K14 Chromatographic and Mass Spectrometric Characteristics of Multiply Derivatized Opiates

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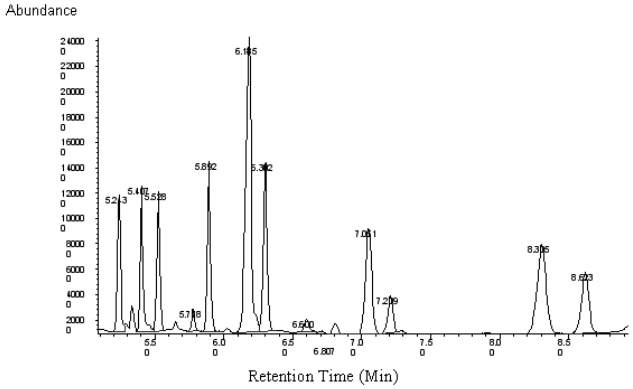
After attending this presentation, attendees will have deeper appreciation on how the analysis of drugs/metabolites in biological media can be facilitated by various chemical derivatization methods.

This presentation will impact the forensic community and/or humanity by illustrating how multiple derivatization approaches can facilitate chromatographic resolution of structurally closely related opiates (see the list below), allowing a single analytical run to analyze all or those that are present. Mass spectrometric characteristics pertinent to quantitative analysis will also be emphasized.

Much attention has been directed to gas chromatography-mass spectrometry (GC-MS) analysis of morphine and codeine. Since other opiates, such as hydrocodone, hydromorphone, oxycodone, and oxymorphone, may interfere with the analysis of morphine and codeine and the analysis of these compounds themselves are also important issues, two double-derivatization approaches utilizing hydroxylamine (HA) and methoxyamine (MA) to first form oxime products with keto- opiates have been reported. The first approach adapted HA, followed by the derivatization with trimethylsilyl (TMS), while the second approach utilized MA, followed by pentafluoropropionyl (PrA) or TMS derivatizations. A review of the literature indicated that studies involving HA were limited, while the MA/PrA studies were (a) unable to chromatographically separate codeine and oxycodone; (b) unable to derivatize the hydroxyl group of oxycodone; and (c) did not include noroxycodone. On the other hand, the MA/TMS studies (a) did not include oxymorphone and noroxycodone; and (b) intensity cross- contributions between the ions designated for the analytes and their deuterated internal standards are generally very significant; thus, limiting the quantitation capability of this approach.

This study included a comprehensive list of compounds: codeine, morphine, 6-acetylmorphine, hydromorphone, oxymorphone, hydrocodone, oxycodone, and noroxycodone. Three-step derivatization approaches involving various combinations of derivatization groups were explored. Combination of MA/acyl/TMS was found to be most favorable. Merits of this approach include: (a) all functional groups in all analytes were derivatized; (b) the resulting products were chromatographically well resolved (Figure 1); and (c) intensity cross- contribution between the ions designated for these analytes and their respective deuterated internal standards were also found favorable (Table 1). Parallel approaches utilizing HA produced inferior results.



Ret. time	Derivatization product	Ret. time	Derivatization product
5.24	Codeine-TMS	5.40	Hydrocodone-MA
5.78	Oxycodone-MA-TMS	5.89	Codeine-PrA
6.16	Oxycodone-MA-PrA	6.18	Morphine-PrA-TMS
6.30	Hydromorphone-MA-PrA	6.60	6-Acetylmorphine-PrA
6.81	Oxymorphone-MA-PrA-TMS	7.21	Morphine-2PrA
8.62	Noroxycodone-MA-PrA-TMS		

Figure 1. Ion chromatogram of multiply derivatized opiate mixture.

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Table 1. Cross-contribution (CC) data of ions (*m/z*) with potential for designating the analyte and the adapted internal standard (IS)

Derivatization product	Ion designating the analyte/IS and CC (in parentheses)
Codeine-TMS	313 (4.53) / 316 (4.83), 343 (4.66) / 349 (0.10), 371 (0.27) / 377 (0.11)
Hydrocodone-MA	297 (0.084) / 303 (0.00), 298 (0.00) / 304(0.00), 328 (0.00) / 334 (0.00), 329 (0.00) / 335 (0.00)
Oxycodone-MA-TMS	326 (4.25) / 332 (3.23), 401 (0.00) / 407 (0.03), 416 (0.00) / 422 (0.07), 417 (0.00) / 423 (0.06)
Codeine-PrA	282 (0.31) / 288 (0.01), 298 (0.35) / 304 (0.04), 355 (0.33) / 361 (0.00), 356 (0.44) / 362 (0.00)
Oxycodone-MA-PrA	230 (0.00) / 236 (0.00), 295 (0.00) / 301 (0.00), 343 (0.00) / 349 (0.00), 400 (0.00) / 407 (0.00)
Morphine-PrA-TMS	357 (1.92) / 360 (1.12), 413 (0.32), 416 (1.43)

Derivatization product	Ion designating the analyte/IS and CC (in parentheses)
Hydromorphone-MA-PrA	283 (0.56) / 289 (0.036), 314 (0.50) / 320 (0.004), 315 (2.32) / 321 (0.21), 339 (0.00) / 345 (0.31), 370 (0.12) / 376 (0.009)
6-Acetylmorphine-PrA	215 (4.19) / 218 (1.83), 268 (1.97) / 271 (1.55), 383 (0.17) / 389 (0.00), 384 (0.21) / 390 (0.00)
Oxymorphone-MA-PrA-TMS	215 (4.96) / 218 (1.87), 402 (0.94) / 405 (1.40), 403 (1.88) / 406 (0.70), 443 (0.085) / 446 (1.52), 458 (0.059) / 461 (1.64)
Morphine-2PrA	268 (2.02) / 274 (0.04), 324 (0.16) / 330 (0.04), 341 (0.24) / 347 (0.00), 342 (0.63) / 348 (0.00), 397 (0.15) / 403 (0.02)
Noroxycodone-MA-PrA-TMS	427 (0.00) / 430 (0.00), 458 (0.00) / 461 (0.00)

Opiate, Derivatization, Internal Standard

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