THE RECEPTION OF PENICILLIN IN PORTUGAL (1945-1950)

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INTRODUCTION

The discovery of penicillin by Alexander Fleming (1881-1955) in 1928, followed by its transformation into a medicine as a result of the work of Howard Florey (1898-1968) and Ernst Boris Chain (1906-1979) (who all shared the Nobel Prize in Physiology or Medicine in 1945) and other collaborators, is one of the most significant moments in the history of 20th century science, medicine and pharmacy (1).
If we consider the combined effects of scientific innovation, the benefits to public health and, consequently, the economic gains, it may be said that the discovery of penicillin was the most important advance in the history of science in the 20th. Century.
Penicillin was not just one more new medicinal product or one more isolated scientific event. It paved the way for new scientific investments in the field of antibiotherapy and consequently the discovery of new antibiotics, boosted scientific research and systematic clinical studies, led to new technical and technological investments in the industrial production of antibiotics, expanded the market for medicines and, most importantly of all, provided a cure for infectious pathologies for which there had been no previous effective treatment and, as such, was reflected in the enhanced quality of peoples' lives or even in the possibility of life itself which, translated into demographic terms, meant that deaths were reduced in all age groups.

THE DISSEMINATION OF PENICILLIN IN PORTUGAL: THE ROLE OF THE PHARMACEUTICAL SCIENTISTS

In searching through the pages of various scientific journals, we found some articles whose essential focus was to explain, through reviews, summaries or clinical studies, the value of penicillin. From the mid 1940s onwards, studies on the applications of penicillin could be found in various portuguese medical periodicals (for example, "Actualidades e Utilidades Médicas", "Gazeta Médica Portuguesa", "O Clínico", "O Médico", "Imprensa Médica", "Portugal Médico", "Clínica Contemporânea", "Jornal do Médico", "Amatus Lusitanus", "Anais Azevedos", "Revista da Sociedade Portuguesa de Estomatologia", "Arquivos do Instituto de Farmacologia e Terapêutica Experimental", "Jornal da Sociedade das Ciências Médicas de Lisboa", "A Medicina Contemporânea", "Coimbra Médica", etc.) and many translations of studies from foreign journals were also published, for example: "The Lancet", "British Medical Journal", "Revista Clínica Española", "Annales de l'Institut Pasteur", "La Presse Médicale", "American Journal of Diseases Children", "Archivos Medico-Quirurgicos y del Trabajo", "Revista Chilena de Pediatria", "Revista Española de Pediatria", "Medicina Española", "American Journal of Medical Sciences", "La France Médicale", "Journal of the American Medical Association", "American Journal of Ophtalmology", etc.. In addition, we found review studies of penicillin, considered by many to be a wonder drug, such were the benefits of its use (2).
In this context, mention should be made of the works published by the doctors José Garrett (3) and Pimentel Barata (4), for example, two leading figures who pioneered the written dissemination of the clinical aspects of penicillin in Portugal; and the works published by the doctors Toscano Rico, Diogo Furtado, Miranda Rodrigues, Domingos Machado, António Braga, Augusto Lamas, João Maia de Loureiro, Armindo Morais, Carneiro de Moura, Cândido Silva, Pereira Varela, Juvenal

Esteves, Alberto Reis, António Bártolo Silva, Mário Trincão, Abílio de Moura, Albertino da Costa Barros, etc.
Some statistical studies also emerged occasionally, which are very interesting from different points of view.
In relation to the work of the pharmaceutical writers, mention should also be made of the studies by Luís da Silva Carvalho, Maria Serpa dos Santos and Raúl de Carvalho, to whom this work is dedicated (5).

Luís da Silva Carvalho was just starting out in his career as a teacher at the University of Coimbra School of Pharmacy. In 1949 he published a large 568-page volume entitled *Penicilina. Propriedades, ensaios e preparações galénicas* ("Penicillin: Properties, trials and galenical preparations") (6). The book was divided into three sections:
1 — The properties of penicillin;
2 — Standards, units and trials;
3 — Galenical preparations for penicillin. In this work, the author provided a thorough overall review of penicillin, including, amongst other topics, chemical structure, synthesis, antibacterial activity and toxicity, absorption and excretion, mechanism of action, stability, standards and units, assessment of penicillin content, resistance and technological questions relating to injectable substances, capsules, pills, medicinal drinks, powders, ointments, pastilles, suppositories, globuli, etc.
At the end of the book, certain pages were reserved for advertising for the pharmaceutical laboratories, both foreign and Portuguese, which manufactured medicines made from penicillin:
—Pfizer (represented in Portugal by the Companhia Portuguesa de Higiene), which advertised penicillin G;
—the Sociedade Industrial Farmacêutica / Laboratórios Azevedos (which offered a penicillin ointment for the first time in Portugal in 1946);
—ophthalmic ointments made from penicillin and penicillin and atropine manufactured under the "Dávi" brand name (from "Laboratórios da Farmácia Jaime Costa");
—CSC-Wander Penicillin, from the "Sociedade Portuguesa de Produtos Wander, Lda";
—."A&H" Penicillin, represented in "Portugal by Coll Taylor, Lda" (Lisbon);
—Penicilina "Avlon" produced by "Imperial Chemical (Pharmaceuticals) Limited", represented in Portugal by the "Companhia União Fabril" and advertised by ICI;
—and Olicilina, advertised by the "Farmácia Barral" laboratories. It should be noted that, from the mid 1940s onwards, it was common to find penicillin advertised in Portuguese publications.

Maria Serpa dos Santos (1916-?), a professor at the University of Coimbra School of Pharmacy, wrote various articles on penicillin, some of which were published in the "Notícias Farmacêuticas" journal and the "Boletim da Escola de Farmácia" (7). This included a study published in 1943, which was evidence of the up-to-date scientific knowledge of the author. It was a general review study of penicillin which included the physical-chemical properties of penicillin, its activity, its actions on human and animal organisms, its therapeutic actions, etc. The author states that Fleming was considered "the greatest of all his peers". Another work published in 1945 by the same author was the result of laboratory studies involving penicillin, undertaken at the Cryptogamy and Fermentation Laboratory at the University of Coimbra School of Pharmacy.

In 1944, Raúl de Carvalho, a professor at the University of Lisbon School of Pharmacy, published an overall review in the "Jornal dos Farmacêuticos" entitled "Penicilina. Seu estudo entre 1929 e 1943"("The Study of Penicillin: 1929 to 1943") (8). The author began with a review of antibiotic substances, then focussed his attention on penicillin. He provided a historical summary of the history of the drug, then discussed its physical-chemical characteristics, antimicrobial properties, industrial production and costs, batching and storage, trials on animals and humans, pharmaceutical formats containing penicillin, dosage, etc.

At the end of the article, the author included a long list of bibliographical references (268 references). Raúl de Carvalho, was fully aware of the great pharmatherapeutic value of penicillin and the economic potential that could be derived from its industrial production, if this could be realised. However the author was also aware of the fact that Portugal had no tradition of chemical industry, which was indispensable to the industrial production of penicillin.

In the early 1940s, penicillin was received in Portugal as an authentic miracle cure. Before it was produced in Portugal, the first batches of penicillin were imported directly from the United States of America via the "Portuguese Red Cross".

PENICILLIN IN THE PORTUGUESE PHARMACOPOEIA: OFFICIAL REGISTRATION OF THE DRUG

Penicillin appeared in the official Portuguese pharmacopoeia for the first time in the *Supplement* to the *Farmacopeia Portuguesa IV* (1961), i.e. in the supplement to the second edition of the *Farmacopeia Portuguesa IV*, which was published in 1946. This supplement included various drugs which urgently needed to be included in the *Farmacopeia* (9).
The Supplement to the Farmacopeia also included, amongst other substances, corticosteroids, vitamins, central analgesics, local anaesthetics, analeptics, tranquilizers, etc. In addition to monographic references on the characterisation of penicillin, the Supplement also included a chapter devoted to the "biological assessment of antibiotics".
Therefore, evaluating the consumption of penicillin in Portugal is a significant factor for the portuguese pharmacy and industry. In Portugal antibiotics was the most used medicine in 1954. Penicillin was an object that generated scientific, medical, pharmaceutical interests etc. but it also fed strong commercial and industrial interests (10).

THE DEATH OF FLEMING AND THE IMPORTANCE OF PENICILLIN: ECHOES IN THE PORTUGUESE PRESS

The death of Fleming was reported in the world's press with a flood of words and images which fuelled the representation of the scientist as a hero and his discovery as a miracle. The Portuguese press, in particular the daily papers, collaborated with great dignity in this process on the occasion of the death of Fleming. In general, the news reports took the following format: information on the death of Fleming, a detailed biography of Fleming, noting his modest background, simple personality and two marriages, the award of the Nobel Prize, the value of his discovery and the benefits to humanity of penicillin.
On the very day of his death, 11 March 1955, the Portuguese evening newspapers, such as the "Diário de Lisboa" (11), the "República" (12) and the "Diário Popular" (13), announced the unexpected death of Fleming. On 12 March and the days which followed, the Portuguese daily papers, such as the "Jornal de Notícias" (14), "O Primeiro de Janeiro" (15), "O Comércio do Porto" (16), "O Século" (17), "Diário da Manhã" (18), "Diário de Notícias" (19), "Novidades" (20) and the "Diário de Coimbra" (21) devoted a great deal of attention to the death of Fleming and the value of penicillin.
In the reports we analysed, Fleming was acknowledged as a: "a benefactor to the world", "discoverer", "inventor", "genius", "outstanding figure in science", "learned mind", "scholar", "scientist", "Humanity's benefactor". They wrote that penicillin was discovered through a "the intuition of genius" and was a "miraculous event", a "a prodigious discovery", "a marvel", "a miracle", "a happy occasion", "a stroke of genius", etc.
Due to its therapeutic properties and benefits to humanity, penicillin was described in the papers as a "wonder cure", "miracle cure", "wonder drug", "extraordinary cure", etc. Fleming would therefore remain for all time in the "ranks of the immortals" and was considered "the greatest figure

in 20th century medicine". In this way, the non-specialist Portuguese press reproduced the international news which focussed on one single name — Fleming — casting a shadow over all the efforts and merits of many other scientists, in particular Florey and Chain.
The specialist press, due to its nature and publication schedules, did not pay so much attention to the death of Fleming in terms of biographies, eulogies and creating a mythical status for his character. However, on 17 March 1955, the journal "O Médico" (22) announced the death of Fleming, stating that he was "one of the most famous figures in medicine of all time, due to his discovery of penicillin which, unlike other famous contemporary discoveries, has no adverse effects, i.e. its benefits come with no harmful effects for humanity".
Pharmaceutical periodicals such as the "Eco Farmacêutico" (23) journal devoted their entire front pages to reporting the death of the scientist, stating that: "unlike so many other scientists who have wasted their time on seeking out processes that can only help Death, Fleming has rescued thousands of lives from an early grave!".

CONCLUSIONS

Since the 1940s, Portugal has remained notably up-to-date from a scientific and technical point of view with regard to the question of penicillin. Penicillin has been received in Portugal without any significant scientific controversy. The first batches of penicillin to arrive in Portugal came from the United States of America via the "Portuguese Red Cross". However, various Portuguese pharmaceutical industries showed an immediate interest in industrial production. The figure of Fleming and the value of penicillin featured heavily in the Portuguese press at the time of Fleming's death in 1955. As with the press worldwide, the Portuguese press contributed towards the construction of the so-called "myth of Fleming" since, whilst Fleming was elevated to the higher status of a genius, other scientists who were equally important to the manufacture of penicillin as a whole were neglected.

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(14) Jornal de Notícias, 12/03/1955, 1
(15) Primeiro de Janeiro(O), 12/03/1955, 1
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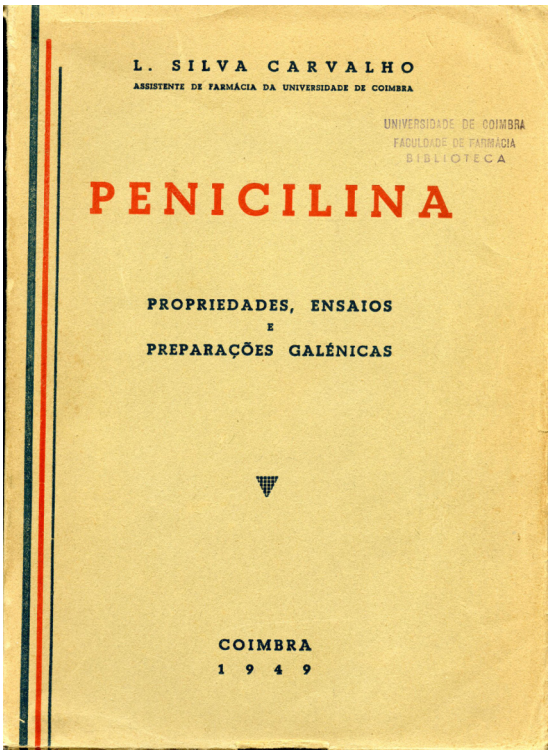

Fig 01 – L. Silva Carvalho and the book "Penicilina" (1949)

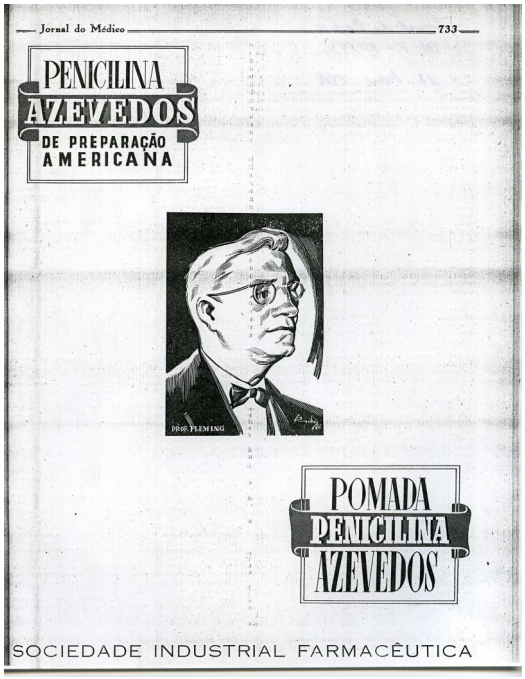

Fig 02 – Portuguese pharmaceutical industry: Sociedade Industrial Farmacêutica – AZEVEDOS (Jornal do Médico).

O prof. Fleming no seu laboratório

MORREU O PROF. FLEMING

— O HOMEM QUE DESCOBRIU A PENICILINA

LONDRES, 11 — «Sir» Alexander Fleming, inventor da penicilina, faleceu repentinamente, nesta cidade, de um ataque cardíaco. Contava 73 anos.

A criada de quarto declara:

«Sir» Alexander ainda ontem parecia gozar de excelente saúde. Esta manhã, levei-lhe, como de costume, o pequeno almoço ao quarto, e pouco depois teve uma crise».

Quando expirou, Lady Fleming estava à sua cabeceira. — (F. P.).

Alexander Fleming contou certo dia a um amigo que foi por simples acaso, um acaso feliz, que descobriu a penicilina. Em 1928, trabalhava em diversas investigações bacteriológicas, no Hospital de Santa Maria, no bairro pobre de Paddington, em Londres. Fazia parte do pessoal clínico, em resultado dos exames universitários que haviam chamado a atenção da direcção e dos chefes de clínica, o ali passou a vida inteira.

Nesse ano de 1928, fazia experiências com lisaimas, as substâncias do corpo humano que têm o poder de matar as bactérias.

Certo dia, um espírito, órgão reproduzor das criptogâmicas, que entrou em dúvida por uma janela, impelido pelo vento, pousou suavemente na lâmina aberta do agar-agar que se examinava.

Deu-se então o milagre científico, proveniente de uma decisão aparentemente sem alcance de maior: em vez da retirar o espírito, como qualquer outro investigador teria certamente feito, aceitou o intruso e colocou-o cuidadosamente sob o microscópio. Qual não seria a surpresa ao descobrir o fenómeno que devia alterar por completo a Medicina no século XX: apareceu uma espécie de halo à volta do bolor, de modo nenhum previsto no âmbito das suas investigações e que parecia devorar literalmente as bactérias ao seu alcance...

O célebre cientista escocês retirou-se da investigação activa em Dezembro passado, ao deixar o seu cargo de chefe do Instituto de Microbiologia Wright-Fleming, no Hospital de Santa Maria, em Londres, mas continuou a trabalhar num pequeno laboratório, que ocupava há muitos anos. Disse então:

«Dedicar-me-ei a trabalhar sobre imunidade — a imunização de pessoas à infecção. Era esse o meu interesse antes de aparecer a penicilina».

«Sir» Alexander Fleming, que foi armado cavaleiro em Junho de 1944 pela descoberta da penicilina e galardoado com o Prémio Nobel de Medicina no ano seguinte, só iniciou a sua carreira médica quando estava perto dos 30 anos. Filho de um jardineiro, foi educado numa pequena escola no Ayrshire, na Escócia, foi para Londres trabalhar numa agência de navegação e, depois, dedicou-se à sua carreira de Medicina. Em seguida a estudos académicos brilhantes, trabalhou sob a direcção de «Sir» Almroth Wright, fundador da terapia pela vacina. Foram ambos a França, durante a primeira guerra mundial, onde estabeleceram um laboratório de investigação no Casino de Boulogne. Entre outros trabalhos notáveis, introduziram o tratamento salino em ferimentos de guerra.

«Sir» Alexander Fleming falou muitas vezes de como o seu serviço durante a guerra desenvolveu o seu interesse por substâncias bactericidas.

Fez um estudo especial de feridas de guerra sépticas, observando propriedades bactericidas de células de glóbulos brancos contidas no pus de feridas sépticas. Depois da guerra, regressou ao célebre Hospital de Santa Maria com «Sir» Almroth Wright e aí permaneceu o resto da sua vida.

Esteve em Lisboa, em Setembro de 1946, vindo do Brasil, onde fez conferências.

A BOMBA «F»

GENEBRA, 10 — Foi hoje inaugurado o Salão Automóvel de Genebra, a que comparecem os mais importantes construtores mundiais, qual deles com os mais sensacionais modelos. Mas a bomba «F» rebentou explodiu literalmente e atraiu todas as atenções.

A presença em Genebra do Centro Europeu de Energia Nuclear poderá fazer crer que a bomba «F» é mais um engenho destruidor, quando afinal se trata de um pacífico meio de apresentação dos povos: o FIAT 600, a pequena maravilha da indústria italiana, o menor pequeno automóvel do Mundo.

A VISITA do Ministro da Economia à Alemanha Ocidental

Fig 03 – Diário Popular, 11 Mars 1955, p. 9

MORREU

um dos grandes benfeitores da Humanidade, o cientista Fleming, que inventou a penicilina

LONDRES, 11 — Sir Alexander Fleming, inventor da penicilina, faleceu repentinamente, nesta cidade, de um ataque cardíaco. Contava 73 anos. A criada de quarto declarou: «Sir Alexander ainda ontem parecia gozar de excelente saúde. Esta manhã, levei-lhe, como de costume, o pequeno almoço ao quarto, e pouco depois teve uma crise».

Quando expirou, lady Fleming estava à sua cabeceira.

Nos últimos anos, Fleming advertiu que a penicilina estava a ser utilizada demasiadamente e que o excesso do seu emprego reduziria a sua eficácia e tornaria alguns doentes insensíveis às doses posteriores.

Nos tempos futuros, o nome de Fleming, ficará, ao lado dos de Pasteur, Koch, Roux e outros cujo génio e demorados trabalhos lhes valeram ficarem imortalizados no panteão do reconhecimento humano.

Sir Alexander Fleming recebeu o Prémio Nobel da Medicina ao mesmo tempo que sir Howard Florey e o dr. Chain, em 1945, pela descoberta da penicilina e das curas obtidas. Feito cavaleiro da Ordem do Império Britânico em 1944, sir Alexander era doutor «honoris causa» de várias universidades europeias e americanas e possuía as mais altas condecorações de diversos países. Escreveu inúmeros livros consagrados à bacteriologia, ao estudo das imunidades e à quimioterapia. Casado duas vezes, ficou viúvo em 1949 de Sarah Marion Mceilroy (irlandesa falecida em 1949), voltando a casar em 1953 com a dr.ª Amália Coussoiris, heroína da resistência grega. — (F. P. e R.).

Fleming no seu gabinete de trabalho

A PENICILINA continuará a ser o remédio mais eficaz EM INÚMERAS DOENÇAS

— escreveu Fleming pouco antes de morrer

LONDRES, 11 — Pouco tempo antes da sua morte, sir Alexander Fleming, tinha escrito no «Practioner» um artigo relevando o valor presente e futuro da penicilina.

Eis a passagem principal desse artigo: «Depois de vários anos de emprego geral, podemos dizer que não assistiremos ao desenvolvimento generalizado de organismos resistentes que tornariam a penicilina inútil. Esta continua a ser o remédio mais eficaz em inúmeras doenças». — (F. P.).

PROJECTA-SE UMA CARREIRA AÉREA PORTO-VIGO

VIGO, 11 — Anuncia-se a presença em Vigo de um representante dos transportes aéreos portugueses, a fim de estudar o próximo estabelecimento de uma linha Porto-Vigo e volta. A inauguração da linha, que teria no princípio um carácter irregular, poderia verificar-se na próxima Primavera e seria servida

Fig 04 – O Primeiro de Janeiro, 12 Mars 1955, p. 1