

HISTORY AND HIGHLIGHTS OF SPANISH PHARMACOLOGY

◆6630

F. G. Valdecasas

Department of Pharmacology, University of Barcelona, Barcelona, Spain

Spain, a country geographically situated by the Mediterranean Sea, which it limits to the west, has followed in all scientific aspects the cultural evolution of the peoples who have inhabited the shores of this sea since very ancient times. Spain especially assimilated Latin culture and has always been considered a representative Latin state.

The great political and military upheavals that first unsettled and then destroyed the Roman Empire in the West about the fourth century AD brought with them a scientific decadence, especially in medicine. The ancient science was almost completely neglected and was only partially saved by some scholars who flourished in isolated parts of the collapsed Empire. Isidore of Seville (560–636), and Cassiodorus (490–583) and Boethius (480–524), both of Rome, recaptured in their works some of the ancient wisdom and passed it on to later centuries. *Etymologiae*, a book by Isidore, contains some pharmacological knowledge in its *Liber Quartus de Medicina* (1).

It was at this time that the different countries heir to the ancient civilization began to emerge politically and culturally in Europe. From this moment we must take into account the Spanish contribution to science in general and pharmacology in particular.

We divide the history of Spanish pharmacology and its relevant facts into three periods: 1. Arabian-Spanish pharmacology; 2. Renaissance and geographic discoveries; and 3. scientific pharmacology.

THE ARABIAN-SPANISH PERIOD

The well-known Arabist M. Levey said (2), "In pharmacology and pharmacognosy, the medieval islamic peoples far surpassed the Greeks and Latins." Actually, the invasion of the Mediterranean countries by Islam from the seventh century AD again promoted the interchange of knowledge between East and West, thus permitting the flourishing of all the sciences but in particular medicine and pharmacology. The Arabs conquered the Iberian Peninsula about the years 710–720 AD and established their capital in Córdoba. The great Arabian-Spanish culture reached its zenith

between the ninth and twelfth centuries in the period of the Caliphate. Most of the natives were converted to Islam although they lived peacefully with the Jewish and Christian peoples. At that time, Córdoba appeared as the most culturally important city of the West. Arabian pharmacology is fundamentally related to the Greek, and the book of Dioscorides (3) serves as a model. The Arabs, however, gained their knowledge also from Syria, Persia, India, and China as the etymology of the adopted names testifies. Moreover they evolved specialized literary forms for their pharmacological texts. One of these was the very useful list of synonyms which gave the equivalent terminology in Greek, Spanish, Persian, Berber, Hindi, and other languages. In Levey's opinion, one of the best-known list of synonyms is that of Maimonides (1135–1204), a Jewish scholar born in Córdoba. A great number of manuscripts on medicaments of this time have been preserved, some still unstudied. For further details of the history of Arabic-Spanish pharmacology we advise consulting Levey (4), Meyerhof (5), Dubler & Terés (3), Hamarneh (6), and Dietrich (7).

Among the numerous scientists of this epoch the following merit mention: Abulcasís, born in Medina-Zahara near Córdoba, wrote the medical encyclopedia *Al-Tasríf* (8). His disciple Abenguefith, born in Toledo, was the author of a treatise on drugs, whose manuscript is preserved in the library of the Escorial—still unstudied but translated in abstract into Spanish and Catalan (9). Ibn Buklārīš, born in Almería, wrote the very famous treatise on drugs called *Al-Musta'ini* (10). Averroes, born in Córdoba, had a great influence in medieval philosophy and authored an encyclopedia called *Al-Kulliyāt* (known in Latin as *Colliget*). Abenpace, born in Zaragoza wrote a book of experiences in medicines. The famous Al-Ghāfiqī, born in Córdoba, was the author of a book of Simples of which there exists only one copy abbreviated by Barhebraeus (11). Maimonides, born in Córdoba, who had to emigrate to the East for reasons of religious persecution, was one of the greatest scholars of his age. Abenvitar (Ibn al-Baitār), born in Seville, authored a treatise called *Yami' al-Mufradāt* or Collection of Simples (12) which has been preserved and has been translated and studied by Leclerc. Finally, it would be possible to quote others whose names have been lost and whose works have reached us anonymously, such as the *'Umdat al-Tabīb* studied by Asín Palacios (13).

This great age was immensely important for future science. On the one hand it served as a connection between the ancient culture and the European Renaissance and on the other it greatly increased the knowledge of drugs as is pointed out by Meyerhof, Levy, Dubler, and many others. The above works were translated into Latin in their own time by schools of translators like the famous one in Toledo. The great influence of these works on the science of medicaments is shown by the etymology of European names of many drugs and compound medicines. [See Meyerhof (5), Valdecasas & Glanzmann (14), and Dubler (15).]

RENAISSANCE AND GEOGRAPHICAL DISCOVERIES

The end of the fifteenth century and the beginning of the sixteenth represents a milestone in Spanish culture. The Spanish-Islamic war had ended with the conquest of the Arab kingdom of Granada in January 1492, and the discovery of America

at the end of the same year by Spanish ships commanded by Christopher Columbus opened a great period of cultural growth and political influence for Spain. Interest in the study of medicines doubled with the knowledge of the new plants found on the American continent and was influenced by the great knowledge of drugs of aboriginal American cultures, especially of the people of Mexico and Peru. Moreover the pharmacological renaissance began again with the study of the work of Dioscorides, of which several editions in Latin have been printed (16). Andrés Laguna (1499–1560) first translated the *Materia Medica* of Dioscorides into Spanish (17) and published it in Antwerp in 1555. Later, several editions were made. Laguna's translation is one of the first in a modern language, and he deserves the credit for spreading the master work of Greek pharmacology among the non-Latin speaking doctors and surgeons (called at his time *romancistas*). However, for us the most important parts of his work are his comments on drugs. In them, synonyms in the different languages are given and all the plants are identified by their popular names. It is worth noting the comments on opium and solanum (18, 19) where he mentions their use by witches. Other authors who must be mentioned are F. L. de Villalobos, who wrote a treatise in Spanish on syphilis that was printed in 1498, and Gaspar Torrella, author of another treatise on the same illness printed in Latin in Rome in 1497. In both books the use of mercury ointment was mentioned, a fact that must be regarded as a positive pharmacological advance in an illness discovered three or four years earlier.

The great novelty of the discovery of America and of the plants and animals, until then unknown, found there, attracted the attention of scholars and stimulated the development of knowledge in all natural sciences (20). Among the more prominent authors, we may mention, on the one hand those who went to America very young and identified themselves with the indigenous learning, thus facilitating the transmission of knowledge between them and the native people, and, on the other those scholars who went as distinguished intellectuals charged by royal command to study the things of the New World.

The early foundation of universities was of primary importance. In 1536 the *Colegio Mayor* (University College) of *Santa Cruz in Tlatelolco* (Mexico) was already functioning and in 1551 the Universities of Mexico and Lima (Perú) were founded. From this first period we have the wonderful *Codex Badiano* of 1552 by a native Mexican author Martin de la Cruz, physician of the *Colegio Mayor*, which was translated into Latin by another native, Juan Badiano, a professor of the same college. We would like to point out the cultural interchange arising at this early date from the existence of a University where pupils and teachers of native and European origin worked together harmoniously. The *Codex Badiano* recently edited in facsimile by the Mexican Social Security (21) represents a beautiful aspect of the pre-Colombian knowledge of drugs describing the plants in such a way that even today many of them are identifiable.

Bernardino de Sahagún (1499–1590) is another author worth mentioning. After studying in Salamanca he went to Mexico very young, living for a time in Tlatamalco. He then became one of the first professors in Tlatelolco, and later traveled to different places, among them Xochimilco and Tepepulco where he studied the knowledge of the native people in every subject but especially in medicine. He

mentions that his informants were experienced doctors. According to Efen del Pozo (21) Sahagún's view of Aztec medicine was genuine. The notes of the indigenous people in their own languages and his translation into Spanish are very valuable for linguistic scholars as well. His work has been published in Mexico recently by Porrua (22) but there remain many original manuscripts by Sahagún that are being studied. His works are, like the *Codex Badiano*, a source of pre-Spanish medical knowledge.

Knowledge of the New World drugs was of capital importance although it was mixed with magic ideas and rites. Among the new drugs there were many with positive actions later used in Europe. The foremost examples include cinchona, coca, curare, rhatany, jalap, and the hallucinogenic drugs derived from fungi and plants that are very much studied today.

Among the cultured authors who went to America charged with the duty of studying the things of the New World, Gonzalo Fernández de Oviedo (1478–1557) and Francisco Hernández (23) merit special mention. The first was a soldier of great culture who had previously been in Italy and the second was the Royal Physician to Philip II. They both wrote guides to natural history that became widely known. In both, the descriptions of medicinal plants are a prominent feature.

Other scholars, without leaving Spain, collected and studied data brought by those who traveled to and from the New World. Outstanding among these was N. B. Monardes (1493–1565) who wrote *A Book on the Things Brought from our West Indies that Are Used in Medicine*. It was published in Seville in 1565 and was an American medical treatise (24). The erudite Italian P. M. Anghiera, canon of the Cathedral of Granada (1459–1526), was the first to mention the existence of the arrow poison curare and its effects in his *De Orbe Novo Decades*, II (25). The complete story would be interminable.

One item of the Renaissance important to the progress of pharmacology was the coding of drugs in officially accepted books first by pharmaceutical guilds and later by European states. We refer to the pharmacopoeias or codes medicamentorum, one of the first of which, the *Concordia Apothecariorum Barcinonensis*, was printed in Barcelona in 1511 and officially used in the kingdom of Aragón.

SCIENTIFIC PHARMACOLOGY

It is certain that pharmacology as an experimental science did not come into being until the midnineteenth century. However, we must consider that the detailed knowledge of plants and their systematic classification by C. Linnaeus in the eighteenth century provided the basis for the future study of the active principles of drugs and their actions. Among the Spanish botanists of the eighteenth century we mention Hipólito Ruíz (1754–1816) and Josef Pavon (1754–1840), his companion on a Peruvian expedition. The first was author of a *Quinologia* (26) or treatise on the cinchona trees in which he clearly describes cinchona. He also discovered and classified many plants, one being *Chondodendron tomentosum* R. P., from which D-tubocurarine is obtained today. José Celestino Mutis was another notable botanist (1732–1808). He described the flora of the Columbian Andes in his book *The Flora*

of Bogota. Through his profession as a doctor he gave many details of the use of these drugs.

Gaspar Casal (1680–1759) was an early student of the deficiency diseases. He wrote a *Historia Natural y Médica del Principado de Asturias* in which he described for the first time a new illness called mal de la rosa (Sickness of the Rose), now known by the name of pellagra. He described its symptoms, including the ultimate stage of insanity. He related this illness to nutrition, noting that the best remedy was the eating of good nutritious foods (27).

The founding of the Colleges of Surgeons in the middle of the eighteenth century was most important for Spanish medicine and pharmacology. The first such school was developed by the well-known Pedro Virgili (1699–1776), assistant to the chief surgeon of the fleet, D. Juan Lacomba. The sad condition of the men in the ships noted in Cádiz by Virgili, their illnesses and wounds, aggravated by the poor quality and scarcity of surgeons of that time, affected him so much that he founded a School of Surgery in Cádiz, which proved to be an enormous success (28).

Naturally, conflicts arose with the faculties of medicine and disputes over the awarding of degrees. The College of Cádiz (29, 30) was followed by those of Barcelona in 1760 and Madrid in 1787, founded by Gimbernat. Unification of the teaching of medicine and surgery was finally reached in 1799. The creation and early years of the colleges were similar to those of the Caroline Medico-Surgical Institute (1810) according to Liljestrand's description of the latter (31).

In the College of Cádiz a modern study of medicine and surgery was begun. Chairs of physiology and therapeutics were created, great attention was paid to chemistry, and an experimental laboratory was set up. Scholars were also sent to Paris to broaden their knowledge as much in chemistry as in botany and other sciences (32).

We must also make reference to the organization of the teaching of physiology by Dr. Blasco, the Rector of the University of Valencia in 1787. He ordered the vivisection of animals for better understanding of physiology by the students (33).

The nineteenth century, which was the period of outstanding medical and therapeutic advance all over Europe, saw in Spain the greatest period of decadence in its history. It was impoverished by continuous civil wars and deprived of the forces necessary to compete in the constantly expanding European scientific progress. The scientific growth of the eighteenth century was halted and Spanish science in general found itself in a doldrum from which it finally emerged with difficulty at the end of the nineteenth century.

A new period of scientific ferment began in 1898. That year, which marked the loss of the last Spanish overseas possessions, was the starting point of a new period. The men who impelled this new renaissance have been called the generation of '98. At that time there were ten relatively inactive medical schools in the whole country. Each had a department of therapeutics but few or no animal experiments were done. The men of '98 took upon themselves the task of changing this state of affairs in all fields of science.

In the field of experimental medicine there was S. Ramón y Cajal (1852–1934), Nobel prize winner of 1906. His descriptions of the microscopic structures of the

central nervous system are still of great importance in the understanding of cerebral physiology and pharmacology. His principal work, *Histologie du Système Nerveux de l'Homme et des Vertébrés*, was published in French in 1909. Cajal's most important contribution to pharmacology was the concept of neuronal articulation, afterwards called synapse by Sherrington. Cajal demonstrated the individuality of the nerve cell and how its extending fibers were in contact but never in continuity with other fibers or bodies of neighboring cells.

Of Cajal's numerous followers several made important contributions to pharmacology by applying Cajal's histologic techniques. We mention Lorente de No, P. Río Hortega, and F. Castro.

T. Hernando, M. D. (1881–) was Associate Professor of Therapeutics in Madrid. He received some experimental training with M. Márquez (later Professor of Ophthalmology). He studied pharmacology with Schmiedeberg in Strasburg and returned to Spain with new ideas about experimental pharmacology. Professor of Therapeutics in Madrid in 1912, he created a Department of Experimental Pharmacology (1928), trained many students, and was co-founder in 1933 of the International Union of Therapeutics with Loeper, La Barre, Bürgi, Gordonoff, Marañón, and others. The major part of his research was concerned with vitamins. He showed in animals the preventive effects of Vitamin C in cases of gastric ulcers and other digestive problems. In collaboration with R. Mendez and P. Cirera in 1934 (34), he demonstrated that lack of sodium in the diet produces hypertrophy of the adrenal cortex, which is supposed to be one of the first works on this sodium-adrenal cortex relationship. Another field cultivated by Hernando was investigation of digitalis, especially in collaboration with T. Alday. He took great interest in the regulation of medicaments and was Director of the Technical Institute of Pharmaco-Biology, a center devoted to this problem.

J. Negrín (1894–1956) was Professor of Physiology in Madrid in 1922. Born in Las Palmas, Canary Islands, he studied medicine in Germany and Italy. Best known for his political activities (in 1939 he was the last President of the Spanish Republic), his scientific work was also very important. With Professor F. Aguilar he was prime mover, under the auspices of King Alfonso XIII, of the construction of the new University City of Madrid and was its Executive Secretary. With Hernando he also helped create the Institute of Pharmaco-Biology. As Professor of Physiology he developed an important undertaking attracting a large group of students. He created (with the collaboration of Guerra and Corral) a small but very productive Institute of Physiology subsidized by the *Junta para Ampliación de Estudios* (Council for the Widening of Studies). His research work was concerned mostly with the physiology and pharmacology of the autonomic nervous system. He devised a stactometer with a graphic register that was a novelty in his time.

A. Pi Suñer, M. D. (1879–1965), Professor of Physiology in Barcelona (until 1939, and later Professor of Experimental Medicine in Caracas, Venezuela), greatly stimulated experimental pharmacology and together with Professor J. M. Bellido, also a research collaborator, he founded the Institute of Physiology in Barcelona in 1921. He founded the Society of Biology in Barcelona in 1913. The greater part of his research dealt with the autonomic nervous system on which he published a very

comprehensive book (35). He published in *Physiological Reviews* a work on regulation of respiratory movements (36).

J. M. Bellido, M. D. (1880–1952), Professor of Pharmacology in the same University and a friend and colleague of Pi Sunyer, contributed equally to the modern development of pharmacology in Spain. Among his works, we must mention the study of the electrocardiographic effects that accompany (37) digitalis poisoning.

J. M. Corral, M. D. (1889–1972), Professor of Physiology in Madrid, was a colleague of Negrín and followed him in the chair in 1939. He founded the Spanish Society of Physiological Sciences (which included pharmacology) and was its first President. He cultivated biochemistry especially. Other authors worthy of note are: J. G. Blanco, Professor of Physiology in the University of Valencia, and J. Sopena, Professor of the University of Seville. All of them contributed to the promotion of research and gathered many followers.

The Spanish Civil War (1936–1939) completely interrupted all work in the Universities. During the postwar period, research facilities were also greatly reduced. The beautiful new buildings of Madrid's University City were totally destroyed, as was all scientific equipment. Worst of all was the dispersal of the researchers. The majority of those young men who had crowded into the recently created research centers in Madrid and Barcelona emigrated, continuing their work in foreign countries and even changing their citizenship. In spite of this I believe that they must figure in a history of Spanish pharmacology not only because of their birth but also because of their scientific training. We shall mention them briefly.

Outstanding among them are: S. Ochoa, Professor of Pharmacology and later of Biochemistry at New York University, a Nobel Prize winner for his work on the enzymatic synthesis of RNA (1959); Jordi Folch, Professor of Neurochemistry at Harvard Medical School; R. Méndez, Professor of Pharmacology in the Institute of Cardiology in Mexico; R. P. Cirera, Professor of Pharmacology in the University of Mexico; Antoni Oriol, Professor of Physiology in the National Polytechnic Institute of Mexico; J. G. Valdecasas, Professor of Physiology of Granada, who later created important pharmaceutical laboratories in Mexico City; J. Puche, Professor of Physiology of Salamanca and later of the National University of Mexico; and many others. This was a true brain drain that added to the impoverishment and to the lack of means of research in Spain.

Those who remained in Spain had to start again from scratch. We have mentioned J. M. Corral, who succeeded Negrín as Professor of Physiology in the University. He founded the Spanish Society of Physiological Sciences and worked hard in the reconstruction of laboratories and the restoring of the library of the University City. However, the facilities for research were not great so the drain of scientists continued. For example after the war F. Grande, Professor of Physiology of Zaragoza (1909–), left to become Professor in the University of Minnesota in Minneapolis; R. Delgado left to become Professor at Yale University. S. Grisolia also later became Professor at the University of Kansas.

F. G. Valdecasas (1910–) succeeded Bellido as Professor of Pharmacology in Barcelona. He began his training in pharmacology in Madrid with Hernando and Negrín, and continued it in the Institute of Physiology in the University of Göttin-

gen under H. Rein and various U. S. Universities. Associate Professor of Physiology of the University of Madrid (1935), he moved to Barcelona in 1940, and later became President of the CINP (1966–1968). His field of investigation has been vitamins and catecholamines. He demonstrated the synthesis of Vitamin C in normal animals (38), the different effects of small doses of epinephrine, and that occluding the carotids did not impede hypotension produced by the rise of the pressure in the carotid sinus if the carotid reflex was blocked by reserpine (39). He also worked on pharmacological effects of enzymes (40).

A. Gallego (1915–), Professor of Physiology in the University of Seville (1950), followed Corral as Professor in Madrid (1961). He founded the Spanish Institute of Pharmacology. He began his research training with Corral and Negrín during the last years before the civil war, continuing later (1947) in the Rockefeller Institute under Lorente de No, where he worked on the effects of ethyl alcohol upon nerves (41). He has also made important contributions in the field of antibiotics.

After the civil war, research facilities improved slowly. The foundation of the High Research Council (CSIC) was an important factor in this, to which has been added the creation of new Universities and scientific posts. Moreover research in the pharmaceutical industry has been greatly helped in its development by the economic improvement of the country during the past years.

A new generation of young scientists has arisen. A great part of their training has been received in U. S. centers under the guidance of Spanish-Americans such as Ochoa, Grisolia, Grande, Folch, Lorente de No, etc, who have helped greatly in the scientific advancement of these young men. Neither must we forget other Professors such as B. B. Brodie, Cori, Furchgott, Greengard, Hazard, Cheymol, and many others in the USA, France, and other countries, who helped Spanish students.

In short, although the level reached can hardly be considered satisfactory for a country with such ancient scientific traditions and more than thirty million inhabitants, we can at least say that scientific research is slowly but surely progressing.

It would be impossible in the space available to enumerate all the centers and all the Spanish researchers in the fields of science related to pharmacology. Biochemistry has reached a particularly advanced stage of development and, as is natural, many of its papers are about pharmacological actions at the molecular level. We shall try to point out what appears to us to be most important so that the present situation of pharmacology in Spain may be appreciated.

In Madrid the Department of Pharmacology of the Complutensis University is directed by Professor P. G. Jalón, M. D. The pharmacological education that he received in Spain was supplemented in England and the USA. His adrenalin assay is well known. In the Autonomous University of Madrid, pharmacology is within the Physiological Sciences Department, which is directed by J. R. Delgado (ex-Professor of Yale). His works on the physiology and pharmacology of behavior are well known. Associate Professor of Pharmacology was P. Sánchez, now Professor in Valladolid. His pharmacological education was completed in the Pharmacology Department of New York's Down State University under Furchgott.

The *Centro de Investigaciones Biológicas* (CSIC) of Madrid is very active. It comprises various institutes and departments. Professor J. L. R. Candela directs the

Department of Molecular Biology. He works on insulin, glucagon, calcitonin, and other hormones. Professor A. Sols is Director of the Institute of Enzymologie (Autonomous University) of Madrid. He received his training with Cori and Ochoa, and he was the first President of the Spanish Society for Biochemistry. He is the author of specialized chapters in different books (42, 43). J. Río, PhD, is Director of the Department of Pharmacology in the Institute of Chemical Medicine (CSIC). He received his research training in Madrid under Professor Lora and Barcelona under Professor Valdecasas. His principal field of investigation is psychopharmacology with drugs prepared in Professor Madroñero institute and belonging to the series thienylpyrimidine and indolylhydrazine. Professor D. Vázquez, PhD, is Director of the Institute of Cellular Biology (CSIC). His field of research is protein and RNA synthesis and he has studied the action of several antibiotics.

In Barcelona the new Autonomous University has departments of clinical and experimental pharmacology. J. A. Salvá, M. D., is Professor of Experimental Pharmacology. His pharmacological training was complemented in Paris under Professors Hazard and Cheymol. His research field is the pharmacology of the steroidal alkaloids (44). J. Laporte, M. D., is the Professor of Clinical Pharmacology. His pharmacology training was obtained in Barcelona and then in Milan under Professor Garattini. His principal research field is the pharmacology of hemostasis (45). S. Erill is Associate Professor of Clinical Pharmacology. He began his training in Clinical Pharmacology in Barcelona and later complemented it in the USA at the Universities of Kansas and Michigan. His principal field of research is in pharmacokinetics and drug interactions. He is dedicated to medical education.

Dr. P. Puig-Muset, Director of Pevya Research Institute, has been one of the pioneers studying the pharmacology of imidazole (46) and other provocative substances (chymotrypsin, hepatocatalase, lipoxidase, etc).

Professor E. Cuenca, M. D., is Chief of the Department of Pharmacology in Cadiz. His pharmacological training was complemented in Bethesda under Professor Brodie. He is the European Secretary of the CINP. His works on the biochemistry of antidepressant drugs are well known (47).

Professor Sánchez de La Cuesta (1907–) is Chief of the Pharmacology Department of Seville. His pharmacological training was begun with Hernando and complemented in Belgium under Professor Zunz. Professor E. Muñoz, Director of the Department of Pharmacology in Granada, and Professor R. Villarino (1905–), Director of the same in Santiago, are also worthy of mention.

Professor E. Herrera, PhD, is Director of the Department of Physiology of the Faculty of Sciences in Barcelona. His field of activity is the metabolism of the carbohydrates and relevant pharmacological actions. Young and very active Directors of Pharmacology Departments are also to be found in the Universities of Valencia (Professor Esplugues), Murcia (Professors Serrano and Jané), Bilbao (Professor Segarra), La Laguna (Professor Flórez) and Salamanca (Professor Bayo).

J. Forn, M. D., is Associate Professor of Pharmacology in the Barcelona University. His training was complemented in Bethesda under Professor Brodie and he is working now in Yale with Professor Greengard. Associate Professor M. Puig, M. D., Associate Professor L. Rodríguez, PhD, Associate Professor E. Rodríguez, M.

D., and Professor E. Planas are very active in Barcelona after complementing their research training abroad. Space does not permit us to give more details of their research activities.

ACKNOWLEDGMENTS

To Professor J. Vernet for his valuable information on the Arabian-Spanish period, to Professor T. Hernando for the data on the first half of the present century, to Dr. Juan Negrín Jr., for the data about his father, to J. G. Valdecasas for having sent to me examples of the new Mexican editions, and in general to all who have sent data to enable me to achieve this difficult task. To Professor D. MacDermott for correction of the English text.

Literature Cited

1. Isidorus Hispalensis. 1945. *Ethimologiarum. Liber IV. De Medicina*. Facsimile from a 1493 printing. Transl. D. Bermúdez, C. E. Arqués. Barcelona: Lab. Norte de España. 92 pp.
2. Levey, M. 1966. *The Medical Formulary of al-Kindi*. Madison/Milwaukee/London: Univ. Wisconsin Press. 410 pp.
3. Dubler, C. E., Terés, E. 1957. *La versión árabe de la "Materia Médica" de Dioscórides*. Barcelona: Dubler. 804 pp.
4. Levey, M. 1973. *Early Arabic Pharmacology*. Leiden: E. J. Brill. 187 pp.
5. Meyerhof, M. 1935. *Al-Andalus* 3:1-41
6. Hamarneh, S. K. 1971. Arabic medicine and its impact on teaching and practice of the healing arts in the West. *Convegno Internazionale; Aprile 1969. Fondazione Alessandro Volta*, 395-429. Roma: Fondazione A. Volta
7. Dietrich, A. 1971. Quelques observations sur la matière médicale de Dioscoride parmi les arabes. *Convegno Internazionale; Aprile 1969. Fondazione Alessandro Volta*, 375-94. Roma
8. Hamarneh, S. K., Sonnedecker, G. 1963. *Janus Suppl.* 5: 1-129
9. Faraudo de Saint-Germain, L. 1943. *Transcripción, estudio proemial y glosarios de: El "Libre de les medicines particulars."* Versión catalana trescentista del texto árabe del "Tratado de los medicamentos simples" de Ibn Wáfid (Abenguefith), autor médico toledano del siglo XI. Barcelona: Real Academia de Buenas Letras de Barcelona. 198 pp.
10. Labarta, A. M. 1972. *El Prólogo de Al-Musta Inī de Ibn Buklārīš según los manuscritos de Madrid y Nápoles*. PhD thesis. Univ. Spain, Barcelona. 221 pp.
11. Meyerhof, M. 1932. *The abridged version of the book of simple drugs of Ahmad ibn Muhammad Al-Ghāfiqī*. Cairo: Egyptian Univ. 719 pp.
12. Leclerc, L. 1877, 1881, 1883. *Ībn al-Baitār (Abemvitar) Traité des simples*. Paris. 3 vols. 1021 pp.
13. Asin Palacios, M. 1943. *Glosario de voces romances registradas por un botánico anónimo hispano-musulmán de los siglos XI-XII*. Madrid-Granada: Consejo Superior Investigaciones. 420 pp.
14. Valdecasas, F. G., Glanzmann, S. 1959. *Planta Med.* 7:122-27
15. Dubler, C. E. 1954. *Glosario Médico castellano del siglo XVI*. Barcelona: Dubler. 939 pp.
16. Hernando, T. 1968. *Introducción y comentarios al "Pedacio Dioscórides Anazarbeo de A. Laguna. 1555. 1:17-133*. Madrid: Instituto de España. 2 vols. 1061 pp.
17. Dubler, C. E. 1955. *La "Materia Médica" de Dioscórides traducida y comentada por D. Andrés Laguna*. Barcelona: Dubler. 621 pp.
18. Rothman, T. 1972. *Bull. Hist. Med.* 46:562-67
19. Valdecasas, F. G. 1968. Opening Address. *VI Int. Congr. CNP, Tarragona. Excerpta Med. Int. Congr. Ser.* 1800:3-8
20. Hanke, L., Mendoza, G. 1965. *Historia de la Villa Imperial de Potosí por Bartolomé Arzans de Osua. 1:XXVII-CLXXV*. Providence, R. I.: Brown Univ. Press. 3 vols. 1637 pp.
21. de la Cruz, M. 1964. *Libellus de Medicinalibus Indorum Herbis*. Ms of 1552. Mexico: Instituto Mexicano del Seguro Social. 394 pp.

22. Garibay, A. M. 1969. *Historia General de las Cosas de Nueva España por Bernardino de Sahagun. 1560*. Mexico: Editorial Porrúa. 4 vols. 1461 pp.
23. Hernández, F. 1969. *Historia Natural de Nueva España, 1571*. México: Univ. Nacional de México. 1010 pp.
24. Monardes, N. B. 1569. *Libro de las cosas que traen de nuestras Indias Occidentales que sirven al uso de la Medicina*. Sevilla. 154 pp.
25. Torres Asensio, J. 1892. *Obras de Pedro Martir Angleria. Segunda Década*. 2: 5-208. Madrid: Torres Asensio. 4 vols. 1729 pp.
26. Ruiz, H. 1792. *Quinología o Tratado del Arbol de la Quina*. Madrid. 103 pp.
27. Casal, G. 1st ed. 1762. 2nd ed. 1900. *Historia Natural y Médica del Principado de Asturias*. Oviedo, Spain: Diputación Provincial. 367 pp.
28. Ferrer, D. 1961. *Historia del Real Colegio de Cirugía de Cádiz*. Cádiz: Colegio Oficial de Médicos. 378 pp.
29. Usandizaga, M. 1964. *Historia del Real Colegio de Cirugía de Barcelona (1760-1843)*. Barcelona: Instituto Municipal de Historia de la Ciudad. 243 pp.
30. Usandizaga, M. 1948. *Historia del Real Colegio de Cirugía de San Carlos de Madrid (1787-1828)*. Madrid: Consejo Superior de Investigaciones. 129 pp.
31. Liljestrand, G. 1960. *Acta Pharmacol. Toxicol.* 17:3-6
32. Puigvert, A. 1970. *Facsimile of the "Estatutos y Ordenanzas para la Enseñanza de la Cirugía" from a original of 1764*. Barcelona: Puigvert. 123 pp.
33. Lain Entralgo, P. 1974. *Historia Universal de la Medicina*. Barcelona: Salvat Ed. 6 vols.
34. Hernando, T. 1934. *XVI Int. Physiol. Congr.*, 85
35. Pi Suñar, A. 1947. *Sistema neurovegetativo*. Mexico: Ed. Hispano-Americana. 817 pp.
36. Pi Suñer, A. 1947. *Physiol. Rev.* 27:1-38
37. Bellido, J. M., Farran, M. 1925-1927. *Treballs Soc. Catalana Biol.* 11:320-25
38. Valdecasas, F. G. 1935. *La vitamina C y las cápsulas suprarrenales*. PhD thesis. Madrid Univ., Madrid. 26 pp.
39. Valdecasas, F. G., Soliva, M., Krenn, R. 1955. Acción farmacológica de diferentes especies de Rauwolfia. Acción sobre el seno carotídeo. *II Reun. Soc. Esp. Cienc. Fisiol. (Barcelona)*. 444 pp.
40. Valdecasas, F. G. 1961. Etude experimentale et pharmacologique de la chymotrypsine. *Les enzymes en thérapeutique. VII Congr. Int. Thérapeut.*, 19-25
41. Gallego, A. 1948. *J. Cell. Comp. Physiol.* 31:97-106
42. Sols, A., Gancedo, C. 1972. *Biochemical Regulatory Mechanisms in Eukaryotic Cells*, ed. E. Kun, S. Grisolia. Chap. 4, 85-114. Kansas City: Wiley
43. Sols, A., Marco, R. 1970. *Curr. Top. Cell. Regul.* 2:227-73
44. Salvá, J. A. 1955. *Actual. Pharmacol.* 8:153-76
45. Laporte, J. 1973. *Actual. Pharmacol.* 26:183-207
46. Puig-Muset, P., Puig-Parellada, P., Martín, J. 1972. *Biochemical and Pharmacological Aspects of Imidazole*. Barcelona: Jims. 198 pp.
47. Cuenca, E., Salvá, J. A., Valdecasas, F. G. 1964. *Int. J. Neuropharmacol.* 3:167-71