Research progress on the anti-tumor mechanism and application of deuterium-depleted water

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Abstract: Deuterium (D) is a stable isotope of hydrogen. By reducing the deuterium content in natural water through specific technology, deuterium-depleted water can be obtained Water, DDW). Multiple in vivo and in vitro studies have shown that drinking deuterium-depleted water can enhance the body's antioxidant capacity and immune regulation, exert anti-tumor effects, and has no toxic side effects. This article focuses on the anti-tumor mechanism of deuterium-depleted water and the progress of related application research, in order to provide new preparations for clinical tumor adjuvant therapy.

Keywords: deuterium-depleted water; anti-tumor; mechanism of action; adjuvant therapy

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Research Progress on the Antitumor Mechanism of Deuterium Depleted Water and Its Application

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Abstract: Deuterium (D) is a stable isotope of hydrogen. Deuterium depleted water (DDW) can be produced by specific techniques as reducing the deuterium content of

natural water. Multiple studies in vivo and in vitro have shown that drinking DDW can enhance the body’s antioxidant capacity and immune regulation, playing an anti-tumor

role. It is non-toxic and convenient to drink. This article focuses on the anti-tumor mechanism and related application research progress of DDW, in order to provide new

formulations for clinical tumor adjuvant therapy. Keywords: deuterium depleted water; anti-tumor; functional mechanism; adjuvant therapy.

Hydrogen exists in nature in three isotopes, consisting of one proton, A neutron is called deuterium (D), also known as heavy hydrogen.It can form heavy water (D2O) with oxygen. Deuterium: hydrogen (D/H) = 1: 6 600, the deuterium volume fraction in water after conversion The value is 0.015%. If the volume fraction is less than this value, it is deuterium-depleted water. (Deuterium Depleted Water, DDW). Reducing the deuterium content in water helps activate immune cells and improve the body's basic metabolism, inhibiting cell mutation, etc. [1-3]. Reducing the volume fraction of deuterium in water by 65% can inhibit tumor growth. Clinical trials have shown that drinking DDW (0.001% to 0.002%) can It can stop tumor growth to a certain extent [4] and significantly prolong the patient's survival time and improve the quality of life [5].

At room temperature and pressure, deuterium is a colorless, odorless, non-toxic, flammable gas. In nature, it mainly exists in the form of heavy water (a liquid compound) [6].

The mass number of deuterium is twice that of protium, so the density of D2O is significantly higher than that of H2O. Both the boiling point and melting point increased, and various physical and chemical properties such as ion mobility and ionization degree In the natural environment, a stable concentration of deuterium can.

The protium contained in the object is replaced and accumulated. After the replacement, C-D The bond is more stable than the C—H bond and is not easily broken [6].

If the deuterium concentration is too high, it will reduce the destructive power of biological enzymes on hydrogen bonds. Damage to DNA repair enzymes, resulting in double helix breaks or mismatches, which in turn lead to Genetic factor mutation and even the formation of malignant tumors.

2 Anti-tumor mechanism of deuterium-depleted water

Under natural conditions, the deuterium concentration in the body is 12 mmol/L. The D/H ratio in the body can affect tumor cell division and proliferation, cell signaling Changes in the D/H ratio in the body can affect tumor cells.

The mitosis of tumor cells is inhibited, thus blocking the growth process of tumor cells[5]. The more accepted view is that DDW regulates the growth cycle of tumor cells and/or apoptosis process, thus exerting anti-tumor effects.

2.1 Regulation of tumor cell growth cycle

Some scholars used 0.003% DDW culture medium to test the L929 cells. Cells (mouse fibroblasts) were cultured and found to be more Cultured cells divide more slowly, which can prolong the cell division hysteresis period 5 to 10 h[7]. This study demonstrated that DDW can regulate the cell division process.

In summary, the specific regulatory mechanism of DDW on the cell cycle may be The following are some of them: (1) Long-term culture of DDW can reduce tumor cells (such as The proliferation and differentiation rate of lung cancer cells A549) is inhibited, resulting in cell cycle arrest In the G1/S phase [8-9]; (2) DDW promotes the D/H ratio inside the cell.

Changes occur, the cell cycle regulatory system is blocked, and the tumor cell mitosis, thereby arresting cell growth; (3) DDW can downregulate PCNA protein (proliferating cell nuclear antigen)[10], PCNA is a cell cycle Antigens expressed

in the nucleus of mid-S phase cells are associated with tumor differentiation, metastasis, invasion, Recurrence and prognosis are closely related; (4) DDW can regulate tumor cells P21 protein [11], P21 protein is involved in cell differentiation, growth and The aging process is associated with the occurrence and development of tumors.

Combined with cyclin D (D-type cell cycle protein)/cdk (cyclin dependent The cell cycle is arrested by forming a complex with P21 can also act on PCNA, inhibits PCNA activation of DNA polymerase, thereby reducing DNA synthesis and cell cycle arrest.

2.2 Regulation of tumor cell apoptosis

Apoptosis is the process by which cells end their life activities. The apoptotic cells are eventually killed by neighboring cells through a complex cascade of gene expression. Therefore, inducing tumor cell apoptosis to fight tumor.

Initiating cell apoptosis is also the mechanism by which DDW exerts its anti-tumor effect.

One of the mechanisms. (1) Regulating the apoptosis rate of tumor cells through p53 protein The p53 gene is a tumor suppressor gene, and the p53 protein is a checkpoint regulator. A regulatory factor that regulates the cell cycle from the G1 phase to the S period, thereby inhibiting excessive cell proliferation and accelerating cell apoptosis. It can reduce the expression of proto-oncogenes Ha-ras and C-myc, and has an inhibitory effect on the p53 gene. Because of its up-regulatory effect, it accelerates tumor cell apoptosis [12].

(2) DDW upregulates caspase-3

Protease Protein, Caspase-3) protein, activates the apoptosis process. Caspase-3 is a core regulatory protein in the process of cell apoptosis. The expression level is closely related to cell apoptosis. Western blot results also suggest that DDW medium can induce lung cancer cells The expression of Caspase-3 in A549 cells was increased, and flow cytometry analysis showed that The results confirmed that DDW with different deuterium concentrations can induce lung cancer cells A549 apoptosis [13].

(3) By inhibiting the activity of ATPase,

Increased intracellular Na+ concentration, Ca2+ overload, and impaired mitochondrial function can The synthesis of DDW is blocked, leading to cell apoptosis. It may activate the Caspase signaling pathway [14], thereby reducing ATPase activity. To regulate the proliferation and apoptosis of melanoma A375 cells.

2.3 Inhibition of vascular endothelial growth factor expression

The formation of new blood vessels is an important factor in tumor invasion and metastasis. The main mechanism of angiogenesis is through the endothelial cells and blood Vascular Endothelial Growth Factor This is achieved by overexpression of VEGF. [15]

Lewis lung cancer model mice, and observed the effects of DDW on the organ system of the tumor. The number of tumors, tumor inhibition rate, and lung tissue pathological morphology under light microscopy confirmed that DDW can Down-regulating the expression of VEGF protein, thereby inhibiting the development of cancer in lung cancer model mice It has a certain inhibitory effect.

In addition, scholars have proposed the anti-tumor mechanism of deuterium-depleted water. Many viewpoints have

been proposed. (1) By regulating tumor cell microRNA (miRNAs) expression, inhibiting cell proliferation and/or metastasis ability, and The invasion and differentiation of tumors were affected.

(Colorectal cancer cells) Compared with standard culture conditions, DDW culture The miRNA pattern of exosomes released by cells in culture medium was significantly changed. DLD-1 colorectal cancer cells have increased mitochondrial activity and apoptosis-promoting effect. Domestic scholars have also found that DDW can significantly upregulate Oncogenic miRNAs expression, down-regulation of proto-oncogenic miRNAs expression, considered as One of the molecular mechanisms that inhibits the proliferation and metastasis of lung cancer cell lines [17].

(2) Deuterium can replace hydrogen atoms within the DNA helix structure, thereby Causes malignant tumors, and its mechanism of action is to accelerate the DNA double helix structure The movement, replacement and breakage process causes abnormal arrangement of RNA. DDW can reduce the sugar-phosphorus residues in the DNA backbone.

Deuteration of the acid salt helps maintain the stability of the hydrogen bond network and reduces DNA Damage [18]. (3) DDW has a promoting effect on the body's cell functions.

It can enhance the body's immunity and tolerance, and accelerate the dissolution of blood lipids. speed, thereby playing an anti-tumor role. (4) Deuterium-depleted water can also reduce Expression of proto-oncogenes c-Myc, Ha-ras, Kras, Bcl2, and Myc [19].

3 Application and research of deuterium-depleted water in anti-tumor

Based on the isotope effect, changes in the content of deuterium and protium in water will cause

The physical and chemical properties of DDW are different.

There are no toxic side effects in animals or humans [20-21]. Some researchers [22] The DDW of the experimental animals was collected and their biochemical indices (transaminase, alanine aminotransferase, alkaline phosphatase, creatinine, bilirubin, etc.)

The results showed that preventive use of deuterium-depleted water could correct its metabolic process.

3.1 In vitro studies

The results of multiple in vitro cell culture experiments showed that reducing The concentration of deuterium in the base can delay the proliferation of various cancer cells and even play a role in Inhibitory effects, such as lung adenocarcinoma cells (A549) [23], prostate cancer cells (PC-3)[11], colon cancer cells (HT-29)[11], breast cancer cells (MDA, MCF-7)[24], melanoma cells [25] , etc. Therefore, the academic community generally It is believed that deuterium may be a natural cell growth regulator, or D/H Changes in the ratio may trigger certain Molecular mechanism of bond action.

3.2 Animal Experimental Studies

In 1990, the Hungarian National Research Institute reported that DDW can induce Spontaneous partial or complete regression of malignant tumors in cats and dogs and first injection Registration application for the use of DDW as an anticancer agent in animals. found that DDW can reduce the growth of L929 fibroblast cell line.

In 2010, domestic research The researchers proposed that DDW has both specific and nonspecific immunity on mice. Function has a certain enhancement effect [27]. Recently, a literature [28] reported that deuterium The reduction of the content of

Slow down the migration of differentiated T cells. The above animal studies confirm that DDW It can activate the immune system and have a certain inhibitory effect on tumor growth.

3.3 Clinical application research

Cancer patients who had symptoms remission and long-term drinking of DDW were followed up for 5 years.

It was confirmed that regular consumption of DDW can prevent cancer recurrence and Long-term consumption of DDW may reduce the recurrence rate and/or reduce

Cancer incidence in healthy people. Patients with brain metastasis, prostate cancer, and 129 patients with lung cancer (including Non-small cell lung cancer, small cell lung cancer, lung cancer without metastasis and lung cancer with brain metastasis

Clinical trials in patients with ovarian cancer, breast cancer, and pancreatic cancer showed Both showed that DDW combined with conventional clinical treatment can delay the onset of cancer The above reports support the efficacy of DDW in The possible beneficial effects in tumor prevention and treatment suggest that DDW may be used as a A new adjuvant therapy agent, combined with other tumor treatment methods, Searching for a new and more effective method for tumor prevention and treatment.

4 Conclusion

With the deepening of research on tumor pathogenesis and pathogenic factors, The number of treatments for tumors has increased, mainly including surgery, chemotherapy, radiotherapy, therapy, targeted therapy and immunotherapy.

There are many options and drugs to choose from, but resistance is inevitable. In the face of the complexity of tumors, how to reduce the burden on cancer patients in treatment?To reduce the side effects of treatment, relieve pain and improve the quality of life. In the field of biomedicine, DDW It has been shown to have anti-oxidation [32], anti-radiation [33], and immune cell activation [33]. A number of gratifying research results have been obtained. I believe that DDW will be of certain benefit in the prevention and treatment of tumors in the future. In the future, we may try to study immunity, tissue metabolism, gene transcription and other research directions. Further demonstrate the clinical value of DDW in order to provide a reference for tumor treatment. A new adjuvant therapeutic agent with no toxic side effects.

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