

## Accepted Manuscript

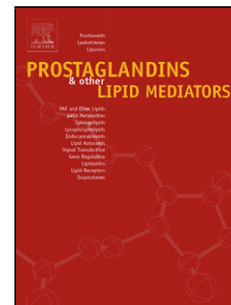
Title: Isolevuglandins and Cardiovascular Disease

Authors: Sean S Davies, Linda S. May-Zhang

PII: S1098-8823(18)30075-3

DOI: <https://doi.org/10.1016/j.prostaglandins.2018.10.002>

Reference: PRO 6308



To appear in: *Prostaglandins and Other Lipid Mediators*

Received date: 1-6-2018

Revised date: 25-9-2018

Accepted date: 3-10-2018

Please cite this article as: Davies SS, May-Zhang LS, Isolevuglandins and Cardiovascular Disease, *Prostaglandins and Other Lipid Mediators* (2018), <https://doi.org/10.1016/j.prostaglandins.2018.10.002>

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

## Isolevuglandins and Cardiovascular Disease

Sean S. Davies<sup>1</sup> and Linda S. May-Zhang<sup>1</sup>

Department of Pharmacology, Division of Clinical Pharmacology, Vanderbilt University, Nashville, TN

To whom correspondence should be addressed: Sean S. Davies [sean.davies@vanderbilt.edu](mailto:sean.davies@vanderbilt.edu)

### Highlights:

- Isolevuglandins form stable pyrrole adducts with the lysyl residues of proteins
- Levels of proteins modified by isolevuglandins are increased by cardiovascular risk factors.
- Modification of HDL by isolevuglandin inhibits its protective functions.
- Dicarbonyl scavengers block myeloperoxidase induced isolevuglandin modification of HDL.

### Abstract:

Isolevuglandins are 4-ketoaldehydes formed by peroxidation of arachidonic acid. Isolevuglandins react rapidly with primary amines including the lysyl residues of proteins to form irreversible covalent modifications. This review highlights evidence for the potential role of isolevuglandin modification in the disease processes, especially atherosclerosis, and some of the tools including small molecule dicarbonyl scavengers utilized to assess their contributions to disease.

### Keywords:

Lipid peroxidation, reactive lipid species, isolevuglandins, cardiovascular disease, HDL

### Introduction

Lipid peroxidation is a constant process within living cells, as a wide variety of cellular processes produce reactive oxygen species (ROS). However, initiating events of pathological processes often exacerbate rates of lipid peroxidation, resulting in accumulation of lipid peroxidation products that contribute to the progression of disease. While abundant in phospholipids of cellular membranes, polyunsaturated fatty acids (PUFAs) are highly susceptible to peroxidation by ROS such as the hydroxyl radical. Peroxidation of linoleic acid and arachidonic acid generates a variety of stable as well as reactive products (**Figure 1**). This mini-review will focus on one particular family of lipid peroxidation products, the isolevuglandins (IsoLG), and their role in cardiovascular disease.

IsoLGs are a family of 4-ketoaldehydes (alternatively referred to as isoketals) that form from the peroxidation of arachidonic acid through bicycloendoperoxide intermediates (termed H<sub>2</sub>-isoprostanes) and undergo concerted rearrangement of the bicycloendoperoxide group to form the 4-ketoaldehyde<sup>1,2</sup>. Because abstraction of the initial hydrogen can occur at 3 different positions on arachidonic acid, subsequent rearrangement and addition of oxygen give rise to four regioisomers of H<sub>2</sub>-isoprostanes. Each of these regioisomers can give rise to two distinct 4-ketoaldehyde isomers, generating a total of eight regioisomers (and 64 stereoisomers) of IsoLG (**Figure 2**). While all regioisomers form to some extent, the formation of certain regioisomers are favored (e.g. 15-E<sub>2</sub>-IsoLG and 5-E<sub>2</sub>-IsoLG versus 8-E<sub>2</sub>-IsoLG and 12-E<sub>2</sub>-IsoLG).

Download English Version:

<https://daneshyari.com/en/article/11026017>

Download Persian Version:

<https://daneshyari.com/article/11026017>

[Daneshyari.com](https://daneshyari.com)