A primary challenge in characterizing the metabolic fate of xenobiotics is distinguishing drug-related material in the presence of the matrix in which metabolism has occurred. A commonly used approach to filter components based on parent drug properties. However, identification of unexpected drug metabolites remains a limiting issue. Unexpected metabolite candidates are components present in analyze samples, and not in controls, but the complex nature of biological systems require many measures to be validated. By characterizing the native complement of biological matrices based on LC-MS conditions, this challenge becomes more tractable and can be used to flag components in samples that are known to be latent present, and are unlikely to be drug metabolites.

Sample preparation

The metabolite library (m/z, drug, and matching isotope pattern) (1 U) and (2 U) were included for 16 HDMSE and (3 U) or (4 U) were prepared in a concentration of (5 U) or (6 U) in the presence/absence of a variety of drug compounds and known NMRs. The three experimental design and their particular purpose are graphically illustrated in Figure 1.

RESULTS

Library creation process

The data were imported, aligned, and aggregated in Progenesis QI from which a relative library was retrieved. The library was filtered on replication and number of fragment ion, converted and imported back into UNIF, as illustrated in Figure 2. The number of diagnostic fragment ions was calculated for each metabolite as the sum of the product ions. Figure 3 shows the distribution characteristics illustrating a high degree of replication precision in all dimensions. A single standard deviation (SD) was used as a rigorous search parameter traditional for DIA search processes. In general, the library was successfully complete and shows good performance of the distribution of the (m/z) search specificity.

Species similarity

Species similarity was assessed by calculating the detection rate of all replicates, (B) detected in all species, whereas in other cases detection was more variable. Figure 4 illustrates the detection frequency of the expected metabolite in all replicates, (B) detected in all species, whereas in other cases detection was more variable. Figure 5 shows the distribution characteristics illustrating a high degree of replication precision in all dimensions. A single standard deviation (SD) was used as a rigorous search parameter traditional for DIA search processes. In general, the library was successfully complete and shows good performance of the distribution of the (m/z) search specificity.

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