*Article*

**Volume 10, Issue 5, 2020, 6167 - 6173**

<https://doi.org/10.33263/BRIAC105.61676173>

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

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Scopus Author ID [36470992900](https://www.scopus.com/authid/detail.uri?authorId=36470992900)

**Received: 23.04.2020; Revised: 7.05.2020; Accepted: 9.05.2020; Published: 12.05.2020**

**Abstract:** Diabetes is a public health problem that affects life quality. Trace elements have a criticalrole 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.



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**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.

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<https://doi.org/10.33263/BRIAC105.61676173>



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

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<https://doi.org/10.33263/BRIAC105.61676173>



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

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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

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<https://doi.org/10.33263/BRIAC105.61676173>



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 apotential 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 importantrole 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.

**Funding**

This research received no external funding.

**Acknowledgments**

We would like to appreciate Mr. Mohmmadhassan Beigi’s kind helps, also we appreciate Kerman Medical University Research Council for their help and support.

**Conflicts of Interest**

The authors declare no conflict of interest.

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<https://doi.org/10.33263/BRIAC105.61676173>



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