# Summary

Hypercholesterolemia (high blood total cholesterol) has been known as one of the most important risk factors of atherosclerosis. It has been shown that hyper-cholesterolemia increases oxidative stress and leads to lipid peroxidation as well as affects red cell membrane structure and function.

The main objective of the present work was to assess the effects of cholesterol administration as well as the effect of a hypolipidemic drug (simvastatin) on some physiological aspect of white male rat. In this regards, four groups (14 rats each) were designed. First group, control group (C-gp), received normal diet for 51 days. Second group (H-gp) received cholesterol (460 mg kg $^{-1}$ b.wt. dissolved in 0.5 ml coconut oil) for 21 days. Third group (S-gp) received simvastatin (1 mg kg $^{-1}$ b.wt.) for 30 days. Fourth group (HS-gp) received cholesterol (460 mg kg $^{-1}$ b.wt. dissolved in 0.5 ml coconut oil) for 21 days then received simvastatin (1 mg kg $^{-1}$ b.wt.) for 30 days. The study includes determination of the following:

**1) Relative organ weights:**

Heart relative weight showed significant increases in H-gp relative to control and HS-gp. Lungs relative weight showed significant decreases in all treated groups related to that of the control one. Liver relative weight showed significant increases in both H-gp and S-gp related to that of C-gp, while liver relative weight of HS-gp showed significant decreases related to those of all other groups. Spleen relative weight showed significant decreases in all treated groups related to that of the control one. Kidney relative weight showed non significant changes in all treated

groups related to that of the control one. Testis relative weight showed significant decreases in all treated groups related to that of the control one.

**2) Hematological parameters:**

The WBCs count showed significant decreases in HS-gp related to those of all other groups. The RBCs count showed significant increases in both H-gp and HS-gp related to that of C-gp. There were non significant changes in Hb content in all treated groups related to that of the control group. Hematocrit value showed significant increases in all treated groups related to that of the control one. Blood indices (MCV, MCH, MCHC) of H-gp showed significant decreases in relation to those of the other groups while blood indices of S-gp and HS-gp showed non significant changes related to those of control one. Platelets count showed significant decline in all treated groups related to that of the control group.

**3) Respiratory functions of blood:**

Blood gases and blood acid-base status revealed that cholesterol and simvastatin treated groups showed respiratory alkalosis indicated by significant increases in blood pH. This alkalosis is compensated by kidney through secretion of bicarbonate, base excess and $TCO_2$. The HS treated group showed non significant change in arterial and venous blood pH which means that cholesterol and simvastatin effects cancel each other. The oxygen equilibrium curves of both cholesterol and simvastatin treated groups were significantly shifted to the right. These shifts indicated by significant increases in $P_{50}$. The Hill's coefficient (*n* value) of the simvastatin treated group showed significant increases compared to other groups.

The OEC of the HS treated group showed non significant right shift compared to the control one and significant left shift compared to cholesterol treated group.

**4) Serum metabolites:**

**a) Serum glucose concentration:**

The serum glucose concentration revealed significant increases in cholesterol and HS treated groups compared to that of the control group.

**b) Serum proteins concentration:**

Serum total protein concentration revealed significant increases in all treated groups. Serum albumin showed significant increases in simvastatin and HS treated groups. Serum globulin revealed significant increases in all treated groups.

**c) Serum lipids:**

Serum triglyceride, total cholesterol, LDL-C and VLDL-C concentration revealed significant increases in cholesterol treated group, while serum HDL-C were significantly lower in cholesterol treated group. The LDL/HDL ratio increased in the cholesterol treated group. Liver total cholesterol concentrations were significantly high in all treated groups.

**5) Liver function:**

**a) Serum transaminases activity:**

The activity of AST revealed non significant changes while ALT revealed significant increases in HS treated group.

**b) Liver transaminases activity:**

Liver AST showed significant decrease in cholesterol treated group while liver AST of simvastatin and HS treated groups revealed significant increases. Liver ALT increased significantly in simvastatin and HS treated groups.

**6) Kidney function:**

Serum urea showed significant decreases in cholesterol and HS treated groups while simvastatin treated group showed significant increase in urea concentration. Serum uric acid revealed significant increases in all treated groups while creatinine showed significant decreases in all treated groups.

**7) Certain hormones:**

**a) Serum levels of thyroid hormones:**

The serum levels of thyroid hormones ($T_3$ & $T_4$) were not affected significantly in all treated groups in relation to those of control one.

**b) Serum level of testosterone:**

Serum testosterone increased significantly in simvastatin treated group compared to that of the control one and to those of other treated groups.

**8) DNA fragmentation %:**

DNA fragmentation % revealed significant increases in cholesterol treated group compared to those of other groups. On the other hand, simvastatin and HS treated groups showed significant decreases in DNA fragmentation % compared to those of other groups.

From this study, simvastatin administration recovers most of the physiological processes which altered due to the cholesterol administration.