century BC. Medical tools that may have belonged to a physician — including a stone mortar, a bronze cupping vessel and numerous tin vessels (*pyxides*) — were among the cargo found on board the *Relitto del Pozzino*, discovered in 1974 off the coast of Tuscany. An Italian-based team led by Erika Ribechini at the University of Pisa have analysed well-preserved discoid tablets of about 4 cm in diameter and 1 cm thick that were stacked in a *pyxis*.

Energy-dispersive X-ray spectroscopy revealed that the tablets mostly consisted of inorganic substances — principally zinc (75%), along with some iron and silicon. Infrared spectroscopy and powder X-ray diffraction enabled the identification of zinc hydroxycarbonate and zinc carbonate as the main compounds present in the sample. These might have been the active ingredients: zinc compounds are known to have long been used for therapeutic applications — zinc oxide obtained as a by-product of copper production, for example, was used for ophthalmologic and dermatologic treatments. Characterization of the organic content of the tablets using infrared spectroscopy indicated the presence of starch, and mass spectrometric analysis was used to identify other ingredients such as both animal and vegetable-derived lipids, beeswax, pine resin and charcoal. Starch grains, resins and charcoal have also been observed in other ancient medicines; resin may have slowed down degradation and microbial growth.

In addition, plant remains (fibres, starch grain and pollen grains) were found using light and scanning electron microscopies, and characterized through botanical analysis. Mainly located in the outer part of the tablets, the fibres may have served to prevent them from breaking apart. Taken together, the tablets' composition and shape — the word for 'small round loaves' in Greek is *kollura* from which the Latin word for eyewash 'collyrium' is derived — suggest that they have been used as an eye treatment. *AP*

BIOCATALYSIS

Promiscuous by nature

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Synthetic chemists have developed a diverse range of metal-catalysed cyclopropanation reactions that involve the addition of a carbene to an olefin. Despite the fact that iron–porphyrin centres, which are common in metalloenzymes, will catalyse this reaction under the right conditions, there are no enzymes that harness similar chemistry for cyclopropanation in their natural biological environment. Some enzymes, however, are known to be promiscuous enough to react with alternative reactants to catalyse a different chemical reaction under the right conditions — albeit normally at a much lower level of activity.

In an effort to see if any metalloenzymes were promiscuous enough to adapt to metallocarbene chemistry, a team led by Frances Arnold at the California Institute of Technology screened a selection of naturally occurring haem proteins (which contain an iron–porphryin moiety) to see if they could be induced to catalyse a cyclopropanation reaction between styrene and ethyl diazoacetate — common reactants for testing catalysts for this transformation. It was found that several of the enzymes could catalyse the cyclopropanation, albeit at low levels. Of these enzymes, cytochrome $P450_{BM3}$ (a monooxygenase from the soil bacterium *Bacillus megaterium*) produced a mixture of *cis* and *trans* diasteroisomers and seemed to be the best candidate for further optimization.

The next step was to identify mutations that improved the catalytic properties. Screening a library of 92 variants resulted in five promising candidates that were further analysed to discover which mutations improved the catalytic turnover as well as the diastereo- and enantioselectivity. Based on these results, Arnold and co-workers started to design new variants that combined advantageous mutations. Designing small-molecule catalysts that favour the *cis* product rather than the *trans* isomer is more challenging and so the team elected to see if a $P450_{BM3}$-based metalloenzyme could be adapted to tackle this problem. Mutations to the amino acids around the active site produced enzymes with enhanced *cis* selectivity and further experiments showed that the variant $P450_{BM3}$ enzymes could tolerate a range of substrates and functional groups. *RJ*

Written by Gavin Armstrong, Stephen Davey, Russell Johnson and Anne Pichon

blogroll

It's time to talk

Is a PhD bad for your health?

Graduate students will be all too familiar with the trials and tribulations that PhD research brings, but is it bad for your health? Chemjobber (http://go.nature.com/FCAet3) and Vinylogous at 'Not the Lab' (http://go.nature.com/gKqFwa) hosted a blog dialogue on 'Is graduate school in chemistry bad for your mental health?' to raise important issues that rarely get discussed. Chemjobber shares his personal experiences including "the feeling that [his] entire life was an utter failure". Vinylogous recounts that his "weekends had been given up, as had hobbies" and "7-day workweeks were expected; dinner was eaten hurriedly at one's desk; stealing was frequent and hoarding of reagents and glassware was necessary". Not only are the five posts excellent, but the comments that the posts have produced are insightful and eye-opening.

Derek Lowe also joined in the mental health discussion at 'In the Pipeline' (http://go.nature.com/dA1576) and at 'Periodic Boundary Conditions', Miss MSE adds her personal viewpoint (http://go.nature.com/PpEfyF). She highlights the need for a life outside her PhD and concludes that "the most important thing I can do for my mental health is this: talk to people who aren't in grad school". Finally, MB at 'Colourblind Chemistry' reveals (http://go.nature.com/4AjdW4) the consequences of picking the wrong principal investigator and how he dealt with that. He summarizes the mental health posts nicely with the comment that "grad school is incredibly difficult, but it doesn't need to be demoralizing".

If the posts described above don't put you off life as a graduate student, then head over to 'The Drew Lab' where Joshua Drew gives out (http://go.nature.com/n7k1nK) some first-rate tips on how to apply to graduate school, from GRE scores to the personal statement, noting that "there are no set formulae as to what makes a good candidate".

Written by JessTheChemist, who blogs at http://theorganicsolution.wordpress.com/