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Study of synergistic bioactivities of leaves of *Coffea arabica* with Copper oxide nanoparticles

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Synergistic bioactivities are the combined actions of two or more substances or compounds that produce a more substantial biological reaction in contrast to their individual effects. When these chemicals interact, their separate effects are amplified or enhanced, producing a more potent result. In this work, leaves of *Coffea arabica* are combined with copper oxide nanoparticles (CuO NPs) to examine the plants' complementary biological activity. *Coffea arabica* leaves were sequentially extracted via maceration with hexane and methanol solvents, and the resulting extract was stored until further use. The methanol extract was used to examine the bioactivities. CuO NPs were synthesized using a chemical synthesis method. UV-visible spectroscopy and Fourier-transform infrared were used to characterize the produced CuO NPs. Determination of total phenolic and flavonoid contents was done and the anti-diabetic activity was examined using α-amylase inhibitory assay, while the anti-oxidant capacity was assessed through DPPH radical scavenging assay. The anti-diabetic, and anti-oxidant effects of the leaf extract and CuO NPs were assessed to determine their synergistic bioactivities. The findings show that the methanol extract of the leaves alone displays good bioactivity in each of the categories where the IC_{50} values of 8.91± 0.01 µg/mL and 171.62± 0.01 µg/mL were observed for anti-oxidant and anti-diabetic activities respectively. Similar to this, the CuO NPs alone show notable bioactivity for anti-oxidant activity where the observed IC_{50} value was 456.15± 0.01 µg/mL yet they do not manifest a notable influence on anti-diabetic activity. However, when copper oxide nanoparticles and the plant extract were combined, strong anti-diabetic effects were seen with an IC_{50} value of 85.25± 0.02 µg/mL, suggesting a potential joint application for the treatment of diabetes through synergistic bioactive interactions. Copper oxide nanoparticles combined with *Coffea arabica* leaves increased antioxidant activity in comparison to individual CuO nanoparticles giving an IC_{50} value of 172.18± 0.01 µg/mL but could not match the natural potency of *Coffea arabica* leaves, indicating a non-amplifying, synergistic interaction. According to this research, combining CuO NPs with *Coffea arabica* leaf extract may be useful for producing bioactive molecules for use in the pharmaceutical and nutraceutical industries. These discoveries help us to better understand how natural resources are used and to create innovative bioactive formulations that are more effective at treating diabetes, and oxidative stress by further improvement. More research is required to fully understand the underlying mechanisms and assess this synergistic combination's toxicity and safety profiles. This research not only advances our comprehension of synergistic bioactivity but also sets the stage for pioneering applications in the realm of therapeutics, bridging the realms of botanical wisdom and cutting-edge nanoscience.

Keywords: *Coffea arabica,* Copper oxide nanoparticles, Synergistic, Anti-oxidant, Anti-diabetic