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Longevity toxicity after chronic α -endosulfan exposure in wild population of *Drosophila melanogaster* Oregon-R (Diptera: Drosophilidae)

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Abstract: The rapid increase in the world population causes different problems such as nutrition and shelter. In this case, people brutally destroy arable land to shelter, and concretization is rapidly spreading. In addition, it is necessary to increase the amount of products to be taken from the limited agricultural areas for the food needs of the increasing population. The decrease in agricultural areas appears as a factor that reduces the amount of product taken from the unit area. In addition, weeds and especially insects reduce the yield, storage, and marketing quality of products obtained from restricted areas. This type of plant products can also be considered a disease carrier vector in the food chain. To increase the yield, various insecticides have been developed against target organisms such as insects and one of these insecticides is α-endosulfan. However, non-target organisms living in the same ecosystem can also be affected by all these insecticides. In the present study, it was researched whether the chronic α-endosulfan application has an effect on longevity in non-target organisms. According to the data obtained, α-endosulfan shortened the maximum and mean lifespan in both male and female populations of the Oregon-R wild strain of *Drosophila melanogaster* based on dose-time interaction. The shortening observed in life span for both populations was statistically significant ($p<0.05$) compared to the control group. This situation can be considered as "population aging".

Keywords: Model organism, Insecticide, Lifespan, Aging

Drosophila melanogaster Oregon-R (Diptera: Drosophilidae) yabanıl popülasyonunda kronik α-endosülfan maruziyetinden sonra in vivo ömür uzunluğu toksisitesi

Özet: Dünya nüfusundaki hızlı artış beslenme ve barınma gibi farklı problemlere de sebep olmaktadır. Bu durumda insanlar barınabilmek için öncelikle tarıma elverişli alanları hunharca tahrip etmekte ve betonlaşma hızla yaygınlaşmaktadır. Ayrıca, artan nüfusun besin ihtiyacı için kısıtlı olan tarım alanlarından alınacak ürün miktarının artırılması da gereklidir. Tarım alanlarındaki azalma, birim alandan alınan ürün miktarını azaltan bir etken olarak karşımıza çıkmaktadır. Ayrıca, yabancı otlar ve özellikle böcekler de kısıtlı alanlardan elde edilen ürünlerin verim, depolama ve pazarlama kalitesini düşürmektedir. Bu tip bitkisel ürünler, besin zincirinde hastalık taşıyıcı vektörler olarak da değerlendirilebilir. Ürün miktarını artırabilmek için böcekler gibi hedef organizmalara karşı çeşitli insektisitler geliştirilmiştir ve bu insektisitlerden birisi de α-endosülfandır. Ancak aynı ekosistemde yaşayan ve hedef olmayan organizmalar da tüm bu insektisitlerden etkilenebilmektedir. Sunulan bu çalışmada kronik α-endosülfan uygulamasının hedef olmayan organizmalarda ömür uzunluğu üzerine etkili olup olmadığı araştırılmıştır. Elde edilen verilere göre, α-endosülfan doz-süre etkileşimine dayalı olarak *Drosophila melanogaster*'in Oregon-R yabanıl soyuna ait hem erkek hem de dişi popülasyonlarında maksimum ve ortalama ömür uzunluğunu kısaltmıştır. Her iki popülasyon için ömür uzunluğunda gözlenen kısalma kontrol grubuna göre istatistiki olarak önemli ($p<0.05$) bulunmuştur. Bu durum "popülasyon yaşlanması" olarak değerlendirilebilmektedir.

Anahtar Kelimeler: Model organizma, İnsektisit, Yaşam süresi, Yaşlanma

1. Introduction

The ecosystem is called the external environment in which organisms live. The physical elements of the ecosystem are soil, water, and air. On the other hand, the biological elements of the ecosystem are humans, animals, plants, and microorganisms. The inability to protect the initial state of the environment with unnatural conditions, especially by human hand, is defined as environmental pollution. Chemicals used in homes, industry, or for medical purposes cause air, water, and soil pollution. All the factors that pollute air and water also increase soil pollution further. The flora and fauna of the soil are affected by acid rainfall, dirty irrigation water, industrial wastes, and even piles of garbage. In particular, microorganisms found in the soil are organisms that are primarily exposed to pollution. Accordingly, the reduction of chemicals performed through soil bacteria may also be inhibited. All these reasons cause cumulative pollution in the soil. Different pollutants accumulated in the soil reach all consumer organisms through the food chain.

Plants, one of the most important rings of the food chain, are important for both animals and humans. For this reason, various pesticides are used to ensure the sustainability of herbal production and to increase the number of products that can be taken from the unit area. However, it is necessary not to ignore the risks to human health caused by pesticides and the preservation of natural balance.

Weeds and animal organisms that damage agricultural products are defined as a pesticide. The first information about the use of pesticides is found in the history of ancient Egypt and Greece. In 1882, French Botanist, Millardet, used the pesticide to prevent vineyard mildew. While the pesticides used in these years were of herbal origin, synthetic pesticides were produced since the 1930s. After 1990s, the usage of prohibitions and restrictions have begun to prevent risks to human health, the environment, or natural balance due to incorrect pesticides (Jayaraj et al. 2016; Affum et al. 2018; Sanlı and Tasdemir 2020). Because all types of pesticides can enter the human body through respiration, as well as passing from the soil to plant or spraying directly to the plant can switch to the human body (Altıkat et al. 2009). The pesticides used in the field of agriculture may remain in nature without disintegration and cause various diseases and even cancer in humans. Organocloric pesticides (OCPs), also defined as endocrine disruptive, are an extremely risky pesticide group (Şık et al. 2012; Zhang et al. 2016). Even low doses of OCPs accumulated in adipose tissue can cause many diseases such as eczema, dermatitis, chronic coronary insufficiency, and hypertonia (Altıkat et al. 2009). Some OCRs are banned by the Ministry of Food and Agriculture and Livestock because people also affect the central nervous system. In a study conducted by Jayaraj et al. (2016), although it was banned in 1987, the OCPs such as DDT, Heptachlor, and Endrin are still found in breast milk and fat tissue shows the dimensions of the danger. Because although they are banned, OCPs are detected in agricultural lands due to their permanent features and/or illegal use (Jiang et al. 2009; Satoh and Gupta 2011; Bozlaker et al. 2013; Yu et al. 2013; Zhang et al. 2015; Serttaş et al. 2021). Although a legal restriction is imposed on the production and use of any pesticide, illegal uses cannot be prevented until existing stocks are consumed. For this reason, it is estimated that α-endosulfan ($C_9H_6CI_6O_3S$), one of the last prohibited OCPs, can also be found in the soil or water as an environmental pollutant. (Tiryaki 2016; Türkyılmaz and Küçükçongar 2021). This insecticide and acaricide (IFCS 2003; Watts 2009) which is moderately toxic and lipophilic, affect organisms through the stomach and respiratory tract (Howland 1998; Kurutaş and Kılınç 2003; Arıkan et al. 2014). Compared to other organochlorine pesticides, α-endosulfan can still be found in threatening amounts in water due to its high solubility in water (Golfinopoulos et al. 2003). Although banned, endosulfan, which can be found in surface waters and underground waters, is potentially toxic to humans and especially aquatic organisms (Türkyılmaz and Küçükçongar 2021). In addition, different insecticides such as Thiodan and Thiotox, which are used today, contain endosulfan as an active ingredient (https://gcrec.ifas.ufl.edu). For this reason, although endosulfan is banned, it continues to exist in agriculture as an active ingredient. According to the EPA (U.S. Environmental Protection Agency), α-endosulfan concentrations above 0.22 μg/L cause adverse effects for aquatic organisms (Mersie et al. 2003). The presence of endosulfan in water, which is one of the most important components of the ecosystem, makes us think that it can also be found in the food chain through plants.

Based on this idea, this study was conducted to determine the effects of α-endosulfan, which has a long half-life and can survive in the ecosystem because it is not used correctly on non-target organisms. For this purpose, it was researched whether chronic α-endosulfan application affects lifespan depending on dose-time interaction in male and female populations of wild type (wt.) of *Drosophila melanogaster* Oregon-R.

2. Materials and Method

2.1. Experimental organism and living conditions

The *D.melanogaster* Oregon-R Meigen (Diptera; Drosophilidae), a model organism in genetics, was used for longevity testing. This strain, which has been inbred for many years at Atatürk University, Faculty of Science, Department of Biology, Genetics Research Laboratory, has no mutant features, long wings, brown body, and round-red eyes. *Drosophila* stock cultures are kept in 250 mL glass bottles in heated-cooled temperature cabinets with 40-60% relative humidity, 25±1 °C temperature, and constant dark conditions. Both main stock cultures and experimental groups are fed with Standard Drosophila Medium (SDM) containing granulated sugar, yeast, agar, cornmeal, and propionic acid to prevent contamination (Uysal et al. 2006). While the media of the main cultures are renewed every ten days, the media of the experimental groups are changed twice a week.

2.2. Insecticide used and lifespan assay

The open formula of α-endosulfan used in the study is given in Figure 1 (Zacharia, 2011). To determine the effects of α-endosulfan on longevity, ♀♀ and ♂♂ populations of the same age (72±4 hours) belonging to the Oregon-R wild strain of *D. melanogaster* were studied separately. First of all, the crosses were made between individuals belonging to this strain and preliminary stocks were prepared and the parents in each culture bottle in which the pupal stage were removed from the medium. The individuals to be used in the experimental groups were collected in different culture bottles, male and female, in every four to five hours for three days, as soon as they emerged from the pupa and before mating.

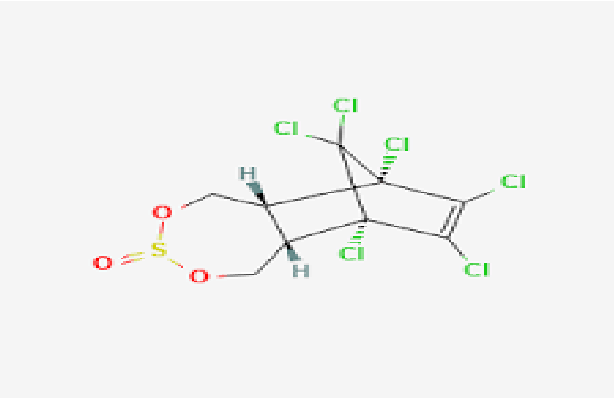


Figure 1. Chemical structure of α-endosulfan.

Then, two separate study setups, control and experimental groups were prepared simultaneously. SDM containing only distilled water and 1% acetone+SDM, the solvent of α-endosulfan (CAS numarası: 959-98-8, Fluka), were used as negative control groups. For the experimental groups containing α-endosulfan+SDM, preliminary trials were carried out and four different application doses (1, 2, 3, and 4 ppm) were determined. It was made in applications of less than 1 ppm, but no change was observed compared to the control groups. Mass deaths within 24 hours were also observed at higher applications than 4 ppm. To determine the longevity, all adult flies belonging to the control and experimental groups were first left to starve for 2 hours in culture bottles. Then, 100 individuals to be used in each application were divided into four groups of 25 individuals for convenience during counting. In the experimental groups, α-endosulfan was applied chronically and media containing different doses of α-endosulfan was renewed twice a week. All control and treatment groups were kept in heated-cooled incubators. Individuals were checked at each transfer and the deceased individuals were recorded by continuing the counts until the last individual died. Ambient conditions were kept stable for both control and experimental groups. The only variable was α-endosulfan, which was added to SDB at different doses.

2.3. Statistical analyses

The experiments were repeated three times for each group. The obtained data were analyzed with SPSS version 16.0 (Statistical Package for the Social Sciences Software, SPSS, Chicago, IL). The mean longevity of the control and experimental groups was compared using Duncan's one-way range test on the probability levels of 0.05.

The materials and methods section should contain sufficient detail so that all procedures can be repeated. Any modifications to existing methods should also be described.

3. Results

In this study, both maximum and mean lifespan were calculated to determine the effects of different doses of α-endosulfan on the ♀ and ♂ population of *D. melanogaster* (Table 1). While the maximum life span of *D. melanogaster* for the ♀ and ♂ populations was 78 and 76 days in the distilled water control group (no 1) respectively, this period was 72 days for both populations in the acetone control group (no 2). According to the data obtained, there was no difference at $p>0.05$ level in terms of maximum lifespan between the distilled water and acetone control groups of both populations.

However, as a result of the chronic application of α-endosulfan at different doses (1, 2, 3, 4 ppm, no 3-6) in the ♀♀ population, the maximum lifespan was shortened to 42, 42, 36, 33 days, respectively (Figure 2b). A similar situation was also observed in the ♂♂ population as a result of α-endosulfan application at the same doses. In the ♂♂ population, the maximum lifespan was shortened with increasing dose of α-endosulfan (Figure 2a), and the observed maximum lifespan decreased to 42, 39, 33, and 30 days (Table 1). The difference between the acetone control group and the application groups was statistically significant for both populations ($p<0.05$).

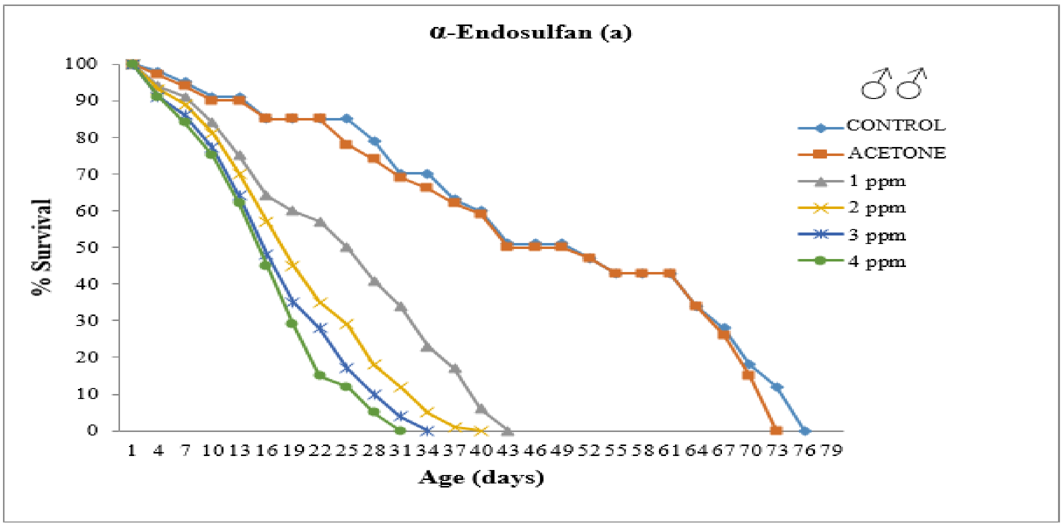
According to the data obtained, the average lifespan for the ♀♀ and ♂♂ populations was also calculated. The mean lifespan in the ♀♀ and ♂♂ populations was 47.49±2.03 (no 1), 47.80±2.14 (no 1), days for the distilled water control group and 46.65±2.03 (no 2), and 46.05±2.14 (no 2), days for the acetone control group, respectively ($p>0.05$). However, these values decreased significantly depending on the dose increase in the α-endosulfan application groups. The mean lifespan for the ♀♀ population was calculated as 24.96±2.03 and 17.43±2.03 days in the lowest (1 ppm, no 3) and highest (4 ppm, no 6) application groups. These values decreased from 23.88±2.14 (no 3) to 15.54±2.14 (no 6) days in the ♂♂ population ($p<0.05$). Negative correlation values for the decline in life span due to the increasing concentration of α-endosulfan were also found as R:-611 and R:-612 for the ♀♀ and ♂♂ populations, respectively (Table 1).

Table 1. Maximum and mean lifespan of male and female populations of *D. melanogaster* and the probability levels between groups.

Chronic α-Endosulfan Application								
	Female population				Female population			
Application groups (no)	No	ML1	ML2±SE	p<	No	ML1	ML2±SE	p<
Control (1)	100	78	47.49±2.03		100	76	47.80±2.14	
Acetone (2)	100	72	46.65±2.03		100	72	46.05±2.14	
1 ppm (3)	100	42	24.96±2.03	1-3,4,5,6* 2-3,4,5,6* 3-4,5,6* 4-5,6*	100	42	23.88±2.14	1-3,4,5,6* 2-3,4,5,6* 3-4,5,6* 4-5,6*
2 ppm (4)	100	42	21.60±2.03		100	39	19.05±2.14	
3 ppm (5)	100	36	17.73±2.03		100	33	16.80±2.14	
4 ppm (6)	100	33	17.43±2.03		100	30	15.54±2.14	
Regression Level			R:-611				R: -612	

SE: Standard error, *: The difference between the groups is significant at the $p<0.05$ level, R: Regression level,

No:Number of individuals, ML1: Maximum lifespan, ML 2: Mean lifespan



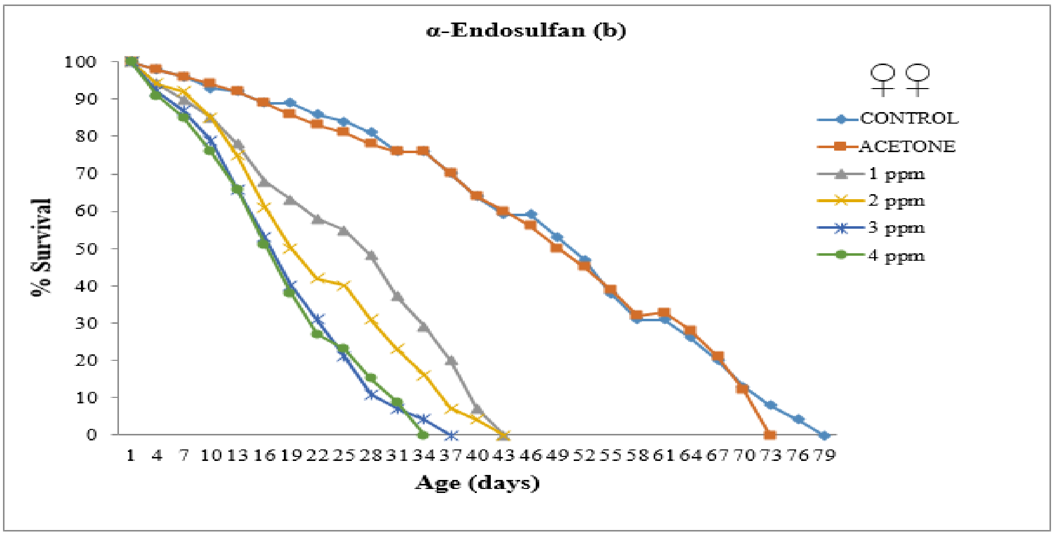


Figure 2. The survival curves of male (a) and female (b) individuals of *D. melanogaster* living medium applied with different concentrations of α-endosulfan during adult stages.

4. Discussion

Insecticides are synthetic or organic chemicals that both increase production in limited agricultural areas and are important for home and public health. Insects reduce the yield, storage, and quality of agricultural products and also act as disease vectors for humans and animals. However, insecticides developed against insects, which are the target organisms, are used unlimitedly and uncontrollably today. α-Endosulfan is a chlorinated hydrocarbon insecticide and acaricide belonging to the cyclodiene subgroup applied to a wide variety of insects and mites in plants, including tea, coffee, cotton, fruit, vegetables, rice, and grain. It has also been used in agriculture to control pests such as white flies, aphids, leafhoppers, Colorado potato beetles, and cabbage worms (Berntssen et al. 2017).

From 1954 to 2000, when α-endosulfan was registered, cumulative use in agriculture is 308,000 tons. Global consumption of insecticide rose from around 9000 tons/year in the early 1980s to 12800 tons in the 1990s. This shows that α-endosulfan is used very widely in different countries. Until 2010, when it was banned globally, it is stated that the worldwide α-endosulfan production was 18000-20000 tons/year (Cone 2010). This semi-volatile insecticide was added to the list of permanent organic pollutants in 2011 with the Stockholm Convention due to its long-range atmospheric transport, especially its accumulation in adipose tissue, and its endocrine disruptor in mammals (Mathew 2011).

In a study by Kristy (2008), this insecticide was even detected in dust from the Sahara desert collected from the Caribbean after being dispersed into the Atlantic Ocean. Therefore, they can be found in air, water, soil, rain, snow, ice, and even fog. Thus, they can affect very wide geographies and the creatures living there. Due to all these negative effects, its production and use have been banned worldwide since mid-2012. Although the legal use of α-endosulfan and its metabolites has been stopped due to the reasons such as high resistance to degradation in nature, bioaccumulation, and environmental transport, they can still be detected in environmental samples and pose a risk to the environment and public health (Kurutaş and Kılınç 2003; Türkyılmaz and Küçükçongar 2021). Although banned according to Türkyılmaz and Küçükçongar (2021), this insecticide can still be found in groundwater. The main concern for human health is that α-endosulfan shows xenoestrogenic (xenohormone) properties. Because xenoestrogens can mimic the effects of endogenous estrogen, they cause early puberty and reproductive system disorders in young people (Herman-Giddens et al. 1997; Aksglaede et al. 2006; Massart et al. 2008). Xenoestrogens found in wastewater treatment plants caused impaired ovarian and testicular histopathology, gonadal intersex, reduced gonadal size, induction of vitellogenin, and altered sex ratios in fish living in these areas (Vajda et al. 2008). Precocious puberty and rapid bone development have also been observed in humans fed contaminated milk or fed fish containing xenoestrogens due to bioaccumulation (Hotchkiss et al. 2008). According to different researchers, early puberty also increases the risk of breast cancer and prostate cancer. Similar effects have been observed not only in humans but also in rats (Darbre 2006; Della Seta et al. 2008; Xu et al. 2010).

Non-target organisms as well as target organisms are affected by the use of α-Endosulfan as an insecticide (Güven and Koç 2020). This causes serious problems in terms of biodiversity (Mossler et al. 2006). The shortening of life span in fruit flies, which is one of the non-target organisms in this study, can be attributed to α-endosulfan. Because the only variable in the optimum living conditions of *D. melanogaster* is α-endosulfan (Material and Method). According to our data, there is a positive correlation between dose increase of α-endosulfan and the shortening of life span (Table 1, Figure 2). It has been shown in previous studies that α-endosulfan concentration and exposure time stimulate the formation of reactive oxygen species (ROS), which in turn causes double-strand breaks in DNA (Bajpayee et al. 2006; Robin and Raghavan 2016). Again, in previous studies, it was determined that different insecticides cause genomic instability by causing genotoxic changes. Chlordane, one of the organochlorine insecticides, also shortened the life span of *D.melanogaster*, just like α-endosulfan. In addition, it was observed that chlordane significantly increased the micronucleus frequency and decreased the nuclear division index in human lymphocyte cells (Özyurt et al. 2018). Again, chlorfenson, one of the organochlorine insecticides, was determined to induce somatic mutations in *D.melanogaster* by somatic mutation and recombination test (Kızılet and Uysal 2019). Similar genotoxic effects were seen after bifenthrin application, and this insecticide caused both micronucleus and sister chromatid exchanges in human lymphocytes (Kızılet and Uysal 2022). According to the same researchers, dimethoate (organophosphorus compounds, sub-group of insecticides) caused similar genotoxic effects (Kızılet et al. 2019). Breaks in DNA can also occur in the telomere regions of chromosomes. When the telomere reaches its critical length, cell division stops. This is called "aging at the cellular level". Cellular aging also accelerates the biological aging of the organism.

Hydroxyl radical, superoxide radical, and hydrogen peroxide are the most well-known ROS. Under normal conditions, organisms are protected from the destructive effect of ROS with the enzymes superoxide dismutase (SOD), glutathione peroxidase (GPx), glutathione reductase (GR), and catalase (CAT) and radical scavengers such as β-carotene, ascorbic acid and α-tocopherol taken with food. However, due to oxidative stress, ROS cause destruction in biomolecules and molecular damage begins in the cell. This accelerates normal biological aging.

There are many different definitions of aging. However, we can define aging in general as the loss of function of tissues and organs necessary for life over time. Intrinsic physiological losses may occur in tissues and organs due to age, and exogenic factors may accelerate the aging process. Biological aging does not depend on a single cause and cannot be explained by a single mechanism. Free radicals theory, somatic mutation, telomere shortening, immunological theory, neuroendocrine theory, the theory of alteration of proteins, and antagonistic pleiotropy theory are some of the theories of aging. In our opinion, *D.melanogaster'*s shortening of lifespan and accordingly, population aging can be explained by the "Theory of Free Radicals". Because *D.melanogaster* Oregon-R is a wild strain in terms of all genotypic properties. In our opinion, "the significant shortening of lifespan observed in adult individuals belonging to experimental groups (p<0.05) indicates the aging of the population".

5. Conclusion

Insecticides applied against various pests in agricultural areas may directly affect cumulatively influenced non-target organisms at any stage of their development (eggs, larvae, or adults). Sometimes insecticides such as α-endosulfan can be found in soil and underground waters, they can affect organisms through the food chain. As a result, insecticides, no matter what purpose it is used, also affect biodiversity. This situation should not be ignored and in our opinion, "organic insecticide use in agriculture should be spread and encouraged by the state".

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None

References

Affum AO, Acquaah SO, Osae SD. 2018. Kwaansa-Ansah EE. Distribution and risk assessment of banned and other current-use pesticides in surface and groundwaters consumed in an agricultural catchment dominated by cocoa crops in the Ankobra Basin, Ghana. Sci Total Environ. 15(633): 630-640

Aksglaede L, Juul A, Leffers H, Skakkebaek NE, Andersson A M. 2006. The sensitivity of the child to sex steroids: possible impact of exogenous estrogens. Hum Reprod Update. 12(4): 341-9

Altıkat A, Turan T, Torun FE. 2009. Türkiye'de pestisit kullanımı ve çevreye olan etkileri. Atatürk Üniv Ziraat Fak Derg. 40(2): 87-92

Arıkan Fİ, Özkan F, Dallar BY. 2014. Fark edilemeyen zehir: endosulfan. Bakırköy Tıp Derg, 10: 179-181

Bajpayee M, Pandey AK, Zaidi S, Musarrat J, Parmar D, Mathur N. 2006. DNA damage and mutagenicity induced by endosulfan and its metabolites. Environ Mol Mutagen 47(9): 682-692

Berntssen MHG, Maage A, Lundebye A. 2017. Chemical contaminants and residues in food (Second Edn) Woodhead Publishing Series in Food Science, Technology and Nutrition U.S.A. pp. 517-551

Bozlaker A, Müezzinoğlu A, Odabaşı M. 2013. Processes affecting the movement of organochlorine pesticides (OCPs) between soil and air in an industrial site in Turkey. Chemosphere. 77(9): 1168-1176

Cone M. 2010. EPA bans pesticide found on cucumbers, zucchini, green beans and other vegetables. The Daily Green.

Darbre PD. 2006. Environmental oestrogens, cosmetics and breast cancer. Best Pract Res Clin Endocrinol Metab. 20(1): 121-43

Della Seta D, Farabollini F, Dessì-Fulgheri F, Fusani L. 2008. Environmental-like exposure to low levels of estrogen affects sexual behavior and physiology of female rats. Endocrinol. 149(11): 5592-8

Golfinopoulos SK, Nikolaou AD, Kostopoulou MN, Xilourgidis NK, Vagi MC, Lekkas DT. 2003. Organochlorine pesticides in the surface waters of Northern Greece. Chemosphere. 50: 507-516

Güven E, Koç I. 2020. Diversity of non-targeted nematode, bacteria and microfungi populations in soil after some pesticide treatment. Yuzuncu Yil Univ Journal of Agric Sci. 30(2): 252-65

Herman-Giddens ME, Slora EJ, Wasserman RC, Bourdony CJ, Bhapkar MV, Koch GG, Hasemeier CM. 1997. Secondary sexual characteristics and menses in young girls seen in office practice: a study from the pediatric research in office settings network. Pediatr. 99(4): 505-12

Hotchkiss AK, Rider CV, Blystone CR, Wilson VS, Hartig PC, Ankley GT, Foster PM, Gray CL, Gray LE. 2008. Fifteen years after "wingspread"-environmental endocrine disrupters and human and wildlife health: where we are today and where we need to go. Toxicol Sci. 105(2): 235-259

Howland MA. 1998. Insecticides: chlorinated, hydrocarbons, pyrethrins, and DEET. In: Goldfrank LR, Flomenbaum NE, Lewin NA, Weissman RS, Howland MA (eds). Goldfrank's Toxicologic Emergencies, 6th edn. Mcgraw-Hill, NewYork, NY, 1451-8

IFCS, 2003. Acutely toxic pesticides: initial input on extent of problem and guidance for risk management, intergovernmental forum on chemical safety. Forum IV, Bangkok, Thailand, 1-5

Jayaraj R, Megha P, Sreedev P. 2016. Organochlorine pesticides, their toxic effects on living organisms and their fate in the environment. Interdiscip Toxicol. 9(3-4): 90-100. doi: 10.1515/intox-2016-0012

Jiang YF, Wang XT, Jia Y, Wang F, Wu MH, Sheng GY, Fu JM. 2009. Occurrence, distribution and possible sources of organochlorine pesticides in agricultural soil of Shanghai. J Hazard Mater. 170(2-3): 989-97

Özyurt E, Kızılet H, Uysal H. 2018. Hedef olmayan organizmalarda klordanın biyo-etkileşimi. Commagene J Biol. 2(1): 48-54

Kızılet H, Uysal H. 2019. Induced somatic mutation during chronic exposure of chlorfenson on *Drosophila melanogaster* Oregon-R (wild type). Drosoph Inf Serv. 102: 4-8

Kızılet H, Uysal H. 2022. Genoprotective role of purslane methanol extract against somatic mutations induced by bifenthrin, a third generation prethyroid insecticide. J Agric Sci. 28(4): 583-591.

Kızılet H, Yılmaz B, Uysal H. 2019. Herbal medicine against genotoxicity of dimethoate, an insecticide, in mammalian somatic cells. Heliyon, 5(3): e01337. doi:10.1016/j.heliyon. e01337

Kristy R. 2008. Harmful elements in Sahara dust. Trinidad and Tobago Express. Retrieved, 05-14

Kurutaş BE, Kılınç M. 2003. Pestisitlerin biyolojik sistemler üzerine etkisi. Arşiv. 12: 215-228

Massart F, Meucci V, Saggese G, Soldani G. 2008. High growth rate of girls with precocious puberty exposed to estrogenic mycotoxins. J Pediatr. 152(5): 690-5

Mathew R. 2011. Stockholm Convention approves recommendation for ban on endosulfan

Mersie W, Seybold CA, Mcnamee C, Lawson MA. 2003. Abating endosulfan from run off using vegetative filter strips: the importance of plant species and flow rate. Agric Ecosyst Environ. 97: 215-223

Mossler M, Aerts MJ, Nesheim ON. 2006. Florida Crop/Pest Management Profiles: Tomatoes: CIR 1238/PI039, Rev. 3/2006. EDIS

Robin S, Raghavan SC. 2016. Induction of DNA damage and erroneous repair can explain genomic instability caused by endosulfan. Carcinogenesis. 37(10): 929-940

Sanlı G, Taşdemir Y. 2020. Seasonal variations of organochlorine pesticides (OCPs) in air samples during day and night periods in Bursa, Turkey. Atmos Pollut Res. 11: 2142-2153

Satoh T, Gupta C. 2011. Anticholinesterase pesticides: metabolism, neurotoxicity, and epidemiology. 1st Edition, Kindle Edition pp.1-9

Serttaş A, Ayaz T, Yurdakul S, Doğan G, Göktaş RK, Civan M. 2021. Sera zirai toprağında toplam pestisit seviyeleri ve sera özellikleri ile pestisit seviyeleri arasındaki ilişkinin değerlendirilmesi. J Engr Sci Desig. 9(3): 900-910

Şık B, Küçükçetin İÖ, Erkaymaz T, Yıldız G. 2012. Gıda güvenliği açışından endokrin sistem bozucu pestisitler. Akademik Gıda. 10(2): 89-95

Tiryaki O. 2016. Türkiye'de yapılan pestisit kalıntı analiz ve çalışmaları. Erciyes Univ J Inst Sci Technol. 32(1): 72-82

Türkyılmaz M, Küçükçongar S. 2021. Endosülfan ve metabolitlerinin su örneklerinde vorteks destekli sıvı-sıvı mikro ekstraksiyon ve yüksek performanslı sıvı kromatografi kullanılarak analizi. Bitlis Eren Univ J Sci. 10(4): 1404-1415

Uysal H, Şişman T, Aşkın H. 2006. *Drosophila* Biology and Crossover Methods (Extended 2nd Edition). Atatürk University Publications, ISBN: 975-442-111-0, Erzurum, Türkiye

Vajda AM, Barber LB, Gray JL, Lopez EM, Woodling JD, Norris DO. 2008. Reproductive disruption in fish downstream from an estrogenic wastewater effluent. Environ Sci Technol. 42(9): 3407-3414

Watts M. 2009. Endosulfan 2nd Edition, PANAP (Pesticide Action Network Asia and the Pacific), Germany, 1-43

Xu X, Dailey AB, Talbott EO, Ilacqua VA, Kearney G, Asal AR. 2010. Associations of serum concentrations of organochlorine pesticides with breast cancer and prostate cancer in U.S. adults. Environ Health Perspect. 118: 60–66

Yu HY, Li FB, Yu WM, Li YT, Yang GY, Zhou SG, Zhang TB, Gao YX, Wan HF, 2013. Assessment of organochlorine pesticide contamination in relation to soil properties in the Pearl River Delta, China. Sci Total Environ. 447:160-68

Zacharia JT. 2011. Identity, Pesticides In The Modern World-Trends In Pesticides Analysis, Margarita Stoytcheva, In Tech, Croatia, 3-10. ISBN 978-953-307-437-5

Zhang A, Luo W, Sun J, Xiao H, Liu W. 2015. Supplementary material for distribution and uptake pathways of organochlorine pesticides in greenhouse and conventional vegetables. Environ Sci Eng. 505: 1142-1147

Zhang J, Zhang J, Liu R, Gan J, Liu J, Liu W. 2016. Endocrine-disrupting effects of pesticides through interference with human glucocorticoid receptor. Environ Sci Technol. 50(1): 435-443