Letter to Editor

Effectiveness of 5-aminolevulinic Acid Combined with Curcumin Mediating Photodynamic Therapy

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Dear Editor

5-aminolevulinic acid (5-ALA) is the mitochondria metabolite produced from glycine and succinyl-CoA, which is converted to protoporphyrin IX (PpIX) by the conjugation of eight itself molecules forming the "heme" group in a porphyrin ring (Figure 1) [1]. The PpIX is used as a photosensitizer (PS) with an absorption wavelength of 410 nm, and 5-ALA acts as a precursor or prodrug for PpIX in photodynamic therapy (PDT). Exogenous administration of excessive amounts of 5-ALA increases the production of PpIX during heme biosynthesis. It is eliminated after 24-48 h with a lower risk of long-term photosensitivity [2]. However, 5-ALA PDT has several disadvantages, including the concentration of ALA is affected by its absorption and pharmacokinetics that are not fully covered the treatment area [3-5], as well as the limited depth of tumor penetration and caused pain symptoms [6].

Unsurprisingly, most plant extracts have no pharmaceutical activity on abnormal cells if they are not exposed to light. Some plant extracts are used as PS and activated through light with a suitable wavelength, which is strongly toxic to malignant cells [7]. Curcumin is a famous PS obtained from herbal plants, consisting of hydrophobic polyphenols found in the turmeric rhizome (*Curcuma longa* L.). It has various pharmaceutical properties, including anti-inflammatory, antioxidant, anti-bacterial, and antiviral properties [8, 9]. Curcumin has a broad absorption spectrum from 300 to 500 nm with a relatively high extinction coefficient [10]. Upon excitation of the wavelength for curcumin, it is produced reactive oxygen species (ROS) and more specifically, singlet state oxygen (^1O), hydrogen peroxide, and hydroxyl radicals [11]. ROS undergoes a destruction process in the PDT for the treatment of cancers and diseases. A PS accumulates in the tumor tissue and illuminates it with light [12].

Curcumin-mediated PDT, combined with autophagy inhibitor, can further suppress epithelial-mesenchymal transition (EMT) in lung cancer cells. It may be a potential strategy against the invasion and migration of lung cancer. Li et al. investigated the apoptosis mechanism of curcumin-mediated PDT by detecting the levels of ROS, mitochondrial membrane potential, and related proteins [13]. Wang et al. examined the effect of curcumin-mediated PDT on oxidized low-density lipoprotein (ox-LDL)-treated vascular smooth muscle cells (VSMCs) to confirm whether these effects are mediated by autophagy. The therapy significantly promoted the autophagy level and inhibited the phenotypic transformation induced by ox-LDL [14]. Paolillo et al. indicated the effect of combined curcumin-mediated PDT and artificial skin on *Staphylococcus aureus* infected wounds in rats. The PDT was performed with a curcumin gel and a blue

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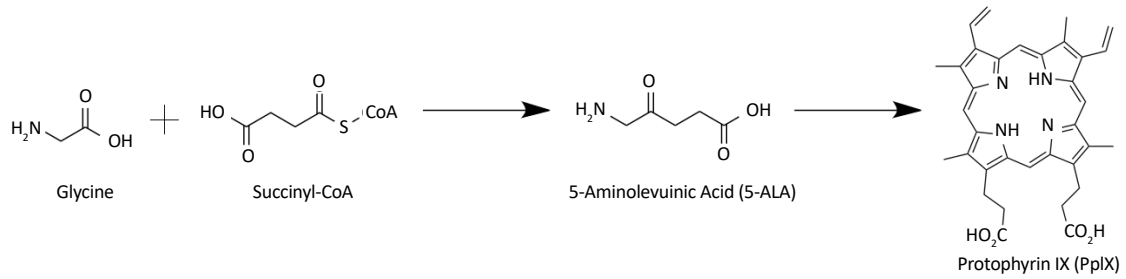

Figure 1. Formation of PpIX through the 5-ALA molecules

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LED light (450 nm, 80 mW/cm^2) at the dose of 60 J/cm^2 which accelerated the wound contraction [15].

Şueki et al. studied the efficacy of 5-ALA-mediated PDT and used 10 µM of non-toxic doses of curcumin, which significantly reduced the resistance of PDT for Caco-2 cells. This identified the 5-ALA-mediated PDT, combined with curcumin, synergistically improves the antitumor efficacy of PDT on Caco-2, which is considered a highly resistive cancer cell line [16]. Tumor cell lines from adult T cell leukemia or lymphoma (ATL) are susceptible to specific cell death by visible light exposure after a short-term culture with 5-aminolevulinic acid, indicating that 5-ALA mediates the efficiency of PDT [17]. It is much better to use the PDT with other conventional therapies such as curcumin. Growing evidence showed that curcumin combined with PDT can overcome the limitation of curcumin's low bioavailability, which is used to enhance the reactivity of curcumin and the efficacy of PDT [18].

The above mentioned information demonstrates that 5-ALA-mediated PDT combined with curcumin may have some positive outcomes, such as enhancing the bioavailability and efficacy of PDT. However, more studies are required on the 5-ALA PDT and curcumin in the human body.

Ethical Considerations

Compliance with ethical guidelines

There were no ethical considerations to be considered in this research.

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Conflict of interest

The author declared no conflict of interest.

References

[1] Wachowska M, Muchowicz A, Firczuk M, Gabrysiak M, Winiarska M, Wańczyk M, et al. Aminolevulinic Acid (ALA) as a prodrug in photodynamic therapy of cancer. Molecules. 2011; 16(5):4140-64. [DOI:10.3390/molecules16054140] [PMCID]

[2] Park J, Lee YK, Park IK, Hwang SR. Current limitations and recent progress in nanomedicine for clinically available photodynamic therapy. Biomedicines. 2021; 9(1):85. [DOI:10.3390/biomedicines9010085] [PMID] [PMCID]

[3] Peng Q, Warloe T, Berg K, Moan J, Kongshaug M, Giercksky KE, et al. 5-Aminolevulinic acid-based photodynamic therapy. Clinical research and future challenges. Cancer 1997; 79(12):2282-308. [DOI:10.1002/(SICI)1097-0142(19970615)79:123.0.CO;2-O]

[4] O'Connor AE, Gallagher WM, Byrne AT. Porphyrin and nonporphyrin photosensitizers in oncology: Preclinical and clinical advances in photodynamic therapy. Photochem Photobiol. 2009; 85(5):1053-74. [DOI:10.1111/j.1751-1097.2009.00585.x] [PMID]

[5] Profio AE, Doiron DR. Dosimetry considerations in phototherapy. Med Phys. 1981; 8(2):190-6. [DOI:10.1118/1.594932] [PMID]

[6] Warren CB, Karai LJ, Vidimos A, Maytin EV. Pain associated with aminolevulinic acid-photodynamic therapy of skin disease. J Am Acad Dermatol. 2009; 61(6):1033-43. [DOI:10.1016/j.jaad.2009.03.048] [PMID] [PMCID]

[7] Kubrak TP, Kołodziej P, Sawicki J, Mazur A, Koziorowska K, Aebisher D. Some natural photosensitizers and their medicinal properties for use in photodynamic therapy. Molecules 2022; 27(4):1192. [DOI:10.3390/molecules27041192] [PMID] [PMCID]

[8] Salem M, Rohani S, Gillies ER. Curcumin, a promising anticancer therapeutic: A review of its chemical properties, bioactivity and approaches to cancer cell delivery. RSC Adv. 2014; 4:10815-29. [DOI:10.1039/c3ra46396f]

[9] Kunnumakkara AB, Bordoloi D, Harsha C, Banik K, Gupta SC, Aggarwal BB. Curcumin mediates anticancer effects

by modulating multiple cell signaling pathways. Clin Sci (Lond). 2017; 131(15):1781-99. [DOI:10.1042/CS20160935] [PMID]

[10] Sreedhar A, Sarkar I, Rajan P, Pai J, Malagi S, Kamath V, et al. Comparative evaluation of the efficacy of curcumin gel with and without photo activation as an adjunct to scaling and root planing in the treatment of chronic periodontitis: A split mouth clinical and microbiological study. J Nat Sci Biol Med. 2015; 6(Suppl 1):S102-9. [DOI:10.4103/0976-9668.166100] [PMID] [PMCID]

[11] Chignell CF, Bilski P, Reszka KJ, Motten AG, Sik RH, Dahl TA. Spectral and photochemical properties of curcumin. Photochem Photobiol. 1994; 59(3):295-302. [DOI:10.1111/j.1751-1097.1994.tb05037.x] [PMID]

[12] Foresto E, Gilardi P, Ibarra LE, Cogno IS. Light-activated green drugs: How we can use them in photodynamic therapy and mass-produce them with biotechnological tools. Phytomedicine Plus. 2021; 1(3):100044. [DOI:10.1016/j.phyplu.2021.100044]

[13] Li Y, Xiao P, Huang Z, Chen X, Yan X, Zhai J, Ma Y. Evaluation of curcumin-mediated photodynamic therapy on the reverse of multidrug resistance in tumor cells. RSC Adv. 2020; 10(1):298-306. [DOI:10.1039/c9ra09996d] [PMID]

[14] Wang G, Zhu Y, Li K, Liao B, Wang F, Shao L, et al. Curcumin-mediated photodynamic therapy inhibits the phenotypic transformation, migration, and foaming of oxidized low-density lipoprotein-treated vascular smooth muscle cells by promoting autophagy. J Cardiovasc Pharmacol. 2021; 78(2):308-18. [DOI:10.1097/FJC.0000000000001069] [PMID]

[15] Paolillo FR, Rodrigues PGS, Bagnato VS, Alves F, Pires L, Corazza AV. The effect of combined curcumin-mediated photodynamic therapy and artificial skin on Staphylococcus aureus-infected wounds in rats. Lasers Med Sci. 2021; 36(6):1219-26. [DOI:10.1007/s10103-020-03160-6] [PMID]

[16] Şueki F, Ruhi MK, Gülsoy M. The effect of curcumin in antitumor photodynamic therapy: In vitro experiments with Caco-2 and PC-3 cancer lines. Photodiagnosis Photodyn Ther. 2019; 27:95-9. [DOI:10.1016/j.pdpdt.2019.05.012] [PMID]

[17] Sando Y, Matsuoka KI, Sumii Y, Kondo T, Ikegawa S, Sugiura H, et al. Author correction: 5-aminolevulinic acid-mediated photodynamic therapy can target aggressive adult T cell leukemia/lymphoma resistant to conventional chemotherapy. Sci Rep. 2021; 11(1):6420. [DOI:10.1038/s41598-021-86066-9] [PMID] [PMCID]

[18] Xie L, Ji X, Zhang Q, Wei Y. Curcumin combined with photodynamic therapy, promising therapies for the treatment of cancer. Biomed Pharmacother. 2022; 146:112567. [DOI:10.1016/j.biopha.2021.112567] [PMID]

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