

## Hunter-gatherers win profit-sharing deal for obesity drug

A groundbreaking agreement has been signed granting the San people (formerly called the Bushmen) a share of profits from a potential obesity-reducing drug extracted from the hoodia cactus. The deal is one of the first to give holders of traditional knowledge a share of royalties from drug sales.

For thousands of years the San, one of the oldest peoples in Southern Africa, have eaten slices of the bitter hoodia to keep them going for long periods without food or drink when they are on hunting trips.

Piet Rooi, a 73 year-old former farm worker, told the *South African Mail and Guardian*: "I eat the xhoba [hoodia] to stave off hunger and thirst and then I no longer feel hungry or thirsty. I eat it when I am feeling weak and then I feel strong and virile. I eat it when I have a bad stomach or flu and then I feel better."

In the 1960s the Council for Scientific and Industrial Research (CSIR), based in South Africa, isolated the appetite suppressant molecule in the hoodia and patented it. In 1997 the CSIR licensed the rights to the molecule, named P57, to a UK-based company, Phytopharm. After initial tests on the drug looked promising, Phytopharm sold on the rights for US\$ 21 million to the pharmaceutical giant, Pfizer.

Shares in Phytopharm and Pfizer rose sharply amid hopes that the drug would revolutionize the US\$ 9.5 billion market in slimming aids. There was an international outcry with the companies accused of biopiracy. The chief executive of Phytopharm, Richard Dixey, told the *Financial Times* at the time that he believed the San "had disappeared."

The San, very much alive and numbering 100 000 in South Africa, Namibia, Botswana and Angola, then launched a legal battle to get a share of the profits. After years of tough negotiation a benefit-sharing agreement was finally signed on 24 March 2003. Under the terms of the agreement the CSIR will pay the San 8% of all milestone payments it receives from its licensee, Phytopharm plc, as well as 6% of all



Hoodia growing in its natural environment

Phytopharm plc

royalties that the CSIR receives once the drug is commercially available.

Even though this represents only a tiny fraction of the net profits, Roger Chennells, lawyer for the South African San Council, told the *Bulletin*: "The San are very happy with the agreement. They expect to get 12 million rand (US\$ 1.6 million) over the next 3–4 years; then if things go well 10–12 million rand per year."

The money is to be deposited into a San Hoodia Benefit Sharing Trust and will be spent on education, skills development and creating jobs for the San, one of the most impoverished and marginalized groups of people in Southern Africa.

Petrus Vaalbooi, chairperson of the South African San Council, says: "We are thankful that the traditional knowledge of our forefathers is acknowledged by this important agreement, and that we are making it known to the world. As San leaders we are determined to protect all aspects of our heritage."

It is possible that P57, like any drug in development, will come unstuck in clinical trials. However, as it has effectively been tested in humans for centuries, it is likely to have few of the adverse side-effects that are common with other slimming products. A UK Phase IIa clinical study in 18 obese patients showed that P57 reduced calorie intake by an average of

1000 calories compared with placebo (see graph [www.phytopharm.com/Platforms/MetabolicSyndrome\\_P57.shtml](http://www.phytopharm.com/Platforms/MetabolicSyndrome_P57.shtml)). Larger studies are now planned and Pfizer hopes to have the drug on the market by 2008.

The San have detailed knowledge of thousands of other indigenous plants, many of which have potential medical uses. They are planning to work in partnership with the CSIR to develop some of these plants commercially. Mr Chennells said: "We are optimistic that this case will serve as a sound foundation for future collaboration, not only for the San but also for other holders of traditional knowledge." ■

Jaqui Wise, *Capetown*

## *Plasmodium falciparum* outwits Malarone, protector of travellers

Doctors in Sweden have reported resistance to Malarone, one of the newest and increasingly relied on products for preventing and treating malaria (*BMJ* 2003;326: 628-9). A study last year (*Malaria Journal* 2002;1:1) indicated that *Plasmodium falciparum*, the parasite that causes most malaria, was resistant to Malarone in vitro. The current finding confirms it: two patients treated at a Gothenburg hospital had ample amounts of the drug in their blood to

wipe out the parasite, yet the infection persisted.

The newfound resistance will affect travellers more than people living in malaria-endemic areas, however. The pink Malarone tablets have become a staple for visitors to climates in which the *Anopheles* mosquito, carrier of malaria-causing parasites, thrives. In trials leading to the drug's registration, its overall efficacy was found to be 98.7%. But the price of the drug severely limits its use in poor regions, including Africa where about 90% of all malaria infections occur.

Malarone is a combination of atovaquone and proguanil, two compounds that interfere with *P. falciparum* metabolism in different ways. Both have been used separately before (proguanil was approved in the US in 1948), but together they have a synergistic effect, and efficiently kill the malaria-causing parasite in red blood cells. Since 1996, more than 35 countries have approved the use of Malarone. Along with prescribing it as a prophylaxis, to prevent *P. falciparum* infection, doctors also administer the drug to treat malaria in travellers who have returned home.

However, resistance to both atovaquone and proguanil has been seen when the compounds are used individually. So it is not surprising that a strain of *P. falciparum* resistant to both could evolve, says David Ubben, a scientific advisor for the Geneva-based Medicines for Malaria Venture. "The malaria parasites are extremely agile at making themselves resistant to antimalarial agents," he says. "It's easy to imagine that *Plasmodium* strains that already carry a certain resistance can develop resistance to a second component."

The two young brothers treated in Sweden became infected with Malarone-resistant parasites during a two-month visit to the Ivory Coast. They had taken chloroquine and proguanil to ward off infection, but after returning north both boys developed a fever. The younger child failed to respond to Malarone, despite having therapeutic levels of atovaquone, proguanil and cycloguanil (the active metabolite of proguanil) in his blood. He recovered when treatment was switched to mefloquine. His four-year-old brother cleared the parasites after three days of Malarone treatment, in which therapeutic drug levels were reached, but the organisms reappeared within a month. The boy also recovered with mefloquine treatment.

To investigate further, researchers led by Anna Färnert of the Division of Infectious Diseases at the Karolinska Institute in Stockholm analysed the parasites in each boy's blood. The scientists found that the older child harboured a strain of *P. falciparum* carrying a genetic mutation that has been implicated in atovaquone resistance, as well as the case of Malarone resistance reported last year. However, the parasite in the younger brother did not have the changed gene, suggesting that "there might be other mechanisms involved," says Färnert.

While finding resistance to Malarone is not setting off alarm bells, it does sound a cautionary note. Physicians using it need to keep a close eye on the possibility of drug failure. "Malarone is a good drug, but it may not always be 100% effective," says Färnert. "But, that is the message for all malaria drugs." ■

Charlene Crabb, *Paris*

## World Water Forum ends in flood of commitments

The eight-day meeting held in the three neighbouring cities of Kyoto, Shiga and Osaka, Japan, ended on 23 March by issuing a statement of commitment. Overall, this was "to facing the global water challenges" and achieving the Millennium Development Goal (MDG) of halving, by 2015, the proportion of poor people without secure access to water and sanitation. To do so, groups participating in the Forum made over 100 commitments, but what these add up to, and the extent to which they are and compatible, remains to be seen.

"The third World Water Forum has become a truly action-oriented conference," said Kenzo Hiroki, its Vice Secretary-General. Over 24 000 participants from 182 countries attended — well over three times as many people as expected. Their main concerns were with meeting the increasing human need for adequate water supplies, and balancing these with the demands of health, sanitation, food production, transportation, energy and environmental protection. Most countries also stressed the need for effective government, improved capacity, and adequate financing to manage these issues.

Global water consumption has increased tenfold in the last century, according to SustainAbility, a develop-

ment consulting firm. Over a billion people in the world have no access to safe drinking-water, and 2.4 billion lack adequate sanitation. A result is that 3 million people die from preventable waterborne diseases every year. The World Trade Organization and industry groups see the market as the only way to organize the distribution of this increasingly scarce resource, by setting a price on it. Others, such as Maud Barlow and Tony Cark, authors of *Blue gold*, see this approach as "the corporate theft of the world's water".

Lyla Mehta, of the Institute of Development Studies in the UK, told the *Guardian* that "Because many people think of water as a basic human right, they react angrily to the idea of private companies making profits out of water provision". She cites protests and revolts in Bolivia, Ghana, Peru, Trinidad and Tobago, and other developing countries, over the privatization of water supply systems.

The participants of the Water Forum had till 30 April to finalize the content and wording of their commitments. These included setting up a global flood warning system, organizing a consortium of institutions to support governments in managing their water supply systems, financing communities to solve or mitigate their water and sanitation problems, and strengthening the capacity of indigenous people to protect their water rights.

The final statement said that increasing the efficiency of water use may not be sufficient to meet the growing demand for water in many developing countries, particularly in cities. "All options to augment the available water supply, including increased storage through the use of groundwater recharge and dams, need to be considered, ensuring that all those who will be affected will also benefit." It concluded: "A wider adoption of good practice is required in order to avoid the environmental and social costs and risks of the past."

More concretely, Sir Richard Jolly, Chair of the Water Supply and Sanitation Collaborative Council, points out that although about US\$ 10 billion a year is currently spent on water and sanitation, meeting the MDG for water and sanitation will require "at least a doubling of this level of investment". ■

Desmond Avery, *Bulletin*