



Thursday, Nov. 18, 2010

## Herbal Healing

By SIMON ELEGANT

**I.** Son Sarun came to the town of Pailin in Cambodia's desolate northwest because of the stories he had heard: the \$100,000 ruby found just over the next hill, the \$25,000 sapphire that tumbled out of trousers being laundered in the river. He hadn't heard that the once gem-rich area had been largely mined out and all that remained was swamp and mosquitoes. When the 38-year-old former soldier came down with a headache and fever last year, he couldn't afford a doctor. He was no richer when blood appeared in his urine, sputum and excrement. One morning in December he collapsed.

**II.** "The doctor said the virus had already entered my brain," says the gaunt, hollow-eyed Sarun. The diagnosis: advanced cerebral malaria. In the past, that would have been a death sentence in Pailin, where the malaria parasite is resistant to all the main forms of quinine, the once miraculous antimalaria agent discovered in the bark of a South American tree four centuries ago. But Sarun's doctor wielded a potent new weapon, a non-quinine-based drug called artemisinin. After a week of daily shots, Sarun was back squatting in the muddy river, sifting rock and sand.

**III.** In the world of disease and medicine, artemisinin is like a gem discovered in a riverbed. For thousands of years, the plant it is derived from was used in traditional Chinese medicine to subdue fever. During China's brief war with Vietnam in 1979, the Chinese government gave its soldiers a crudely distilled antimalaria pill based on artemisinin—and it worked. Today, scientists at the Shanghai Institute of Materia Medica, where artemisinin was first isolated, have further refined the compound into what is now "simply the most effective antimalarial drug we've ever had," says FranCois Nosten, a physician who has spent 16 years combating malaria on the Thai-Burmese border under a program run by Mahidol University in Thailand and Oxford University in England.

**IV.** After a five-year delay caused in part by skepticism that a drug based on a Chinese herbal remedy could be effective, the World Health Organization recently gave official backing for the distribution of an artemisinin-based medicine in Africa. "We have the drug that will save lives," Nosten says. "Now it is a question of getting enough cash to pay for it and then getting it to the people who are sick." The payoff could be huge. In Africa, where resistance to quinine is spreading rapidly, 2 million people, mostly children, die from the disease annually.

**V.** Artemisinin is the biotech world's moniker for qing haosu, a crystalline compound extracted from sweet wormwood, a weedy plant indigenous to China. The curative powers of such plants are the basis of Asian traditional medicine—and from China through the rest of the continent there are literally millions of plants, combinations, shamanistic traditions and household remedies claiming to beat disease or boost health. The vast majority of Asians believe in them, and many use them loyally. For decades, however, this seemingly blind faith has sparked deep suspicion among Western scientists.

**VI.** In some cases, such skepticism is richly deserved. Consider the 30 fretful souls lined up outside a shabby row house in a suburb of Malaysia's capital, Kuala Lumpur. They're waiting eagerly on this steamy afternoon to see a man they call simply Shifu, or master. Inside, a ponytailed Chinese man in his late 50s sits at a wooden table. Each interview, conducted in full view of the expectant throng, takes just minutes. There's a quick feel of the pulse and blood pressure, a scan of the face and eyes, a pause to hear what's wrong, followed by a grim diagnosis ("your intestines are full of toxins, very dirty, your liver is gone, you are full of worms") and a prescription for medicine that will "detoxify" the patient. The Shifu mixes his own medicine upstairs (strictly no entry). He doesn't reveal his ingredients and his patients don't ask; they just glug down the brown liquid obediently. "I think I feel better," ventures a woman in her 40s after three weeks of this daily sludge and little else. "Anyway, I lost weight, though that might be because I spent so much time going to the toilet after I took the medicine."

**VII.** Self-appointed herbal healers like this have long epitomized the world of traditional Asian medicine for many Western scientists: a chaotic, unregulated realm in which for every legitimate practitioner who spent years studying such texts as the "Taiping Royal Prescriptions"—first published in 992 and containing 16,800 formulas—there is some street-corner charlatan sweeping dried leaves and God-knows-what into jars that sell like crazy. All of which has led Western skeptics to dismiss much of traditional Asian healing as little better than witch doctoring.

**VIII.** Even when a herbal prescription has centuries of use behind it, and when its production and sale are closely supervised by government agencies, things can go horribly wrong. Several dozen Japanese died in the late 1990s after taking a popular liver tonic called shosaikoto, which the national health insurance program had certified.

**IX.** In the past few years, a quiet but historic campaign has been under way to subject traditional Asian treatments to rigorous scientific scrutiny. Governments in China, Singapore, Taiwan and Hong Kong are pouring money into hard research on long-accepted cures. In his 1998 annual policy address, Hong Kong Chief Executive Tung Chee-hwa vowed to make the city the world leader in research on traditional remedies, a drive that bore fruit with the opening in 2001 of the Institute of Chinese Medicine. Not to be outdone, Taiwan unveiled a \$100 million plan that year, aimed at transforming itself into a "traditional Chinese medicine technology island" by 2006. Research into traditional cures is also blossoming at universities and other institutions outside Asia. The U.S. government's National Institutes of Health will spend \$220 million on research and training in alternative medicines this year, a chunk of which will go toward the study of Asian remedies.

**X.** The forces driving the burst of interest in Chinese medicine vary from national pride to pure intellectual curiosity. And, of course, money. Herbal and other alternative medicaments clocked up a stunning \$40 billion in sales in the U.S. alone last year.

**XI.** Whatever the reasons, there is mounting evidence that these efforts to unlock the secrets of Asian remedies could produce tangible benefits for sufferers of diseases that have confounded both Western and Eastern schools of medicine—everyone from menopausal women to cancer patients. A number of new drugs spawned by this recent research boom are currently undergoing trials across Asia. The ailments they aim to treat range from the awful side effects of chemotherapy to the crippling pain of arthritis. As with all drug trials, the odds are heavily stacked against success. But if just one of these drugs makes it to the pharmacy shelves alongside artemisinin, the world's medicine chest, compartmentalized for centuries, will have grown immeasurably richer. And it will be yet another sign that what once seemed like two fundamentally opposed approaches to healing have finally begun to work in tandem.

**XII.** It ought to be easy: take drug combinations that have been used for thousands of years and apply strict scientific tests to them to find out what makes them work. Then distill the active compound and make a pill. But life isn't that simple. The very fact that traditional remedies have been used successfully for centuries—precisely what should make them invaluable signposts to researchers—means that drugs developed from those formulas can't be patented. That, in turn, means that no international drug behemoth is driving this research. "Large pharmaceutical companies will only be interested if you can prove the medicine is a new treatment or you can derive new compounds from the traditional form," says Professor Ricky Man, who heads the department of pharmacology at the University of Hong Kong. Another daunting challenge, drugmakers say, lies in getting approval from the notoriously strict U.S. regulatory agency, the Food and Drug Administration (FDA). "The FDA requires that we prove how a certain medicine affects the body," explains a China-based executive with Swiss drug giant Roche. "That's easy with Western medicine but traditional Chinese medicine is like a recipe: you can't prove to the FDA what each ingredient does." Despite such obstacles, a few pharmaceutical titans, including Roche and Merck, do maintain small research projects in China. "We're very interested in traditional Chinese medicine, and we're acting on it," says an executive at Merck. "We're testing some plant ingredients to see how they affect the body."

**XIII.** There are theoretical hurdles too. Western science can't figure out what makes some of the most effective traditional methods work. Take acupuncture. While there is no longer any serious doubt in Western scientific circles that it works in alleviating pain and even lowering blood pressure, there is no convincing explanation of how it does so. As advocates of traditional Asian medicine see it, the West's narrow scientific approach misses the point of such ancient practices, which attempt to treat the body as a complex whole instead of trying to heal a specific illness. This quest for precision leads scientists to disassemble complex formulas in the hope of isolating a single compound that could cure one specific disease. That's anathema to Asian healers. "If you want to be true to traditional medicine, it is mixtures rather than one chemical that work," says Richard Eu, CEO of Singapore's 122-year-old traditional medicine maker Eu Yan Sang.

**XIV.** Western medicine approaches diseases in a "direct and unilateral way," says Ryoo Byung Hwan, vice president of life-science business planning for SK Chemicals, a pioneer company in herbal remedy research. Even when it works, says Ryoo, it fails to take into account the human body's complexity. By contrast, traditional cures are effective in combating chronic diseases caused by a variety of factors. "Traditional medicine doesn't analyze or attack the disease directly but it tries to return the body to balance, to its normal state."

**XV.** In 1995, Ryoo launched the Joins project to develop a new way of treating arthritis, which afflicts 10% of the world's over-60 population. Ryoo decided to submit traditional Korean herbal remedies to stringent tests based on Western scientific methods. "Western medicine can't completely cure arthritis because they don't know its exact cause," he says. Ryoo began by analyzing the causes of arthritis using traditional methods. His studies showed there were three major causes: "wind," "coldness" and "wetness." Imbalance in these three conditions, along with "dryness," is considered the root cause of all diseases in traditional medical practice. Ryoo then scoured the 600 herbs used for centuries in Korea, performing a long screening process that included tests on animals, and finally narrowed the field to three herbs. Ryoo combined them into a yellow pill the size of an aspirin and christened it Joins.

**XVI.** After some encouraging initial results, Ryoo decided to compare Joins with the toughest competition from the West, Voltaren, a powerful anti-inflammatory drug widely prescribed for arthritis. (In 2001, Voltaren raked in sales of more than \$500 million for its Swiss manufacturer, Novartis.) Ryoo was sure Joins would produce fewer side effects than Voltaren, which can cause severe gastric problems, but feared it might not match up as a painkiller: "Comparing the efficacy of a herbal medicine with a chemical medicine like Voltaren is risky. Chemicals are like sharp knives: if you use them properly they will do their jobs perfectly, but if you miss your target, they might cause serious side effects. Herbs are like dull knives—they are not as swift, but they have fewer side effects."

**XVII.** Tests by five major Seoul-based hospitals showed Joins was as good a painkiller as Voltaren and did indeed produce fewer side effects. Ryoo now wants to prove that Joins can also protect the joints, curing arthritis instead of just relieving its symptoms. In vitro experiments conducted at Seoul National University and Cardiff University in Wales show Joins may reduce joint tissue degradation.

**XVIII.** Of course, countless promising drugs have failed after cantering effortlessly through years of trials. But Ryoo's project shows vividly that traditional medicine's strongest advocates are now willing—indeed eager—to subject their cures to stringent scientific examination. Ryoo's method—creating a new formula from a combination of traditional herbs, then subjecting the result to clinical testing—is the reverse of most attempts to unlock the secrets of traditional medicine. The more common approach is taken by Singapore's Eu Yan Sang group. The company commissioned the Chinese University of Hong Kong to subject its best-selling product, Bak Foong or White Phoenix, to three years of scrutiny.

**XIX.** Bak Foong pills are made from a complex traditional formula with no less than 20 exotic ingredients, including flying squirrel feces, deer antler, black sesame seeds, essence of white-feathered chicken and cinnamon bark. Eu Yan Sang wanted to test the original concoction to see how it achieved its supposed benefits, which, aside from helping with menstrual pain, are also characterized by the company as "building resistance to colds, increasing blood and vital life force and settling extreme emotions."

**XX.** Professor Chan Hsiao-chang, who led the study, says tests showed that Bak Foong pills help adjust estrogen levels, lower blood pressure and boost the immune system. While it's no miracle cure, it did prove to have a broad and benign effect on the body. That, she says, helps validate the basic principle of Chinese medicine: "to readjust and balance the elements in our bodies back to a normal and healthy level."

**XXI.** The question remains: How do traditional remedies achieve such results at the molecular level? Liu Jikai, a researcher at the Kunming Institute of Botany, China's premier center for the study of traditional medicine, thinks he has the beginnings of an answer. Liu, who holds degrees in both traditional Chinese and Western medicine, says the common thread running through the most effective traditional formulas is the high proportion of two classes of compounds: polyphenols and saponins. Polyphenols are famously found in wine, tea, chocolate and fruits, while saponins occur in a wide range of grains and vegetables from spinach to tomatoes.

**XXII.** Western laboratories are likewise scrutinizing polyphenols and saponins, which appear to play a role in preventing cancer, killing tumors, lowering cholesterol, fighting infection and even countering depression. So far, science has been unable to explain how they work. The Chinese haven't figured it out either but Liu thinks the same mechanism underlies China's ancient ways of healing: "Western medicine is like a key in a lock. But traditional Chinese medicine is nonspecific, just like polyphenols and saponins. That's why, for example, traditional medicine doctors can prescribe the same formula for different diseases. It also explains why traditional cures are better for disease prevention and the treatment of chronic conditions that are usually caused by a combination of factors, not a single virus or bacterium."

**XXIII.** Yet Liu is also trying to develop a more focused treatment for blood clots, using a method he came across in reviewing classical formulations. Another research team at his institute has produced a treatment for HIV that is now being tested on aids patients in Thailand. Even the die-hard traditionalists at Eu Yan Sang are going modern, using the Chinese University of Hong Kong's research to produce a new herbal formula for postmenopausal women that will combine only a few of the most bioactive herbs from the Bak Foong formula.

**XXIV.** The traditional medicine-based drug that is probably farthest down the testing road comes from Taiwan. Chemist T.S. Jiang is running a trial of a drug there called Xue Bao ("blood treasure") derived from yellow root, a purple flowering plant. Xue Bao reduces the side effects of chemotherapy on cancer patients, says Jiang, so that appetite improves, normal sleep patterns resume and hair grows back. Critically, Xue Bao has produced no

side effects, unlike the two Western drugs G-CSF and EPO, which are most widely used in conjunction with chemotherapy. So far the drug has been tested on 500 patients in Taiwan and China with encouraging results. It still has to pass the third and final trial stages—but Jiang has already taken his faith to the public, floating his company PhytoHealth Corp. on Taiwan's TAISDAQ stock exchange.

**XXV.** "We're kind of excited," says Jiang, and no wonder: the combined market for G-CSF and EPO in 2000 was \$6.8 billion. PhytoHealth's stock has dropped about 30% in value from the giddy heights of its debut on May 13, and all eyes are now anxiously focused on the results of the third—and most difficult—round of tests. "So far the phase-two study results have been pretty good," says Yu Hsiang-lin, secretary general of the government's Development Center for Biotechnology. "The real question is whether they can pass phase three safely. If they do, it's a big market."

**XXVI.** Meanwhile, the promise of artemisinin looks richer than ever. Henry Lai, a bioengineering professor at the University of Washington, recently published a paper detailing experiments in which artemisinin killed virtually all breast cancer cells exposed to it within 16 hours, while having no impact on normal cells. "Not only does it appear to be highly effective," says Lai, "but it's very, very selective." In tests at other universities in the U.S. and Germany, artemisinin has also shown early promise in combating diseases like leukemia and bone cancer.

**XXVII.** In their own studies of artemisinin, Chinese scientists appear to have figured out how it works in fighting malaria. They believe the compound reacts with the high concentrations of iron in the malaria parasite to produce free radicals, a highly destructive form of charged atom that kills the parasite. Lai has built on these observations, using them as the foundation of his work on cancer. He knew that high iron concentrations also exist in cancer cells, which need the metal to do the deadly work of replicating themselves millions of times. Artemisinin, he theorizes, has the same effect on iron-rich cancer cells, seeming to knock them dead within hours.

**XXVIII.** "It all sounds a little too good to be true," says a somewhat bemused Lai, who is currently firing off funding proposals for additional research. And maybe it will in fact prove to be just another losing battle in the endless war against mankind's biggest killer. But as Lai knows, scientists must keep testing all of the weapons in the arsenal—no matter where they come from. If he is right and artemisinin can help vanquish cancer, it will be one of nature's greatest gifts. How strange it would be if the cure were indeed derived from sweet wormwood, a healing plant first mentioned in a Chinese medical text nearly 2,200 years ago.