

Limitation of Experimental Research on Opium Consumption and Cancer Development in Human: Call for Establishment of an International Consortium

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In the previous issue of the Basic and Clinical Cancer Research, Rafipour H. and et al. published a comprehensive systematic review of the experimental research articles published on the carcinogenicity of opium, a narcotic drug (1). The main finding was that experimental studies for the evaluation of opium carcinogenicity are limited. The majority of these studies used noscapine alkaloids as a chemical extraction (n=23), and a few (n=9) used opium and its derivatives. Most in vivo and in vitro studies on opium alkaloids showed a protective effect -shrinking tumors- or no association between exposure to opioids and cancer overall. However, out of 13 tests that applied opium itself in their experiments, 9 (70%) tests showed the carcinogenic effect of opium. Summary of findings from this review paper supports the results of monograph-volume 126-prepared by the International Agency for Research on Cancer (IARC) on the carcinogenicity of opium use. In September 2020, a Working group assigned by IARC concluded that opium consumption is carcinogenic for humans (Group 1) (2). The conclusion was

based on “sufficient evidence” for the carcinogenicity of both smoked and ingested routes of raw, dross, or sap opium consumption. This conclusion has been made based on a thorough evaluation of epidemiological and experimental research published during the last half a century, most of which were performed in Iran, the most prevalent region of opium consumption worldwide. Although associations between opium use and several cancer sites have been reported, the associations have been confirmed for cancers of the larynx, lung, and urinary bladder. It means that the carcinogenicity of opium use is similar to tobacco smoking and requires preventive measures to avoid the further occurrence of cancer among the population exposed to opium and its derivatives. Opium is produced illicitly in approximately 50 countries worldwide, although 84% of global opium is produced in Afghanistan (3). The main opium trafficking flows through Iran to several countries worldwide. Consequently, with over two million users, the highest prevalence of opium use has been reported for the Iranian population who



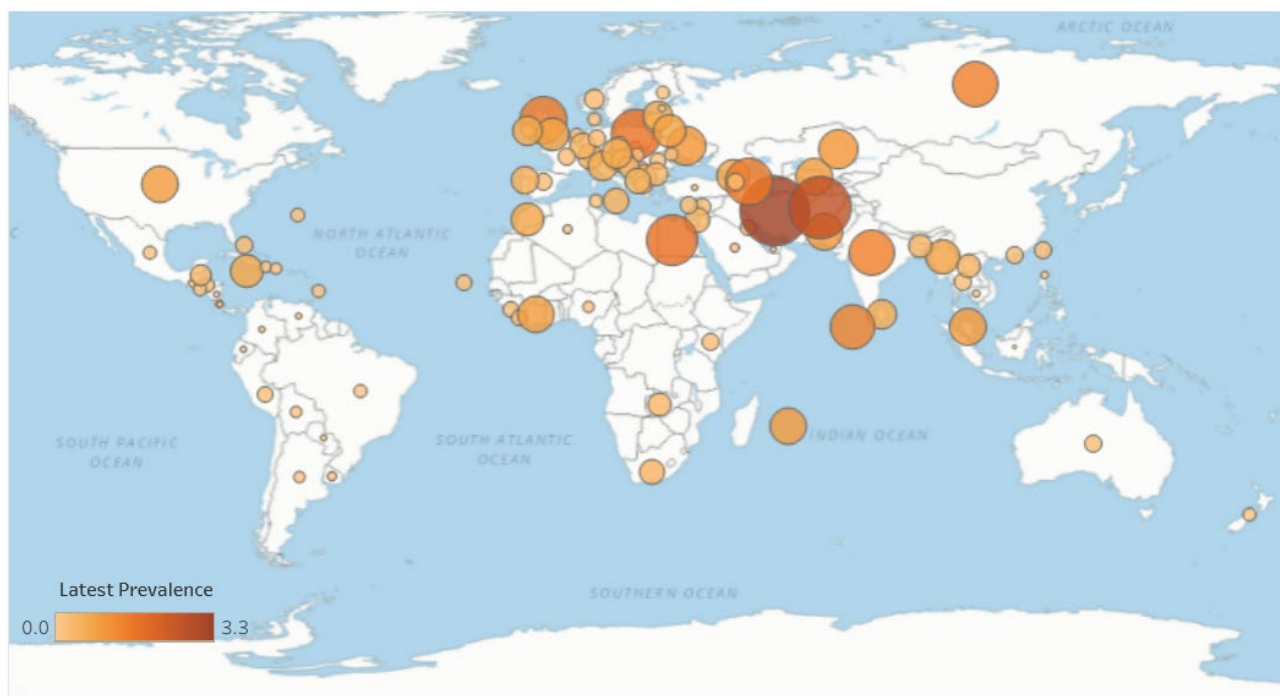


Figure 1. Annual Prevalence of Opiates among Adults in 2010

(Source: ChartsBin statistics collector team 2010, viewed 22nd January, 2021, <http://chartsbin.com/view/z2q>)

can easily access the opium products (**Figure 1**). Despite the worldwide variation, within-country variation also exists for opium consumption. For Instance, opium use is higher in Sistan-e-Baluchestan and Kerman provinces located in the southeastern part of Iran and bordered by Afghanistan. This region is one of the routes for drug smuggling from Afghanistan to Europe, known as the Golden Crescent route. Rafipour H. and et al. highlighted important limitations of experimental research on the carcinogenicity of opium use. Following the IARC's conclusion and classification of opium as group 1 carcinogens, research on the mechanism of opium carcinogenicity should be prioritized. Golestan cohort study in Iran has provided the most convincing evidence for the carcinogenicity of opium

use (4, 5). In addition, we conducted a large multicenter case-control study, the so-called Iranian study of opium and cancer (IROPICAN), to evaluate associations between opium use and the risk of different cancer types (6). The first reports from this project revealed a strong association between opium use on laryngeal cancer among the Iranian population. Although the association between opium use and cancer risk had been established, the mechanism for this association is a black box, and further research is still needed. Rafipour H. et al., in their systematic review, highlighted that because of significant qualitative or quantitative limitations in the published literature, evidence from experimental researches on the carcinogenicity of opium is "inadequate". They concluded that none of the

conducted studies have performed or completed all series of classic laboratory and animal tests. Besides, they reported that the exact pathway of the carcinogenicity of opium is still unclear, and future experimental investigations are required in this regard. They also noted that none of the previous studies used genomic and epigenetic screening techniques. One of the reasons behind this deficiency is that the countries with a high prevalence of opium use suffer greatly from insufficient infrastructure and resources to conduct these types of research. Such advanced laboratory-based studies are beyond the capacities of research in these countries. Given the widespread use of these opioids across the world and the striking dissimilarity of opium production and shady dealers, it is necessary to establish an international research consortium to bridge the gaps to understand the biological mechanisms of opium carcinogenicity in humans. It is also the time to investigate early detection technologies to screen and prevent opium related cancers in high-risk populations,

especially for lung, bladder, and laryngeal cancer.

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