



OPIUM CONSUMPTION

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This publication represents the views and expert opinions of an IARC Working Group on the Identification of Carcinogenic Hazards to Humans, which met remotely, 11–20 September 2020

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OF CARCINOGENIC HAZARDS
TO HUMANS

6. EVALUATION AND RATIONALE

6.1 Cancer in humans

There is *sufficient evidence* in humans for the carcinogenicity of opium consumption. Opium consumption causes cancers of the urinary bladder, larynx, and lung. Positive associations have been observed between opium consumption and cancers of the oesophagus, stomach, pancreas, and pharynx.

6.2 Cancer in experimental animals

There is *inadequate evidence* in experimental animals regarding the carcinogenicity of opium.

6.3 Mechanistic evidence

There is *strong evidence* in experimental systems that opium, specifically *sukhteh* and opium pyrolysates, exhibits key characteristics of carcinogens (it is genotoxic).

6.4 Overall evaluation

Opium consumption is *carcinogenic to humans (Group 1)*.

6.5 Rationale

The evaluation of opium consumption (i.e. smoking or ingestion) as Group 1 is based on a determination of *sufficient evidence* of carcinogenicity in humans. In reaching this determination, the Working Group noted that in a cohort study of 50 045 adults in Golestan Province, a north-eastern province of the Islamic Republic of Iran, self-reported opium consumption was assessed at baseline, validated with urinary levels of opium metabolites, and the cohort was followed for more than a decade to ascertain incident cancers. The risk of several types of cancer – including cancers of the urinary bladder, larynx, and lung – was significantly higher among opium users than non-users and increased in an exposure-dependent fashion with cumulative opium use. The prospective cohort design minimized concerns regarding selection bias and reverse causation, and the detailed assessment of demographic, socioeconomic, and lifestyle factors addressed concerns regarding the major potential confounders of the associations of interest. These cohort study findings are supported by multiple case-control studies that provide evidence of positive associations between opium consumption and these types of cancer, often based upon larger numbers of site-specific cancer cases, ascertained over a larger geographical area in the Islamic Republic of Iran and, in many cases,

derived in studies that used similar exposure assessment tools and covariate adjustments to those used in the Golestan Cohort Study. While individually each study has its limitations, the Working Group concluded that, collectively, these studies provide a basis to rule out chance, bias, and confounding as alternative explanations for the positive association between opium use and cancers of the urinary bladder, larynx, and lung with reasonable certainty; thus, there was *sufficient evidence* of human carcinogenicity for these three cancer types. Additionally, evidence was deemed to be *limited* that opium consumption causes cancers of the oesophagus, stomach, pancreas, and pharynx. While positive associations were seen in the body of evidence for these cancers, chance, bias, and/or confounding

could not be ruled out with reasonable confidence. The *sufficient evidence* of carcinogenicity in humans applies to smoking and ingestion as routes of consumption of raw, dross, and minimally refined opium.

There is also *strong evidence* in experimental systems that opium, specifically *sukhteh* and opium pyrolysates (solid residues of combusted opium), exhibits key characteristics of carcinogens. These opium forms are genotoxic. There is *inadequate evidence* in experimental animals regarding the carcinogenicity of opium consumption because all available studies had major qualitative or quantitative limitations.