ISSN: 0975-8585

Research Journal of Pharmaceutical, Biological and Chemical Sciences

# Laetrile Or Amygdalin (Vitamin B-17) – Nutrient Or A Drug: A Review Of Running Controversies.

**MR Suchitra, and S Parthasarathy*.**

[1]Department Of Biochemistry, SASTRA University, Tamil Nadu, India.
[2]Mahatma Gandhi Medical College And Research Institute, Sri Balaji Vidyapeeth University, Puducherry – South India

**ABSTRACT**

Amygdalin/Vitamin B17/Laetrile is a cyanogenic diglucoside, an active ingredient of several fruit pits and rawnuts was thought to possess anti-cancer properties. Amygdalin is contained in a few stone fruit kernels, such as apricot bitter almond, peach and plum and in the seeds of the apple. Even though there are a few animal and human studies which demonstrate the benefits of amygdalin in cancer, these are not well established in randomized clinical trials. When considering the other diseases like hypertension, pain, and bronchial asthma the role of Laetrile needs to be explored by using this drug as a supplement to regular therapeutic strategies. But as such the intake of apricot kernels and apple seeds should not be discouraged for fear of amygdalin toxicity in view of their other nutritional benefits.

**Keywords:** laetrile, amygdalin, vitamin B17,

***Corresponding author***

ISSN: 0975-8585

## INTRODUCTION AND CHEMISTRY

Vitamin B17/Amygdalin/Laetrile is one of the most controversial vitamins in the last three decades. Chemically, it is a cyanogenic di-glucoside, but with a condensed formula of C20-H27-NO-11, and a MW (molecular weight) of 457. It has a chemical name of DMandelonetrile-betaglucoside-6 beta-D-glucoside. Amygdalin was first invented in the early nineteenth century inFrance as an active component of some fruit pits and rawnuts.[1] Cyanide, one of the important metabolites of amygdalin, wasthought to possess anti-cancer properties and was introduced in the United States as an anti-tumour drug in the 1920s. Several formulations of Laetrile have been used so far over the years, which included oral, peritoneal, intravenous, and intramuscular preparations. The oral formulation is the most potent of the preparations. Anysubstance can be considered a real vitamin only when it is essential for the normal cellular function. Laetrile does not fit into this. Hence to call it a vitamin is a big question. Vitamins are substances that must be compulsorily included in the diet to maintain health and prevent certain diseasesif they are deficient. They cannot be synthesized in the body. Hence the name vitamin is actually a misnomer for amygdalin. Laetrile is a semi synthetic of amygdalin, synthesized from amygdalin by hydrolysis. [2]The name vitamin B-17 was given to laetrile by E.T. Krebs Jr, but it is not approved by the Committee on Nomenclature of American Institute of Nutrition Vitamins. Mandelonitrile refers to the part of the laetrile molecule from which cyanide is released by decomposition. A 500 mg laetrile tablet may contain between 5–51 mg of hydrogen cyanide per gram.[3]

## SOURCES

The preferred commercial source for Laetrile is from the apricot kernels (i.e. Prunusarmeniaca). Amygdalin is contained in a few stone fruit kernels, such as bitter almond (5%), apricot (1.4%), peach (0.68%), and the plum (0.04–1.7%), It's also found in the seeds of apple (0.3%).[4] The stones are taken out of the fruit, cracked to get the kernels, which are dried in ovenor in the sun. The kernels are then boiled in ethyl alcohol and after evaporation and diethyl ether is added. The chemical amygdalin is now precipitated assmall white crystals. [5]

## BENEFITS

### Antitumor benefits

Laetrile has been tested in all the models which includes cultured animal cells (i.e.cells grown in specialized containers present in the laboratory), in whole animals, in xenograft models (i.etumor cells from one species transplanted onto another), and in humans to find outif it has got any specific anticancer properties. As noted earlier, hydrogen cyanide is believed to be the main tumor-killing ingredient in laetrile. Hydrogen cyanide can also be got from prunasin, which is an incomplete breakdown product of amygdalin. Proponents of antitumour activity of laetrile have suggested four different and unique theories. The rationale for the first theory of laetrile use is that the malignant cells have higher than normal levels of an enzyme called beta-glucuronidase and deficient in another enzyme named rhodanese. Laetrile is modified in liver and the enzyme beta-glucuronidase breaks down the modified compound, producing cyanide. This targets the imbalance of the enzyme of the tumour cells. The second theory states that cancer cells may contain more beta-glucosidase activity than the normal cells. As in the case of the first theory, this is being targeted by amygdalin. The third theory states that tumoris the result of a metabolic disorder caused possibly by a vitamin deficiency. It also states that laetrile, or amygdalin/vitamin B-17, is the missing vitamin needed by the body to restore health and to prevent tumor growth. The fourth theory states that the cyanide released by laetrile has some toxic effect which extends beyond its interference with cellular utilization. According to this fourth theory, cyanide increases the acid content of tumors and this leads to the destruction of lysosomes. The released enzymes from lysosomes destroy tumor cells. Amygdalin has been shown to block the growth of bladder cancer cells in vitro. Suppression of cdk2 and cyclin A might be a relevant mechanism defining how amygdalin may arrest or diminish tumor proliferation [6,7,8,9].

Park et al. [10], have shown in their studies that amygdalin inhibited the proliferation of human colon cancer i.eSNU-C 4 cell, and the possible mechanism is the inhibition of expression of cell cycle related genes; Kwon et al. [11] in their study, confirmed that amygdalin can induce apoptosis or cell death in human promyelocyti cleukemia cells. Chang et al. [12] identified that amygdalin can induce apoptosis in prostate cancer cells by regulating the expression of Bax and of Bcl-2. The Bcl 2 proteins are significantly involved in the control of cell apoptosis. Chen, Y. et al.13foundthat amygdalin can inhibit the survival rate of HeLa cells, ina

concentration dependent manner. Amygdalin can induce apoptosis of HeLa cells mediated by endogenous mitochondrial pathway. Amygdalin could also inhibit the growth of HeLa cell in nude mice bearing tumors through inducting tumor cell. HeLa is an immortal cell line used in scientific research. The cell line was derived from cervical cancer cells taken on February 8, 1951 from **He**nrietta **La**cks14, a patient who died of cancer on October 4, 1951.Manuel Navarro [15] treated a total ofover five hundred patients in a terminal state of different malignancies like adenocarcinoma of the breast, lungs, tongue colon etc. and obtained encouraging results with the use of Laetrile and that these results was either comparable or superior to the use of the more toxic yet standard cytotoxic agents. Studies from a few others have given positive results [16,17] with the use of laetrile in different malignancies. The claims that laetrile or amygdalin has beneficial effects for different cancer patients are not currently supported by sound clinical research data. But there is a considerable serious risk of adverse effects from cyanide poisoning after Laetrile or amygdalin,18 especially after oralingestion. The risk-benefit balance of Laetrile as a treatment for cancer is therefore presently clearly negative.

**Other benefits:**

Amygdalin is a potent antifibrotic agent that may have therapeutic potential for patients with fibrotic kidney diseases. J Guo et al [19] in their study proved treatment of the cultured renal interstitial fibroblasts with amygdalin inhibited their proliferation and the production of transforming growth factor (TGF)-β1. In the rat model where there is obstructive nephropathy, after ureteral obstruction, the administration of amygdalin eliminated the extracellular matrix accumulation and alleviated the renal injury on the 21st day. Amygdalin attenuated the kidney fibroblast activation and thus the rat renal interstitial fibrosis. These results clearly indicate that amygdalin is a potent anti-fibrotic chemical that may well have therapeutic potential for patients with fibrotic kidney diseases.

Analgesic effect

The mouse hot plate and acetic acid-induced writhing test confirmed that amygdalin has analgesic effects and no tolerance; mice without tail-erecting response and nalorphine induced jump response after treated with amygdalin. This effect of nalorphine paves the way of concept of opioid role in its action which was countered by others [20,21]. Aprobable anti prostaglandin effect has also been suggested. Inhibition of the nitric oxide production by inhibiting the LPS-stimulated mRNA expressions of COX-2 and iNOS in the mouse BV2 cells is also suggested.

Antihypertensive effect:

Vitamin B17 may cause a low blood pressure reaction due to formation of thiocyanate, a powerful blood-pressure-lowering agent but cannot be used as a therapeutic agent for hypertension [22]. The formation of thiocyanate is the possible explanation of the effect.

Boosting immunity: Amygdalin [22] stimulated the immune system by causing a statistically significant increase in the ability of a patient's white blood cells to attack harmful cells.

In Bronchial asthma:

Amygdalin can promote synthesis of pulmonary surfactant. Amygdalin is decomposed into benzaldehyde and hydrocyanic acid after oral administration which prevent respiratory center to reach certain level and slow down respiratory movement and produce antitussive and antiasthmatic effect [23].

Miscellaneous:

Amygdalin prevents the alloxan induced hyperglycemia which depends on effective concentration of drug inblood [24]. Research has shown therapeutic effect of amygdalin for gastric ulcer, psoriasis and arthritis. A need for a further research on human diabetic control is needed such as in the case of other seeds. [25,26],

**RISKS AND DANGERS**:

Tam Dang et al 27have reported a near fatal case of cyanide poisoning due to excess intake of amygdalin. This patient took 1500mg of amygdalin as prescribed, which contains approximately 90mg of cyanide. This amount is approximately around 1.8 times higher than the minimum described lethal dose of 50mg of cyanide. After that, she presented with multi-organ failure including encephalopathy lactic acidosis, and shock. Individuals who have less capacity to detoxify cyanide to thiocyanate because of either genetic predisposition (e.g. as occurs in patients with Leber's Optic Atrophy) or a diet which is low in sulfur containing amino acids are having increased risk to developing adverse side effects from laetrile, a cyanide producing substance used in cancer treatment.

Side effects of too-high thiocyanate levels include rapid heartbeat, dizziness, muscle weakness, nausea, and possibly shortness of breath. If any of these symptoms occur, all sources of amygdalin (including fruit seeds) should be stopped immediately and a physician should be contacted for further instructions. Usually, symptoms will diminish or completely disappear within 24 hours of amygdalin cessation. Still there are a lot of doubts about the dangerous therapeutic level of thiocyanate. Nausea vomiting and neuropathy have been described as other side effects. Vitamin C hastens the conversion of laetrile into the toxic chemical hydrogen cyanide. It also depletes the body of cysteine reserves, an amino acid that helps the body to detoxify hydrogen cyanide. Hence amygdalin with other fruits and seeds 28with such unproven effects need to be explored.

**CONCLUSION**

Unless randomized controlled clinical trials establish its efficacy along with acceptable side effects, amygdalin/laertile cannot be promoted as an antitumor drug. The formulations, dosage and the methods of administration have to be standardized before contemplating laetrile as a pure drug. Regarding other indications, along with the regular treatment, amygdalin supplementation seems to have a role. This possible space has to be explored with both cell line studies and human trials. It does not imply that the sources of amygdalin like apricots should be discarded. They must be given a role as a nutritional supplement due to their other benefits.

**REFERENCES**

[1] Marinela. Vitamin B17/Laetrile/Amygdalin (a Review). Bulletin UASVM Animal Science and Biotechnologies, 2009, (66)1-2
[2] Viehoever A, Mack H: Bio-chemistry of amygdalin (bitter, cyanogenetic principle from bitter almonds). Am J Pharm:1935; (107)397-450,
[3] Dorr RT, Paxinos J: The current status of laetrile. Ann Intern Med.1978:89 (3): 389-97,
[4] Bolarinwa, Islamiyat F.; Orfila, Caroline; Morgan, Michael R.A. "Amygdalin content of seeds, kernels and food products commercially-available in the UK" Food Chemistry. 2014: 152: 133–139.
[5] Chisholm, Hugh, ed. "Amygdalin".Encyclopædia Britannica. 1 (11th ed.). 1911:Cambridge University Press. p. 900.
[6] Song Z, Xu X. Advanced research on anti-tumoreffects of amygdalin. J Can Res Ther 2014;10:3-7.
[7] Gal em, Fung Fh, Greenberg Dm: Studies on the biological action of malononitriles. II. Distribution of rhodanese (transulfurase) in the tissues of normal and tumor-bearing animals and the effect of malononitriles thereon. Cancer Res.1952. 12 (8): 574-9,
[8] Nitikman M, Duncan K, Yoshida E.Metastatic colorectal cancer and Laetrile in the 21st century:persistence of a 1970s controversy. AME Med J 2017;2:100.
[9] Charles G. Moertel,., Thomas R. Fleming.A Clinical Trial of Amygdalin (Laetrile) in the Treatment of Human Cancer, N Engl J Med. 1982; 306:201–6.
[10] Park HJ, Yoon SH, Han LS, et al. Amygdalin inhibits genes related to cell cycle in SNU-C4 human colon cancer cells. World J Gastroenterol. 2005;11(33):5156-61.
[11] Chang HK1, Shin MS, Yang HY, Lee JW, Kim YS, Lee MH, Kim J, Kim KH, Kim CJ. Amygdalin induces apoptosis through regulation of Bax and Bcl-2 expressions in human DU145 and LNCaP prostate cancer cells. Biol Pharm Bull. 2006;29(8):1597-602.

[12] Yu Chen, Jinshu Ma, Fang Wang, Jie Hu, Ai Cui, Chengguo Wei, Qing Yang & Fan Li Amygdalin induces apoptosis in human cervical cancer cell line HeLa cells, Immunopharmacology and Immunotoxicology,2013: 35:1, 43-51.
[13] Scherer, W.F.; Syverton, J.T.; Gey, G.O. "Studies on the propagation in vitro of poliomyelitis viruses. IV. Viral multiplication in a stable strain of human malignant epithelial cells (strain HeLa) derived from an epidermoid carcinoma of the cervix". Journal of Experimental Medicine. 1953: 97 (5): 695–710.
[14] Navarro MD. Five years experience with laetrile therapy in advanced cancer. ActaUnio Internationalis Contra Cancrum 1959;15:209-21.
[15] Makarević J, Rutz J, Juengel E, Kaulfuss S, Reiter M, Tsaur I, et al. Amygdalin Blocks Bladder Cancer Cell Growth In Vitro by Diminishing Cyclin A and cdk2. PLoS ONE 2014; 9(8): e105590.
[16] Nitikman M, Duncan K, Yoshida E. Metastatic colorectal cancer and Laetrile in the 21st century: persistence of a 1970s controversy. AME Med J 2017;2:100.
[17] Milazzo S, Horneber M, Ernst E. Laetrile treatment for cancer. Cochrane Database of Systematic Reviews 2015, Issue 4. Art. No.: CD005476. DOI:10.1002/14651858.CD005476.pub4
[18] Guo J, Wu W, Sheng M, Yang S, Tan J. Amygdalin inhibitsrenal fibrosis in chronic kidney disease. Molecular MedicineReports.2013: 7: 1453-1457.
[19] Hwang HJ, Kim P, Kim CJ, Lee HJ, Shim I, Yin CS, et al. Antinociceptive effect of amygdalin isolated from Prunusarmeniaca on formalin-induced pain in rats. Biol Pharm Bull 2008;31:1559-64.
[20] Zhu YP, Su ZW, Li CH. Analgesic effect and no physical dependence of amygdalin.ZhongguoZhong Yao ZaZhi 1994;19:105-7, 128.
[21] Biaglow E. J., Durand E. R.The enhanced radiationresponse of an in Vitro tumor model by cyanide releasedfrom hydrolysed Amygdalin. Int. J. Radiat. Biol. 1978: 33, (4)pp. 397-401.
[22] Huaping Z, Liwen C, Wenbin L, Hanchu L. Effect ofamygdalin on the proliferation of hyperoxia-exposed type IIalveolar epithelial cells isolated from premature rat. J HuazhongUnivSciTechnolog Med Sci2004:24: 223-225.
[23] Heikkila RE, Cabbat FS.The effect of alloxan-induceddiabetes by amygdalin. Life sci1980: 27: 659-662.
[24] Perez JJ. Amygdalin analogs for the treatment of psoriasis.2013: Future Med Chem 5: 799-808.
[25] M.R.Suchitra, S.Parthasarathy. Effect of administration of fenugreek seeds on HbA1C levels in uncontrolled diabetes mellitus–a randomized controlled trial.Int J PharmTech Res.2015:8 (2), 180-182
[26] Tam Dang, Cham Nguyen, and Phu N. Tran. Physician Beware: Severe Cyanide Toxicity fromAmygdalin Tablets Ingestion.Case Reports in Emergency Medicine. 2017: Article ID 4289527, 3 pages.
[27] M.R Suchitra, and S Parthasarathy. Sitaphal: Reemergence. Res J Pharm BiolChem Sci.2015;6(3): 1560-1565.