

Microbiology

The insect microbiomes – a new hope against antimicrobial resistance?

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ABSTRACT

Due to the increase in antimicrobial resistance in pathogens, currently used antibiotics are becoming ineffective. Thus, new antibiotics need to be discovered. This study makes light into a yet unexploited source of potent antimicrobials: the insect microbiomes



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Nowadays, more and more antibiotics (also referred to as antimicrobial drugs) are becoming ineffective to fight against bad bacteria and fungi because these organisms are capable of rapidly developing resistance to those compounds. These resistances arise due to the misuse and overuse of antibiotics. In order to counterbalance the emergence of new antibiotic-resistant pathogens, there is an urgent need to discover new antimicrobial compounds. Natural products are the principal source of antimicrobials and they are mainly produced by soil bacteria of the [Actinobacteria group](#). In recent years, sampling campaigns to look for new compounds led to the rediscovery of known antimicrobial compounds. Given the need for more effective therapeutic molecules, there has been growing

interest in host microbiomes as a potential source of discovery for new antibiotics. The microbiome is the collection of microorganisms, such as bacteria, fungi or viruses, colonizing a given habitat, plants or animal hosts. Indeed, antibiotics have been discovered from microbiomes of diverse animals, such as insects or humans; bacterial members of the microbiome produce antimicrobial compounds to protect the host from pathogens. There is a well-known example in the [southern pine beetle](#) where Actinobacteria, typically *Streptomyces*, produce chemical defenses to fight against infections.

Recently, a group of American scientists has investigated the potential of insect microbiomes as a valuable source of new antibiotics. They focused on

Streptomyces bacteria as they are the source of most clinically used antimicrobial drugs. Moreover, they have been shown to form beneficial associations with diverse insect hosts. Their hypothesis was that bacteria of the genus *Streptomyces* from insect microbiomes are a promising source of antimicrobial compounds, which have evolved differently from *Streptomyces* bacteria from soil.

The first thing they did was to try to isolate *Streptomyces* from diverse insect hosts, such as bees or butterflies, for example, sampled from different locations and habitats across America. The research team succeeded in isolating *Streptomyces* from insects. They showed that these bacteria were widespread across the host range and habitats investigated. For comparison, the researchers also isolated *Streptomyces* from soil and plants. By analyzing the genetic material and by comparing the evolutionary relationships of insect-, soil- and plant-*Streptomyces*, they were able to demonstrate that insect-associated bacteria evolved in distinct lineages. Of key importance, the scientists were also able to show that insect-associated *Streptomyces* harbor great potential for uncharacterized antimicrobial compound synthesis.

Investigating further, the researchers tested these insect-*Streptomyces* for their effectiveness against bacterial and fungal pathogens. By confronting the insect-associated *Streptomyces* against clinically-relevant bacteria and fungi, the researchers showed that insect-*Streptomyces* had a stronger ability to inhibit pathogens compared to soil- or plant-associated bacteria. Specifically, insect-associated *Streptomyces* had greater antifungal activity.

Thus, in order to further investigate the inhibitory potential of compounds extracted from insect-*Streptomyces*, the researchers tested their effect in a mouse infection model. First, they identified in an

artificial setting (in-vitro) which extracts were able to inhibit bacterial and fungal pathogens. In the case of inhibitory activity, the extracts were analyzed in order to identify the compounds present. Unknown/novel compounds were then used in the in-vivo mouse infection model. The experimental results showed that insect-*Streptomyces* had potent inhibitory activity in-vivo, for both bacterial and fungal pathogens. Moreover, extracts coming from insect-*Streptomyces* showed no toxicity for the mouse. Finally, in one of the insect-*Streptomyces* extracts, the scientists discovered a new antimicrobial compound – *cyphomycin* – from a Brazilian *Streptomyces* isolated from the microbiome of a fungus-growing ant. Purified cyphomycin was active against multi-resistant fungal pathogens both in-vitro and in-vivo, and in low concentrations.

Through experimental and qualitative laboratory procedures, the research team confirmed their working hypothesis demonstrating that insect microbiomes are a promising source of novel antimicrobial compounds. The implications of their research open a new paradigm for the discovery of new antibiotics with exciting potential for medical applications. The promise of this new source for new antimicrobials products lies in the fact that insects, throughout their evolution, and because of the constant pressure applied by pathogens, have formed associations with *Streptomyces* bacteria that produce effective antimicrobial compounds.

In conclusion, antimicrobial products coming from insect-associated *Streptomyces* are especially suited for medical applications, as their associations with insects appear to favor low toxicity compounds to animals. Are these insect microbiome-derived antimicrobial compounds the key to our success over antimicrobial resistance? Only the future will tell us!