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"How and when Chilean Pharmacology started to be experimental and became a science"

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ABSTRACT

Pharmacology in Chile has about 75 years of history and from its beginning until today has grown exponentially. Today, pharmacology is taught in the biomedical careers of the main Chilean universities and research centers in pharmacology are in the north, central and south of Chile. This editorial offers an overview of the main milestones that have led to the consolidation of Chilean pharmacology in Latin America and the world.

1. "From the mid forties and up to the late sixties"

Main actors of this time-period are those pharmacologists that should be considered fathers and initiators of experimental pharmacology in Chile: Jorge Mardones Restat, a medical doctor and academic from the Universidad de Chile (UCh) and Fernando García-Huidobro also a medical doctor and academic but now from the Pontificia Universidad Católica de Chile (PUC).

1.1. Dr. Jorge Mardones Restat

He was a truly and one of the first experimental pharmacologists in Chile. In addition, he was the first president of the Chilean Society of Pharmacology (SOFARCHI) (1979); awarded the Chilean Prize of Science (1977); and still very young, nominated as minister of health by the Chilean government (1950–1952) (Fig. 1).

Dr. Mardones pioneered and promoted the strict and adequate use of the statistical analysis when evaluating the relative importance of data obtained from biomedical protocols and from experimental designs in physiology and pharmacology in Chile. He was the creator and pushed forward very strongly the formation and consolidation of the first Institute of Pharmacology (later to become a Department at the UCh) with full undergraduate teaching commitments in biomedical- and health-orientated careers and with full dedication to research in experimental Pharmacology, in Chile. A whole generation of prominent Chilean pharmacologists initiated and obtained their training at this Institute; among them: Carlos Muñoz (President SOFARCHI, 1980–1981), Mario Penna (President SOFARCHI, 1985–1986), Sergio Lecannelier (President SOFARCHI, 1991–1992), Natividad Segovia-Riquelme, Lutske Tampier (President SOFARCHI, 1997–1998), María Elena Quintanilla and many others. Along with them, during the mid-1950s, Dr. Mardones compiled a serial of "monographs", the first in Chile, dealing with General Pharmacology and with special topics in System Pharmacology. Under the direction of Dr. Mardones, the Dept. of Pharmacology at the UCh, became an important center of attraction to many fellowship holders, essentially young and newly graduated medical doctors, dentists and pharmacists, coming from all over Chile and other Latin American countries such as Argentina, Uruguay and Perú. In addition, academics from this Dept. of Pharmacology played an important role promoting experimental Pharmacology in other Chilean universities. The task performed by Dr S. Lecannelier during this time-period at the Universidad de Concepción (UDEC), in the mid-south of Chile, is an example of such an important role.

The "monographs" in Pharmacology compiled by J. Mardones, finally led him to generate by the mid-1970s, the first Chilean textbook of Pharmacology, addressed primarily to undergraduate students from medical, dental, pharmacy and other biomedical careers. This textbook was written with the participation of 29 collaborators, all academics and members of the Dept. of Pharmacology, UCh (Fig. 2).

During the 1950s, Dr. Mardones together with Natividad Segovia-Riquelme and Lutske Tampier, were able to develop and isolate through "breeding" techniques two strains of rats which differ in regard to the spontaneous consumption of ethanol. One of those strain was characterized by a spontaneous and high consumption or "appetite" for ethanol (named UChB rats), while the other strain exhibited a low "appetite" and indeed they rejected to consume ethanol (named UChA). These research findings influenced very strongly and in a pioneering way the concept of genetic characteristics as a determinant factor during the consumption and abuse of ethanol and other drugs. These strains of rats are presently being used by research groups at UCh to study the molecular and cellular mechanisms underlying addiction and dependence to ethanol and other drugs of abuse.

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Fig. 1. Dr. Jorge Mardones Restat, first president of SOFARCHI

Fig. 3. Dr. Fernando García-Huidobro. He is a founding member of SOFARCHI and is considered one of the fathers of Chilean pharmacology.

1.2. Dr. Fernando García-Huidobro

This introverted and rather quiet medical doctor from the Pontificia Universidad Católica de Chile (PUC) was the other important experimental pharmacologist in Chile during this time-period, starting at the early-1950s (Fig. 3). This was a time in which Ariens and Stephenson had developed their concepts of "intrinsic activity" and "efficacy" of the drug–receptor complex in order to account for the diversity of biological effects triggered by the interaction of a drug with its receptor. F. García-Huidobro together with H. Croxatto, through an analysis of dose–response curves generated by adrenergic drugs acting upon peripheral organs, proposed that the formation of the drug–receptor complex was associated with a change in the receptor structure within the membrane. Actually, a change to a "crystal-type structure", involving therefore a release of energy which thermodynamically facilitated the biological responses observed in these peripheral organs following the interaction of the drug with its receptor. At this time (1950s) the model of membrane that predominated was that of Danielli and Davson, a rigid membrane model. The findings by F. García-Huidobro also occurred much earlier than the "fluid mosaic model of cell membranes" proposed by Singer and Nicholson in 1972 and the "mobile or floating receptor hypothesis" formulated in 1974. Therefore, the proposition of García-Huidobro and Croxatto, presented in the late-1950s, was indeed pioneering for that time-period.

In addition, during the 1960s, F. García-Huidobro along wih Carmen Maggiolo developed a method to implant morphine "pellets" in mice, which allowed them to induce a rapid physical dependence and addiction to morphine in these animals. This method was one of the first and most successful experimental models to study dependence and central tolerance to drugs like morphine in mice and rats.

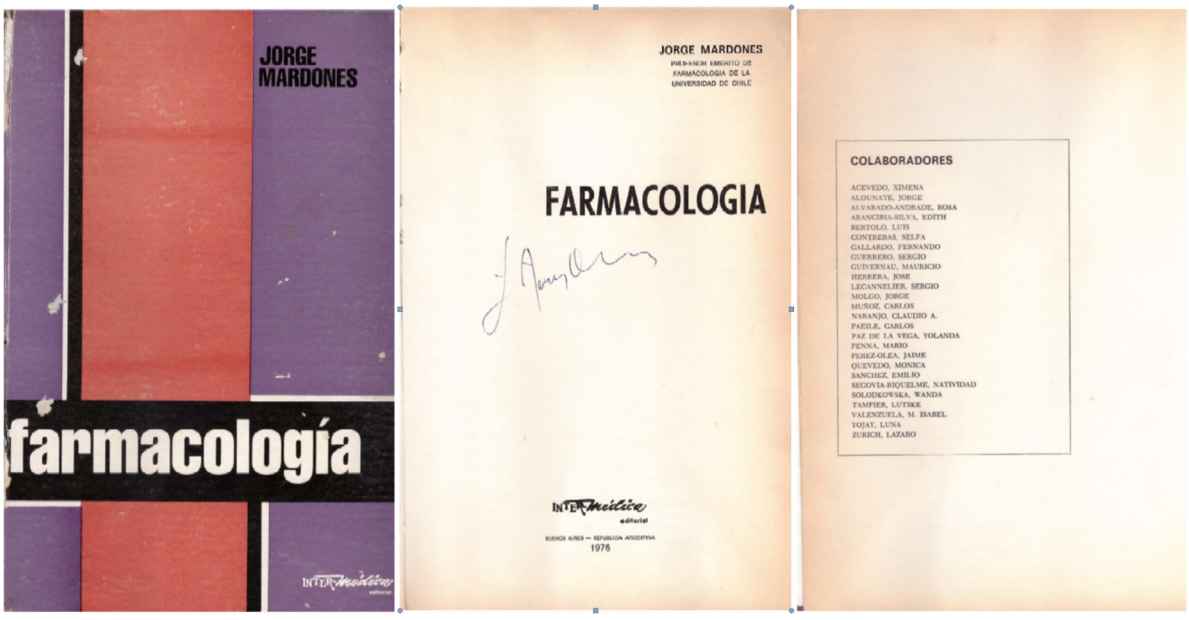

Fig. 2. First Pharmacology book edited in Chile by Dr. Jorge Mardones Restat and colleagues.