Trace Elements Content of Some Traditional Plants Used for the Treatment of Diabetes Mellitus

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Abstract: Diabetes is a public health problem that affects life quality. Trace elements have a critical role in the activity and structure of the enzymes involve in carbohydrate metabolism. Many traditional herbs have been used for the treatment and management of Diabetes Mellitus (DM). Anti-diabetic medicinal plants have a significant lowering effect on blood sugar, then assessment of mineral content of these plants has a great value to judge their mechanism of action. Determination of Cobalt (Co), Chromium (Cr), Ferrum (Fe), Manganese (Mn), Molybdenum (Mo), Selenium (Se), Vanadium (V), and Zinc (Zn) values in twenty-eight anti-diabetic plants were conducted and the estimation carried out by atomic absorption spectrophotometry after wet digestion. We found that the levels of Mn, Mo, Co, and Cr were in trace amount, whereas Fe, Se, V and Zn contents were higher. Because of trace elements variations between the studied plants, the hypoglycemic effect of these herbs is not due to a unique element present in the herbs, it rather a synergic effect of several elements might account for the hypoglycemic nature of these plants. Further work is necessary to evaluate this phenomenon.

Keywords: Trace elements; Diabetes mellitus; Anti-diabetic plants; Selenium; Vanadium.

1. Introduction

Diabetes mellitus (DM) is a public health problem and characterized as a chronic metabolic disease that has a serious effect on the life expectancy and quality in the patients, also DM treatment is a global problem. DM has some secondary long time effects that deteriorating the patient's condition including retinopathy, kidney disorder, and cardiac effects [1,2]. Medicinal plants showed several beneficial effects over wide range diseases and the researchers focus on the medicinal plants properties to find new, safe and potent agents to improve and/or cure diseases including DM [1,3-6]. Traditional and medicinal plants are widely used around the world as a treatment for DM and several studies have proved anti-diabetic effect of many species of plants such as: *Cressa cretica* L. [7], *Trigonella-foenum graecum*, *Syzygium jambolona*, *panax ginseng* [8], *Morus alba* Linn [9], *Allium cepa* [10], *Cinnamomum zeylanicum*, *Cinnamomum cassia* [11], *Melina azadiracta* [12], *Coriandrum sativum* [13], *Rosa damascene, and Quercus infectoria* [5].

Trace elements are necessary and essential for good health [2,7]. Trace elements and some metals serve as cofactors in many enzymatic reactions; they also have some critical roles in the physiological processes in the body including carbohydrate homeostasis and metabolism.

Any abnormalities in essential metabolic elements can cause dysfunction and disorder [3,14]. Trace elements have been identified as potential candidates for some metabolic dysfunction such as DM, insulin resistance, obesity, and metabolic syndrome [3,4,7,10]. It reported that some trace elements deficiencies can promote DM complications and also there reports that proved that some trace elements were reduced in patients with DM [7,14-17]. Several studies have been proved that there is a relationship between the development of DM and some trace elements levels. The most important trace elements that related to the DM are Chromium (Cr), Zinc (Zn), Selenium (Se), and Vanadium (V) [16-18,20].

Cr is related to glucose metabolism and is important for normal glucose homeostasis and involved in insulin action as a part of GTF (Glucose tolerance factor). Cr deficiency is characterized by hyperglycemia, impaired glucose tolerance, and lipid disorders [16-19, 21]. Zn is correlated with insulin biosynthesis and secretion from pancreas β-cells [3,16]. Zn plays a pivotal role in the stabilization of insulin hexamer and insulin storage in the pancreas and increases insulin concentrations in both types of DM (type 1 and 2). On the other hand, Zn also acts as an efficient antioxidant and defends the cells against free radicals [3,17,20]. Se reduction was reported in DM [3,16]. V also possesses anti-diabetic properties and described as an insulin-mimetic element [14,16,18].

Trace element contents of anti-diabetic plants are variable. Narendhirakannan and colleagues studied the elemental composition of four traditional medicinal plants. They found that various trace elements such as V, Zn, Cr, and Nickel (Ni) can be counted for hypoglycemic effect of those plants [10,22]. Mineral contents of some different species of the genus Ficus Linn that have anti-diabetic properties were conducted by atomic absorption spectrophotometry. The results showed that these species of Ficus genus are a good source of required elements for patients and they contain some specific trace elements that can improve insulin action [1].

Currently available therapeutic options for DM such as dietary change, taking oral hypoglycemic agents, and insulin therapy have shown to have their own limitations. Many natural products and herbal medicines have been recommended for the treatment of DM [23]. In Iran, some traditional plants have been consumed by diabetic people to reduce their health problems but their involved active agents are not well known. Probably trace elements can be considered as responsible for these plants' pharmacological effects. For this reason, some plants commonly consumed to reduce blood glucose were analyzed for their trace element contents using atomic absorption spectrophotometry.

2. Materials and Methods

Medicinal plants were purchased from the medicinal herbal markets in Kerman city and all of them were botanically identified and a voucher specimen of each plant was deposited at the herbarium of the Herbal Medicine Research Center Faculty of Pharmacy, Kerman University of Medical Sciences, Iran (Table 1). About 0.5 gr of the dried and grounded plant samples were digested in nitric acid overnight at room temperature. Then samples heated for 4 hours. The digested samples were cooled and dissolved in 50 mL of deionized water and were used for the assay of trace elements through atomic absorption Spectrophotometry. The standard curve of each element was obtained by dilution of stock solutions [24,25].

A Varian flameless atomic absorption spectrophotometer, model 220 AA, equipped with a Varian graphite furnace and auto sampling system were used in all determinations. As the light source, a hollow cathode lamp from Varian was used and pyrolytic coated graphite

tubes was utilized as atomizer. The conditions for analysis were based on the instructions presented by the instrument manual. Samples of 25 µ L were carried to the graphite tube by the auto sampling system and submitted to the furnace established conditions.

3. Results and Discussion

The concentration of elements analysed in this study was ordered and showed in table 1, and mineral contents of the anti-diabetic plants presented in table 2.

Interestingly, *Allium sativum* showed maximum content of Vanadium (V). In five other plants Selenium (Se) was leading trace elements regarding content that they are including: *Apium graveolens*, *Cannabis sativa*, *Juniperus communis*, *Teucrium polium* and *Zataria multiflora*. Fe content of the rest of plants was higher than other elements. The orders of Ferrum (Fe)> Se> Zinc (Zn)> and Fe> Se> Zn> V were more frequent in plants of our study. Minimum and maximum of minerals in studied plants are showed in table 3.

Table 1. Families, Species, used parts and profile of concentration ordered elements in the anti-diabetic plants.

Species	Family	Utilized part	Profile of elements conc.
Allium cepa	Alliaceae	Bark	Fe> Zn> V> Se> Mo> Co> Cr> Mn
Allium Sativum	Amaryllidaceae	Fruit	V> Fe> Se> Zn> Mo> Co> Cr> Mn
Apium graveolens	Umbelliferae	leaves	Se> Fe> Zn> Co> V> Mo> Mn> Cr
Actium lappa	Asteraceae	Root	Fe> Zn> V> Se> Mo> Co> Cr> Mn
Cannabis sativa	Cannabaceae	Seed	Se> Zn> Fe> Mn> Co> V> Cr> Mo
Capparis spinosa	Lauraceae		Fe> V> Zn> Se> Co> Mo> Cr> Mn
Cinnamomum zeylanica	Lauraceae	Bark	Fe> Mn> Se> V> Zn> Co> Mo> Cr
Citrullus colocynthis	Cucurbitaceae	Fruit	Fe> Se> Zn> V> Co> Cr> Mo> Mn
Coriandrum sativum	Alliaceae		Fe> Se> Zn> V> Mo> Co> Cr> Mn
Cucumic sativus	Cucurbitaceae	Bark	Fe> V> Zn> Se> Co> Mo> Cr> Mn
Cuminum cyminum	Alliaceae	Seed	Fe> V> Se> Zn> Co> Cr> Mo> Mn
Datura stramonium	Solanaceae	Seed	Fe> Se> Zn> Co> V> Mo> Cr> Mn
Ficus carica	Moraceae	Leaves	Fe> Se> V> Zn> Mo> Co> Cr> Mn
Fumaria parviflora	Fumariaceae	Arial part	Fe> Se> V> Zn> Mo> Mn> Cr> Co
Glycyrrhiza glabra	Fabaceae	Root	Fe> Se> Zn> V> Mo> Co> Cr> Mn
Juglans regia	Juglandaceae	Leaves	Fe> Se> Zn> Mn> V> Co> Cr> Mo
Juniperus communis	Cupressaceae	Flower	Se> Fe> V> Zn> Mn> Co> Cr> Mo
Lactuca sativa	Asteraceae	Leave	Fe> Se> Zn> Co> V> Mo> Mn> Cr
Morus alba	Moraceae	Leave	Fe> Se> V> Zn> Mn> Co> Cr> Mo
Plantago psyllium	Plantaginaceae		Fe> Zn> Se> V> Co> Mo> Mn> Cr
Punica granatum	Lythraceae	Bark	Fe> Se> V> Zn> Co> Mo> Cr> Mn
Sesamum indicum	Pedaliaceae	Seed	Fe> Se> Zn> V> Co> Mo> Cr> Mn
Spinacia oleracea	Chenopodiaceae	Leave	Fe> V> Se> Zn> Mn> Co> Cr> Mo
Teucrium polium	Lamiaceae	Arial parts	Se> Fe> Zn> Mo> V> Co> Cr> Mn
Trigonella foenum-graecum	Fabaceae	Seed	Fe> Se> Zn> V> Mo> Cr> Co>Mn
Urtica urens	Uricaceae	Arial pars	Fe> Se> Zn> V> Co> Cr> Mn> Mo
Vaccinium arctostaphylos	Ericaceae	Fruit	Fe> Se> Zn> Mn> V> Co> Cr> Mo
Zataria multiflora	Lamiaceae	Arial paarts	Se> V> Zn> Fe> Cr> Mo> Mn> Co

Trace elements have been characterized for a long time as anti-diabetic agents. They are involved in metabolism and enzymatic reactions in the body [3,16]. In this study, we showed elemental contents of some traditional plants which is used as an anti-diabetic sources. We assessed elements that their anti-diabetic properties have already been shown including Cr, Cobalt (Co), Fe, Manganese (Mn), Molybdenum (Mo), Se, V and Zn [3,8]. In one out of 28 plants V content was maximum, and in five out of 28 Se content were maximum and in the rest of plants, Fe was the main element. Zucchi et al. assessed many elements concentration including trace elements we used in this study, in eight hypoglycemic plants [8]. They reported that in some of these plants trace elements like Se, Cr and V were not detected, and this report is challenging this fact that these elements have hypoglycemic effects. They also have reported that Cr, Mo, Se and V were not detected in *Trigonella foenum graecum*, a potent anti-diabetic

plant, which is totally in contrast with our results. On the other hand, they showed the order of Fe> Mn> Zn> Co for other detected elements [8] and we showed this order: Fe> Se> Zn> V> Mo> Cr> Co>Mn.

Table 2. Trace elements concentration of plants (μg/g dry wt).

Plants	Co	Cr	Fe	Mn	Mo	Se	V	Zn
Allium cepa	1.309	0.515	19.45	0.12	1.915	2.4	4.03	4.221
Allium Sativum	0.911	0.476	6.1	0.12	1.12	4.0	10.36	2,868
Apium graveolens	1.346	0.597	6.04	0.64	1.112	7.9	1.28	4.706
Arctium lappa	1.365	0.548	16.23	0.25	1.818	3.1	5.12	5.215
Cannabis sativa	1.408	0.665	22.09	1.57	0.032	9.4	1.27	5.741
Capparis spinosa	1.35	0.497	18.63	0.01	0.615	2.4	5.2	4.388
Cinnamomum zeylanica	1.023	0.835	11.68	5.27	0.99	4.6	4.34	2.693
Citrullus colocynthis	0.9	0.425	11.89	0.03	0.195	8.0	3.61	3.945
Coriandrum sativum	0.899	0.788	22.09	0.52	0.915	13.1	1.58	3.695
Cucumic sativus	1.222	0.487	24.89	0.28	0.717	2.4	5.2	3.776
Cuminum cyminum	1.00	0.835	33.39	0.48	0.815	5.2	7.95	4.074
Datura stramonium	1.27	0.346	36.84	0.16	0.412	9.7	1.27	3.997
Ficus carica	1.42	0.785	10.07	0.11	2.001	5.2	4.62	2.926
Fumaria parviflora	0.147	1.104	20.39	1.19	2.04	7.9	5.14	3.447
Glycyrrhiza glabra	0.911	0.266	22.45	0.17	1.0	5.3	1.29	3.407
Juglans regia	1.281	1.108	43.02	2.63	0.037	14.0	1.43	3.716
Juniperus communis	0.983	0.857	12.79	1.01	0.817	27.0	5.98	3.588
Lactuca sativa	1.471	0.335	8.41	0.86	1.018	6.5	1.36	3.7
Morus alba	1.553	1.205	7.24	1.76	0.989	5.2	4.99	3.151
Plantago psyllium	1.281	0.09	11.52	0.72	1.111	4.3	4.03	6.227
Punica granatum	1.391	0.879	24.87	0.19	1.115	5.8	5.64	3.225
Sesamum indicum	1.156	0.634	30.92	0.23	1.145	14	1.39	5.338
Spinacia oleracea	1.427	1.022	21.1	2.62	1.008	5.2	5.51	3.834
Teucrium polium	1.264	0.905	5.87	0.74	3.001	13	1.3	5.278
Trigonella foenum-graecum	0.852	0.93	9.65	0.75	1.18	7.9	1.7	3.691
Urtica urens	1.329	1.156	13.27	0.24	0.038	13	1.53	3.184
Vaccinium arctostaphylos	0.718	0.159	13.9	1.23	0.095	5.7	1.22	5.361
Zataria multiflora	0.766	1.039	2.53	0.91	1.008	5.8	5.17	3.703

Table 3. Minimum and maximum of minerals in studied plants.

Element	Min	Max
Co	*Fumaria parviflora*	*Morus alba*
Cr	*Plantago psyllium*	*Morus alba*
Fe	*Zataria multiflora*	*Juglans regia*
Mn	*Capparis spinosa*	*Cinnamomum zeylanica*
Mo	*Cannabis sativa*	*Teucrium polium*
Se	*Allium cepa, Cucumic sativus, Capparis spinosa*	*Juniperus communis*
V	*Vaccinium arctostaphylos*	*Allium sativum*
Zn	*Cinnamomum zeylanica*	*Plantago psyllium*

Narendhirakannan and colleagues also investigated the mineral contents of four medicinal plants used in the treatment of diabetes by AAS analysis. They investigated Cr, Zn, V, and Fe. The elements profile of four plants showed that Fe was maximum and Zn was minimum between these four elements. This profile is almost different from the profile that we showed in table 1. The average of Cr contents in our study was lower, and on the other hand, the average of Fe, Zn and V contents of our plants were higher than Narendhirakannan and coworkers study [22].

Investigations support this fact that deficiency of some trace elements in diabetic patients plays a great role in the development of diabetes mellitus [3,17,20]. Zhou et al (2019) have reported that Cr levels were reduced in patients with type 2 DM [18]. Ahmed et al (2018) reported that Cr, Zn and Mg significantly reduced in people with DM, they also reported that between patients with either type 1 or type 2 of DM there was no difference in trace element profile [14]. Kazi et al (2008) have shown that the mean values of Cr, Mn and Zn were

significantly reduced in blood samples of diabetic patients and also they showed that the urinary levels of these elements were higher in diabetic patients than the control group [26]. This study proved the pivotal protective role of trace elements against diabetes mellitus. Then the plants which have insulin-mimetic, hypoglycemic and anti-diabetic properties may conduct these properties by helpful effects of trace elements contents. Our anti-diabetic plants showed great content of essential trace elements. Other studies also showed that some of these anti-diabetic plants are a good source of essential trace elements [8,22,10].

The contents of Fe, Se, V, and Mn are higher than other elements in the current study, and it seems that these elements are more important than other elements in plants that we studied. Altered iron homeostasis is associated with DM [27]. In twenty-two anti-diabetic plants, Fe content was higher than other elements that point to the important impact of Fe on DM. Se reduction observed in DM and there is an association between Se reduction and increased oxidative stress [3]. Se concentrations in some of the plants including; *Juniperus communis*, *Sesamum indicum* and *Juglans regia* were higher than others that indicate a potential negative association of these plants with DM, also these plants are a candidate as anti-oxidant resources. Harati et al (2003) showed that administration of a low dose of Vanadyl sulfate can preserve functional characteristics of β-cells and thereby can be an insulin resistance preventive agent [28]. V has been known because of its insulin-mimetic and anti-diabetic properties [3,16]. *Allium sativum* is the only plant in this study that showed a higher concentration of V than other elements and this supports anti-diabetics properties of *Allium sativum* [29] and anti-diabetic role of V that has been proved earlier [28]. Zn plays an important role in the storage and structure of insulin and the association between Zn deficiency and DM has been documented [3,16,17,20]. In many of our studied plants, Zn was in high concentration and proved that it is an effective ingredient in anti-diabetic plants.

4. Conclusions

Finally, in our study 8 elements were determined in 28 anti-diabetic plants. We showed that the concentration of Fe, Zn, Se and V were in higher than other elements. It seems that hypoglycemic effect of studied plants is not due to a unique element present in the herb. Probably there is a synergic effect of several elements in these plants. Authors suggesting that further study on these plants for their protecting effects against DM regarding elemental content of them are necessary. Also, heavy metal and Mercury content of these plants if exists, should be assessed to be sure that these plants have no toxic effects on human.

Conflicts of Interest

The authors declare no conflict of interest.

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