ACTA SCIENTIFIC BIOTECHNOLOGY (ASBT)

Volume 1 Issue 5 May 2020

Review Article

Nigella sativa L. a Possible Cure to Arsenicosis

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Received: March 24, 2020 Published: April 29, 2020

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Abstract

Nigella sativa is an auspicious herb used from an ancient era as a potential antiseptic. Commonly available in every home and used as an aromatic spice. Thymoquinone is an active agent and has voluminous properties to fight poisoning and carcinogens. This study illustrates that what is arsenic and its toxicity in Bangladesh and what are the uses of Nigella sativa (Black Cumin/Seeds) and how it can be a possible cure to reduce arsenic toxicity. Arsenic rate is fatal in many districts of Bangladesh. One could use Nigella sativa to reduce the affects of arsenic poisoning and eliminate social hazards caused by arsenic thus improving social norms of many arsenic affected people.

Keywords: Nigella sativa; Arsenicosis; Thymoquinone

Introduction

Arsenic poisoning is one of the greatest problems in Bangladesh. High level of arsenic is known to be found in the ground water as per the estimation 125 million inhabitants of Bangladesh are at risk.

It is spread in the maximum areas of the country around 59 out of 67 districts are contaminated and due to its unintentional consumption people suffered and lead to great losses. Many researches and studies revealed the possible diseases and problems it can cause and found various cures to deal with arsenic issues and there is an ongoing research continued further for potential cures and preventive measures.

Arsenic is said to be a 'slow poison' that takes time to have its affects once in high concentration can lead to collateral damage and death. Arsenicosis is one the major disease caused by arsenic poisoning and undue treatment leads to cancer in skin, lung, liver kidney etc.

Talking about arsenic it is not just a health hazard but also a big social hazard in Bangladesh. Due to lack of knowledge in rural areas women and children have traumatized experiences because of their unsupportive family members.

There are several preventive measures taken to deal with the impregnable influence of Arsenic like tube well screening, absorption by using certain activated/coated surfaces, dig deeper wells, coagulation-flocculation and rain water harvesting etc.

But when we talk about preventive measures, we often forget to consider the common things that could potentially be a very useful measure and one such thing is Black Cumin or Black seed (*Nigella sativa* L.).

Black seeds are available in every home and its freshly prepared oils are easily available in the country most of us use it on a daily basis but we lack to address the fact that how much this one ingredient can be useful to prevent the affects of arsenic and avoid further damages like cancer.

Figure A

What is arsenic?

Arsenic is an omnipresent metal like element (metalloid) that is extensively present in the nature. Arsenic was identified by the German alchemist Albertus Magnus around 1250 AD. It was used by the ancient Asians, Egyptians, Greeks, Romans and Chinese.

Arsenic is a highly poisonous carcinogenic element. It has three allotropic forms, yellow, black, and grey. Its name comes from the word arsenikon which is the Greek name for the pigment yellow orpiment. Usually present in two forms organic and inorganic, some forms of arsenic which does not contains carbon are classified as

inorganic other forms that does contain carbon are classified as organic. Arsenic is usually combined with one or more elements such as oxygen, sulphur, chlorine etc. mostly in sulphur form.

Arsenic is also used for many industrial and medical purposes like in pesticides and fertilizers and in colour pigments of paints. Arsenic is often used as anti-inflammatory agents in medicine and to treat acute promyelocytic Leukemia a type of blood cancer which is provided by prescription.

General properties of arsenic

• Elemental Symbol: As

Atomic Number of Arsenic: 33

Atomic Mass: 74.9216 amu

 Melting Point: Arsenic does not melt- it sublimes at 616 degrees C. Which means that it transforms directly from a solid to a vapour by-passing a liquid state

• Number of Protons/Electrons: 33

Number of Neutrons: 42

• Crystal Structure: Rhombohedral

Density @ 293 K: 5.72 g/cm³

Colour: metallic grey, yellow or black.

The semi metal arsenic is present belongs to group VA of the periodic table and can exist in four oxidation states: –3, 0, +3, and +5. Arsenite, AsIII, and arsenate, AsV, are the predominant oxidation states under, respectively, reducing and oxygenated conditions (WHO 2001, IARC 2004).

The other chemical compounds of arsenic are arsenate, arsenite, arsenic trioxide, arsine, arsenic acid, arsenic pentoxide, arsenide and few more. The inorganic As (III) form as $\rm H_2AsO_3$ is 40 - 60 times more toxic than As (V) form as $\rm H_2AsO_4$ (Rashid MR and Mridha MAK 1998).

Other major arsenic containing minerals are arsenopyrites (Fe-AsS), realgar (As_4S_4) , orpiment and arsenic trisulfide (As_2S_3) .

Arsenic in ground water

Arsenic in ground water is one of the biggest problems in Bangladesh as per WHO guidelines the normal arsenic level is 10 $\mu g/L$ but in Bangladesh the level is way higher it is 50 $\mu g/L$. It is still unknown how it is present in the ground waters could be the result of geological sources present naturally like rock sediments.

There is no exact data to state the problems of arsenic in ground waters of Bangladesh but it is assumed to be from 1970's. According to the reports 50 to 60 percent arsenic can be retained by the human body and contamination is very high on villages of Bangladesh.

The water from shallow tube wells (depth of 10 - 70m) contains arsenic in toxic level, which causes a lot of hazards to the human

body. But ground water from deep tube wells (depths > 150 m) is safe and contains arsenic in less concentration.

The inorganic arsenic like arsenic pyrites are said to be found in abundance in rock sediments of ground water and due to its oxidation arsenic acids or its derivatives are released and said to contaminate the ground water. 75 million people of 59 (out of 64) districts are at risk of drinking contaminated water with arsenic above 50 $\mu g/L$. the two main processes of arsenic contamination are oxidation of arsenic pyrites or ferrous hydroxides and oxy-hydroxide reduction.

Oxidation of arsenic pyrites or ferrous hydroxides caused by anthropogenic activities leads to release of acidic molecules in water dropping the PH level of water to be acidic.

Below table describes the entire oxidation process of Arsenic and how it contaminates the ground water.

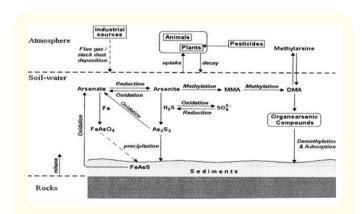


Figure 1: Adopted from article arsenic contamination in groundwater in Bangladesh: An environmental and social disaster.

Oxy-hydroxide reduction: According to this hypothesis, the origin of arsenic rich groundwater is due to a natural process, and it seems that the arsenic in groundwater has been present for thousands of years without being flushed from the delta. Arsenic is assumed to be present in alluvial sediments with high concentrations in sand grains as a coating of iron hydroxide. The sediments were deposited in valleys eroded in the delta when the stream base level was lowered due to the drop in sea level during the last glacial advance. The organic matter deposited with the sediments reduces the arsenic bearing iron hydroxide and releases arsenic into groundwater. Organic matter deposited in the sediments reduce the arsenic adsorbed on the oxyhydroxides and releases arsenic into the groundwater and dissolution occurs during recharge, caused by microbial oxidation of the organic matter as bacteria dissolves surrounding oxygen.

$$H_2AsO_4 - + 3H^+ + 2e^- = = = > H_3AsO_3 + H_2O$$

$$2 H_3 AsO_3 + O_2 ===> HAsO_4 - + H_2 AsO_4^- + 3H^+$$

Health hazards caused by arsenic

Arsenic in toxic to human health its accumulation in larger content leads to diseases like Arsenicosis which is caused by arsenic poisoning and when prolonged leads to cancer.

Arsenicosis is the appearance of black spots (skin lesions) in the body. Undetectable in early stages It generally takes 8 to 14 years for major arsenic poisoning depending upon the ingestion and immune system of the person. When accumulated passes slowly out through hair and nail.

When swallowed the signs and symptoms may be shown in 30 minutes.

These may include:

- Drowsiness
- Headache
- Confusion
- Diarrhoea.

Signs and symptoms associated with more severe cases of arsenic poisoning are:

- A metallic taste in the mouth and garlicky breath
- Excess saliva
- Problems swallowing
- Blood in the urine
- · Cramping muscles
- Hair loss
- Stomach cramps
- Convulsions
- · Excessive sweating
- Vomiting
- Diarrhoea.

Complications linked to long-term arsenic consumption include:

- Cancer
- Liver disease
- Diabetes
- Nervous system complications, such as loss of sensation in the limbs and hearing problems
- Digestive difficulties.

Pathological testing confirms the instance of arsenic poisoning. Urine tests results take 1 to 2 days for the measuring of accurate results of arsenic poisoning. Other tests are blood tests, fingernail samples and hair samples tests.

Tests on hair and fingernails can determine the level of arsenic exposure over a period of up to 12 months. But does not indicate the affects of arsenic on persons health.

Malignancy due to arsenic in Bangladesh

Arsenicosis malignancy is also a major concern in Bangladesh. People in villages are subjected more to arsenic related problems and malignancy because of high water consumptions in summers and also from the food chain.

A 12-year renowned study was conducted by Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, giving an insight about one of the arsenic related cancers. The study was about cutaneous malignancy and the period was from January 2004 to December 2015.

From the research 960 patients had cutaneous malignancy due to arsenic and the tests were for Basal Cell Carcinoma (BCC) Squamous Cell Carcinoma (SCC), Merkel Cell Carcinoma and Melanoma.

The samples of 960 patients stated malignancy from different arsenic contaminated districts of Bangladesh out of which 528 patients (55%) were males and 432 patients (45%) were females. The age group that was affected more was above 40. Cancers were very less below the age of 24. And overall, 520 patients had a family history of malignancy due to arsenic.

Beside cutaneous malignancy there are also other types of cancers reported in Bangladesh due to arsenic like

- · Lung Cancer
- Liver Cancer
- Bladder Cancer
- Pancreatic Cancer etc.

Further researches are carried on due to other various problems related to arsenic and still yet to be reported.

Arsenic toxicity

Arsenic toxicity has been in various levels it is a potential carcinogen. and also known to have genotoxicity and cytotoxicity.

Carcinogenesis is due to oxidative stress caused by arsenic molecules leading to methylation of DNA that alters gene expression. Arsenic metabolites also hinders cell differentiation and distort signal transduction pathways like Protein 53 signalling pathway, Nrf2-mediated redox signalling pathway, and MAPK- Ras-Raf-MEK-ERK pathway.

Cytotoxicity by arsenic have been studied by several researchers. Arsenic induces cytotoxicity by releasing Reactive Oxygen Species which affects lipids and proteins in cells and also modulates signal transduction pathways which affects various biological processes like cell apoptosis, cell growth, cell adhesion etc.

Arsenic induced genotoxicity deteriorates genetic information in cell which leads to mutation. Reactive Oxygen Species reacts with both deoxyribose and bases in DNA, causing base lesions and strand breaks which affects DNA repair and gene regulation mechanism threatening gene stability. Elevated Arsenic also induces S-Adenosylmethionine (SAM) depletion in cells that leads to genomic stability.

A well-known carcinogen arsenic also causes a number of noncancerous diseases including cardiovascular disease, dermal disease, hypertension, and diabetes mellitus.

Nigella sativa L. (Black cumin/seed)

Nigella sativa (Black Seed) is a miraculous herb known for its indigenous medicinal properties. Widely found in Bangladesh and in rest of the Indian subcontinent and West Asia. It is also cultivated in some parts of Europe and Africa. Black Cumin belongs to the family Ranunculaceae.

The seeds and oil have a traditional history for extensive healing properties in medicine.

It is an annual flowering plant which is about 20 to 90 centimetres tall, which usually has white, yellow or pink flowers. An inflated capsule shaped structure fruit bear its marvelous dicotyledon seeds.

A lot of researches support that *Nigella sativa* is rich in antioxidant, anti-inflammatory, anti-histaminic and anti-cancer properties.

Figure B

Chemical properties of Nigella sativa l.

The Chemical properties of *Nigella sativa* seeds is Intense. It has several bioactive compounds i.e. proteins (21 - 31%), carbohydrates (25 - 40%), minerals (3 - 7%), vitamins (1 - 4%) and traces of saponins and alkaloids they also have some major and minor amino acids like glutamate, aspartate, cysteine and methionine respectively. All these constituents together contribute to its biological properties.

Oils of *Nigella sativa* have incredible therapeutic usage in Ayurveda. Externally it is used as an antiseptic and local anaesthetic believed to reduce inflammation on the skin and joint aches, consumption works wonders in the immune system.

The chemical constituents of *Nigella sativa* oil include cholesterol, campesterol, stigmasterol, β -sitosterol, α -spinasterol, (+)-citronellol, (+)-limonene, p-cymene, citronellyl acetate, α -thujene, thymoquinone (TQ), thymohydroquinone (THQ), dithymoquinone, carvacrol, and β -Pinene with various concentration. Nigellone, arachidic, linolenic, linoleic, myristic, oleic, palmitic, palmitoleic and stearic acid and many other unsaturated fatty acids with few other compounds.

Major constituent of *Nigella sativa* seed and its oil is thymoquinone also known as 2-methyl-5-isopropyl-1,4-benzoquinone. it is the main active component infused in the fixed oils with the other biological properties has immense property to deal with carcinogenesis and accelerated other pharmacological researches and cured many ailments.

Thymoquinone content is abundant in freshly extracted oil of *Nigella sativa*. Many researches support the *in-vitro* and *in-vivo* studies of thymoquinone.

It increases the body defence system and targets molecules that inflates the cells hence reducing the inflammation being an active anti-inflammatory agent and other anti-inflammatory diseases, skin disorders, skin eruptions. Also said to have decreased proinflammatory cytokine production with other biological agents.

Also used in the treatment of bronchitis, arthritis, rheumatism hypertension, diabetics, liver disorders, tincture prepared from *Nigella sativa* is used for loss of appetite, diarrhoea etc.

Antimicrobial and antifungal properties are also well elaborated. Further studies constitute its anti-analgesic properties as well.

Thymoquinone obtained from *Nigella sativa* Is known to treat various cancers like Skin, Colon, Cervical, Breast, Renal, Fibrosarcoma and prostrate by reducing oxidative stress in the DNA and also by using various other biological and signalling pathway.

The figure below states the possible mechanisms used by thymoquinone for cancer control.

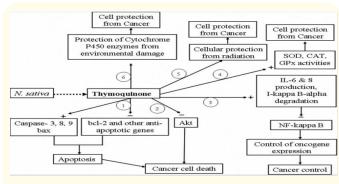


Figure 2: Adopted from article Anticancer activities of Nigella *Sativa (Black Cumin).*

Possible mechanisms of thymoquinone (TQ) action from the figure:

- TQ induces apoptotic cell death in cancerous tissues by upregulating expression of apoptotic genes (caspases and bax) and down-regulating expression of anti-apoptotic genes (e.g. bcl 2);
- 2. TQ suppresses Akt activation by dephosphorylation and thus blocks cancer cell survival;
- 3. TQ deactivates NF-kappa B pathway by inducing cytokine production, and thus control oncogenic expression;
- 4. TQ increases the activities of antioxidant enzymes and protects cell against cancer;
- TQ protects normal cells' injury caused by ionizing radiation in the treatment of cancer; (6) TQ prevents CYP450 enzymes from damage. '+' indicates increasing effect and '-' indicates decreasing effect.

Possible affects of Nigella sativa L. in terms of arsenicosis

Arsenicosis takes longer period of time to appear, affects of arsenic only appear when exposed in larger amount with nascent arsenic molecules.

Releasing reactive oxygen species, it can alter gene function etc., as mentioned above. But antioxidant and scavenging molecules of *Nigella sativa* have the capability to potentially target the arsenic molecules and eliminate them so that it does not create further damage to the cell.

Molecular mechanism of *Nigella sativa* can target arsenic molecules and hence reduce the impact of oxidative stress caused by reactive oxygen species of arsenic. Before it reaches the transduction pathways for cell disruption.

The study reveals that from the tremendous anti-inflammatory, anti-cancer and anti-oxidant properties of Thymoquinone in *Nigella sativa* we could possibly fight arsenicosis.

The scavenging activities of *Nigella sativa* molecules can delay the affects of arsenic.

Possible usage of *Nigella sativa* to reduce the affects of arsenicosis:

- Apply the Nigella sativa oil daily to reduce the possibility
 of the appearance of black spots caused arsenicoisis and
 diminish the first onset of rashes.
- Consumption of oil daily to boost immune system to fight the carcinogens released by arsenic and would reduce the symptoms of arsenic poisoning.

Arsenic molecules in fewer amount could be eradicated by the scavenger molecules of *Nigella sativa* and our immune system will be strong enough to fight the damaging arsenic [1-10].

Conclusion

The motive of this entire study is to link the potential benefits of *Nigella sativa* with arsenic so that to create a booming cure for the people of Bangladesh.

It is a budding preventive measure and cost- effective treatment, if used systematically could diminish arsenicosis in Bangladesh. Often simpler solutions are left unnoticed but they could create a massive impact.

Treatments done by *Nigella sativa* have shown promising results and cured many cancers as per the researches and studies and still further continued.

Rural areas are more arsenic prone in Bangladesh and the lives affected by it are enormous. If we insight the knowledge about the possible uses *Nigella sativa* in people and how they could benefit from it, can change lives and less people will face health as well as social issues.

If used on regular basis it can actually be a potential preventive measure and could ease a lot of inconvenience in rural areas.

A cheaper and social-friendly remedy that can be used by affected area people to reduce the impingement of arsenic and promote well-being.

Future Scope of Research

- A detailed study of the impact of Nigella sativa on arsenic affected people.
- Further pharmacological studies of Nigella sativa mixed with other components to treat arsenicoisis.

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