Title: *In vitro* and *In vivo* analyses of an antidepressant compound as a highly potent antimicrobial agent

Shauroseni Palchoudhuri[1], *Ph.D*; Sujata G. Dastidar[1], Ph.D; Sukhen Das[2], Ph.D

[1]Department of Microbiology, Herbicure Healthcare Bio-Herbal Research Foundation, Kolkata 700154, India

[2]Division of Biophysics, Department of Physics, Jadavpur University, Kolkata 700032, India

Abstract

Statement of the problem: According to the World Health Organization infectious diseases cause almost 50% of all deaths in both developed and developing countries due to the emergence of multi-drug resistant pathogens [1]. Although new antibiotics are being reported, speedy appearance of mutations and acquisition of drug resistance plasmids restrict their usage. However, based on the property of multiplicity of actions in drugs, several researchers have evaluated significant antimicrobial property in drugs belonging to different pharmacological classes. These have been designated as "non-antibiotics"[2]. Intensive studies reveal that the phenothiazine group of chemotherapeutics, possessing three benzene rings along with a halogen moiety in their chemical structure, is the most active class of non-antibiotics [3]. The present study describes a detailed investigation of antimicrobial action of the antidepressant drug doxepin which bears a close structural relationship with a phenothiazine. Methodology: Minimum Inhibitory Concentration (MIC) of doxepin was determined against 250 strains of Gram positive and Gram negative bacteria following international standard guidelines. Tests for synergism were performed between this antidepressant and known antibiotics by disc diffusion method. For *in vivo* tests, doxepin was injected intraperitoneally into albino mice at different concentrations and challenged with virulent pathogen *Salmonella* enterica serovar Typhimurium. Findings: Staphylococci and vibrios were highly sensitive to the drug, following moderate sensitivity in salmonellae and shigellae. Doxepin exhibited effective synergism with chloramphenicol and tetracycline and it is confirmed with the fractional inhibitory concentration index of 0.5 and 0.375 of the respective duo. Doxepin also manifested a significant protection to the challenged mice ($P<0.001$) and potentially reduced the infection in internal organs. Conclusion & significance: Thus, the present study suggests that doxepin has the potential for being developed into a powerful antibacterial agent, the efficacy of which may be enhanced further with a suitable synergistic combination.

References

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Biography

Shauroseni Palchoudhuri is a research professional with 5 years' experience of working in the areas of infectious diseases, antimicrobial resistance and novel antimicrobial search including development of *in-vitro* screening platforms and evaluation in animal models. She completed her Ph.D from Jadavpur University, India (2017). Dr. Palchoudhuri is the author of 14 research articles published in international peer reviewed journals. She also received awards for presenting novel findings in national and international conferences. Dr. Shauroseni Palchoudhuri is a skilled microbiologist with passion towards research for the hope of better therapeutic advances.

Email: shauroseni.micro@gmail.com

Full name: Shauroseni Palchoudhuri

Mobile No.: +16515295142

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Date of Birth: 08/29/1988

Postal address: Department of Microbiology, Herbicure Healthcare Bioherbal Research Foundation, Kolkata 700154, India