Myth-Busting Cane Toads in Australia

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Undeterred by physical and biological control strategies, can cane toads be halted by chemical ecology?

The cane toad (*Bufo marinus*) was introduced into the sugar cane-growing regions of northern Queensland in 1935 in an unsuccessful attempt at biocontrol of the sugar cane beetle (*Dermolepida albohirtum*). The planning and forethought behind this endeavour seem, at least by modern standards, woefully inadequate.

Not only did cane toads fail to control the sugar cane beetle, which was eventually achieved some years later by a synthetic chemical insecticide, but the toad itself went on to become an invasive pest of epic proportion – far outliving and exceeding the sugar cane beetle threat. Since its release, the cane toad invasion front has advanced south along the eastern seaboard from Queensland into northern NSW, and west through the Northern Territory into Western Australia – leading to the colonisation of more than one million square kilometres.

Cane toads are renowned for their ability to produce and deploy cardiotoxic steroids as a form of chemical defence. These steroids act on key enzymes in the heart in much the same way as the well known-toxic plant *Digitalis purpurea*, which is also known as common foxglove. Indeed, the plant preparation known as digitalis has long been used (carefully) as a medication to regulate and jump start irregular heart rhythm. As the gap between beneficial and lethal dose is very narrow, and depends on many factors associated with individual patients, such as their weight, age and health, digitalis treatment is not without serious risk – and fatalities do occur.

It should therefore come as no surprise that many Australian native predator species, including freshwater crocodiles, marsupials, snakes and lizards, are vulnerable to the related poison found in cane toads.

The probability of fatal encounters with cane toads is further enhanced by the presence of specialised parotoid glands that secrete high concentrations of cane toad toxin in response to predatory attack. If this was not enough, the toxin exuded from these glands contains high concentrations of the neurotransmitter adrenaline, providing a double blow to the cardiovascular system of poisoned animals. Adrenaline speeds and stresses the heart, ensuring that the cardiotoxic steroids travel to the heart more rapidly and with greater impact.

Cane toad toxin also contains the hallucinogenic alkaloid bufotenine, whose psychoactive properties and potential for abuse has seen it scheduled in Australia and elsewhere around the world as a Controlled Substance, along with the likes of heroin, LSD and ecstasy.

In summary, the humble cane toad is a pharmacological "nightmare" and, as the invasion front advances across Australia, native predator populations are at serious risk.

Current Control Strategies

Historically, cane toad control strategies can be viewed either as physical or biological. The physical approach favours a low technology, localised containment solution designed to inhibit or delay the movement/presence of toads through the installation of barriers and traps, and through the use of hand collection campaigns. While immediately deployable, and locally effective, physical strategies are labour-intensive, target only a fraction of the colonisation area, and at best only delay the inevitable. They can, however, inspire and engage local communities against a common threat, and attract media attention that serves to alert the public to the cane toad problem. Physical strategies are best characterised as a delaying tactic, buying time for the development of more effective longer-term solutions.

By contrast, the biological approach seeks to develop and deploy lethal self-replicating biological vectors, such as viruses or parasites, with or without genetic modification. Although capturing the public imagination for the "perfect" scientific fix, the reality of biological control is (so far) more promise than substance. As any biological solution by definition lacks a reliable "product recall" option (consider the release of cane toads themselves), it is critical that it be species-specific, effective and without serious adverse side effects – a guarantee that has so far proved impossible to satisfy.

The development of biological solutions suffers from a very high risk of scientific/technical failure, and a high cost and extended time to develop and deploy. This latter point is all the more concerning given the pace of the toad invasion front, which could complete its crossing of northern Australia, from the Pacific to Indian oceans, by 2020. A biological solution that takes an additional 10 years to develop (if at all) would be a Pyrrhic victory indeed!

Adult male cane toad. Photographer: Alexis Barrett

A further challenge to the biological solution is the need to quarantine the effect to Australian cane toads so as to not adversely impact toads in other parts of the world, including adjacent Indonesia.

Cane toad control in Australia has been dominated by limited, short-term and localised success with physical solutions, and the unrealised promise of biological solutions. Clearly, the cane toad is a formidable adversary capable of using chemistry to enhance survival and wreak havoc among Australian predator species.

With the inevitable colonisation of northern Australia, and in the absence of effective control strategies, the search continues for new approaches. In 2006, and with contract research support from the Queensland government via the Invasive Animals Cooperative Research Centre, I led a team of researchers at the University of Queensland's Institute for Molecular Biology in a two-year study of the chemical ecology of the cane toad in Australia, with a view to identifying promising new directions for chemical control.

To start off the project, we reviewed the available literature (scientific peer-reviewed and beyond) to identify gaps in our knowledge that could guide the planning of the research program. To our surprise we found a landscape devoid of detailed analysis of Australian cane toad chemistry but rich in pseudo-knowledge coloured by an almost irrational fear and loathing of toads. This misinformation was compounded by the use of emotive language, a ready acceptance of myths and half-truths (see box, p.41), and a barbaric enthusiasm to apply control solutions (e.g. cricket bats, golf clubs) that would make any animal ethics committee wince. Cane toads really do have a PR problem!

The Indivisible Cane Toad Toxin

Having established that the toad chemistry is better characterised as a toxin rather than venom (see box, p.11), some toad commentators still make the fundamental mistake of referring to the "toxin" as if it were a single chemical entity, demonstrating a failure to see a mixture of chemicals – each if which is present at different (and variable) concentrations with differing biological properties, potency and selectivity – collectively contributing to an ecological outcome. This simplistic categorisation of the "indivisible toxin" historically sidestepped an informed analysis and appreciation of the true ecological role of the various components within cane toad secretions – a serious oversight given that the "toxin" is the underlying cause of the environmental problem.

Our chemical analysis of Australian cane toad toxins revealed a complex mixture of potentially cardiotoxic steroids in adults, with a comparable diversity in eggs and early stage tadpoles. There is almost no overlap in molecular diversity between adults and eggs/tadpoles. Of note, late-stage tadpoles lack cardiotoxic steroids and, contrary to popular belief, are apparently non-toxic to vertebrates.

This raises the question: "How do we actually define or measure toxicity?" Again, popular commentary on cane toad toxicity can be simplistic, presenting measures without due regard to how the toxin was collected and processed, or what species were used to test a toxic response, and how. For example, toxicity testing of cane toad eggs against Australian frog tadpoles would likely return different results compared with testing adult cane toad ingestion by dogs or native predators.

Further to this, the different chemicals within toxin preparations will undoubtedly exhibit differing potency depending on tissue type (e.g. kidney and heart) and species (e.g. pig, quoll, lizard and crocodile). Similarly, because the individual components within the cane toad toxin have different solubility properties, a water preparation would contain different chemistry to one prepared in an organic solvent such as ethanol. Measures of toxicity need to be carefully qualified by what exactly is being measured and how.

Chemical Solutions

But what of chemical control solutions? Despite considerable efforts, to date there is no compelling evidence for a behavioural response consistent with a cane toad sex pheromone. Had such a pheromone existed it would have made an attractive target for control, much as insect sex pheromones have minimised crop damage. Fortunately, the case for a cane toad tadpole

alarm pheromone is strong. It has been demonstrated that injured tadpoles release a chemical cue into the water that triggers an immediate flight response among schooling cane toad tadpoles which take flight when one of their number meets with a violent end. This alarm chemical is species-specific – it does not appear to alarm tadpoles from other species. Importantly it is also non-toxic, biodegradable (or at least easily diluted) and extremely potent.

Could such an alarm pheromone have any merit as a control agent? The answer seems to be a cautious "maybe" – the measured "yes" that only a scientist can warm to. What we now know is that cane toad tadpoles chronically exposed to crushed tadpole extract (the alarm pheromone in its natural state) undergo premature metamorphosis to form underweight metamorphs. These "prem" metamorphs have a lower probability of survival and hence a lower reproductive success.

We take heart from preliminary studies suggesting that the alarm pheromone is a small molecular weight, water-soluble organic molecule. This raises the possibility that the addition of a synthetic tadpole alarm pheromone to controlled waterways (e.g. dams, lakes, streams, irrigation canals) during the breeding season could disrupt normal cane toad development and reduce generational recruitment. While not a national eradication solution, a control solution based around the alarm pheromone could nevertheless be a valuable management tool.

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More recently we turned our attention to the mechanisms for biosynthesis and storage of cane toad toxin to better understand and hopefully identify vulnerable steps in the process. This detailed chemical approach has uncovered some remarkable subtleties of cane toad chemical ecology, including the involvement of bacteria within the toxin glands, and the physical and chemical partitioning of differing chemistry within the gland.

While it is still too early to judge whether investigations into cane toad chemical ecology will inspire the development of practical chemical control solutions, there is cause for hope – a step forward in what has otherwise been seen as a hopeless situation.

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Toad Myth Busting

CANE TOADS SPIT VENOM: FALSE

Venoms are more typically associated with a delivery apparatus, such as fangs or spines, which are absent in toads. Cane toad toxins are exuded from skin glands, predominantly the parotoid glands on the shoulder, in response to predatory attack, and as such are better characterised as defensive secretions and not venoms. To release the toxin requires physical pressure on the gland. True, if you whack a cane toad with a mallet or lump of wood there is a chance the toxic secretion will be expelled with some force and may "get you" in the face, but it's equally the case that whacking a lemon may result in an unpleasant "squirt" to the eye. Toads "spit venom" no more than lemons "spit lemon juice".

CANE TOADS POISON WATERWAYS AND SPREAD DISEASE: FALSE

Toads are poisonous, and they do live in and around waterways, but there is no evidence that they poison waterways as such, nor is there any evidence that cane toads are vectors for human or animal pathogens any more or less than other animals (including many highly poisonous Australian natives). The extreme accusations that persist against cane toads seem to have more to do with an irrational bias against all things toad, perhaps inspired by historical and cultural lore in which toads are often portrayed in a negative light – from warts to witches. These dubious claims are a disappointing distraction since the reality of the toad threat is every bit as unpleasant as the fantasy of venom spitting Typhoid Mary toads lathering up the local creek with poison.