CHAPTER 1

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1.1. Background and rationale

Obesity in general is defined as the presence of excess adipose tissue in the body to such a degree that it may lead to health hazards\textsuperscript{[1-2]}. In developed and developing countries overweight and obesity are most prevalent nutritional problems. The world health organization has described obesity as one of today’s most neglected public health problems, affecting very region of the globe \textsuperscript{[3]}. Overweight and obesity are not only associated with an increased burden of diabetes, hypertension, but also some type of cardiovascular diseases, cancers and premature, social and psychological effects of excess weight\textsuperscript{[4]}.

In general, it is believed that humans are more suited to resist famine than overabundance of food (called the ‘‘thrift gene hypothesis’’) and; hence, it has been argued that the easy and related inexpensive availability of energy-dense food is responsible for the current obesity epidemic\textsuperscript{[5]}. The energy balance is very tightly controlled by hypothalamic factors. Hence, the gut-brain axis and the cross-talk between gut hormones and hypothalamic factors are important in the regulation of food intake, energy balance, and development of obesity \textsuperscript{[5]}. This knowledge has been under utilized in developing experimental murine model of obesity by subcutaneous administration of neonatal rats with monosodium glutamate (MSG). The mono sodium glutamate (MSG)-induced obese mice is a model associated with insulin resistance and dyslipidemia \textsuperscript{[6-8]}. The administration of MSG to newborn mice results indistinctive lesions in hypothalamic arcuate nucleus (ARC) neurons. The neuronal loss impairs insulin and leptin signaling and impacts energy balance as well as pituitary and adrenal activity. In contrast to other models of obesity, MSG-treated mice are characterized by increased plasma levels of
corticosterone as well as increased lipogenesis and reduced lipolysis in the adipose tissue, despite their normophagia\textsuperscript{[9-13]}. This study was therefore aimed at studying the effects of some plant extract on MSG induced obesity disruptions in lipid metabolism.

Sedentary lifestyle and a high-calorie diet are the most prominent factors involved in the development of obesity. Dietary behaviors that promote obesity include frequent consumption of fast food meals; frequent snacking \textsuperscript{[14]}; consumption of oversized portions at home and at restaurants \textsuperscript{[15]}; consumption of high-calorie foods, such as high-fat, low fiber foods \textsuperscript{[16]}; and the intake of sweetened beverages \textsuperscript{[17]}. Furthermore, compared to non-obese individuals, obese individuals tend to consume diets that have a higher energy and fat content \textsuperscript{[18]}. Animal models are useful tools for obesity research as they readily gain weight when fed with high-fat diets \textsuperscript{[19]}. Diet-induced obese (DIO) model is an animal model of choice to study the development of obesity, which relies on high-calorie diet and inactivity to trigger obesity without any genetic involvement \textsuperscript{[20-21]}. The mice fed with high fat develop obesity, hyperphagia, hyperleptinemia, hyperinsulinemia, hyperglycemia, and hypertriglyceridemia. The physiological aspects of this model replicate many of the features observed with the human obesity syndrome \textsuperscript{[22]}. Therefore, the high fat fed model has a good translation potential to extrapolate animal data for clinical studies.

Many attempts have been made to correct the metabolic disparity of the obesity condition, producing a number of reagents including Sibutramine (appetite suppressor), Orlistat (gastrointestinal lipid uptake inhibitor), and Fibrates (PPAR\(\alpha\) agonists) \textsuperscript{[23-24]}. However, administration of these drugs is known to often cause undesirable side effects such as a dry mouth, anorexia, constipation, insomnia, dizziness, and nausea\textsuperscript{[25]}. Therefore, there has been high demand for therapeutically potent, and yet safe, anti-obesity reagents. In spite of an increased awareness of its prevalence and consequences, obesity remains a
complex, difficult to treat condition while bariatric surgery represents a potential, though risky \[^{26}\] alternative for morbidly obese individuals. Owing to the adverse side effects associated with many anti-obesity drugs, more recent drug trials have focused on screening for natural sources that have been reported to reduce body weight and that generally have minimal side effects \[^{27}\]. Although the public enthusiasm for herbal remedies is growing around the world as well as in the Far East, the lack of scientific analysis published on the herbs makes it difficult to determine both the validity of their effects and their mechanisms of action. Due to the limited data concerning the efficacy of herbs and mechanistic explanation of their effects, more detail herbal studies are demanding.

\textit{Foeniculum vulgare} Mill. (\textit{Umbelliferae}) is an annual, biennial or perennial aromatic herb, depending on the variety, which has been known since antiquity in Europe and Asia Minor. \[^{28}\] The preliminary phytochemical screening of fennel showed the presence of up to volatile oil (including about of anethole, estragole, d-limonene, fenchoned-a-pinene, d-a-phellandrene, dipentene, methyl chavicol, anisic acid and anisaldehyde), flavonoids (rosmarinicacid, isorhamnetin, kaempferol, quercetin, rutin and isoquercitrin), phenolic compounds(neochlorogenic acid, chlorogenic acid, gallicacid,caffeic acid, p-coumaric acid, ferulic acid-7-o-glucoside, quercetin-7-o-glucoside, ferulic acid, 1,5 dicafeeylquinic acid, hesperidin), cinnamic acid, rosmarenic acid and apigenin) coumarins (bergapten, imperatorin, xanthotoxin and marmesin), sterols, sugars and 21 fatty acids.\[^{29-33}\] Ethnobotanical information regarding fennel reveals the following medicinal uses: digestive disturbance such as constipation, diarrhoea, flatulence, diabetes, bronchitis, chronic coughs, anemia, treatment of kidney stones, and is considered to have diuretic, stomachic and galactogogue properties.\[^{34-52}\] Furthermore, the Greek name for fennel was marathon was derived from "maraino", to grow thin, reflecting the widely held
belief that drinking fennel tea would have a slimming effect. Drinking a cup of fennel seeds tea 15 minutes before eating a heavy meal, and fennel will take the edge off your appetite. Fennel also tunes up digestion, helping to turn food into energy instead of fat. However, it has not yet been reported whether *Foeniculum vulgare* affects body weight gain in obesity models.

Sea buckthorn (*Hippophae rhamnoides* L.) is thorny nitrogen fixing deciduous shrub. Sea buckthorn (SBT) is primarily valued for its very rich content of vitamin A, B1, B12, C, E, K and P, flavonoid, lycopene, carotenoids, and phytosterols. Therapeutical importance of it is due to rich potent antioxidants. Scientifically evaluated pharmacological effects of it are like anti-inflammation, reduced recurrence of angina, antiatherogenic effect, antiulcer activity, antihypertensive, stress of healing tendons, anti-stress, and adaptogenic activity.[53] There are scientific reports on various pharmacological activities of *Hippophae rhamnoides* L., but anti-obese activity for dried ripe fruits is not reported. The present study is planned to evaluate anti-obesity activity of *Hippophae rhamnoides* L. seeds.

*Pinus sylvestris* is an evergreen coniferous tree growing up to 25 m in height and 1 m trunk diameter.[54-55] Phytochemical information regarding Pine exposed of following constituents: Flavonoid (taxifolin, taxifolin 3′-O-glucoside, and quercetin)[56], Essential oil (α-pinene, camphene, β-pinene, Δ3-carene, limonene, γ-terpene, β-cymene, terpinolene, myrcene, β-amphene, β–phellandrene and smaller amounts of terpinolene, ocimenesabinene and γ-terpinene)[57] while the Merck Index (1968) lists dipentene, pinene, sylvestrene, cadinene and 3-35% bomyl acetate.[58] Phenolic acid (dihydroxybenzoic acid), unsaturated fatty acids (oleic, linoleic and linolenic acids), saturated fatty acids (behenic and lignoceric acids) resin acids (pimaric, dehydroabiatic hydroxyl dehydroabietic acid and abiatic acids), and sterol (sitosterol).[59] The therapeutic properties of pine oil are antimicrobial, anti-neuralgic, anti-rheumatic, anti-septic,
antiviral, bactericidal, balsamic, cholagogue, deodorant, diuretic, expectorant, hypertensive, insecticidal, restorative, rubefacient, adrenal cortex stimulant as well as stimulant to the circulation and nervous system and relieve mental, physical and sexual fatigue. Furthermore, a number of species of the genus Pinus produce large seeds, pine nuts, which are edible and highly nutritious. According to commercial sources who market weight loss products, the pinolenic acid contained in pine nut oil can help limit appetite. However, it has not yet been reported whether *Pinus sylvestris* affects body weight gain in obesity models. The present investigation designs to determine effect of *Pinus sylvestris* bark on body weight in an obese animal model.