////Title: Investigating the Effect of Vitamin C on the Evolution of Insecticide Resistance

////Stand-first: Dietary antioxidants, such as vitamin C, are known to reduce the negative effects of toxins in mammals by preventing cellular damage caused by reactive oxygen species. However, it is not known whether these antioxidants have a similar protective effect in insects. A team led by Dr Barry Pittendrigh [Pit-uhn-dree] at Purdue University have investigated the adaptive responses of fruit flies to insecticide exposure in the presence of vitamin C. Their work has exciting implications for reducing the threat of insecticide resistance in insect pests.

////Body text:

Repeatedly exposing a population of insects to an insecticide often leads to the emergence of new traits that allow the insects to withstand the effects of the chemical. Such traits arise due to genetic mutations, which are then passed to the next generation. Meanwhile, insects without these mutations are more likely to die upon exposure to the insecticide, and are thus less likely to pass on their genes. The increased ability of insects to survive insecticide exposure is known as insecticide resistance, and poses serious societal problems – both in agriculture and human health.

For example, the rise of insecticide resistance means that many agricultural pests can no longer be controlled using chemical treatments, leading to widespread crop damage and threatening our capacity to grow food. Furthermore, resistance amongst mosquitos reduces our ability to manage the spread of life-threatening mosquito-transmitted diseases, such as malaria.

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In nature, many plants produce toxic compounds as a defence against being eaten by insects. In turn, plant-eating insects have evolved corresponding defence systems that allow them to avoid, trap or detoxify such compounds. Research has shown that insects with such defensive mechanisms may also have an increased ability to evolve insecticide resistance.

In addition to defensive toxic compounds, many plants also produce various antioxidants, such as vitamin C. These antioxidants scavenge reactive oxygen species, and thus reduce the oxidative damage that such species can cause in plant cells. Vitamin C has also been implicated in reducing oxidative damage to DNA, and therefore may play a role in suppressing the emergence of genetic mutations.

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DDT is a well-known insecticide that many insect populations have become resistant to. This chemical works by disrupting insect nervous system functioning, causing convulsions and eventually paralysis. DDT also causes oxidative stress. To date, resistance to DDT has been extensively studied in the fruit fly *Drosophila melanogaster* [dro-so-fuh-lah muh-la-now-ga-stir].

Antioxidants including vitamin C have been shown to alter the impacts of DDT and other toxins in mammals. However, the relationship between the protective effects of antioxidants and the increased levels of reactive oxygen species in insects exposed to DDT remains unknown. Furthermore, the degree to which antioxidants reduce the emergence of mutations within insect populations is also unclear.

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To begin to address these questions, Dr Barry Pittendrigh and his colleagues at Purdue University explored the impact of vitamin C on the evolution of DDT-resistant traits in *Drosophila* flies.

His team designed an experiment consisting of four groups – each containing 20 flies. The first group of flies was exposed to a low concentration of DDT only, the second group was given dietary vitamin C alongside the same concentration of DDT exposure, and the third group was fed vitamin C only. The team's control group was given neither of these treatments. These treatments were applied to ten genertions of the flies with each treatment groups.

After allowing the flies to breed for ten generations, Dr Pittendrigh and his colleagues exposed all four study groups to DDT. They then calculated the concentration of DDT needed to kill half of the flies in each group – a parameter known as LC50 [L-C-fifty]. Interestingly, the team found that the LC50 of the DDT-only treatment group was significantly higher than that of the other three groups.

In other words, the highest amount of DDT was needed to kill the flies that had previously been exposed to DDT and no vitamin C over 10 generations, indicating a high rate of insecticide resistance in this group. However, the flies that had been fed vitamin C alongside DDT exposure over 10 generations showed comparatively reduced DDT resistance.

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The research team also examined differences in the genomes of the flies from each of the four groups. Compared to the control group, by the tenth generation, the DDT-only treatment group showed the largest number of genetic mutations, the DDT with vitamin C group had the second-highest number, and the vitamin C group had the fewest.

Overall, the team's results are consistent with previous findings, supporting a hypothesis that dietary vitamin C and other antioxidants may reduce the incidence of inherited genetic mutations induced by exposure to insecticides such as DDT.

Moreover, the team's findings demonstrate that when the flies' diet was supplemented with vitamin C, continuous exposure to a low concentration of DDT generated a lower number of genetic mutations – many of which are assumed to be associated with insecticide resistance. These observations support a hypothesis that decreasing the damage induced by toxins relieves the selection pressure that would otherwise result in the evolution of resistance.

Although other factors likely impact the accumulation of resistance traits in insect populations, the results suggest that antioxidants might reduce the number of genetic mutations and potentially slow the evolution of insecticide resistance. Dr Pittendrigh and his colleagues also note an alternative hypothesis: that antioxidants can act as protectors against cell damage from insecticides, reducing the ability of insecticide chemicals to kill their target insects.

This important work provides a vital step forward in meeting the challenge of insecticide resistance.

The authors concluded with a remark that it remains to be determined whether such interactions occur between plant defensive compounds and plant-produced antioxidants — in other words, whether some plants, or some of their tissues, produce high levels of antioxidants that alter the evolutionary path of resistance in herbivorous insects to those defensive compounds.

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This SciPod is a summary of the paper 'Dietary antioxidant vitamin C influences the evolutionary path of insecticide resistance in *Drosophila melanogaster*', published in the journal *Pesticide Biochemistry and Physiology*. doi.org/10.1016/j.pestbp.2020.104631

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