PLANTS THAT 'RISE FROM THE DEAD' BREATHE LIFE INTO RESEARCH

Resurrection plants can survive almost complete desiccation to bloom again when the rains return. Jill Farrant has devoted her life to understanding these **EXTREMOPHILIC BOTANICALS**, and how they might be useful in medical, cosmetic and agricultural research.

Resurrected *Myrothamnus flabellifolia* plants in the Waterberg Biosphere, Limpopo Province, South Africa.

Unlike most other land plants, resurrection plants have a hidden talent. These unremarkable-looking plants can lose more than 95% of their water content without dying, whereas most other plants die if they lose around half of their water[1].

"Resurrection plants appear, as if by magic, to recover full metabolism 12 to 48 hours after being rehydrated," says Jill Farrant, who heads the Plant Stress Lab at the University of Cape Town, South Africa (see 'A researcher with impact'). She first encountered the plants as a child on her parents' farm in the Limpopo province of South Africa. "It seemed miraculous to me that a plant so dry and apparently dead because of a prolonged period of drought could come alive again when rain did eventually fall." How is this possible?

Resurrection plants have evolved mechanisms that both control water loss and also offer protection against the damage and stress that comes with chronic dehydration. Adaptations include anatomical and subcellular changes in leaf architecture to prevent permanent damage to the cell wall (a process known as cytorrhysis), and proteins and metabolites that protect against damage from reactive oxygen species (ROS) — damaging molecules that arise from various stressors. "These unique plants are ideal models for understanding desiccation-tolerance mechanisms and ultimately for producing crops with similar properties that are more tolerant to drought — predicted to become more prevalent in the coming years because of climate change," Farrant explains.

Developing drought-tolerant crops is not the only use for resurrection plants. One particular species *Myrothamnus flabellifolia* is beloved of

A RESEARCHER WITH IMPACT

Jill Farrant is a professor of molecular and cell biology at the University of Cape Town (UCT) in South Africa. She is internationally recognized for her work on resurrection plants and in 2012 received the African/Arab States L'Oréal-UNESCO Award for Women in Science. She is a fellow of The World Academy of Sciences (TWAS); she holds an A-rating for the quality and impact of her research from South Africa's National Research Foundation (NRF); and she is a member of the UCT College of Fellows. After holding the UCT Research Chair of Molecular Plant Physiology of Desiccation Tolerance for several years, she was awarded the NRF South African Research Chairs Initiative (SARChI) Chair in 2015 at the Molecular and Cell Biology Department at UCT.

traditional African medicine. As researchers dig into the properties of *M. flabellifolia*, they are finding it contains many useful molecules that have health-related implications and might also be able to protect or even reverse skin damage from many different causes.

WAKING FROM THE DEAD

"Of the seven different resurrection plants I have studied, *M. flabellifolia* is definitely my favourite," says Farrant. "As a species it can withstand extremes of temperature (from sub-zero to +55°C) and exposure to ultraviolet (UV) rays." *M. flabellifolia* is an ancient species and one of two woody resurrection plants that grow in Southern Africa and Madagascar.

The Zulu name for the plant is *uvukwabafile*, which translates as 'wakes from the dead'. Indeed, this South African ethnic group believes that the resurrection properties of *M. flabellifolia* transmit to the sick person during treatment. A tea made from its dried leaves is a traditional Zulu remedy for a host of ailments, including colds, mastitis, backache, vascular disorders and abdominal pain. Local people also use its dried powdered leaves to treat burns and wounds, and they inhale the smoke from burning leaves to alleviate chest pains and asthma.

Modern science might not hold entirely the same beliefs as the Zulus, but there is mounting evidence that the plant has medical value. "*M. flabellifolia*'s medicinal and healing properties undoubtedly come from powerful polyphenolic secondary metabolites, made up of *inter alia* essential oils and antioxidants," explains Farrant.

The major antioxidant in *M. flabellifolia* is 3,4,5-tri-O-galloylquinic acid, which protects cell membranes from desiccation-induced structural damage at the microscopic level and is much more effective than vitamin C in preventing free-radical damage[2]. "Antioxidant activation can defend cells against damage caused by pollution, UV rays, dehydration, free radicals and temperature extremes, all of which accelerate skin ageing," says Farrant.

M. flabellifolia also contains a proanthocyanidin-rich extract that has shown activity against the herpes simplex virus in culture[3]. Scientists from Botswana have even found that an extract from the plant might be useful against diabetes, as it seems to inhibit α-glucosidase and α-amylase activity *in vitro*[4].

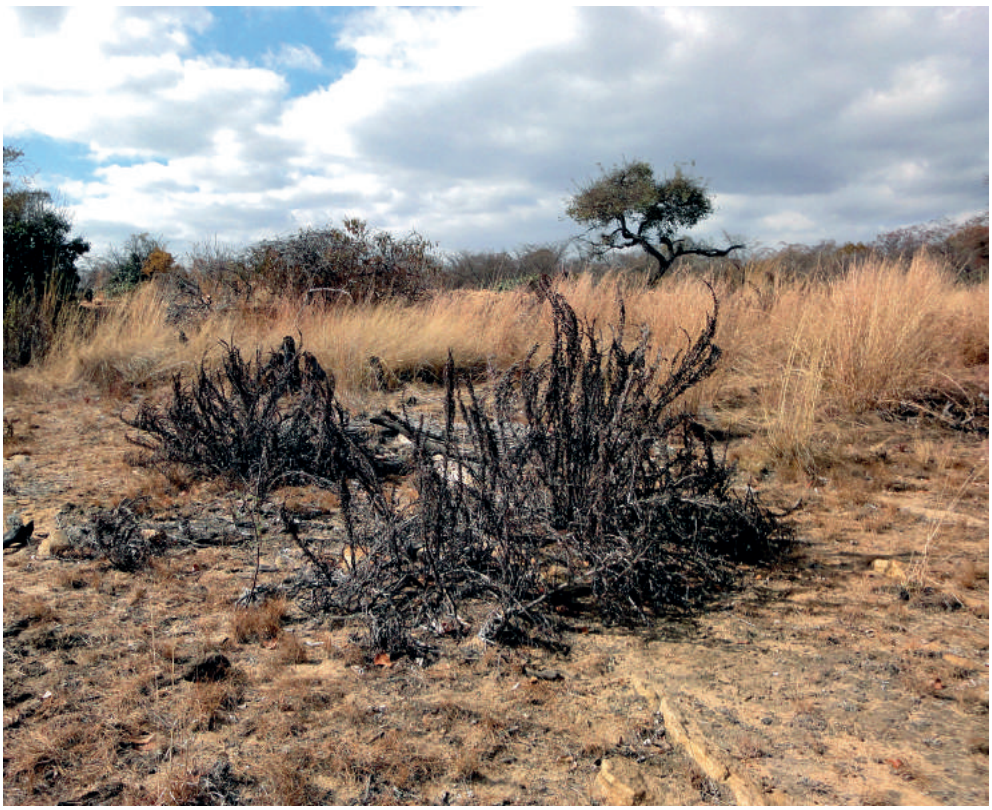
SWEET DREAMS

M. flabellifolia's treasures do not end there. The plant also contains several sugars that serve as cytoplasmic protectants, antioxidants and signalling molecules. The most important of these is trehalose — a simple sugar made of two molecules of glucose. Trehalose does not usually accumulate in measurable quantities in plants but is commonly produced by animals such as tardigrades where it prevents protein and membrane denaturation in cells exposed to environmental stresses such as heat, cold, oxidation and dehydration[5].

In small amounts, trehalose regulates a plant's energy requirements. It also stimulates autophagy, a process in which damaged organelles (tiny structures that perform specific functions within a cell) are broken down and their components recycled into nutrients that help cells survive. In the case of resurrection plants, autophagy prevents senescence (cell ageing) and cell death caused by dehydration[6]. Several cell-based studies have examined the medical properties of trehalose: as an antiviral[7]; as protection against damage caused by dehydration[8]; and in a hydrogel as a treatment for skin burns[9].

"OF THE SEVEN DIFFERENT RESURRECTION PLANTS I HAVE STUDIED, *MYROTHAMNUS FLABELLIFOLIA* IS DEFINITELY MY FAVOURITE."

***Myrothamnus flabellifolia* looks ordinary, but has surprising properties.**



Unlike the grass in the background, these *M. flabellifolia* shrubs are definitely still alive.

As well as activating autophagy, trehalose stimulates a transcription factor called nuclear factor-like 2 (Nrf2) — a master regulator of the antioxidant pathway. Nrf2 upregulates the expression of many other molecules, including the p62 protein complex, which is important for cell growth, and expression of several antioxidant genes[10].

In humans, Nrf2 plays a critical role in protecting a variety of tissues, including the lungs, liver, kidneys, stomach, small intestine, central nervous system and retinal epithelia, from a wide range of toxins and environmental insults. It does this by synthesizing proteins involved in detoxification and elimination of ROS.

SKIN REVIVAL

Of all the organs, the skin might be the most obvious first one to benefit from the molecules found in *M. flabellifolia*, particularly from activation of the Nrf2 pathway. In addition to the general antioxidant effects of Nrf2, the molecule has been found to be crucial for proper functioning of skin cells' barrier junctions and for production of keratinocyte cells, which make up over 90% of the epidermis[11].

What's more, Nrf2 provides protection against upregulation of the collagen-degrading enzyme matrix metalloproteinase-1 (MMP-1, also known as interstitial collagenase or fibroblast collagenase) when skin is exposed to UVA rays. It could thus protect against collagen depletion[12] and provide extracellular matrix support to skin.

Thus, trehalose could boost the antioxidant properties of 3,4,5-tri-O-galloylquinic acid to repair damage in skin cells by stimulating many protective mechanisms. "I see it as inducing the breakdown of damaged organelles and toxins and then recycling key components necessary for skin regeneration," says Farrant. "Since the skin itself performs this regeneration, trehalose effectively promotes self-healing to bring about cell repair and renewal."

In the wild, extreme weather conditions co-occurring with periods of drought concentrate these protective substances within resurrection plants. The metabolites heal the plant, but they can also be exploited for their regenerative properties in skin care. Scientists at Giorgio Armani Beauty have managed to capture these protective molecules in an extract from *M. flabellifolia* they've called Reviscentalis. "The Reviscentalis extract we isolate from dried *M. flabellifolia* leaves contains extremely high levels of 3,4,5-tri-O-galloylquinic acid, as well as other polyphenols," says Farrant.

Adding this extract to cosmetic creams should provide many benefits. "Reviscentalis could protect the skin from oxidative damage caused by pollution, dehydration, extreme temperature changes and other stressors like UV rays," says Farrant.

There is still more to learn from these unique plants. "Further studies are underway to determine the nature and quantities of bio-protective chemicals produced in the leaves of *M. flabellifolia* when they are exposed to different environmental stressors," she says. "These findings will be important for medicine and cosmetics." ■

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