Urinary Excretion of Morphine and Codeine Following the Administration of Single- and Multiple-Dose of Brown Mixture

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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 (10-10.5% morphine), opium tincture (0.9-1.1% morphine), or camphorated opium tincture (0.045-0.055% morphine) and is a popular remedy, while heroin use is considered a serious criminal act, the claim of BM use has to be adequately addressed.

In this study, BM from 7 different manufacturers (5 tablets and 2 solutions) and urine samples from patient and alleged heroin users were analyzed for their morphine and codeine contents. The analytical procedure included hydrolysis, trimethylsilylation, and monitoring of 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 using a six-point calibration protocol (50-2000 ng/mL).

The contents of morphine and codeine and their ratios ([M]/[C]) in: (a) BM tablets ($n = 5$), and BM solution ($n = 2$) available in Taiwan and (b) urine specimens collected from alleged heroin users and patients ($n = 7$) ingesting 1–6 tablets (or 5-20 mL solution) -- one-time single dose or three times per day for two days -- are summarized in Table 1. The contents of morphine and codeine in the tablets are very consistent, but vary considerably in the 2 BM solution. Morphine concentrations found in urine specimens collected from patients ingesting BM tablets or solution are always <4000 ng/mL. The following [M]/[C] ratios 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 for the differentiation of BM tablet ingestion and heroin use.

Table 1. Morphine and codeine contents in Brown Mixture tablet, Brown Mixture solution, and urine specimens collected from alleged heroin users and patients ingesting Brown Mixture

	Brown Mixture		Urine specimen[a] collected users of		
[M]/[C]	Tablet	Solution	Tablet	Solution	Heroin[b]
N	25	10	56	68	90
Range	8.46-9.18	2.56-2.93	4.88-14.8	1.31-9.09	3.15-40.8
Mean	8.77	2.74	7.76	2.62	8.52
Std dev.	0.19	0.15	1.92	0.87	4.03

[a] Only specimens with morphine concentration higher than 300 ng/mL are included.
[b] Alleged heroin users.

Key words: Brown mixture, morphine, codeine.