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Letter to the editor

Drug repositioning, a new alternative in infectious diseases

Dear Editor:

There has been a significant decrease in the number of approved antibiotics in the last two decades, and in parallel, a steady increase of multidrug resistant bacteria (MDR) has been occurring. Thus, MDR have become a global issue of public health, and with this threat, the challenge to develop new antibiotics has emerged in all areas: governmental, scientific, and the private pharmacological industry.[1] In this sense, drug repositioning has arisen as an alternative approach for the faster identification of drugs that are effective against infectious diseases.[2]

The expressions "*Drug repositioning*" and "*drug repurposing*" was first described by Ashburn and Thor (2004)[3] in their paper "*Drug repositioning: identifying and developing new uses for existing drugs*". According to the authors, this is the process to find new uses for clinically approved drugs, and this is also known as *redirecting* and *reprofiling*.

Several studies have signalled that drug repositioning has advantages compared to the traditional way of seeking for active substances,[2,4–7] since pharmacological, toxicological and bioavailability data, among others, are already available. Thus, less time is spent in their development, leading to a significant reduction in costs, and it proves to be a preferred and advantageous alternative strategy to discover drugs more quickly.[4] Other encouraging data are the success rates for repositioned drugs, which are higher when compared to new drugs, reaching 30% in the last few years. Also, together with the positive aspects of repositioning is its recent approval by the *Food and Drug Administration* (FDA).[8]

Comparing repurposing and use off-label, there is a similarity between these practices: a new indication of the drug, other than the usual one. However, the use outside the label goes beyond this, since it may include different age groups, dosage or route of administration. Although this is considered a legal and common application, it is often performed in the

Table 1 – Studies of repositioning non-antibiotic drugs with antibiotic effect.

Drug	Original indication	New indication	Reference
AAS	Non-steroidalAnti-inflammatory	MRSA	Chan et al., 2017[10]
Amitriptiline	Antidepressant	*Staphylococcus* spp.	Mandal et al., 2010[11]
		Enterococcus faecalis	
		Micrococcus luteus	Muthukumar and
		Bacillus spp.	Janakiraman, 2014[22]
		Shigella spp.	
		Salmonella spp.	
		Vibrio cholerae	
		Vibrio parahaemolyticus	
		Escherichia coli	
		Klebsiella pneumoniae Pseudomonas spp.	
		Proteus spp.	
		Citrobacter spp.	
		Providencia spp.	
		Enterobacter cloacae	
		Hafnia spp.	
		Lactobacillus sporogenes	
		Micrococcus flavus	
		Vibriocholerae	
Auranofin	Rheumatoidarthritis	MRSA	Harbut et al., 2015[23]

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– Table 1 (*Continued*)

Drug	Original indication	New indication	Reference
Chlorpromazine	Anti-psychotic	*Corynebacterium urealyticum* *Escherichia coli* *Klebsiella pneumoniae* *Citrobacter freundii*	Munoz-Bellido, Mufioz-Criado and Garcfa-Rodriguez, 1996[12]
		Morganella morganii *Acinetobacter baumanii* *Haemophilus influenzae* *Moraxella catarrhalis* *Campylobacter jejuni* *Staphylococcus aureus* *Staphylococcus epidermidis* *Streptococcus pneumoniae* *Streptococcus pyogenes* *Streptococcus agalactiae* *Enterococcus faecalis* *Clostridium perfringens* *Clostridium difficile* *Bacreroides fragilis* *Prevotella* spp. *Brucella* spp.	Munoz-Bellido, Mufioz-Criado and Garcfa-Rodriguez, 2000[13]
Clofazime	Tuberculosis	*Mycobacterium leprae*	Naylorand Schonfeld, 2014[24]
Clomipramine	Antidepressant	*Serratia marcescens* *Morganella morganii* *Acinetobacter baumanii* *Haemophilus influenzae Campylobacter jejuni* *Staphylococcus aureus* *Staphylococcus epidermidis* *Streptococcus pneumoniae* *Streptococcus pyogenes* *Streptococcus agalactiae* *Enterococcus faecalis* *Clostridium perfringens* *Clostridiumdifficile* *Bacteroides fragilis* *Prevotella* spp. *Brucella* spp.	Munoz-Bellido, Mufioz-Criado and Garcfa-Rodriguez, 2000[13]
Disulfiram	Alcoholism	MRSA *Pseudomonas aeruginosa*	Phillips et al., 1991[25] Velasco-García et al., 2006[26]
Ebselen	Neuroprotector	MRSA VRSA *Streptococcus* spp. *Enterococcus* spp.	Thangamani, Younis e Seleem 2015[6,7]
Escitalopram	Antidepressant	*Klebsiella pneumoniae* *Proteusmirabilis* *Enterobactorcloacae Staphylococcus aureus* *Pseudomonas aeruginosa*	Akilandeswari, Ruckmani and Ranjith, 2013[27]
Fluoxetine	Antidepressant	*Corynebacterium urealyticum* *Haemophilus influenzae* *Moraxella catarrhales* *Campylobacter jejuni*	Munoz-Bellido, Mufioz-Criado and Garcfa-Rodriguez, 1996[12] Munoz-Bellido, Mufioz-Criado and Garcfa-Rodriguez, 2000[13]
Ibuprofen	Non-steroidalAnti-inflammatory	MRSA	Chan et al., 2017[10]
Iproniazid	Antidepressant	*Mycobacterium tuberculosis*	López-Muñozand Alamo, 2009[28]
Loperamide	Diarrhoea	*Salmonella enterica*	Ejim et al., 2011[16]

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