P-216  HISTOMETRIC CHANGES IN CONNECTIVE FIBERS OF THE LUNG FOLLOWING PARAQUAT ADMINISTRATION IN RATS
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Pulmonary fibrosis induction by paraquat was studied histometrically using an image analyzer. Rats were given a subcutaneous injection of paraquat (7 or 25 mg/kg) and autopsied 3, 6 or 9 days later. Histological measurement was performed, using an Olympus-Avio Color Image Analyzer SP500. The percentage of the unit area(22,000 μm²) which was occupied by connective fiber tissue positively stained with aniline blue was measured. Lung prolyl hydroxylase activity was determined as a biochemical parameter. Rats treated with 25 mg/kg of paraquat showed an increase in the percentage of the area of the connective fibers per unit area and also an increase in lung prolyl hydroxylase activity 6 days later. Thus, pulmonary fibrosis was confirmed both morphologically and biochemically. It is concluded that histometric examination using an image analyzer provides a very accurate method for the evaluation of pulmonary fibrosis.


Potential synergism among 5 heterocyclic amines (HAs), which occur in cooked meats and fishes, at low doses in the induction of intestinal tumor was investigated in a multi-organ carcinogenicity bioassay. Rats were sequentially treated with DEN, MNU, BBN, DHPN and DMH for multi-organ initiation during the first 4 weeks, and then given HAs in the diet for 24 weeks as follows: PhIP(300ppm), Glu-P-1(300ppm), Glu-P-2(600ppm), IQ(300ppm) or MeIQ(200ppm) alone at the full-dose(1/1) or lower doses (1/5 or 1/25), or mixtures of all 5 HAs at low doses (1/5 or 1/25). Incidences and multiplicities of both large and small intestinal adenocarcinomas were increased in a dose-related manner. Additive, but not synergistic, effects were observed for multiplicity of colon tumors in the 1/5 and 1/25 combined dose groups. Synergism was found for multiplicity of small intestinal tumor induction at the 1/25 dose level. Slight combination effects of HAs were also observed in the liver and Zymbal glands. The present results indicated that synergistic effects occur in HA intestinal carcinogenesis and that the present assay is useful for evaluation of low dose combination effects of environmental contaminants at the whole body level.