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Antimicrobial/Antiparasitic/Antiviral Agents

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73. ESTABLISHING DRUG COMBINATIONS IN *C. ELEGANS*: INTEGRATING NATURAL AND COMMERCIAL ANTHELMINTICS FOR EFFECTIVE HELMINTHIASIS CONTROL

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Helminthiasis, caused by parasitic infections, are significant neglected diseases that impact millions worldwide, exacerbating poverty and inequality. Combination therapy, which involves using commercial drugs, new agents, or natural products, is an effective approach to broadening treatment effectiveness.

The primary goal of this study is to investigate the effects of combining natural compounds with commercial anthelmintics (levamisole, monepantel, piperazine and ivermectin). Combining bioactive phytochemicals with synthetic compounds has been proposed as a promising strategy for enhancing nematode control in human and veterinary medicine. The concurrent use of natural compounds and synthetic drugs can lead to pharmacodynamic interactions due to the effects of two compounds with different mechanisms of action on the target parasite.

The nematode *Caenorhabditis elegans* is a model system for anthelmintic drug discovery. We performed behavior assays of *C. elegans* strains to identify synergic anthelmintic activities of combinations of natural compounds with commercial anthelmintics. In the experiments, synchronized worms at the adult stage were exposed to various concentrations of selected individual agents on agar plates or multiwell plates. Changes in worm behavior or thrashing rate were observed under a stereoscopic zoom microscope and compared to control conditions. IC_{50} values were determined for the individual natural compounds and anthelmintics as well as for the different combinations. At least three combinations were necessary to assess whether the interactions were synergistic, additive, or antagonistic.

The results suggest that natural compounds, which act through mechanisms different from classical anthelmintics, may help counteract resistance in combined anthelmintic therapies. These findings highlight the potential of multitarget compounds as valuable tools in integrated pharmacological strategies for effective parasite control.