024, 16:2749–2774
2. DÍAZ-ORTEGA P, CALDERÓN-MONTAÑO JM, JIMÉNEZ-ALONSO JJ, GUILLÉN-MANCINA E, JIMÉNEZ-GONZÁLEZ V, BURGOS-MORÓN E ET AL. A diet lacking selenium, but not zinc, copper or manganese, induces anticancer activity in mice with metastatic cancers. *Nutrients* 2024, 16:2249
3. OLIVEIRA HAG, CATARINO CVG, BONFIM GBA, NETO HAP, CARVALHO IM, PEREIRA IB ET AL. Efficacy of triple-negative breast cancer treatments: A systematic review. *RCS Revista Ciências da Saúde – Ceuma* 2024, 2:46–60
4. RADOMSKA D, CZARNOMYSY R, MARCINIEC K, NOWAKOWSKA J, DOMÍNGUEZ-ÁLVAREZ E, BIELAWSKI K. Short communication: Novel di- and triselenoesters as effective therapeutic agents inhibiting multidrug resistance proteins in breast cancer cells. *Int J Mol Sci* 2024, 25:9732
5. RADOMSKA D, CZARNOMYSY R, SZYMANOWSKA A, RADOMSKI D, CHALECKA M, SURAZYNSKI A ET AL. Di- and triselenoesters-promising drug candidates for the future therapy of triple-negative breast cancer. *Int J Mol Sci* 2024, 25:7764
6. SIDIRA D, SIAFAKA A, CHRYSIKOS D, PAPADOPOULOS G, STRATOPOULOS E, FILIPPOU D. Selenium and triple negative breast cancer. *Acta Med Acad* 2024, 53:155–164
7. SOFIANIDI A, DUMBRAVA EE, SYRIGOS KN, NASRAZADANI A. Triple-negative breast cancer and emerging therapeutic strategies: ATR and CHK1/2 as promising targets. *Cancers (Basel)* 2024, 16:1139



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