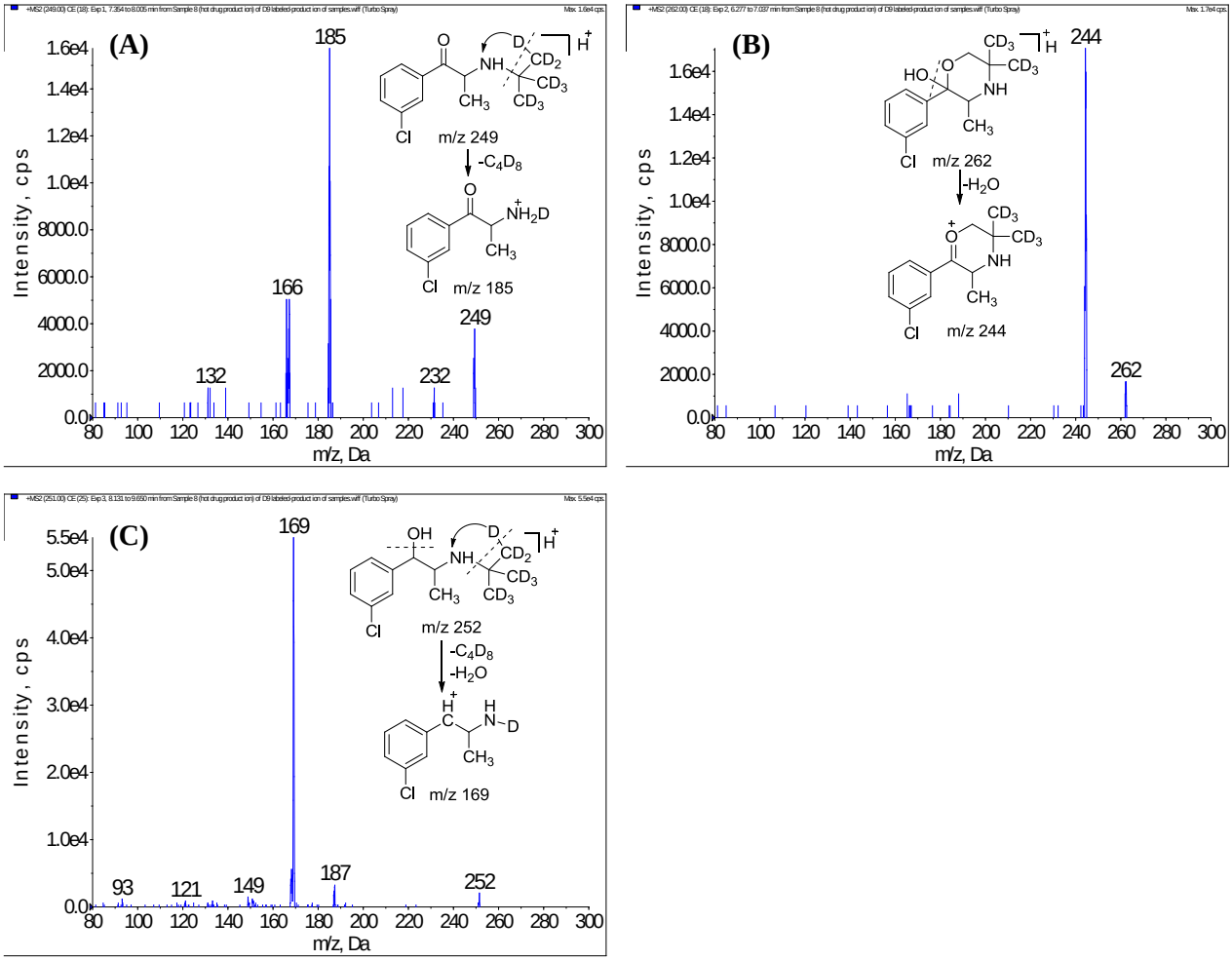Supplementary data Figure 4.