Additive Electrochemical Oxidation of Ascorbic Acid and Glucose in Enzyme Based Blood Electrochemical Meters

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Determining one's blood glucose (GL) using enzyme-based electrochemical meters is very common in a home setting to control diabetes and in treating severe situations in a hospital. Most work using a mechanism where enzymes, such as glucose oxidase or glucose dehydrogenase, present in the test strip oxidize glucose to release free electrons which are then read by electrodes in the meter **[1]**. The higher the electron current, higher the GL concentration read by the meter. Thus, this mechanism is prone to error when electrons are generated by the oxidation of interfering molecules directly at the electrode due to the potential difference between the anode and cathode. One such interfering molecule is Vitamin C (Ascorbic Acid, AA), widely used as a supplement **[2]**, consumed at very high doses in treating trauma in hospitals **[3]**, or during treatment regimes of Covid19 **[4]**. Thus, the objective is to study this proposed interference from AA on meters from five prominent manufacturers, widely available in Switzerland with differing price points. The names of the companies were kept limited to authors for confidentiality reasons. GL concentration used in this study covers the physiological range in fasted state (60-100 mg/dL), fed state (120-140 mg/dL) and diabetes. Similarly, AA covers the physiological range (1-1.5 mg/dL) as a supplement and when given intravenously (approximately 30 mg/dL).

GL reading at 60 mg/dL glucose increases with increasing AA concentration from 0.1 to 25 mg/dL. Similar observations of increasing GL readings were seen at all five GL concentrations (50, 60, 80, 100, 150 mg/dL) and using meters made by all five companies, showing a decrease in specificity due to AA, which is further substantiated when a few meters used gave GL reading with only AA solutions. Using a calibration curve of GL values with only AA solutions, the net GL reading at different AA concentrations could be explained by equation 1, which assumes an additive effect of the concentration-dependent oxidation of GL and AA. The regression line (R^2=0.98) shows good predictions from equation 1 and confirms additive effects (slope=1.06) of oxidation.

Reading on glucose meter = Value at zero AA + [AA]*slope of AA calibration curve

All meters showed a positive deviation in the glucose readings due to the direct oxidation of AA; the extent of this impact varied across the different meters. At low GL (50 mg/dL), the meter from company 1 showed the lowest percent positive error of 16% but other companies showed between a 40 and 65% error (lower specificity), with a similar pattern across the spectrum. This can be explained by the manufacturers designing a very specific patented mutated version of enzyme/co-enzyme systems and/or by advancing the electronics of the meter to increase the specificity by selectively targeting the oxidation of GL. Also, percent error, as expected from equation above, decreased with increasing glucose concentration within each company's meter; e.g. for company 5 there is an error of 65% at 50 mg/dL GL but only 19% at 150 mg/dL GL.

Conclusion: Overall, this study shows that easily oxidizable drugs in the blood will lead to a positive error, lower specificity, while determining one's glucose level and the selection which company's glucometer to use makes a significant impact on the magnitude of this error.

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