Abstract

The use of black seed (Nigella sativa) capsules as a herbal therapy to lower blood glucose in diabetic patients are associated with menstrual cycle irregularities.

The present study was designed to analyses and to compare between two types of Nigella sativa (N.sativa) agricultures in Mosul region and those imports from Saudi Arabia Kingdom, and to investigate the levels of hormones in volatile oil of black seed that regulate menstrual cycle that might be present in Nigella sativa.

Volatile oil of N.sativa was extracted by steam distillation using diethyl ether as an organic solvent. Then, hormones analysis were done using (miniVIDAS software version) instrument.

Results of present study showed a presence of considerable amount of sex hormones estradiol, progesterone, prolactin, testosterone, FSH and LH. This might interpret the cause of menstrual cycle irregularities occur when black seed capsule was taken as a herbal therapy to lower blood glucose in diabetic patients.

Introduction

The understanding of the way in which menstrual cycle works each month is an important step in improving the reproductive health of females. Menstruation is the term given to the periodic discharge of blood, tissue, fluid and mucus from the reproductive organs of sexually mature females. The average length of the menstrual cycle is 28 days, although this can vary between women, and from one cycle to the next in individuals. The flow usually lasts from 3 - 6 days each month and is
caused by a sudden reduction in the sex hormones (as shown in Figure 1) estrogen, progesterone, follicle stimulating hormone (FSH), and luteinizing hormone (LH); the hormones that govern this process. [1,2]

![Figure 1](image1.png)

**Figure 1** Hormone levels in blood at Puberty

The menstrual cycle is complex, controlled by a variety of glands and their associated hormones. A brain structure called the hypothalamus influences the nearby pituitary gland to secrete special chemicals, which prompt the ovaries to secrete their sex hormones, principally estrogen and progesterone. The menstrual cycle is a biofeedback system, which means all of the structures and glands are influenced by the activity of the others. These hormones are usually only present in small amounts and that it is the relationship between the levels of the hormones that is critical. When the balance is upset, menstrual irregularities can occur. The combination contraceptive pill contains the hormones estrogen and progesterone works by altering the bodies natural hormonal balance, thus inhibiting ovulation, preventing implantation of the egg and making the cervical mucus hostile to sperm.[1,3]

Traditionally, the use of black seed *N.sativa* or (Habbet al-suda, Habbah el baraka, or Kamun aswad) capsule as a herbal therapy to lower blood glucose in diabetic patients are associated with menstrual irregularities. [4] From this fact, this study was design to analysis and comparison between two types of *N.Sativa* agricultures in Mosul region and those imports from Saudi Arabia Kingdom, and to investigate the levels of hormones that regulate menstrual cycle might be present in *N.Sativa*.

The black seed or *N.Sativa* is a type of plant that belongs to the *Ranunculaceae* family. [5] It has been used as a herbal medicine for more than 2000 years. It is also used as a food additive and flavor in many countries.[4]
Figure 2 Nigella sativa flower and seeds

It has been reported that a significant decrease in blood glucose was produced by a plant mixture containing *N. sativa* in normal and streptozotocin-induced diabetic rats.[6] *N. sativa* volatile oil has been shown to possess more than 100 constituents, many of which are capable of inducing beneficial pharmacological effects in humans.[7] A decoction comprised of *N. Sativa* seeds, *Hemidesmus indicus* root and *Smilax glabra* rhizome is used to treat cancer patients in Sri Lanka. However, the anti-carcinogenic properties of this decoction have not been experimentally confirmed.[8] Nigella is considered a biological response modifiers because studies show extracts from the seeds are toxic to cancer cells and, in mice, prevent blood cell toxicity caused by the anti-cancer drug cisplatin.[9] The active components of *Nigella* seeds are the volatile oils thymoquinoline and dithymoquinone, both of which inhibit tumor cells in laboratory experiments, even tumor cells resistant to anti-cancer drugs.[10]

**Material and Methods**

Black seed agriculture in Mosul region was considered as sample (1) and black seed imports from Saudi Arabia was considered as sample (2).

Seed sample (20 g) from each sowing were homogenized in 100 mL deionized water, together with 3 g of NaCl to avoid foaming, and the oil was distilled for 3 h by steam distillation using 50 mL of diethyl ether as the organic solvent. The extract was dried over anhydrous Na₂SO₄; the solvent was then evaporated under vacuum in a rotary evaporator.[11] The oil content was determined gravimetrically and expressed on a dry weight basis.

Hormones analysis were done using (miniVIDAS software version) instrument.

**Results**

Essential oil yield was 0.072 g (0.36%) of seed dry weight for sample (1), and 0.0705 g (0.35%) of seed dry weight for sample (2).

Table 1 show the levels of hormones present in *N.Sativa*.
Table 1 Levels of hormones present in *N. Sativa*.

<table>
<thead>
<tr>
<th>Hormone</th>
<th>Sample 1</th>
<th>Sample 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>FSH</td>
<td>0.43 MUI/mL</td>
<td>0.1 MUI/mL</td>
</tr>
<tr>
<td>LH</td>
<td>0.1 MUI/mL</td>
<td>0.1 MUI/mL</td>
</tr>
<tr>
<td>Prolactin</td>
<td>&lt; 0.5 ng/mL</td>
<td>&lt; 0.5 ng/mL</td>
</tr>
<tr>
<td>Progesterone</td>
<td>5.55 ng/mL</td>
<td>0.91 ng/mL</td>
</tr>
<tr>
<td>Testosterone</td>
<td>1.8 ng/mL</td>
<td>0.32 ng/mL</td>
</tr>
<tr>
<td>Estradiol</td>
<td>278.56 pg/mL</td>
<td>113.48 pg/mL</td>
</tr>
</tbody>
</table>

Also, Table 1 shows that black seed agricultural in Mosul region has higher levels of hormones than black seed imports from Saudi Arabia.

**Discussion**

*N. Sativa* grows in temperate and cold climate areas. The seeds of *N. Sativa* contain thymoquinone, monoterpenes such as *p* cymene and *α*-pinene, *Nigellidine*, *Nigellimine* and a saponin [12].

Several therapeutic effects include those on digestive disorders, gynecology, and also anti-asthma and effects have been described for the seeds of *N. Sativa* in ancient Iranian medical books [13]. *N. Sativa* has long been known for its medical use as an antispasmodic, especially against gastrointestinal or respiratory disorders, in many countries.

There is evidence of relaxant effects of volatile oil from this plant on different smooth muscle including rabbit aorta, rabbit jejenum, and isolated tracheal muscles of guinea pigs [12]. Mahfous and El-Dakhakhny (1960) reported that the volatile oil from *N. Sativa* protected guinea pigs against histamine-induced bronchospasm, but it did not affect histamine *H1* receptors in isolated tissues [14]. However, in an in *vivo* study, increasing respiratory rate and intra tracheal pressure of guinea pigs due to administration of volatile oil from *N. Sativa* has been demonstrated [15].

A cell study conducted at the International Immuno - Biology Research Laboratory in South Carolina showed that when incubated with *Nigella* extract, cancer cells were unable to produce fibroblast growth factor and the protein collagenase, both are necessary for blood-vessel growth into the tumor. Without a blood supply, a tumor cannot grow. [16]

*Nigella* also stimulates the immune system, as shown in an experiment conducted with human lymphocytic white blood cells. Cells treated with *Nigella* - seed proteins produced greater amounts of cytokines, specifically interleukin-1-beta and tumor necrosis factor alpha,[17] How and if this is important to treating cancer is not yet established.

Another experiment indicates that thymoquinone may also prevent some toxic side effects of cancer treatments. Scientists from King Saud University in Saudi Arabia found that mice pretreated with thymoquinone were protected from carbon tetrachloride-induced liver toxicity. Carbon tetrachloride is a toxin that in small amounts can kill by causing the liver and kidney to atrophy. Liver toxicity was assessed by measuring the release of liver enzymes in the blood. Thymoquinone also demonstrated antioxidant activity, which may be how it protects the liver.[18]

Recent in vitro studies have demonstrated that *N. sativa* can be cytotoxic to several cancer cell lines. Thymoquinone and dithymoquinone, two isolated active components of *N.*
sativa, have also been shown to be cytotoxic to several parental and multidrug resistant human cell lines. Further N.Sativa and Hemidesmus indicus have been shown to possess anti-oxidant activities [8, 19].

In the present study, the assessment of hormones that exist in volatile oil from N.Sativa was preformed and show a presence of considerable amount of sex hormones estradiol, progesterone, prolactin, testosterone, FSH and LH; the hormones that controlled menstrual cycle. This might elucidate the cause of menstrual irregularities occur when black seed capsule was taken as a herbal therapy to lower blood glucose in diabetic patients [4]

The oral administration of black seed that contain sex hormones is resemble to the oral administration of contraceptive pill contains this hormones works by altering the bodies natural hormonal balance, thus inhibiting ovulation, preventing implantation of the egg and making the cervical mucus hostile to sperm.[1,3]

The higher levels of hormones for black seed agricultures in Mosul region than black seed imports from Saudi Arabia Kingdom may attribute to the mild climate of Mosul region than those of Saudi Arabia Kingdom.

References
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