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## Experimental Atherosclerosis Reductions by Hypolipidemic Drugs

Silvia Saiuli Miki Ihara<sup>1</sup>, Anita L R Saldanha<sup>1</sup>, Leonor do Espírito Santo Almeida Pinto<sup>1</sup>, Ieda Edite Lanzarini Lopes<sup>1</sup>, José Paulo Novazzi<sup>1</sup>, Luis Alberto Barboza<sup>1</sup>, Ana Paula Pantoja Margeotto<sup>1</sup>, André L Varela Gasparoto<sup>2</sup> and Tania Leme da Rocha Martinez<sup>1\*</sup>

<sup>1</sup>Nephrology Department, BP - A Beneficência Portuguesa de São Paulo, São Paulo, Brazil

<sup>2</sup>Intensive Care Unit, BP - A Beneficência Portuguesa de São Paulo, São Paulo, Brazil

**\*Corresponding author:** Tania Leme da Rocha Martinez, BP, Rua Comandante Ismael Guilherme, 358-Jardim Lusitânia, 04031-120 - São Paulo - SP, Brazil.

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### Abstract

This article summarizes the series of experiments done in New Zealand rabbits that developed aortic lesions being fed a high cholesterol diet, varying from 0,5% to 1,5% of the chow. Planimetry in statin treated rabbits showed a reduction of the lesions. Interpreted mainly by its antioxidant properties the probucol drug presented the bigger reduction of the aortic atherosclerotic lesions. The lesions could be proven to be richer in Calcium by a specific coloring technique, von Kossa. This was found in the deep layer of the intima. Fibrates as well were tested and the main observation was the reduction in fibrinogen concentration in this particular experimental model. These findings raised hypothesis leading to the action of antithrombotic drugs. Aiming at the observation of antithrombotic action another group was submitted to aspirin treatment. Although it did not have any effect on the extension of the aortic atherosclerotic lesions, a reduction in the blood aggregation was significant. This effect was interpreted as a probable protection factor in case of ruptured plaques, diminishing the chance of thrombus formation and aortic occlusion in this hypercholesterolemia rabbits. This was confirmed by electron microscopy

showing less fibrin formation on the endothelial surface. It is noteworthy to document that the total cholesterol level ranged from 1400 to 1500 mg% in the high cholesterol diets in the animals and thus causative of the aortic atherosclerotic lesions.

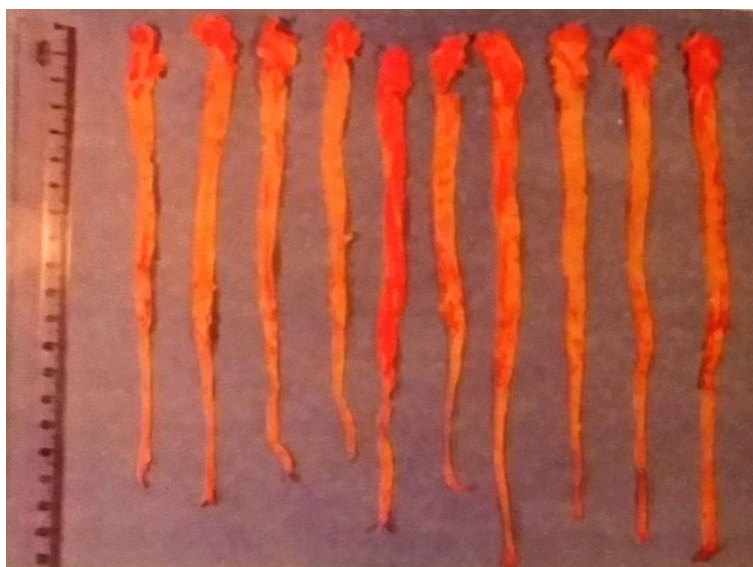
### Keywords

Pathologic Anatomy; Experimental atherosclerosis; Hypolipidemic drugs; New Zealand rabbits; Cholesterol

## Introduction

### Experimental studies of antiatherogenic pharmacological effects of the experimental atherosclerosis laboratory

The experimental atherosclerosis laboratory has proven through experiments with New Zealand rabbits fed a hypercholesterolemia diet at 0.5% to 1.5% cholesterol, the drug action has also been analyzed for the installation and development of atherosclerosis [1-5] (Figure 1). It is noteworthy to document that the total cholesterol level ranged from 1400 to 1500 mg% in the high cholesterol diets in the animals and thus causative of the aortic atherosclerotic lesions. In independent experiments, some drugs with different therapeutic approaches were used in the development of experimental atherosclerosis: Simvastatin, Probucol, Gemfibrozil and Aspirin.



**Figure 1:** Aortas of rabbits fed a hypercholesterolemic diet, cordoned with Sudam III, observing extensive lipid deposition.

**Simvastatin:** at a dose of 10 mg/day, when administered to rabbits with a diet supplemented with cholesterol, showed a reduction in serum cholesterol level, although it did not interfere in the extent of the atherosclerotic lesion in the aorta of these animals. However, lesions with lower volume were installed, with macrophages containing fewer lipids and distributed more homogeneously in the atheromatous plaques [6-10] (Table 1, Figure 2).

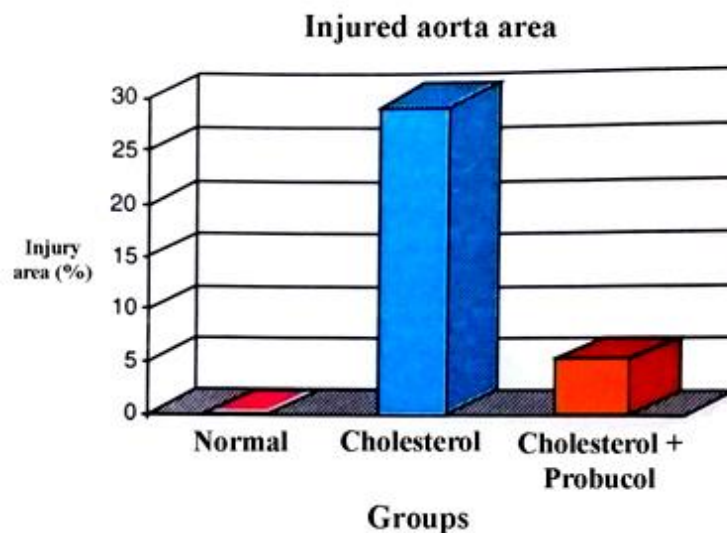
Probucol: at a dose of 1000 mg/day, it has an antioxidant effect, directly interfering in the development of the lesion, with a smaller area of aortic area with atherosclerotic lesions [7,11] (Figure 3).

GROUPS	CHOLESTEROL (mg/dl)	INJURED AREA (%)	THICKNESS (um)	
			Thoracic Fragment	Abdominal Fragment
<b>Cholesterol</b>	1483*	23,33	313*	148*
<b>Simvastatin</b>	661*	19,66	146*	83*
<b>Normal</b>	27*	zero	zero	zero
*p<0,05				

**Table 1:** Cholesterol level, injured aorta area and intimal layer thickness of hypercholesterolemic rabbits treated with simvastatin.

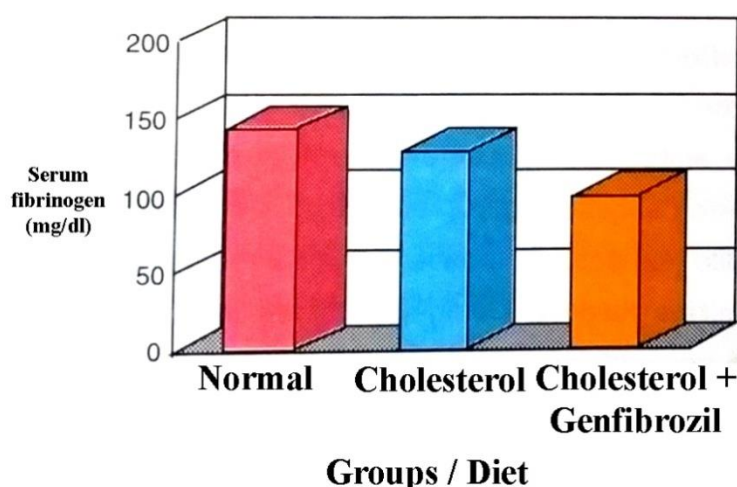


**Figure 2:** Distribution of macrophages in the intima layer of aorta of hypercholesterolemic rabbit treated with simvastatin, evidenced by immunohistochemical reaction - 100x.



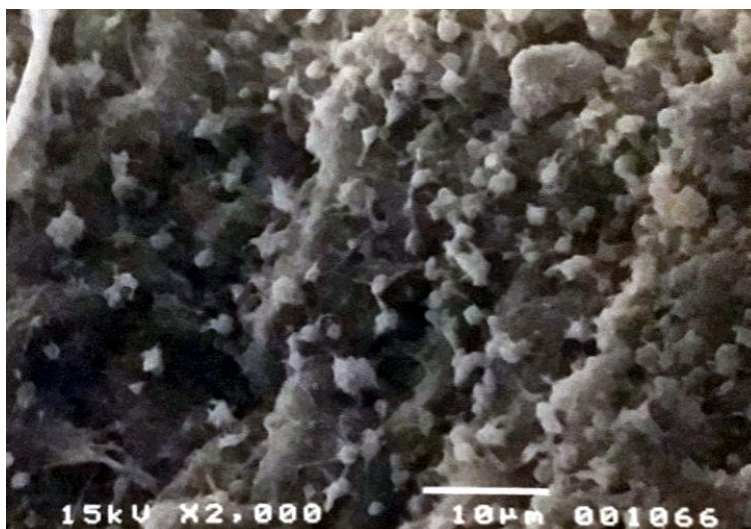
**Figure 3:** Percentage area of aortic involvement of rabbits with hypercholesterolemic diet and Probucol.

Gemfibrozil: up to a dose of 1200 mg/day, there was a reduction in cholesterol levels associated with a decrease in circulating fibrinogen concentration, although atherosclerotic lesions installed in the aorta were similar, suggesting that the reduction of fibrinogen could determine lower thrombotic risk and fewer coronary events [8,12] (Figure 4).



**Figure 4:** Serum fibrinogen levels in rabbits on a hypercholesterolemic diet and treated with Gemfibrozil.

Aspirin: at a dose 100 mg/day, although not a lipid-lowering agent, it is often used in coronary patients for its antithrombotic action. Although it does not act directly in the installation of atherosclerotic lesions, there is lower platelet aggregation, which would provide a protective effect against thrombus formation in cases of plaque rupture. This action was also observed by Scanning Electron Microscopy, with lower fibrin network formation and platelet aggregation on the endothelial surface [9] (Figure 5).



**Figure 5:** Presence of platelets and fibrin network on the endothelial surface of the aorta of hypercholesterolemic rabbits, observed by Scanning Electron Microscopy.

In atherosclerotic lesions in the aorta, in histological sections with special calcium staining (von Kossa) samples with calcium deposits in the deep region of the intima layer of the aorta are apparent [1-3,13] (Figure 6).



**Figure 6:** Presence of calcium salts in the deep region of the intima layer of the aorta of hypercholesterolemic rabbit. Von Kossa reaction 160 x.

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