Evaluation of Active Oxygen Levels in Solid and Liquid Excipients
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Purpose
Screening some excipients for peroxide levels prior to use in a formulation is imperative to ensure adequate stability, safety, and quality of both the excipient and drug product. There is thus a need for an analytical method that can detect the total peroxide level in pharmaceutical excipients even when the identity and structure of the peroxide are unknown. Titrations involving colorimetric detection of organic peroxides have limited applicability. In addition, ferrous ion methods have been shown in the literature to be less accurate than iodometric methods. A modified ASTM E 299-08 standard test method was therefore developed to analyze active oxygen in solid and liquid excipients. The modified ASTM E 299-08 method is an iodometric method and utilizes spectrophotometric analysis to enhance sensitivity. The existing ASTM E 299-08 method was modified to provide an efficient method for use in determining active oxygen content in a wide range of excipients.

Methods
Excipient samples were prepared for analysis by adding 5 mL of a liquid excipient or 5 mL of a methanolic solution of a solid excipient to a 15 mL centrifuge tube and diluting to volume with acid solvent similar to that in ASTM E 299-08. Samples were purged with nitrogen followed by addition of 1 mL of an aqueous potassium iodide (KI) solution. Samples were immediately capped, covered, and protected from light for 1 hour, and then measured using a DU 800 Spectrophotometer. Low and high range iodine calibration curves were used to determine the corresponding active oxygen levels ranging from 0-80 ppm or higher.

Results
Active oxygen levels were measured in both liquid excipients, i.e., polyethylene glycol 400, oleic acid, Kolliphor EL, polysorbate 20, tall oil, and propylene glycol, and solid excipients, i.e., poloxamer 188 and Myrj 52. The liquid excipients were found to contain levels over a range of 0.04 – 79.88 ppm. Active oxygen levels in the solid excipients had levels over a range of 0.38 – 1.00 ppm. The oleic acid and tall oil samples appeared not to be miscible with the 1 mL addition of KI (aq) solution during analysis, forming non-homogeneous mixtures that had higher background absorbances than did the other samples. The duplicates of the fatty acid samples had differences in absorbance of 0.22 (oleic acid) and 0.39 (tall oil), while the other liquid excipients only had a difference in absorbance of 0.08 or less.

Conclusion
The complexity of a formulation and the excipients’ potential reactions can cause unique peroxides to be formed, which can negatively impact the properties of the formulated product. Previously published procedures for measuring active oxygen evaluated excipients for hydrogen peroxide and hydroperoxide levels. The advantages of the active oxygen method presented in this poster over methods in the literature are: the technique is not limited to only specific peroxides, measures peroxide levels directly in the form of active oxygen, has high sensitivity but also a wide dynamic range, does not require numerous procedural steps, and is not time-consuming. The modified active oxygen method demonstrated its benefits by being successfully used to measure active oxygen levels in several excipients that possess widely varying physical characteristics.