

Planta Medica

Journal of Medicinal Plant and Natural Product Research

Editor-in-Chief

Luc Pieters, Antwerp, Belgium

Senior Editor

Adolf Nahrstedt, Münster, Germany

Review Editor

Matthias Hamburger, Basel, Switzerland

Editors

Wolfgang Barz, Münster, Germany
 Rudolf Bauer, Graz, Austria
 Veronika Butterweck, Gainesville FL, USA
 João Batista Calixto, Florianopolis, Brazil
 Thomas Efferth, Mainz, Germany
 Jerzy W. Jaroszewski, Copenhagen, Denmark
 Ikhlas Khan, Oxford MS, USA
 Wolfgang Kreis, Erlangen, Germany
 Irmgard Merfort, Freiburg, Germany
 Kurt Schmidt, Graz, Austria
 Thomas Simmet, Ulm, Germany
 Hermann Stuppner, Innsbruck, Austria
 Yang-Chang Wu, Taichung, Taiwan
 Yang Ye, Shanghai, China

Editorial Offices

Claudia Schärer, Basel, Switzerland
 Tess De Bruyne, Antwerp, Belgium

Advisory Board

Giovanni Appendino, Novara, Italy
 John T. Arnason, Ottawa, Canada
 Yoshinori Asakawa, Tokushima, Japan
 Lars Bohlin, Uppsala, Sweden
 Gerhard Bringmann, Würzburg, Germany
 Reto Brun, Basel, Switzerland
 Mark S. Butler, S. Lucia, Australia
 Ihsan Calis, Ankara, Turkey
 Salvador Cañigueral, Barcelona, Spain
 Hartmut Derendorf, Gainesville, USA
 Verena Dirsch, Vienna, Austria
 Jürgen Drewe, Basel, Switzerland
 Roberto Maffei Facino, Milan, Italy
 Alfonso Garcia-Piñeres, Frederick MD, USA
 Rolf Gebhardt, Leipzig, Germany
 Clarissa Gerhäuser, Heidelberg, Germany
 Jürg Gertsch, Zürich, Switzerland
 Simon Gibbons, London, UK
 De-An Guo, Shanghai, China
 Leslie Gunatilaka, Tucson, USA
 Solomon Habtemariam, London, UK
 Andreas Hensel, Münster, Germany
 Werner Herz, Tallahassee, USA
 Kurt Hostettmann, Geneva, Switzerland
 Peter J. Houghton, London, UK
 Jinwoong Kim, Seoul, Korea
 Gabriele M. König, Bonn, Germany
 Ulrich Matern, Marburg, Germany
 Matthias Melzig, Berlin, Germany
 Dulcie Mulholland, Guildford, UK
 Eduardo Munoz, Cordoba, Spain
 Kirs-Maria Oksman-Caldentey, Espoo, Finland
 Ana Maria de Oliveira, São Paulo, Brazil
 Nigel B. Perry, Dunedin, New Zealand
 Joseph Pfeilschifter, Frankfurt, Germany
 Peter Proksch, Düsseldorf, Germany
 Thomas Schmidt, Münster, Germany
 Volker Schulz, Berlin, Germany
 Hans-Uwe Simon, Bern, Switzerland
 Leandros Skaltsounis, Athens, Greece
 Han-Dong Sun, Kunming, China
 Benny K. H. Tan, Singapore, R. of Singapore
 Ren Xiang Tan, Nanjing, China
 Deniz Tasdemir, London, UK
 Nunziatina de Tommasi, Salerno, Italy
 Arnold Vlietinck, Antwerp, Belgium
 Angelika M. Vollmar, München, Germany
 Heikki Vuorela, Helsinki, Finland
 Jean-Luc Wolfender, Geneva, Switzerland
 De-Quan Yu, Beijing, China

Publishers

Georg Thieme Verlag KG
Stuttgart · New York
 Rüdigerstraße 14
 D-70469 Stuttgart
 Postfach 30 11 20
 D-70451 Stuttgart

Thieme Publishers
 333 Seventh Avenue
 New York, NY 10001, USA
 www.thieme.com

Reprint

© Georg Thieme Verlag KG
 Stuttgart · New York
 Reprint with the permission
 of the publishers only

Medicinal Plants from Jordan in the Treatment of Diabetes: Traditional Uses vs. *In Vitro* and *In Vivo* Evaluations – Part 2

Authors

Fatma U. Afifi-Yazar, Violet Kasabri, Rana Abu-Dahab

Affiliation

Faculty of Pharmacy, University of Jordan, Amman, Jordan

Key words

- traditional medicine
- medicinal plants
- diabetes
- Jordan

Abstract

Diabetes mellitus is the most common metabolic disorder affecting millions worldwide. It is recognized as a global major health problem. As alternatives to the available orthodox medicines, plants are considered a potential source for the treatment of diabetes within traditional ethno-medicine practices. In the Jordanian traditional medicine a significant selection of ethnobotanicals is promoted for their antidiabetic activity. Literature surveys demonstrate the benefit of several ethnobotanicals as antidiabetic agents eval-

uated in *in vitro* and *in vivo* systems in the form of their crude extracts and/or isolated pure compounds with varying degrees of hypoglycemic or antihyperglycemic bioactivities. This mini review discusses the preparatory forms in which these plants are consumed, their reported phytoconstituents, and the results of their reported antidiabetic bioactivity.

Supporting information available online at <http://www.thieme-connect.de/ejournals/toc/plantamedica>

Introduction

Diabetes mellitus (DM), the world's most common metabolic disorder, results from a defect in insulin secretion, insulin action, or both [1]. It is projected that the global prevalence of diabetes is escalating. At least 250 million individuals worldwide suffer from diabetes, and this number will double by 2030. Increases in complications will undoubtedly follow increasing pervasiveness of diabetes [2].

The regional prevalence of diabetes in MENA (Middle Eastern and North Africa) countries is 7.7% [3]. Standing at 10.1%, Jordan has the ninth highest incidence of diabetes. Several national surveys indicated that the prevalence of type 2 diabetes and impaired fasting glycemia is in an unprecedented increase with an epidemiological transition in Jordan [4–6]. More than 80% of diabetes deaths occur in low- and middle-income countries. Endocrine, nutritional, and metabolic diseases represent 7.9% of deaths in Jordan [7–8]. Located in the Middle East, Jordan covers 92 300 km² with high geographical and ecological diversity. Its varied topography and climate result in the junction of four biogeographical regions **Fig. 1S**, and these crossroads engender the coun-

try with substantial biodiversity that is at large understudied or, even worse, left unexplored [9]. The Mediterranean region provides the vast majority of the recorded 2500 wild plant species, including medicinal, poisonous, edible, and ornamental ones. There are more than 140 wild edible plants listed such as *Rumex crispus*, *R. vesicarius*, *Gundelia tournefortii*, *Origanum syriacum*, *Foeniculum vulgare*, and *Chicorium pumilum*. Some of these edible and culinary plants are used by local communities for generations for their medicinal value [10–12].

In Jordan, where traditional medicine plays a partial role in imparting the primary health care, vegetables, culinary herbs, and medicinal plants are among the main choices in the management of diabetes [13, 14]. However, it is officially neither integrated in the health care system nor recognized in national policies of the country. The objective of this mini review is to underline the ethnopharmacological practices related to 30 selected ethnobotanicals with claimed antidiabetic properties in light of their comprehensive scientific evaluation.

received March 17, 2011
revised May 22, 2011
accepted May 24, 2011

Bibliography

DOI <http://dx.doi.org/10.1055/s-0031-1279983>
Published online June 14, 2011
Planta Med © Georg Thieme
Verlag KG Stuttgart · New York ·
ISSN 0032-0943

Correspondence

Prof. Dr. Fatma U. Afifi-Yazar
Department of Pharmaceutical
Sciences
Faculty of Pharmacy
University of Jordan
Queen Rania Al-Abdullah Street
11942 Amman
Jordan
Phone: + 962 6 535 50 00
ext. 233 01
Fax: + 962 6 530 02 50
fatueafi@ju.edu.jo

Discussion

Surveys based on interviews with herbalists and search engines indicated that in the Jordanian traditional medicine almost 70 plant species belonging to 38 families were consumed by diabetic patients. The majority of the used plants are native to Jordan while others like *Zingiber officinalis*, *Terminalia chebula*, or *Embluca officinalis* are recognized as plants of nonindigenous origin [13,15–17].

Reports on the concomitant use of plants accompanying the orthodox therapy are limited. Primarily, interviews with diabetes patients in specialized health centers of Jordan further signified a more diversified list of selected plants [14,18]. The reported plants were: *Camellia sinensis*, *Pimpinella anisum*, *Zingiber officinale*, *Matricaria chamomilla*, *Salvia triloba*, *Trigonella foenum-graecum*, *Nigella sativa*, *Lupinus albus*, *Teucrium polium*, *Allium sativum*, *Cinnamomum zeylanicum*, and *Olea europea*.

Locally, a preliminary screening of the critical pharmacological appraisal of the traditionally utilized botanicals was performed. It demonstrated that reports on diabetes interventional phytotherapies are scarce. Gharaibeh et al. [19] investigated the hypoglycemic effects of *Teucrium polium* in normal and STZ-diabetic rats. Hamdan and Afifi [20], Afifi et al. [21], and Kasabri et al. [22,23] undertook a comprehensive and complementary *in vitro* and *in vivo* testing for a vast array of indigenously recruited herbs, partially consumed as integral to the diet of the traditional communities; *Achillea santolina*, *Eryngium creticum*, *Geranium graveolens*, *Paronychia argentea*, *Pistacia atlantica*, *Rheum ribes*, *Sarcopoterium spinosum*, *T. pollium*, and *Varthemia iphionoides* have been identified as antidiabetic phytomedicines. This line of research findings could link and rationalize the ethnopharmacological use with new approaches in the prevention/modulation of postprandial hyperglycemia emerging from the therapeutic use of α -amylase and α -glucosidase inhibitors. Also, Al-Mustafa and Al-Thunibat [24] investigated the antioxidative potentialities of an extensive list of Jordanian antidiabetic phytomedicines. Moreover, pancreatic mechanistic studies were reported for the hypoglycemic bioactivities of cinchonain Ib from *Eriobotrya japonica* [25] and *Ferula asafoetida* [26]. Additionally, the hypoglycemic effects of *Ballota nigra* [27] and *Artemisia sieberi* [28] were evidenced in alloxan-diabetic rats.

Comparable to conventional diabetes pharmacotherapeutics, the significant efficacy of hypoglycemic herbs is achieved by increasing insulin secretion, enhancing glucose uptake by adipose and muscle tissues, inhibiting glucose absorption from intestine and inhibiting glucose production from hepatocytes [29–31]. Certain herbs may ameliorate overt hyperglycemia substantially in clinical trials with well characterized action mechanisms [32,33]; their test results, however, are subject to several factors. Firstly, each herb contains multiple compounds, only a few of which may be therapeutically effective either alone or synergistically [34]. Secondly, different parts of an herb have different ingredient profiles. Thirdly, different extraction methods may yield different active ingredients [35]. Most recently, the antidiabetic activity of several flavonoids, polyphenols, terpenoids, coumarins and some alkaloids have been reviewed [36–39]. The reported secondary metabolites of the selected 30 plants are listed in **Table 1**. Especially important in the present review, flavonoids are the major class of secondary metabolites detected in most of the plants. Moreover, terpenoids have been reported in the discussed plant species with hypoglycemic activities [29,30].

Locally, one of the common practices is to assign certain species of a given genus a single common Arabic name with the expectation that all of them will perform ethnopharmacologically equally. This unjustifiable practice is based on species availability. In application, and despite scientific invalidity, the three *Artemisia*, both *Cichorium* spp., and the two *Crataegus* species have been the subject of such inappropriate convenience of designation.

Plants compiled in **Table 1**, demonstrating antidiabetic pharmacological activities, can be subgrouped as follows:

1. Spices: (*M. spicata*, *O. syriacum*, *L. nobilis*, *C. sativum*, *C. cyminum*, *C. spinosa*). Spices do not only improve the taste of the foods but do also contribute to the well-being of humans. Influence of the spices on the body metabolism and on the endocrine system has gained importance in the recent years. Numerous spices have been evaluated in animal experiments as well as clinical studies, and evidence has been obtained for their antidiabetic potential [40–43].
2. Vegetables and fruits: (*Cichorium intybus*, *C. pumilum*, *Opuntia ficus indica*, *Allium cepa* *Portulaca oleraceae*, *Crataegus aronia*, *C. azarolus*, *Citrus limon*, *C. paradisi*). Since appropriate diet, exercise, and weight reduction are essential in controlling the blood sugar, antidiabetic activities of many edible fruits and vegetables – in the form of aqueous and alcohol extracts – have been tested in diabetes animal models. Furthermore, clinical evidence for the antidiabetic activity is reported for two vegetables, namely for *C. intybus* and *A. cepa*. *A. cepa* exhibited hypoglycemic effects in type 1 and type 2 diabetic patients (**Table 1**). Exceptionally, *C. intybus*, possessing multiple action mechanisms in controlling the blood glucose level such as alpha amylase inhibitory activity, appetite regulation, and increasing insulin secretion (**Table 1**), has hypoglycemic activity in different animal models and clinically evidenced benefits in the reduction of diabetes risk (**Table 1**).
3. Medicinal herbs and nonedible parts of fruits: (*Artemisia herba-alba*, *A. judaica*, *A. vulgaris*, *Citrullus colocynthis*, *Aloe vera*, *Eucalyptus globules*, *Plantago major*, *P. ovata*, *Ruta chalepensis*, *Eryngium creticum* and *C. sinensis*, *Ceratonia siliqua*, *Juglans regia*, *Morus nigra*). For *A. herba-alba*, hypoglycemic, antihyperglycemic, and preventive effects have been illustrated in various animal models of diabetes. Nevertheless, *A. judaca* exhibited antidiabetic effects in STZ-diabetic rats, but *A. vulgaris* used locally for its antidiabetic activity has not been appraised pharmacologically. The remaining medicinal herbs, with the exception of *R. chalepensis*, have established antidiabetic activities. Richness in flavonoids, such as rutin, may raise plausible anticipation for *R. chalepensis* antidiabetic potentiality (**Table 1**). Several studies indicated the hypoglycemic benefits of flavonoids such as hesperidin, quercetin, luteolin, naringenin, and rutin in STZ-diabetic rats [44–48]. Leaf decoctions of common fruit trees – *C. siliqua*, *J. regia*, and *M. nigra* – and the peels of *C. sinensis* are praised throughout the country for their antidiabetic activities. These substantial efficacies have been clearly verified. Moreover, the antidiabetic efficiency of *C. siliqua* leaf extracts has been confirmed in type 2 diabetic patients (**Table 1**).

Conclusion

Based on hundreds of years of belief and observation, a marked number of plant species are used by the inhabitants of Jordan for the treatment of diabetes. The traditional knowledge of plants

Table 1 Selected plants indigenous to Jordan used for the treatment of diabetes in folk medicine.

No.	– Species – Preparation Method – References of ethno-pharmacological indications	Reported phytoconstituents	Reported antidiabetic efficacy and/or action mechanism
1	Asteraceae <i>Artemisia herba-alba</i> Asso. (syn.: <i>A. inculta</i>) (decoction of flowers, shoots, leaves [15, 49, 50])	Flavonoids [51]. Main essential oil components: β -thujone and α -thujone, 1,8-cineole, camphor, chrysanthemone, <i>trans</i> -sabinyl acetate, <i>trans</i> -pinocarveol, and borneol [52]	Significant and time-dependent hypoglycemic effect in normoglycemic and alloxan diabetic rabbits [53]. Preventive and antihyperglycemic effect in high-fat diet diabetes mice [54, 55]
2	Asteraceae <i>A. judaica</i> L. (infusion of flowering tops [56, 57])	Judaicin: a bitter principle [58]. Piperitone, <i>trans</i> -ethyl cinnamate, ethyl-3-phenyl propionate, spathulenol, <i>cis</i> -ethyl cinnamate, 2,6-dimethyl phenol, methyl cinnamate [59]. Flavonoids [60]	Antidiabetic effect in STZ-diabetic rats via acting as an insulin-mimetic reversing the changes in the enzyme activities of cytochrome P-450 (2E1, 2B, and 2C) on <i>androst-4-ene-3, 17-dione</i> metabolism [61]
3	Asteraceae <i>A. vulgaris</i> L. (infusion of flowering head [15])	Estrogenic flavonoids [62]. Jaceosidine, eupafolin, luteolin, quercetin, apigenin, aesculetin, esculetin-6-methylether, and scopoletin [63]. Yomogin [64]. Dicafeoylquinic acids [65]. Sesquiterpene lactones and a novel aromatic compound [66]. <i>Trans</i> -thujone, <i>cis</i> -thujone, chrysanthemyl acetate, 1,8-cineole, sabinene, β -pinene, artemisia ketone, caryophyllene, oxygenated monoterpenes, sesquiterpenes [67]. Flavonoid aglycon: quercetin 3,7,3'-trimethyl ether [68]	None
4	Asteraceae <i>Cichorium intybus</i> L. (decoction of flowers, roots [69])	Dietary fructans [70]. Anthocyanins [71]. Sesquiterpene lactones of guaiane and germacrane type. Lactucopicrin, 8-desoxylactucin, and three sesquiterpene lactone glycosides: crepidiaside B, sonchuside A, and ixeriside D [72]. Lactucin and lactucopicrin: sesquiterpene lactones [73]. Quercetin, kaempferol, luteolin, apigenin, crysoeriol and caffeoyl derivatives, polyphenols [74]. Flavonoids [75]. A guaianolide sesquiterpene glycoside, cichotyboside [76]. Tannins, chlorogenic acid along with caffeic acid derivatives [77]	Antihyperglycemic effect in alloxan-induced diabetes mice [78] and clinically proven reduction on diabetes risk [79], which can be explained by a reduction in intestinal absorption of glucose [80]. Significant increases in catalytic concentration of <i>glutathione S-transferases</i> in the liver of diabetic NOD mice [81]. Its dietary inulin-type fructans promote secretion of endogenous gastrointestinal peptides involved in appetite regulation [82] and via reduction in the hepatic Glc-6-pase activity thus decreasing hepatic glucose production, with no possibility of inducing insulin secretion from pancreatic beta-cells [83], also through adipogenesis inhibition and PPARgamma upregulation, inhibition of protein tyrosine phosphatase 1B and regulation of insulin signalling markers [77, 84]. α -Glucosidase inhibition [85]. Insulin-sensitizing and insulin-secreting principles [86]. Neuroprotection by stimulating AChE activity in brains of alloxan diabetic rats [87]
5	Asteraceae <i>Cichorium pumilum</i> L. (decoction of aerial parts [50, 69])	Flavonoids [88]; guaianolides [89]; eudesmanolides, eight lactucin-like guaianolides and phenolics, eudesmane-type sesquiterpene lactones [90]	None
6	Cactaceae <i>Opuntia ficus-indica</i> (L.) Mill. (edible fruits [15])	Polyphenols and flavonoids: ferulic acid; the chief derivative of hydroxycinnamic acid, rutin, and isorhamnetin derivatives [91]. Betacyanins and betaxanthins [92]. Kaempferol and isorhamnetin glycosides (glucoside and rhamnoside) [93]	Hypoglycemic effects [94]
7	Capparaceae <i>Capparis spinosa</i> L. (decoction of flowers, fruits [69])	Saccharides and glycosides, flavonoids, alkaloids, terpenoids and volatile oils, fatty acids and steroids [95]. Antioxidative capparoside (4-hydroxy-5-methylfuran-3-carboxylic acid, 1) [96]. Phenolics: rutin, tocopherols, carotenoids, and vitamin C [97]. Flavonoids, indoles, and phenolic acids [98]	Potent antihyperglycemic activity in STZ rats without affecting basal plasma insulin concentrations [99]. Hypoglycemic activity [95]
8	Cucurbitaceae <i>Citrullus colocynthis</i> L. (Schrad) (infusion of dry fruits, seeds [15, 56, 64, 100])	Tertiary and quaternary alkaloids, glycoside and saponin components [101]. Phenolics and flavonoids [102]	Hypoglycemic and antihyperglycemic effects in normal and alloxan diabetic rabbits [101] and STZ diabetic rats [103] by partly preserving or restoring pancreatic beta-cell mass [104] and insulinotropic effect [105]. Clinical beneficial effect on improving the glycemic profile without severe adverse effects in type 2 diabetic patients [106]

continued next page

Table 1 Selected plants indigenous to Jordan used for the treatment of diabetes in folk medicine. (continued)

No.	– Species – Preparation Method – References of ethno-pharmacological indications	Reported phytoconstituents	Reported antidiabetic efficacy and/or action mechanism
9	Fabaceae <i>Ceratonia siliqua</i> L. (decoction of leaves [107])	Flavonoids: mainly myricetin [108]. Phenolics: mainly gallotannins and proanthocyanidins, tannins, flavonol-glycosides, and traces of isoflavonoids [109–112]. Tannins [113]	Significantly decreased the glucose response to and glycemic index of fibers-enriched food in type 2 diabetic subjects. It also tended to decrease their insulinemic response and insulinemic index [114]. Increases total and acylated plasma ghrelin accompanied by enhanced lipid metabolism, thus suggesting higher lipid utilization and suppressed lipolysis, without affecting fasting concentrations of glucose, TAG, total ghrelin, NEFA, insulin, and leptin [115]
10	Graminae <i>Avena sativa</i> L. (infusion of seeds [69])	Beta-glucan, minerals, B complex vitamins, protein, fat, minerals [116]. Avenanthramide [117]	Improving glycemic, insulinemic, and lipidemic responses [118]. Oatmeal test seemed to be a good, noninvasive screening test in diabetic gastropathy in type 1 diabetes, but has no diagnostic value in type 2 diabetes [119]. Depression of the glycemic index by high levels of beta-glucan fiber making it a useful functional food component for reducing postprandial glycemia [120, 121]. Significantly improved whole-body insulin sensitivity [122, 123] induced changes of postprandial peptide YY and ghrelin responses [124] and increased postprandial cholecystokinin levels [125]. Dihydro-avenanthramide D protects pancreatic beta-cells from cytokine and STZ toxicity [117]
11	Juglandaceae <i>Juglans regia</i> L. (decoction of leaves [69, 107])	Ellagic acid [126]. Hydrolysable tannins [127]. Diaryl-heptanoids [128]. Unsaturated fatty acids, tocopherols, phospholipids, sphingolipids, sterols, hydrocarbons, and volatile compounds, phenolic compounds [129]	Dramatic hypoglycemic effect in experimental diabetes rats; where density of islets in pancreatic tissue, percent of beta cells, and islets size increased significantly thereby signifying regeneration of islets or beta cells [130–132], thus, recommended in prevention of DM and its late complications [133]
12	Labiatae <i>Mentha spicata</i> L. (infusion of seeds, oil [56])	Protocatechuic aldehyde, protocatechuic acid, chrysoeriol, 5,6-dihydroxy-7,8,3',4'-tetramethoxyflavone, nodifloretin [134]. Two lignans named spicatolignan A and spicatolignan B [135]. Carvone; monoterpene ketone [136] and menthone [137]; flavonoids [138]; piperitenone oxide 1,8-cineole [139]	None
13	Labiatae <i>Origanum syriacum</i> L. (decoction of leaves [15])	Monoterpene glucosides [140], oxygenated monoterpenes and sesquiterpenes [141]. Polar phenolic analytes; hydroxyl-benzoates, hydroxyl-cinnamates, and flavonoids [142]. Carvacrol, thymol, and thymoquinone [143]. Rosmarinic, oleanolic, and ursolic acids [144]. γ -terpinene and p-cymene [145]	None
14	Lauraceae <i>Laurus nobilis</i> L. (decoction of fruit, leaves [56])	Cinnamtannin B-1 [146]. Flavonoid O-glycosides, flavonoid C-glycoside. Catechin and cinnamtannin B1 [147]	Hypoglycemic effects in normal and alloxan-diabetic rabbits [148]. Improvement of glucose and lipid profile of type 2 diabetes patients [149]
15	Liliaceae <i>Allium cepa</i> L. (raw bulbs, oil, leaves [18, 56, 107])	Flavonoid glycosides [150]; S-alk(en)yl cysteine sulfoxide metabolites [151, 152]; S-allylcysteine sulfoxide, S-methylcysteine sulfoxide, and diallyl trisulfide [153]; quercetin [154]; onionin A [155]	Antidiabetic [41] via stimulating effects on glucose utilization and partly dependent on the stimulation of insulin secretions [156]. Hypoglycemic effect in STZ-diabetic rats coupled to decrease in the total serum lipid, triglyceride, and atherogenic index and increase in HDL-cholesterol/total cholesterol ratio, and reducing renal oxidative stress [157]. Clinical hypoglycemic effects in type 1 and type 2 diabetic patients [158]
16	Liliaceae <i>Aloe vera</i> L. (infusion of leaves, juice [15])	Cinnamoyl, p-coumaroyl, feruloyl, caffeoyl aloesin [159]. Phenols, flavonoids, ascorbic acid, β -carotene and α -tocopherol [160]. Mannose polymers with some glucose and other sugars; mainly acemannan, glycoproteins, enzymes, amino acids, vitamins, and minerals [161]. Anthraquinones: aloesin, aloes-emodin, and barbaloin, N-terminal octapeptide derived from verectin [162] and triglucosylated naphthalene glycoside [163]	Hypoglycemic or antidiabetic effects [164] thereby indicated for the treatment of diabetes and dyslipidemia [165]

continued next page

Table 1 Selected plants indigenous to Jordan used for the treatment of diabetes in folk medicine. (continued)

No.	– Species – Preparation Method – References of ethno-pharmacological indications	Reported phytoconstituents	Reported antidiabetic efficacy and/or action mechanism
17	Moraceae <i>Morus nigra</i> L. (decoction of leaves [107])	Anthocyanins [166]. Olcanolic acid, apingenin, cyclocommunol, morusin, cyclomorusin, kuwanon C, daucosterol [167]. Essential minerals, nutritive components, total phenols, and alkaloid contents [168]. A new 2-arylbenzofuran derivative, mornigrol D, G, and H along with norartocarpetin, dihydrokaempferol, albanin A, albanin E, moracin M, and albafluran C [169]	Antihyperglycemic propensity via significant increases in catalytic concentration of <i>glutathione S-transferases</i> in the liver of diabetic NOD mice [170, 171]
18	Myrtaceae <i>Eucalyptus globulus</i> Labill. (decoction of leaves, oil [18])	Heteroxylan composed of galactosyl, 4-O-methyl-glucuronosyl and xylosyl residues [172]. Ellagic acid derivatives; 3-O-methylellagic acid 4'-O- α -L-2''-O-acetyl-rhamnopyranoside, 3-O-methylellagic acid 4'-O- α -L-rhamnopyranoside, ellagic acid, and 3-O-methylellagic acid [173]. β -sitosterol, betulinic acid, stigmasterol, euscaphic acid, 2a-hydroxybetulinic acid, macrocarpal B, macrocarpal A, oleanolic acid, 3,4,3'-O-trimethylellagic acid, 3-O-methylellagic acid 4'-O-(2''-O-acetyl)- α -L-rhamnopyranoside, camaldulenside (cypellocarpin C, 3-O-methylellagic acid 4'-O- α -L-rhamnopyranoside, 3-O-methylellagic acid, ellagic acid, and gallic acid [174]) and cypellocarpa C [175]	<i>In vitro</i> stepwise enhancement of insulin secretion from the clonal pancreatic beta-cell line (BRIN-BD11) and enhancement of 2-deoxy-glucose transport, glucose oxidation, and incorporation of glucose into glycogen in mouse abdominal muscle [176, 177]. Antihyperglycemic action not exerted via the stimulation of insulin secretion but via enhancement of peripheral glucose uptake, exerting an antioxidative activity demonstrated by the increase of catalase, superoxide-dismutase, and glutathione-peroxidase activities in the liver and kidney, and a lowering of lipids peroxidation level in these organs [178]. Significantly improved the hyperglycemia, polydipsia, polyphagia, and also compensated weight loss of diabetic rats, in addition to treatment of candidiasis in normal and diabetic rats [179]. Noticeably, dose-dependent amelioration of diabetic states by partial restoration of pancreatic beta cells and repair of STZ-induced damage in rats [180]
19	Plantaginaceae <i>Plantago major</i> L. (decoction of seeds [69])	Ursolic acid [181]. Polysaccharides, lipids, caffeic acid derivatives, iridoid glycosides, terpenoids, alkaloids [182]. Phenolic glycoside [183]. Antioxidative flavonoids [184]	Significant antihyperglycemic effect in experimental diabetic rats [185, 186]
20	Plantaginaceae <i>P. ovata</i> Forsk. (decoction of seeds [69])	Neutral arabinoxylan [187]. Phytosterols; β -sitosterol and stigmasterol [188]. Saponin [189]	Fasting blood glucose and HbA1c showed a significant reduction, whereas HDL-Cholesterol increased significantly. LDL/HDL ratio was significantly decreased in diabetic outpatients [190]
21	Portulacaceae <i>Portulaca oleraceae</i> L. (decoction of herb [69, 107])	β -sitosterol, β -sitosterol-glucoside, N,N'-dicyclohexylurea, and allantoin [191]. Portulene; a di-terpene [192]. Phenolic alkaloids; oleracein A, oleracein B, and oleracein E [193]. Betacyanins [194]	Moderate antidiabetic activity via potent antioxidant potential in STZ-diabetic rats [195]
22	Rosaceae <i>Crataegus aronia</i> L. Bosc. ex DC (decoction of flowers, fruits [196])	Phenolics and flavonoids [197]	Hypoglycemic and antiperoxidative bioactivities in experimental diabetic rats [198]
23	Rosaceae <i>C. azarolus</i> L. (decoction of flowers, fruits [107])	Polyphenols [199]	None
24	Rutaceae <i>Citrus limon</i> (Linn.) Burm. (fresh fruits [56])	Hydroxycinnamates and polymethoxylated flavones in citrus peel molasses [200, 201]. Flavonoids: eriocitrin and hesperidin [202]. Phenolics and flavonoids [203]. Naringenin [204]. Limonoids: nomilin and limonin [205]. Ascorbic acid [206]. Flavonoid dimethylnobiletin [207]	Antioxidative in diabetic rats [202, 203]. Increases glucose uptake by skeletal muscle cells in an AMPK-dependent manner [204]. Cardiovascular friendly [208]. Anti-atherogenic bioactivities; inhibiting monocyte-to-macrophage differentiation and foam cell formation as well as hypolipidemic activity via enhancing LDL receptor gene expression and activity and decreasing acyl CoA: diacylglycerol acyltransferase 2 expression in HepG2 liver cells [207]
25	Rutaceae <i>C. paradisi</i> Macfa (raw fruits [69])	Alkaloids, flavonoids, cardiac glycosides, tannins, and saponin [200]. Furanocoumarins [210]. Naringenin [204] and nootkatone [211]. 4'-geranyloxyferulic acid [212]. Limonoids: nomilin and limonin [205]	Hypoglycemic and hypolipidemic effects in normal and alloxan diabetic rats [209, 213]. Improving glycemic control in nondiabetic rats [214]. Increasing glucose uptake by skeletal muscle cells in an AMPK-dependent manner [204], thus significantly reducing high-fat and high-sucrose diet-induced body weight gain, abdominal fat accumulation, and the development of hyperglycemia, hyperinsulinemia, and hyperleptinemia in C57BL/6J mice [211]

continued next page

Table 1 Selected plants indigenous to Jordan used for the treatment of diabetes in folk medicine. (continued)

No.	– Species – Preparation Method – References of ethno-pharmacological indications	Reported phytoconstituents	Reported antidiabetic efficacy and/or action mechanism
26	Rutaceae <i>C. sinensis</i> (L.) Osbeck (decoction of peels [69])	Phenolics: chlorogenic acid, luteolin, myricetin, naringenin, <i>p</i> -coumaric acid, and quercetin; and flavonoids – mainly hesperidine [215, 216]. Flavonones [217]. Cyclic monoterpene, DL-limonene [218]. Ascorbic acid [219]	Maximum glucose lowering and antiperoxidative activities in alloxan diabetic mice [220]. Antithyroidal, hypoglycemic, and insulin stimulatory properties, suggesting its potential to ameliorate both hyperthyroidism and diabetes mellitus [221]. Significant decrease in fasting glucose levels in the overweight treatment group of osteoarthritis patients [222]. Lack of α -glucosidase inhibitory effects [223]. Selective inhibition of aldose reductase [224] and reduction of advanced glycation end products and H_2O_2 induced oxidative stress in human adipocytes [225]
27	Rutaceae <i>Ruta chalepensis</i> L. (decoction of leaves, buds, roots [49])	Alkaloids, flavonoids, coumarins, tannins, volatile oil, sterols and/or triterpenes [226], and rutin, a flavone glycoside [227]	None
28	Umbelliferae <i>Coriandrum sativum</i> L. (decoction of seeds [18, 56])	Polyacetyles [228]. 1- <i>O</i> - β -D-glucopyranoside, 3- <i>O</i> - β -D-glucopyranoside, 4- <i>O</i> - β -D-glucopyranoside, 1- <i>O</i> - β -D-fructofuranoside, 3- <i>O</i> - β -D-fructofuranoside, 4- <i>O</i> - β -D-fructofuranoside, 1- <i>O</i> - β -D-(6- <i>O</i> -4-hydroxybenzoyl)-glucopyranoside, and 1- <i>O</i> - β -D-(6- <i>O</i> -4-methoxybenzoyl)-glucopyranoside of 2-C-methyl-D-erythritol [229]. Monoterpenoids, glycosides, monoterpene glucoside sulfates, and aromatic compound glycosides [230]	Antihyperglycemic, insulin-releasing, and insulin-like activity [231, 232]
29	Umbelliferae <i>Cuminum cyminum</i> L. (dry fruits [18])	Monoterpenoid glucosides [233]. Sesquiterpene lactone glucosides and alkyl glycosides [234]. A flavonoid glycoside; 3',5'-dihydroxyflavone 7- <i>O</i> - β -D-galacturonide 4'- <i>O</i> - β -D-glucopyranoside [235]. Cuminaldehyde, γ -terpinene, α -cymene, β -pinene, 2-carene-10-al, trans-carveol, and myrtenal [236]	Antihyperglycemic effect [237] comparable to glibenclamide and inhibition of advanced glycation end products formation in STZ-diabetic rats [238]. Aldose reductase and α -glucosidase inhibition [239]
30	Umbelliferae <i>Eryngium creticum</i> Lam. (decoction of aerial parts [100])	A unique <i>n</i> -propyl sesquiterpene [240]	Hypoglycemic effects [241] in rat models. Favorable acute antihyperglycemic trend in starch-fed rats despite the lack of <i>in vitro</i> inhibitory activity of α -amylase and α -glucosidase [23]

shown in relation to their medicinal use reflects a striking diversity of species and uses, as well as their importance in popular plant therapy. Pharmacologic and therapeutic evaluation of the selected plants in this review explicitly substantiates the ethno-pharmacological practices in Jordan. These traditions could pave the way for future phytochemical and pharmacological studies, thereby contributing to alternative therapeutic strategies to available drugs with undesirable adverse effects or those lacking in satisfactory efficacy or safety.

Supporting information

In **Table 15** of the Supporting information, the up-to-date reported pharmacological activities of the selected medicinal plants with claimed antidiabetic propensities are discussed. On the other hand, **Table 1** includes the reported antidiabetic efficacy and/or action mechanism of the same selection of medicinal plants.

Conflict of Interest

The authors declare none.

References

- Moore H, Summerbell C, Hooper L, Cruickshank K, Vyas A, Johnstone P, Ashton V, Kopelman P. Dietary advice for treatment of type 2 diabetes mellitus in adults. *Cochrane Database Syst Rev* 2004; 2: CD004097
- Wild S, Roglic G, Green A, Sicree R, King H. Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. *Diabetes Care* 2004; 27: 1047–1053
- International Diabetes Federation (IDF). IDF Diabetes Atlas, 4th edition, Prevalence estimates of diabetes mellitus (DM), 2010 –MENA. IDF [Online]. Available at: <http://www.diabetesatlas.org/content/prevalence-estimates-diabetes-mellitus-dm-2010>. Accessed November 10, 2010
- Bulatova NR, Yousef AF, AbuRuz SM. Antiplatelet therapy for primary and secondary prevention in Jordanian patients with diabetes mellitus. *Thromb Res* 2007; 121: 43–50
- Ajlouni K, Khader YS, Batieha A, Ajlouni H, El-Khateeb M. An increase of diabetes mellitus in Jordan over 10 years. *J Diabetes Complicat* 2008; 22: 317–324
- Zindah M, Belbeisi A, Walke H, Mokdad AH. Obesity and diabetes in Jordan: findings from the behavioral risk factor surveillance system, 2004. *Prev Chronic Dis* 2008; 5: 1–8
- World Health Organization. WHO Publications 2011: Fact Sheet No 312
- Dababneh F, Asad M, Abu Diab A. Information and research newsletter, issue 1, mortality data in Jordan 2007. Jordan: Ministry of Health; 2010
- Al-Eisawi D, El-Oqlah A, Al-Khader IA. Jordan country study on biological diversity. United Nations Environmental Program. Amman: Al-Rai Commercial Press; 2000: 7–11
- Al-Eisawi DM. List of Jordan vascular plants. *Mitt Bot München* 1982; 18: 79–182

- 11 Al Eisawi DM. Vegetation of Jordan. Cairo: UNESCO-Regional Office for Science and Technology for the Arab States; 1996: 266
- 12 Al-Eisawi DMH. Field guide to wild flowers of Jordan and neighbouring countries. Amman: Commercial Press, Jordan Press foundation Al-Rai; 1998: 4–8
- 13 Al-Aboudi A, Afifi FU. Plants used for the treatment of diabetes in Jordan: a review of scientific evidence. *Pharm Biol* 2011; 49: 221–239
- 14 Wazaify M, Afifi FU, El-Khateeb M, Ajlouni K. Complementary and alternative medicine use among Jordanian diabetes patients. *Complement Ther Clin Pract* 2011; 17: 71–75
- 15 Abu Rmailah B, Afifi F. Treatment with medicinal plants in Jordan. *Dira-sat* 2000; 27: 53–74
- 16 Afifi FU, Abu Irmaileh B. Herbal medicine in Jordan with special emphasis on less commonly used medicinal herbs. *J Ethnopharmacol* 2000; 72: 101–110
- 17 Abu-Irmaileh BE, Afifi FU. Herbal medicine in Jordan with special emphasis on commonly used herbs. *J Ethnopharmacol* 2003; 89: 193–197
- 18 Ootom SA, Al-Safi SA, Kerem ZK, Alkofahi A. The use of medicinal herbs by diabetic Jordanian patients. *J Herb Pharmacother* 2006; 6: 31–41
- 19 Gharaibeh MN, Elayan HH, Salhab AS. Hypoglycaemic effects of *Teucrium polium*. *J Ethnopharmacol* 1988; 24: 93–99
- 20 Hamdan II, Afifi FU. Studies on the *in vitro* and *in vivo* hypoglycaemic activities of some medicinal plants used in treatment of diabetes in Jordanian traditional medicine. *J Ethnopharmacol* 2004; 93: 117–121
- 21 Afifi F, Al-Khalidi B, Khalil E. Studies on the *in vivo* hypoglycemic activities of two medicinal plants used in the treatment of diabetes in Jordanian traditional medicine following intranasal administration. *J Ethnopharmacol* 2005; 100: 314–318
- 22 Kasabri V, Afifi FU, Hamdan I. *In vitro* and *in vivo* acute antihyperglycemic effects of five selected indigenous plants from Jordan used in traditional medicine. *J Ethnopharmacol* 2011; 133: 888–896
- 23 Kasabri V, Afifi FU, Hamdan I. Evaluation of the acute antihyperglycemic effects of four selected indigenous plants from Jordan used in traditional medicine. *Pharm Biol*, in press
- 24 Al-Mustafa AH, Al-Thunibat OY. Antioxidant capacity of some Jordanian medicinal plants used traditionally for the treatment of diabetes. *Pakistan J Biol Sci* 2008; 1: 351–358
- 25 Qa'dan F, Verspohl EJ, Nahrstedt A, Petereit F, Matalka KZ. Cinchonain Ib isolated from *Eriobotrya japonica* induces insulin secretion *in vitro* and *in vivo*. *J Ethnopharmacol* 2009; 124: 224–227
- 26 Abu-Zaiton AS. Anti-diabetic activity of *Ferula asafoetida* extract in normal and alloxan-induced diabetic rats. *Pakistan J Biol Sci* 2010; 13: 97–100
- 27 Nusier MK, Bataineh HN, Bataineh ZM, Daradka HM. Effects of *Ballota nigra* on glucose and insulin in alloxan-diabetic albino rats. *Neuroendocrinol Lett* 2007; 28: 470–472
- 28 Irshaid F, Mansi K, Aburjai T. Antidiabetic effect of essential oil from *Artemisia sieberi* growing in Jordan in normal and alloxan induced diabetic rats. *Pakistan J Biol Sci* 2010; 13: 423–430
- 29 Mukherjee PK, Maiti K, Mukherjee K, Houghton PJ. Leeds from Indian medicinal plants with hypoglycemic potentials. *J Ethnopharmacol* 2006; 106: 1–28
- 30 Prabhakar PK, Doble M. A target based therapeutic approach towards diabetes mellitus using medicinal plants. *Curr Diabetes Rev* 2008; 4: 291–308
- 31 Hui H, Tang G, Go VLW. Hypoglycaemic herbs and their action mechanisms. *Chin Med* 2009; 4: 11
- 32 Yin J, Zhang H, Ye J. Traditional Chinese medicine in treatment of metabolic syndrome. *Endocr Metab Immune Disord Drug Targets* 2008; 8: 99–111
- 33 Kuriyan R, Rajendran R, Bantwal G, Kurpad AV. Effect of supplementation of *Coccinia cordifolia* extract on newly defected diabetic patients. *Diabetes Care* 2008; 31: 216–220
- 34 Angelova N, Kong HW, van der Heijden R, Yang SY, Choi YM, Kim HK, Wang M, Hankemeier T, van der Greef J, Xu G, Verpoorte R. Recent methodology in the phytochemical analysis of ginseng. *Phytochem Anal* 2008; 19: 2–16
- 35 Shan JJ, Rodgers K, Lai CT, Sutherland SK. Challenges in natural health product research: the importance of standardization. *Proc West Pharmacol Soc* 2007; 50: 24–30
- 36 Benella W, Bellahcen S, Bnouham M. Antidiabetic medicinal plants as a source of alpha glucosidase inhibitors. *Curr Diabetes Rev* 2010; 6: 247–254
- 37 Qi LW, Liu EH, Chu C, Peng YB, Cai HX, Li P. Anti-diabetic agents from natural products—an update from 2004–2009. *Curr Top Med Chem* 2010; 10: 434–457
- 38 Bedekar A, Shah K, Koffas M. Natural products for type II diabetes treatment. *Adv Appl Microbiol* 2010; 71: 21–73
- 39 Dinda B, Debnath S, Mohanta BC, Harigaya Y. Naturally occurring triterpenoid saponins. *Chem Biodivers* 2010; 7: 2327–2580
- 40 Broadhurst CL, Polansky MM, Anderson RA. Insulin-like biological activity of culinary and medicinal plant aqueous extracts *in vitro*. *J Agric Food Chem* 2000; 48: 849–852
- 41 Srinivasan K. Plant foods in the management of diabetes mellitus: spices as beneficial antidiabetic food adjuncts. *Int J Food Sci Nutr* 2005; 56: 399–414
- 42 Srinivasan K. Spices as influencers of body metabolism: an overview of three decades of research. *Food Res Int* 2005; 38: 77–86
- 43 Mueller M, Jungbauer A. Culinary plants, herbs and spices – a rich source of PPARy ligands. *Food Chem* 2009; 119: 660–667
- 44 Fernandes AAH, Novelli ELB, Okoshi K, Okoshi MP, DiMuzio BP, Guimarães FC, Fernandes Jr. A. Influence of rutin treatment on biochemical alterations in experimental diabetes. *Biomed Pharmacother* 2010; 64: 214–219
- 45 Kamalakkannan N, Prince PSM. Rutin improves the antioxidant status in streptozotocin-induced diabetic rat tissues. *Mol Cell Biochem* 2006; 293: 211–219
- 46 Li YQ, Zhou FC, Gao F, Bian J, Shan F. Comparative evaluation of quercetin, isoquercetin and rutin as inhibitors of α -glucosidase. *J Agric Food Chem* 2009; 57: 11463–11468
- 47 Kim JS, Kwon CS, Son K. Inhibition of alpha-glucosidase and amylase by luteolin, a flavonoid. *Biosci Biotechnol Biochem* 2000; 64: 2456–2461
- 48 Ortiz-Andrade RR, Sánchez-Salgado JC, Navarrete-Vázquez G, Webster SP, Binnie M, García-Jiménez S, León-Rivera I, Cigarroa-Vázquez P, Villalobos-Molina R, Estrada-Soto S. Antidiabetic and toxicological evaluations of naringenin in normoglycemic and NIDDM rat models and its implications on extra-pancreatic glucose regulation. *Diabetes Obes Metab* 2008; 10: 1097–1104
- 49 Aburjai T, Hudaib M, Tayyem R. Ethnopharmacological survey of medicinal herbs in Jordan, the Ajloun Height region. *J Ethnopharmacol* 2007; 110: 294–304
- 50 Al-Khalil S. A survey of plants used in Jordanian traditional medicine. *Int J Pharmacognosy* 1995; 33: 317–323
- 51 Salah SM, Jager AK. Two flavonoids from *Artemisia herba-alba* Asso with *in vitro* GABAA-benzodiazepine receptor activity. *J Ethnopharmacol* 2005; 99: 145–146
- 52 Mighri H, Akrouf A, El-jeni H, Zaidi S, Tomi F, Casanova J, Neffati M. Composition and intraspecific chemical variability of the essential oil from *Artemisia herba-alba* growing wild in a Tunisian arid zone. *Chem Biodivers* 2010; 7: 2709–2717
- 53 Twaij HA, Al-Badr AA. Hypoglycaemic activity of *Artemisia herba-alba*. *J Ethnopharmacol* 1988; 24: 123–126
- 54 Hamza N, Berke B, Cheze C, Agli AN, Robinson P, Gin H, Moore N. Prevention of type 2 diabetes induced by high fat diet in the C57BL/6j mouse by two medicinal plants used in traditional treatment of diabetes in the east of Algeria. *J Ethnopharmacol* 2010; 128: 513–518
- 55 Hamza N, Berke B, Cheze C, Le Garrec R, Lassalle R, Agli AN, Robinson P, Gin H, Moore N. Treatment of high fat diet induced type 2 diabetes in C57BL/6j mice by two medicinal plants used in traditional treatment of diabetes in the east of Algeria. *J Ethnopharmacol* 2011; 133: 931–933
- 56 Lev E, Amar Z. Ethnopharmacological survey of traditional drugs sold in the Kingdom of Jordan. *J Ethnopharmacol* 2002; 82: 131–145
- 57 Hudaib M, Mohammad M, Bustanji Y, Tayyem R, Yousef M, Abuirjeie M, Aburjai T. Ethnopharmacological survey of medicinal plants in Jordan, Mujib nature reserve and surrounding area. *J Ethnopharmacol* 2008; 120: 63–71
- 58 Khafagy SM, Tosson S. Crystallographic, optical and chromatographic studies of judaicin, bitter principle of *Artemisia judaica* L. *Planta Med* 1968; 16: 446–449
- 59 El-Massry KF, El-Ghorab AH, Farouk A. Antioxidant activity and volatile components of Egyptian *Artemisia judaica* L. *Food Chem* 2002; 79: 331–336
- 60 Liu CZ, Murch SJ, EL-Demerdash M, Saxena PK. *Artemisia judaica* L.: micropropagation and antioxidant activity. *J Biotechnol* 2004; 110: 63–71
- 61 Debbri HA. Plant extracts as treatment for diabetes mellitus [dissertation]. Glasgow: University of Glasgow; 1996

- 62 Lee SJ, Chung HY, Maier CGA, Wood AR, Dixon RA, Mabry TJ. Estrogenic flavonoids from *Artemisia vulgaris* L. J Agric Food Chem 1998; 46: 3325–3329
- 63 Lee SJ, Chung HY, Lee IK, Oh SU, Yoo ID. Phenolics with inhibitory activity on mouse brain monoamine oxidase (MAO) from whole parts of *Artemisia vulgaris* L. (Mugwort). Food Sci Biotechnol 2000; 9: 179–182
- 64 Tigno XT, Gumila E. In vivo microvascular actions of *Artemisia vulgaris* L. in a model of ischemia-reperfusion injury in the rat intestinal mesentery. Clin Hemorheol Microcirc 2000; 23: 2–4
- 65 Carnat A, Heitz A, Fraisse D, Carnat AP, Lamaison JL. Major dicaffeoylquinic acids from *Artemisia vulgaris*. Fitoterapia 2000; 71: 587–589
- 66 Tigno XT, de Guzman F, Flora AM. Phytochemical analysis and hemodynamic actions of *Artemisia vulgaris* L. Clin Hemorheol Microcirc 2000; 23: 167–175
- 67 Judzentiene A, Buzelyte J. Chemical composition of essential oils of *Artemisia vulgaris* L. (mugwort) from North Lithuania. CHEMIJA 2006; 17: 12–15
- 68 Nikolova M, Velickovic D. Phenological variations in the surface flavonoids of *Artemisia vulgaris* L. and *Artemisia absinthium* L. Turk J Bot 2007; 31: 459–462
- 69 Oran SA, Al-Eisawi DM. Check list of medicinal plants in Jordan. Dirasat 1998; 25: 84–112
- 70 Roberfroid MB, Delzenne NM. Dietary fructans. Annu Rev Nutr 1998; 18: 117–143
- 71 Nørbaek R, Nielsen K, Kondo T. Anthocyanins from flowers of *Cichorium intybus*. Phytochemistry 2002; 60: 357–359
- 72 Malarz J, Stojakowska A, Kisiel W. Sesquiterpene lactones in a hairy root culture of *Cichorium intybus*. Z Naturforsch C 2002; 57: 994–997
- 73 Bischoff TA, Kelley CJ, Karchesy Y, Laurantans M, Nguyen-Dinh P, Arefi AG. Antimalarial activity of lactucin and lactucopicrin: sesquiterpene lactones isolated from *Cichorium intybus* L. J Ethnopharmacol 2004; 95: 455–457
- 74 Heimler D, Isolani L, Vignolini P, Tombelli S, Romani A. Polyphenol content and antioxidative activity in some species of freshly consumed salads. J Agric Food Chem 2007; 55: 1724–1729
- 75 Lavelli V. Antioxidant activity of minimally processed red chicory (*Cichorium intybus* L.) evaluated in xanthine oxidase-, myeloperoxidase-, and diaphorase-catalyzed reactions. J Agric Food Chem 2008; 56: 7194–7200
- 76 Ahmed B, Khan S, Masood MH, Siddique AH. Anti-hepatotoxic activity of cichotyboside, a sesquiterpene glycoside from the seeds of *Cichorium intybus*. J Asian Nat Prod Res 2008; 10: 223–231
- 77 Muthusamy VS, Saravanababu C, Ramanathan M, Bharathi Raja R, Sudhagar S, Anand S, Lakshmi BS. Inhibition of protein tyrosine phosphatase 1B and regulation of insulin signalling markers by caffeoyl derivatives of chicory (*Cichorium intybus*) salad leaves. Br J Nutr 2010; 104: 813–823
- 78 Petlevski R, Hadzija M, Slijepcevic M, Juretic D. Effect of 'antidiabetic' herbal preparation on serum glucose and fructosamine in NOD mice. J Ethnopharmacol 2001; 75: 181–184
- 79 Sartorelli DS, Fagherazzi G, Balkau B, Touillaud MS, Boutron-Ruault MC, de Lauzon-Guillain B, Clavel-Chapelon F. Differential effects of coffee on the risk of type 2 diabetes according to meal consumption in a French cohort of women: the E3N/EPIC cohort study. Am J Clin Nutr 2010; 91: 1002–1012
- 80 Kim M, Shin HK. The water-soluble extract of chicory reduces glucose uptake from the perfused jejunum in rats. J Nutr 1996; 126: 2236–2242
- 81 Petlevski R, Hadzija M, Slijepcevic M, Juretic D, Petrik J. Glutathione S-transferases and malondialdehyde in the liver of NOD mice on short-term treatment with plant mixture extract P-9801091. Phytother Res 2003; 17: 311–314
- 82 Delzenne NM, Cani PD, Daubouil C, Neyrinck AM. Impact of inulin and oligofructose on gastrointestinal peptides. Br J Nutr 2005; 93 (Suppl. 1): S157–S161
- 83 Pushparaj PN, Low HK, Manikandan J, Tan BK, Tan CH. Anti-diabetic effects of *Cichorium intybus* in streptozotocin-induced diabetic rats. J Ethnopharmacol 2007; 111: 430–434
- 84 Muthusamy VS, Anand S, Sangeetha KN, Sujatha S, Arun B, Lakshmi BS. Tannins present in *Cichorium intybus* enhance glucose uptake and inhibit adipogenesis in 3T3-L1 adipocytes through PTP1B inhibition. Chem Biol Interact 2008; 174: 69–78
- 85 Atta-ur-Rahman, Zareen S, Choudhary MI, Akhtar MN, Khan SN. Alpha-glucosidase inhibitory activity of triterpenoids from *Cichorium intybus*. J Nat Prod 2008; 71: 910–913
- 86 Tousch D, Lajoix AD, Hosi E, Azay-Milhou J, Ferrare K, Jahannault C, Cros G, Petit P. Chicoric acid, a new compound able to enhance insulin release and glucose uptake. Biochem Biophys Res Commun 2008; 377: 131–135
- 87 Ahmed N, Tarannum S. Acetylcholinesterase activity in the brain of alloxan diabetic albino rats: presence of an inhibitor of this enzyme activity in the cerebral extract. Int J Diabetes Dev Ctries 2009; 29: 174–177
- 88 Saleh MR, Metwally AM, Amer MM. Isolation of a flavonoid substance from *Cichorium pumilum* Jacq. Pharmazie 1975; 30: 404
- 89 El-Masry S, Ghazy NM, Zdero C, Bohlmann F. Two guaianolides from *Cichorium pumilum*. Phytochemistry 1984; 23: 183–185
- 90 Kisiel W, Michalska K. Root constituents of *Cichorium pumilum* and rearrangements of some lactucin-like guaianolides. Z. Naturforsch C 2003; 58: 789–792
- 91 Galati EM, Mondello MR, Giuffrida D, Dugo G, Miceli N, Pergolizzi S, Taviano MF. Chemical characterization and biological effects of Sicilian *Opuntia ficus indica* (L.) mill. Fruit juice: antioxidant and antitumorogenic activity. J Agric Food Chem 2003; 51: 4903–4908
- 92 Tesoriere L, Butera D, Gentile C, Livrea MA. Bioactive components of caper (*Capparis spinosa* L.) from Sicily and antioxidant effects in a red meat simulated gastric digestion. J Agric Food Chem 2007; 55: 8465–8471
- 93 Ginestra G, Parker ML, Bennett RN, Robertson J, Mandalari G, Narbad A, Lo Curto RB, Bisignano G, Faulds CB, Waldron KW. Anatomical, chemical, and biochemical characterization of cladodes from prickly pear [*Opuntia ficus-indica* (L.) Mill.]. J Agric Food Chem 2009; 57: 10323–10330
- 94 Butterweck V, Semlin L, Feistel B, Pischel I, Bauer K, Verspohl EJ. Comparative evaluation of two different *Opuntia ficus-indica* extracts for blood sugar lowering effects in rats. Phytother Res 2011; 25: 370–375
- 95 Yang T, Liu YQ, Wang CH, Wang ZT. Advances on investigation of chemical constituents, pharmacological activities and clinical applications of *Capparis spinosa*. Zhongguo Zhong Yao Za Zhi 2008; 33: 2453–2458
- 96 Yang T, Wang C, Liu H, Chou G, Cheng X, Wang Z. A new antioxidant compound from *Capparis spinosa*. Pharm Biol 2010; 48: 589–594
- 97 Tlili N, Khaldi A, Triki S, Munné-Bosch S. Phenolic compounds and vitamin antioxidants of caper (*Capparis spinosa*). Plant Foods Hum Nutr 2010; 65: 260–265
- 98 Zhou H, Jian R, Kang J, Huang X, Li Y, Zhuang C, Yang F, Zhang L, Fan X, Wu T, Wu X. Anti-inflammatory effects of caper (*Capparis spinosa* L.) fruit aqueous extract and the isolation of main phytochemicals. J Agric Food Chem 2010; 58: 12717–12721
- 99 Eddouks M, Lemhadri A, Michel JB. Caraway and caper: potential antihyperglycaemic plants in diabetic rats. J Ethnopharmacol 2004; 94: 143–148
- 100 Dafni A, Yaniv Z, Palevitch Z. Ethnobotanical survey of medicinal plants in northern Israel. J Ethnopharmacol 1984; 10: 295–310
- 101 Abdel-Hassan IA, Abdel-Barry JA, Tariq Mohammeda S. The hypoglycaemic and antihyperglycaemic effect of *Citrullus colocynthis* fruit aqueous extract in normal and alloxan diabetic rabbits. J Ethnopharmacol 2000; 71: 325–330
- 102 Kumar S, Kumar D, Manjusha, Saroha K, Singh N, Vashishta B. Antioxidant and free radical scavenging potential of *Citrullus colocynthis* (L.) Schrad. methanolic fruit extract. Acta Pharm 2008; 58: 215–220
- 103 Al-Ghaithi F, El-Ridi MR, Adeghate E, Amiri MH. Biochemical effects of *Citrullus colocynthis* in normal and diabetic rats. Mol Cell Biochem 2004; 261: 143–149
- 104 Sebbagh N, Cruciani-Guglielmacci C, Ouali F, Berthault MF, Rouch C, Sari DC, Magnan C. Comparative effects of *Citrullus colocynthis*, sunflower and olive oil-enriched diet in streptozotocin-induced diabetes in rats. Diabetes Metab 2009; 35: 178–184
- 105 Nmila R, Gross R, Rchid H, Roye M, Manteghetti M, Petit P, Tijane M, Ribes G, Sauvage Y. Insulinotropic effect of *Citrullus colocynthis* fruit extracts. Planta Med 2000; 66: 418–423
- 106 Huseini HF, Darvishzadeh F, Heshmat R, Jafariaraz Z, Raza M, Larijani B. The clinical investigation of *Citrullus colocynthis* (L.) schrad fruit in treatment of type II diabetic patients: a randomized, double blind, placebo-controlled clinical trial. Phytother Res 2008; 23: 1186–1189
- 107 Said O, Khalil K, Fulder S, Azaizeh H. Ethnopharmacological survey of medicinal herbs in Israel, the Golan Heights and the West Bank region. J Ehnopharmacol 2002; 83: 251–265
- 108 Vaya J, Mahmood S. Flavonoid content in leaf extracts of the fig (*Ficus carica* L.), carob (*Ceratonia siliqua* L.) and pistachio (*Pistacia lentiscus* L.). Biofactors 2006; 28: 169–175

- 109 Balaban M. Identification of the main phenolic compounds in wood of *Ceratonia siliqua* by GC-MS. *Phytochem Anal* 2004; 15: 385–388
- 110 Papagiannopoulos M, Wollseifen HR, Mellenthin A, Haber B, Galensa R. Identification and quantification of polyphenols in carob fruits (*Ceratonia siliqua* L.) and derived products by HPLC-UV-ESI/MSn. *J Agric Food Chem* 2004; 52: 3784–3791
- 111 Alali FQ, Tawaha K, El-Elimat T, Syouf M, El-Fayad M, Abulaila K, Nielsen SJ, Wheaton WD, Falkinham 3rd JO, Oberlies NH. Antioxidant activity and total phenolic content of aqueous and methanolic extracts of Jordanian plants: an ICBG project. *Nat Prod Res* 2007; 21: 1121–1131
- 112 Klenow S, Jahns F, Pool-Zobel BL, Gleis M. Does an extract of carob (*Ceratonia siliqua* L.) have chemopreventive potential related to oxidative stress and drug metabolism in human colon cells? *J Agric Food Chem* 2009; 57: 2999–3004
- 113 Manolaraki F, Sotiraki S, Stefanakis A, Skampardonis V, Volanis M, Hoste H. Anthelmintic activity of some Mediterranean browse plants against parasitic nematodes. *Parasitology* 2010; 137: 685–696
- 114 Feldman N, Norenberg C, Voet H, Manor E, Berner Y, Madar Z. Enrichment of an Israeli ethnic food with fibres and their effects on the glycaemic and insulinaemic responses in subjects with non-insulin-dependent diabetes mellitus. *Br J Nutr* 1995; 74: 681–688
- 115 Gruendl S, Garcia AL, Otto B, Wagner K, Bidlingmaier M, Burget L, Weickert MO, Dongowski G, Speth M, Katz N, Koebnick C. Increased acylated plasma ghrelin, but improved lipid profiles 24-h after consumption of carob pulp preparation rich in dietary fibre and polyphenols. *Br J Nutr* 2007; 98: 1170–1177
- 116 Sadiq Butt M, Tahir-Nadeem M, Khan MK, Shabir R, Butt MS. Oat: unique among the cereals. *Eur J Nutr* 2008; 47: 68–79
- 117 Lv N, Song MY, Lee YR, Choi HN, Kwon KB, Park JW, Park BH. Dihydro-avenanthramide D protects pancreatic beta-cells from cytokine and streptozotocin toxicity. *Biochem Biophys Res Commun* 2009; 387: 97–102
- 118 Pick ME, Hawrysh ZJ, Gee MI, Toth E, Garg ML, Hardin RT. Oat bran concentrate bread products improve long-term control of diabetes: a pilot study. *J Am Diet Assoc* 1996; 96: 1254–1264
- 119 Jüngling B, Schleiffer T, Buttmann A, Kraatz K, Kress S, Vogt M, Windeler J, Riemann JF. Postprandial blood glucose latency after oatmeal is a valid screening test for diabetic gastropathy in type 1 diabetes, but not in type 2 diabetes. *Dig Dis Sci* 2001; 46: 713–722
- 120 Jenkins AL, Jenkins DJ, Zdravkovic U, Wüsch P, Vuksan V. Depression of the glycemic index by high levels of beta-glucan fiber in two functional foods tested in type 2 diabetes. *Eur J Clin Nutr* 2002; 56: 622–628
- 121 Tapola N, Karvonen H, Niskanen L, Mikola M, Sarkkinen E. Glycemic responses of oat bran products in type 2 diabetic patients. *Nutr Metab Cardiovasc Dis* 2005; 15: 255–261
- 122 Weickert MO, Möhlig M, Schöfl C, Arafat AM, Otto B, Viehoff H, Koebnick C, Kohl A, Spranger J, Pfeiffer AF. Cereal fiber improves whole-body insulin sensitivity in overweight and obese women. *Diabetes Care* 2006; 29: 775–780
- 123 Lammert A, Kratzsch J, Selhorst J, Humpert PM, Bierhaus A, Birk R, Kusterer K, Hammes HP. Clinical benefit of a short term dietary oatmeal intervention in patients with type 2 diabetes and severe insulin resistance: a pilot study. *Exp Clin Endocrinol Diabetes* 2008; 116: 132–134
- 124 Weickert MO, Spranger J, Holst JJ, Otto B, Koebnick C, Möhlig M, Pfeiffer AF. Wheat-fibre-induced changes of postprandial peptide YY and ghrelin responses are not associated with acute alterations of satiety. *Br J Nutr* 2006; 96: 795–798
- 125 Beck EJ, Tosh SM, Batterham MJ, Tapsell LC, Huang XF. Oat beta-glucan increases postprandial cholecystokinin levels, decreases insulin response and extends subjective satiety in overweight subjects. *Mol Nutr Food Res* 2009; 53: 1343–1351
- 126 Papoutsis Z, Kassi E, Chinou I, Halabalaki M, Skaltsounis LA, Moutsatsou P. Walnut extract (*Juglans regia* L.) and its component ellagic acid exhibit anti-inflammatory activity in human aorta endothelial cells and osteoblastic activity in the cell line KS483. *Br J Nutr* 2008; 99: 715–722
- 127 Jin ZX, Qu ZY. Study on hydrolysable tannin constituents of seed of *Juglans regia* L. *Zhongguo Zhong Yao Za Zhi* 2008; 33: 1705–1707
- 128 Liu JX, Di DL, Wei XN, Han Y. Cytotoxic diarylheptanoids from the pericarps of walnuts (*Juglans regia*). *Planta Med* 2008; 74: 754–759
- 129 Martínez ML, Labuckas DO, Lamarque AL, Maestri DM. Walnut (*Juglans regia* L.): genetic resources, chemistry, by-products. *J Sci Food Agric* 2010; 90: 1959–1967
- 130 Jelodar G, Mohsen M, Shahram S. Effect of walnut leaf, coriander and pomegranate on blood glucose and histopathology of pancreas of alloxan induced diabetic rats. *Afr J Tradit Complement Alternat Med* 2007; 4: 299–305
- 131 Asgary S, Parkhideh S, Solhpour A, Madani H, Mahzouni P, Rahimi P. Effect of ethanolic extract of *Juglans regia* L. on blood sugar in diabetes-induced rats. *J Med Food* 2008; 11: 533–538
- 132 Said O, Saad B, Fulder S, Khalil K, Kassis E. Weight Loss in Animals and Humans Treated with 'Weighlevel', a Combination of Four Medicinal Plants Used in Traditional Arabic and Islamic Medicine. *Evid Based Complement Alternat Med* 2008; 24: 1–7
- 133 Dzhaferova RE, Garaev GSh, Dzhaferkulieva ZS. Antidiabetic action of extract of *Juglans regia* L. *Georgian Med News* 2009; 170: 110–114
- 134 Chen GT, Gao HY, Zheng J, Wu B, Yang XK, Wu LJ. Study of chemical constituents in active parts of *Mentha spicata* L. *Zhongguo Zhong Yao Za Zhi* 2006; 31: 560–562
- 135 Zheng J, Chen GT, Gao HY, Wu B, Wu LJ. Two new lignans from *Mentha spicata* L. *J Asian Nat Prod Res* 2007; 9: 431–435
- 136 Gonçalves JC, Oliveira Fde S, Benedito RB, de Sousa DP, de Almeida RN, de Araújo DA. Antinociceptive activity of (–)-carvone: evidence of association with decreased peripheral nerve excitability. *Biol Pharm Bull* 2008; 31: 1017–1020
- 137 Soković MD, Vukojević J, Marin PD, Brkić DD, Vajs V, van Griensven LJ. Chemical composition of essential oils of *Thymus* and *Mentha* species and their antifungal activities. *Molecules* 2009; 14: 238–249
- 138 Ke SY, Liu DL, Ma ZD, Liu YJ. Study on the extraction of total flavonoids from *Mentha spicata* by ultrasonic method. *Zhong Yao Cai* 2009; 32: 1288–1290
- 139 Koliopoulos G, Pitarokili D, Kioulos E, Michaelakis A, Tzakou O. Chemical composition and larvicidal evaluation of *Mentha*, *Salvia*, and *Melissa* essential oils against the West Nile virus mosquito *Culex pipiens*. *Parasitol Res* 2010; 107: 327–335
- 140 Kamel MS, Assaf MH, Hasanane HA, Ohtani K, Kasai R, Yamasaki K. Monoterpene glucosides from *Origanum syriacum*. *Phytochemistry* 2001; 58: 1149–1152
- 141 Alma MH, Mavi A, Yildirim A, Digrak M, Hirata T. Screening chemical composition and *in vitro* antioxidant and antimicrobial activities of the essential oils from *Origanum syriacum* L. growing in Turkey. *Biol Pharm Bull* 2003; 26: 1725–1729
- 142 Dorman HJ, Bachmayer O, Kosar M, Hiltunen R. Antioxidant properties of aqueous extracts from selected Lamiaceae species grown in Turkey. *J Agric Food Chem* 2004; 52: 762–770
- 143 Lukas B, Schmiederer C, Franz C, Novak J. Composition of essential oil compounds from different Syrian populations of *Origanum syriacum* L. (Lamiaceae). *J Agric Food Chem* 2009; 57: 1362–1365
- 144 Shen D, Pan MH, Wu QL, Park CH, Juliani HR, Ho CT, Simon JE. LC-MS method for the simultaneous quantitation of the anti-inflammatory constituents in oregano (*Origanum* species). *J Agric Food Chem* 2010; 58: 7119–7125
- 145 Berrehal D, Boudiar T, Hichem L, Khalfallah A, Kabouche A, Al-Freihat A, Ghannadi A, Sajjadi E, Mehrabani M, Safaei-Ghomi J, Kabouche Z. Comparative composition of four essential oils of Oregano used in Algerian and Jordanian folk medicine. *Nat Prod Commun* 2010; 5: 957–960
- 146 Lopez JJ, Jardin I, Salido GM, Rosado JA. Cinnamtannin B-1 as an antioxidant and platelet aggregation inhibitor. *Life Sci* 2008; 82: 977–982
- 147 Dall'Aqua S, Cervellati R, Speroni E, Costa S, Guerra MC, Stella L, Greco E, Innocenti G. Phytochemical composition and antioxidant activity of *Laurus nobilis* L. leaf infusion. *J Med Food* 2009; 12: 869–876
- 148 Yanardag R, Can S. Effect of *Laurus nobilis* L. leaves on blood glucose levels in normal and alloxan-diabetic rabbits. *Chim Acta Turc* 1994; 22: 169–175
- 149 Khan A, Zaman G, Anderson RA. Bay leaves improve glucose and lipid profile of people with type 2 diabetes. *J Clin Biochem Nutr* 2009; 44: 52–56
- 150 Boyle SP, Dobson VL, Duthie SJ, Kyle JA, Collins AR. Absorption and DNA protective effects of flavonoid glycosides from an onion meal. *Eur J Nutr* 2000; 39: 213–223
- 151 Griffiths G, Trueman L, Crowther T, Thomas B, Smith B. Onions – a global benefit to health. *Phytother Res* 2002; 16: 603–615
- 152 Rose P, Whiteman M, Moore PK, Zhu YZ. Bioactive S-alk(en)yl cysteine sulfoxide metabolites in the genus *Allium*: the chemistry of potential therapeutic agents. *Nat Prod Rep* 2005; 22: 351–368
- 153 Kook S, Kim GH, Choi K. The antidiabetic effect of onion and garlic in experimental diabetic rats: meta-analysis. *J Med Food* 2009; 12: 552–560

- 154 Galluzzo P, Martini C, Bulzomi P, Leone S, Bolli A, Pallottini V, Marino M. Quercetin-induced apoptotic cascade in cancer cells: antioxidant versus estrogen receptor alpha-dependent mechanisms. *Mol Nutr Food Res* 2009; 53: 699–708
- 155 El-Aasr M, Fujiwara Y, Takeya M, Ikeda T, Tsukamoto S, Ono M, Nakano D, Okawa M, Kinjo J, Yoshimitsu H, Nohara T. Onionin A from *Allium cepa* inhibits macrophage activation. *J Nat Prod* 2010; 73: 1306–1308
- 156 Kumari K, Augusti KT. Antidiabetic and antioxidant effects of S-methyl cysteine sulfoxide isolated from onions (*Allium cepa* Linn) as compared to standard drugs in alloxan diabetic rats. *Indian J Exp Biol* 2002; 40: 1005–1009
- 157 Bang MA, Kim HA, Cho YJ. Alterations in the blood glucose, serum lipids and renal oxidative stress in diabetic rats by supplementation of onion (*Allium cepa* Linn). *Nutr Res Pract* 2009; 3: 242–246
- 158 Taj Eldin IM, Ahmed EM, Elwahab HMA. Preliminary study of the clinical hypoglycemic effects of *Allium cepa* (red onion) in type 1 and type 2 diabetic patients. *Environ Health Insights* 2010; 14: 71–77
- 159 Yagi A, Takeo S. Anti-inflammatory constituents, aloesin and aloemannan in *Aloe* species and effects of tanshinon VI in *Salvia miltiorrhiza* on heart. *Yakugaku Zasshi* 2003; 123: 517–532
- 160 Ozsoy N, Candoken E, Akev N. Implications for degenerative disorders: antioxidative activity, total phenols, flavonoids, ascorbic acid, beta-carotene and beta-tocopherol in *Aloe vera*. *Oxid Med Cell Longev* 2009; 2: 99–106
- 161 Rodríguez Rodríguez E, Darias Martín J, Díaz Romero C. *Aloe vera* as a functional ingredient in foods. *Crit Rev Food Sci Nutr* 2010; 50: 305–326
- 162 El-Shemy HA, Aboul-Soud MA, Nassr-Allah AA, Aboul-Enein KM, Kabash A, Yagi A. Antitumor properties and modulation of antioxidant enzymes' activity by *Aloe vera* leaf active principles isolated via supercritical carbon dioxide extraction. *Curr Med Chem* 2010; 7: 129–138
- 163 Yang QY, Yao CS, Fang WS. A new triglucosylated naphthalene glycoside from *Aloe vera* L. *Fitoterapia* 2010; 81: 59–62
- 164 Hamman JH. Composition and applications of *Aloe vera* leaf gel. *Molecules* 2008; 13: 1599–1616
- 165 Ngo MQ, Nguyen NN, Shah SA. Oral *Aloe vera* for treatment of diabetes mellitus and dyslipidemia. *Am J Health Syst Pharm* 2010; 67: 1804, 1806, 1808 passim
- 166 Dugo P, Mondello L, Errante G, Zappia G, Dugo G. Identification of anthocyanins in berries by narrow-bore high-performance liquid chromatography with electrospray ionization detection. *J Agric Food Chem* 2001; 49: 3987–3992
- 167 Wang L, Wang HQ, Chen RY. Studies on chemical constituents from bark of *Morus nigra*. *Zhongguo Zhong Yao Za Zhi* 2007; 32: 2497–2499
- 168 Imran M, Khan H, Shah M, Khan R, Khan F. Chemical composition and antioxidant activity of certain *Morus* species. *J Zhejiang Univ Sci B* 2010; 11: 973–980
- 169 Wang L, Yang Y, Liu C, Chen RY. Three new compounds from *Morus nigra* L. *J Asian Nat Prod Res* 2010; 12: 431–437
- 170 Petlevski R, Hadzija M, Slijepcevic M, Juretic D. Effect of 'antidiabetic' herbal preparation on serum glucose and fructosamine in NOD mice. *J Ethnopharmacol* 2001; 75: 181–184
- 171 Petlevski R, Hadzija M, Slijepcevic M, Juretic D, Petrik J. Glutathione S-transferases and malondialdehyde in the liver of NOD mice on short-term treatment with plant mixture extract P-9801091. *Phytother Res* 2003; 17: 311–314
- 172 Shatalov AA, Evtuguin DV, Pascoal Neto C. (2-O-alpha-D-galactopyranosyl-4-O-methyl-alpha-D-glucurono)-D-xylan from *Eucalyptus globulus* Labill. *Carbohydr Res* 1999; 320: 93–99
- 173 Guo QM, Yang XW. A new ellagic acid derivative from the fruits of *Eucalyptus globulus* Labill. *Pharmazie* 2005; 60: 708–710
- 174 Yang XW, Guo QM. Studies on chemical constituents in fruits of *Eucalyptus globulus*. *Zhongguo Zhong Yao Za Zhi* 2007; 32: 496–500
- 175 Yang XW, Guo QM, Wang Y, Xu W, Tian L, Tian XJ. Intestinal permeability of antiviral constituents from the fruits of *Eucalyptus globulus* Labill. in caco-2 cell model. *Bioorg Med Chem Lett* 2007; 17: 1107–1111
- 176 Swanston-Flat SK, Day C, Bailey CJ, Flatt PR. Traditional plant treatments for diabetes. Studies in normal and streptozotocin diabetic mice. *Diabetologia* 1990; 33: 462–464
- 177 Gray AM, Flatt PR. Antihyperglycemic actions of *Eucalyptus globulus* (eucalyptus) are associated with pancreatic and extra-pancreatic effects in mice. *J Nutr* 1998; 128: 2319–2323
- 178 Ahlem S, Khaled H, Wafa M, Sofiane B, Mohamed D, Jean-Claude M, Abdelfattah el F. Oral administration of *Eucalyptus globulus* extract reduces the alloxan-induced oxidative stress in rats. *Chem Biol Interact* 2009; 181: 71–76
- 179 Bokaeian M, Nakhaee A, Moodi B, Ali Khazaei H. *Eucalyptus globulus* (eucalyptus) treatment of candidiasis in normal and diabetic rats. *Iran Biomed J* 2010; 14: 121–126
- 180 Mahmoudzadeh-Sagheb H, Heidari Z, Bokaeian M, Moudi B. Antidiabetic effects of *Eucalyptus globulus* on pancreatic islets: a stereological study. *Folia Morphol (Warsz)* 2010; 69: 112–118
- 181 Ringbom T, Segura L, Noreen Y, Perera P, Bohlin L. Ursolic acid from *Plantago major*, a selective inhibitor of cyclooxygenase-2 catalyzed prostaglandin biosynthesis. *J Nat Prod* 1998; 61: 1212–1215
- 182 Samuelsen AB. The traditional uses, chemical constituents and biological activities of *Plantago major* L. A review. *J Ethnopharmacol* 2000; 71: 1–21
- 183 Egorov TsA, Galkina TG, Balashova TA, Arsen'ev AS, Nikonorova AK, Babakov AV, Grishin EV. Phenolic glycoside isolated from seeds of the greater plantain (*Plantago major* L.). *Dokl Biochem Biophys* 2004; 396: 132–135
- 184 Beara IN, Lesjak MM, Jovin ED, Balog KJ, Anackov GT, Orčić DZ, Mimica-Dukić NM. Plantain (*Plantago* L.) species as novel sources of flavonoid antioxidants. *J Agric Food Chem* 2009; 57: 9268–9273
- 185 Rodríguez J, Loyola JI, Maulen G, Schmeda-Hirschmann G. Hypoglycemic activity of *Geranium core-core*, *Oxalis rosea* and *Plantago major* extracts in rats. *Phytother Res* 1994; 8: 371–374
- 186 Noor H, Jueng M, Chee BJ, Kueh BI, Othman Z. Medicinal properties of *Plantago major*: Hypoglycemic and male fertility studies. *Pertanika J Trop Agric Sci* 2000; 23: 29–35
- 187 Fischer MH, Yu N, Gray GR, Ralph J, Anderson L, Marlett JA. The gel-forming polysaccharide of psyllium husk (*Plantago ovata* Forsk). *Carbohydr Res* 2004; 339: 2009–2017
- 188 Nakamura Y, Yoshikawa N, Hiroki I, Sato K, Ohtsuki K, Chang CC, Upham BL, Trosko JE. Beta-sitosterol from psyllium seed husk (*Plantago ovata* Forsk) restores gap junctional intercellular communication in Ha-ras transfected rat liver cells. *Nutr Cancer* 2005; 51: 218–225
- 189 Miao MS, Zhang GL, Miao YY, Shi JJ, Liu HL. Influence of *Zea mays* L. saponin (ZMLS) on ultrastructure of kidney and pancreas in diabetes rats induced by streptozotocin. *Zhongguo Zhong Yao Za Zhi* 2008; 33: 1179–1183
- 190 Ziai SA, Larijani B, Akhoondzadeh S, Fakhrzadeh H, Dastpak A, Bandarian F, Rezaei A, Badi HN, Emami T. Psyllium decreased serum glucose and glycosylated hemoglobin significantly in diabetic outpatients. *J Ethnopharmacol* 2005; 102: 202–207
- 191 Rasheed AN, Afifi FU, Shaedah M, Taha MO. Investigation of the active constituents of *Portulaca oleracea* L. (Portulacaceae) growing in Jordan. *Pakistan J Pharm Sci* 2004; 17: 37–45
- 192 Elkhayati ES, Ibrahim SR, Aziz MA. Portulene, a new diterpene from *Portulaca oleracea* L. *J Asian Nat Prod Res* 2008; 10: 1039–1043
- 193 Yang Z, Liu C, Xiang L, Zheng Y. Phenolic alkaloids as a new class of antioxidants in *Portulaca oleracea*. *Phytother Res* 2009; 23: 1032–1035
- 194 Wang CQ, Yang GQ. Betacyanins from *Portulaca oleracea* L. ameliorate cognition deficits and attenuate oxidative damage induced by D-galactose in the brains of senescent mice. *Phytomedicine* 2010; 17: 527–532
- 195 Sharma A, Vijayakumar M, Rao Ch V, Unnikrishnan MK, Reddy GD. Action of *Portulaca oleracea* against streptozotocin-induced oxidative stress in experimental diabetic rats. *J Complement Integr Med* 2009; 6: 1–12
- 196 Ali-Shtayeh MS, Yaniv Z, Mahajna J. Ethnobotanical survey in the Palestinian area: a classification of the healing potential of medicinal plants. *J Ethnopharmacol* 2000; 73: 221–232
- 197 Bernatoniene J, Trumbeckaitė S, Majiene D, Baniene R, Baliutytė G, Savickas A, Toleikis A. The effect of *Crataegus* fruit extract and some of its flavonoids on mitochondrial oxidative phosphorylation in the heart. *Phytother Res* 2009; 23: 1701–1707
- 198 Ljubuncic P, Azaizeh H, Cogan U, Bomzon A. The effects of a decoction prepared from the leaves and unripe fruits of *Crataegus aronia* in streptozotocin-induced diabetic rats. *J Complement Integr Med* 2006; 3: 1–11
- 199 Bashri-Sahloul R, Ammar S, Fredj RB, Saguem S, Grec S, Trotin F, Skhiri FH. Polyphenol contents and antioxidative activities of extracts from flowers of two *Crataegus azarolus* L. varieties. *Pakistan J Biol Sci* 2009; 12: 660–668

- 200 Manthey JA, Grohmann K. Phenols in citrus peel byproducts. Concentrations of hydroxycinnamates and polymethoxylated flavones in citrus peel molasses. *J Agric Food Chem* 2001; 49: 3268–3273
- 201 Sultana S, Ali M, Ansari SH, Bagri P. New 4'-substituted flavones from the fruit peels of *Citrus limon* (L.) Burm.f. *J Asian Nat Prod Res* 2008; 10: 1123–1127
- 202 Miyake Y, Yamamoto K, Tsujihara N, Osawa T. Protective effects of lemon flavonoids on oxidative stress in diabetic rats. *Lipids* 1998; 33: 689–695
- 203 Akhila S, Bindu AR, Bindu K, Aleykutty NA. Comparative evaluation of extracts of *Citrus limon* burm peel for antioxidant activity. *Pharmacognosy* 2009; 1: 136–140
- 204 Zygmunt K, Faubert B, MacNeil J, Tsiani E. Naringenin, a citrus flavonoid, increases muscle cell glucose uptake via AMPK. *Biochem Biophys Res Commun* 2010; 398: 178–183
- 205 Hafeez F, Akram W, Shaalan EA. Mosquito larvicidal activity of citrus limonoids against *Aedes albopictus*. *Parasitol Res*, in press
- 206 Pisoschi AM, Pop A, Negulescu GP, Pisoschi A. Determination of ascorbic acid content of some fruit juices and wine by voltammetry performed at pt and carbon paste electrodes. *Molecules* 2011; 16: 1349–1365
- 207 Yen JH, Weng CY, Li S, Lo YH, Pan MH, Fu SH, Ho CT, Wu MJ. Citrus flavonoid 5-demethylnobiletin suppresses scavenger receptor expression in THP-1 cells and alters lipid homeostasis in HepG2 liver cells. *Mol Nutr Food Res* 2011; 55: 733–748
- 208 Shukla SK, Gupta S, Ojha SK, Sharma SB. Cardiovascular friendly natural products: a promising approach in the management of CVD. *Nat Prod Res* 2010; 24: 873–898
- 209 Adeneye AA. Methanol seed extract of *Citrus paradisi* Macfad lowers blood glucose, lipids and cardiovascular disease risk indices in normal Wistar rats. *Nig Q J Hosp Med* 2008; 18: 16–20
- 210 Yu J, Buslig BS, Haun C, Cancelon P. New furanocoumarins detected from grapefruit juice retentate. *Nat Prod Res* 2009; 23: 498–506
- 211 Murase T, Misawa K, Haramizu S, Minegishi Y, Hase T. Nootkatone, a characteristic constituent of grapefruit, stimulates energy metabolism and prevents diet-induced obesity by activating AMPK. *Am J Physiol Endocrinol Metab* 2010; 299: E266–E275
- 212 Genovese S, Epifano F, Carlucci G, Marcotullio MC, Curini M, Locatelli M. Quantification of 4'-geranyloxyferulic acid, a new natural colon cancer chemopreventive agent, by HPLC-DAD in grapefruit skin extract. *J Pharm Biomed Anal* 2010; 53: 212–214
- 213 Adeneye AA. Hypoglycemic and hypolipidemic effects of methanol seed extract of *Citrus paradisi* Macfad (Rutaceae) in alloxan-induced diabetic Wistar rats. *Nig Q J Hosp Med* 2008; 18: 211–215
- 214 Owira PM, Ojewole JA. Grapefruit juice improves glycemic control but exacerbates metformin-induced lactic acidosis in non-diabetic rats. *Methods Find Exp Clin Pharmacol* 2009; 31: 563–570
- 215 Freeman BL, Eggett DL, Parker TL. Synergistic and antagonistic interactions of phenolic compounds found in navel oranges. *J Food Sci* 2010; 75: C570–C576
- 216 Ghafar MFA, Prasad KN, Weng KK, Ismail A. Flavonoid, hesperidine, total phenolic contents and antioxidant activities from *Citrus* species. *Afr J Biotechnol* 2010; 9: 326–330
- 217 Moura LM, de Sylos CM. The effect of the manufacturing process on the *Citrus* juice on the concentrations of flavanones. *Alim Nutr* 2008; 19: 379–384
- 218 Singh P, Shukla R, Prakash B, Kumar A, Singh S, Mishra PK, Dubey NK. Chemical profile, antifungal, antiaflatoxigenic and antioxidant activity of *Citrus maxima* Burm. and *Citrus sinensis* (L.) Osbeck essential oils and their cyclic monoterpene, DL-limonene. *Food Chem Toxicol* 2010; 48: 1734–1740
- 219 Tounsi MS, Wannes WA, Ouerghemmi I, Jegham S, Ben Njima Y, Hamdaoui G, Zemni H, Marzouk B. Juice components and antioxidant capacity of four Tunisian *Citrus* varieties. *J Sci Food Agric* 2011; 91: 142–151
- 220 Parmar HS, Kar A. Antidiabetic potential of *Citrus sinensis* and *Punica granatum* peel extracts in alloxan treated male mice. *Biofactors* 2007; 31: 17–24
- 221 Parmar HS, Kar A. Medicinal values of fruit peels from *Citrus sinensis*, *Punica granatum*, and *Musa paradisiaca* with respect to alterations in tissue lipid peroxidation and serum concentration of glucose, insulin, and thyroid hormones. *J Med Food* 2008; 11: 376–381
- 222 Oben J, Enonchong E, Kothari S, Chambliss W, Garrison R, Dolnick D. *Phellodendron* and *Citrus* extracts benefit cardiovascular health in osteoarthritis patients: a double-blind, placebo-controlled pilot study. *Nutr J* 2008; 7: 16–23
- 223 Gholamhoseinian A, Fallah H, Sharifi-far F, Mirtajaddini M. The inhibitory effect of some Iranian plants extracts on the alpha glucosidase. *Iran J Basic Med Sci* 2008; 11: 1–9
- 224 Saraswat M, Muthenna P, Suryanarayana P, Petrash JM, Reddy GB. Dietary sources of aldose reductase inhibitors: prospects for alleviating diabetic complications. *Asia Pac J Clin Nutr* 2008; 17: 558–565
- 225 Ramful D, Tarnus E, Rondeau P, Da Silva CT, Bahorun T, Bourdon E. Citrus fruit extracts reduce advanced glycation end products (AGEs) and H₂O₂-induced oxidative stress in human adipocytes. *J Agric Food Chem* 2010; 58: 11 119–11 129
- 226 Al-Said MS, Tariq M, al-Yahya MA, Rafatullah S, Ginnawi OT, Ageel AM. Studies on *Ruta chalepensis*, an ancient medicinal herb still used in traditional medicine. *J Ethnopharmacol* 1990; 28: 305–312
- 227 Barboza J, Hilje L, Durón J, Cartín V, Calvo M. Phagodeterrence by a crude extract of common rue (*Ruta chalepensis*, Rutaceae) and its partitions on *Hypsipyla grandella* (Lepidoptera: Pyralidae) larvae. *Rev Biol Trop* 2010; 58: 1–14
- 228 Nakano Y, Matsunaga H, Saita T, Mori M, Katano M, Okabe H. Antiproliferative constituents in Umbelliferae plants II. Screening for polyacetylenes in some Umbelliferae plants, and isolation of panaxynol and faltarindiol from the root of *Heracleum moellendorffii*. *Biol Pharm Bull* 1998; 21: 257–261
- 229 Kitajima J, Ishikawa T, Fujimatu E, Kondho K, Takayanagi T. Glycosides of 2-C-methyl-D-erythritol from the fruits of anise, coriander and cumin. *Phytochemistry* 2003; 62: 115–120
- 230 Ishikawa T, Kondo K, Kitajima J. Water-soluble constituents of coriander. *Chem Pharm Bull (Tokyo)* 2003; 51: 32–39
- 231 Gray AM, Flatt PR. Insulin-releasing and insulin-like activity of the traditional anti-diabetic plant *Coriandrum sativum* (coriander). *Br J Nutr* 1999; 81: 203–209
- 232 Eidi M, Eidi A, Saeidi A, Molanaei S, Sadeghipour A, Bahar M, Bahar K. Effect of coriander seed (*Coriandrum sativum* L.) ethanol extract on insulin release from pancreatic beta cells in streptozotocin-induced diabetic rats. *Phytother Res* 2009; 23: 404–406
- 233 Ishikawa T, Takayanagi T, Kitajima J. Water-soluble constituents of cumin: monoterpene glycosides. *Chem Pharm Bull (Tokyo)* 2002; 50: 1471–1478
- 234 Takayanagi T, Ishikawa T, Kitajima J. Sesquiterpene lactone glucosides and alkyl glucosides from the fruit of cumin. *Phytochemistry* 2003; 63: 479–484
- 235 Sachin BS, Sharma SC, Sethi S, Tasduq SA, Tikoo MK, Tikoo AK, Satti NK, Gupta BD, Suri KA, Johri RK, Qazi GN. Herbal modulation of drug bioavailability: enhancement of rifampicin levels in plasma by herbal products and a flavonoid glycoside derived from *Cuminum cyminum*. *Phytother Res* 2007; 21: 157–163
- 236 Hajlaoui H, Mighri H, Noumi E, Snoussi M, Trabelsi N, Ksouri R, Bakhrouf A. Chemical composition and biological activities of Tunisian *Cuminum cyminum* L. essential oil: a high effectiveness against *Vibrio* spp. strains. *Food Chem Toxicol* 2010; 48: 2186–2192
- 237 Roman-Ramos R, Flores-Saenz JL, Alarcon-Aguilar FJ. Anti-hyperglycemic effect of some edible plants. *J Ethnopharmacol* 1995; 48: 25–32
- 238 Jagtap AG, Patil PB. Antihyperglycemic activity and inhibition of advanced glycation end product formation by *Cuminum cyminum* in streptozotocin induced diabetic rats. *Food Chem Toxicol* 2010; 48: 2030–2036
- 239 Lee HS. Cuminaldehyde: aldose reductase and alpha-glucosidase inhibitor derived from *Cuminum cyminum* L. seeds. *J Agric Food Chem* 2005; 53: 2446–2450
- 240 Ayoub NA, Kubecka KH, Nawwar MA. An unique n-propyl sesquiterpene from *Eryngium creticum* L. (Apiaceae). *Pharmazie* 2003; 58: 674–676
- 241 Twaij H, Abdel-Jalil H, Ibrahim J. Screening methods for the possible hypoglycaemic activity of Jordanian medicinal plants (Part II). *Jordan J Appl Sci (Nat Sci)* 2002; 4: 16–21