Cannabinoid-Driven Structural and Functional Changes in *Trichomonas vaginalis*

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Trichomonas vaginalis, the causative agent of trichomoniasis, is responsible for a widespread sexually transmitted infection affecting approximately 278 million people annually. Current treatment relies on metronidazole (MTZ) but increasing resistance and adverse effects present significant challenges. *Cannabis sativa*, which contains over 100 phytocannabinoids, has gained attention for its therapeutic potential, including applications in parasitic infections such as *Plasmodium* and *Trypanosoma cruzi*. Recent legal and commercial developments have further reinforced interest in its medical applications. This study investigates the anti-parasitic effects of cannabinoids, including WIN 55,212-2, cannabivarin (CBV), and natural extracts of *C. sativa* with distinct phytochemical profiles: EBDRS9, rich in cannabidiol (CBD); EBPWK12, rich in tetrahydrocannabinol (THC); EBCBG30, rich in cannabigerol (CBG); and EBTHCV1MIX, a combination of CBD and THC. Their impact on the growth and morphology of *T. vaginalis* was assessed, along with pharmacokinetic properties. Notably, CBV complies with Lipinski's rules, suggesting favorable characteristics for oral drug delivery. The tested compounds significantly inhibited *T. vaginalis* trophozoite growth, including both synthetic cannabinoids and natural extracts, and impaired parasite adhesion to host cells. Morphological alterations such as membrane projections, blebbing, autophagosome formation, and damaged hydrogenosomes were observed. These findings highlight the antiparasitic activity of cannabinoids and *C. sativa* extracts against *T. vaginalis*, inducing significant cellular alterations and warranting further investigation into their mechanisms of action.

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