

## Structural characterization of phospholipids by radical-driven fragmentations

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Structural characterization of glycerophospholipids (GPLs) at the fatty acid level presents an opportunity to improve the understanding of the complex relationship between lipid metabolism and diseases. The fine structural characterization of GPL ions generated by atmospheric pressure ionization sources is still not accessible without instrumental modification or derivatization [1]. Indeed, the fine description of structures remains challenging since the most popular tandem mass spectrometry (MS/MS) method is built on collision-induced dissociation (CID) of the gas-phase ion. With CID conditions, the weakest chemical bonds will be cleaved, leading to incomplete fragmentation and lack of structural information, especially in locating double bonds (DBs) on the aliphatic chains.

Since radical release can be obtained from copper reduction by CID in the gas phase and yield diagnostic fragment ions to locate DBs on fatty acids, we hypothesize that this alternative could be of interest for a more complete structural characterization of GPLs [2]. Unfortunately, the fragmentation of copper-adducted GPLs produces only even-electron fragments. As a result, no structural information for the DB has been obtained. To allow copper to chelate with DBs and thus generate a DB-reactive radical, we investigated the gas-phase formation of ternary complexes, which would attenuate the attraction of copper to the polar head of these lipids. The ternary complexes formed with an atomic or a molecular anion provided information on the location of the DB but were weakly observed due to their low stability. Adding a stabilizer ligand such as bipyridine to this complex significantly improved the formation of a reactive copper adduct. CID dissociation of these complexes for different classes of GPLs yields diagnostic fragment ions on both sides of the DB, allowing unambiguous location even for highly unsaturated analogs. This methodology was applied to complex GPL samples using LC-MS/MS analysis with a post-column introduction of CuCl<sub>2</sub> and bipyridine.

### References

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2. C. Afonso, A. Riu, Y. Xu, F. Fournier, J.-C. Tabet. J. Mass Spectrom., **40**, 342-349 (2005)