

Mass Spectra and Cross-Contributions of Ion Intensity Between Drug Analytes and Their Isotopically Labeled Analogs — Benzodiazepines and Their Derivatives

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ABSTRACT: With GC-MS as the preferred method and isotopically labeled analogs (ILAs) of the analytes as the internal standards (ISs) of choice for quantitative determination of drugs/metabolites in biological specimens, one important aspect associated with chemical derivatization (CD) is that the CD products derived from the analyte and the selected IS must generate ions suitable for designating the analyte and the IS. These ions must not have significant cross-contribution (CC), i.e., ISs' contribution to the intensities of the ions designating the analytes, and vice versa. With this in mind, the authors have reviewed literature and information provided by manufacturers, searching for suitable CD reagents, CD methods, and ILAs of the analytes related to the following 18 benzodiazepines: oxazepam, diazepam, nordiazepam, nitrazepam, temazepam, clonazepam, 7-aminoclonazepam, prazepam, lorazepam, flunitrazepam, 7-aminoflunitrazepam, *N*-desalkylflurazepam, *N*-desmethylflunitrazepam, 2-hydroxyethylflurazepam, estazolam, alprazolam, α -hydroxyalprazolam, and α -hydroxytriazolam. These analytes and ILAs were derivatized with various derivatization groups, followed by GC-MS analysis. The resulting mass spectrometric data are systematically presented in two forms: (a) full-scan mass spectra; and (b) CC data of ion-pairs with potential for designating the analytes and their respective ILAs (candidates of ISs in quantitative analytical protocols). Many of these full-scan mass spectra are not yet available in the literature and should be of reference value to laboratories engaged in the analysis of these drugs/metabolites. Full-scan MS data were further used to select ion-pairs with potential for designating the analytes and ISs in quantitative analysis protocols. The CC data of these ion-pairs were evaluated using data collected in selected ion monitoring mode and systematically tabulated, making the data readily available for analysts searching for this important analytical parameter.

KEY WORDS: Alprazolam, 7-aminoclonazepam, 7-aminoflunitrazepam, chemical derivatization, clonazepam, cross-contribution, *N*-desalkylflurazepam, *N*-desmethylflunitrazepam, diazepam, estazolam, flunitrazepam, GC-MS, α -hydroxyalprazolam, 2-hydroxyethylflurazepam, α -hydroxytriazolam, internal standard, lorazepam, nitrazepam, nordiazepam, oxazepam, prazepam, temazepam.
