

# DRUG-RESISTANT BACTERIAL CONTAMINATION AND EFFICACY OF SELECTED HERBAL MEDICINES SOLD IN KAMPALA CITY, UGANDA

## ABSTRACT

**Background:** Antimicrobial resistance (AMR), is when pathogens such as bacteria evade activities of drugs to which they were once susceptible, causing treatment failure. The AMR is escalating and is among the leading causes of global mortality, projected at 10 million annual deaths by 2050. Transmission of resistant bacteria to humans may occur through the food chain, the environment, or direct interactions with animals and plants. Effective redress needs thwarting the evolution and spread of resistant bugs, and discovery of effective drug substitutes. With the proliferation of herbal medicines (HM) trade in Kampala city where this study was carried out, it is unclear whether these HM are drivers of resistant bugs, or are possible drug candidates to resolve AMR. Drug-resistance traits of bacteria isolated from HM, and antibacterial activities of some medicinal plants in Kampala were examined, to inform and support intervention design.

**Methods:** The prevalence of selected bacterial strains in 140 HM was examined using conventional culture, following the guidelines of World Health Organization (WHO), and Uganda National Drug Authority (NDA). Drug resistance traits were tested using Kirby Bauer disc diffusion methods, and Polymerase Chain Reaction (PCR). Plants species frequently used in treating ailments potentially caused by bacteria were identified ethnopharmacologically and their in-vitro antibacterial potency was evaluated using agar-well diffusion method. The potential enablers of HM bacterial contamination were examined with semi-structured questionnaires, Key Informant Interviews, and field observations. Data were analysed using D'Agostino-Pearson test, Chi-square, and Mann-Whitney U tests ( $P \leq 0.05$ ), with STATA version-15.0. Graphs were plotted using GraphPad Prism ® version 9.0.0.

**Results:** Fifty-nine bacterial strains were isolated from 45 (32.1%) samples, that is, *Klebsiella pneumoniae*: n=34; 57.6%, *Escherichia coli*: 12; 20.3%, *Staphylococcus aureus*: 7; 11.9%, *Klebsiella oxytoca*: 3; 5.1%, *Bacillus cereus*, *Pseudomonas aeruginosa*, and *Enterobacter* spp. (1; 1.7% each). *Salmonella* spp. and *Shigella* spp. were not encountered. The least potent drugs were the Penicillins: n = 45, 76.2%, Fluoroquinolones: 32, 54.2%, Sulfonamides: 30, 50.8%, Carbapenems: 18, 10.2%, 3<sup>rd</sup> and 4<sup>th</sup> generation cephalosporins: 18; 15.3%, and 8; 30.5% respectively. Majority of the bacteria (43, 72.9%) resisted more than three antibiotics (multidrug resistant/MDR strains), and comprised mostly; *K. pneumoniae* (), *E. coli* (), and *S. aureus* (). *P. aeruginosa*, *K. pneumoniae*, and *S. aureus* had average AMR indices above the critical value (0.2), indicating high risk to the community. The MDR genes: Extended spectrum  $\beta$ -lactamases and Carbapenemases were found in eight and five out of 20 isolates respectively, while AmpC, and *MecA* were not detected. Novel evidence was generated for the high potency of Citrus limon leaf extracts against MDR *S. pneumoniae* NCTC 12977, *K. pneumoniae* ATCC 700606, and clinical isolates of *K. pneumoniae* and *S. pneumoniae*. C. limon fruit juice was equally strong against *S. pneumoniae*. *Momordica foetida* leaves were weak, narrow spectrum antibacterial agents with bacteriostatic effects only on *S. pneumoniae*, while *Conyza pyrrhopappa* leaves had no activity. *E. coli* was resistant to all the plant extracts. Policy, environmental, and herbalist related factors were among the major potential barriers to HM microbial safety.

**Conclusion:** Though this research highlighted quality and efficacy limitations, it has generated novel evidence supporting the possible usefulness of HM in developing powerful biotherapeutics, to manage bacterial diseases which have become incurable with clinical drugs.