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### Background activity of the amygdalin as antitumor

Prasad Meraboina<sup>1</sup>, Saravanan Jaganathan<sup>2</sup>, Dr.N.Sriram<sup>1</sup>, Raju.N<sup>3</sup>, Dr. Vijayakumar Daroji<sup>2</sup>

<sup>1</sup>Holy Mary Institute of Technology & Science College of Pharmacy, Keesara, Telangana 200253

<sup>2</sup>College of Pharmacy, Kannur Medical College, Anjarakandy, Kannur Kerala 670612

<sup>1</sup>Holy Mary Institute of Technology & Science College of Pharmacy, Keesara, Telangana 200253

<sup>3</sup>Vadevi College of pharmacy, Singaram, Telangana 506005

<sup>2</sup>College of Pharmacy, Kannur Medical College, Anjarakandy, Kannur Kerala 670612

\*Corresponding Author: Prasad Meraboina

#### ABSTRACT

Cancer is one of the most deadliest disease in the world nearly 10% of world population is suffering with the various types of the cancerous condition as a growth in the science now a day's scientist has discovered various types of like chemotherapy, radiotherapy, immunotherapy and some other treatment, but in the mid of the 18<sup>th</sup> century an compound called amyglidn was identified as best treatment for cancer condition to many patients but in the starting of the 20<sup>th</sup> century it was thought to be not the safest treatment for the cancer so it was banned to use for the patients. Some scientist has scaled the positives and negatives of the amyglidn and concluded that more number of negatives than that of the positives. But there are few supporters for the treatment of the amyglidn to cancer patients.

**Keywords:** Amygdalin, Antitumor, Benzaldehyde and Hydrocyanic acid.

#### INTRODUCTION

Cancer is a disease which can be presented as an abnormal cell growth by having a power to invade or develop to other body parts. As per the research studies it was found that nearly 22% of cancer patients death are due to having alcohol and/or tobacco and having the unhealthy weight maintenance like obesity and poor diet factors are also one of the major factor for the disease, other factors including exposed to the radiation, toxic materials in some people it can be occurred due to the infections by various organisms, it can also be occurred due to inheritance of the genetic matter [1] it may be as a defects or changes in the gene

from the parents generally genetic changes or the variation in the genetic leads to the cancer.

Generally Cancer begins with a change in the one cell and then it starts growing and multiplying rapidly without any control in its growth it can divide one into two then four and s on until they form a mass of cells which is called as tumour. Tumors are divided into types based on their metastasis capacity. In some tumours, the cells stay in the same place and as the tumour stops growing before it gets very large - often because it simply runs out space to grow. These are called benign tumors and they are not normally dangerous. In some conditions this tumour cells are able to invade the surrounding tissue and spread into nearby

organs where they can cause serious and, eventually, fatal damage. These are called malignant tumors.

They are many types of cancers actually they have been divided based on the type of cell that the tumor cells has been occurred it mean origin of the tumor in the body. They are Carcinoma: in this condition cancers are from epithelial cells. It is most common cancers and this include nearly all those

in the breast, prostate, lung, pancreas and colon.

Sarcoma in this state cancer is developed from the connective tissue which includes bone, cartilage, fat, nerve cells. Lymphoma: both are raised from hematopoietic cells. [2] Germ cell tumor is an condition in which the cancers is developed from pluripotent cells, Blastoma: Cancers derived from immature "precursor" cells or embryonic tissue.

Signs and symptoms of the cancers patients can't be same for all type of the cancers for example in the patient who is having breast cancer will be having the symptoms like lump in the breast, bloody discharge from the nipple. Prostate cancer will includes difficulty with urination but in some times there won't be any symptoms. In case of lung cancer patient will be having the symptoms like cough, chest pain, wheezing, weight loss and so on all the three mentioned are cancer condition but they don't have any common symptoms. But some minute symptoms can be or be n't the same in all the cancer patients but studies has shown few common conditions like unexplained weight loss, fever, fatigue, skin changes (like darker looking skin, reddened skin.), un usual bleeding, pain, hair loss, in digestion or problem in swallowing, nagging cough or hoarseness Symptoms of cancer metastasis depend on the location of the tumor. Generally for easy identification symptoms can be of local symptoms and systemic symptoms

Treatment for the cancer disease can also varied based on the condition, type, location, status of the disease and few other criteria. Generally types of the treatment for the cancer patients include chemotherapy, radiation therapy, hormonal therapy, targeted therapy and palliative care. The treatment intent may or may not be curative. Chemotherapy includes the treatment using various drugs. Radiation therapy includes exposed to the various ranges of the rays and destroying the cancers tumor cell, targeted therapy can be also know as surgery where the specific cell has been identified and they

are removed from the body in most of the cases after the targeted therapy chemotherapy is preferred in order to prevent the further occurrence of the diseases [3]. palliative care is one of the most important care given to the patient who is having the cancer generally Palliative care includes action to reduce physical, emotional, spiritual and psychosocial distress. Unlike treatment that is aimed at directly killing cancer cells, the primary goal of palliative care is to improve quality of life. [4]

Some of the recent advances in the treatment of the cancer diseases in the 20<sup>th</sup> century is Immunotherapy is an advanced treatment for the cancer condition which works to harness the innate powers of the immune system and makes to fight against various diseases. This therapy is most efficient when compared to that of remaining therapies. Because it is based on targeted for systemic treatment and it has fewer side effects. [5]

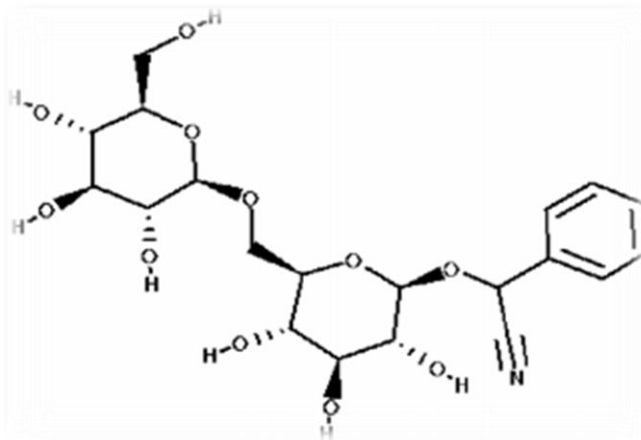
Therefore the anti-tumor effect of amygdalin is one of the hot topic in recent years regarding its anti tumor activity it can be done by decomposing carcinogenic substances in the body, killing cancer cells, blocking nutrient source of tumor cells, inhibiting cancer cell growth, and could also reduce the incidence of prostate cancer, lung cancer, colon cancer and rectal cancer. It were produced and manufactured in countries like America, Germany, Italy, Japan, Philippines and other 20 countries. Amygdalin do have some other effects also like anti-tussive, antiasthmatic, shows an beneficial effects in the digestive system, analgesic effect, it can also promote apoptosis of human renal fibroblast, improves human immune function effect and do have some minute effects in humans

Amygdalin is also known as bitter apricot, laetrile, and almond. Chemical structure of the D-mandelonitrile- $\beta$ -D-glucoside-6- $\beta$ -glucoside. It is widely distributed in the plants mainly in the rosaceae family plants like apricot, cherry, plum and etc.

Generally amygdalin itself is not toxic but when it is decomposed it converts into benzaldehyde and hydrocyanic acid (HCN) but HCN compound is a toxic material. In case of the anti- asthmatic property and the anti-tussive effect of the amygdalin hydrocyanic acid is produced and this compound inhibits the respiratory centre to normal level and it can also produce the pulmonary surfactant which has been observed in the animal models, but no certain evidence in case of humans

[6]. It can also mitigate the symptoms of patients in advanced stage of cancer, and prolong their

survival period.



Chemical structure of amygdalin

### The toxicity of amygdalin

Some toxicological studies have revealed that oral intake of the amygdalin has much toxic effect than that of the intravenous or intraperitoneal intake of the product. The mean lethal doses of the (LD<sub>50</sub>) of the amygdalin is nearly in rats was 880 mg/kg oral intake where as the LD<sub>50</sub> of intravenous injection in mice was about 25 g/kg, where as in case of the intraperitoneal administration of the amygdalin can be up to 8g/kg. The maximum safe dose of intravenous and intramuscular injection of amygdalin in mice 3 g/kg, 0.075 g/kg orally respectively. (Rietjens IMCM,) Many studies has revealed that amygdalin was hydrolyzed by some of the intestinal microbial after oral administration producing more hydrocyanic acid. Human can present systemic toxicity after oral administration of amygdalin 4 g per day, lasted for half a month or intravenous injection of a month.

### History of the amygdalin for the treatment of the cancer

The history of the amygdalin has been started from the past 18<sup>th</sup> century an two chemists named Robiquet and Boutron has separated the compound. In America it was used for the first time in the treatment of cancer during 1820s [7]. In mid 18<sup>th</sup> century intravenous amygdalin named Laetrile, was registered as a patent. USA National institute of cancer has been conducted few clinical studies. In another clinical studies 22 cases are been treated

with the drug and result has shown as only 6 cases had good effects against cancer hence it was concluded that the effect of the anti-tumor effect of the amygdalin was not enough to support FDA has filed the noted against the activity of the laetrile and banned the drug and noted as an toxic product in 1979 that leads to the stop using as a drug. In 1980, 23 states of USA restored application of amygdalin in the treatment of advanced cancer patients [8]. Unfortunately, American FDA approved NCI two clinical trials of amygdalin, the results could not confirmed the effectiveness of amygdalin. In 1987, the imports of amygdalin were banned in USA; afterwards amygdalin was banned in USA and Europe. In the UK, the drug can produce cyanide and has been listed as a prescription drug, which can be used under the supervision of a doctor.

Generally in normal cells rhodanese enzyme which is also known as thiosulfate sulfurtransferase will be present. This enzyme has a capability of neutralize benzaldehyde, hydrogen cyanide and transforming them into utilizable materials like thiocyanate (rhodanide) and benzoic acid. When laetrile is given cancer cells along with glucose then due to the lack of the rhodanese enzyme in cancer cell thiocyanate and benzoic acid were not formed, but instead of them cyanide and benzaldehyde is formed from delivered glucose due to the action of the  $\beta$ -glucosidase. Formed cyanide and benzaldehyde kills the neoplastic cells [9].

Amygdalin can be metabolized by the intestinal enzymes and PH condition of duodenal then a compound will be formed that is D-glucuronic acid and L-mandelonitrile (cyanohydrin). L-mandelonitrile will hydrolyze to cyanide and benzaldehyde. [10]

The controversy of the anti-tumor activity of the amygdalin was from the mid of the 19<sup>th</sup> century few hypothesis has been suggested the activity of the amygdalin in cancer cells.

Few popular hypotheses regarding the activity of the amygdalin are when the compound is taken orally then it is metabolized and formed mandelonitrile then mandelonitrile moves into the hepatic cells. Later  $\beta$ -glucosidase performs its activity and then cyanide compound will be formed, another hypothesis states that neoplastic cells do have a large amount of the  $\beta$ -glycosidase while the normal cells have huge amount of the rhodanese enzyme, which helps in the formation of the thiocynic acid. However some studies has concluded that the both the neoplastic and normal cells do contain equal amount of the rhodaneses and  $\beta$ -glucosidase. [11, 12]

Some scientists had concluded that the cancer is due to the laetrile or vitamin B17 deficiency; hence it was assumed that dietary administration of laetrile would prevent the incidence of the cancer.

An American biochemist, Ernst T. Krebs has suggested that laetrile to be as a vitamin and to categorize as a nutritional supplement to committee on nomenclature of the American institute of nutrition vitamins but it was not approved.

In one of the research study researches has conducted the study on the metastasis blocking properties of amygdalin on bladder cancer cell lines at last it was concluded that the mode of action of the amygdalin varies, depending on the tumor interim composition. Moreover, one study reported that amygdalin blocked bladder cancer cell growth by down-modulating the cell cycle regulating proteins cdk2 and cyclin A [13]

## CONCLUSION

Lot of studies has been done on the activity of the amygdalin in case of various diseases and in some studies they concluded that amygdalin shows a good effect where as the few research studies are vies versa to it. Even through the positives are present in case of cancer treatment, but still there is lot of confusion and controversy in the activity of the amygdalin. So in order to get clarity in this few more in –depth analysis need to be done on the activity of the amygdalin.

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