

# A European pharmacotherapeutic agent Roflumilast exploring integrated preclinical and clinical evidences for SARS CoV-2 mediated inflammation to organ damage

yogendra Singh<sup>1</sup>, Noeraj Fuloria<sup>2</sup>, Shivkanya Fuloria<sup>2</sup>, Vetriselvan Subramanian<sup>3</sup>, Waleed Almalki<sup>4</sup>, Fahad Al-abbasi<sup>5</sup>, Imran Kazmi<sup>6</sup>, Sobhit Rajput<sup>6</sup>, and Gaurav Gupta<sup>7</sup>

<sup>1</sup>Maharishi Arvind College of Pharmacy

<sup>2</sup>AIMST University

<sup>3</sup>MAHSA University

<sup>4</sup>Umm Al-Qura University

<sup>5</sup>King Abdulaziz University

<sup>6</sup>Aligarh College of Pharmacy

<sup>7</sup>Sunsh Gyan Vihar University

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## Abstract

COVID-19 has spread globally, affecting almost 160 million individuals. Elderly and pre-existing patients (such as diabetes, heart disease and asthma), seems more susceptible to serious illness with COVID-19. Roflumilast was licensed for usage in the European Union in July 2010 as a phosphodiesterase-4 (PDE4) inhibitor. Roflumilast has been shown to decrease lipopolysaccharide-induced lung fibrosis, lung hydroxyproline, right heart thickening in animal prophylaxis. The current study reviewed existing data that the PDE-4 inhibitor protects not just lung tissues but also other major organ systems after COVID-19 infection by decreasing immune cell infiltration. These immune-balancing effects of roflumilast were related with a decrease in oxidative and inflammatory burden, response-1 suppression, and increased PKA/cAMP levels in lung and other organ tissue.

## Introduction:

COVID-19 has spread globally, affecting more than 216,867,620 documented occurrences and 4,567,537 fatalities in individuals. Elderly and pre-existing patients (such as diabetes, heart disease and asthma), seems more susceptible to serious illness with COVID-19. Due to changes in blood glucose and other diabetes-related complications, diabetic individuals who become infected can be hard to treat. A significant comorbidity towards the occurrence of SARS CoV-2-related COVID-19 includes inflammatory cytokine storm, acute kidney injury, myocarditis, thrombosis, ARDS, TIA mediated cerebral complication that ultimately leads to multi-organ failure. A recent case report illustrates an atypical initial presentation and subsequent complications throughout the middle-aged man. The person complained of abdominal discomfort and vomiting then was diagnosed with a severe acute renal damage. During the hospitalization, the study participant sustained a myocardial infarction and respiratory failure. This indicates that this patient most likely developed myocardial syndrome as a result of COVID-19-associated acute renal injury.<sup>1</sup> Notably, the main contributor to the above-mentioned consequences of organ damage and death is inflammation.

In an early stage of SARS CoV-2 attack, pro-inflammatory cytokines circulating including IFN- $\gamma$ , IL-1/2/6/8, and TNF- $\alpha$ , directly exacerbate the damage by attracting various leukocyte populations to the site of injury, resulting in a devastating inflammatory pathway. As a result of that excitation of immune cells including the