Amygdalin as a promising therapeutic agent: A review

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Abstract

Amygdalin is obtained from stones (hard seed form) of apricots, bitter almonds, peaches, plums and cherries. Amygdalin is a plant glycoside which is used to treat multi diseased/disorder conditions including cancer. Amygdalin is helpful to induce apoptosis to treat some severe conditions like cancer and human renal fibroblast. US banned amygdalin for cancer cure while this drug is used as prescription drug in UK. Synthesis of hydrocyanic acid (HCN) is the uniqueness of this compound, further metabolism of hydrocyanic acid is proven as toxic for target cells and for cancerous cells.

Keywords: Amygdalin, L-mandelonitrile, benzaldehyde and HCN.

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Introduction

Amygdalin is a cyanogenetic glycoside which is also known as laetrile. Amygdaline is also familiar under the name of vitamin B17. It is a plant glycoside belongs to Rosaceae family. The source of amygdalin is almonds, apricots, cherries, peach and plums. Its chemical formula is C20H27NO11. Molecular weight of this cyanogenetic compound is 457 Daltons. D mandelonitrile-β-D-glucoside-6-β-glucoside is chemical structure of amygdalin. Amygdalin which is obtained from bitter almonds is used as a therapeutic agent since hundreds of years. Amygdalin in bitter almonds was found by Schrader in 1803. This compound is used as anti-pyretic, ant-tussive and anti-cancer. This compound also having some potential benefits in asthma, leprosy and bronchitis [1]. This compound is itself is non-toxic but produces HCN which is poisonous and decomposed by enzymes. Pharmacological effects of amygdaline also possess anti-fibrosis, anti-atherogenic, to treat hypoxia during lung injury anti-tumor and immunity regulator. Anti-tumor effect is one of the novel topics for some recent years [2]. Anti-cancer activity of amygdalin is promoted by production of decomposed compound from HCN in the body which is toxic for the cancer cells and destroys the nutrition value of the cancer cells and resultant cell destroys. Amygdalin is reported in studies effective against prostate cancer. Amygdalin is used as an anti-cancer in many countries for 20 years viz. Italy, Japan, China and America. But the use of amygdalin is evoked in US by the US-FDA due to some toxic effects of amygdalin to the normal cells and less potency to kill tumor cells.

Reported potential effects of Amygdalin

1. Anti-asthmatic effect: Amygdalin is reported to synthesize some pulmonary surfactants. Amygdalin is hydrolyzed in benzaldehyde and hydrocyanic acid (HCN) in body and HCN is responsible to slow down the respiratory movements through which it acts as anti-tussive and anti-asthmatic agent. Amygdalin does...
not put effect on type-1 helper T-cells but kills type-2 helper T-cells. Route of administration for amygdalin affect the potency for anti-asthmatic effect because airways infection lowers the potency of amygdalin for anti-asthmatic effect [3].


3. **Effect on immune system**: Amygdalin induce proliferation of T-lymphocytes and blood lymphocytes motivated by polyhydroxyl alkanoates. Proliferation of T-lymphocytes and blood lymphocytes are responsible to secret interleukin and interferon and these both will prevent the TGF-β1 and will boost the immunity [6].

4. **Anti-atherosclerosis effect**: A study reveals that due to activation of T-cells amygdalin also having anti-atherosclerotic effects on Apo-lipoprotein E (Apo-E) deficient mice. This study reveals that amygdalin having a potential effect to treat atherosclerosis [4, 5].

5. **Amygdalin as pain reliever**: This analgesic activity of amygdalin is performed on mice by using hot plate method. When animal is placed on hot plate that animal experience pain due to production of acetic acid. Amygdalin obtained from bitter almonds lowers the pain due to formation of less formalin content. With the release of anti-inflammatory cytokines and tumor necrosis factor and blocking cyclo-oxygenase (COX) amygdalin inhibits prostaglandins. Amygdalin produces nitric oxide by blocking lipo-oxygenase (LOX) [6]. Therefore amygdalin is having potential analgesic and anti-inflammatory effects. According to the studies it is reported that benzaldehyde unit of amygdalin is responsible to slow down CNS oriented pain [7].

6. **Potential effects on digestive tract**: Amygdalin when administered orally then it is converted into prunasin by enzymes present in digestive tract by passing through salivary glands and various sites of gastrointestinal tract. Further prunasin is converted into mandelonitrile by β-glucosidase and hydroxy mandelonitrile by hydroxylase in GIT. Benzaldehyde is an important functional moiety for amygdalin, decomposition of benzaldehyde results in lowering of pepsin activity and retardation in digestive tract activity. Pepsin hydrolysate is obtained from almond water and 500 mg/kg dose of pepsin hydrolysate on rats inhibits the level of AST (Aspartate Transaminase) and ALT (Alanine Transaminase) and raise the hydroxy proline content which is responsible for multiplication of connective tissues of liver. Almond water is responsible to stop multiplication of connective tissues of liver. This study had reported in rats [8-10].
7. **To inhibit hyperglycemia:** Amygdalin is helpful to low the blood sugar level induced by alloxan. This study was conducted on male mice. Amygdalin with a dose of 3mg/kg is given to the male mice before 1 hour prior to the administration of alloxan. It was revealed from the study that amygdalin is helpful to low the blood sugar level. Amygdalin is helpful to scavenge the hydroxyl free radical of alloxan which is responsible to harm the β-cells of pancreas.

8. **Amygdalin as anti-tumor agent:** Amygdalin is one of the most used anti-cancer agents since many years. First time amygdalin used as anti-cancer agent by Russian doctor in 1845. In US trial on amygdalin was started in 1820 and in 1850 amygdalin is patented as official compound. US national cancer institute used amygdalin through oral and intra-venous routes for cancer treatment but this drug through these routes fails to fulfill the standards for USFDA. In context of this situation clinical trials on amygdalin had started and study revealed that 6 out of 22 patients treated with cancer. Study did not support the significance outcome of amygdalin for cancer treatment. In 1979 USFDA proved toxic effects of amygdalin. Import of amygdalin is stopped in US in 1987. In UK amygdalin is prescription drug for cancer and to be used under the supervision of doctor because it produces cyanide which is toxic. It is also believed that cyanide which is produced from amygdalin is toxic for cancerous cells. Some studies revealed that amygdalin can start apoptosis in human leukemia cells (HL-60 cells) and also having potential effects to treat colon cancer.

**Toxicity of Amygdalin**

Therapeutic index of amygdalin showed that drug is potent and more toxic through oral route than intra-venous route. According to studies toxic dose (LD₅₀) for oral route is 880 mg/kg of body weight for rats. For intravenous injection toxic dose (LD₅₀) of amygdalin is 25 gm/kg of body weight for rats. For intraperitoneal injection toxic dose (LD₅₀) of amygdalin is 8 gm/kg of body weight for rats. Toxic dose of amygdalin through i.v. route for humans is 5 gm. Through oral route amygdalin produces more hydrocyanic acid than parenteral routes and hydrolyzed by intestinal microbes. Toxicity of amygdalin will be induced in humans through oral route is 4 gm for 15 days and through i.v. route for 30 days.

**Chemistry of Amygdalin**

It is cyanogenetic glycoside obtained from aromatic amino acid phenylalanine. Amygdalin generally obtained from apricots (8%), bitter almonds (5%) and plums (2.5%). Melting point of amygdalin is 223°C to 226°C and solubility of amygdalin in hot water is 0.1 g/ml. Seeds in the form of stones are taken out from fruit and dried either in sun light or in oven. Dried seed is boiled with ethanol and evaporate whole the content of ethanol after that add diethyl ether and get the amygdalin in white precipitated form. Amygdalin is degraded by intestinal glucosidase. Amygdalin is converted in gentibiose and L-mandelonitrile. Gentibiose is converted in glucose and L-mandelonitrile is converted in benzaldehyde and hydrocyanic acid. Decomposed form of hydrocyanic acid is fetal for target cells.
Conclusion

Amygdalin shows its primary potential effects to treat asthma, to boost immunity, to treat atherosclerosis and to lower blood sugar. Amygdalin is proven as secondary agent to cure cancerous situation. Its anti-cancer effect is not steady and exact mechanism of amygdalin to treat the cancerous conditions is to be understood. Efforts in the future need to put to expand the pharmacokinetic profile of amygdalin. Also need to improve the PK profile of amygdaline administrated through oral route and topical route. Compounds like amygdalin are anticipated to overcome present difficulties to enter in clinical trials in future.

References