IJNRD.ORG ISSN : 2456-4184
INTERNATIONAL JOURNAL OF NOVEL RESEARCH AND DEVELOPMENT (IJNRD) | IJNRD.ORG
An International Open Access, Peer-reviewed, Refereed Journal

THE REVIEW ON FLAXSEED AS AN ANTICANCER AGENT

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ABSTRACT

Flaxseed, also known as Linseed (Linum usitatissimum L.), is one of the oldest cultivated crops with significant nutritional and medicinal value. It is primarily cultivated for its oil, fiber, and bioactive compounds. The nutritional profile of flaxseed includes a high content of omega-3 fatty acids, especially alpha-linolenic acid (ALA), lignans, dietary fibers, phenolic compounds, and proteins, which confer multiple health benefits. The presence of these components, particularly ALA, has been associated with anti-inflammatory, antioxidant, antihypertensive, and anti-diabetic properties. Flaxseed is increasingly utilized in the prevention and management of various diseases such as cardiovascular diseases, diabetes, and even cancer. Its bioactive components have shown promising results in preventing cancer cell proliferation, inducing apoptosis, and inhibiting tumor metastasis. This paper discusses the potential role of flaxseed in cancer prevention and its health benefits, focusing on its anticancer effects, especially in colorectal, prostate, and breast cancers. The composition of flaxseed and its molecular mechanisms in combating cancer are reviewed to highlight its therapeutic potential.

KEYWORDS:- Cancer, Flaxseeds, Alpha linolenic acid.

1. INTRODUCTION

1.1 Flaxseed:

Flax seeds, also known as linseed (Linum usitatissimum L.), is one of the oldest cultivated crops in the world, which is specially famous for its oil, fiber, and nutritional benefits. Flaxseed is actually the term which is usually used when we refer to flax for human consumption.While linseed is particularly used in industrial applications.Flaxseed is an adaptable whole grain seed that ranges in color from golden yellow to dark brown. It is grown over (around/through) Canada and North Dakota.Nowadays, it is grown in over 50 countries, mainly in the Northern Hemisphere. India is a topmost country when it comes to the leading flaxseed-producing countries, accounting for an average of 23.8% of the total population & it comes third in production, contributing 10.2% of the world's production. The cultivation of flaxseed is mainly focused in Madhya

Pradesh, Maharashtra, Chhattisgarh, and Bihar in India.[1] Flaxseed consist of high amount of lignans compare to all other plant foods. With upto 800 times more than other consumed by humans.[2] Flaxseed gives a nutty taste and crispy texture it is perfect for improving breads, crackers and other bakery delights.It can also be ideal Integrated into one's daily diet by sprinkling it over cereal,mixing it with drinks or yogurts and adding it to salads or soups.[3]

Fig No.1.Flax seeds [27]

fig No.2.Flax seed tree [28]

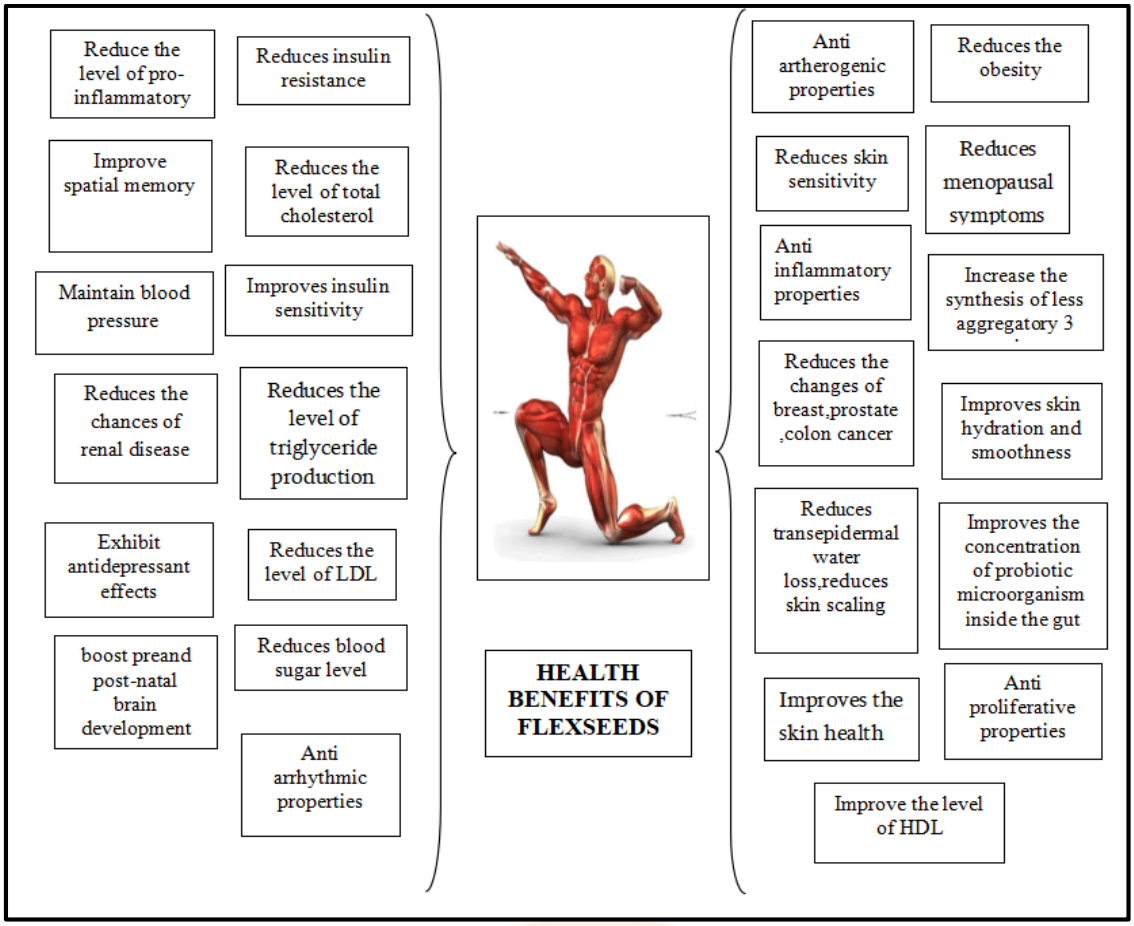
The seed of the flax crop is rich in functional ingredients.These Contains proteins, a-linolenic acid, lignans, mucilage, phenolic compounds, fiber, and small amounts of Show case significant orbitides all of which shows biological activity.The wide range of biomolecules found in flaxseed gives its exceptional nutritional value.Therefore, the components of flaxseed have been utilized as food additives because of their distinctive functional characteristics.Besides, studies have shown that the protein and cyclic peptides found in flaxseed exhibit beneficial antioxidant, antihypertensive anti-inflammatory, Immune- suppressive and anti diabetic qualities.flaxseeds have gained popularity as dietary supplements due to their reported benefits in promoting human health and easing symptoms related to various conditions such cardiovascular disorders, diabetes, neural disorders, menopause, skin problems, gastro-Intestinal disorders and even **cancer.**[4]

1.2 Cancer: Cancer was recognized as a significant disease ages ago. In the ages that followed, patient battling cancer found themselves with limited possibility for recovery and long term survival, challenging reality that survive for certain type of cancer,highlighting the urgent need for advancements in medical interventions. In worldwide, cancer is a significant contributor to mortality, with analyse that indicating a rise from 14 million new cases per year in 2012 to an anticipated 19.3 million cases annually by 2025.one of the primary causes of deaths widely is attributed to various forms of cancer.colorectal, liver, breast, gastric, prostate, cervical and lung cancers stand out as primary suspect in cancer-related facilities.The majority of deaths due take place in low & middle Income countries Surgery, radiotherapy, Immune therapy and targeted therapies form the primary arsenal against cancer.[5]In advanced stages, cancer cells travel from their original location to other organs via circulation, giving rise to metastatic lesions and secondary tumors.This process Includes primary tumor or dissociation, migration, Invasion, adhesion and proliferation at a distant location.[6]Unfortunately in several cases, these therapies are unsuccessful, leading to cancer ensuring as a significant obstacle for clinical treatments. one way to deal with Issue is by focusing on halting the Spread of other parts of the body.This can be fulfilled by gaining insights into the complex molecular and cellular processes responsible for malignancy and the rapid advancement of the disease.Further Investigation is required to identify more cancer efficient methods for treating cancer.[7]Exploring novel strategies in disease management could present promising opportunities.[5]

2. HEALTH BENEFITS OF FLAXSEED :

Apart from being packed with essential nutrients, flaxseed provides valuable health benefits due to its high levels of omega-3 alpha-linolenic acid, dietary fibers, and lignans. Many clinical studies have shown that polyunsaturated fatty acids have substantial anti-inflammatory properties and are beneficial in preventing conditions like rheumatoid arthritis, asthma, atherosclerosis, and coronary heart disease. Fatty acids (ALA, DHA, and EPA) may provide health benefits in combating a range of diseases, such as neurological disorders, atherosclerosis, cardiovascular disease, cancer, osteoporosis, immunology, arthritis, diabetes, and hypertension. In addition to enhancing vascular function, research shows that flaxseed also has antiatherogenic, antiproliferative, and antiarrhythmic qualities. Numerous clinical studies have shown that

EPA and DHA are crucial in relieving symptoms of depression.[8] Flaxseed oil is thought to help prevent tumors because of its high content of alpha-linolenic acid. The tumors' fatty acid composition showed heightened levels of alpha-linolenic acid, which resulted in inhibiting the growth of tumor cells. The water-binding capacity of insoluble fiber in flaxseed enhances intestinal bulk, providing assistance in managing constipation, irritable bowel syndrome, and diverticular disease. Flaxseed fiber plays a vital role in lowering blood glucose levels.[1]



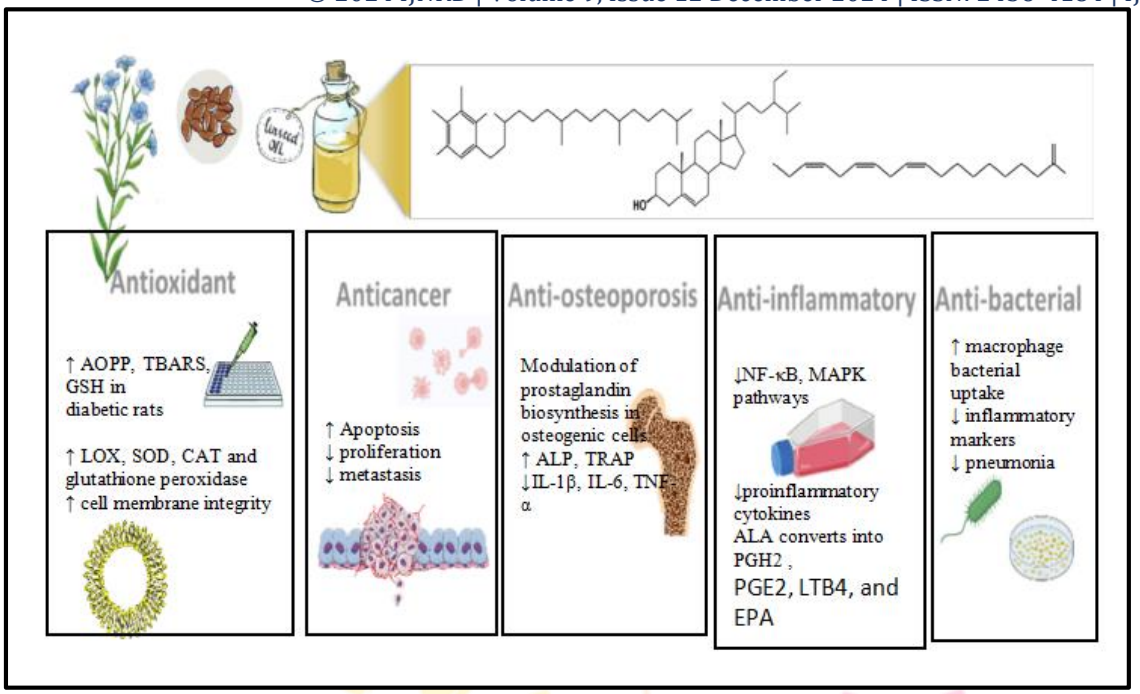


Fig No. 3: Various Health Benefits of Flaxseeds [8,36]

3. NUTRITIONAL COMPOSITION :

Flaxseed is considered a promising functional food because of its rich nutritive composition. It contains high levels of lignins, soluble fiber, phenolic compounds, alpha-linolenic acid, and high-quality protein. Flaxseeds provide a rich array of minerals, including calcium, magnesium, phosphorus, and salt. Flaxseed stands out as the most abundant source of phytoestrogens, specifically lignans. Flax lignins display antioxidant properties, which could be the primary factor behind their anticancer effects.[8] High levels of cysteine and methionine contribute to enhancing antioxidant levels, consequently lowering the risk of cancer.[1] The discussion on the chemical composition of flaxseed highlights a well-balanced blend of proteins, fats, dietary fiber, and carbohydrates. This combination makes it an ideal option for consumers who prioritize their health[9]

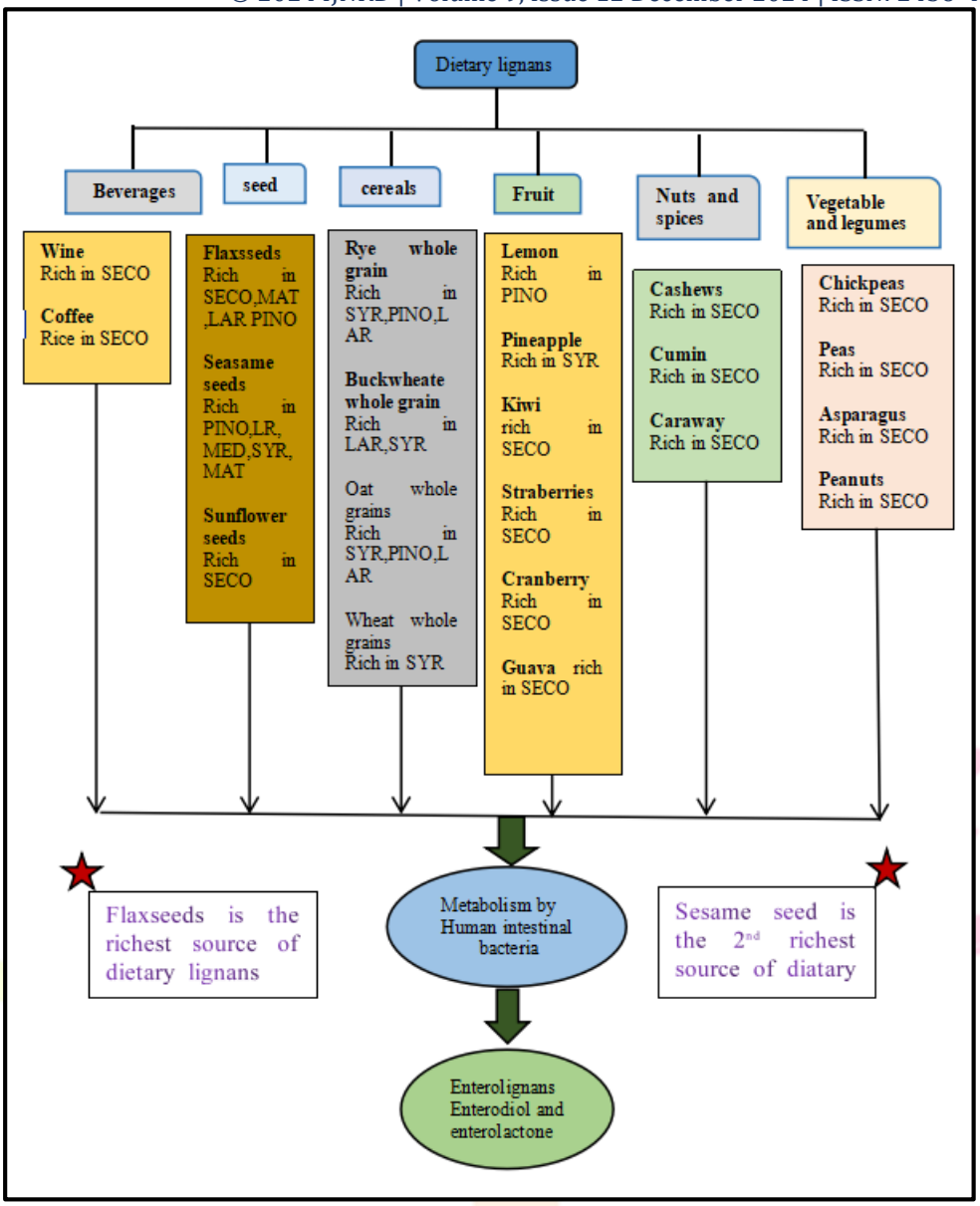


Fig No. 4: Sources of Dietary Lignans [5]

Name	Amount	Name	Amount	Name	Amount
Water	5.32-8.89g	Panthonic acid	0.57-1.4	Fatty acids,total polyunsaturated	28.7g
Energy	534kcal	Vitamin B-6	0.3-0.61mg	PUFA 18:2ssss	5.17-6.67g
Energy	2230KJ	Folate,total	35-112	PUFA 18:3	18.7-26.2g
Protien	17-21.3g	Folate,DFE	87	PUFA 20:2 n-6 c,c	0-0.015g
Total lipid(fat)	36.8-45.8g	Choline,total	78.7mg	stigmasterol	9-14mg
Ash	3.42-4.07g	Betaine	3.1mg	Campesterol	40-50mg
Carbohydrtes,by the difference	28.9g	Lutein + zeaxanthin	500-970	Beta-sitosterol	84-96mg
Fiber ,total dietary	25.3-28.6g	Vitamin E(alpha - tocopherol)	0.23-0.45mg	Tryotophan	0.297g
Sugar ,total including NLEA	1.55g	Tocopherol, Gamma	14.3-25.8mg	Threonine	0.766g
Sucrose	0.84-1.51g	Tocopherol,Delta	0.21-0.55mg	Isoleucine	0.896g
Glucose	0.21-0.73g	Vitamin K (phylloquinone)	3.7-4.8	Leucine	1.24g
Calcium,Ca	200-340mg	Fatty acids,total saturated	3.66g	Lysine	0.862g
Iron,Fe	3.67-7.32mg	SFA 14:0	0-0.016g	Methionine	0.37g
Magnesium,Mg	354-431mg	SFA 15:0	0.005g	Cystine	0.34g
Phosphorus,P	603-722mg	SFA 16:0	1.67-2.58g	Phenylalanine	0.957g
Potassium,K	673-1000mg	SFA 17:0	0.018g	Tyrosine	0.493g
Sodium,Na	21-45mg	SFA 18:0	1.12-1.17g	Valine	1.07g
Zinc,Zn	3.95-4.92mg	SFA 20:0	0.043-0.057g	Arginine	1.92g
Copper,Cu	1.07-1.52mg	SFA 22:0	0.04-0.064g	Histidine	0.472g
Manganese,Mn	1.64-3.08mg	SFA 24:0	0.031-0.032g	Alanine	0.925g
Selenium,Se	4.8-46	Fatty acids,total monounsaturated	7.53g	Aspartic acid	2.05g
Niacin	2.7-3.21mg	MUFA 16:1	0.018-0.031g	Glutamic acid	4.04g
Vitamin C,total ascorbic acid	0.5-0.7mg	MUFA 18:1	6.86-7.91g	Glycine	1.25g
Thiamin	0.533-3.2mg	MUFA 20:1	0.051-0.083g	proline	0.806g
Riboflavin	0.161mg	MUFA 22:1	0-0.027g	Serine	0.97g
Niacin	0.07-0.232mg	MUFA 24:1 c	0.009-0.121g	Hydroxyproline	0.13-0.22g

Table No. 1: Nutritional Composition of Flaxseed

3.1 Chemical Composition of Flaxseed :

Flaxseed comprises of three distinct components: the germ or embryo, a hull, and two cotyledons. These components represent 4%, 55%, and 36% of the seed weight. Usually, whole flaxseed includes around 3–4% ash, 4–8% moisture, 20–35% dietary fiber, 20–30% protein, 30–41% fat, and 1% simple sugars. The key bioactive components in flaxseed are carbohydrates (mucilage), oil, lignans, protein/peptides, and a small amount of CGs and linatine. Minor components consist of phytic acid, trypsin inhibitor, phenolics, minerals, cadmium, vitamins, and selenium. [4]

3.1.1 Dietary Fiber in Flaxseed :

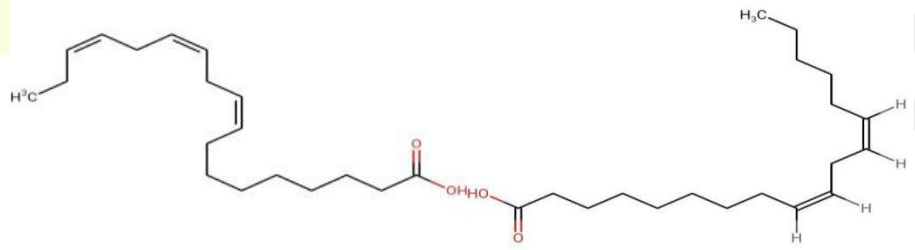
Dietary fiber, found in flaxseed up to 40%, comprises of 25% soluble fiber and 75% insoluble fiber. Gums, pectin, and β-glucan are examples of soluble fiber that play a crucial role in lowering blood sugar levels and absorbing cholesterol and triglycerides. These fibers are essential in preventing diabetes and cardiovascular disease. Flaxseeds are an excellent source of both soluble and insoluble dietary fiber. Cellulose, lignin, and hemicellulose are the primary elements found in insoluble fiber.[9] Soluble fiber is located in a mucilaginous substance comprised of water-soluble polysaccharides. Flaxseed mucilage consists of both acidic and neutral polysaccharides. Flaxseed reveals a remarkably low carbohydrate content of 28.9g/100g; with 27. 3g of it is dietary fiber the rest is sugar. The flaxseed proteins demonstrate greater lipophilicity in comparison to soy proteins. Flaxseed fiber is crucial for reducing blood glucose levels. Flaxseed cake, recognized for its rich dietary fiber content, has been utilized for extracting both soluble and insoluble fibers.[8]

Dietary fibres	g/100 g of flaxseed
Soluble fibres	4.3-8.6
Insoluble fibre	12.8-17.1

Table No. 2: Composition of Dietary Fibres in Flaxseed [29]

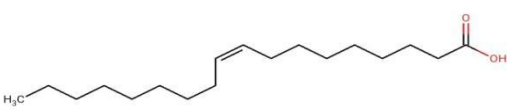
3.1.2 Fatty Acids Profile of Flaxseed:

Flaxseed oil is divided into monounsaturated and polyunsaturated components according to the number of carbon atoms and double bonds in the fatty acids. Flaxseed oil is abundant in unsaturated fatty acids, ranging from 87. 8 to 89. 8%, while containing only a small amount of saturated fatty acids. An FA analysis of the petroleum ether extract of flaxseed revealed significant presence of key fatty acids: α-linolenic acid at 42. 4% (with a chemical formula of 18:3, Omega-3), linoleic acid at 26. 2% (with a chemical formula of 18:2, Omega-6), palmitic acid at 12. 9% (with a chemical formula of 16:0), and stearic acid at 10. 7% (with a chemical formula of 18:0). Another research revealed the fatty acid composition of flaxseed to be 47. 44 – 53. 67% linolenic acid, 19. 56 – 24. 33% oleic acid, 12. 8 – 15. 01% linoleic acid, 5. 01 – 9. 57% stearic acid, and 5. 14 – 6. 43% palmitic acid. During metabolism, ALA is transformed into docosahexaenoic acid (DHA) and eicosatetraenoic acid (EPA), playing a crucial role in facilitating the optimal growth of the central nervous system, particularly in the myelination of neurons. Omega-3 PUFA plays a crucial role in the regulation of epigenetic gene expression, making it vital in managing various health issues such as coronary heart disease, type II diabetes mellitus, and cancer.[9,10,11,12,13]

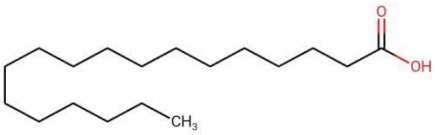


Alpha linolenic Acid

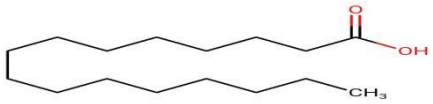
Linolenic Acid



Oleic Acid



Stearic Acid



Palmitic Acid

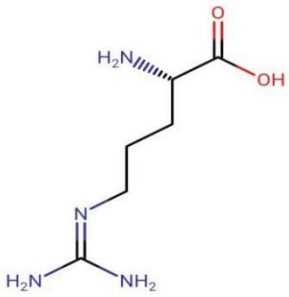
Fig No. 5: Structures of Various Fatty Acids

Fatty Acids	g/100 g of Flaxseed
Alpha linolenic Acid	22.8
Linolenic Acid	5.9
Oleic Acid	7.3
Stearic Acid	1.3
Palmitic Acid	2.1

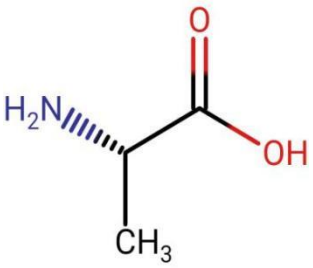
Table No. 3: Fatty Acids Composition of Flaxseed [29]

3.1.3 Proteins in Flaxseed :

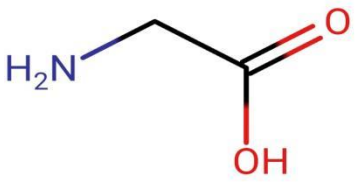
Flaxseed serves as a rich protein source, accounting for up to 23% of the total seed mass. This percentage increases to 35 to 40% following oil extraction.[9] Flaxseed offers complete proteins, meaning it contains all essential amino acids in sufficient quantities. This can help address any protein deficiencies. A recent study conducted an amino acid analysis of flaxseed and found that it contains high levels of several important amino acids. These include arginine, alanine, glycine, isoleucine, histidine, lysine, and leucine. Cysteine and methionine, both sulfur-based amino acids, can be found in flaxseed. In FPI (flaxseed protein isolates) the lysine to arginine ratio is much lower (0. 25) compared to other proteins like soy protein and whey protein, etc. This highlights the potential of flaxseed protein as a favorable option for pharmaceutical formulations and infant formula.[14,15]With plant-based protein being notably more environmentally friendly, sustainable, and greener compared to animal protein, it has become a prominent trend in the food industry. Flaxseed is highly regarded as an excellent protein source due to its significant levels of sulfur-based amino acids like cysteine and methionine, as well as branched-chain amino acids such as leucine and isoleucine, and essential amino acids including tyrosine, threonine, and lysine. Flaxseed boasts an abundance of storage proteins like aspartic acid, glutamine,asparagine, and arginine, akin to other seeds, elevating its amide content.[9]



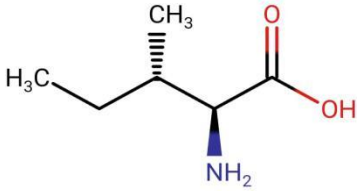
Arginine



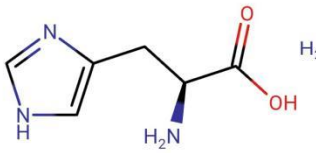
Alanine



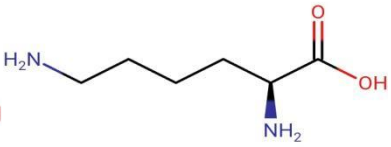
Glycine



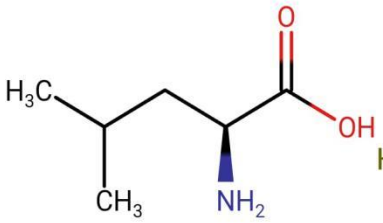
Isolucine



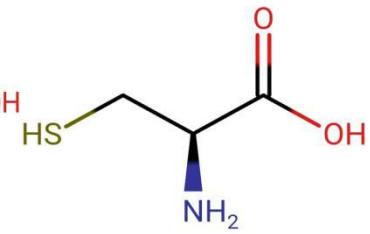
Histidine



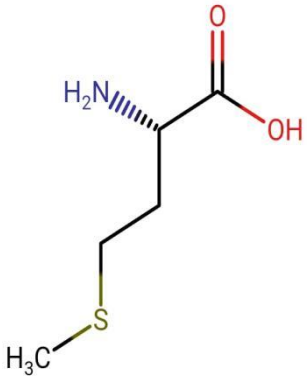
Lysine



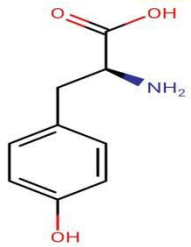
Leucine



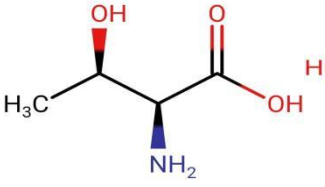
Cysteine



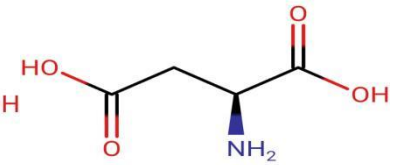
Methionine



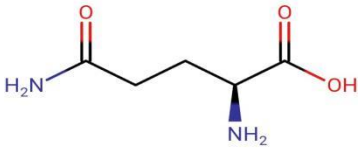
Tyrosine



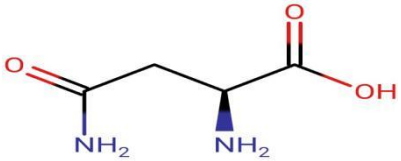
Threonine



Aspartic Acid



Glutamine



Asparagine

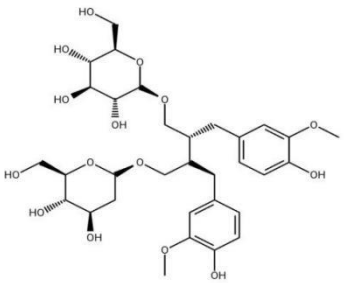
Fig No.6: Structures of Various Amino Acids

Amino acids	Flaxseed protein meal (g/100g)
Arginine	10.63
Alanine	4.59
Glycine	6.14
Isolucine	5.21
Histidine	2.45
Lysine	4.18
Leucine	6.82

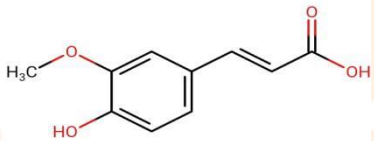
Table No.4: Protein Composition of Flaxseed [10]

3.1.4 Phenolic Compounds and Carotenoids :

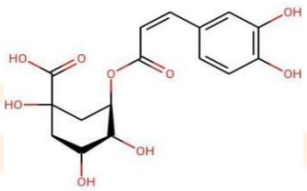
Flaxseeds possess a significant amount of phenolic compounds. These phenolic compounds are highly esteemed for their remarkable anti-cancer and antioxidant properties. Some of the significant phenolic acids discovered in defatted flaxseed are ferulic acid, chlorogenic acid, and gallic acid. Other phenolic acids consist of p-coumaric acid glucosides, hydroxycinnamic acid glucosides, and 4-hydroxybenzoic acid, all found in small quantities. It serves as a valuable mineral source, abundant in phosphorous and magnesium, with minimal sodium content. When petroleum ether is utilized in the extraction process of flaxseed oil, researchers discovered that the predominant components are stearic acids, palmitic acid, and α-linolenic acid.[8] Phenolic substances offer a wide range of health benefits. Flaxseed boasts a diverse range of phenolic compounds, specifically categorized into two groups: phenolic acids and lignans. Lignans, as low molecular weight phenolic dimers, consist of a base structure known as 2,3-dibenzylbutane. They typically reside in the outer coat of the seed. Secoisolariciresinol diglucoside (SDG) is a significant lignan found in flaxseed, typically ranging from 610 to 1300 mg per 100 g. The phenolic acid composition of flaxseed is detailed in Table 5, highlighting that whole seeds contain lower phenolic acid content compared to meal after oil extraction.[10]



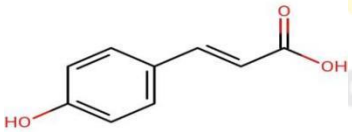
Secoisolariciresinol diglucoside



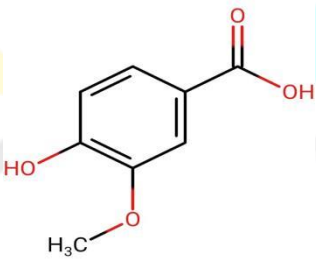
Chlorogenic acid



Ferulic Acid

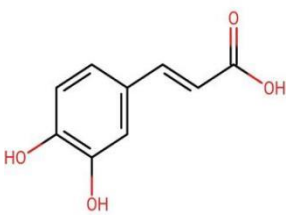


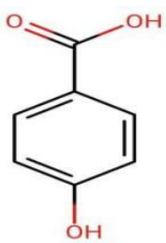
Coumaric acid

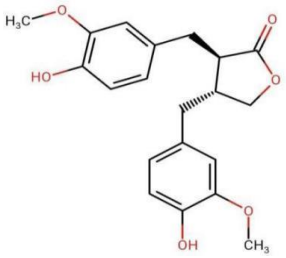


Vanillic acid

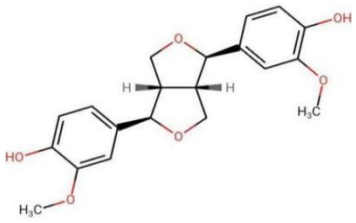
Sinapic acid

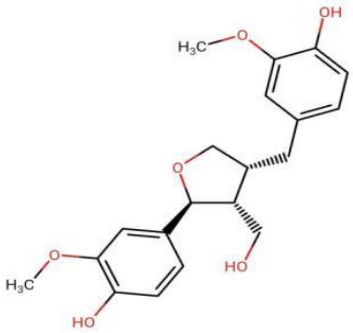


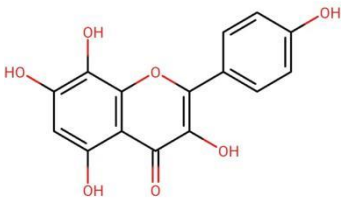




Caffeic acid p-Hydroxybenzoic acid Matairesinol







Pinoresinol Laricinesol Herbacetin

Fig No.7: Structures of Various Phenolic Compounds

Phenolic acids	Non-defatted extracts	Defatted extracts
p-Hydroxybenzoic acid	1719	6454
Chlorogenic acid	720	1435
Ferulic acid	161	313
Coumaric acid	87	130
Vanillic acid	22	42
Sinapic acid	18	27
Caffeic acid	4	15
Secoisolariciresinol diglucoside	1300	n.a *
Laricinesol	1.7	n.a *
Matairesinol	3.1	n.a *
Pinoresinol	0.8	n.a *

Table No.5: Phenolic Acid Composition of Flaxseed[10]

3.1.5. Vitamins :

Flaxseed contains both water and fat-soluble vitamins.[16]Gamma-tocopherol, recognized for its antioxidant properties, safeguards cell proteins and fats against oxidation. It also helps regulate sodium elimination in urine, potentially reducing its levels in the blood. Moreover, it plays a crucial role in lowering the risk of heart disease, certain types of cancer, and Alzheimer's disease.[17]Vitamin K can be found in flaxseed as 2-methyl-1,4-naphthoquinone, also known as phylloquinone.Vitamin K plays a fundamental role in the blood clotting process, working in conjunction with various proteins that regulate blood clotting and manage calcium levels in the bones.[18]

Fat soluble vitamins	Mcg/100 g	Mg/tbsp./milled flax
Vitamin E		
• Alpha tocopherol	7	0.10
• Delta-tocopherol	10	0.14
• Gamma-tocopherol	552	7.73
Vitamin K	-	0.3
Water soluble vitamins		
Ascorbic acid (Vit. C)	0.50	0.04
Thiamine (Vit. B1)	0.53	0.04
Riboflavin (Vit. B2)	0.23	0.02
Niacin acid	3.21	0.26
Pyridoxine (Vit. B6)	0.61	0.05
Pantothenic acid	0.57 Mcg/100 g	0.05 Mcg/100 g
Folic acid	112	9.0
Biotin	6	0.5

Table No.6: Composition of flaxseed vitamins, fat soluble and water soluble.[9]

3.1.6 Polysaccharide :

FM is divided into two categories of polysaccharide fractions according to their net charge: acidic and neutral. Arabinoxylans, along with β-D-(1,4)-xylan, form the backbone of a neutral fraction. This portion is devoid of uronic acid. Conversely, the acidic fraction primarily consists of sugars like galactose, rhamnose, and galacturonic acid, which are essential components of pectic substances.[10] Upon examining the chemical composition of FM from various genotypes, it was observed that FM derived from yellow seeds contained lower galacturonic acid (13–16%) and rhamnose (12–14%) levels, but higher amounts of neutral sugars such as xylose (39–48%) compared to FM sourced from brown seeds.[19]

3.1.7 Phytic acid:

Phytic acid plays a crucial role in seedling germination and development by containing 60–90% of the phosphorus found in the seed. Phytic acid seems to help in reducing blood sugar levels and lowering the risk of colon cancer.[20] The potent chelating characteristics of phytic acid with monovalent or divalent minerals could potentially result in deficiencies of calcium, zinc, and iron.[21]

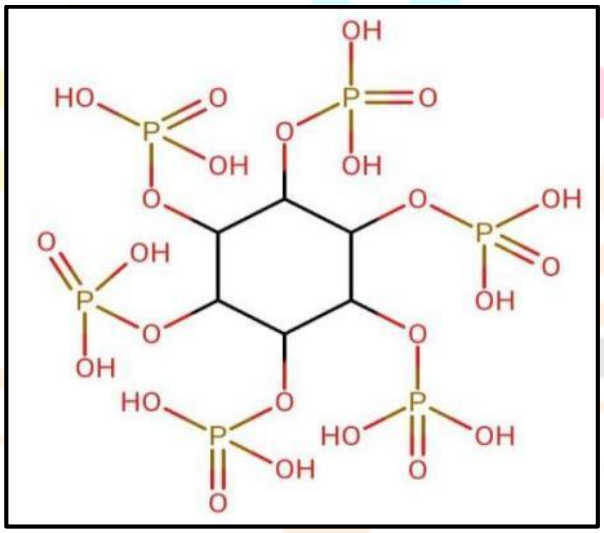
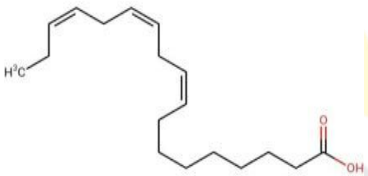
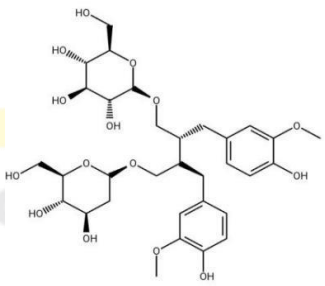


Fig No.8 : Structure of Phytic Acid

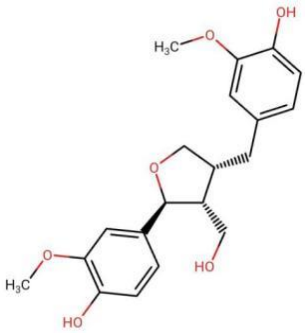
3.2 Structure of Chemical Compounds:



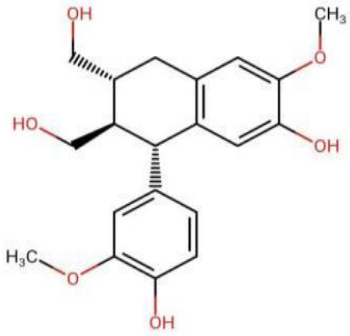
Alpha linoleic acid



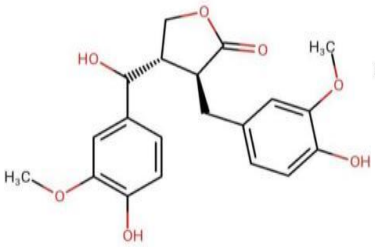
Secoisolariciresinol Diglucoside



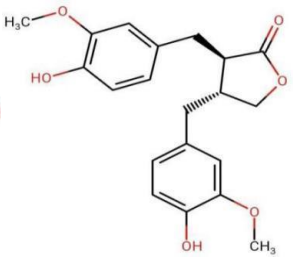
Laricinesol



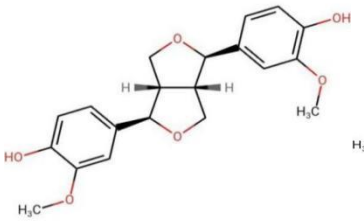
Isolariciresinol



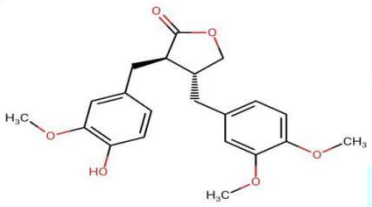
7-Hydroxymatairesinol



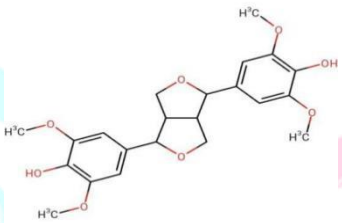
Matairesinol



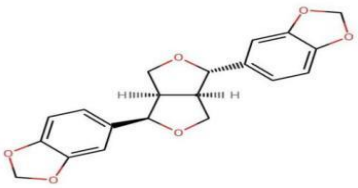
Pinoresinol



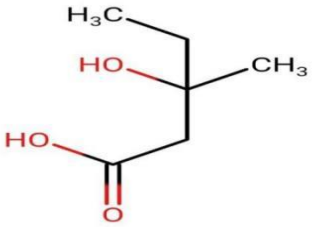
Arctigenin



Syringaresinol



Asarinin



Hydroxymethylglutaric acid

Fig.No.9: Structure of Various Chemical Compounds

Sr No	Name of Constituents	Chemical Formula	IUPAC Name	Molecular Weight
1.	Alpha-Linolenic Acid	C18H3002	Cis,cis-9,12-octadecadienoic acid	278.43g/mol
2.	Secoisolariciresinol Diglucoside	$C_{32}H_{46}O_{16}$	(2R,3R,4S,5S,6R)-2-[(2R,3R)-2,3-bis[(4-hydroxy-3-methoxyphenyl)methyl]-4-[(2R,3R,4S,5S,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)oxan-2-yl]oxybutoxy]-6-(hydroxymethyl)oxane-3,4,5-triol.	686.70
3	Lariciresinol	C20H24O6	4-[[(3R,4R,5S)-5-(4-hydroxy-3-methoxyphenyl)-4-(hydroxymethyl)oxolan-3-yl]methyl]-2-methoxyphenol	360.40 g/mol
4	Isolariciresinol	C20H24O6	(6R,7R,8S)-8-(4-hydroxy-3-methoxyphenyl)-6,7-bis(hydroxymethyl)-3-methoxy-5,6,7,8-tetrahydronaphthalen-2-ol	360.40g/mol

5	7-Hydroxymatairesinol	C20H22O7	(3R,4R)-4-[(S)-hydroxy-(4-hydroxy-3-methoxyphenyl)methyl]-3-[(4-hydroxy-3-methoxyphenyl)methyl]oxolan-2-one	374.38–374.4 g/mol
6.	Matairesinol	C20H22O6	(3R,4R)-3,4-Bis[(4-hydroxy-3-methoxyphenyl)methyl]oxolan-2-one	**358.39 g/mol**
7.	Pinoresinol	C20H22O6	4-[(3S,3aR,6S,6aR)-6-(4-hydroxy-3-methoxyphenyl)-1,3,3a,4,6,6a-hexahydrofuro[3,4-c]furan-3-yl]-2-methoxyphenol	358.39g/mol
8.	Arctigenin	C21H24O6	(3R,4R)-4-[(3,4-dimethoxyphenyl)methyl]-3-[(4-hydroxy-3-methoxyphenyl)methyl]oxolan-2-one	372.41g /mol
9.	Syringaresinol	C22H26O8	4,4′-[(1R,3aS,4R,6aS)-Tetrahydro-1H,3H-furo[3,4-c]furan-1,4-diyl]bis(2,6-dimethoxyphenol)	418.442g/mol
10.	Asarinin	C20H1806	5-[(1R,3aR,4S,6aR)-4-(2H-1,3-benzodioxol-5-yl)-hexahydrofuro[3,4-c]furan-1-yl]-2H-1,3-benzodioxole	354.4 g/mol
11.	Hydroxymethylglutaric acid.	C6H10O5	3-hydroxy-3-methylglutaric acid, β-hydroxy-β-methylglutaric acid, and dicrotalic acid)	162.14g/mol

Table No.7: Chemical Properties of chemical compounds

3.3 Potentially toxic/non-Nutritional Compounds in Flaxseed :

Flaxseeds have suggested that certain components of flaxseed, such as cyanogenic glycosides (CGs) and linatine, could have toxic properties.

3.3.1. Linatine :

Flaxseed cotyledons are rich in linatine, with a concentration of around 100 parts per million. This polar compound containing amines is linked to the development of vitamin B6 deficiency symptoms in chicks fed with flaxseed, including issues like stunted growth, reduced appetite, neurological complications, and anemia.[22,23]

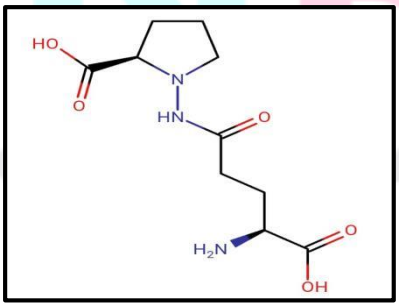


Fig No.10: Structure of Linatine

3.3.2 Cynogenic glycosides :

Flaxseed contains cynogenic glycosides compounds known as Linustatin, Linamarin, and neolinustatin, which have the potential to realease approximately 7. Flaxseed boast a content of 8 µM of cynogenic compounds per gram. The amount of CGs in different flax seed varities may vary, with some containing none at all. The ratio stands at 74 to 1. The cynide concentration amounts to 60 grams per kilogram.[24]

3.3.2.1 Linustatin and Neolinustatin :

Linustatin and neolinustatin are the primary glycosides found in flaxseed, while mature seeds typically have small amounts of the monoglycosides linamarin and lotaustralin.[25] In a study, a one-time dose of 30 grams of flaxseed (equivalent to 9 mg of HCN) was given, and the levels of HCN and thiocyanate in the blood were observed for 180 minutes. Weekly monitoring was carried out after consuming 15 grams of flaxseeds (equal to 4. 5 mg HCN) thrice daily over a five-week period. The levels of HCN in the serum did not display a predictable trend. Likewise, after the volunteer ingested 100 grams of flaxseed (equivalent to 30 mg of cyanide compounds), their plasma cyanide levels did not show a notable increase from the initial baseline[26]

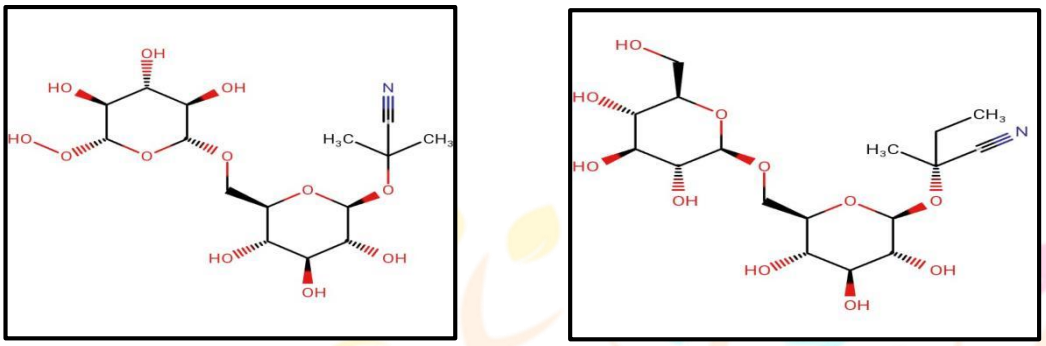


Fig No.11 : (A) Structure of Linustatin (B) Structure of Neolinustatin

3.3.2.2 Linamarin and Lotaustralin :

Linamarin has been characterized as a glucoside of acetone cyanohydrin that might bring about negative physiological effects if ingested in its raw form due to its elevated cyanide levels.[24] Furthermore, studies have shown that linamarin or its methylated form lotaustralin can break down into hydrogen cyanide (HCN) when acted upon by naturally occurring β-glycosidase enzymes in the human digestive system.[30]

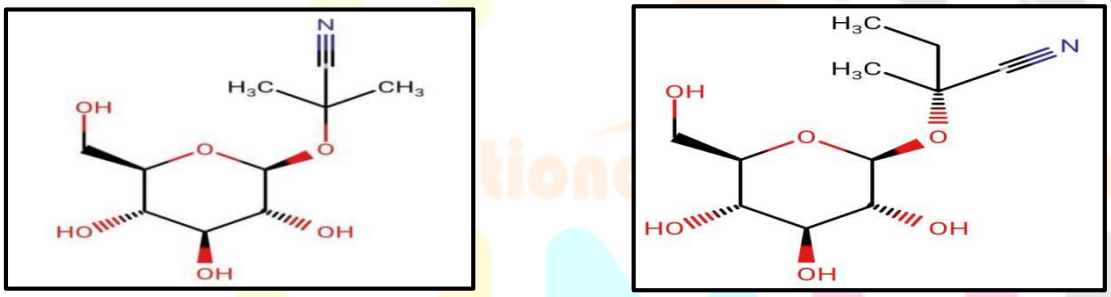


Fig No. 12: (A) Structure of Linamarin (B) Structure of Lotaustralin

4. EFFECT OF FLAXSEED ON DIFFERENT TYPES OF CANCERS :

4.1 Colorectal Cancer :

This cancer type arises in the colon or rectum, both of which are sections of the large intestine. Colorectal cancer (CRC) ranks as the third most frequently diagnosed malignancy in the United States. The likelihood of developing colorectal cancer throughout one's lifetime is consistent for both men and women. Factors that increase the likelihood of developing the disease are grouped into categories of modifiable and non-modifiable. Non-modifiable factors typically consist of ethnicity (African Americans and individuals of Jewish descent), age (over 50 years), and a personal or family history of colorectal polyps, cancer, or inflammatory bowel disease. Adjustable factors that can contribute to the development of the disease are having a body mass index (BMI) over 25, lack of physical activity, and consuming a diet rich in saturated fats and red meat but lacking in fiber, fruits, and vegetables. Smoking and excessive alcohol intake is significant influencers in the cause of this condition. It has been recommended to include one to three tablespoons of ground Flaxseeds in your daily diet, equivalent to 8-24g per day, as a beneficial addition to a balanced eating routine. According to the Food and Drug Administration's Estimated Daily Intake guidelines, Flaxseed can be

incorporated as an additional ingredient in various baked goods, breakfast cereals, salad dressings, yogurt, and other food items, at a recommended rate of 4g per serving, consumed 3 to 4 times daily, not exceeding 16g per day. The nutritional content of 100g of Flaxseed consists of 20. 3g of protein, 37g of fat, 29g of carbohydrates, and a total of 530 kcal. The chemical composition of it varies based on processing, leading to an increase in protein, carbohydrates, and minerals, and a decrease in lipid content.[31]

4.1.1 Mechanism of Action :

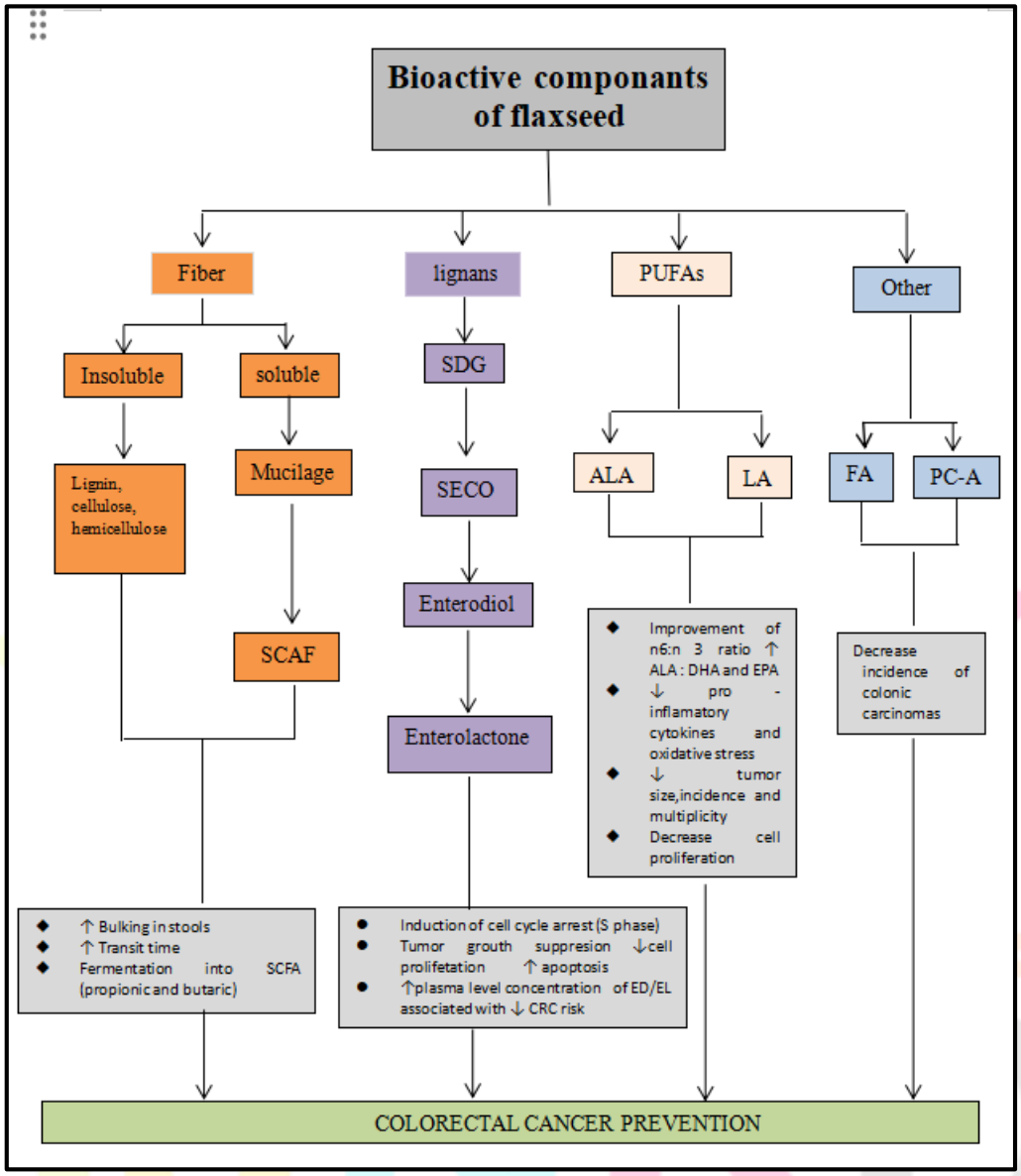


Fig No. 13: Mechanism of Action of Colorectal Cancer Prevention [31]

4.2 Liver Cancer:

Liver cancer continues to be a significant global health concern, with its prevalence increasing on a global scale. It is projected that more than 1 million people will be diagnosed with liver cancer every year by 2025. Hepatocellular carcinoma (HCC) stands out as the prevalent type of liver cancer, representing approximately 90% of all cases. The most significant risk factor for the development of hepatocellular carcinoma (HCC) is the infection with Hepatitis B virus (HBV), contributing to approximately 50% of cases. Due to patients achieving sustained virological response with antiviral drugs, the risk associated with hepatitis C virus infection has significantly diminished.[32]

4.2.1 Mechanism of Action:

Model illustrating how flaxseed augments one-carbon metabolism in a manner that accelerates SAM biosynthesis, resulting in an elevated AMP/ATP ratio and an elevated ADP/ATP ratio.

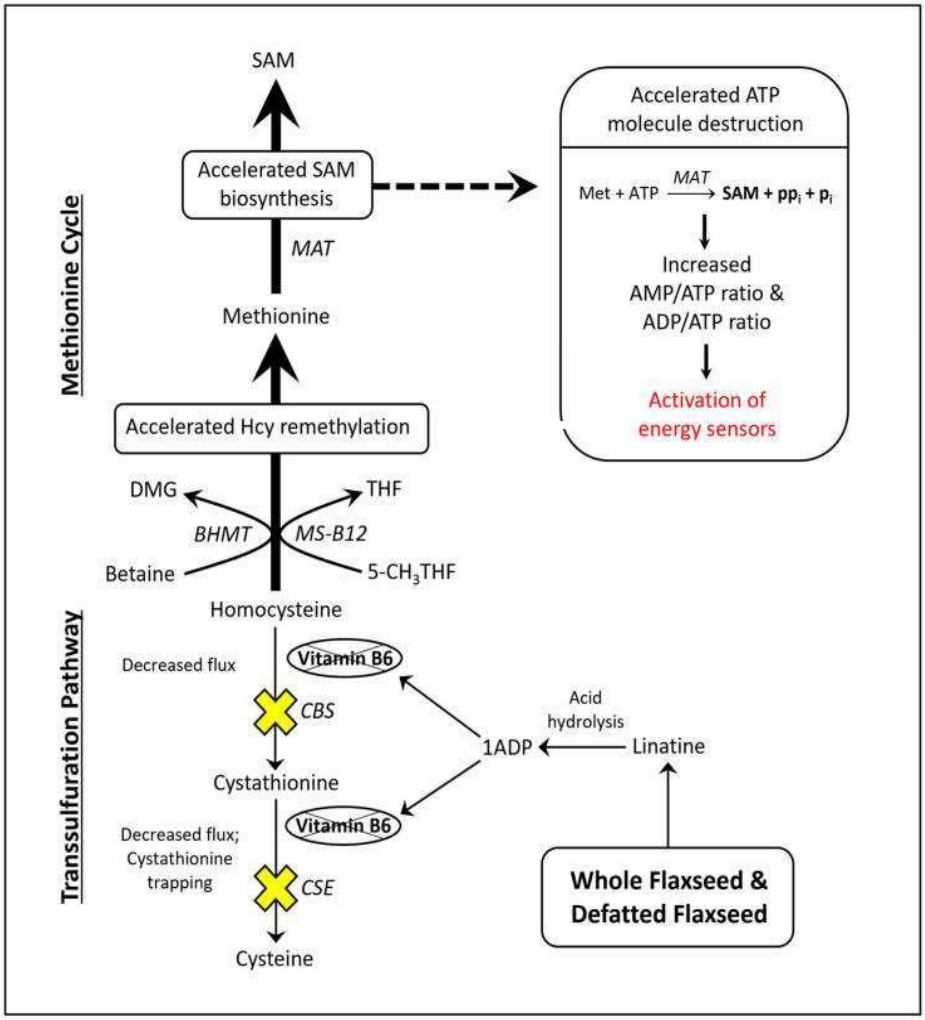


Fig No. 14: Mechanism of Action of Liver Cancer[33]

4.3 Breast Cancer:

It's a form of cancer that arises when breast cells proliferate uncontrollably, leading to the formation of a tumor. Breast cancer is widely recognized as one of the most prevalent forms of cancer resulting in the highest fatality rates globally. The World Health Organization estimated that over 1. 68 million women globally were diagnosed with breast cancer in 2012. Approximately 521,000 individuals lost their lives to this cause, with Europe seeing over 464,000 new cases diagnosed and about 131,000 women passing away within the same year. Numerous factors can contribute to the development of breast cancer, including gender, poor dietary choices and lifestyle habits, family history, alcohol or tobacco use, lack of breastfeeding, hormone therapy, being overweight, and obesity, among various others.Secoisolariciresinol diglucoside (SDG) is the main lignan found in flaxseeds, constituting approximately 95% of the seed's lignan content. The remaining 5% is made up of lariciresinol, pinoresinol, and matairesinol. Upon ingestion of SDG lignan, the bacteria in the colon work their magic by transforming the lignan into mammalian lignans known as enterolactone and enterodiol. They share a structural resemblance with estrogen, exhibiting both antioxidant properties and a mild estrogenic effect (Figure 15). It functions as an antiestrogen because it closely resembles the primary type of estrogen, enabling it to bind to the cell receptors and consequently impede the proliferation of cancer cells.[34]

4.3.1 Mechanism of Action:

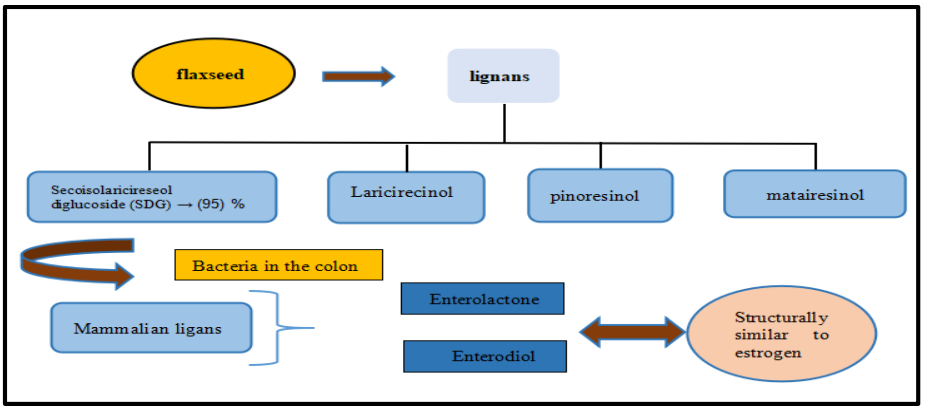


Fig No 15: Metabolism of Lignans in Flaxseed[34]

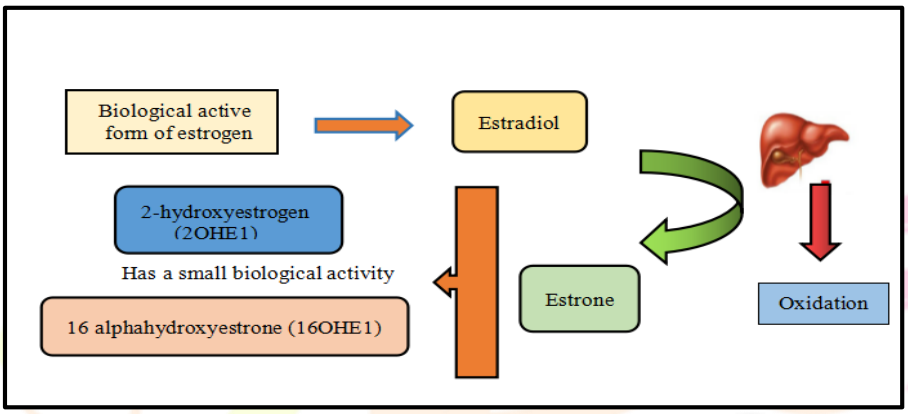


Fig No. 16: Influence of Estrogen Metabolism in Cancer [34]

5. ANTICANCER EFFECT OF ALPHA LINOLENIC ACID :

Cancer has possed a constant risk to human life ever since it was identified and even when manageable, it significantlyreduces the quality of life. Various Studies have demonstrated that ALA has a notable Impact in combating various types of cancers.Table 8- Show cases a selection of ALA sensiive cancers such as hepatocellular carcinoma, prostate cancer, colorectal cancer.Moreover, ALA also ·influences various gastrointestinal malignancies & bladder carcinoma.as represented in fig.17, ALA demonstrates a range of anticancer attributes such as inhibiting proliferation, triggering apoptosis,curbing tumor spreads blood vessel formation, and displaying antioxidant properties.[35]

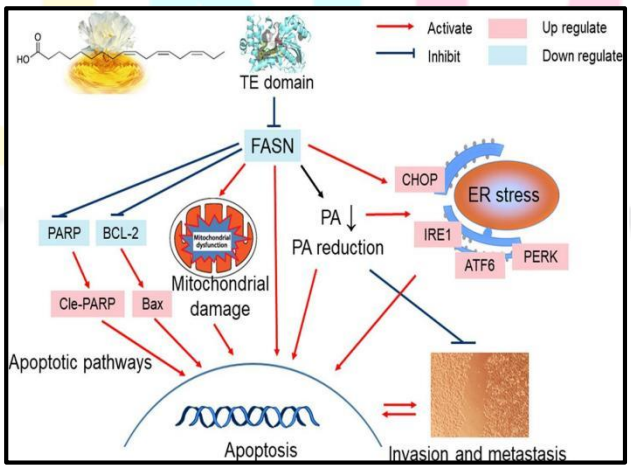


Fig. No. 17 Mechanism of Alpha linoleic Acid[35]

Cancer	Effect	Effective molecules	Change in Ex-Pression
Colorectal Cancer[31]	Induction of apoptosis	caspase 3	Downregulation
Hepatocellular Carconoma [32,33]	Inhibition of proleferatio n	Farnesoid X receptor	Upregulation
Breast Cancer [34]	Inhibition of tumor metastasis	COX2/PGE2/Twist 1	Downregulation

Table No. 8: The mechanism of the antitumor effects of ALA in various cancer

6. CONCLUSION :

Flaxseeds contain excellent bio-active compounds with various health benefits such as preventive and treating capability against various diseases, including cancer. Food products are increasingly including flaxseed in the list of nutritive and functional ingredients. Flaxseed shown promising results due to its rich composition of lignans, omega-3 fatty acids (especially alpha-linolenic acid, or ALA), and dietary fiber, all of which contribute to its potential anticancer properties. Numerous studies highlight that these components may play a role in reducing cancer risk and progression, particularly in hormone-related cancers such as breast,liver,colorectal cancers. The anticancer effect appears to be largely linked to the lignan secoisolariciresinol diglucoside (SDG), which can act as a phytoestrogen, modulating estrogen metabolism and reducing estrogen receptor-positive cancer risks. Additionally, ALA may inhibit tumor cell proliferation and induce apoptosis, further contributing to flaxseed's anticancer potential.

7. REFERENCES :

1. Priyanka Kajla & Alka Sharma & Dev Raj Sood, Flaxseed—a potential functional food source, J Food Sci Technol ; Association of Food Scientists & Technologists (India) 2014, doi: 10.1007/s13197-014-1293-y

2. Stephanie Tannous, Tony Haykal, Jana Dhaini, Mohammad Hassan Hodroj, Sandra Rizk* Department of Natural Sciences, Lebanese American University, Byblos, Lebanon, The anti-cancer effect of flaxseed lignan derivatives on different acute myeloid leukemia cancer cells , Biomedicine & Pharmacotherapy 132 (2020) 110884 , https://doi.org/10.1016/j.biopha.2020.110884.

3. Shireen Chikaraa, Sujan Mamidib, Avinash Sreedasyamb, Kishore Chittemc, Ralph Pietrofesad, Athena Zuppae, Ganesh Moorthye, Neil Dyerf, Melpo ChristofidouSolomidoud, and Katie M. Reindla, A review on flaxseeds:Nutritional profile,health benefits ,value added products,and toxicity (2017), DOI: 10.1002/efd2.114

4. Abdul Mueed, Sahar Shibli, Muhammad Jahangir, Saqib Jabbar & Zeyuan Deng ;A comprehensive review of flaxseed (Linum usitatissimum L.): health-affecting compounds, mechanism of toxicity, detoxification, anticancer and potential risk, (2022) ,Critical Reviews in Food Science and Nutrition, https://doi.org/10.1080/10408398.2022.2092718

5. S. Franklyn De Silva * and Jane Alcorn Flaxseed Lignans as Important Dietary Polyphenols for Cancer Prevention and Treatment: Chemistry, Pharmacokinetics, and Molecular Targets,Drug Discovery & Development Research Group, College of Pharmacy and Nutrition, 104 Clinic Place,(2019), doi:10.3390/ph12020068

6. Jian Han1,2, Shan-Shan Lu3, Zhi-Jie Wang1, You-Lin Li1, Flax seed oil inhibits metastatic melanoma and reduces lung tumor formation in mice,The Key Institute of State Administration of Traditional Chinese Medicine (2015).

7. Aniket V. Malia, Subhash B. Padhye, Shrikant Anant ,Mahabaleshwar V. Hegde, Shivajirao S. Kadamb, Anticancer and antimetastatic potential of enterolactone: Clinical, preclinical and mechanistic perspectives,European Journal of Pharmacology 852 (2019) 107–124, https://doi.org/10.1016/j.ejphar.2019.02.022.

8. Jhilam Pramanik,Akash Kumar, Bhupendra Prajapati,A review on flaxseeds :Nutritional profile, health benefits, value added products, and toxicity, (2023),https://doi.org/10.1002/efd2.114

9. Samina Kausera, Ashiq Hussaina, Shahmir Ashrafa, Ghulam Fatimaa, Ambreena, Sadaf Javariab, Zain Ul Abideena, Khurram Kabirc, Shazia Yaquba, Saima Akrama, Anjum Shehzada, Sameh A. Kormad , Flaxseed (Linum usitatissimum); phytochemistry, pharmacological characteristics and functional food applications, Food Chemistry Advances 4 (2024) 100573, https://doi.org/10.1016/j.focha.2023.100573

10. Abdul Mueed, Sahar Shibli , Sameh A. Korma , Philippe Madjirebaye , Tuba Esatbeyoglu ,and Zeyuan Deng ,Flaxseed Bioactive Compounds: Chemical Composition, Functional Properties, Food Applications and HealthBenefits-Related GutMicrobes,(2022), https://doi.org/10.3390/foods11203307

11.Qiu, C., Wang, H., Guo, Y., Long, S., Wang, Y., Abbasi, A. M., et al. (2020). Comparison of fatty acid composition, phytochemical profile and antioxidant activity in four flax (Linum usitatissimum L.) varieties. Oil Crop Science, 5(3), 136–141,

12.DiNicolantonio, J. J., & O'Keefe, J. H (2020). The importance of marine omega-3s for brain development and the prevention and treatment of behavior, mood, and other brain disorders. Nutrients, 12, 2333,doi:10.3390/nu12082333

13.Fan, L., Xu, J., Guan, X., Li, R., & Wang, S. (2023). Developing radio frequency pretreatment technology for improving yield and quality of flaxseed oil extractions. Innovative Food Science & Emerging Technologies, 86, Article 103363,https://doi.org/10.1016/j.ifset.2023.103363

14.Kaushik, P., Dowling, K., McKnight, S., Barrow, C. J., Wang, B., & Adhikari, B. (2016). Preparation, characterization and functional properties of flaxseed protein isolate. Food Chemistry, 197, 212–220 , http://dx.doi.org/10.1016

15.Noreen, S., Tufail, T., Bader Ul Ain, H., Ali, A., Aadil, R. M., Nemat, A., et al. (2023). Antioxidant activity and phytochemical analysis of fennel seeds and flaxseed. Food Science & Nutrition, 11(3), 1309–1317,https://doi.org/10.1002/fsn3.3165

16.Shams, R., Pandey, V. K., Dar, A. H., Tripathi, A., & Singh, R. (2022). A descriptive review on nutraceutical constituents, detoxification methods and potential health benefits of flaxseed. Applied Food Research, 2(2), Article 100239.http://dx.doi.org/10.1016/j.afres.2022.100239

17.Sen, C. K., Khanna, S., & Roy, S. (2006). Tocotrienols: Vitamin E beyond tocopherols. Life Sciences, 78(18), 2088–2098. doi:10.1016/j.lfs.2005.12.001

18.Plissonneau, C., Sivignon, A., Chassaing, B., Capel, F., Martin, V., Etienne, M., et al. (2022). Beneficial effects of linseed supplementation on gut mucosa-Associated microbiota in a physically active mouse model of Crohn's disease. International Journal of Molecular Sciences, 23(11), 5891.https://doi.org/10.3390/ijms23115891

19.Cui, W.; Kenaschuk, E.; Mazza, G. Influence of genotype on chemical composition and rheological properties of flaxseed gums. Food Hydrocoll. 1996, 10, 221–227,https://doi.org/10.1016/S0268-005X(96)80038-5

20.Bekhit, A. E.-D A., A. Shavandi, T. Jodjaja, J. Birch, S. Teh, I. A. M. Ahmed, F. Y. Al-Juhaimi, P. Saeedi, and A. A. Bekhit. 2018. Flaxseed: composition, detoxification, utilization, and opportunities. Biocatalysis and Agricultural Biotechnology 13:129–52. doi: 10.1016/j. bcab.2017.11.017.

21.Harland, B. F., and E. R. Morris. 1995. Phytate: a good or a bad food component? Nutrition Research 15 (5):733–54. doi: 10.1016/0271-5317(95)00040-P
22.Daun, J., V. Barthet, T. Chornick, and S. Duguid. 2003. Structure, composition, and variety development of flaxseed. Flaxseed in Human Nutrition 1–40. doi: 10.1201/9781439831915.ch1.

23.Kratzer, F. 1946. The treatment of linseed meal to improve its feeding value for chicks. Poultry Science 25 (5):541–2. doi: 10.3382/ ps.0250541.

24.Russo, R., and R. Reggiani. 2014. Variation in the content of cyanogenic glycosides in flaxseed meal from twenty-one varieties. Food and Nutrition Sciences 05 (15):1456–62. doi: 10.4236/fns.2014.515159.

25.Bacala, R., and V. Barthet. 2007. Development of extraction and gas chromatography analytical methodology for cyanogenic glycosides in flaxseed (Linum usitatissimum). Journal of AOAC International 90 (1):153–61.
doi: 10.1093/jaoac/90.1.153.

26.Cressey, P., and J. Reeve. 2019. Metabolism of cyanogenic glycosides: a review. Food and Chemical Toxicology: An International Journal Published for the British Industrial Biological Research Association 125:225–32. doi: 10.1016/j.fct.2019.01.002.

27.https://images.app.goo.gl/YH2EzpM8h52N5X5f8

28.https://images.app.goo.gl/XzYLhAK8DczGH9a37

29.Bernacchia R, Preti R and Vinci G ,Review Article Chemical Composition and Health Benefits of Flaxseed ,Austin Journal of Nutrition and Food Sciences(2014),www.austinpublishinggroup.com
30.Baker, A., M. Garner, K. Kimberley, D. Sims, J. Stordock, R. Taggart, and D. Walton. 2018. Cyanide toxicity of freshly prepared smoothies and juices frequently consumed. European Journal of Nutrition & Food Safety 8 (4):215–24.
doi: 10.9734/EJNFS/2018/44004.

31.Jennifer A. A. DeLuca1 & Erika L. Garcia-Villatoro1 & Clinton D. Allred,Flaxseed Bioactive Compounds and Colorectal Cancer Prevention, Current Oncology Reports (2018) 20:59,https://doi.org/10.1007/s11912-018-0704-z

32.Josep M. Llovet , Robin Kate Kelley, Augusto Villanueva , Amit G. Singa, Eli Pikarsky, Sasan Roayaie, Riccardo Lencioni, Kazuhiko Koike, Jessica Zucman- Rossi and Richard S. Finn , https://doi.org/10.1038/s41572-020-00240-3

33.William C. Weston 1 , Karen H. Hales and Dale B. Hales , Flaxseed Reduces Cancer Risk by Altering Bioenergetic Pathways in Liver: Connecting SAM Biosynthesis to Cellular Energy (2023),https://doi.org/10.3390/metabo13080945

34.Ana Calado, Pedro Miguel Neves, Teresa Santos and Paula Ravasco ,The effect of Flaxseed in Breast Cancer: A Literature Review (2018), doi: 10.3389/fnut.2018.00004

35.Wenyuan Huanga, Xing Guoa, Chunyan Wanga, Amantay Alzhana, Zhengan Liub, Xiaofeng Maa, Qingyan Shub,α-Linolenic acid induces apoptosis, inhibits the invasion and metastasis, and arrests cell cycle in human breast cancer cells by inhibiting fatty acid synthase, Journal of Functional Foods 92 (2022) 105041 ,https://doi.org/10.1016/j.jff.2022.105041.

36.Somaia Al-Madhagy, Naglaa S. Ashmawy2, Ayat Mamdouh, Omayma A. Eldahshan and Mohamed A. Farag , A comprehensive review of the health benefits of flaxseed oil in relation to its chemical composition

and comparison with other omega-3-rich oils , Al-Madhagy et al. European Journal of Medical Research (2023) 28:240 , https://doi.org/10.1186/s40001-023-01203-6