

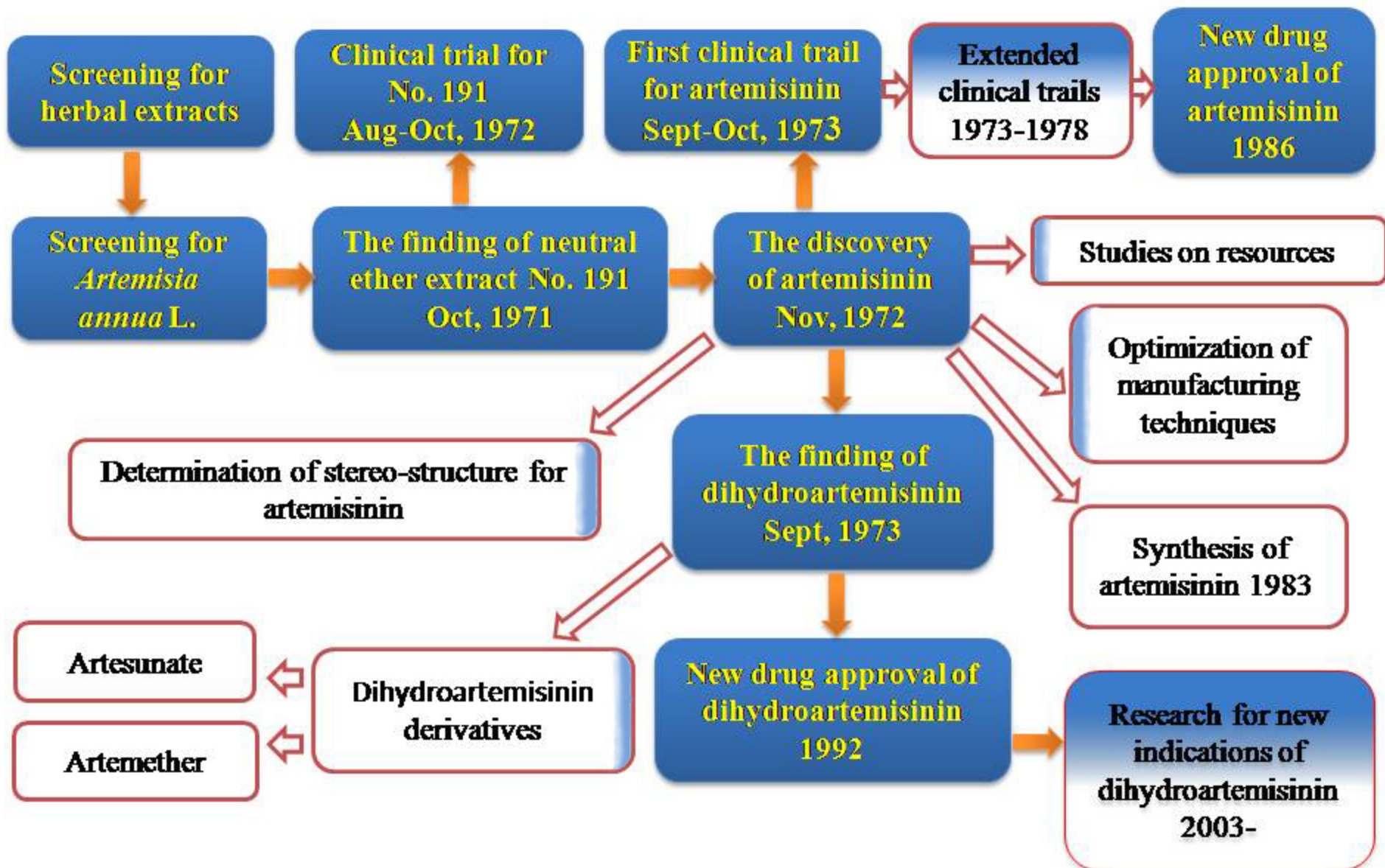
Artemisinin– A Gift from Traditional Chinese Medicine to the World

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Academy of Chinese Medical Sciences,
Beijing, 100700, China**

**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)



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

186	1/2 185	→ 1:1	$\frac{0.5g}{0.3ml}$	"	"	1/5	040	540	570	640	602%	-30%	
187	青蒿子 AEC+H ₂ O 1:4	→ 1:2	$\frac{0.4g}{0.2ml}$	"	"	2/5	330	400	340		357%	22%	
188	1/2 187	→ 1:1	$\frac{0.25g}{0.25ml}$	"	"	0/5	500	420	410	370	416%	9%	
189	石打穿 AEC+H ₂ O 1:2.5		$\frac{0.5g}{0.2ml}$	"	"	0/5	480	420	400	600	426%	7%	
190	1/2 189	→ 1:2.5	$\frac{0.31g}{0.25ml}$	"	"	0/5	550	260	290	600	420%	9%	
✓ 191	青蒿 Et ₂ O 1:4		$\frac{0.8g}{0.2ml}$	"	"	4/5	0	(5/4 7/16)			100%		
192	1/2 191	→ 1:2	$\frac{0.6g}{0.3ml}$	"	"	2/5	0	(1-2/4)	205	0	(1-2/4)	68%	85%
193	青蒿 -Et ₂ O 1/2 AEC+H ₂ O P ₂ S ₅ 1:4		$\frac{1.2g}{0.3ml}$	"	"	1/5	293	0	(1/4)	132	0	106%	77%
194	1/2 193		$\frac{0.8g}{0.2ml}$	"	"	0/3	511	509	10		343%	26%	
195	土茯苓 Et ₂ O+EtOH 1:10	→ 1:2.5	$\frac{0.875g}{0.35ml}$	"	"	1/5	400	560	420	460	455%	1.3%	
196	1/2 195	→ 1:2.5	$\frac{0.625g}{0.25ml}$	"	"	0/5	580	386	380	395	520	452%	2%

中国医学科学院药物研究所

分析化学室

微量有机元素分析报告

样品原编号: 青蒿素(IV)

分析编号:

送样人: 中药研究所 屠呦呦

工作领导人签字:

样品干燥情况: 已干燥

样品主要性质:

感光 _____; 吸水 _____; 挥发性 _____; 爆炸性 _____

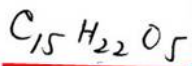
沸点 _____; 熔点 _____; 其他 _____

样品含有元素:

要求分析项目: C, H, O

要求分析元素的百分比范围

或化合物的可能结构式:



送样日期: 73年4月24日

(分析结果见

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



(Back side)

分析结果:

样品在分析前的处理:

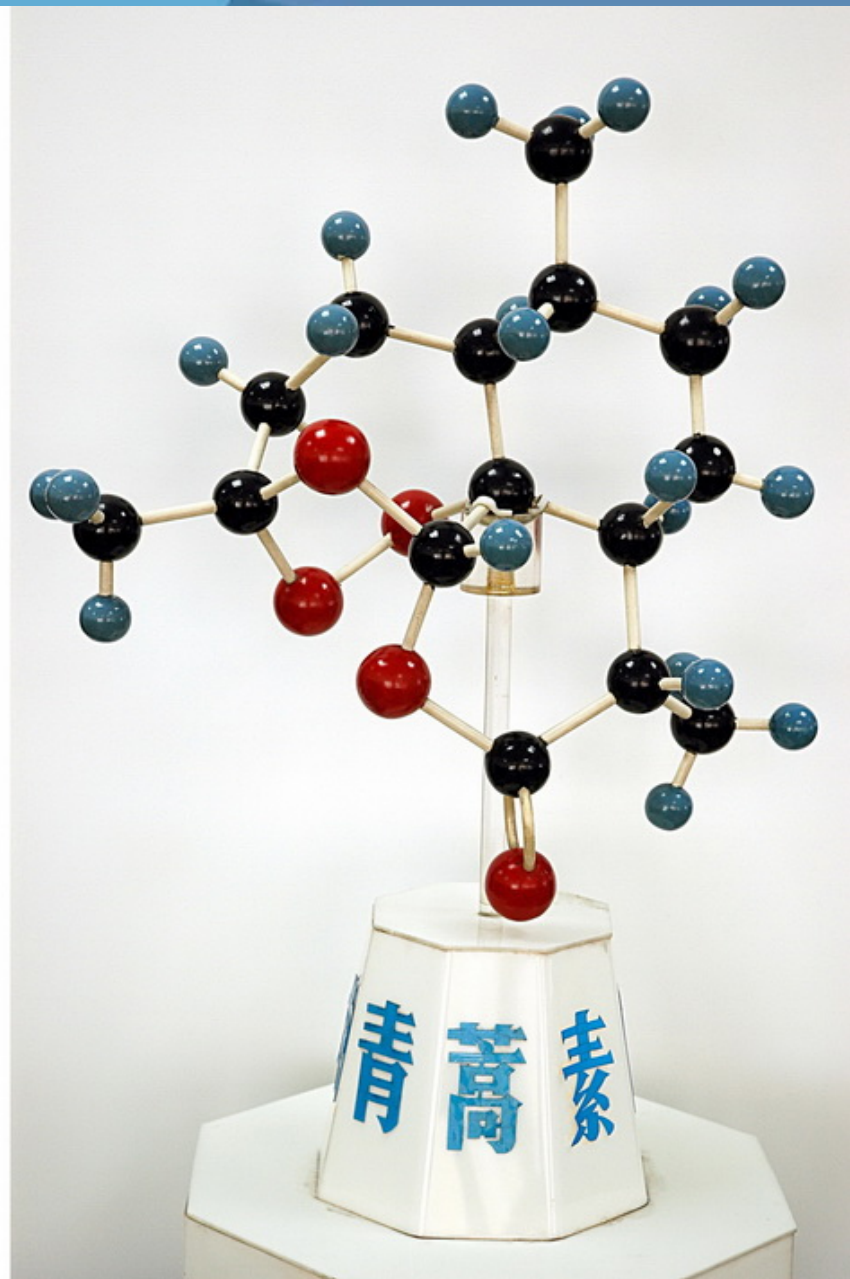
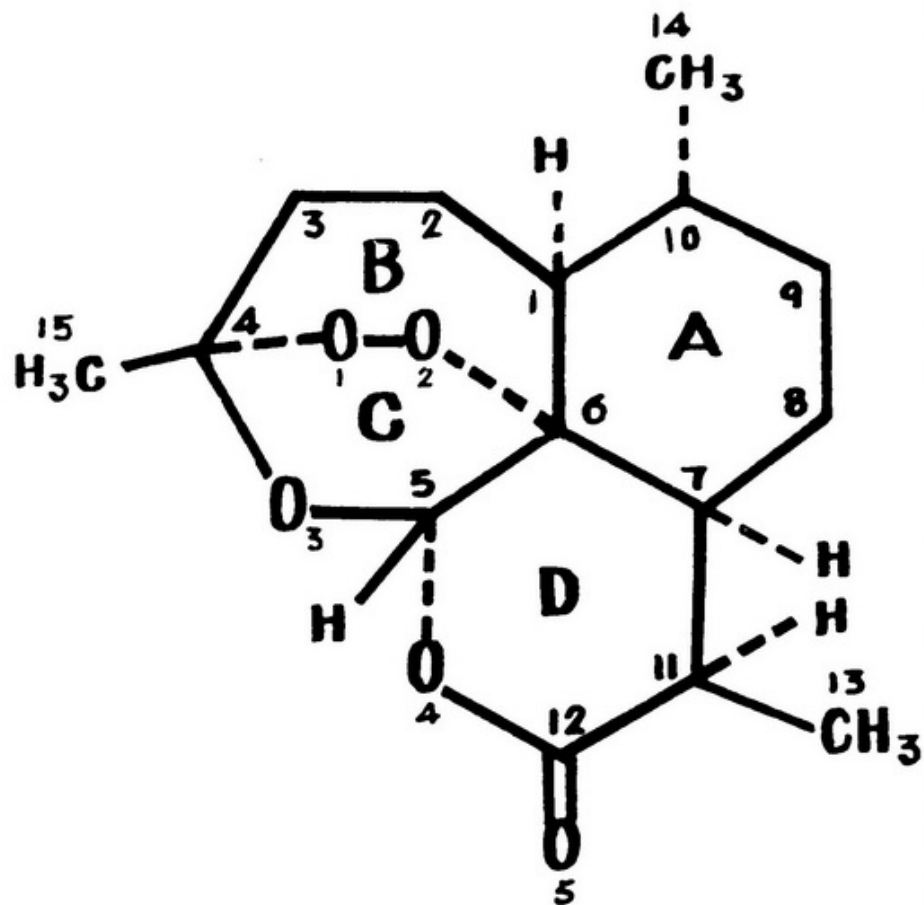
样品重(Mg)	CO ₂ 重(Mg)	H ₂ O重(Mg)	%C	%H	註
2.531	5.923	1.928	63.86	8.52	
3.173	7.411	2.422	63.59	8.54	
样品重(Mg)	温度(°C)	压力(MM/Hg)	氮气体积(Ml)	%N	
样品重(Mg)	()沉淀重(Mg)	MI	N	%	

分析室意见: _____

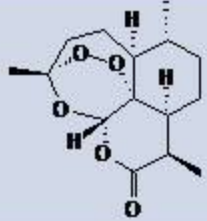
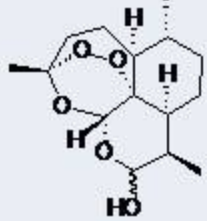
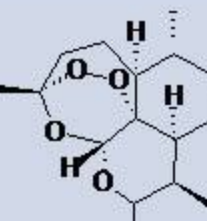
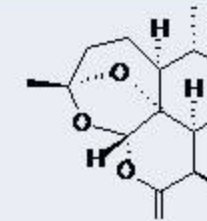
分析人: 李秀兰

分析日期: 73年4月27日

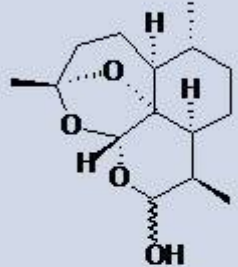
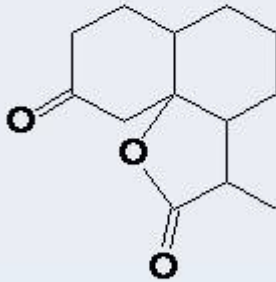
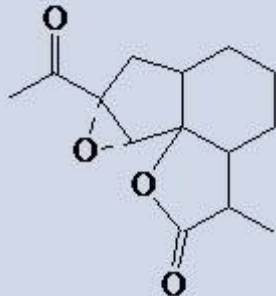
The Molecular Structure and the Stereo-structure of Artemisinin



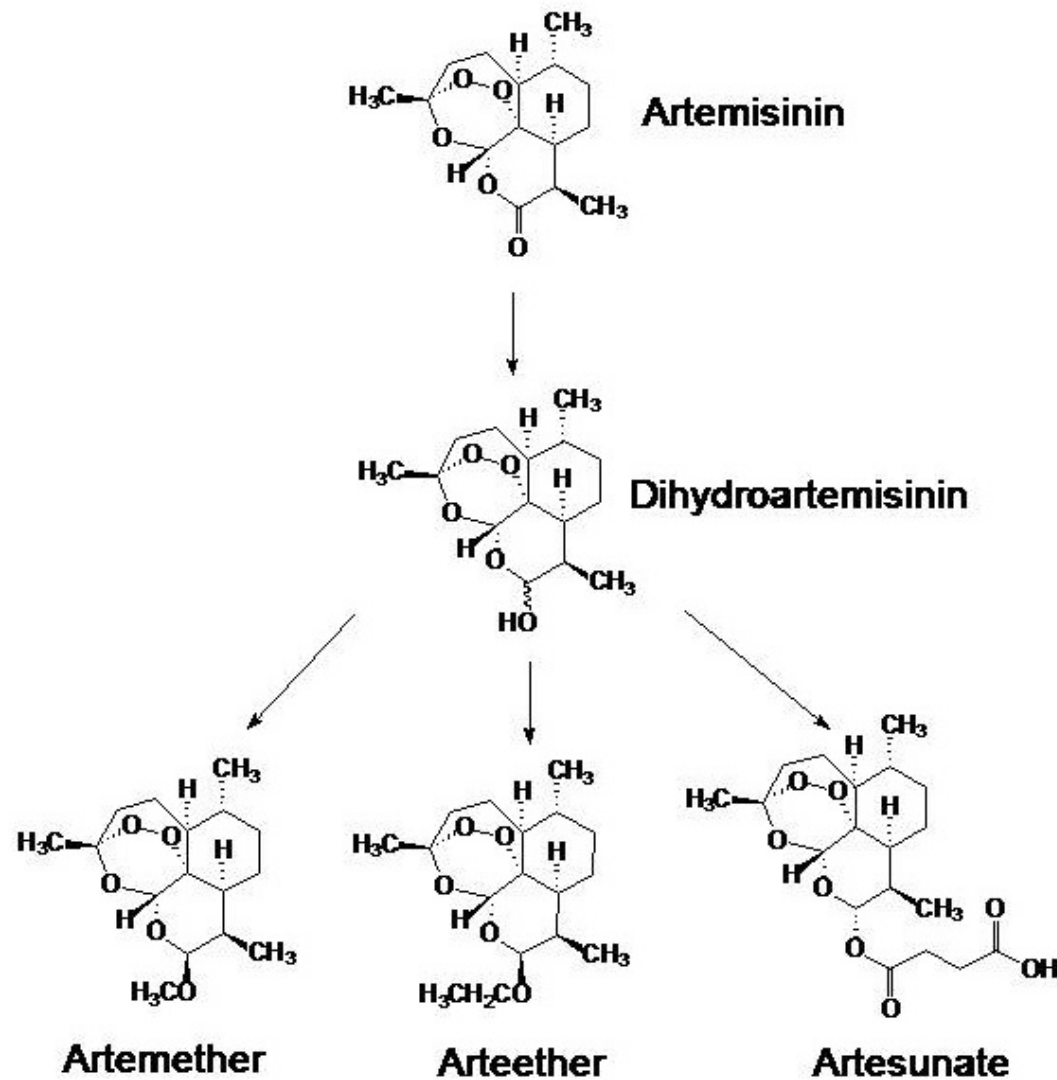
Structure - Activity Relationship of Compounds from Artemisinin

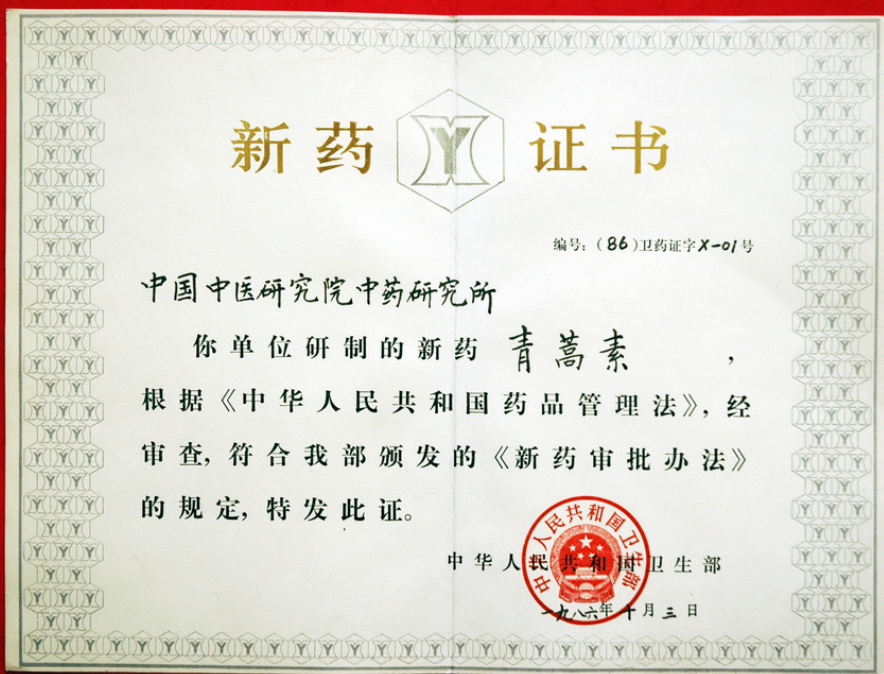
Compound	Graph of chemical structures	Dose mg/kg/day \times 3	Clearance of parasites
Artemisinin	 The chemical structure of Artemisinin is a complex polycyclic molecule with a bicyclic peroxide bridgehead system, a lactone ring, and a ketone group. It features a decalin core with a peroxide bridge and a lactone ring fused to it.	50-100	Yes
Dihydroartemisinin	 The chemical structure of Dihydroartemisinin is similar to Artemisinin but with the peroxide bridgehead system reduced to a dihydroperoxide bridgehead system.	12.5	Yes
Acetate of dihydroartemisinin	 The chemical structure of Acetate of dihydroartemisinin is similar to Dihydroartemisinin but with an acetate group (OCOCH ₃) attached to the lactone ring.	6	Yes
Deoxyartemisinin	 The chemical structure of Deoxyartemisinin is similar to Artemisinin but with a hydroxyl group instead of a ketone group at the C-12 position.	100	No

Structure - Activity Relationship of Compounds from Artemisinin (continued)

Compound	Graph of chemical structures	Dose mg/kg/day \times 3	Clearance of parasites
Dihydrodeoxyartemisinin	 <p>The structure shows a complex polycyclic system with a central oxygen atom bridged between two rings. It features several hydroxyl groups, including one at the bottom and two others on the left side, and two hydrogen atoms explicitly shown on the top rings.</p>	100	No
Acid treatment product of artemisinin	 <p>The structure is a polycyclic system with a central oxygen atom. It features a carbonyl group on the left side and another carbonyl group at the bottom, with a methyl group attached to the carbon of the bottom carbonyl.</p>	100	No
Base treatment product of artemisinin	 <p>The structure is a polycyclic system with a central oxygen atom. It features a carbonyl group at the top left and another carbonyl group at the bottom, with a methyl group attached to the carbon of the bottom carbonyl.</p>	100	No

Molecular Structures of Artemisinin and its Derivatives





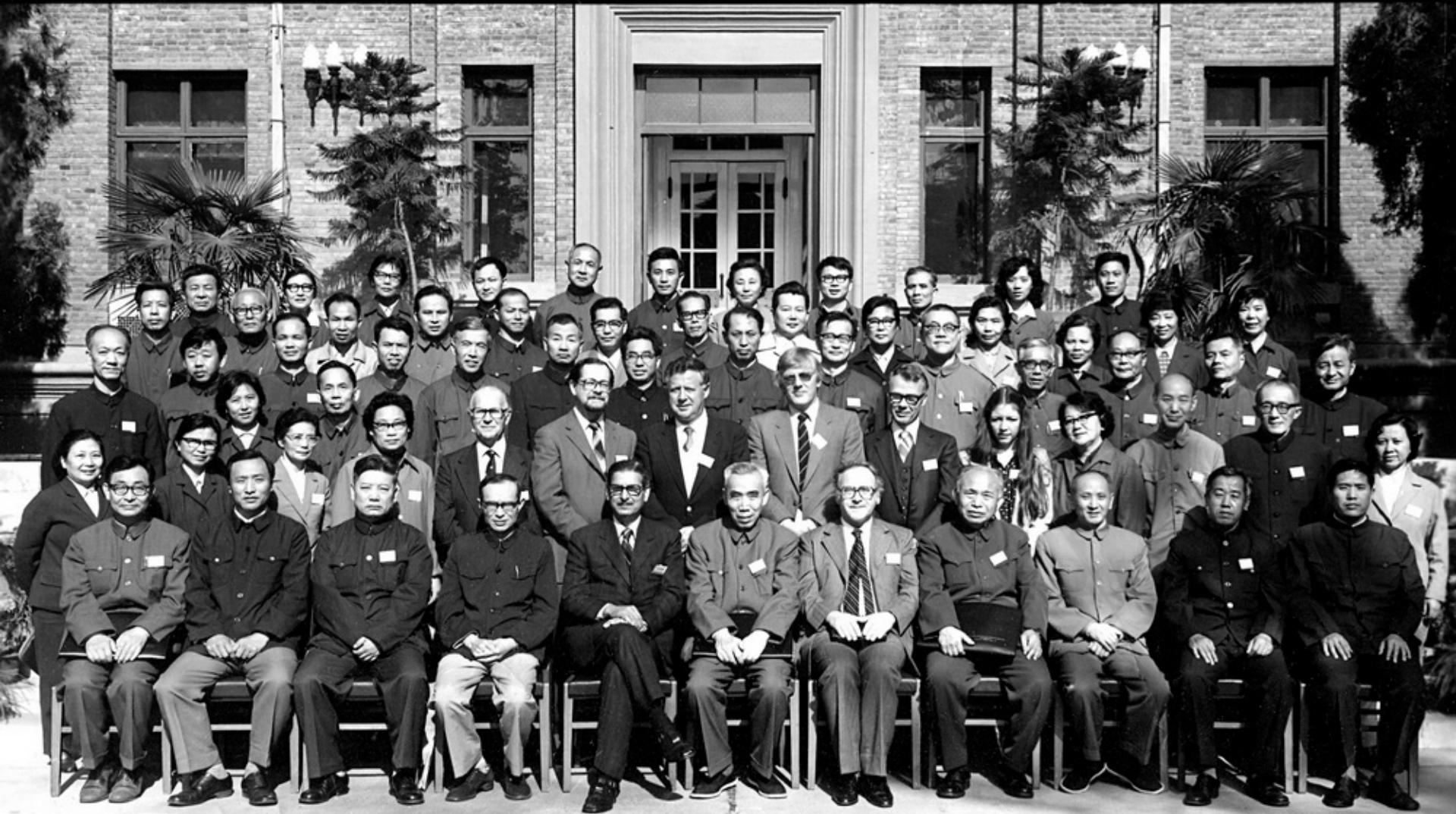
New drug certificate of artemisinin issued by the Ministry of Health (1986) (left)

New drug certificate of dihydroartemisinin issued by the Ministry of Health (1992) (Right)



Worldwide Attention to Artemisinin

The 4th Meeting of The SWG-Chemal "Qinghaosu"
Beijing · China October · 1981



Commitment to the Clearly Defined Goal

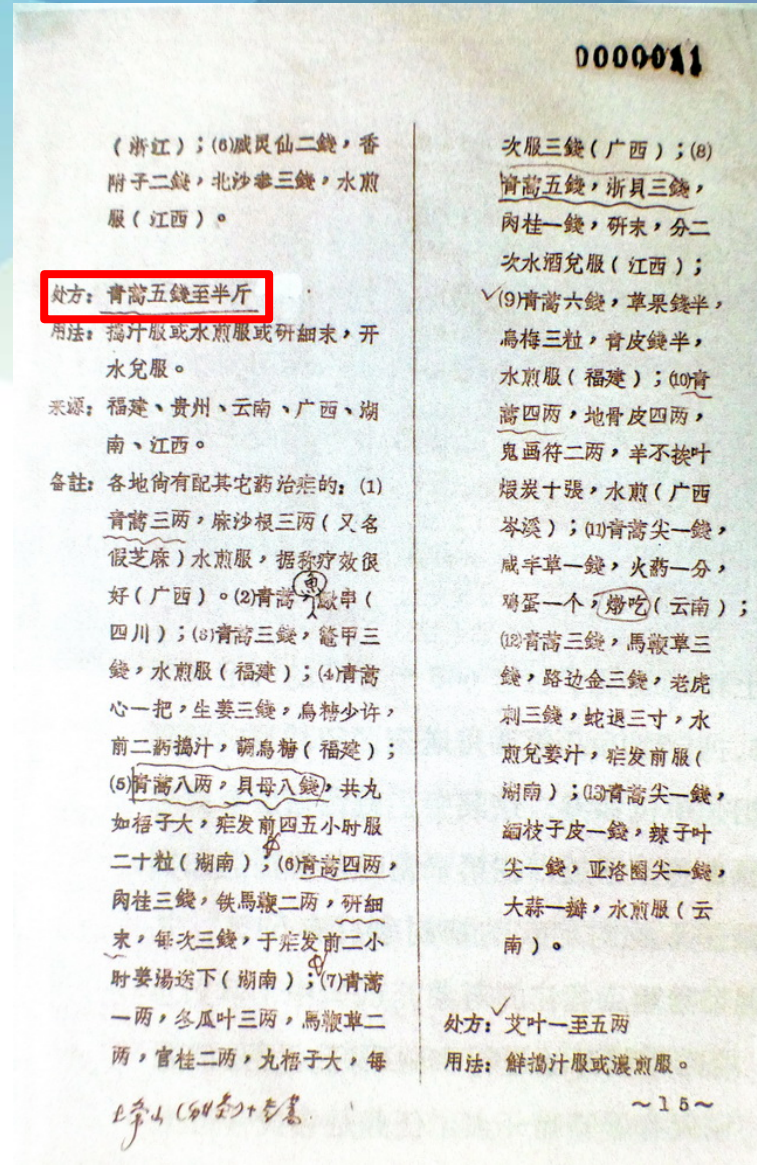
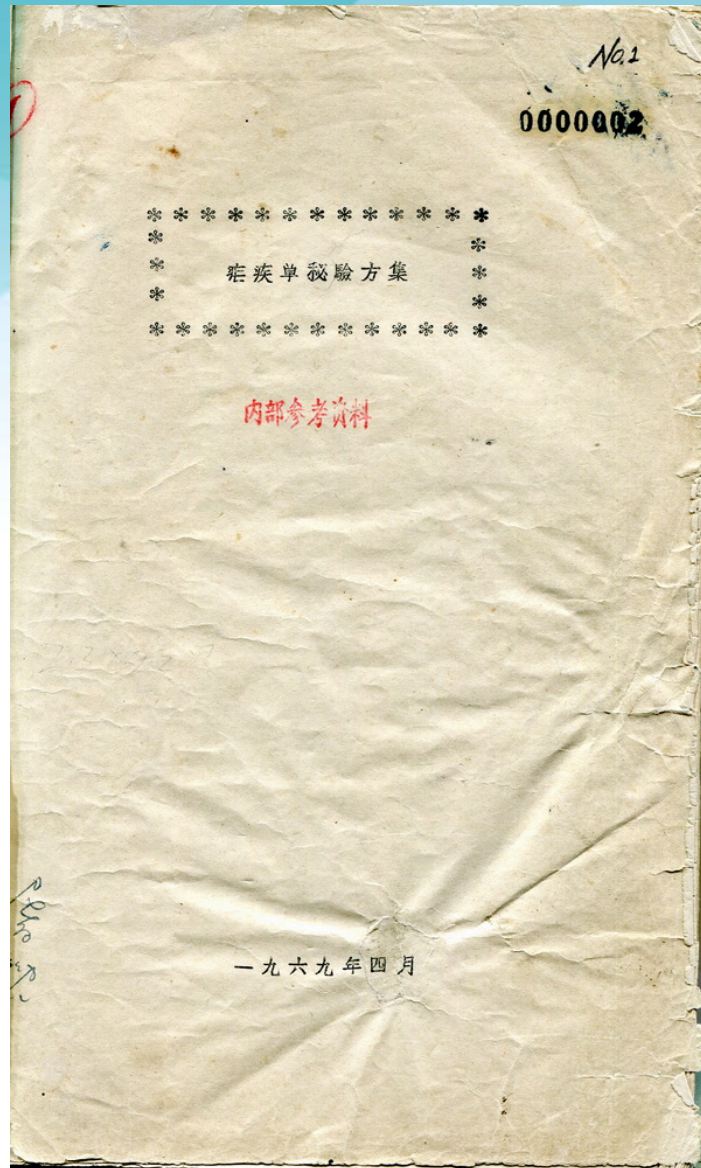


Knowledge is Prologue in Discovery



Antimalarial Collections of Recipes and Prescriptions

April, 1969



A Handbook of Prescriptions for Emergencies

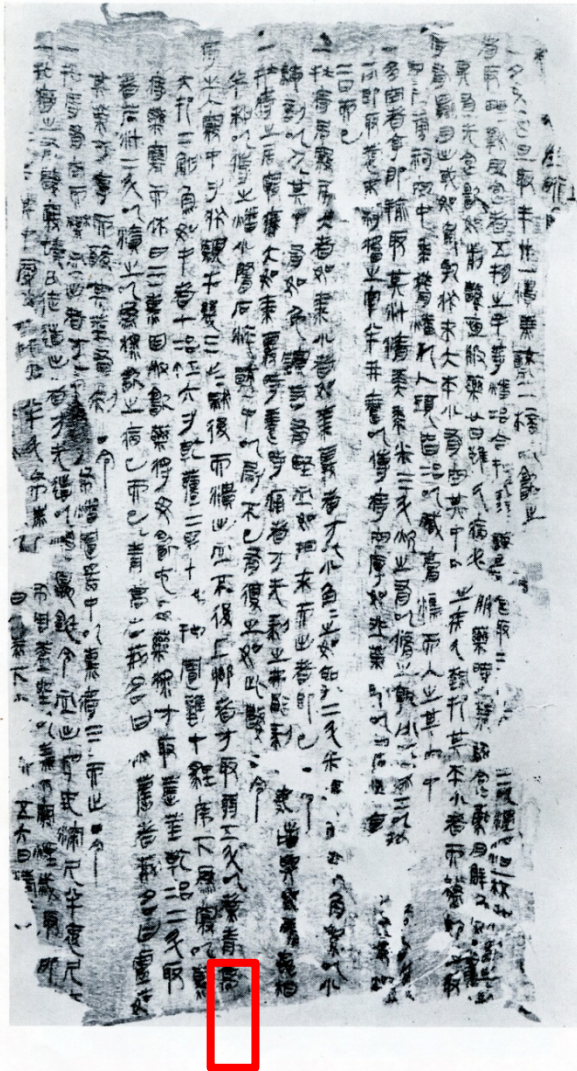


葛山翁肘後備急方卷之三
治寒熱諸瘧方第十六
二丸欲發時服一丸
又方青蒿一握以水二升漬絞取汁盡服之
又方用獨父蒜於白炭上燒之末服方寸匕
又方五月五日蒜一片去皮中破之刀割令容巴豆
一枚去心皮內蒜中令合以竹挾以火炙之可
熱搗爲三丸未發前服一丸不止復與一丸
又方取蜘蛛一枚蘆管中密塞管中以縮頸過發時

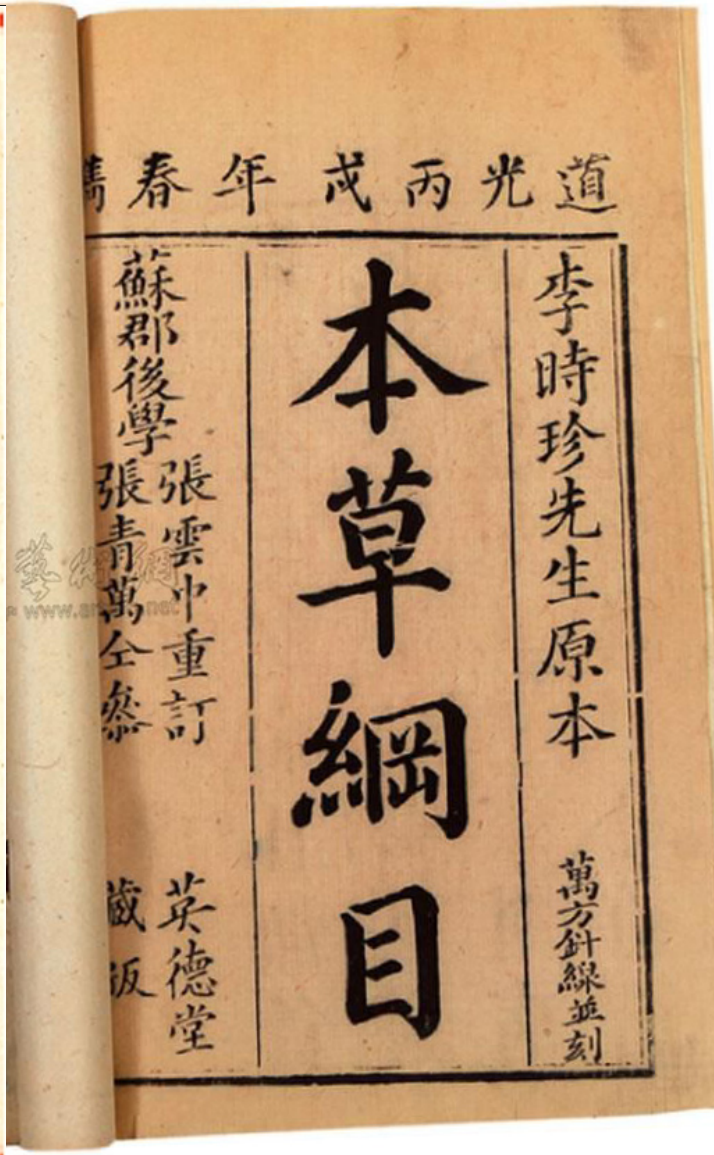
Qinghao Has a Long History of Clinical Application

图版拾贰

马王堆三号汉墓出土的帛书



《五十二病方》(部分)



Simple Resarech Facilities in the 1970s



Invention Certificate for Progress in Anti-malarial Research Issued by National Congress of Science and Technology, 1978



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.

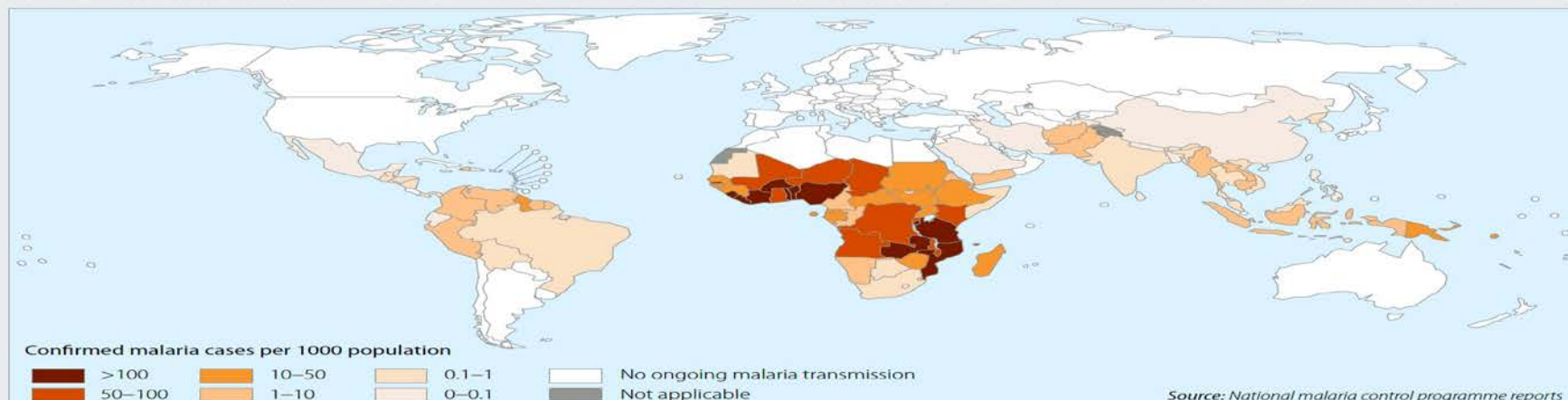
Malaria mortality rates have decreased by **47%** worldwide and by **54%** in the WHO Africa Region.

By 2015

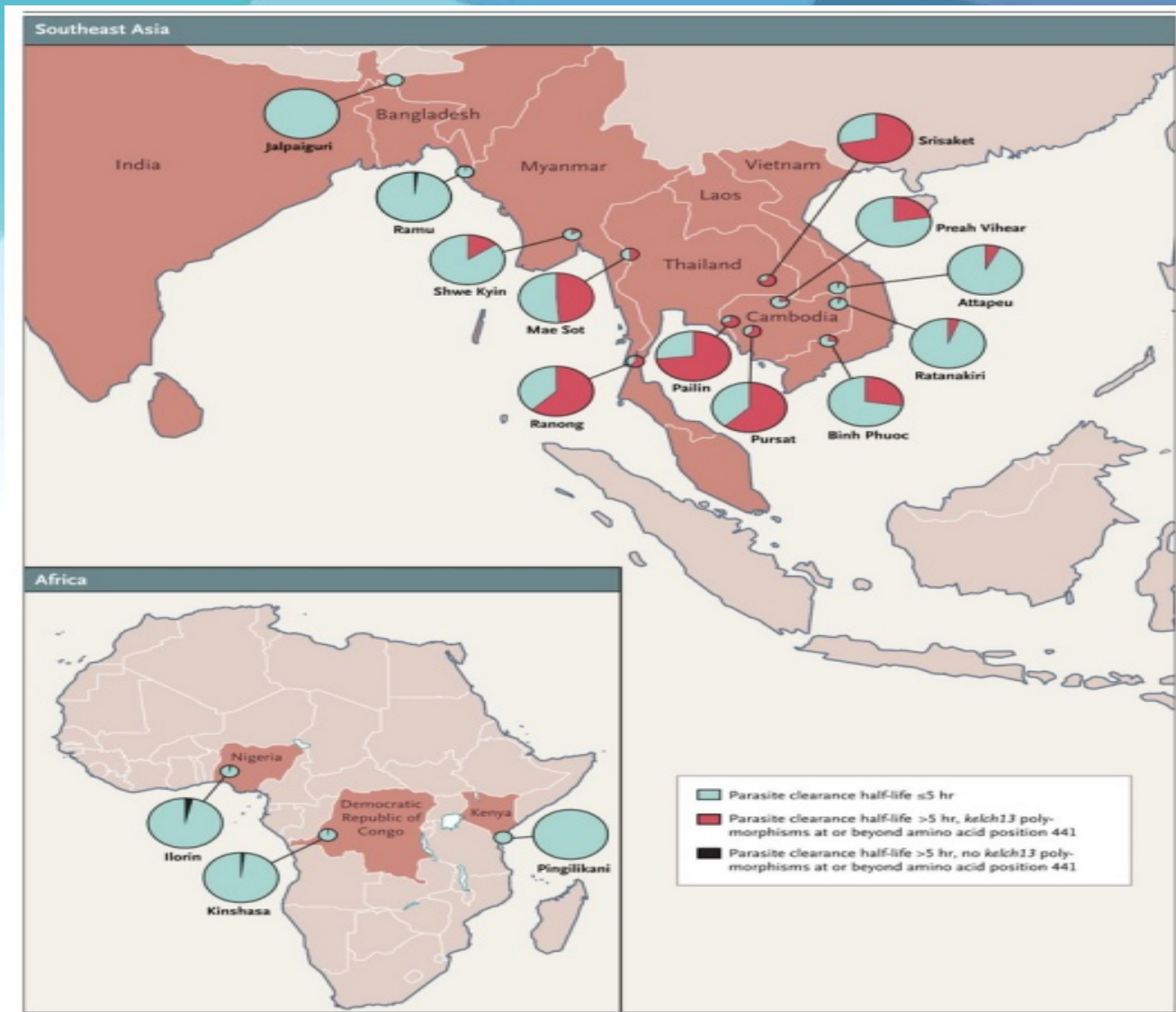
If the annual rate of decrease over the past 13 years is maintained, malaria mortality rates are projected to decrease by **55%** globally and by **62%** in the WHO Africa Region.

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

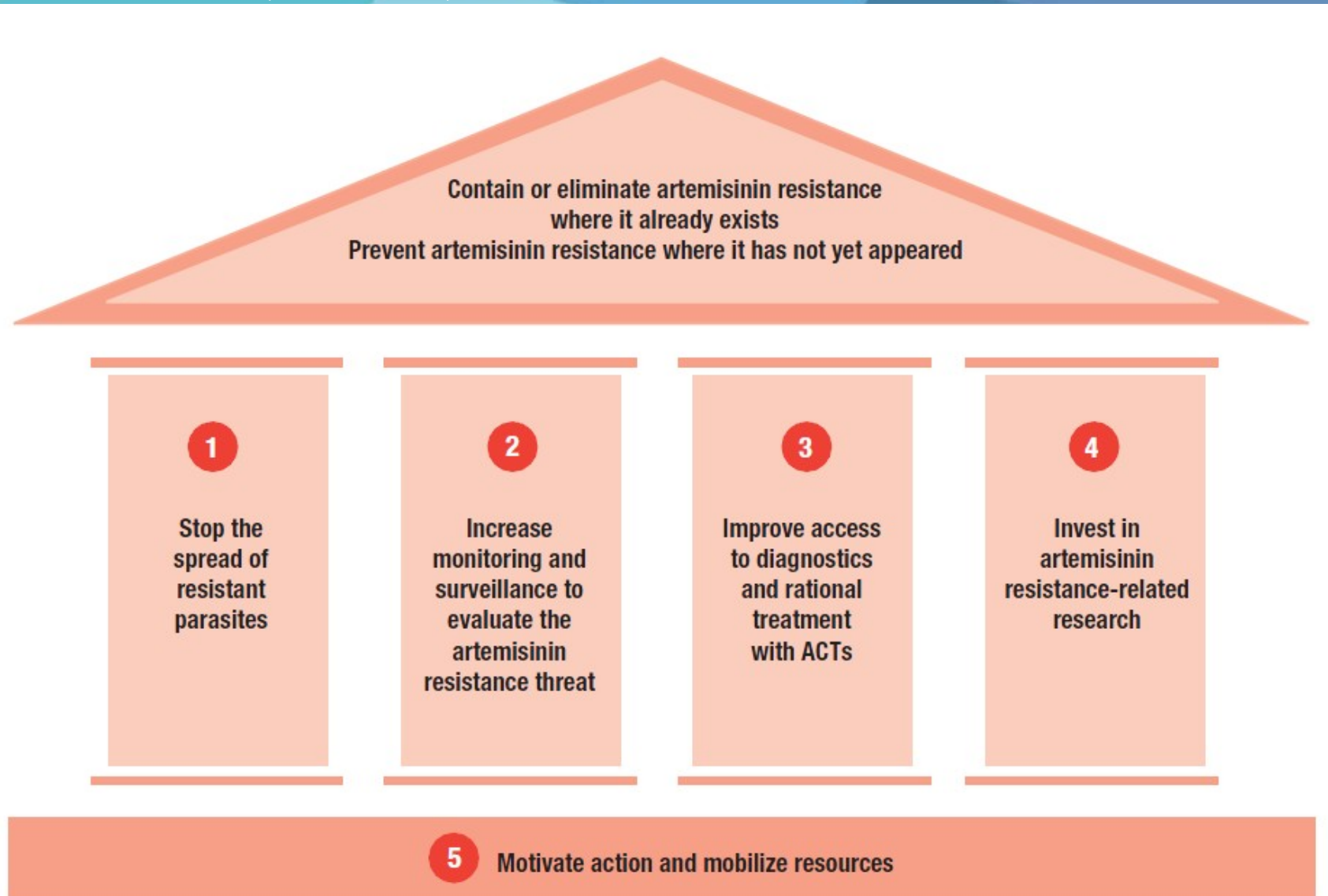


Spread of *P. falciparum* Resistance to Artemisinin



Ashley E A et al, Spread of Artemisinin Resistance in *Plasmodium falciparum*
Malaria N Engl J Med. 2014, 371(5): 411–423

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



中國醫學是
一個偉大的寶庫，
應當努力發掘，加
以提高。
毛澤東

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



白日依山尽，

The sun along the mountain bows,



黄河入海流，

The Yellow River seawards flows,



欲穷千里目，更上一层楼。

**You will enjoy a grander sight,
By climbing to a greater height.**

On the stork tower,
Wang Zhihuan (Tang dynasty)

Acknowledgements

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!