CHEM 4800
Seminars Fall 2019

October 28

Tramadol: its structure, metabolites, and ability to induce seizures
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Tramadol hydrochloride is a commonly prescribed narcotic for chronic pain management. Tramadol and its three main metabolites: O-desmethyltramadol (M1), N-desmethyltramadol (M2), and N,O-didesmethyltramadol (M5) are known to induce seizures when taken in high prescription or abuse concentrations. Tramadol seizures were once thought to be caused by serotonin toxicity, however recent studies on tramadol-induced seizures have shown that this theory is unlikely. In this study, tramadol and its metabolites will be investigated for their structure and ability induce seizures. A study was performed in which blood samples of 120 tramadol-intoxicated patients were collected and analyzed. The samples were evaluated using high performance liquid chromatography to detect tramadol and its metabolites blood concentration. It was found that the elevated concentrations of tramadol, M1, and M2 metabolites directly correlated with and elevated incidence of seizures [1]. Another study was performed in which tramadol's effect on mitochondria was evaluated in a qualitative assessment on 70 male rats. The study showed that tramadol, when taken in abuse doses, significantly decreased the activity of complex I, III, and IV of the electron transport chain and increased the number of red neurons (histopathologic markers for cell death)[2]. This finding led the researchers to conclude that tramadol-induced seizures may be caused by its inhibitory effect on ECT activity, causing ATP depletion and decreasing mitochondrial integrity [2]. Overall, the direct cause of tramadol-induced seizures is still under investigation. The evaluated research indicated that the ETC and tramadol metabolites, excluding M5, are involved in seizure induction. An understanding of how tramadol induces seizures is critical to finding a way to prevent and stop tramadol-induced seizures in the future.

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Comparative analysis of urine and sweat patch testing for the detection of heroin in opioid users
Katherine Pinkerton

Over the past decade and a half, the number of heroin abuse related deaths has increased exponentially in the United States.[1] As a result, more treatment programs have been implemented across the country as a means to lower and/or stop opioid abuse. In these treatment programs routine drug testing is done in order to track patient progress and hold accountability in the chance of relapse. Urine analysis is the most common analytical method used for drug testing. However, there are several disadvantages of urine analysis such as the short time window of drug detection, the adulteration of sample by outside sources, and false positives due to the ingestion of opiate-containing foods.[2] These were aspects taken into consideration when designing a new method of detection. Sweat Patch analysis has been recently offered as a new detection method that acknowledges and corrects these disadvantages seen in Urine analysis. A comparative study was conducted to compare the two analytical methods, Urine analysis and Sweat Patch Testing, by analyzing opioid users in treatment programs for heroin detection.[2,3,4] Established chemistry techniques were employed to confirm correlations between the two detection methods.[2,3,4] From prior studies, Sweat Patch Testing proves as a reliable source for long term detection of opioids for programs such as out-patient treatment programs; however, Urine analysis proves most effective for reliable short term detection of opioids for situations such as DUIs.[2,3,4]

Work Cited
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October 30

Solving the high risk of addiction and abuse of morphine
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An estimated 1.7 million individuals in the United States suffers from substance abuse disorders related to prescription opioid pain relievers.[1] Morphine, a commonly used opioid medication, has a high likelihood of addiction and abuse due to its fast acting nature. The rate at which a psycho-active drug occupies, or binds to, brain receptor sites for that drug determines the intensity of its rewarding effects and its potential for abuse and addiction. Due to the opioid addiction crisis, scientists have started looking into solutions to resolve the issues of misuse and abuse of opioid medications. By making morphine biologically inactive through SAR methods of a prodrug addition, the half-life of the medication can be increased and prevent dangerous alternative methods of administration.[2] Through the modification of morphine's pharmacokinetic profile with a prodrug, the euphoria experienced by abusers through alternative routes of administration can be eliminated or reduced.[3] The addition of lysine or arginine as a prodrug onto the morphine structure will make morphine inactive until enzymatic cleavage by the enzyme, trypsin, in the GI tract. Through the application of the prodrug concept, potential abuse-deterrent opioids may be developed to aid the opioid epidemic.

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Effectiveness of matrix versus reservoir fentanyl transdermal systems

Hannah Roberson

Transdermal delivery has increasingly become the preferred route for drug delivery, due to having a controlled rate of absorption and distribution, and having higher efficacy and safety. It is important to control fentanyl's rate of delivery, because it is highly potent and has had an increasing amount of reports of overdose and death. There are two types of fentanyl transdermal systems (FTS), matrix systems (M-FTS) and reservoir systems (R-FTS).[1] Both systems have had reports of death from use, so research on the effect of many variables that interfere with FTS is studied.[1] Research on the effect of heat and compromised skin on both FTS suggests that under normal, as prescribed conditions, the effectiveness of both are equal without harmful effects. Both FTS were then tested on compromised skin and skin with an elevated temperature at 40 ˚C.[1] Both tests affected the rate of release of fentanyl for M-FTS and only slightly for R-FTS. M-FTS is a less reliable mode of delivery than R-FTS based on the results of the research, given that most users will not use the systems under intended, normal conditions.

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