

## Combination of Selected PPI's With Antibiotics to Explore their Potential Role as Adjuvant to Combat Antibiotic Resistance

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**SUMMARY.** The aim was to investigate the effect of different protein-pump inhibitors (PPIs) including omeprazole, pantoprazole, dexlansoprazole and efflux-pump (EP) inducer and inhibitor on the antibacterial efficacy of well-known antibiotics including levofloxacin, ciprofloxacin and moxifloxacin against which microbial resistance has already been reported. The minimum inhibitory concentration (MIC) of ciprofloxacin, moxifloxacin and levofloxacin were determined by using disc diffusion method. Zone of inhibition (ZoI) of these antibiotics were determined against *Salmonella typhi* using disc diffusion method. Statistical analysis was performed to elaborate the significance ( $p < 0.05$ ) of difference among the acquired data. ChemDIS-Mixture was also used to identify the common protein targets of the selected antibiotics and the PPIs in human. The results showed that the selected antibiotics had different susceptibility effects against *S. typhi*. The ZoI and MIC of ciprofloxacin and moxifloxacin against *S. typhi* were significantly ( $p < 0.05$ ) higher in the presence of adjuvants than that of antibiotics alone. While, this increase was non-significantly higher in the presence of pantoprazole. On the other hand, levofloxacin and co-amoxiclav did not show any improvement in their efficacy in the presence of adjuvants against the selected strain of *S. typhi*. ChemDIS-Mixture revealed common protein targets (CYP1A2, CYP3A4, CXCL8, UDPGT, HAT and SPGT) of the selected antibiotics and the PPIs. Based on the above findings, it can be concluded that there could be an improvement in the antibacterial efficacy of ciprofloxacin and moxifloxacin in the presence of omeprazole, pantoprazole, and dexlansoprazole.

**RESUMEN.** El objetivo era investigar el efecto de diferentes inhibidores de la bomba de proteínas (IBP), incluidos el omeprazol, el pantoprazol, el dexlansoprazol y el inductor e inhibidor de la bomba de expulsión (EP), sobre la eficacia antibacteriana de antibióticos bien conocidos, incluidos levofloxacina, ciprofloxacina y moxifloxacina contra los cuales los microbios ya se ha reportado resistencia. La concentración inhibitoria mínima (MIC) de ciprofloxacina, moxifloxacina y levofloxacina se determinó utilizando el método de difusión en disco. La zona de inhibición (ZoI) de estos antibióticos se determinó frente a *Salmonella typhi* utilizando el método de difusión en disco. Se realizó un análisis estadístico para elaborar la significación ( $p < 0,05$ ) de la diferencia entre los datos adquiridos. ChemDIS-Mixture también se utilizó para identificar los objetivos proteicos comunes de los antibióticos seleccionados y los IBP en humanos. Los resultados mostraron que los antibióticos seleccionados tenían diferentes efectos de susceptibilidad contra *S. typhi*. La ZoI y la MIC de ciprofloxacina y moxifloxacina contra *S. typhi* fueron significativamente ( $p < 0,05$ ) más altas en presencia de adyuvantes que con antibióticos solos. Mientras que este aumento no fue significativamente mayor en presencia de pantoprazol. Por otro lado, levofloxacina y co-amoxiclav no mostraron ninguna mejora en su eficacia en presencia de adyuvantes frente a la cepa seleccionada de *S. typhi*. ChemDIS-Mixture reveló dianas proteicas comunes (CYP1A2, CYP3A4, CXCL8, UDPGT, HAT y SPGT) de los antibióticos seleccionados y los IBP. Con base en los hallazgos anteriores, se puede concluir que podría haber una mejora en la eficacia antibacteriana de ciprofloxacina y moxifloxacina en presencia de omeprazol, pantoprazol y dexlansoprazol.

**KEY WORDS:** adjuvants, antibiotic resistance, disc diffusion method, efflux-pumps, minimum inhibitory concentration (MIC), protein-pump inhibitors (PPIs), zone of inhibition (ZoI).

# Equal contribution

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