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A Review: Contribution of Vitamin B17 as Oncological Inhibitor and its Pharmacological Ameliorative Activity

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Abstract: ***Vitamin B17 is also known as Amygdalin. Source of vitamin B17 are stone fruit kernels, bitter almond, apricot, peach, and the plum. Vitamin B17 is often considered as cure of cancer. Cancer is a disease caused by an uncontrolled proliferation of tumour cells. The scientific name of Vitamin B17 is mandelonitrile beta-D-gentiobioside, is known as a nitriloside (a natural cyanide-containing substance).Above and beyond the beneficial effects, it can be extremely poisonous because of the high level of cyanide, In the past this was the main cause of the failure of many clinical trials linked with anticancer effects of vitamin B17. Vitamin B17 produces hydrogen cyanide and its release in the tissue of the body and targets the tumour cells. In this review we will discuss about the natural source of B17, pharmacological effects, mechanism of action of vitamin B17.***

Keywords: Vitamin B17, Amygdalin, cancer cells, tumour cells, pharmacological effects

1. Introduction

Vitamin B17/Amygdalin/Laetrile is the greatest contentious vitamins in the previous three decades. Chemically, it is a cyanogenic di-glucoside, on the other hand a condensed formula of $C_{20}H_{27}NO_{11}$, and a MW (molecular weight) of 457. The chemical name of D Mandelonetrile-betaglucoside-6 beta-D-glucoside. Initially Amygdalin was invented in the early nineteenth century in France as a vigorous component of several fruit pits and raw nuts [1]. Vitamins are a assemblage of organic molecules required in minute quantities for normal metabolic utility and growth. The word vitamin is consequent of the Latin word “vita” which means life, Vitamins is not synthesized in the body and are obtained from plant and animal sources. They assist in concoction of hormones, blood components and neurochemicals. In combination with proteins catalyze thousands of reactions in the body by activating different metabolic enzymes. There are various vitamins such as A, B-complex, C, D, E, K [2]. Primarily, Two French chemists isolated Amygdalin (Vitamin B17) in 1830 [3], [4]. Moreover this vitamin is used as anticancer agent in Russia before 1845 [5], [6], whereas the first recorded utilization of amygdalin in the United States as a treatment for cancer happen in the early 1920s [7]. E.T. Krebs Jr gave the name vitamin B-17 to laetrile, although it was not permitted via the Committee on Nomenclature of American Institute of Nutrition Vitamins.

By the process of decomposition cyanide is released from Mandelonitrile which is referred as the constituent of the laetrile molecule. A 500 mg laetrile tablet could have between 5–51 mg of hydrogen cyanide per gram.[8] The cytotoxic effects of amygdalin in opposition to cancer cells are related with the release of hydrogen cyanide (HCN), which is an antitumor complex, decomposing carcinogenic substances in the body, inhibiting cancer growth and blocking nutrient source of tumor cells [9] Leatrile isdelivered to cancer cells along with glucose are not neutralized to rhodanide and benzoic acid due to requirement of rhodanese enzyme in neoplastic cells. As a substitute, neoplastic cells liberate cyanide and benzaldehyde from delivered glucose by the accomplishment of β-glucosidase found in cancer cells. In turn, the released cyanide and benzaldehyde cells by development of a killing targeted poison [10].

Neoamgdaline is therapeutically as inadequate as amygdaline and a viable combination of each is called isoamygdaline [10], [11].

2. Sources

Different source of vitamin B17 is the apricot kernels (i.e. Prunusarmeniaca). Amygdalin is present in a small amount of stone fruit kernels, like bitter almond (5%), apricot (1.4%), peach (0.68%), and the plum (0.04–1.7%), It’s also present in the seeds of apple (0.3%).[12] The stones are taken out of the fruit, cracked to get the kernels, that are desiccated in oven or in the sun. Af ter that the kernels are boiled in ethyl alcohol and evaporated and then diethyl ether is added. The chemical amygdalin at this time precipitates as miniature white crystals. [13]

3. Pharmacological activity of vitamin B17

Amygdalin is very useful part of the traditional Chinese medicine (TCM) found in bitter almond, which has been studying on from two hundred years. As near the beginning in 1803, Schrader found this material in learning the bitter almond ingredients. In anticipation of 1830, Robiquet extracted amygdalin from the bitter almond, which has always been used as auxiliary medicine of cough expectorant agent and cancer remedy. [14], [15]

3.1 The anti-tumor effect of amygdalin

Cancer is also known as a malignant tumor, this is defined by

uncontrolled cell growth which have the potential to attack on the other tissues of the body. Along with chemotherapy, radiotherapy and surgery, immunotherapy also grips a capable coverage for cancer therapy; although, formation of an effectual and proficient technique is one of the most interesting matter in the modern research area. [16], [17]. As vitamin B17 have cytotoxic and anti-cancer effects which can treat human cancerous cells [18] Amygdalin is generally used as a alternate therapy for treatment of cancer, or in combination with an additional nonconventional treatment, like metabolic therapy, urine therapy, dietotherapy, intake of fruit seeds, and intravenous injection of β-glucosidases and so on. [19]-[21] β-glucosidases is an enzyme which was initiated from the intestinal bacteria, [22] it can also be found in edible plants, with the purpose of decomposing amygdalin into benzaldehyde, glucose and hydrocyanic acid. [23] Amygdalin also exists in the correlated products of amygdalin and Laetrile, which is the active constituent of drugs. [24], [25]

3.2 Analgesic effect

The mouse hot plate and acetic acid-induced writhing test showed that amygdalin has analgesic effects and no tolerance; mice lack tail-erecting response and after treatment with amygdalin nalorphine induced jump response. This effect of nalorphine paves the way of concept of opioid role in its action which was confronted by others [26], [27]. This method might connect with inflammatory cytokines such as tumor necrosis factor-α (TNF-α) and interleukin-1β (IL-1β), as well as c-Fos. [28], [29] Likewise, in mouse BV2 microglial cells, amygdalin produced antiinflammatory and analgesic effects probably by inhibiting prostaglandins E2 and nitric oxide synthesis through suppressing lipopolysaccharide (LPS) induced expression of cyclooxygenase (COX)-2, inducible nitric oxide synthase (iNOS) on mRNA levels. [30], [31]

3.3 The effects on the digestive system

Benzaldehyde is an additional constituent which is decomposed by amygdalin through the enzyme decomposition. It is used to inhibit the activity of pepsin and have an effect on the digestive function. Administration of pepsin hydrolysate of almond water-solution at a dose of 500 mg/kg on CCl 4 treated rats, which found that it could inhibit the level of AST, ALT and increase hydroxyproline content, inhibiting the extention of euglobulinlysis time. In pathology, the soluble pepsin hydrolysate of almond water can inhibit the proliferation of connective tissue of rat liver, but could not inhibit D2 D-galactosamine induced the increase of rats' AST, ALT level. In addition, it is reported that amygdalin has a good therapeutic effects on rats with chronic gastritis and chronic atrophic gastritis. [32]-[34].

3.3 Improve the defense system of organism

Amygdalin can considerably enlarge polyhydroxyalkanoates (PHA) induced human peripheral blood T lymphocyte proliferation; and can also promote peripheral blood lymphocytes stimulated by PHA secrete IL-2 and IFN-g, and then inhibit the secretion of TGF-β1, therefore enhance immune function. [35] Amygdalin also take part in the expression of regulatory T cells for the treatment of atherosclerosis, and this can also enlarge the lumen area, reduce aortic plaque coverage. [36]-[38].

3.4 Antiasthmatic effects

Pulmonary surfactant synthesis can be encouraged by Amygdalin. After oral administration Amygdalin is decomposed into benzaldehyde and hydrocyanic acid which could inhibit lungs to reach assured level and result in steadily respiratory movement and attain antitussive and antiasthmatic effect [39], [25].

3.5 Other effects

Amygdalin have capability to slow down the alloxan induced hyperglycemia, the useful intensity be interconnected to the drug concentration in blood. According to the research amygdalin has shown the therapeutic effect on gastric ulcer, psoriasis and arthritis. Amygdalin can also calm down angiogenesis in the cultured endothelial cells of diabetic rats. [25] Although there is need for an advance research on human diabetic control. Like as in the case of other seeds. [39].

3.6 Side effects

Amygadlin, may result in fast heartbeat due too-high thiocyanate levels, dizziness, muscle weakness, nausea, and possibly shortness of breath. If there is any of these symptoms happen, then without delay stop taking different sources of amygdalin (including fruit seeds) and for advance advice contact specialized physician. Generally, symptoms may reduce or totally disappear within 24 hours of amygdalin cessation [39]. The common toxicity is in digestive of human, if the daily intake of dose is reduced to daily oral doses of 0.6 ~ 1g, then it can avoid toxicity [25].

4. Theories of anticancer activities

Many researchers have proposed different theories regarding anticancer mechanism of amygdalin named as, Trophoblast theory, Enzyme balance theory and lysosomes theory.

4.2 Trophoblast theory

According to this theory intake of amygdalin in adequate amount may prevents the metamorphosis of rogue egg/sperm cell into cancerous tissue. Amygdalin have one unit of cyanide and benzaldehyde, two unit of glucose strongly bonded with each other. β- Glucosidase, an enzyme that metabolizes amygdalin which is profoundly found in cancerous cells rather than normal tissues. Due to the presence of β-glucosidase in Amygdalin unlocks itself to liberate cyanide and benzaldehyde in the tissue and it destruct the cancerous cells by inhibition process. rhodanese is one more enzyme which can completely metabolize cyanide and benzaldehyde into useful components. That usually present in normal tissues as compared to cancerous

tissue. [40]

4.3 Enzyme balance theory

According the Enzyme balance theory state that the imbalance between the enzymes cause cancer. The cancer cells have higher amount of β- glucosidase and may also have need of rhodanese enzyme therefore, cancer cells negatively affected on administration of amygdalin while normal cells are protected by rhodanese enzyme [41].

4.4 Lysosome theory

Lysosome theory states that, there is the decrease in the pH unit by 0.97 when the cyanide amount of amygdalin decreases, with a total decrease of up to 1.6 pH units by increasing the acidic level which result in destruction of lysosomes in cancerous cells. lysosomal enzymes which are released from the lysosome results in devastation of cancerous cells, in that way inhibit the development of the cancerous cell. Though there is no scientific record to support these theories [42].

5. Mechanism of action of vitamin B 17

According to ErnestT. Krebs Jr. human have Rhodanese enzyme in their body which is present in full body apart from in the tumour cells. And this enzyme can convert cyanhydric acid which is found in B17 into thiocyanate. Thiocyanate is beneficial for the organism as it lowers the blood pressure and on the other side the enzyme Beta-Glucosidase is found in cancer cell in large amount except in normal body cells. So there will be no presence of Beta-Glucosidase enzyme in normal healthy person as there will no cancer cell in the body [43], [44]. Vitamin B17 is made up from one molecule of benzaldehyde (which act as a analgesic) and another molecule is hydrogen cyanide (cyanhydric acid) which have two molecules of glucose.

Hydrogen Cyanide and Benzaldehyde are the two by products are formed in the body when Vitamin B17 is introduced in the body this break down is occurring by the action of Rhodanese enzyme. Thiocyanate and benzoic acid are used for the nourishment of healthy cells and to forms the metabolic pool production for vitamin B17.

But Rhodanese enzyme doesn't act when cancer cells are present and vitamin B17 get in contact with cancer cells, on the other hand Beta-Gucosidase is the only enzyme that present in large amount in the cancer cells.

A chemical reaction starts when B 17 and Beta-Glucosidase get in touch with each other and a poison is produced with the combination of Hydrogen Cyanide and benzaldehyde this is used to damage and kill the cancer cells This complete process is known as selective toxicity. Particularly the tumour cells or cancer growth are targeted and damaged by this process [44]-[46].

Cancer Epidemiology Biomarkers and Prevention (CEBP) reported that, a simple diet can change or reduce their risk of developing disease that has family history of colon cancer. A diet should contain high content of folic acid, methionine (an essential amino acid), and no alcohol intake, this can reduce colon cancer risk in those who have family history of the cancer disease [47], [44]

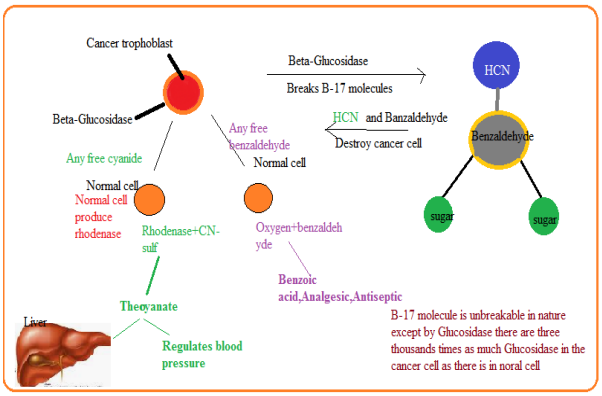

Figure1: Mechanism of action Amygdalin/Laetrile [48]

6. Conclusion

This paper reviews latest research of vitamin B17 in cancer treatment. Vitamin B17 is a compound which is found in stone fruit kernels, bitter almond, apricot, peach, and the plum. The properties of vitamin B17 leads to interpret that B17 could help in providing nourishment to healthy cells and lethal for cancer cells. So we can say that vitamin B17 can be used as natural chemotherapy in cancer treatment. But there a lot of study is necessary to show that vitamin B17 have anticancer properties as there is no proof that vitamin B17 have anticancer activity.

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