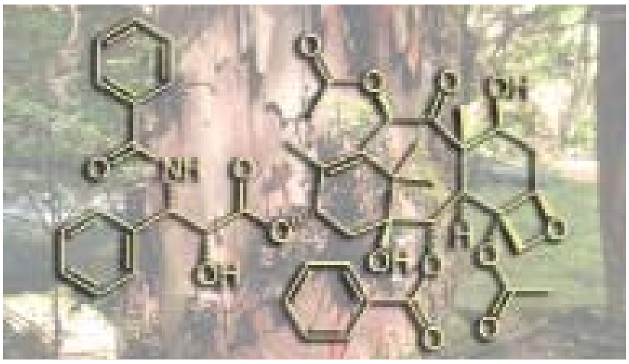
Chemical science

E. coli bacteria engineered to produce precursors of a widely used cancer drug

Bacteria factories for Taxol precursors

US researchers have engineered bacteria to produce precursors of Taxol (paclitaxel), one of the most widely used cancer drugs. The work could lead to quicker and cheaper synthetic routes to Taxol, and could improve commercial access to terpenoids used in food, cosmetic and chemical products.

The researchers from Massachusetts Institute of Technology (MIT) and Tufts University in Boston broke down the synthesis into two parts. First, they amplified four bacterial genes in *Escherichia coli* to increase production of isopentenyl pyrophosphate (IPP), a building block of an important Taxol precursor, taxadiene. They then inserted two plant genes to convert the IPP to taxadiene, achieving 1g per litre in the fermentation mixture. Furthermore, they also produced taxadien-5α-ol from *E. coli,* the next compound on the route to Taxol for the first time.



***E. coli* could now be used to make paclitaxel, a cancer drug originally isolated from the bark of the Pacific yew tree**

Reference
P K Ajikumar *et al, Science*, 2010, **330**, 70 (DOI: 10.1126/science.1191652)

Taxol is made naturally by the Pacific yew tree, *Taxus brevifolia*. In the early years, production relied on the tree bark as a feedstock, which devastated the population. But in the 1990s, several scientists developed synthetic and semi-synthetic approaches. US pharmaceutical firm Bristol-Myers Squibb brought Taxol to market in 1992 and it quickly became a first-line treatment for a range of cancers.

Now it could be possible to get *E. coli* to do the work. The key, the researchers say, was metabolic engineering: careful balancing of the effects of the numerous genes. 'By mimicking nature, we can now begin to produce these intermediates that the plant makes, so people can look at them and see if they have any therapeutic properties,' says author Gregory Stephanopoulos.

'This is a remarkable study,' says Lai-Xi Wang, a molecular biologist at the University of Maryland School of Medicine, US. 'The combined modular engineering approach, which enables the balancing of multiple metabolic reactions simultaneously for the production of the key Taxol precursor, may be generally applicable for other targets.' *Andrew Turley*

'Organic' aqua regia that could selectively recycle noble metals

Challenging aqua regia's throne

An 'organic' aqua regia which can selectively dissolve noble metals has been discovered by researchers in the US. This could lead to new ways to recycle noble metals from industrial processes and aid the manufacture of nanomaterials, they say.

Traditional aqua regia is a mixture of concentrated nitric and hydrochloric acids in a ratio of 1:3 that can dissolve noble metals such as gold, platinum and palladium, even though the metals are not soluble in either acid alone. However, such inorganic acid compounds cannot dissolve one noble metal in preference to another, making recycling noble metals with inorganic acids a challenge.

Now, Wei Lin and colleagues at the Georgia Institute of Technology in Atlanta, have demonstrated an organic solvent which achieves high dissolution rates of noble metals under mild conditions, with the added benefit of being tunable to a specific metal.

The team discovered that gold dissolves when it is left in a mixture of thionyl chloride ($SOCl_2$) and the organic solvent pyridine. Further experiments on the system revealed that other organic solvents and reagents – such as *N,N*-dimethylformamide (DMF), imidazole, and pyrazine – could achieve similar effects when mixed with thionyl chloride, with the gold recoverable by subsequent calcination. In addition, a $SOCl_2$–DMF mixture dissolves gold but not palladium or platinum. 'The selectivity may be beneficial in improving the purity of the recycled noble metals from catalysis and the electronics industry,' Lin suggests.

'The spectacular dissolution selectivity relies on the intrinsic versatility of organic chemistry so that soon selective organic aqua regia mixtures will be used to dissolve the noble metal of interest,' says Mario Pagliaro a chemist at Italy's National Research Council (CNR). 'One immediate application will be full recovery of platinum from exhaust catalytic converters today, and from fuel cells tomorrow,' he suggests.

The teams organic aqua regia can selectively dissolve a range of noble metals

Reference
W Lin *et al, Angew. Chem.*, 2010, **49**, 7929 (DOI: 10.1002/anie.201001244)

However, in terms of efficiency and cost, Lin concedes that his organic aqua regia is currently unable to compete with traditional aqua regia. But it does offer a safer alternative and it could have uses beyond recycling, such as synthesis of noble metal nanostuctures and selective removal of nanocoatings.

The team is now working to further understand the chemistry of the dissolution process.
James Urquhart