

DNA damage by benzo(a)pyrene in human cells is increased by cigarette smoke free radicals and decreased by their removal.

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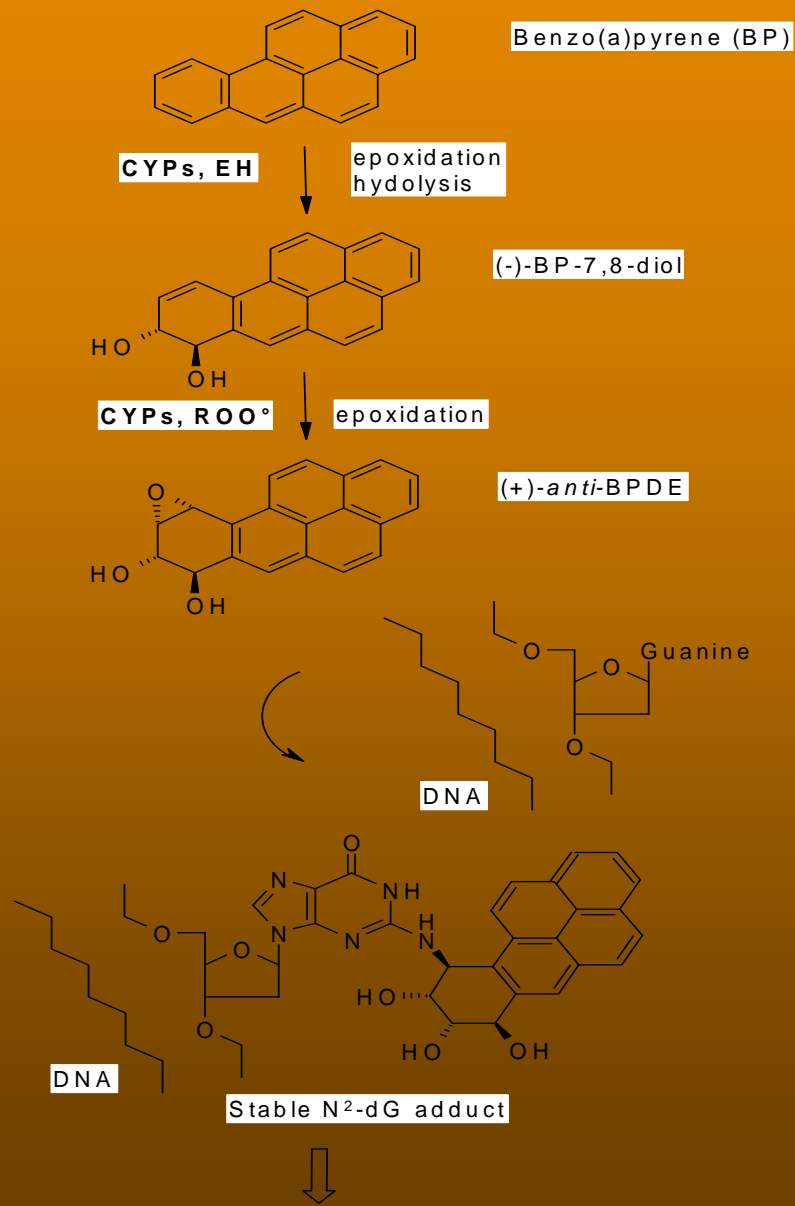
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Cigarette smoking is causally associated with a large number of human cancers (1).. Benzo(a)pyrene (BP) is a highly carcinogenic polycyclic aromatic hydrocarbon (PAH) present in cigarette smoke, typically less than 10 ng per cigarette. BP is one of more than 60 carcinogens in cigarette smoke that is involved in the aetiology of lung cancer. It is metabolically activated into benzo(a)pyrene-7,8-diol-9,10-epoxide (BPDE) which reacts with DNA predominantly at the N2-position of guanine to produce primarily N2-guanine lesions, e.g. benzo(a)pyrene-7,8-diol-9,10-epoxide-N2-deoxyguanosine (BPDE-dG) adduct. The presence of BPDE-DNA adducts in human tissues has been conclusively established and BPDE-dG adduct concentrated exclusively in bronchial cells and thus implicated in the initiation of human lung cancer





**Mutations within tumor genes (e.g p53, ras)**

# Study's Goal

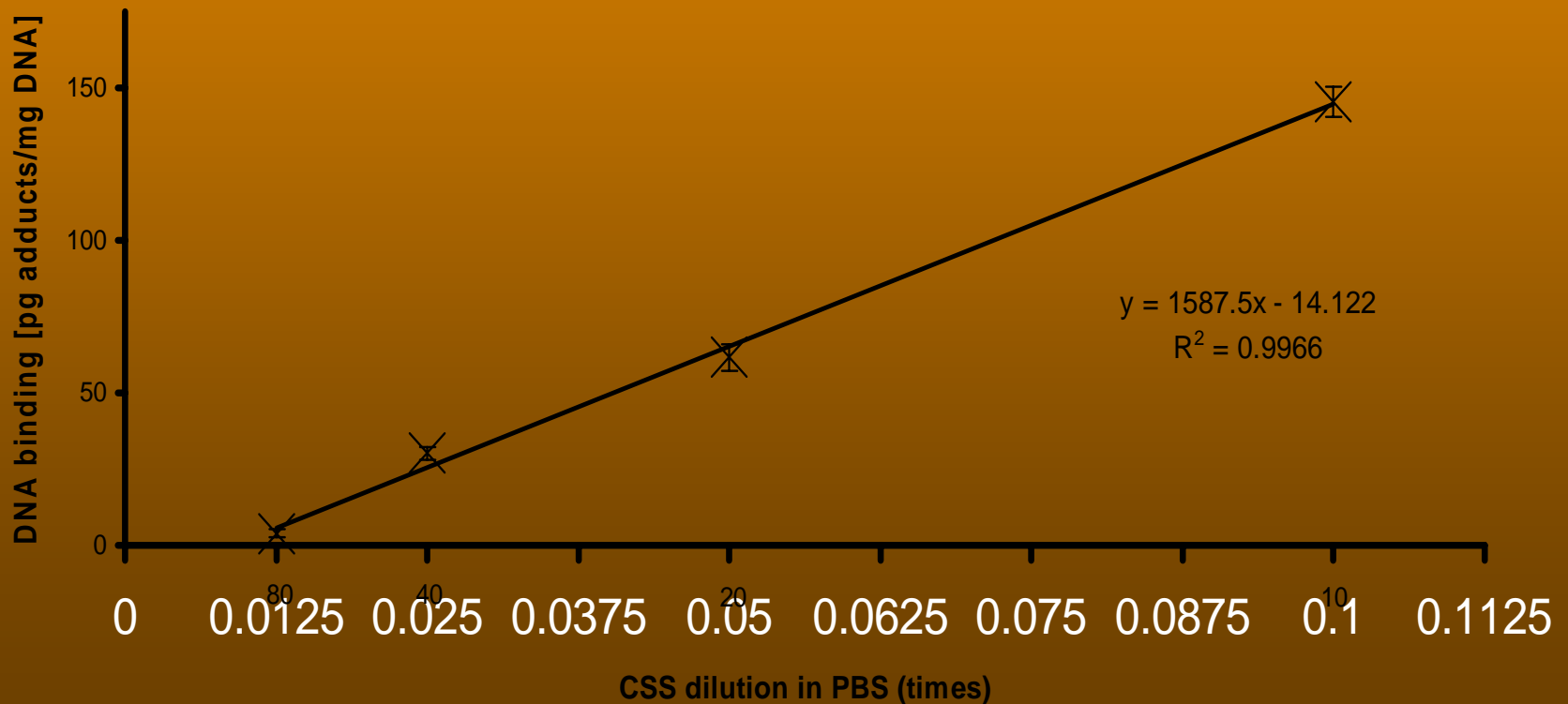


- Our study was designed to (i) determine the relative contribution of ROS in the cigarette smoke on the activation of BP-7,8-diol in comparison with cytochrome P450; (ii) to apply the method used in this study to answer the following questions; (iii) does cigarette smoke's ROS promote the carcinogenic process by contributing to the metabolism of BP-7,8-diol resulting in an increase in the formation of the critical lung BPDE-dG? (iv) Can a filter containing a scavenger of cigarette free radicals affect the formation of BPDE-dG?

# Preparation of Cigarette Smoke/PBS Solution (CSS).

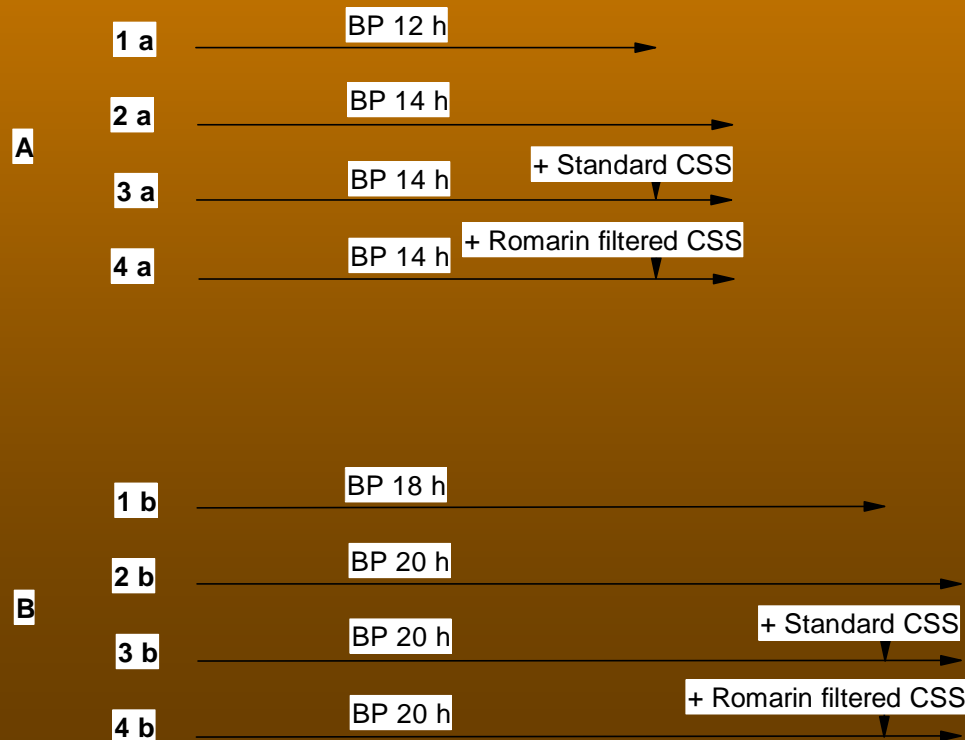
Smoking was performed according to Pryor et al without the Cambridge filter. Essentially the same smoke collecting method has been used earlier by Nakayama et al. The smoke from burning 8 cm of one cigarette (Marlboro) during 3.8 min with the help of constant vacuum generated from a water pump was bubbled through 10 ml of phosphate-buffered saline (PBS) solution which traps both the gas-phase and tar cigarette smoke chemicals. As there were no water-insoluble tar compounds present on the walls of the wash bottles, a major part of the water-soluble compounds from the smoke of a single cigarette was contained in the 10 ml PBS solution. This aqueous solution named cigarette smoke solution (CSS) was reacted immediately with exogenous DNA or added to MCF-7 cells in culture in the presence of benzo (*a*) pyrene or its proximate metabolite (+)-BaP-7,8-diol. Different dilutions of CSS were used .

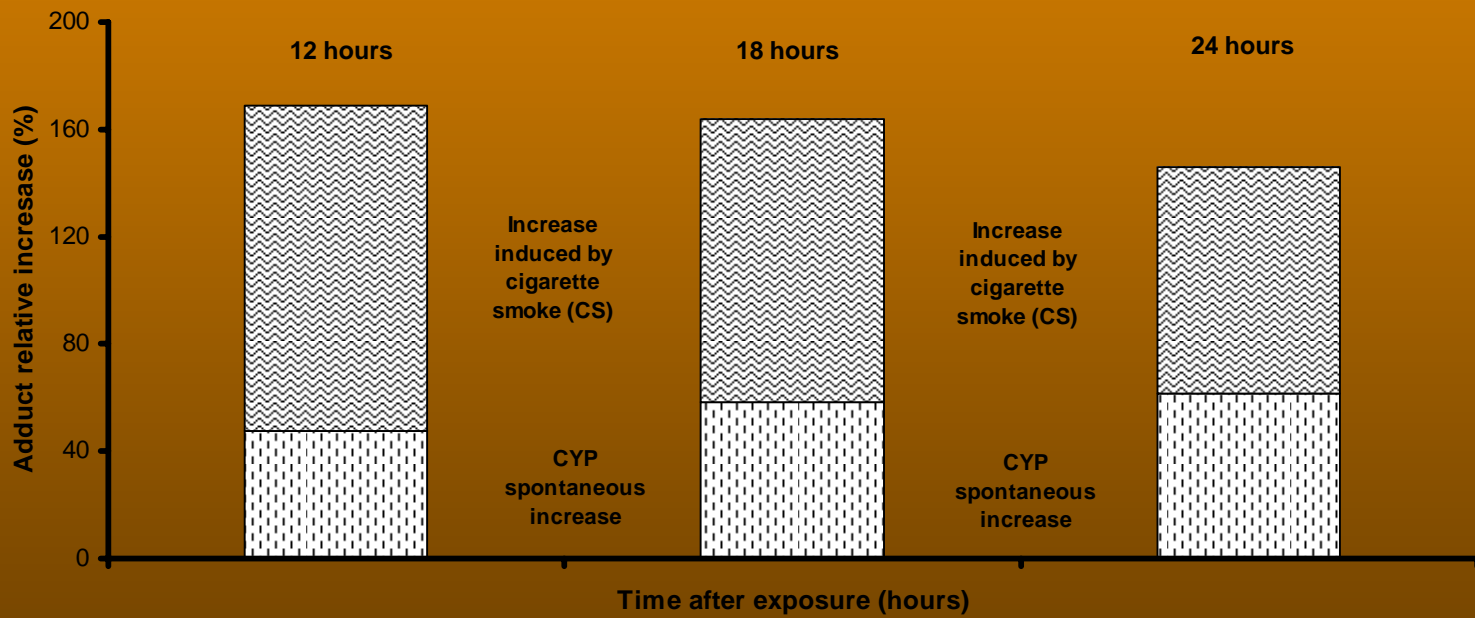
# The Effect of Cigarette Smoke on (-)-anti-BPDE-dG Adduct Formed in MCF-7 Cells Treated with (+)-BP-7,8-diol



# Treatment of MCF-7 Cells with BP and Cigarette Smoke.

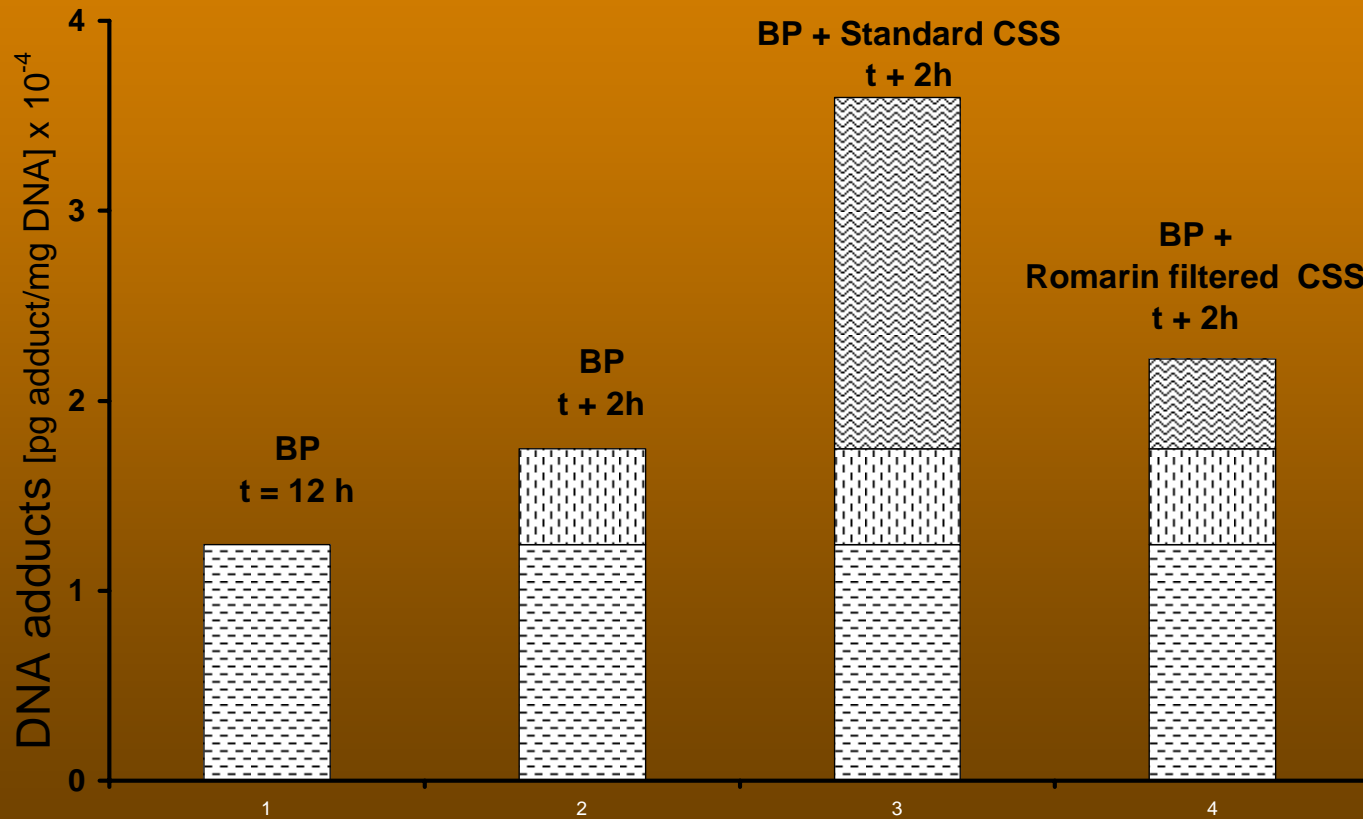
- To see the effect of CS the following scheme was performed.. The cells were treated with BP (2.5  $\mu$ M) and CSS







# Filter's effect



# Filter's effect

