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# Amygdalin as a Complementary and Alternative Medicine: (Review)

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*Abstract: The alternative and complementary medicine (CAM) is considered as one of the most popular therapies worldwide. It has been used to treat different types of illness and diseases including tumors. Traditional medicine still does not provide patients with permanent solution to their suffering, especially in terminal cases cancers. Amygdalin, extracted from the seeds of apricot and almond, is under debate as to its effectiveness in cancer treatment. This review will focus on amygdalin as an alternative medicine and the researches that have investigated its role in healing.*

*Keywords: Complementary and alternative medicine, amygdalin, cancer, treatment, apricot seeds.*

## **Introduction:**

Complementary and alternative medicine (CAM) includes a wide range of healing methods, approaches, and therapies. A therapy is called complementary when it is used in addition to conventional treatments; on the other hand, it is called alternative when it is used instead of conventional treatment. Complementary and alternative therapies are used in an effort to prevent illness, reduce stress, reduce the side effects, or cure diseases. Nearly four in ten American use complementary or alternative medicine (CAM) each year. (2002, Owens, 2015)

According to the National Health Interview Survey (NHIS), nearly 40 % of adults in the United States are actively using some form of CAM, and over 70 % will use CAM at some time during their life.(Barnes et al., 2008)

The most frequently used CAM therapies were natural products, followed by deep breathing and meditation, and chiropractic treatment. Approximately 50 % of adults in the National Health and Nutrition Examination Survey (NHANES)



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reported using dietary supplements such as multivitamins, omega-3 or fish oil supplements, and calcium, and the most common reasons for using supplements was to improve or maintain general health. (Bailey et al., 2013) (Greco et al., 2013)

Conventional approaches to cancer treatment have generally been studied for safety and effectiveness through a scientific process that includes clinical trials. Few CAM therapies have undergone a proper evaluation. Yet, treatment outcomes of CAM are found to vary significantly between medical trials in different social environments. (2002, Shim, 2015) (2002)

### **Amygdalin:**

Amygdalin, D-mandelonitrile- $\beta$ -D-glucoside-6- $\beta$ -glucoside, belongs to the aromatic cyanogenic glycoside group and is widely distributed in the rosaceous plant seed, for example, apricot, peach, apple, cherry, plum, *etc.* Mounting evidence has supported the anti-cancer effects of amygdalin. Amygdalin induces apoptosis process in various cancer cells such as leukemia, prostate cancer, cervical and liver cancer cells and breast cancer. (Lee and Moon, 2016, Chen et al., 2013)

### **Chemical and physical properties:**

It is a cyanogenic glucoside isolated from almonds and seeds of other plants of the family Rosaceae. (Newmark et al., 1981) It is converted by plant emulsion (a combination of a glucosidase and a nitrilase) or hydrolic acid into benzaldehyde, D-glucose, and hydrocyanic acid (figure 2). The chemical names are: amygdalin, R-amygdalin, amygdalosite, beta-gentiobioside. The molecular formula is  $C_{20}H_{27}NO_{11}$  (figure 1). It is molecular weight is 457.42848 g/mol. (Newmark et al., 1981, Milazzo et al., 2007, Li et al., 2015)

It was isolated for the first time in the 19th century. Amygdalin is called interchangeably vitamin B17 or laetrile. Scientists evaluate the positive influence of amygdalin on many diseases like: bladder cancer, prostate cancer, cervical cancer, colon cancer, promyelocytic leukemia, chronic kidney disease, psoriasis and other. (Zdrojewicz et al., 2015).



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### **Amygdalin and cancer researches:**

Amygdalin reduced the growth of tumor cells at 10mg/ml. Apoptosis was triggered in those cancer cells, whereas colony formation was suppressed in all cell lines. The cell cycle proteins cdk 1, cdk 2 and cdk 4 as well as cyclin A, cyclin B and cyclin D3 were modulated by amygdalin after both 24h and 2weeks.(Makarevic et al., 2016).

It was proved that amygdalin inhibits cell growth in breast carcinoma cells. it regulates apoptosis-related proteins. Cancer cell lines Hs578T were treated with amygdalin at the indicated concentrations (0, 10, 20 and 40 mg/mL). The results indicated that amygdalin induces apoptosis by increasing the expression of Bax and decreasing the expression of Bcl-2 in Hs578T breast cancer cells. (Lee and Moon, 2016)

The inhibitory effect of amygdalin on the growth of renal cell carcinoma (RCC) cells was assessed. Amygdalin (10 mg/ml) was applied to the RCC cell lines for 24 h or 2 weeks. Amygdalin caused a significant reduction in proliferation of RCC. Amygdalin also induced a marked decrease in cell cycle activating proteins, in particular cdk1 and cyclin B. Amygdalin also modulated the differentiation markers, E- and N-cadherin. Hence, the study revealed that exposing RCC cells to amygdalin inhibited cell cycle progression and tumor cell growth by impairing cdk1 and cyclin B expression.(Juengel et al., 2015).

In vitro, proliferability of cell line of non-small cell lung carcinoma; NSCLC was inhibited after they were treated by amygdalin with higher concentration. So it was suggested that amygdalin was likely to have anti-metastatic effect.(Qian et al., 2015)



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A case report was published of severe cyanide poisoning arising from CAM use. A severely agitated, encephalopathic, unresponsive 4-year-old boy with a history of metastatic ependymoma. The use of CAM including intravenous and oral amygdalin and oral apricot kernel was reported. Serum cyanide level was markedly elevated. Cyanide poisoning can be the cause of severe encephalopathy in children receiving CAM treatment with substances containing cyanogenic glycosides. (Sauer et al., 2015)

Another study investigated the role of amygdalin in the treatment of bladder cancer. Amygdalin (10 mg/ml) was applied bladder cancer cell lines for 24 h or for 2 weeks. Integrin knock-down was carried out to evaluate integrin influence on migration and adhesion. A 24 h or 2 week amygdalin application distinctly reduced tumor cell adhesion and migration of cancer cells. Integrin subtype expression was significantly and specifically altered by amygdalin. Knock down of beta4 integrin caused a significant decrease in migration of bladder cancerous cells (Makarevic et al., 2014)

The effect of amygdalin on cervical cancer cells has also been studied. The viability of human cervical cancer cell line was significantly inhibited by amygdalin. It was revealed that amygdalin-treated cervical cells developed typical apoptotic changes. (Chen et al., 2013)

Integrins are studied because of they regulate cell adhesion to the extracellular matrix, a cellular process that mediates cell differentiation, metastasis and angiogenesis. (Bendas and Borsig, 2012)

Treatment with amygdalin increased expression of Bax, a pro-apoptotic protein, decreased expression of Bcl-2, an anti-apoptotic protein, and increased caspase-3 enzyme activity in prostate cancer cells. The study has shown that amygdalin



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induces apoptotic cell death in human prostate cancer cells by caspase-3 activation through down-regulation of Bcl-2 and up-regulation of Bax.(Chang et al., 2006).

Microarray showed that amygdalin downregulated especially genes belonging to cell cycle category. RT-PCR analysis revealed that mRNA levels of these genes were also decreased by amygdalin treatment in human colon cancer cells. This study suggested that amygdalin have an anticancer effect via downregulation of cell cycle-related genes in SNU-C4 human colon cancer cells, and might be used for therapeutic anticancer drug.(Park et al., 2005)

### **Conclusion:**

Cancer patients considering complementary and alternative therapies should discuss this decision with their doctor, nurse, or pharmacist as they would any therapeutic approach, because some complementary and alternative therapies may interfere with their standard treatment or may be harmful when used with conventional treatment.

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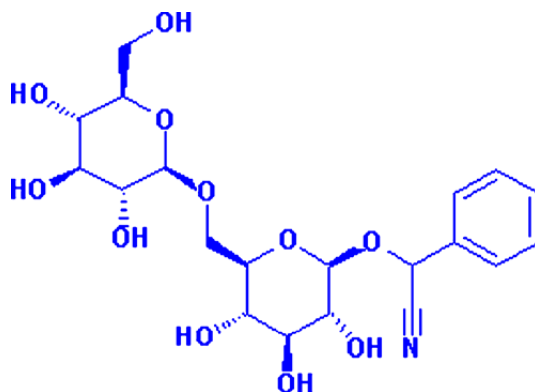


Figure 1: chemical structural of amygdalin

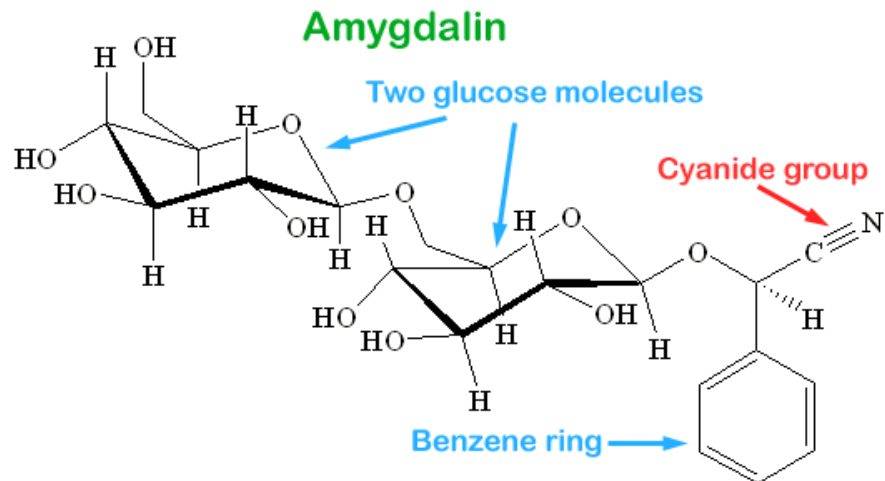


Figure 2: hydrolysis of amygdalin to its three main components