

Free Radicals in Pharmacology and Toxicology— Selected Topics

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I. Introduction	189
II. Novel free radical metabolites	189
A. Semiquinoneimine free radicals	189
B. Thiyl free radicals	192
C. Nitrogen oxide free radicals	194
D. Sulfur oxide free radicals	196
E. Peroxy free radicals	196
F. Ethanol free radicals	196
G. Triarylmethane dye carbon-centered free radicals	197
III. Free radical pathways in the metabolism of xenobiotics	198
A. One-electron enzymatic reduction of xenobiotics	198
B. One-electron enzymatic oxidation of xenobiotics	201
IV. Prostaglandin synthetase and lipoxygenases: Examples of enzymatically controlled stereospecific lipid peroxidation	201
V. Free radicals in drug-induced cutaneous photosensitization	206
A. Halogenated salicylanilides	206
B. Chlorpromazine	206
C. Sulfanilamide	207
VI. Conclusion	208

I. Introduction

A FREE RADICAL is any molecule that has an odd number of electrons (12). Although most free radicals are organic, it is also possible to form inorganic free radicals, e.g. \dot{O}_2^- . A simple organic molecule like benzene may be transformed into a free radical by three different mechanisms. One-electron oxidation of benzene (removal of one of the pi-electrons) results in the formation of the benzene cation radical.



The addition of an electron, the one-electron reduction of benzene, generates the benzene anion radical.



Finally, the homolytic cleavage of one of the C—H bonds in benzene by ultraviolet or other radiation forms a hydrogen atom and the neutral phenyl radical.



Although extreme chemical reactions are required to form free radicals from benzene, many other molecules

may be converted into radicals under relatively mild conditions including those that are encountered in biological systems. Thus it is not surprising that free radicals are found in many metabolic pathways involving both naturally occurring and foreign compounds.

In previous reviews, 14 different classes of free radical metabolites have been discussed (89, 90). In this review, seven additional novel free radical metabolites are described in detail (section II). This section is followed by a summary in tabular form (tables 2 and 3) of all known free radical pathways classified by chemical class and enzyme (section III). The next section (IV) describes in greater detail the free radicals formed by the action of prostaglandin synthetase and lipoxygenase on fatty acids. The final section (V) is concerned with the role of free radicals in drug-induced photosensitization. The technique of spin labeling, which employs stable nitroxide radicals as probes, will not be discussed in this review. The application of spin labeling to pharmacological and toxicological problems has already been reviewed recently (24).

II. Novel Free Radical Metabolites

A. Semiquinoneimine Free Radicals

The one-electron oxidation of phenylenediamine by the horseradish peroxidase/ H_2O_2 system forms a cation radical. The same system also catalyzes the formation of semoquinone from hydroquinone. Thus a free rad-

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Table of Contents Quantitative Toxicology Selected Topics

1. Understanding the eBook Quantitative Toxicology Selected Topics
 - The Rise of Digital Reading Quantitative Toxicology Selected Topics
 - Advantages of eBooks Over Traditional Books
2. Identifying Quantitative Toxicology Selected Topics
 - Exploring Different Genres
 - Considering Fiction vs. Non-Fiction
 - Determining Your Reading Goals
3. Choosing the Right eBook Platform
 - Popular eBook Platforms
 - Features to Look for in an Quantitative Toxicology Selected Topics
 - User-Friendly Interface
4. Exploring eBook Recommendations from Quantitative Toxicology Selected Topics
 - Personalized Recommendations
 - Quantitative Toxicology Selected Topics User Reviews and Ratings

- Quantitative Toxicology Selected Topics and Bestseller Lists
- 5. Accessing Quantitative Toxicology Selected Topics Free and Paid eBooks
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 - Quantitative Toxicology Selected Topics eBook Subscription Services
 - Quantitative Toxicology Selected Topics Budget-Friendly Options
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 - ePub, PDF, MOBI, and More
 - Quantitative Toxicology Selected Topics Compatibility with Devices
 - Quantitative Toxicology Selected Topics Enhanced eBook Features
- 7. Enhancing Your Reading Experience
 - Adjustable Fonts and Text Sizes of Quantitative Toxicology Selected Topics
 - Highlighting and Note-Taking Quantitative Toxicology Selected Topics
 - Interactive Elements Quantitative Toxicology Selected Topics
- 8. Staying Engaged with Quantitative Toxicology Selected Topics
 - Joining Online Reading Communities
 - Participating in Virtual Book Clubs
 - Following Authors and Publishers Quantitative Toxicology Selected Topics
- 9. Balancing eBooks and Physical Books Quantitative Toxicology Selected Topics
 - Benefits of a Digital Library
 - Creating a Diverse Reading Collection Quantitative Toxicology Selected Topics
- 10. Overcoming Reading Challenges
 - Dealing with Digital Eye Strain
 - Minimizing Distractions
 - Managing Screen Time
- 11. Cultivating a Reading Routine Quantitative Toxicology Selected Topics
 - Setting Reading Goals Quantitative Toxicology Selected Topics
 - Carving Out Dedicated Reading Time
- 12. Sourcing Reliable Information of Quantitative Toxicology Selected Topics
 - Fact-Checking eBook Content of Quantitative Toxicology Selected Topics
 - Distinguishing Credible Sources

13. Promoting Lifelong Learning
 - Utilizing eBooks for Skill Development
 - Exploring Educational eBooks
14. Embracing eBook Trends
 - Integration of Multimedia Elements
 - Interactive and Gamified eBooks

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