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Pharmacology in China: a brief overview

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Pharmaceutical science has been an important part of Chinese civilization for more than 5000 years. As the gold standard for proof of therapeutic value, pharmacology has laid a solid foundation towards the development of pharmacy. In China, the advancement of pharmacology has its own trajectory and paths that differ from those in other countries.

Formation (1923–1949)

Contemporary pharmacology in China began in the third decade of the past century. Dr K.K. Chen, a pharmacologist of Peking Union Medical College (PUMC), started his research on the mechanism of biological actions of *Ephedra sinica stapf*. He purified ephedrine alkaloids and proved that they were active constituents for the therapeutic effect in asthma. In 1924, he published this work in *The Journal of Pharmacology and Experimental Therapeutics* [1] showing that ephedrine alkaloids had pharmacological effects similar to that of epinephrine on the cardiovascular system. It is the first example of using modern technologies to identify active components in traditional Chinese herbs and to translate a laboratory discovery to bedside practice. The finding was highly regarded then by the pharmaceutical community and paved the way for subsequent exploration in sympathomimetics, thereby exerting a long-lasting impact on modern pharmacology.

The Chinese Society of Physiology was established in 1926 and included a pharmacological subgroup. The prospect of pharmacology as an emerging scientific discipline thus began to appear in China. Between the 1930s and the 1940s, Chinese pharmacologists were engaged in studies of biological effects of approximately 90 commonly prescribed herbs, with identification of some previously unknown active ingredients. A good example is the unveiling of the therapeutic value of sodium nitrite and sodium thiosulfate. Both are effective in detoxification of acute cyanide poisoning, a method that is still in use today [2].

Growth (1949–1985)

Pharmacological sciences in China has experienced a steady growth since 1949. Pharmacology departments began to be established in most medical schools, and a group of scholars who returned from abroad in the 1950s, together with domestic specialists, formed the core of the Chinese pharmacology community, leading to the emergence of a research infrastructure with Chinese characteristics.

Major discoveries in this period include sodium dimercaptosuccinnate, an antidote for heavy metal toxicity by lead, mercury, arsenic, and antimony [3], tetrahydropalmatine as the analgesic ingredient of *Rhizoma corydalis* [4] and antitumor agents such as camptothecins, hydroxycamptothecins, harringtonine, and homoharringtonine [5], among others. It is especially noteworthy to mention that localization of the analgesic action site of morphine in the gray matter surrounding the third ventricle and cerebral aqueduct, described some 40 years earlier in China than the Western laboratories, is considered a milestone in morphine research [6]. Treatment of acute promyelocytic leukemia with all-trans retinoic acid was another original discovery made in China [7], which is now routine clinical therapy throughout the world.

From 1966 to 1976, China was in the middle of the notorious ‘Cultural Revolution’ and research activities stalled nationwide. A bright spot was the revelation and successful development of artemisinin, a major breakthrough in antimalaria drug research [8] that was recognized recently by the 2011 Lasker–DeBakey Clinical Medical Research Award for ‘saving millions of lives across the globe, especially in the developing world’. Meanwhile, the biological basis of traditional Chinese medicine (TCM) was the only focus of many pharmacologists during this time and produced some social–economic benefits (e.g., discovery of the liver-protective effect of schisandra [9] that led to the successful development and eventual launching of bifendata to treat hepatitis B).

The Chinese Pharmacological Society was established in 1979 and started to publish a journal in English – *Acta Pharmacologica Sinica* in 1980. The society finally joined the International Union of Pharmacology (IUPHAR) in 1985, signaling China’s entry onto the international stage of pharmacology.

Expansion (1986–present)

With a booming Chinese economy, especially after China joined the World Trade Organization (WTO) in 2001, funding for scientific research has risen steadily. This allows the establishment of drug discovery technology platforms that confer international standards, as exemplified by the National Center for Drug Screening (NCDS) along with a number of other state-owned organizations specializing in preclinical research, clinical studies, and

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pilot manufacturing of biopharmaceuticals. The NCDS was jointly set up in 1997 by the Ministry of Science and Technology, Chinese Academy of Sciences (CAS), and Shanghai Municipality. It is the only national entity dedicated to screening bioactive substances with potential therapeutic value through offering assay services and technical consultations to universities, research institutions, and pharmaceutical companies nationwide. This allows the country to innovate in an area that was lagging behind the developed world for years in a coordinated and resource-sharing manner. The capability of the NCDS has been further strengthened recently via the foundation of the Chinese National Compound Library (CNCL). Of the ~1.3 million sample collection, approximately 38% was derived from a generous donation from Novo Nordisk A/S of Denmark in 2008 [10]. Today, the CNCL, in conjunction with its six satellite libraries across the country, is becoming a center of key resources for China's indigenous drug discovery efforts, which have been one of the focuses of the 'National Science and Technology Major Project' (also known as the 'Mega Project').

Over the past two decades, specialized infrastructure, technical competence, and talent pool have been developed for drug innovation, particularly in high-tech park clusters located in different geographical regions [11]. As a result, development in several pharmacology disciplines in China has matched the global pace, and new breakthroughs [12–14] are not uncommon. Many of these highlights are systematically reviewed in this series to illustrate the current status of pharmacological research in China.

It is worthwhile to note that the development of contemporary pharmacology in China has two unique features. First, it began some 80 years behind that in Western countries. The initial stage was filled with hardships, including a lack of funds and shortage of essential equipment. Knowledge dissemination was heavily dependent upon the core group of scientists who previously studied in Europe, North America, and the former Soviet Union. They brought with them new concepts and technologies to China. Second, owing to historical and cultural reasons, many Chinese pharmacologists started their careers by studying bioactive components from TCM aimed at making novel drugs from their discoveries. This combination of traditional knowledge and modern technologies has therefore become a widely accepted research model. The latter feature, together with the large and rapid improvements of clinical trial capacity in China, has begun to draw attention of the international pharmaceutical industry.

Outlook

Although pharmacological studies on TCM (herbs in particular) will continue to be a focal point, strong emphases will be directed towards basic and original research, thereby narrowing the gap between Chinese pharmacological research and those in developed countries. Implementation of this strategy is an important task of the National Science and Technology Major Project, and two of the programs, one on 'drug discovery and development' and the other on 'combating major infectious diseases' are associated with pharmacology. By attracting drug makers and small- to medium-sized biotech companies as principal players in technology innovation, scientists, venture capitalists, and entrepreneurs would converge to take advantage of translational medicine. In this regard, clinical pharmacology is an area that will be substantially strengthened, especially for pharmacogenomics, via initiation of another multimillion dollar 'Lead Project' on personalized medicine at the Chinese Academy of Sciences, with an aim to better guide clinical use of therapeutics at grass root levels. Finally, we should closely monitor how these areas are trending so we may develop new theories, advanced techniques, and novel methodologies as the historical transformation of the Chinese pharmaceutical industry proceeds from imitation to innovation.

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