IMPACT OF AGROCHEMICALS ON SOIL ENVIRONMENT: AN OVERVIEW

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Abstract

In the modern day, agrochemicals are regarded as a crucial component of agriculture. On the basis of their intended uses, agrochemicals are broadly divided into pesticides (chemicals that protect plants), plant growth regulators (PGRs, plant hormones, stimulants, retardants, and additives), fertilizer (chemicals that promote plant growth), soil conditioners (antibiotics and hormones), and acidifying agents (chemicals that maintain the pH of the soil). These compounds are used by our farmers to defend against pre- and post-harvest losses and to improve crop yield. A major source of pollution that persists and biomagnifies in nature and affects the sustainability and soil properties is the extended and intensive use of agrochemicals. The role of soil microorganisms in the agricultural ecosystem is essential for preserving soil fertility and health as well as increasing crop productivity. Agrochemicals, either directly or indirectly, change the diversity, richness, and evenness of non-targeted beneficial microorganisms, systematically reducing the nutrition available to plants and accelerating the spread of disease in agricultural crops. The classification of agrochemicals and their effects on the soil are mainly emphasized in this article.

Keywords: Agrochemicals, pollution, agricultural yield, and soil health

Introduction

Chemicals used in agriculture are referred to as agrochemicals or agrichemicals. These substances include insecticides, fertilizers, soil improvers, liming agents, and plant growth hormones. The current world population is 7.2 billion, but that number might rise to 9.3 billion by 2050, significantly boosting the demand for food worldwide. Boxall et al. also stated that pathogenic microorganisms, weeds, and pests contribute to a 25% loss in agricultural productivity globally. Weeds and insects are therefore important reducing biotic sources in agriculture. In contrast to conventional or modern farming systems, which are

entirely dependent on the use of agrochemicals, organic farming systems, which safeguard the environment without the use of agrochemicals, were in use prior to the Industrial Revolution. These agrochemicals are typically used in all parts of the world to improve crop production. On the one hand, pesticides are used to control pests, diseases, pathogens, and weeds. On the other hand, fertilizers are used to give nutrients to the soil [1-4]. As a result, the majority of complex agrochemical chemicals, some of which are toxic to non-target, beneficial soil microorganism activities. Since they are treated equally throughout the entire field, regardless of the affected areas, more than 95% of applied herbicides and 98% of applied insecticides reach non-target soil microorganisms than their target pest [5-6]. Therefore, only around 0.1% of the entire number of applied pesticides reach the target species, while the remainder pollutes the soil and environment. Pesticides are being used carelessly, which disrupts not just the biodiversity of the soil but also the ecosystem and soil microcosms, which include the soil microfauna in field communities [7]. Pesticides used in large quantities that reach the soil have a direct impact on the soil microbiota, a biological indicator of soil fertility that affects plant growth and development [8-9]. Similar to this, multiple studies have documented how different pesticides affect soil enzyme activity, including hydrolyzes, nitrate reductase, urease, oxidoreductases, nitrogenase, and dehydrogenase activities. Pesticide applications also have an impact on biological nitrogen fixation (BNF) and the biotransformation's that are linked to it (such as ammonification, nitrification, denitrification, phosphorus solubilization, and S-oxidation). In addition, the extensive use of pesticides in modern agriculture has a negative impact on reduced microbial carbon biomass (MCB) and functional diversities of many non-target soil microbial species [10-11]. Through evaporation in the air, volatilization in the soil, and discharge in water, agrochemicals absorbed by plants are dispersed into the ecosystem. Agrochemicals, particularly pesticides, not only pollute the environment but also harm microflora and microfauna. Additionally, they prevented plants from absorbing crucial minerals and nutrients from the soil [12]. Various agrochemical types used in agriculture According to their intended uses, agrochemicals are broadly categorized as pesticides (chemicals that protect plants), plant growth regulators (PGRs, plant hormones, stimulants, retardants, and additives), fertilizers (chemicals that promote plant growth), soil conditioners (antibiotics and hormones), and acidifying agents (chemicals that maintain the pH of soil) [13].

International Journal of Engineering & Scientific Research

Vol. 5 Issue 7, July 2017,

ISSN: 2347-6532 Impact Factor: 6.660

Journal Homepage: http://www.esrjournal.com Email: esrjeditor@gmail.com

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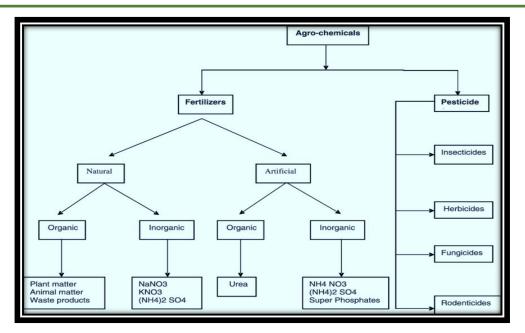


Figure-1 Classification of Agrochemicals

Pesticides

Pesticides are categorized as "plant protectors" since they shield plants from pest-caused illnesses and diseases while also increasing agricultural yields. These are also described as sophisticated chemicals that are used to prevent or eliminate pests. The ideal insecticide would be biodegradable, act on the intended hazardous species, and not leach into the ground water [13]. The majority of pesticides used in agriculture release vapors that pollute the air and are also absorbed into the soil through surface runoff from treated plants. When these pesticides are deposited in soil, they directly affect the soil microorganisms and have a negative impact on the local ecosystem, plants, people's health, and water bodies [14]. Pesticides are further divided into algicides, fungicides, herbicides, insecticides, molluscicides, nematicides, and rodenticides based on the mechanism of the target organisms [15]. Insecticides are chemical substances that are used to kill insects at various life stages, including eggs (ovicides), larvae (larvicides), and adults (adulticides), which interfere with moulting and maturation stages (insect growth regulators), which interfere with pheromone-based mating behaviors. Organic nitrogen, organic phosphorus, organic chlorine, pyrethroids, and carbamates are typical examples. Molluscicides, such as metaldehyde, niclosamide, Slug-

Tox, and limatox, are substances used to suppress gastropod pests (snails and slugs), which harm plants by eating on them. Nematicides are substances that are used to eradicate plant parasitic nematodes. Typical examples include Aldicarb, Nimitz, Velum Prime, and Mocap [16]. Rodenticides are substances that are either used to prevent the growth of rodents like rats, mice, and domestic pests including chipmunks, woodchucks, and squirrels or to kill them. Difenacoum, bromadiolone, warfarin, and zinc phosphide are a few examples of rodenticides.

Herbicides

Depending on the type of herbicidal chemicals used, herbicides cause a drop in the overall microbial population between 7 to 30 days of application. They also have a negative impact on microbial biodiversity indirectly by changing their physiology or metabolic processes. This in turn impacts the amount of plant growth regulators (gibberellins production, transportation of Indoleacetic Acid (IAA), ethylene concentration, etc.) as well as soil enzymatic activity, cellular membrane composition, protein biosynthesis, and others [17–18]. Numerous delicate bacteria have been documented to perish as a result of the administration of excessively high dosages of herbicides.

Fungicides

Numerous studies have documented their detrimental impact on soil microbial activity, growth, and survival [19]. Bavistin, a fungicide, inhibits a number of soil microbial communities, however the effect is negligible. Not all fungicide compounds can cause AMF to become sensitive [20]. Carbendazim, a benzimidazole fungicide and a metabolite of benomyl, and emisan, which contains 6% 2-methoxyethylmercury chloride, both negatively affect AMF in groundnut. However, groundnut mycorrhizae may be stimulated by Cu treatments. Metalaxyl applications encourage AM colonization in the roots of soybean and maize [21].

Insecticides

Insecticides are chemical substances that are used to kill insects at various life stages, including eggs (ovicides), larvae (larvicides), and adults (adulticides), which interfere with moulting and maturation stages (insect growth regulators), which interfere with pheromone-

based mating behaviors. When used at field-recommended amounts, pesticide residues have no negative effects on nitrification [22]. But what raises questions are the quantities and prolonged use of such insecticides. However, at greater rates, it prevents the nitrification process and the bacteria that are engaged in it [23]. For instance, when sprayed at concentrations between 0.02 and 10 times the field recommended dose, the biochemical processes of nitrification and denitrification in soils polluted with monocrotophos, lindane, dichlorvos, endosulfan, malathion, and chlorpyrifos are reduced [24]. The extent and degree of toxicity of insecticides can vary depending on the kind and group of insecticides used, and they have a negative effect on soil bacteria that are crucial to the transformation of nitrogen in soils [25]. Pesticide pollution has a big impact on the ecosystem of the soil [26]. Repeated use of these sophisticated chemicals (fertilizers, weedicides, insecticides, etc.) invariably results in the microbial life that is essential to a healthy soil ecosystem being destroyed [27]. Through the use of insecticides, soil-dwelling microorganisms can be genetically altered in a way that is detrimental to the soil ecology and may eventually develop a resistance to the chemicals used to eradicate them.

Rodenticides

Pesticides formulated to kill rodents are known as rodenticides. There are specific products for pocket gophers and voles, but they mostly target commensal mice and rats. Rodenticides can poison animals other than rodents as well, though. Anticoagulants and non-anticoagulants are the two basic groups into which rodenticides can be placed. Because an anticoagulant stops or lowers blood coagulation, which lengthens the clotting time in affected animals, it is frequently referred to as a blood thinner. The first-generation anticoagulants are those that were created as rodenticides prior to 1970. When feeding takes place over multiple days instead of just one, these chemicals are substantially more harmful. The first-generation anticoagulants chlorophacinone, diphacinone, and warfarin are approved in the US for the management of rats and mice. Beginning in the 1970s, second-generation anticoagulants were created to treat rodents resistant to first-generation anticoagulants. Additionally, second-generation anticoagulants have a higher likelihood of being able to kill with just one feeding than first-generation anticoagulants.

Table-1 Examples of Some Rodenticides

International Journal of Engineering & Scientific Research

Vol. 5 Issue 7, July 2017,

ISSN: 2347-6532 Impact Factor: 6.660

Journal Homepage: http://www.esrjournal.com Email: esrjeditor@gmail.com

Double-Blind Peer Reviewed Refereed Open Access International Journal - Included in the International Serial Directories Indexed & Listed at: Ulrich's Periodicals Directory ©, U.S.A., Open J-Gage as well as in Cabell's Directories of Publishing Opportunities, U.S.A.

Rodenticides	Example
Alkaloid Rodenticides	strychnine
Botanical Rodenticides	scilliroside
Calciferol	<u>cholecalciferol</u>
	ergocalciferol
Coumarin	brodifacoum
	bromadiolone
	<u>alpha-bromadiolone</u>
	coumachlor
	<u>coumafuryl</u>
	<u>coumatetralyl</u>
	dicoumarol
	difenacoum
	difethialone
	flocoumafen
	warfarin
Fumigant	<u>calciumcyanide</u>
	hydrogencyanide
	phosphine
	sodium cyanide
Halogenated Alkanoic Acid	fluoroacetamide
	fluoroaceticacid
	sodium fluoroacetate
Indandione	chlorophacinone
	diphacinone
	naphthylindane-1,3-diones
	pindone
	valone

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Inorganic	aluminiumphosphide
	magnesiumphosphide
	phosphorus
	<u>thalliumsulfate</u>
	zinc phosphide

Fertilizers

In general, compounds that encourage plant development are referred to as fertilizers. Any organic or inorganic mixture that gives crops soluble versions of key nutrients is called fertilizers. Fertilizers that are organic or natural include animal dung, compost, Human dung, recyclable materials, and industrial byproducts are preferred to synthetic fertilizers are phosphate fertilizers, nitrogen fertilizers (urea and ammonium sulphate), Potash fertilizers and potash sulphate (K2SO4) are examples [28].

Agrochemicals Used and Their Impact on Soil Quality

The Natural Resource Conservation Service of the (USDA) states that "Soil quality is how well soil does what we want it to do." One aspect of soil quality is soil fertility. Plant growth requires nutrients, which fertile soils may supply. These are the chemical elements that make up soil. The presence of synthetic chemicals or other changes to the natural soil environment are the main causes of soil contamination or soil pollution. It is generally brought on by industrial activity, agricultural chemicals, or inappropriate waste disposal. Agrochemicals are applied in agricultural settings to help assure a plentiful supply of food. Agrochemicals are used to achieve a number of significant benefits. These are mostly linked to higher plant and animal crop yields and reduced storage spoilage. These advantages are significant. Agrochemicals have significantly aided the success of the "green revolution," especially when used in conjunction with crop species that have undergone genetic improvement. Because of this, there is now more food available for Earth's rapidly growing human population. However, the usage of some agrochemicals has also been linked to some significant ecological and environmental harms. Degradation of soil quality results from the extensive use of outside agricultural inputs in agricultural production systems. Pesticides are

an example of organic (carbon-based) contaminants that affect soil quality. Due to their high persistence in soil, pesticides progressively degrade and become a source of contamination [29]. With the aid of soil organic carbon, soil functions as a filter, buffer, and a potential site for pollutant degradation [30]. However, it is also known that soil is a potential route for pesticide transport that could contaminate water, air, plants, food, and ultimately humans through runoff and sub-surface drainage, interflow, and leaching, as well as the transfer of mineral nutrients and pesticides into the plants and animals that make up the human food chain [31].

Pesticides have the potential to enter the environment when they are used on a target plant or when they are discarded. Pesticides can go through processes including transfer (or mobility) and degradation after being released into the environment [32–34]. New compounds are created by the breakdown of pesticides in the environment [35]. Adsorption, leaching, volatilization, spray drift, and runoff are just a few of the transfer processes that allow pesticides to move from the target site to other environmental media or non-target plants [36]. The many chemical kinds reveal their disparities in environmental behavior. For instance, whereas organochlorine substances like DDT have minimal acute toxicity, they exhibit a substantial capacity to accumulate in tissues and continue to harm organisms over the long term. Most nations have outlawed their sale, but because to their nature, their leftovers linger in the environment for a very long time. Organophosphate insecticides exhibit a noticeable acute toxicity in mammals despite having a low persistence [37].

The water solubility, soil sorption constant, octanol/water partition coefficient, and half-life in soil (DT50) of pesticides all have a strong correlation with the persistence of pesticide residues in the soil [38]. Strongly bound pesticides have high K_{ow} values that lead to high K_{oc} values, and both of these characteristics lead to strong sorption to the organic matter in the soil. As a result, it would be reasonable to anticipate that pesticides that are hydrophobic, persistent, and bio-accumulable would persist in soil [39].

Conclusion

Long-term use of agrochemicals in agriculture may have a fatal impact on soil microbial activities that affect nutrient cycle and crop productivity. As a result, it's critical to use agrochemicals at the right concentration to sustain soil health and the environmental balance. It is essential to use pesticides wisely and selectively because the majority of negative effects are brought on by application levels that are higher than what is advised. Reducing the negative impacts on people and the environment requires education of farmers, distributors, industry, legislators, and other stakeholders in the selective use of pesticides. The long-term impact of pesticides on microbial populations and their long-term eco-toxicological effects requires well-designed trials. It would be appropriate to use current techniques for better pesticide use to reduce lethal assets and prevent threats to human safety. Additionally, to avoid the careless use of agrochemicals, the application of biopesticides, nano fertilizers, nano biofertilizers, and nano pesticides should be emphasized in order to conserve the beneficial natural microflora that is crucial for sustaining soil fertility. Many of the most recent eco-friendly strategies to combat the threat of chemical pollution have placed biological pest control at the forefront.

References

1. FICCI (Federation of Indian Chambers of Commerce and Industry). Ushering in the 2nd green revolution: Role of crop protection chemicals. Fine Chemicals Corporation. What areAgrochemicals?JayhawsNews.2016.https://www.jayhawkchem.com/2018/05/11/whatarea grochemicals/

2.Boxall AB, Hardy A, Beulke S, Boucard T, Burgin L, Falloon PD, Williams RJ. Impacts of climate change on indirect human exposure to pathogens and chemicals from agriculture. Environment Health Perspectives 2009, 117, 508–514.

3.Oliveira CM, Auad AM, Mendes SM, Frizzas MR. Crop losses and the economic impact of insect pests on Brazilian agriculture. Crop Protection 2014, 56, 50–54.

4. Varma D, Meena RS, Kumar S. Response of mungbean to fertility and lime levels under soil

acidity in an alley cropping system of Vindhyan Region, India. International Journal of Chemical Studies 2017, 5, 1558–1560.

5. Wang, M.-C.; Gong, M.; Zang, H.-B.; Hua, X.-M.; Yao, J.; Pang, Y.-J.; Yang, Y.-H. Effect of Methamidophos and Urea Application on Microbial Communities in Soils as Determined by Microbial Biomass and Community Level Physiological Profiles. J. Environ. Sci. Health B 2006, 41, 399–413.

6. Miller, G.T. Sustaining the Earth; Brooks/Cole: Monterey County, USA, 2004; ISBN 9780534400880.

7. Lo, C.-C. Effect of pesticides on soil microbial community. J. Environ. Sci. Health Part B 2010, 45, 348–359.

8. Santos, A.; Flores, M. Effects of glyphosate on nitrogen fixation of free-living heterotrophic bacteria. Lett. Appl. Microbiol. 1995, 20, 349–352.

9. Fabra, A.; Duffard, R.; Duffard, A.E. de Toxicity of 2,4-Dichlorophenoxyacetic Acid to Rhizobium sp in Pure Culture. Bull. Environ. Contam. Toxicol. 1997, 59, 645–652.

10. Hussain, S.; Siddique, T.; Saleem, M.; Arshad, M.; Khalid, A. Chapter 5 Impact of Pesticides on Soil Microbial Diversity, Enzymes, and Biochemical Reactions. Adv. Agron. 2009, 102, 159–200.

11. Monkiedje, A.; Spiteller, M. Degradation of Metalaxyl and Mefenoxam and Effects on the Microbiological Properties of Tropical and Temperate Soils. Int. J. Environ. Res. Public. Health 2005, 2, 272–285.

12. Van der Werf HM. Assessing the impact of pesticides on the environment. Agriculture Ecosystems Environment 1996, 60, 81–96.

13. FICCI (Federation of Indian Chambers of Commerce and Industry). Report on use of agrochemicals for sustainable farming. 8th Agrochemicals Conference 2019 – July 16, 2019, New Delhi, India. http://ficci.in/past-event-page.asp?evid¹/₄24230

14. Johnsen K, Jacobsen CS, Torsvik V, Sørensen J. Pesticide effects on bacterial diversity in agricultural soils–a review. Biology and Fertility of Soils 2001, 33, 443–453.

15.Agnihotri NP, Gajbhiye VT, Kumar M, Mohapatra SP. Organochlorine insecticide residues in Ganga river water near Farrukhabad, India. Environmental Monitoring and Assessment 1994,

30, 105–112.

16.Dhananjayan V, Jayakumar S, Ravichandran B (2020). Conventional methods of pesticide

application in agricultural field and fate of the pesticides on the environment and human health. Eds (Thomas S et al.), In: Controlled Release of Pesticides for Sustainable Agriculture.

ISBN 978-3-030-23395-2, Cham, Springer.

17. Milosevic, N.; Govedarica, M. Effect of herbicides on microbiological properties of soil. MaticaSrp. Proc. Nat. Sci. 2002, 102, 5–21.

18. Kremer, R.J.; Means, N.E. Glyphosate and glyphosate-resistant crop interactions with rhizosphere microorganisms. Eur. J. Agron. 2009, 31, 153–161

19. Cycoń, M.; Piotrowska-Seget, Z.; Kaczyńska, A.; Kozdrój, J. Microbiological characteristics of a sandy loam soil exposed to tebuconazole and λ -cyhalothrin under laboratory conditions. Ecotoxicology 2006, 15, 639–646.

20. Datta, R.; Anand, S.; Moulick, A.; Baraniya, D.; Pathan, S.I.; Rejsek, K.; Vranova, V.; Sharma, M.; Sharma, D.; Kelkar, A.; et al. How enzymes are adsorbed on soil solid phase and factors limiting its activity: A Review. Int. Agrophysics 2017, 31, 287–302

21. Monkiedje, A. Soil quality changes resulting from the application of the fungicides mefenoxam and metalaxyl to a sandy loam soil. Soil Biol. Biochem. 2002, 34, 1939–1948.

22. Niewiadomska, A. Effect of Carbendazim, Imazetapir and Thiram on Nitrogenase Activity, the Number of Microorganisms in Soil and Yield of Red Clover (Trifolium pratense L.). Pol. J. Environ. Stud. 2004, 13, 4.

23. Gundi, V.A.K.B.; Narasimha, G.; Reddy, B.R. Interaction Effects of Insecticides on Microbial Populations and Dehydrogenase Activity in a Black Clay Soil. J. Environ. Sci. Health Part B 2005, 40, 69–283.

24. Madhaiyan, M.; Poonguzhali, S.; Hari, K.; Saravanan, V.S.; Sa, T. Influence of pesticides on the growth rate and plant-growth promoting traits of Gluconacetobacterdiazotrophicus. Pestic. Biochem. Physiol. 2006, 84, 143–154.

25. Madhaiyan, M.; Poonguzhali, S.; Hari, K.; Saravanan, V.S.; Sa, T. Influence of pesticides on the growth rate and plant-growth promoting traits of Gluconacetobacterdiazotrophicus. Pestic. Biochem. Physiol. 2006, 84, 143–154.

26. Das, A.C.; Mukherjee, D. Influence of Insecticides on Microbial Transformation of Nitrogen and Phosphorus in TypicOrchragualf Soil. J. Agric. Food Chem. 2000, 48, 3728–3732.

27. Zhu, G.; Wu, H.; Guo, J.; Kimaro, F.M.E. Microbial Degradation of Fipronil in Clay Loam Soil. Water. Air. Soil Pollut. 2004, 153, 35–44.

28. Fox, J.E.; Starcevic, M.; Kow, K.Y.; Burow, M.E.; McLachlan, J.A. Nitrogen fixation: Endocrine disrupters and flavonoid signalling. Nature 2001, 413, 128–129.

29. G.A. Stephenson, K.R. Solomon, Pesticides and the Environment. Department of Environmental Biology, University of Guelph, Guelph, Ontario, Canada, 1993.

30.P. Burauel, F. Bassmann, Soils as filter and buffer for pesticides: Experimental concepts to understand soil functions, Environ Pollut., 133, 2005, 11–6.

31 P.W. Abrahams, Soils: their implications to human health, Sci. Total Environ., 291, 2002,1-32

32. Singh, D.K. Pesticides and Environment. Pestic. Chem. Toxicol. 2012, 1, 114–122.

33. Scholtz, M.; Bidleman, T.F. Modelling of the long-term fate of pesticide residues in agricultural soils and their surface exchange with the atmosphere: Part II. Projected long-term fate of pesticide residues. Sci. Total Environ. 2007, 377, 61–80. [CrossRef]

34. Liu, Y.; Mo, R.; Tang, F.; Fu, Y.; Guo, Y. Influence of different formulations on chlorpyrifos behavior and risk assessment in bamboo forest of China. Environ. Sci. Pollut. Res. 2015, 22, 20245–20254. [CrossRef]

35. Marie, L.; Payraudeau, S.; Benoit, G.; Maurice, M.; Gwenaël, I. Degradation and Transport of the Chiral Herbicide S-Metolachlor at the Catchment Scale: Combining Observation Scales and Analytical Approaches. Environ. Sci. Technol. 2017, 51, 13231–13240.

[CrossRef]

36. Robinson, D.E.; Mansingh, A.; Dasgupta, T.P. Fate and transport of ethoprophos in the Jamaican environment. Sci. Total Environ. 1999, 238, 373–378. [CrossRef]

37. Damalas, C.A.; Eleftherohorinos, I. Pesticide Exposure, Safety Issues, and Risk Assessment Indicators. Int. J. Environ. Res. Public Health 2011, 8, 1402–1419. [CrossRef] [PubMed]

38. Zhang, F.; He, J.; Yao, Y.; Hou, D.; Jiang, C.; Zhang, X.; Di, C.; Otgonbayar, K. Spatial and seasonal variations of pesticide contamination in agricultural soils and crops sample from an intensive horticulture area of Hohhot, North-West China. Environ.

Monit. Assess. 2013, 185, 6893-6908. [CrossRef] [PubMed]

39. Aktar,W.; Sengupta, D.; Chowdhury, A. Impact of pesticides use in agriculture: Their benefits and hazards. Interdiscip. Toxicol. 2009, 2, 1–12. [CrossRef] [PubMed]