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# THE POTENTIAL OF ROSUVASTATIN IN STABILIZING LIPID PROFILE AND IMPROVING CLINICAL OUTCOMES IN COVID-19 PATIENTS WITH CORONARY HEART DISEASE

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## ARTICLE INFO

## ABSTRACT

*Introduction : The novel coronavirus disease (COVID-19) pandemic, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), remains a global challenge since December 2019 cause by its severe symptoms and high mortality rate. Some comorbidities are associated with clinical outcomes in COVID-19 patients, one of them is cardiovascular disease, including coronary heart disease (CHD). Statins are popularly used as the lipid controller in CHD patients. Not only controlling the lipid profile, statins also can reduce the inflammation process in COVID-19 patients. This review aims to determine the activity of statins and its potential to improve the clinical manifestation of COVID-19 patients with CHD. Methods : The method used in this paper is to examine and review the literature journal that has been published last 10 years. Results : Recent studies have shown that statins capable to control the lipid, also lowering the LDL cholesterol and increasing the HDL cholesterol. And other trials have shown that statin also have ability to reduce the inflammation and inhibit further cell damage by binding mpro, a protease produced by SARS-COV2. Conclusions: Based on those studies, we conclude that*

*statins have the potential effect as adjuvant therapy for clinical improvement in COVID-19 patients with CHD.*

## 1. INTRODUCTION

Corona Virus Disease 2019 (COVID-19) is caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) infection that leads to several symptoms such as fever, dry cough, tachypnea, [1] starting from second day to the 14th after the first exposure[2]. COVID-19 was first discovered in December 2019 in Wuhan, China and has been spread to more than 180 countries. [3] The first COVID-19 cases in Indonesia were identified on March 2nd 2020 and the positive-confirmed cases of COVID-19 continues to occur rapidly by then.

In Indonesia, thousands cases of COVID-19 have been identified. [4] Several studies have found that poor clinical symptoms of COVID-19 were caused by cytokine storm phenomenon that is characterized by high levels of pro-inflammatory cytokines such as Tumor necrosis factor-α (TNF-α), Interleukin-6 (IL-6), and other pro-inflammatory cytokines [5][6]

Several studies have reported that some comorbids such as chronic obstructive pulmonary disease (COPD), hypertension, cardiovascular diseases, and brain disorders can affect the condition of COVID-19 patients. Patients with any comorbidity yielded poorer clinical outcomes than those without.[2]

Coronary heart disease (CHD) is one of the comorbidities that can worsen clinical manifestation in COVID-19 patients. [7] This disease is caused by atherosclerotic plaques due to high level low density lipoprotein (LDL) cholesterol.[8] Dyslipidemia becomes one of the conditions that can increase cardiovascular disease incidence, including coronary heart disease that can worsen clinical manifestation in COVID-19 patients. So this makes regular lipid control necessary to evaluate in COVID-19 patients, especially for those with cardiovascular comorbidity.[9]

Statin is one of the popular medical therapy options to treat patients with coronary heart disease by lowering LDL cholesterol.[10] Besides lowering LDL cholesterol level, statins can also suppress the inflammation, including in COVID-19 patients. [11] In addition, statins can increase the level of High Density Lipoprotein (HDL) cholesterol and it can bind to SARS-CoV-2 Main proteinase (SARS-CoV-2 M Pro), a protease enzyme of SARS-CoV-2 that can cause tissue damage. [12] Those evidences support the potential effect of statin as an adjuvant therapy to control lipid profile and to improve clinical outcomes in COVID-19 patients with coronary heart disease.

## 2. METHODS

In this literature review, the authors searched Google Scholar and PubMed databases using some keywords: COVID-19, statin, and coronary heart disease. The latest journals are collected and then the selection process is based on chosen topic and the inclusion and exclusion criteria are considered to sort the results.

The inclusion criterias used in this study are: references that match with keywords and published in the last 10 years. Exclusion criteria are limitations in accessing journals. After finding the criterias, the contents of selected journals were used as references in

compiling this literature review. In total, there are 42 journals used as references in this study.

## 3. COVID-19 AND POTENTIAL OF ROSUVASTATIN IN CORONARY HEART DISEASE PATIENTS

### 3.1. COMORBIDITY LEADS TO CLINICAL DETERIORATION OF COVID-19

The COVID-19 pandemic presents an unprecedented challenge to public health due to its high morbidity and mortality rates. Currently, more than 180 countries have reported 10,533,779 COVID-19 cases with 512,842 deaths on the 2nd of July 2020. SARS COV-2 has infected various groups of ages, ethnicities, and sexes that spreads rapidly among the community. [3]

COVID-19 has a broad spectrum of clinical manifestations, ranging from asymptomatic to severe symptoms. There is 80% of mild to moderate COVID-19 cases globally, 13,8% of severe cases, and 6,1% of critical cases. Most of infected patients experience mild respiratory symptoms such as dry cough and sneezing, to the most severe symptoms such as difficulty breathing or shortness of breath. Other symptoms that can be found in COVID-19 patients are productive cough, sore throat, myalgia or arthralgia, chills, nausea or vomiting, nasal congestion, hemoptysis, conjunctival congestion, abdominal pain, and diarrhea. [13]

The initial course of COVID-19 begins with incubation period that lasts for about 3-14 days. The white blood cell count and lymphocytes are still normal or can be slightly decreased in the early period of COVID-19. In this period, most of patients usually do not show any clinical symptoms. SARS-COV-2 enter host cells via the angiotensin-converting enzyme 2 (ACE2) receptor, which is expressed in various human organs, include respiratory tract, gastrointestinal tract, and heart. Symptoms found in this phase are relatively mild. The second wave of symptoms occurs within four to seven days after the initial symptom. Difficulty of breath will be experienced by the patients in this phase as a result of lesions in lung parenchyma. Lymphopenia also can be found in this phase. Various inflammation markers and hypercoagulopathy tends to increase in this phase. Uncontrolled or unresolved inflammation can trigger cytokine storm that can lead to acute respiratory distress syndrome (ARDS), sepsis, and other complications.[13]

The pathophysiology of COVID-19 infection is not fully understood yet. Some studies have shown that the spike protein of SARS-COV-2 plays an important role in the viral invasion to target cells through Angiotensin Converting Enzyme 2 (ACE2) receptor as the port d' entree.[14] One of principal mechanism of the clinical deterioration in COVID-19 patients is cytokine storm phenomenon. This mechanism is supported by several studies that shows increasing level of some pro-inflammatory cytokines in patients with severe symptoms compared to patients with mild to moderate symptoms. [5][6]

In the study of Bo Diao et al , it was found that increasing level of Interleukin-6 (IL-6), Tumor Necrosis Alpha (TNF-α), and IL-10 in COVID-19 patients was directly comparable to the demand of patient for intensive care. [5]. Other study by Guang Chen et al also has stated that the level of pro-inflammatory cytokines such as IL-6, IL-10, and TNF-α was higher in COVID-19 patients with severe symptoms than in patients with

moderate symptoms.[6]. These two studies confirmed that cytokine storm may contribute in clinical deterioration of COVID-19 patients.

SARS-CoV-2 infects host cells by binding to the ACE-2 receptor then cause aggressive inflammatory response that leads to cytokine storm. After entering host cells, SARS-CoV-2 will release its RNA and begin to replicate. After replicating, new viruses will be released. The viral antigen will be recognized by the immune system, then trigger the response of Natural Killer (NK) cells and CD8 cytotoxic cells through major histocompatibility (MHC). Once this process occurs, pro-inflammatory cytokines will be produced and lead to cytokine storm. [15]

In addition to the pathogenicity of COVID-19, some comorbidities also affect the clinical manifestation of COVID-19 patients. Several studies have reported that COVID-19 patients with comorbidity show worse clinical condition with higher mortality rate. One study have shown that comorbidity is common (57,7%) among individuals with COVID-19. Patients with comorbid disease show more clinically fatal, 84,1% of patients have at least one comorbid disease.[3]

Comorbidities such as hypertension, COPD, cardiovascular disease, and diabetes are at risk to trigger clinical deterioration in patients with COVID-19. The United States was reported as a country with highest mortality rate worldwide with the top five comorbidities among the death cases of COVID-19: hypertension (55,4%), diabetes mellitus (37,3%), hyperlipidemia (18,5%), and coronary heart disease (12,4%) [2]

## 3.2. COVID-19 WITH CORONARY HEART DISEASE

Cardiovascular disease plays a role in increasing the risk of morbidity and mortality in patients with COVID-19 [30] Coronary heart disease is one of the major comorbidity that can worsen the clinical manifestation of COVID-19. In China, 14,2% of 44.672 confirmed COVID-19 patients have coronary heart disease. It was also reported that 5,8% of patients with severe symptoms had history of coronary heart disease compared to 1,8% patients with mild to moderate symptoms. Previous studies have also reported that coronary heart disease has identified as the 4th highest comorbidity in COVID-19 [7] [16]

Several studies have shown the high risk of clinical deterioration in COVID-19 patients with coronary heart disease. [17] The acute systemic inflammatory response and large amount of pro-inflammatory cytokines in COVID-19 patients with coronary heart disease can trigger plaque rupture, thrombus formation, and coronary varcular spasm that leads to myocardial infarction. Aggrasive inflammation will stimulate macrophages to produce collagenase, an enzyme that can degrade collagen which is one of the main components of atherosclerotic plaqu which is normally found in blood vessels, including coronary arteries. After the atherosclerotic plaque inside coronary artery ruptures, thrombus can easily form. Besides that, activated macrophage will produce tissue factors which are strong procoagulant that will surge the thrombus formation. Furthermore, SARS-CoV-2 can also cause direct damage to the endothelium dan vasculature, leading to force the thrombus formation. It is supported by several metalloproteinases that are related to cytokines recruitment and inflammation that will basically mediated in coronary heart disease. Combination of these processes lead to worse clinical outcomes in COVID-19 patients with coronary heart disease.[18]

### 3.3. STATIN AS A LIPID STABILISATOR FOR COVID-19 PATIENT WITH CORONARY HEART DISEASE

Coronary heart disease is triggered by atherosclerotic plaque that causes obstructive coronary artery and block the blood supply to the myocardium. This atherosclerotic plaque is built up because of the high level of LDL cholesterol which transport lipid from liver to peripheral tissues and the low level of High-Density Lipoprotein (HDL) cholesterol which transport lipid from peripheral tissues to liver. This plaque formation leads to myocardial hypoperfusion and infarction [8][19]

The use of statin is one of optional medical therapy in the treatment of coronary heart disease globally, it becomes the first line lipid-lowering agent. [10] Besides lowering the level of LDL, its other target in controlling lipid is to increase the level of HDL in patients with coronary heart disease. Statins reduce the level of LDL by inhibiting the HMG CoA reductase, an enzyme which is important in producing LDL. The inhibition of HMG CoA reductase will reduce the production of cholesterol in the liver and reduce the level of cholesterol in endoplasmic reticulum. This will result in the translocation of Sterol Regulatory Element Binding (SREB) from the endoplasmic reticulum to the golgi apparatus. SREB clevage is caused by some proteases and translocated to the nucleus and it will activate the transcription factors for some genes such as HMG CoA Reductase and LDL receptor genes that stimulates LDL receptors in the liver. Along with the increase of LDL receptors, the clearance of Apoliporotein A dan B which containing LDL dan VLDL will increase and affect the level of LDL in plasma. [20] [31] This will reduce the formation of atherosclerotic plaque in blood vessels. Besides lowering LDL level, statin also has the ability in inducing the level of HDL by enhancing the activation of peroxisome α proliferator receptor. [21] [32] [33] [34]

Moreover, statins can also prevent atherosclerotic plaque rupture that is common in COVID-19 patient with coronary heart disease. Statins have a mechanism of action that can reduce the production o Nitric Oxide Synthase (NOS) in the endothelium that can trigger inflammation and atherosclerotic plaque rupture in the vascular endothelium, including in the coronary arteries. Statin also have the ability in stabilizing atherosclerotic plaque and preventing the rupture. [40][41]

Several studies have demonstrated the effectiveness of statin in combating virus infection and its potential mechanism. In some virus infection, statin-induced reduction of cholesterol in the plasma membrane will supress the viral titer and inhibit the virus to invade the cells. These data indicate that cholesterol can also bring an effect on the early stages of infection. The virus will bind to the specific receptor that are concentrated in lipif rafts, an area of plasma membrane that has large amount of cholesterol.

Statins can reduce the percentage of cholesterol in the cell membrane, affecting receptor binding and altering the adhesion of viral agents into the host cells significantly. Lipid rafts are also involved in virus replication because it can concentrate the viral replication factors. [35] Lipid rafts with high concentrated cholesterol provide a platform for focusing ACE2 on host cell membrane by facilitating the binding of COVID-19 spike protein in order to invade the host cells. Statin is potential to be the lipid stabilitator as well as an antiviral for COVID-19 patients with coronary heart disease because of its therapeutic target is to disrupt the lipid rafts [36]

### 3.4. STATIN AS ANTI-INFAMMATORY AGENT FOR COVID-19 PATIENTS WITH CORONARY HEART DISEASE COMORBIDITY

Besides having a lipid controlling effect, statin can also play a role as an anti-inflammatory agent. Some studies have conducted that patients who consume statin show lower C-Reactive Protein (CRP) levels than the groups who do not receive statin therapy. [12]

The clinical deterioration in COVID-19 is caused by cytokine storm phenomenon that involves IL-6, TNF-α, IL-1β, and other pro-inflammatory cytokines [4][5]. Statin has the potency in reducing the level of pro-inflammatory cytokines and improving the clinical outcomes in COVID-19 patients through several mechanism. [11] Statin can reduce cytokines storm in COVID-19 patients by normalizing the expression of Myeloid differentiation primary *response* 88 (MyD88) gene which is the result of the interaction of SARS-CoV with Toll Like Receptor (TLR). The interaction of SARS-CoV with Toll Like Receptor (TLR) will activate NF-κB signaling pathway that will trigger the production of some pro-inflammatory cytokines. [22] Furthermore, statin can inhibit the progression of elevated pro-inflammatory levels (IL-6, TNF-α, IL-10, dan IL-8) in some cells such as mononuclear cells, synovial cells, and endothelial cells.[23] Through these two mechanism, statin can be an effective reductor for cytokine storm that causes acute respiratory distress syndrome (ARDS) in COVID-19, especially for patients with coronary heart disease.

### 3.5. ROLE OF STATIN IN INHIBITING TISSUE DAMAGE AND ENDOTHELIAL DISFUNCTION IN COVID-19 PATIENTS WITH CORONARY HEART DISEASE

Aside from controlling lipid profile and suppressing the inflammation, statin also have the ability to inhibit tissue damage that happens in COVID-19 by binding to Mpro, a molecule protease produced by SARS-COV-2.[12]

Invasion of SARS COV-2 can generate endothelial dysfunction due to its binding to the ACE-2 receptor in various organs.[24] Statin can improve the endothelial dysfunction by depressing the amount of adhesion molecules such as Intercellular Adhesion Molecule-1 (ICAM-1) and E-selectin; reducing the attachment of platelets dan leukocytes to the endothelial cells. These mechanisms will maintain the function of endothelium and improve the clinical outcomes of COVID-19 patients with coronary heart disease. [25] [26]

Statin can also act as an antioxidant that is important for restoring vascular redox balance that is initiated by the inflammatory process of COVID-19, this is based on the ability of statin to decrease redox-sensitive proinflammatory transcription factors like *Nuclear Factor Kappa B* (NF-κB). [27] Reactive oxygen species (ROS) has a negative impact to cardiac structure that can lead to contractility dysfunction, myocardial hypertrophy and fibrosis. Statin can reduce the production of ROS by suppressing the expression of miRNA-221 and miRNA-222 and promoting BH4 cofactor, which relates to endothelium nitric oxide synthase *3* (eNOS). Moreover, disrupted blood flow that is caused by atherosclerotic plaque can enhance ROS by increasing endothelium shear stress and stimulating *Krüppel-like Factor 2* (KLF-2) and activating cystathionine-lyase (CSE). Statin can also suppress the production of ROS by normalizing blood flow in blood vessels. [37] [38] [39]

Statin can also regulate some molecular pathways that control the activity of adenine dinucleotide phosphate oxidase and endothelium nitric oxide synthase which can help repairing the redox homeostasis. [38]

Other mechanism of statin in inhibiting tissue damage and endothelial dysfunction is impairing NOD-, LRR- and pyrin domain-containing protein 3 (NLRP3) inflammasome, that is potent pro-inflammatory structures in endothelium cells, by stimulating pregnane X receptor (PXR). By this way, statin will prevent tissue damage and maintain the endothelial function. [39]

Regeneration process becomes very important when endothelium damage happens as the result of severe tissue damage. This regeneration process is supported by endothelium progenitor cell (EPC) that will replace damaged cells naturally and have important role in preventing and treating cardiovascular disease. Statin has the ability to increase EPC as its pleiotropic effects. [39]

In addition, statin is able to reduce oxidized LDL. That supports the reduction of LDL atherogenicity. These antioxidant and LDL-lowering effects of statin will support tissue repair in COVID-19 patients with coronary heart disease. [37]

### 3.6. POTENTIAL OF ROSUVASTATIN IN CLINICAL IMPROVEMENT OF COVID-19 PATIENTS WITH CORONARY HEART DISEASE

The effect of statin in improving clinical outcomes of COVID-19 patients is supported by a study in China that conducted a trial of statin administration to 13,981 COVID-19 patients. The result of the study showed decreased C Reactive Protein (CRP), IL-6, and neutrophil level in statin group compared to control group. The decreased pro-inflammatory cytokines will effect the symptoms that associate to high inflammatory process which caused by COVID-19 such as fever, cough, fatigue, and all severe symptoms such as shortness of breath, respiratory distress syndrome, and other signs of severe pneumonia. This evidence proves the effectiveness of statin as an anti-inflammatory agent for COVID-19 patients. This mechanism is crutial to prevent the rupture of atherosclerotic plaque and the formation of thrombus due to aggrasive inflammation in COVID-19 patients with coronary heart disease. [42]

A study conducted by Zhang et al in China, shows shorter length of hospital stay, low demand for mechanical ventilation and intensive care unit (ICU) in statin group compared to control group. [28] This finding indicates the ability of statin in inhibiting the progression of COVID-19 directly by inhibiting viral replication with the inhibision mechanism of SARS-CoV-2 main protease (Mpro) and RNA-dependent RNA polymerase (RdRp) . Statins also can inhibit the progression of COVID-19 indirectly by its immunomodulatory effects, such as balancing the inflammation response by decreasing IL-6 via TLR-4, repairing endothelium function, as well as its lipid stabilizing effect by preventing the rupture of atherosclerotic plaque and the formation of thrombus due to the aggressive inflammation. [39] [40] [41]

Furthermore, statin can also enhance the immune response of macrophage that can be beneficial to ward off Macrophage Activation Syndrome (MAS), that is common in COVID-19 and causes hyperproduction of pro-inflammatory cytokines and can induce thrombosis. By optimizing the function of macrophage, statin can reduce the risk of thrombosis in COVID-19 by suppressing PAI-1 level in serum. Moreover, pulmonary

fibrosis can also be suppressed by statin with its ability in supressing TGF-β signaling pathway. [39]

Statin is one of pharmacological therapy that can improve clinical outcomes, reduce the demand of mechanical ventilator and shorten the length of hospital stay for COVID-19 patients with coronary heart disease based on some previous described mechanisms of statin.

In order to compare several types of statins on reducing LDL levels, Y J Jeong et al conducted a clinical trial that shows the performance of rosuvastatin is significantly more effective in lowering LDL cholesterol compared to other statins in low-intensity statins , moderate-intensity statins, and moderate to high intensity statins such as atorvastatin, simvastatin, pitavastatin, dan pravastatin as listed in tabel 1. [29]

Željko Reiner et al conducted a study in 2020 to compare the binding affinity between several statins and SARS COV-2 Mpro. Statins that involved in the study were rosuvastatin, pravastatin, simvastatin, pitavastatin, lovastatin, fluvastatin, and atorvastatin. The method of the study was in vitro molecular docking test. The result of the study shows that pitavastatin, rosuvastatin, and fluvastatin have stronger binding affinity compared to other statins.[12]

Tabel 1. Comparation of LDL-lowering efficacy of statins

| | | LDL cholesterol | | | | |
| | | Baseline (mg/dL) | Visit 1 (mg/dL) | Reduction rate (%) | References[11] | Statin classification (ACC/AHA 2013[17]) |
| | $n$ | | | | | |
| --- | --- | --- | --- | --- | --- | --- |
| Class A statins (high-intensity statins) | | | | | | |
| Atorvastatin (40 mg) | 52 | 149 ± 5 | 71 ± 4 | 51·3 ± 2·2 | >50%,[21] 48%,[8,22] 46%[23] | High |
| Rosuvastatin (20 mg) | 146 | 165 ± 4 | 83 ± 3 | 49·4 ± 1·6 | >50%[22,23] | High |
| Class B statins (moderate-to-high-intensity statins) | | | | | | |
| Atorvastatin (20 mg) | 290 | 147 ± 2 | 80 ± 2 | 44·4 ± 1·0 | 40%–50%[22,23,25] | Moderate |
| Rosuvastatin (10 mg) | 1366 | 150 ± 1 | 78 ± 1 | 47·6 ± 0·5 | 40%–50%[8,22,23,26] | Moderate |
| Class C statins (moderate-to-low-intensity statins) | | | | | | |
| Atorvastatin (10 mg) | 1118 | 138 ± 1 | 85 ± 1 | 38·4 ± 0·5 | 30%–40%[22,23,25] | Moderate |
| Pitavastatin (2 mg) | 650 | 145 ± 1 | 89 ± 1 | 38·0 ± 0·6 | 30%–40%[24] | Moderate |
| Pravastatin (40 mg) | 307 | 150 ± 2 | 101 ± 2 | 32·1 ± 0·9 | 30%–40%[8,22,26] | Moderate |
| Rosuvastatin (5 mg) | 104 | 141 ± 3 | 82 ± 3 | 41·5 ± 1·6 | 30%–40%,[23] >40%[25] | Moderate |
| Simvastatin (20 mg) | 326 | 137 ± 1 | 85 ± 1 | 36·5 ± 1·0 | 30%–40%[23–25] | Moderate |
| Class D statins (low-intensity statins) | | | | | | |
| Pravastatin (20 mg) | 324 | 150 ± 2 | 108 ± 2 | 27·6 ± 0·8 | 20%–30%[8,22,25] | Low |
| Pravastatin (10 mg) | 129 | 144 ± 2 | 111 ± 2 | 22·4 ± 1·2 | <20%,[25] 20%[22] | Low |
| Etcetera | | | | | | |
| Simvastatin (20 mg) + Ezetimibe (10 mg) | 209 | 151 ± 1 | 77 ± 2 | 51·4 ± 1·2 | | |
| Simvastatin (10 mg) + Ezetimibe (10 mg) | 434 | 162 ± 2 | 86 ± 1 | 42·6 ± 0·8 | | |

*Source: Jeong YJ, Kim H, Baik SJ, Kim TM, Yang SJ, Lee SH, et al. J Clin Pharm Ther. 2017;42(3):292–300*

Table 2. Comparisons of statins' binding affinity to SARS-CoV-2 Mpro and its amount of binding interaction

| No. | Statin | Affinity (kcal / mol) | Amount of interactions |
|---|---|---|---|
| 1. | Pitavastatin | -8,2 | 2 |
| 2 | Fluvastatin | -7,7 | 2 |
| 3. | Rosuvastatin | -7,7 | 7 |
| 4. | Lovastatin | -7,4 | 2 |
| 5. | Simvastatin | -7.0 | 2 |
| 6. | Atorvastatin | -6.8 | 3 |
| 7. | Pravastatin | -6.6 | 4 |

*Source: Willim HA, Ketaren I, Supit AI. e-CliniC [Internet]. 2020;8(28):237–45.*

Based on previous research results, it can be concluded that rosuvastatin is potential to improve clinical outcomes in COVID-19 patients with coronary heart disease through its multiple ability to significantly reduce the level of LDL, to prevent tissue damage by its high-binding affinity to SARS-CoV-2 Mpro, to suppress cytokine storm, and to repair endothelial dysfunction comparing to other statins. Therefore, based on these potential mechanisms, we recommend the use of rosuvastatin as a treatment for COVID-19 patients with coronary heart disease.

## 4. CONCLUSION

This literature review elucidates the role of statins as lipid stabilizer in coronary heart disease patients, cytokine storm suppressor, and SARS-CoV-2 Mpro binder, and its contribution in improving endothelial function in COVID-19 patients. This review also conclude that rosuvastatin was superior to other statin in reducing LDL level and reinforcing binding affinity to SARS-CoV-2 Mpro. Based on these reasons, rosuvastatin is potential to be a propitious treatment approach for COVID-19 patients with coronary heart disease. Therefore, further in vivo research related to the use of rosuvastatin in COVID-19 patients with coronary heart disease is still needed.

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**Conflict of Interest Statement:**

The author declares that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.