

# HIGHLIGHTS OF PHARMACOLOGY IN MAINLAND CHINA<sup>1</sup>

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This review was based mainly on scientific literature collected from the major medical libraries in the United States, the Office of Technical Services of the U. S. Department of Commerce, and the Library of Congress. Most of the material surveyed was obtained from four publications: the *Chinese Medical Journal*, which appears in English and contains an abstract section on articles published in various other Chinese medical journals including pharmacologic papers; the Chinese-language periodical *Yao-hsueh T'ung-pao* (*Pharmacology Bulletin*), which was first published in 1955 by the Chinese Pharmacology Society and is primarily concerned with the pharmacognosy, pharmacology, and therapeutic uses of traditional Chinese drugs (1); *Acta Pharmaceutica Sinica*; and *Acta Physiologica Sinica*; the latter two Chinese journals often contain English summaries of manuscripts dealing with pharmacodynamics and toxicity of plant drugs.

As in all other branches of science, pharmacologic research in mainland China is carried out on planned programs. During the past decade, pharmacologists have been directed to concentrate their research efforts on chemotherapy and traditional Chinese medicine. Although the primary emphasis in chemotherapy was directed toward eradicating parasitic and infectious diseases, medical personnel, particularly pharmacologists, were urged to intensify studies on Chinese materia medica. Numerous compounds 葯草 medicinal herbs have been screened for possible therapeutic uses (2). These efforts have been further accelerated since the big "leap forward" in 1958.

In order to promote training and research in traditional medicine, the Academy of Traditional Chinese Medicine was established in Peking. Recent publications indicate that research institutes of Chinese medicine now exist in most of the provinces and major cities and that all medical schools offer courses in traditional medicine. Physicians trained in Western medicine have been requested to co-operate with the traditional practitioners and to learn and apply traditional medicine including therapy using acupuncture and moxibustion [Li (3); Hsu (4)]. That this crash program has affected the Chinese pharmacologic contributions at both the basic and applied levels is reflected in the literature by the increasing number of manuscripts describing the pharmacologic effects or therapeutic efficacy of a great number of herbs for a variety of conditions. With the exception of some of the studies on parasitocidal agents, the great majority of trials with traditional medicine were conducted on a relatively small number of patients, and, more importantly, without proper controls, reference standards, adequate follow-up

<sup>1</sup> The survey of the literature pertaining to this review was concluded in July 1961. A few important publications which appeared during 1959 and 1960 are included.

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studies, and quantitative evaluation of drug action. One cannot help but view these clinical testimonials with reservations.

The current status of pharmacology in mainland China was described in 1957 by Chou & Chin (5), summarized in 1959 by Chin, Sung & Hsu (6), and more recently critically surveyed by Way (7). Space limitations in this short review permit only brief mention of the highlights of pharmacology in mainland China in recent years. Some of the more important contributions will be dealt with in greater detail.

In the December 1959 issue of the *Chinese Medical Journal*, a comprehensive survey of the "Achievements in the Fight Against Parasitic Diseases in China" was made by Hou *et al.* (8). Nationwide campaigns were conducted one after another for the eradication of the five major parasitic diseases, schistosomiasis, malaria, filariasis, ancylostomiasis, and kala-azar. Of these prevalent diseases, the greatest attention has been given to schistosomiasis, as indicated by the abundance of literature on new and effective antischistosomal remedies. These efforts have resulted in perhaps the most important basic pharmacologic contributions of China in the last decade.

More than 1000 antischistosomal compounds have been synthesized, selected, and screened. Through animal experimentation and clinical trials, the more promising antimonials were reported to include the intramuscular preparations (antimony ammonium gluconate, antimony sodium dimercaptosuccinate, and antimony dithiopropionate) and the oral compounds (thiouracil-antimony-1 and antimony quinine hydrochloride). Of the non-antimonial preparations, rosaniline, hexachlorophene, and *para*-amino-oxybenzene-heptane were found to have therapeutic potential. Among the traditional Chinese remedies, *Cucurbita pepo* (pumpkin seeds), *Hemerocallis thumberggi*, and wild daylily were reported to possess definite therapeutic effects in experimental and clinical schistosomiasis. The effectiveness of pumpkin seed was said to be enhanced by the concomitant use of antimony potassium tartrate. Compared with the latter, pumpkin seed was claimed to be safer and more effective [(6, 8, 9); Chi (10); Chou & Huang (11)].

As a result of the intensive research on the chemotherapy of schistosomiasis, some basic information was obtained on the pharmacology and toxicology of antimonials, especially with respect to the mechanisms involved in their antischistosomal action, their cardiac arrhythmic, emetic, and central nervous system effects, and their effects on carbohydrate metabolism and thyroid function. Some useful methods were described for direct observation of drug action on adult schistosome worms by inoculation of the parasites into the anterior chamber of the rabbit eye and through transillumination of the portal veins of the infected rabbits (8). Of interest is the report that antimonial-induced myocarditis, manifested mainly in the form of Adams-Stokes syndrome, was successfully treated with large intravenous doses of atropine [Huang (12)]. Judging from the literature, considerable work has also been done on antidotes for antimonial drugs. It has been reported that the toxicity of antimony potassium tartrate in mice could be reduced by the administration of thiouracil, procaine, and dithiosuccinate (6).

With respect to other parasitic diseases, in vivax malaria radical cure was reported to have been achieved in almost 100 per cent of the large series of cases treated with primaquine (15 mg daily for 14 days) simultaneously with chloroquine (300 mg daily for the first four days) or cyclochloroguanide (a total dosage of 600 mg given in four days). In a control group given chloroquine alone, there was a relapse rate of 50 per cent. In animal experimentation, the schizonticide potency of cyclochloroguanide was found to be ten times that of chloroguanide or paludrine, whereas its toxicity was only one-tenth of the latter (8). Recently, in animal experimentation, marked antimalarial activity and low toxicity were noted for dichlorophenyltriazine and other halogen-substituted derivatives [Yao & Tang (13)]. Of the medicinal plants, *Orixa japonica*, T. and *Brucea javanica*, L. showed significant antimalarial effect in experimentally infected animals (6). In filariasis, the treatment course appeared to have been successfully shortened to three days with hetrazan in dosages of 300 mg three times daily. In the mass treatment of ancylostomiasis, tetrachloroethylene in a single dose of 3 to 4 ml before bedtime has been generally used with satisfactory therapeutic results. 1-Bromo-2-naphthol was also reported to have been widely employed with fewer side effects [Li (14); Wang (15)]. More difficult to evaluate is the claim that "Kuan Chung T'ang," a mixed concoction of *Aspidium falcatum* or *Polystichium falcatum* has been found effective in about 85 per cent of ancylostomiasis and 55 to 85 per cent of filariasis. Kala-azar is generally treated with antimonial compounds, especially sodium antimonial gluconate. In the antimony-resistant cases, stilbamidine or the less toxic pentamidine is used [(8); Wang & Wu (16)]. During the last few years, there appeared several apparently convincing reports testifying to the high efficacy of the combined use of *Cucurbita pepo*, L. (pumpkin seeds) and *Areca* nuts in the treatment of taeniasis; the former was said to paralyze the cephalic half of the tapeworm and the latter the caudal half [Chiang *et al.* (17); Hsieh (18); Hsieh (19)]. Mention should also be made of the clinical observation from a large series of cases that chloroquine by far surpasses emetine or gentian violet in the therapy of clonorchiasis sinensis, even though prolonged treatment with large dosages is still necessary [Weng *et al.* (20)].

In order to meet the ever-increasing demands for antibiotics which have been extensively used in bacterial infections, the various penicillins, tetracyclines, streptomycin, and chloramphenicol as well as the sulfa drugs have been mass-produced in modern factories. Pilot plants have also been set up for the manufacture of erythromycin, neomycin, polymyxins, and nystatin. According to a recent report by the Chinese Pharmaceutical Association, the output of antibiotics in 1959 rose to 10.6 times that of 1957, sulfa drugs 1.8 times, and antipyretics 3.2 times (21). A new anticancer antibiotic, actinomycin K, isolated in 1957, showed promising therapeutic effects on experimental tumors in mice. However, in 24 patients with malignant tumors only partial remission of short duration was obtained following actinomycin K therapy (daily intravenous doses of 100 to 200 mg). The observation periods appeared to be too short and the number of cases too few for a proper clinical assessment of this cytostatic agent [Chang & Chang (22)].

Among the medicinal plants exhibiting antibacterial activity, *Coptis teeta* and *Coptis chinensis* have been most extensively studied both experimentally and clinically. They are bacteriostatic against most Gram-positive and Gram-negative microorganisms. Recent studies have reportedly shown that staphylococci resistant to penicillin and "streptomycin-resistant dysentery" proved still sensitive to *Coptis* [Ho *et al.* (23); Chin (24); Tsou *et al.* (25); Ch'i (26)]. The modern Chinese and Western pharmacologic literature dealing with the medical use of *Coptis*, particularly in bacillary dysentery, and its alkaloid, berberine was reviewed by Yeh *et al.* (27). Other plants showing significant antibacterial activity include *Rhus javanica*, L., *Prunus mume*, S., Chinese redbud bark, *Cornus officinali*, etc. With respect to antifungal medicinal herbs, *Polygonatum giganteum* appeared to possess definite fungicidal activity in athlete's foot (6).

Some of the herbs which have been claimed to have useful therapeutic attributes other than antiparasitic and antibacterial activity and which have at least been studied to some extent in the pharmacologic laboratory may be briefly mentioned as follows [(6); Gerasimenko (28)].

Plants reported to possess hypotensive properties include *Rauwolfia verticillata* (grown in South China and Hainan Island), *Veratrum schindleri* (containing a new alkaloid, tien mulilminine) [Chin & Hsu (29)], *Veratrum nigrum*, *Ervatamia divaricat*, L., *Salsola ruthenica*, *Cleodendron trichotomum*, T., *Paeonia moutan*, and *Conioselinum univittatum*. Diuretic effects were noted in *Lobelia radicans*, T., *Akebia quinata*, *Phyllostachys puberia*, M., *Lagenaria vulgaris*, S., and *Loranthus parasiticus*, L. [Chang *et al.* (30)]. Cardiac stimulant effects were reported for *Strophanthus divaricatus*, *Periploca sepium*, and *Nerium indicum*. Analgesic properties were noted in *Cordalis ambigua*, *Cocculus diversifolius*, and *Scolopia japonica*. Uterine stimulant effects were reported for *Ligusticum acutitlobum* and *Leonurus sibiricus*. *Panax ginseng*, the well-known Chinese universal tonic, has recently been reported to show hypoglycemic as well as cardiogenic activity, to reduce cocaine-induced convulsions, and to promote recovery from experimental hemorrhage and asphyxia in dogs. Sung (31) found that rats given ginseng withstood heat stress better than untreated controls, suggesting that the drug reduced endogenous corticosteroid requirements. *Justicia gendassa* and *Sinomenium acutum*, two herbs commonly used by the Chinese traditional practitioners for the treatment of painful joints and rheumatism, have been found to contain alkaloids showing activity similar to that of the salicylates and causing depletion of adrenal ascorbic acid. Cortisone-like properties were also noted for *Glycyrrhiza glabra*, L. (licorice) (32). One of its constituents, hypoglycyrrhic acid, appeared to possess action similar to that of desoxycorticosterone. There are favorable clinical reports on the use of licorice in a variety of disorders, notably Addison's disease in which this drug caused retention of serum sodium, rise in blood pressure, and general well-being. Another interesting property of licorice reported to have been demonstrated in animal experimentation is its antidotal effect against tetanus toxin. This antidotal action is said to be increased when used in conjunction with oil of turpentine.

Mainland China's vast health needs and desperate shortage of trained scientific personnel, particularly pharmacologists, are being met by a crash program that combines modern medicine with the lore of the traditional herb. This stress on applied and developmental rather than fundamental research, and on quantity rather than on quality has apparently helped the nation to make important strides in achieving and expanding its health services on a large scale, especially in the field of parasitic diseases. For instance, schistosomiasis, which used to be a disease seriously endangering the health of about ten million people distributed in 13 provinces, is now claimed to have been practically wiped out in approximately 60 per cent of the former areas of prevalence. The prevalence of malaria, filariasis, and kala-azar has also been reported to have been brought under control in many areas [(8); Du (33)].

Chinese traditional medicine is of great interest as a rich source of potential therapeutic agents. Developed over the course of more than 3000 years, there are now about 3000 traditional drugs, of which some 800 are in common use. Approximately two-thirds of these are of vegetable origin. Chinese popular folk medicine presents a complex problem for study because their prescriptions usually consist of many ingredients of vegetable and often partially animal and mineral origin. The task of studying scientifically such complex prescriptions must be approached in four different ways: (a) by examining a number of complex formulae used for the same or similar disorder and selecting the best of them; (b) by re-examining the ingredients of the formula and eliminating those which have proved to be inactive; (c) by individual study of the ingredients which play the main therapeutic role in the prescription; and (d) by a combined use of modern and traditional drugs.

To meet the increasing demands for traditional Chinese drugs, their cultivation has recently been greatly accelerated. Intensive campaigns have been launched to encourage people to grow medicinal plants. According to a recent official estimate, in 1959 the plantations aggregated over three million *mu* (*mu* = 1/15 hectare), an increase of 52 per cent over that of 1958, while the total value of production rose by 39 per cent (21). Also a number of medicinal plants are reported to have been successfully transplanted. To cite one example, the tonic ginseng, which was thought to be adaptable for cultivation only in the northeastern provinces, is said to have been successfully planted in other areas, such as Shansi, Hopei, and Yunnan. In this connection, it is of interest to mention that ginseng has been grown in the United States (in Wisconsin and Minnesota) for many years and has supplied the China market until the present decade.

With the current mass alignment of medical personnel to study Chinese folk medicine, progress will certainly be made toward discovering useful traditional drugs, if the pharmacologic and clinical research programs are carried out on a more scientific level. Perhaps in the ancient Chinese art of herbalism will be found the key to unlock mysteries that have confounded Western medical science for years. Only time and intensive research will provide the answer.

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## CONTENTS

THE PHARMACOLOGISTS OF EDINBURGH, <i>J. H. Gaddum</i> . . . . .	1
HIGHLIGHTS OF PHARMACOLOGY IN MIDDLE CHINA, <i>James Y. P. Chen</i>	11
HIGHLIGHTS OF PHARMACOLOGY IN INDIA, <i>B. Mukerji, N. N. De, and J. D. Kohli</i> . . . . .	17
HIGHLIGHTS OF PHARMACOLOGY IN CENTRAL EUROPE, <i>Helena Ráskova</i>	31
BIOCHEMICAL MECHANISMS OF DRUG ACTION, <i>James A. Bain and Steven E. Mayer</i> . . . . .	37
THE RELATIONSHIP BETWEEN CHEMICAL STRUCTURE AND PHARMA- COLOGICAL ACTIVITY, <i>B. M. Bloom and G. D. Laubach</i> . . . .	67
MECHANISMS OF DRUG ABSORPTION AND EXCRETION, <i>David P. Rall and C. Gordon Zubrod</i> . . . . .	109
METABOLIC FATE AND EXCRETION OF DRUGS, <i>E. Boyland and J. Booth</i>	129
INVERTEBRATE PHARMACOLOGY SELECTED TOPICS, <i>Frederick Cresci- telli and T. A. Geissman</i> . . . . .	143
PARASITE CHEMOTHERAPY, <i>Edward F. Elslager and Paul E. Thompson</i>	193
SITES OF ACTION OF SOME CENTRAL NERVOUS SYSTEM DEPRESSANTS, <i>Edward F. Domino</i> . . . . .	215
DRUGS AFFECTING THE BLOOD PRESSURE AND VASOMOTOR TONE, <i>W. S. Peart</i> . . . . .	251
RENAL PHARMACOLOGY, <i>Alfred E. Farah and Tracy B. Miller</i> . . .	269
PHARMACOLOGICAL CONTROL OF ADRENOCORTICAL AND GONADAL SECRETIONS, <i>Pieter G. Smelik and Charles H. Sawyer</i> . . . .	313
TOXICOLOGY: INORGANIC, <i>Harry Foreman</i> . . . . .	341
THE SMALLER HALOGENATED HYDROCARBONS, <i>Maynard B. Chenoweth and Carl L. Hake</i> . . . . .	363
RECENT DEVELOPMENTS IN CHEMICAL AND BIOCHEMICAL ASSAY TECH- NIQUES APPLICABLE IN PHARMACOLOGY, <i>R. P. Maickel and H. Weissbach</i> . . . . .	399
REVIEW OF REVIEWS, <i>Chauncey D. Leake</i> . . . . .	415
AUTHOR INDEX . . . . .	431
SUBJECT INDEX . . . . .	456
CUMULATIVE INDEXES, VOLUMES 1-2 . . . . .	475