Review Article

Potential effect of Foeniculum vulgare (fennel seeds) in obesity and weight management - An overview

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Abstract

Obesity, a metabolic health concern owing to fat deposition, results in development of various chronic diseases like cardiovascular disease and diabetes. Observing this, nutraceuticals have gained popularity in effectively managing and reducing obesity. Nutraceutical like Foeniculum vulgare (fennel seeds) enriched with bioactive ingredients offer the best anti-obesity means. Therefore, the aim of this study was to provide an overview of the metabolic pathways tailed by fennel seeds which eventually reduce obesity and regulate weight gain. Also to observe gaps in past studies regarding foeniculum vulgare anti-obesity effect. For this, recent research articles delivering information about the fennel seeds and their impact on obesity were considered. Mainly, glucose metabolism pathway tailed regarding fennel seeds is extensively studied, showing insulin receptor signalling, coupled with pancreatic β-cell upregulation, ensuring enhanced insulin sensitivity and reduced gluconeogenic enzymes regulation. Additionally, lipid metabolism illuminating the inhibition of specific lipid enzymes and fatty acid oxidation reducing serum low density lipoprotein, triglyceride and increasing serum high density lipoprotein levels were studied. Leptin receptor modulation with antioxidants and anti-inflammatory property mitigate obesity and its related syndromes. Despite the known mechanisms, investigation reporting human trails is still required revealing the synergistic effect of fennel seed with other phytochemicals.

Keywords: Fennel Seeds, Bioactive Ingredients, Anti-oxidation, Anti-inflammation, Metabolism.

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Introduction

Obesity appears as a critical health concern, prevailing and affecting lives globally [1]. As World Health Organization (WHO) reported in 2022 around 16% of adults were classified obese while 43% were considered overweight, underscoring the progression of obesity worldwide [2, 3]. The redundant accumulation of adipose tissues in body, is considerably linked with trigging long-term health conditions like type 2 diabetes mellitus [4], cardiovascular diseases [5] and metabolic disorders [6, 7], which is mounting the urge to combat adipogenesis [8]. Nutraceuticals effects and drawbacks of pharmacological medications and intervention for weight control,

nutraceuticals have emerged as a cure to treat obesity effectively [9]. Fennel seeds (Foeniculum vulgare) have attained popularity, attributable to their enrichment in bioactive compounds like flavonoid, essential oils, dietary fibres and phytosterols, rendering it as a potent natural bio-remedy for weight management. The relevance of foeniculum vulgare lies in various studies and in past cultures of Egypt, Greek and Rome [10, 11]. Many past studies demonstrated the weight controlling property of fennel seeds achieved by regulating satiety and blood cholesterol levels [12]. Recent studies clinically investigated that there was a moderate significant influence of fennel seeds on lowering body mass index [13]. Furthermore, other studies indicated a positive impact of fennel seeds coupled with black cumin and chia seeds [14, 15]. This anti-adipogenic property of foeniculum vulgare is a result of its potential to modulate lipid functioning and appetite regulation [16]. Therefore, the promising effect of weight management and control provided by foeniculum vulgare have aligned itself for advanced research to explore its optimum potential for obesity mitigation [17]. Thus, the aim of this review is to illuminate the physiological and mechanistic pathways adopted by foeniculum vulgare (fennel seed) in inhibiting adipogenesis by influencing glucose and lipid metabolism. Additionally, to reveal recent scientific gaps in the field of nutraceuticals regarding fennel seeds with respect to obesity management.

Origin of foeniculum vulgare

From past millennium, Foeniculum vulgare, a symbol of strength, originated from the Mediterranean region [18, 19]. Egyptian civilization used fennel seeds post meal for digestion discomfort and was recognized for its pro-longevity effect [20, 21]. In Greek tradition it was assumed that these seeds bring courage and longevity [22]. While, in Rome culture foeniculum vulgare was supplemented in meals for flavour enhancement [23] and was believed that it exclusively offered strength and stamina [24]. In India, fennel seeds were adopted to treat inflammation and gut problems [25, 26]. Since then, foeniculum vulgare has held a marked position in food industry and is now being incorporated in nutraceuticals and home remedies [27, 28].

Bioactive compound and nutrients in foeniculum vulgare

Foeniculum vulgare is recognized for its diverse range of active ingredients and nutrients that classify them as a bioactive functional cuisine. These seeds are enriched with phenols, essential oils along with a whole bunch of micronutrients [29, 30]. The active ingredients are having a copious amount of trans-anethole and estragole, along others like limonene, α-pinene, fenchone and α-thujone are present as essential oils in fennel seeds [31]. The distinguished aroma of fennel seed is attributable to the volatile compounds like β-fenchol and ρ-anisaldehyde [32, 33]. The role of fennel seeds in inflammation is on account of the phenolic compounds found in them, such as, chlorogenic acid, vanillic acid, flavonoids (apigenin, kaempferol and quercetin) and rosmarinic acid playing part as antioxidants [34, 35]. Additionally, 87 other volatile compounds are characterized by their profound protective action from metabolic diseases [36].

Regarding nutrients, foeniculum vulgare is augmented with carbohydrates (52g/100g) and fibres (40g/100g) making it a good source for resolving gut problems [37, 38]. Moreover, protein (16g/100g) and fats (15g/100g) notably offer tissue repair and growth property. Vitamin A, Vitamin E and Vitamin C plus thiamine, riboflavin, niacin and pyridoxine work for skin improvement and immunity [39, 40]. While minerals particularly calcium (196mg/100g) and iron (19mg/100g) aid in bone support and blood

formation [41]. Along with a pool of other micronutrients counting as zinc, magnesium, manganese, selenium, copper, potassium and phosphorus propose resolution for chronic diseases [42, 43].

The synergistic impact of all these ingredients contributes to weight loss and obesity management. Encapsulated with profuse number of fibres and minerals (calcium and iron), essential oils, phenols and flavonoids offer foeniculum vulgare role in, controlling appetite [44], improving satiety, enhancing digestion [45], lowering lipid profile [46, 47], along with modulating receptor pathways (leptin receptor) involved in calorie control to overall reduce obesity [48].

Mechanism of action

Incorporating foeniculum vulgare into your nutritional regimes bids a positive impact by tailing physiological and mechanistic pathways regulating obesity and metabolic syndromes.

Glucose metabolism

Insulin receptor signalling

Bioactive ingredients in foeniculum vulgare are recognized for their outcome of enhancing insulin receptor signalling for glucose metabolism [49]. This pathway particularly encompasses the activation of insulin receptor β-subunit which leads to activation of cascade of different protein (phosphorylation of Akt and glycogen synthase kinase-3 alpha/beta (GSK-3α/β) involved in the generation and release of insulin [50]. Followed by recent study conducted on hyperglycaemic rat models perceived the effect of foeniculum vulgare extract. The report showed that the bioactive compounds like essential oils and phenolic acids indirectly enhanced the expression of insulin receptor, ultimately triggering the endogenous insulin signalling pathway, leading to glucose active uptake by cells [51]. Also, a study was conducted on induced fructose insulin resistance, aiming to explore the impact of bioactive compounds in foeniculum vulgare. The research reported about the upregulation of Insulin Growth Factor-1 (IGF-1) gene which was directly involved in insulin signalling pathway [52] This enhanced insulin receptor stimulation led to autophosphorylation of insulin synthesis proteins and ultimately resulted in further glucose metabolism [53]. Additionally, a study indicated that foeniculum vulgare can upregulate insulin receptor activation which is linked to tyrosine phosphorylation (protein involved in insulin receptor activation) eventually augmenting insulin secretion ensuring enhanced glucose homeostasis [54]. This additional stimulation of insulin receptor provided by foeniculum vulgare extract amplifies the amount of serum insulin which primes the surplus glucose flow in cells subsequently dropping glycaemic level [55].

Upregulation of pancreatic β cells

Foeniculum vulgare gained popularity attributable to its exclusive feature of enhancing pancreatic β-cell functioning which is linked with insulin secretion [56]. Pancreatic β- cells are engaged in the secretion of insulin in response to glycaemic levels eventually dropping the likelihood of developing chronic obesity related syndrome [57]. Fennel seeds being enriched in bioactive compounds like essential oils and phenolic acids exhibit antioxidant properties that decline oxidative stress in cells [58]. Additionally, these active ingredients alleviate apoptosis leading towards neogenesis mostly via the progenitor islets (pancreatic β-cells) which triggers hyperplasia of β-cells [59]. Supported by clinical studies on hyperglycaemic animal models, foeniculum vulgare like other phytochemicals lowered fasting glycaemic levels by endorsing pancreatic β- cells replication to reinstate enhanced insulin

secretion which was suppressed by the oxidative stress in obese animal models [60]. This feature of foeniculum vulgare grounds additional insulin release and improves insulin sensitivity, subsequently lowering metabolic stress instigated by fat deposition [61]. The antioxidant property of fennel seeds led to reduce obesity and its progression into chronic diseases [62]. Various studies testify that the active compounds found in foeniculum vulgare (fennel seeds) amplifies insulin release which inclusively recover the lipid and blood glucose profile tailed by weight loss but the direct association of foeniculum vulgare to regenerate pancreatic β-cells in humans is limited which prerequisites advanced experimental research to deliver strong evidence restoring pancreatic cells.

Enzyme modulation

Foeniculum vulgare characterized by its antioxidant property also exhibit enzyme regulation of biochemical pathways ensuring glycaemic level in body [63]. Gluconeogenesis, a biomechanism adopted in response to hypoglycaemia, which results in enhancing hepatic glucose productivity [64, 65]. Fennel seeds undisputably inhibit gluconeogenic enzymes leading to declined liver glucose production [66]. A recent study on diabetic rats given foeniculum vulgare extract suppressed gluconeogenesis, optimizing insulin sensitivity while research on defining the consequence of fennel seeds extract on humans showing the inhibition of gluconeogenesis is limited [67, 68]. Additionally, existence of active compounds like phenolic acid and flavonoids in foeniculum vulgare upregulated glycolytic enzymes (engaged in glucose catabolism), subsequently lowering blood glucose [69, 70]. Many studies examining obese and hyperglycaemic rat models reported that fennel seeds extract dropped glucose level in rat models by enzyme modulation but there is incomplete or limited study investigating human trails [71, 72]. This enzyme regulation effect of foeniculum vulgare compounds, inhibiting gluconeogenic enzymes and upregulating glycolytic enzymes as shown in Figure 1, inclusively rallies glucose metabolism and supports obesity management [73].

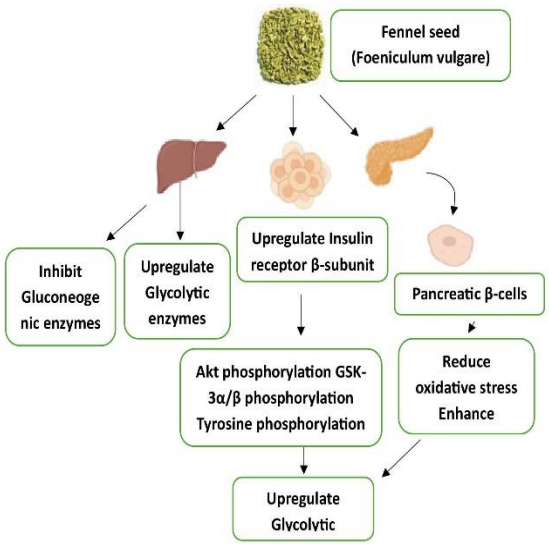

Figure 1: Illustration of Glucose metabolism by Fennel seeds.

Lipid metabolism

Lipid enzymes regulation

The antioxidant component of foeniculum vulgare indirectly downregulates a significant enzyme Lipase, engaged in lipid metabolism [74]. Lipase is acknowledged to breakdown triglyceride (TGA) into fatty acid and glycerol which is a rate limiting step in cholesterol synthesis [47] . By downregulating lipase functioning, foeniculum vulgare certifies low serum cholesterol and fatty acid [44]. A study directed on rat models treated with foeniculum vulgare extract exhibited a reduction of 35 to 50% of lipid profile counting low-density lipoprotein (LDL), triglyceride (TGA) and total blood cholesterol [75]. Recently human experimental study verified the synergistic effect of fennel seeds and chia seeds in dropping lipid profile (blood cholesterol, LDL and TGA). The study evidenced

improved lipid biomarkers braced with a significant correlation between fennel seeds and cholesterol level, safeguarding the positive impact of foeniculum vulgare on declining obesity risk [44]. Anethole, a bioactive compound in foeniculum vulgare predominantly downregulates HMG-CoA reductase enzyme functioning, regulating rate of cholesterol synthesis [76]. It inclusively attenuates hepatic endogenous cholesterol synthesis, declining obesity and its progression into chronic diseases [77]. Additionally, anethole boosts the expression of LDL receptor on hepatocytes, ensuring the surplus influx of LDL eventually diminishing serum LDL levels [78]. Supported by many studies on rats, projecting the influence of anethole on dropping serum lipid profile. Moreover, an updated study on mice verified that post 6 weeks of anethole (from foeniculum vulgare extract) exposure directed reduced serum cholesterol by blocking LDL receptors and by downregulating HMG-CoA reductase activity suppressing serum TGA and LDL [79]. Furthermore, the antioxidant factor of foeniculum vulgare ensures the inhibition of lipid oxidation conquering oxidative stress on lipid catabolic enzymes [80].

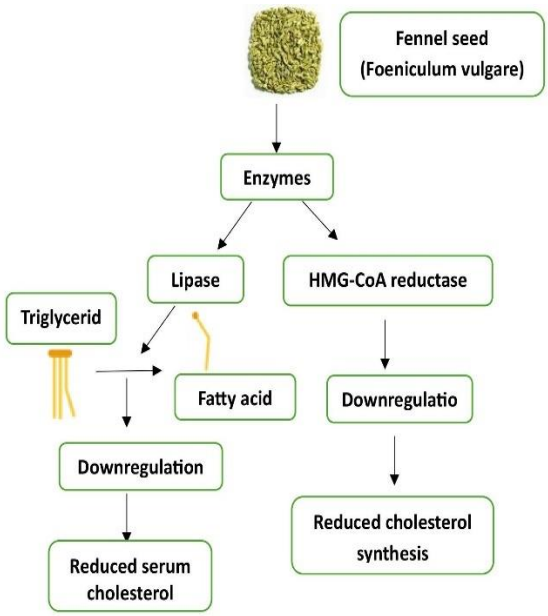

Figure 2: Illustration of Lipid enzyme regulation by Fennel seeds.

A study on human trails evidenced that consumption of fennel seeds fortified crackers in obese adults for 45 days dramatically reduced serum lipid profile and overall upgraded lipid metabolism [81]. These studies attest the antioxidant role of foeniculum vulgare lowering lipid profile, fat accumulation and eventually diminishing obesity related chronic syndromes illustrated in Figure 2.

Phytosterol absorption

Phytosterols are plant-based sterols found in foeniculum vulgare that can competently reduce dietary cholesterol absorption [15]. Being structurally similar with plasma cholesterol, it competes for absorption via intestine, overall lowering LDL level [83]. Improved lipid profile with reduced serum LDL drove as anti- obesity factor diminishing fat deposition and improving lipid homeostasis [84]. There are several studies that focus on phytosterols being a crucial compound in reducing total plasma cholesterol. A recent study was conducted perceiving obesity management property of fennel seeds which reported about the significant lowering cholesterol behavior of phytosterol [85]. Another study from 2021-2025, focusing on phytosterols mechanism of action showed that about 30-50% of reduced serum cholesterol absorption was ensued by the enterocytes of intestine, offering a major edge in declining cholesterol and improving lipid profile [85]. Moreover, studies are documented that emphasize the transport protein action for transferring cholesterol in body. A study on phytosterols inhibiting cholesterol transport protein reported the relocation and absorption of cholesterol was reduced by incorporating fennel seeds in diet. Another research supporting this highlights behavior of foeniculum vulgare phytosterol in reducing cholesterol transport directly engaging it in obesity and weight control management [85]. Additionally, few studies exist signifying plant-based sterols indorsing plasma cholesterol excretion via

intestinal lumen. An updated review focusing on blood cholesterol excretion through intestine reported and delivered perception to the mechanistic pathways trailed by the transporter protein to remove cholesterol from plasma directly targeting obesity and weight management [86]. Furthermore, studies reveal the compensatory onset of hepatic cholesterol synthesis in response to decreased plasma cholesterol level, overall reducing cholesterol load and eventually increasing plasma HDL levels [87]. Conferring to this compensatory mechanism of liver does not fully commence cholesterol back to original level and subsequently offers promising weight loss and obesity control behavior [88].

Fatty acid oxidation

Foeniculum vulgare enriched with unsaturated fatty acid (oleic acid and linoleic acid), flavonoids and phenolic acids offer antioxidant property for hepatocytes and adipocytes [89]. The antioxidant property of fennel seeds commenced by reducing the oxidative stress triggered by fat accumulation [90]. This is achieved by enhanced β-oxidation of fatty acid, which is the catabolism of fatty acid into energy chiefly in mitochondria of liver and adipose cells [37]. A study assessed the chemical analysis of foeniculum vulgare extract revealing the active compounds that augment lipid oxidation in targeted cells [91]. Past study on dairy milk cow supplemented by fennel seeds led to improved lipid metabolism primarily linked to fatty acid oxidation in hepatocytes [92]. A recent human food product study done to evaluate obesity biomarkers evidenced that foeniculum vulgare fortified food had the potential benefit of reducing obesity on account of the existing active compounds via lipid metabolic enzyme modulation [93]. It is proposed that fatty acid oxidation is improved by upregulating key enzymes involved in beta oxidation as shown in Figure 3 [94], but direct study showing this behavior of fennel seeds in hepatocytes is limited and more experimental study is needed to verify this.

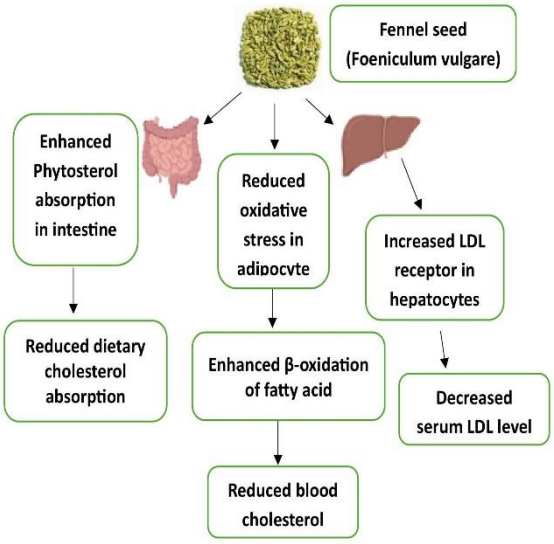

Figure 3: Lipid metabolism by Fennel seeds.

Appetite and satiety regulation

Leptin receptor modulation

Leptin is a satiety hormone that suppresses hunger and enhances feeling of fullness. Foeniculum vulgare parts by upregulating leptin receptor in hypothalamus not affecting serum leptin level [95]. This upregulation of receptor augments brain stimulation of leptin by specifically sensing additional serum leptin [96]. A study conducted on mice examining leptin upregulation reported about amplified leptin signaling not interfering with the serum leptin levels [47]. This assists in limiting calorie intake by generating a sense of satiety, generally reducing the likelihood of obesity. Though study on human samples to assess the modulation of satiety hormone is not in detail and thus additional clinical trials are suggested [15]. It is proposed that the direct influence of leptin receptor upregulation circuitously down regulates ghrelin receptor genes, resulting in low ghrelin signaling [97]. Ghrelin is a hormone accountable for hunger

stimulation [98]. Its reduced expression eventually leads to low food intake. A past study on mice models, given 100 mg/kg of fennel seeds resulted in the body weight reduction accompanied by the ghrelin receptor downregulation [99]. Another study on human samples revealed enhanced leptin and ghrelin signaling as shown in Figure 4 favoring in depth experimental research studying satiety hormone signaling [100].

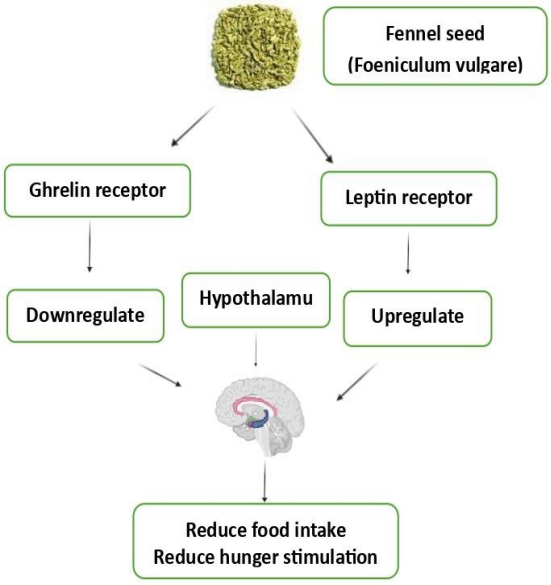

Figure 4: Illustrating receptor modulation by Fennel seeds.

Neurotransmitter and oxidative stress

Bioactive compounds like saponins and estragole present in foeniculum vulgare offer antioxidant property to neural cells engaged in satiety regulation [101]. These phytochemicals guard neural cells form oxidative stress regulating satiety and hunger [102]. By offering satiety control, it cuts the calorie intake generally reducing binge eating behavior [103]. Conferring to a recent study on mice models assessing phytochemical extracts impacting neurons, it reported about neuroprotection from oxidant stress potentially beneficial for managing obesity related oxidative stress [102]. Furthermore, these active ingredients affect neurotransmitter signalling pathway allocating additional support regulating food consumption and hunger cues [104]. A study on phytochemicals (especially flavonoids) impact on nervous system testified the inhibition of neurotransmitter (acetylcholine and serotonin) generally reducing nausea and delivering appetite regulation [105].

Gastric emptying and hormone secretion

Foeniculum vulgare augmented with essential oils and anethole deliver feeling of fullness and satisfaction post meal [106]. The mechanism encompasses the relaxation of gastric muscles, triggering surplus gastric hormones secretion, comprising Cholecystokinin (CCK), a peptide hormone [107]. This hormone enhances the absorption of nutrients from the gastric track and reduces gastric emptying rate. There are studies that propose satiety regulation granted by foeniculum vulgare extracts via cholecystokinin and other hormones regulation (leptin and ghrelin) [108] as shown in Figure 5 favouring additional experimental studies analysing deceleration of postprandial gastric emptying.

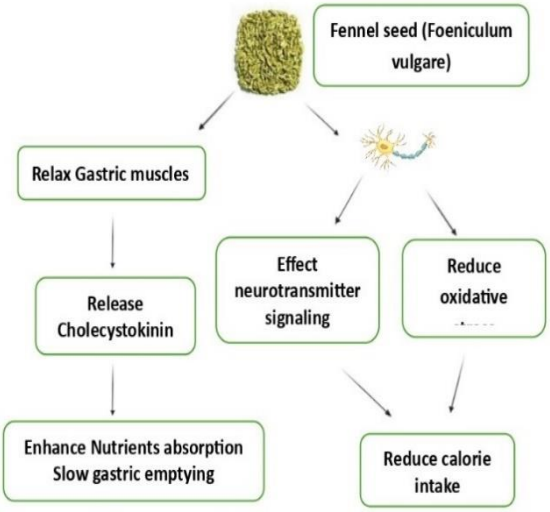

Figure 5: Appetite regulation by Fennel seeds.

Antioxidant effect of fennel seeds

The bioactive component of foeniculum vulgare like essential oils, phenolic acids

and flavonoids deliver the antioxidant effect. Chiefly trans-anethole which makes 38% of the active part of fennel seeds significantly offer free radical scavenging [109]. Free radicals like (hydrogen peroxide and hydroxide radical) are neutralized efficiently by foeniculum vulgare active ingredients [110]. A study presenting the chemical analysis and antioxidant property of foeniculum vulgar reported that the free radical scavenging property of bioactive components exists in fennel seeds reducing overall obesity related chronic diseases [111]. Flavonoids like quercetin derivative stabilize the reactive oxygen species by donating hydrogen atom thus foiling lipid oxidation and peroxidative damage caused to the cellular components of body [112]. These key ingredients in foeniculum vulgar lower the oxidative damage caused by fat deposition and thus provide weight control and management. While trans-anethole, neutralize the free radical intermediates declining the oxidative stress damage [113]. A previous study on hyperglycemic rats demonstrated the effect of trans-anethole from fennel seed extract reporting in enhanced antioxidant enzyme activity [109]. Moreover, the components of fennel seeds upregulate key enzymes engaged in antioxidation like superoxide dismutase (SOD), glutathione peroxidase (GSH) and catalase (CAT) [114]. Evidenced by research on mice, impact of trans-anethole on lipid metabolism resulted in improved CAT and SOD functioning [115]. Therefore, foeniculum vulgar extract augmented free radical scavenging by stabilizing oxidative damage triggered by adipose tissue accumulation [99].

Anti-inflammatory effect of fennel seeds

Flavonoid and trans-anethole found in foeniculum vulgar are responsible for anti-inflammatory action as prolonged inflammation is caused by the activation of pro-inflammatory cytokines [116]. Fennel seeds extract rich in trans-anethole inhibits pro-inflammatory cytokine leading to the mitigation of chronic inflammation [117]. Several studies reported support the anti-inflammatory behaviour of foeniculum vulgar. A study based on in-vitro human neutrophils reported the potential of fennel seed reducing tissue inflammation [116]. Another human trail research investigated the effect of fennel seeds fortified cracker consumption by obese adults and reported in reduced inflammation related complications caused by overweight and fat deposition [118]. Moreover, essential oils in foeniculum vulgar downregulate enzymes involved in metabolic tissue inflammation inclusively offering reduced inflammation in body. Numerous studies are available showing expression of fennel seed extract in lowering chronic inflammation by downregulating enzymes. Another study on obese rat models reported abridged number of liver enzymes causing metabolic inflammation, eventually reducing systemic inflammation. Thus, insulin sensitivity and metabolic function of body is improved due to the anti-inflammatory potential of foeniculum vulgar phytochemicals [116].

Limitation and future prospective

However, along with all of the mechanistic pathways tailed by foeniculum vulgar still remains some gaps in the research and experimental field. Present studies reported are either ensuring restraint sample size or confirms animal model trails. More investigation is needed regarding human and fennel seeds effect. Moreover, there is limited research explaining the explicit pathways and mechanism trailed by the phytochemicals found in foeniculum vulgar. Additionally, lab research is required to display the correlation of fennel seeds and other phytochemicals. Furthermore, exploring the dosage, treatment and cure offered by fennel seeds are vital to uncover its safety and practical application in regular meals. Studying these gaps will grant robust evidence offering

regular usage of foeniculum vulgar.

Conclusion

Foeniculum vulgar confirms a significant positive relation with lowering obesity and in offering weight control management. Active compounds of fennel seeds enhance and transform glucose and lipid metabolism pathways by either modulating enzymes or downregulating the expression of transporter and receptor genes. Furthermore, the antioxidant and anti-inflammatory property of foeniculum vulgar suggests additional assistance to mitigate obesity-related chronic diseases. Despite these benefits there are still uncovered research areas concerning health and wellness offered by fennel seeds.

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