Answer to bacterial antibiotic resistance may be found in plants

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Bacterial resistance to antibiotics is an ever-growing problem for healthcare, agriculture and hygiene, thanks to their indiscriminate and often excessive use.

While natural, plant-derived antimicrobial small molecules may offer a potential solution, they often lack sufficient activity and selectivity to fulfil antibiotic requirements, and their conventional methods activation may not be compatible with biomedical applications.

Now, however, an international team of researchers believe they have discovered an answer to these problems.

In a new study, published in the journal *Nano Futures*, the team show it is possible to use atmospheric-pressure plasma for rapid, single-step potentiation of activity of select terpenes – the volatile unsaturated hydro/carbons found in the essential oils of plants – without the need for chemicals or heating.

Co-lead author Dr Kateryna Bazaka, from Queensland University of Technology (QUT), Australia, said: "Bacteria are the ultimate survivors. They have unmatched capacity to produce new generations in just 20 minute, rapidly develop resistance to even the most potent drugs, including targeted antibiotics, and extraordinary genetic, metabolic, and physiological diversity and evolutionary adaptive capabilities.

"It's no surprise, therefore, that despite the development of potent synthetic antibiotics, bacteria remain one of the leading causes of mortality globally."

Co-lead author Professor Ken Ostrikov, from QUT, said: "There are of course downsides to antibiotics. They are overused; they interfere with commensal microbiota; and have potentially adverse dose-dependent and idiosyncratic side effects, particularly in young, elderly, and immuno-compromised patients. Most alarmingly, they contribute to the development of antibiotic-resistant pathogens.

"The development of novel antibiotic strategies and materials is, therefore, crucial."

The team's approach was to use plant secondary metabolites (PSMs). PSMs are highly diverse, with more than 12,000 alkaloids, 8,000 phenolic compounds, and 25,000 terpenoids currently known. Additionally, the natural role of many plant secondary metabolites is to inactivate bacteria – something they have evolved to do effectively over an extremely long period. Lastly, the microbial processes and components they target may be different from those of conventional antibiotics, potentially minimising the incidence of cross-resistance.

However, 'activating' the antimicrobial properties of the PSMs at safe doses often requires either heating or chemical manipulation, making the process either impractical, costly, or leaving a reduced effectiveness.

To overcome this, the team experimented with the using non-equilibrium conditions of atmospheric-pressure plasma to achieve rapid, single-step activation of select terpenes, without the use of chemicals or heating.

They then tested the effectiveness of the activated PSMs against a variety of bacteria, including Staphylococcus aureus, the bacteria often responsible for staphylococcal infections.

Dr Bazaka said: "We found that an activated terpinen-4-ol, a PSM with documented broad-spectrum activity, produced a statistically significant decrease in the number of colony forming bacterial units, with complete inactivation achieved within five minutes of exposure.

"Our results demonstrate that plasma treatment can be potentially used to enhance the ability of PSM to reach and modify the membrane of the bacterial microorganism, and interact with intracellular targets.

"Significantly, the activation approach is generic, and could therefore potentially be applied to other molecules and their mixtures in an effort to expand the range of effective antimicrobial agents for deactivation of pathogenic organisms in hygiene, medical and food applications."

More information: Kateryna Bazaka et al. Plasma-potentiated small molecules—possible alternative to antibiotics?, *Nano Futures* (2017). DOI: 10.1088/2399-1984/aa80d3

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