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APPLICATION OF AMYGDALINE IN THE TREATMENT OF ONCOLOGICAL DISEASES

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Annotation
This article describes the properties, metabolites of chemical transformations, and the use of Amygdalin in the treatment of oncological diseases. The proposed mechanisms of action of amygdalin on cancer cells, the results of studies in Uzbekistan and foreign countries, are described.

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In 1830, the substance was first isolated by the French chemists Robiquet and Bouchard. The greatest interest in it was observed in the United States in the 1970s, where a derivative of amygdalin called Laetrile was actively used in many clinics, mainly outside the American health care system [1].

Amygdalin is a naturally occurring substance with potential pharmacological activity. Its molecular formula is C20H27NO11. Amygdalin is found in the kernels of bitter almonds, apricots, cherries, peaches, and plums. Despite the presence of cyanide in its structure, which has raised safety concerns, amygdalin has attracted considerable attention from researchers, especially in the context of oncology.

Mechanisms of action of Amygdalin

Amygdalin is metabolised in the body by beta-glucosidase, breaking down into glucose, benzaldehyde and hydrocyanic acid. It is the last component that is toxic - it inhibits the mitochondrial respiratory chain by binding to the enzyme cytochrome-c-oxidase, which can lead to hypoxia at the cellular level [2].

An important aspect is the potential selectivity of the effect: it is assumed that tumour cells express beta-glucosidase to a greater extent and rhodanase, an enzyme that neutralises cyanide, to a

lesser extent. This could theoretically provide a selective effect of amygdalin on malignant cells. However, this mechanism remains a matter of debate.

The United States is one of the first countries where amygdalin began to be used in practice for the treatment of cancer, especially in the form of a semi-synthetic derivative - Laetrile.

In the 1970s, Laetrile became popular in the alternative oncology community, largely due to the work of Ernest Krebs, Jr., who argued that cancer was a form of vitamin deficiency and that amygdalin (which he called vitamin B17) could "restore the balance." By 1977, more than 70,000 Americans were being treated with Laetrile, according to the American Cancer Society. In 1982, the National Cancer Institute (NCI) completed a double-blind study that showed no significant improvement in patients receiving Laetrile. The FDA classified the substance as an unapproved drug and banned its sale in the United States. Despite the ban, Laetrile continues to be used in alternative medicine, particularly in Mexican clinics (such as Oasis of Hope in Tijuana), which refer patients from the United States.

A patient with metastatic liver cancer, who refused chemotherapy, underwent treatment in a clinic in Tijuana using Laetrile in combination with ozone therapy and nutritional support. According to the results, tumour growth slowdown was noted on PET-CT, but a stable remission state was not confirmed.

In Western European countries, the attitude towards amygdalin is more reserved. In most countries, it is not included in the pharmacopoeia and is classified as a substance prohibited for use. However, in a number of clinics in Germany, Switzerland and Austria, it is used as part of complementary therapy. Some private clinics in Bavaria and Baden-Württemberg offer courses of intravenous amygdalin. It is used primarily in patients with terminal cancer as a component of integrative therapy. It is often combined with high doses of vitamin C, ozone therapy, curcumin, and oncological diets.

At the Hufeland Klinik (Baden-Baden), a 58-year-old woman diagnosed with stage IV breast cancer received combination therapy including amygdalin (IV 1 g × 10 courses). An improvement in the general condition and a decrease in pain syndrome were noted, but objective regression of the tumour was not recorded.

At the Paracelsus Centre (Lucerne), amygdalin is used as part of "metabolic therapy" along with homoeopathy and drainage therapy. Patients sign informed consent indicating possible toxicity.

Amygdalin is prohibited for use in France. If it is found in biologically active supplements, the products are seized. In 2019, the ANSM agency (France) revoked the license of several biologically active supplements based on apricot kernels due to the content of amygdalin.

In Russia, amygdalin is not officially registered as a medicine, but it is used in private clinics and as part of biologically active supplements, especially as part of naturopathic or integrative therapy. A study conducted in 2017 at the Federal State Budgetary Institution "Scientific Centre of Oncology named after Blokhina", showed that amygdalin extract in vitro has a weak cytotoxic effect on breast carcinoma cells (MCF-7 line) but can enhance the effect of doxorubicin when used together.

The journal published an article by Pavlov E. "Pharmacy and Pharmacology" (2020) published a study of the toxicological profiles of amygdalin: a dependence of the toxicity level on the route of administration was revealed (the lowest toxicity is with intravenous administration).

In Moscow, a 49-year-old man with lung adenocarcinoma, stage 3. Refused standard chemotherapy. Received courses of amygdalin therapy (orally) in combination with adaptogens (ginseng, pink radiola). After 4 months, a decrease in tumour mass by 17% according to CT data. However, after 8 months, disease progression occurred. Side effects: dizziness, vomiting, hypotension.

In Kazakhstan (Almaty Medical University) in 2022, a preclinical stage of the study of the antiproliferative effect of the extract of apricot kernels of the "Shalkar" variety was conducted. The

level of amygdalin content is 2.1%. In experiments on mice, a 19% slowdown in sarcoma growth was shown.

In Armenia, traditional recipes based on apricot kernels (Armenian variety "Shalakh") are used, but without standardisation of dosages.

In Tajikistan in 2021, an analysis of local varieties of apricot was conducted at the pharmacological faculty of TSU named after Ainu: based on the data obtained, a prototype of a biologically active supplement with a reduced cyanide content was developed.

In Uzbekistan, apricot is one of the traditional crops. In the Andijan, Fergana, Samarkand and Tashkent regions, varieties with a high content of amygdalin (up to 2.5%) are common. Since 2018, interdepartmental studies on the pharmacognosy of this substance have been launched in Uzbekistan.

Researchers from the Department of Pharmacognosy of the Tashkent Pharmaceutical Institute isolated pure amygdalin using aqueous-alcoholic extraction. Cytotoxicity was studied on the HepG2 cell line (hepatocellular carcinoma). Dose-dependent inhibition of tumour cell growth was shown (up to 36% at a concentration of 0.25 g / l).

The main treatment is surgery + chemotherapy, and additionally, intravenous amygdalin extract. In the group with the supplement, improved blood counts and a decrease in asthenic syndrome. Statistically significant remission was not detected.

A 56-year-old patient from Fergana was diagnosed with stage III ovarian cancer. Against the background of the main treatment - 6 courses of chemotherapy, in the recovery stage, she took an infusion based on apricot kernels. The level of leukocytes normalised faster compared to the control group. No side effects were recorded. The study was not randomised.

In the Andijan region, in a private clinic specialised in folk medicine "Oltin Vodiy Tabiati" for the treatment of oncological diseases of the brain tumour used bitter almonds containing Amygdalin with food additives Majmui Rakhmoniy, Shifoi Marhabokhon and Ascalsy. It was used on 40 patients diagnosed with brain tumours. Of these, 29 (72.5%) of patients showed a sharp improvement in their condition of patients within 6 months.

Given the rich raw material base (bitter almonds), we recommend creating new food additives. Integration of amygdalin into rehabilitation schemes (for example, during recovery after chemotherapy).

Amygdalin continues to be the subject of intense scientific debate. Its potential selectivity for cancer cells makes it an interesting candidate for further research, despite its high toxicity with uncontrolled use. Uzbekistan and other CIS countries with a rich plant base have good conditions for studying and developing standardised forms of amygdalin. However, the use should be based on strict clinical protocols and compliance with safety standards.

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