Computational Modeling of Cannabidiol and Δ⁹-Tetrahydrocannabinol Derivatives from the Thermal Degradation of Cannabis sativa

Cannabis sativa is an intricate plant biomass that comprises over 400 chemicals, including at least 61 cannabinoids that undergo pyrolytic degradation during smoking, generating thousands more than 2000 chemical compounds with potential toxicological effects. Despite widespread use, the mechanistic pathways of cannabinoid decomposition, particularly for Δ⁹-tetrahydrocannabinol (Δ⁹-THC) and cannabidiol (CBD), remain poorly understood. This study investigates the thermal degradation of Δ⁹-THC and CBD, with a focus on their electronic structures, stability, and potential toxic byproducts. Computational modeling was performed using Gaussian 09 at the density functional theory (DFT) level with the B3LYP/6311G++ basis set to evaluate molecular orbital behavior and energetics. Toxicity estimations of degradation products were carried out using the HyperChem platform. CBD was found to decompose into reactive species such as α-terpinyl radical, limonene, and olivetol, which are associated with oxidative stress and carcinogenic potential. The geometry optimizations converged after 40 (CBD) and 68 (THC) steps, with energies stabilizing at −968.519 and −968.727 Hartrees, respectively. Frontier molecular orbital analysis showed Δ⁹-THC has a wider HOMO-LUMO band gap than CBD, suggesting greater electronic stability. Solubility modeling revealed CBD is markedly more soluble in octanol than in water compared to its radical derivatives, while degradation byproducts displayed elevated toxicity indices. Computational evidence indicates that CBD thermal degradation produces toxic radicals with significant biological risks, including oxidative stress and impaired pulmonary function. These findings provide novel insight into cannabinoid pyrolysis pathways and highlight the need for experimental validation to better understand their health impacts in humans.