EFFECTIVENESS OF APPLES AND STATINS IN REDUCING TOTAL CHOLESTEROL LEVELS IN HYPERCHOLESTEROLEMIA PATIENTS IN NORTH GORONTALO REGENCY

EFICÁCIA DE MAÇÃS E ESTATINAS NA REDUÇÃO DOS NÍVEIS DE COLESTEROL TOTAL EM PACIENTES COM HIPERCOLESTEROLEMIA NA REGIÃO DE NORTH GORONTALO

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Abstract
Apples are a type of fruit rich in bioactive polyphenols and dietary fiber. These bioactive components possess significant health potential. The first-line therapy for hypercholesterolemia is typically statin medication. The purpose of this study was to analyze the effectiveness of apples and statins in reducing total cholesterol levels in patients with hypercholesterolemia. Methode research, This study employed a quasi-experimental design the sample consisted of 30 respondents divided into two intervention groups: apples and statins. This experimental study was conducted over 14 days. The study lasted two weeks. Baseline total cholesterol levels were measured before the intervention, after which subjects received one of three interventions for two consecutive weeks. The first group was given one Malus domestica (Red Delicious variety) apple per day (approximately

Resumo
As maçãs são um tipo de fruta rica em polifenóis bioativos e fibras alimentares. Esses componentes bioativos possuem um significativo potencial para a saúde. O tratamento de primeira linha para a hipercolesterolemia geralmente envolve medicamentos com estatina. O objetivo deste estudo foi analisar a eficácia das maçãs e das estatinas na redução dos níveis de colesterol total em pacientes com hipercolesterolemia. Método: Este estudo empregou um delineamento quase-experimental. A amostra foi composta por 30 participantes divididos em dois grupos de intervenção: maçãs e estatinas. Este estudo experimental foi conduzido ao longo de 14 dias. O estudo durou duas semanas. Os níveis basais de colesterol total foram medidos antes da intervenção, após a qual os participantes receberam uma das três intervenções por duas

150 grams), the second group received 20 mg of simvastatin daily, taken at night, and the third group received both interventions—one Red Delicious apple (approximately 150 grams) per day and 20 mg of simvastatin taken nightly. After the 2-week intervention period, The results showed that the intervention group consuming apples exhibited the most significant reduction in total cholesterol levels (p-value = 0.000) compared to the statin group (p-value = 0.188). The conclusion of this study is that apples can produce a greater reduction in cholesterol levels than statins.

Keywords: Apples. Statins. Hypercholesterolemia. Polyphenols. Pectin. Antioxidants.

semanas consecutivas. O primeiro grupo recebeu uma maçã Malus domestica (variedade Red Delicious) por dia (aproximadamente 150 gramas), o segundo grupo recebeu 20 mg de sinvastatina diariamente, tomada à noite, e o terceiro grupo recebeu ambas as intervenções — uma maçã Red Delicious (aproximadamente 150 gramas) por dia e 20 mg de sinvastatina à noite. Após o período de intervenção de duas semanas, os resultados mostraram que o grupo que consumiu maçãs apresentou a redução mais significativa nos níveis de colesterol total (p-valor = 0,000) em comparação com o grupo que utilizou estatinas (p-valor = 0,188). A conclusão deste estudo é que as maçãs podem produzir uma redução maior nos níveis de colesterol do que as estatinas.

Palavras-chave: *Maçãs. Estatinas. Hipercolesterolemia. Polifenóis. Pectina. Antioxidantes.*

1 INTRODUCTION

Lipids, including cholesterol, are essential compounds for the human body. Lipids are fat-derived molecules absorbed by the intestines from daily food intake and distributed throughout body tissues with the assistance of apolipoproteins. Lipids function as an energy source, precursors for steroid hormone synthesis, and play a role in bile acid production.

The first-line therapy for hypercholesterolemia is the use of statin drugs. Statins act by competitively inhibiting the enzyme HMG-CoA reductase, which converts HMG-CoA into mevalonate, an early precursor in cholesterol biosynthesis. However, the use of statins is often associated with several serious adverse effects, including myopathy, liver dysfunction, diabetes mellitus, cognitive decline, and acute kidney injury (Cheon & Jo, 2022; Stanley *et al*., 2024).

Apples are a type of fruit rich in bioactive polyphenols and dietary fiber, both of which have significant health potential. The main polyphenolic compounds found in apples include flavanols (such as catechins and proanthocyanidins or Pas), followed by hydroxycinnamates, flavonols, dihydrochalcones, and anthocyanins (particularly in red apples). PAs and flavanols have been shown to reduce serum cholesterol, increase HDL cholesterol, inhibit LDL oxidation, activate endothelial nitric oxide synthase, prevent

platelet aggregation, and suppress inflammatory responses involved in atherosclerosis (Pappan *et al*., 2024).

Research has demonstrated that consuming apples or their bioactive compounds is associated with improved lipid metabolism and a reduced risk of cardiovascular disease. An intervention study involving patients with mild hypercholesterolemia showed that consuming 2 apples per day for 8 weeks, followed by a 4-week washout period, significantly decreased total cholesterol, triacylglycerol, and intercellular cell adhesion molecule-1 (Pappan *et al*., 2024). Ervina's study also reported a significant reduction in blood cholesterol levels after green apple juice administration among hypercholesterolemic residents in Bekasi. Similarly, Damayanti *et al*. (2016) found that Manalagi apples effectively reduced cholesterol levels among individuals with hypercholesterolemia in Sleman, Yogyakarta.

In contrast, a study conducted by Roza *et al*. (2013) found no significant effect of apple consumption—whether whole, peeled, or juiced—on the reduction of LDL cholesterol or the increase of HDL cholesterol after 14 days of administration in hypercholesterolemic rats. Furthermore, a vascular mortality modeling study among adults aged 50 years and older demonstrated that consuming 1 apple per day had an effect comparable to taking a daily statin in reducing vascular mortality. However, choosing apples over statins could prevent approximately 1,200 cases of myopathy, 200 cases of rhabdomyolysis, and 12,300 cases of diabetes (Briggs *et al*., 2013).

2 METHOD

This study employed a quasi-experimental design. A quasi-experimental study is a research method that does not use randomization in selecting study samples (Sugiyono, 2012). The research was conducted on 30 subjects aged ≥18 years who were diagnosed with hypercholesterolemia, confirmed by total cholesterol levels ≥200 mg/Dl using the point-of-care testing (POCT) method with capillary blood samples. Participants were instructed not to modify their dietary patterns during the study period. Prior to participation, all subjects provided both oral and written informed consent and received a detailed explanation of the study procedures.

The study lasted two weeks. Baseline total cholesterol levels were measured before the intervention, after which subjects received one of three interventions for two

consecutive weeks. The first group was given one Malus domestica (Red Delicious variety) apple per day (approximately 150 grams), the second group received 20 mg of simvastatin daily, taken at night, and the third group received both interventions—one Red Delicious apple (approximately 150 grams) per day and 20 mg of simvastatin taken nightly. After the 2-week intervention period, total cholesterol levels were remeasured using POCT with capillary blood samples. In this study, 30 respondents were included, with a 5% margin of error, yielding a minimum required sample size of 28 participants. Ultimately, 30 subjects were enrolled and divided into three groups: the first received the apple intervention, the second received the statin intervention, and the third received the combined apple and statin intervention.

3 RESULTS AND DISCUSSION

3.1 Results

History of Hypercholesterolemia

Tabel 1

Analysis of Respondent Characteristics Based on History of Hypercholesterolemia

History of Hypercholesterolemia	Total (n)	Percentace (%)
Never	21	70
< 12 months	3	10
≥ 12 monnths	6	20

Source: Primary Data, 2025

Based on the previous history of hypercholesterolemia, 21 respondents (70%) had no prior history of high cholesterol, 3 respondents (10%) had a history of hypercholesterolemia for less than 12 months, and 6 respondents (20%) had a history of hypercholesterolemia for 12 months or longer.

Tabel 2

Analysis of Respondent Characteristics Based on Total Cholesterol Levels Before Intervention

Cholesterol level (mg/dl)	Apel	Statin	Apel and Statin
Desired (<200)	-	-	-
Slightly high (200-239)	7 (70%)	7 (70%)	1 (10%)
High (□ 240)	3 (30%)	3 (30%)	9 (90%)
Total	10	10	10

Source: Primary Data, 2025

Based on the table above, in the apple group, 7 respondents (70%) have slightly elevated total cholesterol levels (200-239 mg/dL), and 3 respondents (30%) have high total cholesterol levels (≥ 240 mg/dL). In the statin group, 7 respondents (70%) have slightly elevated total cholesterol levels (200-239 mg/dL), and 3 respondents (30%) have high total cholesterol levels (≥240 mg/dL). In the apple and statin group, 1 respondent (10%) has slightly high total cholesterol (200-239 mg/dL), and 9 respondents (90%) have high total cholesteroL.

Tabel 3

Analysis of Respondent Characteristics Based on Total Cholesterol Levels After Intervention

Cholesterol level (mg/dl)	Apple	Statin	Apple and Statin
Desired (<200)	1 (10%)	-	3 (30%)
Slightly high (200-239)	5 (50%)	8 (80%)	4 (40%)
High (□ 240)	4 (40%)	2 (20%)	3 (30%)
Total	10	10	10

Source: Primary Data, 2025

Based on the table above, it is known that in the apple group there is 1 respondent (10%) with a desirable total cholesterol level (<200 mg/dl), 5 respondents (50%) with slightly high total cholesterol levels (200-239 mg/dl), and 4 respondents (40%) with high total cholesterol levels (≥ 240 mg/dl). In the statin group, 8 respondents (80%) have slightly elevated total cholesterol levels (200-239 mg/dl), and 2 respondents (20%) have

high total cholesterol levels (≥ 240 mg/dl). In the apple and statin group, there are 3 respondents (30%) with desirable total cholesterol levels (<200 mg/dl), 4 respondents (40%) with slightly high total cholesterol levels (200-239 mg/dl), and 3 respondents (30%) with high total cholesterol levels (≥ 240 mg/dl).

4 ANALYSIS OF THE DIFFERENCE IN TOTAL CHOLESTEROL LEVELS BEFORE AND AFTER CONSUMING STATINS

Before conducting the statistical difference test, normality and homogeneity tests were carried out with the following results:

Tabel 4

Normality and Homogeneity Test of Statin Groups

Cholesterol	Normality Test	Homogeneity Test
Before statin	0,439	0,666
After statin	0,754	

Source: Primary Data, 2025

Based on the results of the normality test, a significance value of 0.439 was obtained for the group before statin use and 0.754 for the group after statin use. Since the p-values are > 0.05, the data are normally distributed. The homogeneity test results showed a significance value of 0.666; because the significance value is > 0.05, the data are homogeneous. After both data groups were found to be normally distributed and homogeneous, a parametric statistical test, the paired-samples T-test, was conducted to analyze differences in total cholesterol levels before and after statin treatment. The results obtained are as follows:

Tabel 5

Analysis of Differences in Total Cholesterol Levels Before and After Consuming Statins

Cholesterol	mean	SD	P value
Before statin	235,60	11,42	0,188
After statin	233,90	13,97	

Source: Primary Data, 2025

From the table above, it can be seen that in the statin intervention group, the average cholesterol level before the intervention was 235.60 mg/dl with a standard deviation of 11.42. After the statin intervention, the average cholesterol level decreased to 233.90 mg/dL with a standard deviation of 13.97. Statistical testing using a paired sample T-test yielded a P value of 0.188. Since the P value is> α (0.05), it can be concluded that there is no difference in total cholesterol levels before and after statin use.

Analysis of the Difference in Total Cholesterol Levels Before and After Consuming Apples

Before conducting the statistical difference test, normality and homogeneity tests were performed with the following results:

Tabel 6

Normality and Homogeneity Test of Apple Groups

Cholesterol	Normality Test	Homogeneity Test
Before apel	0,717	
		0,858
After apel	0,749	

Source: Primary Data, 2025

Based on the normality test results, the significance value was 0.717 in the group before apples and 0.749 in the group after apples. Since the significance value is > 0.05, the data are normally distributed. In the homogeneity test, the significance value was 0.858. Since the significance value is > 0.05, the data are homogeneous. After both data groups were found to be normally distributed and homogeneous, a paired-samples T-test was conducted to analyze differences in total cholesterol levels before and after consuming apples. The results obtained are as follows:

Tabel 7

Analysis of Differences in Total Cholesterol Levels Before and After Consuming Apples

Cholesterol	mean	SD	P value
Before apel	258,60	21,69	0,000
After apel	239,20	22,56	

Source: Primary Data, 2025

From the table above, it can be seen that in the group receiving the apple and statin intervention, the average cholesterol level before the intervention was 258.60 mg/dl with

a standard deviation of 21.69. After receiving the apple and statin intervention, the average cholesterol level decreased to 239.20 mg/dL, with a standard deviation of 22.56. Statistical testing using a paired-samples T test yielded a P value of 0.000. Since the P value is less than the α value (0.05), it can be interpreted that there is a difference in total cholesterol levels before and after consuming apples.

5 DISCUSSIONS

5.1 Difference in total cholesterol levels before and after consuming statins

The results of the study showed that the mean total cholesterol level before the intervention was 235.60 mg/dL with a standard deviation of 11.42. After statin administration, the mean cholesterol level decreased to 233.90 mg/dL, with a standard deviation of 13.97. Statistical analysis using a paired-samples t-test yielded a p-value of 0.188. Since the p-value was greater than the significance level (α = 0.05), it can be interpreted that there was no significant difference in total cholesterol levels before and after statin administration. The findings suggest that total cholesterol levels did not decrease following the intervention, which may be attributed to several factors, including the duration of the intervention, the type of statin used, individual metabolic variations, and daily dietary cholesterol intake, all of which can influence statins' cholesterol-lowering effect.

According to Alvarez *et al*. (2024), the maximal effect of statins in lowering cholesterol levels typically requires 4–6 weeks of continuous therapy. An experimental study also reported that, even with a statin dose of 40 mg, a minimum of 6 weeks is required to achieve reductions of 41% in LDL cholesterol, 21% in triglycerides, and a 6% increase in HDL cholesterol (Davidson *et al*., 1997). To achieve a significant reduction in atherosclerotic plaque volume, a higher statin dosage is necessary—such as atorvastatin>10 mg or its equivalent, simvastatin >20 mg—and a longer treatment duration of at least 6 months (Tian *et al*., 2012).

Simvastatin has relatively low bioavailability —approximately 5% —which is lower than that of atorvastatin (12%) and rosuvastatin (20%) (Schachter, 2004). When compared at the same dosage (10 mg), atorvastatin reduced LDL cholesterol by 8% more, total cholesterol by 6% more, triglycerides by 5% more, the LDL/HDL ratio by 11% more,

and apolipoprotein B by 7% more than simvastatin (Insull *et al*., 2001). Similarly, rosuvastatin 10 mg produced a 12.8% greater reduction in LDL cholesterol compared to simvastatin 20 mg (47.4% vs. 34.6%). However, when compared with pravastatin 20 mg, simvastatin 20 mg achieved an 8.1% greater LDL reduction (34.6% vs. 26.5%) (Brown *et al*., 2002).

The pharmacological effect of statins is also influenced by individual metabolic characteristics. Since most statin compounds are metabolized by the CYP450 enzyme system in the liver, hepatic function plays a major role in statin metabolism. Renal function also contributes significantly, particularly for simvastatin, as its metabolites are primarily excreted via the kidneys. Furthermore, approximately 95% of simvastatin molecules bind to plasma proteins to exert their effect; therefore, plasma albumin concentration can also influence statin metabolism (Egom & Hafeez, 2016).

Difference in Total Cholesterol Levels Before and After Consuming Apples

The results of the study showed that the mean total cholesterol level before the intervention was 232.20 mg/dL with a standard deviation of 13.84. After the apple intervention, the mean total cholesterol level decreased to 230.40 mg/dL with a standard deviation of 15.24. Statistical analysis using the paired sample t-test yielded a p-value of 0.00. Since the p-value was less than the significance level ($\alpha = 0.05$), it can be interpreted that there was a significant difference in total cholesterol levels before and after apple consumption.

However, the findings indicated that total cholesterol levels did not show a meaningful reduction following the intervention. This may be attributed to several factors, including the duration of the intervention. Although there is no established minimum duration for apple intervention, most studies have used interventions lasting at least 4 weeks to achieve significant reductions in cholesterol levels. In addition, participant compliance with apple consumption may have also influenced the results. Although daily follow-up monitoring of apple consumption was performed in this study, there was no direct observation of the consumption process, which may have introduced bias in the intervention outcomes.

A study by Nagasako-Akazome *et al*. (2005) using apple polyphenol tablets for a four-week intervention reported significant reductions in total cholesterol and LDL levels, along with an increase in HDL levels. Similarly, a study by Koutsos *et al*. (2019) in which participants consumed two apples daily for four weeks demonstrated that apple

consumption effectively reduced total cholesterol, LDL, and triacylglycerol levels. In another experiment, Susilowati *et al*. (2020) found that in 25 test rats, administering apple extract for 4 consecutive weeks significantly decreased total cholesterol and LDL levels while increasing HDL levels.

Habu *et al*. (2023) used a shorter intervention duration: 15 elderly participants received Granny Smith green apple juice for 7 days and observed a significant reduction in cholesterol levels after the intervention. Similarly, Izzati *et al*. (2018) reported a significant effect of consuming green apple juice for 7 days on lowering total cholesterol levels. On a molecular level, the Red Delicious apple variety exhibits higher free radical scavenging activity compared to the Granny Smith variety. This effect is primarily attributed to its polyphenol content—100 grams of Granny Smith apples contain 202.8 mg gallic acid equivalents (GAE), whereas Red Delicious apples contain 1187 mg GAE. Furthermore, the Red Delicious variety has been shown to possess stronger antitumor activity than Granny Smith (Mustafa *et al*., n.d.; Rosenblat *et al*., 2013).

The differing results in this study may be explained by participants' compliance with apple consumption. Although daily follow-up monitoring of apple intake was performed, the lack of direct observation during consumption could have introduced bias and affected the accuracy of the intervention outcomes.

6 CONCLUSIONS

There was no difference in total cholesterol levels before and after consuming statins in hypercholesterolemia patients with a p-value of 0.188, while there was a difference in total cholesterol levels before and after consuming apples in hypercholesterolemia patients with a p-value of 0.000.

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Data availability

All datasets relevant to this study's findings are fully available within the article.

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