Toxicological investigation of organosulfur compounds in rats: a histopathological and biochemical approach

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Dibenzothiophene is an organosulfur compound present as a fuel contaminant and considered a reference molecule for bioremediation studies. DBT and its oxidized derivative, dibenzothiophene-sulfone (DBTO₂), are considered potentially carcinogenic compounds, although their specific cellular toxicity has not been clearly demonstrated. Altered homeostasis may generate tissue inflammation and ultimately promote tumor formation. At the cellular level, these processes are often associated to increased expression of proteolytic enzymes. This study refers to a toxicological investigation of DBT and DBTO₂ in Wistar rats intended to analyze the proteolytic activity profile in the induced tumor tissues. Ten injections of DBT and DBTO₂ were administered intraperitoneally at 30 mg/kg, in male Wistar rats for 10 weeks. In parallel, their effects were compared to that of dimethylhydrazine (DMH), a known cancer inducer, given under the same regimen. Macroscopic analyses revealed polyp formation restricted to the large intestine for DMH-treated animals, whereas for those treated with DBT and DBTO₂ polyps were mainly observed in the small intestine. Histopathological analyses demonstrated the presence of cellular atypias associated to treated animals, particularly for those administered DBT and DMH. In addition, proteolytic activity contained in the lysosomal fraction, isolated from DBT-treated rat, was significantly inhibited in the presence of soybean Bowman-Birk inhibitors. This finding is in agreement with previous reports on DMH treatment and suggests increased expression of trypsin and chymotrypsin-like proteases during DBT-treatment. Future experiments aim to address the transcriptomic and proteomic alterations promoted by exposure to DBT and DBTO₂ to gain insight into their cellular toxicity.

Keywords: DBT/DBTO₂, cancer, tumor-markers.