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Pancreatic Lipase Inhibition by Edible Plants Used in Three Middle East Countries: A Mini-Review

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ABSTRACT

Obesity is considered a serious prevalent disease that is accelerating at an alarming rate. It has drawn worldwide attention and many approaches have been suggested to reduce dietary lipid hydrolysis and absorption. One of the substantial approaches is to inhibit pancreatic lipase (PL) that is the major responsible enzyme for fat digestion in the gastrointestinal lumen. Unfortunately, till now, the only pharmaceutical drug approved for obesity management is "Orlistat", which has many unpleasant side effects. During the last decade, a massive effort has been dedicated to discovering safe lipase inhibitors from natural sources to avoid undesired drawbacks. The Middle East region is well known for its highly diverse flora with vast potential medicinal value. In this review, we try to provide an overview of the edible plants with potent anti-lipase activities and comprise a number of common ingredients in the Middle Eastern cuisine.

Keywords: Pancreatic lipase; edible plants; obesity; Jordan, Palestine, Tunisia, Middle East.

INTRODUCTION

According to WHO definition, obesity is defined as an abnormal or excessive accumulation of fat that forms a risk to health. It has become a worldwide serious challenge since the overweight rate has been increasing dreadfully. A recent fact sheet from WHO reported that in 2016, out of the 7.5 billion world population then, more than 1.9 billion adults, were overweight and more than 650 million were obese.[1] In addition, the prevalence of obesity has been increasing dramatically in children and adolescents in both developed and developing countries.[2] Indeed, over 340 million children and teenagers aged 5-19 were overweight or obese in 2016. Moreover, 41 million children under the age of 5 were overweight or obese.[3]

The pathogenesis of obesity is multifactorial. It comprises both modifiable and non-modifiable risk factors. One of the major risk factors is a chronic surplus in the daily intake of calories to the maximum fat burning capacity of the body. Such negative balance is nourished by a triad of unhealthy lifestyle habits, high-fat diet and inadequate physical activity. The clinical outcomes of

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obesity are diverse ranging from no symptoms to complications with tremendous risks for morbidity and mortality such as type 2 diabetes, hypertension, coronary heart diseases, dyslipidemia, atherosclerosis, gall bladder and liver diseases and a number of cancers.[4] Obesity has also been linked to infertility and menstrual dysfunction and anovulation.[5]

Obesity represents a heavy burden on the healthcare systems and national expenditures worldwide. In USA for example, obesity and its associated chronic diseases were estimated to have direct healthcare costs of more than $480 billion and more than $1.24 trillion in indirect cost of work loss in 2016.[6] Despite of expansions in public awareness campaigns against obesity and regulatory changes, the prevalence rates globally are still rising. Hence, the need for new treatment modalities and novel pharmacologic options has never been greater.

A plausible pharmacologic target to manage obesity is reducing the digestion and absorption of dietary fat in the digestive tract. Lipases are enzymes that catalyze the breakdown of ester bond in triglycerides to form monoglycerides and free fatty acids, the more absorbable forms, which will then be stored in adipose tissues, leading to obesity.[7] Pancreatic lipase (PL) is the key enzyme of fat digestion accounting for the hydrolysis of 50-70% of dietary fat.[8] Not surprisingly, it drew the attention of researchers to develop natural or synthetic drugs to selectively inhibit the enzyme and halt its actions. This latter is an intriguing approach to help conquer obesity ameliorate many of its related public health concerns.

Nonetheless, pharmaceutical drugs combating obesity are still limited on the market due to non-negligible adverse effects of drugs in development. Therefore, the need for therapeutic remedies with safe, non-toxic ingredients is highly sought after. Such remedies have been explored in complementary and alternative medicine (CAM) products worldwide. According to World Health Organization (WHO), around 21,000 plant species can be used as medicinal plants and around 7000 compounds used in modern medicine come from medicinal plants.[9] Moreover, around 80% of the population of developing countries use folk medicine to meet their primary health care needs and around 25% of prescriptions in USA contain one or more plant products.[9]

The current article, best to our knowledge, is the first review of the pancreatic lipase (PL) inhibition activity of edible plants from the Middle East region aiming to provide promising strategies of reducing obesity.

HUMAN PANCREATIC LIPASE STRUCTURE

Different types of lipases (triacylglycerol hydrolases) are members of human lipase superfamily such as endothelial, lingual, hepatic, lipoprotein, lungs, kidney, skeletal muscles, adipose tissue, placenta, gastric and pancreatic lipases.[10]

The three-dimensional structure of human pancreatic lipase was first determined and published in Nature journal.[11] X-ray crystallography was used to determine its structure and the results showed that it consisted of a single chain glycoprotein, with 449 amino acids. The primary structure was deduced using sequencing complementary DNA clones. The structural results have proved that Ser152 was the nucleophilic residue essential in the enzyme activity as the catalytic function was lost after a chemical alteration of this residue. Ser152 is a part of an Asp-His-Ser triad. The previous finding was emphasized by another study which had used X-ray technique to support the identification of the Ser 152, His 263, Asp 176 catalytic triad.[12] Bioinformatics studies revealed the tertiary structure of human pancreatic lipase with α-helices, β sheets and random coils.[13] A surface lid or flab covers the presumptive active site which makes it unreachable by solvents. This flap is re-oriented upon activation.

LIPASE MECHANISM OF ACTION

Lipid metabolism starts with partial hydrolysis of ingested dietary fat by lingual lipase and stomach gastric

lipase to convert triacylglycerol into diacylglycerol and free fatty acids. The partially digested fat will be emulsified by the bile salts, secreted from the duodenum, into small fat micelles to increase the surface area and enzymatic hydrolysis efficiency. Triglycerides occupy the center of the droplet while the surface is covered with polar lipids, fatty acids, phospholipids, cholesterol and bile salts.

Hydrolytic action of gastric lipase continues in the duodenum in synergy with pancreatic lipase to convert lipids into monoglycerols and free fatty acids. Eventually, the fat micelles will be absorbed by intestinal enterocytes. Pancreatic protein co-lipase is a cofactor that facilitates hydrolytic activity of the pancreatic lipase and stabilizes its conformation.[10]

PL MECHANISM OF INHIBITION

The mechanism of PL inhibition is based on impairing the catalytic role of PL in triglyceride hydrolysis and inhibition of fat breakdown into monoglyceride and fatty acids.[14]

NATURAL AND SYNTHETIC LIPASE INHIBITORS

Extensive research in anti-obesity effects of natural and synthetic products has been profoundly progressing. A meta-analysis review of data spanning the years 2000-2018 was published in 2019, revealing that most of the plants exhibit their anti-obesity mode of action through regulating lipid profile and inhibiting pancreatic lipase.[15] There is a large pool of plant phytochemicals that have potent PL inhibitory actions, such as saponins, terpenes, phenolics, glycosides, alkaloids, carotenoids and polysaccharides.[16,10,17,18] On the other hand, robust studies on synthetic lipase inhibitors such as phosphonates, boronic acids and fats analogues have been carried out.[19] The most potent synthetic lipase inhibitor reported was 2-[(2-oxohexadecanoyl) amino]-1-[[(2-oxohexadecanoyl)-amino] methyl] ethyl decanoate that decreased the activity of human pancreatic and gastric activities to the half at 0.076 and 0.020 surface molar fractions, respectively.[10] Other studies have documented the promising roles of pharmacological agents like novel fluoroquinolones and triazolofluoroquinolones in lipase inhibition and obesity management.[19-22] In addition, a recent study has shown, for the first time, the fundamental potential of the agrochemical quinclorac as a potent synthetic and safe lipase inhibitor via *in vivo* bioactivity experiments.[23] So far, Orlistat is the first and only drug that was approved by US FDA in 2000 and introduced to the market under the name Xenical and later approved as an over-the–counter drug.[24] It is considered a semi-synthetic PL inhibitory drug from microbial origin, as it is a saturated derivative of lipstatin, the natural, irreversible lipase inhibitor from *Streptomyces toxytricini*.[25] It inhibits gastric and pancreatic lipases in the gastrointestinal tract, by competing with dietary fat molecules for the active sites of lipases, blocking fat hydrolysis pathway, thus eliminating fat absorption and storage inside adipocytes. So far, orlistat is the only anti-obesity drug on the market. Nevertheless, it still has many undesirable side effects, such as oily stools, diarrhea, abdominal pain and fecal spotting.[26]

PL INHIBITORS IN EDIBLE PLANTS

Many of the culinary herbs and plants used in the Middle East have been widely studied and claimed to have medicinal benefits. Indeed, in the last decade,[27] numerous screening studies of edible plants from Middle East region have been conducted to investigate their potential anti-lipase activity.

Jordan, Palestine and Tunisia are characterized by their high diversity and the abundance of edible flora that have substantial potential therapeutic roles as complementary and alternative medicines.

Jordan

Bustanji and colleagues (2010) studied the lipase inhibition action of *Rosmarinus officinalis* L. (Rosemary), which is a native perennial plant to Jordan that is used extensively in the Mediterranean cuisine as a cooking seasoning. It is used also in folkloric medicine, as a

treatment for dysmenorrhea,[28] respiratory disorders and hair growth stimulant.[29-30] Its anti-inflammatory and anti-oxidant effects have been studied thoroughly and it is known to have a hypo-glycemic and hypo-lipidemic dual effect. The latter effects were attributed to the presence of active phytochemicals like monoterpenes, diterpenes and the phenolics, mainly caffeic acid derivative, acids like rosmarinic acid (RA). The results of Bustanji et al revealed a significant PL inhibitory effect of rosemary extract with a low IC_{50} dose (13.8 µg/mL). The active constituents of rosemary are rosmarinic acid (RA), chlorogenic acid (CA), caffeic acid (CaA) and gallic acid (GA). They all showed inhibitory actions but the most potent one was GA with the lowest IC_{50}.[31]

Another experimental study was carried out by Issa and collaborators (2011) to investigate the effect of methanolic extract of *Lavandula angustifolia* (lavender) on diabetic dyslipidemia. This plant is native to northern regions of Jordan and is well known in this area as a folkloric medicine to diabetes. Their results showed a concentration-dependent manner inhibitory activity of lavender on PL with an IC_{50} 56.5 µg/mL. The authors inferred that this inhibitory effect could be associated with the presence of RA (IC_{50} 125.2 µg/mL) and GA ($IC_{50}$of 10.1 µg/mL).[32]

Bustanji and co-workers (2011b) have also investigated the anti-lipase activity of 23 medicinal plants, belongs to 15 plant families from Jordan, and compared their potential anti-lipase effects. Thirteen species demonstrated anti-lipase activity with IC_{50} less than 1.0 mg/mL. These were *Anthemis palaestina* 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. (234µg/mL), *Hypericum triquetrifolium* Turra (236.2 µg/mL), *Malva nicaeensis* All. (260.7 µg/mL), *Chrysanthemum coronarium* L. (286.1 µg/mL), *Paronychia argentea* Lam. (342.7 µg/mL), *Convolvulus althaoieds* L. (664.5µg/mL), *Reseda alba* L. (738 µg/mL), and *Adonis palaestina* Boiss (937.5 µg/mL). Some of these medicinal plants are edible.

The two most potent PL inhibitors among the aforementioned plants were *A. palaestina* and *S. spinosa*. With IC_{50}107.7 µg/mL and 156.2 µg/ml for *A. palaestina and S. spinosa*, respectively. The results were deemed pharmacologically significant in comparison with the reference drug orlistat IC50 (0.65 µg/mL) by using spectrophotometric assay to measure the PL inhibition activity.[33]

Another study from Jordan investigated the lipase inhibition activities of methanolic extracts of *Ginkgo biloba* L. (Ginkgoaceae) leaves.[34] The authors documented by virtual studies that the active phytochemical terpenetrilactones, including ginkgolides and bilobalide, fit into the active site of PL. Moreover, the experimental studies reported the PL inhibition activity of the active constituents with IC_{50} = 22.9, 90.0 and 60.1 µg/mL, respectively.[34]

In vitro and *in vivo* investigations of anti-obesity activities of another edible plant called *Crataegus aronia* L. (Rosaceae) from Jordan were conducted.[35] Crude aqueous extract of *C. aronia* was tested for its anti-lipase profiles. A significant concentration-dependent anti-lipase activity was demonstrated compared to orlistat. An *In vivo* experiment was conducted to examine the effect of the diet-supplemented with *C. aronia* crude extract on the body weight, compared with the regular diet of rats. They reported a significant decrease in the body weight of rats having the crude extract of *C. aronia,* in comparison with the control group. Their findings proposed that *C. aronia* has a substantial effect on PL in inhibition of fat digestion.

In 2015, Mohammad and co-workers virtually and experimentally examined the PL inhibitory efficacy of turmeric (*Curcuma longa* Linn.) from the family Zingiberaceae, a well- known natural antioxidant that is widely used in Mediterranean cuisines as a food additive. They concluded via the docking studies that curcumin, the active phytochemical, fits the binding site of the PL enzyme, along with anti-pancreatic lipase activity (IC_{50}

value of 7.3 µg/mL). These results support the robust use of curcumin as a promising PL inhibitor.[36]

Dietary *Salvia triloba* (Lamiaceae), known in Jordan as sage, was also studied for its lipid-lowering effects in experimental rats. Methanolic extract of the leaves exhibited a PL inhibitory potency in a dose-dependent manner and an IC_{50} of (100.80 ± 9.07 µg/mL), compared to orlistat IC_{50} (0.114 ± 0.004 µg/ml). These inhibitory effects were largely attributed to the phytochemical constituents of *S. triloba*, as flavonoids, phenolic acids and triterpenes (oleanolic acid, carnosic acid, and ursolic acid). The effect of methanolic extract of *S. triloba* on plasma triacylglyceride levels was measured in rats received high fat diet and the results revealed a marked reduction in serum triacylglyceride levels, compared to the orlistat treated group. *In vitro* results were supported by the *in vivo* findings and the authors suggested dual hypotriglyceridemic and antilipolytic properties of the sage leaves with a significant potential as an anti-obesity treatment.[37]

Palestine

A screening study from Palestine was published by Jaradat *et al*. in 2017 for PL inhibtion effects of some native medicinal and edible plants. Their results showed that *Urtica urens*, *Brassica napus*, *Portulaca oleracea* have inhibitory activity against PL. The organic and aqueous extracts of *U. urens* showed the highest anti-lipase activity with IC_{50}157 µg/mL and 157.1 µg/mL, respectively. The organic extracts of *P. oleracea* came next with IC_{50}262.03 µg/mL and the least active were the aqueous extracts of *B. napus* and *P. oleracea* that had IC_{50} 296.87 µg/mL and 417.62 µg/mL, respectively. They recommended that these three edible plants can be used as food additives in dietary industry to regulate body weight by reducing the hydrolysis and absorption of fatty food.[38]

Jaradat and co-workers conducted another study in 2017, to screen the anti-lipase activity of ten medicinal and edible plants collected from West Bank area of Palestine. The tested plants are: *Arum palaestinum* Boiss, *Crataegus azarolus* L., *Malva parviflora* L., *Taraxacum syriacum* Boiss, *Rhus coriaria* L., *Rosmarinus officinalis* L., *Psidium guajava* L., *Origanum dayi* Post, *Brassica nigra* (L.) K. Koch, *and Vitis vinifera* L. The inhibition activity was assessed by using UV-visible spectrophotometer, and it was compared to the reference drug orlistat, which had an IC_{50} value 12.38 µg/mL. Among the ten screened native plants, they found that aqueous extracts of *V. vinifera* and *R. coriaria* were the most potent inhibitors with IC_{50} values of 14.13 and 19.95 µg/mL, respectively. The organic extract of *O. dayi* was also considered a potent PL inhibitor with an IC_{50} value of 18.62 µg/mL. This study was the first in screening the lipase inhibition activity of these three potent natural inhibitors which may play a significant role in obesity prevention.[39]

A recent article was published in 2018 about the anti-obesity potential of selected species from Palestine. The authors examined 90 plant species and found that the top active species in PL inhibtion in terms of minimum IC_{50} value are *Camellia sinensis*, *Ceratonia siliqua, Curcuma longa, Sarcopoterium spinosum, Mentha spicata*. These findings promote the use of the natural resources in overweight regulation.[40]

Tunisia

An in vitro study to assess the lipase inhibitory ability of *Juniperus phoenicea* L. was conducted in 2014. Its berries are used in cooking seasoning as well as in traditional medicine in the Middle East area. The results of the study revealed a powerful inhibitory effect of *J. phoenicea* extracts against PL, compared to the positive control, orlistat. These findings are consistent with the presence of phenolic phytochemicals in *J. phoenicea* leaves.[41]

Sellami and colleagues screened different extracts from various spices used in Tunisian cuisine, besides some aromatic beverages as coffee, green and black tea that are used commonly in Tunisia. Seventy-two plant extracts

were examined *in vitro* for their anti-lipase inhibitory effects, out of which, cinnamon *(Cinnamomum verum)* and mint (*Mentha aquatic*) showed the most potent and powerful PL inhibitory activities with the IC_{50} of 45 and 62 µg/ml, respectively. The strong PL inhibitory potency of both cinnamon and mint was suggested to be due to the presence of active constituents such as polyphenols, saponins, tannins, terpenes, flavonoids and alkaloids. Moreover, the inhibition effect was irreversible in presence of bile salts and colipase. The authors suggested that these two culinary plants could be a good source for new progenitors of anti-obesity drugs.[42]

CONCLUSION

A tremendous work is carried out to find an efficient and safe pancreatic lipase inhibitor from natural origin. This research mania is driven by the ascending worldwide awareness of the pathological consequences of obesity as a life-threatening disease. Currently, orlistat (Xenical) is the only drug available on the market for obesity. It should be emphasized that obesity is not synonymous with hyperlipidemia, even though it's considered a risk factor for hyperlipidemia. The possible explanation for the scarcity of anti-obesity drugs compared to lipid lowering drugs is the fact that obesity is multifactorial. Hence, the success rate of any pharmacologic intervention is highly variable among individuals. This has discouraged major pharmaceutical companies from investing in the development of new drugs for that indication. Another limiting factor is the inability of pharmaceutical manufacturers to patent drugs extracted from natural plants since these are already found naturally without any credit to the manufacturers. A third reason is the variabilities in the constituents of natural plants from one geographic area to another which further complicates the manufacturing process and quality validation. Nonetheless, the need for an alternative treatment strategy for obesity has driven a wealth of investigations of potential natural progenitors that can be synthetically modified to create potential drug candidates. An overview of the Middle Eastern food reveals the high correlation of the consumable plants with the inhibition of fat digestion. Undoubtedly, many edible plants from the Middle East region are good candidates for the discovery of new influential and harmless lipase inhibitor drugs.

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Conflicts of interest

The authors declare no conflicts of interest.

Authorship

All authors contributed equally to the literature search, participated in writing the review and approved the submission.

REFERENCES

1. World Health Organization (WHO), World Health Organization Factsheets, 2019; https://www.who.int/topics/obesity/en/
2. Blüher M. Obesity: global epidemiology and pathogenesis. *Nat. Rev. Endocrinol*. 2019; 15: 288–298.
3. World Health Organization (WHO), World Health Organization Factsheets, Obesity and overweight, 2017; http://www.who.int/mediacentre/factsheets/fs311/en/
4. Kopelman P.G. Obesity as a medical problem. *Nature.* 2000; 404:635–643.
5. Silvestris E., Pergola G., Rosania R. and Loverro G. Obesity as disruptor of the female fertility. *Reprod. Biol. Endocrin*. 2018; 16:22.
6. Ramasamy A., Laliberte´ F., Aktavoukian S., Lejeune D., DerSarkissian M., Cavanaugh C., Smolarz G., Ganguly R. and Duh M. Direct and indirect cost of obesity among the privately insured in the United States:

A Focus on the impact by type of industry. *J. Occup. Environ. Med.* 2019; 61: 877-886.

7. Ado M., Abas F., Mohammed A. and Ghazali H. Anti- and Pro-Lipase Activity of Selected Medicinal, Herbal and Aquatic Plants, and Structure Elucidation of an Anti-Lipase Compound. *Molecules.* 2013; 18:14651-14669.
8. Bajes, H.R., Almasri, I. & Bustanji, Y. Plant Products and Their Inhibitory Activity Against Pancreatic Lipase. *Rev Bras Farmacogn.* 2020**;** 30:321–330 (2020).
9. World Health Organization (WHO), World Health Organization Factsheets, Traditional Medicine: Definitions, 2008; Retrieved 2014-04-20.
10. Lunagariya N., Patel N., Jagtap S., Kamlesh K. and Bhutani K. Inhibitors of pancreatic lipase: state of the art and clinical perspectives. *EXCLI Journal.* 2014; 13: 897-921.
11. Winkler F., Darcy A. and Hunziker W. Structure of human pancreatic lipase. *Nature.* 1990; 343: 771–774.
12. Ltithi-Peng Q., Marki H. and Hadvary P. Identification of the active-site serine in human pancreatic lipase by chemical modification with tetrahydrolipstatin. *FEBS J.* 1992; 299 (1): 111-115.
13. Mukherjee A. Hydrophobic-hydrophilic interaction in lipase catalytic triad and possibility of a cofactor mediated catalysis. *IJAFS*. 2014; 4(3): 84-89.
14. Shahu R., Mhatre S., Rathod P., Kulkarni C. and Yadav R. Pancreatic lipase inhibitors from plant sources for possible use as antiobesity drugs. *MGM J. Med. Sci*. 2017; 4(4): 177-184.
15. Karri S., Sharma S., Hatware K. and Patil K. Natural anti-obesity agents and their therapeutic role in management of obesity: A future trend perspective. *Biomed. Pharmacother*. 2019; 110: 224–238.
16. Bustanji Y., Issa A., Hudaib M., Moulay A., Tawaha K., Mohammad M., Hamed S., Masri I. and Alali F. Hormone Sensitive Lipase Inhibition by Selected Medicinal Plants. *J. Med. Plants Res.* 2011a; 5: 4405-4410.
17. Mohammad M., Al-masri M., Issa A., Khdair A. and Bustanji Y. Inhibition of pancreatic lipase by berberine and dihydroberberine: An investigation by docking simulation and experimental validation. *Med Chem Res*. 2013; 22: 2273–2278.
18. Singh G., Suresh S., Bayiyeni V. and Kadeppagari R. Lipase inhibitors from plants and their medical applications. *Int. J. Pharm. Pharm. Sci.* 2015; 7(1): ISSN: 0975-1491
19. Kasabri V., Arabiyat S., Al-Hiari Y., Zalloum H., Almaliti J., Telfah A., Bustanji Y., Alalawi S. Fluoroquinolones as a potentially novel class of antidiabesity and antiproliferative compounds: synthesis and docking studies. Can. J. Chem. 2020, 98: 635-645.
20. Arabiyat S., Al-Hiari Y., Bustanji Y., Zalloum H. and Kasabri V. In Vitro Modulation of Pancreatic Lipase and Proliferation of Obesity Related-Colorectal Cancer Cell Line Panel by Novel Synthetic Triazoquinolones. *Rev. Roum. Chim.* 2016a; 61 (11-12):871-879.
21. Arabiyat S., Kasabri V., Al-Hiari Y., Bustanji Y., Albashiti R., Almasri I. and Sabbah D. Antilipase and antiproliferative activities of novel fluoroquinolones and triazolofluoroquinolones. *Chem. Biol. Drug. Des.* 2017; 90(6): 1282-1294.
22. Arabiyat S., Kasabri V., Al-Hiari Y., Al-Masri I., Alalawi S. and Bustanji Y. Dual Glycation-Inflammation Modulation, DPP-IV and Pancraetic Lipase Inhibitory Potentials and Antiproliferative Activity of Novel Fluoroquinolones. *Asian Pac. J. Cancer P*. 2019; 20: 2503-2514.
23. Dahabiyeh L., Bustanji Y. and Taha M. The herbicide quinclorac as potent lipase inhibitor: Discovery via virtual screening and in vitro/in vivo validation. *Chem. Biol. Drug Des.* 2019; 1–11.
24. Heck A., Yanovski J. and Calis K. Orlistat. a new lipase inhibitor for the management of obesity. *Pharmacotherapy*. 2000; 20(3): 270–279.
25. Mohammad M., Aiedeh K., AlKhatib H, Tawaha K., AlKhalidi B., Al-Masr Ii, Hamed S., Bustanji Y. A comparative enzymatic inhibition assay as a surrogate indicator of pharmaceutical and potency equivalence of two

orlistat formulations 2010. *Jordan J Pharm Sci.* 3, 69-74

26. Filippatos T.D., Derdemezis C.S., Gazi I.F., Nakou E.S., Mikhailidis D.P. and Elisaf M.S. Orlistat-associated adverse effects and drug interactions: a critical review. *Drug Saf*. 2008; 31(1):53-65.
27. Adisakwattana S., Jiphimai P., Prutanopajai P., Chanathong B., Sapwarobol S. and Ariyapitipan T. Evaluation of α-glucosidase, α-amylase and protein glycation inhibitory activities of edible plants. *Int. J. Food Sci. Tech*. 2010; 61 (3): 295-305.
28. Takaki I., Bersani-Amado L.E., Vendruscolo A., Sartoretto S.M., Diniz S.P., Bersani Amado C.A. and Cuman R.K.N. Anti-inflammatory and anti-nociceptive effects of *Rosmarinus officinalis* L. Essential Oil in Experimental Animal Models**.** *J. Med. Food*. 2008; 11: 741-746.
29. Al-Sereiti M.R., Abu-Amer K.M. and Sen P. Pharmacology of rosemary (*Rosmarinus officinalis* Linn.) and its therapeutic potentials. *Indian J. Exp. Biol*. 1999; 37:124-130.
30. Fabio A., Cermelli C., Fabio G., Nicoletti P. and Quaglio P. Screening of the antibacterial effects of a variety of essential oils on microorganisms responsible for respiratory infections. *Phytother. Res.* 2007; 21: 374-377.
31. Bustanji Y., Issa1 A., Mohammad M., Hudaib M., Tawah K., Alkhatib H., Almasri I. and Al-Khalidi B. Inhibition of hormone sensitive lipase and pancreatic lipase by *Rosmarinus officinalis* extract and selected phenolic constituents. *J. Med. Plants Res*. 2010; 4 (21): 2235-2242.
32. Issa A., Mohammad M., Hudaib M., Tawah K.H., Abu Rjai T., Oran S. and Bustanji Y. A potential role of *Lavandula angustifolia*in the management of diabetic dyslipidemia*. J Med. Plants Res.* 2011; 5(16): 3876-3882.
33. Bustanji Y., Mohammad M., Hudaib M., Tawaha K., Al-Masri I., AlKhatib H., Issa A. and Alali F. Screening of some medicinal plants for their pancreatic lipase inhibitory potential. *Jordan J. Pharm. Sci.* 2011b; 4(2): 81-88.
34. Bustanji Y., Al-Masri I., Mohammad M., Hudaib M., Tawaha K., Tarazi H. and Al-khatib H. Pancreatic Lipase Inhibition Activity of Trilactone Terpenes of *Ginkgo biloba. J Enzym Inhib Med Ch*. 2011c; 26(4): 453-459.
35. Al-Hallaq E., Kasabri V., Abdalla S.H., Bustanji Y. and Afifi F. Anti-Obesity and Antihyperglycemic effects of *Crataegus aronia*extracts: *In Vitro* and *in Vivo* Evaluations. *Food Nutr. Sci*. 2013; 4:972-983.
36. Mohammad M., Kasabri V., Zalloum H., Tayyem R., Aburish E., Al-Hiari Y. and Bustanji Y. Antilipolytic property of curcumin: Molecular docking and kinetic assessment. *Rev. Roum. Chim.* 2015; 60(10): 983-989.
37. Arabiyat S.H., Al-Rabi'ee A., Zalloum H., Hudaib M., Mohammad M. and Bustanji Y. Antilipolytic and hypotriglyceridemic effects of dietary *Salvia triloba* Lf (Lamiaceae) in experimental rats. *Trop. J. Pharm. Res*. 2016b; 15(4): 723-728.
38. Jaradat N., Zaid A. and Zaghal E. Anti-lipase activity for *Portulaca oleracea, Urtica urens, Brassica napus*and *Lathyrus hierosolymitanus* wild plants from Palestine. *Marmara Pharm. J*. 2017a; 21(4): 828-836.
39. Jaradat N., Zaid A., Hussein F., Zaqzouq M., Aljammal H. and Ayesh O. Anti-Lipase Potential of the Organic and Aqueous Extracts of Ten Traditional Edible and Medicinal Plants in Palestine; a Comparison Study with Orlistat. *Medicines.* 2017b; 4: 89.
40. Jamous R., Abu-Zaitoun S., Akkawi R. and Shtayeh M. Antiobesity and Antioxidant Potentials of Selected Palestinian Medicinal Plants. *Evid-Based Compl. Alt.* 2018; ID 8426752, 21 pages.
41. Keskes H., Mnafgui K., Hamden K., Damak M., El Feki A. and Allouche N. In vitro anti-diabetic, anti-obesity and antioxidant proprieties of *Juniperus phoenicea* L. leaves from Tunisia. *Asian Pac. J. Trop. Biomed*. 2014; 4(2): 649-655.
42. Sellami M., Louati H., Kamoun J., Kchaou A., Damak M. and Gargouri Y. Inhibition of pancreatic lipase and amylase by extracts of different spices and plants. *Int. J. Food Sci. Nutr*. 2017; 86(3): 313-320.
43. Mohammad M., Aiedeh K., AlKhatib H, Tawaha K.,

AlKhalidi B., Al-Masr Ii, Hamed S., Bustanji Y. A comparative enzymatic inhibition assay as a surrogate indicator of pharmaceutical and potency equivalence of two orlistat formulations 2010. Jordan J Pharm Sci. 3, 69-74

44. Bustanji Y., Mohammad M., Hudaib M., Tawaha K., Al-Masri I., AlKhatib H., Issa A., Alali F. Screening of Some Medicinal Plants for their Pancreatic Lipase Inhibitory Potential. Jordan Jordan J Pharm Sci. 2011; 4:81-88.
45. Bustanji Y, Hudaib M., Tawaha K., Mohammad M., Almasri I., Hamid S. and Oran S. In vitro Xanthine Oxidase inhibition by selected Jordanian medicinal plants. Jordan J Pharm Sci.. 2011; 4:29-34
46. Alhourani N., Hudaib M, Bustanji Y., Alabbassi R., Kasabri V. Chemical Composition of Essential Oil and Screening of Antiproliferative Activity of Paronychia argentea Lam. Aerial Parts: an Ethno-Medicinal Plant from Jordan. Jordan J Pharm Sci. 2020; 13:291

تثبيط انزيم الليباز البنكرياسي بواسطة النباتات الصالحة للأكل المستخدمة في ثلاث دول في الشرق الأوسط: مراجعة مصغرة

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ملخص

تعتبر السمنة من الأمراض الخطيرة المنتشرة والتي تتسارع عالميا بوتيرة تنذر بالخطر. و هذا الانتشار السريع لفرط السمنة نبه المجتمعات في جميع أنحاء العالم لايجاد حلول جذرية للسمنة لما لها من مخاطر كبيرة على صحة الافراد و المجتمعات. و تم اقتراح العديد من من الأساليب لتقليل التحلل المائي للدهون الغذائية للحد من امتصاصها. و من اهم هذه المقترحات عمل تثبيط للأنيم الليباز البنكرياسي **(PL)**. وهو الإنزيم الرئيسي المسؤول عن هضم الدهون في تجويف الجهاز الهضمي. و لكن للاسف الدواء الصيدلاني الوحيد المسجل لهذه الغاية هو "أورليستات" ، و الذي له العديد من الآثار الجانبية. خلال العقد الماضي ، تم تكريس جهد كبير لاكتشاف مثبطات جديدة لأنزيم الليباز البنكرياسي الآمنة من المصادر الطبيعية لتجنب الآثار الجانبية غير المرغوب فيها. تشتهر منطقة الشرق الأوسط بنباتاتها المتنوعة ذات القيمة الطبية الكبيرة المحتملة لعلاج العديد من الامراض المزمنة. في هذه المراجعة ، نحاول تقديم لمحة عامة عن النباتات الصالحة للأكل ذات الأنشطة القوية المضادة لليباز البنكرياسي وتشتمل على عدد من المكونات الشائعة في مطبخ الشرق الأوسط.

الكلمات الدالة: الليباز البنكرياسي، النباتات التي تؤكل، السمنة، الاردن، فلسطين، تونس، الشرق الاوسط.

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