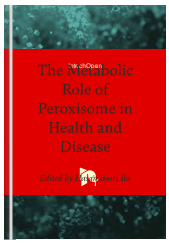
OPEN ACCESS PEER-REVIEWED CHAPTER

Peroxisomal Modulation as Therapeutic Alternative for Tackling Multiple Cancers

Submitted: April 6th, 2022 , Reviewed: April 11th, 2022 , Published: May 11th, 2022

DOI: 10.5772/intechopen.104873

WRITTEN BY
Shazia Usmani, Shadma Wahab, Abdul Hafeez, Shabana Khatoon and Syed Misbahul Hasan



FROM THE EDITED VOLUME

The Metabolic Role of Peroxisome in Health and Disease

Edited by Hasan Basri İla

Book Details | Order Print

Abstract

Peroxisomes are indispensably involved as a central player in the metabolism of reactive oxygen species, bile acids, ether

Sectio

Chapter

Peroxisomal Modulation as Therapeutic Alternative for Tackling Multiple Cancers

Shazia Usmani, Shadma Wahab, Abdul Hafeez, Shabana Khatoon and Syed Misbahul Hasan

Abstract

Peroxisomes are indispensably involved as a central player in the metabolism of reactive oxygen species, bile acids, ether phospholipids, very-long-chain, and branched-chain fatty acids. The three subtypes of PPARs are PPAR-alpha, PPAR-delta, and PPAR-gamma which have been found to be instrumental in the control of cancer metabolism cascades. Any disproportionate expression of PPAR can lead to the progression of cell growth and survival in diverse types of cancers. It can be exploited both as an agonist or antagonist for utilization as a potential therapeutic alternative for the treatment of cancer. Therefore, the multifunctional PPAR modulators have substantial promise in various types of cancer therapies. Many recent studies led to the observations that a variety of phytochemicals, including phenolics, have been implicated in anticancer effects. Plant phenolics seem to have both palliative and treatment opportunities in combating cancer which requires deep insight into the proposed mechanisms. Henceforth, this chapter highlights the role of peroxisomal subtypes as an activator or suppressor followed by its modulation through bioactive obtained from a variety of crude drugs. A discussion on various challenges restricting proper utilization has also been incorporated.

Keywords: peroxisome, metabolism, PPARs, herbal, cancer

1. Introduction

Peroxisomes are small membrane-bound organelles with simple structures but contain enzymes that display a wide range of metabolic activities. About 50 peroxisomal enzymes have been identified where major [1, 2] pathways for metabolism involve α- and β-oxidation of fatty acids, biosynthesis of ether lipids, polyamines, D-amino acids, glyoxylate, and purines. The synthesis and assembly of peroxisomal proteins occur on free ribosomes which are then imported into these tiny organelles as completed polypeptide chains. The disorders related to peroxisomal functions can be attributed to a disturbance in the formation of the organelles or might be related to defects in either a particular peroxisomal enzyme or a related transporter [3, 4]. The metabolic disorders promote the accumulation of substrates that are usually degraded

by specific peroxisomal enzymes. A variety of clinical symptoms has proven to be very severe leading to an early death.

2. Metabolic implications of peroxisomes, a druggable target

Peroxisome-related homeostatic balance is an indispensable mechanism of health where the removal of worn-out and defective peroxisomes occurs through autophagy. Association with mitochondria is reflected when commotion of peroxisomal function results in disruption of mitochondrial function. The impaired peroxisomal function has been found to be instrumental in special conditions of neurodegenerative disorders and diabetes, while dysregulation in peroxisomal function can result in cancer [5, 6]. There has been increasing evidence linking peroxisomal misregulation to the eruption of several diseases which potentiate an elevated possibility of targeting peroxisomal involvement in disease prevention or treatment.

Peroxisomes are amazingly active organelles, which have an important role in lipid and hydrogen peroxide metabolism making them elemental for human health [7]. Despite great advances in identification of essential components and related molecular mechanisms, an understanding of the process by which peroxisomes are incorporated into metabolic pathways is of elementary importance. The interaction of peroxisomes with other subcellular compartments, metabolic co-operations, peroxisome–peroxisome interactions, and the interaction of peroxisomes with microtubules needs to be addressed to utilize this information directly to combat the process of disease development.

Peroxisomes are consigned to clearing up the reactive oxygen chemical debris cast off by other organelles, where their functions extend far beyond hydrogen peroxide metabolism [8]. Peroxisomes are closely associated with mitochondria, and their ability to carry out fatty acid oxidation and lipid synthesis may be highly implicated in generating cellular signals required for normal physiology. The biology of peroxisomes and their relevance to human disorders, including cancer, obesity-related diabetes, and degenerative neurologic disease cannot be undermined [9].

Peroxisomes are multifarious where they invariably modulate the metabolism of reactive oxygen species and primary homeostatic mechanisms, such as oxidation of fatty acid, synthesis of bile acid, and transport of cholesterol. Henceforth, it is implicative that peroxisomal homeostasis is an important regulator of health, and disruption of peroxisomal function can lead to mitochondrial dysfunction, reflecting the intimate link between the two organelles [10].

The impaired peroxisomal function leads to neurodegenerative disorders and diabetes, but dysregulation may have far-reaching effects, such as the development of cancer [11]. The peroxisomal function is also transformed with aging owing to deviations in the expression and/or localization of peroxisomal matrix proteins.

The homeostatic mechanisms of peroxisomes are undermined by the existence of distressing genetic disorders attributed to impaired peroxisomal function. However, with amplified evidence connecting peroxisomal dysfunction to the pathogenesis of these acquired diseases, it can be utilized as a druggable target in disease prevention or treatment [12].

The immune system evasion is one of the mainstays of cancer, and peroxisomes have an indispensable role in the regulation of cellular immune responses.