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Effect of Nigella Sativa on Growth and IGF-1 Levels in Rats Prenatally Exposed to Pesticides

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Abstract

Nigella sativa contains antioxidants and can potentially improve growth disorders due to prenatal pesticide exposure. Pesticides affect the work of thyroid hormone, insulin, and Insulin-like Growth Factor that play essential roles in the growth and development processes. This study aimed to determine the effect of Nigella sativa supplementation on body weight and IGF-1 levels in mice, with a history of pesticide exposure in the womb. This study was conducted from October 14, 2023 to December 1, 2023 at the laboratory of the Center for Food and Nutrition Studies, Inter-University Center, Gajah Mada University, Indonesia. This experimental study used a cohort design and involved 20 pregnant female rats as the experimental animals. These rats were divided into several groups: K0 (control group with standard feed), K1 (group exposed to pesticides during pregnancy), and P1 and P2 (group exposed to pesticides. Followed by 10.8 mg/200gBW/day and 21.6 mg/200 gBW/day of Nigella sativa after birth, respectively). The pesticide dose used was 10 mg/200gBW/day orally. Anthropometric examinations was conducted at birth, and on day 7, day 14, day 21, and day 28. The examination of IGF-1 levels was performed on day 28 using the ELISA method. Results showed that the mean birth weights (g) of the rats by group were as follows: K0:6.09±0.12; K1:4.03±0.03, P1:4.03±0.02 P2:4.05±0.03. On day 28, the mean body weights (g) were as follows: K0:104.0±1.79; K1:65.17±1.47; P1:92.17 ± 3.19; and P2:102.00±1.41. The mean IGF-1 level (pg/mL) were as follows: K0:23.76±0.68; K1:9.03±0.24, P1:14.94±0.37; and P2:19.51±0.56. The ANOVA test presented a p-value of <0.001. Hence, Nigella sativa supplementation after birth significantly affects body weight and IGF-1 levels in rat model of prenatally exposed to pesticides.

Keywords: Body weight, IGF-1, nigella sativa, pesticide, womb

Introduction

Stunting is a chronic condition of stunted growth determined by calculating the Z score of the Height for an Age index of less than -2 Standard Deviation World Health Organization Child Growth Standards median.[1] Stunting increases the risk of various other health problems, delays in motor development, neurodevelopmental disorders, and cognitive function.[1] Stunting begins in the first thousand days of life, from the womb until 2 years post-natal life.[2] Stunting prevalence based on the results of the 2017 Nutritional Status Monitoring, in Indonesia reached 29.6 percent (aged 0-59 months), which potentially causes maternal nutritional status and sanitation.[3] Stunting is a health problem in Indonesia, with a prevalence of more than 20%, especially in 14 provinces, which exceeds the national figure.[3] Research by Aryastami et al.[4] found that low birth weight increases the risk of stunting by 1.74 times compared to normal birth weight. Prenatal exposure to pesticides also increases the risk of low birth weight. In a study conducted in Brebes, Central Java, Widyawati et al.[5] reported an odds ratio of 6.8 (95% CI: 2.0–22.9) for low birth weight in pesticide-exposed pregnancies. They also observed significantly lower IGF-1 levels among exposed subjects (OR 3.6; 95% CI: 1.2–11.1).

Organophosphate and carbamate class pesticides, which farmers in Indonesia widely use, are classified as endocrine-disrupting chemicals (EDCs), which can affect the work of hormones that play an essential role in the growth and development process, such as thyroid hormone, insulin, and Insulin-Like Growth Factor-1 (IGF-1).[5,6] IGF-1 affects placental trophoblast cells' metabolism, mitogenesis, and differentiation,

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affecting the fetus in pregnancy.[5]

Nigella sativa is an herbal ingredient known for a long time because it is useful as an antioxidant, anti-inflammatory, and immunomodulator, and it improves metabolism to prevent low birth weight and stunting.[7] Nigella sativa, known as black cumin, has been used as an adjuvant therapy since the time of the Prophet Muhammad, SAW, as stated in the hadith: "In black cumin, there is a cure for every disease except death." Black cumin is also mentioned in the Holy Bible as a "Curative black seed" and is described as *'Melanthion by Hippocrates and Dioscorides'* and as *'Gitch of Pliny.*[7] The content of active substances in black cumin such as thymoquinone (TQ), dithymoquinone (DTQ), carvone, limonene, transanethol , p-cymene, indazole alkaloids such as nigellidine and nigellicine , and isoquinoline alkaloids including nigellicimine, nigellicimine-N-oxide and α-Hederin has various benefits such as antioxidant, anti-inflammatory, immunomodulatory, antitussive, antihypertensive and balancing blood sugar levels.[7] Pesticides induce ROS and pro-inflammatory responses.[8] High oxidative stress in endothelial cells of placentae impairs cell function and angiogenesis, reducing fetal growth by poor placental blood vessel development and weakening the blood flow and exchange of nutrition or oxygen.[9] The antioxidants in Nigella sativa are expected to be able to prevent this.

Growth is a dynamic process involving nutritional, hormonal and nervous system factors. Linear growth in the first year of life is mainly influenced by nutrition, although hormonal factors such as IGF-1 and leptin also play a role. Research in Bangladesh compared the control group of stunted children and found significant differences in leptin levels, leptin: adiponectin ratio, and IGF-1 levels.[10]

Thymoquinone, the active compound in *Nigella sativa,* is believed to help repair cell, tissue, and organ damage that occurs during pregnancy. It acts through the production of thymohydroquinone via a two-step one-electron reduction or a one-step two-electron reduction process. These mechanisms enable it to scavenge free radicals and prevent oxidative damage.[11] As a result, *Nigella sativa* supplementation is thought to increase body weight and IGF-1 expression in offspring that were exposed to pesticides in utero. This study aims to investigate the effect of *Nigella sativa* supplementation on body weight and IGF-1 expression in rats prenatally exposed to pesticides.

Methods

This research has received approval from the Bioethics Commission for Medical/Health Research, Faculty of Medical, Sultan Agung Islamic University, Semarang, with number. 467/XI/2023/Bioethics Commission. This research is an experimental study on experimental animals, pregnant white Wistar rats, using a cohort design. Animal models are used to evaluate the efficacy, safety, and potential side effects of drugs or chemicals, including teratogenicity, toxicity, and carcinogenicity, before advancing to human trials.[12]

The study was carried out at the Laboratory of the Center for Food and Nutrition Studies, Inter-University Center (PAU), Gadjah Mada University, Yogyakarta, from October 14, 2023 to December 1, 2023. The rats underwent a one-week acclimatization period starting on October 7, 2023. Mating and confirmed pregnancy began on October 14, 2023. The pregnant rats were exposed to pesticides from October 14 to November 3, 2023 (21 days), followed by Nigella sativa supplementation from November 4 to December 1, 2023 (28 days).

The study involved 24 pregnant Wistar white rats, randomly divided into four groups, with each group consisting of six rats.

The K0 group (negative control) received only standard feed and water *ad libitum*. The K1 group (positive control) received standard feed and water *ad libitum* along with pesticide exposure at a dose of 10 mg/200 g body weight (BW) per day during pregnancy. The P1 group (treatment group 1) received standard feed and water ad libitum, pesticide exposure at 10 mg/200 g BW per day during pregnancy, followed by *Nigella sativa* supplementation at a dose of 10.8 mg/200 g BW per day for 28 days. The P2 group (treatment group 2) received standard feed and water *ad libitum*, pesticide exposure at 10 mg/200 g BW per day during pregnancy, followed by *Nigella sativa* supplementation at a dose of 21.6 mg/200 g BW per day for 28 days.

Gramoxone, a herbicide liquid (LD50 1,098 mg/gBW) was used in this research, administrated orally by sonde from fertilization (day 1 of pregnancy marked by a vaginal plug after mating) until day 20. Herbicides are well absorbed from the Gastrointestinal tract but are not well absorbed after inhalation or dermal exposure.[13]

After giving birth (21st day), the average number of children born and the average body weight were calculated. Observations were

Table 1 Mean Body Weight of Rats (Grams) According to Age and Treatment Group

Group	Day 1	Day 7	Day 14	Day 21	Day 28
K0	6.09±0.12	21.33±0.82	48.83 ± 1.69	76.67±1.63	104.0±1.79
K1	4.03±0.03	14.50±0.55	30.67±4.18	46.00±0.89	65.17±1.47
P1	4.03±0.02	16.67±0.52	39.17±0.98	63.17±0.75	92.17±3.19
P2	4.05±0.03	20.33±0.82	45.67±0.82	73.33±0.82	102.00±1.41

Noted: K0: Control group which only received standard feed and drink ad libitum; K1: Positive control group that received standard feed + drinking ad libitum and exposure to pesticides at a dose of 10 mg/200gBW/day during pregnancy; P1: Treatment Group 1: received standard feed + drinking ad libitum + exposure to pesticides 10 mg/200g BW/day in the womb followed by Nigella sativa 10.8 mg/200g BW/day for 28 days; P2: Treatment Group 2: received standard feed + drinking ad libitum + exposure to pesticides 10 mg/200gBW/day in the womb followed by Nigella sativa 21.6 mg/200gBW/day for 28 days

continued to determine the growth of the rat pups by providing standard feed and drinking ad libitum and Nigella sativa for 28 days. IGF-1 levels were measured with blood samples taken from the orbital vein. Measuring body weight using electronic scales brand: Mettler Toledo, checking levels IGF-1 using the spectrophotometric method (ELISA). The data obtained were tested for normality and homogeneity; the data were normal and homogeneous using the Kolmogorov Smirnov test and the Levene test. The data were normally distributed and homogeneous, so a statistical test was carried out using one-way ANOVA followed by LSD post hoc test to determine the differences between groups, which were considered statistically significant if $p<0.05$.

Results

On the 21st day of pregnancy, all pups gave birth safely, and no pregnant rats died during the study. The average number of pups in the K0 group=9.67; K1=8.7; P1=8.8, and P2=8.7. To reduce bias in the number of pups, six individuals were taken to equalize the number of samples for each group, as samples for further treatment in the form of Nigella sativa at a dose of 10.8 mg/200 gBW/day (P1 group) and Nigella sativa at a dose of 21.6 mg/200 gBW/day ((P2 group) given for 28 days. Nigella sativa oil is administrated orally by sonde. Body weight of rats' children monitoring was carried out on days 1, 7, 14, 21, and 28.

The increase in body weight in the group that received *Nigella sativa* supplementation was superior when compared with the group that

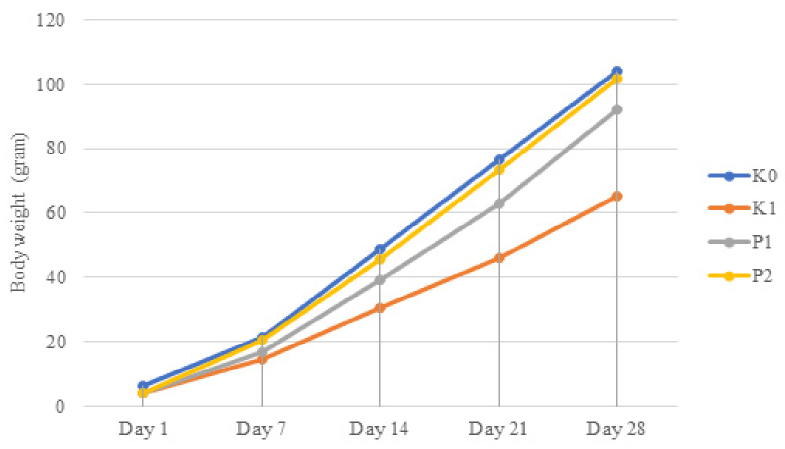

Figure 1 Rat Body Weight Growth (Grams) On Days 1, 7, 14, 21, and 28 According to Treatment Groups

Table 2 Mean IGF-1 levels (pg/mL) on day 28 based on treatment group

Group	n	IGF-1 Levels (pg/mL)
K0	6	23.76±0.68*
K1	6	9.03±0.24*
P1	6	14.94±0.37*
P2	6	19.51±0.56*

Noted: K0: Control group which only received standard feed and drink ad libitum; K1: Positive control group that received standard feed + drinking ad libitum and exposure to pesticides at a dose of 10 mg/200gBWday during pregnancy; P1: Treatment Group 1: received standard feed + drinking ad libitum + exposure to pesticides 10 mg/200g BW/day in the womb followed by Nigella sativa 10.8 mg/200g BW/day for 28 days; P2 : Treatment Group 2: received standard feed + drinking ad libitum + exposure to pesticides 10 mg/200gBW/day in the womb followed by Nigella sativa 21.6 mg/200gBW/day for 28 days

received exposure to pesticides without *Nigella sativa* supplementation, but lower than a control group that had no pesticides exposures. Post hoc test found significant differences in all groups (p<0.001), except for body weight between the control group and the group that received Nigella sativa supplementation at a dose of 21.6 mg/ 200gBW/day (p=0.114)

IGF-1 levels in the group that received the exposure to pesticides were significantly lower when compared with other groups (p<0.001), while the levels in the control group that only received standard feed had the highest levels. In the ANOVA test, the p-value was obtained < 0.05, followed by the LSD post hoc test, the p-value was obtained <0.05 in all groups (p<0.001) including between P1 and P2 groups.

Discussion

Research in the agricultural area of Magelang Regency show a significant relationship between children's habits of playing in agricultural areas (p=0.011), storing pesticides in the house (p=0.036), mother's involvement in spraying (p=0.040), washing spray tools (p=0.040), mixing pesticides (p=0.040) with the incidence of *stunting*. There was no significant relationship between the incidence of stunting and the use of insecticides in the house (p=0.304).[1]

Pesticide-induced oxidative stress is caused by Reactive oxygen species (ROS) and Reactive Nitrogen Species (RNS) which activate signaling pathways in mitochondria and induce apoptosis.[14] Epidemiological studies on workers exposed to pesticides found increased oxidative stress and damage at the gene level caused by free radical reactions, characterized by a positive relationship between levels of Thiobarbituric Acid Reactive Substances (TBARS), Total Glutathione (TG), oxidized glutathione (GSSG) and 8-oxo-7,8-dihydro-2′-deoxyguanosine (8-oxodG), this situation explains that exposure

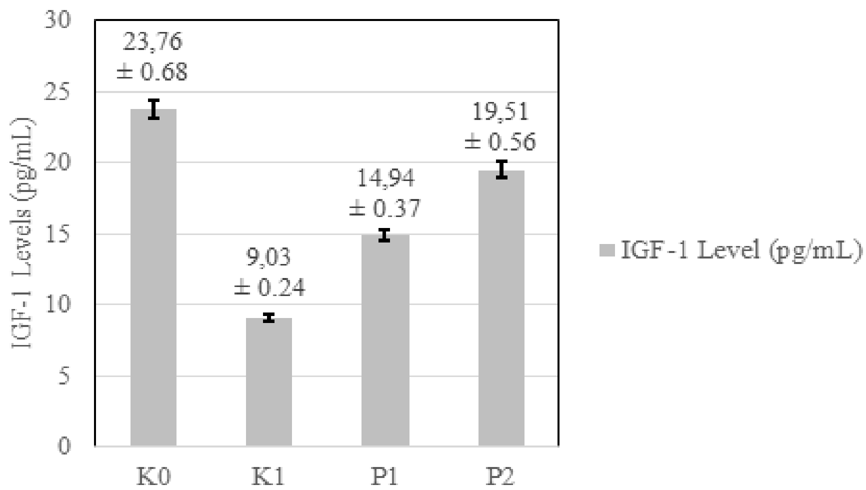

Figure 2 IGF-1 Levels on Day 28, According to the Treatment Group

to pesticides can induce oxidative stress by increasing the production of free radicals which can accumulate in cells and damage biological systems including macromolecules, RNA, DNA, DNA repair systems and modifying detoxification systems and antioxidant defense systems.[15]

Some pesticides such as Organophosphate and carbamate identified as Endocrine Disrupting Chemicals (EDCs) can bind to steroid hormone receptors such as the glucocorticoid receptor (GR) which play an essential role in metabolic processes, hormonal function, the immune system, and the central nervous system. Research on 34 types of pesticides in their role in the effects of glucocorticoids and antiglucocorticoids on the glucocorticoid receptor found 12 chemicals that showed real antagonistic effects.[16]

Endocrine Disrupting Chemicals has an indirect influence on the fetus through the placenta, it can interfere with the synthesis and metabolism of steroid hormones and disrupt the hypothalamic-pituitary-adrenal axis during the fetal growth process, resulting in delayed fetal growth.[17,18] EDC is lipophilic so that it can accumulate longer in adipose tissue.[18] Exposure to pesticides increases oxidative stress, damaging cell biological systems such as macromolecules, proteins, DNA, RNA, and other proteins in the detoxification and antioxidant systems.[15]

Epidemiological studies show that there is a relationship between pesticide exposure and impaired intrauterine growth, fetal death, premature birth, and congenital abnormalities.[19] In this study, all pups were born safely and had no birth defects.

This research shows that growth disorders during pregnancy can still be corrected with supplementation after birth, and Nigella sativa is a natural ingredient that has the potential to improve stunting and the consequences it causes in later life, such as cognitive disorders and degenerative diseases. Nigella sativa contains important minerals such as potassium, phosphorus, calcium, Mg, Na, Fe, Zn, Mn, and Cu. Nigella sativa is also a source of fatty acid esters such as arachidonic acid, myristic acid, stearic acid, palmitic acid, oleic acid, linoleic acid, linolenic acid, DHA, EPA, Thymoquinone (TQ) which has broad pharmacological effects as an antioxidant: reducing lipid peroxidation and levels of oxidative stress in body tissues, anti-inflammatory, anti-diabetic, anti-cancer, antimicrobial, hepatoprotective and has a kidney protective effect.[7,20,21]

Exposure to pesticides is also a risk factor for stunting in children in rural areas. Research conducted by Kartini found a significant relationship between exposure to pesticides and stunting and low levels of insulin-like growth factor-1 (IGF-1) in children exposed to it. Pesticide.[6] Children with low IGF-1 levels have a risk of stunting 8.35 times higher than the group with normal IGF-1 levels.[6] Insulin-like growth factor-1 (IGF-I) is a polypeptide hormone produced mainly by the liver but also secreted by other tissues as autocrine/paracrine. IGF-1 plays an active role in intrauterine fetal growth, proliferation and differentiation, until after birth. IGF-I, in response to growth hormone stimulation, is partly responsible for systemic GH activity, although it has several other cellular activities (anabolic, antioxidant, anti-inflammatory, and cytoprotective).[22]

Previous research shows that IGF-1 influences intrauterine linear growth. This hormone deficiency has an effect from the beginning of birth until childhood, causing skeletal maturation and stunted organ growth. This growth abnormality causes small brain volume (visible from head circumference), small heart size, and acromicria (small chin, undeveloped facial bones, small hands, and feet). IGF-1 deficiency also causes developmental delays and weakness of the muscular system.[22]

The results of this research give rise to a new optimism in treating stunting in the future by utilizing the potential of herbs such as Nigella sativa because supplementation with Nigella sativa in mice with a history of pesticide exposure succeeded in increasing body weight by catch-up growth as evidenced by the average body weight on day 28. However, the average was slightly lower than the control group which only received standard feed there was no significant difference ($p=0.114$). Nigella sativa supplementation was able to increase IGF-1 levels, although not as high as the control group. The increase in body weight and IGF-1 levels in the group that received Nigella sativa supplementation was not able to improve growth disorders caused by exposure to pesticides during pregnancy. Genetic factors also play a role in the pathophysiology of stunting, this situation is to the findings of research conducted by Mweetwa et al which states that genetic variations are associated with stunting and the state of enteropathy that precedes it and various part ways related to gene expression, glycosylation, nerve signaling, sensitivity to nutrients and changes in the microbiota.[23]

Higher IGF-1 levels in the group that received Nigella sativa supplementation when compared to the control group that received pesticide exposure prove that the active substance content in Nigella sativa can repair cellular level damage that occurs due to pesticide exposure. Mitochondria are one of the cell organelles that can be damaged due to pesticide exposure, characterized by low IGF-1 levels. Previous research has shown that IGF-1 is protective of mitochondria. Treatment with low doses of IGF-1 shows several beneficial effects, including restoring physiological levels of IGF-1, improving insulin resistance and lipid metabolism, providing mitochondrial protection, and having hepatoprotective, neuroprotective, antioxidant, and antifibrogenic effects.[24]

In this study, it was found that low birth weight and the lowest post-natal weight gain (day 28) in the (K+) group who only received exposure to pesticides, this situation is possible due to the effect of free radicals exposure in the womb, decrease in hemoglobin and total protein levels, such as research conducted by Masuda Sultana in 2020, which proved that total protein and hemoglobin levels are related to low birth weight and poor nutrition in the fetus.[25]

This research has various limitations that may affect the research results. It is hoped that future research will measure hemoglobin levels and other blood profiles, observing part ways that may occur, for example, epigenetic modifications that affect gene expression, especially genes responsible for growth, intestinal microbiota profiles that occur due to nigella sativa supplementation, which can affect the immune system and gene expression, the repair mechanism that occurs due to Nigella sativa supplementation.

In conclusion, Nigella sativa supplementation can improve growth that is disrupted due to exposure to pesticides during pregnancy, characterized by an increase in body weight approaching normal growth (catch-up growth). The mean body weight of the group that received Nigella sativa supplementation of 21.6 mg/200gBW/day was not significantly different compared to the control group that received standard feed (p=0.114). The mean body weight of the group exposed to pesticides during pregnancy was the lowest compared to other groups in the ANOVA test, with a value of p<0.001. Increased IGF-1 levels prove that there is an improvement in cellular levels. Hormonal dysfunction that occurs due to exposure to pesticides is still reversible, so with Nigella sativa supplementation, which contains bioactive compounds as antioxidants, anti-inflammatory, anti-diabetic, immunomodulatory, and other mineral content in critical periods in the first 1000 days of life, the damage that occurs can still be repaired.

References

1. Mardiyana R, Darundiati YH, Dangiran HL and HLD. Hubungan paparan pestisida dengan kejadian stunting pada anak usia 2-5 tahun di Kabupaten Magelang (Studi Kasus di Kecamatan Ngablak). Media Kesehatan Masyarakat Indonesia. 2020;19(1):77–82. https://doi.org/10.14710/mkmi.19.1.77-82
2. de Onis M, Branca F. Childhood stunting: a global perspective. Matern Child Nutr. 2016;12 Suppl 1(Suppl 1):12–26. doi:10.1111/mcn.12231
3. Akrom A, Hidayati T, Kencana OW, Kurniawan NU. Infection and undernutrition increase the risk of stunting among rural children. Int J Public Heal Sci. 2022;11(3):920–6. doi:10.11591/ijphs.v11i3.21592
4. Aryastami NK, Shankar A, Kusumawardani N, Besral B, Jahari AB. Low birth weight was the most dominant predictor associated with stunting among children aged 12 – 23 months in Indonesia. BMC Nutr. 2017:1-6. doi:10.1186/s40795-017-0130-x
5. Widyawati SA, Suhartono S. The relationship between pesticide exposure and umbilical serum IGF-1 levels and low-birth weight: A case-control study in Brebes, Indonesia. Int J Occup Env Med. 2020;11:15–23. doi:10.15171/ijoem.2020.1809
6. Kartini A, Subagio HW, Hadisaputro S, Kartasurya MI, Suhartono S, Budiyono B. Pesticide Exposure and Stunting among Children in Agricultural Areas. Int J Occup Env Med. 2019;10:17–29. doi:10.15171/ijoem.2019.1428
7. Yuniarti H, Fasitasari M, Wibowo JW. Potensi nigella sativa dalam pengobatan covid-19. Ind J Clin Nutr Physic. 2020;3(1):89-102.
8. Shah HK, Sharma T, Banerjee BD. Organochlorine pesticides induce inflammation, ROS production, and DNA damage in human epithelial ovary cells: An in vitro study. Chemosphere. 2020;246:125691. doi:10.1016/j.chemosphere.2019.125691
9. Hu C, Wu Z, Huang Z, Hao X, Wang S, Deng J, et al. Nox2 impairs VEGF-A-induced angiogenesis in placenta via mitochondrial ROS-STAT3 pathway. Redox Biol. 2021;45:102051. doi:10.1016/j.redox.2021.102051
10. Hossain M, Nahar B, Haque MA,

Mondal D, Mahfuz M, Naila NN, et al. Serum adipokines, growth factors, and cytokines are independently associated with stunting in Bangladeshi Children. Nutrients. 2019;11(8):1827. doi: 10.3390/nu11081827.
11. Darakhshan S, Bidmeshki Pour A, Hosseinzadeh Colagar A, Sisakhtnezhad S. Thymoquinone and its therapeutic potentials. Pharmacol Res. 2015;95-96:138–58. doi:10.1016/j.phrs.2015.03.011
12. Kiani AK, Pheby D, Henehan G, Brown R, Sieving P, Sykora P, et al. Ethical considerations regarding animal experimentation. J Prev Med Hyg. 2022;63(2 Suppl 3):E255–266. doi:10.15167/2421-4248/jpmh2022.63.2S3.2768.
13. Roberts JR, Karr CJ; Council On Environmental Health. Pesticide exposure in children [published correction appears in Pediatrics. 2013 May;131(5):1013-4]. Pediatrics. 2012;130(6):e1765-e1788. doi:10.1542/peds.2012-2758
14. Sule RO, Condon L, Gomes AV. A Common Feature of Pesticides: Oxidative stress-the role of oxidative stress in pesticide-induced toxicity. Oxid Med Cell Longev. 2022;2022:5563759. doi:10.1155/2022/5563759
15. Ledda C, Cannizzaro E, Cinà D, Filetti V, Vitale E, Paravizzini G, et al. Oxidative stress and DNA damage in agricultural workers after exposure to pesticides. J Occup Med Toxicol. 2021;16(1):1. doi:10.1186/s12995-020-00290-z
16. Zhang J, Zhang J, Liu R, Gan J, Liu J, Liu W. Endocrine-disrupting effects of pesticides through interference with human glucocorticoid receptor. Environ Sci Technol. 2016;50(1):435–43. doi:10.1021/acs.est.5b03731
17. Tang ZR, Xu XL, Deng SL, Lian ZX, Yu K. Oestrogenic endocrine disruptors in the placenta and the fetus. Int J Mol Sci. 2020;21(4):1519. doi:10.3390/ijms21041519
18. Yilmaz B, Terekeci H, Sandal S, Kelestimur F. Endocrine disrupting chemicals: exposure, effects on human health, mechanism of action, models for testing and strategies for prevention. Rev Endocr Metab Disord. 2020;21(1):127–47. doi:10.1007/s11154-019-09521-z
19. Roberts JR, Karr CJ; Council On Environmental Health. Pesticide exposure in children [published correction appears in Pediatrics. 2013 May;131(5):1013-4]. Pediatrics. 2012;130(6):e1765-e1788. doi:10.1542/peds.2012-2758
20. Khan MA. Thymoquinone, a constituent of prophetic medicine-black seed, is a miracle therapeutic molecule against multiple diseases. Int J Health Sci (Qassim). 2019;13(1):1–2.
21. Rasoli MS, Khalili M, Mohammadi R, Soleimani A, Kohzadi R, Heidari R, et al. The chemical composition of nigella sativa l and its extract effects on lipid peroxidation levels, total antioxidant capacity and catalase activity of the liver and kidney in rats under stress. Gene Cell Tissue. 2018;5(1):1–6. doi:10.5812/gct.61323.Research
22. Puche JE, Castilla-Cortázar I. Human conditions of insulin-like growth factor-I (IGF-I) deficiency. J Transl Med. 2012;10:224. doi:10.1186/1479-5876-10-224
23. Mweetwa MN, Haritunians T, Dube S, Chandwe K, Amadi B, Zyambo K, et al. Genetic variation in environmental enteropathy and stunting in Zambian children: A pilot genome wide association study using the H3Africa chip. PLoS One. 2023;18(9):e0291311. doi:10.1371/journal.pone.0291311
24. Sádaba MC, Martín-Estal I, Puche JE, Castilla-Cortázar I. Insulin-like growth factor 1 (IGF-1) therapy: mitochondrial dysfunction and diseases. Biochim Biophys Acta. 2016;1862(7):1267–78. doi:10.1016/j.bbadis.2016.03.010
25. Sultana M, Jahan N, Sultana N, Doha M. Low level of serum Hemoglobulin concentration associated with neonatal birth weight. Bangladesh J Med Sci. 2020;19(2):278–83. doi: 10.3329/bjms.v19i2.45008