

Evaluation Summary of Coffee Extract for Use as a Cigarette Ingredient

Coffee extract is derived from the roasted beans of the *Coffea* species and, as such, contains the full complement of chemicals that constitute plant cells. To date, over 1000 chemicals have been identified in brewed coffee, although the chemical composition varies widely depending on its origin, processing method, roasting technique and brewing method used.^{1,2} The most pharmacologically relevant constituents are considered to be caffeine, caffeic acid, cafestol and kahweol.³⁻⁶ Coffee extract is generally recognized as safe (GRAS) for use in food by U.S. Food and Drug Administration (21 CFR § 182.20).

Caffeine metabolism has been well-documented and varies between species. Caffeine is rapidly absorbed from the intestines, and its elimination follows first-order kinetics when consumed in doses that are common to average daily consumption rates.⁷⁻²¹ The pharmacokinetics of caffeic acid and the coffee diterpenes, cafestol and kahweol, are not as well-understood in humans. Caffeic acid undergoes significant metabolic transformation by intestinal microflora in mammals,²² whereas the metabolic fate of cafestol or kawool is unknown.

The acute toxicity of coffee extract is unknown and is likely influenced by its caffeine content. In rodents, the oral dose of caffeine causing 50% lethality is 200 - 355 mg/kg body weight,²³⁻²⁵ whereas in cats and dogs the mean lethal dose is 100 - 150 mg/kg body weight.^{26,27} Short- and long-term studies of coffee consumption by rodents did not reveal any carcinogenic potential.²⁸⁻³⁵ Rats administered caffeic acid in their diet were found to have forestomach lesions (hyperplasia),^{36,37} but this was not confirmed by similar findings in other studies which used brewed coffee.³⁵

The absence of any carcinogenic effect of coffee consumption was reflected in the low genotoxicity of coffee in *in vitro* assay systems. Although individual chemicals found in coffee have been reported as mutagenic in microbial assays, the majority of studies using whole coffee indicate a low mutagenic or genotoxic potential.³⁸⁻⁶⁸

The teratogenic effects of coffee and caffeine have been studied in a number of animal species, however, no clear overall pattern of effects has emerged. Those studies demonstrating teratogenic effects are predominantly associated with large doses of caffeine equivalent to 15 to 23 cups of coffee per day in humans.^{69,70} The relevance of the teratogenic or potential anti-teratogenic effects of coffee in animals to the human condition is highly questionable, because the susceptibility of rodents to the teratogenic effects of coffee are not reflected in the human population by epidemiological studies.⁷¹ No consistent results or conclusions were obtained among studies analyzing effects of coffee or caffeine on fertility, fecundability or risk of delayed conception.⁷²⁻⁷⁷

Epidemiologic studies on the relation between coffee consumption and cancer risk have predominantly focused on cancers of the urinary bladder, pancreas and colorectum. Studies examining the relation between coffee and bladder cancer have been contradictory, despite the large number of reports published over the last three decades.⁷⁸⁻⁹⁴ In most of these studies, the risk tends to be higher in coffee drinkers than among non-drinkers, but the excess risk is generally moderate and is not dependent on either dose or duration. For other cancer sites, including buccal cavity and pharynx,^{82,94-98} stomach and small intestines,^{82,87,94,97,99,100}

colorectal,^{82,87,94,97,101-113} pancreas,^{82,87,94,97,114-128} lung,^{82,87,94} breast,^{82,94,108,129-139} ovaries,^{82,94,140-142} and lymphatic system,^{82,94,143,144} the relation between cancer risk and coffee drinking has been less extensively investigated, but the evidence does not indicate any strong correlation.

Currently, coffee 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). Coffee extract is applied directly to the tobacco as an additive, flavoring, flavoring agent, or solvent, and as such, coffee extract may be subject to pyrolysis-type reactions when smoked. Coffee 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,¹⁴⁵ coffee extract applied to tobacco would not be expected to significantly distill at 100°C. At the higher temperatures used in the pyrolysis studies conducted by PM USA, the results suggest coffee extract would pyrolyze extensively to yield products similar to those seen when many organic natural products combusted.¹⁴⁶

Coffee extract was part of a PM USA 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.¹⁴⁷⁻¹⁵⁰ Three pairs of test cigarettes were produced, each containing different groups of ingredients. Coffee extract was added to two pairs at target levels of 13 ppm, 32 ppm, 39 ppm and 95 ppm. 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 coffee 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 coffee extract) added to tobacco do not add significantly to the overall toxicity of cigarettes.

Currently, information is only available for tests utilizing coffee extract in a mixture of ingredients applied to cigarette tobacco. Studies are ongoing to address the use of coffee 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 coffee extract up to 2,700 ppm¹⁵¹) compared to the smoke from cigarettes without added ingredients.¹⁴⁷⁻¹⁵⁵ Based on the best data available, ingredients used in PM USA and/or PMP SA cigarettes do not increase the overall toxicity of cigarette smoke.

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