Research Article

# Thiourea Derivatives Restore Dysfunctional Mitochondria in Chronic Hepatitis B Infection

Jitendra Kumar<sup>1</sup>, Purnima Tyagi<sup>1</sup>, Raghwendra Pratap Singh<sup>1</sup>, Akhilesh k Saini<sup>1</sup>, Deepti Sharma<sup>1</sup>, Jaswinder Singh Maras<sup>1</sup>, Vijay Kumar<sup>1</sup>

Department of Molecular and Cellular Medicine, Institute of Liver and Biliary Sciences, New Delhi, India; Immunology Laboratory, Council for Scientific and Industrial Research-Institute of Microbial Technology, Chandigarh, India; Department of Chemistry, Sri Venkateshwara College, University of Delhi, New Delhi, India

#### ABSTRACT

Backgrounds Chronic Hepatitis B (CHB) infection and the Hepatitis B virus X protein (HBx) are major risk factors associated with Hepato Cellular Carcinoma (HCC). In CHB infection, HBx induces mitochondrial dysfunction, exhaustion and impaired function in hepatocytes. Restoring hepatocyte health along with reduction in virus replication could be an ideal treatment for CHB. Thiourea derivatives are well known for their antiviral properties, though their effect on mitochondrial and/or hepatocyte health remains obscure. This study focuses on the repurposing of thiourea derivatives (DSA-00, DSA-02 and DSA-09) for hepatocyte replenishment.

Methods: HepG2.2.15 cells were treated with thiourea derivatives, alongside Entecavir (ETV). HBV DNA, RNAs and antigens, measured by qPCR, Quantitative Reverse Transcriptuse Polymerase Chain Reaction (RT-qPCR) and Engune-Linked Immunosorbent Assay (ELISA), respectively. Followed by proteomic analysis by Weighted Protein Co-expression Network Analysis (WPCNA) and Fluorescence Activated Cell Sorting (FACS) used for the validation of results.

Results: The proteomics analysis showed both DSA-00 and ETV were enriched with proteins associated with antiviral responses. In addition, DSA-00 additionally showed an increase in proteins linked to mitochondrial response. Whereas DSA-02 exhibited associations with the innate immune system and citric acid cycle and DSA-09 displayed pathways similar to DSA-00 and ETV. The treated groups exhibited an enhanced bio-energetic and antiviral response as compared to the untreated group. EACS analysis revealed the restoration of exhausted hepatocytes by thiourea derivatives through targeting mitochondria.

Conclusions Our findings suggest that thiourea derivatives hold potential as a novel therapeutic agent that seems to restore mitochondrial health along with an anti-viral response in CHB.

Keywordse Antiviral; Thiourea derivatives; Hepatitis B virus; Chronic hepatitis B infection; Mitochondria dysfunction; Exhausted hepatocytes

#### INTRODUCTION

Chronic Hepatitis B (CHB) infection is caused by Hepatitis B Virus (HBV) that lasts for more than six months and leading to longterm liver disease. Currently, 257 million people around the world had a CHB infection [1,2]. CHB often leads to major problems with the liver, such as circhosis, liver failure and liver cancer. As the illness persists longer, there is more liver inflammation

Correspondence to Jitendra Kumar, Department of Molecular and Cellular Medicine, Institute of Liver and Biliary Sciences, New Delhi, India, E-mail: jkumar1@ilbs.in, jna.gupts@gmail.com

Jawinder Singh Maras, Departments of Molecular and Cellular Medicine, Institute of Liver and Biliary Sciences, New Delhi, India, Email: justi2param@gmail.com

Vijay Kumar, Departments of Molecular and Cellular Medicine, Institute of Liver and Biliary Sciences, New Delhi, India, Email: vijakumar98@gmail.com

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# **Surgical Materials To Thiourea And Thiourea Derivatives**

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