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Argentinean Society of Experimental Pharmacology: Brief history and main scientific contributions to the discipline

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Zolpidem, a selective full agonist of the alpha-1 subunit of the benzodiazepine-GABA-A receptor
Mizolastine, a peripherally acting histamine H-1 receptor antagonist
Glutaprodil, a noncompetitive antagonist of the iononotropic NMDA receptor

ABSTRACT

Argentina Biomedical Science has been historically strong. The development of Human and Veterinary Pharmacology in our country as a pivotal discipline has been acknowledged worldwide because of the quality of its contributions. Argentinean Society of Experimental Pharmacology (SAFE) is a non- profit association whose research fields include Experimental and Clinical Pharmacology. SAFE main goals are described as follow (a) To meet active researchers for studying concerns regarding Experimental and Clinical Pharmacology (b) To launch an initiative for development of the discipline in mainly our country and other collaborative countries worldwide (c) To spread the pharmacological know-how obtained from different research teams (d) To strengthen relations between pharmacologists (e) To facilitate the presentation and discussion of scientific papers. This current article shows the SAFE's more important scientific contribution to pharmacology through its former research scientists to the present.

1. Introduction

The development of Human and Veterinary Pharmacology sciences in our country has been acknowledged worldwide because of the quality of its contributions. The Argentinean Society of Experimental Pharmacology (SAFE) was founded in 1968 by those who, at the time, led the investigation of the discipline of Physio-Pharmacology in our country.

Scientist researchers such as Juan A. Izquierdo, Iván Izquierdo, Alfredo Coviello, Luis María Zieher, Francisco Stefano, Salomón Langer, Edda Adler-Graschinsky, María Amelia Enero, Otto Orsingher, Alfredo Donoso, Alvaro Gimeno, Martha Fernández de Gimeno, Modesto C. Rubio, Daniel Cardinali, Rodolfo Rothlin, Damasia Becú, José Tessler, Carlos Baratti among other garner a tradition in basic neuropharmacological research of international importance. Most of them were involved on the SAFE's creation at the end of the 60s.

2. SAFE's former Board Committee in 1968

1 President: Dr. Juan A. Izquierdo (Buenos Aires)

Abbreviations: 5-HT, serotonin; ADH, antidiuretic hormone; ANS, autonomic nervous systems; ATP, Adenosine triphosphate; CNS, central nervous system; DA, dopamine; IUPHAR, Union of Pharmacology; NE, norepinephrine; PUCRS, Pontifical Catholic University of Rio Grande do Sul; SAFE, Argentinean Society of Experimental Pharmacology; UBA, University of Buenos Aires; UFRGS, Universidade Federal do Rio Grande do Sul; UNC, University of Córdoba.

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2 Executive Secretary: Dr. Iván Izquierdo (Córdoba)
3 Secretary I: Dra. Amanda Pellegrino de Iraldi (Buenos Aires)
4 Secretary II: Dr. Luis M. Zieher (Buenos Aires)
5 Tresaurer I: Dr. Augusto V. Juorio (Buenos Aires)
6 Tresaurer II: Dr. Otto Orsingher (Córdoba)

Argentinean Society of Experimental Pharmacology is a non-profit association whose research fields include Experimental and Clinical Pharmacology. SAFE has also been an associate-member of the International Union of Pharmacology (IUPHAR) since the last 30 years.

SAFE's main goals are described below:

- To meet active researchers for studying issues regarding Experimental and Clinical Pharmacology.
- To launch an initiative for development of the discipline mainly in our country but also in collaboration with countries worldwide.
- To spread the pharmacological know-how obtained from different research teams.
- To strengthen relations between pharmacologists.
- To facilitate the presentation and discussion of scientific papers.

3. SAFE's key contributions to the scientific International Community

Argentinean Society of Experimental Pharmacology was created in 1968 by initiative of Prof. Iván Izquierdo, Chief of the Department of Pharmacology, University of Córdoba (UNC). SAFE obtained relevant results which had been pivotal for the better understanding the physio-pharmacology of different systems, although the pharmacology of the Nervous System predominated for the first decades. A summary of relevant research is described below and illustrated in Figs. 1, 2 and 3.

- **Prof Juan A. Izquierdo,** was the first President of SAFE in 1968. He was a chief of the Department of Pharmacology, University of Buenos Aires. He and his co-workers made the first approaches contributing to the understanding of the neurotransmission in central (CNS) and autonomic (ANS) nervous systems [1–12].
- **Prof. Iván Izquierdo (J.A. Izquierdo's son)**, was the first SAFE's Executive Secretary. It is an Argentine and a pioneer in the study of the neurobiology of memory. Born in 1937 in Buenos Aires, Argentina, he completed the course of Medicine in 1961 and received his PhD in Pharmacology in 1962, University of Buenos Aires (UBA). For some years he served as professor at the National University of Córdoba (UNC), Argentina, but, according to a confluence of factors, both political (the Argentina dictatorship) as personal (his marriage, Ivone, it is from Brazil), he went to Brazil at the beginning of the seventies, and since 1978 lives in Porto Alegre, state of Rio Grande do Sul, Brazil. For over twenty years, he led the "Memory Center", Department of Biochemistry, ICBS, Universidade Federal do Rio Grande do Sul (UFRGS), where he has had a great influence on a whole generation of young scientists: he has trained 42 doctors over the years, most of whom working in universities in Brazil and abroad. Recently retired from the public university and he moved to the Pontifical Catholic University of Rio Grande do Sul (PUCRS), where he continues his work of basic research and training of future scientists. Iván Izquierdo has made numerous original contributions to the understanding of the cellular basis of storage and memory recall. He worked from 1957 to 1959 and from 1959 Endocrinology Neuroscience. He contributed to the discovery of several of the fundamental mechanisms of memory formation, memory differentiation between short and long term ones, and reliance on endogenous state. His extensive career has been recognized in different parts of the world and in different ways. In addition to receiving numerous awards he has been appointed member of scientific academies from different countries; he teaches as a visiting professor at universities in Brazil, Chile, Canada and the United States. He has been invited to speak at over 100 international congresses in Argentina, Australia, Brazil, Canada, Germany, Italy, France, Japan, Mexico, United States and England, among other countries. Also, the Institute of Scientific Knowledge (ISI) honored him as the most cited scientist in Latin American literature from 1995 to 2005. Some of his more relevant articles are stated in Refs. [13–20].
- **Prof. Alfredo Coviello.** In 1969 he showed for the first time that angiotensin II increases the reabsorption of sodium and water in the proximal convoluted tubule of the kidney isolated toad *Bufo arenarum* by an independent direct effect of its vascular action. This observation was then tested in the dog, rat, rabbit and man. In 1973 demonstrated for the first time that angiotensin II increased water reabsorption in the presence of an osmotic gradient on a functional model of the distal nephron (fur isolated toad) effect subsequently found in the kidney of the dog. In this tissue he also showed that angiotensin II stimulates sodium transport as measured by the short circuit current, proven action by other authors in the distal nephron of the rat. The effect of angiotensin II on the water permeability, similar to the antidiuretic hormone, is mediated by cyclic AMP formation. This effect of angiotensin II is blocked by antagonists of AT1 receptors and antidiuretic hormone (ADH) antagonists and, in turn, losartan blocksade at ADH, suggesting a common receiver for both hormones. These effects of angiotensin II in the transport of sodium and water provide evidence about their role as intrarenal hormone, with modulating effects on pressure natriuresis and diuresis, which has been attributed an important role in regulating the blood pressure. His works were key steps for the further understanding of the physiological role of Angiotensin II, see Refs. [21–30].
- **Profs. Salomón Z. Langer, Francisco J.E. Stefano, María Amelia Enero, Edda Adler-Graschinsky and Rodolfo P. Rotlhin.** The great contribution of these prestigious scientists' team into physio-pharmacology of the CNS and ANS has been pivotal for understanding the Presynaptic Regulation. A selection of the more representative articles of the 70's decade about this topic is shown below. The last review article written by Langer [36] reflects almost 50 years of work in this area. Furthermore, the work of this team the above article was recognized by the *British Journal of Pharmacology*, in a special volume entitled "Landmarks in Pharmacology", as one of the 25 more relevant papers of the last 50 years. During the years 1975–1976, Dr. Langer provided the first extensive and rigorous evidence "in vitro" and "in vivo" of co-transmission (norepinefrine (NE) and Adenosine triphosphate (ATP)) in the cat's nictitating membrane. In June 1976, Dr. Langer became Head of the Department of Pharmacology at the Wellcome Research Laboratories in Beckenham, Kent, U.K. In 1977, Dr. Langer was appointed Director of Biology at Synthélabo Research in Paris where he was later appointed Research Director and Vice-President. In 1977 Synthélabo was number 81 in the world ranking of Pharmaceuticals. Today through growth and merger, it has become Sanofi, which is number 5 in the ranking worldwide. The research team directed by Dr. Langer discovered in 1979 and 1980 a specific, high-affinity binding site labeled with for [^{3}H]-imipramine and later with [^{3}H]-paroxetine, which is associated with the serotonin transporter in the brain and in blood platelets of various species including man. The [^{3}H]-paroxetine binding was subsequently used as a marker in the purification of the serotonin transporter for cloning and expression. During the years 1980–1990 Dr. Langer continued his work on presynaptic autoreceptors regulating NE, DA (dopamine) and 5-HT (serotonin) release and reported the interactions in neurotransmission between the neuronal transporter and the corresponding