Review Article

Impact of Antibiotics on Plants

Ekta Bhatt, Dr. Pammi Gauba*
Department of Biotechnology, Jaypee Institute of Information Technology, India.
***Corresponding author's E-mail:** pammi.gauba@jiit.ac.in

Received: 25-07-2018; **Revised:** 22-08-2018; **Accepted:** 05-09-2018.

ABSTRACT

Any unwanted substances introduced in the environment are referred as contaminants. Organic compounds in environment are a worldwide problem because most of them compounds are harmful and carcinogenic. They may be clinical wastage, released via human excretion. There are multiple studies which show that these pharmaceutical drugs may cause a variety of problems leading to harming of animals and plants who take it via contaminated water. Due to the consumption of pharmaceuticals in our day to day life, their presence in our environment is obvious. There are various studies which shows that the accumulation of chemical compound in plants. Phytoremediation that shows the capabilities of plant species in the removal of chemical compounds is the most promising, relatively effective technology but limited work has been performed towards the toxic effect of these pharmaceutics on plants. This review article mainly examines and provides a critical view on the knowledge and limitations in field application strategies, approaches about phytoremediation technique. And the use of plant species and assays for monitoring and testing the impact of pharmaceutics on contaminated area.

Keywords: Pharmaceuticals, Phytoremediation, Organic pollutants.

INTRODUCTION

Antibiotics play important role as a pollutant in environment. They are designed to control the growth of bacteria in human or animals thereby protecting their health. Every year, humongous amount of pharmacologically active substances are used all over the globe to create chemicals and compounds curing and preventing illness. Most antibiotics remain bioactive as a metabolite , even after being excreted from the treated individual's body, there by posing a threat to the nature and various microbes (including varied forms of bacteria).Most unaltered drugs find their way to nature by the means of natural fertilizers, where unaltered animal manure is added directly to the fields[1]. Also, wastewater from various sewage treatment plants even after treatment host some antibiotics which finally reach the water bodies. The antibiotics have still not been graded as dangerous pollutants but the bacterial resistance has been a big issue in terms of human and animal health known ecotoxicological activity [1,2] Phytotoxicity is another issue to be discussed as very few tests have been developed till date to measure this phenomenon caused by the accumulation of antibiotics (e.g. sulphadimethoxine, enrofloxacin and oxytetracycline) in plants. As per studies the effects of antibiotics on plants was found to be different between varying compounds and between plant species. The antibiotics namely: tetracycline's (chlortetracycline and tetracycline, as well as tylosin commonly used in combination with tetracycline's) and sulfonamides (sulfamethoxazole and sulfamethazine, as well as trimethoprim commonly used in combination with sulfonamides) Studies shows that phytotoxicity and plant growth tests in soil were also performed. Measurement of soil microbial respiration and phosphatase activity is useful for measuring soil microbial activity[2].

What are Antibiotics?

Antibiotics are biologically active molecules with an increasing use in human, plants and animals. Antibiotics are used to treat infections or diseases caused by bacteria, antibiotics have saved millions of lives since they were first introduced [3]. However, as they have been overused many antibiotics are no longer effective against the bacteria they once killed.

Antibiotics are designed to control the growth of bacteria in human or animals thereby protecting their health. Every year, humongous amount of pharmacologically active substances are used all over the globe. Chemicals and compounds are created for curing and preventing illness.[3]

The studies was conducted that seed germination test on filter paper and plant growth test in soil, soil respiration and phosphatase activity tests were conducted to check the potential impact of six antibiotics (chlortetracycline, tetracycline and tylosin; sulfamethoxazole, sulfamethazine and trimethoprim) on plant growth and soil quality.The studies conducted have shown that the phototoxic effects varies from antibiotic to antibiotic and also varying plant species. Studies have been done that plants like sweet oat, rice & cucumber collected from different side. It was seen that rice turned out to be most sensitive to sulfamethoxazole with the effective concentration value (EC10 value of 0.1 mg/L). Two sulfonamides (sulfamethoxazole and sulfamethazine) and trimethoprim have shown significant effects on soil

respiration in comparison to the effects of tetracyclines and tylosinX . Also, soil microbial and enzyme activities were affected by antibiotic residues in manure and soils.

Phytotoxicity of antibiotics

Root length of germinated seeds is used as the endpoint in statistical analysis in seed germination tests. Sweet oat and rice seeds presented more susceptibility to the antibiotics as per the results with cucumber seeds being less sensitive to all antibiotics. Chlorotetracycline and tetracycline inhibited germination of the three plant seeds and rice was the most sensitive to sulfamethoxazole. Tylosin with EC50 values more than 300 mg/L is seen to be the least toxic compound towards rice and cucumber seeds.[3,4] Sulfamethoxazole and sulfamethazine also inhibited seed germination of most plants. Antibiotics could negatively affect plant seed germination, with varying effects between different plant species and between the antibiotics used in the tests, sweet oat being the most sensitive with varying toxicity values. Tetracyclines increased radish yields, but decreased pinto bean yields and Tetracyclines (strong adsorption onto soil components) and sulfonamides topped the toxicity chart with tylosin and trimethoprim causingtoxicity in seed germination[4] .When grown in chlortetracycline-treated soil, a significant increase in the activities of the plant stress proteins glutathione S-transferases and peroxidases was observed in maize plants, but not in pinto beans.

Antibiotic effects on soil microbial and enzyme activity

Reduced microbial activity by antibiotic sulfadiazine in manure was observed by author CO_2 decreased significantly in soil with increasing concentrations of sulfamethoxazole,sulfamethazine and trimethoprim[1] (exhibited strong adsorption onto soil) in the soil. All this Indicates that the effect of antibiotics (sulfamethoxazole, sulfamethazine and trimethoprim) on soil microbial respiration was time dependent. The bioavailable antibiotic fraction was responsible for increase in soil respiration. Effects of the antibiotics were reduced by sorption and degradation.[4]The heterogeneous nature of soil caused inhibition of soil phosphatase on addition of various antibiotics. Enzymatic activities and other microbial factors could be influenced by various factors are not specific for antibiotics.

The continuous release of pharmaceuticals into the environment is making them pseudo-persistent contaminants, posing a dangerous threat to ecosystems, despite their low concentration in wastewater or agricultural land.[5] The recent studies have reported the presence of low levels of various pharmaceuticals, including antibiotics, analgesic, hormones, steroids, and parasiticides, in treated wastewater, surface water, groundwater, and agricultural soil. The low concentration of pharmaceuticals from the environment can be further accumulated in plants and thus may result into bio-magnification. The release of antibiotics in the environment may result in the selection and abundance of antibiotic resistance bacteria in the environment, which can further affect the microenvironment of the plant. Antibiotic-resistant bacteria may reach the environment through the excretions of treated patients, it may also evolve through horizontal gene transfer via conjugation, transduction, and transformation.[6] It is now evident that the wastewater is a most important source of pharmaceuticals pollutant. The conventional methods for its treatment are not efficient to irradiate the pharmaceuticals.[7] It is assumed that around 50% of the pharmaceuticals are removed and rest end up in the environment. The advanced techniques of wastewater treatment, such as, advanced oxidation processes in combination with ozonation and UV-irradiation help in degradation of pharmaceuticals through hydroxyl radical, and are capable of removing most of the active pharmaceuticals from wastewater.[8] Due to its expensive nature (due to costly chemicals reagent used in this method), this method is only used at few places in Europe and USA. Therefore there is a need to develop a more cost-effective method/improve the existing methods for efficient removal of the pharmaceutical contaminant from the wastewater.

It was observed that there is significant decrease in the strength of pinto beans and growth of wheat with an increase in antibiotic concentrations whereas no significant effect was observed in corn plant.Also a considerable decrease in morphology of plants (such as, plant yields, plant heights, shoot and root dry-weights) and chemical (reduction in Ca, Mg, K, and N contents was observed[9].

In soil, antibiotics get adsorbed along with various micro and macro nutrients and soil organic matters which effects of the plants. Sulphadimethoxine reduced the growth of roots, hypocotyls, and leaves in plants of *Panicum miliaceum*, *Pisum sativum*, and *Zea mays*.[10] bioaccumulation of this antibiotic was seen in plants.[11,12] Enrofloxacin was observed to be beneficial for plant growth with low concentration whereas at higher concentration it was toxic for the growth of different plants like cucumber and lettuce.[13] The effect of antibiotics also shows the metabolic interaction in plants, which can degrade the lower concentration of enrofloxacin in some beneficial compound whereas when presence in higher concentration the plant is unable to process the pharmaceuticals and it exhibits the toxic effect. Different studies on many plants also have shown the beneficial effect of antibiotics at the lower concentrations whereas at the higher concentrations it can be toxic.[14,15] It has been also observed that different parts of the plants show the different activity to the pharmaceuticals interaction[16], which can be contributed to the different groups of pharmaceuticals and different metabolism of the tissues. Chloroquine, quinacrine, and metronidazole were observed to be toxic to soybean, where metronidazole was observed to highly toxic, whereas chloroquine was least toxic.[17,18] Root growth was

observed to be more sensitive to oxytetracycline than shoot, this response is supposed to be due to higher accumulation of pharmaceuticals in root than shoot. But Oxytetracycline when mixed in solution for plant growth showed significant inhibitory effect at concentrations higher than 0.02 mM.[19,20] The study shows that the phytotoxicity might be due to the inhibition of the translational activity of chloroplast and chloroplast (p)ppGpp synthase activity by tetracycline, which is almost similar to oxytetracycline.[20,21] A study showed that the phytotoxic effects of antibiotics on lettuce, alfalfa, and carrot. phytotoxic effects of different antibiotics was found in the order: levofloxacin > chlortetracycline > tetracycline > sulfamethoxazole > tylosin > oxytetracycline > sulfamethazine > lincomycin > amoxicillin > trimethoprim.[22]A significant change in primary and secondary metabolite properties and morphological characteristic of plants have been seen after interact with pharmaceuticals.

Table 1: Phytotoxic effect of different pharmaceuticals in the plants.

S.No	Group	Pharmaceuticals compound	Plants	Phytotoxic effects	References
1.	Nonsteroidal anti-inflammatory drug	Acetaminophen	Barley	Reduction of fresh and dry mass of root and leaves.	23,24
		Diclofenac	Horseradish Flax	Viability was observed to be reduced by 65%. Viability was observed to be reduced by 48%.	24,25
		Ibuprofen	*Lemna minor* L.	25% inhibition of growth in plant culture exposed to 1 mg L-1 of Ibuprofen.	27
2.	Antibiotic	Amoxicillin	Carrot Lettuce Alfalfa	Higher concentration of drug was observed to be toxic for root growth	25
		Chlortetracycline	Pinto beans	Plant growth was affected when grown in sandy loam but no effect was observed. Increasing concentration of antibiotic was observed to be toxic for root growth	22,23
		Enrofloxacin	*Cucumis sativus* *Lactuca sativa* *Phaseolus vulgaris*	High concentration was observed to have toxic effect on Postgerminative Development of plant.	26
		Levofloxacin	Lettuce Alfalfa Carrot	Higher concentration was observed to be toxic for root and shoot growth.	28
		Lincomycin	Lettuce Alfalfa Carrot	Higher was observed to be toxic for root growth	29
		Metronidazole	Soybean	With increase in drug concentration (0-4g/Kg of soil) plant growth decreases	29
3.		Oxytetracycline	*Phragmites Autralis*	Higher concentration cause toxic effect to root and photosynthetic activities.	29,30
		Sulfamethazine	*Phragmites autralis* Carrot Lettuce Alfalfa	Higher concentration cause toxic effect to root and photosynthetic Activities in all listed plants.	31, 32
		Sulfamethoxazole	Carrot Lettuce	Highly toxic for root and shoot in both plants.	32
		Sulphadimethoxine	*Amaranthus*	post germinative	32

			retroflexus *Pisum Sativum*	development was seen.	
		Tetracycline	Carrot	Toxic for root and shoot growth.	33
		Trimethoprim	Carrot Lettuce	Toxic for root growth at high Concentration.	34
		Tylosin	Carrot Lettuce Alfalfa	It was observed to be toxic for root growth.	34
4.	**Anti-malaria Drug**	Chloroquine	Soybean	With increase in drug concentration plant growth decrease.	26
5.	**Anti-protozoal**	Quinacrine Dihydrochloride	Soybean	Higher concentration was observed to be very toxic for seed germination	30

The interaction of antibiotics in plants can be a main cause of production of reactive oxygen species (ROS). Metabolic activity drugs may generate a reactive intermediate which can reduce molecular oxygen to form ROS. These reactive species can then interact with nucleic acids, proteins and carbohydrates to cause toxicity response. The rise in ROS grade due to pharmaceutical contact is not clearly define in studied topic but it has been frequently shown in animals cases.[37]

If pharmaceutical compounds are contaminating the soil, there is also a need to find out the ways to extract these contaminants from the environment. Phytoremediation is a method, which utilizes plants and the associated rhizosphere microorganisms to remove or transform toxic chemicals from the environment[35] Plants for phytoremediation are selected on various factors such as the ability to extract or degrade the contaminants of concern, adaptation to local climates, high biomass, deep root structure, compatibility with soils, growth rate, easy for planting and maintenance, and ability to take up a large amount of water through their roots. Reports have shown plants can be very useful for remediation of pharmaceutical compounds.

CONCLUSION

One of the most prominent effect of these contaminations and overuse and abuse of antibiotics especially in animal feed can be seen by the resistance that bacteria are developing and with each time a stronger dose of antibiotic is required to eliminate these threats and sometimes the drug itself previously successful in killing the bacteria must be switched, and the bacteria affecting human health and animal health being so closely related developing resistance is as much f a threat to the human population as it is to the animals that we cultivate, this is all indicates that “the more the antibiotics will pollute the environment, as much of a waste they’ll become”

There is a continuous debate whether the low concentration of pharmaceuticals detected in drinking water are enough to cause potential environment and human health issues. Nevertheless, there is enough evidence to show that antibiotics do have deleterious impact on microbial community structure and function when exposed to such low concentrations of pharmaceuticals. Hence many current infrastructures are being re-examined to improve the efficiencies of removal of pharmaceuticals and other organic micro contaminants in the aquatic system. Several European countries have banned the use of antibiotics in animal feeds. Further studies are also required in plant physiology and molecular biology level, pharmaceuticals interaction in plant as this is very important in metabolic process. The behavior of production of reactive oxygen species (ROS) in plants as the result of pharmaceutical exposure is needed to explore further. Not much work is done on the direct effect of plants by pharmaceutical removal from wastewater treated area. The plant studies are mainly on plant uptake of pharmaceutical drugs and public health problems. Phytoremediation is cost effective and environmental friendly way to treat polluted areas. Therefore, the process of phytoremediation is gaining popularity to decontaminate the pharmaceutical-contaminated environment.

REFERENCES

1. Liu, F., Ying, G.G., Tao, R., Zhao, J.L., Yang, J.F. and Zhao, L.F., Effects of six selected antibiotics on plant growth and soil microbial and enzymatic activities. *Environmental pollution*, *157*(5), 2009, 1636-1642.
2. Golet, E.M., Xifra, I., Siegrist, H., Alder, A.C. and Giger, W., Environmental exposure assessment of fluoroquinolone antibacterial agents from sewage to soil. *Environmental science & technology*, *37*(15), 2003, 3243-3249.
3. Mishra, A. and Choudhuri, M.A., Monitoring of phytotoxicity of lead and mercury from germination and early seedling growth indices in two rice cultivars. *Water, Air, & Soil Pollution*, *114*(3), 1999, pp.339-346.
4. Kong, W.D., Zhu, Y.G., Fu, B.J., Marschner, P. and He, J.Z., The veterinary antibiotic oxytetracycline and Cu influence functional diversity of the soil microbial community. *Environmental Pollution*, *143*(1), 2006, 129-137.
5. Grassi, Mariangela, Luigi Rizzo, and Anna Farina. "Endocrine disruptors compounds, pharmaceuticals and personal care products in urban wastewater: implications for agricultural reuse and their removal by adsorption process." *Environmental Science and Pollution Research* 20.6, 2013, 3616-3628.

6. Monteiro, S. C., & Boxall, A. B. Factors affecting the degradation of pharmaceuticals in agricultural soils. *Environmental Toxicology and Chemistry*, *28*(12), 2009, 2546-2554.

7. Fatta-Kassinos, D., et al. "The risks associated with wastewater reuse and xenobiotics in the agroecological environment." *Science of the Total Environment* 409.19, 2011, 3555-3563.

8. Kumar, R. R., Lee, J. T., & Cho, J. Y, Fate, occurrence, and toxicity of veterinary antibiotics in environment. *Journal of the Korean Society for Applied Biological Chemistry*, *55*(6), 2012, 701-709.

9. Kinney, Chad A., Edward T. Furlong, Steven D. Zaugg, Mark R. Burkhardt, Stephen L. Werner, Jeffery D. Cahill, and Gretchen R. Jorgensen. "Survey of organic wastewater contaminants in biosolids destined for land application." *Environmental science & technology* 40, no. 23, 2006, 7207-7215.

10. Herklotz, Patrick A., et al. "Uptake of human pharmaceuticals by plants grown under hydroponic conditions." *Chemosphere* 78.11, (2010), 1416-1421.

11. Kalaji, Hazem M., et al. "Pharmaceutical Compounds: An Emerging Pollutant (A Review on Plant-pharmaceuticals Interaction)." *CHIANG MAI JOURNAL OF SCIENCE* 44.2, 2017, 287-297.

12. Batchelder, A. R. Chlortetracycline and Oxytetracycline Effects on Plant Growth and Development in Liquid Cultures 1. *Journal of Environmental Quality*, *10*(4), 1981, 515-518.

13. Batchelder, A. R. "Chlortetracycline and Oxytetracycline Effects on Plant Growth and Development in Soil Systems 1." *Journal of environmental quality* 11.4, 1982, 675-678.

14. Migliore, Luciana, et al. "Effect on plants of sulphadimethoxine used in intensive farming (Panicum miliaceum, Pisum sativum and Zea mays)." *Agriculture, ecosystems & environment* 52.2-3, 1995, 103-110.

15. Migliore, Luciana, et al. "Effect of sulphadimethoxine contamination on barley (Hordeum distichum L., Poaceae, Liliposida)." *Agriculture, ecosystems & environment* 60.2-3, 1996, 121-128.

16. Migliore, Luciana, Salvatore Cozzolino, and Maurizio Fiori. "Phytotoxicity to and uptake of enrofloxacin in crop plants." *Chemosphere* 52.7, 2003, 1233-1244.

17. Migliore, Luciana, et al. "Hormetic effect (s) of tetracyclines as environmental contaminant on Zea mays." *Environmental Pollution* 158.1 (2010), 129-134.

18. Migliore, Luciana, et al. "Phytotoxic antibiotic sulfadimethoxine elicits a complex hormetic response in the weed lythrum salicaria L." *Dose-response* 8.4 (2010).

19. Jjemba PK. The effect of chloroquine, quinacrine, and metronidazole on both soybean plants and soil microbiota. Chemosphere. Feb 1, 46(7), 2002, 1019-25.

20. Liu, Feng, et al. "Effects of six selected antibiotics on plant growth and soil microbial and enzymatic activities." *Environmental Pollution* 157.5, 2009, 1636-1642

21. Liu, Feng, et al. "Effects of six selected antibiotics on plant growth and soil microbial and enzymatic activities." *Environmental Pollution* 157.5, (2009), 1636-1642.

22. Schmidt, Wiebke, and Clare H. Redshaw. "Evaluation of biological endpoints in crop plants after exposure to non-steroidal anti-inflammatory drugs (NSAIDs): Implications for phytotoxicological assessment of novel contaminants." *Ecotoxicology and environmental safety* 112, (2015), 212-222.

23. Hillis, Derek G., et al. "Effects of ten antibiotics on seed germination and root elongation in three plant species." *Archives of environmental contamination and toxicology* 60.2, (2011), 220-232.

24. Kalaji HM, Carpentier R, Allakhverdiev SI, Bosa K. Fluorescence parameters as early indicators of light stress in barley. Journal of Photochemistry and Photobiology B: Biology. 112, 2012, Jul 2, 1-6.

25. Soares, C., Branco-Neves, S., de Sousa, A., Pereira, R., & Fidalgo, F., Ecotoxicological relevance of nano-NiO and acetaminophen to Hordeum vulgare L.: combining standardized procedures and physiological endpoints. *Chemosphere*, *165*, 2016, 442-452.

26. Hoang, Thuy Thi Thanh, et al. "A preliminary study on the phytoremediation of antibiotic contaminated sediment." *International journal of phytoremediation* 15.1, 2013, 65-76.

27. Kalaji, Hazem M., et al. "Pharmaceutical Compounds: An Emerging Pollutant (A Review on Plant-pharmaceuticals Interaction)." *CHIANG MAI JOURNAL OF SCIENCE* 44.2, 2017, 287-297.

28. Hickey, E. J., et al. "Diclofenac induced in vivo nephrotoxicity may involve oxidative stress-mediated massive genomic DNA fragmentation and apoptotic cell death." *Free Radical Biology and Medicine* 31.2, 2001, 139-152.

29. Boelsterli, Urs A. "Diclofenac-induced liver injury: a paradigm of idiosyncratic drug toxicity." *Toxicology and applied pharmacology* 192.3, 2003, 307-322.

30. Stirnimann, Guido, Kerstin Kessebohm, and Bernhard Lauterburg. "Liver injury caused by drugs: an update." *Swiss Med Wkly* 140, 2010, w13080.

31. Susarla, S., Medina, V. F., & McCutcheon, S. C., Phytoremediation: an ecological solution to organic chemical contamination. *Ecological Engineering*, *18*(5), 2002, 647-658.

32. Teixeira, J., Ferraz, P., Gouveia, C., Azevedo, F., Neves, S., Fidalgo, F., & Silva, A. M. Targeting key metabolic points for an enhanced phytoremediation of wastewaters pre-treated by the photo-Fenton process using Solanum nigrum L. *Ecotoxicology and environmental safety*, *120*, 2015, 124-129.

33. de Sousa, Alexandra, et al. "Metalaxyl-induced changes in the antioxidant metabolism of Solanum nigrum L. suspension cells." *Pesticide biochemistry and physiology* 107.2 (2013): 235-243.

34. Teixeira, Jorge, et al. "Targeting key metabolic points for an enhanced phytoremediation of wastewaters pre-treated by the photo-Fenton process using Solanum nigrum L." *Ecotoxicology and environmental safety* 120, 2015, 124-129.

35. Datta, R., Das, P., Smith, S., Punamiya, P., Ramanathan, D. M., Reddy, R., & Sarkar, D. Phytoremediation potential of vetiver grass [Chrysopogon zizanioides (L.)] for tetracycline. *International journal of phytoremediation*, *15*(4), 2013, 343-351.

36. Gujarathi, Ninad P., Bryan J. Haney, and James C. Linden. "Phytoremediation potential of Myriophyllum aquaticum and Pistia stratiotes to modify antibiotic growth promoters, tetracycline, and oxytetracycline, in aqueous wastewater systems." *International journal of phytoremediation* 7.2, 2005, 99-112.

Source of Support: Nil, **Conflict of Interest:** None.