



Vitamin B17: Cancer Cure or Quackery? A Comprehensive Review

Kangkana Sharma¹, Rituraj Bharadwaj²

¹Department of Zoology, Gauhati University, Guwahati, Assam, India

²Rahman Institute of Pharmaceutical Sciences and Research, Sonapur, Assam, India

Corresponding Author's*Email: bharadwajrituraj@gmail.com

ABSTRACT

Cancer continues to be a formidable global health challenge, necessitating the exploration of novel therapeutic avenues. Amygdalin, a naturally occurring cyanogenic glycoside abundant in seeds of various fruits, has garnered considerable attention as a potential anticancer agent. The review begins by providing an overview of amygdalin's historical use as a traditional remedy for cancer and delves into its controversial status within the medical community. It explores the molecular mechanisms proposed for amygdalin's anticancer effects, including its conversion into hydrogen cyanide and subsequent cytotoxicity, as well as its potential to induce apoptosis, inhibit angiogenesis, and modulate immune responses. The cellular and molecular pathways influenced by amygdalin are discussed in detail, shedding light on its multifaceted actions within cancer cells. The interaction of amygdalin with key molecular targets within cancer cells, such as Bcl-2 family proteins. Clinical perspectives on amygdalin's efficacy and safety profile are also critically evaluated. While early studies hinted at promising results, the lacks of rigorous clinical trials and inconsistent methodologies have raised scepticisms. Moreover, the controversial metabolism of amygdalin and its potential to release toxic cyanide compounds warrant thorough investigation. In conclusion, this comprehensive review provides a balanced synthesis of the current literature surrounding amygdalin's potential as an anticancer agent. While preclinical evidence suggests its promise, the translation of amygdalin into a clinically viable treatment option necessitates rigorous investigation into its mechanisms, potential toxicity, and synergistic interactions with established therapies. By shedding light on the intricate molecular pathways and clinical challenges associated with amygdalin, this review serves as a foundation for future research endeavours aimed at harnessing its therapeutic potential in the fight against cancer.

Keywords: Amygdalin, Vitamin B17, Cancer, Cyanogenic Glycoside, Apoptosis.

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INTRODUCTION

Diseases associated with industrial civilization are one of the greatest problems in developing and developed countries. Technological advances and the resulting environmental pollution are implicated in an increase in diseases such as cancer, diabetes, osteoporosis, obesity, cardiovascular disease, neurodegenerative disease and autoimmune diseases [1]. Cancer is a series of diseases characterized by uncontrolled growth and metastasis of malignant cells throughout the body [2]. From the 20th century to 21st century, cancer was one of the leading causes of death. Cancer patients around the world continue to face significant challenges in their journey towards recovery. In general, approximately 5-10% of cancers can be attributed to genetic defects, while 90-95% are associated with smoking, diet, obesity, lack of physical activity, excessive alcohol consumption, sun exposure, pollution [2, 3]. It is due to environmental and lifestyle factors such as infectious diseases, and so on stress. Although cancer is widely recognized as a preventable disease, cancer-related deaths continue to increase worldwide [3, 4]. In response, the World Health Organization (WHO) is stepping up research, early detection and prevention-focused campaigns to identify lifestyle changes and medical interventions to treat cancer. According to the World Health Organization (WHO), cancer is a leading cause of morbidity and mortality globally, with an estimated 9.6 million cancer-related deaths in 2018 [5, 6]. The physical and emotional toll on cancer patients, as well as their families, is immense, often requiring a multidisciplinary approach to treatment and care. Despite advancements in medical research and technology, access to quality cancer treatment remains unequal across regions, exacerbating the burden for patients in lower middle income countries. Organizations like the Union for International Cancer Control (UICC) and the National Comprehensive Cancer Network (NCCN) are working tirelessly to address these disparities, promote early detection, and provide comprehensive care for cancer patients across the globe [6, 7].

There are many established options for cancer treatment, including radiation, chemotherapy, and surgery. However, herbal medicines have few side effects, high pharmacological effects, and are available at low cost, so they are expected to be future cancer treatments. Natural products are promising resources for the development of chemo-preventive and chemotherapeutic agents. About 80% of all drugs approved by the FDA in the last 30 years are derived from natural sources [6, 7].

The most common medical approach to treating cancer involves surgery. Radiation therapy, chemotherapy, and some methods often used together to achieve synergy. The most common alternative approaches include modified approaches like use of diet, acupuncture, hypnotherapy, bioenergetic therapy, and natural energy therapy [8, 9]. Chemotherapy can cause a range of side effects, including nausea, vomiting, fatigue, and hair loss, anemia, and immune system suppression. These side effects can significantly impact a patient's quality of life [10]. Moreover, chemotherapy drugs target rapidly dividing cells, which includes cancer cells. However, they can also affect healthy rapidly dividing cells, leading to damage in the bone marrow, digestive tract, and other tissues [10]. Further, chemotherapy drugs are systemic, affecting the entire body, which can result in damage to healthy cells and tissues. This lack of selectivity contributes to side effects and complications. Cancer cells can develop resistance to chemotherapy drugs over time, reducing the treatment's effectiveness and requiring alternative approaches [10].

Herbal medicine is rooted in the use of plants and plant-derived compounds to promote health and healing. Many plants contain bioactive compounds with potential anti-cancer effects. One of the key advantages of herbal medicine is its potential to minimize the harsh side effects often associated with conventional cancer treatments such as chemotherapy and radiation therapy [11]. These remedies may offer a gentler approach, targeting cancer cells while sparing healthy ones. Herbal treatments may enhance a patient's overall well-being by alleviating symptoms, reducing pain, and supporting the body's natural healing processes. This can lead to an improved quality of life during and after cancer treatment. Herbal medicine could be used in combination with standard cancer treatments to enhance their efficacy and reduce side effects [11]. This integrative approach is gaining traction among healthcare practitioners. Moreover, herbal treatments can be tailored to individual patients based on their specific cancer type, genetic makeup, and overall health. This personalized approach has the potential to yield better outcomes [11].

Cancer continues to be a formidable health challenge, prompting ongoing research into potential treatments and preventive measures. Amid this pursuit, a substance known as Vitamin B17, also referred to as amygdalin or laetrile, has garnered attention as a potential anti-cancer agent. However, the use of Vitamin B17 in cancer treatment remains controversial, with conflicting viewpoints on its effectiveness and safety. Vitamin B17 gained prominence due to its association with apricot kernels, which contain a compound called amygdalin. Advocates of Vitamin B17 propose that this compound, when ingested, releases cyanide, a toxic substance, which purportedly selectively targets and destroys cancer cells while sparing normal cells. This mechanism, often touted as "targeted chemotherapy," has led to widespread interest in using Vitamin B17 as a natural and holistic alternative to conventional cancer treatments.

Amygdalin, a disaccharide found in mostly in fruit kernels of peach, bitter almond and apricot. We have seen the use of these fruits since ancient time as for treatment of many diseases [12, 13]. Beta-glucosidase, which is stored in plant cell compartments and is also present in the human small intestine, degrades amygdalin to prunasin, mandelonitrile, glucose, benzaldehyde, and hydrocyanic acid [14, 15]. Hydrogen cyanide (HCN), benzaldehyde, prunasin and mandelonitrile can be absorbed into the lymphatic and portal circulation. Amygdalin's anticancer activity is believed to be related to the cytotoxic effects of enzymatically released HCN and unhydrolyzed cyanoglycosides [16].

Derived from amygdalin, laetrile has been used as a complementary and alternative natural therapy in the treatment of cancer for over 30 years. Studies of amygdalin on various cancer cell lines have shown its anti-cancer effects, and claims of patient studies conducted by the US Food and Drug Administration in the late 1970s confirmed this [17, 18].

Exploring the Cyanogenic Glycosides

Amygdalin belongs to the cyanoglycosides (CG) group of organic compounds composed of sugars and aglycones containing a 1-cyanobenzyl moiety. The 1-cyanobenzyl moiety is attached to the hemiacetal OH group located at the anomeric carbon atom of the sugar moiety [19, 20]. The primary function of cyanogenic glycosides is to protect plants from insects and large herbivores. Amygdalin levels typically increase during fruit enlargement and remain constant or slightly decrease during ripening. In peach seeds, the amygdalin content is higher in the endocarp than in the mesocarp. The bitterness of almond grains is determined by the content of cyanogenic amygdalin diglucosides [19, 20].

Medical uses of CG are primarily associated with amygdalin, which was discovered in 1830. French chemists Pierre-Jean Robiquet and Antoine-François Boutron-Charlard. The theory of Dr. Ernst T. Krebs Sr., Amygdalin Could Be an Effective Anticancer Agent, but It actually Works Toxic to humans, published in 1920 [21, 22, 23]. Despite this statement, his son became Ernst Theodore. Krebs his Jr. in 1952 synthesized a less toxic single-subunit amygdalin derivative. He named it Laetrile. Amygdalin and a mixture of its modifications are literally not amygdalin or amygdalin, but is described as "vitamin B17" by cancer. Laetrile is also not a vitamin. In 1977, the FDA (USA) issued a statement pointing this out. There was no evidence regarding the safety and efficacy of laetrile [21, 22, 23].

Amygdalin and laetrile banned in US and Europe. It is a Mexican laboratory and clinic that provides amygdalin preparations and treatments. Over the years (e.g. Cyto Pharma De Mexico, 40 years on the market), but there there are no solid clinical data proving the effectiveness of these treatments in patients [24]. In contrast, in-vitro cell culture studies have shown the presence of various amygdalin activities beneficial in cancer treatment. For example, amygdalin can: Apoptotic proteins and signalling molecules, which may justify their decline in tumor growth [24]. Treatment with amygdalin increased and decreased Bax expression Bcl-2 expression and induced caspase-3 activation in DU15 and LNCaP human prostates cancer cells, induced apoptosis of his HeLa cervical cancer cells via endogenous substances reduced adhesion and migration of mitochondrial pathways, UMUC-3 and RT112

Bladder cancer cells by activation and regulation of focal adhesion kinase (FAK) β -1 by integrins. Amygdalin also has the ability to inhibit anti-apoptotic expression genes including Survivin and XIAP genes. Other biological activities of Amygdalin antibacterial, antioxidant, anti-atherosclerosis, anti-asthma, prevent lung and liver fibrosis. Amygdalin also improves microcirculatory disturbances, reduces pancreatic fibrosis. It has anti-inflammatory and analgesic properties and stimulates muscle cell growth [24].

Glimpse into the mechanism of Amygdalin as anticancer

According to research by Ernest T. Krebs, Jr., rhodanese is a human enzyme that is present throughout the body, except in tumor cells. This enzyme can convert hydrocyanic acid (found in vitamin B17) to thiocyanate. Thiocyanate has a positive effect on the body by lowering blood pressure and is a precursor of vitamin B12 and the enzyme beta-glucosidase. Beta-glucosidase is abundant in cancer cells but absent in other normal cells of the body [25, 26, 27]. The β -glucosidase enzyme is absent in normal healthy volunteers without cancer. Vitamin B17 consists of: the chemical composition of B17 consists of one molecule of benzaldehyde (an analgesic), one molecule of hydrocyanic acid (hydrocyanic acid), and two molecules of glucose. When vitamin B17 is added to the body, it is broken down by the enzyme rhodanese. This enzyme breaks hydrocyanic acid and benzaldehyde into two by-products, thiocyanate and benzoate [25, 26, 27]. These have a positive effect on the nutrition of healthy cells generation of a metabolic pool of vitamin B17. When B17 comes into contact with cancer cells, there is no rhodanese to degrade and neutralize it, only the enzyme β -glucosidase, which is abundant in cancer cells, works. Thus, when B17 and beta-glucosidase come into contact with each other, a chemical reaction is initiated that synergistically combines hydrogen cyanide and benzaldehyde to produce a toxin that destroys and kills cancer cells. This whole process is called selective toxicity. Only cells exhibiting tumor or cancerous growth are specifically attacked and destroyed [25, 26, 27].

Amygdalin as immunomodulator

In other words, amygdalin greatly increases the secretion of polyhydroxyalkanoates through the proliferation of circulating T lymphocytes [28]. This process results in the secretion of interleukin (IL) 2 and interferon (IFN) γ [29]. However, β 1 secretion of transforming growth factor beta 1 (TGF) is inhibited, ultimately leading to improved immune function. However, the regulatory role of amygdalin in monitoring T lymphocyte cell expression should not be overlooked. In clinical studies, 10 mg/kg amygdalin inhibited immune cell proliferation. In other studies, this dose also reduced immunosuppressive activity in kidney-transplanted mice [30, 31]. Her two aspects of immune system function are observed in patients after ingestion or injection of amygdalin. According to some findings, amygdalin increases the efficiency of immune cells. However, in some cases, patients have an increased organ transplant success rate [32, 33]. Thus, it can be a beneficiary action of amygdalin as it may help the immune compromised patient during the chemotherapy.

Amygdalin in cell cycle

It has been reported that, uncovered prostate cancer (PCa) cell lines LNCaP, DU-145 and PC3 to diverse concentrations of amygdalin, and found that cell multiplication was repressed particularly as spoken to by a noteworthy diminish in G2/M stage and S stage cells whereas a critical increment within the number

of stage and G0/G1 stage cells by stream cytometry [34]. In expansion, the expressions of cell cycle proteins such as CKD1, CKD2, cyclin A, and cyclin B were diminished after amygdalin organization, demonstrating that amygdalin restrained cell multiplication by controlling the cell cycle of PCa cells. So also, amygdalin applied its antitumor impact by influencing the cell cycle of human colon cancer. The result of cDNA microarray examination appeared critical contrasts in quality expression of SNU-C4 cells after amygdalin treatment at a dosage of 5 mg/mL for 24 hours [35]. They found that amygdalin down-regulated the cell cycle-related qualities: ATP-binding cassette, exonuclease 1 (EXO1), sub-family F and topoisomerase (DNA) I (TOP1) in SNU-C4 human colon cancer cells, in this manner influencing tumor cell cycle, restraining cell expansion and applying its antitumor impact. These comes about illustrated that amygdalin may avoid threatening expansion of tumor cells by controlling tumor cell cycle-related proteins or qualities, influencing cell cycle and restraining cell expansion, particularly in human PCa and colorectal cancer.

Amygdalin in trials

One of the early proponents of laetrile, a chemically modified form of amygdalin, claimed that it is effective, which he cited as one of the reasons for its continued popularity over the years [35]. Additionally, Sir Ernst Krebs Jr., who believed that cancer is caused by a vitamin deficiency, suggested that amygdalin could be the missing vitamin. He publicly declared that laetrile is vitamin B17, a claim that gained acceptance among many Americans and political figures in the mid-1970s, but was later refuted [35]. A recent review titled "Amygdalin: quackery or cure" by Blaheta et al. provides a comprehensive overview of current knowledge on amygdalin trials. The review, based on an analysis of numerous journals from the reputed database and other relevant internet sources, concludes that there is insufficient evidence to support the notion that amygdalin can effectively treat cancer, and therefore, the matter remains inconclusive. The review reports that clinical trials in cancer patients showed no induction of apoptosis or tumor regression, particularly in advanced stages of the disease. However, the authors also note that purified amygdalin does not appear to be toxic to normal cells. The therapeutic potential of amygdalin with multiple administrations was not determined. Another group of researchers from Cancer Networks discredited laetrile as a cancer cure, comparing it to false beliefs about AIDS being a disease created to target black people and autism being caused by vaccines.

Challenges and opportunities for Amygdalin in cancer therapy

The efficacy of amygdalin as a cancer treatment lacks robust scientific evidence from well-designed clinical trials. Most claims are based on anecdotal reports and testimonials, which do not meet the rigorous standards required to establish its effectiveness. Amygdalin contains a compound called cyanide, which is toxic to the body even in small amounts. While proponents argue that the cyanide is released selectively to target cancer cells, the potential for cyanide poisoning and harm to healthy cells remains a significant safety concern. Many health regulatory authorities, including the U.S. FDA, have banned or restricted the use of amygdalin-containing products due to safety concerns and the lack of scientific evidence supporting its efficacy. This limits its availability and use as a cancer therapy. Relying solely on amygdalin as a cancer treatment could lead to delays in receiving evidence-based and clinically proven therapies, which may be more effective in treating cancer. Delayed or inadequate treatment can have serious consequences for patient outcomes. Promotional efforts and misinformation about amygdalin may lead patients to believe it is a legitimate cancer treatment, potentially diverting them from well-established and effective therapies. The quality and purity of amygdalin-containing products can vary widely, as they are not regulated with the same rigor as pharmaceutical drugs. This poses risks for patients who may not know what they are actually ingesting. Pursuing amygdalin treatment can be costly, and patients may spend significant amounts of money on an unproven therapy, diverting resources from evidence-based treatments. Promoting and administering unproven or potentially harmful treatments like amygdalin raises ethical concerns, as patients may be vulnerable and seek alternative options out of desperation. In some cases, individuals promoting or providing amygdalin treatment may face legal challenges due to the lack of scientific validation and potential risks to patients' health. The promotion of unproven therapies like amygdalin can erode public trust in the medical and scientific communities, as patients may become disillusioned if promised outcomes are not achieved.

While amygdalin, also known as Vitamin B17 or laetrile, has faced significant challenges and controversies as a potential cancer therapy, there are some perceived opportunities for its use. It's important to note that these opportunities are subject to scientific research and validation, and any potential use of amygdalin should be approached with caution and in consultation with qualified healthcare professionals.

Amygdalin contains cyanide and other compounds that, in theory, could have anti-cancer properties. Research is on-going to investigate whether these compounds could be modified or utilized in a way that selectively targets cancer cells while minimizing harm to healthy cells. Some proponents of amygdalin suggest that it could be used in combination with conventional cancer treatments to enhance their efficacy while potentially reducing side effects. This integrative approach is being explored to determine if there are synergistic effects. Amygdalin is derived from certain plant sources, including apricot kernels and bitter almonds. These natural sources could provide a foundation for the development of new compounds or drugs with potential anti-cancer properties. Some research suggests that amygdalin may be more effective against certain types of cancer cells. Identifying these specific cancer types and mechanisms could lead to targeted therapies in the future. Amygdalin may have a role in supportive care for cancer patients by alleviating symptoms, managing pain, and improving overall well-being. This could contribute to enhancing the quality of life during cancer treatment. As research progresses, it's possible that amygdalin or its derivatives could be part of personalized treatment plans based on an individual patient's cancer type, genetic makeup, and overall health. Scientific exploration of how amygdalin interacts with cancer cells and the potential mechanisms behind its effects could lead to valuable insights into cancer biology and treatment strategies. Some studies have looked at amygdalin as a potential preventive measure against cancer. Research into its effects on cancer development and initiation could contribute to preventive strategies. Research is exploring the possibility of combining amygdalin with other natural compounds, conventional treatments, or targeted therapies to create more effective and tailored treatment regimens. This approach could capitalize on the strengths of different treatments and enhance overall outcomes. Some studies suggest that amygdalin may have immunomodulatory effects, meaning it could influence the body's immune response against cancer cells. Further research into these effects could open up avenues for immunotherapy strategies. As research advances, it's conceivable that certain patient profiles or genetic markers could help identify individuals who might respond positively to amygdalin-based treatments. This could contribute to personalized medicine approaches. The specific mechanisms by which amygdalin may affect cancer cells are still not fully understood. Further investigation into these mechanisms could provide valuable insights into potential therapeutic targets for cancer treatment. In the realm of integrative and holistic medicine, amygdalin may have a place in patient-centred care, where patient preferences and beliefs are considered alongside evidence-based treatments. This approach respects patients' autonomy while ensuring their safety and well-being. While not a replacement for proven cancer treatments, amygdalin might have a role in cases where standard therapies are not suitable due to a patient's health status, preferences, or specific circumstances. Regardless of its ultimate efficacy as a cancer therapy, research into amygdalin and its effects on cancer cells contributes to our understanding of cancer biology and treatment options. Findings from such studies could pave the way for the development of entirely new classes of anti-cancer agents.

CONCLUSION

The perceived opportunities for amygdalin as a potential cancer therapy underscore the complexity of the field and the on-going quest for innovative approaches to cancer treatment. While these opportunities offer a glimmer of potential, it is crucial to approach amygdalin and similar alternative treatments with scepticism, scientific rigor, and a deep commitment to patient safety. Rigorous clinical trials, evidence-based research, and transparent communication are essential to determine whether amygdalin can truly fulfil its potential as a viable cancer treatment. Until then, patients are strongly advised to prioritize proven and well-established cancer therapies in consultation with knowledgeable healthcare professionals.

The Conflict of Interest: Nil

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