服用複方甘草合劑於尿液中嗎啡及可待因含量分析

Urinary Excretion of Morphine and Codeine Following the Administration of Brown Mixture

中文摘要

如同罌粟子因素（poppy-seed defense）在美國所引起之爭議，在臺灣當尿液檢測結果呈現鴉片類陽性反應時，受檢者常辯稱是因爲服用複方甘草合劑（Brown mixture）而導致尿液中 morphine 和 codeine 成分的出現。複方甘草合劑乃一常用之藥品，在藥品處方中含有鴉片粉、鴉片酊或鴉片樟腦酊成分，而由於海洛因的使用爲持續存在的嚴重社會問題，所以對於服用複方甘草合劑所導致的尿液檢驗結果必須與之作一明確區隔。

本篇論文分析方法爲將檢品經水解、萃取、衍生，最後以氣相層析質譜儀（GC/MS）檢測。所用 trimethylsilyl (TMS)衍生之 codeine、morphine 和 nalorphine (IS)選擇監測之離子分別爲 m/z 371、356、343；429、414、401 和 455、440、414，上列化合物之第一個離子用於定量。結果顯示此分析方法對於複方甘草合劑製劑及尿液中 morphine 和 codeine 濃度的定量具有相當好的靈敏度與再現性；在檢量線濃度 50-1500 ng/ml的範圍之內呈現良好的線性關係，其回收率可達 80%。精密度評估同日內及異日間確效的偏差各在 0.99~5.69% 及 0.81~3.58% 之間；準確度評估同日內及異日間確效的偏差各在-3.96~2.52% 及 -5.33~7.84% 之間，顯示此分析條件適合用於分析複方甘草合劑製劑及尿液中微量的 morphine 和 codeine。

蒐集八種不同廠牌複方甘草合劑（含錠劑和溶液劑）及收集病患尿液檢體分析其內 morphine 和 codeine 含量，實驗結果顯示複方甘草合劑不同廠牌錠劑間其嗎啡和可待因含量相等，而在二種溶液劑間則有明顯差異。在正常治療情況下，不管是服用複方甘草合劑錠劑或溶液劑，尿液中 morphine 濃度通常不會大於 4000 ng/ml。當尿液中嗎啡濃度大於 300 ng/ml時，其嗎啡/可待因比值可歸納爲以下二種情況：(1)小於 3.0 爲複方甘草合劑溶液劑使用者；(2)大於 3.0 爲複方甘草合劑錠劑或海洛因使用者。綜上所述，顯示(1)服用複方甘草合劑不易導致尿液中嗎啡濃度高於 4000 ng/ml；(2)無法利用尿液中嗎啡/可待因比值作爲分辨複方甘草合劑錠劑和海洛因使用者之指標。

英文摘要

Parallel to the "poppy-seed defense" strategy commonly reported in the United States, donors of urine samples tested positive for opiates in Taiwan often claimed the consumption of Brown Mixture (BM) as the source of the observed morphine and codeine. Since BM contains opium powder, opium tincture, or camphorated opium tincture and is a popular remedy, while heroin use is considered a serious criminal act, the claim of BM use has to be adequately addressed.

The analytical procedure included hydrolysis, trimethylsilylation and GC-MS analysis, monitoring the following ions designated for TMS-derivatized codeine,

morphine, and nalorphine (internal standard)：m/z 371, 356, 343；429, 414, 401；455, 440, 414, respectively. The first ion listed for each compound was used for quantitation. A linear relationship was found in the range from 50 to 1500 ng/ml with absolute recovery about 80%. Precision for intraday and interday is from 0.99% to 5.69% and from 0.81% to 3.58%, respectively. Accuracy for intraday and interday is from −3.96% to 2.52% and from −5.33% to 7.84%, respectively.
In this study, BM from eight different manufacturers (tablets and solutions) and urine samples from patients were analyzed for their morphine and codeine contents. The contents of morphine and codeine in tablets are very consistent, but vary considerably in the BM solutions. Morphine concentrations found in urine specimens collected from volunteer patients ingesting BM tablets (or solutions) are always < 4000 ng/mL. The following morphine/codeine concentration ratios ([M]/[C]) were observed for urine specimens with morphine concentration ? 300 ng/mL：(a) < 3.0 for patients ingesting BM solution; (b) > 3.0 (mostly > 5.0) for patients ingesting BM tablets and alleged heroin users. It appears that (a) BM ingestion (tablet or solution) is unlikely to result in morphine concentration > 4000 ng/mL; and (b) [M]/[C] ratio may not be an effective parameter to differentiate heroin use from BM tablet ingestion.