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Reduction of nitroxides in whole blood, erythrocytes, and plasma

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The appropriate use of nitroxides for *in vivo* EPR techniques or as contrast agents for *in vivo* NMR techniques, requires an adequate understanding of the metabolism of the nitroxides in blood and its constituents. To determine the effects of key variables on the rate of reduction in whole blood, plasma, and erythrocytes we studied a set of 19 nitroxides selected to provide representative variations of ring structure, charge, and lipophilicity. No essential differences were observed between reduction in rat or human blood components and the same structure/reduction and charge/reduction relationships were observed as in nucleated mammalian cell lines. In order to get more insights into the processes which influence the metabolism of nitroxides in blood, we also studied the effect of various potential inhibitors of the metabolism of nitroxides in blood. The inhibitors (ascorbate oxidase, desferal, N-ethylmaleimide, heat, and combinations of these) were selected on the basis of the different mechanisms by which they should act; they were studied in intact and freeze-thawed erythrocytes and plasma. In contrast to nucleated cells it was found that the main source of reduction in erythrocytes and plasma is ascorbic acid. In erythrocytes some other nonenzymatic and enzymatic mechanisms also are involved, but at least 65-90% of the reduction could be attributed to ascorbate.