

# Traditional Medicine

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For millennia, people have healed with herbal or animal-derived remedies, using knowledge handed down through generations. In Africa, Asia, Latin America and the Middle East, 70-95 per cent of the population still use traditional medicine (TM) for primary healthcare. And some 100 million people are believed to use traditional, complementary or herbal medicine in the European Union (EU) alone — as high as 90 per cent of the population in some countries<sup>2</sup>.

The industry is worth big money. In 2012, global sales of Chinese herbal medicine reached US\$ 83 billion, up more than 20 per cent from 2011<sup>3</sup>. The global market for all herbal supplements and remedies could reach US\$ 115 billion by 2020, with Europe the largest and the Asia-Pacific the fastest growing markets. **The demand is driven by women as the main consumers of dietary supplements, by growing emphasis on healthy living and concerns over the side-effects of mainstream drugs.**

### Desperately Seeking Drugs

Meanwhile, modern medicine is desperately short of new

treatments. Drugs take years to get through the research and development pipeline, at enormous cost. And rising drug resistance, partly caused by misuse of medicines, has rendered several antibiotics and other life-saving drugs ineffective. So scientists and pharmaceutical companies are increasingly searching TM for new drug sources.

A few triumphs have stoked this interest. The best known is artemisinin, used to treat malaria (see Box 1). Ethnobotanical and other studies are now seeking other anti-malarials. For example, a team at the University of Cape Town, South Africa, has identified a compound that could evolve into the first single-dose cure for malaria.

#### Box 1: Artemisinin: traditional medicine's blockbuster drug

- Artemisinin, which is extracted from *Artemisia annua* (Chinese sweet wormwood), is the basis for the most effective malaria drugs in the world.
- Long-used in China, the medicine was first noticed by Western researchers in the 1980s. But its worldwide use wasn't endorsed by the WHO until 2004, largely because of scepticism: research groups spent years validating the claims of Chinese traditional healers. Artemisinin is also proving useful against other diseases, including cancers and schistosomiasis
- But it is showing signs of fallibility. There are reports of growing resistance to artemisinin in South-East Asia, and fears that if resistant parasites spread to Africa they could trigger a public health catastrophe
- Meanwhile, work on artemisinin-based therapies continues. The Centre for Novel Agricultural Products' Artemisia Research Project, at the UK's University of York, is developing high-yielding varieties of *A. annua*.

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<sup>2</sup> Molly Meri Robinson and Xiaorui Zhang The world medicines situation 2011 (WHO, 2011)

<sup>3</sup> WHO traditional medicine strategy 2014-2023. (WHO, 2013)

<sup>4</sup> Sahdeo Prasad and Amit Kumar Tyagi Traditional medicine: the goldmine for modern drugs (Advanced Techniques in Biology and Medicine, 2015)

Across the globe, researchers, policymakers, pharmaceutical companies and traditional healers are joining forces to bring TM into the twenty first century. In some ways, it is already here. Nearly a quarter of all modern medicines come from natural products, many of which were first used in traditional remedies (see Table 1). And of 121 prescription drugs used worldwide against cancer, 90 are derived from plants<sup>4</sup>.



Table 1: Selected modern drugs that come from traditional medicine<sup>5</sup>

Drug	What is It for?	Derived from	Originally Used in
Artemisinin	Antimalarial	Produced from the Chinese herb Qinghao or sweet wormwood	Traditional Chinese medicine for chills and fevers
Cromoglycate	Asthma prevention	Based on the plant <i>Khella</i> , whose active ingredient is khellin	Traditional Middle Eastern remedy for asthma. Also traditionally used in Egypt to treat kidney stones
Etoposide	Anticancer	Synthesised from podophyllotoxin, produced by the American mandrake plant	Various remedies in Chinese, Japanese and Eastern folk medicine
Hirudin	Anticoagulant	Salivary glands in leeches, now produced by genetic engineering	Traditional remedies across the globe, from Shui Zhi medicine in China to eighteenth and nineteenth century medicine in Europe
Lovastatin	Lowers cholesterol	Foods such as oyster mushrooms and red yeast rice, also used to synthesize other compounds such as pravastatin	Mushrooms are used to treat a wide range of illnesses in traditional medicine in China, Japan, Eastern Europe and Russia
Opiates	Painkilling	Unripe poppy seeds	Traditional Arab, Chinese, European, Indian and North African medicines as pain relief and to treat a range of illnesses including diarrhea, coughs and asthma
Quinine	Antimalarial	Bark of the cinchona tree	Traditional remedies to treat fevers and shivers in South America
Vinca alkaloids (vincristine, vinblastine)	Anticancer	Synthesized from indole alkaloids produced by the rosy periwinkle	Folk remedies across the world use periwinkle plants, including as an antidiabetic in Jamaica and Madagascar, to treat wasp stings in India, as eyewash in Cuba, as love potion in medieval Europe

<sup>5</sup> Bertrand Graz and others To what extent can traditional medicine contribute a complementary or alternative solution to malaria control programs? (Malaria Journal, 2011)

Table 2: Key differences between traditional and modern medicine

	Traditional Medicine	Modern Medicine
Knowledge protection	Open access but social or legal restrictions may govern who can use certain knowledge, under what conditions and with what benefit for knowledge holders	Closed, patent-protected
Formulation	Ad hoc during consultation with the patient	Predetermined and, once approved in clinical trials, formulas cannot be changed unless retested
Regulation	Usually loose. In some cases with restrictions on use or dissemination. Rules and standardization are being introduced but vary between countries	Extremely tight
Testing	No formal testing: understanding of effectiveness is handed down through generations	Rigorous trials that happen in different phases (first testing for safety, then efficacy) mean bringing a drug to market costs billions of dollars
Dosage	Unfixed: the amount of medicine given might be roughly similar, but the amount of active ingredient (which is what dosage really is) can vary hugely	Standardized medicines given in fixed doses that vary with age or weight, or disease severity
Consultation	Lengthy, and the patient is asked a wider range of questions than just about their symptoms	Consultations in both primary and secondary care tend to be brief and focused, especially as national health systems come under financial strain
Training	Lengthy training over many years but knowledge is often passed one-to-one through families, and practitioners are often born into a family of healers	Lengthy and often vocational: health professionals go through formal training in schools and universities

**Modernizing tradition**

But efforts to incorporate TM’s knowledge into modern healthcare and ensure it meets safety and efficacy standards are far from complete. And conservationists worry that a growing TM market threatens biodiversity by overharvesting medicinal plants or using body parts from endangered animals. Integration also faces other challenges stemming from key differences in how traditional and modern medicine are practiced, evaluated and managed (see Table 2).

**Inherently variable**

It can be extremely difficult to apply modern tests — developed for standardized drugs — to TM’s inherently diverse range of products.

Many traditional medicines are made by crushing leaves or bark, and the resulting mixture can contain hundreds of potentially active molecules. Identifying these is hard enough, and testing each one for safety and effectiveness

is practically impossible. Unlike many modern pharmaceuticals, the quality of material for traditional medicines varies enormously between, and even within, source countries and plants. This is both because of genetic differences and other factors such as environmental conditions, harvesting, transport and storage.

Dosage is similarly varied. Modern medicine demands dosages that are standardized based on factors such as bodyweight or disease severity. Traditional healers are more likely to give patients a unique dosage or combination of medicines that is decided during the consultation. So when modern evaluations of traditional drugs give poor results, it may be due to many factors: from mistakenly using the wrong plant to contamination or dosing problems.

**Protection and bio-piracy**

Perhaps the most striking difference between traditional and modern medicines is the legal protection given to knowledge. Traditional practitioners have historically

shared their knowledge and experience freely — defining ‘open-access’ before the term even existed. Modern medicine, on the other hand, has stringent intellectual property laws and a highly evolved protective patenting system.

Scientists searching indigenous sources for new drugs — ‘bioprospecting’ — have to navigate these differences. Researchers have sometimes sought patents for compounds that had already been used for centuries. An example is the 1995 patent on an antifungal neem derivative commonly used in Indian traditional remedies. The European Patent Office (EPO) granted a patent to the US Department of Agriculture and the multinational WR Grace and Company. It took the Indian government five years and millions of dollars to convince the EPO to revoke the patent on the basis of prior use.

Research into traditional medicines remains controversial. A fresh example is the possible medical applications of sabara (*Guiera senegalensis*), a plant common in the Sahel and widely used by Mali’s Dogon people. French researchers looked for active ingredients and isolated Guieranon B, which showed anti-cancer activity in preclinical studies. The researchers filed patent claims in 2014 and are looking for partners to develop a drug — but without including the African people with whom the knowledge originates. Plundering unprotected indigenous resources has been termed ‘biopiracy’ and highlights the challenges facing efforts to integrate traditional and modern approaches to medicine.

**Legal frameworks and sharing benefits**

There is an urgent need for both global and local legal frameworks to regulate bioprospecting activities and avoid biopiracy. However, protecting intellectual property (IP) rights of indigenous peoples and local communities to traditional medical knowledge is a thorny issue.

Schemes that provide IP protection in the classic sense — against un-authorized use by third parties — are seldom easy to apply to traditional knowledge systems because their property/non-property distinctions rarely fit indigenous cultures. Also, patent protection is typically time-limited, while traditional medical knowledge should

be protected retroactively or indefinitely or both. Further, IP protection must not restrict people’s access to traditional medical practices that are a form of cultural expression. And it must allow research and innovation that enhances traditional medicine’s status as a healthcare option.

The problem is so complex that the World Intellectual Property Organization (WIPO) has established an ad hoc committee to develop an international legal instrument to protect traditional medical knowledge, and address the IP aspects of benefit-sharing and access to genetic resources. The Nagoya Protocol is an existing international legal tool that offers some protection for traditional knowledge of medicines. The protocol came in to force on 12 October 2014 as a supplement to the Convention for Biological Diversity (CBD), and was ratified by 59 countries and the EU. Its main objective is to equitably share the benefits gained from using genetic resources and it clearly addresses the associated rights of indigenous communities. It forces countries to ensure that anyone under their jurisdiction who benefits from traditional knowledge has obtained prior informed consent and negotiated a fair and equitable deal to share those benefits.

**National initiatives**

While the Nagoya Protocol works internationally, countries use a mix of other IP tools to protect traditional medical knowledge. These include trademarks, geographical indications and registration systems<sup>6</sup>. For example, Thailand’s Act on Protection and Promotion of Traditional Thai Medicinal Intelligence protects recipes and texts drawn from traditional Thai medicine.

Enacting laws is another strategy. For example, Peru has legislated to protect indigenous people’s collective knowledge without barring knowledge licensing contracts. The country’s Cusco region has outlawed exploitation of native species for commercial gain, including patenting genes or other resources. India’s Council for Scientific and Industrial Research takes a more pragmatic approach. In 2001, it launched a traditional knowledge digital library (TKDL) of remedies and medicinal plants. From 2009, the EPO has been able to consult the 34 million page, multilingual database before granting patents and has cancelled or withdrawn 36 applications to patent

<sup>6</sup> Ryan Abbott Documenting traditional medical knowledge (World Intellectual Property Organization, 2014)

<sup>7</sup> Anand Chaudhary and Neetu Singh Intellectual property rights and patents in perspective of Ayurveda (Ayu, 2012)

traditionally known medicinal formulations in just under

	1999	2003	2005	2007	2012
WHO member states with Traditional Medicine	25	39	45	48	69
WHO member states regulating herbal medicine	65	82	92	110	119

two years<sup>7</sup>.

**National initiatives**

Efforts to make traditional medicines mainstream also have to cope with varying regulation. Every country has a national drug authority of sorts, but with different rules.

Research data	<b>105</b>
Mechanisms to control and regulate advertising claims	83
Mechanisms to control and regulate herbal products	78
Mechanisms to monitor and regulate providers	75
Financial support for research	68
Expertise within national health authorities	67
Mechanisms to monitor safety of practices	65
Cooperation for information sharing	63
Mechanisms to monitor safety of products	60
Education and training of providers	58
Others	15

The WHO has recorded a steady and marked increase in countries with national policies on traditional and complementary medicine, or national regulations on herbal medicines, over the past 15 years<sup>8</sup>.

But about half the countries that responded to a global survey in 2012 reported regulating traditional and complementary medicine practitioners, and there are several obstacles to effective regulation<sup>9</sup>.

	1999	2003	2005	2012
WHO member states with national research institutes in Traditional Medicine	19	56	58	73

**Deficit areas that limit the effective regulation of T and C medicine by member states:**

And traditional medicine often means different things to different people. A single medicinal plant may be classified as a food, a dietary supplement or a herbal medicine.

Education and research have also advanced. Some 39 countries now provide high-level education and training programs on traditional medicine.

**Progress in university education and research capacity:**

**Room for improvement**

But much still needs to be done before a global standard for TM is agreed. Loose regulation means there are as many fake remedies and false practitioners as genuine treatments and practitioners. It is often difficult to distinguish between traditional treatments backed by research and those with unproven claims or even ‘extras’ that may lead to harm.

Contaminated and adulterated products are common. Many herbal products, especially those purchased online, contain toxic heavy metals such as lead, mercury and arsenic<sup>10</sup>. Conventional drugs such as Viagra and estrogens are sometimes added to herbs, to make them ‘more effective’. All this exacerbates concerns over unknown but potentially harmful drug-herb interactions —and over substituting tested conventional with untested herbal medicine.

In response, the WHO has been working to develop international guidelines and technical standards to help countries formulate policy and regulations to control traditional medicines. A key first step, according to the WHO, is to acknowledge the role TM already plays in people’s healthcare, identifying which forms are most popular, and whether people rely on TM on their own or seek advice from health professionals.

**Testing times**

Like regulation, methods for evaluating and testing medicines also vary widely. Modern drugs go through

rigorous laboratory tests and clinical trials designed to prove effectiveness, test for safety and standardize manufacturing practices. In contrast, traditional medicines undergo few scientific tests, production standards tend to be less rigorous or controlled, and practitioners are often

not certified or licensed.

Some argue that drugs which have been tried and tested in thousands of people for decades or centuries don’t need the same tests as a brand new chemical. And some argue

Justifiable social need for the research	The rationale for trialing a traditional medicine cannot simply be that it already exists as a treatment. There must be both a social need and some preliminary evidence that the medicine will not counteract other conventional medicines used to treat the same disease. Stakeholders will define social need in varying ways — for example a government may want to prevent any other party from commercializing the treatment and health campaigners may want the clinical trial to try to produce better drugs.
Appropriate definitions of inclusion and exclusion criteria, and outcome measures	Concepts of health and sickness differ between modern and traditional medicine. For example, Western researchers would use the New York Heart Association classification for heart failure, but traditional Chinese medicine (TCM) practitioners would see heart failure as a heart yang chi deficiency or a kidney yang deficiency, categorizing patients based on pulse or tongue examination. Researchers testing a herbal remedy for heart failure would need to take both biomedical and TCM criteria into account for the results to be valid from both perspectives
Innovative protocol design	Drugs brought to market by putting traditional medicines through clinical trials must be rigorously tested, but standard methodologies may not be appropriate for a medicine that contains a mixture of active ingredients or in treatments that vary between practitioners. Standard protocols could adapt to accommodate many of these issues
Establishing standards for safety and evidence	The familiarity of traditional medicines, and their widespread use, could lead some researchers to wrongly assume they are safe. Care is needed early on to determine safety requirements

**\*Derived from an ethical analysis by Jon Tilburt and Ted Kaptchuk**

that traditional knowledge is itself a science.

standard methods to adapt to cope with ethical issues that do not arise with conventional drug development. US researchers Jon Tilburt and Ted Kaptchuk have, for example, suggested that clinical trials of traditional medicines must follow different ethical rules<sup>11</sup>.

But many agree that traditional medicines need reassessment before being integrated into a conventional framework of pharmaceuticals. Sometimes, this requires

Table 3: How to create modern drugs from traditional compounds<sup>13</sup>

Technique	Process
Reverse pharmacology	Researchers start with the end product, a clinically useful compound for example, and work backwards to find out what it contains and how it functions. This can offer clues about how a medicine works and where it acts in the body
High-throughput screening	High-speed data processing and sensitive detectors conduct millions of biochemical, genetic or pharmacological tests in a few minutes, quickly identifying active compounds that affect particular biological pathways

<sup>8</sup> Ethel Chitindingu and others A review of the integration of traditional, complementary and alternative medicine into the curriculum of South African medical schools (*BMC Medical Education*, 2014)

<sup>9</sup> WHO traditional medicine strategy 2014-2023. (WHO, 2013)

<sup>10</sup> José O Rivera and others Use of herbal medicines and implications for conventional drug therapy medical sciences (*Alternative and Integrative Medicine*, 2013)

<sup>11</sup> Jon Tilburt and Ted Kaptchuk Herbal medicine research and global health: an ethical analysis (Bulletin of the World Health Organization, 2008)

<sup>12</sup> Bhushan Patwardhana and Ashok D. B. Vaidya Natural products drug discovery: Accelerating the clinical candidate development using reverse pharmacology approaches (*Indian Journal of Experimental Biology*, 2010)

<sup>13</sup> Alan Harvey and others The re-emergence of natural products for drug discovery in the genomics era (*Nature Review Drug Discovery*, 2015)

Ethno-pharmacology (ethnobotany)	The systematic study of how specific ethnic groups use medicinal plants
Systems biology	A holistic approach aiming to understand how chemicals and metabolic processes interact in the body. It could be used to measure the whole body's response to the mixtures of active compounds often found in TM
Genome mining	This searches a genome (often a microbe's) for DNA sequences that encode enzymes involved in synthesizing biologically active natural products. The active ingredients of some medicinal plants are actually made by microorganisms living within the plant
Metabolomics	This offers a rapidly advancing approach to drug discovery that can systematically study how a complex mixture, such as a plant extract, is metabolized in the body, and so identify bioactive secondary metabolites

**Rules of research ethics for clinical trials of traditional medicines\***  
**New techniques for old treatments**

New scientific techniques are also being applied to traditional medicine in the search for modern drugs (see Table 3). In India, for example, the Council for Scientific and Industrial Research has teamed up with several public and private partners to conduct clinical trials on herbal products generated through reverse pharmacology. It says this has resulted in wider acceptance of Ayurvedic traditional medicines and promises cheaper, faster and more effective drugs<sup>12</sup>.

**Gaining ground**

Top research bodies worldwide are serious about integrating traditional medicine into modern healthcare. And many countries are working actively to harness and regulate TM.

The US National Institutes of Health, for example, houses an organization called the National Center for

**Traditional medicine: Definitions**

<b>Allopathic medicine</b>	The modern, mainstream system of medical practice in Western countries. It targets disease with remedies that treat or suppress symptoms or the condition itself. It tends to produce effects different from those produced by the disease under treatment.
<b>Complementary/alternative medicine</b>	The terms complementary and alternative medicine are sometimes used interchangeably with the term traditional medicine. They refer to the healthcare practices that are not part of a country's own tradition and are not integrated into the dominant healthcare system.

<sup>14</sup> Caroline da Rosa Traditional medicine and complementary/alternative medicine in primary health care: the Brazilian experience In: Oreste Capelli (editor) *Primary Care at a Glance – Hot Topics and New Insights* (InTech, 2012)

<b>Herbal medicines</b>	These include herbs, herbal materials, preparations and products that contain plant materials or combinations of plants as active ingredients. Herbalism is the practice of making or prescribing plant-based herbal remedies for medical conditions and is considered a form of alternative medicine.
<b>Integrative medicine</b>	The term refers to the blending of conventional and natural/complementary medicines and/or therapies along with lifestyle interventions in a holistic approach, taking into account the physical, psychological, social and spiritual wellbeing of the person.
<b>Traditional medicine</b>	The overall body of knowledge, skills and practices based on the theories, beliefs and experiences indigenous to different cultures, whether they can be explained or not. These might be used to maintain health as well as prevent, diagnose, improve or treat physical and mental illness.

coordinated implementation of the Nagoya Protocol by African countries, which African ministers have recently officially adopted.

And in the Middle East, the Eastern Mediterranean Drug Regulatory Authorities Conference (EMDRAC) in May 2014 addressed the need to harmonize regulation of medical products, including traditional medicines, in the region. The Zayed Complex for Herbal Research and

Traditional Medicine, based in the United Arab Emirates, is one of the WHO's collaborating centers for traditional medicine.

Certainly, traditional medicine has much to offer global health. If both developed and developing countries joined research capacities in equitable collaborations, new scientific techniques could spark a revival in global health research and development.

