

# Science Communication Competition

The Science Communication Competition is now in its fifth year. As in previous years, it aims to find young talented science writers and give them the opportunity to have their work published in *The Biochemist*. In 2015, a new branch of the competition was launched to include video entries. Overall, this year's competition attracted 47 entries and these were reviewed by our external panel of expert judges. The third prize in the written category was awarded to Rosemary Chamberlain, University of Oxford, whose article is presented here; the runner up of the video category was Milana Trepetova, Imperial College London. Milana Trepetova's video can be viewed on the Society's website: <http://bit.ly/1kxt8eH>. The Science Communication Competition will open again in January 2016. Please visit our website for more details: [www.biochemistry.org/GetInvolved/ScienceCommunicationCompetition](http://www.biochemistry.org/GetInvolved/ScienceCommunicationCompetition)

## From bark to bacteria: the natural sources of modern medicine

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Nature; it's all around us. We eat it, we wear it and we are part of it. But do we really appreciate the benefits for our health concealed in the natural world, and the contribution that some organisms are making to modern medicine, as they have done for millennia? If we appreciate the valuable medicine chest that the natural world proves to be, should we be treating it with more care?

Let's start with aspirin, one of the most widely used drugs today, with an estimated 40 000 metric tonnes produced each year<sup>1</sup>. For thousands of years, willow leaves and bark containing salicylic acid have been used for their anti-inflammatory and pain-killing effects, with descriptions of their use being found on tablets from the Sumerian period (around 4000 BC) and Ancient Egyptian papyrus. It is also thought that they were used for this purpose by both Ancient Greek and Chinese civilizations. However, it was only in 1763 that the first scientific description of the treatment appeared; the Reverend Edward Stone of Oxfordshire described the beneficial effects of willow bark on feverish patients. In 1859, a way to artificially synthesize salicylic acid was devised, and demand quickly grew. However, salicylic acid can significantly irritate the stomach and has an unpleasant taste. Felix Hoffman, a German chemist, worked to modify salicylic acid to reduce these side effects, without reducing the drug's benefits. He succeeded in 1897, producing acetylsalicylic acid (ASA), and named this aspirin<sup>2</sup>. More recently, aspirin has been discovered to have 'anti-platelet' properties, meaning that it reduces the likelihood of clots forming in the blood<sup>3</sup>. It is therefore now widely used for prevention of heart attacks and strokes and has also been shown to have some effect in preventing some cancers<sup>4</sup>. Not bad for a few leaves and pieces of bark!

Another natural medicine is quinine, the first effective anti-malarial. It is found in the bark of the Cinchona tree, known as 'quina-quina' ('bark of barks') to the Quechuan

people of South America, hence 'quinine'. The bark was traditionally used to reduce shivering due to cold temperatures, as it also acts as a muscle relaxant (although perhaps we might question the wisdom of this, as shivering is one of the body's tricks to warm us up). In an ultimately serendipitous leap, it seems that someone saw the coincidental connection between shivering due to a malarial fever and shivering due to cold, and it was discovered that the bark was an effective anti-malarial. In the 17th Century, the remedy was brought from Peru to Europe, where malaria was then common. Quinine extracted from Cinchona bark remained the top antimalarial drug until the 20th Century, when alternatives were found that had fewer side effects<sup>5</sup>. It is still used for severe malaria in some cases today, or in areas where alternatives are unaffordable.

We have seen that both aspirin and quinine entered mainstream medicine in centuries past and are still in use today. Since their introduction, in a time when the vast majority of medicines were created using natural products, the powerful technique of 'combinatorial chemistry' emerged on the scene in the late 1980s<sup>6</sup>. This involves the production of huge numbers of synthetic compounds to produce a 'library' that can then be tested for medical effectiveness. This reduced the emphasis on natural products for a time, but, more recently, the two approaches have begun to merge, with natural products being used as the 'templates' for combinatorial chemistry<sup>6</sup>. Identification of new natural products is still essential and new medicines are being developed all the time using previously unknown medicinal properties of plants.

Medicinally active plants can be found all around us. For example, the humble daffodil, found in our parks and gardens every spring. You may have noticed that adding cut daffodils to a vase of other flowers rapidly results in some drooping, slightly dead-looking, blooms. One of the headline stories this spring, was 'Keep daffodils away from



food, supermarkets told<sup>7</sup>. Perhaps it's not so surprising then that there are some potent compounds hidden away in these innocent-looking bulbs.

One of these is the drug galanthamine, made from a compound extracted from daffodil bulbs. It is now licensed for use in the treatment of mild to moderate Alzheimer's disease, and has been shown to be effective in slowing the progression of the condition. It works by preventing the breakdown of acetylcholine, a chemical that is necessary for communication between nerve cells, and that is generally present at lowered levels in the brains of patients with Alzheimer's disease<sup>8</sup>. There are other exciting daffodil-related compounds currently in clinical trials, including a potential anti-cancer drug extracted from a plant in the same family as the daffodil<sup>9</sup> and it has been seen that some daffodil compounds have inhibitory effects on HIV infection<sup>10</sup>

The examples discussed here only show a fraction of the plants, animals and micro-organisms that contain compounds used in modern medicine. Between 2005

and 2010 alone, 19 drugs based on natural products were approved worldwide, for conditions ranging from Type 2 diabetes and cystic fibrosis, through attention-deficit hyperactivity disorder (ADHD), to ovarian and breast cancer, as well as others with pain-relieving, antibacterial or antifungal properties<sup>11</sup>. Sources of these drugs include green tea, the cannabis plant, chilli peppers and the saliva of a poisonous lizard known as the Gila monster.

Looking at the world of micro-organisms, there's a wealth of new promise and possibility, as well as a whole realm of natural products that have been used for decades. Let's first look at antibiotics, probably the most well-known of these. Antibiotics are compounds produced naturally by some bacteria and fungi, but the reasons for them being produced are not universally agreed upon. It has been traditionally thought they are secreted to kill neighbouring bacteria and so reduce competition for food, water and other limited resources, a sort of chemical warfare on the microscopic scale. But it now seems that, in most cases, the concentrations of antibiotics found naturally are too low to

kill bacteria. It has been suggested that they are instead a part of a bacterium's 'signalling system'. A lone bacterium doesn't exist in its own little world, blissfully ignorant of all going on outside, there is a network of communication both within and between species<sup>12</sup>.

Probably the most famous antibiotic is penicillin. It was discovered by Alexander Fleming in 1928 and was the first antibiotic that was shown to work effectively against bacterial species that infect humans. Fleming discovered it accidentally on a Petri dish of *Staphylococcus aureus* bacteria, an antibiotic-resistant form of which is what we know today as the 'superbug' MRSA (methicillin-resistant *Staphylococcus aureus*). He observed a bacteria-free clear circle on the dish, around a growth of a mould that had contaminated the plate. Crucially, he appreciated the importance of this, that the mould could kill *S. aureus*. The mould was isolated and identified as *Penicillium notatum*, and the 'antibiotic' compound that it produced was named penicillin. Mass production and treatment of patients became possible after Howard Florey and Ernst Chain developed a method of extraction and purification, and led to the Nobel Prize being awarded jointly to all three in December 1945, following extensive use to treat infection during World War II<sup>13</sup>.

Although penicillin is probably the most well-known, it is not a 'classic' antibiotic, in that it is produced by a fungus, whereas most other natural antibiotics are made by soil bacteria, such as those in the *Streptomyces* family. In some cases, antibiotics that were originally isolated from bacteria are now made synthetically, sometimes with small modifications. Others are still produced by fermentation, meaning that they are harvested from huge vats of the bacteria, effectively 'antibiotic farming'. Unsurprisingly, compounds produced by microbes have other medicinal

properties too. Cyclosporin and rapamycin are two drugs that were first discovered as naturally occurring antibiotics, but are also powerful immunosuppressants, meaning that they dampen down the immune system. They are now central to transplant medicine, reducing the risk that donor organs are rejected<sup>14</sup>.

Antibiotics are becoming increasingly ineffective, so the discovery of new antibiotics is more important now than ever. The search for antibiotic-producing bacteria is turning to ever more diverse environments, from marine sediments to mangroves and several potential leads have been identified. Bacteria from marine environments are also producing exciting leads for anti-cancer compounds<sup>15</sup>.

We've glimpsed only a tiny proportion of the natural products that are fundamental to modern medicine, but, even so, the vital importance of preserving biodiversity around the world seems obvious. We must do all we can to avoid destroying sources of potentially life-saving drugs, oblivious to their existence and potential. Projects such as Kew Garden's Millennium Seed Bank<sup>16</sup> are crucial; storing the seeds of thousands of plant species will allow future investigation and exploitation of their potential medicinal benefits, even if they disappear from their natural habitats. ■

## Further links

In developed countries around 25% of all prescribed medications contain materials that originate from plants. However, despite this only 20% of known plant species have been investigated for their medicinal potential.

**Kew Gardens** are a centre for research into the properties of plants and fungi. You can read more about the importance of plants in medicine here: [www.kew.org/science-conservation/plants-fungi/medicine](http://www.kew.org/science-conservation/plants-fungi/medicine).

**Chelsea Physic Garden** was founded in 1673 and has focused on research and education about natural sources of medicine for many years. You can read more about the garden and the work they do here: <http://chelseaphysicgarden.co.uk/the-garden/>.

### Other articles of interest:

A history of aspirin: [www.pharmaceutical-journal.com/publications/previous-issues/cp-september-2014/a-history-of-aspirin/20066661.article](http://www.pharmaceutical-journal.com/publications/previous-issues/cp-september-2014/a-history-of-aspirin/20066661.article)

Cinchona: a short history <http://www.lib.cam.ac.uk/deptserv/rcs/cinchona.html>

Treating Alzheimer's Disease with daffodils <http://jncc.defra.gov.uk/page-5721>

## References

1. Warner, T.D. and Mitchell, J.A. (2002) Cyclooxygenase-3 (COX-3): filling in the gaps toward a COX continuum? *Proc. Natl. Acad. Sci. U.S.A.* **99**, 13371–13373
2. Jack, D.B. (1997) One hundred years of aspirin. *Lancet* **350**, 437–439
3. [www.nhs.uk/conditions/Anti-platelets-aspirin-low-dose-/Pages/Introduction](http://www.nhs.uk/conditions/Anti-platelets-aspirin-low-dose-/Pages/Introduction)
4. Cuzick, J., Otto, F., Baron, J.A. et al. (2009) Aspirin and non-steroidal anti-inflammatory drugs for cancer prevention: an international consensus statement. *Lancet Oncol.* **10**, 501–507
5. Sherman, I.W. (2010) *Magic Bullets to Conquer Malaria: from Quinine to Qinghaosu*, ASM Press, Washington, DC
6. Cragg, G. and Newman, J. (2013) Natural products: a continuing source of novel drug leads. *Biochim. Biophys. Acta* **1830**, 3670–3695
7. [www.theguardian.com/business/2015/feb/07/keep-daffodils-away-from-food-supermarkets-told](http://www.theguardian.com/business/2015/feb/07/keep-daffodils-away-from-food-supermarkets-told)
8. Anon (2001) Galantamine (Reminyl) for Alzheimer's disease. *Med. Lett. Drugs Ther.* **43**, 53–54
9. Nair, J.J., Bastida, J., Codina, C., Viladomat, F. and van Staden, J. (2013) Alkaloids of the South African Amaryllidaceae: a review. *Nat. Prod. Commun.* **8**, 1335–1350
10. Akkouch, O., Ng, T.B., Singh, S.S. et al. (2015) Lectins with anti-HIV activity: a review. *Molecules* **20**, 648–668
11. Mishra, B.B. and Tiwari, V.K. (2011) Natural products: an evolving role in future drug discovery. *Eur. J. Med. Chem.* **46**, 4769–4807
12. [www.sgm.ac.uk/en/publications/microbiology-today/index.cfm/publication/antimicrobials/article/0DC7B109-3D72-452B-A62C7465DEDD32C8](http://www.sgm.ac.uk/en/publications/microbiology-today/index.cfm/publication/antimicrobials/article/0DC7B109-3D72-452B-A62C7465DEDD32C8)
13. Wennergren, G. and Lagercrantz, H. (2007) "One sometimes finds what one is not looking for" (Sir Alexander Fleming): the most important medical discovery of the 20th century. *Acta Paediatr.* **96**, 141–144
14. [www.sgm.ac.uk/en/publications/microbiology-today/index.cfm/publication/antimicrobials/article/C1FD8C70-FA3C-4829-8E8DC35E8BD2F470](http://www.sgm.ac.uk/en/publications/microbiology-today/index.cfm/publication/antimicrobials/article/C1FD8C70-FA3C-4829-8E8DC35E8BD2F470)
15. Manivasagana, P., Kanga, K.H., Sivakumar, K., Li-Chan, E.C., Oh, H.M. and Kim, S.K. (2014) Marine actinobacteria: an important source of bioactive natural products. *Environ. Toxicol. Pharmacol.* **38**, 172–188
16. [www.kew.org/science-conservation/collections/millennium-seed-bank/about-millennium-seed-bank](http://www.kew.org/science-conservation/collections/millennium-seed-bank/about-millennium-seed-bank)