CANCER CAUSING CHEMICAL AGENTS FROM THE CIGARETTE SMOKE

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Keywords: *cangerigen agents, benzopyrene, Michael receptors, radioactive compunds*

Abstract: *Giving up smoking is the best decision and there should be no other alternative. This is what science people say. According to them, one single cigarette contains not less than 70 cancer agents. Even the exposure to passive smoking may cause secondary effects that trigger long term diseases and even death. The risk is higher even with occasional smoking. According to some international reports, any cigarette contains a mixture of over 7,000 substances, out of which hundreds are toxic and less than 70 of them are cancer causing. Each exposure to the cigarette smoke and, therefore to these chemicals, affects the DNA. As for the regular exposure, each new cigarette shatters the efforts of the body to repair what has been destroyed. Cancer causing substances reach with each and every inhaled „puff" the smokers' lungs and the lungs of those around them, with effects soon to be recorded. It is not without reason that we consider smoking, guilty of 85% of the pulmonary cancer cases. And there is clear evidence that smoking is also responsible for other types of cancer, too.*

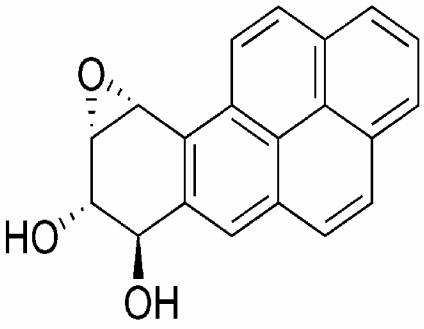
Cuvinte cheie: *agenţi cancerigeni, benzopiren, receptori Michael, compuşi radioactivi*

Rezumat: *Renunţarea la fumat este cea mai bună decizie şi nu ar trebui să aibă alternative, spun oamenii de ştiinţă. Potrivit acestora, o singură ţigară conţine nu mai puţin de 70 de agenţi cancerigeni.Chiar şi expunerea la fumul de ţigară poate avea efecte secundare imediate la nivelul organismului, putând cauza boli pe termen lung şi chiar moartea. Riscul este mare chiar şi atunci când se fumează doar ocazional. Conform umor rapoarte internaţionale ţigara conţine un amestec de peste 7.000 de substanţe, din care sute sunt toxice şi cel puţin 70 sunt cancerigene. Fiecare expunere la fumul de ţigară şi, prin urmare la aceste chimicale, afectează ADN-ul. În ceea ce priveşte expunerea regulată, fiecare nouă ţigară zădărniceşte eforturile organismului de a încerca să repare ceea ce s-a distrus. Substanţele cancerigene ajung cu fiecare "fum" inhalat în plămânii fumătorilor şi a celor care fumează pasiv, efectele fiind imediate. Nu degeaba fumatul este vinovat de 85% dintre cazurile de cancer pulmonar, existând dovezi că este responsabil şi de alte câteva tipuri de cancer*

Smoke, or any organic matter partially burnt, contains cancer causing agents. The potential effects of smoking, pulmonary cancer for instance, might appear even after 20 years through clinical manifestations. The death rate due to pulmonary cancer in men has lowered in 1975 to approximately 20 years, after the initial decline of cigarette consumption by men. The decline of cigarette consumption in women started also in 1975, but till 1991, mortality caused by pulmonary cancer has not lower in women.(1) Cigarette smoke contains several cancer causing pyrolytic products, which in combination with the DNA brings about genetic mutations. Particularly, a powerful cancer causing agent is represented by the cyclic aromatic hydrocarbonates (PAH). There are 19 cancer causing agents that we are aware of and which are present in the cigarette smoke. Among them, the most powerful are:

The polycyclic aromatic hydrocarbures (PAH) – it is the most important category of cancer causing substances in the tobacco smoke. They are born through a combustion process of the tobacco and the layer under special conditions: low oxygen and temperatures of 450-700°C. PAH are retained partially by the gudron left in the filter, but around ¾ of them reach the lungs. In the tobacco smoke, there are approximately 150 PAH. The first PAH identified as a cancer causing agent in the tobacco smoke is the benzopiren.(2) (figure no. 1) which irreversibly links the DNA (3) (figure no. 2) either destroying the cell or creating a genetic mutation.

Figure no. 1. Chemical structure of benzopyrene



If the mutation inhibits the programmed death of the cell, the cell can survive, becoming a cancer cell. The benzopyren is 50.000 times more powerful in terms of cancer causing, than saccharine, which has been given a greater attention in this senses.(4)

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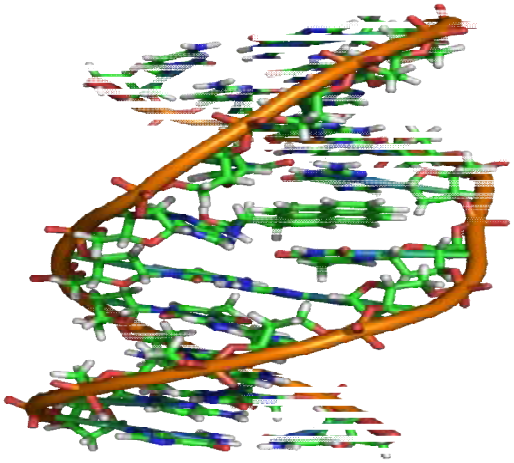
Article received on 28.10.2011 and accepted for publication on 31.01.2012
ACTA MEDICA TRANSILVANICA March 2012;2(1):253-255

Figure no. 2. Benzopyren - a major mutation agent by linking it to the DNA



The DNA contains information on the cell functioning. In practice, it contains ingredients for proteins synthesis. If the mutation inhibits the programmed death of the cell, the latter can survive and becomes a cancer cell, a cell functioning just like a normal one. Carcinogenesis is radiomimetic, for instance it is similar to the one produced by the ionization caused by the nuclear radiation. Tobacco producers have experimented the consumption of the cigarettes without benzopyren, using the technology based on non-combustion vapours, These products have not become popular.

a) Acrolein is a pyrolysis product, predominant in the cigarette smoke, conferring it a pungent smoke and an irritating, tear causing effect. It contributes dramatically to the cancer causing effect. As with the PAH, acroleine is an alkaline electrophilic agent, which permanently links with guanine, in the structure of DNA, causing the creation of a cyclic structure of hemiamine type. The acrolein-guaninic link provokes mutations during the ADN-copying, and this fact determines cancers in a way similar to those produced by the PAH. Anyway, the acrolein is 1000 times more abundant in the cigarette smoke, comparative to the PAH and is capable of acting individually, without any metabolic activation. It has been demonstrated that acrolein is a mutating and cancer causing agent in the human cells. Carcinogenesis of acroleine has been difficult to study by experiments on animals, due to its toxicity which kills the animals before the cancer occurrence.(5) In general, the compounds capable to react through conjugated electrophile links (the so-called Michael receptors - after the reaction of Michael) are toxic and cancer causing because they may permanently alchilate the DNA, similarly with the toxic gases or the alphatoxin. Michael's receptors contribute to the chronic inflammatory processes within the diseases caused by tobacco.(6)

b) Nitrosamines represent a group of cancer causing compounds found in the tobacco smoke, but not in the tobacco raw leaves.

The nitrosamines are formed on the tobacco leaves during their processing through a chemical reaction between the nicotine and other compounds contained by the leaf and with other hydrogen oxides in all the combustion gases. By the free burning of the cigarette, a reduction in the nitrosamine levels to less than 0.1 parts/million (7) has been proven. Some of the nitrosamines are shown as volatile gases (diethylnitrosamine = 0,01-0,171 μg). Most of them are yet nonvolatile (N-nitrosonornicotine (0,14-3,70 μg/cigarette N-nitrosonatabine, N-nitrosodietanolamine, nitrosopiperidine etc).

c) Using the determination by chemiluminiscence, D. Hoffmann has found important differences in the contents of nitrosamine in the cigarettes, according to their nitrate contents, to the smoke blow they collected from through aspiration (primary or secondary blow), the stand-by cigarette etc. (8) (table no. 1).

d) Aza-arenes or *heterocyclic hydrocarbons* are represented by dibenz (a,h) acridine, dibenz (a,j) acridine and dibenz (c,g) carbazole, known as cancer causing substances. To these other substances with a mutation role, the following are added: quinolina, benzo (f) quinidine, benzo (h) quinoline and fenantridine. Their concentrations are of nanogramme order, 10-20 times higher than in the smoke released by the stand-by cigarette.

e) There are 33 known nitriles in the cigarette smoke, most of them aromatic.(9)

f) Aromatic amines, such as beta-naftilamine, 4-aminodifenile and ortotoluidine, are present in very small concentrations (1-3 ng/cigarette), and they can highly increase in the smoke of the cigarette kept in stand-by (for example: ortotoluidine reaches concentrations of 100-200 ng/cigarette in the inhaled smoke and 2000-3000 ng/cigarette in the smoke of a stand-by cigarette).

Table no. 1 – Nitrosamines in the cigarette smoke (μg/cigarette)

Type of cigarette	Nitroso-dimetilamine	Nitroso-etilimetilamine	Nitroso-dietilamine	Nitroso-pirolidine	Nitroso-nornicotine
Common (l,l g) Through inhaling, Free burning, stand-	13 6800	1,8 9,4	1,5 53	11 300	250 -
Cigar, small (l,l g) Through inhaling, free burning, stand-by	30 1770	3,1 75	- 29	20 610	550 -
Cigar, Columbia (6,8g) through inhaling, free burning, stand-by	370 2350	52 75	21 -	61 640	1690 13100
cigar, common (7,5g) Through inhaling	70	10	-	10	890

g) Other nitrogen compounds. It is estimated that in the cigarette smoke, there are more than 600 nitrogen compounds, out of which some are cancer causing: nitrophenols, some aromatic and aliphatic nitrohydrocarbures acetonitrile, aliphatic and aromatic amines (metilamine, aniline, pyrolidine). Some of them may be predecessors of nitrosamines such as urethane, or hydrazine belonging to the maleic hidrazide used in the treatment of tobacco for preventing the growing of lateral branches and the proper development of the leaves. The hydrazine is found in quantities of 20-40 μg /cigarette, and 1,1-dimetilhidrazine and urethane is found in quantities of tens of nanogrames order.

h) Radioactive agents. In addition to the chemical cancer causing nonradioactive agents, tobacco and cigarette smoke contains small quantities of Pb^{210} and Po^{210}, both being cancer causing radioactive agents. The presence of Po^{210} in the cigarette smoke has been experimentally measured at the levels of 0,0263-0,036 pCi (0,97-1,33 mBq), and this is equivalent to about 0,1 pCi/mg smoke (4 mBq/mg); or around 0,81 pCi ^{210}Pb/g of dry condensed smoke (30 Bq(kg).

The research undertaken by the chemist Ed Martell has shown that the radioactive substances in the cigarette smoke are deposited in the hot spots where the bronchia separate from each other. Since the gudron in the cigarette smoke is resistant to dissolving, under the action of the fluid in the lungs, the radioactive compounds have enough time to pass through the mucosa before they are cleaned in a natural way. In the interior, these radioactive compounds persist in the passive smoking and, therefore, a large exposure takes place when they are inhaled during the normal inhaling and this is deeper and longer than when inhaled from cigarettes. The destructions caused by smoking, at the level of the protective epithelial tissue, enhance the retention of insoluble Po210, which is produced through tobacco burning. Martell estimated that a dose of carciogenetic of 80-100 razi is freed in the lung tissues by most of the smokers who die of pulmonary cancer.(10) The idea that Po^{210} is responsible for many cancer cases among smokers is accepted by at less one researcher.(11,12)

In order to highlight the effects caused by Po210 from the cigarette, we can make a comparison with what happens with Xrays used in a usual thoracic radiography. A modern thoracic radiography uses a dose of 0,034 mSv/radiography, therefore, a smoker of 20 cigarettes per day receives during a whole year a radiation dose equivalent to 300 thoracic radiographies.(13)

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