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Amygdalin - A Nascent Vitamin B17: A Review

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ABSTRACT
Amygdalin, or vitamin B17 or laetrile, is a naturally occurring compound in raw fruits, nuts, and seeds. This review examines amygdalin's chemistry, history, and pharmacological effects. It was first isolated in the early 1800s and used to treat cancer in 1845. Amygdalin is shown to break down into toxic hydrogen cyanide, which is thought to target cancer cells selectively. Proposed pharmacological effects include treating asthma, pain, inflammation, and anticancer properties. Anticancer mechanisms promote apoptosis, inhibiting proliferation, metastasis, and angiogenesis in cancer cells. However, human trials are limited, and the FDA has not approved amygdalin for cancer treatment due to concerns about its safety. While preclinical studies are promising, further research is needed to demonstrate amygdalin's safety, dosing, and clinical anticancer effects conclusively.

Keywords: Amygdalin, Antitumor, Cyanogenic, Toxicity, Vitamin B17

I. INTRODUCTION

The compound known as amygdalin, also called "mygdalin" and "dietary B17," is believed to possess potential anticancer properties, which is of significant concern given the prevalence of cancer as a major health challenge. Amygdalin is a cyanophytoloside belonging to the Rosaceae family and can be found in the seeds of various raw fruits (Chen Y. 2013). The manifold medicinal uses of amygdalin encompass anti-atherosclerotic activity, anti-renal and pulmonary fibrosis, anti-inflammatory effects, as well as potential antitumor properties. Today, the efficacy of amygdalin in anticancer therapy is a subject of both importance and debate. Despite limited clinical research and some evidence of amygdalin's effectiveness against cancer, the FDA does not fully endorse its use for cancer treatment.

II. MEDICAL CARE THROUGH AMYGDALIN IN INDIVIDUALS.

Manuel Navarro (1957, 1971) administered amygdalin to over 490 patients, employing intravenous and oral delivery methods (M. et al. MD, 1984). Many successfully treated cancers included gastric, lung, breast, rectal, esophageal adenocarcinoma, lymphosarcoma, and fibrosarcoma. Binzel PE treated cancer patients from 1974 to 1991, employing syringes with doses ranging from three to nine grams and one gram of oral amygdalin at bedtime. Contreras E. et al. (1980) found that amygdalin effectively prevented cancer, and its non-toxic nature allowed its use during surgical procedures, radiation therapy, and chemotherapy. When combined with vitamin A and enzymes, amygdalin demonstrated effectiveness (WJ, 1980). Schacter M et al. recommended using cysteine in conjunction with vitamin B17 to mitigate the cyanogenic effects of vitamin B17. The most compelling case series, published between 1953 and 1962, provided strong evidence for using amygdalin. However, the need for a sufficient number of control groups and the positive outcomes being primarily based on subjective improvements in health were noted as limitations. Amygdalin was initially isolated by French chemists in 1830 and was first used as an anti-cancer treatment in Russia in 1845. It gained use in the United States in the 1920s. The National Cancer Institute (NCI) conducted over 20 case studies on the potential benefits of amygdalin as an alternative treatment, with less than seven yielding successful results. Nevertheless, the FDA banned the use of amygdalin in 1979.

III. CHEMISTRY OF LAETRILE

Amygdalin's chemical composition consists of several components:

- Cyanogenic Glycoside: Amygdalin is classified as a cyanogenic glycoside, a compoun no d composed of a sugar molecule (glycoside) linked to a cyanide group. Its potential therapeutic benefits and toxic

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properties are attributed to the presence of the cyanide group.

- Sugar Component: Typically, the sugar portion in amygdalin comprises a glucose molecule bonded to the cyanide group.
- Aromatic Rings: The structure of amygdalin includes aromatic rings, placing it within the broader category of compounds known as benzylisoquinoline alkaloids. This feature is commonly found in various plant-derived compounds.
- Hydroxyl Groups: Hydroxyl groups (OH) are also part of amygdalin's structure, and they can participate in various chemical reactions.

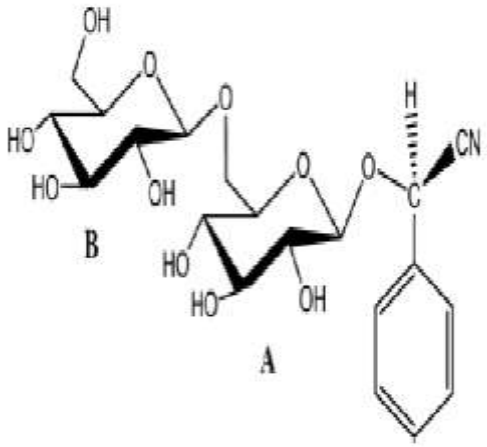

Figure 1: Chemical structure of amygdalin

IV. MECHANISM OF ACTION

Ernst T. Krebs Jr. introduced a regimen involving Vitamin B17, also known as amygdalin, asserting that rhodanese is typically found within normal cells. It is composed of two parts glucose, one part hydrogen cyanide (HCN), and one part benzaldehyde. In contrast, rhodanese interacts with Vitamin B17, converting HCN and benzaldehyde into non-toxic compounds, thiocyanate, and benzoic acid, which nourish healthy cells (T. et al. J, 2016). Most cancer cells contain the enzyme beta-glucosidase. When it comes to laetrile, a compound related to Vitamin B17, it approaches most cancer cells. However, it is broken down by beta-glucosidase into benzaldehyde and HCN, creating a toxic effect that selectively destroys cancer cells in a harmful manner. The transportation mechanism of amygdalin within the body relies on zinc. Manner et al. suggest that cancer can be effectively managed with dietary interventions, specific nutrients, pancreatic enzymes, and amygdalin. Li Yun-long et al. focused on amygdalin, observing that cancer cell nuclei exhibited positive signs of HCN release and cancer treatment through beta-glucosidase activity.

V. PHARMACOLOGICAL EFFECTS

5.1. Bronchial asthma affects

Vitamin B17 Became utilized in historic Korean remedies to prevent allergies. After oral management, amygdalin breaks down into benzaldehyde and cyanic acid, which is obtuse respiratory and has an allergy and cough suppressant sequel. Laetrile kills kind two helper T cells that inhibit Th2 reaction to allergen. (T. I. Makarević J 2016) (Dorr RT 1978)

5.2. Consequences on human kidney fibroblasts

Amygdalin inhibits the expression and production of positive collagenase kind 1 in human kidney fibroblasts, which promotes apoptosis of human kidney fibroblasts.

5.3. Position in immunity

Polyhydroxyalkanoate stimulates human T lymphocytes to produce IL-2, inhibit viruses, and counteract TGF-B1, thereby boosting the immune response. Vitamin B17 plays a role in regulating T cells, according to Navarro, M. (1971), aiding in the treatment of psoriasis and atherosclerosis, and also has the potential to increase the inner surface area of blood vessels, reducing aortic plaque buildup.

5.4. Outcomes on digestion

Research has found that prunasin is a crucial element of vitamin B17 in digestive fluids. In the mobile culture gadget. It changed into degraded within the small gut to mandelonitrile with the aid of β-glucosidase and hydroxylase, yielding hydroxymandelonitrile. Amygdalin breaks down benzaldehyde via enzymatic degradation, which could inhibit the motion of pepsin and influence the digestive device (Park HJ 2005). Additionally, amygdalin has a remarkable healing effect in rats with continual gastritis and persistent atrophic gastritis.

5.5. Pain relieving effect

Studies have indicated that isolating vitamin B17 from Prunus armeniaca can alleviate formalin-induced pain in rats. This effect may be associated with anti-inflammatory cytokines, such as TNF and IL-1, as well as the c-Fos protein. Investigations into the impact of amygdalin have

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demonstrated its influence through the modulation of pro-inflammatory expression. Anti-inflammatory cytokines seasoned-IL-1 beta. Hypoglycemic effect: Amygdalin prevents alloxan-precipitated hyperglycemia (Qadir M 2017). That is due to removing detrimental and diplomatic hydroxyl radicals fabricated by alloxan.

5.6. Antitumor effect

Schrader discovered this activity in 1803 in Almonds. A Russian doctor used it for the first time in a cancer remedy in 1845. It became utilized in Mexico and manufactured in massive quantities as an anticancer drug (R. J. Makarević J 2014). Amygdalin can provoke apoptosis in HL-60 cells and inhibit cancer in the human colon. SNU-C4 manufacturing can initiate apoptosis by synchronizing the expression of Bax and Bcl-2 in most prostate cancers. It also lessen the presence of Hela cells by apoptosis in rats through an endogenous mitochondrial pathway. Human genome microarray observation effects confirmed that during Hela cells (Liu C 2017), Five hundred seventy-three genes exhibited distinct expression patterns in the group treated with amygdalin compared to the control group. Notably, the JNK-c jun pathway was among those genes affected. Vitamin B17 has been proposed as a 2nd line of protection.

5.7. Bronchogenic cancer

Qian et al. suggested demonstrated anti-cancer effects in Non-Small Cell Lung Cancer (NSLC) by suppressing the AKT-mTOR signalling pathway. Amygdalin was employed in treating metastatic cell lines dad/M and and dad/M, inhibiting all proliferative and migratory capabilities (Li X, 2016). Vitamin B17 has been identified as a factor that reduces the levels of critical agents like beta 4, beta 1, ILK, and beta-catenin, which are known to promote cancer metastasis. It also regulates the expression of E-cadherin and decreases AKT phosphorylation (Do JS, 2006).

5.8. Bladder most cancers

Makeravic et al. observed the adhesion of vascular tumour cells, collagen, and the migration of tumour cells. They investigated the impact of amygdalin on various integrin alpha and beta subtypes, as well as ILK and FAK (Park HJ, 2005). Following the treatment of bladder cancer nuclei with specific doses, they noted a significant reduction in cell adhesion and migration.

5.9. Hypernephroma

Juengel et al. observed reduction in S phase with amygdalin and substantially decreased the proliferation of RCC cells (EJ, 1980). Additionally, it notably diminished the levels of cell cycle regulators, such as cyclin B, CDK 1, N-cadherin, and E-cadherin.

5.10. Squamous cell carcinoma

Juengel et al. suggested proapoptotic influence on HeLa cancer cells of the cervix through the intrinsic mitochondrial pathway was contributed by amygdalin (Juengel E, 2016).

5.11. Malignant tumour of the breast

Research indicates that Vitamin B17 exhibits anti-proliferative effects in ER sensitive MCF7 cells and in Hs578T-TNBC and MDA-MB-231 cells. It reduces Bcl-2 and Bax levels, activates caspase-3, and cleaves PARP. Amygdalin induces a cytotoxic impact on human breast cancer cells and hinders the growth of MCF7, Hs578T and MDA-MB-231 cells. A MTT assay conducted after a 24-hour treatment with laetrile at various concentrations resulted in cytotoxic effects on ER-positive MCF7 cells and Hs578T-TNBC and MDA-MB-231 cells (Navarro, 1971). In experiments, amygdalin was administered at varying concentrations for one day, and the levels of Bax, pro-caspase-3, Bcl-2, and PARP were quantified through immunoblotting. It was observed that an elevated levels of the proapoptotic protein Bax while decreasing the expression of the antiapoptotic Bcl-2. These findings suggest that amygdalin triggers apoptosis in Hs578T cells, potentially involving a signalling pathway mediated by p38 MAPK. Amygdalin interferes with the adhesion of Hs578T in cancer cells of the breast (Dorr RT 1978). It successfully stopped the invasive phenotype of Hs78T breast cancer cells. Amygdalin treatment decreased α5-integrin stages. (M. M. Holzbecher MD 1984) it is commonly believed that amygdalin has apoptotic and adhesive consequences on breast cancer cells. For that reason, this shows that amygdalin can be used as a chemotherapeutic agent within the remedy of most breast cancers, especially TNBC, in the future.

5.12. Prostate most cancers

Makerevice identified prostate cancer cell lines' response to Vitamin B17, noting that cell

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proliferation ceased due to a significant reduction in the G2M-phase and S-phase nuclei, as observed through cytometry.

5.13. Bowel or rectal cancers

Vitamin B17 exerts an impact on cancer of the human colon. Park et al. observed alterations in the gene expression on the cells of SNU-C4 following the treatment. Amygdalin downregulates cell cycle-related genes, including exonuclease 1, ATP-binding cassette, and topoisomerase, in colon cancer cells of SNU-C4 (Chittranjan et al.). Research has confirmed that amygdalin treatment has demonstrated effectiveness in cancer by impeding cell proliferation and disrupting the telomerase feedback mechanism in human cancer cell lines, achieved through an increase in β-glucosidase activity.

5.14. Ovarian most cancers

The study observed that the optimal dosage iniciated the release of estradiol-17β by ovarian GC. However, no changes in GC-induced progesterone release were detected after adding amygdalin.

VI. CONCLUSION

In summary, amygdalin is a naturally occurring compound used in cancer treatment despite some concerns regarding its safety. The preclinical evidence presented in this review indicates several mechanisms, such as promoting apoptosis, inhibiting proliferation, preventing metastasis, and regulating signalling pathways. Amygdalin may be well-tolerated, but its cyanide content poses risks of toxicity that require further study. More high-quality human trials with large sample sizes and standardized amygdalin preparations are needed to understand its role in integrative oncology better.

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TU, VM and SAP contributed equally in manuscript preparation. All authors have read and approved the manuscript.
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