

## Review on the effect of the opium drug in the body

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**ABSTRACT:** Opium are the second most prevalent abused illicit substance after cannabis in the world. The latest United Nations Office on Drugs and Crime (UNODC) report estimated 30% increment in opium cultivation worldwide. High prevalence of opium consumption in eastern countries may be due to the high availability and traditional misconceptions. Opium consumption has been linked to hypertension, diabetes mellitus, dyslipidemia, and coronary artery diseases (CAD). In this review, we will review the association between opium use, cardiovascular diseases, and clinical outcomes. The present evidence suggests that chronic opiate consumption may increase the risk of cardiovascular diseases and related mortality.

**Keywords:** Opium, Cardiovascular disease, Drug interactions, Metabolic effects, Mortality

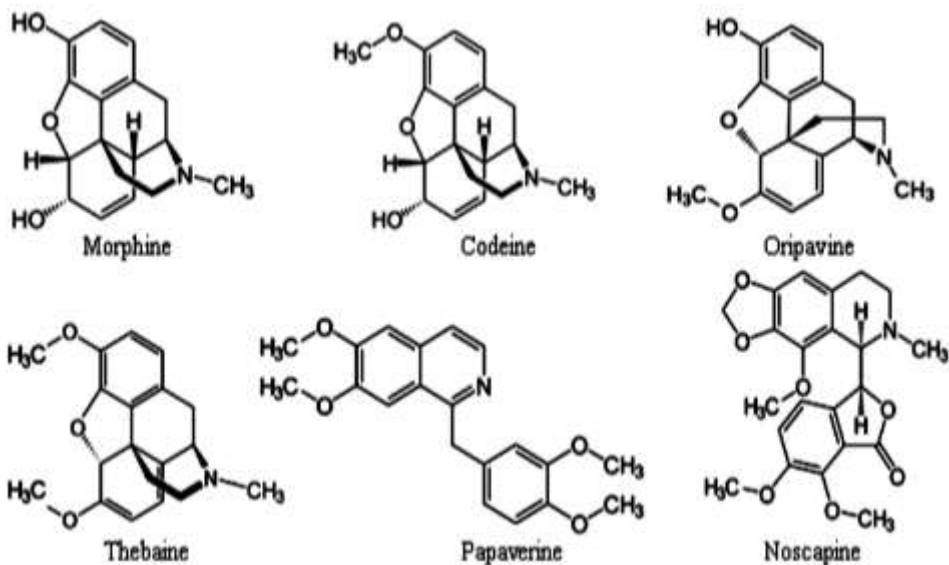
### I. INTRODUCTION

Poppy (*Papaver somniferum* L.) is one of the ancient plants that was cultivated for millennia and used for both medicinal and recreational purposes. Opium is a dark sticky or crumbly mass exuded from the ripening capsule of opium poppy and consists of several alkaloids including approximately twelve percent morphine with lesser amounts of noscapine, codeine, papaverine and thebaine.

Raw opium is the second most prevalent abused substance after tobacco in most Asian countries. The 2017 report of the United Nations Office of Drugs and Crime (UNODC) estimated the overall production of opium to be 6,380 tons worldwide with 30% increase compared to the previous year and they reported the number of illicit users to be up to 17.7 million in 2015.



### Structure



### Blood pressure and hypertension

There are misconceptions in the general population or even among some medical professionals, that opium could have favorable impacts on lowering blood pressure in hypertension while many experts may disagree. Opium use had no significant ameliorative effect on hypertension in either occasional or dependent users

Similarly, several other studies failed to find a correlation between opium consumption and hypertension prevention. However, not all of these studies were consistent. A cohort study of 9,264 adults showed a lower prevalence of hypertension in opium users as compared to their counterparts, probably because of the younger age of opium users in that study population. In the contrary, in a cohort study on 5,332 participants, high systolic and diastolic blood pressures were more prevalent in opium users than in others (3). A case-control study reported the rate of hypertension to be significantly higher in addict patients with ischemic stroke than controls

Endogenous opioid systems and opioid receptor agonists are purported to modulate the arterial pressure to some extent.

### Effects on coronary disease and myocardial infarction

Opium users have shown to have a higher susceptibility to coronary artery disease compared to non-users with a dose-response relationship reported between these two (9, 33). Chronic opium

consumers have an overall increase in their ECG abnormalities. The ECG abnormalities are more frequently observed in male opiate consumers than in females. QTc prolongation (13%), R and/or S wave abnormalities (11%), and poor R progression (10%) were the most reported ECG changes. Niaki et al. showed that opium consumption was a significant risk factor of MI with an adjusted odds ratio of 26.3. However, they did not find any association between opium abuse and extent of MI. In patients admitted with the diagnosis of MI the prevalence of opium addiction was 19%, while it was 2.8% in general population. Sadeghian et al. presented the opium abuse as a major risk factor for ischemic heart disease

### Pharmacology of Opiates

In 1806, Friedrich Wilhelm Sertürner isolated morphine as the active component of the opium poppy, and there the modern opioid pharmacology was born (More than 40 alkaloids exist in the milky latex fluid obtained from the opium poppy. The six major alkaloids that account for almost all of the natural alkaloid composition in opium are morphine, noscapine, codeine, papaverine, thebaine, and narceine (16). Thebaine is not used therapeutically, but several drugs such as naloxone, naltrexone, oxycodone, and buprenorphine are synthesized from the baine.

The opioid receptors are categorized according to the International Union of Pharmacology (IUPHAR) recommendation to  $\mu$ -

(MOP),  $\kappa$ -(KOP), and  $\delta$ -opioid (DOP) receptors, which are G-protein-coupled receptors Cyclic AMP and/or ion channels (K<sup>+</sup>) are second messenger systems of opiate receptors. Studies suggested that modifications in the levels of cyclic AMP during chronic opiate consumption are associated with the development of tolerance and physical dependence (18).

#### Interactions with cardiovascular medications

Opioid addicted patients may concurrently suffer from other comorbidities. Cardiovascular and pulmonary diseases are common among chronic opiate abusers but dose-dependent exact interactions are not studied well. Hence, the use of opiates (either therapeutic or on an abusive basis) along with cardiovascular medications (including anticoagulants, antiarrhythmic, cardiotoxic, and antihypertensive drugs) may increase the risk of drug-drug interactions.

#### Effect on heart failure

Heart failure and functional class seem to be no different in opium-addicted patients after MI than in non-addicted individuals. Davoodi et al. reported no difference between addicted and non-addicted patients regarding functional class, angiographic findings, and the need for CABG. Similarly, post-MI LVEF was not different between addicted and non-addicted patients ( $p = 0.4$ ). Safaei also reported no difference between the LVEF of addicted and non-addicted patients before and 6 months after CABG.

The effect of opium in patients with heart failure (HF) is still unclear. Morphine can lower some of the symptoms occurring in the late stages of HF such as dyspnea. Similarly, morphine seems to relieve the ischemia symptoms in patients with cardiovascular risk factors. The underlying pharmacological mechanism of morphine has encouraged some of the researchers to conclude that morphine may be cardioprotective in HF patients. However, one study revealed that patients with HF who use morphine along with nitroglycerine and furosemide had higher mortality rates (48). However, there is not enough data to provide evidence-based recommendations regarding the cessation of opium abuse in cardiac patients (49).

#### Effects on cerebrovascular disease and stroke

A few studies assessed the effect of chronic opium consumption on the development of ischemic stroke. A case-control study showed a

significant rise in ischemic stroke in opium-addicted patients in Kerman ( $P < 0.0001$ ) (50). In another cross-sectional sonographic study conducted on 97 patients with ischemic stroke shown that there was no significant difference in the frequency of atherosclerosis and the type of involved vessels among opium addicts and non-addict patients. Rezvani and Ghandehari studied 558 opium users with a mean age of 56.2 years. They claimed that opium inhalation did not have a significant effect on occurrence cerebrovascular events and they concluded that opium may have a protective effect on ischemic stroke (40). Khademi et al in Golestan cohort study conducted on 5000 Iranian adults demonstrated that chronic abuse of opium was associated with an increased risk of ischaemic heart disease and cerebrovascular events. A recent case-control study presented opium addiction and hypertension as two independent predictors of stroke.

## II. CONCLUSION

The incremental rise of opioid abuse requires us to inform and educate the patients regarding its possible detrimental effects. Several large-scale studies imply that opium is hazardous cardiovascular and metabolic disorders and even may worsen these complications.

Successive data demonstrated that there is an association between habitual opium consumption and the risk of ischemic events. While vernacular wrong believes and short-term and small-sized studies accentuate the usefulness of opium consumption. Therefore, clinicians and patients should be noticed about the deleterious effects of opium addiction on various vascular events.

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