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Antinutrient Phytic acid: Can be proved to be a Boon for Colorectal Cancer

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Abstract: Phytic acid also known as inositol hexa-phosphate, is a simple ringed bioactive sugar molecule with six phosphate groups attached to each carbon. Cereals, pulses, and oil seeds contain considerable amounts of Phytic acid. Phytic acid is known as a potent anti-nutrient that binds with the minerals and forms chelates thus leading to mineral deficiency diseases if administered in excess dosage. The phytase (enzyme) containing foods can reverse the reaction and increase the bioavailability of minerals. In-spite of having anti-nutritional properties, phytic acid can be a boon for colorectal cancer. Colorectal cancer, the third most often malignant carcinoma, progresses sporadically in the setting of hereditary cancer syndromes, or on the basis of inflammatory bowel disease. Nutrients can directly affect the fundamental cellular processes and is considered as the most important risk factors in colorectal cancer. Colorectal Cancer occurs with the formation of polyps. Various mechanisms have been proposed for Phytic Acid as anti-tumorigenic abilities that are antioxidant properties, gene alteration, increase natural killer activity and cell cycle inhibition. Different studies suggest phytic acid can suppress tumour growth and prevent colorectal cancer. Phytic acid supplementation with its potential anti-inflammatory, antioxidant activity, and metal chelation capacity are of great deal of interest to improve the anticarcinogenic activity of chemotherapeutic drugs in combination or alone. Further studies are needed to establish the safe dosage of phytic acid in daily diet as well as for preventing colorectal cancer.

Keywords: Phytic Acid, Phytic Acid Extraction, Anti-Nutrient, Phytic Acid: min molar ratio, Cancer,Colorectal Cancer

Introduction :

Phytic acid is a simple ringed carbohydrate with six phosphate groups attached to each carbon (Norazalian et al.2009), It is also known as inositol hexaphosphate (Kaur et al.2020). Phytic acid is a natural compound discovered in 1903. (Farahnaz et al.2017). Phytic acid is a natural compound found in soya beans, oil seeds, nuts, and grains. It is a major form of phosphorylated

inositol present in food, finding 1-5% by weight of most cereals, nuts, oilseed, legumes, and grains. Phytic acid occurs at 9.5-14.5 % by weight in Rice Bran.(Norazalian et al. 2009). Phytic acid has anti-nutritional properties. Anti-nutritional factors bind essential nutrients and reduce the bioavailability of them. The phytic Acid present in legume and cereals also decrease the digestibility of proteins and minerals absorption in the body causing deficiency disorder. (Mirinal et al .2019). Cancer is a frightening disorder or set of disorders. Unlike infectious diseases, parasites, and many environmental diseases, cancer is not primarily caused by some entity that is foreign to our bodies. Its agents of devastation are human cells that have, as it were, slipped their reins, and have been conscripted and to some extent transformed into pathological organisms or the building blocks of tumors.

Several types of cancers have occurred in the human body such as Breast Cancer, Colorectal Cancer, Skin Cancer, Blood Cancer etc (Hausman et al.2019**).** Colorectal Cancer is the third most often malignant carcinoma (Lui et al.2018). Nutrition plays a considerable role in the development of colorectal cancer. People who consume more red

meat, poultry, and processed meat are prone to develop colorectal cancer.(Aguirre-Portolés et al. 2017). Colorectal Cancer develops gradually, and initially does not produce any symptoms until reaching a considerable size of several centimetres. Some common symptoms of colorectal cancer are cramping,

pain, and bleeding along with stool. The development of colon tumors is a multi-step process that involves histological, morphological, and genetical changes. (Balchen et al 2016). Therefore, Many studies have shown that phytic acid can reduce the growth of cancer cells in leukaemia, breast, poster, liver, colon and skin cancer. (Farahnaz et al.2017).

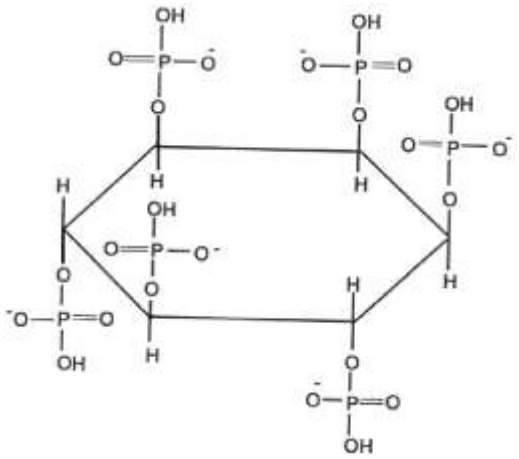

Figure 1:Chemical Structure Of Inositol Hexaphosphate (Phytic Acid)(Kaur et al.,2020)

Phytic Acid and Its Sources:

Phytic Acid is one of many derivatives of phosphorylated inositol hexaphosphate. The molar mass of phytic acid is 660.04 mol-1. In x-ray crystallographic analysis, it can be observed that the phosphate groups are axially and equatorially attached to carbon at the positions of 1,2,3,4,5and 6.The molecular formula is $C_6H_{18}O_{24}P_6$ The various studies it has been shown that the effect of phytic acid on the mallard reaction and the formation of the acrylamide were observed. Phytic acid and phosphate both them enhance the browning in the glucose/B alanine system, but the effectiveness of phosphorus is more than phytic acid. The molecules of phytic acid are inert and highly stable. Phytic acid has a very high ability to form chelate by reacting with polyvalent cations such as $Cu^{2+,}$ $Zn^{2+,}$ Ni^{2+}, Co^{2+}, Mn^{2+}, Fe^{2+}, and Ca^{2+} respectively. After reacting to the Phytic acid with different ions forms insoluble phytate salt, and it inhibits the

absorption of the following minerals, so the phytic acid is known to be a potent anti-nutrient. The lower amount of inositol with fewer phosphate groups can help to regulate various cellular actions such as cellular differentiation, cell division, endocytosis, and exocytosis.

Table :1 Phytic Acid sources (plant based)

Plant Name	Composition in 100gm	References
Lupine	1.38g	Hidvegi and Lastily ,2002
Pigeon Pea	0.22 g	Igbedioh et al.,2002
Cow Pea	0.42g	Hidvegi and Lastily ,2002
Lentils	0.86g	Elhardallou and Walker,2002
Cherry Tomato	0.11282g	Oyetayo and Libitoye ,2012
Citrus fruit juices	0.06g	Ani and Abel ,2018
Potato	0.111-0.296g	Phillipy et al.,2004

- Phytic Acid Extraction:

Phytic acid extracted from rice bran .The solid-liquid extraction of the phytic acid from the rice bran by using of response surface methodology. Box Behncon design was to monitor the processing parameters of yielding phytic acid that are as follows

a.Ratio of acid solution to raw materials (mg/g)

b.Hydrochoric acid concentration (mol/l)

c.Extraction time(h)

the result concluded that the optimal conditions ware HCL concentration 0.62 (ml/g) and the time of extraction was 5.5h .The validation test would indicate the possible yielding of phytic acid under optimization condition.The antioxidant assays recommended that the extracted phytic acid had the scavenging capabilities than vitamin-c at the very same condition of 0.5mg/ml.The acids wewre mostly use in solid-liquid phytic acid extraction from bran are hydrochloric acid and sulphuric acid.(Wu et al.,2009)

Phytic Acid as potent anti-nutrient:

Phytic Acid inhibits the absorption of iron, zinc, and calcium can lead to mineral deficiencies. At a time it can bind with two or more minerals. It can bind with other minerals due to the presence of six negatively charged phosphate groups. These negatively charged phosphate groups can bind with positively charged metal ions. The molar ratio between calcium, zinc and iron, and phytic acid can provide information about the availability of minerals comparing the molar ratio with the critical molar ratio can indicate the bioavailability of particular minerals. (Ibrahim et al.,2019)

$$\text{Phytic Acid:Min Molar Ratio} = \frac{PA/MwPA}{Min/MwMin}$$ (Ibrahim et al.,2019)

PA: Calculated amount of Phytic Acid in the sample.

MwPA: Molecular Weight of Phytic Acid (600Da).

Min= mineral present in the sample.

MwMin: Molecular weight of minerals are as follows Zinc – 65, Iron – 56, Calcium – 40.

Table:2 Phytic Acid to mineral molar ratio(Ibrahim et al.,2019)

Molar Ratio	Critical Level
[Phytic Acid]/Calcium	0.2
[Phytic Acid]/Iron	0.4
[Phytic Acid]/Zinc	10
[Phytic Acid] [Calcium][Iron]	0.5

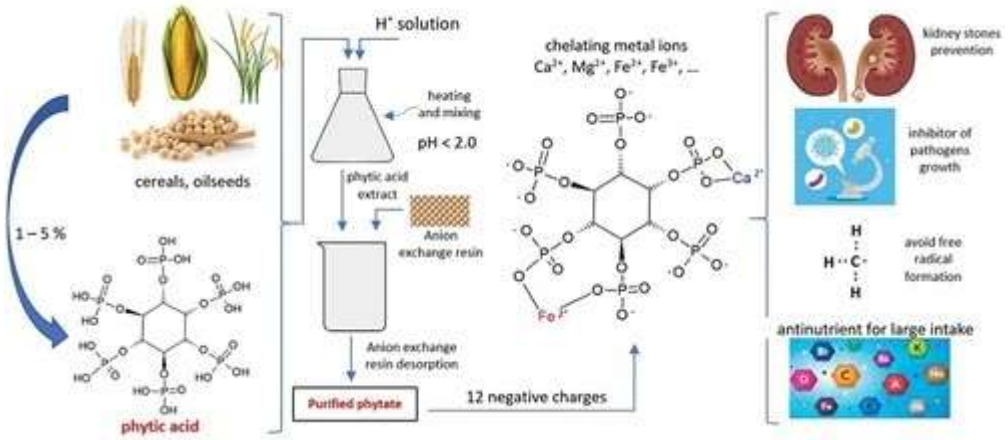

Figure 2:Anti-Nutrition Property Of Phytic Acid(Gupta et al.,2015)

Role of Phytase to increase bioavailability of minerals & phytase extraction:

Phytate needs to be phosphorylated to a higher extent for iron and calcium release as compared to other minerals. Studies have shown that the activity of phytase enzymes in the human body is very low. So the presence of a considerable amount of phytase in the gastrointestinal tract can degrade phytate. Initially in the phytate degradation intestinal phosphatase plays a considerable role.(Kryukor et al.,2021).It has been observed during the study that the phosphorus is released from the phytate (complex)through a sequential cleavage of the phosphate group. Previously it was believed that regardless of the properties of the phytase(enzyme), the rate of the dephosphorylation of phytate is limited by the first cleaved of phosphate depending on the specificity of phytase(enzyme). The inhibition mechanism of phytase does not depend on the enzyme, it depends on the bioavailability of phytase enzyme. phytic acid binds with the essential positively charged metal ions and makes them unavailable, phytase releases the ions and makes them available. The extra phosphatic effect has no other scientific justification, phytase only exhibits the phosphohydrolase action and is not able to catalyze any other reaction.(Kryukor et al.,2021)

- Phytase Extraction:

The production of Fungal Phytase**:**
Different fermentation methods have to be performed to obtain fungal phytase, the process is semi-solid state fermentation, solid fermentation, and submerged fermentation. (Han et al., 1987; Shivanna and Venkateswaran,2014).The production of fungal phytase has to be done through solid-state fermentation. Huang et al., 2018). It is a process where the production of phytase occurs on solid material surfaces with the presence or little presence of water. The

process required enough moisture to stimulate the growth of microorganisms. This process results in high quantity production of phytase. (Bhargav et al., 2008).

Development of colorectal cancer:

Colorectal cancer (CRC)is one of the most common cancer diagnosed among males and females. It has been observed that people in developed countries are more likely to develop colorectal cancer than in developing countries**(**Lui et al.2018). It has been estimated that the lower consumption of whole grain food in developed countries may be the reason for the high rate of colorectal cancer. Initially, colorectal cancer does not show any symptoms until the tumor reaches a considerable size of several centimetres which may block the excretion of stool which causes abdominal pain, bleeding, and black or bloody stool. The occurrence of colorectal cancer can be the cause of mutation of exact genes. The mutation may occur in the tumor-suppressing gene, oncogene, and gene involved in the repairing mechanism of DNA. 70% of colorectal cancer
follow a definite sequence of mutation. Later it will be promoted into an exact morphological sequence. Initially, the mutation occurs at the gene that suppresses the mutation known as Adenomatous Polyposis Coli. It will result in non-malignant adenomas known as polyps. It starts with the formation of adenoma and ends at the state of carcinoma. It can be predicted that 15%of these kind of these kinds of adenomas tend to be promoted to carcinoma stage within 1 decades. **(**Inés et al.2017**)**

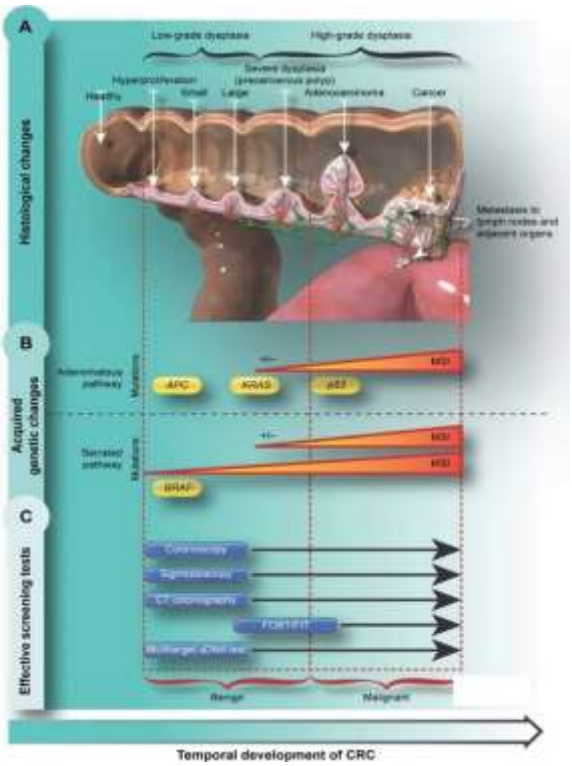

Figure 3:Development Of Colorectal Cancer(Balchan et al.2016)

Role of Phytic acid on colorectal cancer:

Phytic acid has anti-cancer,anti-inflammatory and anti-oxidenrt properties(Kaur et al.,2020).Phytic acid generally effect the cell cycle by decreasing the S-Phase of the mitosis.It kind of cease the cell cycle in the G0/G1 Phase .Shamsuddin and Ullahithas reported their

observation about phytic acid that is significantly decreased the mitosis in the AOM influenced colon tumors .Saied and Shamsuddin describe about the role for up regulation of tumor suppressor in fisher 344 rats .Phytic acid can inhibit colon cancer in rodents .Dietary fibre has kind of negative risk factor of colorectal cancer,it also improves the environment of colon.It also improves the organic acid and micro flora in colon.Studies have show that in the combonation of high fat diet phytic acid can improve the colonic environment.When 30% beef meat allow with 2.04% sodium =phytic acid along with 0.4% of monoinositol(mi) or 0.2% of MI+sodium +phytic acid 1.2% .The study concluded that it can supress the serum tumor necrosis factor.

Conclusion:

In Various studies in clinical nutrition conducted over 10-15 years have established the direct and indirect role, of PHYTIC ACID IN COLORECTAL CANCER. It has also established the anti-nutritional role of phytic acid in human health. From this study, it has been observed that metal chelates are found to be an attractive channel to improve the cytotoxic activity of the chemotherapeutic drug. The study further highlights inhibiting redox enzymes, which could be an effective strategy to break the defence mechanism of cancer cells, leading to improved therapeutic activity. Delivery of anticancer drugs using pH-sensitive polymer ensures high local drug concentration to achieve selective cytotoxic activity and also minimizes systemic exposure to the drug, which could help to reduce the risk of drug-dependent systemic toxicity. The present

Studies open a new avenue for effective treatment of colon cancer. However, organ-specific toxicity will need to be investigated for further clinical prospects. The administration of proper doses of phytic acid along with foods and in combination with drugs can prevent the risk of developing colorectal cancer. From the study, it has been observed that the Proper doses of phytic acid also help in treating colorectal cancer. The study has computed that phytic acid not only helps in preventing and treating colorectal cancer but also helps to prevent other types of cancer such as breast cancer, skin cancer, gastric cancer etc. Phytic Acid may have beneficial effects that are similar to dietary fibre. Phytic acid may beneficially modify the composition of cecal organic acids, micro flora, and mucins and could decrease the serum levels of pro-inflammatory cytokines has been observed in different studies .Though phytic acid has various health benefits, especially suppressing cancer it has various anti-nutritional roles too. It decreases the absorption of iron in the body which can lead to anemia, consumption in the prescribed amount is recommended for cancer-developing risk groups and all individuals, and also the study has shown different kinds of processes that can reduce the anti-nutritional activity of phytic acid containing sources

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