Electronic Supplementary Material (ESI) for Analytical Methods.

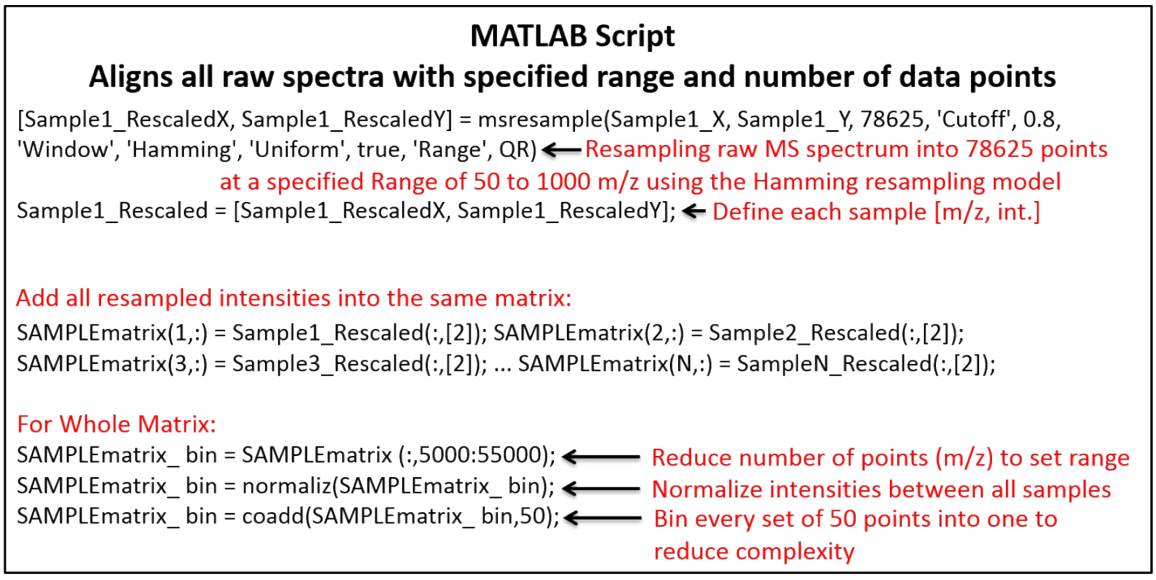

Figure S1: MATLAB script for resampling and processing DART mass spectral data prior to PCA analysis.

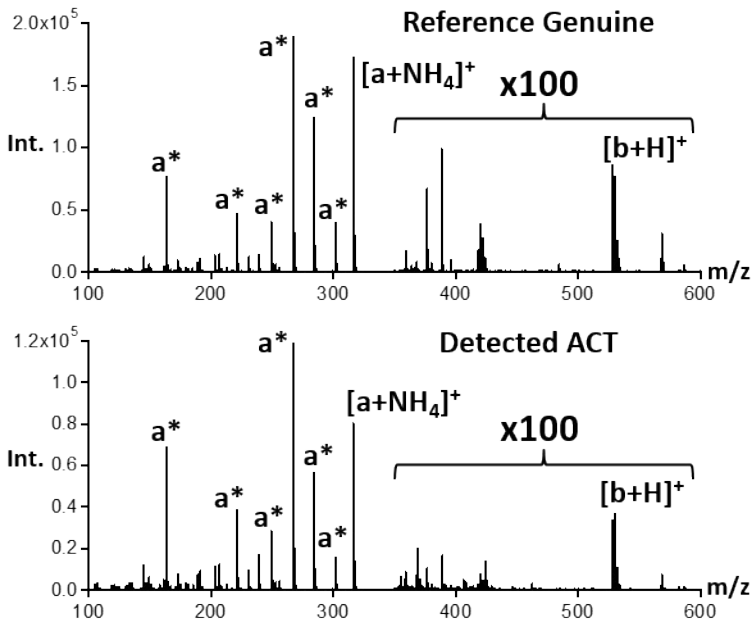

Figure S2: DART-MS of a reference genuine artemether-lumefantrine tablet (top) and a detected artemether-lumefantrine containing seized tablet sample (bottom).

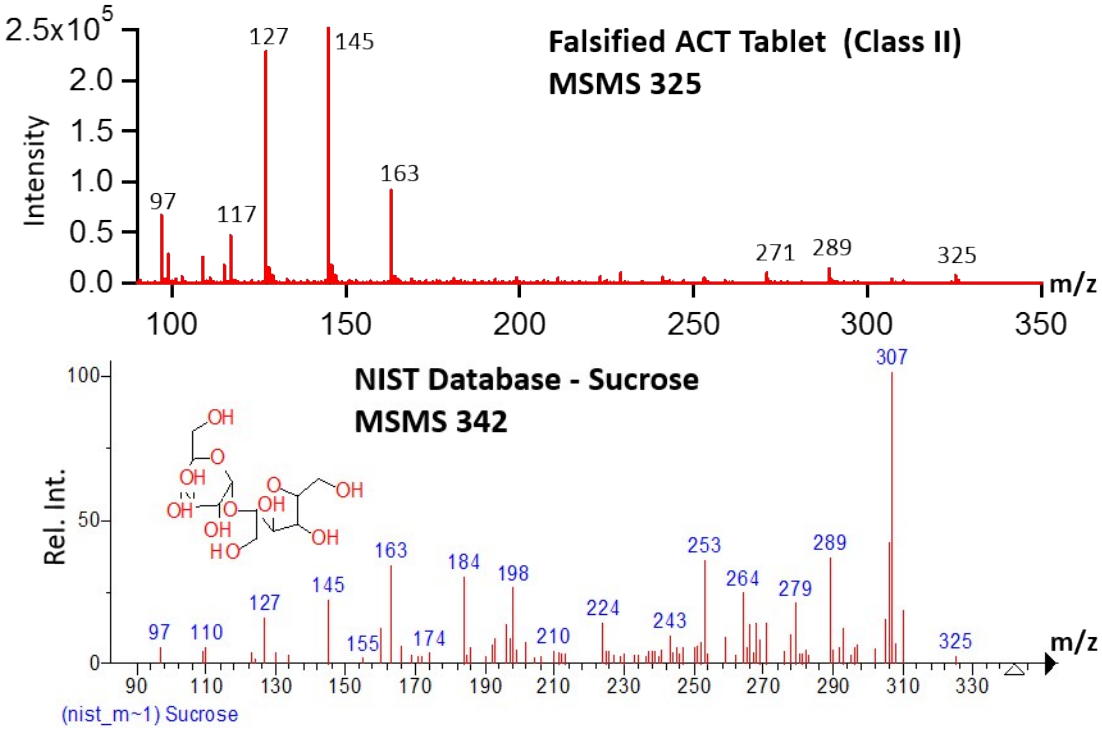

Figure S3: Experimental MS/MS spectrum of the m/z 325 species of a Class II falsified anti-malarial tablet obtained on the QTOF mass spectrometer (top) and corresponding NIST database MS/MS spectrum for sucrose (bottom) showing matches in the fragmentation pattern, suggesting that the m/z 325 species is a sugar that possesses a similar structure to the larger sucrose ($C_{12}H_{22}O_{11}$), or is a fragment itself that forms via DART ionization of sucrose (or a structural isomer).

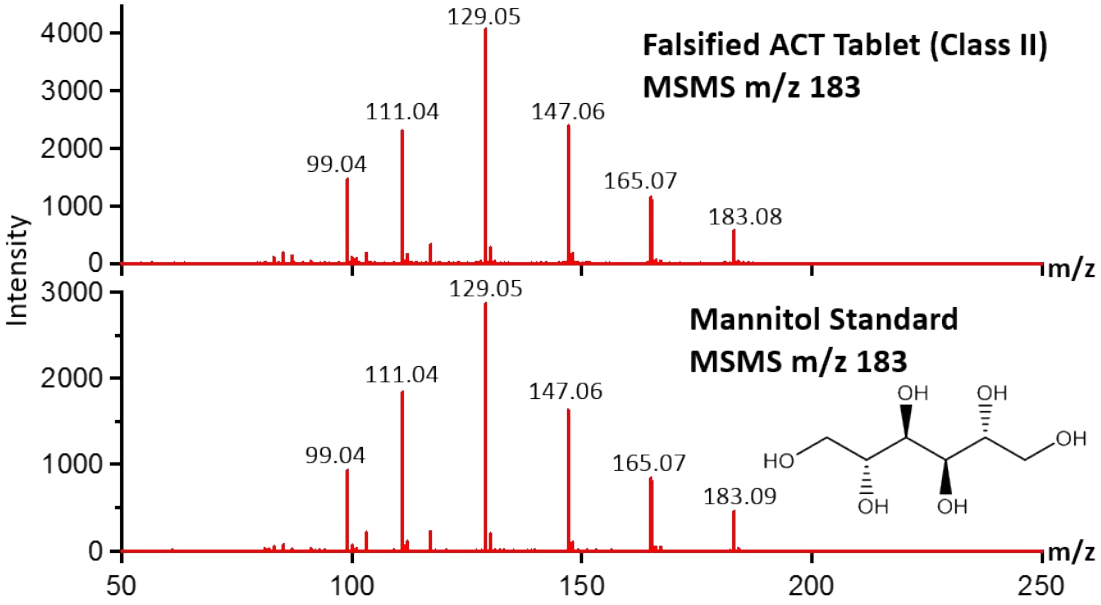

Figure S4: Experimental DART-MS/MS of the species at m/z 183 of a Class II falsified anti-malarial tablet obtained on the QTOF mass spectrometer (top) and DART-MS/MS of a standard pure powder of mannitol with chemical formula $C_6H_{14}O_6$ (bottom), showing confident assignment of this sugar-alcohol (or an indistinguishable structural isomer).

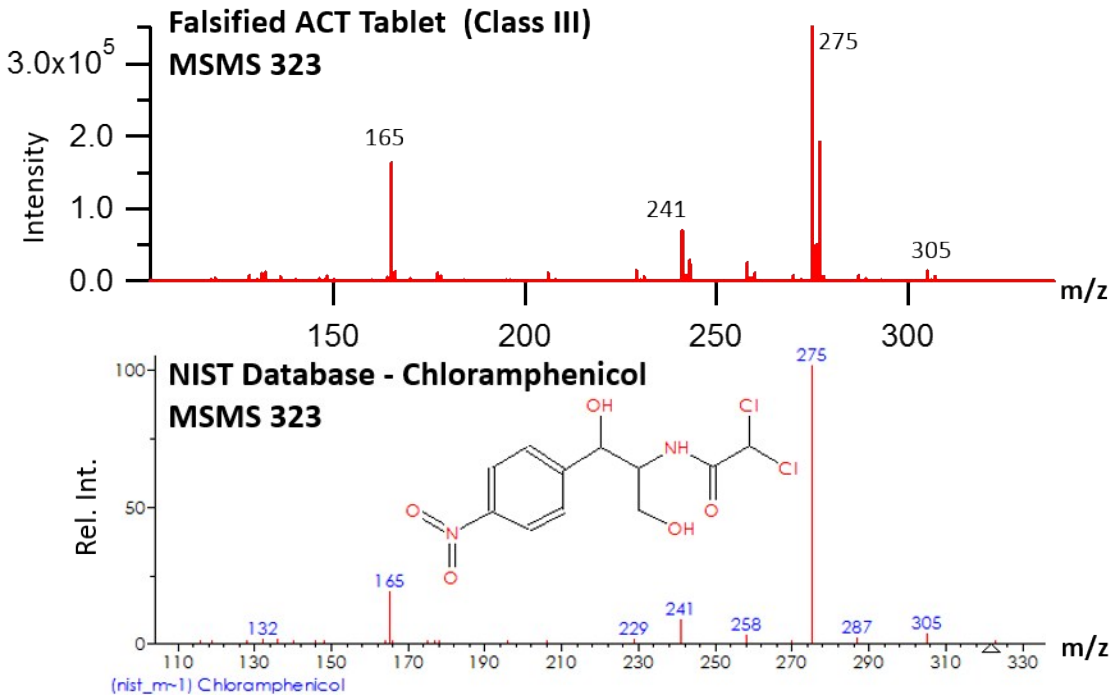

Figure S5: Experimental MS/MS of the species at m/z 323 for a Class III falsified anti-malarial tablet obtained on the QTOF mass spectrometer (top) and the NIST database MS/MS spectrum of chloramphenicol (bottom) showing confident assignment of this antibiotic compound.

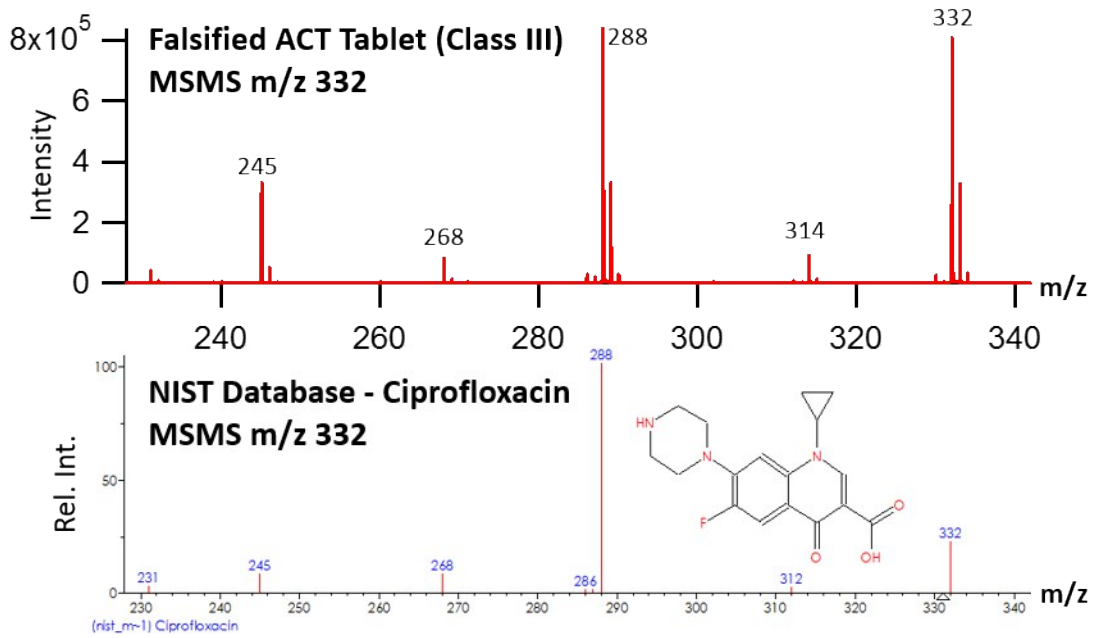

Figure S6: Experimental MS/MS of the species at m/z 323 in a Class III falsified anti-malarial tablet obtained on the QTOF mass spectrometer (top) and the matching NIST database MS/MS spectrum for ciprofloxacin (bottom).

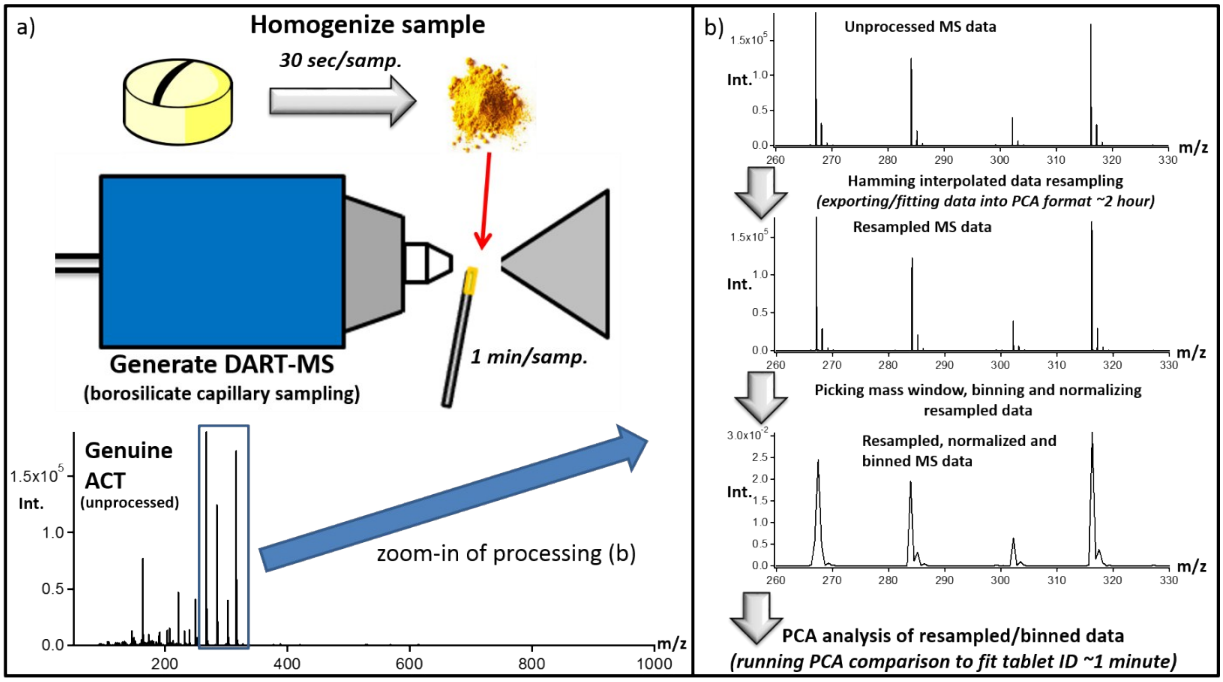

Figure S7: Workflow used to fingerprint ACTs showing a) the time-costs associated with homogenizing and sampling each tablet powder prior to DART-MS analysis and b) the data processing steps allowing for PCA comparison of resampled, normalized, and binned MS data. The overall time associated with analyzing each tablet is ~ 1.5 minutes, with the data analysis step requiring ~ 1-2 hours after sampling all tablets within a batch.

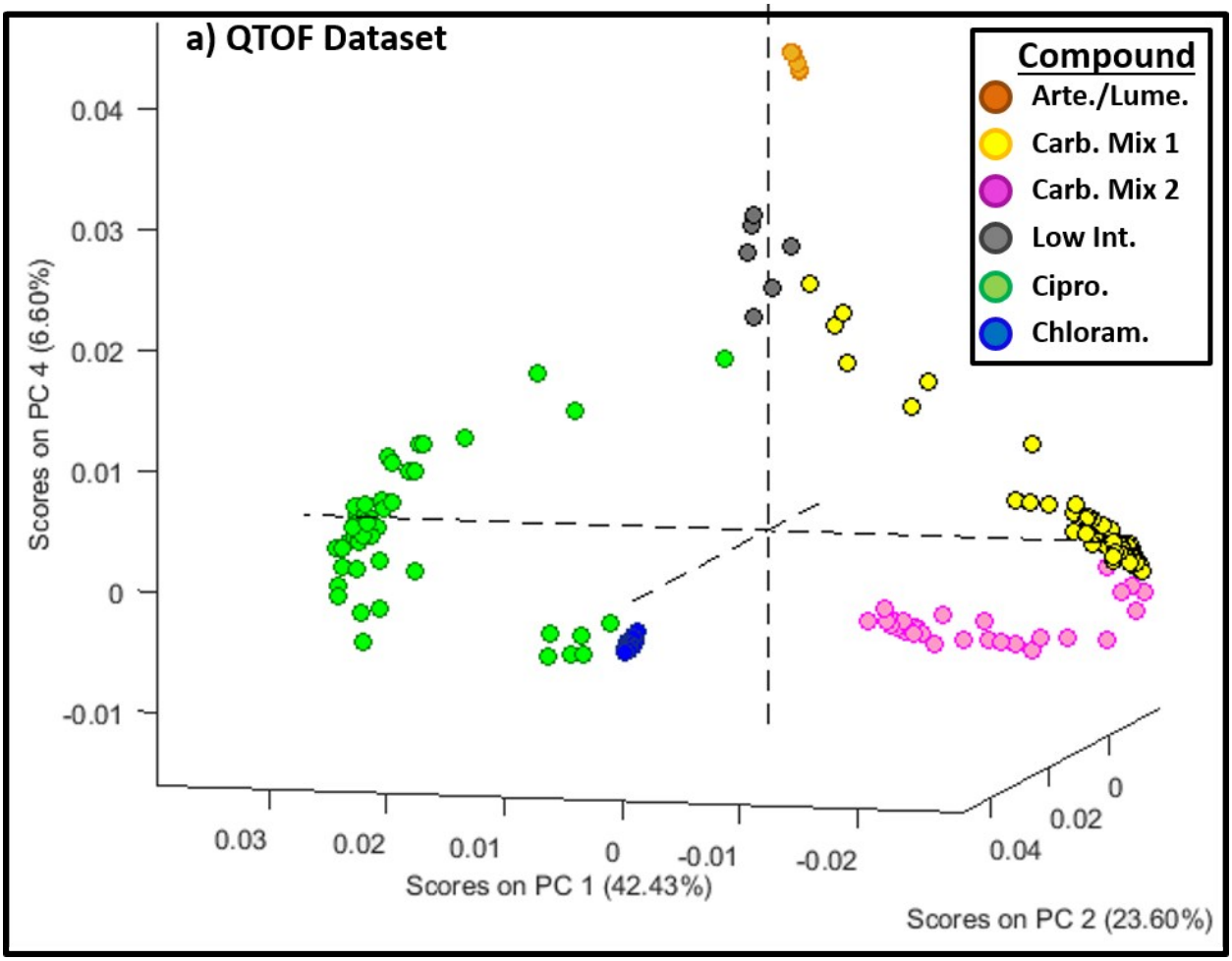

Figure S8: PCA scores plots (PC1-PC2-PC4) of the high-resolution DART QTOF spectral data. The artemether/lumefantrine containing tablets are shown in the plot in orange, carbohydrate mix 1 (simple sugars) in yellow, carbohydrate mix 2 (simple + alcohol sugars) in pink, low intensity carbohydrate-containing tablets in gray, ciprofloxacin in green, and chloramphenicol in blue.

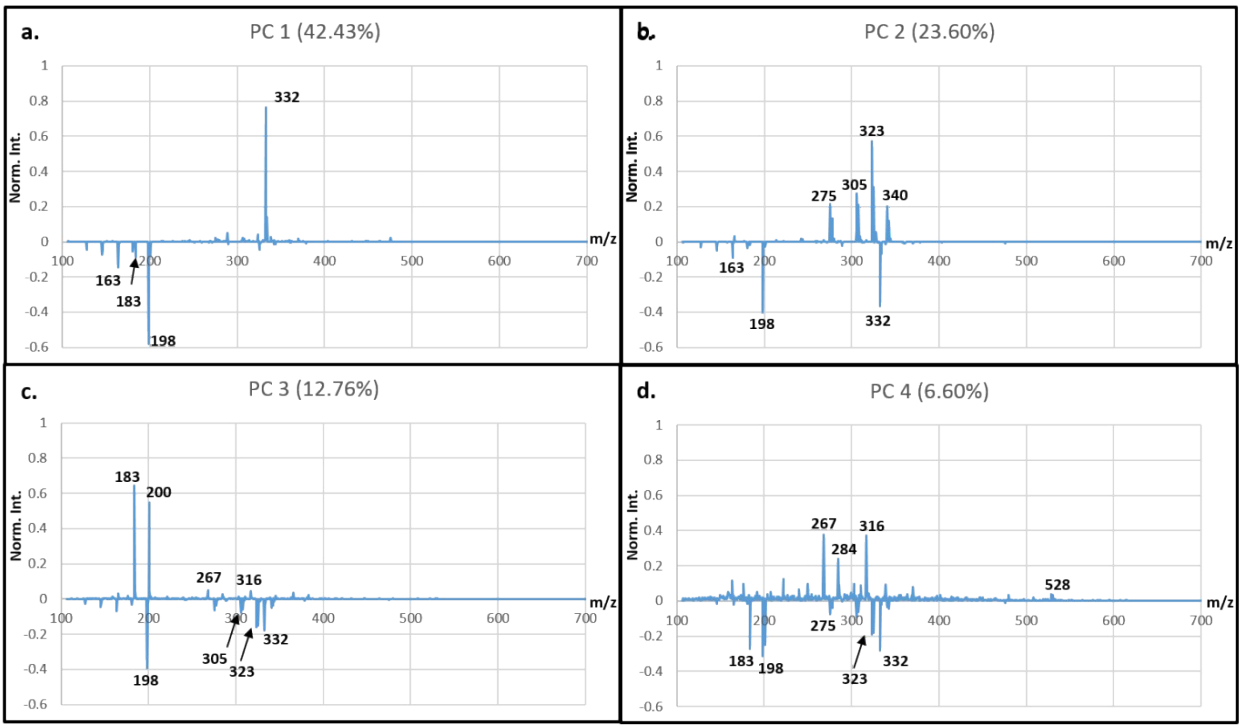

Figure S9: Loadings plots for the first four principal components from the QTOF fingerprinted dataset.

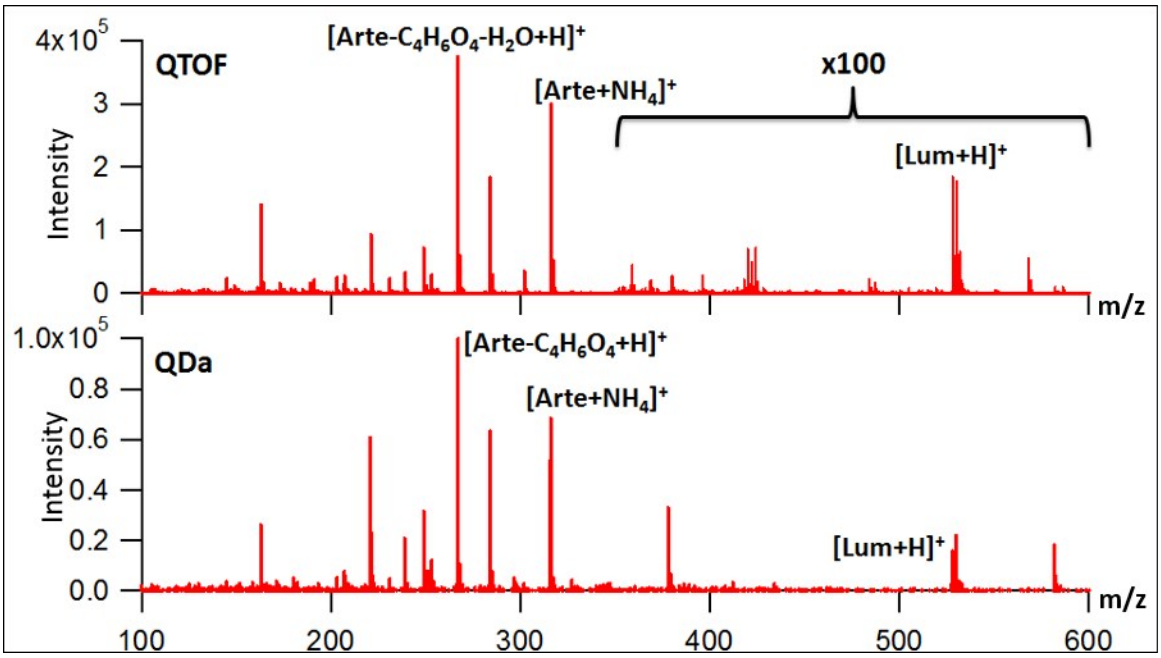

Figure S10: Comparison of the DART QTOF (top) and DART QDa (bottom) mass spectra for crushed genuine artemether/lumefantrine tablets.

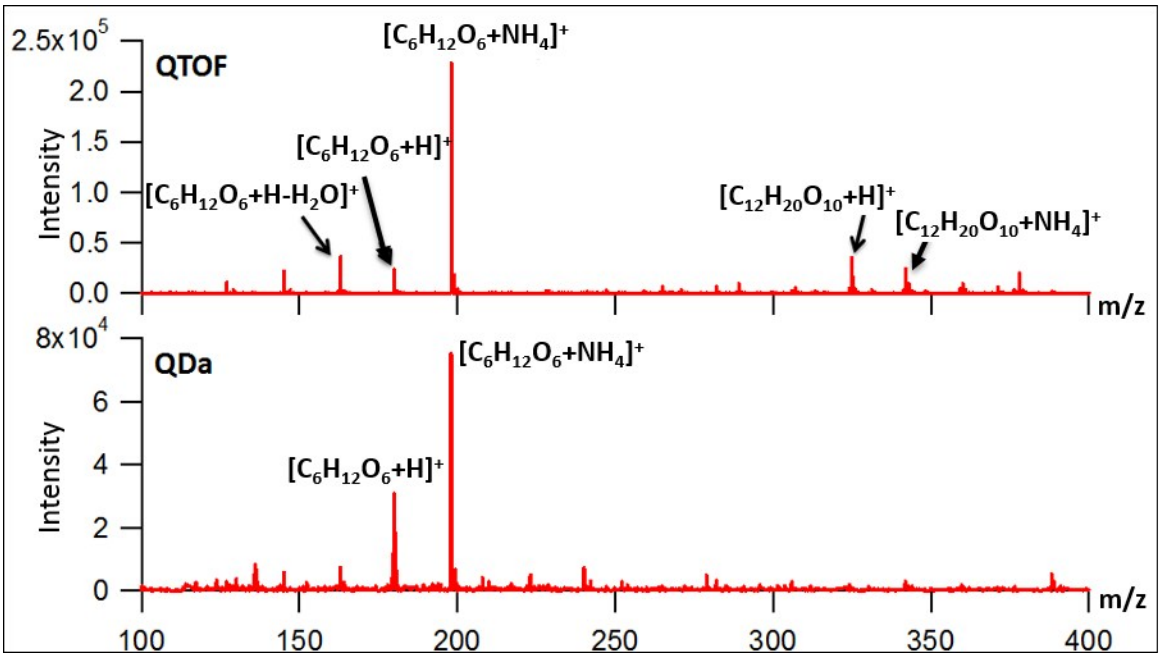

Figure S11: Comparison of the DART QTOF (top) and DART QDa (bottom) mass spectra for representative sugar-containing falsified anti-malarial tablets.

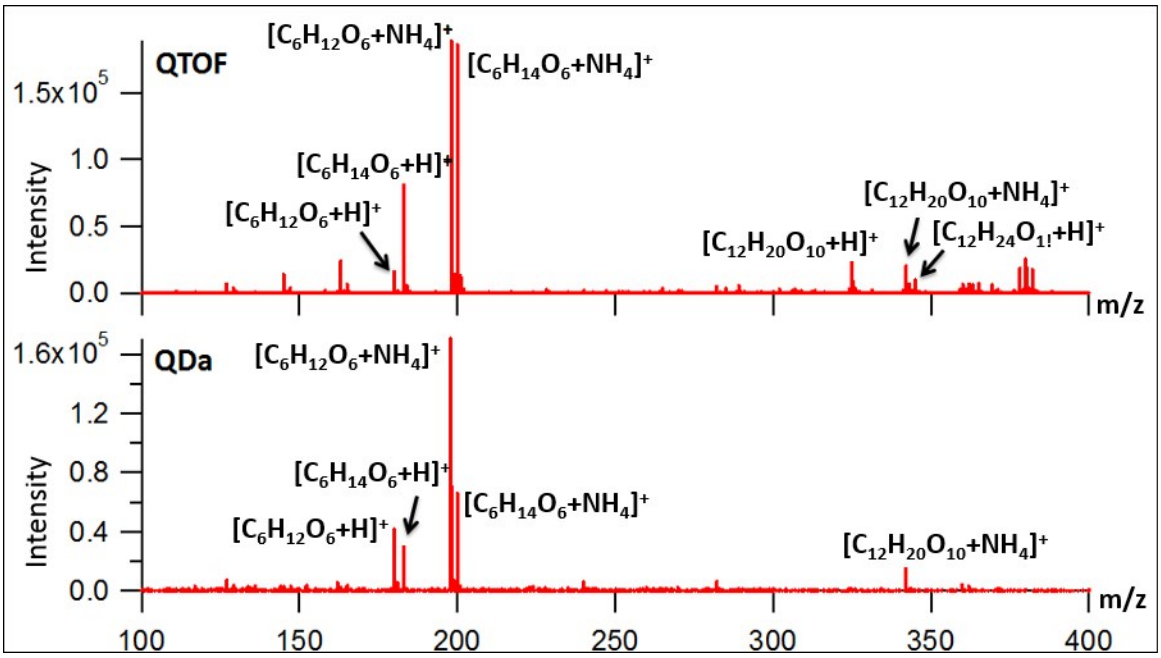

Figure S12: Comparison of the DART QTOF (top) and DART QDa (bottom) mass spectra for representative mannitol-containing falsified anti-malarial tablets.

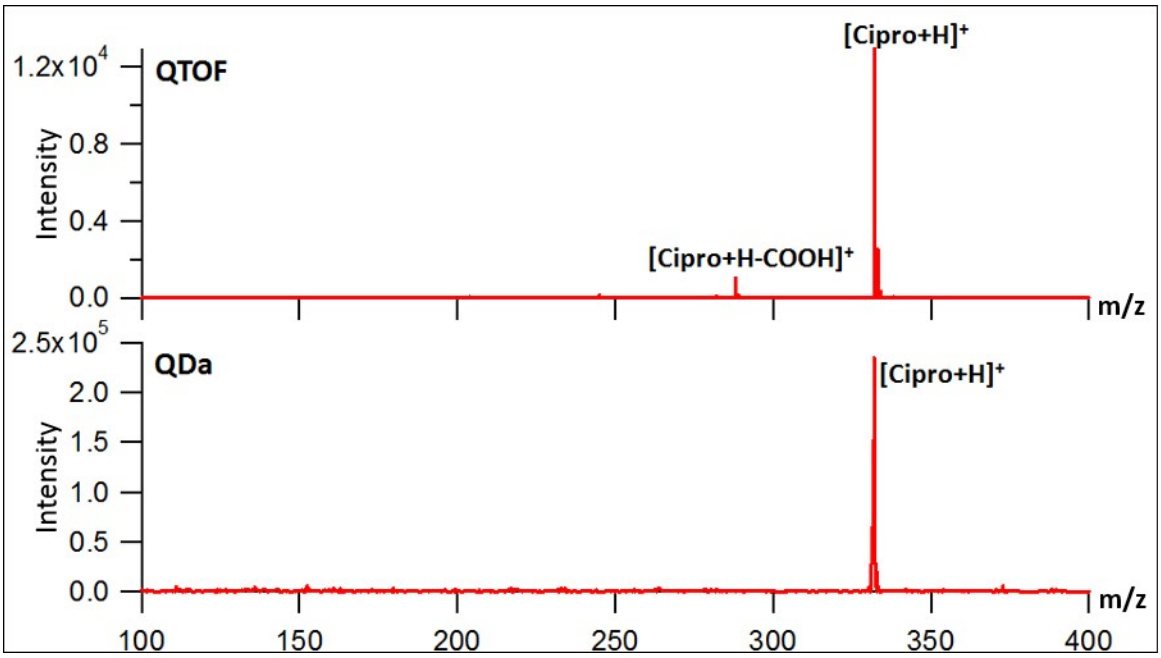

Figure S13: Comparison of the DART QTOF (top) and DART QDa (bottom) mass spectra for representative ciprofloxacin-containing falsified anti-malarial tablets.

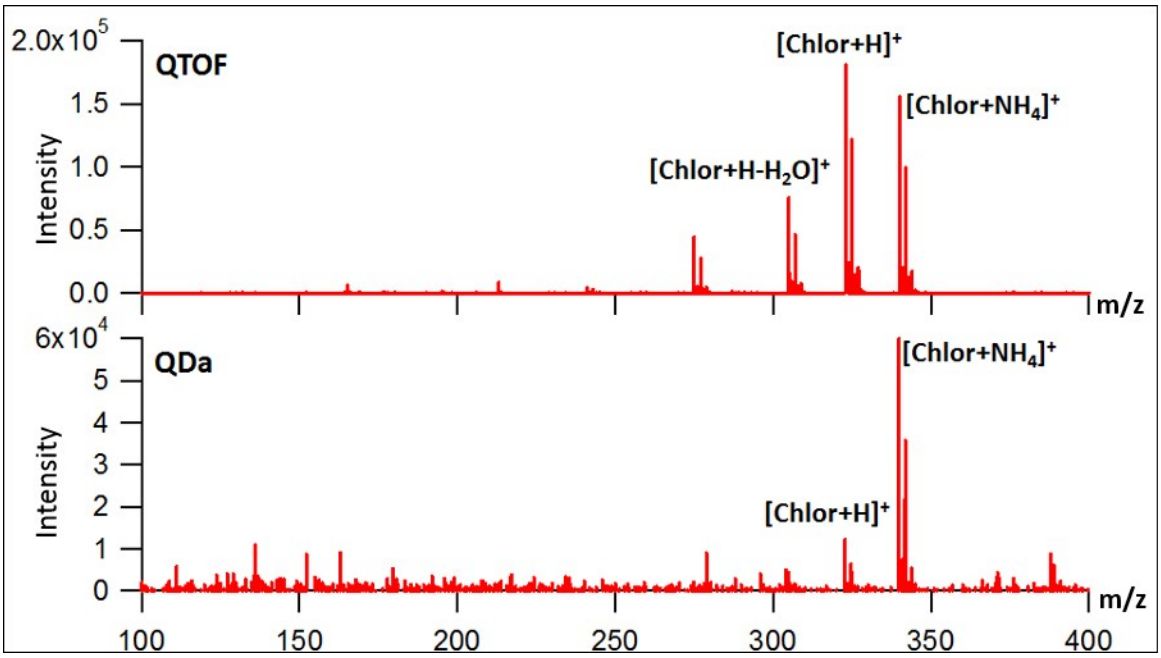

Figure S14: Comparison of the DART QTOF (top) and DART QDa (bottom) mass spectra for representative chloramphenicol-containing falsified anti-malarial tablets.

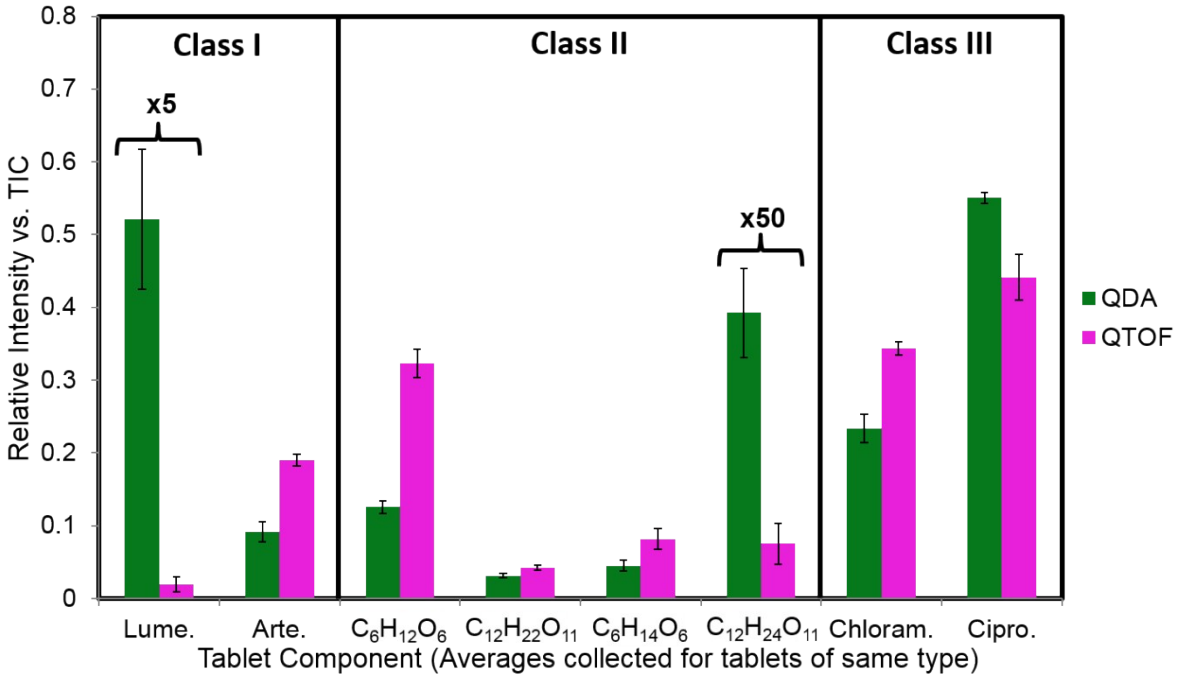

Figure S15: Relative intensities of each major component detected in Class 1, 2, and 3 tablets averaged over all tablets sampled. Comparisons are shown between the QDa set of results (green), and the QTOF results (purple). Ion abundances were normalized by dividing the peak area of the corresponding ion over the sum of all ions. Error bars were calculated using the standard error by considering each tablet as a separate measurement.

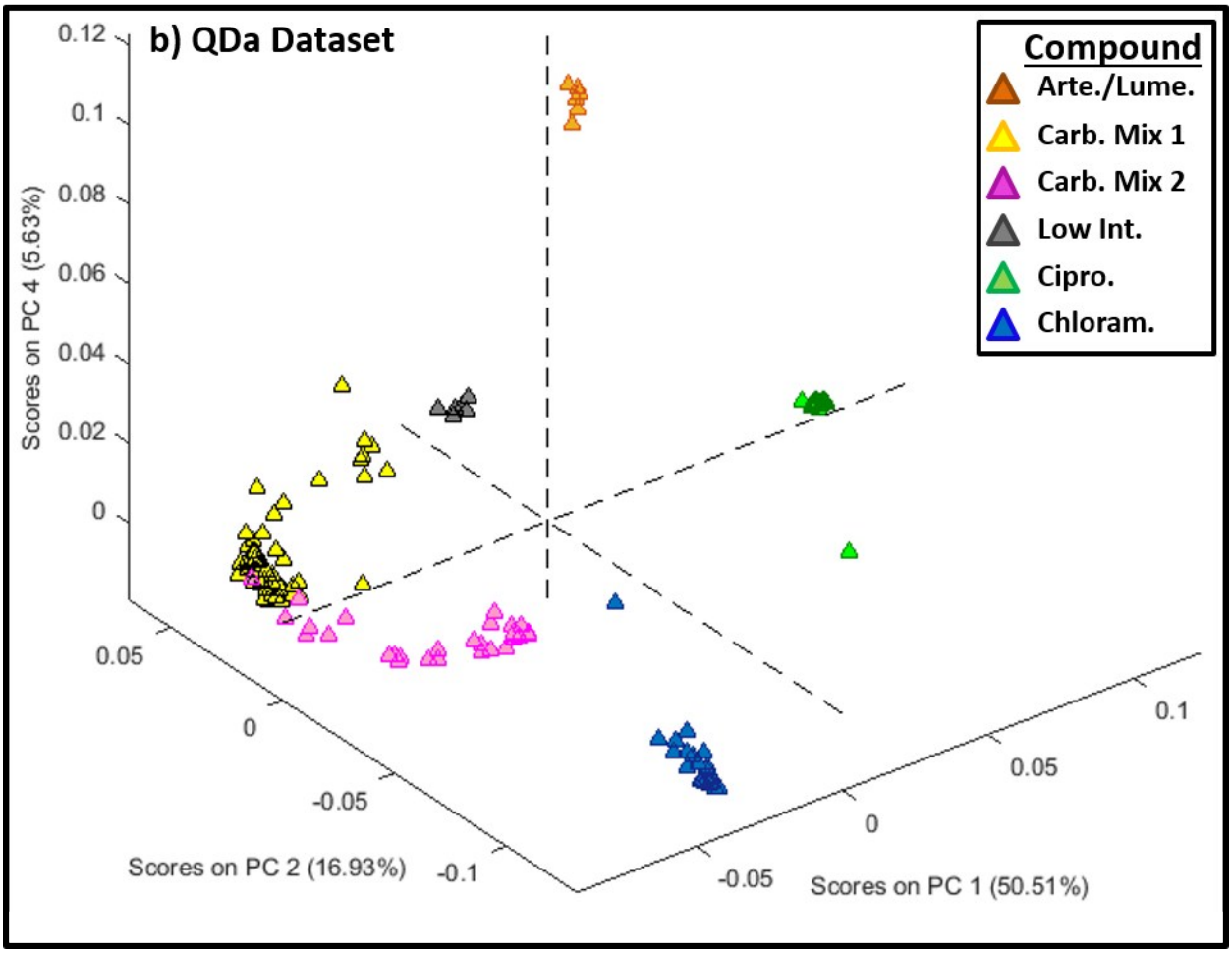

Figure S16: Principal component analysis scores plot (PC1-PC2-PC4) for the QDa dataset. The artemether/lumefantrine containing tablets are shown in the plot in orange, carbohydrate mix 1 (simple sugars) in yellow, carbohydrate mix 2 (simple + alcohol sugars) in pink, tablets with low carbohydrate abundances in gray, ciprofloxacin in green, and chloramphenicol in blue.

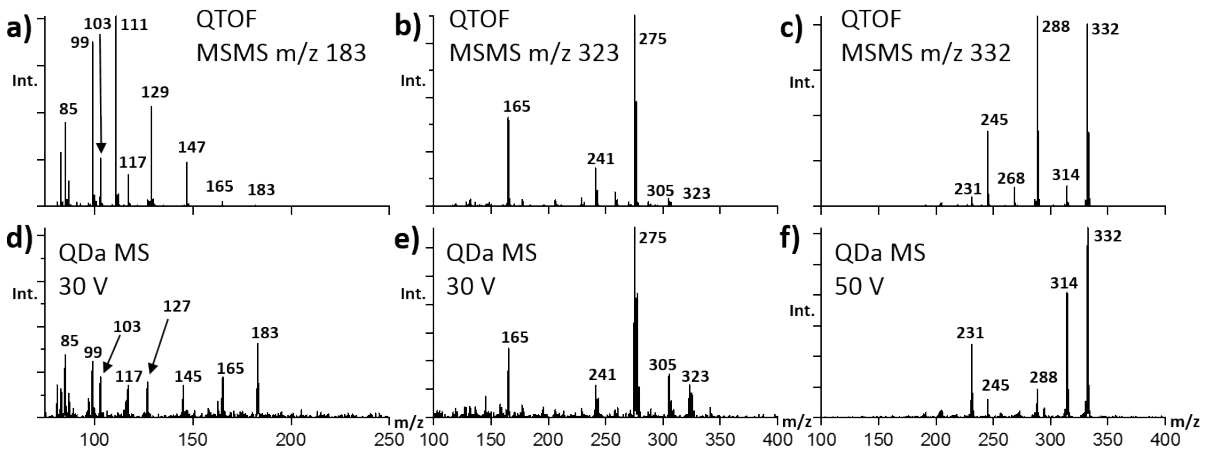

Figure S17: Comparison of DART-MS/MS spectra collected on the QTOF at higher mass resolution for specific chemical components found in the investigated anti-malarial tablets: a) m/z 183 (sugar alcohol $C_6H_{14}O_6$), b) m/z 323 (chloramphenicol), and c) m/z 332 (ciprofloxacin). The bottom panels (e-h) show in-source CID fragmentation spectra obtained on the QDa.

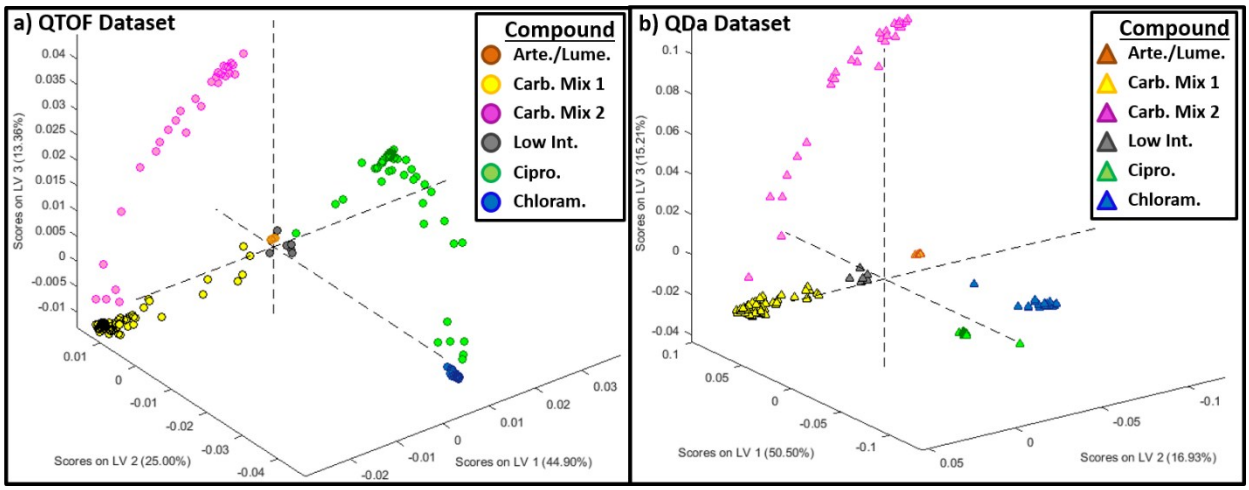

Figure S18: Partial least squares Discriminant Analysis (PLS-DA) from the QTOF and QDa fingerprinted dataset. Mean-centering preprocessing was performed and all 5 classes (genuine, sucr./gluc., mann/malti, low intensity gluc, cipro, and chloram) were loaded for data processing.