# Study the Histopathological Effect Associated with Oral Overdose of Opioid Derivatives - on Liver and Kidney Tissue in Male Rats

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## Abstract

The current study aimed to ascertain the impact of acute codeine dose (0.50 and 1 ml/ 250g), on the histolopathological profile of the liver and kidney in male rats. A synthetic antispasmodic substance with comparatively low toxicity is opioid derivatives (Codeine), In present study results found that normal histological structure, except Some minor changes were shown in the control group (antihistamine syrup, which does not contain codeine), while the groups II and III contain overdose treatment of codeine were reveal that the over dose of codeine involved inflammation cells infiltrations in the liver parenchyma, congestion of blood vessel, fatty degeneration, cytoplasmic vacuolation, and pyknotic of hepatocytes nuclei. However, renal damage profiles were seen in the kidneys of treated rats, kidney reveal necrosis, cytoplasmic degeneration of lining of the renal tubules, and enlarged lumen intracellular space. Red blood cells flooded the intertubular gaps and congested the renal blood vessels. conclusion that opioid derivatives (Codeine) poisoning caused renal and hepatocellular damage.

**Keywords:** Codeine, Liver, Kidney, rats.

## Introduction

includes (Glyceryl gluatacolate, chlorpheniramine maleate, and phenylephrine HCL), which is represented by Tussilet cough syrup, does not contain codeine in its composition, Group II administrated codeine orally at a dose amount of 0.5ml/250g/day, two time daily, While the Group III through oral administrated codeine in a dose amount of 1ml /250g/day, two time daily after 30 days, this dosage is comparable to human addictive dosages.

Light microscopy processing: After 30 days of therapy, liver and kidneys were quickly removed after the rats were murdered under diethyl ether anesthesia. For light microscope preparations, specimens were fixed in 10% formalin, then dehydrated in a graded series of ethanol (70%, 85%, 95% and 100%), clearing by xylin encased in paraffin wax and sectioned at 4um thickness. Mallory stain was used to stain slides for histological study. (9).

## Results

### light microscope results:

Throughout the experiment, there was no fatalities. noticed in either the control or treated groups, group I (control) Sections of liver tissue of control group showed that, semi normal structure of hepatocytes and central veins that were organized in the hepatic cord around blood sinusoids (Fig. 1-A). Histological analysis of the livers of Groups II and III revealed a variety of negative effects on morphology and histopathology, which increased with increasing dose quantity. Group II was found a little enlarged and cirrhotic, few of hepatocytes showed ballooning degeneration, veins congestion and few of inflammatory infiltrate showed diffuse between liver lobular (Fig.1-B, C and D). While group III reveal enlarged and cirrhotic, sinusoidal dilatation, aggregation of Kupffer cells, fibrosis, more of hepatocyte's degeneration and hemorrhage (Fig. 1- E, F and G). Sections of kidney tissue of control group that revealed a semi-normal shape of focal tubules and glomerulus. ( Fig.2- A ). Groups II showed cytoplasmic degeneration and necrosis of **renal** tubules epithelial, with a few interstitial heamorrahge. While, group III showing the acute necrosis of renal tubules epitheliual, acute haemorrage, and hypertrophy of renal tubular epithelial.

**1.C**

fib

d

**1.D**

-

**Figure 1. (1.A.) Section in control rats livers central veins (V) as well as hepatocytes (h), There was arranged in hepatic cord around blood sinusoids ( ch) and few degeneration of hepatocytes ( Mallory stain 400X). (1. B, C and D) group II showing few of hepatocytes showed ballooning degeneration (D), veins congestion (VC), aggregation of kupffer cells (kup) and sinusoidal dilatation (SD) ( Mallory stain 400X). (1. E. F. and G) group III showing Sinusoidal dilatation (sd), aggregation of Kupffer cells (kup) , fibrosis (fib), more of hepatocytes degeneration (d), inflammation infiltration cells (inf) and congestion (cg) ( Mallory stain, 400X origina**

**Figure 2. (2.A.) The section in the control rats' kidneys contains normal glomerulus (g) and renal tubules (r) . (2.B.) (Mallory stain 400X). (2. B. and C) group II showing renal tubule epithelial degeneration (dg) and necrosis (nc). Few interstitial hemorrhages (He) ( Mallory stain 400X). (2. D and E) group III showing acute necrosis of renal tubules epitheliual (ne), acute haemorrage (he), hypertrophy of renal tubular epithelial (hyp) ( Mallory stain, 400X original magnification).**

r

g

**2.A**

addiction, and its effect on metabolic profiles is quite scant, it's crucial to look into and comprehend how cough syrup affects these metabolic patterns. Although opioids have been widely used for a long period, their long-term effects, particularly at the histological profile, are unknown. (12). One of the natural plant alkaloids known as codeine is found in opium extracts and is commonly used to treat coughs and mild to moderate pain. Despite its widespread usage, codeine has not been linked to blood enzyme increases throughout therapy for a long time, and there have been no compelling reports of idiosyncratic acute, clinically obvious liver impairment linked to its use. (13). As with other opiates, codeine produces respiratory depression and physical and psychological addiction (14). Following parenteral and oral administration, codeine and its salts are effectively absorbed. Codeine is largely processed in the liver by endoplasmic reticulum enzymes, where it passes through partial conjugation with glucuronic acid, O-demethylation, and N-demethylation. Most of the drug's excretion is found in the urine as inactive metabolites, with trace levels of free and conjugated morphine also present. The feces contain very small levels of codeine and its metabolites (15). morphine and its derivatives have been widely employed as opioid analgesics for the treatment of both acute and chronic pain (16). All morphine derivatives undergo liver metabolism before being eliminated by the kidneys; nevertheless, this process can result in hepatotoxicity and nephrotoxicity (17). However, the lethal dose of codeine in rats is 427 mg/kg body weight orally, 130 mg/kg intraperitoneally, 229 mg/kg subcutaneously, and 75 mg/kg intravenously, while in the mice, the corresponding lethal dose values are 250 mg/kg (18). According to a time- and dose-dependent leakage of lactate dehydrogenase, codeine was caused cytotoxicity in isolated rat hepatocytes (19). Cell death started at doses of 0.5 or 1.25 mM after 60 minutes from treatment with codeine, and viability fell to less than 10% after 120 to 150 minutes. Metyrapone, a cytochrome P450 metabolism inhibitor, was added, which prevented hepatotoxicity, proving that a codeine metabolite produced by P450 was the cause of the cytotoxicity (20). The different doses of codeine (2.5 mg/250 g and 5.55mg/250g) exhibited a variety of negative impacts on the liver's histology, including vacuolation, hyperplasia, hypertrophy, degeneration, and necrosis. These effects got worse as the dose level grew. These findings supported those of. (21), who found that varying dosages of opium derivatives caused histological alterations in the liver of mice. In addition to causing histological lesions inflammatory infiltration, necrosis, hyperpigmentation, degeneration, and vessel congestion, the administration of morphine and its derivatives like codeine and tramadol also revealed pathocytological changes like torn and convoluted nuclear membranes, the distance between nuclei and irregular chromatin. Our findings agree with those of earlier research (22). The metabolism and excretion of morphine are carried out by the liver and kidneys, (23 and 24). During its metabolism, morphine has the potential to be toxic to the kidneys and the liver (25). Long-term usage of LAAM has been linked to renal damage, including focal cortico-medullary mineralization, focal tubular epithelium renewal, and mineral/crystal deposition in the intertubular region of the kidney (26). In the tubular cells of the kidneys, they manifested histopathologic alterations (27).

Conclusion: The present study contends that hepatic and renal damage is observed in the histological assessments following an overdose of cough medicine containing codeine. The long-term consequences of these immediate harmful effects could, be

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