

## Discovered in China

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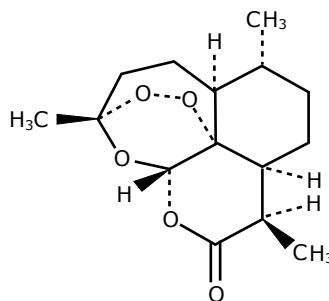
If one wants to associate China with an animal symbol, he or she might immediately think of the panda. However, for thousands of years, the official Totem for China was not the panda but the dragon, or as some scholars recently suggested, the “Loong”.

Loong is an imaginative animal. Its body is formed by parts from different animals. It has the head of a camel or horse, eyes of a turtle, horns of a deer, body of a python, skin of a fish, legs of a tiger, and paws of an eagle. Different from the western dragon, it does not have wings but can still fly high in the clouds. According to Chinese historians, the creation of Loong is not purely by human imagination; it was a combination of different Totems from various tribes many thousands years ago when they merged together.

Like the Loong, Chinese culture itself is a melting pot of many cultures. Although the melting process often caused bloody clashes between cultures, it eventually produced a society that flourished with innovation and prosperity. Western culture, including its advanced science and technology, is the latest to meet the Chinese culture; the two are now melting into a global culture.

This is exactly what is happening in the biotechnology and pharmaceutical industry in China.

The foundation of traditional Chinese medicine (TCM) can be traced back to as early as two thousand years ago with the publication of the <Huang Di Nei Jin> or the <Royal Internal Medicine>. Many basic theories that we still know today, such as “Ying and Yang,” were originally described in therein. The literature even included thirteen drug formulations. The study of pharmaceutical properties and the usages of natural products peaked in the 16th century with the publication of <Ben Chao Gang Mu> or the <Pharmacopeia of Herb Medicine>. A total of 1,892 medicinal plants were documented and 11,000 medicinal formulations were described. Even today, it still holds tremendous value for modern drug discovery. The successful discovery of Qinghaosu (Artemisinin), an anti-malaria drug, is one such example. However, as with traditional medicines from other cultures, CTM suffers from the lack of mechanism and pharmacological studies at the molecular and cellular level. Most of the active ingredients were still obtained by extraction from parent plants rather than by chemical synthesis.



Structure of Qinghaosu (Artemisinin)

Modern chemistry and pharmacology were introduced to China early last century, not long after the first chemically synthesized drug, Aspirin, came to market. However, the country was then torn apart by civic war and later by outside forces. The political and economic environment at the time gave the pharmaceutical industry little chance to grow. Nonetheless, China started its modern pharmaceutical and chemical industry during the wartime. The first college of pharmacy was established in 1936. Seventy years later, it became the China Pharmaceutical University, the largest pharmaceutical university in China, with over 10,000 students and 1,500 educators. In addition, there are thirty or so Departments of Pharmacy and thirty or so Colleges of CTM educating tens of thousands of students every year, preparing them for medical, pharmaceutical, and healthcare related careers.

The modern practice of sending Chinese students abroad to study began as early as the 18th century, when China was still ruled by the Qing dynasty. However, the movement did not gain momentum until one hundred years later. In late 1970s, China finally abandoned its century long “close door policy” and openly embraced the international world and modern science and technology. China has since sent over one million students abroad to study the sciences, including pharmaceutical sciences and technologies. According to the Institute of International Education (IIE), the number of Chinese students studying in U.S. has increased from just above 10,000 in 1985 to about 70,000 in 2006. Most students are engaged in higher education programs.

Increasingly, however, Chinese students are now returning to China with their newly acquired knowledge and skill in modern science and technology. Such returnees are known in Chinese as “hai-gui,” which literally means “sea turtles.” As the phrase suggests, such returnees are like sea turtles returning to shore again after leaving to grow up in the sea. About 1.21 million Chinese studied abroad from 1978 to 2007, and roughly a quarter of them or 0.33 million returned back to China during the same period. In the last year alone, 44,000 “sea turtles” landed on the China’s shores. These returnees become the seeds for the growing of modern biotechnology and pharmaceutical industry. Many of them are in healthcare and drug discovery.

Returning “sea turtles,” however, are not the only ones rushing in to China’s healthcare industry. Foreign companies and multinational companies in particular have seized the historic opportunity to open the world largest healthcare virgin land. While expanding markets for their products, they have also helped to build up a modern biotech and pharmaceutical industry in China

Take Novartis as an example. The company initially focused its efforts on sales and has seen its sales in the Chinese market grow by 25 percent annually since 1999. In 2006, Novartis broke ground for its manufacturing center in Suzhou. It was the first active pharmaceutical ingredients (API) export base built by a multinational pharmaceutical giant in China. Following the Suzhou site, Novartis opened its R&D facility in Shanghai’s Zhangjiang Hi-Tech Park in 2007.



**Empress Chi’xi (right first) photographed with Princess DerLin who was educated in German and is credited by many today as among the first generation of “hui gui”s.**



“The level of scientific expertise in China is rising rapidly. At the same time, the healthcare needs of the Chinese are growing, primarily the result of urbanization, lifestyle changes and associated chronic diseases,” said Dr. Daniel Vasella Chairman and CEO of Novartis. “The Shanghai center will allow us to combine modern drug discovery approaches with those of traditional Chinese medicine that have been used to treat patients in China for thousands of years. This new research center will help Novartis contribute to the needs of patients in China and elsewhere and has the potential to become a global center for biomedical innovation.” As the Chinese name of Novartis says: Novartis is “Committed to China.”

Novartis is not alone in establishing its own drug discovery center in China. Major multinational giants, including Roche, Astrazeneca, Pfizer, GSK, BMS, Nova Nordiks, and lately Abbott and Aventis, have all recently invested heavily in their R&D centers in China. This trend reflects a major shift in the outlook of major pharmaceutical companies. “(China is) not only a market, it is also an enormous resource of science. There is a new science base emerging in this country. And I think China has a lot to offer to the world, in terms of its capacity, its capability to find new drugs and new medicines,” said Franz Humer, CEO of Roch in 2007.

Meanwhile, Chinese research institutes are also rapidly being equipped with modern technologies and instrumentations. Not far from the Novartis and Roche R&D centers stands The National Center for Drug Screening. The center was created by the joint investments of the Ministry of Science and Technology, the Chinese Academy of Sciences, and the Shanghai Municipality Government. As a public technology platform, the Center offers drug screening services and technical consultation to universities, research institutions, and pharmaceutical companies nationwide. The National Center of Drug Screening is a part of the drug discovery infrastructure of Shanghai Institute of Materia Medica (SIMM). That is a major drug research center in China. Companies like Novartis have committed to long-term collaborations with the Institutes.

In addition to multinational pharmaceutical companies and Chinese pharmaceutical research institutes,

cities like Shanghai also host several internationally renowned drug discovery and development CROs. At the leading edge are companies such as Wuxi Pharmatechs and ChemPartner. Both companies are led by returnees, the “sea turtles,” from US. These companies provide services from drug discovery to development for mostly multinational companies. Wuxi Pharmatech for example, has its primary facilities in Shanghai that include a 630,000 square-foot R&D center and a 220,000 square-foot process development and cGMP-quality manufacturing plant. In addition, a 130,000 square foot R&D center in Tianjin and a similar center at Suzhou are been built up. Alone with Wuxi, there are dozens of well-established CRO companies that are specialized services in areas, such as preclinical research including chemistry, bioassay, formulation, pharmacology and toxicology and clinical trials. An CRO Service Alliance was recently formed at Shanghai that include companies such as Sundia Meditech, United



SIMM's new R&D labs in Zhangjian Sci-tech park



Wuxi Pharmatech's new R&D facilities at Shanghai

PharmaTech, and HD BioSciences. HD BioSciences is known for its expertise in assay development, high-throughput screening (HTS) and natural product-based lead identification.

It is of interest to notice that the growing Chinese CRO companies are now taking their first step out of China. Wuxi Pharmatech recently purchased Apptec (San Paul, MN) that offers integrated, GLP/GMP-compliant discovery, testing and contract manufacturing services. Almost at the same time, VenturePharm Service, a leading CRO company in China that offers clinical trial services, acquired majority shares of Commonwealth Biotechnology Inc. (Richmond, VA). The CBI group include companies, such as Exelgen (previously Tripos), a leader in computer-aided library designing and synthesis and

Mimotopes, the pioneer in combichem and peptide library. These companies all made significant impact to drug discovery in the past. A merger of East with West will bring the strengths of both world together. We will likely see more of such Alliances in the near future.

Drug discovery and development is here in China and it is flourishing at light speed. The industry has a growing appetite for technologies and talent. Several SBS members are now leading drug screening and discovery efforts in China. Dr. Bin Li who joined ChemPartner last year and soon to become the R&D Director in the newly established Abbott R&D Center in Shanghai. When asked why he decided to go back to work at Shanghai, he pointed out that "Shanghai is at the forefront of rapid growth in drug discovery research activities with multinational pharmas setting up their own R&D centers and CROs expanding into biology service areas. With a young and energetic workforce, the business-friendly environment, and numerous overseas returnees, who bring back knowledge, experience, and leadership that are needed to build the discovery capabilities and train the local scientists, Shanghai will undoubtedly become a hub for drug discovery research in the future. While multinational R&D centers set their goals on discovering innovative drugs, CROs strive to provide quality service at competitive prices and fast turnaround times, and provide solutions for more and more integrated and program-based discovery research. I can foresee myself working and enjoying Shanghai for many more years".

When GSK opened its R&D center in China, Dr. Moncef Slaoui, the Head of Research, said, "We intend to be part of a future in which the phrase 'discovered in China' is heard as often as 'made in China' is heard today."

Back to the story of "Loong", have you ever watched the dragon dance during Chinese New Year parade? If you had, you would have noticed that the dragon is constantly chasing a fireball. If the dancing dragon represents the modern China, the fireball is a NEW DRUG discovered in China. At least that is how I see it.



The traditional Dragon Dance chasing the fireball