

## A Narrative Review of Codeine and Preventive Measures in Mitigating against the Widespread of its Abuse and Misuse

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### Abstract

Codeine is a phenanthrene extracted naturally from opium; it can also be produced artificially by the methylation of morphine. Among opiate drugs, codeine is the most frequently consumed around the world, broadly used for its pain relieving, antitussive properties, and its ability to prevent diarrhea. The abuse of codeine products is a major developing general health challenge in numerous nations around the globe, this is because such items are available in the range of over the counter medications (OTC) which are consistently, and easily gotten in the market even without prescription. This paper discusses Codeine and the Preventive measures in mitigating against its Abuse and Misuse. It is a review study in which the prevalence rate of codeine misuse, motives for misuse of codeine, Side effects of codeine abuse and Prevention of codeine abuse was discussed extensively under; Pharmacovigilance, drug education, monitoring and screening. It was concluded that the importance and uses of codeine are numerous, but the abuse of codeine and codeine products, for example the codeine cough syrup is a general health problem all over the world, and it remains necessary that codeine is regulated in each respective countries to reduce the prevalence rate of its misuse and abuse.

**Keywords:** Codeine; Preventive measures; Abuse; Misuse

### Introduction

The name codeine is gotten from the Greek word kodeia (κώδεια) for 'poppy head' and it is found normally in the poppy plant 'Papaver somniferum var. collection' [1]. Codeine is a phenanthrene extracted naturally from opium; it can also be produced artificially by the methylation of morphine [1]. Among opiate drugs, codeine is the most frequently consumed around the world, broadly used for its pain relieving, antitussive properties and its ability to prevent diarrhea [2,3]. The fundamental pharmaceutical form of codeine is the tablet which is usually (60%); however, codeine is additionally accessible in form of capsule, effervescent tablet, syrup, suppository and solution [4]. Also, Codeine products may be marketed for subcutaneous or intramuscular infusion. Although, the Intravenous use of codeine is not recommended and advised as it might cause hypotension and muscular contraction [5].

The importance and uses of codeine are numerous. The aforementioned statement is affirmed by Campbell, Iedema, Kelly and Madadi, Cartabuke et al., EMA, Hall et al., Anderson, [4,6-11] as codeine could be used for the treatment of cancer pain, and for the management of minor pains in adults and children. Also, Codeine is used as a component of a stepwise regimen for the management of mild to moderate non-cancer pain, usually in mixture with paracetamol or potentially with Non-Steroidal Anti-inflammatory Drugs after there is inadequate pain control with the agents alone [1]. According to Semple et al. [12], codeine was recommended for pediatric use because of the lower rate of narcotic related symptoms in circumstances where airway management and neurological assessment are critical. In addition, given codeine's simplicity of usage as an oral

syrup or tablet, it has been used in mild to moderate pain management in children [3].

The non-therapeutic use of codeine is on the high as various researches demonstrated that the attention to codeine's abuse potential in the hazardous drug using networks is higher than in the general population, and it can possibly alleviate withdrawals from more grounded opium products, for example, heroin [13,14]. Recreational codeine use is described by the use of high dosages of codeine in 'binge' form with nasal, rectal and oral, with the subcutaneous use frequently done [15]. The abuse of codeine items is a major developing general health challenges in numerous nations around the globe, this is because such items are available in the range of over the counter medications (OTC) which are consistently and easily gotten in the market even without doctor's prescription [16]. For instance, thousands of Nigeria youth and women are addicted to codeine [17]. Codeine is a medicine that has become a street drug, unfortunately, drug abuse, misuse or overuse are usually not detected until the person and society at large suffers from the consequences. In light of the aforementioned, and the upsurge in the abuse of codeine in our societies, this paper did a narrative review on the Preventive measures in mitigating against the Abuse and Misuse of codeine.

### Literature Review

This is a theoretical research and the review focuses on Codeine and Preventive measures in mitigating against the widespread of its Abuse and Misuse. Literature review was majorly performed in Google, PubMed, Web of Science and Springer Link data bases. These data bases were searched so as to get the latest and valid information for the topic at discourse. Year of publication was not a factor in the literature search, but the articles were limited just to those written in English.

## Prevalence rate of codeine misuse

It is a known fact that codeine is misused in pill or syrup shape [18], but the abuse of codeine cough syrup is a general health problem all over the world, and this is very much archived; for instance in countries like the USA [19], India [20,21], Hong Kong [22,23], and Japan [24-27]. Over the counter and prescribed types of codeine cough syrup exists and contains diverse rates of codeine, dextromethorphan and promethazine hydrochloride, an antihistamine with narcotic properties. In the USA, and especially in Southern States, codeine cough syrup is dangerously blended by users with liquor (alcohol) or soda pops (i.e. Sprite), which are usually called varying names which are; 'Purple Drank', 'Syrup', 'Barre', 'Purple Tonic', 'Purple Sizzurp'; Texas tea, 'Tsikuni' and 'Lean or Southern Lean' [28,29].

Multi-drug users and clients in the USA reported using codeine syrup because of lack of legal sanctions, it is seen to be a safe drug, can be gotten cheaply or inexpensive, and can be broadly acquired from pharmacists, doctors and hospitals [28]. Agnich et al. Elwood and Peters et al. [28-30] research findings affirmed that codeine cough syrup use is entrenched among males in urban dark ethnic groups and lesbian, gay, bisexual, transgender (LGBT) minorities, and is related with negative health behaviors like poly substance use, abnormal amounts of sexual action, and abuse of new psychoactive substances. A survey research by Agnich et al. looking at the pervasiveness of misuse of codeine cough syrup of 2,349 students was carried out in the USA. The sample involved White (69%), African American (24%), Hispanic (3%), Native American (3%) and Asian (1%), with participants with a normal age of 20. Results from the research study revealed that notable gaps in treatment may exist for both Hispanic and Native American students. The researchers recommended that urban male youth of every single racial background are potential misusers of codeine syrup, and abuse might be frequent among the LGBT group.

## Motives and reasons for misuse of codeine

Reasons for abuse of narcotic drugs including codeine can be alluded to self-treatment for pain and the recreational use of the drug [18,31-38]; with more predominance rate of recreational use motives found among men [39]. Although, the number of researches that explicitly investigate what persuades individuals to misuse and abuse codeine is constrained. Nevertheless, some research studies which expressly looked into people's motives for codeine abuse are established. For instance, Daniaulaityte et al. [33] carried out a comprehensive and detailed interview with twenty-four individuals who had a background marked by narcotic abuse (Figure 1). Their use of codeine was associated with self-curing for physical pain related with day to day duties, and for psychological well-being. In addition, some began taking codeine for lubbish reasons, and after some time got addicted, while others took codeine to substitute their dependence on heroin, particularly when heroin was not promptly accessible [33]. Furthermore, another comparative study by McCabe et al. [39] discovered that reasons for codeine abuse includes but not limited to self-treatment of physical and emotional pain, rest and nervousness problems and quest for delight. Also, easy accessibility of codeine and individuals identity types (for instance, addictive personality) may likewise be a factor. Furthermore, the use of codeine for its pleasurable impacts, to unwind or decrease stress was likewise revealed as a factor for its misuse [40].

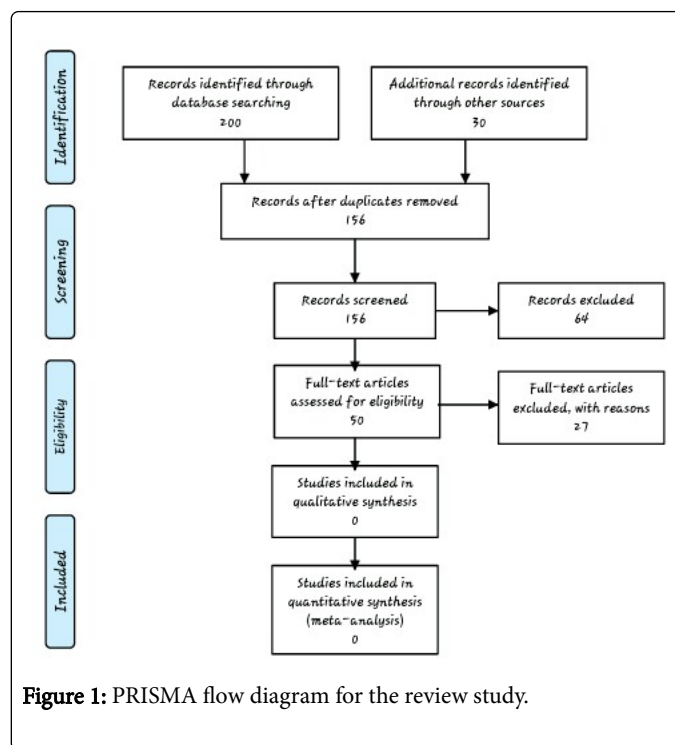


Figure 1: PRISMA flow diagram for the review study.

## Side effects of codeine abuse

Like all medications, codeine is not free from health problems and consequences. Outcomes of codeine abuse, for example; dependence and untoward reactions in the use of opiate drugs affects the manner by which they are prescribed or recommended for patients, with doctors been careful by prescribing lower doses than required to create pain relieving impacts [41]. As indicated by Iedema, codeine is viewed as a capricious medication with expanded danger of harmfulness when mixed or blended with other products. Furthermore, some of the consequences of codeine abuse are discussed under the following headings;

**Ability to cause impairment:** Bachs et al. [42] observed carefully the impacts of codeine alone, on a clinical test for tipsiness in connection to suspected sedated driving. Forty-three instances of suspected drugged drivers from a national database that tested positive for codeine in blood tests were inspected, but negative for morphine and different drugs. From findings of the study, codeine seemed to have a dose-dependent effect on the central nervous system (CNS) that may have prompted impairment. Furthermore, the result of this study bolsters the view that some codeine effects do not appear to be mediated by morphine. Also, Hou et al. [43] carried out an intervention study looking at the brain images of codeine cough syrup addicts, and matched it with that of the healthy people. Brain scans, the volume and weight of the respective corpus striatum and the proportion of the corpus striatum to the entire brain were measured in the 22 codeine cough syrup participants who are addicted members, and contrasted it with that of the 27 healthy participants. The result indicated changes to the respective corpus striatum, and a diminished weight, volume and proportion to the entire brain in the codeine cough syrup addict members. The aftereffect result of the scan suggested that changes occurred in the dopaminergic system which is in charge of the cognitive and motor action; this implies that chronic codeine cough syrup abuse may induce grave damage to the brain and

the neuro-imaging. Also, this finding additionally buttresses the point that codeine cough syrup causes codeine dependence.

**Ability to cause injury or damage:** Buckeridge et al. [44] analyzed clinic and medical records from 2001-2003 in Quebec, the second biggest territory in Canada. Populace based health databases were used to quantify previous risk factors for injuries in 2001/2002, and drug use and injuries during follow-up in 2003. The records analyzed included professionally prescribed medications, amount, length, diagnosis, procedure and location. Altogether 403,339 adults of more than 65 years of age were followed up over a one year time span to evaluate the risk of damage related with narcotic use. The findings showed that 3.7% of the entire population had injuries, with fractures and laceration being the most widely recognized. 15.3% of this population was prescribed a sedative drug of which 10.8% was codeine. Furthermore, In Denmark, a study that analyzed the impacts of morphine and opiates on fracture risk revealed that codeine was among sedative drug related with frequent fracture risks [45].

**Other Adverse health effects:** The adverse health consequences of codeine use were affirmed, and have been reported by many researchers around the world. The detailed health consequences of inordinate, long period or dependent on the use of codeine or codeine product incorporates gastric ulcers, intestinal or internal bleeding, hepatotoxicity, hypokalaemia, inflammatory stomach conditions, and significant hypokalaemia related with an extreme myopathy, which is usually seen in clients with no history of substance use disorder [15,16,40,46-51]. Critical chronic health problems relating to gastrointestinal bleeding, nephro-toxicity, hypokalaemia and narcotic dependence are usually related with the abuse of ibuprofen-codeine products [15,46,49,52].

### Prevention of codeine abuse

As it is often said, prevention is better and less expensive than cure. In reducing the widespread Abuse and Misuse of Codeine, workable preventive measures for health professionals are discussed under the following headings;

**Pharmacovigilance:** Expanded pharmacovigilance in primary care settings is essential and needed [53,54]. Although, there is expanded attention on "responsible prescribing" in the literature on the misuse of prescribed narcotic analgesics (codeine inclusive), to include risk assessments, prescribing agreements and treatment contracting without compromising legitimate access to opioids for analgesic uses [55,56]. Nevertheless, prescribed codeine or codeine products must be monitored after they have been licensed for use. The monitoring is important in order to identify and evaluate the progress of the medications and get the previously unreported adverse reactions from patients.

**Drug education:** Education in administration of medicine containing codeine is required [9]. For example, pediatricians taking care of pediatric patients using codeine or codeine products needs to be educated and informed to look for alternative medical assistance if signs and symptoms of toxicity occur.

**Monitoring:** Health experts involved in codeine prescriptions need to monitor use in vulnerable groups. For example in patients with incessant and serious non-malignant pain, patients with cancer pain and illegal drug users or clients. The target of such checking is to establish whether narcotic drugs, for example, codeine are substituting for or convoluting pain, the psychological health and addiction

treatment outcomes; in this manner reducing the risk of overdose [57-61].

**Screening:** Effective and Standard screeners, for instance, the Screener and Opioid Assessment Tool for Patients with Pain (SOAPP), the Opioid Risk Tool (ORT), the Prescription Misuse Index and the current opioid misuse measure are used for pain patients on long term opioid treatment to screen for patient abnormal behaviour [62]. Patient education, monitoring, testing, adjunct support, treatment of co-morbid conditions is needed in the Management of aberrant opioid behaviours [63]. For example, breastfeeding is discouraged and requires close screening and checking if a breastfeeding mother is prescribed codeine or codeine products, given the potential dangers related with CYP2D6 ultrafast metabolism [64]. Codeine use by nursing mothers while breastfeeding affects the infant and is related with apnoea, bradycardia, drowsiness and cyanosis [65]. Furthermore, Ladies with the cytochrome P450 2D6 (CYP2D6) genotype quickly process codeine into morphine, bringing about high breast milk and plasma levels in neonates, and can cause newborn and child death due to high opioid poisonous concentration [66].

Also, as a form of Codeine abuse prevention, Awareness may be created among the general public, particularly among public drivers, Okada riders, adolescent and university students and event miscreants.

### Conclusions

This paper has revealed that the importance and uses of codeine are numerous when used as prescribed by a medical doctor, as it is used for the treatment of cancer pain, and for the management of minor pains in adults and children. However, codeine is the most abused opioid drugs as it is misused in pill or cough syrup form. The abuse of codeine cough syrup is a general health problem all over the world and the abuse of codeine cough syrup is more entrenched among male in the urban dark ethnic groups and lesbian, gay, bisexual, transgender (LGBT) minorities. It remains necessary however that codeine is regulated in each respective country to reduce prevalence rate of its misuse and abuse.

### Recommendations

Following the review of literature, the following among many other recommendations were proffered;

Codeine and other codeine products should not be sold at pharmacy to patients unless prescribed by a medical doctor.

Parents should endeavor to always keep prescribed medications such as codeine and codeine products away from the reach of children at home.

Self-medication should be totally discouraged and prescribed codeine and codeine products should be used as recommended by the medical doctor.

Strict rules and regulations banning people from accessing codeine and other codeine products that are not prescribed should be put in place, and such rules and regulations should be strictly enforced.

Since codeine and other codeine products may be gotten by people illegally, law enforcement agencies should intensify patrol to making sure that where the dealings of these drugs takes place are combed and the perpetrators of the business are arrested.

The public should be health educated on the health and social consequences of drug abuse and misuse.

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