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Gardner H W. Decomposition of linoleic acid hydroperoxides. Enzymic reactions compared with nonenzymic. *J. Agr. Food Chem.* 23:129-36, 1975.
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This literature review described the transformation of lipid hydroperoxides by both chemical and enzymic methods. Certain of the enzymic hydroperoxide reactions had comparable chemical models, but others appeared to be uniquely restricted to enzymes. Novel reaction mechanisms were proposed. [The *SCI*® indicates that this paper has been cited in over 130 publications.]

Chemistry and Biochemistry of Lipid Hydroperoxides

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Following research assignments in Hawaii and California, I accepted a position at the Northern Regional Research Center in Peoria (from whence all roads lead to soybean and cornfields), in order to reduce unnecessary but tempting distractions. My time, in those early US Department of Agriculture years, was divided between mission-oriented work and maverick research on the chemistry and biochemistry of lipid hydroperoxides. Attendance at a symposium on the latter topic resulted in an invitation to write this review, of which I now share some personal thoughts. The citation rate of this article, and that of another highly cited paper of mine appearing in the same journal,[1] illustrate the impact of timely journal-published reviews. By comparison, my book chapters have been condemned to near oblivion.

Personal research into previously unknown reactions of lipid hydroperoxides furnished recency to the review. For example, investigation of an iron-catalyzed redox reaction between cysteine and linoleic acid hydroperoxide suggested a novel pathway to isomeric epoxyhydroxy and epoxyoxo fatty acids. The mechanism, an intramolecular rearrangement of an alkoxyl radical into an epoxyallylic radical, was incorporated into a research manuscript that reported the work, but it was promptly rejected by a well-meaning reviewer who objected to a figure showing the postulate. And so, via this review, the contested mechanism found its way into print anyway. Dogged persistence is sometimes necessary to overcome entrenched resistance, but it is not always without hazard.

Certain structural features of products from the iron-catalyzed reaction were similar to those of products isolated from a reaction of soybean lipoxygenase under anaerobic conditions. Since lipoxygenase contains iron at the active site, it seemed a good bet that the enzyme mechanism might be similar to that of the nonenzymatic reaction. My proposal for the aerobic and anaerobic mechanisms of lipoxygenase was nearly identical to the model eventually adopted. However, my review has rarely, if ever, been cited specifically regarding the lipoxygenase proposal, because preeminent lipoxygenase investigators simultaneously published their own mechanism.[2]

Two other postulates offered in the review proved to be notably inaccurate. First, I flatly stated that lipoxygenase activity was absent in animal tissue. M. Hamberg and B. Samuelsson,[3] by incredible coincidence, submitted their first definitive paper on animal lipoxygenase in human platelets on the exact day my review manuscript was submitted. Science is not static, even for a day! Second, I regret postulating that trihydroxy fatty acids originate from hydroperoxide fatty acids via 1,4-addition of hydroxyl radicals to conjugated hydroperoxydiene. Apparently, trihydroxy fatty acids arise predominantly from hydration of epoxyhydroxy intermediates.[4]

Science continues to make inroads into lipid oxidation dogma. In particular, advances have been considerable in areas of physiologically active products from the action of animal lipoxygenases,[5] the odor-producing hydroperoxide lyase of fish[6] and plants, and the chemical reactions of lipid hydroperoxides.[4] In the latter category, much of the chemistry of peroxyl radical rearrangements into cyclic peroxides and prostaglandin-like endoperoxides has been developed since 1975.

Finally, proofreading can have its perils. When the galleys of my review arrived, many free radical symbols were missing. Evidently, the printer meticulously removed all of those annoying "fly specks." The fly specks were successfully restored, except for one in Figure 4.

1. **Gardner H W.** Lipid hydroperoxide reactivity with proteins and amino acids: a review. *J. Agr. Food Chem.* 27:220-9, 1979. (Cited 135 times.)
2. **de Groot J J M C, Veldink G A, Vliegenthart J F G, Boldingh J, Wever R & van Gelder B F.** Demonstration by EPR spectroscopy of the functional role of iron in soybean lipoxygenase-1. *Biochim. Biophys. Acta* 377:71-9, 1975. (Cited 120 times.)
3. **Hamberg M & Samuelsson B.** Prostaglandin endoperoxides. Novel transformations of arachidonic acid in human platelets. *Proc. Nat. Acad. Sci. USA* 71:3400-4. 1974. (Cited 1,320 times.) [See also: **Hamberg M & Samuelsson B.** Citation Classic. Commentary on *Proc. Nat. Acad. Sci. USA* 71:3400-4, 1974. *Contemporary classics in the life sciences. Volume 2: the molecules of life.* Philadelphia: ISI Press, 1986. p. 185.]
4. **Gardner H W.** Oxygen radical chemistry of polyunsaturated fatty acids. *Free Radical Biol. Med.* (In press.)
5. **Samuelsson B, Hammarström S, Hamberg M & Serhan C N.** Structural determination of leukotrienes and lipoxins. *Adv. Prostag. Thromb. Leuktr. Res.* 14:45-71. 1985. (Cited 5 times.)
6. **Josephson D B & Lindsay R C.** Enzymic generation of volatile aroma compounds from fresh fish. (Parliment T H & Croteau R. eds.) *Biogeneration of aromas.* Washington, DC: American Chemical Society, 1986. p. 201-19. (Cited 5 times.)