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Thiram Effects on HeLa TI Cells

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INTRODUCTION & AIM

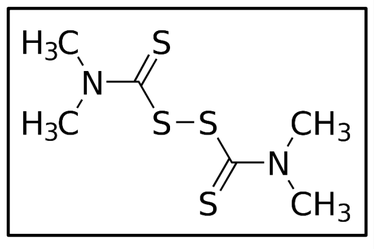
Dithiocarbamate pesticides possess a diverse array of molecular mechanisms, making them multifunctional substances. Among the commonly used dithiocarbamates, there is the fungicide thiram, employed for safeguarding plants and seeds against fungal diseases. The limited solubility of thiram in water facilitates its accumulation in the soil, thereby raising concerns about its potential impact on human health. Despite the widespread use of thiram, there is still a paucity of knowledge regarding its toxic effects on humans.

This study aimed to assess the genotoxic effects of thiram, its influence on cell colony formation, and its effect on the expression profile of genes associated with proliferation and repair. Additionally, we conducted an analysis of thiram's integral epigenetic activity under different time exposures.

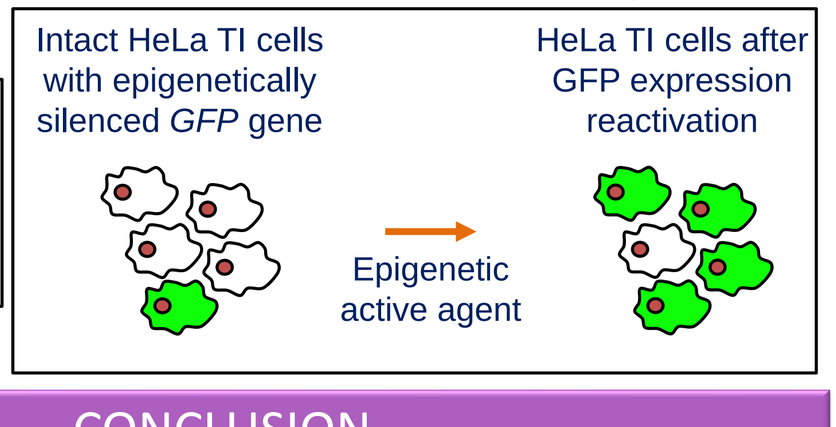
METHOD

HeLa TI cells were used in the study. DNA damage was assessed using the DNA comet assay, while the clonogenic assay was utilized to evaluate the colony-forming ability of cells after thiram treatment. Gene expression levels were measured by real-time PCR. The epigenetic activity of thiram was assessed by quantifying the reactivation level of the epigenetically silenced GFP gene utilizing flow cytometry.

Thiram structure



HeLa TI cell-based assay



CONCLUSION

Thus, thiram exhibits genotoxic and cytotoxic effects, influences on the expression of proliferation and repair genes, and induces dose- and time-dependent epigenetic modifications in HeLa TI cells.

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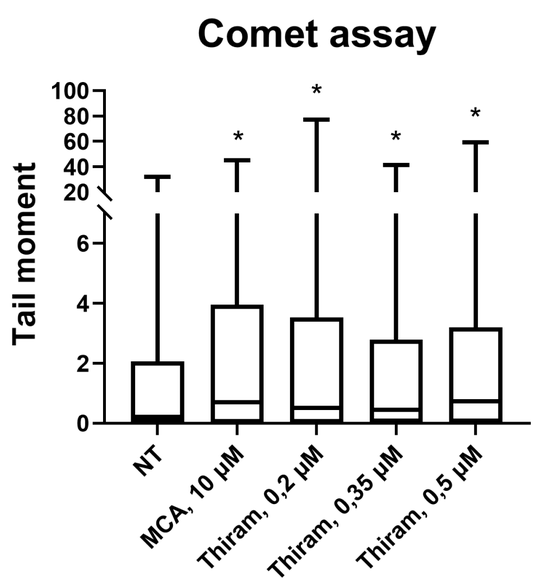
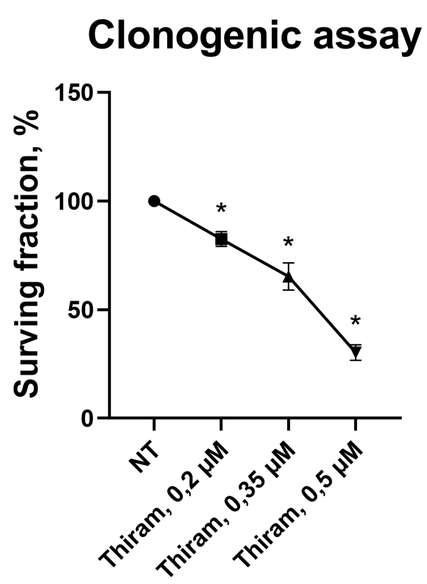
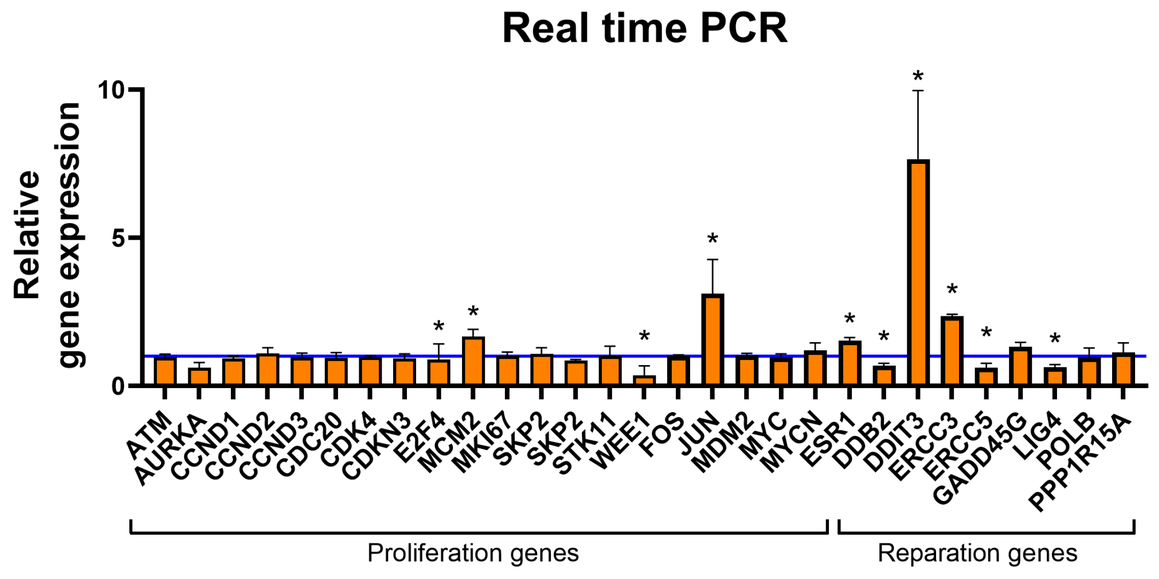
RESULTS & DISCUSSION

Using HeLa TI cells, we observed that thiram significantly increased tail moment in the DNA comet assay and caused a significant decrease in cell survival as determined by the clonogenic assay.





Additionally, thiram downregulated gene expression levels of DDB2, ERCC5, LIG4, and WEE1, while upregulating the expression levels of MCM2, DDIT3, ERCC3, JUN1, and ESR1.



The analysis of epigenetic activity revealed that thiram induced statistically significant increase in the GFP+ cells amount after exposures of 24, 72, and 96 hours.