Artemisinin– A Gift from Traditional Chinese Medicine to the World

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Nobel Lecture, Dec 7, 2015
Karolinska Institutet
Summary of the Work Completed by the Research Team in Academy of Traditional Chinese Medicine (Boxes in Blue Background)

- Screening for herbal extracts
- Clinical trial for No. 191 Aug-Oct, 1972
- First clinical trial for artemisinin Sept-Oct, 1973
- Extended clinical trials 1973-1978
- New drug approval of artemisinin 1986

- Screening for Artemisia annua L.
- The finding of neutral ether extract No. 191 Oct, 1971
- The discovery of artemisinin Nov, 1972
- The finding of dihydroartemisinin Sept, 1973
- New drug approval of dihydroartemisinin 1992
- Research for new indications of dihydroartemisinin 2003-

- Determination of stereo-structure for artemisinin
- Studies on resources
- Optimization of manufacturing techniques
- Synthesis of artemisinin 1983

- Artesunate
- Dihydroartemisinin derivatives
- Artemether

- New drug approval of artemisinin 1986

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The Breakthrough in the Research of *Artemisia annua* L for Discovery of Artemisinin

Archive, Institute of Chinese Materia Medica
The elements analysis by the collaborative institution, Institute of Matria Medica, Chinese Academy of Medical Sciences, on April 27th, 1973. (Front side)

<table>
<thead>
<tr>
<th>分析结果</th>
<th>样品在分析前的处理：</th>
</tr>
</thead>
<tbody>
<tr>
<td>样品重(Mg)</td>
<td>CO₂重(Mg)</td>
</tr>
<tr>
<td>2.531</td>
<td>5.93</td>
</tr>
<tr>
<td>3.173</td>
<td>7.42</td>
</tr>
<tr>
<td>样品重(Mg)</td>
<td>温度(℃)</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

分析室意见：

分析人：李华
分析日期：1973年4月27日

Archive, Institute of Chinese Materia Medica
The Molecular Structure and the Stereo-structure of Artemisinin
## Structure - Activity Relationship of Compounds from Artemisinin

<table>
<thead>
<tr>
<th>Compound</th>
<th>Graph of chemical structures</th>
<th>Dose mg/kg/day × 3</th>
<th>Clearance of parasites</th>
</tr>
</thead>
<tbody>
<tr>
<td>Artemisinin</td>
<td><img src="image" alt="Artemisinin Structure" /></td>
<td>50-100</td>
<td>Yes</td>
</tr>
<tr>
<td>Dihydroartemisinin</td>
<td><img src="image" alt="Dihydroartemisinin Structure" /></td>
<td>12.5</td>
<td>Yes</td>
</tr>
<tr>
<td>Acetate of dihydroartemisinin</td>
<td><img src="image" alt="Acetate of Dihydroartemisinin Structure" /></td>
<td>6</td>
<td>Yes</td>
</tr>
<tr>
<td>Deoxyartemisinin</td>
<td><img src="image" alt="Deoxyartemisinin Structure" /></td>
<td>100</td>
<td>No</td>
</tr>
<tr>
<td>Compound</td>
<td>Graph of chemical structures</td>
<td>Dose mg/kg/day $\times 3$</td>
<td>Clearance of parasites</td>
</tr>
<tr>
<td>-----------------------------------------------</td>
<td>------------------------------</td>
<td>----------------------------</td>
<td>------------------------</td>
</tr>
<tr>
<td>Dihydrodeoxyartemisinin</td>
<td><img src="image" alt="Dihydrodeoxyartemisinin" /></td>
<td>100</td>
<td>No</td>
</tr>
<tr>
<td>Acid treatment product of artemisinin</td>
<td><img src="image" alt="Acid treatment product of artemisinin" /></td>
<td>100</td>
<td>No</td>
</tr>
<tr>
<td>Base treatment product of artemisinin</td>
<td><img src="image" alt="Base treatment product of artemisinin" /></td>
<td>100</td>
<td>No</td>
</tr>
</tbody>
</table>
Molecular Structures of Artemisinin and its Derivatives
New drug certificate of artemisinin issued by the Ministry of Health (1986) (left)

New drug certificate of dihydroartemisinin issued by the Ministry of Health (1992) (Right)
Worldwide Attention to Artemisinin
Commitment to the Clearly Defined Goal

应该把最完善的药
提供给世界人民
Knowledge is Prologue in Discovery
Antimalarial Collections of Recipes and Prescriptions
April, 1969

(浙江)：(8)吴灵仙二钱，香附子二钱，北沙参三钱，水煎服。

处方：青蒿五钱至半斤

来源：福建、贵州、云南、广西、湖南、江西

备注：各地均有配制方药治疗的：(1)青蒿三钱，麻黄根三钱（又名 toughest 三钱，水煎服，据报疗效很好（广西）。(2)清膏药散（四川）；(3)清膏三钱，绿豆三钱，水煎服（福建）；(4)清膏三钱，生姜三钱，乌药少许，前二药煎汁，调白糖（福建）；

(5)清膏三钱，白术三钱，共丸如绿豆大，治发前四五小时服二十粒（湖南）；(6)清膏四两，向桂三钱，细马连二两，研细末，每次三钱，于发前二小时服下（湖南）。(7)青蒿一两，冬瓜子三钱，马蹄草二两，官桂二两，九香子大，每

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Archive, Institute of Chinese Materia Medica
A Handbook of Prescriptions for Emergencies

治癒病方

寒熱诸癒方第十六

二丸欲發時服一丸

又方青蒿一握以水二升煎絞取汁盡服之

又方用獨父蔥於白炭上燒之末服方寸匕

又方五月五月蒜一片去皮中破之以竹挾以火炙之更可

熱癒為三丸未發前服一丸不止復與一丸

又方取蜘蛛一枚置羹中以絹頭過發時

治癒病方鼠婦豆豉二枚合搗令相和末服服之
Qinghao Has a Long History of Clinical Application
Simple Research Facilities in the 1970s
Invention Certificate for Progress in Anti-malarial Research
Issued by National Congress of Science and Technology, 1978

Archive, Institute of Chinese Materia Medica
The World Is Continuing to Make Impressive Progress in Reducing Malaria Cases and Deaths.

Dr. Margaret Chan, 2014

Since the year 2000
- Average malaria infection prevalence declined **46%** in children aged 2–10, from 26% to 14% in 2013.
- The number of malaria infections at any one time dropped **26%**, from 173 million to 128 million in 2013.
- Malaria mortality rates have decreased by **47%** worldwide and by **54%** in the WHO Africa Region.

By 2015
- If the annual rate of decrease over the past 13 years is maintained, malaria mortality rates are projected to decrease by **55%** globally and by **62%** in the WHO Africa Region.
- Malaria mortality rates in children aged under 5 years are projected to decrease by **61%** globally and **67%** in the WHO Africa Region.

Figure 1.1 Countries with ongoing transmission of malaria, 2013

<table>
<thead>
<tr>
<th>Confirmed malaria cases per 1000 population</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;100</td>
</tr>
<tr>
<td>50–100</td>
</tr>
<tr>
<td>10–50</td>
</tr>
<tr>
<td>1–10</td>
</tr>
<tr>
<td>0.1–1</td>
</tr>
<tr>
<td>No ongoing malaria transmission</td>
</tr>
<tr>
<td>0.01–0.1</td>
</tr>
<tr>
<td>Not applicable</td>
</tr>
</tbody>
</table>

*Source: National malaria control programme reports*
Spread of *P. falciparum* Resistance to Artemisinin

WHO Global Plan for Artemisinin Resistant Containment (GPARMC) Goals and Recommendations

1. Stop the spread of resistant parasites
2. Increase monitoring and surveillance to evaluate the artemisinin resistance threat
3. Improve access to diagnostics and rational treatment with ACTs
4. Invest in artemisinin resistance-related research
5. Motivate action and mobilize resources
Chinese medicine and pharmacology are a great treasure-house. We should explore them and raise them to a higher level.

Hand writing by Mao Zedong
You will enjoy a grander sight, By climbing to a greater height.

白日依山尽，
The sun along the mountain bows,

欲穷千里目，更上一层楼。

On the stork tower,
Wang Zhihuan (Tang dynasty)
Finally, I would like to acknowledge all colleagues in both China and overseas for their contributions in the discovery, research and clinical application of artemisinin.

I am grateful for all my family members for their continuous understanding and support.

I sincerely appreciate your kind attention.

Thanks you all!