Review Article *ISSN: 2277-8713*
Subha Ganguly, IJPRBS, 2013; Volume 2(3): 333-342 *IJPRBS*

ISSN: 2277-8713
IJPRBS
A Path for horizing your innovative work
INTERNATIONAL JOURNAL OF PHARMACEUTICAL RESEARCH AND BIO-SCIENCE

LONG TERM EXPOSURE TO CHEMICALS, INSECTICIDES AND HEAVY METALS CAUSING TOXICITY: A REVIEW

SUBHA GANGULY

IJPRBS-QR CODE

PAPER-QR CODE

AICRP on Post Harvest Technology (ICAR), Department of Fish Processing Technology, Faculty of Fishery Sciences, West Bengal University of Animal and Fishery Sciences, 5, Budherhat Road, P.O. Panchasayar, Chakgaria, Kolkata - 700 094, WB, India

Accepted Date:

23/06/2013

Publish Date:

27/06/2013

Keywords

Chemical,

Exposure,

Heavy metal,

Toxicity

Corresponding Author

Dr. Subha Ganguly

Abstract

Insecticides are used worldwide for crop protection especially in the developing nations. Neonicotinoid insecticides, which are one of the most important classes of commercial insecticides worldwide are systemic in plants and animals and are used to manage crop pests and control fleas on cats and dogs. Acetamiprid belongs to the class of chloronicotinyl neonicotinoid insecticides used to control insects and ectoparasites *viz*., Hemiptera, particularly aphids, thysanoptera and leptoptera on a wide range of crop species. The indiscriminate and injudicious use of second generation fluoroquinolones *viz.,* enrofloxacin produced anemia, leucopenia, hypoglycaemia, hypoproteinemia, increased enzymatic activity and hepatotoxic and nephrotoxic effects in broiler chickens. Exposure to heavy metals results in congestion and hemorrhages in the lungs, tubular degeneration in kidneys and occasional hemorrhages in the brain. The present article was conducted to review the various pharmaceutical, physiological and toxicopathological effects of different chemical agents and heavy metals due to environmental exposure and through feed on poultry birds. Heavy metals possess high density and toxicity towards living beings. Heavy metals like arsenic, chromium, lead and mercury are point popular and relevant. Heavy metals constitute the crust of the earth which resists degradation. Human get inflicted with heavy metals through the agency of food, water and atmosphere. Mercury poisoning by eating fishes is a prominent cause for public health hazard.

Introduction

Neonicotinoid insecticides, which are one of the most important class of commercial insecticides worldwide, are systemic in plants and animals are used to manage crop pests and control fleas on cats and dogs. The selective toxicity of neonicotinoids is attributed for nicotinic acetylcholine receptors of insects to that the mammals to the fundamental differences between the receptors. Whereas nicotine binds at an anionic subside in the mammalian nicotinic Ach receptors, the negatively tipped (Magic nitro or Ciano) neonicotinoid interact with a proposed unique subside consisting of cationic amino acid residues in the insect nicotinic Ach R. Nicotine and imidacloprid share the same structural moiety, the same mode of action, and essentially the same structural activity relationships. Several analogs including acetamiprid, thiamethoxam and thiacloprid, have since been discovered and have been shown to have the same mode of action as imidacloprid. Neonicotinoid are those compounds which have an essential moiety like nitroimine, cyanoimine or nitromethylene.[1]

Enrofloxacin is a second generation quinolone derivative which belongs to the group fluoroquinolone. The fluoroquinolones are metabolized in the liver and excreted in urine through the kidney. The liver and kidney develop the highest drug concentration though concentrations in essentially all tissues, including the skeletal and central nervous system reach therapeutic levels. That is why it is relevant to detect the pathological alteration in the visceral tissues and organs.

Selenium function is closely associated with Vitamin E. Both have antioxidant property and protect the biological membranes from oxidative degeneration. Glutathione peroxidase is the enzyme which has selenium as its constituent with 4 gm Se atoms per mole. Out of the total body selenium, 40 per cent is in the enzyme glutathione peroxidase as observed in rats. Both glutathione peroxidase and vitamin E prevent the formation of lipid hydroperoxides which damage the

cellular membrane and disturbed the structural integrity of the cells. Selenium and vitamin E are mutually replaceable to some extent but up to a particular limit.[2,3,4]

Fish serves as an important and rich source of easily digestible protein supplement to our body. Also fish oil serves as an important source of omega-3 fatty acids also contains traces of mercury, as reported by the Environmental Protection Agency. Mercury generally does not pose its deleterious effect alone. It combines with carbon to form organic compounds, like methylmercury. It is formed in water and soil as per reports of while diets should include fish as part of a nutritional regimen, this protein source rich in omega-3 fatty acids also contains traces of mercury, as put forth by the Environmental Protection Agency. Mercury, a metal that exhibits several forms, combines with carbon to form organic compounds. The most familiar one is methylmercury, which is created by microorganisms found in soil and water as per reports of the *Agency for Toxic Substances and Disease Registry*. Methylmercury generally accumulates in the fish muscles on over exposure.[5]

Research reports and findings

Cases of acute ciprofloxacin toxicity of birds have been reported earlier by many investigators[6,7], in human[8] and in broiler birds[9]. Birds treated with therapeutic dose develop mild diarrhea and depression which simulated the reports[6,7]. Broiler birds of control group had no clinical manifestation at any stage during the experimental period.

Anemia in human treated with ciprofloxacin has been reported[6,8]. Broiler birds treated with ciprofloxacin develop leucopenia[9]. Hypoproteinemia in broiler birds treated with overdoses of ciprofloxacin was reported[4].

Niyogi[9] and Sugawara et al.[10] also reported an elevated serum enzymatic activity in broiler birds and monkey respectively after therapy with ciprofloxacin both in therapeutic dose and higher doses of the drug. An increased level of serum enzymatic activity is known to occur in a wide range of inflammatory/degenerative

disease conditions particularly in hepatic and nephrotic diseases. An experimental study was conducted by Niyogi et al. to estimate the residual concentration of arsenic in different tissues / organs of broiler birds induced with arsenic trioxide @ 1/10th of acute LD_{50} i.e. 16.25 mg/kg bw 6 weeks. All the induced birds had widespread distribution of arsenic in the organs/ tissues. However, the residual concentrations were not uniform in various tissues, possibly due to variation in the rate of accumulation and/or clearance of residues from the individual tissues/organs. The largest residual concentration of arsenic was found in liver, next largest in proventriculus, followed by intestine, kidneys, feather, skin, spleen, bursa of Fabricius, skeletal muscles, heart, lungs, brain and lowest in the blood. In this study, control birds had least amount (0.02-0.39 µg/g) of arsenic in various organs or tissues, possibly due to environmental contamination. The accumulation of arsenic in organs/tissues of treated birds varied from 0.124-36.89 µg/g of wet tissue which was abnormally higher than the values in the tissues of normal birds.[11]

Salyi et al.[12] induced acute experimental selenium poisoning in broiler chicks and concluded that oral LD_{50} of selenium in the form of sodium selenite was 9.7 mg/kg body weight. Earlier workers have reported significant decline in body weight of selenium fed chickens. The organic form of selenium is known to be accumulated in higher quantities and persist for longer periods in tissues as compared to inorganic toxicity[13-15]. Increasing trends in the liver concentration of selenium in chicks, hens, cockerels and sheep have been reported by other workers.[12-14] According to Cousins and Cairney, the increased intake of selenium resulted in steady rise in tissue selenium concentrations until levels as high as 5-7 ppm in liver and kidneys.[16]

Paul et al. conducted with sixty healthy day old broiler chicks to determine the effect of induced enrofloxacin toxicity. The birds were divided into four groups keeping the first group as control. Clinically, the broiler birds in all the

treatment groups administered with therapeutic dose of enrofloxacin expressed the clinical symptoms of systemic toxicity. Hematological studies indicated that the hemoglobin concentration, packed cell volume, total erythrocytic count and total leucocytic count showed significant variation ($P<0.01$) between the treatment groups. Biochemically, all treated groups of birds induced with graded dose level of enrofloxacin, had significantly ($P<0.01$) decreased levels of total plasma protein with simultaneous reduction in albumen-globulin (A:G) ratio than in controls.[3]

An investigation was conducted by Kumar et al. on 300 day-old apparently healthy broiler chicks of either sex procured from a commercial hatchery in Kolkata, India. All the chicks were from the same hatch and also from the same breeding stock. The birds were maintained under standard feeding and management conditions. The oral LD_{50} of selenium in sodium selenite in broiler chickens is 9.590838 mg per kg body weight, contained in that compound. The oral ALD_{50} of sodium selenite was determined by Karber's method and was found to be 9.59038 mg/kg body weight.[16].[4]

Acetamiprid is a broad spectrum, high effective, safety, insecticide with good contact and stomach poisoning to pests, activity. As neonicotinoids insecticides persist in crops, biotransformation of these insecticides represents a promising approach for improving the safety of food. The neonicotinoids possess common characteristics that distinguish them from conventional insecticides suggested that after uptake of imidacloprid by sucking pests, feeding ceases and an avoidance behavior results.[1]

Clinical signs

Acetamiprid having low hazards for mammals and high potency to pests, are essential requirements for safe and effective pesticides though few studies has done at different dose levels in rats, goat, bees, mice[1] etc. However in mammals poisoning of neonicotinoid insecticides may cause trembling, emaciation, staggering, labored breathing, apathy, convulsion etc.

Dilation of pupils, weakness, paralysis of hind legs, gasping and tonic clonic convulsions were also observed.[1]

Hematological reports

There are reports of reduction in RBC count and PCV in rat's when cypermethrin and permethrin were administered at a single dose of 10mg/kg b.wt of each pyrethroid. A significant increase counts in white blood cells (WBCs) is noticed in male mice treated with these insecticides, while RBCs decreased when the animals were treated with formulated insecticides. Reduction in hemoglobin concentration and the hematocrit values in general takes place. All three insecticides caused a significant increase in the mean cell volume.[1]

Pathomorphological studies

Gross changes in liver of insecticide treated birds show enlarged, pallor or yellowish discoloration. Marked areas of hemorrhages necrosis, congestion, and fatty changes were also observed, congestion of upper respiratory tract and myocardium, mild enteritis in small and large intestines in all treated birds. Histopathologically, significant alterations in the liver is observed, such as mild fatty changes, congestion and degeneration of hepatocytes, in kidneys including marked congestion, tubular cell degeneration and sloughing of epithelial cells .The cerebral hemisphere revealed changes comprising of mild neuronal degeneration with surrounding glial cells, satellitosis and vacuolation. Mild congestion and hemorrhages is also observed in lungs and myocardial tissues following oral administration.

Mondal studied the pathology of induced acetamiprid daily orally for a period of 28 days at the dose rate of 25, 100, and 200mg/kg b.wt respectively and observed liver is the most affected organ followed by lungs, heart, spleen, brain, kidney and ovary. In heart there was hemorrhage, degenerative and necrotic changes in cardiac muscles cells, heart showed edema, mild hemorrhages in epicedium and edema at higher dose i.e. 200mg/kgb.wt/day.[17] Bhardwaj et al. administered imidacloprid orally daily to female rats for a period of 90 days with doses of 0,

5 ,1 0, 20mg/kg/day .And observed hepatocellular damage in the higher dose treated animals. Repeated exposure of high dose of imidacloprid (20mg/kg/day) for 90 days produced mild focal necrosis with swollen cellular nuclei and cytoplasmic lesions in the hepatocytes of liver. There were slight degeneration of tubules and glomeruli of the kidney of female rats compared with control and also resulted to necrosed Purkinje cells with loss of dendrites and granules in granular layer of cerebellum. However, no pathological changes were observed in brain, liver and kidney of rats exposed to imidacloprid at 5 and 10mg/kg/day.[18]

Goyal et al. studied the histopathological alterations induced after oral sub acute thiacloprid toxicity in *Gallus domesticus* on repeated oral administration of 10mg/kg/day thiacloprid for 28 days. Results showed that gross changes in liver of treated birds with enlarged, pallor or yellowish discoloration. Marked areas of hemorrhages necrosis, congestion, and fatty changes were also observed, congestion of upper respiratory tract and myocardium, mild enteritis in small and large intestines in all treated birds. Histopathologically, significant alterations in the liver were observed, such as mild fatty changes, congestion and degeneration of hepatocytes, in kidneys included marked congestion, tubular cell degeneration and sloughing of epithelial cells .The cerebral hemisphere revealed changes comprising of mild neuronal degeneration with surrounding glial cells, satellitosis and vacuolation. Mild congestion and hemorrhages was observed in lungs and myocardial tissues following oral administration of thiacloprid. Zhang et al[20] investigated the short term toxicity of acetamiprid in male mice which showed vacuolation of the seminiferous tubules, number of spermatids, and interstitial Leydig cells were obviously decreased. Moreover some cells sloughed from the lumen of the seminiferous tubules, some primary spermatocytes vacuolated with widened interstitium.

The effect of consumption of mercury toxicity is immense on human health. It primarily affects the kidneys and brain

of growing fetus. Poisoning due to mercury can cause injury not only to the brain and kidneys but also to a growing fetus. The *Agency for Toxic Substances and Disease Registry* has reported the toxic effect of mercury on primarily the human nervous system and that of growing fetus in particular. Contact with the metal causes difficulties with memory and distortions in hearing and vision including tremors and irritability. As per reports of EPA and FDA, the toxicity from heavy metals due to fish consumption According to the EPA, the dangers of mercury poisoning from eating fish are not a major concern. The risk depends on the amount of fish intake coupled with levels of mercury in the fish. EPA and FDA recommends pregnant and nursing mothers to avoid the consumption of such type of infected fishes and are recommended for intake of fish low in mercury content.[5,21]

Conclusion

Insecticide chemicals and heavy metals possess basic and clinical toxicity towards living beings. Heavy metals constitute the crust of the earth which resists degradation. Human get inflicted with heavy metals through the agency of food, water and atmosphere. Mercury poisoning by eating fishes is a prominent cause for public health hazard. Based on the review and analysis of physiological effects of different pharmaceutical chemicals and heavy metals, it was suggested that their indiscriminate and injudicious use produces anemia, leucopenia, hypoglycaemia, hypoproteinemia, increased enzymatic activity and hepatotoxic and nephrotoxic effects in broiler chickens.

References:

1. Singh TB, Mukhopadhayay SK, Sar TK, Ganguly, S Acetamiprid induces toxicity in mice under experimental conditions with prominent effect on the hematobiochemical parameters. J Drug Metab Toxicol 2012;3(6): 1-5, 134. doi:10.4172/2157-7609.1000134.

2. Ganguly S. Effect of induced toxicopathological effect of pharmaceutical agents and heavy metals on broiler birds: A Review. Int

Res J Pharm 2013a;4(5): 24-25. DOI/CrossRef Prefix: 10.7897/2230-8407.04507.

3. Paul A, Mukhopadhayay SK, Ganguly S, Pal S, Niyogi D. Study on induced enrofloxacin toxicity in broiler birds. Int J Adv Innov Res 2013;2(5): 675-79.

4. Kumar D, Mukhopadhayay SK, Ganguly S, Niyogi D, Jana S, Pal S. Effect of acute selenium toxicity in broiler birds. Int J Adv Innov Res 2013;2(5): 680-82.

5. Ganguly S. Human health benefits from fish consumption and environmental
toxicity issues in fish flesh. Int Res J Biol Sci 2013b;In press.

6. Flanner KDP, Aucoin, Whitt DA, Pras SA. Plasma Concentration of Enrofloxacin in African grey parrots. Avian Dis 1990;34:1017-22.

7. Zhou S, Wang D. Study on acute toxicity of norfloxacin nicotinate in chickens. J HAU Agril Univ 1994;13(1):80-83.

8. Sharma AK, Khosla R, Kela AK, Mehta VL. Fluoroquinolones: Antimicrobial agents of the 90's. Indian J Pharmacol 1994;26:249-61.

9. Niyogi D. Toxicopathology and immune response of broiler chickens induced with ciprofloxacin toxicity, 1999;M.V.Sc thesis submitted to West Bengal University of Animal and Fishery Sciences, India.

10. Sugawara T, Yoshida M, Takada S, Miyamoto M., Nomura M. One month oral toxicity study of the new quinolone Antibacterial agent in rats and cynomalgus monkeys. Arzneimitted forschung 1996;46(7):705-10.

11. Niyogi, D, Mukhopadhayay SK, Ganguly S. Bioavailability of arsenic in chronic induced arsenic toxicity in broiler birds. Indian Vet J 2013;90(6): 23-25

12. Salyi G, Banhidi G, Szabo E, Gonye S, Ratz F. Acute selenium poisoning in broilers. Magy Allatorv Lap 1993;48:22-26. (Vet Bull 64:2969).

13. Khan MZ, Szarek J, Markiowicz, K. Concurrent oral administration of

monensin and selenium to broiler chickens : effects on concentrations of different elements in the liver. Acta Vet Hung 1993a;41: 365-79. (Nutr Abstr Rev 64: 4790).

14. Khan MZ, Szarek J, Krasnodebska-Depta A, Konicicki A. Effect of concurrent administration of lead and selenium on some haematological and biochemical parameters of broiler chickens. Acta vet Hung 1993b;41:123-37 (Nutr Abstr Rev 64: 5060).

15. Rosenfeld I, Beath OA. Selenium. Geobotany, Biochemistry, Toxicity and Nutrition. Academic Press, New York, 1964.

16. Cousins FB, Cairney IM. Some aspects of selenium metabolism in sheep. Flust J Agr Res 1961;12:927-42. [*cited by* Shamberger. 1983].

17. Mondal S. Studies on the toxicopathology of acetamiprid in rats. MVSc Thesis submitted to College of Veterinary Science and Animal Husbandry, Indira Gandhi Krishi Vishwavidyalya, Durg, India. 2007.

18. Bhardwaj S, Srivastava MK, Kapoor U, Srivastava LP. A 90 days oral toxicity of Imidacloprid in female rats: morphological, biochemical and histopathological evaluations. *Food and Chem Toxicol* 2010;48(5): 1185-90.

19. Goyal BS., Garg SK, Garg BD. Effect of low levels of malathion administration on blood glucose erythrocytes concentration in WLH chiks. Indian J Poult Sci 1986; 21: 156-58.

20. Zhang Jiao-Jiao, Wang Yi, Xiang Hai-Yang, Li Meng Xue, Li Wen Hao, Ma Kai Ge, Wang Xian- Zhong and Zhang Jia-Hua. Oxidative stress: Role in acetamiprid induced impairment of the male mice reproductive system. Agricultural Sciences in China 2010;10(5), 786-96.

21. Ganguly S. A Handbook on Basic and Clinical Toxicology of Livestock, Birds and Fishes. Research India Publications, Delhi, India. 2013c;Book Proposal Accepted. ISBN xxx-xxxx-xxx-xxx. In press.