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The tobacco industry's past role in weight control related to smoking

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Background: Smoking is thought to produce an appetite-suppressing effect by many smokers. Thus, the fear of body weight gain often outweighs the perception of health benefits associated with smoking cessation, particularly in adolescents. We examined whether the tobacco industry played a role in appetite and body weight control related to smoking and smoking cessation. Methods: We performed a systematic search within the archives of six major US and UK tobacco companies (American Tobacco, Philip Morris, RJ Reynolds, Lorillard, Brown & Williamson and British American Tobacco) that were Defendants in tobacco litigation settled in 1998. Findings are dated from 1949 to 1999. Results: The documents revealed the strategies planned and used by the industry to enhance effects of smoking on weight and appetite, mostly by chemical modifications of cigarettes contents. Appetite-suppressant molecules, such as tartaric acid and 2-acetylpyridine were added to some cigarettes. Conclusion: These tobacco companies played an active and not disclaimed role in the anti-appetite effects of smoking, at least in the past, by adding appetite-suppressant molecules into their cigarettes.

Introduction

Tobacco is a major cause of death in developed countries. 1,2 Smoking is thought to produce an appetite-suppressing effect by many smokers, particularly in adolescents.³ Most smokers want to stop smoking, but the fear of body weight gain might outweigh the perception of potential health benefits associated with smoking cessation, particularly in women. 4-7 For instance, female students concerned about their weight are at an increased risk of initiating smoking.⁸ In general, smokers have a lower body mass index (BMI) than non-smokers.9 Six months after smoking cessation, the mean body weight gain is estimated ~3.5 kg. 10 Among sedentary smokers, weight gain might even be higher. 11,12 Smoking and weight share a complex relationship.¹³ On one hand, on average, smokers have a lower BMI than non-smokers and sustained quitters have the same BMI than never smokers. On the other hand, heavier smokers defined as either nicotine-dependent smokers or smokers of more than a pack a day, have a higher BMI than lighter smokers. 14-17 In longitudinal studies, smoking cessation is associated with weight gain. 18,19 Hypotheses about the cause of post-cessation weight gain involve increased energy intake by alteration of food preferences, food intake as a substitute for cigarette, as well as decreased energy expenditure by suppression of the stimulating effect of nicotine on

Following the 1998 'Master Settlement Agreement' between US tobacco industry and 46 States, US tobacco companies made their internal documents available on the Internet. Previous research into the archives of tobacco companies have helped the health-care community to understand the industry's strategies. To our knowledge, no study has explored the industry's knowledge of the link between smoking and appetite or body weight and how such a link was used to promote tobacco products.

The objective of our study was to answer the following questions: did the tobacco industry try to take advantage of the relationships between body weight, appetite, smoking and smoking cessation? Did it go as far as modifying its products to obtain such advantages?

Methods

We conducted a systematic search within the archives of six major tobacco companies (American Tobacco, Philip Morris, RJ Reynolds, Lorillard, Brown & Williamson and British American Tobacco) that were defendants in tobacco litigation settled in 1998. 20,22 We retrieved the documents online from the Legacy Tobacco Document Library. The search identified documents by means of a search using keywords such as Body weight gain', 'Appetite', 'Weight control', 'Relapse', etc. Then, using a 'snowball sampling method', 20 other documents were found. Our results are presented and grouped by theme; they do not follow a strict chronological order. Documents presented in this article are dated from 1949 to 1999.

Results

Industry's projects to add substances to cigarettes with effects on body weight and appetite

Since the 1960s, tobacco companies intended adding appetite suppressant in cigarettes to attract new smokers concerned about their body weight. PM stated in a 1965 internal memorandum: 'If we were able to develop cigarettes which are much "safer" than the existing ones [...] and which also act as appetite depressants, then we may uncover a new market of smokers. The potential smokers would be the non-smokers who are more concerned with losing weight than with contracting respiratory or blood circulatory illnesses. [...] To develop new smoking products which will be low in tobacco tar, low in tobacco gas and rich in appetite-depressing factors' (Bates no. 2056159412). In a 1971 internal memorandum about 'New Product Ideas', PM discussed the possibility of creating a cigarette that controlled appetite, either by stimulating or reducing it. Under 'Specific Appetite Inducers' they contemplated the following course of action: 'Incorporate special herbs or medications in a cigarette form as appetite stimulants or possibly for tension release. Especially for people who live alone (elderly) or business men to stimulate appetite'. PM also considered an 'Alternate product' containing an 'appetite suppressant ingredient' (Bates no. 1000300217/0220). One year later, this company

envisaged the creation of 'cigarette products which are marketed as appetite reducers (sweet tasting) or thirst-inducing companion for beer or other beverages (salty). The former relies its efficacy on the empirical evidence that conventional cigarets [sic] depress appetite; the sweet taste is not intended to change blood sugar levels, but merely to provide a sensory confirmation that appetite is being reduced' (Bates no.1000110930/0933). In 1988, PM investigated the possibility of creating 'a slimmer Marlboro', an 'updated Marlboro that's more attractive to female', in which it would 'make it an appetite depressant' (Bates no.506656719–506656749).

The PM documents contained also some drawings—seemingly resulting of a brainstorming—showing how addition of 'appetstat [sic] grains' could be put inside the cigarette filter: the 'sweet' ones depress appetite, and the 'salt' ones stimulate thirst and appetite (Bates no. 1000110840/0922). In 1981, PM stated in an internal report: 'It was noted that one beneficial attribute ascribed to smoking is appetite suppressance [sic]. A thorough study of this effect and publication of the results may have a beneficial impact on the image of smoking. If particular compounds responsible of this effect could be found, it might be possible to enhance the effect in a cigarette aimed at people desiring help with weight control. Care must be taken not to make specific claims or to invoke a "drug additive" image. This is simply a natural effect of the product and/or its use' (Bates no.1003395096/5101). The company was aware that advertising the appetite suppression characteristic of cigarettes as a benefit would entail the risk of potential Food and Drug Administration (FDA) interference (Bates no. 01587028/ 7036; Bates no. 500417387; Bates no. 1003395088/5092; Bates no. 621007557).

During the 1970s, Lorillard also explored the 'technical feasibility of [...] use of active agents beyond nicotine which might provide an additional dimension of physiological effect—facilitate/depress sleepiness, enhance/ reduce appetite feeling [...]' (Bates no. 81564000/4004). In 1976, its scientists suggested a new brand that would 'give smokers an additional benefit that is different, but compatible with traditional cigarette benefits. (An example here might be the addition of an appetite depressant to the cigarette to help dieting)' (Bates no. 80635192/5195). Lorillard scientists raised the following questions: 'How to enhance whatever effect elements like nicotine already has for benefits like weight control', 'How to help with weight control', 'How to address weight control without adding pharmacological agency' and 'How to convince consumer[s] [a] cigarette is [a] weight control agent' (Bates no. 83910635/0661). They concluded in 1979 that: 'Revolutionary Next Era possibilities suggested by our Agencies [included]: [...] Use of the cigarette to deliver another benefit like an appetite depressant' (Bates no. 03547249/7251; Bates no. 01399043/9049). This company thought of turning the prospective appetite-reducing cigarette into a marketing advantage. Already, in 1974, Lorillard devised the following slogan regarding the Trims cigarettes: 'This new longer length cigarette actually contains an appetite depressant to keep you looking and feeling as slim and trim as your cigarette' (Bates no. 01587028/7036). Tartaric acid was added to its Trims cigarettes for its appetite-suppressant effect. However, this tobacco product was no longer considered only as a cigarette but as a drug by the FDA that won a case against the Lorillard Company in 1977. The description of the judgement was the following: 'the product is intended to affect for the ingestion of food and thereby achieving a reduction in the body's weight', and 'based solely upon that claim held that it was a drug' (Bates no. 1003045052/5092).

The RJR Company also launched the development of a weight control cigarette product. In 1982, they searched ideas about 'a cigarette concept that turns build-up into an appetite suppressant' (Bates no. 502788460–502788508). In 1988, they devised new cigarettes, which suppressed appetite: 'For diets as well as for when you are hungry but it's not time [to] break for lunch yet' (Bates no. 521386038/6045). A RJR scientist, in a memorandum about 'Project FD' [Future Dimensions], reported 'the psychological and physiological state of human[s] can be strongly influenced by both aromatic and odourless compounds. Herein lies a fascinating new business/product opportunity for both the tobacco and food operation[s] of RJR Nabisco'. The author explained one of the

concepts of Project FD: 'Hunger control—food aromas with "mouth fullness" stimulation' (Bates no. 521386038/6045).

Specific industry's projects to add substances with an effect on appetite

Our research identified several substances with an effect on appetite, used, or intended to be used, by the industry (table 1).

As mentioned above, 'tartaric acid' has been the anti-appetite molecule added to the Lorillard Trims cigarettes (Bates no. 1003045052/5092). Before that case, in 1961, a PM document entitled 'Additives to smoking tobacco' listed numerous patents of substances that were added to cigarettes, and gave the reasons for their use. The patent 'Ferguson 2773785' was then used as 'an appetite reducer which dries and puckers the mouth, etc. comprising additive of tartaric acid' (Bates no. 2028665546/5552). The patent description of this additive found in the PM archives explained in details the putative mechanism of action of this 'new and improved therapeutic appetite satient composition designed to curb the appetite without supplying calories to the body and particularly to a therapeutic appetite satient composition in combustible from which can be smoked and upon smoking causes loss of appetite' (Bates no. 2026479779-780). We did not find any other arguments suggesting a link between Edgar A. Ferguson and the tobacco industry. Tartaric acid has also been claimed as an ingredient on the 'UK Tobacco Additives' list (of unknown date) held in BAT documents (Bates no. 321973087-321973167).

2-Acetylpyridine is a molecule patented for its appetite-suppressant effect.²⁴ It has been used as a cigarette ingredient, as by PM, B&W, BAT and RJR (its chemical codename is 1122-62-9) (Bates: 605006573; Bates no. 2078541185; Bates no. 508403623; Bates no. 508403623/3699; Bates no. 2078541185/1198; Bates no. 321973087–321973167). In a confidential 1995 memorandum, PM researchers expressed their interest in the appetite-suppressant effect of 2-acetylpyridine and reported some independent scientific research about its effect. This molecule 'smells like corn chips', and might have anti-smoking properties²⁵ (Bates no. 2075008887/8888).

Tobacco industry investigated additional substances for their antiappetite effects, but they were not found in cigarette ingredients lists: 'Ephedrine and amphetamine', two well-known sympathicomimetic appetite suppressants, were considered as cigarette ingredients in the 1960s. In 1968, a RJR scientist wrote: 'SM67A, an ephedrine congener, was tested for anorexic activity in rats. In comparison with standard anorexics, SM67A was found to have some anorexic activity' (Bates no. 502799201). In 1972, RJR sent a list of ingredients containing SM67A to a company called Uniroyal Chemical for chemical analysis (Bates no. 508370235/0237). In 1969, American Tobacco was also interested in ephedrine through 'Project PAC-S-P-69', where PALL MALL cigarettes were evaluated with the following additives: 'caffeine 10%, theophylline 10%, theobromine 10% and ephedrine 5%' (Bates: 950077074). A PM scientist, reporting on his participation at the Tenth Annual Meeting of the Society of Toxicology, made the following recommendations: 'As a result of the meeting I would suggest the following studies: (i) the combined effects of nicotine and ethanol on metabolism of each one; (ii) the combined effects of nicotine and barbiturates; (c) the combined effects of nicotine and caffeine; (d) the combined effects of nicotine and amphetamines' (Bates no. 1003702971/2974). In 1967, RJR performed the synthesis of molecules where the phenyl group of drugs such as amphetamine was replaced by a pyridyl group. This new compound was thought to 'conceivably lead to an appetite depressant (anorexient) without undesirable nervous stimulation' (Bates no. 500613441). Nevertheless, the potential increase in the risk of cardiac arrhythmias when combining caffeine, ephedrine, etc, with nicotine was known by the industry. For example, this medical information about nicotine and heart disease toxicity that mentions the role of ephedrine (Bates no. 517585341/5810) was held by RJR.

"N₂O ('laughing gas')" was investigated by Lorillard, as an appetite suppressant (Bates no. 80635192/5195). In April 1976, during a discussion on new brand possibilities, Lorillard researchers mentioned: 'Additional positive benefits—1. A cigarette that helps weight reduction

Table 1 Substances investigated and/or added for body weight control by tobacco industry and their putative mechanism(s) of action

Substances	Putative mechanism(s) of action
Tartaric acid	Appetite-suppressant effect via drying of the mouth: tartaric acid volatilizes and is reformed in the mouth. Tartaric acid acts on the membranes in the mouth and produces a dryness that has an appetite-reducing effect.
2-Acetylpyridine	Appetite-suppressant effect via neutralization of the olfactory stimulus.
Catecholamine: ephedrine, amphetamine	Appetite-suppressant effect via dopaminergic stimulation.
Laughing gas	Appetite-suppressant effect via modifications of the taste of food.
Menthol	Appetite modifications via diminution of upper airways irritation.
Mariolide	Anorectic effect not eventually described.
Propylene glycol	Potential appetite-suppressant effect not eventually described.
Reserpine	Decrease of brain activity resulting in a decrease in salty food intake in rats.

by increasing some component already in the smoke, e.g. $NO_2 \ [sic]$. This cigarette either depresses appetite or makes all foods taste flat; acting as an anti-MSG [monosodium-glutamate]. This cigarette is endorsed by weight watchers' (Bates no. 80635192/5195). In June of the same year, during the 'Lorillard Problem Laboratory', 'ideas' were discussed, notably the 'use of laughing gas (already in tobacco) as appetite depressant' (Bates no. 01345589/5596).

'Menthol' was mentioned in a 1952 letter from B&W to an expert, entitled 'Effect of mentholated cigarettes on appetite', asking whether the menthol added to mentholated cigarettes could 'take the edge off the smoker's appetite any more than a similar cigarette without menthol'. The expert answered that menthol had an inconclusive effect on smoker's appetite (Bates: 650203535). In 1971, Liggett & Myers, looking at 'New Opportunities in the Menthol Cigarette Market', observed: 'weight control' has substantial appeal [...]. Filters-with-and-without menthol are credited with suppressing appetite. Salem, as the cross-over "bridge" between filters-and-menthols, in combination with Salem's feminity, fulfils weight control expectations' (Bates no. LG0110469–LG0110548).

'Mariolide' was studied by the tobacco industry and described as a 'brain stimulant compound' (Bates no. 504175618/5619). In 1966, RJR scientists investigated mariolide as an appetite suppressant: 'An experiment was conducted to determine whether mariolide has any appetite-suppressing properties or not. [...] This experiment shows that the mariolide does have an ability to decrease food intake but that it occurs at very high doses. The mariolide would not be expected, in the light of these experiments, to have value as an anorexic agent' (Bates no. 504724009/4012).

'Propylene glycol' was listed in Lorillard's documents in 1981, and one of its major pharmacological effects was 'appetite depressant' (Bates no. 88698405/8407).

'Reserpine', an anti-hypertensive and a tranquilizer, was mentioned in the famous 'Project HIPPO II' conducted by the Battelle Institute in Geneva for BAT—which investigated the addictive role of nicotine for the first time—as having some effects on appetite. It was observed that reserpine 'decreased very slightly the appetite in our "appetite test" on rats [...]' (Bates no. 680143705/3741).

Discussion

Our search inside the tobacco documents uncovers the tobacco industry's attitude towards weight control related to smoking. The industry made plans and strategies on how to enhance the effects of smoking on appetite and body weight through adding substances acting as anti-appetite agents. Additionally, we found that the industry has added some substances acting as appetite suppressants into cigarettes.

PM put during the 1960s a substance containing tartaric acid into its cigarette in order to reduce smokers' appetite. Tartaric acid was considered as an appetite suppressant and removed from the market in 1977 by a decision of a US court. This substance was also added to BAT cigarettes, although we did not find at which date, and if it is still the case.

The Ferguson's patent description was the only information we can find on the anti-appetite putative role of tartaric acid in the medical and chemical literature. The substance 2-acetylpyridine is also claimed as an appetite-reducing molecule and is one of the tobacco additives, disclosed on many past lists of cigarette ingredients. No independent studies about the role on appetite of other substances mentioned in our study were found in Medline or Cheminfo databases.

Our findings must help smokers and the health-care community to understand at least partially why cigarette smoking is producing the effect of reducing appetite, and could explain in part why smokers weigh in general less than non-smokers. Although little is known in the medical literature about the anti-appetite effect of the above cited substances, we can make the hypothesis that the weight gain following smoking cessation could be a 'rebound effect' of discontinuation of the daily consumption of an anti-appetite substance through cigarette smoking, as it is known for the use of other anti-appetite substances. ²⁶

The tobacco industry, as we saw it with the Lorillard Trims cigarettes case, has had no advantage to claim the use of their anti-appetite additive. In a PM memorandum dated from 1969, M. H. Wakeham, a scientific director, simply explained why they did not need to declare which additives are put into cigarettes: 'In the response to Roger's [Fagan] question concerning FDA requirements on the introduction of a substance into cigarettes, I told him that the FDA had no requirements until a health claim is made. Then there must be studies on safety, efficacy, mechanism of action, metabolism, etc. If a substance is simply added to a product and no claims are made there is no need for FDA approval' (Bates no. 1001880474).

The major limitation of our study is the scattered nature and relatively small volume of tobacco industry documents related to our topic. Clearly, the restrictions inherent to the filing and indexing system of the industry's archives are problematic when conducting a systematic review of documents; the indexing system of archives is not always consistent and full-text research tools might not recognize words due to the poor quality of scanned documents. However, this alone is not sufficient to explain the relative scarcity of the documents we retrieved. It can be hypothesized that large amounts of material have disappeared, either by exclusion from the database or destruction by the industry. Indeed, some documents that we retrieved can only be understood in the context of activities or projects, which must have generated further documents of which no trace was found, in spite of our varied attempts. Another shortcoming is the lack of current documents, the most recent document on which our work is based dates back to the late 1990s—this is a general problem that affects all research topics: since it knows its internal documents may turn up publicly (i.e. since 1998), the industry can be expected to be much more wary about leaving a written trace of activities that may be compromising. In spite of these shortcomings, we are confident that we used the research method recognized by the scientific community as the most suitable for obtaining a good understanding of the general attitudes, knowledge and activities of the tobacco industry regarding the issue of weight control. 22,27-29

In conclusion, we found clear evidence that every one of the six US and UK tobacco companies elaborated the idea to put appetite depressants molecule inside cigarettes to enhance this effect. They all investigated various substances for such a use. At least two of them, PM and BAT has actually modified its products to affect appetite and body weight. We already knew the industry modified its products to enhance addiction and dependence.³⁰ In addition, specific analyses of cigarette contents could be performed, looking especially for substances that could modify food intake or body weight, such as ephedrine. Research into the tobacco industries' archives should be pursued to improve understanding of companies' strategies, although we should take into account that it is highly possible that the past and present more sensitive documents are being removed from these databases by the industry. 31,32 The scientific community is most probably powerless towards this issue. As recommended by the World Health Organization's Framework Convention on Tobacco Control, strict regulation of cigarette and tobacco additives is needed as part of the fight against tobacco dependence and smoking induced diseases.³³

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Conflicts of interest: None declared.

Key points

- The tobacco industry has added into cigarettes some appetite suppressants substances, e.g. tartaric acid.
- The tobacco industry made strategies on how to enhance the effects of smoking on appetite and body weight through adding substances acting as anti-appetite agents.
- These findings are new arguments to implement a strict regulation of cigarette and tobacco additives.

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