

EFFECTS AND BENEFITS OF VITAMIN B17 OR AMYGDALIN IN CANCER TREATMENT***Deeksha Meelu, Nitish Chaudhary, Shakti Bhadauriya and Vinod Kumar Gupta**

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ABSTRACT

Cancer is a group of disease which contain the abnormal growth of cells. Vitamin B17 or Amygdalin have anti-cancer property it is consider as cure of cancer. The source of Vitamin B17 are Apricots, Seeds of Apples, peaches, pears, Lima beans, fava beans, Almonds, Staw-berries, Black berries. Amygdalin/Laetrile is different names of Vitamin B17. Chemical its structure consists two glucose rings having Chemical formula $C_{20}H_{27}NO_{11}$. The main anti-cancer activity of amygdalin compound is due to cyanide group. Amygdalin or Vitamin B17 contain Cyanide group due to this group it destroy the cancer cells. In this review we will discuss about the history of amygdalin, pharmacological effects, mechanism of vitamin b17, natural source of vitamin B17 and potential benefits.

KEYWORDS: Vitamin B17, Amygdalin, Cancer, Therapeutic effects, potential benefits, Pharmacological effects.**INTRODUCTION**

Cancer refers to collection of large group of disease which involving the abnormal growth of cells. These abnormal cells enter to anywhere in the body and caused cancer cells. In 2020, Cancer is a leading cause of nearly 10 million deaths worldwide.^[1] It is one of the most fearful disease with exorbitant treatment cost which is render the patients helpless, and a condition in which alternative therapies come in the pictures. This is the most awful disease found among people and the largest single cause of death in human. Amygdalin or Vitamin B17 has beneficial effect for cancer patients.^[2] There are many cancer therapies known as chemotherapy and radiation which kills cancer cells by inducing apoptosis however they can adversely affect the life of patients and cause a death.^[3, 4, 5, 6, 7, 8, 9] In 2007, there are more than 8 million deaths were estimated which is occurred and by 2030 it is projected to increment to 17 million cancer death per year. Breast cancer, lung, colon /rectum, liver cancers are no largely longer confined to only Western Industrialized countries but also known as most common cancer worldwide.^[10] There are different types of cancer present in human body. But most common types of cancer in male are colorectal cancer (colon cancer), prostate cancer, lung cancer, stomach cancer and in female the most common types of cancer are breast cancer, lung cancer, cervical cancer, colon cancer. Where colon cancer is third most common cancer worldwide which is often found in patients aged 50 years or older. The approved cancer treatment does not depend upon diagnostic methods or medical therapies.

In 1830 Amygdalin (Vitamin B17) was first isolated by two French chemists.^[11, 12] Amygdalin is a controversial anti-cancer agent, it is a Cynogenic plant compound which is extract from apricot and peach kernels fruit.^[13] Amygdalin/Laetrile is different names of Vitamin B17. Chemical its structure consists two glucose rings having Chemical formula $C_{20}H_{27}NO_{11}$ on other hand molecular mass of amygdalin has 457.43 g/mol. It is easily soluble in hot water. And Synonyms of Amygdalin are: (R)-Amygdalin; D-Amygdalin; (R)-Laenitrile. Vitamin B17 is considered as a natural Cyanide substance which is known as nitiolide, the scientifically named of amygdalin is Mandelonitrile beta D-gentiobioside. The main anti-cancer activity of amygdalin compound is due to cyanide group. The correct dose of amygdalin can reduce the pain and complications of cancer cells therapy are indicated by many different studies.^[14, 15, 16, 17, 18, 19] There are many studies which highlighted the activity of anticancer by amygdalin with reference to its specificity of tissues, activity of telomerase and effect of anticarcinogenic on many types of cells: for eg. bladder cancer cell growth.^[20]

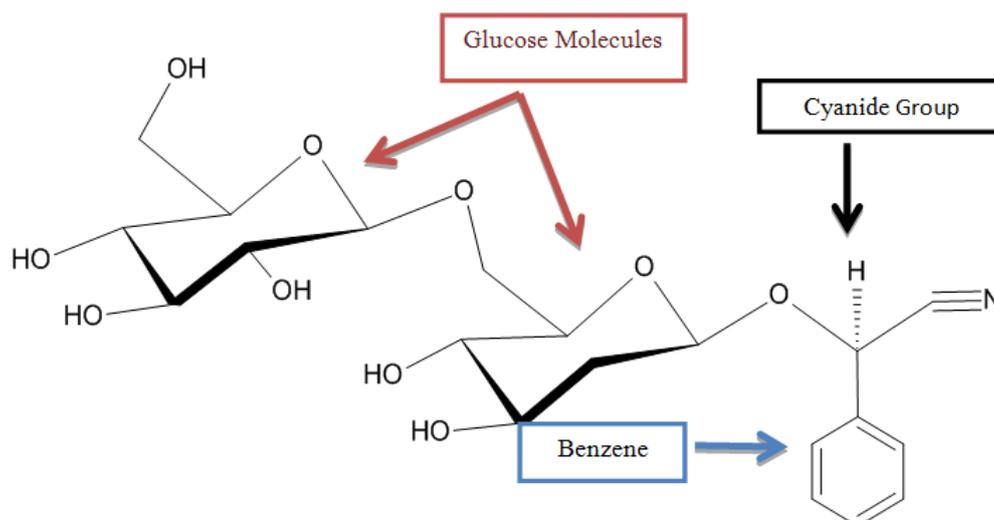


Figure 1. Structure of Amygdalin.

CONVERSION OF AMYGDALIN TO LAETRILE

Due to hydrolysis process or hydrolysis of amygdalin, laetrile compound is synthesized which is known as semisynthetic form of amygdalin. It is also known as anti-cancer agent or anti-cancer drug. In the medical history, this drug is one of the most controversial subjects.^[21, 22, 23] Hydrolysis processes converted the amygdalin into Laetrile.

HISTORY

In 1830s amygdalin was first isolated from bitter almonds by French Chemists Robiquet and Boutron-Charlard. Later, Liebig and Wohler observe that the hydrolyzation of amygdalin with the evolution of aldehyde group of Benz and Hydrogen Cyanide during enzyme preparation and this process is known as emulsion.^[24]

In 1845, amygdalin was first used as an antineoplastic agent in Russia^[25] where the patient who was treated shows/reported as positive results.^[26] In the 1920s, Dr. Ernst Krebs was working on techniques to discover a method for enhancing the taste of bootleg Whiskey where he observed that apricot kernels extract to minimized tumours of rodents.^[27] In the United State, Initial reports an administration of amygdalin dates back to 1920s^[28] where at that time oral compose (formulation) was determined to be too toxic so it is fallen into disused.^[29] In 1950s in United State of America, Laetrile was patented as non-toxic form of amygdalin.^[30]

In 1970s, the unconventional antineoplastic therapies, one of the most widespread was amygdalin and 1978 almost 70,000 US cancer patient used it^[31] so transport of amygdalin in US was put banned but In 23 states of USA, were permissible to use amygdalin for cancer patients.^[32]

In 1980s, the United State Supreme Court acted to uphold a federal ban on interstate shipment of

Laetrile/Amygdalin because of owing to the large number of toxicities reported.^[33] Later National Cancer Institute (NCI) planned to analyse the efficiency of amygdalin therapy and it sponsored a clinical trial with FDA consent, but it was unsuccessful to prove the efficacy of amygdalin as anti-cancer drug.^[34] By that time for sale as pharmaceutical product, it was illegal instead of this restriction; it is still used as an anti-cancer agent.^[35]

MECHANISM

How Vitamin B17 kills Cancer cells?

According to conducted research by Ernest T. Krebs Jr. the mechanism of how vitamin B17 kills cancer cells or amygdalin action is following:

Rhodanese is one particular human body enzyme which is found in everywhere in the body except at cancer cells. On the other side the enzyme Beta-Glucosidase found in only cancer cells with very large quantities but not found in anywhere in the human body. If there is no enzyme Beta-Glucosidase present in body it means there is no cancer in body.^[36] For normal healthy volunteer who have no cancer, then there is no enzyme present.^[37, 38, 39]

Vitamin B17 is made up of two chemical composition of glucose one is Hydrogen Cyanide and another one is Benz aldehyde.

When vitamin B17 is introduced to the body, it is breakdown by the Rhodanese enzyme. This enzyme breakdown the hydrogen cyanide and Benz aldehyde into 2 by products, Benzoic acid and Thiocyanate which is forms the metabolic pool production for Vitamin B17 and beneficial in nourishing healthy cells.

When Vitamin B17 comes into contact with cancer cells then there is no breakdown and neutralize the enzyme Rhodanese but only the enzyme Beta-glucosidase is present in very large quantities.

A chemical reaction initiated when Vitamin B17 and Beta-glucosidase are comes into contact each other, and

the hydrogen cyanide and Benzaldehyde groups are combine together synergistically to produce a toxin which kills the cancer cells (as shown in Figure 2.).^[40, 41, 42, 43] This whole process is known as selective toxicity process which is especially target and broken cancer cells only.^[44]

Another study related to mechanism is reported by Cancer Epidemiology Biomarkers and Prevention, who studied family history of Colon Cancer people, may be able to reduce the risk of disease developing with a few dietary changes. It appears when a diet high in an essential amino acid (methionine) and high in folic acid

and low in alcohol intake.^[45] In this way control the growth of cancer cells and prevent spreading of it to other organs.

Zinc is the mechanism of transportation for laetrile. The laetrile would get into the tissues of the body because patient did not have sufficient level of Zinc. They also found that vitamin A, B and C, selenium, magnesium all played important role in body to maintaining the defence mechanism.^[46] The total nutritional program consisting of diet, minerals, vitamins, laetrile and pancreatic enzymes are best treated for cancer.^[47, 48]

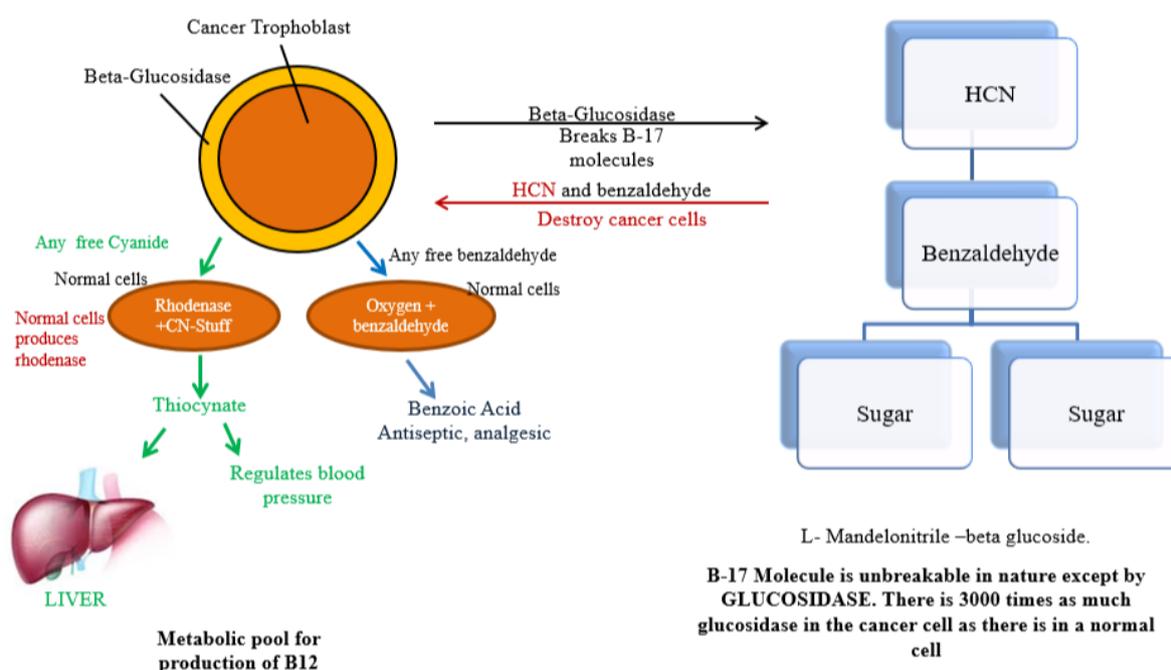


Figure 2. Mechanism of vitamin B17.

SOURCES

(Apricots, Seeds of Apples, peaches, pears, Lima beans, fava beans, Almonds, Staw-berries, Black berries)

There are many different sources which contain Vitamin B17 or amygdalin known as:- seeds, fruits, sprouts, nut and the very best source of amygdalin is found in apricots. While soil and climate play important role to identify how much quantity of Vitamin B17 present in any foods so it can be difficult to determine. Amygdalin is present in small amount of fruits in kernels such as plum (2.5%), bitter almonds (5%), peaches (6%) and apricots (8%).^[49] It is also present in seed of apple (0.3%)^[50], Lima beans Sorghum and clover.^[51] Leaves/leafy green, sweet potatoes and yams are best sources.

THERAPEUTIC EFFECT OF AMYGDALIN

For many years, amygdalin is traditional drug whose antitussive, anti-inflammatory, antipyretic and other therapeutic effects are known^[52] a recent study explained that the amygdalin treatment was helpful for alcohol induced gastric ulceration and gastric mucosal and protection might be mediated by TNF- α suppression and gastric mucosal nitric oxide production.^[53] Also used for preventing and treating inflammatory disorders, migraine.^[54] Another study related to amygdalin was conducted to analyse the antigenic efficiency of amygdalin on endothelial cells of diabetic rats which explain that the inhibitory effects on angiogenesis in rats is induced by amygdalin where vital hallmark of cancer cells is known as angiogenesis.^[55] In this anti-agnogenic activity of amygdalin is investigated which play important role in growth of cancer cells.^[56]

POTENTIAL BENEFIT

Some research studies found that vitamin B12 or amygdalin is the natural Laetrile form and it has some benefits. There are many potential benefits of amygdalin for health: - Lower blood pressure:- The amygdalin help in lower the blood pressure. These effects will be improved when it is taken by vitamin.^[57]

Relieve pain: - According to study, vitamin B12 stimulated the immune system by stimulate the activity of white blood cells to attack harmful cells.^[58] May be it helps to relieve pain caused by any inflammatory disorders or conditions such as joint pain, arthritis. But for human, clinical studies related to human being is still awaited.^[59]

Boost immunity: - To fight with cancer cells, a test tube study found that the amygdalin enhance the ability of immune cells. It provides strength and boost to immunity system to fight with cancer.^[60]

Protect against cancer: - Vitamin B12 have ability to kill the cancer cells more easily than killing normal,

healthy cells. By the department of physiology at Kyung Kee University in south Korea, explain that the amygdalin extract was combined with human prostate cancer cells, this extract helped induced apoptosin in the prostate cancer cells, apoptosis is a mechanism of “programmed cell death” and considered important part of cancer treatment. Researcher concludes that the natural option for prostate cancer treatment is amygdalin.^[61] On other animal studies show that the amygdalin compound is combined with other antibody – enzyme complex it is effectively killing cancerous brain and bladder cells under certain condition.^[62]

PHARMACOLOGICAL EFFECTS

Amygdalin is most useful part of Traditional Chinese Medicine (TCM) which is normally found in bitter almond, it has been studying on from two hundred years. For cough and Cancer, the extracted amygdalin from bitter almond which has been used as auxiliary medicine that is explained by First Schrader In 1803 and later Robiquet.^[63, 64] Pharmacological effects of amygdalin are shown in Figure 3.

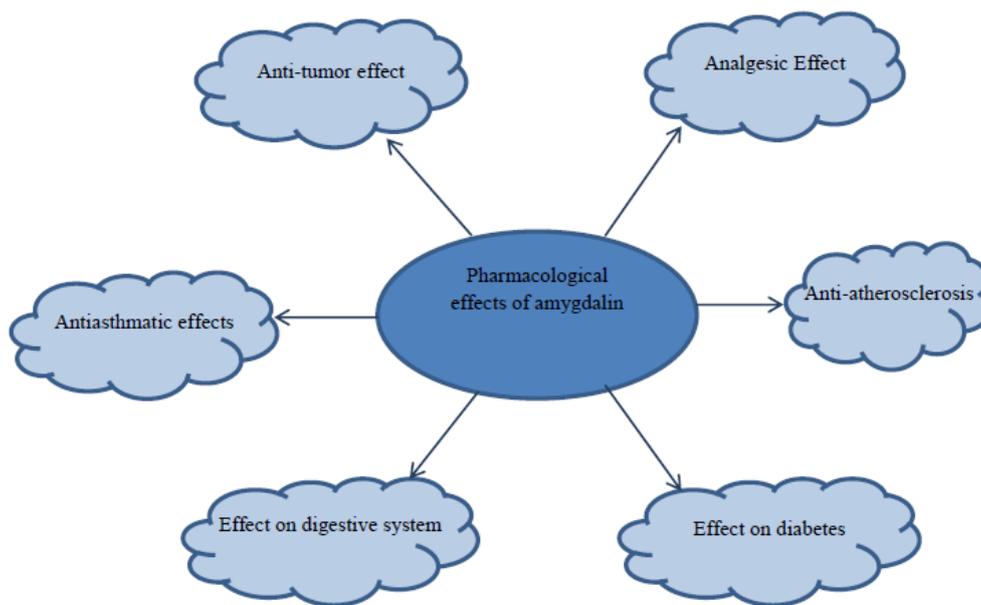


Figure 3. Pharmacological effects of amygdalin.

Anti-tumor effect: In 1970s, for improving the efficiency of cancer cells therapy, amygdalin was prescribed as a complementary drug. Anti-tumor effect may be depend upon the cell cycle process, the induction of apoptosis, the production of toxins to reduce or

eliminate the activity of cancer cells and regulating the immune function [Table 1]. Recent studies explain that the choosing an effective dose of amygdalin has lethal effect with minimum side effects on surrounding cells.^[65, 66, 67, 68, 69, 70]

Table 1: Anti-tumor effect of Amygdalin.

Types of cancer	Cell types & Dosage of amygdalin	Treatment time	Cellular effects	Ref.
Renal cell carcinoma cancer	RCC cell line type; KTC-25; 10mg/kg	24 hours or 2 weeks	Apoptosis, adhesionand Proliferation.	[71]
Bladder	Human cells; 10mg/ml (UMUC-3 or RT112 blander cancer cells)	24 hours or 2 weeks	Proliferation, Adhesion, invasion, cell cycle, migration, cytotoxicity.	[72]

Prostate	LNCaP cells (Castration-sensitive), DU-145 and PC3 cells (castration-resistant); 0.1mg/ml, 1mg/ml, 10mg/ml.	24 hours or 2 weeks	Proliferation, apoptosis, cell cycle. Dose of amygdalin dependently diminished tumor cell growth at 10mg/ml (maximum effects)	[73]
Colon	Rat model colon cancer; 5 mg/ml	24 hours	Proliferation, cell cycle, cytotoxicity proliferation, apoptosis.	[74]
Cervical cancer	Hela Cells of cervical cancer; 1.25mg/ml, 5mg/ml, 20mg/ml.	24 hours	Apoptosis, Proliferation. Through mechanism of apoptosis amygdalin inhibit the growth of Hela cells.	[75]

Anti-atherosclerosis effect: It refers to the build-up of cholesterol, fats and other substances on the artery walls, which is restricted to blood flow.^[76] The combination of amygdalin in apolipoprotein E- knockout mice fed and probucol with a fat diet is mediated the Anti-atherosclerosis effect. Result showed that this combination is effectively reducing atherosclerotic progress.^[77]

Analgesic effect: After treatment with amygdalin nalorphine induced jump response and mice lack tail-erecting response found that the mouse hot plate and acetic acid-induced writhing test which shows that the amygdalin has no tolerance and analgesic effect.^[78, 79]

Anti-atherosclerosis: Atherosclerosis explains cholesterol, fats and other substances on the plaque, which shows resistant on blood flow.^[80] The combination of probucol and amygdalin in apolipoprotein E-knockout mice fed with high-fat diet is mediated the Anti-atherosclerosis effects. Study showed that amygdalin and probucol effectively decrease the anti-atherosclerosis effect.^[81]

Effect on diabetes: Amygdalin increases the activity of pancreatic enzymes. This compound enhances the lower blood sugar and insulin secretion in body.^[82] Within 4 to 8 hours, the treatment of diabetic mice with amygdalin and almond extract significantly reduced their blood serum glucose.^[83]

Effect on digestive system: Through the enzyme decomposition amygdalin is decomposed the benzaldehyde. Amygdalin play important role in inhibit the activity of digestion cycle and pepsin. After enzymatic breakdown formed compound was essential in improving the acute gastric and atrophic diseases in mice.^[84] Amygdalin protected gastric mucosa from alcohol induced gastric ulcers.^[85]

CONCLUSION

This review paper shows study of vitamin B17 in cancer treatment. Amygdalin is natural source found in apricot where vitamin B17 is also natural source found in nuts, apple seeds, fruits and other sources. Vitamin B17 act as nutrition for healthy cells and lethal for cancer cells. So it is act as natural chemotherapy in treatment of cancer treatment. There are lots of study who explain that vitamin B17 have anti-cancer activity property. Vitamin

B17 is also known as Amygdalin. The concentration of amygdalin is low as compare to concentration needed in vivo experimental condition. We hope this review helps in future research for use of amygdalin or vitamin B17 in pharmacy.

REFERENCES

1. Ferlay J, Ervik M, Lam F, Colombet M, Mery L, Pineros M, et al. Global Cancer Observatory: cancer today. Lyon: International Agency for Research on Cancer; 2020, accessed February 2021).
2. Milazoo S, Horneber M. Laetrile treatment for cancer. The Cochrane Library. 2015. 1.
3. Basuony M, Hafez E, Tousson E, Massoud A, Elsomkhraty S and Eldakamawy S (2015). Beneficial role of Panax ginseng root aqueous extract against Cisplatin induced blood toxicity in rats. Am. J. Biol. Chem., 3(1): 1-7.
4. Al-Rasheed NM, El-Masry TA, Tousson E, Hassan HM and Al-Ghadeer A (2017). Protective potential of Grape Seed Proanthocyanidins Extract against Gleevec (Imatinib Mesylate) Induced Liver Toxicity and Oxidative Stress in Male Rats. Annual Res. & Review in Biol., 20(6): 1-9.
5. Al-Rashed NM, El-Masry TA, Tousson E, Hassan HM and Al-Ghadeer A (2018). Hepatic protective effect of grape seed proanthocyanidin extract against Gleevec-induced apoptosis, liver Injury and Ki67 alterations in rats. Brazilian Journal of Pharmaceutical Sci., 54(2): e17391.
6. Tousson E, Hafez E, Zaki S and Gad A (2014). P53, Bcl-2 and CD68 expression in response to amethopterin-induced lung injury and ameliorating role of L-carnitine. Biomed. Pharmacoth., 68(5): 631-9.
7. Tousson E, Hafez E, Zaki S and Gad A (2016). The cardioprotective effects of L-carnitine on rat cardiac injury, apoptosis, and oxidative stress caused by amethopterin. Environm. Sci. Pollution Res., 23(20): 20600-20608.
8. Tousson E (2016). Histopathological alterations after a growth promoter boldenone injection in rabbits. Toxicol. Industrial Health, 32(2): 299-305.
9. Tousson E, Bayomy MF and Ahmed AA (2018a). Rosemary extract modulates fertility potential, DNA fragmentation, injury, K167 and P53 alterations induced by etoposide in rat testes. Biomed. Pharmacoth., 98(2): 769-74.

10. Thun M.J. et al., 2010. The global burden of cancer. Priorities for prevention. *Carcinogenesis*, 31(1): 100-110.
11. Dorr R.T., Paxinos J (1978). The current status of laetrile. *Ann. Intern Med.*, 89(3): 389-97.
12. Viehoveer A, Mack H. (1935). Bio-chemistry of amygdalin (bitter, cynogenetic principle from bitter almonds). *Am. J. Pharm.*, 10: 397-450.
13. Curt G. A. (1990). Unsound methods of cancer treatment. *Princ. Pract. Oncol. Updates*, 4(12): 1-10.
14. He XY, Wu LJ, Wang WX, Xie PJ, Chen YH, Wang F. Amygdalin- A pharmacological and toxicological review. *J Ethnopharmacol*, 2020; 254: 112717.
15. Mani J, Neuschäfer J, Resh Ch, Rutz J, Maxeiner S, Roos F, et al. Amygdalin modulates prostate cancer cell adhesion and migration in vitro. *Nutr Cancer*, 2020; 72(3): 528-37.
16. El-Masry T, Al-Shaalan N, Tousson E, Buabeid M, Al- Ghadeer A. Potential therapy of vitamin B17 against Ehrlich solid tumor induced changes in Interferon gamma, Nuclear factor kappa B, DNA fragmentation, p53, Bcl2, surviving, VEGF and TNF- α Expressions in mice. *Pak J Pharm Sci.*, 2020; 33(1 Suppl): 393-401.
17. El-Kholy WB, Abdel-Rahman SA, Abd El-Hady El-Safti FEN, Issa NM. Effect of vitamin B17 on experimentally induced colon cancer in adult male albino rat. *Folia Morphol*, 2021; 80(1): 158-69.
18. Kolesar E, Tvrda E, Halenar M, Schneidgenova M, Charstinova L, Ondruska L, et al. Assessment of rabbit spermatozoa characteristics after amygdalin and apricot seeds exposure in vivo. *Toxicol Rep.*, 2018; 5: 679-86.
19. Bailly Ch. Anticancer properties of prunus mume extracts (Chinese plum, Japanese apricot). *J Ethnopharmacol*, 2020; 246: 112215.
20. Ragga H.S. H, Agr.bdEl Rahman, A.A Tasneem, O.H. Mohammed, M.F. Omnia, and A.A. Aya 2019. Experimental and Therapeutic Trials of amygdalin. *International Journal of Biochemistry and Pharmacology*, 1(1): 21-26.
21. Hydrolysis reaction of amygdalin. Available from: <http://www.chm.bris.ac.uk/motm/amygdalin/amygdalin.htm>.
22. Ross W.E. (1985). Unconventional cancer therapy. *Compr. Ther.*, 11(9): 37-43.
23. Moertel C.G., Fleming T.R., Rubin J., Kyols L.K., Sarna G., Koch R., currie V. E., Young C.W., Jones S.E., Davignon J. (1982). A clinical trial of amygdalin (laetrile) in the treatment of human cancer. *N. Engl.J. Med.*, 306(4): 201-206.
24. Greenberg DM (1975) The vitamin fraud in cancer quackery. *West J Med*, 122(4): 345-348.
25. Blaheta RA, Karen N, Axel H, Eva J (2016) Amygdalin, Quackery or cure? *Phytomedicine*, 23(4): 367-376.
26. The laetrile controversy. In: Moss RW: *The Cancer Industry: The Classic Expose on the Cancer Establishment*. Brookly, NY: First Equinox Press, 1996; 131-52.
27. Lerner IJ (1990) Laetrile: A lesson in cancer quackery. *CA Cancer J Clin*, 31(2): 91-95.
28. Moss RW (2005) Patient perspectives: Tijuana cancer clinics in the post-NAFTA era. *Integr Cancer ther*, 4(1): 65-86.
29. Davignon JP, Trissel LA, Kleinman LM (1978) Pharmaceutical assessment of amygdalin (laetrile) products. *Cancer Treat Rep*, 62(1): 99-104.
30. Chandler RF, Anderson LA, Phillipson JD. Laetrile in perspective. *Can Pharm J.*, 1984; 117(11): 517-20.
31. Curran WJ (1980) Laetrile for the terminally ill: Supreme court stops the nonsense. *N Engl J Med*, 302(11): 619-621.
32. Davignon JP, Trissel LA, Kleinman LM (1978) Pharmaceutical assessment of amygdalin (laetrile) products. *Cancer Treat Rep*, 62(1): 99-104.
33. Curt GA. Unsound methods of cancer treatment *Princ Pract Oncol Updates*, 1990; 4(12): 1-10.
34. Curran WJ (1980) Laetrile for the terminally ill: Supreme court stops the nonsense. *N Engl J Med*, 302(11): 619-621.
35. Davignon JP, Trissel LA, Kleinman LM (1978) Pharmaceutical assessment of amygdalin (laetrile) products. *Cancer Treat Rep*, 62(1): 99-104.
36. George M (2016) *Practical Organic Chemistry* (4th edn), London, UK, 509-517.
37. <https://cancercompassalteroute.com/therapies/vitamin-b17-laetrile/>
38. Barrie R, Cassileth. Amygdalin (Vitamin B17). *IOOJ.*, 2009; 23(5).
39. Various methods of cancer management. Available from: <http://cochranelibrary-wiley.com/doi/10.1002/14651858.CD005476.pub4/pdf>.
40. Barrie RC (2009) Amygdalin (Vitamin B17). *IOOJ*, 23(5): 1-2.
41. Unproven methods of cancer management. *Cancer J of Clinician*, 1991; 41(3): 187-192. Available from: <https://onlinelibrary.wiley.com/doi/pdf/10.3322/canjclin.41.3.187>.
42. Mora A, et al. Application of the Prunus spp. Cyanide Seed Defense System onto Wheat: Reduced Insect Feeding and Field Growth Tests. *J Agric Food Chem.*, 2016; 64: 3501-3507.
43. Bolarinwa F, et al. Amygdalin content of seeds, kernels and food products commercially-available in the UK. *Food Chem.*, 2014; 152: 133-139.
44. Walaa FE (2018) Mechanism action of amygdalin as natural chemotherapy to prevent colon cancer, *RRJPTS*, 6(1): 47-51.
45. Mohammed Elbossaty WF. Mechanism action of amygdalin as natural chemotherapy to prevent colon cancer. *RRJPTS*, 2018; 6(1): 47-51.
46. Binzel, p.e. (1994). *Alive and Well*, American Media, California, 21-23.
47. Manner, H.W., T. L. Michaelson, S. J. DiSanti (1978). *Enzymatic Analysis of normal and malignant Tissues*, presented at the Illinois state Academy of science.

48. Manner, H.W., T. L. Michaelson, S. J. DiSanti (1978). Amygdalin, Vitamin B.
49. I.F. Bolarinwa, C. Orfila, M.R.A. Morgan, "Amygdalin content of seeds, kernels and food products commercially-available in the UK" *Food Chemistry*, 2014; 152: 133-139.
50. Nitin S (2016) Vitamin B17 and its proposed application in treating cancer. *Interdisciplinary Journal of Contemporary Research*, 3(6): 2393-8358.
51. Bolarinwa F, Orfila C, Morgan R (2014) Amygdalin content of seeds, kernels and food products commercially available in the UK. *Food Chem*, 152: 133-139.
52. Chang HK, yang HY, Lee TH, Shin MC, Lee MH, et al. (2005) Armeniacae semen extract suppresses lipopolysaccharide-induced expressions of cyclooxygenase-2 and inducible nitric oxide synthase in mouse BV2 microglial cells. *Biol Pharm Bull*, 28(3): 449-454.
53. Nabavizadeh F (2011) Gastroprotective effects of amygdalin on experimental gastric ulcer: Role of NO and TNF- α . *J Med Plants Res.*, 5(14): 3122-3127.
54. Yan J (2006) Preparative isolation and purification and amygdalin from *Prunus armeniaca* L. with high recovery by high-speed countercurrent chromatography. *J Liq Chrom Rel Tech*, 29(9): 1271-1279.
55. Eichholz A, Merchant S, Gaya A, (2010) Anti-angiogenesis therapies: Their potential in cancer management. *Onco Targets Ther.*, 3: 69-82.
56. Marianpour H, Shahnaz K, Ali Z, Omid K, Siavash GN, et al. (2012) Amygdalin inhibits angiogenesis in the cultured endothelial cells of diabetic rats. *Indian J Pathol Microbiol*, 55(2): 211-214.
57. Milazo S, Horbener M, (2015) Laetrile treatment for cancer. *Cochrane Database Syst Rev.*, (4): 54-76.
58. Shalayel M. Epigenetic Mode of Bacterial Drug Resistance. *Br. Biomed Bull*, 2017; 5: 296: 1-2.
59. Suchard JR, Wallace KL, Gerkin R (1998) Acute cyanide toxicity caused by apricot kernel ingestion. *Ann Emerg Med*, 32(6): 742-744.
60. Liczbinski P, Bukoswaka B (2018) Molecular mechanism of amygdalin action *in vitro* review of latest research. *Immunopharmacol Immunotoxicol*, 40(3): 212-218.
61. Chang H.K., Shin M.S., Yang H.Y., Lee J.W., Kim Y.S., Lee M.H., Kim J., Kim K.H., Kim C.J. (2006). Amygdalin induces apoptosis through regulation of Bax and Bcl-2 expressions in human DU145 and LNCap prostate cancer cells. *Biol. Pharm. Bull.*, 29(8): 1597-1602.
62. Biaglow E.J., Durand E.R. (1978). The enhanced radiation response of an *in vitro* tumor model by cyanide released from hydrolysed Amygdalin. *Int. J. Radiat. Biol.*, 33(4): 397-401.
63. Halenár M, Medved'ová M, Maruníaková N, Kolesárová A. Amygdalin and its effects on animal cells. *J Microbiol Biotechnol Food Sci.*, 2013; 2: 1414-23. http://www.jmbfs.org/wp-content/uploads/2013/04/31_jmbs_halenar_fbp_b.pdf
64. Hwang HJ, Kim P, Kim CJ, Lee HJ, Shim I, Yin CS, et al. Antinociceptive effect of amygdalin isolated from *Prunus armeniaca* on formalin-induced pain in rats. *Biol Pharm Bull*, 2008; 31(8): 1559-64.
65. Chen Y, Ma J, Wang F, Hu J, Cui A, Wei Ch, et al. Amygdalin induces apoptosis in human cervical cancer cell line HeLa cells. *Immunopharmacol immunotoxicol*, 2013; 35(1): 43-51.
66. Qian L, Xie B, Wang Y, Qian J. Amygdalin-mediated inhibition of non-small cell lung cancer cell invasion *in vitro*. *Int J Clin Exp Pathol*, 2015; 8(5): 5363-70.
67. Makarević J, Rutz J, Juengel E, Kaul Fuss S, Tsaur I, Nelson K, et al. Amygdalin influences bladder cancer cell adhesion and invasion *in vitro*. *PLoS one.*, 2014; 9(10): e110244.
68. Juengel E, AFschar M, Makarević J, Rutz J, Tsaur I, Mani J, et al. amygdalin blocks the *in vitro* adhesion and invasion of renal cell carcinoma cells by an integrin-dependent mechanism. *Int J Mol Med.*, 2016; 37(3): n 843-50.
69. Sohail R, ABBAS SR. Evaluation of amygdalin-loaded alginate-chitosan nanoparticles as biocompatible drug delivery carriers for anticancerous efficacy. *Int J Biol Macromol*, 2020; 153: 36-45.
70. Du Hk, Song FC, Zhou X, Li H, Zhang JP. [Effect of amygdalin on serum proteinic biomarker in pulmonary fibrosis of bleomycin-induced rat (chinese)]. *Zhonghua Lao Dong Wei Shenf Zhi Ye Bing Za Zhi.*, 2010; 28(4): 260-3.
71. Sohail R, Abbas SR. Evaluation of amygdalin loaded alginate-chitosan nanoparticles as biocompatible drug delivery carries for anticancerous efficacy. *Int J Biol Macromol*, 2020; 153: 36-45.
72. Juengel E, AFschar M, Makarević J, Rutz J, Tsaur I, Mani J, et al. amygdalin blocks the *in vitro* adhesion and invasion of renal cell carcinoma cells by an integrin-dependent mechanism. *Int J Mol Med.*, 2016; 37(3): n 843-50.
73. Qian L, Xie B, Wang Y, Qian J. Amygdalin-mediated inhibition of non-small cell lung cancer cell invasion *in vitro*. *Int J Clin Exp Pathol*, 2015; 8(5): 5363-70.
74. EI- Kholy WB, Abdel-Rahman SA, Abd EI-Hady EI-Safti FEN, Issa NM. Effect of vitamin B17 on experimentally induced colon cancer in adult male albino rat. *Folia Morphol*, 2021; 80(1): 158-69.
75. Qian L, Xie B, Wang Y, Qian J. Amygdalin mediated inhibition of non-small cell lung cancer cell invasion *in vitro*. *Int J Clin Exp Pathol*, 2015; 8(5): 5363-70.
76. He XY, Wu LJ, Wang WX, Xie PJ, Chen YH, Wang F. Amygdalin-A pharmacological and toxicological review. *J Ethnopharmacol*, 2020; 254: 112717.

77. Qu SL, Fang Q, Chen GX, Wang ZH. Effects of terandrine, tetramethylpyrazine and amygdalin in on human kidney fibroblast. *Chin J nephrol*, 2000; 16(3): 186-9.
78. Zhu Y.P, Z.W. Su, C.H. Li. "Analgesic effect and no physical dependence of amygdalin." *ZhongguoZhong Yao ZaZhi*, 1994; 19: 128.
79. Biaglow E.J, E.R. Durand, "The enhanced radiation response of an in vitro tumor model by cyanide released from hydrolysed Amygdalin." *Int. J. Radiat. Biol.*, 1978; 33(4): 397-401.
80. He XY, Wu LJ, Wang WX, Xie PJ, Chen YH, Wang F. Amygdalin-A pharmacological and toxicological review. *J Ethnopharmacol*, 2020; 254: 112717.
81. Qu SL, Fang Q, Chen GX, Wang ZH. Effect of tetrandrine tetramethylpyrazine and amygdalin on human kidney fibroblast *Chin J Nephrol*, 2000; 16(3): 186-9.
82. Bailey CJ, Day C. Traditional plant medicines as treatments for diabetes. *Diabetes care*, 1989; 12(8): 553-64.
83. Shim SM, Kwon H. Metabolites of amygdalin under simulated human digestive fluids. *Int J Food Sci Nutr.*, 2010; 61(8): 770-9.
84. Nabavizadeh F, Alizadeh AM, Sadroleslami Z, Adeli S. Gastroprotective effects of amygdalin on experimental gastric ulcer: Role of NO and TNF- α . *J Med Plant Res.*, 2011; 5(14): 3122-7.
85. Cai Y, Li YM, zhong L. Effect of amygdalin on gastric ulcers in experimental models. *Journal-China Pharmaceutical University*, 2003; 34(3): 254-6.