# Evaluation Summary of Fenugreek Extract for Use as a Cigarette Ingredient

Fenugreek extract, derived from *Trigonella foenum-graecum* L., has been approved as a Generally Recognized As Safe (GRAS) substance for food use as a flavorant by U.S. Food and Drug Administration (21 CFR § 182.20) and the Flavor and Extract Manufacturers' Association (FEMA No. 2485).[1] Fenugreek extract is also approved as a flavoring substance for use in food by the Council of Europe (CoE No. 460).[2] Fenugreek seeds and extracts have a widespread and varied use as a food, as flavoring substances and in medicinal products to treat multiple ailments.[3-5] It is recognized as an effective treatment for diabetes mellitus and hypercholesterolemia in India.[6]

A fairly extensive toxicological database exists for fenugreek seed and various aqueous or alcohol extracts. The $LD_{50}$ (half maximal lethal dose) of fenugreek powder and fenugreek absolute extract in rats was > 5 g/kg, indicating that it is relatively non-toxic.[7-12] With the exception of an occluded application to rabbit skin, fenugreek absolute was non-irritating and non-sensitizing to animals and humans.[6]

Subchronic feeding studies have shown essentially no adverse effects when fenugreek powder was fed to rats or mice at doses up to 10,000-20,000 mg/kg/day in the diet. Twice weekly gavage dosing for four weeks of an aqueous extract at 1,000 mg/kg was reported to cause tubular necrosis of the kidney in rats. Fenugreek extracts or oils were not mutagenic in bacterial assays.[6,10]

No adverse effect in growth of dams or fetuses or in any fertility index was seen with dietary administration of fenugreek powder up to 10,000 mg/kg/day in the feed. Repeated oral dosing (60 days) of male rats at 100 mg/kg with a crude non-polar steroidal fraction of fenugreek seed resulted in complete infertility, significant decreases in reproductive organ weights, sperm counts and motility and histopathological alterations in the testicular semeniferous tubules and cauda epididymis tubular epithelium. However, because fenugreek extract and fenugreek oleoresin are products of polar solvent extraction, negligible amounts of these steroidal constituents would be expected to be present in these extractive products. Further, large amounts of fenugreek spice (1 kg) would have to be consumed to ingest an equivalent amount of steroids, assuming they were as bioavailable when taken in as the whole spice. Circulating $T_3$ was significantly reduced by oral dosing of rats at 110 mg/kg of an ethanol extract for two weeks.[6,12-15]

Multiple studies in humans and animals have demonstrated the beneficial antihyperglycemic and hypercholesterolemic properties of fenugreek powder and extracts. No adverse effects on liver or kidney function were observed in humans with diabetes mellitus taking 25 g/day of fenugreek powder.[6,16-18]

Currently, fenugreek extract is used worldwide at levels below 100 ppm in selected cigarette brands manufactured and/or distributed by Philip Morris USA Inc.(PM USA) and/or Philip Morris Products SA (PMP SA). Fenugreek extract is applied directly to the tobacco as an additive, flavoring, flavoring agent, or solvent, and as such, fenugreek extract may be subject to pyrolysis-type reactions when smoked. Fenugreek extract may also be applied to the filter as a flavoring material where it would not be subjected to pyrolysis temperatures.

As suggested by the purge and trap studies conducted by PM USA,[19] fenugreek extract applied to tobacco would not be expected to significantly distill at 100°C. In pyrolysis studies conducted by PM USA, with fenugreek extract exposed to higher temperatures, the solvent, propylene glycol, appeared to be the major peak identified.[20] The major fenugreek extract pyrolysis products included glycoaldehyde, 1-hydroxy-2-propanone, 5-(hydroxymethyl)-2-furfural, and levoglucosan. The results of this analysis suggest that fenugreek extract would be pyrolyzed extensively at the burning temperatures of a cigarette and would not be delivered in the smoke intact.[20]

Fenugreek extract was part of a PM USA ingredient testing program that was designed to evaluate the potential effects of 333 ingredients added to typical commercial blended test cigarettes on selected biological and chemical endpoints.[21-24] Three pairs of test cigarettes were produced, each containing different groups of ingredients. Fenugreek extract was added as part of the ingredient mixture to two pairs at target levels of 99, 104, 297 and 311 ppm on tobacco. No significant effects were noted in cytotoxicity, mutagenic studies or in respiratory tract endpoints in 90-day rat inhalation studies. In addition, smoke chemistry studies from cigarettes containing a mixture of flavors including fenugreek extract did not significantly alter the smoke chemistry profile compared to control cigarettes. Based on the results of these studies, the authors concluded that these ingredients (including fenugreek extract) added to tobacco do not add significantly to the overall toxicity of cigarettes.

Currently, information is only available for tests utilizing fenugreek extract in a mixture of ingredients applied to cigarette tobacco. Studies are ongoing to address the use of fenugreek extract as a single ingredient. Published studies show there is no meaningful difference in the composition or toxicity of smoke from cigarettes with added ingredients (including fenugreek extract) compared to the smoke from cigarettes without added ingredients.[21-28] Based on the best available data, the ingredients used in PM USA and/or PMP SA cigarettes do not increase the overall toxicity of cigarette smoke.

## References


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