In this manuscript, Shahpoury et al. report a chromatographic (LC-MS) method of analyzing oxidative potential (OP) of airborne particulate matter (PM) in simulated epithelial lining fluid (SELF). In the introduction section, the authors reviewed the current state of analyzing OP of airborne PM and raised a few existing problems as following.

1. The commonly used DDT method is not a good indicator for OP because its reaction does not well represent those antioxidants (e.g., ascorbic acid, GSH and CSH) in biological fluids.
2. Existing studies using real biological antioxidants to probe OP did not fully consider the autooxidation of them and thus carried uncertainty.
3. Existing methods have disadvantages of 1) being time-consuming and expensive and 2) measurement variability among different assays.

Other than these problems, the authors also proposed to explore the validity of using electrochemical potential as an indicator of PM's OP, which I took as the 4th aspect of this paper beside the three problems.
Below are my reviewing report with focuses on evaluating how far each aspect (numbered 1-4) above has been addressed.

Aspect 1
A major merit of this study is that the authors evaluated OP with three common antioxidants in SELEF and thus made their method more approximating the actual redox environment in biological fluids. LCMS analysis of the three antioxidant and their oxidized products is more accurate in quantification. However, I would recommend the authors to make comparison of their method to DDT method to directly demonstrate their method's advantage. Moreover, how is LCMS analysis compared with HPLC with absorbance detection? What is the necessity of using MS instead of a cheaper diode array detector?

Aspect 2
Page 3 L10-15: Giving a little more detailed explanation on the chemistry of autooxidation and how it causes analytical uncertainty will be helpful for readers to understand the issue.
Page 7 L6-7: Specifying "those reported by Crobeddu et al." is recommended and a quantitative comparison of the "precision" here would make the argument more plausible. I am not fully certain how the autooxidation is avoided by the authors. Is it because a "reference" (without PM) is subtracted from a PM-contained sample? By skimming the cited Crbeddu's work, I found that study also considered the subtraction of blank. The authors should better justify the improvement of their method here.

Aspect 3
I did not find much demonstration in this paper of the method's advantage in saving analysis time and cost. The use of LCMS will probably increase the cost. It also did not discuss on the analytical variance across different assays.

Aspect 4
I have most concerns on the content related to "electrochemical oxidation-reduction potential (ORP)".

First, on Page 3 L29-30, Flohe's review paper in 2013 was cited, yet the "controversy" was not clarified. In that paper, Flohe argued the point that electrochemical potential does not generate more new information than the concentration ratio of a redox couple, since chemical equilibrium hardly exist in biological environment. I hold the same opinion with Flohe and thus have doubts in the necessity of probing redox potential on top of measuring the concentrations of a redox couple. If the authors can provide their insights into this question, that'll substantiate the use of electrochemical potential beyond simply piling up data.
Second, more description of the electrode measurement method is required to confirm the validity of the measured ORP. The key missing information includes how long the electrode takes to achieve a stable reading, and what is the principle of determining the stable reading. In Figure 3, it is obvious that the redox is in non-equilibrium up to 240 min and I would not expect the time scale for establishing equilibrium between a particle solution and an electrode is much shorter than the redox reaction occurring in the system. In other words, a stabilized OPR is hard to be obtained if redox reactions are taking place. The authors should justify whether the measured OPR is in equilibrium (,whose likelihood is low from my perspective).
Figure 3c: Which AO species is this figure representing? Is it AA? The decrease of ORP_ref is an indication that the reaction is taking place toward reducing, i.e., the oxidized AO species is gaining electrons. This means oxidized AO species exists at a very initial phase of the reaction. How does this happen? Where is the oxidized AO species from at t0?
Figure 5: What is the solution matrix of this figure? What is the reference of the potential scale? I would recommend the authors provide raw concentration data for calculating Eh.

Lastly, I have some other supplementary comments as below.

In Figure 2, the % depletion and % formation should sum to 100%, if the assumed reaction stoichiometry (Page 6 L 25) is true, but this is not the case. Although the author suggested a possible reason at a later place (Page 7 L30-35), I would recommend it to be discussed and clarified earlier when the stoichiometry firstly appeared.
Page 3 L 17: What does "the same chemical species" mean? (what chemical species?)
Page 7 L 1-2: In the sentence "The mean consumption for AA, …", is this referring to the Ref sample or PM-contained sample?