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Behavior of antibiotic resistance genes under extremely high-level antibiotic selection pressures in pharmaceutical wastewater treatment plants

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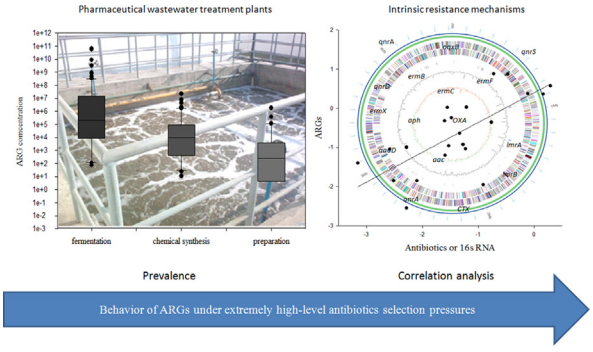
HIGHLIGHTS

- The ARGs would proliferate or attenuate in different treatment units of pharmaceutical wastewater treatment plants (PWWTPs).
- A big part of the ARGs may be transported to the dewatered sludge.
- The bacterial abundance and antibiotic concentration within the PWWTPs influenced the fate of the associated ARG together.
- The intrinsic resistance mechanisms of corresponding ARGs play a key role in their fate.
- ARGs concentration in the wastewater from fermentation was significantly higher than chemical synthesis and preparation.

GRAPHICAL ABSTRACT



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ABSTRACT

Pharmaceutical wastewater treatment plants (PWWTPs), which receive wastewater containing extremely high levels of antibiotics, are regarded as potential hot spots for antibiotic-resistance development in the environment. Six sampling campaigns in six PWWTPs in Southeastern China were carried out to assess the prevalence and fate of antibiotic resistance genes (ARGs). Different genes were monitored in different PWWTPs (PWWTP A: lincosamides; PWWTP B: aminoglycosides and macrolides; PWWTP C: quinolones; PWWTP D: macrolides and quinolones; PWWTP E: cephalosporins; and PWWTP F: quinolones and macrolides) using real-time quantitative polymerase chain reactions (PCRs), according to the antibiotic type produced. The levels of typical ARG subtypes in the final effluents ranged from $(1.03 \pm 0.91) \times 10^1$ to $(6.78 \pm 0.21) \times 10^7$ copies/mL. The absolute abundance of ARGs in effluents accounted for 0%–577% of influents to the six PWWTPs with a median value of 6%. Most of the ARGs are transported to the dewatered sludge, with concentrations from $(1.38 \pm 0.21) \times 10^5$ to $(6.84 \pm 0.43) \times 10^{10}$ copies/g dry weight (dw). In different treatment units (before/after biological units), a clear trend of proliferation or attenuation was not observed for the ARGs, aside from a strong attenuation in moving bed bio-film reactor (MBBR) in PWWTP C. Through correlation analyses, this study demonstrated that the bacterial abundance and antibiotic concentrations within the PWWTPs influenced the fate of the associated ARGs, and this was possibly related primarily to the intrinsic resistance mechanisms of corresponding ARGs. Macrolide ARGs, which tend to locate in plasmids and

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transposons, positively correlate weakly with total macrolide antibiotic concentrations but positively correlate strongly with 16S rRNA concentrations. Furthermore, ARG concentrations in the wastewater from fermentation were significantly higher than in the wastewater from chemical synthesis and preparation. This is the first comprehensive study on the behavior of antibiotic resistance genes under extremely high-level antibiotic selection pressures in pharmaceutical wastewater treatment plants (PWWTPs) in Southeastern China.

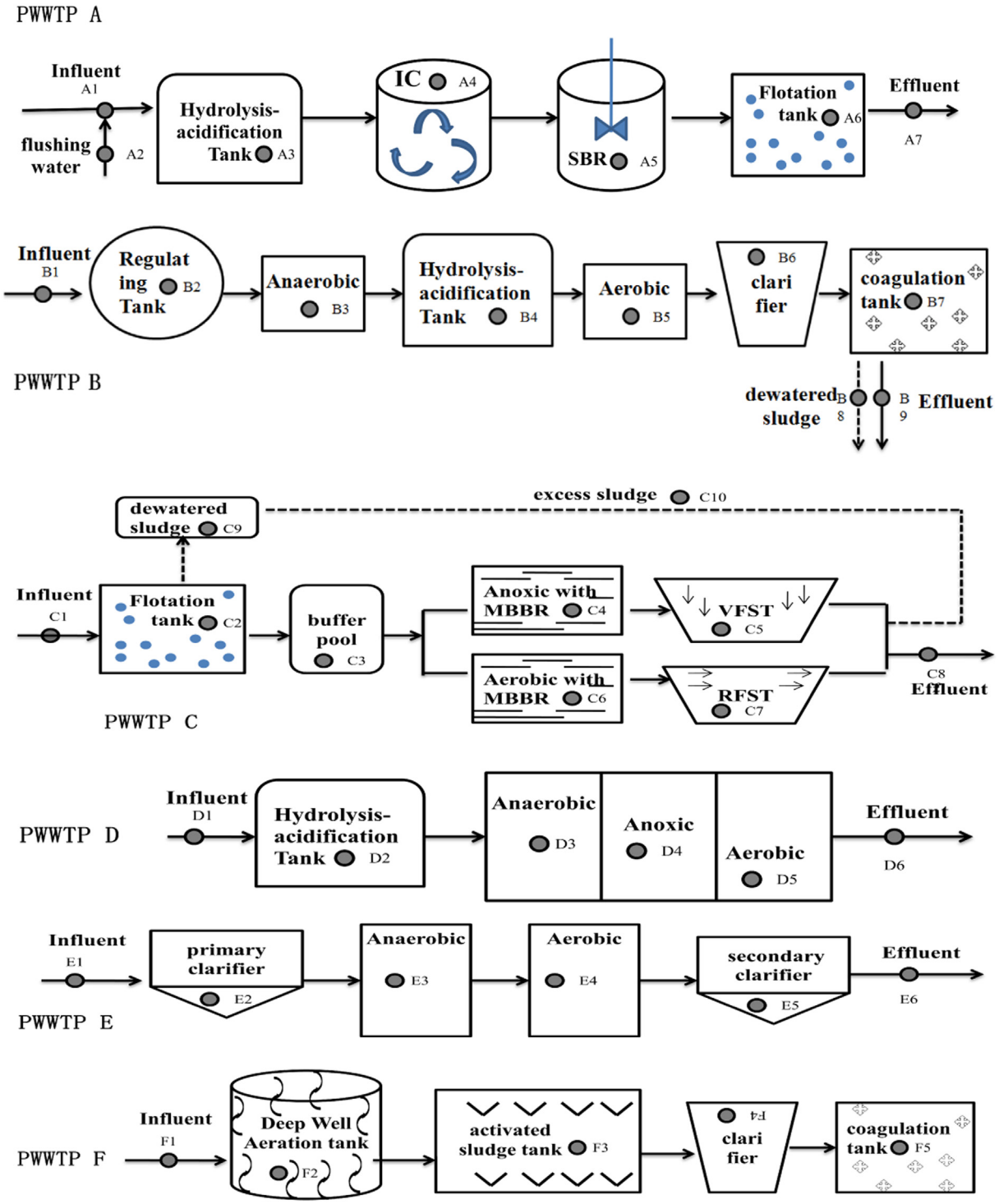

Fig. 1. The flow chart layouts of the treatment processes in the six pharmaceutical wastewater treatment plants and the sampling site location. The black dot represents the specific sampling location and the dotted line represents the recycled sludge. IC: internal circulation anaerobic reactor; SBR: sequencing batch reactor; VFST: vertical flow sedimentation tank; RFST: radial flow sedimentation tank; MBBR: moving bed bio-film reactor.