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Acidic pH amplifies iron-mediated lipid peroxidation in cells.

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The goal of our study was to investigate the mechanism by which changes in extracellular pH influence lipid peroxidation processes. Ferrous iron can react with hydroperoxides, via a Fenton-type reaction, to initiate free radical chain processes. Iron is more soluble at lower pH values, therefore we hypothesized that decreasing the environmental pH would lead to increased iron-mediated lipid peroxidation. We used Photofrin, a photosensitizer that produces singlet oxygen, to introduce lipid hydroperoxides into leukemia cells (HL-60, K-562, and L1210). Singlet oxygen reacts with the PUFA of cells producing lipid hydroperoxides. Using EPR spin trapping with POBN, free radical formation from HL-60 cells was only detected when Photofrin, light, and ferrous iron were present. Free radical formation increased with increasing iron concentration; in the absence of extracellular iron, radical formation was below the limit of detection and lipid hydroperoxides accumulated in the membrane. In the presence of iron, lipid-derived radical formation in cells is pH dependent; the lower the extracellular pH (7.5-5.5), the higher the free radical flux; the lower the pH, the greater the membrane permeability induced in K-562 cells, as determined by trypan blue dye exclusion. These data demonstrate that lipid peroxidation processes, mediated by iron, are enhanced with decreasing extracellular pH. Thus, acidic pH not only releases iron from "safe" sites, but this iron will also be more damaging.