High prevalence and global distribution of fosfomycin resistance genes in *Salmonella* serovars

Fosfomycin, an old antimicrobial agent with a broad spectrum of activity, has been reintroduced into clinical use for the treatment of patients with difficult-to-treat-infections,[1] including those due to carbapenem-resistant Enterobacterales.[2] However, fosfomycin-resistant bacterial strains (including *Salmonella* spp) have emerged and spread, potentially posing a crucial threat to public health[3] as *Salmonella* spp are a major culprit of diarrhoeal and invasive diseases globally and fosfomycin represents an attractive treatment option.[4,5] We therefore tested whether fosfomycin resistance in *Salmonella* spp is a substantial concern for the One Health framework by analysing 550 780 publicly available *Salmonella* spp genomes in the NCBI Pathogen Detection system.

Alarmingly, we uncovered a high prevalence of fosfomycin resistance genes among *Salmonella* spp strains, with a total of 26 165 strains harbouring at least one *fosA*-group fosfomycin resistance gene encoding glutathione S-transferase. Specifically, the identified genes were *fosA7* (n=13963), *fosA7.2* (n=5247), *fosA3* (n=3762), *fosA7.3* (n=2453), and *fosA7.4* (n=740). Of these *Salmonella* spp strains, 21 were *Salmonella enterica* subsp *salamae*. The remaining strains fell under *Salmonella enterica* subsp *enterica* and were further subdivided into 73 distinct serovars (appendix p 2–3). 36 of these serovars were rare and were reported for the first time in this Correspondence (appendix p 4–5).

Upon comprehensive examination of the global distribution of *Salmonella* spp strains carrying fosfomycin resistance genes, our genomic analysis revealed their presence across 47 countries, spanning six continents (appendix p 6). This distribution indicates a global problem and raises concerns about the potential effect of fosfomycin resistance on public health within the One Health framework. The emergence and spread of fosfomycin-resistant *Salmonella* strains poses a crucial threat, as they restrict treatment options for this common infection and could lead to increased morbidity and mortality rates. The effectiveness of antimicrobial therapy has already been threatened by the emergence and expansion of antimicrobial-resistant *Salmonella* serovars.[6]

Understanding the mechanisms underlying fosfomycin resistance in *Salmonella* spp is crucial for developing strategies to combat this problem. Further research is needed to investigate the genetic determinants responsible for the widespread dissemination of fosfomycin resistance genes in these bacteria. The identification of these genes provides valuable insights into the molecular basis of resistance, which could inform the design of new therapeutic approaches or the enhancement of existing antibiotic therapies. Moreover, efforts to monitor and control the spread of fosfomycin-resistant *Salmonella* strains should be intensified, with a focus on enhancing surveillance systems and implementing stringent infection control measures. A One Health approach is particularly relevant in this context, as antibiotic resistance is a complex issue that transcends human, animal, and environmental boundaries. Collaborative efforts between human and veterinary medicine, agriculture, and environmental sectors are vital to effectively address this growing problem.

The findings presented in this Correspondence underscore the substantial importance of fosfomycin resistance in *Salmonella* spp within a One Health framework. The high prevalence and global distribution of *fosA* resistance genes among *Salmonella* serovars raise serious public health concerns and necessitate immediate action to preserve the effectiveness of antibiotics and protect human and animal health worldwide.

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For more on the **NCBI Pathogen Detection system** see https://www.ncbi.nlm.nih.gov/pathogens/

See **Online** for appendix