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 country with substantial biodiversity that is at large understudied or, even worse, left unexplored [9].

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 ethnomedicine 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 evaluated 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
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 *Emblica 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 officinalis*, *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. Gharabeh et al. [19] investigated the hypoglycemic effects of *Teucrium polium* in normal and STZ-diabetic rats. Hamdan and Affii [20], Affii 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 cultivated 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. polium*, 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 ethnomedically 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. syracicum*, *L. nobilis*, *C. sativum*, *C. cymiu*, *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*, *P. 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*, *Citrus coloynthis*, *Aloe vera*, *Eucalyptus globules*, *Plantago major*, *P. ovata*, *Ruta chalepensis*, *Eryngium ceticum* 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. judaica* 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

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**Table 1**

<table>
<thead>
<tr>
<th>Herb</th>
<th>Summary</th>
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</thead>
<tbody>
<tr>
<td><em>Achillea santolina</em></td>
<td>Hypoglycemic bioactivity of cinchonain Ib from <em>Eriobotrya japonica</em></td>
</tr>
<tr>
<td><em>Eryngium creticum</em></td>
<td>Hypoglycemic bioactivities of <em>Paronychia argentea</em></td>
</tr>
<tr>
<td><em>P. pumilum</em></td>
<td>Hypoglycemic bioactivities of <em>Ferula asafoetida</em></td>
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<tr>
<td><em>Ballota nigra</em></td>
<td>Hypoglycemic effects of <em>Artemisia sieberi</em></td>
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<tr>
<td><em>A. herba-alba</em></td>
<td>Hypoglycemic, antihyperglycemic, and preventive effects</td>
</tr>
<tr>
<td><em>A. judaica</em></td>
<td>Hypoglycemic, antihyperglycemic, and preventive effects</td>
</tr>
<tr>
<td><em>A. vulgaris</em></td>
<td>Hypoglycemic, antihyperglycemic, and preventive effects</td>
</tr>
<tr>
<td><em>Citrus coloynthis</em></td>
<td>Hypoglycemic, antihyperglycemic, and preventive effects</td>
</tr>
<tr>
<td><em>Aloe vera</em></td>
<td>Hypoglycemic, antihyperglycemic, and preventive effects</td>
</tr>
<tr>
<td><em>Eucalyptus globules</em></td>
<td>Hypoglycemic, antihyperglycemic, and preventive effects</td>
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<tr>
<td><em>Plantago major</em></td>
<td>Hypoglycemic, antihyperglycemic, and preventive effects</td>
</tr>
<tr>
<td><em>P. ovata</em></td>
<td>Hypoglycemic, antihyperglycemic, and preventive effects</td>
</tr>
<tr>
<td><em>Ruta chalepensis</em></td>
<td>Hypoglycemic, antihyperglycemic, and preventive effects</td>
</tr>
<tr>
<td><em>Eryngium ceticum</em></td>
<td>Hypoglycemic, antihyperglycemic, and preventive effects</td>
</tr>
<tr>
<td><em>C. sinensis</em></td>
<td>Hypoglycemic, antihyperglycemic, and preventive effects</td>
</tr>
<tr>
<td><em>Ceratonia siliqua</em></td>
<td>Hypoglycemic, antihyperglycemic, and preventive effects</td>
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<tr>
<td><em>Juglans regia</em></td>
<td>Hypoglycemic, antihyperglycemic, and preventive effects</td>
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<tr>
<td><em>Morus nigra</em></td>
<td>Hypoglycemic, antihyperglycemic, and preventive effects</td>
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<tr>
<td><em>C. siliqua</em></td>
<td>Hypoglycemic, antihyperglycemic, and preventive effects</td>
</tr>
<tr>
<td><em>J. regia</em></td>
<td>Hypoglycemic, antihyperglycemic, and preventive effects</td>
</tr>
<tr>
<td><em>M. nigra</em></td>
<td>Hypoglycemic, antihyperglycemic, and preventive effects</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>No.</th>
<th>Family</th>
<th>Species</th>
<th>Reported phytoconstituents</th>
<th>Reported antidiabetic efficacy and/or action mechanism</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Asteraceae</td>
<td><em>Artemisia herba-alba</em> Asso. (syn.: <em>A. inculta</em>) (decocition of flowers, shoots, leaves [15, 49, 50])</td>
<td>Flavonoids [51]. Main essential oil components: β-thujone and α-thujone, 1,8-cineole, camphor, chrysanthene, trans-sabinyl acetate, trans-pinenocarveol, and borneol [52]</td>
<td>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]</td>
</tr>
<tr>
<td>2</td>
<td>Asteraceae</td>
<td><em>A. judaica</em> L. (infusion of flowering tops [56, 57])</td>
<td>Judaicing: a bitter principle [58]. Piperitone, trans-ethyl cinnamate, ethyl-3-phenyl propionate, spathulenol, cis-ethyl cinnamyl, 2,6-dimethyl phenol, methyl cinnamate [59]. Flavonoids [60]</td>
<td>Antidiabetic effect sin 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 androst-4-ene-3,17-dione metabolism [61]</td>
</tr>
<tr>
<td>3</td>
<td>Asteraceae</td>
<td><em>A. vulgaris</em> L. (infusion of flowering head [15])</td>
<td>Estrogenic flavonoids [62], jacosidine, eupafolin, luteolin, quercetin, apigenine, aesculetin, esculetin-6-methylene, and scopoletin [63], Yomogin [64]. Dicaffeoylquinic acids [65]. Sesquiterpene lactones and a novel aromatic compound [66]. Trans-thujone, cis-thujone, chrysanthene, 1,8-cineole, sabine, β-pinene, artemisia ketone, carophyllene, oxygenated monoterpines, sesquiterpenes [67]. Flavonoid aglycon: quercetin 3,7,3′-trimethyl ether [68]</td>
<td>None</td>
</tr>
<tr>
<td>4</td>
<td>Asteraceae</td>
<td><em>Cichorium intybus</em> L. (decoction of flowers, roots [69])</td>
<td>Dietary fructans [70]. Anthocyanins [71]. Sesquiterpene lactones of guaiane and germacrane type. Lactucoporicin, 8-desoxylactucin, and three sesquiterpene lactone glycosides: crepidiaside B, sonchuside A, and ierioside D [72]. Lactucin and lactucopricin: sesquiterpene lactones [73]. Quercetin, kaempferol, luteolin, apigenin, coryssoeriol and caffeoyl derivatives, polyphenols [74]. Flavonoids [75]. A guaianolide sesquiterpene glycoside, cichotyboside [76]. Tannins, chlorogenic acid along with caffeic acid derivatives [77]</td>
<td>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 glutathione S-transferases in the liver of diabetic NOD mice [81]. Its dietary fructan 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 adipo genesis 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-secretion promoting principles [86]. Neuroprotection by stimulating AChE activity in brains of alloxan diabetic rats [87]</td>
</tr>
<tr>
<td>5</td>
<td>Asteraceae</td>
<td><em>Cichorium pumilum</em> L. (decoction of aerial parts [50, 69])</td>
<td>Flavonoids [88]; guaianolides [89]; eudesmanolides, eight lactucin-like guaianolides and phenolics, eudesmane-type sesquiterpene lactones [90]</td>
<td>None</td>
</tr>
<tr>
<td>6</td>
<td>Cactaceae</td>
<td><em>Opuntia ficus-indica</em> (L.) Mill. (edible fruits [15])</td>
<td>Polyphenols and flavonoids: ferulic acid, the chief derivative of hydroxycinnamic acid, rutin, and isorhamnetin derivatives [91]. Betacynans and betaxanthins [92]. Kaempferol and isorhamnetin glycosides (glucoside and rhamnoside) [93]</td>
<td>Hypoglycemic effects [94]</td>
</tr>
<tr>
<td>7</td>
<td>Capparaceae</td>
<td><em>Capparis spinosa</em> L. (decoction of flowers, fruits [69])</td>
<td>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]. Phytochemistry: rutin, tocopherols, carotenoids, and vitamin C [97]. Flavonoids, indoles, and polyphenolic acids [98]</td>
<td>Potent antihyperglycemic activity in STZ rats without affecting basal plasma insulin concentrations [99]. Hypoglycemic activity [95]</td>
</tr>
<tr>
<td>8</td>
<td>Cucurbitaceae</td>
<td><em>Citrullus colocynthis</em> L. (Schrad) (infusion of dry fruits, seeds [15, 56, 64, 100])</td>
<td>Tertiary and quaternary alkaloids, glycoside and saponin components [101]. Phenolics and flavonoids [102]</td>
<td>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]</td>
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<thead>
<tr>
<th>No.</th>
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<th>Reported antidiabetic efficacy and/or action mechanism</th>
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<tr>
<td>9</td>
<td>Fabaceae</td>
<td><em>Ceratonia siliqua</em> L. (decoction of leaves [107])</td>
<td>Flavonoids: mainly myricetin [108]; Phenolics: mainly gallotannins and proanthocyanidins, tannins, flavonol-glycosides, and traces of isoflavonoids [109–112]; Tannins [113]</td>
<td>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]</td>
</tr>
<tr>
<td>10</td>
<td>Gramineae</td>
<td><em>Avena sativa</em> L. (infusion of seeds [69])</td>
<td>Beta-glucan, minerals, B complex vitamins, protein, fat, minerals [116]; Avenanthramide [117]</td>
<td>Improving glycemic, insulinemic, and lipemic 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] and induced changes of postprandial peptide YY and ghrelin responses [124] and increased postprandial cholecystokinin levels [125]. Dihydroavenanthramide D protects pancreatic beta-cells from cytokine and STZ toxicity [117]</td>
</tr>
<tr>
<td>11</td>
<td>Juglandaceae</td>
<td><em>Juglans regia</em> L. (decoction of leaves [69, 107])</td>
<td>Ellagic acid [126]; Hydrolysable tannins [127]; Daryl-Heptanois [128]; Unsaturated fatty acids, tocopherols, phospholipids, sphingolipids, sterols, hydrocarbons, and volatile compounds, phenolic compounds [129]</td>
<td>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]</td>
</tr>
<tr>
<td>12</td>
<td>Labiatae</td>
<td><em>Mentha spicata</em> L. (infusion of seeds, oil [56])</td>
<td>Protocatechualdehyde, protocatechuic acid, chrysoeriol, 5,6-dihydroxy-2,8,3′,4′-tetramethoxylflavone, niflorellin [134]. Two lignans named spicatolignan A and spicatolignan B [135]. Carvone; monoterpene ketone [136] and menthone [137]; Flavonoids [138]; Piperitene oxide 1,8-cineole [139]</td>
<td>None</td>
</tr>
<tr>
<td>13</td>
<td>Labiatae</td>
<td><em>Origanum syriacum</em> L. (decoction of leaves [15])</td>
<td>Monoterpenes glucosides [140], oxygenated monoterpenes and sesquiterpenes [141]; Polar phenolic analytes; hydroxyl-benzoates, hydroxyl-cinnamates, and flavonoids [142]. Carvacrol, thymol, and thymoquinone [143]. Rosmarinic, oleolic, and ursolic acids [144], γ-terpinene and p-cymene [145]</td>
<td>None</td>
</tr>
<tr>
<td>15</td>
<td>Liliaceae</td>
<td><em>Allium cepa</em> L. (raw bulbs, oil, leaves [18, 56, 107])</td>
<td>Flavonoid glycosides [150]; α-alk(en)yl cysteine sulfoxide metabolites [151, 152]; S-allylcysteine sulfoxide, S-methylcysteine sulfoxide, and dialyl trisulfide [153]; quercetin [154]; onionin A [155]</td>
<td>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]</td>
</tr>
<tr>
<td>16</td>
<td>Liliaceae</td>
<td><em>Aloe vera</em> L. (infusion of leaves, juice [15])</td>
<td>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: aloeisin, aloe-emo din, and barbaloin, N-terminal octapeptide derived from verectin [162] and triglucosylated naphthalene glycoside [163]</td>
<td>Hypoglycemic or antidiabetic effects [164] thereby indicated for the treatment of diabetes and dyslipidemia [165]</td>
</tr>
</tbody>
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### Table 1 Selected plants indigenous to Jordan used for the treatment of diabetes in folk medicine.

<table>
<thead>
<tr>
<th>No.</th>
<th>Family</th>
<th>Species</th>
<th>Preparation Method</th>
<th>Reported phytoconstituents</th>
<th>Reported antiidiabetic efficacy and/or action mechanism</th>
</tr>
</thead>
<tbody>
<tr>
<td>17</td>
<td>Moraceae</td>
<td>Morus nigra L. (decoction of leaves [107])</td>
<td>Anthocyanins [166], Oleanolic acid, apigenin, cyclocommunol, morusin, cyclomorusin, kuwanon C, daucosterol [167], Essential minerals, nutritive components, total phenols, and alkaloid contents [168]. A new 2-arylhentofuran derivative, monigrol D, G, and H along with nororacarpin, dihydrokaempferol, albanin A, albanin E, moracin M, and albafluran C [169].</td>
<td>Antihyperglycemic propensity via significant increases in catalytic concentration of glutathione S-transferases in the liver of diabetic NOD mice [170, 171]</td>
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<tr>
<td>18</td>
<td>Myrtaceae</td>
<td>Eucalyptus globulus Labill. (decoction of leaves, oil [18])</td>
<td>Heteroxylan composed of galactosyl, 4-O-methylglucuronosyl and xylosyl residues [172], Ellagic acid derivatives; 3-O-methylflavaglucic acid 4′-O-α-L-rhamnopyranoside, ellagic acid, and 3-O-methylflavaglucic acid 4′-O-α-L-rhamnopyranoside, camaldulenside (cycloprocacop C, 3-O-methylflavaglucic acid 4′-O-α-L-rhamnopyranoside, 3-O-methylflavaglucic acid, ellagic acid, and gallic acid [174]) and cypellocarpa C [175].</td>
<td>In vitro stepwise enhancement of insulin secretion from the clonal pancreatic beta-cell line (BRIN-BD11) and enhancement of 2-deoxyglucose 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, polypidipia, 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]</td>
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<tr>
<td>19</td>
<td>Plantaginaceae</td>
<td>Plantago major L. (decoction of seeds [69])</td>
<td>Ursolic acid [181], Polysaccharides, lipids, caffeic acid derivatives, stigmasterol, betulinic acid, and saponins [182].</td>
<td>Significant antihyperglycemic effect in experimental diabetic rats [185, 186]</td>
<td></td>
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<tr>
<td>20</td>
<td>Plantaginaceae</td>
<td>P. ovata Forsk. (decoction of seeds [69])</td>
<td>Neutral arabinofuranos [187], Phytoesters; β-sitosterol and stigmasterol [188], Saponin [189].</td>
<td>Fasting blood glucose and HbA1c showed a significant reduction, whereas HDL-Cholesterol increased significantly. LDL/HDL ratio was significantly decreased in diabetic outpatients [190]</td>
<td></td>
</tr>
<tr>
<td>22</td>
<td>Rosaceae</td>
<td>Crataegus aronia L. Bosc. ex DC (decoction of flowers, fruits [196])</td>
<td>Phenolics and flavonoids [197].</td>
<td>Hypoglycemic and antioxidative bioactivities in experimental diabetic rats [198]</td>
<td></td>
</tr>
<tr>
<td>23</td>
<td>Rosaceae</td>
<td>C. azarolus L. (decoction of flowers, fruits [107])</td>
<td>Polyphenols [199].</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td>24</td>
<td>Rutaceae</td>
<td>Citrus limon (Linn.) Burm. (fresh fruits [56])</td>
<td>Hydroxycinnamates and polymethoxylated flavonoids 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 dimethylellagic acid [207], 3′-O-methylellagic acid, 3-macrocarpal A, oleanolic acid, 3,4,3′-O-trimethylellagic acid, 3-O-methylflavaglucic acid 4′-O-(2′-O-acetyl)-α-L-rhamnopyranoside, camaldulenside (cycloprocacop C, 3-O-methylflavaglucic acid 4′-O-α-L-rhamnopyranoside, 3-O-methylflavaglucic acid, ellagic acid, and gallic acid [174]) and cypellocarpa C [175].</td>
<td>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]</td>
<td></td>
</tr>
<tr>
<td>25</td>
<td>Rutaceae</td>
<td>C. parodii Macfa (raw fruits [69])</td>
<td>Alkaloids, flavonoids, cardiac glycosides, tannins, and saponin [200, Fanuracoumarins [210]. Naringenin [204] and nootkatone [211], 4′-geranylxyferolic acid [212]. Limonoids: nomilin and limonin [205].</td>
<td>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-induced body weight gain, abdominal fat accumulation, and the development of hyperglycemia, hyperinsulinemia, and hyperleptinemia in C57BL/6J mice [211]</td>
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</table>
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
7 World Health Organization. WHO Publications 2011: Fact Sheet No 312

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

<table>
<thead>
<tr>
<th>No.</th>
<th>Species</th>
<th>Preparation Method</th>
<th>Reported phytoconstituents</th>
<th>Reported antidiabetic efficacy and/or action mechanism</th>
</tr>
</thead>
<tbody>
<tr>
<td>26</td>
<td>Rutaceae C. sinensis (L.) Osbeck (decoction of peels [69])</td>
<td>Phenolics: chlorogenic acid, luteolin, myricetin, naringenin, p-coumaric acid, and quercitin; and flavonoids – mainly hesperidin [215, 216]. Flavanones [217]; Cyclic monoterpenes, DL-limonene [218]; Ascorbic acid [219]</td>
<td>Maximum glucose lowering and antiperoxidative activities in alloxan diabetic mice [220]; Antihyperglycemic, 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 H2O2 induced oxidative stress in human adipocytes [225]</td>
<td></td>
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<tr>
<td>27</td>
<td>Rutaceae Ruta chalepensis L. (decoction of leaves, buds, roots [49])</td>
<td>Alkaloids, flavonoids, coumarins, tannins, volatile oil, steroids and/or triterpenes [226], and rutin, a flavone glycoside [227]</td>
<td>None</td>
<td></td>
</tr>
</tbody>
</table>
Afifi Yazar Fu et al. Medicinal Plants from... Part 2... Planta Med 2011; 77: 1210–1220


88 Saleh MR, Metwally AM, Amer MM. Isolation of a flavonoid substance from Cichorium pumilum Jaq. Pharmazie 1975; 30: 404


91 Gabor EM, Mondello MR, Giuffrida D, Dugo G, Miceli N, Pergolizzi S, Tavio MA. Chemical characterization and biological effects of Sicilian Opuntia ficus indica (L.) mill. Fruit juice: antioxidant and anticycloc-


97 Tili N, Khalidi A, Trili S, Munne-Bosch S. Phenolic compounds and vita-
min antioxidants of car (Capparis spinosa). Plant Foods Hum Nutr 2010; 65: 260–265


99 Eddouks M, Lernhadi A, Michel JB. Car: potential anti-


101 Abdel-Hassan IA, Abdel-Bary JA, Tarig Mohammmed S. The hypogly-

102 Kumar S, Kumar D, Manjusha, Saroha K, Singh N, Vashishta R. Antioxid-


108 Vaya J, Mahmood S. Flavonoid content in leaf extracts of the fig (Ficus carica L.), carob (Ceratonia silique L.) and pistachio (Pistacia lentiscus L.). Biofactors 2006; 28: 169–175
139 Kodzoe FT, Kofi TK, Akoto BO. Chemical composition of essential oils against the West Nile virus mosquito Culex pipiens. Parasitol Res 2010; 107: 327–335

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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 Zhen Yao Za Zhi 2007; 32: 496–500


177 Gray AM, Flat PR. Antihyperglycemic actions of Eucalyptus globulus (eucalyptus) are associated with pancreatic and extra-pancreatic effects in mice. J Nutr 1998; 128: 2319–2323


181 Samuelsen AB. The traditional uses, chemical constituents and biological activities of Plantago major L. A review. J Ethnopharmacol 2000; 71: 1–21


209 Genovese S, Epifano F, Carlucci G, Marcotullio MC, Curini M, Locatelli M. New 4


212 Parmor HS, Kar A. Antidiabetic potential of Citrus sinensis and Punica granatum peel extracts in alloxan treated male mice. Biofactors 2007; 31: 17–24

213 Parmor HS, Kar A. Medicinal values of fruit peels from Citrus sinensis, Punica granatum, and Musa paradisica with respect to alterations in tissue lipid peroxidation and serum concentration of glucose, insulin, and thyroid hormones. J Med Food 2008; 11: 376–381


217 Ramofu D, Ternus E, Rondoule 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: 1119–1129


219 Barboza J, Hilje L, Duron J, Carth V, Calvo M. Phagodeterrence by a crude extract of common rue (Ruta chalepensis, Rutaceae) and its par
tions on Hipsyipyla grandella (Lepidoptera: Pyralidae) larvae. Rev Biol Trop 2010; 58: 1–14

220 Nakano Y, Matsuenga H, Saita T, Mori M, Katano M, Okabe A. Anti-proliferative constituents in Umbelliferae plants II. Screening for polycy

221 Kitajima J, Ishikawa T, Fujimata E, Kondo H, Takeyamani T. Glycosides of 2-C-methyl-D-erythritol from the fruits of anise, coriander and cumin. Phytochemistry 2003; 62: 115–120

222 Ishikawa T, Kondo K, Kitajima J. Water-soluble constituents of cori

223 Gray AM, Freti PR. Insulin-releasing and insulin-like activity of the tradi


225 Ishikawa T, Takeyamani T, Kitajima J. Water-soluble constituents of cu
m; monoterpenoid glucosides. Chem Pharm Bull (Tokyo) 2002; 50: 1471–1478

226 Takeyamani T, Ishikawa T, Kitajima J. Sesquiterpene lactone glucosides and alkyl glycosides from the fruit of cumin. Phytochemistry 2003; 63: 479–484

227 Sachin BS, Sharma SC, Sethi S, Tasaqa SA, Tikoo MK, Tikoo AK, Satti NK, Gupta BD, Suri KA, John RK, Gazi GN. Herbal modulation of drug bio


229 Roman-Ramos R, Flores-Saenz JL, Alarcon-Aguilar FJ. Anti-hyperglyce

230 Jagtap AC, Patil PR. Anti hyperglycemic activity and inhibition of ad

231 Lee HS. Cuminaldehyde: aldose reductase and alpha-glucosidase inhib

232 Ayoub NA, Kubeckzka KH, Nawwar MA. An unique n-propyl sesqui
pene from Eryngium cicutricum L. (Apiaceae). Pharmazie 2003; 58: 674–676