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### Laetrile: A wonder drug or farce?

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#### Abstract

Cancer is one of the most feared diseases with exorbitant treatment costs which render the patients helpless, a condition in which alternative therapies come in the picture.

A number of companies come up with a wide variety of agents which claim to cure cancer with lesser side effects and at a lower cost. One such drug is 'Laetrile', also known as 'Amygdalin' and popularly marketed as 'Vitamin B17'. The effectiveness of this drug, however, is crucially questionable.

The toxic effects of this drug have been found to be more severe in individuals consuming high amounts of Vitamin C. Toxicity of this drug is also associated with Vitamin B12 deficiency, which is a commonly found state in India. It is presently an easily available drug within India. Indian population is thus at great risk from consumption of this drug due to the possible adverse effects.

India is the country with a major part of population below the poverty line, which forces the individuals toward alternative therapies. The ambiguity of the nature of this drug has led to turmoil amongst the oncologists and the suffering patients, and strict laws till the time this drug has not been proved to be harmless and effective, along with more advanced research is the need of the hour.

**Keywords:** Cancer, Laetrile, Amygdalin, Vitamin B17

#### Introduction

'Cancer' is a word which in itself is capable of instilling fear in any individual. Being a disease of aggressive nature, treatment modalities are consuming and associated with dire side effects. Exorbitant treatment costs, high morbidity and indefinite cure are concordant concerns which bother the patients as well as their families.

Consequently, the affected individuals often seek alternative therapies which seem promising at the time of need. Indian ancient literature comprises of a number of agents which can be used for various ailments, with a significantly lower incidence of adverse effects. Such therapies attract the patients due to their primordial existence and an inherent inclination of people towards indigenous or 'herbal' medicines.

Conventional anti-cancer drugs and treatment strategies are associated with a high degree of apprehension. Hence, with a ray of hope, a large number of patients choose these alternative therapies for treatment of cancer.

One such drug that has been commonly talked about lately is 'Laetrile'. It is a semi-synthetic derivate of the parent compound 'Amygdalin', which is a natural agent found within seeds of fruits such as peaches, bitter almonds and apricots. Both Laetrile and Amygdalin have similar structures and contain cyanide, which is known to target the cancer cells<sup>[1]</sup>.

However, the activity and effectiveness of Laetrile is crucially questionable. According to the Cochrane review published in 2015, the claims that laetrile or amygdalin have beneficial effects for cancer patients are not supported by sound clinical data<sup>[2]</sup>.

#### Indian scenario

According to Jonathan Bromley *et al.*<sup>[3]</sup> the risk of harm that is parallel with Amygdalin consumption becomes even more remarkable when it occurs in patients who concomitantly consume Vitamin C, which is a widely consumed vitamin in its natural form as well as a nutritional supplement.

According to Crampton RF *et al.*<sup>[4]</sup> the risk of toxicity has also been found to be greater in patients who have a deficiency of Vitamin B12, which is commonly observed in vegetarians, meat being the primary source of this Vitamin.

In 2007, the Food and Agriculture Organizations of the United Nations ranked India as the lowest consumer of meat in the world (3.2 kg per person per year, a value 120 kg less than the United States of America) [5]. A study done by Eimear Leahy in 2010 revealed that more than 34% of the Indian population is vegetarian [6]. According to Edelstein S, India has more vegetarians than the rest of the world put together, corresponding with a large number of Vitamin B12 deficient population [7].

According to a report published by the World Bank in 2016, India had 30 per cent of its population living below poverty line. The cancer survival rate in India is among the lowest in the world, despite having better and advanced treatment modalities. The major reason behind this is the lack of affordability of these advanced treatments.

Living in a country with exorbitant conventional cancer treatment costs, it is not surprising to find people drifting toward any other alternative therapy which they come across in the time of need.

The propaganda of Laetrile or Amygdalin profoundly influences people worldwide through social media and YouTube. Laetrile, being endorsed as an aboriginal anti-cancer agent, is sold in India via pharmaceutical companies over the counter. The drug can easily be procured over the counter in some states of India and through online marketing as well. It is available in the form of tablets for oral administration and injections which can be given intravenously or intramuscularly. It has been found that the incidence of cytotoxicity associated with this drug is much higher when this drug is taken orally [8, 9, 10].

The benefits of this technique seem plenty; however, the risk-benefit balance of this drug as an alternative treatment for cancer is “unambiguously negative” [2]. With a large amount of literature in favour as well as against the consumption of this drug as an anti-cancer agent, it becomes a critical dilemma whether or not to prescribe this drug to the patients in need.

### Definition

The words ‘Amygdalin’, ‘Laetrile’ and ‘Vitamin B17’ are often used interchangeably for one common supposed anti-cancer agent. There exists, however, a difference between them. The word ‘Amygdalin’ ( $C_{20}H_{27}NO_{11}$ ) refers to the naturally occurring chemical compound which is found in raw nuts and seeds of plants and fruits belonging to the Rosaceae family, such as almond, apricot, peach, apple and plum.

‘Laetrile’ ( $C_{14}H_{15}NO_7$ ) is a semi-synthetic derivative of Amygdalin, which was patented in the 1950s and is still promoted as an anti-cancer agent. The word is derived from laevorotatory (‘lae’) and mandelonitrile (‘trile’), which is the common structural component of both Amygdalin and Laetrile.<sup>11</sup>

‘Vitamin B17’ is the name given to Laetrile and Amygdalin compounds by E.T. Krebs Jr., as an attempt to pass these agents off as necessary vitamins for human health. Another reason to label these drugs as vitamins was to avoid FDA screening and regulations which apply to medicines but not to vitamins. At present these drugs are not classified as a vitamin and the claim that Laetrile is an essential component is not backed by any scientific evidence.

### History

Amygdalin was first isolated in 1830 by two French chemists [12], and was first used in Russia in 1845, where positive results were reported for the patient who was treated [13]. The

use of Amygdalin soon became known to large population. In the 1950s in United States of America, Laetrile was patented as a non-toxic form of Amygdalin [14]. Owing to the large number of toxicities reported, the U.S. Supreme Court acted to uphold a federal ban on interstate shipment of laetrile in 1980 [15]. Since then, the ambiguity pertaining to the use of this drug has been going on.

Laetrile is commonly marketed and promoted as Vitamin B17. However, according to the U.S. National Library of Medicine in 2017, Laetrile is not scientifically categorized as a vitamin by the Committee on Nomenclature of the American Institute of Nutrition Vitamins. After its ban from the United States of America, it was a mere strategy to label the compound as vitamin in order to promote its usage as a safe and necessary anti-cancer agent, and to bypass approval of the FDA.

### Mechanism of action

Laetrile is a cyanogenic agent, which breaks down to form cyanide on interacting with an enzyme Beta-glucuronidase, which is a member of the glycosidase family of enzymes that catalyze the breakdown of complex carbohydrates [16].

Hydrogen cyanide is reported to be the main agent in Laetrile which is responsible for killing of cancer cells [17], and when the drug hydrolyzes in the presence of Beta-glucuronidase, hydrogen cyanide is formed.

However, according to Dorr RT, the concentration of Beta-glucuronidase in malignant cells is no more in abundance than in normal healthy body cells [12].

Another suggested enzyme to play a role is Rhodanese, which is responsible for converting cyanide into thiocyanate to render it harmless within the human body. It has been postulated that this enzyme is exclusive to non-cancer cells, thereby preventing the non-cancer cells from cyanide toxicity, and the toxic effects of Laetrile on cancer cells are because of an imbalance in these two enzymes [18].

According to the CA- A Cancer Journal for Clinicians, Rhodanese levels are equal in both cancer and non-cancer cells, therefore, refuting this theory as well.

However, experimental evidence does exist supporting the idea that the normal and malignant tissues do differ significantly in their concentrations of Beta-glucuronidase and Rhodanese [8, 19].

### Concomitant intake of vitamin C

Vitamin C is widely consumed by individuals in natural form, as well as in the form of dietary supplements. Cyanide, once inside body, needs to be converted to thiocyanate as quickly as possible to have minimal side effects. Therefore, individuals with reduced capability to convert cyanide to thiocyanate face greater risk of experiencing adverse effects of Laetrile.

According to Calabrese EJ [20], large doses of Vitamin C are associated with diminished body Cysteine, which is a sulphur containing amino acid, known to facilitate the detoxification of cyanide. Consequently, people who are consuming high doses of Vitamin C are at a risk of even more severe side effects from consumption of Laetrile.

### Deficiency of vitamin B12

Vitamin B12, also known as Cobalamin, is a member of B-complex vitamins, and is known to maintain normal functioning of nerve cells and formation of red blood cells. Major sources of Vitamin B12 include animal products such as fish, meat, eggs etc. Given the large proportion of

vegetarian population in India, it is not uncommon to find individuals with deficiency of vitamin B12.

According to the Cochrane Review on Laetrile, the risk of cyanide toxicity associated with Laetrile consumption increases with deficiency of Vitamin B12.

The theory which supports this relationship was proposed by Houeto *et al.* [21] It states that cyanide is converted to cyanocobalamin by Vitamin B12, which is excreted from the kidneys. In the absence of this conversion or detoxification of cyanide, the risk increases.

### Discussion

A study was conducted by CG Moertel *et al.* on 178 cancer patients who were treated with Laetrile. All of these patients had never undergone chemo or any other form of anti-cancer therapy. At the end of the study, no benefit was found in any patient. Along with that, there was a lethal elevation of cyanide levels in several patients. The authors thus concluded that Laetrile has no value in the treatment of cancer.

A systematic review was published in 2007 by Stefania Milazzo, Stephane Lejeune, and Edzard Ernst to assess the clinical evidence for Laetrile efficacy in cancer [22]. The authors collected and compiled all the scientific data available from various portals where Laetrile was used for treatment of cancer. They found 36 studies matching their inclusion criteria and evaluated them. No Randomized controlled trial was found. On compiling the results, it was found that the effectiveness of Laetrile was proved in none of these studies.

The Cochrane Review for Laetrile treatment for cancer was published by Milazzo S, Horneber M. in 2015. The authors reviewed available literature and concluded that the efficacy of Laetrile or Amygdalin in cancer is not currently supported by sufficient sound clinical data. Along with having no beneficial effects, there lies a significantly high risk of adverse effects arising from cyanide poisoning after laetrile or amygdalin.

Conventional cancer treatment modalities such as chemotherapy, surgery and radiotherapy used to treat cancers are also associated with a high rate of morbidity; however, there is sufficient evidence to prove their efficacy in reduction of cancer cells as well. Therefore, the risk of adverse effects is justified due to the benefits that may be obtained from the conventional therapies. On the contrary, along with the perilous side effects of Laetrile, there is no conclusive evidence that it works as an anti-cancer agent.

Laetrile is not approved from the US Food and Drug Administration because of its potential toxicity and was banned for sale in 1980s. It is sold as a natural extract of Amygdalin in Mexico currently. However, in India there are no particularly stringent laws pertaining to the manufacture and sale of this drug. Through online retailers, this drug can easily be bought in bulk for consumption.

Social media, including websites like YouTube and Facebook, are used by proponents of Laetrile to promote this drug. Since the accessibility of general population to such websites is much more than the accessibility to scientific literature, it is highly common for people to get influenced and fall for the idea of such alternative therapies for cancer in the time of need.

With a large proportion of the country's population below the poverty line, the affordability of costly treatment procedures leave the patients with very limited options and these alternative therapies play a role in such situations. Further conclusive research is of paramount importance to ascertain the efficacy and safety of this drug.

However, as a precautionary measure, till the time there is insufficient scientific data available, strict laws should be implemented within the country pertaining to the manufacture and sale of dubious drugs over the counter.

Therefore, an increased level of awareness is of paramount importance among the general population. All clinicians who deal with patients with cancer should meticulously counsel the patients and their family members to not get influenced by marketing strategies of scientifically unproven drugs. More research in this field is the need of the hour in the Indian population, where conventional cancer treatments are out of reach of many.

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