

# **Research Article**

# The role of flax seed in prevention and management of diabetes mellitus type I and type II

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#### **Abstract**

Diabetes mellitus is a common metabolic disorder. Statistics of individuals who are suffering from diabetes mellitus and its outcomes show the importance of concentration on the approaches of prevention and management of diabetes mellitus. World health organization emphasize on the using the traditional drugs with the lowest side effects to control diabetes symptoms. The consumption of flax seed as a rich source of phytoestrogens, isoflavones, lignin and omega 3 fatty acids can be helpful in controlling diabetes by the interaction of these nutrients. So, we reviewed the related articles in systemathic review method.

Keywords: Diabetes mellitus; insulin resistance; flax seed; secoisolariciresinaol.

#### Introduction

Diabetes mellitus is a growing worldwide epidemic. This %4 of people are suffering from this life span metabolic disorder and it is predicted that the number of diabetic patients will rise to %5.4 till 2025 (1-10). Studies reflect this concern that diabetes will become the most common cause of death (11). Diabetes prevalence doubled in the recent two previous decades (12) and unfortunately it is predicted that this prevalence will be doubled in two future decade, too (13). Diabetes is one of the forth primary causes of chronic diseases-related disorders (14). Altering lifestyle, physical activity levels and dietary patterns in Asian countries cause that the prevalence of diabetic patients reach to 10.6 persons per one thousand persons (15). So, focus on prevention approach and hyperglycemic management should be the basic priority in health care systems. Using traditional remedies and herbal seeds have effective roles in disease control. World health organization suggests the usage of effective and non-toxic traditional remedies with the lowest side effects in diabetes management (16). Flax seed is one of the natural and traditional sources of diabetes control (17).

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This is one of the last ancient herbal remedies which are known as functional food (18). Several studies shows that its' useful effects in health promotion and cardiovascular disorders, hyperlipidemia and various cancer types. We aim to systematically review the effect of flax seed consumption on diabetes mellitus type I and type II prevention and management, in addition the related hyperglycemic parameters were studied in the association with flax seed intake, too.

#### Methods

This systematic review assessed the sources which are published in journals, electronic books, seminars and symposiums between 1992 and 2015. We searched ISI (Web of Science) ,Pubmed ,Iran Medex, and MagIran. Our keywords that we searched contain "diabetes mellitus", "insulin resistance", "flax seed", "Linseed", "secoisolariciresinol".

We assessed articles that were about fasting blood sugar, homeostasis model assessment of insulin resistance, and HbA1C. In the current review, we assessed the studies which were performed on animal and human, too. The studies were screened based on their title, abstract and full text. The primary searched showed that 111 articles were related to the mentioned matter. In the second phase, after assessment of these articles based on the title, abstract and major purpose, 66 articles extracted from our study. The references of related articles were assessed, too.

#### Results

Linum usitatissimum is a member of Linasea family rich of omega 3 fatty acids (19) contains %50-62 of seed weight α-linolenic acid (18:3, n-3) as its major fatty acids (20,21) which contains %22 of flax seed (22). This seed contains %15-18 linoleic acid (23,24). The consumption of α-linolenic acid (ALA) increases serum ω 3-fatty acids levels of EPA acid (20:5; n-3); DPA acid (22:5; n-3); and also DHA acid (22:5; n-3). This increase is based on linoleic acid content (18:2; n-6) (25,26). There are a nonsignificant difference between the forms of flax seeds consumption on its' bioavailability (27). Its stability is not different significantly between various types of its' products (27,28) and all are effective in diabetes managements based on its' strong antioxidant roles. Flax seeds contain phytoestrogens as the main content which can control obesity, insulin resistance, menopause effects, CVD disorders, different types of cancers, hyperlipidemia, osteoporosis and various stages of chronic kidney disorders (29-35). Phytoestrogens is similar to estrogen or 17-B estradiol effects which can bind to different tissues (36) and adipocyte tissues (38). Phytoestrogens bind to their receptors especially 17-β estradiol receptor that cause its' main anti-diabetic and hyperglycemic effects (39). Phytoestrogens can affect via non estrogenic receptors and blocks the thyrosin kinase (40), DNA polymerase I and II (41, 42) and ribozyme S6 kinase (43) activation which is effective in cell signaling, their division. Flax seeds have 3 types of phytoestrogens as isoflavones (ginstein, didzein), lignin (meta-ieisinol, secoisolarisinol) and conmestan (44). Its' active and basic isoflavones are ginstein, didzein which block glucose uptake in cell membrane of brush borders and its' dependent on its' dosage (45). Studies showed that it cause the increase of Na-dependent transporter 1 and diffusion of glucose transporter 2 in diabetic patients. Increasing transporters higher glucose uptake in lumen and after food intake hyperglycemia (46,47). Experimental studies showed that thyrosin kinase enzymes control insulin secretion from pancreatic cells. Ginstein blocks thyrosin kinase enzymes function and 100 µmol/L of ginstein can increase insulin secretion; moreover it lower pancreatic cell division (48). It can stimulate insulin release via gloose and sulphonyl urea levels (48,49). Didzein can increase pancreatic cell secretion. Comestrol and isoflavones are similar to estrogen. Nogowaski et al. showed comestrol can effect on carbohydrate metabolism, lower muscle glycogen mass and insulin adhesion to its' cell membrane, so it can effect on insulin receptor function (56). Lignane block cell membrane structure in plants (57). Flax seed is the rich source of lignane and its concentration is 100 times of its amount in other sources (44). Secoisolariciresinaol (SDG) is the major lignan of flax seed (58,59). In addition it contains isolariciresinaol pinoresinol 9 matairesinol lignanes (60). flax seed lignin contain % 34-38 SDG, %15-21 cinammic acid, and % 9-11 of its'body weight from hydroxy methyle glutaric acid. SDG can be extracted from this seeds with %98 sincerity (61). Its range is 0.6-1.8/100 gr in different types of flax seeds (62). Lignan like isoflavones hydrolysis via β glucosidase

and it convert to entrolactone and entradiole (63). Diglucosided SDG (64) and entrolactone and entradiole SDG show antioxidant effects and control the free radical effects in diabetes.

The antioxidant effects of SDG and entradiole is more than antioxidant effects of vitamin E (65). It decreased diabetes risk %71 in rats (66). Lignan consumption of 22 mg/Kg BW during 24 hours led to %25 lower DM risk and its intake from 3 days before till 21 days after streptozotocin (STZ) intake in the same dosage lower %75 the risk of diabetes promotion and serum malone dialdehyde level, it also increase antioxidant level in pancreatic cells (67). SDG lower oxidative stress (62) and prevent DM (63,64). So, it can prevent and decay DM type I and II outcomes (68-71). It decreases limited enzymes of gluconeogenesis expression, phosphoenole pyruvate kinase (PEPCK), blood sugar level and hypoglycemia in diabetic animal (72). Intakeof 360 mg SDG/ day lignane of flax seeds in cross over RCT in diabetic patients (contains %20 SDG, %15.6 oil, %3.2 protein, %2.6 fiber and %30 carbohydrate) during 12 weeks lower HbA1C and CRP levels (73) and similar findings were seen in Hallund et al. study (74). In a pilot study on healthy young men intaking flax seeds mucilage lowered BS level (75). Intaking 50 grams of flaxseeds or 25 grams of its mucilage lowered BS level till %27 in healthy women (76). These effects were seen in hypercholesterolemic menopause women, too (77). Consuming 2 maffins (78), 13.5 grams of flax seeds in 6 bread spice (79) and 10 grams of its powder in 2-3 serving (80) increases urinary lignin excretion of flax seeds and its effects are dependent to dosage and time of its consumption (81).

## Conclusion

In conclusion, DM as a common metabolic disease with basics of hyperglycemia and glycosylated and oxidative metabolits and free oxygen radical and oxidative stress can manage its' glucose intolerance, insulin resistance and ß pancreatic cells damage. Flax seed has major antioxidant sources such as linolenic acid, phytoestrogens. These contents generate and protect ß-pancreatic cells. Linolenic acid lower voltage of K+-dependent gate of pancreatic cells via effecting protein kinase A and cyclic monophosphate adenosine functions, it increases calcium concentrations and insulin secretion. SDG naturalizes free radicals and control DM incidence and improper future outcomes

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