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Short Communication

Rediscovering fosfomycin in its 50th anniversary (1969-2019)

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sent it to Merck & Co., Inc., in Kenilworth, NJ in the USA to verify if it produced the highly antibacterial substance she had found.

The result of this collaboration between the United States and Spain was the discovery three years later of Fosfomycin (originally called *Phosphonomycin* or 833A) a new bactericidal antibiotic with a very strong antimicrobial effect, finding that HENDLIN *et al* published in "Science" 3rd October 1969 [3]. In the article appear eleven North American researchers: HENDLIN, STAPLEY, JACKSON, WALLICK, MILLER, WOLF, MILLER, CHAIET, KAHAN, FOLTZ, WOODRUFF and the Spaniards MATA, HERNANDEZ and MOCHALES. The said WOODRUFF, in an article published in 1979, paid tribute to Justo MARTÍNEZ MATA for his contribution with his antibiotic screening program [4].

Fosfomycin was discovered in Spain and definitely developed in the USA by a team of researchers formed by an agreement between Merck and CEPA. As an analogue of Phosphoenol Pyruvate (PEP), it irreversibly inhibits the cytosolic enzyme MurA (N-acetyl-glucosamine enol-pyruvyl transferase), which takes part in the formation of N-acetylmuramic acid from the cell wall peptidoglycan. In addition, the formation of penicillin-fixing proteins (PBP) decreases. Fosfomycin is water soluble, has a low molecular weight (PM 138) and also a low protein fixation, which allows high tissue diffusion, CANDEL and CANTÓN 2019 [5].

2019 marks 50 years since its discovery, a milestone in the History of Medicine, which coincidentally concurs with another milestone in the History of Humanity, the arrival of man to the Moon 20th July 1969 at 20:17:40 UTC, in the Apollo 11 mission: Neil A. Armstrong, Edwin "Buzz" Aldrin and Michael Collins. For both events you can extrapolate the words that mission commander Neil A. Armstrong pronounced when setting foot on the lunar surface: "That's one small step for man, one giant leap for mankind."

Dear director

2019 marks the 50th anniversary of the discovery of fosfomycin, an antibiotic widely used in urological and systemic diseases.

As a urologist, I have some reasons to dedicate this short article to it:

- *Streptomyces fradiae*, the gram-negative bacteria that naturally produces fosfomycin, was discovered in 1969 in a soil sample from Mount Montgó, located in front of Dénia, my city of residence.
- Many doctors and urologists use phosphomycin in our patients,, being the "gold standard" of oral treatment in a single dose of uncomplicated acute cystitis in healthy women.
- Fosfomycin is an antibiotic that has been around for 50 years and that today has not lost its validity but has gained it, being used in non-urological and systemic infections of all kinds.
- My admiration for fosfomycin and its discoverers, remembering its 50th birthday.

On the occasion of this event, a brief study and personal commentary on the history of its discovery is made, highlighting the old articles and a current monograph from 2019.

MARTÍNEZ MATA, National Health Doctor, Pharmacist and Scientific Director of the Spanish Company of Penicillin and Antibiotics (CEPA), had been searching since 1957 for microbiologically active substances, antibiotics [1,2].

At the end of July 1966, the Spanish microbiologist of CEPA, Sagrario MOCHALES del VAL, identified the strain of *Streptomyces fradiae* in a sample of soil collected on the southern slope of Mount Montgó in Jávea (Alicante), lyophilized it and



Recalling the history of the discovery of Fosfomycin from the filamentous bacteria *Streptomyces fradiae* and having celebrated its fiftieth anniversary in 2019, I personally have three reasons to remember such an event and give my thanks to all the researchers who took part in the discovery of this antibiotic.

First, as an urologist, I know that "Phosphomycin Tromethamine" is one of the most commonly used antibiotics, to the point that it is the "universal antibiotic" and "gold standard single dose" in the treatment of non-complicated acute cystitis in healthy women, both in Europe and in Latin America. In the USA, Fosfomycin is only approved by the Food and Drug Administration as Fosfomycin Trometamol for the oral treatment of non-complicated cystitis, currently awaiting approval for its intravenous presentation as disodium salt, CANDEL and CANTÓN 2019 [5].

The second reason is the fact that the soil sample collected by Spanish doctor Sebastián HERNÁNDEZ FERNÁNDEZ in April 1966, and the confirmation in the USA of the finding of *Streptomyces fradiae* by Dr. MOCHALES, was obtained on the southern slope of Mount Montgó, located north in the province of Alicante (Spain) between the towns of Dénia and Jávea, a rocky mass that rises 753 meters above sea level, and where on its north face, in the town of Dénia, I have lived for over 30 years and feel very lucky to see its green slopes covered with Mediterranean pine-trees and its crowning, vertical, white summit, every day from the windows in my house (Figure 1).

The third reason is to express my admiration for the productive cooperation between American Company Merck & Co., Inc., in Kenilworth, NJ and the Spanish Company of Penicillin and Antibiotics (CEPA), whose research yielded such good results with the development of this antibiotic, that today, 50 years after its discovery, has not lost any of its validity but rather the opposite, as the treatment for multidrug-resistant microorganisms infections, and to which the Spanish Journal



Figure 1: View of the southern slope of Mount Montgó from the AP-7 motorway.

of Chemotherapy has dedicated a monographic issue this May 2019 under the title: "Current aspects in Fosfomycin" [6].

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