Kafkas Üniversitesi Fen. Bil. Enst. Derg.
9 (1): 33 – 38, 2016

Organofosforlu Pestisitlerin Yüksek Omurgalı Karaciğer Üzerindeki Etkileri

Özlem ÖNEN[1],*, Yasemen ADALI[2], Hatice BEŞEREN[3]

[1] *Kafkas Üniversitesi, Fen Edebiyat Fakültesi, Biyoloji Bölümü, Kars*
[2] *Kafkas Üniversitesi, Tıp Fakültesi, Tıbbi Patoloji Anabilim Dalı, Kars*
[3]*Kafkas Üniversitesi, Veteriner Fakültesi, Patoloji Anabilim Dalı, Kars*

Yayın Kodu (Article Code): 9-1A-5

Özet: Organofosforlu pestisitler, fosfor içeren asitlerin ester, tiol ester veya anhidrit türevleri olup tarımda, evlerde, bahçelerde ve veterinerlikte kullanılmaktadır. Bu derlemede, öncelikle organofosforlu pestisitlerin yüksek omurgalıların karaciğer histolojisi üzerindeki etkilerine ilişkin güncel raporların değerlendirilerek ileride yapılacak çalışmalara ışık tutabilmesi amaçlanmıştır.

Mevcut literatür bilgileri, Kafkas Üniversitesi, Fen-Edebiyat Fakültesi, Biyoloji Bölümü, Zooloji ve Ekotoksikoloji Laboratuvarları ve Tıp Fakültesi, Tıbbi Patoloji Anabilim Dalı Laboratuvarlarındaki çalışmalar ışığında gözden geçirilerek derleme halinde düzenlenmiştir.
Çeşitli kimyasalların etkilerini ortaya koymak için karaciğer, omurgalılarda detoksifikasyon merkezi olması bağlamında histopatolojik olarak öncelikli incelenmesi gereken alanlardandır. Burada, organofosforlu pestisitlerin yüksek omurgalıların karaciğerlerindeki histopatolojik etkileri derlenmiştir. Gözlemlenen başlıca histopatolojik etkiler, sinüzoidal dilatasyon, konjesyon, steatoz, alkolik hepatit benzeri bulgular ve sentrolobüler nekroz olarak özetlenmiştir.

Bu derlemede anlatılan çalışmalar doğrultusunda, organofosforlu pestisitlerin son derece toksik oldukları ve diğer pestisite nazaran doğada daha hızlı parçalansalar da akut toksisitelerinin yüksek olduğu ortaya konmuştur. Organofosforlu pestisit maruziyetiyle yüksek omurgalıların karaciğerlerinde izlenen histolojik değişimlerin özgül nitelik taşımadığı, ancak sürekli artan pestisit kullanımı uzantısında, biyoçeşitliliğin korunmasına yönelecek tüm çalışmalarda bu değişimlerin izlenmesinde yarar olduğu açıktır. Gelişmiş tekniklerin kullanıldığı ileri düzeydeki bütün araştırmalar, histolojik düzeyde temel verilere dayanarak gerçekleştirilebilir ve histopatoloji; özel alanlardaki araştırmaların altın anahtarıdır.

Anahtar Kelimeler: Organofosforlu pestisitler, yüksek omurgalılar, karaciğer, histopatoloji.

The Effects of Organophosphorous Pesticides on the Liver of Advanced Vertebrates

Abstract: Organophosphorus pesticides are the esters, thiol ester or anhydride derivatives of acids containing phosphor; and are used in agriculture, houses, gardens and veterinary medicine. Primarily, it was aimed to able to shed light on future studies, evaluating the current reports regarding the effects of organophosphorus pesticides on the liver of advanced vertebrates.

The available literatural information arranged as compilation by revised in accordance with the works in the Kafkas University, Faculty of Arts and Sciences, Department of Biology, Zoology and Ecotoxicology Laboratories and Faculty of Medicine, Department of Medical Pathology Laboratories.

To expose the effects of various chemicals, the liver is the area that should be examined for histopathologically priority in the context of being a detoxification center in vertebrates. Here, histopathological effects of organophosphorus pesticides in the lungs of advanced vertebrates were compiled. The major histopathological effects observed in the liver were summarized as sinusoidal dilation, congestion, steatosis, alcoholic hepatitis like findings and centrolobular necrosis.

It was demonstrated that organophosphorus pesticides is highly toxic and their acute toxicities are high although they break down more quickly in nature than many other pesticides in accordance with the researches described in this review. It is clear that histologic changes in the liver of high vertebrates with organophosphorus pesticide exposure are not specific, but it is obvious that the monitoring of these alterations is useful in all the activities that will lead to the conservation of biodiversity. All advanced researches that uses developed techniques may be carried out basing on the fundamental data on the histological level and histopathology is the golden key of the researches in specialized fields.

Keywords: Organophosphorus pesticides, advanced vertebrates, liver, histopathology.

*****(Corresponding author) **e-mail:** onenozlem@gmail.com

Introduction

Organophosphate pesticides come from heterogeneous chemicals specially designed for pests, weeds and plant diseases (Bolognesi, 2003; Kumar et al., 2010). Organophosphate pesticides have been widely used in agriculture for years for plant protection and pest control, and thousands of these compounds are marketed for these purposes [Mansour et al., 2009; Eleršek and Filipič, 2011]. Insecticides such as malation, paration, diazinon, forat, terbufos, phthionine and chlorpyrifos; nerve gases such as soman, sarin and tabun; ecotriphate and isoprofloxacin used in eye treatment and trichlorfon used against parasites are examples of organophosphorus insecticides (Kats and Brooks, 2009).

The toxicity of organophosphorous pesticides depends on their chemical structure, their metabolism in the target organism, their exposure to concentration (or dosage), their degree of fragmentation, the entrance pattern to organism, etc. (Eleršek and Filipič, 2011). The best described toxic effects of organophosphate pesticides are neurological manifestations following acute poisoning as a consequence of the primary target (acetylcholinesterase). Potential secondary targets and toxic effects outside the nervous system are very important for risk assessment, although they have not been studied adequately. Unlike other man-made chemicals, organophosphate pesticides can affect a large part of the human population as a result of domestic consumption, agricultural activities and contaminant food and water consumption (Maroni et al., 2000).

According to World Health Organization records, about 3 million people worldwide are exposed to toxicity due to pesticides and it is reported that this toxicity causes a high rate of death. Among them, organophosphorus pesticides are known to suppress the enzyme acetylcholinesterase and cause neurotoxicity (Demirdöğen, 2010).

The aim of this review is to evaluate and summarize the damages caused by organophosphate pesticides especially on the liver structure histopathologically in the context of being a detoxification center in mammals from high vertebrates.

Material and Method

The current literature is compiled and reviewed in the light of the studies in the Kafkas University, Faculty of Arts and Sciences, Department of Biology, Zoology and Ecotoxicology Laboratories and Faculty of Medicine, Department of Medical Pathology Laboratories.

Results

In all vertebrates, the liver is composed of smooth, polygonal hepatocytes which has prominent dark nucleus and distinct cell borders around the central vein and sinusoids extending between them (Ganser et al., 2003; Junqueira and Carneiro, 2003; Gartner and Hiatt, 2006; Ross and Pawlina, 2006; Aroud, 2011; Önen et al., 2011; Amaral et al., 2012; Yao et al., 2012; Holy et al., 2015; Muikham et al., 2016; Odokuma and Omokaro 2015; Okle et al., 2016).

Organophosphorus compounds are known to seriously affect the liver. Common changes in the liver in high vertebrates caused by organophosphorus compounds are necrosis and steatosis. The general conclusion is that the findings in the liver do not change and are not specific to the chemical being exposed (Kerem et al., 2007; SutayandTirpude, 2008; Kumar et al., 2010; Alarami, 2015; Holy et al., 2015).

Liver is the organ where activation and detoxification of organophosphorus compounds takes place (Barr et al., 2005; Khogali, 2005).

Pesticides can directly kill high vertebrates which are not targeted organisms, also impair liver function in the adverse effects of all metabolic processes.

For example, in rat livers which are exposed to fenthion, an organophosphate pesticide; minimal cellular changes like congestion, Kupffer cell activation and centrolobular damage were seen in low-dose exposure groups while swelling and vacuolization in hepatocytes and moderate centrolobular degeneration were observed in high dose groups (Kerem et al., 2007, Figure 1).

In this frame , according to some studies taken as reference (Holy et al., 2015; Saha and Das, 2015), it is reported that in the liver of rats exposed to dichlorvos, an organophosphate pesticide, differ from control group by the presence of feathery changes in hepatocytes, congestion, sinusoidal dilatation, steatosis-like fatty change and centrolobular necrosis around the central vein and an increase in toxicity due to dose escalation has been reported.

In diabetic rats with organophosphorus insecticide exposure to monocrotophyx, prominent changes in liver like congestion in central vein, enlargement of hepatocytes as well as focal necrosis, sinusoidal dilatation, fatty degeneration, congestion in sinusoids around the central vena, swelling and vacuolization in hepatocytes, picnosis like degenerations (Figure 2) were reported (Benjamin et al., 2006).

Within the scope of a study on humans as the most advanced high vertebrates, congestion, centrolobular necrosis, fatty degenerations, alcoholic hepatitis-like findings, and sinusoidal dilation were reported in human livers examined in forensic laboratories (Sutay and Tirpude, 2008).

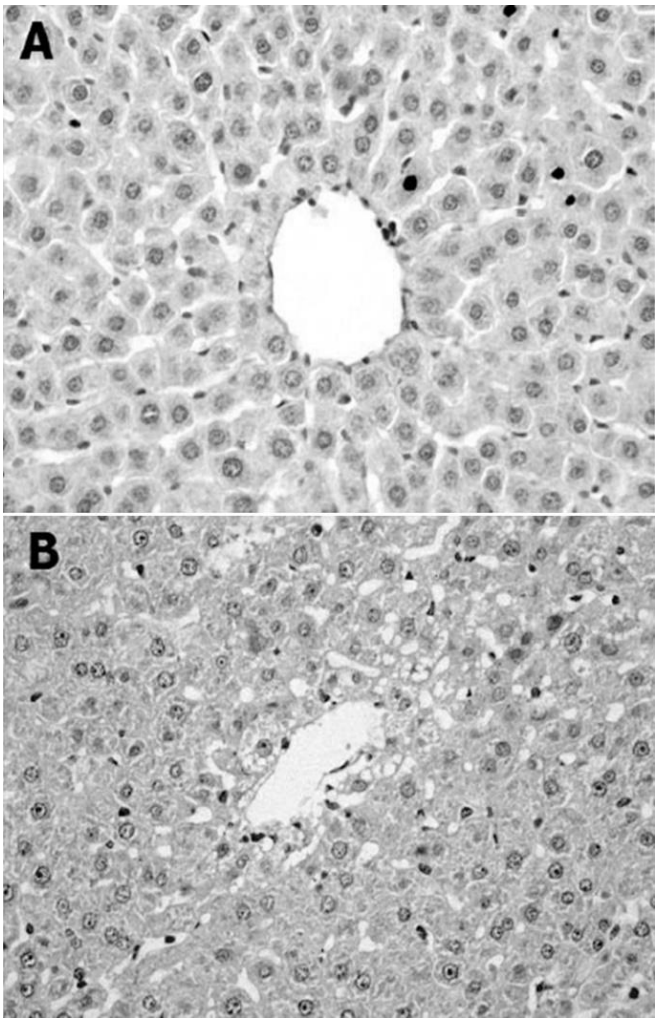

Figure 1. Histopathological changes observed in rat liver with fenthion exposure. **A.** Low dose fenthion exposure, no cell damage present, **B.** High dose fenthion exposure, swelling and vacuolization of hepatocytes, and centrolobular deformation evaluated as moderate damage, HE x 200 (Kerem et al., 2007).

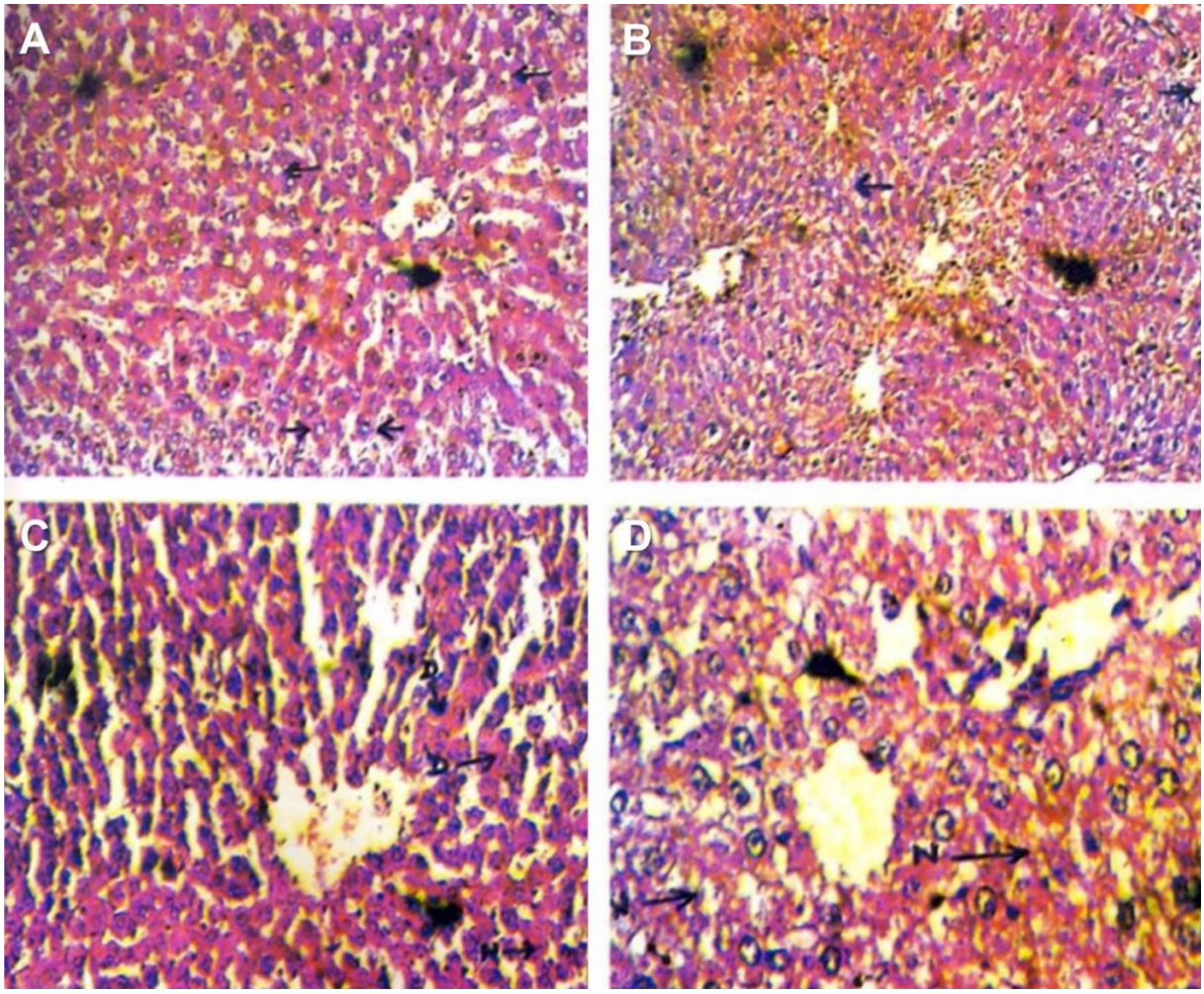

Figure 2. Histopathological changes in albino rat liver exposed to monocrotophos **A-B.** Fat degeneration: arrow **C.** Necrosis and degeneration in parenchyma cells: N, sinusoidal dilatation: D, **D.** centrolobular necrosis: N, A-C x 200, D x 400 (Benjamin et al., 2006).

Discussion and Conclusion

Along with the common histological alteration steatosis observed in the livers of high vertebrates as a result of various chemical applications, the changes observed are not as specific as many times emphasized. However, there is definitely benefit in monitoring these changes in all studies that will lead to the conservation of biodiversity in the context of ever-increasing chemical use. All advanced studies using advanced techniques can be performed on the basis of histological histology and histopathology; Is the starting line of research in specific areas. Agricultural governments of developed countries should focus on the monitoring and optimization of the use of organophosphorus compounds as pesticides and, most importantly, the promotion of the use of organic pesticides from chemical pesticides.

References

Alarami AMJ 2015. Histopathological Changes in the Liver and Kidney of Albino Mice on Exposure to Insecticide, Dimethoate. *International Journal of Current Microbiology and Applied Sciences*, 4(7): 287-300.

Amaral MJ, Bicho RC, Carretero MA, Sanchez-Hernandez JC, Faustino AMR, Soares AMVM, Mann RM 2012. The use of a lacertid lizard as a model for reptile ecotoxicology studies: Part 2 – Biomarkers of exposure and toxicity among pesticide exposed lizards. *Chemosphere*, 87(7): 765–774. http://dx.doi.org/10.1016/j.chemosphere. 2012 .01.048

Aroud M 2011. Biological Markers of Human Exposure to Pesticides. Chapter: 10. In: Pesticides in the Modern World – Pests Control and Pesticides Exposure and Toxicity Assessment. pp. 191-212. Editor: Margarita Stoytcheva ISBN: 978-953-307-

457-3,InTech,Available from:http://www.intechopen.com/books/pesticides-in-the-modern-world pests-control-and-pesticides-exposure-and-toxicity-assessment/biological-markers-of-human-exposure-topesticides

Barr DB, Allen R, Olsson AO, Bravo R, Caltabiano LM, Montesano A, Nguyen J, Udunka S, Walden D, Walker RD, Weerasekera G, Whitehead Jr RD, Schober SE, Needham LL 2005. Concentrations of selective metabolites of organophosphorus pesticides in the United States population. *Environmental Research*, 99: 314-326. doi:10.1016/j.envres.2005.03.012

Benjamin N, Kuswah A, Sharma RK, Katiyar AK 2006. Histopathological changes in liver, kidney and muscles of pesticides exposed malnourished and diabetic rats. Indian Journal of Experimental Biology, 44: 228-232.

Bolognesi C 2003. Genotoxicity of pesticides: a review of human biomonitoring studies. *Mutation Research*, 543: 251–272.

Demirdöğen BC 2010. Organofosfatlı-pestisit-zehirlenmeleri ve serum paraoksonaz 1 (PON1) enziminin organofosfat metabolizmasındaki rolü. *Türk Hijyen ve Deneysel Biyoloji Dergisi*, 67(2): 97-112.

Eleršek T, Filipič M 2011. Organophosphorous Pesticides - Mechanisms of Their Toxicity. Chapter 12. In: Pesticides - The Impacts of Pesticides Exposure. (ed. M Stoytcheva), Published: January 21, 2011 under CC BY-NC-SA 3.0 license, pp. 243-290. doi: 10.5772/14020, ISBN: 978-953-307-531-0

Ganser LR, Hopkins WA, O'Neil L, Hasse S, John H. Roe JH, Sever DM 2003. Liver Histopathology of the Southern Watersnake, Nerodia fasciata fasciata, Following Chronic Exposure to Trace Element-Contaminated Prey from a Coal Ash Disposal Site. *Journal of Herpetology*, 37(1): 219-226. doi: 10.1670/0022-1511(2003)037[0219:LHOTSW]2.0.CO;2

Gartner LP, Hiatt JL 2006. Color Textbook of Histology. 3rd Edition. Philedelphia, Pennsylvania, W.B. Saunders Company, 577 pp.

Holy B, Kenanagha B, Onwuli DO 2015. Haemato-pathological effect of Dichlorvos on blood Picture and liver cells of albino rats. *Journal of Toxicology and Environmental Health Sciences*, 7(2): 18-23. doi: 10.5897/JTEHS2015.0327 ISSN: 2006-9820.

Junqueira LC, Carneiro J 2004. Basic Histology: 10. Edition. Text & Atlas. Lange Medical Books/McGraw-Hill, New York.

Katz KD, Brooks DE 2009. Organophosphate Toxicity. In: Medscape. Editors: Talavera F, Tarabar A, Kirkland L, http://emedicine.medscape.com/article/167726-overview (Erişim tarihi: 10.12.2009)

Kerem M, Bedirli N, Gürbüz N, Ekinci Ö, Bedirli A, Akkaya T, Şakrak Ö, Paşaoğlu H 2007. Effects of Acute Fenthion Toxicity on Liver and Kidney Function and Histology in Rats. *Turkish Journal of Medical Sciences*, 37(5): 281-288.

Khogali FA, Sheikh JB, Rahman SA, Rahim AA, Daghestani MH, 2005. Histopathological and Hematological Effects of Dimethoate 40EC on Some Organs of Albino Mice. *Journal of King Saud University - Science*, 18(2): 73-87.

Kumar SV, Fareedullah Md, Sudhakar Y, Venkateswarlu B, Kumar EA, 2010. Current review on organophosphorus poisoning. *Archives of Applied Science Research*, 2(4): 199-215.

Mansour SA, Mossa AH 2009. Lipid peroxidation and oxidative stress in rat erythrocytes induced by chlorpyrifos and the protective effect of zinc. *Pesticide Biochemistry and Physiology*, 93(1): 34–39. doi: 10.1016/j.pestbp.2008.09.004

Maroni M, Colosio C, Ferioli A, Fait A 2000. Chapter 1 – Organophosphorous pesticides, In: *Toxicology*, 143: 5-37.

Muikham I, Srakaew N, Chatchavalvanich K 2016. Microanatomy of the digestive system of Supachai's caecilian, *Ichthyophis supachaii* Taylor, 1960 (Amphibia: Gymnophiona). *Acta Zoologica*, 1-19 pp. doi: 10.1111/azo.12173, online ISSN: 1463-6395, John Wiley and Sons.

Odokuma EI, Omokaro EI 2015. Comparative histologic anatomy of vertebrate liver. *Annals of Bioanthropology*, 3(1): 1-5. doi: 10.4103/2315-7992.160728

Okle OSE, Derbalah A, Omnia El Euonya OE 2016. Hepatic damage associated with fatal zinc phosphide poisoning in broiler chicks. *International Journal of Veterinary Science and Medicine*, 4: 11–16. http://dx.doi.org/10.1016/j.ijvsm.2016.10.002

Önen Ö, Gündüz Ö, İşisağ Üçüncü S 2011. Ham Petrolün Suda Çözünebilen Kısımlarının *Pelvicachromis pulcher* (Boulenger, 1901) (Cichlidae, Teleostei) Bağırsak ve Karaciğeri Üzerindeki Etkileri. *Kafkas Üniversitesi Veteriner Fakültesi Dergisi*, 16(Suppl-B): 197-203.

Ross MH, Pawlina W 2006. Histology A Text and Atlas, Fourth Edition, Lippincott Williams & Wilkins Company, Baltimore.

Saha S, Das D 2015. Changes in Liver in Case of Insecticidal and Alcohol Poisoning: An Autopsy Study*". Journal of Evolution of Medical and Dental Sciences*, 4(27): 4622-4628, doi: 10.14260/jemds/2015/669 , pISSN- 2278-4748

Sutay SS, Tirpude BH 2008. Pattern of histo pathological changes of liver in poisoning. *Journal of Indian Academy of Forensic Medicine*, 30(2): 63-68.

Yao Y, Lin J, Yang P, Chen Q, Chu X, Gao C, Hu J 2012. Fine Structure, Enzyme Histochemistry, and Immunohistochemistry of Liver in Zebrafish. Advances in Integrative Anatomy and Evolutionary Biology, 295(4): 567-576. doi: 10.1002/ar.22416