Menthol's potential effects on nicotine dependence: a tobacco industry perspective

Valerie B Yerger

Department of Social and Behavioral Sciences, Center for Tobacco Control Research and Education, University of California, San Francisco, San Francisco, California, USA

Correspondence to
Dr Valerie B Yerger, Department of Social and Behavioral Sciences, Box 0612, University of California, San Francisco, San Francisco, CA 94143-0612, USA; valerie.yerger@ucsf.edu

This manuscript will be useful for the *Tobacco Control* readership in all countries that are parties to the FCTC, as they implement the product regulation provisions of the FCTC.

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ABSTRACT

Objective To examine what the tobacco industry knows about the potential effects menthol may have on nicotine dependence.

Methods A snowball strategy was used to systematically search the Legacy Tobacco Documents Library (http://legacy.library.ucsf.edu/) between 22 February and 29 April, 2010. Of the approximately 11 million documents available in the Legacy Tobacco Documents Library, the iterative searches returned tens of thousands of results. We qualitatively analysed a final collection of 309 documents relevant the effects of menthol on nicotine dependence.

Results The tobacco industry knows that menthol overrides the harsh taste of tobacco and alleviates nicotine's irritating effects, synergistically interacts with nicotine, stimulates the trigeminal nerve to elicit a 'liking' response for a tobacco product, and makes low tar, low nicotine tobacco products more acceptable to smokers than non-mentholated low delivery products.

Conclusion Menthol is not only used in cigarettes as a flavour additive; tobacco companies know that menthol also has sensory effects and interacts with nicotine to produce tobacco products that are easier to smoke, thereby making it easier to expose smokers, especially those who are new and uninitiated, to the addictive power of nicotine.

INTRODUCTION

The isomer *l*-menthol, which has been used as an additive in cigarettes since 1926,[1] is extracted from the peppermint plant, *Mentha arvensis*.[2] The concentration of menthol in cigarettes varies according to the product and the flavour or effect desired,[3] but is present in 90% of all tobacco products, both 'mentholated' and 'non-mentholated'.[4] Menthol added to cigarettes at appropriate levels imparts a minty flavour and sensory effects on the smoker.[5 6] The market share of filter-tipped identifiably mentholated products increased from 1.1% in 1956 to 20% in 2006.[7]

Menthol cigarettes are overwhelmingly popular among African American smokers (83% compared with 24% of US white smokers),[8] owing to, at least in part, tobacco companies' disproportionately promoting their menthol brands in African American communities.[9–13] It may not yet be clear what are the relative risks of smoking menthol cigarettes;[14 15] however, African Americans, who smoke fewer cigarettes per day[16] and generally have a later onset of smoking initiation compared to white people,[17] have higher rates of lung cancer and other tobacco-related diseases.[18 19] Cotinine, a biomarker of nicotine exposure,[20–22] is higher in African American smokers than in white smokers,[23] suggesting African Americans metabolise nicotine more slowly,[23 24] which could be because they smoke mentholated cigarettes.[25–27]

The issue of menthol goes beyond the African American population. Analysing data from the 2003 and 2006–7 Tobacco Use Supplement to the Current Population Surveys, Lawrence *et al* noted some other racial/ethnic groups were also more likely than white smokers to consume mentholated cigarettes.[28] Menthol cigarettes have been specifically designed to attract youths,[29 30] whose use of mentholated cigarettes has increased from 2000 to 2008.[8 31] Tobacco companies also targeted their menthol marketing campaigns at women,[9 32] who use mentholated cigarettes at much higher rates than their male counterparts.[17] Additionally, mentholated cigarettes are actively promoted in other parts of the world and make up a substantial proportion of the market in many developing countries.[4 33]

Several studies published in the open literature suggest there is a relation between menthol and nicotine dependence. Fagan *et al* demonstrated that despite smoking fewer cigarettes per day, menthol smokers showed greater signs of nicotine dependence as evidenced by being more likely to smoke their first cigarette within 5 minutes of waking.[34] The time to first cigarette is a more robust indicator of dependence than the number of cigarettes smoked in a day or the Fagerström test of nicotine dependence (FTND).[35 36] Other public health researchers have also shown that menthol smokers have a significantly shorter time to the first cigarette of the day than non-menthol smokers.[37–39] Muscat *et al*, however, did not find a significant association between smoking mentholated cigarettes and FTND scores[39] and Hyland *et al* did not find an association between the use of mentholated cigarettes and quitting, the amount smoked, or the time to first cigarette upon waking.[40]

Menthol's sensory and respiratory effects may lead to greater nicotine dependence in adult smokers[5 6 41–44] and in adolescents who smoke.[30 31 38 45] Smoking mentholated cigarettes produces a cooling sensation in the upper airway,[46] which is innervated by trigeminal somatosensory neurons.[47] Menthol activates the cold sensitive ion channel TRPM8,[48] which is the underlying mechanism for the trigeminal detection of menthol in the head and neck regions such as the nasal and oral cavities.[49] Menthol's cooling action depresses respiratory activity, resulting in breath holding, which then leads to increased lung exposure to nicotine.[5 42] The addictive properties of nicotine have been clearly demonstrated.[50 51] It has been

suggested by public health researchers that menthol potentiates nicotine dependence by making the "poisons [eg, addictive nicotine] go down easier".[52]

Evidence from internal tobacco company documents leads to a similar conclusion: tobacco companies not only knew menthol has sensory effects and interacts with nicotine, but that they used this knowledge to produce tobacco products that would be easier to smoke. Including menthol in cigarettes makes it easier to expose smokers, especially those who are new and uninitiated, to the addictive power of nicotine.

METHODS

As described in detail elsewhere,[53] we used a snowball sampling design[54] to search the Legacy Tobacco Documents Library (LTDL) (http://legacy.library.ucsf.edu/) between 22 February 2010 and 29 April 2010. We combined traditional qualitative methods[55] with iterative search strategies tailored for the LTDL dataset.[56] Initial keyword searches combined terms related to: menthol, nicotine, dependence and addiction; and brand names such as Kool, Newport and Salem. This initial set of keywords resulted in development of further search terms and combinations of keywords (eg, 'menthol pharmaco*', 'menthol/nicotine interaction', and 'nicotine delivery'). For each set of results, the first 100–200 documents were reviewed to locate documents relevant to the research questions. A final collection of 309 documents was analysed for this paper, of which 50 were deemed representative and cited.

RESULTS

Menthol is not just a flavour additive

In a 1982 RJ Reynolds interoffice memo written in anticipation of questions from consumers concerned about menthol, RJ Reynolds biochemist Charles Nystrom told Tim Cahill of the company's public relations department that menthol has been 'used as a flavour additive in cigarettes' since 1926 and that 'there is no evidence that menthol has any effect on the smoker other than the effect of menthol on the taste and flavour of the cigarette'.[1] Cahill subsequently responded to consumer letters inquiring about the effects of menthol in cigarettes, assuring consumers that menthol was used as a flavour additive and had no other effect or addictive properties.[57]

Sensory properties of menthol

Three years earlier, in 1979, the Roper Organization conducted a study of 1367 menthol and non-menthol smokers for Philip Morris, which concluded that the addition of menthol to cigarettes masked the harshness of tobacco, which makes cigarettes more desirable to some smokers.[58]

The Roper report concluded that menthol smokers are attracted to menthol's drug-like properties: 'cooling effects; clean, antiseptic effects; slightly numbing, anaesthetic effects; and heady, lifting effects'.[58] Menthol's cooling effect appears to be a result of chemical action that occurs at or near nerve endings which are associated with the sensation of cold.[59] These nerve endings are located in the nasal, oral and skin membranes. When menthol is added to cigarettes and smoked, this cooling sensation is also experienced in the lungs. The cooling sensation is dose sensitive. Increasing the amount of menthol beyond a certain limit would not generally result in a greater degree of cooling, but would cause an increase in other sensations such as tingling, stinging and burning.[60]

Because of its sensory properties, menthol is able to mask the harshness of tobacco.[61] In 1982, the Creative Research Group (CRG) conducted for British American Tobacco discussion groups with menthol smokers or 'potential users' aged 18–50 years on consumer perceptions of mentholated cigarettes. CRG concluded in its report 'Project Crawford' that mentholated cigarettes "undeniably impart a cooling influence, and … a by-product of this is to reduce harshness and to modify or mask the tobacco taste".[61] Supporting this notion that menthol is more than a flavour additive, CRG concluded that the flavour of menthol was not a 'significant reward' and that menthol smokers build tolerance to the taste of menthol but continue to get menthol's sensory effects.[61]

Regarding menthol's ability to mask tobacco taste, CRG concluded:

> There is no question that menthol has a significant masking effect on both the taste of the tobacco and the harshness of the smoking experience. Some menthol smokers seek as much masking effect as possible, attempting to eradicate the tobacco taste altogether.
>
> …
>
> [Mentholation] can still function in its masking role and yet can have lost a large portion of its own [flavour].[61]

The report included quotes from some of the discussion group participants that reveal the part menthol plays in covering up tobacco taste. For example, one participant said, *"As far as I am concerned, I want the menthol to completely cover up the taste of the tobacco. I don't like the taste of tobacco"*. Another participant reported, *"If the menthol was gone, I wouldn't be able to stand the cigarette!"* [Emphasis in original.][61]

In addition to making cigarettes smoother and less harsh, menthol's cooling effect alleviates nicotine's irritating effect. The tobacco companies were well aware that younger, inexperienced smokers had low tolerance for irritation and tobacco taste.[62 63] RJ Reynolds conducted studies in 1983 on nicotine and menthol to better understand the "independent and joint effects of nicotine and menthol on smoker perception".[64] One of its studies concluded, "Nicotine [is]…a major irritant in cigarette smoke while menthol is known to produce a cooling effect and is often used to alleviate sensations of irritation".[64] In contrast to what RJ Reynolds was telling its customers in 1982,[57] a 1976 confidential RJ Reynolds research report written by chemist Dr Mary Evelyn Stowe to Dr Donald H Piehl, manager of the company's Chemical Research Division, indicates that RJ Reynolds had known for more than three decades that menthol, even at subliminal levels too low to be detected by smokers, reduced 'that nasal sting, tongue bite, and harshness' of tobacco.[65]

Tobacco industry research on menthol and nicotine

As consumers were becoming increasingly more concerned about the harmfulness and addictiveness of nicotine, Philip Morris, for example, sought to design denicotinised cigarettes and menthol played a crucial part in the company's research.[66] During the late 1980s, Philip Morris scientists conducted in-house testing of various prototypes of ART, an "alkaloid [nicotine] reduced tobacco" product.[67 68] ART cigarettes had 0.12 mg nicotine/cigarette, compared to 0.20 mg or more of nicotine per cigarette in conventional cigarettes. One ART prototype, the ART-extracted, was completely denicotinised. Owing to the absence or decreased nicotine delivery, non-mentholated ART prototypes lacked 'impact'. Impact, perceived by the smoker as a 'kick' or 'grab' in the back of the mouth and throat when inhaling a cigarette,[6 69] is crucial in providing much of the immediate satisfaction gained from smoking.[70] Phillip Morris

found the mentholated prototypes of ART to be 'subjectively superior' to the non-mentholated versions because they were the only ART prototypes that provided any impact.[71] When further testing the mentholated ART prototypes, Philip Morris scientists found menthol provided this perceived impact because it produced some nicotine-like effects.[68]

Menthol and nicotine interaction

In 1989, Philip Morris scientists discovered that 'menthol and nicotine interact in a very interesting fashion'.[72]

> Specifically, perceived impact seems to vary as a function of the delivery levels of menthol and/or nicotine in smoke…it seems *that menthol level almost exclusively determines degree of impact*. In low nicotine delivery cigarettes, *it appears that nicotine and menthol combine in an additive manner to determine degree of impact* [emphasis added].[72]

Philip Morris continued its research on menthol cigarettes by combining menthol with varying levels of nicotine.[73 74] Philip Morris found in a factorial study that combined four levels of menthol (0.00 mg, 0.41 mg, 0.85 mg and 1.95 mg per cigarette) and three levels of nicotine (0.08 mg, 0.41 mg and 0.91 mg per cigarette) that the addition of menthol either increased or decreased impact, depending on whether, and to what degree, nicotine was present.[75] The study concluded that cigarettes without nicotine were preferred more when menthol was added. Those cigarettes that had low or intermediate levels of menthol were preferred over those cigarettes with the highest menthol level.

Between 1989 and 1991, Philip Morris scientists conducted smoking panel tests as part of product development to determine specific combinations of menthol and nicotine needed in low nicotine delivery cigarettes to attain a desired impact.[76–79] In 1990, Philip Morris scientists conducted electrophysiological studies to record and measure objective information about the effects of nicotine on the central nervous system (CNS).[68 75 80] Smokers were attached by electrodes to a machine that recorded brain activity impulses.[81] These pattern-reversal evoked potential measurements were 'very sensitive to nicotine delivery in a dose-related manner'.[68] While conducting these studies, menthol's electrophysiological effects on the CNS became apparent. In a memo they distributed to other company researchers, Philip Morris research scientists Frank Gullotta, C S Hayes and B R Martin concluded, "as we had seen before, adding menthol to the [nicotine] extracted model had the effect of increasing impact. More interestingly, and something we had not seen before however, menthol had the effect of low[er]ing impact in those cigarettes containing nicotine".[68]

In 1990, Philip Morris conducted a study on menthol-nicotine interactions. Varying the amount of menthol and nicotine delivery affected impact scores.[82] Test cigarettes with the highest level of menthol but the lowest level of nicotine delivery had the highest impact score (figure 1).[82] As the nicotine level decreases while the menthol level increases, impact increases (figure 2).[79]

What became apparent to Philip Morris scientists from these studies in the late 1980s and early 1990s is that impact increased when nicotine per puff was low and menthol per puff was high.[79 82] Therefore, in 1991, Philip Morris took into account the levels of all three variables—tar, nicotine and menthol—when predicting and manipulating the impact of low nicotine delivery cigarettes.[83] An abstract of Gullotta's work, which he faxed in 1995 to Philip Morris' research scientist Gerry Nixon,[84] concluded, "menthol increased 'impact' for the low nicotine

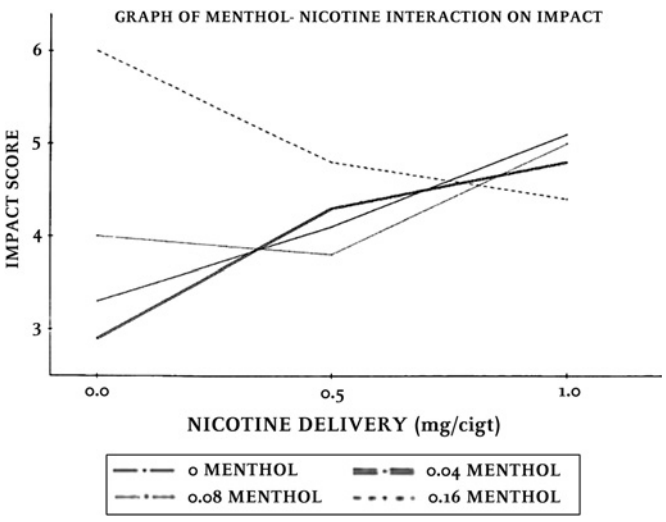

Figure 1 Philip Morris test cigarettes with the highest level of menthol but the lowest level of nicotine delivery had the highest impact scores.[82]

delivery cigarettes….The effect of menthol was most pronounced for the cigarette with the lowest nicotine delivery… It was concluded that menthol has a pronounced effect on nicotine-derived 'impact'. Therefore, menthol levels must be considered when targeting cigarettes for degree of perceived impact".[85]

In 1985, RJ Reynolds conducted product development studies of full flavour and low tar cigarette prototypes among full flavour menthol smokers. RJ Reynolds produced a report (lacking the names of any authors or contributors) containing the findings from these studies.[86] These qualitative studies indicated that higher overall acceptance among full flavour menthol smokers was associated with high nicotine flavour, regardless of menthol delivery. The report also concluded, "At

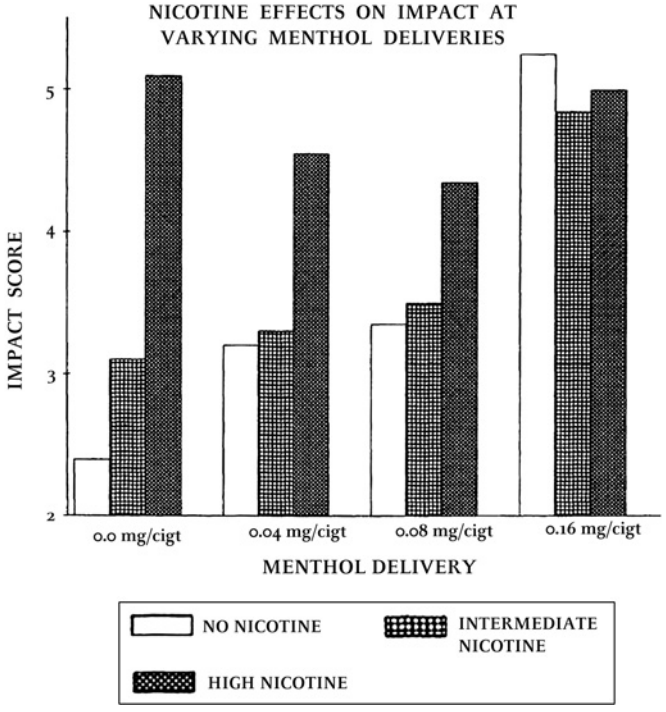

Figure 2 As nicotine levels decrease and menthol levels increase, impact score increases.[79]

moderately high tobacco nicotine levels (~2.00%), almost any pack menthol…approximates the mean ideal strength. However, at lower tobacco nicotines (~1.45%–~1.83%), pack menthols must increase (from 0.34% to 0.62%), in conjunction with tobacco nicotines, to maintain mean ideal strength".[86] Menthol was also shown to ease the flow of smoke through the filter.[86]

Menthol's role in cigarettes containing low levels of nicotine and tar

In order to achieve substantial reductions in nicotine and tar yields, tobacco companies developed and used a number of manufacturing and design techniques,[87] which included 'highly efficient filters, perforations of the filter tipping paper, adjusted porosities and burn characteristics of the cigarette rod wrapping paper, and the use of expanded tobacco'.[88] In 1972, Philip Morris considered how a reduction in tar level would affect a cigarette's nicotine/tar ratio and if such a change in the ratio would affect that cigarette's acceptability and marketability.

> The nicotine/tar ratio of all cigarettes…is .07±0.01. We have no acceptability data for nicotine/tar ratios outside this range. Since the trend in tar delivery is downward, and since nicotine is presumed to be that which is sought by the smoker, does a cigarette with a high nicotine/tar ratio have market potential?[89]

Lorillard Tobacco Company was also aware of the increasing market demand for cigarettes that would deliver lower levels of tar. In 1975, Lorillard received a report of the Marketing Corp of America's marketing study that discussed the market demand for and a 'strong likelihood of continued growth' of low tar/nicotine brands.[90]

Though the industry may have been aware that there was the likelihood that low tar/nicotine cigarettes would be attractive to a growing number of smokers concerned about effects of cigarettes on their health, some of the findings from the 1979 Roper study conducted for Philip Morris in 1979 revealed low tar cigarettes were tasteless, failed to satisfy the smoker and were harder to smoke.

> The appeal of low tars is simple and single—better for you, less harmful, easier on the lungs, throat, etc. The weakness or objection to low tars is also simple—tasteless, lacking in satisfaction.… But since lack of taste is the #1 drawback to low tars, the question occurs as to whether it is possible to "spray" or "inject" extra taste into low tars.
>
> …
>
> [L]ow and ultra low tar menthol smokers are better satisfied by their cigarettes than their non-menthol counterparts…menthol makes up in some way for the light or "pale" qualities of a low tar cigarette.[58]

Tobacco companies discovered they could manipulate the level of tar and nicotine in their cigarettes, and with the help of menthol, design 'light', 'mild' and 'ultra light' cigarettes that would be acceptable to consumers.[91] According to the 1979 Roper report, for example, menthol compensated for the reduced taste in 'light cigarettes', which otherwise would have been less satisfying to smokers.[58] In 1982, Philip Morris conducted a focus group study with menthol smokers of various menthol brands. The study revealed:

> People want to know they are smoking a cigarette, not just sucking air…Many of the smokers describe the non-menthol low delivery cigarette as lacking taste, papery, or like burning leaves…Most of the smokers believed menthol cigarettes are smoother and less harsh than non-menthol.[92]

Consistent with what other tobacco companies reported, Brown and Williamson (B&W) recognised the role menthol played in making mild, light and ultra light cigarettes more attractive to smokers than non-mentholated counterparts. According to an undated product development report, when B&W increased filtration and ventilation to decrease the amount of tar delivered to the smoker, it increased the amount of menthol to maintain the appeal of low tar cigarettes (table 1).[91]

An undated document indicates that British American Tobacco also recognised the need for an optimal balance between menthol and nicotine:

> Another aspect to consider is the balance between the menthol and the nicotine in the smoke. This should not be a problem in lower delivery products as the combined effects, remembering menthol produces a physiological effect 'menthol impact', would not be unacceptably high. Problems can arise if there is a high level of either or both. The theory is that the two components stimulate the same receptors and compete with one another.[93]

Menthol's sensory stimulation

Menthol affects the response of many receptors to stimulation. Physiological effects of menthol are dose sensitive.[60] Small concentrations of menthol are more effective than large quantities, which will depress receptor stimulation. After prolonged, chronic exposure, response to receptor stimulation is also depressed. By 1990, Philip Morris understood menthol was a complex compound and that liking mentholated cigarettes was complex. Philip Morris scientists produced a 199-page research and development report on their chemical senses research, which encompassed 'the development of a fundamental understanding of those physical/chemical and biological system interactions that result in a favourable subjective response to the product'.[73]

Philip Morris scientists were, however, limited in their ability to measure these feeling factors and realised that product development would require a more focused research programme on chemical senses. Menthol was an integral part of this plan. The 1993 operational plans for its Sensory Technology Program revealed that Philip Morris scientists—represented by scientific affairs director Richard Carchman in an internal memo—intended to utilise their knowledge of the 'synergistic interaction' between menthol and nicotine to develop a product that was low tar yet had superior sensory characteristics.[94] Philip Morris' strategic plan for 1993–1997 described the development of molecular models to identify the processes that lead to human sensory perceptions, including the mechanisms by which nicotine and menthol bind to receptor sites to elicit sensory effects.[87] Philip Morris was specifically interested in understanding these mechanisms to improve the 'sensory efficacy' of both nicotine and menthol in order to increase the company's menthol market share.[87]

Mechanism underlying menthol's sensory effects

The trigeminal nerve is the fifth cranial nerve and is widely distributed throughout the head. Trigeminal chemoreception

Table 1 The transfer efficiency rate of menthol decreases with increasing filtration and ventilation[91]

Tar range	% Transfer efficiency	% Menthol applied
Full flavour	15–16	0.35–0.45
Milds	12–13	0.45–0.55
Lights	8–10	0.60–0.80
Ultras	1–5	0.80–1.25

was of interest to the tobacco industry because nicotine stimulated this nerve,[95] and the trigeminal is essential to eliciting a 'liking' response for a tobacco product.[73] According to 1988 Philip Morris interoffice correspondence, the impact provided by menthol is probably mediated by the nociceptive fibres of at least two nerves: glossopharyngeal and trigeminal.[71]

In 1989, Philip Morris established its 'Trigeminal Panel', composed of smoking employees in the company's research and development department,[68] to conduct research 'to screen for compounds [including menthol] which might possess nicotine-like sensory characteristics'.[96] The panel identified compounds which elicited trigeminal responses and exhibited nicotine-like sensory characteristics.[97] The panellists were assessed for their electrophysiological and subjective effects on the CNS.[98–101] Menthol produced some nicotine-like CNS and subjective effects in humans[71 97] and was found to be a 'partial replacement' for nicotine.[78]

RJ Reynolds also conducted in-house research on menthol and demonstrated menthol elicited taste and smell responses by stimulating the trigeminal cold fibres, the gustatory (taste) and olfactory (smell) nerves and nociceptors (sensory receptors that respond to pain).[60] These combined actions provide what RJ Reynolds called the 'total menthol response' in an undated document.[60]

Menthol and nicotine metabolism

It is unclear if tobacco companies conducted research on menthol's effects on nicotine metabolism. An undated B&W study on nicotine and cotinine intentionally excluded menthol smokers from the sample,[102] as did a report on a plasma cotinine study done for RJ Reynolds.[103] Although in 1985 B&W considered doing comparative blood cotinine testing on menthol and non-menthol smokers,[104] subsequent searching in the LTDL did not reveal evidence that this research was done. Such research, if rigorously designed, could provide understanding of menthol's role, if any, in nicotine metabolism. Industry scientists reviewed scientific articles published in the open literature, including research showing menthol may increase toxic exposure by inhibiting nicotine metabolism and detoxification of tobacco-specific lung carcinogens.[15]

Tobacco companies understood menthol to be metabolised primarily in the liver, via its conjugation with glucuronic acid, and subsequent excretion in the urine as glucuronide.[105] The amount excreted varies, depending on the dose of menthol and the specific animal.[105] A study on the metabolism of *l*-menthol in rats by organic chemists in India found in the Philip Morris collection reported that there was "[m]aximal induction of cytochrome P-450 and its reductase…upon 3 days of repeated treatment with *l*-menthol".[106] Although the study was done on rats, it had relevance for humans because—in most smokers—nicotine is eventually metabolised to cotinine via a pathway that is catalysed by hepatic cytochrome P4502A6 (CYP2A6).[107 108]

According to a published non-industry study on menthol glucuronidation in humans,[109] cited in a 1986 privileged and confidential attorneys' work product report on menthol that was created by the industry law firm Covington & Burling,[105] human subjects given 500 g of *l*-menthol rapidly but incompletely metabolised it into menthol glucuronide. In all, 77.5% of the 10–20 mg of menthol administered orally to the human subjects was recovered in the urine in 11 hours, with no additional menthol recovered in the subsequent 25 hours. The authors of the study concluded that not all of the menthol appears to be conjugated, and 'the metabolic fate of the menthol that is not conjugated is unknown'.[105] Conjugation with glucuronic acid (glucuronidation) serves as an essential mechanism for eliminating numerous drugs and chemicals, including menthol, in humans and other animals.[110 111] A 2001 report prepared by Philip Morris' product integrity team on the use of menthol as an ingredient in cigarettes presents evidence that Philip Morris continued to cite published studies that concluded menthol had no effect on nicotine metabolism.[112] There was no indication that Philip Morris conducted its own in-house studies of menthol and nicotine absorption.

DISCUSSION

In 1982, RJ Reynolds was telling consumers there was no evidence menthol had any 'effect on the smoker other than the effect of menthol on the taste and flavour of the cigarette',[1] a position the tobacco industry still maintained in 2010. At the 15 July 2010 FDA Tobacco Products Scientific Advisory Committee (TPSAC) meeting in Bethesda, Maryland, Jane Y Lewis, senior vice president for Altria Client Services, on behalf of Philip Morris (PM) USA, publicly stated "menthol is a flavor [and that] PM USA only adds menthol to the flavor recipes of cigarettes labeled as menthol cigarettes".[2]

The companies' internal documents tell a different story. Tobacco companies have known at least since the early 1980s that the flavour of menthol is not a 'significant reward' for menthol smokers.[61] Rather, menthol's ability to provide an 'extra something' beyond its flavour to smokers[58] has been of interest to tobacco companies. The evidence presented in this paper shows menthol is not just an ingredient added in a proprietary recipe to make cigarettes taste a certain way, as suggested in the 15 July 2010 public presentations by the tobacco industry to the FDA TPSAC.[2 113]

William R True, senior vice president of Lorillard Tobacco Company's Research and Development, also publicly stated on 15 July 2010 at the FDA TPSAC meeting that his company uses 'menthol at very low levels' in non-menthol brands.[113] Our research of the internal tobacco documents supports True's statement. As a cooling or anaesthetic agent, menthol, even at low or subliminal levels, masks the harshness of tobacco and alleviates the irritation associated with nicotine.[61 64 65] Adding menthol to cigarettes makes them easier to smoke, which is a strategy to attract young and inexperienced smokers.[30 62 63]

Tobacco companies' in-house studies on menthol showed that menthol has some nicotine-like sensory effects. Stimulating sensory receptors can strengthen the conditioned aspects of smoking.[50] Tobacco companies explored a number of ways to manipulate levels of menthol and took advantage of menthol's physiological effects on the trigeminal cold fibres, the gustatory and olfactory nerves, and nociceptors to make the smoking experience more pleasurable for some smokers.

Prompted by consumer concerns of the harmfulness of cigarettes, tobacco companies sought to design cigarettes with lower delivery levels of nicotine and tar. Tobacco companies experimented with varying ratios of tar, nicotine and menthol in product prototypes and discovered menthol synergistically interacted with nicotine. Subsequent in-house research showed nicotine levels could be reduced in cigarettes and with the appropriate level of menthol added, low nicotine delivery cigarettes could be produced that would be appealing to consumers.[64 114] Menthol's role in the design of low nicotine delivery cigarettes became apparent in the 1980s, when tobacco companies determined the amount of menthol needed to attain a desired impact at any given nicotine level. By increasing the amount of menthol up to a certain threshold level, tobacco

companies designed cigarettes with lower nicotine content without sacrificing impact. The use of menthol, especially in low nicotine delivery cigarettes, provides the strength and impact that higher nicotine level cigarettes deliver. These findings suggest adjusting menthol levels compensates for the reduced appeal of non-mentholated low nicotine cigarettes.

Industry documents retrieved for this study did not reveal the companies conducted their own studies on how menthol affected dependence measures such as FTND or the biomarkers of tobacco smoke exposure such as cotinine, carbon monoxide (CO), carboxyhaemoglobin or thiocyanate.[115] However, a search of the open scientific literature identified two industry studies on menthol and smoke exposure biomarkers. One study compared 112 menthol and non-menthol smokers and found no difference in the level of biomarkers between moderately heavy menthol and non-menthol cigarette smokers.[116] The second one, a cross-sectional, observational study in 3341 adult cigarette smokers, also reported not finding any differences in the level of smoke exposure biomarkers between menthol and non-menthol smokers.[117] Also identified in the literature search were numerous articles written by industry research scientists on the effects of non-mentholated smoking on the biomarkers of exposure.[118–128] Since none of these industry-funded studies included menthol as a variable, there were missed opportunities to contribute to the understanding of menthol's role in nicotine dependence, nicotine metabolism, nicotine exposure or cigarette consumption. However, studies published by peer-reviewed public health researchers have increased the knowledge base of how menthol affects biomarkers of exposure. Several of these public health studies show that menthol smokers, when compared with non-menthol smokers, have higher carbon monoxide levels,[27 129–133] which correlates highly with nicotine exposure.[134]

Tobacco companies did not appear to conduct in-house studies on menthol to assess how menthol may affect dependence or exposure measures. Instead, tobacco companies, concerned about how to increase their share of the cigarette market, focused on testing new products and manipulating the menthol and nicotine levels in cigarettes. Internal industry research indicates that menthol has some nicotine-like effects, interacts directly with nicotine to produce cigarettes that are easier to smoke and makes low nicotine delivery products more acceptable to consumers. The cooling and local anaesthetic effects of menthol make mentholated cigarettes easier to smoke than non-mentholated cigarettes. Menthol, therefore, facilitates smoking and contributes to smoking initiation among inexperienced and uninitiated smokers.[29] Because of its effects on smokers, who thus are exposed to the addictive power of nicotine, menthol contributes to the overall burden of tobacco-related disease. Banning the use of menthol in all cigarettes will lead to fewer people starting to smoke[29] and more people quitting,[135] which will have a positive impact on the public health.

What is already known about this topic

Tobacco companies manipulated the level of menthol to reduce the harshness and irritation that come with smoking non-mentholated cigarettes.

What this study adds

Despite tobacco industry claims that menthol is only used as an ingredient in a proprietary recipe to make cigarettes taste a certain way, publicly available documents reveal industry research showing that menthol has some nicotine-like effects, interacts directly with nicotine to produce cigarettes that are easier to smoke and makes low nicotine delivery products acceptable to consumers.

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