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Bioenzyme based on nanobiotechnology for cancer treatment: A mini-review

Navid Mousavinejad

Department of Clinical Biochemistry, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran

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Abstract

Biological enzymes, also known as organic catalysts, play an effective role in the treatment of cancer, especially when combined with nanoparticles using nanobiotechnology methods, their anti-tumor effect improves. Nanoparticle-based bioenzymes play an important role in improving cancer treatment by affecting tumor tissue microenvironment such as pH, glucose concentration, hypoxia and redox reaction. Moreover, by degrading the extracellular matrix of tumor tissue, nanoparticle-based enzymes cause increased accumulation of immune cells in this area, thus enhancing the efficacy of treatments based on chemotherapy, photothermal therapy, radiotherapy, and immunotherapy.This mini-review summarizes the recent progress in the field of enhancing cancer treatment methods based on nanoparticle-conjugated enzymes, presents the structure of nanoparticle-based bioenzymes and the various applications of bioenzymes, advantages and disadvantages, challenges, and conclusions.

Keywords: Bioenzyme, NanoTechnology, Cancer Therapy

1 Introduction

Bio enzymes, which play an essential role in speeding up biological reactions, have recently been used as a new treatment method to treat cancer[1-6]. Also, bio-enzymes improve the efficiency of cancer treatment methods such as chemotherapy and Immunotherapy[7-11]. Enzymes can destroy cancer cells by changing the microenvironment of tumor tissue, such as changes in pH, changes in redox reactions, and changes in glucose concentration[12-18]. However, the use of bio-enzymes to treat cancer or to increase the efficiency of cancer treatment methods such as Immunotherapy and chemotherapy is facing problems, and the most important of these problems include maintaining the stability of the enzyme structure, the weak membrane permeability of bio enzymes, and Poor passage of bio-enzymes in the bloodstream[19-24]. On the other hand, nano drugs have been widely used to treat cancer[25-32]. Nanoparticles alone or binding to other molecules such as proteins, enzymes, nucleic acids, or other molecules can help treat cancer[33-41]. Conjugating bio-enzymes to nanoparticles increases the stability of the bio-enzymes structure, the specific connection of bio-enzymes to the target tumor tissue, and improves the movement of bio-enzymes in the bloodstream and, as a result, increases the efficiency of cancer treatment methods[42-46]. This mini-review discusses the types of bio-enzymes based on nano-biotechnology, their mechanisms in cancer treatment, and the types of nanoparticles used.

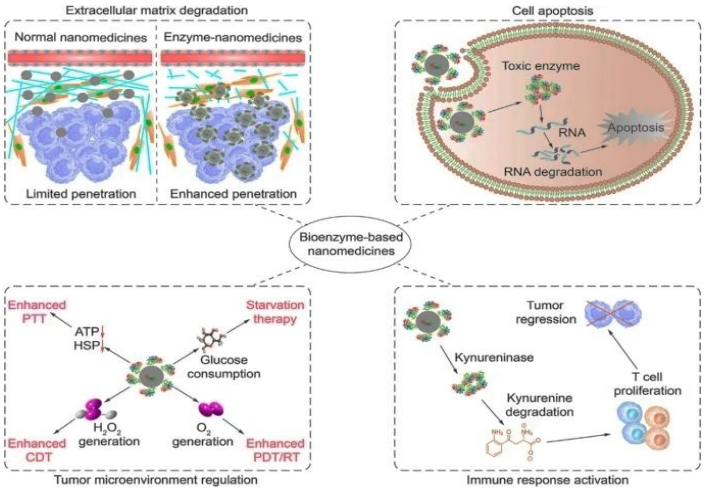

Figure 1. Different mechanisms of Bioenzymes based on nanobiotechnology for cancer treatment

Corresponding: Navid Mousavinejad Department of Clinical Biochemistry, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran
E-mail: Navid.mousavi.njd@gmail.com

2 Application and mechanisms

Assembly of natural glucose oxidase (GOD) onto CoFe-layered double hydroxides (CoFe-LDHs) monolayer nanosheets based on nano biotechnologies methods that increase the dispersion of the GOD. GOD increases the production of hydrogen peroxide, hydrogen peroxide convert to hydroxyl radical ion with the help of Fenton's reaction , which Fe3+ within the host layer, the CoFe-LDHs nanosheets exhibit a collaborative enhanced Fenton catalytic activity, increasing the production of hydroxyl ion stimulates the apoptosis system of tumor cells and causes cell death[14, 47-52].

Recently, the anticancer role of RNase has been recognized, but poor membrane permeability, slow movement in blood flow and poor structural stability have limited the use of RNase in cancer therapy. To overcome these problems, a nanogel consisting of azobenzene (Azo) and β-cyclodextrin (βCD) conjugated to poly(L-glutamic acid)-graft-poly (ethylene glycol) methyl ether (PLG-g-mPEG) has been used that RNase placed inside it. This nanogel structure is sensitive to hypoxia, and as a result, the specificity increases. Also, with the help of this nanogel structure, the half-life of the enzyme in the bloodstream is increased[53-59].

Tumor extracellular matrix often acts as a barrier, limiting the access of drugs and immune cells to cancer cells. A new approach to overcome this problem that has attracted a lot of attention today is the use of nanomedicines. Bio enzyme based on nanobiotechnology can improve cancer therapy due to their special features, including their small size. There are two ways for nanobiotechnology to pass through the extracellular matrix and reach cancer cells: decomposition the extracellular matrix and preventing its formation. Enzymes such as catalase and hyaluronidase conjugated with nanoparticle are used in improving cancer treatment methods by destroying the extracellular matrix of the tumor[60-66].

Photodynamic therapy is a type of phototherapy that involves light and a chemical drug called, photosensitizer, which converts oxygen to singlet oxygen under light irradiation and induces cell death. However, some challenges such as non-specific delivery of PSs (photosensitizers) to the tumor tissue, hypoxic tumor microenvironment, and reduction of O_2 produced by intracellular antioxidants Glutathione (GSH) compromise the efficacy of this method. a smart multifunctional synergistic nanoplatform (CMGCC) for T1-weighted magnetic resonance (MR) imaging-guided enhanced PDT is presented, which is composed of nanoparticles composed of catalase (CAT) and manganese dioxide (MnO_2) integrated into chlorin e6-modified glycol chitosan (GC) polymeric micelles. In this system, GC polymers with the ability to change the pH-sensitive surface charge from neutral to positive can improve PS accumulating in the tumor area, CAT could effectively reoxygenate the hypoxic tumor through endogenous catalysis of hydrogen peroxide to O_2, MnO_2 can consume intracellular GSH while simultaneously releasing Mn^{2+} as a Contrast material for T1-weighted MR imaging. Both in vitro and in vivo experiments showed that CMGCC significantly increased the efficacy of PDT against HeLa cells and HeLa subcutaneous tumors. also, It shows that it is a promising synergistic nanoplatform with highly efficient PDT activity for cancer treatment[67-73].

Glucose oxidase, which is known as an effective factor in the treatment of cancer, with the mechanism of producing hydrogen peroxide and glucuronic acid in the presence of oxygen, causes the depletion of glucose and the production of active oxygen radicals, as well as increasing the production of acid, and in this way, it is used in the treatment of cancer. The cancer cell survives through the autophagy system of these mechanisms**.** Studies prove of an anti-cell adaptation strategy based on dendritic mesoporous organosilicate nanoparticles (DMONs) loaded with GOx and 3-methyladenine (3-MA) (an autophagy inhibitor) to target DMON@GOx /3-MA. This formulation can inhibit cell-adaptive autophagy after starvation therapy. Us *in vitro* and *in vivo* results demonstrate that inhibition of autophagy increases the efficacy of starvation therapy and results in tumor growth suppression. This anti-cell adaptation strategy will provide a new avenue to improve the efficacy of starvation cancer therapy[74-81].

A smart nanocarrier responsive to the tumor microenvironment (TME)-responsive biotin/R8 peptide co-modified nanocarriers (BRNC) loading paclitaxel (PTX)/glucose oxidase (GOx) were constructed. The way that first attached the cell-penetrating peptide (R8) to the surface of the nanocarrier, giving it strong penetration capability and also enabling it to escape from endosomal capturing. Simultaneously, long-chain polyethylene glycol (PEG) was introduced into the nanocarrier through an acid-sensitive hydrazone linkage to protect the positive charges of the peptide. In addition, for optimization of the tumor specificity of this nanocarrier, modified biotin was added to the end of the long chain PEG. GOx catalyzes the oxidation of intracellular glucose to gluconic acid and GOx can catalyze the oxidation of intracellular glucose to toxic gluconic acid which finally H2O2 worsen the microenvironment of tumor survival. Both in vitro and in vivo studies showed that simultaneous administration of GOx-BRNC and PTX-BRNC can significantly improve the effectiveness of cancer treatment [82-89].

3 Advantages and Disadvantages

The use of enzymes for the treatment of cancer is associated with many limitations, such as low half-life in the bloodstream, multiple injection times, structural confusion, and low specificity in binding to the target tissue. Conjugating enzymes used in cancer treatment with particles Nano increases the half-life of the enzyme, negligible multidrug resistance, low side effect, increases the stability and speed of the enzyme while passing through the bloodstream, and with the help of special nanoparticle technology, it is possible to increase the specificity of binding of the enzyme to the target tumor tissue[90-93].

The best drug delivery method is the method that has the most accumulation in the tumor tissue without harming the healthy tissues around the tumor. Tumor tissue increases angiogenesis to increase oxygenation and nutrition to its own cells. The vessels produced in this way have larger pores so that nanomedicines with a diameter of 8 to 100 nanometers can pass through. Also, due to the lack of lymphatic system in the tumor tissue, the release of nano drugs is greatly reduced, which called Enhanced Permeability and Retention (EPR)which increases the efficiency of cancer treatment methods based on biolenzymes based on nanoparticles[94-97].

4 Conclusion

The use of enzymes in cancer treatment has always faced problems, such as low half-life in the bloodstream, weak specific binding to the target tumor tissue, low accumulation in the target tissue. But in this mini-review, we learned that by conjugating enzymes with nanoparticles, drugs are produced that have a high specificity to bind to the target tumor tissue and cause drug accumulation in the target tumor tissue, and also have a high half-life in the circulation. are blood and cancer treatment methods such as chemotherapy, photothermaltherapy, immunotherapy, hormone therapy, and radiotherapy can help.

Ethical issue

Author is aware of, and comply with, best practice in publication ethics specifically with regard to authorship (avoidance of guest authorship), dual submission, manipulation of figures, competing interests and compliance with policies on research ethics. Author adheres to publication requirements that submitted work is original and has not been published elsewhere in any language.

Competing interests

The author declares that there is no conflict of interest that would prejudice the impartiality of this scientific work.

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