Food and Agriculture Organization of the United Nations

Antimicrobial Resistance and Foods of Plant Origin

Summary Report of an FAO Meeting of Experts

FAO Antimicrobial Resistance Working Group

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Abstract

Genes conferring resistance to antimicrobials, including resistance to drugs used to treat human and animal infections, are found among bacteria isolated from foods of plant origin. Soil, water, insects, animal intrusion, manure used as fertilizer, and human handling are probable sources of contamination. The extent to which antimicrobial use in plant production selects for the emergence and maintenance of antimicrobial resistant (AMR) organisms in plant production is unclear. Surveillance and further testing are needed to conduct comprehensive risk assessments and to monitor progress in implementing more sustainable plant health practices that reduce reliance on antimicrobials. Integrated Pest Management (IPM) is one such example that helps reduce reliance on pesticides (including antimicrobials) in horticultural cropping systems. There is increasing recognition that a wide range of stakeholders have a role to play in safegaurding human and animal health as well as protecting the environment against AMR. Communicating the negative consequences of overusing and misusing antimicrobials across in all sectors, including among farmers, the food industry, and regulators will help to promote more responsible use of these products worldwide. Training users in responsible application of antimicrobials and consequences of irresponsible use is a critically high priority in countries with developed economies and in resource-limited countries alike.

Introduction

Bacteria and fungi cause significant plant disease and production losses worldwide, especially in low- and middle-income countries (LMICs). Climate change is predicted to exacerbate this problem and the use of antibiotics and antifungal agents is expected to rise concomitantly as older treatments become ineffective and are discontinued and as disease burden continues to climb. There is growing concern that antimicrobials[1] are losing their effectiveness in all sectors, not only in horticulture, but also in veterinary and human medicine. Extensive use and misuse of antimicrobials drives the development and transmission of antimicrobial resistance (AMR), but it is unclear the extent to which antimicrobial use (AMU) is driving the development of AMR specifically in plant pathogens, soil organisms, spoilage organisms, and non-pathogenic contaminants and zoonotic agents present on foods of plant origin.

Some of the same drugs that are used in human and veterinary medicine (*e.g.*, streptomycin, tetracyclines, triazoles) are also used to control plant diseases. Thus, resistance that develops in one sector can be transferred and clinically relevant across sectors and species. Through processes of co-selection and cross-resistance, resistance that develops to one antibiotic may also render an organism resistant to several unrelated drugs and chemicals. Bacteria, notably zoonotic organisms with

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[1] Any substance of natural, semi-synthetic, or synthetic origin that at *in vivo* concentrations kills or inhibits the growth of microorganisms (bacteria, fungi, viruses, parasites) by interacting with a specific target.

resistance to one or multiple antibiotics, are found on fruits, vegetables, and other edible plants, as well as in soils. The frequency with which plant-origin resistant bacteria colonize the human gastrointestinal tract and serve as reservoirs of AMR genes in the gastrointestinal tract needs to be determined. There is convincing evidence that agricultural AMU is driving the emergence of AMR fungi that are increasingly transmitted from the environment to humans.

Antibiotics – antimicrobials that specifically inhibit or kill bacteria – are approved for use to treat plant diseases in at least 20 countries. In countries where regulations and oversight of antibiotic use are strong, the use of antimicrobials and their residues on foods of plant origin is minimal. However, in LMICs, the quantity and types of antimicrobials being used for agronomic application are undocumented – a problem compounded by challenges of access to quality-assured antimicrobials, including a growing industry of fraudulent and substandard products. The consequences of AMU in plant production resulting in occupational exposure, food, and environmental contamination need to be assessed in order to develop science-based recommendations for mitigating the negative public health impacts of AMR.

Reducing AMU and minimizing the AMR risk for foods of plant origin

Resistant bacteria from multiple sources can contaminate foods of plant origin. The soil is replete with bacteria that harbour AMR genes. Direct contact of edible portions of plants with soil and soil splash can contribute to food contamination. Animal and human wastes introduced intentionally as soil amendments or through animal intrusion provide another pathway for AMR bacteria to contaminate foods of plant origin. Water used for irrigation may also be contaminated with AMR organisms. Importantly, the adoption of good agricultural practices that limit total microbial contamination of foods of plant origin is a critical first step in reducing the introduction of AMR organisms into the food chain.

Contributing to the problem of antimicrobial resistance is the fact that there are very few reagents to treat bacterial infections of plants. The risk of development of resistance in plant pathogen populations is widely understood in horticultural production systems: Among bacterial plant pathogens, resistance is reported for products commonly used to treat bacterial diseases (*e.g.*, streptomycin, tetracycline, kasugamycin, and copper). With regard to antifungals, resistance to triazole fungicides is also well documented and relatively common, although there is a great deal of variation in the frequency of resistance between regions and among pathogens.

There are programs are in place to minimize AMR risks. Biological control (introduction of organisms that provide direct antagonism, competition, hyper-parasitism, or induction of host plant resistance) and biorational products, such as plant extracts, are alternatives to antimicrobials that may prevent and treat plant diseases. These products are considered to be lower risk to the environment and human health. However, biological and biorational products are generally far less effective than antimicrobials and their performance is inconsistent over time and across locations. As more is learned about phytobiome functions in food crop systems, more effective pre- and pro-biotic agents against plant pathogens may be developed to reduce the need for conventional antibacterial and antifungal agents.

By far the most effective approach to limit the use of antimicrobials in plant production is through the use of the well-established measures of “Integrated Pest Management” (IPM) – a systems approach designed to minimize economic losses to crops, as well as to minimize risks to people and the environment. Key components of IPM for preventing and managing plant diseases are:

1. **Accurate diagnosis and monitoring**, which can also include disease modelling and predictive systems to optimize timing of plant protection product applications;
2. **Use of disease resistant crop varieties**, including resistant rootstocks in both fruit and vegetable systems;
3. **Exclusionary practices** that prevent the introduction of pathogens into a crop, such as using pathogen-free true seed and vegetative planting material, clean irrigation water and sanitation practices that prevent the movement of pathogens from plant to plant and field to field;
4. **Careful site selection and soil improvement** to maximize plant health and minimize environmental factors that favour pathogens;
5. **Crop rotation** and other cultural practices to prevent pathogen build-up;
6. **Use of biological and biorational products**; and
7. **Judicious use of antimicrobials**, including both antibiotics and fungicides.

While many growers in developed countries are aware of and practice disease management strategies, improved uptake of these specific practices, especially in LMICs, will help to reduce infection pressure and consequently the need for antimicrobials. IPM should continue to be emphasized in grower and gardener education programs in developed economies and should be widely encouraged through governmental and non-governmental programs in LMICs. The importance of IPM for slowing the development of AMR and promoting food security and human and animal health cannot be overstated.

Innovation needs for sustainable production

Additional information, tools, and activities are urgently needed to better understand and mitigate the risks associated with AMR from agronomic sources, especially in LMICs. For example, advances in surveillance, good practices, awareness and strengthened government regulation and oversight for antimicrobial use and surveillance will contribute to a more effective One Health approach to combat AMR.

The largest barrier to understanding the role of plant-based agriculture in the holistic picture of AMR ecology is the lack of relevant data. Information is particularly lacking for LMICs. Systems to record AMU and AMR in fruits and vegetables at the national level are virtually absent. Surveillance systems for foods of plant origin should be developed in such a way that they can be integrated and harmonized with surveillance in other sectors, including AMR programmes in humans, animals, and foods of animal origin, to better assess risks and priority areas for intervention. In addition to AMR among plant pathogens, it is important to monitor animal, human, and zoonotic pathogens on plants as well as the resistome[2] of other organisms in the plant production environment, which may also contribute resistance genes to the food chain. The creation of new, rapid, and inexpensive tests and tools to diagnose plant diseases and characterize the resistome of the plant production environment will help to establish more appropriate surveillance strategies and AMU guidelines. To this end there are challenges that need to be addressed in developing these surveillance programmes. One key challenge will be determining an appropriate standard denominator to characterize AMU (*e.g.,*

[2] The collection of all the antimicrobial resistance genes and their precursors in both pathogenic and non-pathogenic microorganisms.

kilograms of oxytetracycline used per tonne of dates or apples produced) so that trends within and across countries can be monitored in kind.

Few methods are available to reduce or eliminate bacteria or AMR genes from fruits and vegetables that are consumed raw or with minimal processing. Therefore, prevention of contamination at all stages of production and processing is paramount to minimize the introduction of AMR into the food chain from plant-based foods. Development, validation, and application of additional contamination prevention strategies along the entire food chain could greatly reduce AMR in foods of plant origin.

Due to the limited number of medicines available to effectively treat plant diseases, additional strategies to prevent, control and treat plant diseases need to be developed, especially interventions and products with systemic effects. Examples of valuable innovations may include the following:

1. **Selective breeding** to decrease host plant susceptibility to diseases or to degrade antimicrobials;
2. **Discovery of antifungals and antibacterials** with different modes of action not shared with drugs used in human medicine;
3. Use of **effective biologicals** (probiotics, prebiotics, bacteriophages) **and biorational compounds** for disease control;
4. **Exploitation of the microbiome and soil health** to control plant diseases; and
5. More effective **integrated disease and pest management strategies**.

Additional information is specifically needed to quantify the relationship between the use of antimicrobials, other plant protection products, and other influences on the selection, transmission, and persistence of AMR among organisms on plants and in the surrounding food production environment.

AMR is a problem that affects everyone. A paradigm shift in behaviour and production management is needed to reduce AMU. Awareness of the severity of the problem and adoption of sustainable solution pathways at all stages in the food chain is critical to slow the development of AMR and mitigate its negative consequences. For food producers, this means recognizing that AMR can contribute to production and economic losses at all scales of production. Resistance can also cause direct and serious health impacts on producers who apply antimicrobials, and their families and customers who consume products contaminated with antimicrobial residues and AMR bacteria. In some countries, buyers are demanding commodities produced with strong antimicrobial stewardship practices, such as treating only after a correct diagnosis, appropriate application and dosing, respecting pre-harvest intervals, and incorporating IPM practices. Understanding and incentives for producers to employ better practices remains an obstacle to effective management of AMR and this problem is further complicated by misinformation and availability of products on the market that are fraudulent, substandard, or otherwise without evidence of effectiveness.

Endnote

This overview of AMR and horticulture is based on the discussions of a technical meeting of experts on these issues that was convened by FAO in October 2017. A more detailed technical paper is forthcoming.

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