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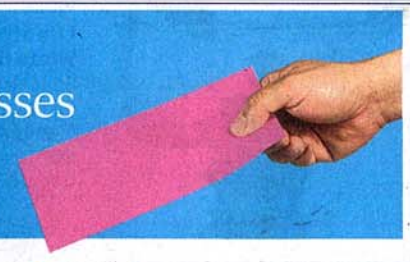

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NATURAL BORN 'KILLERS'

Venom in animals and plants offers treasure trove of cures and drugs to tackle many ailments

A Russell's viper (top) and venom being extracted from a cobra (above). Venom from the jararaca pit viper has been used to produce drugs that can treat hypertension and cardiac failure. PHOTOS: AGENCE FRANCE-PRESSE

Nicole Lim and George Kanianthara Chandy

Dripping from bared fangs, exposed barbs or prickly tentacles, venom is nature's most efficient killing technique. Animals inject venom into prey to immobilise or kill, or use it in self-defence.

At least 20,000 people are killed each year by snakes alone, according to estimates.

Venom is made up of tens to hundreds of toxins mixed with other molecules. These concoctions have been honed over years to give an animal an advantage over its predators and prey.

Venom has a range of deadly effects, from preventing nerve-muscle communication (resulting in paralysis) to stopping the heart from beating and interrupting blood clotting.

Toxins can be lethal but as 15th century physician and philosopher Paracelsus put it: "There are no poisons, just poisonous dosages."

Modifying the mechanisms these toxins employ has become a surprisingly fertile starting point for new drugs.

To date, some 16 drugs derived from venom have been approved for use in people while several more are undergoing clinical trials.

These include a whole class of cardiovascular drugs as well as novel treatments for diabetes and severe chronic pain.

These drugs are now being taken by millions of people around the globe.

They were derived from studying around 1,000 toxins contained in venom. That's just a drop in the ocean. It is estimated that the animal kingdom alone is the source of more than 20 million toxins produced by at least 100,000 species.

Using venom in treatments is not new. Bee venom was one of the earliest remedies for ailments such as gout and baldness, and was used by the ancient Greeks, Chinese and Egyptians.

Snake venom also has a long history of use in healing. For example, cobra venom has been used in traditional Chinese and Indian medicine for centuries.

The jararaca pit viper's venom also provided modern medicine's first venom-derived drug, the angiotensin-converting enzyme inhibitor captopril, better known as an ACE inhibitor, used to treat hypertension and cardiac failure.

However, it was not until the turn of the century that the field began to blossom, as technology empowered scientists to work more easily with these precious substances.

Advances in fields such as molecular biology and in technologies such as mass spectrometry and next-generation sequencing have made the identification of novel toxins much more accessible.

In addition, breakthroughs in structural biology have defined the molecular structures of toxins as well as their targets in our bodies.

With a toxin blueprint in hand, and knowledge about the body's many biological pathways, scientists can now recreate the material to study and adapt it into possible new drugs.

The painkiller Prialt, derived from the magical cone marine snail, was approved in 2004. The carnivorous sea snail's bite is laced with a powerful venom that paralyses its prey, usually fish, instantly.

The painkiller, developed from one of the toxins in the venom, is administered straight into the spine where, unlike other painkillers, it inhibits pain signal transmission.

This novel mode of action reduces the risk of addiction.

Another example is the "tumour paint" derived from the deathstalker or yellow scorpion. The toxin, Chlorotoxin, behaves differently in insects and mammals.

In insects, the scorpion's usual prey, it triggers paralysis.

In mammals, it binds to chloride channels found in tumour cells.

By adding a fluorescent dye, the new compound, called BLZ-100, can help doctors see exactly which cells are cancerous, ensuring that no cancer cells are left behind after surgery to remove a tumour.

It is now in phase one testing.

Snake venom continues to be studied intensively by many researchers, including Professor Manjunatha Kini from the National University of Singapore, who is modifying snake toxins to develop drugs to prevent clot formation.

Meanwhile, Emeritus Professor P. Gopalakrishnakone is developing venom-derived drugs to prevent tissue adhesion following surgery, and to treat arthritis.

Scientists are now trawling the skies, lands and seas to track down venomous species.

Melittin, found in bee venom, is being investigated to treat diseases such as HIV; glucagon-lie-peptide-1 from the male platypus is a promising lead candidate for a better diabetes treatment; a peptide from the Chilean rose tarantula's venom holds promise for a treatment for muscular dystrophy; while a peptide from the venom of the 20cm-long Chinese red-headed centipede has the potential to be a more potent and non-addictive alternative to morphine.

But just as this field is taking off, it is facing its biggest threat.

The fragile environments which are home to creepy-crawlies, tentacled sea creatures and even monsters (the Gila monster's saliva contains a toxin that helps diabetics control glucose and lose weight; it was turned into an anti-diabetes drug in 2005) are deteriorating and shrinking.

It is not just animal venom that is slipping through our fingers. The medicinal potential of poisonous plant species and toxins produced by micro-organisms and fungi is also evaporating.

Close to 50 per cent of plant and animal species have experienced localised extinctions due to factors such as urbanisation, poaching and climate change. The most heavily affected areas are the tropics.

If we do not halt the countdown to extinction, we are at risk of throwing this treasure chest away without ever having fully opened the lid.

ABOUT THE WRITERS

- Ms Nicole Lim is a medical writer at the Lee Kong Chian School of Medicine (LKCMedicine) at Nanyang Technological University.
- Professor George Kanianthara Chandy is professor of molecular physiology at LKCMedicine. In his work on the potential of potassium channels for treating autoimmune diseases such as psoriasis, multiple sclerosis and rheumatoid arthritis, venom provided the solution. One of the toxins in the venom of the sun sea anemone is an effective inhibitor of a T lymphocyte potassium channel called Kv1.3. When this channel is overactive, it triggers autoimmune diseases. The compound, dalazatide, has been licensed to a start-up and is beginning phase two testing (having cleared the first safety hurdle and shown efficacy in treating psoriasis).

Toxic healers

GILA MONSTER

- The saliva contains a toxin that helps diabetics control glucose and lose weight.
- It was turned into an anti-diabetes drug in 2005.

ST FILE PHOTO

PLATYPUS

- The ancient, patchworked platypus is a relatively unchanged animal from which researchers are learning about mammalian gene regulation and immune systems.
- Glucagon-lie-peptide-1 from the male platypus is a promising lead candidate for better diabetes treatment.

PHOTO: GERRY PEARCE/AUSTRALIAN-WILDLIFE.COM

BRAZILIAN LANCEHEAD

- One of several pit vipers whose venom is a powerful blood coagulant.
- Scientists have combined a derivative of the venom with injectable hydrogels to create a material that can quickly stop bleeding and protect wounds.

PHOTO: GREG HUME

POLYBIA PAULISTA

- This Brazilian social wasp protects itself against predators by producing venom known to contain a powerful cancer-fighting ingredient.

PHOTO: MARIO PALMA/SAO PAULO STATE UNIVERSITY