# Nobel Prize for artemisinin brings phytotherapy into the spotlight

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Editorial

# Nobel Prize for artemisinin brings phytotherapy into the spotlight

It is a great news for the entire scientific community dedicated to natural products that the Nobel Prize in Physiology or Medicine 2015 was awarded by the Nobel Assembly at Karolinska Institutet (Stockholm, Sweden) for the discovery of two main natural products: (1) avermectin, a macrocyclic lactone isolated from the soil microorganism *Streptomyces avermitilis* (and its derivative ivermectin) and (2) artemisinin, a sesquiterpene lactone containing an unusual peroxide bridge, isolated from the plant *Artemisia annua* L. (Asteraceae).

Both these compounds have established new therapies to treat parasitic diseases such as lymphatic filariasis and onchocerciasis (avermectin) and malaria (artemisinin). The prize was divided, one half jointly to William C. Campbell and Satoshi Ōmura *for their discoveries concerning a novel therapy against infections caused by roundworm parasites* and the other half to Youyou Tu *for her discoveries concerning a novel therapy against malaria* (http://www.nobelprize.org/nobel_prizes/medicine/laureates/2015/advanced-medicineprize2015.pdf).

The editors and editorial board members of *Phytomedicine* wish to congratulate the awardees cordially for their crowning success after dedicating their lives to finding treatments for diseases that plague much of humanity.

**Satoshi Ōmura** screened *Streptomyces* strains isolated from soil samples in Japan for novel bioactive compounds. The bacterial culture containing *Streptomyces avermitilis* revealed the best antiparasitic activity and contained *avermectin* (Burg et al., 1979).

**William C. Campbell** and colleagues have isolated avermectin from Ōmura's Streptomyces culture and modified it to *ivermectin*, which was highly effective against several parasitic diseases including river blindness and lymphatic filariasis (elephantiasis) (Egerton et al., 1979).

**Youyou Tu** studied herbs that have been used in traditional Chinese medicine (TCM) for >2000 years to treat fever and chills with the aim of treating malaria. As a result, her group (Fig. 1) discovered that low-temperature extraction of sweet wormwood (*qinghao, A. annua*) provides the most effective preparation against malaria parasites (Tu et al., 1981a, 1981b). Artemisinin, the active ingredient of *A. annua*, revealed a profound activity against malaria, and its derivatives artesunate and artemether are part of the established malaria combination treatment protocols worldwide. It is noteworthy that Youyou Tu is the first Chinese scientist to be awarded the Nobel Prize in Physiology and Medicine. It is not surprising that this award is related to phytomedicine – a research area that has a remarkable background in China, where TCM represents a major medicinal system of the largest population in the world.

The Nobel Assembly awarded scientists not only for breakthrough inventions that may lead to therapy improvements in the future (as they did in the past) but also for already established therapies.

The fact that avermectin and artemisinin are both natural products is promising and highly significant, reinforcing the well-known fact that a considerable portion of drugs produced in current clinical practice have been derived from natural resources (Newman and Cragg, 2012; Cragg and Grothaus, 2014).

Furthermore, the Nobel Assembly pointed to the importance of novel treatment options for communicable tropical diseases. The three most severe communicable diseases are malaria, AIDS, and tuberculosis, which attract some attention concerning treatment and research funding, although not adequate to eradicate them from the planet. Another category of communicable diseases is the neglected tropical diseases, which are common in tropical and subtropical countries, where their prevention and cure are not sufficiently available. Phytotherapy has a high potential in the fight against communicable diseases. As stated by the World Health Organization, up to 80% of the population in developing countries depends on the use of traditional medicine and medicinal herbs for primary health care (WHO, 2007, 2013).

Therefore, it is imperative that rational phytotherapy remove nonscientific elements from traditional herbal medicine and make medicinal herbs accessible to modern research trends in pharmacology, analytical chemistry, medicine, and molecular biology. The chemical profiling of plant constituents (e.g., fingerprinting), the exploration of mechanistic modes of action, synergistic interactions, animal experimentation, and clinical trials in patients are the important and indispensable elements of phytotherapeutic research.

In contrast to the oral transmission of knowledge on medicinal plants in many traditional medicines worldwide, TCM relies on written textbooks and an educational system of TCM scholars. The investigation of Youyou Tu provides an astonishing example: how precise and reproducible the instructions in the TCM textbooks were. Rather than the standard hot decoction procedure for most other medicinal herbs, *A. annua* has been recommended to be used as pressed juice. Youyou Tu obtained reproducible results as she referred to the corresponding passages in the textbooks and found that the preparation of the plant differed from the standard recipes. On 23 May 1967, Mao Zedong initiated a secret research project (No. 523) to find a drug against malaria to treat the malaria-infected Vietnamese soldiers in their fight against the US army. Youyou Tu was one among 500 scientists from 60 laboratories who identified plant extract No. 191 (*qinghao*). She tested 640 out of 2000 traditional recipes and found

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**Fig. 1.** Tu Youyou and Lou Zhicen in 1951 (taken from Wikimedia).

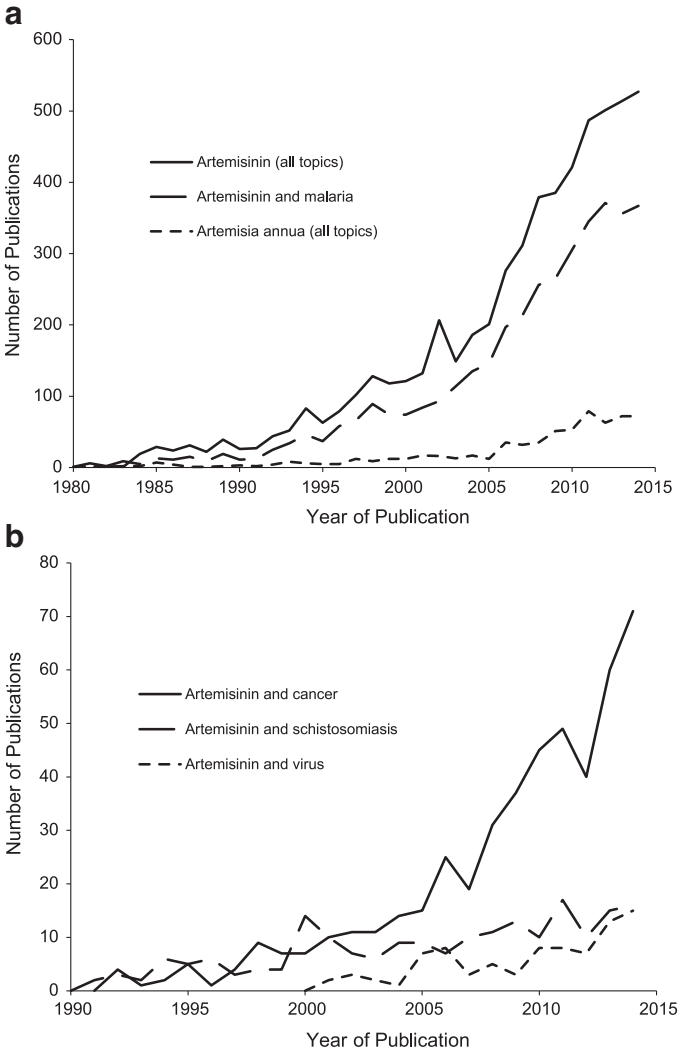


**Fig. 2.** Survey of the literature deposited in the PubMed database from 1980 to 2014 for (a) artemisinin, *Artemisia annua*, and malaria; (b) artemisinin and other diseases.

*A. annua* as the most active drug against malaria in her animal experiments. This was the breakthrough and starting point for thriving research conducted on *A. annua*, artemisinin, and malaria (Fig. 2a).

Herbal products are rather multi-specific than monospecific and most frequently target different cells. Hence, phytochemicals are found to be active against several diseases. This is also true for artemisinin and its derivatives, artesunate and artemether. As uncovered in the past years, artemisinin-type compounds are also active against cancer cells, human cytomegalovirus (HCMV) infections, and other viral infections, as well as schistosomiasis (Efferth, 2005; Efferth et al., 2008; Liu et al., 2011; Efferth and Krishan, 2016) (Fig. 2b). Randomized double-blind clinical phase II trials on the activity of artemisinin against human cancer and schistosomiasis, as well as preliminary clinical data on HCMV-infected patients, provide striking evidence that the bioactivity of this class of sesquiterpenes goes far beyond malaria treatment (Jansen et al., 2011; Wolf et al., 2011; Pérez del Villar et al., 2012; Krishna et al., 2014). The application of artemisinin for new disease indications has to be further explored in the future.

It is fortunate for the entire field of phytotherapy and medicine that artemisinin attracted the attention of scholars and public. In fact, *Phytomedicine* published 31 articles on artemisinin, of which 21 were on artemisinin in the context of malaria treatment. Two articles published the latest results on artemisinin to our readership (Cocquyt et al., 2011; Sen and Chatterjee, 2011). The scope of this journal includes research on not only isolated phytochemicals but also total plant extracts.

In the spirit of Youyou Tu's recent recognition, the scientific community should strengthen further strengthen phytotherapy by high-quality research. *Phytomedicine* is the right platform for that purpose. It is noteworthy that awarding scholars working on natural products will foster the scientific development of this field of research in the future.

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