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Review Article

Anti-inflammatory Mechanisms Beyond Cholesterol-Lowering Capabilities of Statins: Evidence from *in vitro* and *in vivo* Studies

Running Title: Statin and anti-inflammatory effects

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Abstract

Hypercholesterolemia is a major contributor to the risk of developing a range of severe health conditions, including cardiovascular diseases (CVDs), brain diseases, nephropathy, retinopathy, and neuropathy. The primary function of statins is to mitigate cholesterol content via suppressing 3-hydroxy-3-methylglutaryl coenzyme A reductase (HMG-CoA-R). This study aims to evaluate the anti-inflammatory mechanisms underlying the cholesterol-reducing capabilities of statins. The effects of statins beyond their cholesterol-lowering action are referred to as pleiotropic effects. Anti-inflammatory effects are among the pleiotropic roles of statins. These effects include lowering triglyceride (TG) concentrations, elevating high-density lipoprotein cholesterol (HDL-C) and interleukin 10 (IL-10), and downregulating inflammatory markers. Part of the anti-inflammatory effects results from the suppression of the activity of the Rho and Ras protein families, thus inhibiting nuclear factor kappa-light-chain enhancer of activated B cells (NF-κB) and activating protein-1 (AP-1). In recent years, the anti-inflammatory effects of atorvastatin, simvastatin, and rosuvastatin have been studied more extensively than those of other statins. In fact, these statins are more prominent.

Keywords: Statin, TG, HDL-C, Rho, Ras, NF-κB, AP-1, Anti-inflammatory.

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Introduction

Hypercholesterolemia is a major contributor to the risk of developing a range of severe health conditions, including cardiovascular diseases (CVDs), brain disorders, nephropathy, retinopathy, and neuropathy (1, 2). The main task of statins is to lower cholesterol levels by inhibiting 3-hydroxy-3-methylglutaryl coenzyme A reductase (HMG-CoA-R) (3). Atorvastatin, lovastatin, fluvastatin, simvastatin, pravastatin, pitavastatin, and rosuvastatin are commonly used statins in clinical practice (4). Atorvastatin, lovastatin, fluvastatin, simvastatin, and pitavastatin are lipophilic statins with high permeability in non-hepatic cells. In contrast, hydrophilic statins, such as rosuvastatin and pravastatin, have low permeability to non-hepatic cells. Generally, the effects of statins that extend beyond cholesterol synthesis inhibition are referred to as pleiotropic effects. Statins show anti-inflammatory effects as part of their multiple pleiotropic roles (5). According to the Adult Treatment Panel III (ATP III), rosuvastatin and atorvastatin are more effective than other statins in lowering total cholesterol and low-density lipoprotein cholesterol (LDL-C) (6). This study aims to evaluate the anti-inflammatory mechanisms beyond the cholesterol-mitigating capabilities of statins. Understanding the anti-inflammatory effects beyond statins' cholesterol-synthesis inhibition helps clarify their role in the abatement of cardiovascular, cerebral, neuronal, hepatic, renal, and ocular complications in patients.

Methods

This study is a narrative review. A comprehensive search was conducted across PubMed, MeSH, Scopus, and Google Scholar to identify relevant studies examining the anti-inflammatory effects of statins and their cholesterol-lowering properties. Studies published between 2010 and 2025 were included. The keywords used were statin, atorvastatin, rosuvastatin, pitavastatin, fluvastatin, simvastatin, pravastatin, lovastatin, cholesterol, triglycerides, HDL-C, GGPP, FPP, Rho, RhoA, ROCK, Ras, NF-κB, IL-1β, TNF-α, IL-6, IL-8, IL-18, IFN-γ, MCP-1, VCAM-1, selectin, TLR-4, MMP, PAI-1, CRP, and COX-2. The initial investigations were conducted in both preclinical and human clinical trial phases. Additionally, the review studies were thoroughly examined. Approximately 120 articles were assessed, of which approximately 84 were selected for further review.

Results

Statins as Potent Anti-Inflammatories

Statins not only lower cholesterol and LDL-C levels but can also reduce triglyceride (TG) levels. Conversely, they can augment high-density lipoprotein cholesterol (HDL-C). Given that fatty acids and their metabolites, such as diacylglycerol (DAG), activate protein kinase C (PKC), and that activation of PKC leads to the activation of the nuclear factor kappa-light-chain enhancer of activated B cells (NF-κB), (7, 8). Statins may help lessen TG and raise high-density lipoprotein cholesterol HDL-C by attenuating the synthesis of triglyceride metabolites. The role of NF-κB will be explained in more detail below.

Andevari et al. reported that atorvastatin (20 mg/day) decreased TG in patients with type 2 diabetes mellitus

(T2DM) and prediabetes over 12 weeks. However, it improved HDL-C levels (9). Velarde et al. reported that triglyceride (TG) and apolipoprotein B (Apo-B) concentrations were reduced in women with metabolic syndrome after 6 and 12 weeks of atorvastatin 80 mg (10). In a study published by Ciucanu et al., increasing the dose of rosuvastatin (5, 10, 20, and 40 mg) resulted in a further decrease in the content of TG and Apolipoprotein B100 (Apo-B100), along with an increase in the concentrations of HDL-C and Apolipoprotein A1 (Apo-A1) (11). Furthermore, Xu et al. reported that 12 weeks of simvastatin (20 mg/day) treatment in patients with coronary heart disease (CHD) reduced triglyceride (TG) levels (12). Moreover, Farnier et al. reported that HDL-C concentrations were elevated in dyslipidemic patients after 12 weeks of simvastatin (10, 20, or 40 mg) (13).

In a study by Aydin et al., rosuvastatin (20 mg/day) notably increased HDL-C in patients with ST-elevation myocardial infarction (STEMI) (14). Karkeet et al. reported that administration of rosuvastatin at 20 mg daily for six months led to a substantial decrease in TG concentrations in patients with metastatic prostate cancer (mPC) (15).

Besides cholesterol production, the mevalonate pathway also produces isoprenoid-like compounds, such as farnesyl pyrophosphate (FPP) and geranylgeranyl pyrophosphate (GGPP). Consequently, statins hinder the production of both cholesterol and isoprenoids (16). The large family of Ras GTPases includes two members. For activation, these G proteins must be transported intracellularly, positioned in the plasma membrane, and interact with various protein effectors; this process requires isoprenylation (17). Members of the Ras and Rho families serve as primary substrates for isoprenylation. GGPP is required for the activation of the Rho family, whereas FPP is essential for the activation of the Ras family (18, 19). Inside non-liver cells, such as those associated with blood vessels, lipophilic statins, particularly, block the functioning of Ras and Rho family proteins. The inhibition results in the accumulation of their inactive forms within the cytoplasm, which helps attenuate inflammation and vascular issues (20). Members of the Ras and Rho family participate in the inflammation of blood vessels (21, 22). One factor activated in the Ras and Rho signaling pathways is NF-κB, which upregulates a wide range of inflammatory mediators (23). The NF-κB-triggered constituents are listed below.

The Role of the Rho Family in Vascular Inflammation

RhoA is part of the Rho family, which plays a crucial role in the inflammatory process. RhoA forms a complex with Rho-dependent kinase (ROCK), which subsequently activates NF-κB (24).

Relationship Between Statins and NF-κB Target Factors

NF-κB upregulates a wide range of inflammatory factors, as listed below.

Inflammatory Cytokines

NF-κB enhances the production of inflammatory cytokines, such as tumor necrosis factor alpha (TNF-α), interleukin-1 beta (IL-1β), interleukin-6 (IL-6), interleukin-8 (IL-8), interleukin-18 (IL-18), and interferon-gamma (IFN-γ). TNF-α and IL-1β can be released from vascular endothelial cells and exert autocrine effects. Consequently, by engaging their

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receptors on endothelial cell surfaces, they activate NF-κB a second time and upregulate inflammatory mediators, thereby promoting the progression of vascular pathologies (25).

Du et al. declared that simvastatin attenuated apoptosis in endothelial progenitor cells caused by TNF-α (26) **Table 2**. Moreover, Liu and colleagues showed that the use of atorvastatin at doses of 20 mg and 40 mg in CAD (coronary artery disease) patients with coronary atherosclerosis diminished TNF-α (27) **Table 1**.

Table 1. Research into the impact of atorvastatin on inflammatory factors

Study	Type of statin	Doses	Model	Downregulation of various inflammatory factors
(27)	Atorvastatin	20 and 40 mg/day	in vivo CAD patients	TNF-α
(28)	Atorvastatin	-	in vitro PBMCs of T2DM patients	IL-1β secretion
(31)	Atorvastatin	10 mg/day	in vivo CKD patients	IL-6, IL-8
(33)	Atorvastatin	20 mg/day	in vivo T2DM patients	IL-18
(36)	Atorvastatin	20 mg/day	in vivo ACS patients	IFN-γ
(42)	Atorvastatin	20 mg/day	in vivo Overweight/obese women with polycystic ovary syndrome	MCP-1, IL-6
(79)	Atorvastatin	1 μmol/l	in vitro Endothelial cell model	VCAM-1 expression
(46)	Atorvastatin	10 mg/day	in vivo Young subjects with successfully repaired coarctation of the aorta	VCAM-1
(49)	Atorvastatin	40 mg/day	in vivo ACS patients	E-selectin
(55)	Atorvastatin	10 mg/kg/d	in vivo spontaneously hypertensive rats	MMP-2, MMP-9
(57)	Atorvastatin	0.001–10 μmol/l	in vitro HUVECs	TF expression
(59)	Atorvastatin	80 mg/day	in vivo Platelet-derived microparticles in patients with peripheral arterial occlusive disease	TF, P-selectin expression
(80)	Atorvastatin	0.3 μmol/l	in vitro HUVECs	PAI-1
(66)	Atorvastatin	10 mg/day 40 mg/day	in vivo Renal patients	CRP
(68)	Atorvastatin	0.1–10 μmol/l	in vitro HUVECs	COX-2 expression and activity

Researchers led by Dosanjos found the in vitro stimulation of atorvastatin in peripheral blood mononuclear cells (PBMCs) from patients with T2DM blocked the secretion of IL-1β from these cells (28) **Table 1.** In a study conducted by Erkan et al., fluvastatin 40 mg/day notably lowered TNF-α and IL-1β in patients positive for antiphospholipid antibodies (29) **Table 3.** Moreover, Marino and colleagues demonstrated that simvastatin diminished the production of IL-8 by neutrophils in individuals with dyslipidemia (30) **Table 2.**

Table 2. Research into the effects of simvastatin on inflammatory factors

Study	Type of statin	Doses	Mode	Downregulation of various inflammatory factors
(26)	Simvastatin	10^{-7} and 10^{-8} mol/l	in vitro EPCs	TNF-α
(30)	Simvastatin	-	in vitro Neutrophils in dyslipidemic patients	IL-8
(32)	Simvastatin	10 μmol/l	in vitro Vascular SMCs	TNF-α, IL-18
(81)	Simvastatin	20 mg/day	in vivo patients with myocardial injury	TNF-α, IL-6, IL-8
(43)	Simvastatin	100 μmol/l	in vitro HUVECs	MCP-1 expression
(44)	Simvastatin	80 mg/day	in vivo patients undergoing esophagectomy	MCP-1
(51)	Simvastatin	40 mg/day	in vivo Hypercholesterolemic patients	IL-6, IFN-γ, E-selectin, and P-selectin
(53)	Simvastatin	20 mg/day	in vivo Obese women	MMP-9
(82)	Simvastatin	20 mg/day	in vivo T2DM patients	CRP
(65)	Simvastatin	40 mg/day	in vivo Hypercholesterolemic men	CRP
(83)	Simvastatin	10 μmol/l	in vitro 3T3-L1 differentiated adipocytes	PAI-1
(68)	Simvastatin	0.1–10 μmol/l	in vitro HUVECs	COX-2 expression and activity

Fassett et al. stated that patients with chronic kidney disease experienced decreased blood concentrations of IL-6 and IL-8 when taking 10 mg/day of atorvastatin (31) **Table 1.** Simvastatin was shown by Lin et al. to counteract the enhanced growth of

cultured aortic smooth muscle cells caused by a combination of TNF-α and IL-18. (32) **Table 2.**

Kadoglou and colleagues reported that atorvastatin (20 mg/day) reduced serum IL-18 levels in patients with T2DM (33) **Table 1.** Furthermore, Liu et al. found that IL-18 concentrations declined in patients with acute coronary syndrome (ACS) after receiving fluvastatin treatment (34). In a study by Fujioka et al., pitavastatin (1-2 mg/day) was found to attenuate serum IL-18 levels in hypercholesterolemic subjects (35) **Table 3.**

Table 3. Studies on the effects of rosuvastatin, fluvastatin, pitavastatin, pravastatin, and lovastatin on inflammatory factors

Study	Type of statin	Doses	Model	Downregulation of various inflammatory factors
(34)	Fluvastatin	40 mg/day	in vivo ACS patients	IL-18
(35)	Pitavastatin	1-2 mg/day	in vivo Hypercholesterolemic subjects	IL-18
(37)	Rosuvastatin	20 mg/day	in vivo Blood monocytes in healthy subjects	TLR-4, TNF-α expression
(63)	Pitavastatin	2 mg/day	in vivo Hyperlipidemic patients	MCP-1
(47)	Rosuvastatin	10 mg/day	in vivo Ankylosing spondylitis patients	ICAM-1, IL-6, TNF-α
(84)	Rosuvastatin	40 mg/day	in vivo Patients with mixed dyslipidaemia	IL-8
(29)	Fluvastatin	40 mg/day	in vivo Antiphospholipid antibody-positive patients	TNF-α, IL1β
(54)	Rosuvastatin	10 mg/day	in vivo CHF patients	MMP-2, MMP-9
(58)	Rosuvastatin	20 mg/day	in vivo Hypercholesterolemic patients	TF activity
(62)	Rosuvastatin Pitavastatin	2.5 mg/day 2 mg/day	in vivo Patients with T2DM	PAI-1, TNF-α
(64)	Pravastatin	40 mg/day	in vivo HIV-infected persons with combined hyperlipidemia	PAI-1
(82)	Rosuvastatin	20 mg/day	in vivo T2DM patients	CRP
(66)	Lovastatin	10 mg/day 40 mg/day	in vivo Renal patients	CRP

IFN-γ is a cytokine upregulated by NF-κB and plays a substantial role in overseeing immune responses. Wang et al. reported that administering atorvastatin (20 mg/day) in patients with acute coronary syndrome (ACS) reduced serum IFN-γ levels (36) **Table 1. Toll-Like Receptor 4 (TLR-4)**

Additionally, NF-κB upregulates toll-like receptor 4 (TLR-4) in macrophages, endothelial cells, and vascular smooth muscle cells (VSMCs). The TLR-4 signaling pathway again directs NF-κB. R. McGuire et al. reported that TLR-4 expression declined with rosuvastatin (20 mg/day) in blood monocytes of healthy subjects; furthermore, rosuvastatin downregulated plasma TNF-α levels (37) **Table 3.** Alizadeh-Tabrizi et al. stated that atorvastatin lowered paraquat-induced cytotoxicity in alveolar macrophages by decreasing TLR-4 expression (38).

Chemokines and Cell Adhesion Molecules

NF-κB amplifies the upregulation of monocyte chemoattractant protein-1 (MCP-1) and various cell adhesion molecules, including intracellular adhesion molecule-1 (ICAM-1), vascular cell adhesion molecule-1 (VCAM-1), and selectins (39). These molecules enable monocytes and T lymphocytes to adhere to and penetrate the vascular endothelium, eliciting an inflammatory response. On endothelial cells, ICAM-1 interacts with two distinct ligand pairs: CD11a/CD18 and CD11b/CD18. These ligands are abundantly expressed in leukocytes, leading to subsequent leukocyte attraction and incorporation into endothelial cells (40). Upon entering the tissue, monocytes transform into macrophages. These macrophages can engulf LDL-C particles, leading to their conversion into foam cells. The formation of foam cells enlarges the extracellular matrix and contributes to the development of atherosclerotic plaques. Additionally, macrophages and T lymphocytes play a crucial role in the

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progression of inflammation by releasing adhesion molecules, chemokines, proinflammatory cytokines, and growth factors (41).

Research conducted by Sathyapalan et al. found that following a 12-week course of atorvastatin 20 mg in overweight or obese women with polycystic ovary syndrome, plasma levels of MCP-1 and IL-6 declined substantially (42) **Table 1.** Simvastatin has been shown to reduce inflammation in human umbilical vein endothelial cells (HUVECs) by dampening IL-33-induced MCP-1 mRNA and protein production, as well as activating c-Jun N-terminal kinase (JNK) and c-Jun phosphorylation, as reported by Umebashi et al. (43). Moreover, Shyamsundar et al. showed that intake of simvastatin at 80 mg resulted in a notable reduction of plasma MCP-1 levels by day 3 in patients who were undergoing esophagectomy (44) **Table 2.** Chen et al. found that giving of pitavastatin at a dosage of 3 mg/kg in low-density lipoprotein receptor knockout (LDLR-/-) mice on a high-fat diet (HFD) substantially lowered the contents of MCP-1 and TNF-α (45). In a study by Brili et al., atorvastatin 10 mg/day reduced VCAM-1 levels in young individuals who had undergone successful repair of coarctation of the aorta (46) **Table 1**. Garg et al. demonstrated that treatment with rosuvastatin (10 mg/day) significantly decreased levels of ICAM-1, IL-6, and TNF-α in patients with ankylosing spondylitis (47) **Table 3**. Du et al. demonstrated that atorvastatin downregulated ICAM-1 in atherosclerotic rabbits (48).

E-selectin and P-selectin are other cell adhesion molecules. In a study published by Altun et al., taking atorvastatin 40 mg per day for 3 months in patients with acute coronary syndrome (ACS) resulted in notable decreases in E-selectin (49) **Table** 1. Also, Shen et al. published that rosuvastatin substantially lowered neuroinflammation in the brains of septic mice by downregulating IL-6, MCP-1, VCAM-1, E-selectin, and TNF-α (50). Furthermore, Barale and colleagues demonstrated that simvastatin (40 mg/day) in hypercholesterolemic patients reduced IL-6, IFN-γ, E-selectin, and P-selectin (51) **Table 2.**

Extracellular Matrix Metalloproteinases (MMPs)

Atherosclerotic plaques are degraded by metalloproteinases found in the extracellular matrix (MMPs), which also play a key role in the development of atherosclerosis and glomerulosclerosis (52). In a study by Andrade et al., obese women treated with simvastatin showed substantial decreases in MMP-9 levels (53) **Table 2.** Tousoulis and colleagues declared that the use of rosuvastatin in patients with chronic heart failure significantly lowered the concentrations of MMP-2 and MMP-9 (54) **Table 3.** In a study by Lu et al., spontaneously hypertensive rats showed a attenuation in the expression of MMP-2 and MMP-9 following daily treatment with atorvastatin at a dose of 10 mg/kg. (55) **Table 1**.

Platelet Tissue Factor (TF)

Platelet tissue factor (TF) is the most crucial mediator in blocking the coagulation cycle. Consequently, it significantly triggers the conversion of prothrombin to thrombin during blood clotting (56). Martínez-Sales et al. demonstrated that atorvastatin counteracts thrombin-induced TF expression in endothelial cells (57) **Table 1.** Panes and colleagues stated that administering rosuvastatin at a dose of 20 mg per day

for one month neutralized platelet tissue factor activity in hypercholesterolemic patients (58) **Table 3.** Also, atorvastatin administration has been shown to lower thrombin generation and the expression of TF and P-selectin on microparticles in patients with peripheral arterial occlusive disease, according to Mobarrez et al. (59) **Table 1.**

Plasminogen Activator Inhibitor-1 (PAI-1)

Plasminogen activator inhibitor-1 (PAI-1) hinders the breakdown of blood clots by inhibiting plasminogen activators (60). Ni et al. reported that simvastatin and atorvastatin blocked glucose-triggered PAI-1 expression by modulating the activities of RhoA and NF-κB in cardiac microvascular endothelial cells (61). Moreover, Yanagi et al. demonstrated that rosuvastatin (2.5 mg/day) and pitavastatin (2 mg/day) reduced PAI-1 and TNF-α in T2DM patients. There were no notable differences between the two drugs in their effects on reducing these factors (62). Furthermore, Nomura et al. found that pitavastatin attenuated PAI-1, E-selectin, and VCAM-1 in patients with T2DM (63). Fichtenbaum et al. reported that PAI-1 concentrations declined in individuals taking 40 mg/day of pravastatin (64) **Table 3**.

C-Reactive Protein (CRP)

C-reactive protein (CRP) is another inflammatory agent induced by NF-κB. It notably affects endothelial cell inflammation. Bellia et al. demonstrated that administering 20 mg of rosuvastatin or simvastatin reduced CRP in T2DM patients. In a study published by Nilsson et al., simvastatin 40 mg/day significantly lowered CRP concentrations in hypercholesterolemic individuals (65). Also, in a study by Soleymani et al., this reduction effect was observed in patients with renal disease taking atorvastatin 10 mg/day and lovastatin 40 mg/day (66) **Table 1** and **3.**

Cyclooxygenase-2 (COX-2)

The next factor is the enzyme cyclooxygenase-2 (COX-2), which contributes to the development of inflammation by producing prostaglandins and thromboxanes (67). Massaro and colleagues demonstrated that expression and activity of COX-2 were attenuated in human endothelial cells via atorvastatin and simvastatin. This effect was counteracted by mevalonate and GGPP (68) **Table 1** and **2.** Zhang et al. reported that simvastatin (0.1, 1, or 10 μM) downregulated COX-2 in human mesangial cells (69).

Published studies indicate that statins effectively downregulate a wide range of inflammatory factors.

In addition to their effects on inflammatory cytokines and chemokines, Statins also increase IL-10 levels, an anti-inflammatory cytokine that suppresses NF-κB and, consequently, the expression of proinflammatory cytokines. Hernández et al. demonstrated that atorvastatin (10 or 40 mg/day) elevated IL-10 in hypercholesterolemic patients (70). In a study by Maneechotesuwan et al., simvastatin (20 mg/day) demonstrated the same effect in patients with chronic obstructive pulmonary disease (COPD) (71). Moreover, Liu et al. declared that fluvastatin at a dosage of 40 mg per day substantially enhanced the concentrations of IL-10 in patients with ACS (34) **Table 3**. Also, Ozguler et al. published that rosuvastatin (20 mg/day) upregulated IL-10 levels in patients undergoing coronary bypass surgery (72).

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The Involvement of the Ras Family in Vascular Inflammation

According to the information above, the inhibitory effects of statins on Ras activity may be linked to their ability to block FPP synthesis. Ras triggers the activation of various components, including MAPKKKs, MAPKKs, and mitogen-activated protein kinases (MAPKs), such as JNK, p38, and ERK. The phosphorylation of IkB is initiated by these MAPKs, causing it to separate from NF-κB and move from the cytoplasm to the nucleus. Subsequently, NF-κB upregulates inflammatory factors (73). Moreover, the MAPKs can activate the transcription factor activating protein-1 (AP-1) in the nucleus. AP-1 augments the production of cytokines and inflammatory agents, including TNF-α, IL-1β, IL-6, IL-8, VCAM-1, ICAM-1, transforming growth factor-β (TGF-β), and Bax (74). TGF-β notably increases the synthesis of extracellular matrix proteins, including fibronectin, collagen, proteoglycans, and PAI-1. Consequently, this leads to the expansion of the extracellular matrix and a reduction in arterial wall flexibility (75). On the other hand, Bax is a protein that is involved in apoptosis. Bax can contribute to vascular complications by inducing endothelial cell apoptosis (76). Chen and colleagues demonstrated that pitavastatin suppressed AP-1 signaling in human T cells, leading to potent anti-inflammatory effects (77). In a study by Fu et al., simvastatin inhibited sepsis-induced apoptosis in HUVECs by downregulating Bax (78).

Conclusion

Anti-inflammatory effects are part of the pleiotropic roles of statins. These effects include attenuation of triglyceride (TG) concentrations, increasing high-density lipoprotein cholesterol (HDL-C) and interleukin-10 (IL-10), and downregulating inflammatory markers. Part of the anti-inflammatory effects results from the suppression of the activity of the Rho and Ras protein families **Figure 1**. In recent years, the anti-inflammatory effects of atorvastatin, simvastatin, and rosuvastatin have been studied more extensively than those of other statins. In fact, these statins are more prominent in this regard. Given the reported anti-inflammatory effects of statins, future studies can examine these effects in more detail, particularly through systematic and meta-analytic reviews. These studies would be better suited to examine in detail the effects of a specific statin type in a specific study model, especially in patients. Of course, given that endocrinologists are increasingly using atorvastatin and rosuvastatin to prevent cardiovascular complications, more clinical trials are being conducted on the relationship between these drugs and inflammatory agents.

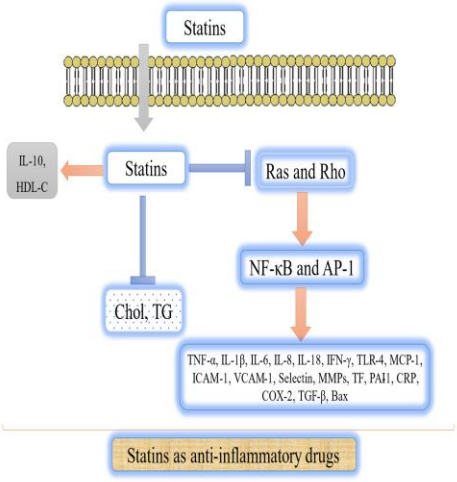

Fig.1. Anti-inflammatory mechanisms of statins. The anti-inflammatory effects of statins are due to downregulation of Ras, Rho, Chol, and TG and upregulation of IL-10 and HDL-C.

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