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Full Length Research Paper

Major and trace elements in *Nigella sativa* provide a potential mechanism for its healing effects

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The seeds of *Nigella sativa* are used commonly in the Middle East as a traditional medicine to treat a variety of health conditions. Its seeds and oil have been used for centuries in the Islamic World, as sacred and holistic medicine. It has been also used in India and other countries for similar purposes. In the Middle East, it is a popular addition to the traditional diet, and is often mixed with either bread or honey. Commercial use of these seeds has recently been extended to many products including shampoos, oils, soaps, etc. The plant is also commonly known as black seeds, black cumin and black caraway seed. Twenty five seed samples of *Nigella sativa* were collected from four Middle Eastern countries: Qatar, Palestine, Egypt and Syria. Two analytical methods (XRF and ICP/OES) were used for the determination of Ag, Al, As, Ba, Br, Ca, Cl, Cd, Co, Cr, Cu, Fe, K, Mg, Mn, Ni, P, Pb, Rb, S, Se, Si, Sr, Th, Ti, Zn and U. Concentrations of Ca and K were found in all samples at the percentage levels. Ag, As, Co, Pb, Se, Si, Th and U were below the lower limit of detection of both analytical methods. The remaining elements were found in considerable concentrations in all the samples from the four countries. *Nigella* seeds provide relatively high amounts of some essential nutrients including Mn, Zn, Cu and Fe. Although the therapeutic mechanism of *Nigella sativa* is unknown, the presence of the trace elements that are essential nutrients and important for immune functioning, such as Mn, Fe, Cu, and Zn, suggests one possible mechanism.

Key words: *Nigella sativa*, trace metals, ICP/OES, EMMA/XRF.

INTRODUCTION

In recent times, interest in medicinal properties of traditional plant-based therapeutics has increased worldwide resulting in a growing body of evidence showing therapeutic potential of traditional medicinal plants. *Nigella sativa* (black cumin or black seed) offers a good example.

The name *N. sativa* comes from the Latin word, *nigellus*, meaning black. *N. sativa* is an annual flowering plant that grows 20-30 cm tall and is native to Asia and the Middle East. The plant has small black seeds that have a slightly rough texture and an oily interior. They have a pungent bitter taste and a faint smell of strawberries. The seeds have been used extensively in all levels and religions in Asia, the Middle East and Africa as herbal medicine, in religious ceremonies, and for cooking. In Islam, the seeds are regarded as a prophetic remedy with immense healing power. The prophet Muhammad once stated that the black seed can heal every disease except death. Consequently, it was used by both Muslims and non-Muslims for thousands of years. The seeds were also used by the ancient Romans in cooking and by Asian herbalists for many remedies, including migraines. The seeds have been found in several sites from ancient Egypt, including Tutankhamun’s tomb.

The seeds and the oil are considered to be the greatest healing herb of our time in the east and thousands of scientific studies have been published on all aspects of medicine. *N. sativa* is used therapeutically to strengthen the immune system, fight cancer, purify the blood and increase longevity. Since 1959, over 5000 studies at international universities and articles published in various journals have shown positive results supporting its traditional uses (Cheikh-Rouhou et al., 2007). Examples of plant medical uses mentioned in recent publications are: antiasthmatic (Kanter, 2009; Boskabady et al., 2010), antidermatophytic (Aljabre et al., 2005), antiepileptogenic (Ilhan et al., 2005), antioxidant (Zaoui et al., 2002; Mariod et al., 2009), antimetastatic (Al-Jishi and

Abuo Hozaifa, 2003), immunomodulatory (Salem, 2005), blood glucose regulator (Meddah et al., 2009), leukocyte phagocytic regulator (Haq et al., 1995), lipid peroxidation level regulator (Hosseinzadeh et al., 2007), therapeutic of liver damage (Mahmoud et al., 2002), neuropharmacological activity regulator (Al-Naggar et al., 2003), therapeutic for pancreatic cancer (Banerjee et al., 2009). Moreover, while studies document the effectiveness of the black seed by itself, ongoing studies with the combination of other herbs have also documented healing potential.

N. sativa's chemical composition is diverse. In addition to its primary ingredient, crystalline nigellone, the seeds contain 15 amino acids, complete proteins, carbohydrates, both fixed oils (84% fatty acids, including linolenic, and oleic), and volatile oils, alkaloids, saponin, and crude fiber, as well as minerals such as calcium, iron, sodium and potassium (Ghosheh et al., 1999; Cheikh-Rouhou et al., 2007; Al-Bataina et al., 2003). There are still many components in the plant seeds that have not been identified (Özcan and Akbulut, 2007).

This study was undertaken to determine comprehensively major and trace elements in the seeds of *N. sativa* using two analytical methods. Moreover, the study aimed to provide an insight to the suggested healing properties of *N. sativa* seeds by highlighting the importance of some of the analyzed elements in the human body.

METHODOLOGY

Sample collection

Five samples were collected from each of the following countries: Qatar, Palestine, Egypt and Syria where the seeds are locally grown and it was found that the seeds have been stored under similar conditions. The samples were purchased from five different large plant stores in November and December 2009 and they were preserved as they used to be sold in each country. Samples of 100 g each were put in plastic bags or cups as sold (that is, without processing or preserving) and shipped to the Institute of Earth Sciences at Heidelberg University, Germany for analysis.

Sample preparation and analysis

Once the samples were in Germany, they were ground manually and treated similarly. Sample aliquots (approximately 200 mg) were weighed to 0.1 mg into 20-mL polytetrafluoroethylene (PTFE) vessels. The acid mixtures contained 3 mL of HNO_3 and 0.1 mL of HBF_4. A starting pressure of 50 bar (with Ar) was applied to the reaction chamber. Vessels were then heated in the microwave autoclave for 76 min, increasing the temperature up to 240°C; during this phase the pressure in the reaction chamber reached about 120 bars. After cooling for about 90 min to well below the boiling point of the acid mixture at atmospheric pressure, the reaction chamber was opened. Colorless, homogeneous digestion solutions were obtained, indicating efficient destruction of the organic matter. The contents of the digestion vessels were quantitatively transferred into graduated 15-mL polypropylene tubes (Falcon, Becton Dickinson, Meylan Cedex, France) and filled to the mark with high-purity water. The digested samples, blanks and reference materials were analyzed using Inductively Coupled Plasma-Optical Emission Spectrometer (ICP/OES) VISTA-MPX, VARIAN.

Quality control

For additional quality control, plant standard reference materials (SRM), spinach and apple leaves (NIST 1570a and NIST 1515, respectively), with certified elemental concentrations were analyzed with every batch of samples (Table 1). Analysis of SRM (NIST 1570a) was performed for validation of the applied analytical procedure ICP/OES. Concentrations of elements were measured in samples mineralised by mixture of HNO_3 and HBF_4 in a closed system with the aid of microwave energy. Each plant sample was digested twice. Each diluted digestion solution was analyzed for trace elements by ICP/OES twice, yielding a total of four analytical values per sample that agreed within an uncertainty of <5%.

As a complementary measurement and for further quality control, a second measurement technique, the Energy-dispersive miniprobe X-ray fluorescence multielement analysis (EMMA) was used. The XRF was carried out with a conventional X-ray tube with Mo anode, focused concave LiF (220) variable wavelength monochromator, and sample holder (EMMA Analytical Inc., Elmvale, Ontario, Canada). Aluminum, Si, K, Ti, Cr, Mn, Fe, Ni, Cu, Zn, Ga, As, Br, Rb, Sr, Y, Pb, Ca, P, Cl, Th, Zr, U, S, and Se were measured in the microprobe mode directly on dried, milled seed samples with no further sample preparation, using a beam size of 0.1×6.0 mm and a rotating sample holder allowing samples 25 rotations per minute, with a 600 s analysis time. With this configuration, samples were rotated 250 times per analysis. Calibration, lower limits of detection, accuracy, and precision of this method are given elsewhere (Cheburkin and Shotyk, 1996; Shotyk et al., 2000).

RESULTS AND DISCUSSION

Results of the analyses for the plant standard reference material (NIST 1570a) are shown in Table 1. For most of the examined elements, good agreement between obtained data and certified values was observed. For Al and Cu, the differences in concentrations (measured and certified) were within the limits of standard deviation (± 5%); while the differences in concentrations of Cd, Mn and Ni were ±10%. The differences in concentrations for the rest of the tested parameters were 20%. Table 2 shows findings for the two methods of analysis (XRF and ICP/OES). Generally, the two methods showed a very good agreement which is consistent with previous studies of Shomar (2006, 2009). Figure 1 shows the comparison between average tested parameters for the four countries.

Ag, As, Cr, Pb, Se, Si and U were below the lower limit of detection. Several trace elements (Fe, Cu, Zn, Mn, etc.), which are essential micronutrients required for various body functions and well-being of the immune system, were within the normal ranges (Table 2). It is well known that Fe, Cu, Zn, Mn, etc., have immunomodulatory functions and thus influence the susceptibility to the course and the outcome of a variety of viral infections (Chaturvedi et al., 2004; Devi et al., 2008).

Al-Bataina et al. (2003) found the following

Table 1. Certified values and experimental results of standard reference material (SRM) by ICP/OES.

Parameter	Certified SRM (1) Spinach leaves	Experimental data (n=12)
Ag (mg/kg)	ND	< 0.24
Al (mg/kg)	310 ± 11	298 ± 10
As (mg/kg)	0.068 ± 0.012	< 2.5
Ba (mg/kg)	ND	7.3 ± 0.2
Br (mg/kg)	ND	< LLD
Ca (%)	1.527 ± 0.041	NM
Cl (mg/kg)	ND	NM
Cd (mg/kg)	2.89 ± 0.07	3.2 ± 0.3
Co (mg/kg)	0.39 ± 0.05	0.5 ± 0.1
Cr (mg/kg)	ND	2.0 ± 0.1
Cu (mg/kg)	12.2 ± 0.06	12 ± 0.3
Fe (mg/kg)	ND	242 ± 11
K (%)	2.903 ± 0.052	NM
Mg (%)	ND	< LLD
Mn (mg/kg)	75.9 ± 1.9	67 ± 1.6
Ni (mg/kg)	2.14 ± 0.10	2.6 ± 0.2
P (mg/kg)	0.518 ± 0.011	NM
Pb (mg/kg)	ND	0.5 ± 0.2
Rb (mg/kg)	ND	NM
S (mg/kg)	ND	NM
Se (mg/kg)	0.117 ± 0.009	NM
Sr (mg/kg)	55.6 ± 0.8	37 ± 18
Th (mg/kg)	0.048 ± 0.003	NM
Ti (mg/kg)	ND	NM
Zn (mg/kg)	82 ± 3	95 ± 8
U (mg/kg)	ND	NM

ND: No data, NM: not measured by this method, LLD: lower limit of detection.

concentrations (mg/kg dry weight) for *N. sativa* seeds from Jordan: K, 12000; Mg, 3800; Ca, 9000; P, 5700; Fe, 220; Cu, 85; Zn, 94; Mn, 64; Al, 72; S, 2900; Rb, 8 Sr, 13. More recent study of Cheikh-Rouhou et al. (2007) analyzed several elements in seeds collected from Tunisia and the average concentrations (mg/kg, dry weight) were: K, 783; Mg, 235; Ca, 572; Na, 21; P, 50; Fe, 9; Cu, 1.7; Zn, 8; and Mn, 4.4 mg/kg.

Summary of the major findings of this study could be categorized according to their average concentrations (Figure 1) on the following:

Aluminum and Copper

Compared to the study of Özcan and Akbulut (2007), Al contents were high in all samples of the four countries and ranged from 67 mg/kg in Palestine to 136 mg/kg in Syria. At an average of 10 mg/kg copper concentrations were lowest in the samples from Palestine (10 mg/kg) while (average) concentrations in the other three countries ranged from 13 - 18 mg/kg. The plants were able to accumulate the highest amount of copper in a considerable amount (Sheded et al., 2006). Reddy and Reddy (1997) reported that the range of Cu contents in 50 medicinally important leafy materials growing in India were 17.6-57.3 mg/kg. Copper is an essential nutrient for people because it is required for a wide range of biological functions such as enzymatic and redox reactions (McLaughlin et al., 1999).

Barium, Bromine and Chlorine

Although Ba is reported to be commonly present in plants, it apparently is not an essential component of plant tissues. The Ba concentrations in all samples were low (6-17 mg/kg), but with the normal plants ranges of 1 to 200 mg/kg (DW) (Kabata-Pendias and Pendias, 2001). Bromine, on the other hand, could be bound into miscellaneous small molecules of the plants, including antibiotics and porphyrins. It is documented that marine plants contain more Br than do land plants and the natural Br contents of plants seems not to exceed 40

Table 2. Major and trace elements in *Nigella sativa* collected from four Middle Eastern countries Using ICP/OES and EMMA-XRF.

Parameter	Unit	Qatar (n=5)		Palestine (n=5)		Egypt (n=5)		Syria (n=5)	
		ICP/OES	XRF	ICP/OES	XRF	ICP/OES	XRF	ICP/OES	XRF
Ag	mg/kg	<0.24	NM	<0.24	NM	<0.24	NM	<0.24	NM
Al		95 ± 8	NM	67 ± 9	NM	99.2 ± 10	NM	136 ± 29	NM
As		<2.5	<1.5	4.5 ± 1	<1.5	<2.5	<1.5	<2.5	<1.5
Ba		14.1 ± 2	NM	5.6 ± 1	NM	14 ± 3	NM	16.8 ± 4	NM
Br		NM	2.0 ± 0.2	NM	2.8 ± 0.6	NM	1.8 ± 0.2	NM	1.3 ± 0.2
Ca		NM	7100 ± 1005	NM	4200 ± 902	NM	8500 ± 1119	NM	8500 ± 1230
Cl		NM	433 ± 99	NM	430 ± 88	NM	467 ± 98	NM	696 ± 187
Cd		0.1	NM	0.1 ± 0.05	NM	1.0 ± 0.2	NM	0.3 ± 0.1	NM
Co		<0.23	NM	0.5 ± 0.1	NM	<0.23	NM	<0.23	NM
Cr		0.3 ± 0.1	<1.5	1.7 ± 0.03	<1.5	4.2 ± 0.5	<1.5	<0.23	<1.5
Cu		16.6 ± 3	15.1 ± 4	10 ± 2	10.2 ± 3	14.5 ± 3	15.9 ± 3	14.6 ± 3	17.5 ± 4
Fe		96	89 ± 14	2461 ± 688	3342 ± 795	114 ± 44	135 ± 65	149 ± 33	179 ± 68
K		NM	8800 ± 897	NM	4800 ± 877	NM	9900 ± 1017	NM	9300 ± 1000
Mg		2405 ± 850	NM	1200 ± 358	NM	2356 ± 413	NM	2342 ± 768	NM
Mn		43 ± 11	48.1 ± 8	44 ± 7	47.4 ± 8	47.4 ± 8	52.1 ± 10	43 ± 6	46.4 ± 8
Ni		6.1 ± 1.5	6.1 ± 1.2	3.0 ± 0.8	3.6 ± 1	6.3 ± 2	6.0 ± 2	5.0 ± 2	4.9 ± 1
P		NM	4804 ± 789	NM	2281 ± 649	NM	4823 ± 698	NM	4329 ± 888
Pb		0.8 ± 0.1	<0.8	0.6 ± 0.1	<0.8	<0.25	<0.8	0.8 ± 0.1	<0.8
Rb		NM	6.5 ± 2	NM	3.3 ± 0.9	NM	6.6 ± 2	NM	<0.7
S		NM	3238 ± 775	NM	1566 ± 288	NM	3183 ± 839	NM	2961 ± 998
Se		NM	<0.7	NM	<0.7	NM	<0.7	NM	<0.7
Sr		30 ± 7	32.8 ± 6	22 ± 5	23.7 ± 4	34 ± 5	39.4 ± 8	21 ± 3	23.6 ± 5
Th		NM	<2.5	NM	<2.5	NM	<2.5	NM	<2.5
Ti		NM	7.2 ± 2	NM	42.4 ± 8	NM	9.3 ± 2	NM	10.9 ± 3
Zn		65 ± 9	59.6 ± 13	30 ± 4	33.7 ± 5	62.2 ± 7	59.9 ± 11	67 ± 9	64.8 ± 8
U		NM	<2.5	NM	<2.5	NM	<2.5	NM	<2.5

NM: Not measured by this method.

mg/kg. Higher values should be related to pollution (Kabata-Pendias and Pendias, 2001). All samples showed very low concentrations of Br (1-3 mg/kg). Chloride was detected in considerable concentrations in all samples for the four countries.

The concentration was much lower than that measured in more than 30 medicinal plants for the same countries (Shomar, 2010, Unpublished data).

Calcium, Potassium and Magnesium

The range of Ca varied up to two-fold, with values between 0.42% in Palestine and 0.85% in Egypt and Syria. Qatar samples showed 0.71% of Ca.

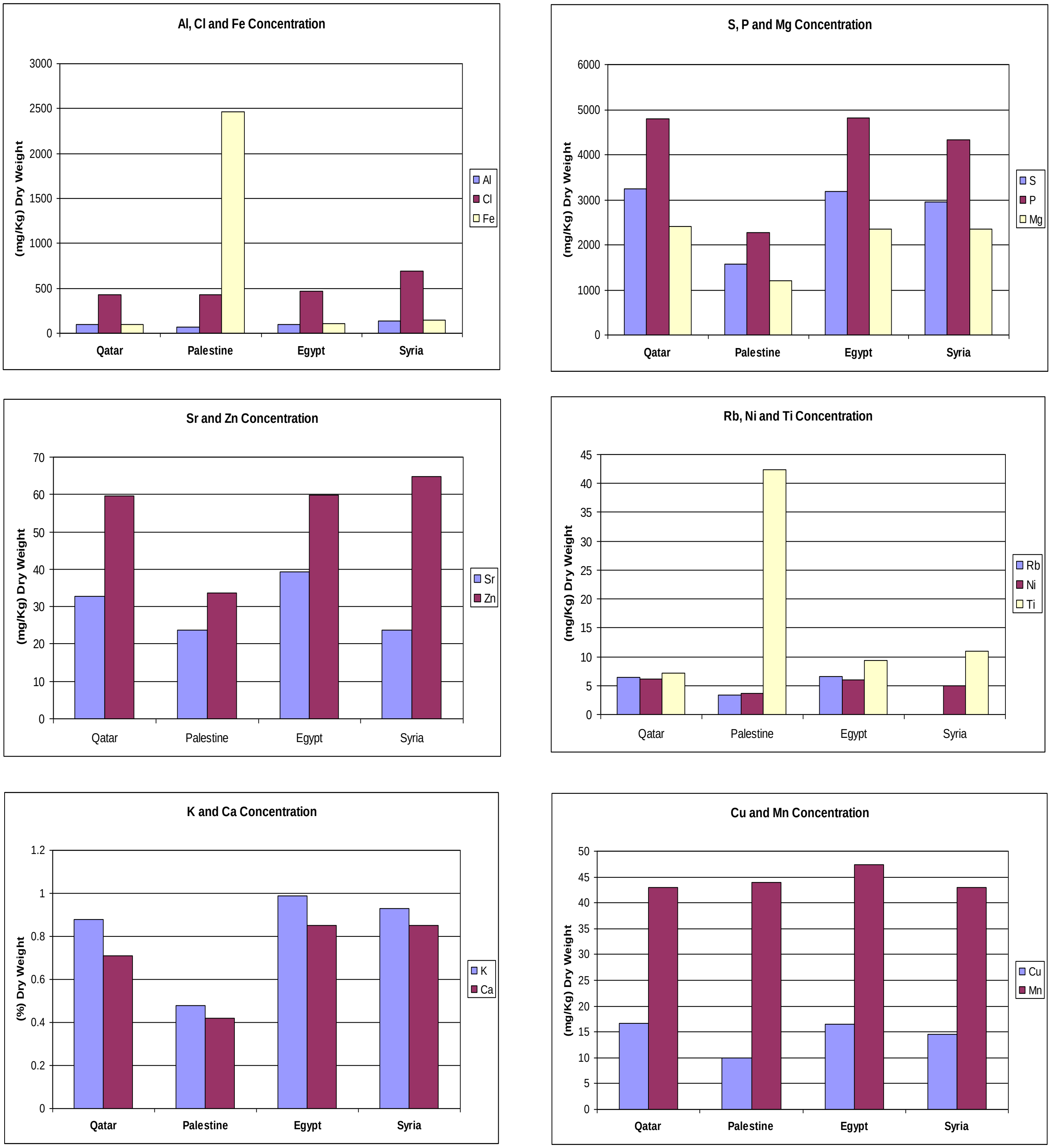

Figure 1. Comparison between tested elements for the four countries.

High amounts of Ca are important because of its role in bones, teeth, muscle system and heart functions (Brody, 1994). It is well known that Ca is essential for bones, etc., and these concentrations in the seeds are high enough to be a good source of Ca.

From Table 2, it is observed that appreciable concentrations of K (ranging from 0.5 to 1%) were found in all samples from the four countries. Potassium is a multifunctional nutrient and forms an essential part of many important enzymes (Sizer and Whitney, 1999).

Magnesium is critical to many cell functions. It assists in the operation of more than 300 enzymes, is needed for the release and use of energy from the energy-yielding nutrients, and directly affects the metabolism of K, Ca and vitamin D (Devi et al., 2008). It is important for healthy bones and acts in the cells of soft tissues, where it is part of the protein-making machinery and is necessary for the release of energy. A magnesium concentration of 1200 mg/kg was found in the samples from Palestine which is half of the concentrations found in the other three countries (2400 mg/kg).

Arsenic, Cadmium, Cobalt, Chromium, Lead and Nickel

Concentrations of As, Cd, Co, Cr, Pb and Ni were very low or not detected in all samples (Table 2). These toxic elements cause both acute and chronic poisoning, and can adversely affect the kidney, liver, heart, vascular and immune system (Heyes, 1997). Low levels of these toxic elements in the seeds from the four countries are a benefit.

Iron and Manganese

Samples from all countries showed considerable concentrations of Fe which supports the use of the seeds for treating anemia. The samples from Qatar showed the lowest concentration of Fe (93 mg/kg), while the highest concentration was found in the seeds from Palestine (3000 mg/kg). Samples from Egypt and Syria showed similar concentrations of 110 and 180 mg/kg, respectively. Iron is an important element in human body and plays a role in oxygen and electron transfer. It is necessary for the formation of haemoglobin (Dalziel, 1936; Kaya and Incekara, 2000).

All samples showed similar Mn concentrations averaging about 45 mg/kg. This value is within normal concentrations of Mn in plants of 20-300 mg/kg (Kabata-Pendias and Pendias, 2001). Manganese is one out of three toxic essential trace elements, which means that it is not only necessary for humans to survive, but it is also toxic when too high concentrations are present in a human body. The adult human body contains about 10 to 20 mg of Mn most of this is concentrated in the pancreas, bone, liver, and kidneys. Mn acts as a catalyst and cofactor in many enzymatic processes involved in the synthesis of fatty acids and cholesterol. Mn is an important cofactor in the enzymes necessary for mucopolysaccharide synthesis and an essential cofactor of important enzymes active in the mitochondria, and in the synthesis of glycoproteins, which coat body cells and protect against invading viruses. Moreover, many of the metabolic functions in which manganese is an important cofactor can use magnesium and manganese interchangeably (Dobson et al., 2007; Au et al., 2008; Cabrera et al., 2010).

Phosphorus and Zinc

Phosphorous was found in all samples with a range of 2300 to 5000 mg/kg. The high levels are indicative that it is essential for plant growth. In humans, phosphorus compounds carry, store and release energy and they assist many enzymes and vitamins in extracting the energy from nutrients (Devi et al., 2008).

The concentration of Zn ranged between 30 mg/kg in samples from Palestine and 67 mg/kg in samples from Syria (Table 2); the concentrations of Zn in the samples from Qatar and Egypt were similar. The physiological activities of the plant influence Zn absorption and the interactions with many elements like Fe, Mn and Cu also affect Zn uptake (Sheded et al., 2006).

Zn is a dietary trace mineral that, in addition to its many essential functions in growth and development, is essential for the function of the immune system cells. Zinc has been shown to be effective in the treatment of the common cold (Kumari and Chandra, 1993; Mossad et al., 1996).

Selenium and Titanium

Although Se is essential for the growth of certain plants (Shrift, 1969); the accumulation of Se in the plant may cause toxicity (Rios and Waterman, 1997). Selenium was below the instrumental detection limit for all samples. Al-Saleh et al. (2006) found that the average concentration of Se in the dry seeds of *N. sativa* was 0.177 ± 0.10 mg/kg fresh weight.

The Ti concentration was 7 mg/kg in the samples from Qatar, 10 mg/kg in the samples from Egypt and Syria and 42 mg/kg in the samples from Palestine. Little attention has been given to Ti in plants and there is currently no clear evidence of biochemical role for Ti (Kabata-Pendias and Pendias, 2001; Szentmihályi and Then, 2007), although Chapman (1972) and Shkolnik (1974) described its possible catalytic function in N fixation by symbiotic microorganisms and photooxidation of N compounds by plants.

Conclusion

Nigella seeds from the four Middle Eastern countries contained significant amounts of important minerals. Calcium, K, Mg, P, S, Zn, Fe, Mn, are the most abundant element in the black cumin seeds, followed by Ba, Br and Cl. Levels of toxic elements, including As, Cd, Co, Cr, and U, were very low or not detected. These results agree with those found by Takruri and Dameh (1998) for five varieties of black cumin seeds (Iranian, two Syrian, Turkish and Jordanian). However, the nutritional content of these minerals cannot be predicted from the quantity of black cumin consumed.

The present study adds to previous information about the presence of some major and trace elements in the seeds of *N. sativa*. The concentrations of some of these elements were differed by the country of origin of the *N. sativa.* These differences could be explained by local growing conditions such as differences in soil type, and differences in water/soil/plant interactions due to ambient temperature.

This study indicates that *N. sativa* accumulates a diverse array of elements, some of which are important for biological functioning. The elucidation of element specification in *N. sativa* seeds helps interpret the potential therapeutic properties of the seeds. However, beyond elements, the chemical composition of *N. sativa* has not been well characterized. There could be phyto-chemicals with therapeutic properties that act alone or in conjunction with the elements that are important. Nonetheless, the presence of several elements important for immune functioning in *N. sativa* indicated this as one possible mechanism for the therapeutic effects of the seeds. The dosage for consumption of the seeds by the local people, as prescribed by some physicians is based on experience gathered over generations of practicing physicians and lacks proper scientific and clinical validation. The present data on elemental concentration in these medicinal seeds might be useful to set standards for prescribing the dosage and duration of administration of these herbal medicines.

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