

## Understanding the Mechanisms of *Salmonella typhimurium* Resistance to Cannabidiol

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**Abstract :** The emergence of multidrug resistance poses a huge risk to public health globally. Yet these recalcitrant pathogens continue to rise in incidence rate, with resistance rates significantly outpacing the speed of antibiotic development. This, therefore, presents an aura of related health issues such as untreatable nosocomial infections arising from organ transplants and surgeries, as well as community-acquired infections that are related to people with compromised immunity, e.g., diabetic and HIV patients, etc. There is a global effort to fight multidrug-resistant pathogens spearheaded by the World Health Organization, thus calling for research into novel antimicrobial agents to fight multiple drug resistance. Previously, our laboratory demonstrated that Cannabidiol (CBD) was an effective antimicrobial against *Salmonella typhimurium* (*S. typhimurium*). However, we observed resistance development over time. To understand the mechanisms *S. typhimurium* uses to develop resistance to Cannabidiol (CBD), we studied the abundance of bacteria lipopolysaccharide (LPS) and membrane sterols of both susceptible and resistant *S. typhimurium*. Using real-time quantitative polymerase chain reaction (RT-qPCR), we also analyzed the expression of selected genes known for aiding resistance development in *S. typhimurium*. We discovered that there was a significantly higher expression of *bla*TEM, *fimA*, *fimZ*, and integrons in the CBD-resistant bacteria, and these were also accompanied by a shift in abundance in cell surface molecules such as lipopolysaccharide (LPS) and sterols.

**Keywords :** antimicrobials, resistance, cannabidiol, gram-negative bacteria, integrons, *bla*TEM, Fim, LPS, ergosterols

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