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Cigarette Smoke

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Abbreviation
ACT, agueous cigarette extract solution.
DMPO, 5,5-dimethyl-l-pyrroline-N-oxide.
$HO^{\bullet}$, hydroxyl radical.
$NO^{\bullet}$, nitrogen oxide.
$NO_2^{\bullet}$, nitrogen dioxide.
Q, quinone.
QH_2, hydroquinone.
$QH^{\bullet}$, semiguinone.

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Abstract

Cigarette smoke can be divided into two phases, tar and gas-phase smoke, by the use of filter. The radicals in these two fractions differ. Tar contains more than 10^{17} stable, long-lived radicals per gram, such as catechol and hydroqunone radicals. Gas-phase smoke contains more than 10^{15} radicals per puff. Gas phase smoke contains high concentration of nitric oxide, reactive olefins and dienes. Damage to DNA appears to involve a complex of polyphenolic tar components with DNA, followed by production of the hydroxyl radical that nicks DNA. Cigarette smoke can cause many diseases. The radicals in cigarette smoke can be directly detected by electron spin resonance (ESR).

Introduction

Smoking-related diseases account for approximately 440,000 American deaths every year. This number includes both the direct effects of smoking on the smoker, but also indirect effects of smoking, such as premature births and the effects of secondhand smoke. The costs are enormous. Estimates of the costs of smoking, both in terms of health care costs and costs related to lost productivity, are between 100-150 billion dollars each year. Smoking is the cause of the majority of cases of chronic bronchitis and emphysema, and accounts for almost 90% of all cases of lung cancer [1].

Cigarette smoke is a composite of numerous pollutants in rather high concentrations. Well over one thousand constituents of smoke, including many oxidants, prooxidants, free radicals and reducing agents, have been identified [2]. Nitrogen dioxide, one of the major oxidant air pollutants present in photochemical smog, for example, is found in cigarette smoke at levels as high as 250 ppm [3]. Also, Pryor and associates have identified two different populations of free radicals, one in the tar and one in the gas phase, in cigarette smoke [4]. These include poisons and over 50 cancer causing substances, many of which have been strongly connected to a variety of diseases,

In this paper, we will focus on chemistry of cigarette smoke, damage of DNA caused by radicals in cigarette smoke and the mechanisms of diseases produced by cigarette smoke.

Oxidants in Cigarette Smoke

Gas-phase cigarette smoke and cigarette particulate matter (Tar)

Tobacco scientists divide cigarette smoke into two phases, tar and gas-phase smoke, by the use of a filter, typically a Cambridge glass-filter that retains 99.9% of the particles larger than 0.1 μm [5]. Figure 1 illustrates the separation of cigarette smoke into gas-phase smoke (which goes through the filter) and tar (which is trapped in the filter). A typical cigarette weighs about 1 g and yields about 20 mg of wet tar (sometimes called total particulate matter) and, in the human smoking pattern, about 350 mL puffs of gas-phase smoke from a cigarette, taken one per min, and each 2 s in duration.

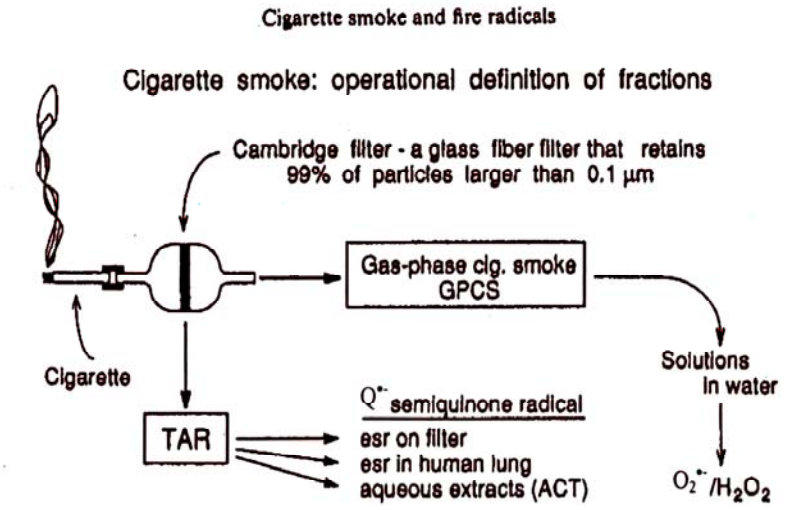

Figure 1. The separation of gas-phase cigarette smoke from cigarette tar by the use of Cambridge filter [4].

The cigarette tar radical

Cigarette tar contains remarkably high concentrations of quite stable, long–lived radicals per gram. They can be directly observed by electron spin resonance. At least four different radical species can be identified [6]. The radical species with most interesting chemical properties is semiquinone in equilibrium with quinines and hydroquinones in the relatively viscous cigarette tar matrix. This quinone/semiquinone/hydroquinone equilibrium is shown in reaction 1, where Q is a quinone, QH_2 a hydroquinone, and $QH^{\bullet}$ a semiquinone.

$$Q + QH_2 \leftrightarrow 2QH^{\bullet} \quad (1)$$

As is typical of quinone radicals, tar extracts in aqueous buffers and other solvents can reduce oxygen to form superoxide (reaction 2), and superoxide can dismutate to form hydrogen peroxide (reaction 3)

$$QH^{\bullet} + O_2 \rightarrow Q + O_2^{\bullet -} + H^+ \quad (2)$$

$$2\,O_2^{\bullet -} + 2\,H^+ \rightarrow O_2 + H_2O_2 \quad (3)$$

Thus, aqueous cigarette tar extract solutions (ACT) consume oxygen and produce a series of activated oxygen species that can cause biological damage.

The radicals in gas-phase cigarette smoke

In contrast to the stable radicals in cigarette tar, the organic radicals in gas-phase cigarette smoke are reactive carbon- and oxygen-centered radicals that would expected to have lifetimes of less than 1 s. These radicals are too short-lived to be observed by direct ESR, but they can be

studied by the ESR spin trap method [2]. There are more than 10^{15} organic radicals per puff in gas-phase cigarette smoke. Gas-phase smoke contains high concentrations of nitric oxide, reactive olefins and dienes [6]. It is a paradox that despite their short lifetime, radical concentrations are maintained at high levels in gas-phase cigarette smoke for more than 10 min; in fact smoke radicals actually increase in concentration with time. To explain this paradox, the radicals in gas-phase cigarette smoke were suggested to exist in a steady state in which they are continuously formed and destroyed [4].

The steady-state mechanism for radical production in cigarette smoke is based on nitrogen oxide ($NO^{\bullet}$) chemistry [6]. In this mechanism, $NO^{\bullet}$ is slowly oxidized to nitrogen dioxide (reaction 4), which reacts with smoke constituents such as isoprene to form carbon-centered radicals (shown as $R^{\bullet}$ in reaction 5).

$$2NO^{\bullet} + O_2 \rightarrow 2NO_2^{\bullet} \quad (4)$$

$$NO_2^{\bullet} + \text{isoprene} \rightarrow R^{\bullet} \quad (5)$$

Damage to DNA Caused by Cigarette-tar Derived Radicals

The fraction of cigarette tar that contains the tar radical is complex mixture that contains polyhydroxyaromatics; this faction could bind to DNA, generate the hydroxyl radical in a site – specific manner, and nick DNA, as shown in Figure 2. Furthermore, these nicks may be a type that leads to error-prone repair, explaining the mutagenic properties of smoke.

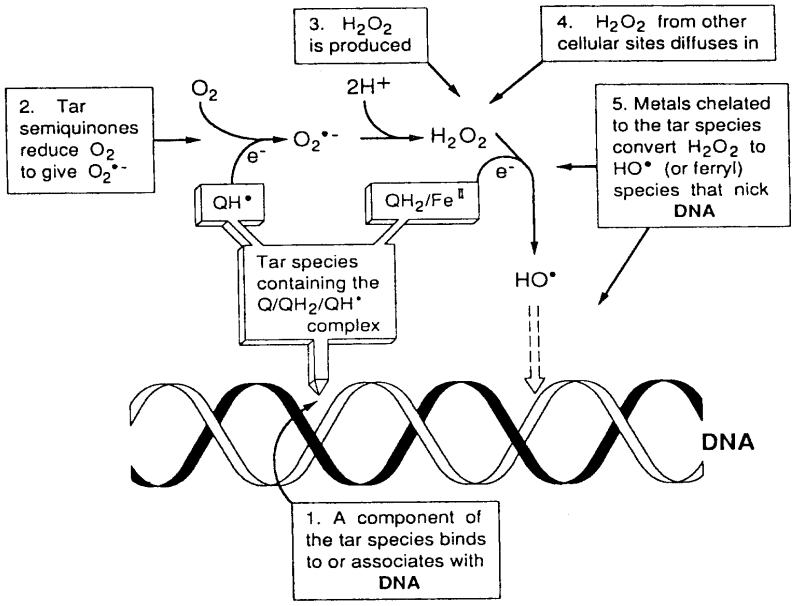

Figure 2. A cartoon showing the binding of a tar species that contains a polyhydroxyaromatic component to DNA [6].

Diseases Caused by Cigarette Smoke

Smoking is now identified as a major cause of heart disease, stroke, several different forms of cancer, and a wide variety of other health problems. Heart disease and lung cancer comprise of the vast majority of deaths caused by smoking, followed by chronic bronchitis, stroke, peripheral vascular disease, and other cancers [7]. As described above, cigarette smoke contains many radicals that can cause various diseases. Here, we focus on the mechanism for cigarette smoke damage in the lungs. Figure 3 shows us that cigarette flame produces different radicals reaching the lung and then causes damage to lung.

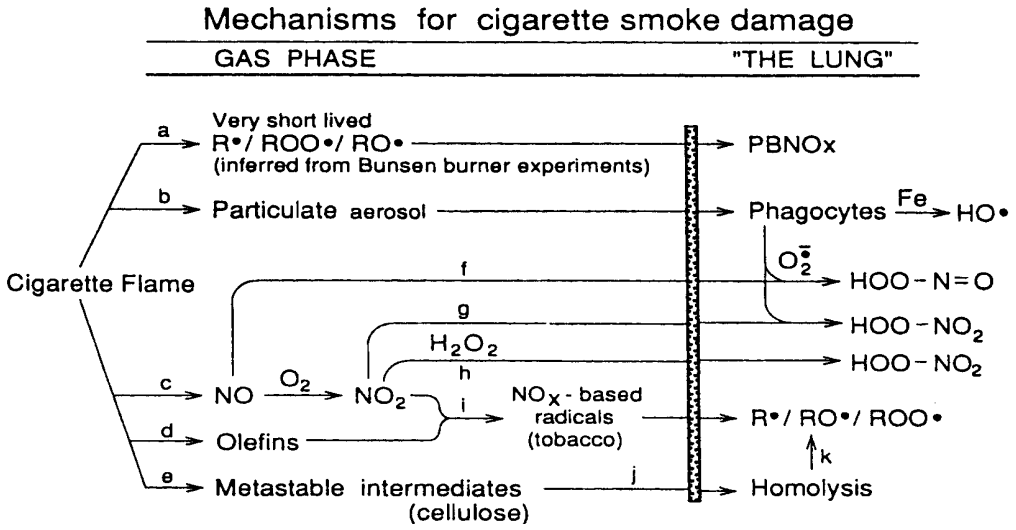

Figure 3. Mechanisms for radical production in smokes [3].

Detection of Free Radicals Generated by Cigarette Smoke

When aqueous extracts of cigarette tar are allowed to react with spin traps, spin adduct spectra are obtained that show the presence of the hydroxyl radical. The spin adduct ESR spectra obtained using DMPO are shown in Figure 4.

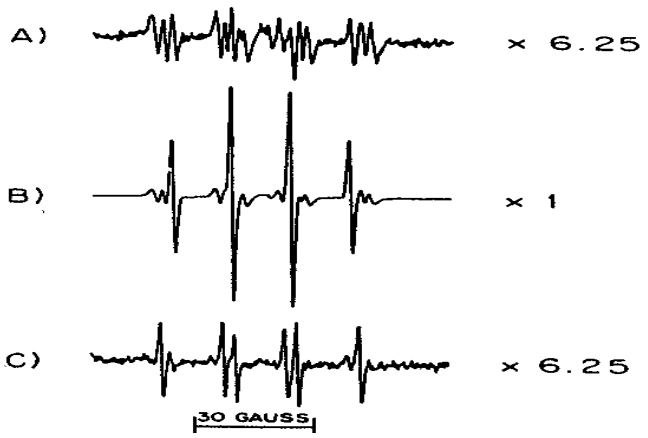

Figure 4. The ESR spectra of the spin adducts obtained when aqueous extracts of cigarette tar (ACT) and the radicals produced are allowed to react with 0.04 M 5,5-dimethyl-1-pyrroline-N-

oxide (DMPO). Panel A shows a complex spectrum that can be resolved as the signals of three spin adducts assigned to the hydroxyl radical, an alkyl radical, and the carbon dioxide radical anion. In panel B, the spectrum of the hydroxyl radical is intensified in the presence of EDTA. Spectrum C shows that a weaker alkyl radical signal is obtained if the solution is passed through a column containing Chelex-100 before mixing with DMPO [5].

Summary

Cigarette smoke radicals are of two distinct classes: 1) Long-lived radicals associated with the particulate phase (tar). 2) Short-lived radicals associated with the gas-phase that are strongly oxidizing radicals. These radicals are capable of initiating or promote oxidative damage including DNA damage and organs injury. Many diseases are related to cigarette smoke, such as lung cancer and heart diseases and so on. The radicals in cigarette smoke can be directly detected by electron spin resonance (ESR).

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