



Smoke generation inside a burning cigarette: Modifying combustion to develop cigarettes that may be less hazardous to health[☆]

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Abstract

The formation of smoke from a burning cigarette depends on a series of mechanisms, including generation of products by pyrolysis and combustion, aerosol formation, and physical mass transfer and filtration processes. Each mechanism, and their interactions, has a profound effect on the levels of chemical constituents in tobacco smoke. An enormous amount of research has been done on these subjects over the last 50 years. This work is briefly reviewed.

A burning cigarette is a complex system in which many types of chemical reactions and physical processes occur. There are two main regions inside the burning zone: a combustion zone and a pyrolysis/distillation zone. Inside the combustion zone, oxygen reacts with carbonised tobacco producing simple gases such as carbon dioxide, carbon monoxide and hydrogen, together with the heat that sustains burning. Temperatures up to 950 °C are generated when the cigarette is puffed. Immediately downstream of the combustion zone is the cooler pyrolysis/distillation zone, where the bulk of the 5000 or so chemicals in smoke are generated. As the super-saturated vapour generated rapidly cools within a few milliseconds it condenses into the aerosol particles that make up the smoke.

From the 1950s onwards many attempts have been made to selectively remove or reduce the chemicals in smoke that are thought to be associated with adverse health effects. Some new cigarettes have been developed in which the combustion and smoke formation processes have been modified, with the aim of producing cigarettes that may be potentially less hazardous. An overview is presented of the approaches taken.

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Contents

1. Introduction	374
2. Smoke generation mechanisms	374

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3. The chemical nature of cigarette smoke	377
4. Approaches to developing cigarettes that may be potentially less hazardous to health	378
References	383

1. Introduction

A burning cigarette is a classic example of an incomplete combustion system and the adverse health effects of its combustion products are well known. The combustion processes occurring inside a cigarette, and approaches to modelling them, have been described in detail elsewhere [1–3]. The objectives of this paper are to outline those aspects of cigarette combustion and smoke chemistry that are believed to be relevant to smoking-related diseases, and to summarise some attempts that have been made to modify combustion and develop smoking products that may be less hazardous to health. A historical approach will be taken.

Fifty years ago things happened that were to change the perception of smoking completely and forever. Firstly, five case-controlled studies were published in 1950, one in the UK [4] and four in the USA [5–8] in which the authors demonstrated that there was a strong statistical association between cigarette smoking and lung cancer. Before 1950 there had been suspicions, based largely on anecdotal evidence, that smoking might be injurious to health, going back to the statement by King James I of England (also known as King James VI of Scotland) in his 1604 book “A Counter-Blaste to Tobacco” that smoking was “lothsome to the Eye, Hatefull to the Nose, harmful to the braine, dangerous to the Lungs (sic)....”. Secondly, Wynder et al. [9] published the results of biological work showing the generation of tumours on mice following skin painting with tobacco smoke particulate matter. Thirdly, Cooper and Lindsey [10,11] and Cooper et al. [12] reported the presence of a known carcinogen, benzo[*a*]pyrene, in the particulate matter of tobacco smoke. Although their spectral evidence was criticised by Feiser [13] as inadequate, the issue was eventually resolved in 1959 by the isolation of crystalline benzo[*a*]pyrene from cigarette smoke particulate matter by Wynder and Hoffmann [14,15].

We now know that cigarette smoking is associated with an increased incidence of a variety of diseases. For each of these diseases, epidemiology suggests dose–response relationships. This means that groups of smokers that start smoking later, quit

earlier and smoke fewer cigarettes per day tend to have lower incidences of these diseases than people who smoke more. The incidence of disease in low dose smokers is still higher than in people who do not smoke. The only way to avoid a smoking-related risk is not to smoke. For those that do smoke, the risks are primarily modified by the amount and duration of consumption. However, within this context, the design of cigarettes may also modify risks, and efforts to design “less hazardous” cigarettes have been conducted by tobacco companies for many years, often in collaboration with public health groups. One essential element of this work has been the development of a greater understanding of smoke chemistry.

2. Smoke generation mechanisms

In the 1950s, relatively little was known about the chemical nature of smoke or its generation. Since that time an enormous amount of work has been done to unravel the physical and chemical mechanisms occurring as the cigarette burns. This work has been done essentially to answer two questions [16]:

1. Which components of smoke are responsible for the human health risks associated with smoking?
2. Which components of smoke are important to the flavour, sensory experience and consumer acceptance of tobacco products?

To some, the second question may seem irrelevant. However, in seeking to produce cigarette modifications that may be regarded as “less hazardous”, the second point remains important. Any tobacco product modification that may be accepted as “less hazardous” would be of little value unless it provided an acceptable alternative to conventional products to those people who decide that they want to smoke. The answers to these questions are the “holy grail” of tobacco research. However, after 50 years of research neither question can be answered completely.

Tobacco is a plant material and consists of some 3800 constituents, ranging from small organic and inorganic molecules to biopolymers [17]. The small molecules belong to numerous classes of

compounds such as hydrocarbons, terpenes, alcohols, phenols, acids, aldehydes, ketones, quinones, esters, nitriles, sulphur compounds, carbohydrates, amino acids, alkaloids, sterols, isoprenoids, Amadori compounds, etc. The biopolymers consist of cellulose, hemicellulose, pectin, lignin, starch, proteins and peptides, nucleic acids, etc. During smoking, these are all subjected to temperatures up to 950 °C in the presence of varying concentrations of oxygen in the burning zone of the cigarette or other tobacco product [2]. About 4800 individual substances have been identified in tobacco smoke [16]. Most of these are at trace levels and current limits of detection for smoke components are of the order of about 100 pg (i.e. 100×10^{-12} g). Many of the smoke components arise from a variety of different routes including distillation from tobacco, combustion, pyrolysis and pyrosynthetic reactions. Approximately 2800 constituents are found in tobacco smoke but not tobacco, indicating the importance of pyrolysis, pyrosynthetic and combustion formation mechanisms.

The approximate relationships of the major combustion processes involved in smoke generation have been described by Muramatsu [3] and are shown in Fig. 1. Many studies have been under-

taken to determine the conditions inside the burning zone of the cigarette that influence product formation mechanisms. These include determination of the temperature and gas formation contour distributions at various times in the smoking cycle of a burning cigarette, using temperature probes and small sampling tubes inserted inside the burning zone and connected to a mass spectrometer [18–23]. This work has been summarised by Baker [1,2] and, from it, a pictorial representation of the major smoke formation mechanisms occurring inside the cigarette can be obtained (Fig. 2). The interior of the burning zone is oxygen-deficient and hydrogen-rich and can be effectively divided into two regions: an exothermic combustion zone and an endothermic pyrolysis/distillation zone. As air is drawn into the cigarette during the puff, oxygen is consumed by combustion with carbonised tobacco and the simple combustion products carbon monoxide, carbon dioxide and water are formed, together with the release of heat which sustains the whole burning process. Temperatures in this region of between approximately 700 and 950 °C are generated and heating rates as high as 500 °C s^{-1} are achieved. Immediately downstream of the combustion region is the pyrolysis/distillation

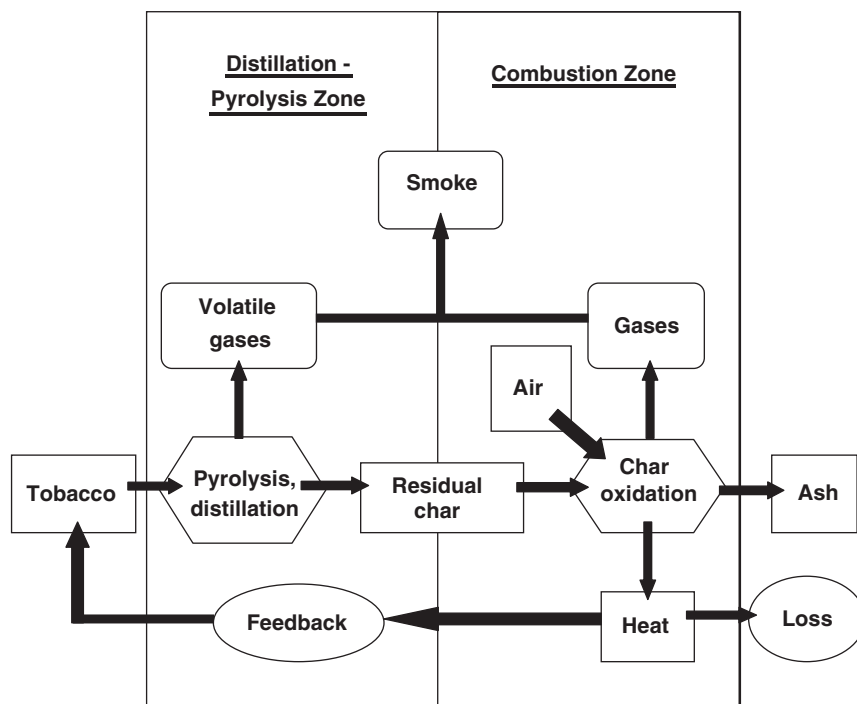


Fig. 1. Schematic diagram of the major processes occurring during cigarette combustion, after Muramatsu [3].

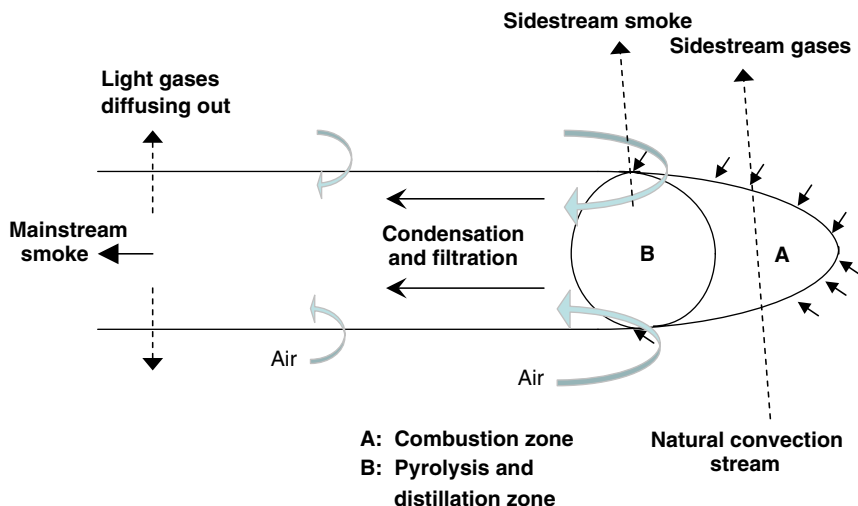


Fig. 2. The burning cigarette during a puff.

zone, where the temperatures are between approximately 200 and 600 °C and which is still low in oxygen. The majority of smoke products are generated in this region by a variety of mechanisms which are essentially endothermic. A highly concentrated, probably supersaturated, vapour is generated and, during a puff, is drawn down the tobacco rod to form the mainstream smoke. Its residence time in the formation region is only a few milliseconds.

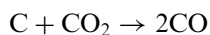
As the generated vapour is drawn out of the pyrolysis/distillation region during the puff, it cools very rapidly in the presence of diluting air entering at the paper burn line. This brings the vapours of the less volatile compounds quickly to their saturation point and condensation occurs as the vapour cools below about 350 °C. A dense aerosol consisting of growing droplet particles is formed. The mainstream smoke emerging from the mouth-end of the cigarette during a puff is a highly concentrated, dynamic aerosol system. The smoke particles are liquid, with water making up approximately 20% of the droplet volume and, consequently, they have spherical shapes. There are some 10^9 – 10^{10} particles per ml in fresh mainstream smoke, making it an extremely dense aerosol. Initially the particles vary in diameter from less than 0.1 to 1.0 μm [24–26]. These very high concentrations and small sizes are such that the particles will rapidly coagulate, resulting in sizeable decreases in number concentra-

tion and increases in average particle diameter within fractions of a second.

The size of smoke particles will also increase in moist environments due to absorption of water vapour. This will be particularly important in the respiratory tract where the relative humidity is estimated to be 99.5% [27]. The relative humidity of mainstream smoke is 60–70% and little particle growth due to water absorption occurs below 90% relative humidity [25,26]. Particle growth increases sharply with humidity above 90% due to the absorption of water and smoke particles double in size at 99.5% relative humidity [28]. Smoke particle growth by absorption is a complex process dependent on the chemical composition of both the particles and surrounding gas phase. It occurs in milliseconds [29].

Carbon monoxide and dioxide are the major products in cigarette smoke and are formed by both thermal decomposition and combustion of many of the components of tobacco: starch, celluloses, sugars, carboxylic acids, esters, amino acids, etc. Studies in which the cigarette was smoked or pyrolysed in isotopically labelled oxygen and carbon dioxide [21,30,31] have shown that approximately 30% of the carbon monoxide is formed by thermal decomposition of tobacco constituents, about 36% by combustion of tobacco and at least 23% by the endothermic carbonaceous reduction of carbon

dioxide:



3. The chemical nature of cigarette smoke

Cigarette smoke is a complex mixture. Of the approximately 4800 identified substances in tobacco smoke [16], 45 are believed by Regulatory Authorities in Canada and the USA to be relevant to smoking-related diseases [32–34]. These include, inter alia, some volatile carbonyl compounds, tobacco-specific *N*-nitrosamines, aromatic amines, phenols, volatile alkenes, benzo[*a*]pyrene and metals. A summary of these substances, together with their approximate amounts in cigarette smoke and their phase in smoke, are listed in Table 1. These substances are sometimes colloquially called “Hoffmann analytes” since similar lists of toxicological substances have been proposed by Dietrich Hoffmann and co-workers of the former American Health Foundation in New York since the mid-1980s (e.g. [36–38]). The latest compilation by Hoffmann and colleagues in fact lists 82 substances. Those substances on the list of “Hoffmann analytes” are not necessarily the only cigarette smoke constituents that have toxicological properties. Rodgman and Green [39] have listed 149 substances in smoke, including more extensive lists of polynuclear aromatic hydrocarbons, *N*-nitrosamines, *N*-heterocyclic amines and other organic molecules. In addition, free radicals may also be important, (e.g. [40]).

Much effort has been devoted to determining the conditions under which smoke components are generated and the mechanisms by which they are formed, especially those that are believed to be implicated in tobacco-related diseases [2,41]. For example, tobacco smoke contains a large variety of hydrocarbon compounds. The type of hydrocarbon generated from tobacco is dependent on the temperature of the tobacco. The general results from a large number of studies indicate that, at temperatures between about 300 and 550 °C in the cigarette burning region, small hydrocarbon molecules (C_1 to C_3) are generated. Longer chain *n*-alkanes and alkenes are formed at temperatures between about 400 and 700 °C. At temperatures above about 500 °C, benzene and alkylbenzenes are formed. At temperatures above about 700 °C naphthalenes are formed. More than 75 monocyclic aromatic hydrocarbons such as benzene and toluene

are formed from the pyrolysis of amino acids, fatty acids, cinnamic acid, sugars and paraffins, precursors with an aromatic or cyclohexane ring, and pyrosynthesis from primary hydrocarbon radicals. There are at least 80 naphthalenes present in smoke. Polynuclear aromatic hydrocarbons are formed at temperatures above 800 °C. Over 300 individual polynuclear aromatic hydrocarbons have been identified in tobacco smoke. The polynuclear aromatic hydrocarbons are formed by pyrolysis and pyrosynthetic reactions of long-chained hydrocarbons, terpenes, phytosterols such as stigmaterol, paraffins, sugars, amino acids, celluloses and many other tobacco components. They are also formed by pyrosynthetic reactions involving small, primary hydrocarbon free radicals in the high temperature region of the burning zone [42,43].

As a further example, tobacco smoke contains two general types of nitrosamines:

- (1) Tobacco-specific nitrosamines, which are found only in tobacco and tobacco smoke particulate phase, are derived from tobacco alkaloids, and are non-volatile.
- (2) Non tobacco-specific nitrosamines, which are found in many systems, are volatile and are present in the vapour or semi-volatile fraction of smoke.

Tobacco specific nitrosamines are not present in freshly harvested green tobacco. They are formed during curing by nitrosation of tobacco alkaloids. The nitrosating agent is nitrite, derived from tobacco nitrates by bacteria and enzymes during curing. When the cigarette is smoked, some of the nitrosamine transfers to smoke, some decomposes and some tobacco-specific nitrosamines are also formed pyrosynthetically in the burning zone. There is some conflict in the scientific literature on exactly how much is formed pyrosynthetically. The levels of non tobacco-specific nitrosamines in mainstream smoke are much lower than those of the tobacco-specific nitrosamines. They are not present in tobacco and are formed pyrosynthetically during tobacco combustion. These pyrosynthetic reactions involve nitrosation of amino acids and tobacco protein. The nitrosating agent is believed to be N_2O_3 , formed by reaction of NO and NO_2 . Thus amino acids, protein in tobacco (which can generate amines on burning), and nitrate (which can generate nitrogen oxides) are important precursors of the volatile nitrosamines.

Table 1
Modified ‘Hoffmann List’ of smoke toxins^a

Class, constituents	Number in class	Yield ^b	Smoke phase ^c
Major components	3		
“Tar”		9.2 mg	P
Nicotine		0.77 mg	P
CO		13 mg	V
Inorganic gases	3		
NH ₃		14 µg	V
HCN		140 µg	V–P
NO _x		310 µg	V
Tobacco-specific nitrosamines	4		
<i>N</i> '-Nitrosonornicotine (NNN)		100 ng	P
<i>N</i> '-Nitrosoanabasine (NAB)		23 ng	P
<i>N</i> ' Nitrosoanatabine (NAT)		110 ng	P
4-(Methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK)		89 ng	P
Phenols	7		
Phenol, <i>o</i> -cresol, <i>m</i> -cresol, <i>p</i> -cresol		3–10 µg	V–P
Catechol, hydroquinone		39 µg	P
Resorcinol		0.7 µg	P
Carbonyls	8		
Formaldehyde		19 µg	V–P
Acetaldehyde, acetone		610, 290 µg	V–P
Propionaldehyde, methyl ethyl ketone, acrolein		51–72 µg	V–P
Butyraldehyde, crotonaldehyde		32, 25 µg	V–P
Polynuclear aromatic hydrocarbons	1		
Benzo[<i>a</i>]pyrene		7.0 ng	P
Aromatic amines	4		
1-Aminonaphthalene, 2-aminonaphthalene		15, 10 ng	P
3-Aminobiphenyl, 4-aminobiphenyl		3.4, 2.1 ng	P
Semi-volatiles	3		
Pyridine, styrene		8 µg	P
Quinoline		0.4 µg	P
Vapour phase	5		
1,3-Butadiene, benzene, toluene, acrylonitrile		15–90 µg	V–P
Isoprene		400 µg	V–P
Metals	5		
Pb, Cr, Ni, Hg, As, Cd, Se		1–52 ng	P
Total	45		

^aAbbreviated list as used in Canada and Massachusetts [33,34].

^bUniversity of Kentucky 1R4F reference cigarette, ISO machine-smoking conditions [35]. Many modern, commercial cigarettes have lower levels than these quoted reference cigarette levels. For example, in the European Union all cigarettes must have “tar”, nicotine and CO yields below 10, 1 and 10 mg, respectively.

^cP—particulate phase of smoke, V—vapour phase, V–P—partitioned between the vapour and particulate phases.

4. Approaches to developing cigarettes that may be potentially less hazardous to health

From the 1950s onwards the scientific literature on tobacco smoke, patent literature and internal

tobacco company research reports have contained descriptions of many attempts to remove or reduce the identified biologically active chemicals in cigarette smoke. Unfortunately, many of the methods described were based on either an incomplete view

of smoke chemistry or produced adverse effects to the smoke, or both.

The earliest attempts were to remove benzo[*a*]pyrene and the other polynuclear aromatic hydrocarbons (PAHs) from smoke. As discussed in Section 3, from the large amount of work done on the generation of these materials in tobacco smoke, it had become clear by the mid-1960s that their formation involved pyrosynthetic reactions of long-chained hydrocarbons, terpenes and phytosterols, and pyrosynthetic reactions involving small, primary hydrocarbon free radicals in the high temperature region of the burning zone. It is well known that high-temperature free radical reactions can be quenched by the presence of nitric oxide, itself a free radical. Nitric oxide is generated from the thermal decomposition of nitrites and nitrates. Consequently, the addition of nitrites, nitrates and high-nitrate tobacco material to the tobacco blend was found to be an effective method of significantly and selectively reducing the level of benzo[*a*]pyrene and PAHs in smoke relative to “tar”, (e.g. [44]). In addition, removal of waxes from tobacco by solvent extraction reduced the proportion of long-chained hydrocarbons in tobacco, known precursors of benzo[*a*]pyrene and PAHs [45,46]. Thus, in the 1960s the belief was that removal of tobacco waxes and increasing the tobacco nitrate levels should be undertaken as a means of reducing the levels of polynuclear aromatic hydrocarbons in smoke.

However, as discussed above, nitrate is a precursor for the generation of nitrosamines in tobacco. Consequently, increasing the nitrate in the tobacco increases the level of both tobacco-specific and volatile nitrosamines in tobacco smoke [47,48]. In addition, selection of tobaccos with relatively high levels of long-chained hydrocarbons was also suggested as a means of reducing formation of nitrogen oxides and nitrosamines [47]. Thus, by 1982 the belief was that increasing tobacco waxes and reducing the tobacco nitrate was the best means of reducing the levels of nitrosamines in smoke.

Consequently, removal of tobacco waxes and adding nitrate to tobacco reduce the levels of the PAHs, and increase the levels of the nitrosamines, in tobacco smoke. This is just one example of the dilemmas facing those trying to produce acceptable product modifications. There are many separate processes involved in the generation of different smoke components, often interacting in a complex manner. Making a modification to reduce the level of one group of substances in smoke usually also

produces other undesirable effects. That is why, historically, the most promising approach to the development of cigarettes that might be associated with reduced health risks has been to reduce all of the smoke components rather than selective reduction of specific substances. Thus for 30 years the tobacco industry has continuously sought to develop cigarettes with progressively lower “tar” yields. Indeed, it is possible that some of the health risks of smoking are not actually associated with individual compounds, or classes of compound, in smoke. Rather, these health risks may be associated with the smoke as a whole. If this were the case, total smoke yield would be more indicative of adverse health effects than individual chemical constituent. “Tar” is a collective term for all of the particulate matter of smoke, collected on an analytical filter, with the amounts of water and nicotine subtracted. Indeed, after considering the epidemiological and biological data available at the time, Wynder [49], a pioneer in the study of smoking epidemiology and biological activity, stated:

It may be predicted that if the average smoker were exposed to only half the amount of tobacco tar to which the smoker of regular-sized cigarettes is now exposed, his cancer risk would be considerably reduced. Any measure designed to thus reduce man’s exposure to tobacco tar, whether through modification of the tobacco or the cigarette, or through more efficient filtration, can significantly contribute to the decrease in risk.

Wynder re-emphasised this conclusion in a paper in the British Medical Journal in 1957 [50], and emphasised the importance of cigarette filtration, removal of precursors of smoke carcinogens and modification of tobacco pyrolysis. In the UK the development of lower “tar” cigarettes has been undertaken in association with various government bodies, in particular the UK Independent Scientific Committee on Smoking and Health. It has been accomplished by the use of filters and filter ventilation, modified cigarette paper and modified forms of tobacco and tobacco blends. In the UK the sales-weighted average “tar” yield has been gradually reduced from about 38 mg in the mid-1950s to below 10 mg today, when measured with the standard ISO smoking regime method [51]. In the USA the sales-weighted average “tar” yield has been reduced to about 12 mg. In fact there is now a “tar” ceiling of 10 mg for all cigarettes within the

European Union, i.e. all cigarettes sold must have a “tar” yield below 10 mg. Very low “tar” cigarettes are currently available with yields of below 1 mg. “Tar” is a collective term for the particulate-phase material in cigarette smoke (specifically, total particulate matter minus nicotine and water). Consequently, as “tar” levels have fallen over the last 40 years, all of the particulate-phase constituents listed in Table 1 will have been reduced to the same extent as the “tar”, to a very good first approximation. The use of filters containing activated carbon also reduces the gas-phase constituents of cigarette smoke. However, the most effective means of reducing gas-phase components in smoke is by the use of porous cigarette papers and ventilated filters. In a ventilated cigarette filter, a zone of microscopic ventilation holes is provided around the circumference of the filter. Such filters have been available for over thirty years and were developed to reduce the yields of all smoke components. The effects of ventilation are more than just dilution of the smoke since the various smoke products are reduced by different amounts [52]. Increasing the level of ventilation at the filter causes a smaller proportion of the puff volume to be drawn in through the cigarette burning zone. The intensity of combustion is consequently reduced, less tobacco is burnt during the puff and the level of most mainstream components generated is decreased. The average velocity of flowing smoke/gases through the cigarette decreases so that the outward diffusion of light gases such as carbon monoxide, and the filtration of smoke aerosol particles are increased. All of these processes will reduce the levels mainstream smoke components. In addition, of course, the levels of all the mainstream smoke products will be diluted with incoming air as they are drawn along the cigarette.

For an 11-year period in the USA, from 1968 to 1979, the National Cancer Institute had a multi-million dollar Smoking and Health Programme on research into the development of less hazardous cigarettes, recently reviewed by Gori [53], one of the principal leaders of the programme. The programme had an advisory committee that included top academic and government researchers in the field as well as the research directors of the major US cigarette manufacturers. The programme had two main objectives:

1. Understanding the pharmacological aspects of smoke.

2. Identifying the hazardous components of cigarette smoke and the development of methods for minimising or eliminating those components.

The major concern of the programme was on the cancer-causing properties of cigarette smoke, i.e. the carcinogenicity or tumorigenicity of smoke. Within the programme, co-ordinated, broadly based research projects were carried out that included determining the detailed chemical composition of mainstream smoke and the biological properties of the smoke using the only standardised animal biological test available at the time, the skin painting of cigarette smoke “tar” onto the shaved backs of mice, to determine how fast and how severely tumours were produced. These studies were done on smoke from more than 150 differently modified cigarettes and 30 reference cigarettes that involved the manufacture of over 70 million experimental cigarettes. These design changes were brought about by modifications to the tobacco, tobacco fractions such as leaves and stem, the paper wrapper of the cigarette, filters, adding or removing nicotine, the use of additives and design changes that could affect the combustion of the cigarette, as well as the use of tobacco substitutes. From this programme it was determined that there were eight design technologies that could be utilised in the development of less hazardous cigarettes. These were modification of the tobacco blend, incorporation of reconstituted tobacco sheet into the blend, the use of additives such as citrates to cigarette paper, the use of filters to reduce smoke yields, the use of expanded tobacco and incorporation of additives such as triacetin as plasticizer in the filter, the use of paper of higher permeability to reduce smoke yields and the use of ventilated filters. In fact, all of these design technologies were developed by the tobacco industry and had begun to be used commercially before the National Cancer Institute’s programme had started in 1968 [39,54]. The National Cancer Institute Programme gave independent confirmation that the technologies were likely to be in the right direction. The use of these technologies eventually permitted the mainstream yield of “tar” in commercial cigarettes to be reduced from 40 to less than 1 mg in some brands, with corresponding reductions in the yields of those smoke components considered harmful. Sadly, the programme was abandoned in 1979 before some of its projects were completed, when the prevailing philosophy of the National Institute of Cancer

changed from modification of cigarettes to abolition of smoking [53].

Concerns have been raised recently by some public health scientists as to whether the low “tar” approach is appropriate on the basis that people switching from higher to lower “tar” cigarettes may adjust their smoking behaviour, for example by taking more intense puffs or inadvertently blocking some of the filter ventilation zone with their lips or fingers. In this way, the reduction in smoke yields obtained by the human smoker would be less than the reduction indicated by smoke yields obtained on a smoking machine. This phenomenon, known as compensation, has been known for decades (e.g. [55]) and was considered as part of the UK’s product modification programme in the 1970s. That programme determined that while compensation was likely to occur to some extent, it was not complete and hence lower “tar” was likely to be associated with some reduction in risk for some diseases. Scherer [56] has more recently reviewed all of the scientific literature on smoking compensation. He concluded that while human smoking behaviour is highly variable, on average partial compensation does occur shortly after smokers switch to cigarettes with different yields to their usual brand. Changes in the puff volume are the most probable mechanism of compensatory smoking. Baker and Lewis [57] have also shown that inadvertent blocking of the filter ventilation zone by the smoker’s fingers or lips as it occurs in practice has only a relatively minor effect on human smoker yields compared to other smoker behaviour factors. Scherer has concluded from all of the available data taken as a whole that the mean compensation is about 50%. Thus, for example, on average a smoker who switches to a cigarette with a “tar” yield 50% lower than his/her current brand as measured on a smoking machine (ISO standard conditions) will actually receive a “tar” yield 25% lower than that received from their original cigarette. Consequently, it may be expected that, in general, smokers switching from a higher to a lower “tar” yield cigarette will obtain a reduction in smoke component uptake.

In the 1970s, several years of intense research and development in the UK led to the production of tobacco substitutes. These were developed jointly by tobacco companies and chemical companies and the substitutes contained cellulose, chalk, glycerol and other materials that were simpler than tobacco. The tobacco substitutes were known by various names, such as NSM (New Smoking Material, developed

by ICI in the UK), *Tabelle*[®] (developed by Courtaulds, UK), *Cytrel*[®] (developed by the Celanese Corporation in the USA) and *BAT-FLAKE* (developed by British American Tobacco in the UK). Cigarettes were made containing mixtures of tobacco and the substitute material. The substitute material acted essentially as a diluent for the smoke generated by the burning tobacco. Smoke from the cigarettes had lower levels of many smoke constituents, and gave lower responses in various bioassays, than the equivalent all-tobacco, conventional cigarette (e.g. [58–60]). The chemical and testing regimes for the new cigarettes were developed by the tobacco industry in collaboration with a committee of independent scientists set up by the British Government [61]. Twelve cigarette brands containing various types of tobacco substitutes were launched in 1977. After some initial interest by the smoking public, smokers quickly decided that they did not like their taste and all the brands failed to gain any appreciable market share. Because of this market failure, all of the brands were subsequently withdrawn from sale.

In the 1980s a cigarette was developed by the R.J. Reynolds Tobacco Company in the USA that heated tobacco rather than burnt it. The cigarette consisted of four main parts. The first section consisted of a carbon fuel element, about 13 mm long and the same diameter (8 mm) as the cigarette. The next section contained a central aluminium capsule, which was partly ventilated, containing α -aluminium oxide spheres which were impregnated with spray-dried tobacco, glycerol and a small amount of flavour, and the capsule was wrapped in tobacco. The third section consisted of folded paper reconstituted tobacco made from tobacco fibre and softwood pulp. The last section, the mouth-holding section, consisted of a specifically designed polypropylene filter. When the carbon section at the front of the cigarette was lit, the hot air generated was drawn through the second section, where it vaporised nicotine and flavours and these were cooled, augmented and filtered in the next two sections. Since no products of tobacco combustion were generated the cigarette gave a much simpler smoke chemistry than conventional cigarettes. The levels of many of the toxic substances in its smoke were much lower than those in an equivalent conventional cigarette, or completely eliminated. The smoke gave significantly lower responses in a variety of bioassays than a conventional cigarette. Also, very little sidestream smoke was generated.

All of the results were published in a very comprehensive review [62]. The cigarette, known as Premier, went on sale in 1988. The cigarette was not liked by its consumers, who complained of the smoke flavour, its difficulty in lighting, and the nuisance problem of disposing of the spent cigarette. It was subsequently withdrawn from sale.

The R.J. Reynolds Tobacco Company subsequently developed the “heat but not burn” tobacco concept further and launched a modified version known as Eclipse in the USA in 1995, and later in Germany, Sweden and Japan. In this version, the second section of the cigarette contained a band cast reconstituted filler with added tobacco extracts, glycerol and flavours. The smoke from Eclipse is 75–80% water and glycerol and consequently the total “tar” content of 4 mg (US Federal Trade Commission machine-smoking conditions, effectively the same as ISO conditions [51]) has less than 1 mg “tar” from the pyrolysis of tobacco. There are much less smoke constituents in the smoke from Eclipse than those from an equivalent conventional low “tar” cigarette, and the overwhelming majority of the toxic compounds listed by health officials are reduced. These include carcinogens, tumour promoters, cytotoxins, mutagens, irritants and vapour-phase free radicals. Smoke and total particulate matter from Eclipse cigarettes have markedly reduced toxicity compared to conventional “low tar” cigarettes when evaluated in widely used and scientifically accepted biological tests. These tests included a battery of *in vitro* assays, Ames, sister chromatid exchanges, chromosome aberrations and cytotoxicity; *in vivo* assays, subchronic inhalation toxicology and 30-week dermal tumour promotion studies; and studies in human smokers. An independent panel of independent scientists, convened by the R.J. Reynolds Tobacco Company, concluded that all the chemical and biological data available indicated that the Eclipse cigarette may have the potential to significantly reduce the health risks compared to conventional cigarettes [63]. The Eclipse cigarette is still on sale in the USA.

In 1998 the Philip Morris Company in the USA marketed another version of a cigarette that heats tobacco rather than burns it, known as Accord. They have developed a hand held device about the same size as a small cell (mobile) phone, which contains a series of battery-operated electric heating elements. The Accord unfiltered cigarette is inserted into the device and the heating elements are activated when the smoker sucks on the cigarette.

The heating elements then generate smoke from the cigarette by a low level of pyrolysis/combustion [64]. The smoke chemistry and responses in various bioassays were significantly reduced relative to a conventional reference cigarette. On a per cigarette basis, almost two thirds of 69 toxic chemicals in smoke identified by regulatory scientists as relevant to smoking-related diseases were reduced by at least 80% [65]. The total particulate matter from the electrically heated cigarette was up to 90% lower in an *in vitro* mutagenicity bioassay (Ames) than the reference cigarette on an equal particulate matter basis, and 40% less active in a cytotoxicity (neutral red uptake) bioassay [66]. In a 90-day rat inhalation study, the biological activity of mainstream smoke from the electrically heated cigarette was equal to that from the reference cigarette on an equal particulate matter basis and 65% lower on an equal cigarette basis [67]. Consumer acceptance of the Accord cigarette has been low although it is still on sale in parts of the USA.

As a final example of cigarette developments to potentially reduce the adverse health effects of smoke, in the late 1990s methods were developed which greatly reduced the formation of nitrosamines during the flue-curing of tobacco, leading to extremely low levels in the smoke from cigarettes made with the tobacco. One method, known as the “Star Process” after the American company that developed it, uses modified heating during tobacco curing, together with microwave heating in their original description of the process, to eliminate the bacteria that produce the nitrite that converts the tobacco alkaloids into nitrosamines [68]. The modified curing process developed by Star also replaces direct heating of the tobacco with indirect heating so that the NO_x , produced as a by-product of the combustion of liquid propane gas, does not have contact with the tobacco and so nitrosates the tobacco alkaloids during curing. The R.J. Reynolds Tobacco Company in the USA has also developed a modified flue-curing process that relies entirely on indirect heating to suppress formation of tobacco specific nitrosamines [69]. In 2001 the Brown and Williamson Tobacco Corporation in the USA (at that time the American company in the British American Tobacco Group) launched a cigarette brand called Advance. This cigarette incorporated tobacco cured by the Star process as well as a three section filter that contained cellulose acetate and activated charcoal/ion exchange resin that selectively reduced carbonyl compounds in the smoke.

The smoke from the cigarette had significantly reduced levels of nitrosamines and carbonyl compounds compared to smoke from conventional commercial cigarettes available in the USA. However, Doolittle et al. [70] have demonstrated that marked reductions in nitrosamines in tobacco do not alter the biological activity of the smoke particulate matter in Ames mutagenicity and neutral red cytotoxicity in vitro bioassays. Thus, the health consequences to the smoker of reducing levels of nitrosamines in tobacco or tobacco smoke are unclear. However, the selective reduction of such substances in tobacco and smoke, where possible, would seem a sensible advance. That cigarette is no longer on sale in the USA.

Apart from the development of reduced “tar” cigarettes, the development of cigarettes to address the adverse health risks of smoking has not been commercially successful to date. However, the development of such cigarettes is continuing in tobacco companies and new cigarettes will continue to be marketed in the future. In 2001 the US Institute of Medicine published a report which stated that reducing the risk of disease from cigarettes is feasible by reducing exposure to tobacco toxins [71]. The report also stated that Potentially Reduced Exposure Products (PREPs) should be developed and that they need to be assessed for their reduced risk of disease compared to conventional cigarettes. The report also reiterated the message that the safest option was not to smoke at all, but that less hazardous cigarettes should be developed for those people who choose to smoke. The report is prefaced with the following words of Goethe:

Knowing is not enough; we must apply.

Willing is not enough; we must do.

This seems a fitting objective for the future direction of research and development in tobacco, where vast amounts of work have been done on the mechanisms of smoke formation and composition. In the future, this work will be enhanced and applied for the development of cigarettes that may be potentially less harmful to health.

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