



# **EFFICACY AND SAFETY OF ATORVASTATIN IN SEPTIC PATIENTS**

**Thesis**

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# ABBREVIATIONS

ALT	Alanine aminotransferase
APACHE	Acute Physiology and Chronic Health Evaluation
APC	Activated protein C
ARDS	Acute respiratory distress syndrome
AST	Aspartate aminotransferase
ATP	Adenosine triphosphate
BUN	Blood Urea Nitrogen
CD	Cluster of differentiation
CPK	Creatine phosphokinase
CRP	C- reactive protein
CRRT	Continuous renal replacement therapy
CVP	Central venous pressure
CYP	Cytochrome P
DIC	Disseminated Intravascular Coagulopathy
DNA	Deoxyribonucleic acid
DO <sub>2</sub>	Oxygen delivery
DVT	Deep venous thromboembolism
EGDT	Early Goal directed therapy
FiO <sub>2</sub>	Fraction of inspired oxygen
GAGs	Glycosaminoglycans
G-CSF	Granulocyte colony-stimulating factor

<b>GM-CSF</b>	Granulocyte macrophage colony-stimulating factor
<b>HIV</b>	Human Immune Deficiency Virus
<b>HMGB1</b>	High-mobility group box 1
<b>HMG-CoA</b>	3-hydroxy-3-methylglutaryl-coenzyme A
<b>HO</b>	Heme oxygenase
<b>HR</b>	Heart rate
<b>ICAM</b>	Intercellular adhesion molecule
<b>ICU</b>	Intensive care unit
<b>IL</b>	Interleukin
<b>INF</b>	Interferon
<b>LDL</b>	Low density lipoprotein
<b>LFA</b>	Lymphocyte function-associated antigen
<b>LPS</b>	Lipopolysaccharide
<b>LVEF</b>	Left ventricular ejection fraction
<b>MABP</b>	Mean Arterial Blood Pressure
<b>MAPK</b>	Mitogen-activated protein kinase
<b>MCPI</b>	Monocytic chemoattractant protein
<b>MDR</b>	Multi Drug Resistant
<b>MHC</b>	Major Histocompatibility Complex
<b>MIF</b>	Macrophage inhibitory factor
<b>NO</b>	Nitric oxide
<b>PAF</b>	Platelet activating factor



<b>PAI-1</b>	Plasminogen activator inhibitor-1
<b>PaO2</b>	Arterial O2 tension
<b>PGE2</b>	Prostaglandin E2
<b>PGI2</b>	Prostaglandin I2
<b>POAP</b>	Pulmonary artery occlusion pressure
<b>PPAR</b>	Peroxisome proliferator-activated receptor gamma
<b>PT</b>	Prothrombin time
<b>PTT</b>	Partial thromboplastin time
<b>SaO2</b>	Arterial oxygen saturation
<b>SBP</b>	Systolic Blood Pressure
<b>SIRS</b>	Systemic inflammatory response syndrome
<b>SOFA</b>	Sequential organ failure assessment
<b>Scvo2</b>	Central venous O2 saturation
<b>Svo2</b>	Mixed venous O2 Saturation
<b>TF</b>	Tissue factor
<b>Th cell</b>	T helper cell
<b>TLR</b>	Toll like receptor
<b>TNF</b>	Tumour necrosis factor
<b>VO2</b>	Oxygen uptake
<b>WBC</b>	White blood cell

# INTRODUCTION

Sepsis is considered one of the leading causes of mortality in the hospital setting. Although some advances have been made in treating patients with sepsis, the mortality of patients with sepsis remains extremely high (**Stephen et al., 2011**).

Sepsis is a process consisting of numerous inflammatory cascades and it is initiated by the presence of bacterial toxins and results in systemic inflammation and multiple organ and tissue damage. Cytokines have a prominent role in the defense mechanisms of the host. Their production is mediated by numerous metabolic pathways, which are independent from each other. In order to treat sepsis effectively, intervention should be made at multiple levels, as controlling just one or two pathways does not impede the overall process (**Terblanche et al., 2007**).

Inhibitors of 3-hydroxy-3-methylglutaryl coenzyme A reductase, namely statins, are a class of drugs used for their ability to lower cholesterol levels. Their primary indication is the prevention of cardiovascular disease. Recently statins have been attributed to have anti-inflammatory and immunomodulatory pleiotropic effects. They inhibit the synthesis of products of mevalonate pathway such as isoprenoids and geranyl-geranylpyrophosphate (**Gao et al., 2008**).

They also modify the intercellular interactions and the cellular chemotaxis of the immune system. Furthermore, statins reduce the release of cytokines and acute-phase proteins. They demonstrate antioxidant properties and an anti-apoptotic action,

contributing to the stabilization of the atheromatic plaque, modifying cell activity by inhibition of the expression of certain genes and participate in various other mechanisms of the inflammatory response (**Gao et al., 2008**).

Having all these properties, statins have been suggested as an adjunct in the treatment of patients with sepsis. Thus, we sought to examine the efficacy and safety of atorvastatin in the treatment of patients with sepsis.



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# INTRODUCTION

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