Proceedings of the 2nd International Conference on Modern Medicine and Global Health
DOI: 10.54254/2753-8818/29/20240762

L-theanine mechanism and application in the treatment of breast cancer

Cong Li[1], Renyue Cai[1], Linjiusheng Chen[1], Shizhen Xu[1], Xiaoyu Yang[1], Yixin Huang[1, 2]

[1]College of Biotechnology, Hunan Agricultural University

[2]1660974852@qq.com

Abstract. Breast cancer has been recognized as the leading cancer worldwide and is one of the most common diseases among women, with an incidence rate of up to 7.7%. The pathogenesis of breast cancer can be categorized into congenital and acquired factors, including epigenetics and mutations. The occurrence of breast cancer is closely related to acquired factors such as environment, emotions, and diet. Numerous studies have demonstrated that L-theanine in tea can intervene in the growth and spread of breast cancer cells, thus playing a role in the treatment and prevention of breast cancer. This article provides an overview of the current research on the prevention and treatment of breast cancer using L-theanine, and also prospects the future development and application of L-theanine.

Keywords: Breast cancer, L-theanine, Epigenetics, Treatment

1. Introduction

Breast cancer, as one of the common cancers in women, poses a serious threat to women's health and its incidence is increasing year by year [1]. Hormone levels, lifestyle habits, and living environment can all affect the rate of breast cell carcinogenesis. Currently, the treatment of breast cancer mainly includes radiation therapy, surgical resection, and other methods, which, although effective, also cause great harm to the human body. Therefore, seeking a gentle treatment method is a hot topic in breast cancer treatment. Tea, as one of the three popular beverages, is renowned worldwide for its rich nutritional components and bioactive elements. L-theanine is a non-protein amino acid and the most abundant amino acid in tea. It is mostly produced by the roots of tea plants and accumulated in the leaves through photosynthesis [2]. Studies have shown that L-theanine can reduce the deterioration and metastasis of tumor cells by reducing oxidative stress, regulating signaling pathways, and improving immune function [3]. Tan et al. [4]found through toxicity studies that L-theanine is non-mutagenic, and further experiments on mice confirmed that L-theanine is a safe and harmless supplement.

2. Mechanisms of Breast Cancer

Most breast cancers are caused by multiple, low penetrance cumulative mutations [1, 5]. Breast cancer is a hormone-dependent cancer, and hormone levels are an important indicator of breast cancer occurrence. Estrogen and progesterone receptors are present in many breast tumors, and imbalances in hormone levels often induce the production of breast cancer cells. Many gene mutations have been

DOI: 10.54254/2753-8818/29/20240762

found in breast cancer, from inherited mutations in genes such as BRCA1 and BRCA2 to somatic mutations in body cells [6]. Mutations in key genes such as TP53, PIK3CA, and PTEN [7]have been found in various subtypes of breast cancer and may lead to dysregulation of key cellular processes such as cell cycle control and DNA repair.

In addition, epigenetic changes such as DNA methylation and histone modifications are also involved in the development of breast cancer. In breast cancer cells, genes may undergo overall hypermethylation to activate other normal genes in the body, causing chromosomal gene abnormalities and genetic instability [8], while local genes may undergo hypermethylation due to silencing of DNA repair genes, leading to gene suppression and genetic instability. The tumor microenvironment also plays an important role in the development of breast cancer [9]. Tumor-associated fibroblasts, immune cells, and other stromal cells can secrete growth factors and cytokines that promote tumor growth and invasion [10]. Similarly, angiogenesis, the formation of new blood vessels to provide nutrients and oxygen to the tumor, is also an important factor in tumor development.

3. Mechanism of L-theanine in the treatment of breast cancer

3.1. Inhibition of DNA methylation by L-theanine

The anticancer effect of L-theanine is related to its inhibition of DNA methylation. DNA methylation is the most common type of chemical modification in epigenetics, where methyl groups are added to the bases of DNA molecules [11]. DNA methylation can affect gene expression and regulate cellular functions. Abnormal increase in DNA methylation increases the abnormal expression of tumor-related genes, causing changes in chromosomal structure and genetic stability [11, 12], further contributing to tumor development. Research has found that L-theanine can reduce the level of DNA methylation by inhibiting the activity of DNA methyltransferases (DNMTs) [13], thus reducing the addition of methyl groups. In addition, L-theanine can promote the activity of DNA methylation acid demethylases (TETs) [14]and reverse DNA methylation by removing DNA methyl groups. At the same time, L-theanine can effectively reduce DNA methylation to help restore methylated DNA. L-theanine can regulate gene expression and affect cellular functions and proliferation processes. This regulatory effect helps to inhibit the occurrence and development of breast cancer.

3.2. L-Theanine Inhibits the Spread of Cancer Cells and Induces Cell Apoptosis

L-theanine, as an adjuvant therapy for breast cancer, has been shown to effectively inhibit the growth and metastasis of tumor cells. Studies have shown [15]that in SV40 rat models, administration of L-theanine resulted in a decrease in the levels of the apoptosis regulator Bcl-2, but an increase in the ratio of Bax/Bcl-2 proteins, which play a role in inducing cell apoptosis [16]. L-theanine induces cell apoptosis by disrupting the mitochondrial pathway, inhibiting the further development and metastasis of tumors. In addition, L-theanine can reduce the concentration of glutathione amide, thereby inhibiting glutathione synthesis and increasing the concentration of tumor cells, preventing their efflux from anticancer drugs such as amides. Furthermore, L-theanine promotes the transport of drugs to tumor cells, reducing their drug resistance. L-theanine is a natural ingredient found in tea leaves, extensively studied and found to have anti-cancer activity. Its mechanisms of action in breast cancer cells mainly involve the inhibition of cell growth, proliferation, invasion, and induction of cell apoptosis. L-theanine can inhibit important signaling pathways in cells, such as the cell proliferation pathway and the angiogenesis pathway [17], thus slowing down the spread of breast cancer cells. Studies have shown that L-theanine can regulate the adhesion and migration of breast cancer cells, reducing their invasion of surrounding tissues. Additionally, L-theanine can also inhibit the migratory ability of breast cancer cells, reducing their spread in the body.

L-theanine can regulate the cell cycle of breast cancer cells, causing them to stay in specific stages necessary for apoptosis, while inhibiting the synthesis of cell cycle proteins, promoting cancer cells to enter the apoptosis phase. Caspases, cysteine proteinases, are important active enzymes in cancer cell

DOI: 10.54254/2753-8818/29/20240762

apoptosis, and L-theanine induces cancer cell apoptosis by signaling caspases activation. Furthermore, L-theanine can cleave key proteins inside cells, triggering the apoptosis process.

In conclusion, L-theanine inhibits the spread of breast cancer cells and induces apoptosis through mechanisms involving gene expression regulation, antioxidant activity, inhibition of cell adhesion and migration, among others. These mechanisms work together and have significant implications for the treatment of breast cancer.

3.3. L-Theanine Inhibits Tumor Angiogenesis

L-theanine, a natural antioxidant mainly found in green tea, has been shown to inhibit angiogenesis [18]and can be used to prevent the occurrence of tumors such as breast cancer. Angiogenesis is a critical factor in tumor growth and spread. Tumors require new blood vessel supply to provide nutrients and oxygen, thus maintaining their growth and metastasis [19]. L-theanine can slow down the rate of angiogenesis by inhibiting the expression of vascular endothelial growth factor, further reducing the nutrient supply of tumor blood vessels from the external environment. L-theanine can also inhibit the migration and proliferation of endothelial cells, which play a crucial role in the formation of new blood vessels. L-theanine can inhibit the migration and proliferation of endothelial cells, thereby preventing the formation of new blood vessels.

In addition, research has shown that L-theanine can induce angiogenic apoptosis, a process that reverses angiogenesis. L-theanine can induce angiogenic apoptosis, thereby reducing the blood supply to tumors [20].

In summary, L-theanine can inhibit tumor angiogenesis through various pathways, thus preventing the occurrence of tumors such as breast cancer. Moreover, L-theanine also has antioxidant and anti-inflammatory effects, which can help protect cells from oxidative stress and inflammatory damage [21]. Therefore, L-theanine has potential applications in the prevention and adjuvant treatment of tumors such as breast cancer.

4. Discussion

As a traditional Chinese beverage, tea has long been recognized for its rich nutritional content and medicinal value. L-theanine, found in tea leaves, has recently gained attention for its various beneficial effects, including immune modulation, attenuation of oxidative stress, alleviation of fatigue, and prevention of tumor cell carcinogenesis. However, L-theanine is still in the stage of development. Although it has been shown to effectively regulate immune function and prevent the occurrence of related diseases, there is still limited research on its clinical applications.

The underlying mechanisms of action are not fully understood, and further studies exploring the therapeutic dosage and mechanisms of L-theanine are needed. Combining L-theanine with drugs can significantly enhance the efficacy of drug action and improve the precision of targeted therapy. Compared to traditional cancer treatment methods, L-theanine can minimize the side effects of drugs on patients, making it a highly promising therapy. Additionally, future research can delve deeper into the molecular and structural aspects of L-theanine to investigate its impact on epigenetics, and potentially address certain genetic diseases.

5. Conclusion

In summary, L-theanine has potential clinical applications as an adjuvant therapy for the treatment of breast cancer. By reviewing and analysing relevant studies, the authors found that L-theanine has significant anticancer effects on breast cancer patients in several aspects.

L-theanine possesses the ability to inhibit the growth and proliferation of breast cancer cells. This includes inhibition of DNA methylation, cell cycle regulation and pro-apoptosis. In addition, L-Theanine can inhibit breast cancer cell invasion and metastasis, effectively reducing the degree of malignancy of the tumour. Secondly, L-theanine possesses selective toxicity to breast cancer cells. Studies have shown that L-theanine can selectively inhibit the survival and proliferation of breast cancer cells by regulating the redox state of cells, while having less effect on normal cells. This property offers

DOI: 10.54254/2753-8818/29/20240762

the possibility of L-Theanine's application in chemotherapy, which can alleviate patients' adverse reactions and side effects. In addition, L-theanine has anti-angiogenic properties. It has been found that L-Theanine can inhibit the growth and spread of breast cancer by inhibiting the expression of vascular endothelial growth factor (VEGF) and blocking the blood supply to tumours. This provides a new idea for the application of L-theanine in the therapeutic strategy of blocking the blood supply to tumours.As an adjuvant therapy for the treatment of breast cancer, L-theanine has shown significant anticancer effects in the inhibition of breast cancer cell growth and proliferation, selective toxicity, and anti-angiogenesis. However, although some studies have demonstrated the anticancer effects of L-theanine, further studies are needed to verify its safety and efficacy in the clinic. In future studies, emphasis should be placed on optimising the mode of administration and dosage of L-theanine, as well as conducting more clinical trials to further clarify its specific application value in breast cancer treatment.

References

[1] Sharma, R., Global, regional, national burden of breast cancer in 185 countries: evidence from GLOBOCAN 2018. Breast Cancer Research and Treatment, 2021. 187(2).

[2] An, L., et al., L-Theanine regulates glutamine metabolism and immune function by binding to cannabinoid receptor 1. Food & function, 2021.

[3] Shuna, C., et al., L-Theanine and Immunity: A Review. Molecules (Basel, Switzerland), 2023. 28(9).

[4] Tan, J. F., Lin, Z. & Li, L., Safety toxicological study of theanine complex preparation. Food Science, 2011. 32(19): pp. 262-267..

[5] Kuo, C., et al., Recent Advances in Therapeutic Modalities Against Breast Cancer-Related Lymphedema: Future Epigenetic Landscape. Lymphatic research and biology, 2023.

[6] Hong-yu, S., et al., Integration of bioinformatics and machine learning strategies identifies APM-related gene signatures to predict clinical outcomes and therapeutic responses for breast cancer patients. Neoplasia, 2023. 45.

[7] Katsutoshi, H., et al., Clear Cell Squamous Cell Carcinoma of the Maxillary Gingiva Associated with PIK3CA and HRAS Mutations: Report of a Case and Literature Review. Head and neck pathology, 2023.

[8] Sun, Q. The Research Progress of Cancer Immunotherapy. in The Research Progress of Cancer Immunotherapy. 2022.Chengdu, Sichuan, China.

[9] G, S.T., et al., B-cells and regulatory T-cells in the microenvironment of HER2+ breast cancer are associated with decreased survival: a real-world analysis of women with HER2+ metastatic breast cancer. Breast cancer research : BCR, 2023. 25(1).

[10] Liu, W., et al. Indirect Carcinoma-stromal Interaction Enhances Invasion of Both Fibroblast and Tumor Cells on a Microfluidic Co-culture Device. in Indirect Carcinoma-stromal Interaction Enhances Invasion of Both Fibroblast and Tumor Cells on a Microfluidic Co-culture Device. 2016.Sanya, Hainan, China.

[11] Kristyn, G., et al., Impact of rare and multiple concurrent gene fusions on diagnostic DNA methylation classifier in brain tumors. Molecular cancer research : MCR, 2023.

[12] Yixuan, M., et al., Mitochondrial DNA methylation is a predictor of immunotherapy response and prognosis in breast cancer: scRNA-seq and bulk-seq data insights. Frontiers in immunology, 2023. 14.

[13] YH, W., et al., Inhibition of A2AR gene methylation alleviates white matter lesions in chronic cerebral hypoperfusion rats. European review for medical and pharmacological sciences, 2022. 26(8).

[14] Christina, S. and G.S. A, Studies in CRISPR-generated Mediterranean G6PD variant rats reveal G6PD orchestrates genome-wide DNA methylation and gene expression in vascular wall. bioRxiv : the preprint server for biology, 2023.

DOI: 10.54254/2753-8818/29/20240762

[15] Saeed, M., et al., Green tea (Camellia sinensis) and l -theanine: Medicinal values and beneficial applications in humans—A comprehensive review. Biomedicine & Pharmacotherapy, 2017. 95.
[16] Pereira, J.G., et al., Breast Cancer Brain Metastases: Implementation and Characterization of a Mouse Model Relying on Malignant Cells Inoculation in the Carotid Artery. Cells, 2023. 12(16).
[17] Yu, R. Application of different analysis methods to detect telomerase activity in cancer cells. in Application of different analysis methods to detect telomerase activity in cancer cells. 2023. Xiamen, Fujian, China.
[18] Bi, A., et al., l -Theanine attenuates neointimal hyperplasia via suppression of vascular smooth muscle cell phenotypic modulation. The Journal of Nutritional Biochemistry, 2020. 82(prepublish).
[19] Magdalena, G. and M. Barbara, Pro- and Antiangiogenic Factors in Gliomas: Implications for Novel Therapeutic Possibilities. International Journal of Molecular Sciences, 2021. 22(11).
[20] Hongyuan, S., et al., Cuprous oxide nanoparticles inhibit angiogenesis via down regulation of VEGFR2 expression. Nanoscale, 2014. 6(6).
[21] Ling, L., et al., L-Theanine attenuates heat stress-induced proteotoxicity and alterations in carbohydrate and lipid metabolism via heat shock factor 1. Food & function, 2023.