Medicinal Plants and Their Inhibitory Activities against Pancreatic Lipase: A Review

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Obesity is recognized as a major lifestyle disorder especially in developing countries and it is prevailing at an alarming speed in new world countries due to fast food intake, industrialization, and reduction of physical activity. Furthermore, it is associated with a vast number of chronic diseases and disabilities. To date, relatively effective drugs, from either natural or synthetic sources, are generally associated with serious side effects, often leading to cessation of clinical trials or even withdrawal from the market. In order to find new compounds which are more effective or with less adverse effects compared to orlistat, the drug that has been approved for obesity, new compounds isolated from natural products are being identified and screened for antiobesity effects, in particular, for their pancreatic lipase inhibitory effect. Pancreatic lipase inhibitory activity has been extensively used for the determination of potential efficacy of natural products as antiobesity agents. In attempts to identify natural products for overcoming obesity, more researches have been focused on the identification of newer pancreatic lipase inhibitors with less unpleasant adverse effects. In this review, we consider the potential role of plants that have been investigated for their pancreatic lipase inhibitory activity.

1. Introduction

Obesity, which has been termed as the “New World Syndrome,” is now considered a global problem by the World Health Organization (WHO) and is associated with a vast number of chronic diseases and disabilities like dyslipidemia, fatty liver disease, osteoarthritis, hypertension, obstructive sleep apnea, gallstones, type 2 diabetes, reproductive and gastrointestinal cancers, coronary artery disease, heart failure, and stroke [1, 2]. Furthermore, it has also been recently claimed to promote breast cancer (in postmenopausal women) and also cancers of the endometrium, colon/rectum, pancreas, kidney, esophagus, gallbladder, liver, and prostate [3, 4].

Obesity is now recognized as the main lifestyle disorder especially in developing countries and it is prevailing at an alarming speed in new world countries due to fast food intake, industrialization, and reduction of physical activity [5]. According to WHO, obesity kills more people than underweight and 65% of the population who live in developed countries are overweight [6]. It has been reported by the World Health Organization (WHO, 2014) that over 1.4 billion adults at the age of 20 and older were overweight, among whom almost 300 million women and more than 200 million men were obese [7]. In the United States, it has been reported that about one-third of the adult population is obese, and it has been considered a significant cause of human deaths [8]. In 2013, it was reported that in developing countries such as Malaysia about 44% of the adult men at the age of 20 and older were overweight and around 12% were obese. Rates are higher even among women, around 49% of the adult women at the age of 20 and older were overweight and around 17% were obese [9]. Obesity is considered an extremely costly health problem which in developed nations accounts for 2–6% of total health care costs [10].
Many medications have been used to prevent and manage obesity over the years. However, despite the seemingly unescapable progression of this disease and the promising results of some drugs on lowering of body weight and amendment of numerous cardiometabolic factors, in the last few years, most of the approved and marketed antiobesity drugs have been withdrawn from the market due to serious side effects [11]. In 2000, phentermine, an appetite-suppressant drug belonging to the family of β-phenethylamine, has been withdrawn by the European Medicines Agency (EMA), due to an undesirable risk to benefit ratio [11, 12]. Besides, mazindol and diethylpropion (amphetamine-like analogues) were withdrawn by the EMA in 2000 [12]. Rimonabant, an appetite-suppressant drug, is the first selective cannabinoid-1 (CB1) receptor blocker, and CB1 receptor plays a role in the regulation of appetitive behavior. In 2008, the use of rimonabant was suspended by EMA due to an increased risk of psychiatric side effects such as anxiety, suicidal ideation, sleep disorders, and depression. It is an appetite suppressant and was available in 56 countries from 2006 but it was never approved by the Food and Drug Administration (FDA) [13].

In 1997, sibutramine which is an anorectic or appetite suppressant, a selective noradrenaline-serotonin reuptake inhibitor, was used widely after approval by the FDA. In October 2010, FDA withdrew it from the market due to association with increased risk of serious nonfatal cardiovascular events like stroke and myocardial infarction [14]. Subsequently, in 2010 EMA also suggested suspending the use of sibutramine [14]. Common side effects of sibutramine are due to activation of the sympathetic nervous system such as insomnia, dry mouth, constipation, anorexia, headache, palpitation, and hypertension [15].

Currently only orlistat (Xenical), a drug which is considered to be acting through inhibition of pancreatic lipase enzyme, a key enzyme for the digestion of dietary triglycerides, has been approved by FDA and is available for long-term treatment of obesity. Orlistat is an inhibitor of gastrointestinal and pancreatic lipases which is able to prevent the absorption of approximately 30% of dietary fat [16]. Orlistat is the saturated derivative of lipstatin (isolated from a Gram-positive bacterium Streptomyces toxytrichi) [17]. Apart from its antiobesity activity, it can also modestly decrease blood pressure, prohibit the onset of diabetes type 2, and improve oral glucose tolerance. In 1998, it was approved and is considered the only existing drug for the long-term control of obesity. The mechanism of lipase inhibition by orlistat is via covalent bonding to the lipase’s active site serine [18].

Despite the promising results of orlistat for obesity treatment, it is associated with certain unpleasant gastrointestinal side effects [19]. These side effects result from orlistat’s mode of action and the most important adverse effects are flatulence, liquid stools, diarrhea, oily spotting, incontinence or fecal urgency, and abdominal cramping [20]. Due to the adverse effects of orlistat, it may not be well tolerated. Hence, it is crucial to discover novel inhibitors, derived from natural sources particularly plants that are not associated with these serious side effects.

Several strategies have been applied for development of antiobesity agents including increase of energy expenditure (by blocking adipogenesis or inducing lipolysis followed by fat oxidation) and reduction of energy intake (by suppressing appetite and delaying or inhibiting absorption of nutrition). In this review, we consider the potential role of plants as antiobesity agents through investigation of their pancreatic lipase inhibition property.

2. Appetite Regulation

Appetite restriction is considered first line in obesity management [21]. Regulation of body weight via appetite control acts as a multifactorial action resulting from hormonal and neurological interrelationships. It is well known that dopamine, histamine, serotonin, and their related receptor activities are correlated with regulation of satiety [22].

A complex regulation of human appetite and satiety is made up of nearly 40 orexigenic and anorexigenic hormones, enzymes, neuropeptides, other cell signaling molecules, and their receptors [23]. The hunger and satiety signaling molecules are produced in the brain (centrally) and in liver, digestive tract, and adipose tissue (peripherally) [24]. The hypothalamus arcuate nucleus (ARC) is considered the most important area of the brain which plays a key role in appetite regulation. The appetite in the short term can be regulated by neural and endocrine signaling from gastrointestinal tract, while the information about adiposity level and acute nutritional status, from peripheral hormones, can be received and translated by the ARC and brainstem neurons [25].

Some substances like beta-adrenergic agonists are known to enhance hepatic fatty acid oxidation and decrease voluntary food intake in rats [26]. It is believed that, in the liver, energy status, mainly through production of ATP, activates signals via the vagal sensory neurons, to the appetite regulating centers of the brain [27]. Accordingly, once hepatic fatty acid oxidation is reduced, there is simultaneous reduction in ATP level which will then enhance appetite. Moreover, ingredients which enhance hepatic fatty acid oxidation like consumption of 1,3-diacylglyceride oil and medium-chain fatty acids lead to the reduction of food intake in human subjects [28].

The mechanism of appetite suppression in the brain is usually through affecting hunger control centers and is associated with a sense of fullness. However, reduction of food intake may increase ghrelin secretion in the stomach of animals and humans which leads to stimulation of increased intake. Thus, ghrelin antagonism might reduce or blunt the increased appetite which possibly happens with reduced feeding and, hence, might be considered an important target for treatment of obesity [29]. Besides, Melanin-Concentrating Hormone (MCH) receptor antagonism can also be considered a potential target for treatment of obesity via appetite regulation.

Moreover, fatty acid synthase (FAS) is the sole protein in the human genome, produced from acetyl coenzyme A and malonyl-CoA, known to catalyze the reductive synthesis of long chain fatty acids. Evidence indicates that inhibition of FAS in mice treated with FAS inhibitors leads to the reduction of food intake and hence reduction of body weight. Therefore,
suppression of FAS can be a potential therapeutic target to inhibit appetite thereby inducing weight loss [30].

3. Inhibitors of Adipogenesis

Adipocytes, also known as fat cells and lipocytes, play a significant role in the control of energy balance and lipid homeostasis, through storing triglycerides and releasing free fatty acids in response to changing energy demands [31]. On the other hand, their long-term increased intake is associated with progression of obesity and leads to the serious comorbidities [32]. Therefore, adiposity mass and size are included as important markers of obesity. There are two types of obesity in which the first one is due to increase in adipocyte number (hyperplasic) and the second one is increase in adipocyte volume (hypertrophic). Hyperplasia is correlated more strongly with obesity severity and is most marked in severely obese individuals. However, hypertrophy, to a certain degree, is characteristic of all overweight and obese individuals [33]. Similar to adipose tissue and muscles, peripheral tissues deal with energy production and nutrient metabolism, whereas the central nervous system (CNS), specifically the hypothalamus, integrates and regulates energy expenditure and food intake [34]. Treatment which leads to the regulation of number and size of the adipocytes and the expression of signals related to energy balance and enhancement or inhibition of special adipokines has been suggested to express antiobesity-related bioactivities. On the other hand, latest research findings indicated that inhibition of adipose tissue or adipogenesis expansion is associated with diabetes type 2 and other metabolic disorders, like atherosclerosis [35].

4. Inhibition of Fat Absorption

The digestion and absorption of nutrients should be decreased in order to reduce energy intake. As fat contributes more than protein or carbohydrate to unwanted calories deposition, inhibition of fat absorption can be considered the most common target to decrease energy intake. Among the existing treatments for obesity, development of nutrient digestion and absorption inhibitors is considered important strategies in the effort to decrease energy intake via gastrointestinal mechanisms [36]. Inhibition of digestion and absorption of dietary lipids, through an inhibitory action on pancreatic lipase, can be targeted for development of antiobesity agents [37].

Pancreatic lipase (triaclyglycerol acylhydrolase), which catalyzes the digestion of dietary triglycerides, is an important lipolytic enzyme which is synthesized and secreted through the pancreas. In humans, pancreatic lipase (PL), encoded by the PNLP gene, plays a significant role in dietary triacylglycerol absorption, hydrolyzing triacylglycerols to monoacylglycerols and fatty acids [38]. It is responsible for the hydrolysis of 50–70% of total dietary fats and is secreted into the duodenum via the duct system of the pancreas [36]. Pancreatic acinar cells secrete pancreatic lipase and this enzyme releases fatty acids from the triglyceride skeleton at the C-1 and C-3 position. These fatty acids are incorporated into bile acid-phospholipid micelles and further absorbed at the level of the brush border of the small intestine, to finally enter the peripheral circulation as chylomicrons. Interference with fat hydrolysis leads to decreased utilization of ingested lipids; hence, lipase inhibition reduces fat absorption.

5. Pancreatic Lipase Inhibitors from Natural Products

Pancreatic lipase inhibitory properties have been extensively examined for the determination of the potential effect of natural products as antiobesity agents. Due to the huge success of natural products for management of obesity, more research has been focused on the identification of newer pancreatic lipase inhibitors with less unpleasant adverse effects. So far, many natural products (plant extracts and isolated compounds) have been reported for their pancreatic lipase inhibition property including protamine [39], e-polylysine [40], polysaccharides like chitosan [41], dietary fibers from wheat bran and cholestyramine [42], soya proteins [43], and synthetic compounds. The summary of medicinal plants as potential antiobesity agents with pancreatic lipase inhibitory activities reported in this review is presented in Table 1.

Sahib et al. [44] evaluated the in vitro antipancreatic lipase activity of ethanolic extract of Centella asiatica, Morinda citrifolia, and Momordica charantia (fruits) at various concentrations (7.81–250 ppm) using orlistat and epicatechin as synthetic and natural positive controls, respectively. The plant extracts Morinda citrifolia, Momordica charantia, and Centella asiatica fruits inhibited pancreatic lipase activity with 21.0 ± 1.3, 25.8 ± 0.1, and 25.3 ± 0.4% inhibition, respectively.

Bustanji et al. [45] screened the methanolic extracts of 23 traditional medicinal plants belonging to 15 families for their antipancreatic lipase activity regardless of their claimed ethnopharmacological uses. These plants were collected from several areas of Jordan. The inhibition of pancreatic lipase activity of plant extracts (12.5, 25, 50, and 200 µg/mL) and orlistat (positive control) were measured using the spectrophotometric assay. Thirteen of the plant extracts inhibited the PL dose dependently, with an IC50 range between 108 and 938 µg/mL, and these include Anthemis palestina Boiss. (107.7 µg/mL), Salvia spinosa L. (156.2 µg/mL), Ononis natrix L. (167 µg/mL), Fagonia arabica L. (204.1 µg/mL), Origanum syriaca L. (234 µg/mL), Hypericum triquetrifolium Turra. (236.2 µg/mL), Malva nicaensis All. (256.7 µg/mL), Chrysanthemum coronarium L. (286.1 µg/mL), Paronychia argentea Lam. (342.7 µg/mL), Convolvulusalthaeoides L. (664.5 µg/mL), Reseda alba L. (738 µg/mL), and Adonis palaestina Boiss. (937.5 µg/mL). The positive control, orlistat, exhibited an IC50 value of 0.65 µg/mL.

Ado et al. [46] evaluated the antilipase activity of the crude methanolic extracts of different parts (leaves, fruits, roots, seeds, stems, and flowers) of 98 plants from Malaysia, considered to be either herbal or aquatic plants. The obtained results showed that 19.4% of the extracts exhibited antilipase activity of more than 80%, while 22.4% showed moderate
| Plant's name       | Family            | Type of extract | Inhibitory activity against pancreatic lipase | Reference(s)                      |
|-------------------|-------------------|-----------------|-----------------------------------------------|-----------------------------------|
| Acer ginnala      | Aceraceae         | Ethanol extract | IC_{50} between 30 and 50 mg/mL               | Lee et al. [61]                   |
| Acer mono         | Aceraceae         | Ethanol extract | IC_{50} less than 10 mg/mL                    | Kim et al. [48]                   |
| Adonis palustris  | Ranunculaceae     | Aqueous ethanol | IC_{50} 14.9 mg/mL                           | Ekanem et al. [55]                |
| Alpinia zerumbet  | Zingiberaceae     | Acetone extract | IC_{50} 5 mg/mL                              | Chomphoo et al. [59]              |
| Anchusa azurea    | Boraginaceae      | Aqueous ethanol | IC_{50} more than 80 mg/mL                    | Bustanji et al. [45]              |
| Anacardium occidentale | Sapindaceae   | Ethanolic extract | IC_{50} more than 10 mg/mL                   | Lee et al. [61]                   |
| Anacardium occidentale | Sapindaceae   | Ethanolic extract | IC_{50} less than 10 mg/mL                    | Kim et al. [48]                   |
| Arctium lappa     | Asteraceae        | Ethanolic extract | IC_{50} less than 10 mg/mL                    | Gholamhoseinian et al. [76]       |
| Artocarpus lakoocha | Moraceae         | Ethanolic extract | IC_{50} more than 10 mg/mL                    | Raghavendra et al. [62]           |
| Asparagus acutifolius | Asparagaceae | Ethanolic extract | IC_{50} more than 10 mg/mL                    | Lee et al. [61]                   |
| Averrhoa carambola | Oxalidaceae       | Ethanolic extract | IC_{50} more than 10 mg/mL                    | Lee et al. [61]                   |
| Baccharis trimera | Asteraceae        | Ethanolic extract | IC_{50} more than 10 mg/mL                    | Lee et al. [61]                   |
| Bergenia crassifolia | Saxifragaceae | Ethanolic extract | IC_{50} more than 10 mg/mL                    | Lee et al. [61]                   |
| Bunium persicum   | Apiaceae          | Ethanolic extract | IC_{50} more than 10 mg/mL                    | Lee et al. [61]                   |
| Camellia japonica | Theaceae          | Ethanolic extract | IC_{50} more than 10 mg/mL                    | Lee et al. [61]                   |
| Centella asiatica | Apiaceae          | Ethanolic extract | IC_{50} more than 10 mg/mL                    | Lee et al. [61]                   |
| Chukrasiatabularis | Meliaceae         | Ethanolic extract | IC_{50} more than 10 mg/mL                    | Lee et al. [61]                   |
| Cichorium intybus | Asteraceae        | Methanolic extract | Methanolic extract | Lee et al. [61]                   |

**Table 1:** Summary of medicinal plants that showed inhibitory activity against pancreatic lipase.
| Plant's name | Family | Plant part | Types of extract | Inhibitory activity against pancreatic lipase | Reference(s) |
|-------------|--------|------------|------------------|---------------------------------------------|--------------|
| *Cinnamomum zeylanicum* | Lauraceae | Derrms | Methanol extract | 25–50% inhibition | Gholamhoseinian et al. [76] |
| *Clematis vitalba* L. | Ranunculaceae | — | Hydroalcoholic extract | IC<sub>50</sub> (0.99 µg/mL) | Marrelli et al. [54] |
| *Convulvulus althaeoides* L. | Convolvulaceae | — | Methanol extract | IC<sub>50</sub> (664.5 µg/mL) | Bustanji et al. [45] |
| *Cornus officinalis* | Cornaceae | Fruits | Ethanolextract | 31.4% inhibition | Roh and Jung [57] |
| *Coscinium fenestratum* | Menispermaeae | Stems | Ethanolextract | IC<sub>50</sub> (160 µg/mL) | Kaewpiboon et al. [58] |
| *Cadonia tricuspidata* | Moraceae | Leaves | Ethanolextract | IC<sub>50</sub> (9.91 µg/mL) | Kim et al. [48] |
| *Cyclocarya paliurus* | Juglandaceae | Leaves | Aqueous extract | IC<sub>50</sub> 9.1 mg/mL | Kurihara et al. [73] |
| *Cynometra cauliflora* L. | Fabaceae | Leaves | Ethanolextract | 100% inhibition | Ado et al. [46] |
| *Dicranopteris linearis* | Gleicheniaceae | Aerial part | Methanol extract | IC<sub>50</sub> between 40 and 50 µg/mL | Kwon et al. [77] |
| *Dioscorea nipponica* | Dioscoreaceae | Roots | Methanol extract | 50% inhibition | Kim and Kang [74] |
| *Eucalyptus galbie* | Myrtaceae | Leaves | Methanol extract | IC<sub>50</sub> more than 10 mg/mL | Gholamhoseinian et al. [76] |
| *Euonymus alatus* | Celastraceae | Roots | Aqueous and ethanol extracts | IC<sub>50</sub> between 40 and 50 µg/mL | Kim and Kang [74] |
| *Fagonia arabica* | Zygophyllaceae | Aerial parts | Methanol extract | IC<sub>50</sub> (204.1 µg/mL) | Bustanji et al. [45] |
| *Ferula asafoetida* | Apiaceae | Resin | Ethanol extract | 72.5% inhibition | Kumar et al. [56] |
| *Ficus carica* | Moraceae | Leaves | Methanol extract | 25–50% inhibition | Gholamhoseinian et al. [76] |
| *Foeniculum vulgare* Miller subsp. | Apiaceae | Leaves and seeds | Aqueous ethanol | IC<sub>50</sub> more than 10 mg/mL | Conforti et al. [50] |
| *Geranium nepalense* | Geraniaceae | Whole grass | Ethanol extract | 38% inhibition | Roh and Jung [57] |
| *Ginkgo biloba* L. | Ginkgoaceae | Leaves | Aqueous extract | IC<sub>50</sub> (0.05 ± 0.01 µg/mL) | Adisakwattana et al. [47] |
| *Hypericum trifoliatum* Turra. | Clusiaceae | Aerial parts | Methanol extract | IC<sub>50</sub> (236.2 µg/mL) | Bustanji et al. [45] |
| *Illicium religiosum* Sieb. et Zucc. | Schisandraceae | Woods | Aqueous and ethanol extracts | IC<sub>50</sub> (21.9 µg/mL) | Kim and Kang [74] |
| *Ilex chinensis* Lam. | Rubiaceae | Flowers | Methanol extract | 66.0% inhibition | Kumar et al. [56] |
| *Juglans mandshurica* Maxim. | Juglandaceae | Fruits | Water extract | IC<sub>50</sub> (2.3 mg/mL) | Han et al. [70] |
| *Juniperus communis* | Cupressaceae | Barks | Aqueous and ethanol extracts | IC<sub>50</sub> (20.4 µg/mL) | Kim and Kang [74] |
| *Jurticia gendarussa* Burm. F. | Acanthaceae | Whole plant | Ethanol extract | 61.1% inhibition | Kumar et al. [56] |
| *Lagerstroemia indica* (L.) Pers. | Lythraceae | Fruits | Dichloromethane extract | 61.2% inhibition | Kumar et al. [56] |
| Plant's name          | Family               | Plant part            | Types of extract          | Inhibitory activity against pancreatic lipase | Reference(s) |
|----------------------|----------------------|-----------------------|---------------------------|-----------------------------------------------|--------------|
| Lepidium sativum L.  | Brassicaceae         | —                     | Hydroalcoholic extracts   | IC$_{50}$ (1.28 µg/mL)                        | Marrelli et al. [54] |
| Levisticum officinale| Apiaceae             | Roots                 | Methanol extract          | More than 50% inhibition                      | Gholamhoseinian et al. [76] |
| Malva nicaeensis All. | Malvaceae           | Aerial parts          | Methanol extract          | IC$_{50}$ (260.7 µg/mL)                       | Bustanji et al. [45] |
| Mangifera indica L.  | Anacardiaceae        | Leaves and stem bark  | Ethanol extract           | 75% inhibition                                | Moreno et al. [71] |
| Melastoma candidum   | Melastomataceae      | Aerial part           | Methanol extract          | 20% inhibition                                | Lai et al. [49] |
| Mentha spicata L.    | Lamiaceae            | Leaves                | Aqueous ethanol           | IC$_{50}$ (7.85 mg/mL)                        | Conforti et al. [50] |
| Millettia reticulata Benth. | Leguminosae       | Rattan cane           | Methanol extract          | 30–40% inhibition                             | Zheng et al. [5] |
| Momordica charantia L.| Cucurbitaceae       | Fruits                | Ethanol extract           | 25.8% inhibition                              | Sahib et al. [44] |
| Morinda citrifolia L.| Rubiaceae            | Fruits                | Ethanol extract           | 21% inhibition                                | Sahib et al. [44] |
| Moringa stenopetala  | Moringaceae          | Leaves                | Ethanol extract           | IC$_{50}$ more than 5 mg/mL                   | Toma et al. [52] |
| Morus alba           | Moraceae             | Leaves                | Aqueous extract           | IC$_{50}$ (0.01 ± 0.01 μg/mL)                 | Adisakwattana et al. [47] |
| Myristica fragrans   | Myristicaceae        | Mace                  | Methanol extract          | 18–20% inhibition                             | Lai et al. [49] |
| Myrtus communis      | Myrtaceae            | Leaves                | Methanol extract          | 25–50% inhibition                             | Gholamhoseinian et al. [76] |
| Nelumbo nucifera Gaertn. | Nymphaeaceae       | Leaves                | Aqueous and ethanol extracts | IC$_{50}$ 0.46 mg/mL | In vivo: it reduced plasma triacylglycerol level in rats | Ono et al. [72] |
| Nigella sativa       | Ranunculaceae        | Seeds                 | Methanol extract          | 25–50% inhibition                             | Gholamhoseinian et al. [76] |
| Oignon natrix L.     | Fabaceae             | Aerial parts          | Methanol extract          | IC$_{50}$ (167 μg/mL)                         | Bustanji et al. [45] |
| Origannum syricata L.| Lamiaceae            | —                     | Methanol extract          | IC$_{50}$ (234 μg/mL)                         | Bustanji et al. [45] |
| Origannum vulgare L. | Lamiaceae            | Stem and leaves       | Aqueous ethanol           | IC$_{50}$ more than 80 mg/mL                  | Conforti et al. [50] |
| Oriza japonica Thunb.| Rutaceae             | Whole plants          | Methanol extract          | More than 80% inhibition                      | Sharma et al. [75] |
| Rosmarinus officinalis L. | Lamiaceae       | Leaves                | Aqueous ethanol           | IC$_{50}$ (700 mg/mL)                         | Conforti et al. [50] |
| Oostegia persica     | Lamiaceae            | Aerial parts          | Methanol extract          | 25–50% inhibition                             | Gholamhoseinian et al. [76] |
| Papaver rhoas L.     | Papaveraceae         | Leaves                | Aqueous ethanol           | IC$_{50}$ more than 80 mg/mL                  | Conforti et al. [50] |
| Paronychia argentea L.am. | Illiciaceae       | Aerial parts          | Methanol extract          | IC$_{50}$ (342.7 µg/mL)                       | Bustanji et al. [45] |
| Passiflora nitida Kunth. | Passifloraceae    | Leaves                | Hydroethanolic extract    | IC$_{50}$ (21.2 µg/mL)                        | Teixeira et al. [53] |
| Phyla nodiflora L.   | Verbenaceae          | Whole plant           | Methanol extract          | 18% inhibition                                | Lai et al. [49] |
| Pistacia vera L.     | Anacardiaceae        | Fruits hall           | Methanol extract          | 25–50% inhibition                             | Gholamhoseinian et al. [76] |
| Pimpinella anisum    | Apiaceae             | Seeds                 | Methanol extract          | 25–50% inhibition                             | Gholamhoseinian et al. [76] |
| Polygonum cuspidatum Sieb. et Zucc. | Polygonaceae | Root and rhizome     | Methanol extract          | 30–40% inhibition                             | Zheng et al. [5] |
| Portulaca okraea L.  | Portulacaceae        | Leaves                | Aqueous ethanol           | IC$_{50}$ (5.48 mg/mL)                        | Conforti et al. [50] |
| Prunella vulgaris L. | Labiatae             | Ear                   | Methanol extract          | 74.7% inhibition                              | Zheng et al. [5] |
| Punica granatum L.   | Lythraceae           | Leaves                | Ethanol extract           | 50% inhibition                                | Adnyana et al. [68] |
Table 1: Continued.

| Plant’s name                      | Family    | Plant part      | Types of extract      | Inhibitory activity against pancreatic lipase | Reference(s) |
|-----------------------------------|-----------|-----------------|-----------------------|-----------------------------------------------|--------------|
| *Pyrus pyrifolia* (Burm.) Nak.    | Rosaceae  | Bark and leaf   | Aqueous and ethanol extracts | $IC_{50}$ between 40 and 50 $\mu$g/mL | Kim and Kang [74] |
| *Quercus infectoria*             | Fagaceae  | Galls           | Methanol extract      | More than 50% inhibition                      | Gholamhoseinian et al. [76] |
| *Raphanus raphanistrum* L.       | Brassicaceae | Leaves     | Aqueous ethanol         | $IC_{50}$ more than 80 $\mu$g/mL | Conforti et al. [50] |
| *Reseda alba* L.                 | Resedaceae | Aerial parts    | Methanol extract      | $IC_{50}$ (738 $\mu$g/mL)                   | Bustanji et al. [45] |
| *Rheum palmatum* L.              | Polygonaceae | Root and rhizome | Methanol extract     | 53.8% inhibition                             | Zheng et al. [51] |
| *Rheum rhizom*                   | Polygonaceae | Rhizomes     | Methanol extract      | 25–50% inhibition                            | Gholamhoseinian et al. [76] |
| *Rosa damascena*                 | Rosaceae  | Flowers         | Methanol extract      | More than 50% inhibition                      | Gholamhoseinian et al. [76] |
| *Ruei Fructus*                   | Rosaceae  | Fruits          | Ethanol extract       | 32.5% inhibition                             | Roh and Jung [57] |
| *Salicis Radiatus Cortex*        | Ulmaceae  | Bark            | Ethanol extract       | 34.8% inhibition                             | Roh and Jung [57] |
| *Salacia reticulata*             | Celastraceae | Roots       | Hot water-soluble extract | $IC_{50}$ 264 mg/mL | Yoshikawa et al. [65] |
| *Salvia miltiorrhiza* Bge.       | Labiatae  | Root and rhizome | Methanol extract     | 30–40% inhibition                            | Zheng et al. [51] |
| *Salvia spinosa* L.              | Lamiaceae | Aerial parts    | Ethanol extract       | $IC_{50}$ 156.2 $\mu$g/mL                   | Bustanji et al. [45] |
| *Satureia italica* (L.) Palib.    | Poaceae   | Whole plant     | Methanol extract      | More than 80% inhibition                      | Sharma et al. [75] |
| *Shorea roxburghii*               | Dipterocarpaceae | Bark     | Methanol extract       | $IC_{50}$ (31.6 $\mu$g/mL)                  | Morikawa et al. [60] |
| *Silene vulgaris* (Moench) Garcke | Caryophyllaceae | Leaves   | Aqueous ethanol         | $IC_{50}$ more than 10 $\mu$g/mL             | Conforti et al. [50] |
| *Smyrnium alsatrum* L.           | Apiaceae  | Leaves          | Aqueous ethanol         | $IC_{50}$ more than 80 $\mu$g/mL             | Conforti et al. [50] |
| *Sonchus oleraceus* L.           | Asteraceae | Leaves          | Aqueous ethanol         | $IC_{50}$ (9.75 mg/mL)                       | Conforti et al. [50] |
| *Solidago serotina*              | Compositae | Whole plant    | Ethanol extract       | $IC_{50}$ less than 10 $\mu$g/mL             | Kim et al. [48] |
| *Sonchus asper* (L.) Hill         | Asteraceae | Leaves          | Aqueous ethanol         | $IC_{50}$ more than 80 $\mu$g/mL             | Conforti et al. [50] |
| *Sorbus commixta* Hedl.          | Rosaceae  | Leaves and stem | Ethanol extract       | $IC_{50}$ (29.6 $\mu$g/mL)                  | Lee et al. [68] |
| *Spathes acmella*                | Compositae | Flower buds    | Ethanol extract       | 40% inhibition                               | Ekanem et al. [55] |
| *Thuja orientalis*               | Cupressaceae | Leaves       | Aqueous and ethanol extracts | $IC_{50}$ between 40 and 50 $\mu$g/mL       | Kim and Kang [74] |
| *Trigonella foenum-graecum*      | Fabaceae  | Seeds           | Methanol extract       | 25–50% inhibition                            | Gholamhoseinian et al. [76] |
| *Uncaria macrophylla* Wall.      | Alismatraceae | Aerial parts | Methanol extract       | 30–40% inhibition                            | Zheng et al. [51] |
| *Urtica arvens*                  | Urticaceae | Aerial parts    | Methanol extract       | 25–30% inhibition                            | Gholamhoseinian et al. [76] |
| *Vigna radiata*                  | Fabaceae  | Roots           | Ethanol extract       | 64.6% inhibition                             | Kumar et al. [56] |
| *Viscum album* L.                | Loranthaceae | Whole plant | Ethanol extract       | $IC_{50}$ (33.3 $\mu$g/mL)                  | Lee et al. [61] |
| *Vitis vinifera* L.              | Vitaceae  | Seeds           | Ethanol extract       | 30% inhibition                               | Moreno et al. [66] |

$IC_{50}$: inhibition concentration 50.
inhibition (41–80%) and 2% were neutral towards porcine pancreatic lipase (PPL) activity. The results indicated that the leaves of *Cynometra cauliflora* (nam-nam), the ripe fruit of *Averrhoa carambola*, leaves of *Aleurites moluccana* (L) Willd. (candle nut/buah kera), and fruits of *Archidendron jiringa* (Jack) Nielsen L. showed the highest antilipase activity (100%) and are equivalent to 0.11 µg orlistat/mL. Orlistat at 0.1 µg/mL showed 95% inhibition of pancreatic lipase activity.

Adisakwattana et al. [47] evaluated the inhibitory activity of aqueous extract of different parts of 9 edible plants on pancreatic lipase *in vitro* using orlistat as positive control. The obtained result indicated that the *Ginkgo biloba* (ginkgo) and *Morus alba* (mulberry) exhibited promising inhibitory activities against pancreatic lipase. Among the plants, mulberry extract was considered the most effective pancreatic lipase inhibitor, whereas *Cassia angustifolia* (Senna) extract was considered the least potent inhibitor with IC\textsubscript{50} of 0.01 ± 0.01 and 0.81 ± 0.03 µg/mL, respectively. On the other hand, all extracts were less potent inhibitors as compared to orlistat with IC\textsubscript{50} of 1.34 ± 0.13 µg/mL.

Kim et al. [48] screened 115 herbal ethanol extracts for porcine pancreatic lipase inhibitory activity *in vitro*. Among the 115 plant species examined, eighteen extracts showed IC\textsubscript{50} values of less than 50 µg/mL, and three of these plants extracts, namely, *Solidago serotina* (whole plant), *Acer mono* (branches and leaves), and *Cudrania tricuspidata* (leaves), exhibited IC\textsubscript{50} values of less than 10 µg/mL. Remarkably, *Cudrania tricuspidata* showed an IC\textsubscript{50} value of 9.91 µg/mL. Then, the pancreatic lipase inhibitory effect of ethanol extract of *Cudrania tricuspidata* leaves (50 and 250 mg/kg) was investigated *in vivo*. The obtained results showed that *Cudrania tricuspidata* (50 mg/kg) decreased plasma triacylglycerol levels and the plant extract at the highest concentration (250 mg/kg) delayed lipid absorption significantly; however, these effects were weaker than that of orlistat (positive control).

Lai et al. [49] screened lipase inhibitory activity of methanolic extracts of different parts of 32 selected medicinal plants in Malaysia using porcine pancreatic lipase and p-nitrophenyl butyrate in an *in vitro* assay. Among the thirty-two extracts, twenty-seven crude extracts exhibited inhibitory activity against porcine pancreatic lipase *in vitro*. *Eleusine indica* exhibited the highest inhibitory effect against pancreatic lipase with 31.36 ± 0.58%, in comparison to the orlistat (34.49 ± 5.39%). Besides, *Myristica fragrans* (mace, 18–20%), *Melastoma candidum* 20%, *Phyla nodiflora* 18%, and *Dichroantepis linearis* 14% showed moderate activity (10–20%). On the other hand, nineteen crude extracts exhibited weak inhibitory activity (<10%) against PL.

Conforti et al. [50] screened pancreatic lipase inhibitory activity of 18 species of edible plants by monitoring the hydrolysis of p-nitrophenyl caprylate (p-NPC), which releases the yellow chromogen, p-nitrophenol. Among those examined, twelve extracts exhibited IC\textsubscript{50} value more than 10 mg/mL: *Asparagus acutifolius*, *Silene vulgaris*, *Origanum vulgare*, *Raphanus raphanistrum*, *Smyrnium olsatum*, *Sonchus asper*, *Foeniculum vulgare*, *Cichorium intybus*, *Papaver rhoas*, and *Anchusa azurea*, while nine extracts exhibited IC\textsubscript{50} value of less than 10 mg/mL. Orlistat at final concentration of 18 mg/mL was tested for comparison of inhibitory activity. The data indicated that, among plant extracts, those belonging to Lamiaceae (*Rosmarinus officinalis* and *Mentha spicata*) exhibited inhibitory activity with IC\textsubscript{50} values of 7.00 mg/mL and 7.85 mg/mL, respectively. Among all plant extracts belonging to Asteraceae, only *Sonchus oleraceus* exhibited inhibitory activity (IC\textsubscript{50} value of 9.75 mg/mL). The extract from *Diplotaxis tenuifolia*, belonging to Brassicaceae, exhibited inhibitory activity with IC\textsubscript{50} value of 7.76 mg/mL. Besides, the aqueous ethanol extracts *Portulaca oleracea* (leaves) showed the highest inhibitory activity on lipase with IC\textsubscript{50} value of 5.48 mg/mL.

Zheng et al. [51] screened lipase inhibitory activity of methanolic extracts of different parts of 37 traditional Chinese herbal medicines (0.2 mg/mL) against PPL *in vitro* using spectrophotometry with 2,4-dinitrophenyl butyrate. Among the 37 plant extracts examined, six extracts exhibited moderate to strong antilipase activity more than 30%. *Prunella vulgaris* L. (Labiateae) and *Rheum palmatum* L. (Polygonaceae) showed the highest inhibitory effect against PPL with 74.7% and 53.8%, respectively. *Polygonum cuspidatum* Sieb. et Zucc. (Polygonaceae), *Uncaria macrophylla* Wall. (Alismataceae), *Salvia miltiorrhiza* Bge. (Labiateae), and *Millettia reticulata* Benth. (Leguminosae) exhibited moderate activity with 30–40%. The result of inhibitory effects of *Rheum palmatum* L. and *Prunella vulgaris* L. at various concentrations revealed increasing inhibitory activities as concentration increased from 5 to 200 µg/mL.

Toma et al. [52] investigated the inhibitory activity of the ethanolic extract of leaf of *Moringa stenopetala* on pancreatic lipase using spectrophotometric assay. The plant extract slightly inhibited pancreatic lipase with IC\textsubscript{50} value of more than 5 mg/mL.

Teixeira et al. [53] studied the inhibitory activity of hydroethanolic extract of leaf of *Passiflora nitida* Kunth (1, 10, and 100 µg/mL) on pancreatic lipase by a spectrophotometric assay using orlistat as positive control. *Passiflora nitida* extract at the highest concentration (100 µg/mL) showed (67.6 ± 2.3%) pancreatic lipase inhibition and orlistat exhibited an inhibition of (74.0 ± 5.3%) at 1.6 µg/mL. IC\textsubscript{50} values for pancreatic lipase inhibition for *Passiflora nitida* extract and orlistat were 2.1 ± 0.8 and 0.1 ± 0.01 (µg/mL), respectively.

Marrelli et al. [54] screened lipase inhibitory activity of hydroalcoholic extracts of five species of edible plants from Calabria region (Italy) against PPL *in vitro* using orlistat (20 µg/mL) as control. Lipase activity was measured by monitoring the hydrolysis of p-NPC. *Clematis vitalba* L. and *Lepidium sativum* L. showed the highest inhibitory activity on pancreatic lipase with IC\textsubscript{50} value of 0.99 ± 0.18 and 1.28 ± 0.29 mg/mL, respectively. Hence, the *Clematis vitalba* extracts can be considered a good candidate for more studies to isolate pancreatic lipase inhibitors.

Ekanem et al. [55] investigated the inhibition of pancreatic lipase of ethanolic extracts of *Aframomum melegueta* (seeds) and *Spilanthes acmella* (flower buds) at concentrations of 0.75–2.0 mg/mL using *in vitro* assay. *A. melegueta* and *S. acmella* (2 mg/mL) showed lipase inhibitory activities of 90% and 40%, respectively.

Kumar et al. [56] screened lipase inhibitory activity of different parts of 33 medicinal plants from India (n-hexane,
dichloromethane, methanol, and ethyl acetate extracts) in vitro. Among the 33 plant extracts examined, the ethanolic extract of Cassia siamea roots (250 mg/mL) exhibited the highest pancreatic lipase inhibition with 74.3 ± 1.4%. In addition, dichloromethane extract of Lagerstroemia indica fruits showed 61.2 ± 1.0% inhibition, and the ethyl acetate extract of Chukrasia tabularis leaves and bark showed 67.6 ± 2.1% and 63.7 ± 4.4% inhibition, respectively. Similarly, the ethanolic extract of Vigna radiata roots, L. indica fruits, Justicia gendarussa whole plant, and Ferula asafoetida resin showed 64.6 ± 0.2%, 70.1 ± 1.2%, 61.1 ± 2.6%, and 72.5 ± 3.5% PL inhibition, respectively. The methanol extract of Ixora chinensis flowers also showed 66.0 ± 2.1% enzyme inhibition.

The screening of the ethanolic extracts of 400 plants (100, 50, 25, 10, 5, 2.5, and 1.25 μg/mL) using porcine pancreatic lipase assay in vitro led to the identification of several extracts with potential activity against PPL. Of the screened extracts, 44 extracts at the concentration of 100 μg/mL exhibited high antilipase effect using 2,4-dinitrophenylbutyrate as a substrate in porcine pancreatic lipase assay. Among the extracts, four exhibited a relatively high antilipase activity of more than 30%. Rubi Fructus fruit, Salicis Radicis Cortex bark, Geranium nepalense whole grass, and Corncus officinalis fruit showed the significant inhibition of PPL with 32.5%, 34.8%, 38%, and 31.4%, respectively, compared to the orlistat (100 μg/mL) as a positive control with 42% [57].

Kaewpiboon et al. [58] screened lipase inhibitory activity of 52 plant species (ethanol and water extracts) of Thai medicinal plants in vitro. The obtained data showed that, out of all the extracts, only ethanol extract of Coscinium fenestratum stems showed a weak lipase inhibitory activity (IC50 value of 160 μg/mL) which had a 17.3-fold lower IC50 value than that of orlistat with 9.25 ± 1.25 μg/mL.

Chompoo et al. [59] investigated the ability of acetone extract from flowers, seeds, leaves, pericarps, stems, and rhizomes of Alpinia zerumbet to inhibit pancreatic lipase in vitro. The obtained data showed that the seed extract (IC50 = 5.00 ± 0.07 μg/mL) had the highest inhibitory effect on PL activity, amongst all different parts.

Morikawa et al. [60] investigated the ability of the methanol extract from bark of Shorea roxburghii to inhibit pancreatic lipase in vitro. The obtained result showed that the plant extract inhibited pancreatic lipase activity with IC50 of 31.6 μg/mL compared to orlistat with IC50 of 0.056 μg/mL.

Lee et al. [61] screened the in vitro lipase inhibitory effect of different parts of 61 medicinal plants (as ethanolic extract) from Korea by measuring the hydrolysis of p-nitrophenyl butyrate to p-nitrophenol. Among the 61 plant extracts examined, Sorbus commixta (leaf, stem) and Viscum album (whole plant) showed the best antilipase activity with IC50 values of 29.6 mg/mL and 33.3 mg/mL, respectively. Of the screened extracts, Camellia japonica (stem, leaf), Castanea crenata (staminate flower), and Acer ginnala (fruit) showed the inhibitory activity with IC50 value of 30–50 mg/mL. However, it was not more effective than positive control (orlistat) with IC50 value of 0.076 mg/mL.

Ragavendra et al. [62] studied the pancreatic lipase inhibitory activity of methanol extract of fruit pericarp Artocarpus lakoocha (10, 100, and 1000 mg/mL) in vitro. The plant extract inhibited pancreatic lipase in a dose dependent manner and highest inhibition (82.49%) was observed at concentration of 1000 mg/mL.

de Souza et al. [63] investigated the effect of the Baccharis trimera Less. leaf (ethanol, methanol, and aqueous extracts) on inhibition of pancreatic lipase activities in vitro. The aqueous and infused extracts did not exhibit inhibitory effect on the PL; however, the methanol extract considerably inhibited the PL activity by 78% and the ethanol extract presented low inhibition of 16% only.

Ivanov et al. [64] investigated the pancreatic lipase inhibitory activity of the crude aqueous ethanol extracts of Bergenia crassifolia rhizomes against human pancreatic lipase in vitro using fluorometric microplate reader. The plant extract inhibited human pancreatic lipase with IC50 value of 3.4 μg/mL.

Yoshikawa et al. [65] investigated the effect of hot watersoluble extract from Salacia reticulata roots on inhibition of pancreatic lipase and lipoprotein lipase from adipose tissue using in vivo and in vitro assays. The plant extract inhibited pancreatic lipase and lipoprotein lipase (LPL) from adipose tissue with IC50 value of 264 mg/mL and 15 mg/mL, respectively. The plant extract inhibited LPL porcine and PL in rat adipocytes dose dependently.

Moreno et al. [66] assessed the pancreatic lipase and lipoprotein lipase activities of the Vitis vinifera L. (grape seeds) ethanol extract using in vitro assay. The plant extract inhibited pancreatic lipase activity dose dependently. At a concentration of 1 mg/mL, it exhibited the highest inhibitory effect against pancreatic lipase and lipoprotein lipase by 30% and 80%, respectively.

Moreno et al. [67] studied the inhibitory effects of ethanol extract of peanut (Arachis hypogaea L.) shells (hulls, seed coats) on lipoprotein lipase and human pancreatic lipase using in vivo and in vitro assays. The plant extract exhibited inhibitory activity on pancreatic lipase dose dependently (1 mg/mL = 42% inhibitory effect) and also exerted a mild inhibitory effect on lipoprotein lipase activity. Besides, the plant extract could prevent the body weight gain induced by feeding a high-fat diet to male Wistar rats for 12 weeks.

Adunya et al. [68] assessed the effect of ethanol extract of pomegranate (Punica granatum L.) leaves with different concentrations on inhibition of pancreatic lipase using in vitro assay. The plant extract at concentration of 20.64 μg/mL inhibited significantly the pancreatic lipase activity with IC50 of 50% compared to the orlistat as standard drug with various concentrations.

Habtemariam [69] investigated the inhibitory effects of ethanol extract of Cassia auriculata (aerial parts) on pancreatic lipase using in vitro assay. The plant extract inhibited pancreatic lipase in a dose dependent manner. It showed inhibitory activity against pancreatic lipase with IC50 value of 6.0 ± 1.0 mg/mL.

Han et al. [70] assessed the pancreatic lipase inhibitory activity of the water extract of Juglans mandshurica fruit using in vitro assay by measuring the rate of release of oleic acid from triolein. The plant extract strongly inhibited pancreatic lipase dose dependently. It inhibited pancreatic lipase activity with an IC50 value of 2.3 μg/mL.
Moreno et al. [71] investigated the inhibitory effect of ethanolic extract of mango tree (*Mangifera indica* L.) (leaves and stem bark) on pancreatic lipase, lipoprotein lipase, and hormone-sensitive lipase using *in vitro* assays. The plant extracts (stem bark and leaves) at a concentration of 1 mg/mL exhibited a significant inhibition of pancreatic lipase. The extract of stem bark (1 mg/mL) decreased LPL activity by 75%. The plant extract of both parts reduced the isoproterenol-stimulated lipolysis in 3T3-L1 adipocytes.

Ono et al. [72] assessed the effect of *Nelumbo nucifera* leaves (aqueous and ethanol extracts) on pancreatic lipase inhibition using *in vitro* and *in vivo* assays. The plant extracts inhibited lipase activity with IC$_{50}$ value of 0.46 mg/mL and it promoted lipolysis in 3T3-L1 adipocytes. The obtained *in vivo* results showed that the plasma triacylglycerol level at 1 h after oral administration of a lipid emulsion to rats was elevated considerably and was reduced significantly in the group treated with the plant extract.

Kurihara et al. [73] investigated the inhibitory effect of *Cyclocarya palliata* water extract (leaves) on pancreatic lipase activity. The plant extracts inhibited pancreatic lipase activity with IC$_{50}$ value of 9.1 mg/mL. Besides, the extract (250 mg/kg) reduced plasma triacylglycerol levels in mice when fed with 5 mL/kg of lard and olive oil.

Kim and Kang [74] screened lipase inhibitory effect of the aqueous and ethanol extracts of different parts of 19 selected medicinal plants in Korea in an *in vitro* assay by a continuous-monitoring pH-Stat technique using tributyrin as a substrate. Among the nineteen plant extracts examined, *Illicium religiosum* (wood) and *Juniperus communis* (bark) showed the highest activity with an IC$_{50}$ value of 21.9 and 20.4 µg/mL, respectively, compared to the orlistat, with IC$_{50}$ value of 0.750 µg/mL. Meanwhile, *Thuja orientalis* (leaf), *Pyrus pyrifolia* (bark and leaf), and *Euonymus alatus* (root) exhibited pancreatic lipase effect with IC$_{50}$ value of 40–50 µg/mL.

Sharma et al. [75] investigated antilipase activity of different parts of 75 medicinal plants belonging to different families using a radioactive method. Of all the tested extracts, methanolic extracts of whole part of three plants, namely, *Setaria italica* (L.) Palib., *Orixia japonica* Thunb., and *Eriochloa villosa* (Thunb.) Kunth., showed strong *in vitro* antilipase activity (above 80%).

Gholamhoseinian et al. [76] investigated antilipase activity of methanol extract of 100 plants (various parts) using turbidimetric assay. Of the extracts tested, *Quercus infectoria* (galls), *Eucalyptus galbie* (leaves), *Rosa damascena* (flowers), and *Levisticum officinale* (roots) exhibited antilipase activity of more than 50%. On the other hand, the methanolic extracts of *Myrtus communis* (leaves), *Pistacia vera* (fruits hall), *Carthamus oxyacantha* (aerial parts), *Nigella sativa* (seeds), *Trigonella foenum-graecum* (seeds), *Urtaica urens* (aerial parts), *Cinnamomum zeylanicum* (derm), *Rheum ribes* (rhizomes), *Pimpinella anisum* (seeds), *Ficus carica* (leaves), *Alhagi camelorum* (aerial parts), *Bunium persicum* (seeds), *Arctium lappa* (roots), and *Otostegia persica* (aerial parts) exhibited an inhibitory activity between 25 and 50% on pancreatic lipase.

Kwon et al. [77] investigated the inhibitory effect of *Dioscorea nipponica* methanol extract (roots) on pancreatic lipase activity by using 4-MU oleate as a substrate. The plant extracts inhibited lipase activity in a dose dependent manner. The extract at the concentration of 10 µg/mL (IC$_{50}$) inhibited pancreatic lipase significantly with 50% inhibition of enzyme activity compared to orlistat as standard drug with various concentrations.

### 6. Summary

Although there has been huge growth in the incidence of obesity over the last 25 years, progress in the discovery and development of new antiobesity drugs is rather limited. The only approved drug, orlistat, an inhibitor of gastrointestinal and pancreatic lipases, is associated with certain unpleasant gastrointestinal side effects. Hence, in search of nontoxic therapeutic, plant-based clinical products are considered an alternative option.

As drugs have failed to give desirable long-term results, it is significant to say that, in the last 10–20 years, a pervasive inspection began in order to clarify the most helpful source of new antiobesity compounds of natural products and to take over the present relative drug of doubtful effectiveness. In the last few years, interest in herbal medicines has increased and about 500 various plant species are used as key ingredients, while most are still being collected from the wild [78]. In recent years, treatments based on natural products and prevention of diverse pathologies have been the focal point and the vision has constantly spread globally. At the same time, proof and documentations have been gathered to support massive possibilities of medicinal plants which had been applied in various traditional systems [79]. For this reason, a focus on natural products among scientists is viewed as an appropriate alternative to multiple medications, and many are of the belief that natural products are potential source of new chemical substances with potential therapeutic efficacy, taking into account that traditional medicine is considered a significant source that may be utilized to control diverse diseases including obesity. Lately, different natural products and plants have been evaluated for their potential antiobesity effect both *in vivo* and *in vitro*. Today, the natural products seem to have the most interesting source of modern drugs and have revealed hopeful outcomes to combat obesity. Various studies identified new compounds and natural products for their PL inhibitory effect which are more potent compared to orlistat. Some of these plant extracts showed profound inhibition effects on fat digestion and are rich in polyphenols, saponins, and terpenes [37]. Many pancreatic lipase inhibitors from nature are under preclinical investigations; unfortunately, none of these have reached clinical level. In fact, it can sometimes be very challenging to extrapolate the results from *in vivo* or *in vitro* studies to human subjects, because they have not been found in many cases to be significantly effective. Therefore, the main limitation of previous studies is that most of the studied compounds have been shown to be more potent than orlistat.
but there have been no clinical studies to show their adverse effects as compared to orlistat.

In this paper, we have reviewed some natural products which have been investigated as a source of potential molecules with PL inhibitory activity. Hence, for all of them concerted efforts are required to define activities, mechanism of action, and optimal dose required as well as their possible toxic or side effects to nominate them as new antiobesity agents. Ideally, such research and exploration will lead to a more effective and safer pharmacological treatment of obesity.

Undoubtedly, there is a huge need for studying medicinal plants and their compounds as a therapeutic treatment to control obesity. Globally, there are huge numbers of unstudied medicinal plants, some of which have been used traditionally to control body weight, while only few of these ever reached the drug development stage due to the lack of scientific and clinical pharmacology data. Hence, it has not been possible for most of these to reach the stage of drug development in which it would be possible to determine the safety and efficacy of the herbal medicines. It is suggested that investigations should be increased to identify, isolate, and collect the compounds reported from plants so that their efficacy and pharmacological activities could be illuminated thoroughly, particularly those used as condiments and spices, in treating and overcoming obesity in humans. Improving knowledge on the use of antiobesity medicinal preparations is needed by continuously testing of the identified medicinal plants for bioactivity and toxicity, developing commercial formulations, and standardizing such extracts [80].

Conflict of Interests
The authors declare no conflict of interests.

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Entrepreneurial opportunities in the green economy. Small and medium-sized enterprises (SMEs) have the potential to play a leading role in addressing environmental challenges and contributing to sustainable development. According to the United Nations, SMEs account for more than two-thirds of the global workforce and contribute to more than 50% of global GDP in many countries.

The green economy is a model of sustainable development that seeks to minimize or reverse environmental degradation, reduce social inequalities, and promote economic growth. SMEs can contribute to the green economy by adopting environmentally friendly practices, developing eco-friendly products and services, and investing in renewable energy and other sustainable technologies.

Small businesses have a unique advantage in the green economy because they are more flexible and can respond quickly to market changes and customer demands. They can also benefit from government incentives and subsidies for environmentally friendly practices.

However, SMEs often face challenges in accessing the necessary resources and capital to invest in green technologies and practices. This can be overcome by accessing government grants, loans, and tax credits, as well as private investors who are interested in supporting green initiatives.

In conclusion, SMEs have a critical role to play in the green economy. With the right support and resources, they can contribute to sustainable development and help create a more environmentally friendly and prosperous future.
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