

Cold turkey, Vietnamese style

It was invented by a healer familiar with the horrors of opiate addiction, and refined by Vietnam's leading chemistry lab. Can this novel herbal cocktail ease withdrawal and reduce drug cravings? Peter Aldhous investigates.

ung doesn't ask for much in life: he dreams of finding a job, getting married, and becoming, as he puts it, a "normal person". But the dark stains on his arms mark him out as a social pariah. Tung was once so desperate for his regular fix of opium that he would first smoke the drug, and then mix the residue with water to create an injectable paste that has discoloured his veins. Now 28, this is Tung's second time in rehab.

In the West, doctors might try to wean Tung off drugs by putting him on a substitute opiate such as methadone, and then gradually reducing the dose. But this is Vietnam, where the authorities take a tough line on what they view as a social evil. At the staterun drug-treatment clinic in Hoa Binh, some two hours' drive into the hills west of Hanoi, abrupt detoxification is the order of the day. Recovering addicts must first go 'cold turkey'

in concrete cells furnished with only a mattress. Many, including Tung, have been forcibly detained.

The conditions may be harsh, but the Hoa Binh clinic is at the centre of an experiment in drug rehabilitation that has sparked the curiosity of clinicians worldwide. Here, hundreds of addicts have been treated with a cocktail of herbal extracts called Heantos. It is claimed that it makes withdrawal tolerable and, in the longer term, reduces the craving for drugs.

From its crude beginnings as a thick brown syrup, Heantos has been refined into a series of subtly different formulations, given at different stages of detoxification and recovery. They are produced in a pilot plant at the Vietnamese Academy of Science and Technology's Institute of Chemistry in Hanoi. And within a year, a clinical trial in Germany may reveal whether the hopes that the

institute has invested in Heantos are justified.

In many countries, Heantos would have remained on the medical fringes. But in Vietnam, there is little of the tension that, in the West, divides the practice of herbalism from the high-tech world of pharmaceutical chemistry. So in the mid-1990s, when Tran Van Sung, now director of the Institute of Chemistry, was approached by a herbalist touting a concoction that could allegedly reform hardened drug addicts, his first instinct wasn't to dismiss the healer as a quack.

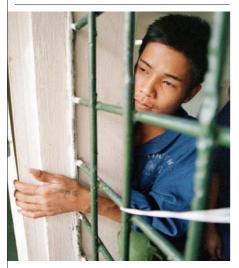
Refined approach

Instead, Sung engaged with the herbalist, Tran Khuong Dan, as a collaborator. "We had difficulties understanding one another in the beginning," Sung admits. Dan's focus on the overall blend of plant extracts in his creation initially jarred with Sung's desire to standardize and improve techniques for extracting the main compounds present. But slowly, their goals coalesced. Dan is today an associate of the chemistry institute, and is named as co-inventor, with Sung and his colleagues, on a German patent application.

The Heantos story began more than a decade before Dan's initial contact with Sung, when Dan was practising in Ho Chi Minh City. After seeing his brother and father fall foul of drugs, Dan travelled the country, investigating remedies used to treat addicts. Individually, none worked very well. But by the end of the decade, Dan had come up with a cocktail of herbal extracts that — judging from tests he conducted on himself, after deliberately getting hooked on various



Social pariahs: Vietnamese opium addicts are shunned by society, but it is claimed that a cocktail of herbs has helped some in state-funded rehabilitation (below) to beat their problem.



opiates — provided relief from drug with-drawal. "It was dangerous, but there was no other choice," says Dan.

Whether this tale has been embellished is hard to say. But flashy showmanship doesn't seem to be Dan's style. On our trip to Hoa Binh, he is quiet and detached; facts about his work on Heantos have to be coaxed from him through an interpreter.

Perhaps Dan has grown tired of telling the story, given the tortuous road that Heantos has travelled. The treatment first came to international attention in 1997, when the United Nations Development Programme (UNDP) decided to invest US\$400,000 in its scientific development. Since then, a similar

sum has come from the Norwegian government, with additional support from the United Nations Educational, Scientific and Cultural Organization.

By local standards, this is lavish funding. And it has caused some tensions within Vietnam, where there are competing approaches to drug detoxification. "Heantos has certainly been contentious," says Ayo Wahlberg, a graduate student at the London School of Economics who is interested in the regulation of herbal medicines, and has made several trips to Vietnam. In the late 1990s, for instance, rumours circulated that some patients had died following adverse reactions. But subsequent safety evaluations by the Vietnamese authorities have given Heantos a clean bill of health.

In parallel, Sung and his colleagues have refined the techniques used to produce Heantos, replacing Dan's method of grinding the plants in water with solvent extraction and freeze-drying. They have also begun characterizing the chemical constituents of the resulting formulations. "We have several hundred pure compounds," says Sung. But

"If Heantos is shown to

have some therapeutic

value, it would boost the prospect of a

treatment that seems

for the past few years

to have become stuck

in limbo."

their identity, and that of the 13 plants from which Heantos is derived, is being kept under wraps until the German patent application is published.

Shortly after the UNDP got involved, there was a flurry of publicity when a group of foreign journalists interviewed Dan and met addicts who had

been treated with Heantos. Some of the resulting articles painted Heantos as a miracle cure, citing positive results from Vietnamese trials — including a study of 110 veterans of what is known here as the American War, who had become addicted to the morphine used to ease the pain of their wounds.

Outside influence

But the Vietnamese clinical studies of Heantos have all failed to meet the gold standard of double blind, placebo-controlled trials. Clinical research is weak in Vietnam. So if the effectiveness of Heantos was to be assessed to internationally recognized standards, it seemed that this would require a trial outside Vietnam.

Initially, this was going to be carried out by a team led by Donald Jasinski at the Johns Hopkins School of Medicine in Baltimore, Maryland. But the planned trial's US proponents failed to secure funding. Eventually, the government of the state of North Rhine Westphalia in Germany, where attitudes to herbal medicine are more positive than in many other Western countries, came to the rescue. In 2001, it agreed to fund a trial to test the ability of Heantos to ease withdrawal symptoms.

The protocol, designed by psychiatrist Norbert Scherbaum of the University Hospital in Essen, calls for the treatment to be given to 30 heroin addicts, while another 30 are given a placebo. But before the trial could go ahead, the German authorities demanded analysis of the Heantos formulations by the Institute of Plant Biochemistry in Halle.

Given that Heantos is such a complex mixture, satisfying the demands of regulatory authorities has been a persistent problem, says Wahlberg. Even a 2004 European Union (EU) directive, designed to lower the hurdles for certain herbal remedies, doesn't provide much assistance. It offers a simplified registration procedure, with few requirements for lengthy preclinical tests and clinical trials, for products that have "a well-established medicinal use" within the EU. Heantos is the product of Dan's invention and Sung's chemical expertise, so it doesn't qualify.

Scherbaum hopes to begin enrolling patients in the trial within the next few months, and to have results by the end of this year. Experts who have followed the progress of Heantos are taking a cautious view. "I've seen a lot of 'magic bullets' come and go," says Gabrielle Welle-Strand of the Centre for Medication-Assisted Rehabilitation in Oslo,

Norway, who was a member of an international team of addiction specialists that visited Vietnam in 1999 to witness the treatment's use.

Scherbaum's trial also isn't designed to test the claims that Heantos can reduce the underlying craving for drugs that prevents many reformed addicts

from keeping clean in the long term. Here, there is no such thing as a miracle cure — as Tung can testify. After his first spell in rehab, aided by Heantos, he returned to his hometown of Mai Chau, in the mountains near the border with Laos. Unable to find work, Tung soon fell in with his old drug-taking friends, and was enslaved to opium once more.

But if Heantos is shown by Scherbaum's trial to have some therapeutic value, it would provide a boost to the prospect of a treatment that seems for the past few years to have become stuck in limbo. Even the Vietnamese authorities have yet to decide whether to approve Heantos for general use.

There's certainly a growing demand in this part of the world for treatments to aid drug rehabilitation. A few years back, Vietnamese drug addicts were few in number, and mostly rural users of opium. Today, there's a burgeoning heroin problem, both in the rapidly expanding cities and along the roads from Laos, used to transport the drug for illegal export.

This trade blights the region, and the wider world. Will Dan and Sung's efforts one day allow Vietnam to be known for exporting an antidote to addiction, rather than merely being a trade route for the criminals who feed it? The answer may lie in Essen.

Peter Aldhous is *Nature*'s chief news & features editor.