






Review

# Natural Bioactive Compounds Targeting NADPH Oxidase Pathway in Cardiovascular Diseases

Siti Sarah M. Sofiullah <sup>1</sup>, Dharmani Devi Murugan <sup>2</sup>, Suhaila Abd Muid <sup>3,4</sup>, Wu Yuan Seng <sup>5,6</sup>, Sharifah Zamiah Syed Abdul Kadir <sup>2</sup>, Razif Abas <sup>7,8</sup>, Nurul Raudzah Adib Ridzuan <sup>1</sup>, Nor Hisam Zamakshshari <sup>9</sup> and Choy Ker Woon <sup>1,\*</sup>

- <sup>1</sup> Department of Anatomy, Faculty of Medicine, Universiti Teknologi MARA (UiTM), Sungai Buloh 47000, Selangor, Malaysia
- <sup>2</sup> Department of Pharmacology, Faculty of Medicine, Universiti Malaya, Kuala Lumpur 50603, Malaysia
- <sup>3</sup> Institute of Pathology Laboratory Medicine and Forensic Sciences (I-PPerForM), Universiti Teknologi MARA (UiTM), Sungai Buloh 47000, Selangor, Malaysia
- <sup>4</sup> Department of Biochemistry and Molecular Medicine, Faculty of Medicine, Universiti Teknologi MARA (UiTM), Sungai Buloh 47000, Selangor, Malaysia
- <sup>5</sup> Centre for Virus and Vaccine Research, School of Medical and Life Sciences, Sunway University, Subang Jaya 47500, Selangor, Malaysia
- <sup>6</sup> Department of Biological Sciences, School of Medical and Life Sciences, Sunway University, Subang Jaya 47500, Selangor, Malaysia
- <sup>7</sup> Department of Human Anatomy, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia, Seri Kembangan 43400, Selangor, Malaysia
- <sup>8</sup> Department of Anatomy and Embryology, Faculty of Medicine, Leiden University Medical Centre, 2333 ZC Leiden, The Netherlands
- <sup>9</sup> Department of Chemistry, Faculty of Resources Science and Technology, University Malaysia Sarawak, Kota Samarahan 94300, Sarawak, Malaysia
- \* Correspondence: choykerwoon@uitm.edu.my



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**Abstract:** Cardiovascular disease (CVD) is the leading cause of death worldwide, in both developed and developing countries. According to the WHO report, the morbidity and mortality caused by CVD will continue to rise with the estimation of death going up to 22.2 million in 2030. NADPH oxidase (NOX)-derived reactive oxygen species (ROS) production induces endothelial nitric oxide synthase (eNOS) uncoupling and mitochondrial dysfunction, resulting in sustained oxidative stress and the development of cardiovascular diseases. Seven distinct members of the family have been identified of which four (namely, NOX1, 2, 4 and 5) may have cardiovascular functions. Currently, the treatment and management plan for patients with CVDs mainly depends on the drugs. However, prolonged use of prescribed drugs may cause adverse drug reactions. Therefore, it is crucial to find alternative treatment options with lesser adverse effects. Natural products have been gaining interest as complementary therapy for CVDs over the past decade due to their wide range of medicinal properties, including antioxidants. These might be due to their potent active ingredients, such as flavonoid and phenolic compounds. Numerous natural compounds have been demonstrated to have advantageous effects on cardiovascular disease via NADPH cascade. This review highlights the potential of natural products targeting NOX-derived ROS generation in treating CVDs. Emphasis is put on the activation of the oxidases, including upstream or downstream signalling events.

**Keywords:** natural products; cardiovascular diseases; oxidative stress; NADPH signalling pathway

## 1. Introduction

Cardiovascular disease (CVD) remains the major cause of mortality and premature death worldwide [1]. In 2019, according to the World Health Organization, 17.9 million deaths were reported from cardiovascular disease, accounting for 32% of all global fatalities, and 85% of these deaths are the result of a heart attack or a stroke [2]. It has