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Iranian Medicinal Plants for Diabetes Mellitus: A Systematic Review

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Abstract: In the Iranian traditional medicine a significant usage of herbs is promoted for their anti-diabetic activity. The aim of this review to assess the efficacy of glucose lowering effects of medicinal plants cultivated in Iran. An electronic literature search of MEDLINE, Science Direct, EMBASE, Scopus, Web of Science, Cochrane Library Database, Ebsco and Google Scholar from database inception conducted up to May 2012. A total of 85 studies (18 humans and 67 animals) examining 62 plants were reviewed. The quality of Randomized Controlled Trials (RCTs) assessed by using the Jadad scale. Among the RCTs studies, the best results in glycemic control was found in *Aloe vera*, *Citrullus colocynthus*, *Plantago ovata*, *Silybum marianum*, *Rheum ribes* and *Urtica dioica*. The majority of plants that have been studied for antidiabetic activity showed promising results. However, efficacy and safety of the most plants used in the treatment of diabetes are not sufficient.

Key words: Diabetes mellitus, medicinal plant, herbal medicine, traditional medicine

INTRODUCTION

Diabetes mellitus is a group of metabolic disorders which are characterized by chronic hyperglycemia, resulting from defects in insulin secretion or insulin action (Patel *et al*., 2012). The disease causes substantial morbidity, mortality, long term complications and is defined as an important risk factor for cardiovascular disease (Yeh *et al*., 2003). It is predicated that the number of diabetic patients in the world could reach up to 366 million by the year 2030 (Patel *et al*., 2012). Approximately two million people (7.7%) of Iranian adults, aged 25-64 years, have been diagnosed as diabetic and about 4.4 million(16.8%) of them have impaired fasting glucose (Mirbadalalzadeh and Shirdel, 2010). Since, ancient times, plants have played an important role in the treatment of many diseases. Different parts of medicinal plants such as leaf, root, flower and seed are used as extracts and chemical compounds to produce drugs (Nikbakht *et al*., 2008). Properties of medicinal plants are due to the presence of various complex chemical substances categorized as alkaloids, glycosides, flavonoids, saponins, tannins, carbohydrate and essential oils (Najafi *et al*., 2010). Today, more than 400 plants in traditional medicine are reported for the treatments of diabetes, although only some of them have been evaluated (Modak *et al*., 2007). The use of plants for the treatment of diabetes has been common among the Iranian population (Hasani-Ranjbar *et al*., 2008). Plants which have been shown to have hypoglycemic activity affect on blood glucose through different mechanisms (Estakhr and Javdan, 2011). Many medications currently used in conventional medicine are obtained from natural plants. For instance, Metformin which is the common drug for management of type 2 diabetes with hypoglycemic activity is derived from the plant, *Galega officinalis*. However, there isn't so many evidence about efficacy and safety of medicinal plants glycemic control (Yeh *et al*., 2003). Our objective was to review and summarize the literature on Iranian native medicinal plants which are used to control of glycemia in diabetes, to guide patients and practitioners in advising their patients and to provide recommendations for future research.

MATERIALS AND METHODS

We searched MEDLINE, Science Direct, EMBASE, Scopus, Web of Science, Cochrane Library Database, Ebsco and Google Scholar databases for studies investigating Iranian medicinal plants in prevention and treatment of diabetes from 1998 up to May 2012. The search terms were the reference lists of articles were also

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reviewed for additional relevant studies. The search terms were diabetes, hyperglycemia, plants, herb, traditional and herbal medicine. To assess quality of RCTs we employed the Jadad scale, a previously validated instrument that assesses trials based on appropriate randomization, blinding and description of study withdrawals or drop outs (Jadad *et al*., 1996) (Table 1).

Included criteria: We included randomized control trials studies which evaluate hypoglycemic effect of medicinal plants in diabetic subjects (humans and animals) with the outcome of change in Fasting Blood Glucose (FBG), Postprandial Blood Glucose (PBG) and HbA1c.We limited studies to those published in the English language and restricted search to Iran affiliation. In addition, we did hand search references of key articles.

Excluded criteria: We excluded trials that examined other diabetic complications such as neuropathy, nephropathy, or retinopathy. Studies on type 1 diabetic patients, herbal component, *in vitro* studies, review articles and letters to the editor, unpublished data such as thesis, studies in subjects with impaired glucose tolerance and studies that published by non-Iranian authors. Two reviewers examined the title and abstract and references of each article. The reviewers independently extracted data on the medicinal plant, dose, intervention, trial duration, sample size, outcome and results.

RESULTS

A total of 85 (18 humans and 67 animals) studies were found examining 62 plants. The most common outcomes measures encountered in these trials included Fasting Blood Glucose (FBG), Postprandial Blood Glucose (PBG) and HbA1c. Of publications identified in the initial database search, 18 trials on the efficacy of medicinal plants in type 2 diabetic patients were reviewed. Table 2 presents the controlled clinical trials of medicinal plans for glycemic control in patients with type 2 diabetes. The higher quality RCTs (with Jadad scores of 3 or greater) are available for *Aloe vera*, *Citrullus colocynthus*, *Plantago ovata*, *Silybum marianum*, *Rheum ribes* and *Urtica dioica*.

Aloe vera: Beneficial effect of *Aloe vera* gel on blood glucose and lipid parameters in diabetic patients has been demonstrated in several randomized clinical trials and no adverse effects were reported in these trials (Huseini *et al*., 2012; Williamson *et al*., 2011; Yeh *et al*., 2003). Aloe gel, obtained from the inner portion of the leaves, contains glucomannan, a hydrosoluble fiber which may in part account for its hypoglycemic effects (Yeh *et al*., 2003). The Natural Standard Research Collaboration reported that the oral use of *Aloe vera* gel for its hypoglycemic effects is possibly safe (Williamson *et al*., 2011).

Urtica dioica: The most animal studies have been shown the beneficial effect of *Urtica dioica* in diabetes but only two human studies have been shown this (Mehri *et al*., 2011; Tarighat *et al*., 2012b). *Urtica dioica* can decrease blood glucose both pancreatic and extra pancreatic pathways. Regarding to pancreatic effects, have been suggested that it is a potent stimulator of insulin release from β-cells and has shown protective effect on β-cells in diabetic rats (Fazeli *et al*., 2008; Mehri *et al*., 2011). Inhibited intestinal absorption of glucose and inhibitory effects on the alpha amylase activity are extra-pancreatic mechanisms (Bnouham *et al*., 2003; Nickavar and Yousefian, 2011).

***Silybum marianum*:** *Silybum marianum* is a member of the Asteraceae family and its seed extract contains large numbers of chemical constituents including several flavonolignans collectively known as silymarin. Glycemic control effect of *Silybum marianum* has been demonstrated in four RCTs that decreased FBS and HbA1C significantly (Fallah Hoseini *et al*., 2004, 2005; Huseini *et al*., 2006). *Silybum marianum* improve insulin resistance and ameliorate β-cell restoration (Huseini *et al*., 2006; Soto *et al*., 2010). Adverse effects related to silymarin have been published in several studies involving a total of over 7000 patients and those confirmed that it is safe. Only three reports of significant adverse reactions (Kalantari *et al*., 2011).

***Citrullus colocynthis*:** *C. colocynthis* (L.) Schrad is a member of the Cucurbitaceae family and is used traditionally as an antidiabetic medication (Huseini *et al*., 2009). Two RCTs, in this review demonstrated that *C. colocynthis* significantly decreased FBG and HbA1c in the dose of 300 mg kg^{-1}. The glycemic control effect of *C. colocynthis* mechanisms is not well known, but it may be have an insulin tropic effect on isolated pancreatic islets (Nmila *et al*., 2000) or inhibited the toxic effect of streptozotocin on pancreatic cells in rats (Al-Ghaithi *et al*., 2004; Huseini *et al*., 2009). The toxicity of large doses of *C. colocynthis* has been reported in some animals and humans studies (Huseini *et al*., 2009).

***Rheum ribes*:** *Rheum ribes* known as an α-amylase and α-glucosidase inhibitor (Kasabri *et al*., 2011). One of the RCT studies was conducted on 36 type 2 diabetic

Table 1: Effects of Iranian medicinal plants in animal diabetic models

Plant (scientific name)	References	Target	Other groups	Intervention	Duration	Outcome
Achillea santolina	Yazdanparast *et al.* (2007)	STZ-induced diabetic rats	Diabetic control rats	0.1 g kg^{-1} ethanolic extract of aerial parts	30 days	Sig. decrease FBG
Alium sativum L.	Eidi *et al.* (2006a)	STZ-induced diabetic rats	normal and glibenclamide treated diabetic rats	0.1-0.25-0.5 g kg^{-1} ethanolic extract	14 days	Sig. decrease FBG
Alium sativum L.	Masjedi *et al.* (2010)	STZ-induced diabetic rats	Normal and diabetic control rats	1 mL/100 g BW/day Garlic juice	3 week	Sig. decrease FBG
Allium ampeloprasum	Roghani and Aghaie (2007)	STZ-induced diabetic rats	Normal and diabetic control rats	plant-mixed pelleted food (6.25%)	4 week	Sig. decrease FBG
Allium porrum L.	Eidi *et al.* (2007)	STZ-induced diabetic mic	Normal and diabetic control mic	100, 200, 250, 300 mg kg^{-1} i.p., ethanolic leaves extract	14 days	Sig. decrease FBG
Aloe vera	Jadidoleslami *et al.* (2006)	STZ-induced diabetic rats	Normal and diabetic control rats	100,200,300,400 mg kg^{-1} aqueous extract+5 mg kg^{-1} glibenclamid	4 week	Sig. decrease FBG
Anethum graveolens	Madani *et al.* (2005)	alloxan-induced diabetic rats	Normal and diabetic control rats	300 mg kg^{-1} i.p. hydroalchoholic extract	48 h	Sig. decrease FBG
Asafoetida	Akhlaghi *et al.* (2012)	STZ-induced diabetic rats	Normal and diabetic control rats	50, 100 and 300 mg kg^{-1} root extract	4 week	Sig. decrease FBG
Berberis vulgaris	Hajzadeh *et al.* (2011b)	STZ-induced diabetic rats	Diabetic control rats	3.5% and 7.5% drinking water from a 100 mg mL^{-1} fruit aqueous extract	6 week	No sig. change in FBG
Camellia sinensis L.	Haidari *et al.* (2012)	STZ-induced diabetic rats	Normal and diabetic control rats	100, 200 mg kg^{-1} alcohol extract of leaves	4 week	Sig. decrease FBG,
Carum carvi	Haidari *et al.* (2011)	STZ-induced diabetic rats	Normal and diabetic control rats	1 g kg^{-1} orally	3 week	Sig. decrease FBG
Coriandrum sativum L.	Eidi and Eidi (2009)	STZ-induced diabetic rats	Normal and diabetic control rats	200, 250 mg kg^{-1} i.p., ethanolic seeds extract	1.5, 3, 5 h	Sig. decrease FBG
Cornus mas L.	Shamsi *et al.* (2011)	alloxan-induced diabetic rats	Normal, diabetic control and glibenclamide treated diabetic rats	2 g day^{-1} fruit	4 week	Sig. decrease FBG
Cucumis sativus L.	Minaiyan *et al.* (2011)	STZ-induced diabetic rats	Normal and diabetic control rats	0.2,0.4,0.8 g kg^{-1} hydroalcoholic and buthanolic seed extrac	9 days	Sig. decrease FBG
Cucurbita pepo L.	Asgary *et al.* (2011)	alloxan-induced diabetic rats	Diabetic control rats	1, 2 g kg^{-1} fruit powder	4 week	Sig. decrease FBG
Cucurbita pepo L.	Asgary *et al.* (2011)	alloxan-induced diabetic rats	Normal, diabetic control and glibenclamide treated diabetic rats	1, 2 g kg^{-1} powder	4 week	Sig. decrease FBG
Cyamopsis tetragonolobus L.	Saeed *et al.* (2012)	STZ-induced diabetic rats	Diabetic control and glibenclamide treated diabetic rats	5%, 10%, 20% (w/w) diet	4 week	Sig. decrease FBG
Cynara scolymus	Heidarian and Soofiniya (2011)	STZ-induced diabetic rats	Diabetic control rats	200, 400 mg kg^{-1} leaf aqueous extract	21 days	Sig. decrease FBG
Cynara scolymus	Mahmoodabadi *et al.* (2006)	Alloxan-induced diabetic rats	Normal, diabetic control and glibenclamide-treated rats	300 mg kg^{-1} i.p., hydroalcoholic extract	48 h	Sig. decrease FBG
Equisetum arvense L.	Safiyeh *et al.* (2007)	STZ-induced diabetic rats	Diabetic control rats	50, 100, 250, 500 mg kg^{-1} methanol, n-hexan and dichloromethan extracts	5 week	Sig. decrease FBG
Equisetum arvense L.	Soleimani *et al.* (2007)	STZ-induced diabetic rats	Diabetic control rats	50, 250 mg/kg/day methanolic extract	5 week	Sig. decrease FBG
Eucalyptus globulus L.	Eidi *et al.* (2009b, c)	STZ-induced diabetic rats	Normal and diabetic control rats	0.05, 0.1, 0.2 and 0.4 g kg^{-1} leaves alcoholic extract	21 days	Sig. decrease Chol, ↓ TG
Ficus carica L.	Rashidi and Noureddini (2011)	STZ-induced diabetic rats	Normal and diabetic control rats	0.05, 0.1, 0.4 mg dL^{-1} aromatic water of leaves	3, 6, 12, 24 h	Sig. decrease FBG
Hordeum vulgare L.	Naseri *et al.* (2010)	STZ-induced diabetic rats rats	Normal and diabetic control	Aqueous seed extract	4 week	Sig. decrease FBG
Juglans regia L.	Asgary *et al.* (2008)	Alloxan-induced diabetic rats	Normal, diabetic control and glibenclamide treated rats	200 mg kg^{-1} ethanolic leaves extract	-	Sig. decrease FBG
Juglans regia L.	Kamyab *et al.* (2010)	STZ-induced diabetic mic	Diabetic control mic	400 mg kg^{-1} leaf and ridges extract	5 h	Sig. decrease FBG
Juglans regia L.	Shirdel *et al.* (2009)	Alloxan-induced diabetic rats	Normal and diabetic control rats	100 mg kg^{-1} i.p, hydroalcoholic extract of green husk	10 days	Sig. decrease FBG
Juglans regia L.	Mohammadi *et al.* (2011)	STZ-induced diabetic rats	Normal and diabetic control rats	200,400 mg kg^{-1} alcoholic leaves extract	28 days	Sig. decrease FBG
Juglans regia L.	Rahimi *et al.* (2011)	Alloxan-induced diabetic rats	Normal control rats	0.6 mg kg^{-1} walnut oil	6 week	Sig. decrease FBG

Table 1: Continue

Plant (scientific name)	References	Target	Other groups	Intervention	Duration	Outcome
Juglans regia L.	Teimoori *et al.* (2010)	Alloxan-induced diabetic rats	Diabetic control rats	250, 500 mg kg^{-1} leaves methanolic extract	3 week	Sig. decrease FBG
Juglans regia L.	Jelodar *et al.* (2007)	Alloxan-induced diabetic rats	Diabetic control rats	60 g kg^{-1} Walnut leaf	15 days	Sig. decrease FBG
Morus alba	Hosseinzadeh and Sadeghi (1999)	Alloxan-induced diabetic mice	Normal and diabetic control mic	500 mg kg^{-1} dried plant	7 days	Sig. decrease FBG
Morus nigra	Hoseini *et al.* (2009b)	STZ-induced diabetic rats	Diabetic control rats	5, 10, 100, 200, 400, 600, 800 and 1000 mg kg^{-1} hydro alcoholic extract	2 month	Sig. decrease FBG (only 400, 600 mg kg^{-1} doses)
Morus nigra	Hosseinzadeh and Sadeghi (1999)	Alloxan-induced diabetic mice	Normal and diabetic control mic	500 mg kg^{-1} dried plant	7 days	Sig. decrease FBG
Nasturtium officinale	Hoseini *et al.* (2009a)	STZ-induced diabetic rats	Glibenclamide-treated diabetic rats	100,800, 1000 mg kg^{-1} methanol and ethyl acetate extract	2 month	Sig. decrease FBG
Olea europaea L.	Eidi *et al.* (2004)	STZ-induced diabetic rats	Normal and glibenclamide-treated diabetic rats	0.1, 0.25, 0.5 g kg^{-1} alcoholic leaves extract	14 days	Sig. decrease FBG
Olea europaea L.	Eidi *et al.* (2009a)	STZ-induced diabetic rats	Normal and diabetic control rats	0.1, 0.25, 0.5 g kg^{-1} leaves extract	14 days	Sig. decrease FBG
Opuntia ficus-Indica L.	Kianbakht and Fallah Huseini (2008) and Fallah Huseini *et al.* 2008)	STZ-induced diabetic rats	Normal, diabetic control and glibenclamide treated diabetic rats	6,12 g/kg/day seeds and pulp of the fruit	4 week	Sig. decrease FBG
Otostegia persica	Hedayati *et al.* (2010)	STZ-induced diabetic rats	Normal, diabetic control and glibenclamide treated diabetic rats	100, 200, 300 mg kg^{-1} methanolic extract	14 days	Sig. decrease FBG
Otostegia persica	Hedayati *et al.* (2012)	STZ-induced diabetic rats	Normal, diabetic control and glibenclamide treated diabetic rats	100, 200, 300 mg kg^{-1} extract	14 days	Sig. decrease FBG
Peucedanum pastinacifolium	Movahedian *et al.* (2010)	STZ-induced diabetic rats	Normal and diabetic control rats	125, 250, 500 mg kg^{-1} hydroalcoholic extract	30 days	↑TG, ↑Chol, ↑LDL, ↑HDL
Phlomis anisodonta	Sarkhail *et al.* (2007)	STZ-induced diabetic rats	Diabetic control rats	100, 200, 400 mg kg^{-1} methanolic extract of aerial parts	10 days	Sig. decrease FBG
Phlomis persica	Sarkhail *et al.* (2010)	STZ-induced diabetic rats	Diabetic control and glibenclamide treated diabetic rats	100, 200 mg kg^{-1} Methanol extract of the aerial parts	10 days	Sig. decrease FBG
Physalis alkekengi	Javdan and Estakhr (2011), and Estakhr and Javdan (2011)	Alloxan-induced diabetic rats	Diabetic control rats	25, 50,100 mg kg^{-1} ethanolic extract	30 days	Sig. decrease FBG
Punica granatum L.	Najafzadeh *et al.* (2011)	STZ-induced diabetic rats	Diabetic control and glibenclamide treated diabetic rats	200, 400, 600 mg kg^{-1} Hydroalcoholic peel extract i.p and 600 mg kg^{-1} orally	8 days	Sig. decrease FBG
Pyrus biossieriana Buhse	Shahaboddin *et al.* (2011)	Alloxan-induced diabetic rats		500, 1000 mg kg^{-1} leaf extract	24, 48, 72 h	Sig. decrease FBG
Rhus coriaria	Mohammadi *et al.* (2010)	Alloxan-induced diabetic rats	Normal control, diabetic control and metformin treated rats	200, 400 mg kg^{-1} fruit ethanolic extract	3 week	Sig. decrease FBG
Rumex patientia	Sedaghat *et al.* (2011)	STZ-induced diabetic rats	Normal and diabetic control rats	6%/w seed powder	4 week	Sig. decrease FBG
Salvia hypoleuca	Estakhr and Javdan (2011)	Alloxan-induced diabetic rats	Normal and diabetic control rats	250-450 mg kg^{-1} ethanolic extracts	2 week	Sig. decrease FBG
Salvia lenifolia	Hosseinzadeh *et al.* (1998)	Alloxan-induced diabetic mic	Normal control mic	2 g kg^{-1} leaf extract	-	Sig. decrease FBG
Salvia officinalis L	Eidi *et al.* (2005)	STZ-induced diabetic rats	Normal and placebo treated rats	100, 250, 400, 500 mg kg^{-1} i.p., methanolic extract	1,3,5 h	Sig. decrease FBG
Salvia officinalis L	Eidi *et al.* (2005)	STZ-induced diabetic rats	Normal, diabetic control and glibenclamide treated rats	0.1, 0.2, 0.4 g kg^{-1} ethanolic leaf extract	2 week	Sig. decrease PBG
salvia officinalis L.	Hajzadeh *et al.* (2011a)	STZ-induced diabetic rats	diabetic control rats	430 mg kg^{-1} aqueous and ethanolic extracts i.p,	6 days	No sig. change in FBG
Salvia verticillata L.	Eidi *et al.* (2011)	STZ-induced diabetic rats	Normal control rats	0.05, 0.1, 0.2 g kg^{-1} ethanolic extract orally	2 week	Sig. decrease FBG
Satoreja khozestanica	Abdollahi *et al.* (2003)	STZ-induced diabetic and diet-induced hyperlipidaemic rats	Normal control rats	500-1000 ppm day^{-1} orally	15 days	Sig. decrease FBG

Table 1: Continue

Plant (scientific name)	References	Target	Other groups	Intervention	Duration	Outcome
Satureja khuzestanica Jamzad	Shahsavari *et al.* (2009)	STZ-induced diabetic mic	Diabetic control rats	100 mg kg^{-1} essential oil	3 week	Sig. decrease FBG
Teucrium polium	Esmaeili and Yazdanparast (2004)	STZ-induced diabetic rats	Diabetic control rats	0.5 g kg^{-1} plant powder	6 week	Sig. decrease FBG
Teucrium polium	Shahraki *et al.* (2006)	STZ-induced diabetic rats	Diabetic control rats	50 mg kg^{-1} suspension of aerial parts	30 days	Sig. decrease FBG
Teucrium polium	Yazdanparast *et al.* (2005)	STZ-induced diabetic rats	Diabetic control rats	1 mL day^{-1} plant extract orally	6 week	Sig. decrease FBG
Trigonella foenum graecum	Zahedi-Asl *et al.* (2006)	STZ-induced diabetic rats	Normal and diabetic control rats	4 g kg^{-1} carbon tetrachloride seed extract	3 day	Sig. decrease FBG
Trigonella foeum graecum L.	Eidi *et al.* (2006b)	STZ-induced diabetic rats	Normal and glibenclamide-treated diabetic rats	0.1-0.25-0.5 g kg^{-1} ethanolic extract	14 days	Sig. decrease FBG
Urtica dioica	Golalipour *et al.* (2007)	STZ-induced diabetic rats alloxan-induced diabetic rats	Normal and diabetic control rats	100 mg kg^{-1} i.p., hydroalCholic leaf extract	5 days	Sig. decrease FBG
Vaccinium arctostaphylos	Feshani *et al.* (2011)	STZ-induced diabetic rats	Normal and diabetic control rats	1 mL day^{-1} Ethanolic extract	3 week	Sig. decrease FBG
Vaccinium myrtillus	Roghani *et al.* (2007)	Alloxan-induced diabetic rats	Normal and diabetic control rats	Plant-mixed pelleted food (6.25%)	4 week	Sig. decrease FBG
Ziziphus Jujuba	Shirdel *et al.* (2009)	STZ-induced diabetic rats	Normal and diabetic control rats	100 mg kg^{-1} i.p., hydroalcoholic extract of leaves	5 days	Sig. decrease FBG
Ziziphus vulgaris L.	Solati and Soleimani (2010)	STZ-induced diabetic rats	Normal and diabetic control rats	0.25, 0.5, 1, 1.5, 2 g kg^{-1}, fruit water extracts orally	2 week	Sig. decrease FBG
Zizyphus spina-christi	Avizeh *et al.* (2010)	Alloxan-induced Diabetic Dogs	Diabetic control rats	500 mg kg^{-1} fruit hydroalcoholic extract	10 days	Sig. decrease FBG

Table 2: Effects of Iranian medicinal plants in type 2 diabetic patients

Plant (scientific name)	References	Design	Sample	Intervention (Intervention/control)	Control	Duration	Outcome
Allium sativum	Parastouei *et al.* (2006)	Before-after clinical trail	50 T2DM with hyperlipidaemia	900 mg day^{-1} garlic powder tablet	-	6 week	No sig. change in FBG and HbA1c
Aloe vera L.	Huseini *et al.* (2012)	Double-blind RCT	30/30 T2DM	600 mg day^{-1} Leaf gel capsule	Placebo	2 month	Sig. decrease FBG, HbA1c
Camellia sinensis	Mirzaei *et al.* (2009)	Double-blind RCT	26/46 T2DM	1500 mg day^{-1} green tea extract	Placebo	8 week	No sig. change in FBG and HbA1c
Citrullus colocynthis L	Fallah Huseini *et al.* (2006b)	RCT	22/22 T2DM	300 mg day^{-1} capsule	Placebo	2 month	Sig. decrease FBG and HbA1c
Citrullus colocynthis L.	Huseini *et al.* (2012)	Double-blind RCT	25/25T2DM	300 mg day^{-1} fruit capsules	Placebo+ Antidiabetic drugs	2 month	Sig. decrease FBG and HbA1c
Hibiscus sabdariffa	Mozaffari-Khosravi *et al.* (2009)	Sequential-RCT	27/27 T2DM	15 g day^{-1}		1 month	No sig. change in FBG
Plantago ovata L.	Ziaei *et al.* (2004)	Double-blind -RCT	21/15 T2DM	10 g day^{-1} psyllium husk fiber+low fat diet	Placebo+low fat diet	8 week	Sig. decrease FBG and HbA1c
Rheum ribes L.	Fallah Huseini *et al.* (2008)	Double-blind RCT	18/18 T2DM	1200 mg day^{-1} stalk extract	Placebo	1 month	Sig. decrease FBG
Satureja khuzestanica	Vosough-Ghanbari *et al.* (2010)	Double-blind-RCT	11/10 T2DM	250 mg day^{-1} Dried leaves	Placebo	2 month	No sig. change FBG
Securigera securidaca	Fallah Huseini *et al.* (2006a)	Double-blind -RCT	35/35 T2DM	1500 mg day^{-1}	Placebo+antidiabetic drugs	2 month	No sig. change in FBG and HbA1c
Silybum marianum	Ziai *et al.* (2005)	Double-blind-RCT	21/15 T2DM	10.2 g day^{-1} psyllium husk fiber+antidiabetic		8 week	Sig. decrease FBG and HbA1c
Silybum marianum	Huseini *et al.* (2006)	Double-blind-RCT	25/26 T2DM	600 mg day^{-1} silymarin tablet+antidiabetic	Placebo + antidiabetic drugs	4 month	Sig. decrease FBG and HbA1c
Silybum marianum	Fallah Hoseini *et al.* (2004)	Double-blind RCT	29/25 T2DM	600 mg day^{-1} silymarin tablet	Placebo	4 month	Sig. decrease FBG
Silybum marianum	Fallah Huseini *et al.* (2005)	Double-blind RCT	30/30 T2DM	750 mg day^{-1} silymarin+ standard therapy	Placebo + standard therapy	4 month	Sig. decrease FBG and HbA1c
Trigonella foenum graecum L.	Kassaian *et al.* (2009)	Before-after clinical trial	24 T2DM	10 g day^{-1} powdered seeds	-	8 week	Sig. decrease FBG
Urtica dioica	Tarighat *et al.* (2012a)	Single-blind RCT	25/25 T2DM	100 mg kg^{-1} hydro alcoholic extract	Placebo	8 week	Sig. decrease FBG and HbA1c

RCT: Randomized control trial, T2DM: Type 2 diabetes mellitus, FBG: Fasting blood glucose and HbA1c: Glycosylated hemoglobin

patients. One group received 1200 mg *Rheum ribes* daily in three 400 mg capsule and other received placebo similarly. The results showed a significant decreased in FBS in *Rheum ribes* treated patients compared with control (Fallah Huseini *et al*., 2008). *Rheum ribes* has anti-hyperlipidemic properties and decreased serum lipids significantly (Fallah Hoseini *et al*., 2004; Fallah Huseini *et al*., 2008; Huseini *et al*., 2012; Huseini *et al*., 2006; Vosough-Ghanbari *et al*., 2010).

***Plantago ovata*:** The seeds and the husks of *Plantago ovata* contain high levels of fiber (Hannan *et al*., 2006). *Plantago* psyllium significantly reduce glycemic index of carbohydrate foods. In one clinical trial showed that 8 weeks treatment with 5.1 g psyllium (*Plantago ovata*) two times daily could reduce FBS and HbA1c significantly (Ziai *et al*., 2005). It seems that glucose-lowering effect of *P. ovata* is due to inhibition of glucose absorption in the gut (Hannan *et al*., 2006).

DISCUSSION

Asian continents have 56% share of the worldwide distribution of therapeutic herbal plants (Chan *et al*., 2012). Iran with 1.64 million km^2 areas has 7500-8000 plant species and is an ancient country in usage of medicinal plants. Several medicinal species are cultivated in Iran (Zahedi-Asl *et al*., 2006). This review focuses on some medicinal plants that used to management of diabetes. In this review, a total of 85 human and animal trials of Iranian medicinal plants used for glycemic control were obtained. *Aloe vera*, *Citrullus colocynthus*, *Plantago ovata*, *Silybum marianum*, *Rheum ribe* and *Urtica dioica* have enough efficacy to decrease blood glucose and really effective in reducing blood glucose in diabetic patients (Fallah Hoseini *et al*., 2004, 2005, 2006b, 2008; Huseini *et al*., 2006, 2009, 2012; Sarkhail, 2011; Tarighat *et al*., 2012a; Ziaei *et al*., 2004; Ziai *et al*., 2005).

The obtained information from the various parts of the plants indicated that leaves are the most favorable storage sites for active components. The extraction methods commonly employed in anti diabetic plant extraction are conventional methods involving solvents (Chan *et al*., 2012). Several animal studies also have shown that some medicinal plants are even more effective than chemical drugs such as glibenclamide (Asgary *et al*., 2008; Eidi *et al*., 2006a, 2004; Hedayati *et al*., 2010; Najafzadeh *et al*., 2011). *Salvia officinalis*, *Nasturtium officinale* and *Phlomis anisodonta* have similar effects of glibenclamide in reducing blood glucose (Sarkhail *et al*., 2010). Chemical medicines, because of their harmful and irreversible effects on people, are slowly being replaced by active substances of plants. Despite of beneficial effects, hypoglycaemic effect of these medicinal plants can interfere with hypoglycaemic drugs and insulin. Therefore, physicians should have adequate knowledge about medicinal plants effects on blood glucose to manage patients who are at risk. Any consumption of medicinal plants must be under the supervision of physicians (Hasani-Ranjbar *et al*., 2008).

CONCLUSION

A considerable number of plant species are traditionally used for the treatment of diabetes mellitus in Iran. The majority of those plants that have been studied for anti-diabetic activity showed promising results. However, efficacy and safety of the most plants used in the treatment of diabetes are not sufficient.

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