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Key Words

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The Anti-proliferative Effect of Prolinethiuramdisulfide on HT-29 Colon Cancer Cells

ABSTRACT

Background. Previous work showed that diethyldithiocarbamate (DDTC) could reduce the proliferation rate of human hepatoma HepG2 cells. However, prolinedithiocarbamate (PDTC) is a better analog of DDTC. PDTC was found to act as a cancer chemopreventive agent and can be biotransformed to prolinethiuramdisulfide (PTDS).

Aims. Herein we studied the action of PDTC and PTDS on colon adenocarcinoma HT29 cells, with the long-term goal of understanding their chemopreventive actions.

Methods. HT29 cells were incubated with PDTC or PTDS, and the cell growth and cell differentiation were analyzed.

Results. In this study we found that PTDS inhibited cell proliferation of HT29 cells, as measured by the cell growth assay, [³H]thymidine incorporation, and clonogenic assay. These results suggest that PTDS has the capacity to reduce linear or clonogenic cell growth. Alkaline phosphatase is a well-established marker in colon cancer cells. We found that PTDS could not induce alkaline phosphatase activity.

Conclusion. Thus, we conclude that PTDS does not induce differentiation in HT29 cells, and its effect on proliferation is exerted through mechanisms independent of cell differentiation.

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INTRODUCTION

Colorectal cancer is a common cause of cancer death. Although advances in radiotherapy, chemotherapy, and surgery have improved 5-year survival, mortality caused by colorectal cancer remains very high and has decreased only slightly.¹ Colon cancer originates from the epithelial cells (colonocytes) that line the bowel. These cells are in direct contact with the

contents of the lumen. The development of colon cancer is a multi-step process involving both somatic mutations and increased rates of cell proliferation.²

Disulfiram(bis[diethylthiocarbamyl]disulfide, DTDS) and its major metabolite, diethyldithiocarbamate (DDTC), were found to protect rodents against the damaging effects of alkylating carcinogens and some antineoplastic drugs.³⁻⁶ It was found that DTDS administered for 2 h before N-nitrosodiethylamine

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