IJPSR (2022), Volume 13, Issue 2 (Review Article)

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 17 February 2021; received in revised form, 08 June 2021; accepted, 09 June 2021; published 01 February 2022

IMPACT OF FLAX ON METABOLIC SYNDROME AND RELATED ENVIRONMENTAL FACTORS

Supriyo Saha [1] and Dilipkumar Pal [*2]

School of Pharmaceutical Sciences and Technology [1], Sardar Bhagwan Singh University, Dehradun - 248161, Uttarakhand, India.
Department of Pharmaceutical Sciences [2], Guru Ghasidas Vishwavidyalaya (A Central University), Bilaspur - 495009, Chhattisgarh, India.

Keywords:

Flax, Hyperglycemia, Hormonal imbalance, Cardiovascular diseases, Biodiesel

Correspondence to Author:
Dr. Dilipkumar Pal

Associate Professor, Department of Pharmaceutical Sciences, Guru Ghasidas Vishwavidyalaya (A Central University), Bilaspur - 495009, Chhattisgarh, India.

E-mail: drdilip71@gmail.com

ABSTRACT: Flax (*Linum usitatissimum*) is an annual herb with a huge source of essential fatty acids, amino acids, vitamin E, organic acids, and cyanogenetic glycosides. Flax is primarily observed with antioxidative and cell rejuvenating properties. Due to the major ups and downs of lifestyle, metabolic syndrome is the most common terminology associated with humans. Metabolic syndrome is amplified by unhealthy food consumption, less physical activity, alcohol consumption, smoking, *etc*. Heart attack, hyperglycemia, insulin resistance, cancer, *in-vitro* fertility and other hormonal or neuronal problems are the medusa's snakes of metabolic syndrome. The constantly changing environment, pollution, bad air quality index, greater amount of carbon footprints, and exhaustion of greenhouse gases are the sources of maladies associated with environmental breakdown. Environmental calamities like consumption of non-renewable fossil fuel, pollutions, melting of the ice age are collectively flowed towards metabolic syndrome. After prolonging intake of Flax (seed or oil) it was observed with greater impacts on mitigation of Diabetes mellitus, occurrence of inflammation, ulcer, atherosclerotic plaque, and maintained the normal levels of hormones also increased the positive biochemical factors secreted from different organs.

INTRODUCTION: In this fast-forward and readymade lifestyle, humans are very prone to a lifestyle disorder known as metabolic syndrome [1]. Metabolic syndrome is amplified by unhealthy food consumption, less physical activity, alcohol consumption, smoking, *etc*. [2]

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.13(2).531-42

This article can be accessed online on www.ijpsr.com

DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.13(2).531-42

As well as, it is a constellation of other problems such as resistance towards insulin sensitivity [3, 4], increased blood pressure, deposition of visceral fat, dyslipidemia [5, 6] and increase amount of oxidative inflammatory markers, higher incidence of hormonal imbalance, polycystic ovarian disease, cancer and other neurological disorders with this syndrome [7]. Major organs like the liver, pancreas, spleen, and heart are highly affected by this syndrome [8, 9]. Hyperglycaemia, hepatic disorders, cancer, inflammation, hormonal disorders, polycystic ovarian syndrome, cardiac arrhythmia, atherosclerosis, ventricular fibrillation, and weight

gain are the principle manifestations of metabolic syndrome **Fig. 1** [10]. Peoples with a large waistline (greater than 35 inches for women and 40 inches for men), high blood pressure (greater than 180/120 mm Hg) [11], less active daily routine, intake of high carbohydrate or fatty foods, higher fasting blood level (greater than 100 mg/dL) [12], greater than 150 mg/dL of triglycerides and lower than 40 mg/dL of HDL level are very much prone towards the disorder (https://www.hopkinsmedicine.org/health/conditions-and-diseases/metabolic-syndrome) [13, 14].

The scientific name of Flax (FL) is *Linum usitatissimum* belongs to the family Linaceae with more than 14 genera. FL is an annual self-pollinated herb with haploid chromosome with simple, sessile, linear-lanceolate leaves and flowers with five petals and sepals [15, 16]. FL seeds are mainly smooth, shiny, oval, lenticular in shape about six mm in length with golden-brown colour. The seed was used as medicine for more than 800 decades [17, 18].

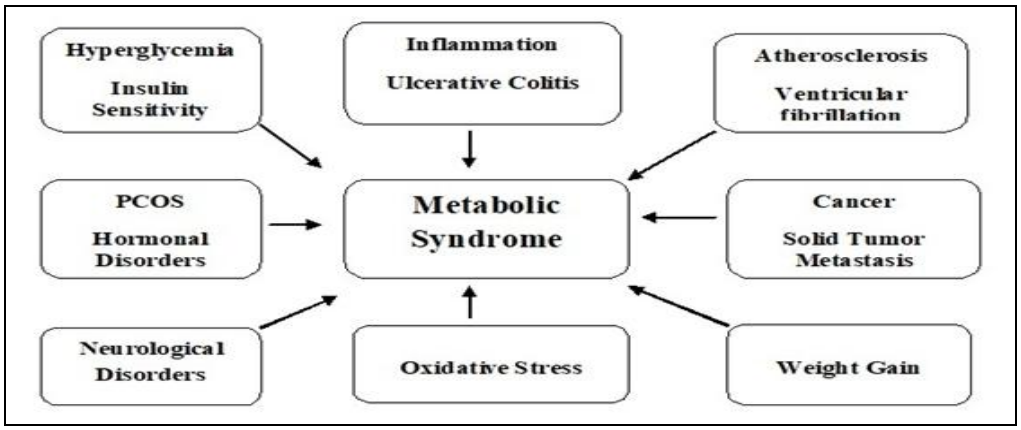

FIG. 1: METABOLIC SYNDROME

Actually, Flax (seed or oil) is the cheap alternate of chia and quinoa seeds, and people follow healthy foods with a balance between carbohydrates, fats, proteins and fibers [19]. This drive causes a serious positive slope in the use of Flax [20]. A recent market report on the sale of Flax (seed or oil) after surveys on five geological areas (Asia-Pacific, Europe, North-America, South-America, and the Middle East & Africa), it was clearly observed that market demand will reach by 30 million USD by 2023 (Report ID: 290219). India, China, Australia, Kazakhstan and Iraq are the giant producer of Flax [21, 22]. Another critical situation that arises with this fast life is environmental calamities. Now the question is what is Environment? The environment is our surroundings, where humans, animals, birds, insects, plants, trees, planktons, corals, fossils and many more organisms are live in a symbiotic way [23, 24]. The rapid change in temperature, shortfall of rain, floods, tornadoes, eruptions of volcanoes, shrinking of river width, lesser amount of fresh oxygen and drinkable water are not the curses of environment; these are the maturity benefits of manmade pollutions [25]. Too much emission of greenhouse gases, huge consumptions of non-renewable fossil fuels, and create much darker carbon footprints are the crusades of the environment [26, 27]. The land and ocean temperature index observed with 0.8°C temperature rise in 2018, followed by 3.3 mm/year rise in global mean sea level, an increase in 1.8 and 1.1 mm/year in ocean mass and steric height [28], respectively, and a decrease in 286 Gt/year and 126 Gt/year in Greenland and Antarctica ice mass, respectively (Data provided by NASA) [29]. Greater consumption of biofuel, biodiesel, and solar energy, lesser consumption of energy, minimization of carbon fuel usages are the principle mitigation process of environmental pollution [30]. Environmental mismanagement creates a direct pavement towards metabolic syndrome. Higher levels of ultraviolet irradiation, nitrogen oxides, sulphur dioxides, particulate matter (< 1.0 µM), and carbon di/mono oxides leads to cardiac arrhythmia, ischemia, cardiomyopathy [31] diabetic mellitus and insulin resistance; alteration of DNA base pairing, skin and lung cancer; inflammatory bowel disease, Crohn's disease and ulcerative colitis, hormonal irregularities and dementia, Alzheimer and Parkinson's diseases [32, 33]. This work mainly focuses on the importance of Fl (whole, seed or oil)

in the management of metabolic syndrome and creates a positive impact on our environment.

Chemical Constituents of FL: FL is composed of essential fatty acids such as alpha linoleic acid, linolenic acid, oleic acid; histidine, isoleucine, leucine, lysine, methionine, valine, threonine, arginine, aspartic acid, cysteine, proline, serine as essential amino acids; alpha and gamma tocopherols; ferulic acid, gallic acid, chlorogenic acid as organic acids and linustatin, linamarin as cyanogenetic glycosides also rhamnose, galactose, fructose, D-xylose, arabinose and cellulose, lignin are the observed polysaccharides obtained from soluble and insoluble fibers of FL seed **Fig. 2.**

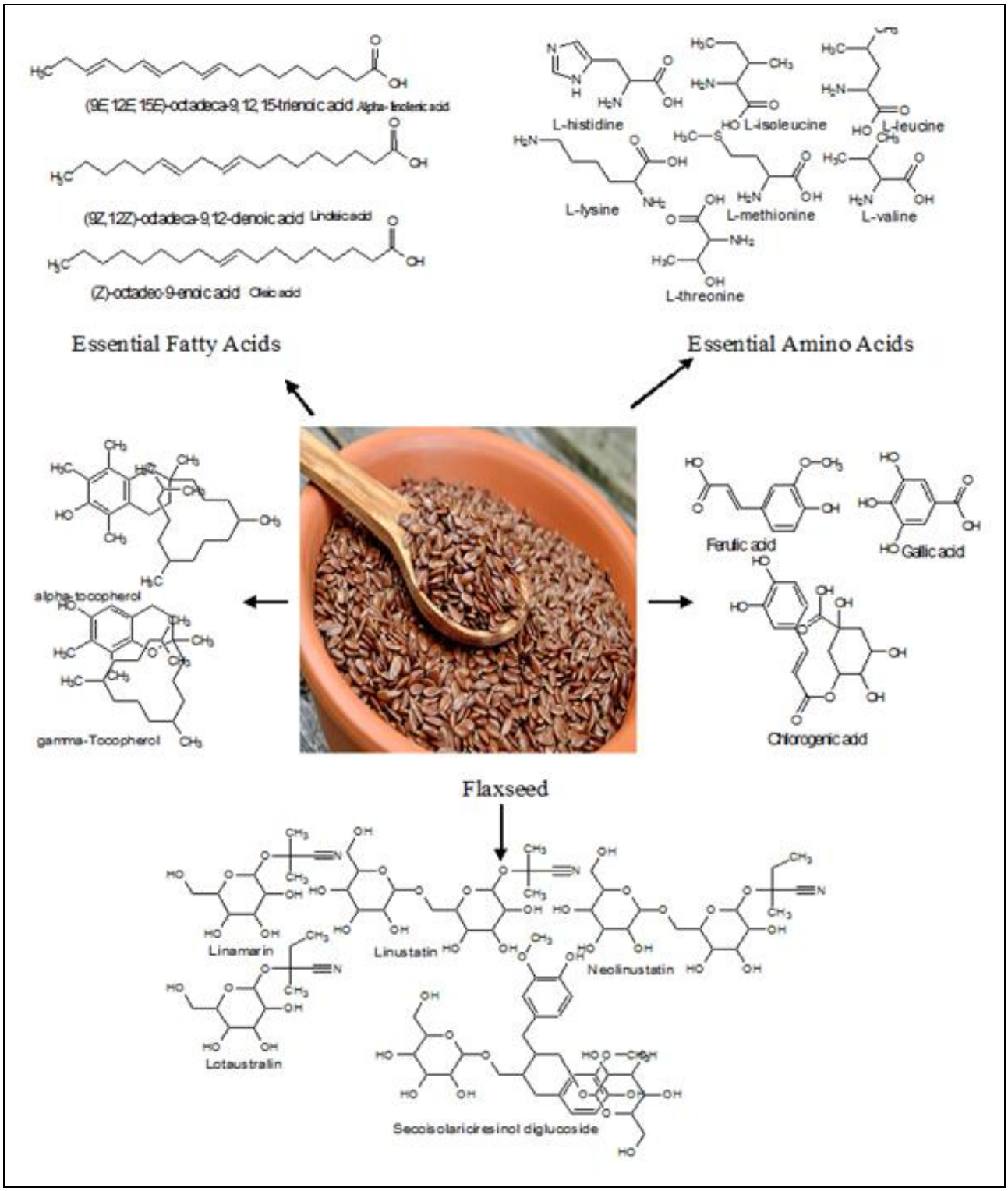

FIG. 2: FLAXSEED AND ITS CHEMICAL CONSTITUENTS

Effects of FL on Metabolic Syndrome:

Effect of FL Seed on Hyperglycemia: High fructose-fed animals were administered with (50 mg/kg body weight) of FL, (25 mg/kg body weight) of quercetin and dual administration of (25 mg/kg body weight of both) for a period of four weeks; followed by estimation of blood glucose, insulin, leptin, and adiponectin level. The outcomes revealed that level of glucose, insulin, cholesterol, triglyceride, leptin and adiponectin were slightly modified whereas level of high- and low-density lipoproteins was marked changed **Fig. 3**.

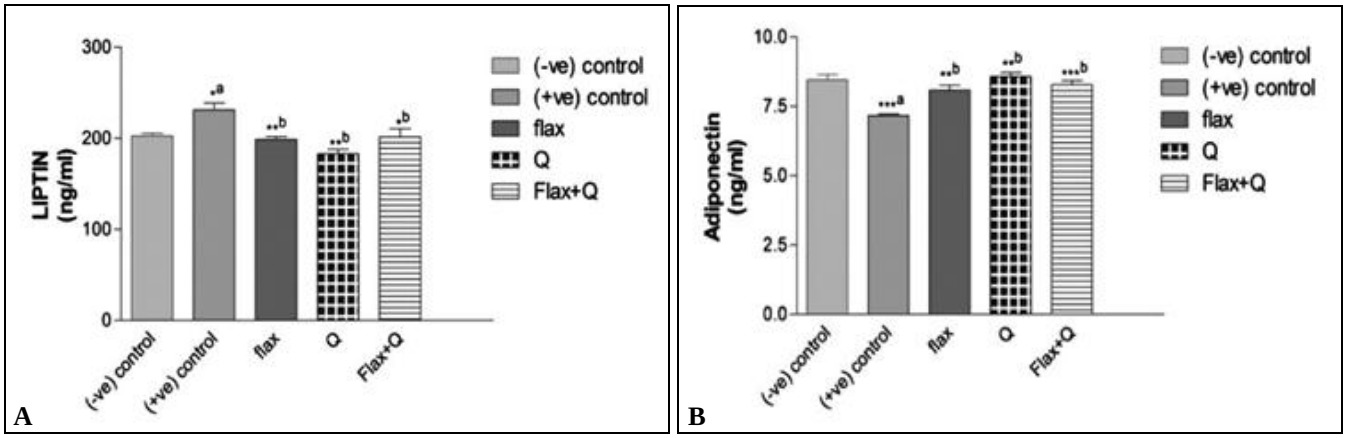

FIG. 3: THE LEPTIN AND ADIPONECTIN LEVELS AFTER ADMINISTRATION OF FLAXSEED, QUERCETIN AND IN COMBINATION IN FRUCTOSE-FED RATS FOR 4-WEEKS. [Copyright @ Abdelkarem *et al.* 2017 with permission from Elsevier B.V].

These data confirmed the effectiveness of FL and quercetin in the management of hyperglycemia [34]. Electrodialysis using ultrafiltration membrane technique of FL with potassium chloride solution was obtained two protein hydrolysates as F1 (300-400) Da and F2 (400-500) Da molecular weight. Then the effect of the fraction on glucose transport and systolic blood pressure was estimated, which revealed that F2 showed greater uptake of glucose transport and F1 showed blood pressure-lowering effect [35]. Another experiment indicated the effect of FL oil on minimization of genetic hyperglycemic conditions. Here at first, hyperglycemic was induced on female rats and processed for pregnancy, after confirmation animals were divided into three parts, fed with a high-fat diet, FL oil, and non-hyperglycaemic diet, respectively. When the male infants were accustomed to nature, then natural death was promoted in two phases as 100 days and 180 days; followed by histopathology of the pancreas. The outcomes revealed that muscle of pancreas was abnormally thick with high-fat diet and a small quantity of islets with lowers insulin density; whereas FL oil diet observed with greater islets and insulin immunodensity [36].

Effect of FL Seed on Inflammation and Hepatic Disorders: A design confirmed the effect of aqueous and hydro-alcoholic extract of FL on ulcerative colitis (induced by acetic acid). The selected animals were divided into four groups as placebo, control, treated, and infected with prednisolone (standard); followed by sacrificed to examine the condition of colon and spleen, the presence of blood in stool, Disease Activity Index (DaI); also the presence of leukocyte and ability for generation of free radical were the scavenging parameters of FL. The intake of (300) mg/ml and (500) mg/ml of FL, parameters like weight loss, DaI, percent affected area, macroscopic colonic lesion, and ulceration index was markedly decreased. Histopathological sections of colon showed the proper presence of neutral and acidic mucin with a reduction in goblet cell depletion along with improved catalase, superoxide dismutase, and glutathione activity **Fig. 4** [37].

Also, inflammatory markers as erythrocyte sedimentation rate (lowered by 6.99 digits), interleukin 6 and interferon-gamma (lowered by 7.32 and 13.18 digit respectively), transforming growth factor-beta (increased by 173.29 digits), and calprotectin (minimized by 192.20 unit) were markedly affected [38]. Another study revealed the antiulcer effect of FL lignan secoisolariciresinol diglucoside on dextran sodium sulphate induced rat model considering amino salicylic as standard. The assessment of DaI, myeloperoxidase assay,

histopathological evaluation of colon (using heamtoxylin and eosin stains) and invasive intestinal inflammation (using fluorescein isothiocyanate dextran stain) were the assessment parameters. Lower DaI and colon weight, higher colon length, lower myeloperoxidase, and slightly higher intestinal permeability were observed with high diglucoside content **Fig. 5** [39].

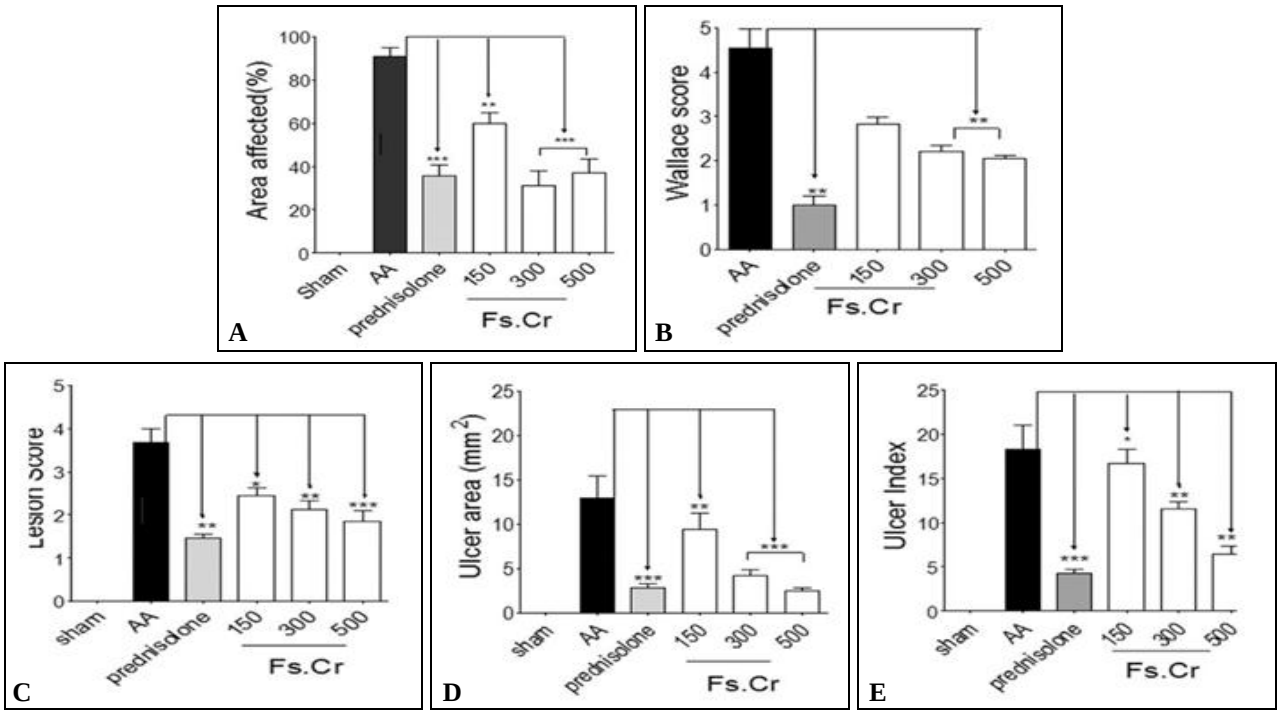

FIG. 4: PRETREATMENT WITH FS.CR IMPROVED THE MACROSCOPIC DAMAGE PARAMETERS OF COLONIC TISSUES IN BALB/C MICE INDUCED WITH AA COLITIS. [Copyright@ Palla *et al.*, 2018 with permission from Elsevier B.V].

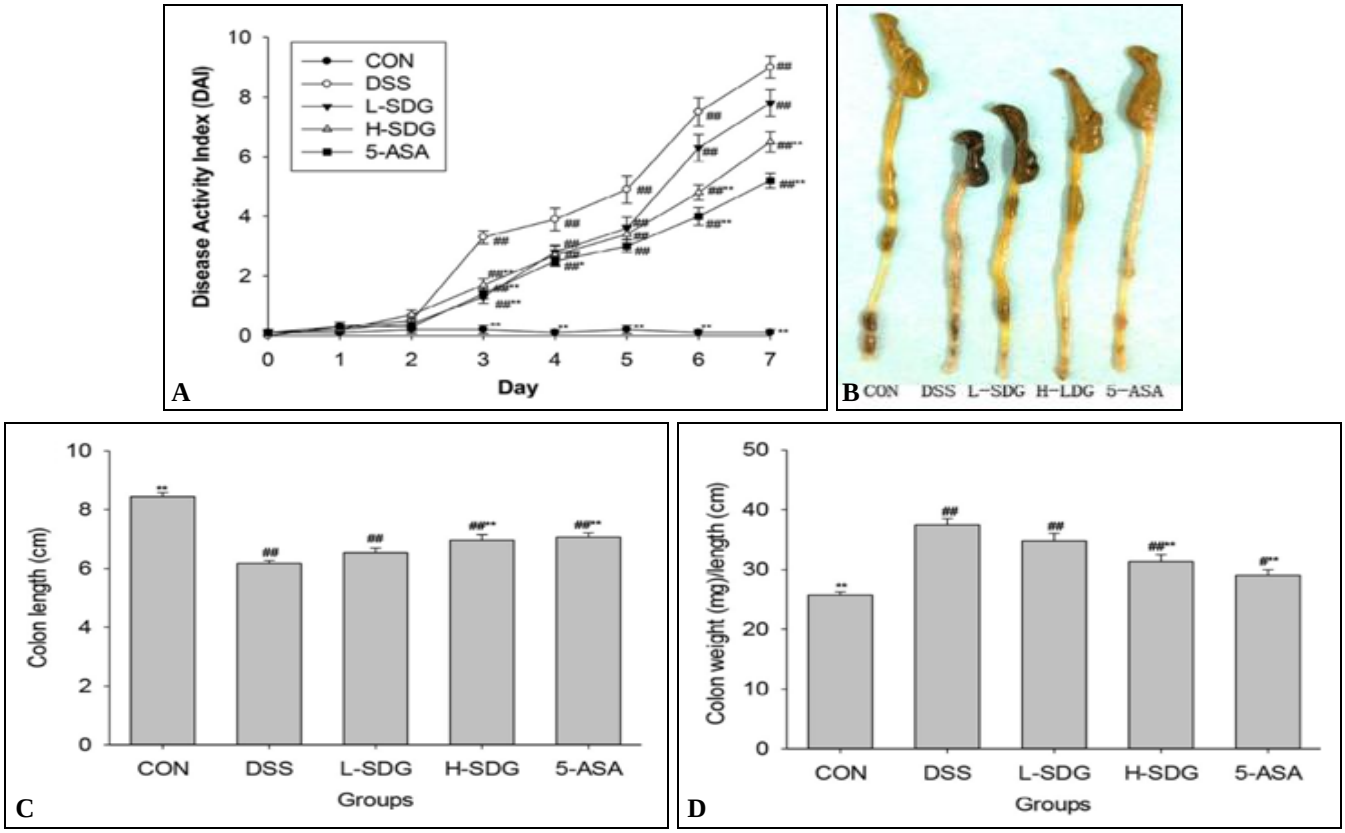

FIG. 5: ORAL SDG TREATMENT AMELIORATED DSS-INDUCED COLON INJURY. [Copyright @ Xu *et al.*, 2016 with permission from Elsevier Ltd].

A study on the effects of FL and corn oil on high ethanol-fed animals followed by assessing the levels of plasma enzyme, hepatic steatotic and inflammatory factors, endotoxin (lipopoly-saccharide greatly linked with toll-like receptor-4 associated inflammatory response). The outcomes revealed that levels of serum alanine aminotransferase, alkaline phosphatase, serum bilirubin, plasma triglyceride, thiobarbituric acid reactive substance (reactive product of lipid peroxidation), tumor necrosis factor-alpha, and endotoxin were markedly decreased with FL oil. This data confirmed the effectiveness of Fl oil on alcoholic liver disease [40].

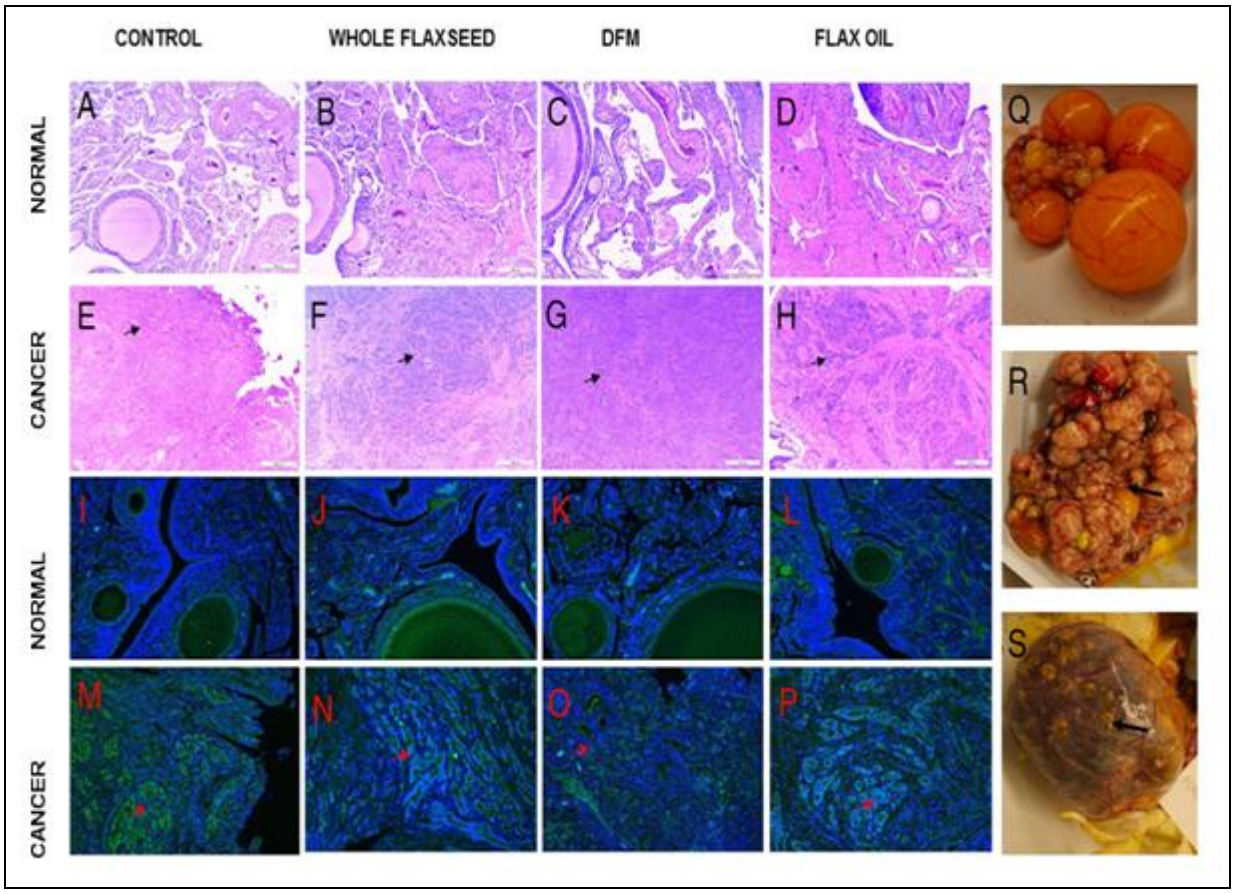

FIG. 6: H AND E STAINING DEPICTING NORMAL AND CANCEROUS OVARIAN TISSUE HISTOLOGY AND IMMUNOFLUORESCENCE DEMONSTRATING ER ALPHA PROTEIN EXPRESSION FROM CONTROL, WHOLE FLAXSEED, DFM AND FLAX OIL DIETS. [Copyright @ Dikshit *et al.*, 2017 with permission from Elsevier Inc.].

Effect of FL Seed on Cancer: A study on chloroform Fl extract (20 µg/ml, 40 µg/ml, 80 µg/ml, 160 µg/ml and 320 µg/ml) and methyl esters of FL fatty acids (hexadecanoic methyl ester, methyl stearate, trans-13-octadecanoic methyl ester, 9,12-octadecadienoic methyl ester, and 9,12,15-octadecatrienoic methyl ester) on breast cancer cell line (MCF 7); followed by determination of different antiproliferation parameters such as programmed cell death and generation of reactive oxygen species (ROS). The outcomes showed a dose-dependent decrease on antiproliferative parameters [41]. In another experiment evaluated the effects of FL oil (200 µl and 400 µl) on tumor growth factor of C57BL/6 mice cervical cancer model along with the level of expression of viral E6 and E7 oncogenes related to ovarian cancer progression. Here five different animal groups were introduced (control, 4 mg/kg of cisplatin-treated, 200 µl of FL oil treated, 400 µl of FL oil treated and 400 µl of FL oil with 4 mg/kg of cisplatin-treated), and the outcomes observed that last treated group showed maximum inhibition of tumor weight, decreased expression of E6 and E7 (tubulin as loading control) along with decreased and increased expression of p53 and Rb genes, respectively with co-administration of cisplatin and FL oil. The increasing expression on cytokines and oxidative stress (thiobarbituric acid-related substances) by cisplatin and oil correlated with cell

toxicity behaviour along with higher trolox value was observed with high concentration of FL oil directly confirmed the effect of FL oil on ovarian cancer cell line proliferation [42]. The metastasis of solid tumor was evaluated using Fl (seed and oil) and secoisolariciresinol diglucoside on human breast cancer cell line (MDA-MB-435) for seven days and it was mainly applicable when size of solid tumors of 0.9 gm and 110 square meters after the scissor of tumor.

The outcomes revealed that the issue of spreading for lung and lymph nodes was statistically minimized **Table 1** [43]. FL seed, defatted FL meal, and FL oil were minimized the expression of estrogen receptorα and higher concentration of microsomal enzyme with the altered genetic information of decapentaplegic homolog7 protein expressions by cascading the mechanism of caspase3 enzyme and phosphorylated the p38 gene **Fig. 6** [44].

TABLE 1: EFFECT OF FL AND FL SECOISOLARICIRESINOL DIGLYCOSIDE AND FLAXSEED OIL (FO), ON THE RECURRENCE OF EXCISED PRIMARY TUMOR

Parameters	Total	Recurrence of tumor (%) Primary tumor less than 0.9 g	Primary tumor greater than 0.9 g	Recurrence of tumor size Volume (cc)	Weight (gm)
Basal diet	7/24 (29.2)	4/14 (28.6)	3/10 (30.0)	0.72	0.89
FL seed	7/24 (29.2)	2/14 (14.3)	5/10 (50.0)	1.30	1.70
Sdg	8/24 (33.3)	3/15 (20.0)	5/9 (55.6)	0.55	0.81
FL oil	8/23 (34.8)	3/13 (23.1)	5/10 (50.0)	0.50	0.79
Sdg with FL oil	6/22 (27.3)	3/14 (21.4)	3/8 (37.5)	0.74	1.09

The ω-3 fatty acid of FL was minimized the occurrence of cancer for 3.5 years old hen and without any observable difference in the expression of cyclooxygenase-1 enzyme for FL presence/ absence diet but lowering in the expression of cyclooxygenase-2 enzyme for FL fed animals. These data confirmed the importance of FL for minimizing the incidence of ovarian cancer [45]. Another study of four previously linoorbitides were isolated from FL oil were assessed against breast cancer cell lines (Sk-Br-3 and MCF 7) and human skin cancer cell line (A375) for a period of two days. The outcomes pointed that first linorbitides (LOB3) showed greater cell toxicity against A375, Sk-Br-3 and MCF 7 with percentage greater that 55%, 45% and 5% after 2 days of treatment. Another parallel examination of peptides on cellular phospholipids binding came with the conclusion of hydrophobic interaction between peptides and cell membrane. These data confirmed the cell toxic nature of FL orbited against breast and skin cancer [46]. Another two orbitides as [1–9-NαC]- linus orb B3 (molecule A) and [1–9-NαC]-linus orb B2 (molecule B) were isolated from Fl oil using hexane as a solvent, evaluated against human gastric cell lines SGC-7901 and GES-1 epithelial cells, decreased cell viability confirmed the anti-proliferative effect [47].

Effect of FL Seed on Oxidative Stress: The oligosaccharides of FL showed good radical scavenging property using inhibition of free radical generation was assessed by hydroxyl radical scavenging, diphenyl picrylhydrazyl, and azino-bis (ethylbenzothiazoline sulphonic acid) methods. Outcomes observed with maximum dose-dependent inhibition observed with sulphonic acid method (rate of inhibition: 92%) followed by hydroxyl scavenging (rate of inhibition: 82.6%) and diphenyl picrylhydrazyl method (rate of inhibition: 58.2%) [48]. Also, four different peptide sequences (QGRGG QGGQGQ, NGSGYPGSDLDSSPPGAKVP, GRE EIGNVMRSLM, and GVKVEGDGGLVRRDEI) with another thirteen amino acid sequence (GFPGRLDHWCASE) were identified from FL hydrolysate, observed with greater scavenging activity by peptide sequence (GFPGRLDH-WCASE) **Table 2** [49].

TABLE 2: ISOLATED PEPTIDES FROM FLAXSEED HYDROLYSATE

Fraction no.	Observed mass	Calculated mass	Peptide sequence	Source protein	Fragment
F2	1012.455 (+1)	1028.475	QGRGGQGGQGQ	Conlinin	35-47
F5	634.600 (+3)	1900.880	NGSGYPGSDLDSSPPGAKVP	Cellulose synthase 6D	144-163
F5	1491.741 (+1)	1490.733	GREEIGNVMRSLM	UDP- Glycosyltransferase-1	426-438
F6	850.000 (+2)	1697.906	GVKVEGDGGLVRRDEI	UDP-Glycosyltransferase-1	367-382

Effect of FL Seed on Cardiovascular Disorders: FL seed and psyllium fibre were lowered the waist circumference by 2.8 cm and 1.18 cm, respectively; HbA1c level was minimized by 0.5 unit by FL and increased by 0.1 unit by psyllium; fasting blood glucose level was increased by 15.4 mg/dl by FL and decreased by 1.6 mg/dl level by psyllium; insulin resistance was increased by 2.2 unit by FL and 1.7 unit by psyllium; serum cholesterol level was lowered by 15.3 mg/dl by FL and increased by 0.7 mg/dl by psyllium; low density lipoprotein was decreased by 13.1 mg/dl by FL and lowered by 0.5 mg/dl by psyllium; tumor necrosis factor and malondialdehyde levels were decreased by FL whether psyllium fibre has not any prominent effect; the most important parameter nitric oxide was markedly increased (2.4 nM/L) by FL whether decreased by 0.8 nM/L unit by psyllium [50]. The effects of FL seed (10% milled), oil (4.4%), and lignan (0.44%) on myocardial infracted animals by assessing on the level of plasma fatty acids, ventricular arrhythmia, ventricular dilation, and myocardial inflammation. The outcomes revealed that FL oil enhanced the level of alpha-linolenic acid and eicosapentaenoic acid without any effects on docosahexanoic acid also the incidence of arrhythmia, ventricular fibrillation, and ventricular tachycardia were markedly decreased by FL oil, and dilation of the ventricle was slightly modified with FL treatment, but myocardial fibrosis was greatly reduced and contraction-relaxation behaviour of heart muscle with all types of FL supplements [51, 52]. FL oil was administered on three groups of animals as control (fed normal prescribed animal diet), WTD (high cholesterol western diet), and FO (high cholesterol western diet with flaxseed oil) showed a markedly decrease in the levels of serum and liver total cholesterol, triglycerides, low-density lipoprotein-cholesterol, malondialdehyde and expression of tumor necrosis factor-α-messenger ribonucleic acid **Fig. 7** [53].

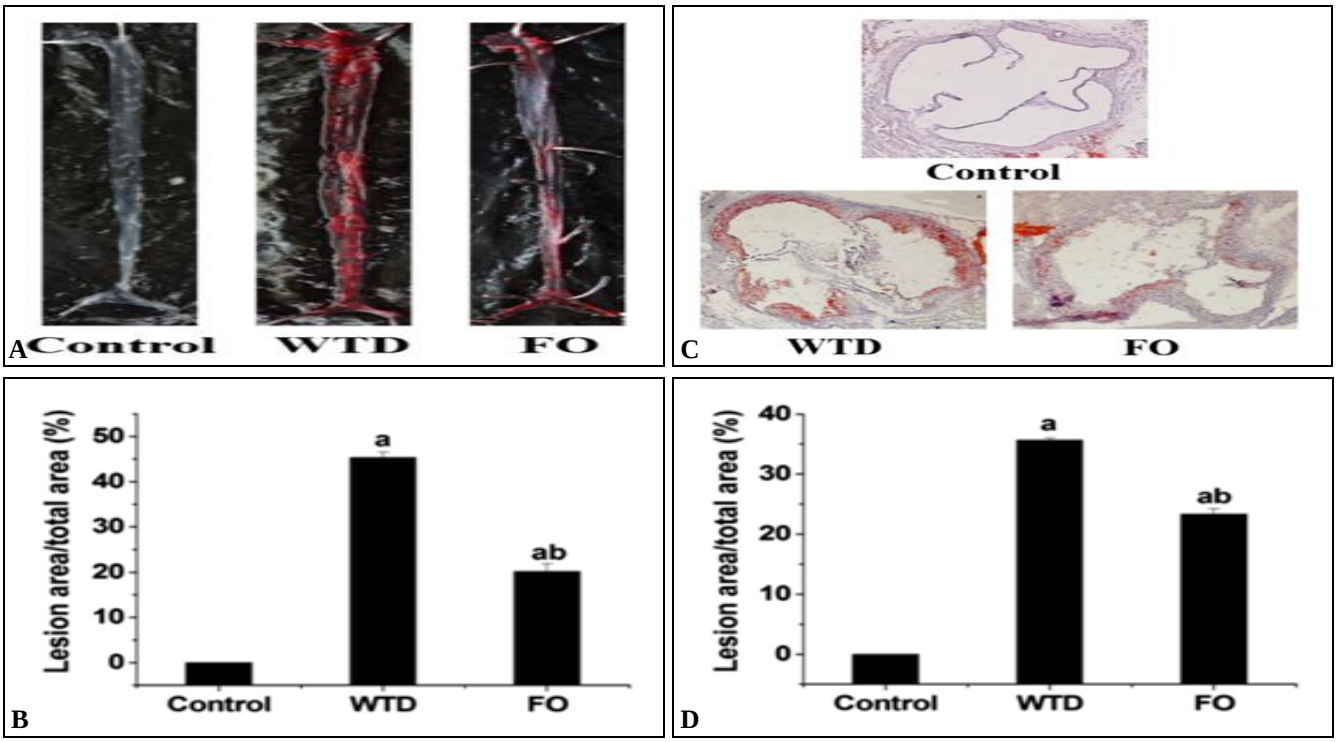

FIG. 7: EFFECTS OF DIETARY FLAXSEED OIL ON AMELIORATING ATHEROSCLEROSIS IN WTD-FED MICE. PHOTOMICROGRAPHS OF REPRESENTATIVE OIL-RED O-STAINED AORTAS OF MICE IN CONTROL, WTD, AND FO GROUPS. [Copyright @ Han *et al.*, 2018 with permission from Elsevier Ltd.]

Another experiment of FL oil on zucker (fa/fa) rats, followed by assessment of level of cytokine, haptoglobin, monocyte chemoattractant protein-1 and adipokine were evaluated from the tissue and serum sample and the lower expression of markers confirmed the beneficial effects of Fl on hyperlipidemia [54]. Also FL spread and 20 mg of FL lignanfed animals observed with 40% lower weight gain and 60% lowered ratio of total cholesterol/high-density lipoprotein and low

density/high-density lipoprotein, and outcomes revealed that no prominent effects on haematological parameters like uric acid [55], creatinine, blood urea nitrogen and albumin level. So, the data confirmed the cholesterol and body weight lowering effects of FL [56, 57].

Effect of FL Seed on polycystic ovarian syndrome and hormonal imbalance: A group of white females with polycystic disease was administered with FL (10 gm/day for first 3 days, 20 gm/day for next 3 days and 30 gm/day for four-month period) and hydroalcoholic FL extract followed by measuring the level of insulin, serum and free testosterone, estradiol, progesterone, testosterone and dehydroepiandrosterone along with number of ovarian follicles and corpus luteumin blood samples. The outcomes revealed that level of insulin was increased whereas level of testosterone in serum and free condition were markedly decreased after four months by FL and increased level of estradiol, testosterone, dehydroepiandrosterone along with decreased number of ovarian follicles and corpus luteum were observed with hydroalcoholic FL extract administration [58, 59]. Also a group of scientist experimented on the modulatory effects of Fl on ovarian parameters like serum progesterone, testosterone, weight and volume of the ovary, number of oocytes and germinal vesicles in primordial, primary, and secondary follicles, level of PCNA, cyclin B1 (markers of G1-S and G2-M phase in cell cycle) Bax and caspase-3 (markers of cytoplasmic / mitochondrial apoptosis) after 10 days and 24 days treatment with 10% of FL seed.

The outcomes revealed that body weight was increased but weight and volume of ovary did not visibly change whereas level of oocytes and germinal vesicles in primordial, primary and secondary follicles were markedly increased; marked decrease in PCNA, cyclin B1 was observed in primordial, primary and secondary follicular oocytes whereas increased values were observed with Bax and caspase-3 levels after 10 to 24 days of FL treatment. These data confirmed the ovarian nourishment effect of FL [60]. Long-term use of FL was reduced the area of corpus cavernosum, corpus spongiosum but testosterone was slightly reduced along with an increased level of 17β-estradiol with FL group [61].

Effect of FL Seed on Neurological Disorders: Scientists also experimentally confirmed the increased levels of genetic expression of BDNF and GDNF along with decreased level of percent dark neurons in ischemic brain cortex by FL oil supplementation; which confirmed the neuro-protective activity of FL on ischemic brain stroke [62]. Also, a group of neonatal hypoxic-ischemic (HI) encephalopathic wistar rats were administered with Fl diet followed by evaluation of brain mass, percent climbing, immobility and swimming as per modified forced swim test (behavioral test) and time of immobility in tail suspension test (correlate with stress) and latency period in morris water maze (correlated with cognitive behavior). The outcomes revealed that the highest brain mass observed with FL-fed animals in induced HI case, swimming capacity was greatly influenced after FL treatment climbing and immobility were more often decreased and latency period was also minimized with FL administration. These data confirmed the effects of FL on HI [63].

Effects of FL on Environmental Factors: Environment-friendly biodiesel was developed after reaction between FL oil and methanol ratio using potassium hydroxide as a catalyst with 98% and 94% of maximum yield [64]. The optimized ratio of biodiesel production was 5.9:1 and (6:1) between methanol and Fl oil [65]. Another study revealed that waste of ethyl esters of polyunsaturated fatty acids of flaxseed oil was used to produce biomass using *Yarrowia lipolytica* S6 yeast. The biomass was generated from 25 g/L and 40 g/L of glycerol. A total yield of 0.51 g/g was developed from 21.3 g/L of strain with (19.4-48.2)% of protein and (7.38-30.51)% of cellular lipids 66. Industrial waste and effluents were managed with FL mucilage (100 mg/L) using sodium dodecyl sulphate as standard effluent. The coagulation process was optimized at pH 7.0 with 76.0 mg of nanocatalyst and 1.07 ml of hydrogen peroxide. This data observed with greater industrial effluent management [67]. Zinc oxide nanosheet was developed using FL mucilage followed by removal of methylene blue. The sheet was 75 nm thick with the removal of 80% of methylene blue within 2 h of exposure [68]. Al soan another water-soluble onion shaped nanoparticle (4-8) nm size was developed using pyrolysis of FL oil with emission of stable green luminescence with greater photocatalytic

efficiency of methylene blue. The nanoparticle was observed with specific detection of aluminium with (Limit of Detection: 0.77µM), which was used as a waste management tool 69. Hydro-alcoholic extract of deoiled FL was used to develop silver nanoparticle for the evaluation of antimicrobial effects against gram (-) ve Escherichia coli, gram (+) ve *Staphylococcus aureus*, and mycotoxin producing fungi *Aspergillus flavus* and *Aspergillus parasiticus*. The nanoparticle was face-centered cubic structure with 9.22 nm. This material was observed with greater efficiency in food and health product industries [70, 71]. FL was used to protect pregnant rats and foetus against diesel exhaust particles (1.5 mg/kg/day) and/or an oral gavage of fenitrothion (1/200 of LD_{50}=3.76mg/Kg/day) [72, 73]. These data clearly stated the importance of the seed on the environment and related factors.

CONCLUSION: In these modern genera, metabolic syndrome is the most common disease among the population. The abnormal lifestyle, inadequate sleep-awake cycle, less physical activity, intake of oily foods, alcohols are the key factors of this syndrome. Flax was cultivated for around 5000 years' timeline in India, China, and Egypt. The development of biodiesel and biomass from seed waste and flaxseed was also helped to develop nanoparticles with greater removal efficiency of dye with antimicrobial effect. The fibre and oil of Flax are normally taken by ancients to mitigate the spectrum of metabolic syndrome. Here we also noticed that the seeds and oils of Flax were highly effective against hyperglycemia, inflammations, ulcer, insulin resistance, ovarian cancer, expression of papilloma, atherosclerosis, hormonal imbalances, and neurological disorders also maintained health of liver, pancreas, spleen, and genital organs. So, in this spectrum of activity, the urban are inclined towards the intake of Flax. These-article emphasized that the shine of Flax (seed or oil) alleviates different conditions linked with metabolic syndrome.

ACKNOWLEDGEMENT: Declared none

CONFLICTS OF INTEREST: The authors declare no conflict of interest.

REFERENCES:

1. Elder SJ, Lichtenstein AH, Pittas AG, Roberts SB, Fuss PJ, Greenberg AS, McCrory MA, Bouchard Jr TJ, Saltzman E and Neale MC: Genetic and environmental influences on factors associated with cardiovascular disease and the metabolic syndrome. J Lipid Res 2009; 50: 1917-26.
2. Hutcheson R and Rocic P: The Metabolic Syndrome, Oxidative Stress, Environment, and Cardiovascular Disease: The Great Exploration. Exp. Diabetes. Res 2012; 1-13. doi:10.1155/2012/271028.
3. Mendrick DL, Diehl AM, Topor LS, Dietert RR, Will Y, Merrill MAL, Bouret S, Varma V, Hastings KL, Schug TT, Hart SGE and Burleso FG: Metabolic Syndrome and Associated Diseases: From the Bench to the Clinic. Toxicol Sci 2018; 162(1): 36-42.
4. Cosselman KE, Ana Navas-Acien A and Kaufman JD: Environmental factors in cardiovascular disease. Nat Review Cardiol 2015; 12: 627-42.
5. Yomralioglu T, Colak EH, Arif C and Aydinoglu AC: Geo-Relationship between Cancer Cases and the Environment by GIS: A Case Study of Trabzon in Turkey. Int. J. Environ. Res. Public. Health 2009; 6: 3190-204.
6. Cancer and the Environment. What You Need to Know What You Can Do. U.S. Department of Health and Human Services. National Institutes of Health. NIH Publication No. 03-2039, 2003.
7. Papazafiropoulou AK, Kardara MS and Pappas SI: Environmental Pollution and Diabetes Mellitus. Recent. Patent. Biomarker 2011; 1: 44-8.
8. Cook CB, Wellik KE and Fowke M: Geoenvironmental Diabetology. J Diabetes Sci Tech 2011; 5(4): 834-42.
9. Whitworth KW, Baird DD, Steiner AZ, Bornman RMS, Travlos GS, Wilson RE and Longnecker MP: Anti-Mullerian Hormone and Lifestyle, Reproductive, and Environmental Factors Among Women in Rural South Africa. Epidemiology 2015; 26(3): 429-35.
10. Vedamurthy A and Ananthakrishnan AN: Influence of Environmental Factors in the Development and Outcomes of Inflammatory Bowel Disease. Gastroenterol Hepatol 2019; 15(2): 72-82.
11. Jorg S, Grohme DA, Erzler M, Binsfeld M, Haghikia A, Muller DN, Linker RA and Kleinewietfeld M: Environmental factors in autoimmune diseases and their role in multiple sclerosis. Cell Mol Life Sci 2016; DOI 10.1007/s00018-016-2311-1.
12. Pal D and Saha S: Chondroitin: a natural biomarker with immense biomedical applications. RS. Adv 2019; 9(48): 28061-077.
13. Pal D, Saha S, Nayak AK and Hasnain MS: Marine-Derived Polysaccharides: Pharmaceutical Applications. Volume 2: Marine- and Microbiologically Derived Polymers, Natural Polymers for Pharmaceutical Applications, Hard ISBN: 9781771888448, E-Book ISBN: 9780429328121, Apple Academic Press, CRC Press.
14. Pal D, Nayak AK, Hasnain MS and Saha S: Pharmaceutical Applications of Chondroitin. Volume 3: Animal-Derived Polymers, Natural Polymers for Pharmaceutical Applications, Hard ISBN: 9781771888448, E-Book ISBN: 9780429328121, Apple Academic Press, CRC Press.
15. Mendrick DL, Diehl AM, Topor LS, Dietert RR, Will Y, Merrill MAL, Bouret S, Varma V, Hastings KL, Schug TT, Hart SGE and Burlesona FG: Metabolic Syndrome and Associated Diseases: From the Bench to the Clinic. Toxicol. Sci 2017; 1-7. doi: 10.1093/toxsci/kfx233.
16. Anuurad E, Semrad A and Berglund L: Human immunodeficiency virus and highly active antiretroviral therapy associated metabolic disorders and risk factors for cardiovascular disease. MSRD 2009; 7: 401-10.

17. https://www.hopkinsmedicine.org/health/conditions-and-diseases/metabolic-syndrome accessed on 12th October 2020.
18. Shim YY, Gui B, Arnison PG, Wang Y and Reaney MJT: Flaxseed (*Linum usitatissimum* L.) bioactive compounds and peptide nomenclature: A review. Trends Food Sci Technol 2014; 38(1): 5-20.
19. Global Flaxseed Oil Market Status and Future Forecast Report 2019-2024. Report ID: 290219 Jul 2019 No. of Pages: 127.
20. Bekhit AEA, Shavandi A, Jodjaja T, Birch J, Teh S, Ahmed IAM, Al-Juhaimi FY, Saeedi P and Bekhit AA: Flaxseed: Composition, detoxification, utilization, and opportunities. Biocatalysis. Agricult. Biotechnol 2018; 13: 129-52.
21. Alpaslan M and Hayta M: The effects of flaxseed, soy and corn flours on the textural and sensory properties of a bakery product. J. Food. Qual 2006; 29: 617-27.
22. Pal D: Antioxidant Potentials and Pharmacological Activities of Marking Nuts: *Semecarpusana cardium* Lf" In "Nuts and Seeds in Health and Diseases Prevention", ISBN Number: 978-0-12-375688-6, 1st Ed Chapter 89, Preedy VR, Watson RR, Patel V; Elsevier London 2011; 749-57.
23. Pal D: Sunflower (Helianthus annuus L.) Seed in Health and Nutrition" In "Nuts and Seed in Health and Diseases Prevention", 1st Ed., Chapter 130, Preedy VR, Watson RR, Patel V; Elsevier: London, 2011, 1097-1105.
24. Pal D, Chandra P, Sachhan N, Hansain S and Nayak A: Pharmaceutical Applications of Fenugreek seed gum, In Natural polymers for Pharmaceutical Applications in Natural polymers for Pharmaceutical Applications. Volume 1, Chapter 9, Nayak AK, Hasnain HS, Pal D; Apple Academic Press: USA, 2019, 201-19.
25. Pal D, Singh H and Kumar MA: Preliminary study on the in vitro antioxidant activity of seeds of *Aesculus indica* and barks of Populuseuphratica. Int J Pharm Pharmaceut Sci 2012; 4(4): 249-50.
26. Nayak A and Pal D: Fenugreek seed gum-alginate mucoadhesive beads of metformin-HCl: Design, optimization and evaluation. IJBM 2013; 54: 144-54.
27. Nayak A and Pal D: Formulation, optimization and evaluation of jackfruit seed starch-alginate mucoadhesive beads of metformin HCl. Int J Biol Macr 2013; 59: 264-72.
28. Nayak A, Pal D and Das S: Calcium pectinate-fenugreek seed mucilage mucoadhesive beads for controlled delivery of metformin HCl. Carbohydr Polym 2013; 96: 349-57.
29. Nayak A and Pal D: Blends of Jackfruit seed starch-pectin in the development of mucoadhesive beads containing metformin HCl. Int. J. Biol. Macromol 2013; 62: 137-45.
30. Nayak A and Pal D: Tamarind seed polysaccharide-gellan mucoadhesive beads for controlled release of metformin HCl. Carbohydr Polym 2014; 103: 154-63.
31. Nayak A and Pal D: *Artocarpus heterophyllus* L. seed starch bivebeas of metformin HCl: Development by response surface methodology. IJBM 2014; 65: 329-39.
32. Nayak A, Pal D and Santra K: Screening of polysaccharides from tamarind, fenugreek and jackfruit seeds as pharmaceutical excipients. Int J Biol Macromol 2015; 79: 756-60.
33. Nayak A and Pal D: Tamarind Seed Polysaccharide: An Emerging Excipient for Pharmaceutical use. Ind J Pharmaceut Edu Res 2017; 51(3): 136-47.
34. Abdelkarem HM and Fadda LH: Flaxseed and quercetin improve anti-inflammatory cytokine level and insulin sensitivity in animal model of metabolic syndrome, the fructose-fed rats. Arabian J Chem 2017; 10(2): S3015-020.
35. Doyen A, Udenigwe CC, Mitchell PL, Marette A, Aluko RE and Bazinet L: Anti-diabetic and antihypertensive activities of two flaxseed protein hydrolysate fractions revealed following their simultaneous separation by electrodialysis with ultrafiltration membranes. Food Chem 2017; 145: 66-76.
36. Correia-Santos AM, Suzuki A, Vicente GC, Saraiva dos Anjos J, Pereira AD, Lenzi-Almeida KC and Boaventura GT: Effect of maternal use of flaxseed oil during pregnancy and lactation on glucose metabolism and pancreas histomorphometry of male offspring from diabetic rats. Diabetes Res Clin Prac 2014; 106(3): 634-42.
37. Palla AH, Iqbal NT, Minhas K and Gilani AH: Flaxseed extract exhibits mucosal protective effect in acetic acid induced colitis in mice by modulating cytokines, antioxidant and anti-inflammatory mechanisms. Int Immunopharmacol 2016; 38: 153-66.
38. Morshedzadeh N, Shahrokh S, Aghdaei HA, Pourhoseingholi MA, Chaleshi V, Hekmatdoost A, Karimi S, Zali MR and Mirmiran P: Effects of flaxseed and flaxseed oil supplement on serum levels of inflammatory markers, metabolic parameters and severity of disease in patients with ulcerative colitis. CTM 2019; 46: 36-43.
39. Xu J, Tian G, Ma C, Gao H, Chen C, Yang W, Deng Q, Huang Q, Ma Z and Huang F: Flaxseed lignin secoisolariciresinol diglucoside ameliorates experimental colitis induced by dextran sulphate sodium in mice. J Functional Food 2016; 26: 187-95.
40. Wang M, Zhang XJ, Yan C, He C, Li P, Chen M, Su H and Wan JB: Preventive effect of α-linolenic acid-rich flax seed oil against ethanol-induced liver injury is associated with ameliorating gut-derived endotoxin-mediated inflammation in mice. J Functional Food 2016; 23: 532-41.
41. Hu T, Linghu K, Huang S, Battino M, Georgiev MI, Zeng in G, Li D, Deng Y, Wang YT and Cao H: Flaxseed extract induces apoptosis in human breast cancer MCF-7 cells. Food Chemical Toxicol 2019; 127: 188-96.
42. Deshpande R, Raina P, Shinde K, Mansara P, Karandikar M and Kaul-Ghanekar R: Flax seed oil reduced tumor growth, modulated immune responses and decreased HPV E6 and E7 oncoprotein expression in a murine model of ectopic cervical cancer. Prostaglandin Other Lipid Mediator 2019; 143: 106332.
43. Chen J, Wang L and Thompson LU: Flaxseed and its components reduce metastasis after surgical excision of solid human breast tumor in nude mice. Cancer Lett 2006; 234: 168-75.
44. Dikshit A, Hales K and Hales DB: Whole flaxseed diet alters estrogen metabolism to promote 2-methoxtestradiol-induced apoptosis in hen ovarian cancer. J Nutritional Biochem 2017; 42: 117-25.
45. Eilati E, Bahr JM and Hales DB: Long term consumption of flaxseed enriched diet decreased ovarian cancer incidence and prostaglandin E2 in hens. Gynecologic Oncol 2013; 130: 620-28.
46. Okinyo-Owiti DP, Dong Q, Ling B, Jadhav PD, Bauer R, Maley JM, Reaney MJT, Yang J and Sammynaiken R: Evaluating the cytotoxicity of flaxseed orbitides for potential cancer treatment. Toxicol Rep 2015; 2: 1014-18.
47. Zou XG, Hu JN, Li J, Yang JY, Du YX, Yu YF and Deng ZY: I Cellular uptake of [1–9-NαC]-linusorb B2 and [1–9-NαC]-linus orb B3 isolated from flaxseed, and their antitumor activities in human gastric SGC-7901 cells. J Functional Food 2018; 48: 692-703.
48. Liang S, Liao W, Ma X, Li X and Wang Y: H_2O_2 oxidative preparation, characterization and antiradical

activity of a novel oligosaccharide derived from flaxseed gum. Food Chem 2017; 230: 135-44.
49. Drummond e Silva FG, Hernandez-Ledesma B, Amigo L, Netto FM and Miralles B: Identification of peptides released from flaxseed (*Linum usitatissimum*) protein by Alcalase® hydrolysis: Antioxidant activity. LWT Food Sci. Tech 2017; 76A: 140-46.
50. Ricklefs K, Johnston CS and Sweazea KL: Ground flaxseed increased nitric oxide levels in adults with type 2 diabetes: A randomized comparative effectiveness study of supplemental flaxseed and psylliumfiber. Obesity Med 2017; 5: 16-24.
51. Parikh M, Raja P, Austria JA, Yu L, Garg B, Netticadan T and Pierce GN: Dietary flaxseed protects against ventricular arrhythmias and left ventricular dilation after a myocardial infarction. J. Nut Biochem 2019; 71: 63-71.
52. Daleprane JB, Batista A, Pacheco JT, FE da Silva A, Costa CA, Resende AC and Boaventura GT: Dietary flaxseed supplementation improves endothelial function in the mesenteric arterial bed. Food Res Int 2010; 43: 2052-056.
53. Han H, Qiu F, Zhao H, Tang H, Li X and Shi D: Dietary flaxseed oil improved western-type diet-induced atherosclerosis in apolipoprotein-E knockout mice. J Functional Food 2018; 40: 417-25.
54. Baranowski M, Enns J, Blewett H, Yakandawala U, Zahradka P and Taylor CG: Dietary flaxseed oil reduces adipocyte size, adipose monocyte chemoattractant protein-1 levels and T-cell infiltration in obese, insulin-resistant rats. Cytokine 2012; 59: 382-91.
55. El-Waseif MA, Abd El-Dayem HH, Hashem HA and El-Behairy SA: Hypolipidemic effect of fat spreads containing flaxseed oil. Anna Agri Sci 2014; 59(1): 17-24.
56. Fukumitsu S, Aida K, Shimizu H, Toyoda K: Flaxseed lignan lowers blood cholesterol and decreases liver disease risk factors in moderately hypercholesterolemic men. Nutrition Res 2010; 30: 441-46.
57. Luo J, Li Y, Mai Y, Gao L, Ou S, Wang Y, Liu L and Peng X: Flaxseed gum reduces body weight by regulating gut microbiota. J. Functional. Food 2018; 47: 136-42.
58. Nowak DA, Snyder DC, Brown AJ and Wahne-fried WD: The Effect of Flaxseed Supplementation on Hormonal Levels Associated with Polycystic Ovarian Syndrome: A Case Study. Curr Top Nutraceut Res 2007; 5(4): 177-81.
59. Jelodar G, Masoomi S and Rahmanifar F: Hydroalcoholic extract of flaxseed improves polycystic ovary syndrome in a rat model. Iran J Basic Med Sci 2018; 21: 645-50.
60. Vckova R, Andrejcakova Z, Sopkova D, Hertelyova Z, Kozioł K, Koziorowski M and Gancarcikova S: Supplemental flaxseed modulates ovarian functions of weanling gilts via the action of selected fatty acids Animal. Reproduction Sci 2018; 193: 171-81.
61. Medeiros de Franca Cardozo LF, Boaventura GT, Brant LHC, Pereira VA, Velarde LGC and Chagas MA: Prolonged consumption of flaxseed flour increases the 17β-estradiol hormone without causing adverse effects on the histomorphology of Wistar rats' penis. Food Chem Toxicol 2012; 50: 4092-96.
62. Bagheri A, Talei S, Hassanzadeh N, Mokhtari T, Akbari M, Malek F, Jameie SB, Sadeghi Y and Hassanzadeh G: The Neuroprotective Effects of Flaxseed Oil Supplementation on Functional Motor Recovery in a Model of Ischemic Brain Stroke: Upregulation of BDNF and GDNF. Acta Medica Iranica 2017; 55(12): 785-92.
63. Mucci DB, Fernandes FS, Souza AS, Sardinha FLC, Soares-Mota M and Tavares do Carmo MG: Flaxseed mitigates brain mass loss, improving motor hyperactivity and spatial memory, in a rodent model of neonatal hypoxic-ischemic encephalopathy. Prostaglandin. Leukotriene Essential Fatty Acid 2015; 97: 13-9.
64. Ahmad T, Danish M, Kale P, Geremew B, Adeloju SB, Nizami M and Ayoub M: Optimization of process variables for biodiesel production by transesterification of flaxseed oil and produced biodiesel characterizations. Renewable Energy 2019; 139: 1272-80.
65. Mandal S and Kundu K: Synthesis of biodiesel by KOH-catalyzedmethanolysis of flaxseed oil and determination of fuel properties. Biofuels 2019; DOI: 10.1080/17597269. 2019.1573603.
66. Juszczyk P, Rymowicz W, Kita A and Rywinska A: Biomass production by *Yarrowia lipolytica* yeast using waste derived from the production of ethyl esters of polyunsaturated fatty acids of flaxseed oil. Industr Crop Product 2019; 138: 111590.
67. Mirbahoush SM, Chaibakhsh N and Moradi-Shoeili Z: Highly efficient removal of surfactant from industrial effluents using flaxseed mucilage in coagulation/photo-Fenton oxidation process. Chemosphere 2019; 231: 51-9.
68. Moghaddas SMTH, Elahi B, Darroudi M and Javanbakht V: Green synthesis of hexagonal-shaped zinc oxide nanosheets using mucilage from flaxseed for removal of methylene blue from aqueous solution. JML 2019; 111834.
69. Tripathi KM, Tran TS, Kim YJ and Kim TY: Green Fluorescent Onion-Like Carbon Nanoparticles from Flaxseed Oil for Visible Light Induced Photocatalytic Applications and Label-Free Detection of Al (III) Ions. ACS Sustainable Chem Eng 2017; 5: 3982-92.
70. Sharbidre AA and Kasote DM: Synthesis of silver nanoparticles using flaxseed hydroalcoholic extract and its antimicrobial activity. Current Biotechnol 2013; 2(2): 1-5.
71. Fahmi AA, El-Desouky MA, Ibrahim KA and Abdelgaid HA: Flaxseed alleviates toxic effects of some environmental pollutants on pregnant rats and their foet uses. Biosci Res 2018; 15(3): 1832-44.
72. Palla AH, Gilani AH, Bashir S and Rehman NU: Multiple Mechanisms of Flaxseed: Effectiveness in Inflammatory Bowel Disease. Evidence. Based. Complementary Alternative Medicine 2020; 2020. https://doi.org/10.1155/ 2020/7974835.
73. Kaur S, Singh AK, Honparkhe M, Kumar A, Singh P and Singh U: Effect of flaxseed supplementation on metabolic state, endocrine profiles, body composition and reproductive performance of sows. Asian Pacific J Reproduction 2021; 10(3): 127-36.

How to cite this article:
Saha S and Pal D: Impact of flax on metabolic syndrome and related environmental factors. Int J Pharm Sci & Res 2022; 13(2): 531-42. doi: 10.13040/IJPSR.0975-8232.13(2). 531-42.