Additives in low tar ('light') and e-cigarettes may reinforce nicotine dependence

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Pyrazine additives in low tar ('light') and e-cigarettes may be reinforcing the addictive qualities of nicotine, and should be strictly regulated, concludes research published online in the journal *Tobacco Control*.

The evidence suggests that pyrazines have sensory and pharmacological effects which act independently of, and in tandem with, nicotine, and

were developed by the tobacco industry to make low tar ('light') cigarettes taste richer and smoother, and boost sales.

Nicotine dependence is a complex process, but is primarily caused by the ability of nicotine to prompt the release in the brain of dopamine, a chemical involved in pleasure, arousal, and mood change.

But a growing body of evidence suggests that nicotine alone is not responsible for the intense addictive properties of tobacco smoking and the high relapse rate among people attempting to stub out their habit for good using nicotine replacement products.

The researchers scoured internal tobacco industry documents made available in the late1990s as a result of litigation and reviewed scientific research on the composition and role of cigarette additives.

The tobacco industry developed low tar cigarettes following increasing concerns about the deleterious impact on health of smoking, and a continuing decline in cigarette sales since World War II. But these low tar versions lacked the taste, aroma, and flavour of regular cigarettes.

The documents reveal that Philip Morris wanted to develop cigarettes with even lower tar yields, but with a taste and flavour that would satisfy smokers' "palates and needs."

The company carried out research to pinpoint the components that were associated with the strongest odour intensity from among the many aromatic chemicals and substances in regular tobacco smoke and then made synthetic versions to be included in low tar cigarettes.

The result was the highly successful MERIT brand, which was the first 'light' cigarette and marketed as a full flavour product yielding less than 9 mg of tar.

Philip Morris called the new flavour combination 'Super Juice'. This was made up of five additives, including three pyrazines—aromatic compounds formed at temperatures of 100 degrees or more and generated during the curing of the tobacco leaf and during smoking, and now widely used in cigarette brands.

Pyrazines are said to be among the most important compounds characterising the flavour and aroma of tobacco and tobacco smoke, contributing the 'brown notes' in general, and in some cases, cocoa, nutty and popcorn type flavours.

Apart from flavour and aroma, pyrazines are known to act on sensory receptors. The documents show that industry identified a role for pyrazines in smoothing, which may ease the inhalation, uptake, and delivery of nicotine by curbing the harshness and irritating effects of nicotine and other tobacco smoke ingredients, say the researchers.

Industry documents indicate that these compounds would promote high consumer acceptance and continued use. An RJ Reynolds report in 1986 describes the company's targeting of 18-24 year old men by increasing the smoothness and masking the harshness and irritation of tobacco smoke.

Laboratory research also suggests that pyrazine stimulation of receptors in the lining of the nose may enhance learned behaviour, either by acting alone or in combination with other sensory stimuli.

And several pyrazine derivatives seem to have a role in boosting the amount of dopamine released during smoking—an effect that is independent of nicotine—studies indicate.

"The sensory inputs of pyrazine flavour additives might also provide cues for reward-related learned behaviours and could play a critical role

in the development, maintenance, and relapse of tobacco dependence," write the researchers. "They could increase the attractiveness of smoking, particularly among youth," they suggest.

Currently the US regulator, the Food and Drug Administration (FDA), bans the use of cigarette additives that are characterising flavours, such as sweet, sour, etc. Yet that hasn't stopped the continued use of flavourings such as liquorice, cocoa or vanilla, which were present in products before the ban took effect, they point out.

A distinction needs to be made between the characterising flavours whose effects are mainly about taste and those whose effects are mainly about smoothing and cooling, they add.

"Taken together, pyrazines appear to increase product appeal and make it easier for non-smokers to initiate smoking, more difficult for current smokers to quit, much easier for former smokers to relapse into smoking, and may mask the risks of both active and passive smoking," they conclude.

They call on regulators around the world to take swift action to regulate pyrazines and other similar ingredients.

More information: A study of pyrazines in cigarettes and how additives might be used to enhance tobacco addiction, DOI: 10.1136/tobaccocontrol-2014-051943

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