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Fenugreek, ingredient added to cigarettes Literature review A preliminary scientific summary

In any brand sold, the maximum use value applied in the tobacco blend is:

- 0,011 mg/cigarette or 0,003% expressed on a dry weight basis.

Summary

Fenugreek^{1,2,3} is a product derived from the herbaceous plant indigenous to western asia, from steam distillation to solvent extraction (volatile hydrocarbon, weak alcohol). Extract is registered as CAS 84625-40-1, FEMA 2485 and Oleoresin as CAS 977018-53-3, FEMA 2486. It is an approved European food-additive³, generally recognized as safe by the Food and Drug Administration⁴. Studies^{5,6,7,8,9,10} have shown a broad margin of safety for fenugreek seed extract. The extract is used primarily for food flavoring.

Composition^{3,11} of fenugreek extract is complex and vary naturally, registered as a "Substances of Unknown or Variable Composition, Complex Reaction Products and Biological Materials". According to its use as a tobacco additive, constituents¹² of relevance were recently determined, showing mainly fatty constituents (around 60%), carbohydrates (around 20%), water and proteins (less than 10%).

Pyrolysis study¹³ referring to the burning of the tobacco rod was performed on fenugreek extract, showing high amounts of fatty esters and traces of volatiles organics constituents (VOC). Nevertheless, no significant and reliable increase of these VOC in mainstream smoke was observed after addition of fenugreek in tobacco blend.

The effect of addition of fenugreek on the composition of tobacco smoke and its biological properties was assessed by key studies^{14,15,16,17,18,19,20,21,22,23,24}. Most of the studies are based on the comparison of test cigarettes with and without fenugreek extract, isolated or in combination with other ingredients. Outcomes were consistent across the studies^{25,26,27}, despite the identified limitations^{28,29,30}. The addition of fenugreek (from 0.001% to 0.6%) didn't result in significant adverse changes in the cigarette smoke composition and biological activity as detailed below:

- *Smoke chemistry*: no significant change was observed in smoke emission of the 39 priority WHO³¹ constituents compare to the control cigarette without ingredient.
- *In vitro assays*: Addition of fenugreek from 0.01% to 0.03% had no significant effect on cytotoxicity (Neutral Red Uptake assay), mutagenicity (Ames Assay *Salmonella typhimurium* strains TA98, TA100, TA102, TA1535, TA1537; with and without metabolic activation) and genotoxicity (*in vitro* Micronucleus assay) of the cigarette smoke.
- *In vivo assays*: Sub-chronic inhalation studies have shown no discernible effect on the character and the extent of the biological responses normally associated with inhalation

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of mainstream cigarette smoke in rats. No effect was observed on reproductive and developmental toxicities.

Influence of the addition of fenugreek at a high application level (0.02%) was assessed by a clinical study^{23,32} including smoking behavior and nicotine pharmacokinetics:

- No significant effect of the addition of fenugreek was observed on inhalation patterns or nicotine uptake,
- Addition of fenugreek did not alter the smoking behavior as an indicator for a change in the sensory properties of the smoke.

Fenugreek contains carbohydrates and can generate by thermal degradation carbonyls³³ as acetaldehyde. Such carbonyl is a potential inhibitor of the enzyme mono-amine oxidase, suspected to act on nicotine dependence. It was shown previously that mainstream smoke emissions of carbonyls^{13,24} were unchanged following the addition of fenugreek extract. Consequently, addition of fenugreek cannot increase nicotine addiction due to its thermal degradation.

Additionally, epidemiological studies^{34,35,36} shown that there was no statistical evidence that ingredients used in traditional blended cigarettes affect smoking cessation patterns.

To conclude, gaps identified previously^{37,38} seem to be fully filled by the literature. Addition of fenugreek seed extract, especially at the current used levels does not discernibly alter the biological effects normally associated with cigarette mainstream smoke.

SYNAPCION
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