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THE EFFECTS OF PAPAYA LEAVES JELLY IN LIPID PROFILE AMONG OVERWEIGHT WOMEN

Choirun Nissa[1*], Syafira Noor Pratiwi[1], Siti Majidah[1], Nadia Rahma[1], Ratih Paramastuti[2], Nadhea Alriessyanne Hindarta[2], Ahmad Syauqy[1], Hartanti Sandi Wijayanti[1], Diana Nur Afifah[1]

[1] Nutrition Department, Faculty of Medicine, Universitas Diponegoro. Jl. Prof Soedarto SH Tembalang, Semarang, Indonesia 50275
[2] Department of Community Nutrition, Faculty of Human Ecology, Bogor Agricultural University. Jl. Kamper, Kampus IPB Darmaga, Bogor, Jawa Barat 16680
***Corresponding author**: E-mail : choirun.nissa@live.undip.ac.id

ABSTRACT

Background *: Insulin resistance that occurred in diabetic state could promote endothelial dysfunction which lead to metabolic disease in obese subjects. Although several studies showed papaya leaves had antidiabetic and antihyperlipidemic agent, the effect of papaya leaves jelly is rarely studied on lipid profiles among overweight women.*
Objectives *: We aimed to examine the effect of papaya leaves jelly on lipid profiles in women with overweight.*
Methods *: This study was a pre-posttest controlled group design with both of the groups were overweight. The treatment group consumed papayq leaves jelly with 24.6 grams papaya leaves jelly that contains 182.4 mg chlorophyll, while the control group consumed 24.6 grams jelly with green dye for 20 days in a row. Three-day recall in three non-consecutive days and physical activity using International Physical Activity (IPAQ) were taken three times. Fasting blood sugar was measured using Glucose Oxidase Phenol 4-Aminophenazone (GODPAP). LDL, HDL, total cholesterol, triglyceride levels were measured using Cholesterol Oxidase Para Aminophenazone (CHOD-PAP). Statistical analysis using Paired t-test was used within group, while Independent t-test and Mann-Whitney were used in between groups. Papaya leaves jelly effects on lipid profiles was analyzed using multiple linear regression after considering energy, protein, fat, and carbohydrate intakes.*
Results *: Triglyceride levels was reduced significantly (p=0.014) in the treatment group despite there were no differences in triglyceride (p= 0.407), LDL (p= 0.923), HDL (p= 0.749) and total cholesterol (p= 0.277) between 2 groups.*
Conclusion *: Papaya leaves jelly consumption could lower triglyceride levels significantly in the treatment group.*

Key words: *Papaya leaves; lipid profile; overweight; women*

INTRODUCTION

Diabetes has become a major health problem worldwide, including in Indonesia. Data from Basic Health Research from Ministry of Health of Republic of Indonesia describes that the prevalence of diabetes in 2013 is 1,5% and increase 2% in 2018.[1]. The magnitude of the incidence, prevalence, and complication of diabetes shows the importance of early prevention and diabetic management, especially during prediabetic stage. Prediabetes is identified as a reversible circumstance which increases risk of diabetes and comorbidities.[2] American Diabetes Association (ADA) postulated that prediabetes is defined as a condition in which glucose levels do not meet the criteria for diabetes but are too high to be considered normal. Individual with prediabetes have fasting blood glucose levels between 100 to 125 mg/dl and / 2-hr postprandial glucose level between 140 to 199 mg/dl.[3]

Subject with prediabetes has a greater risk for the development of diabetes and cardiovascular disease (CVD).[4] Diabetes generally occurred with increased production of reactive oxygen species (ROS) and suppression of antioxidant through glucose autoxidation, polyol pathway, and non-enzymatic glycation of proteins.[5–7]

Evidence suggests that underlying disorder including metabolic syndrome is manifested during prediabetes and type 2 diabetes.[4] Several markers such as obesity, triglycerides, high total cholesterol, high LDL cholesterol, low HDL cholesterol, and hypertension are higher in subjects with prediabetes than those without prediabetes.[4,8]

Lipid abnormalities are common in diabetes since insulin deficiency causes excessive metabolism of free fatty acids and insulin resistance which reduces lipoprotein lipase (LPL) activity that causes hyperlipidemia (hypertriglyceridemia, low HDL cholesterol, elevated LDL cholesterol and elevated serum cholesterol) [9]. Moreover, the increase in lipid profile may be a result of increased lipid breakdown and mobilization of free fatty acids from peripheral deposits [10,11].

Diabetes and hyperlipidemia may be prevented during reversible condition at prediabetic state by consuming green leafy vegetables that contain chlorophyll which inhibits oxidative DNA damage and lipid peroxidation both by reducing

reactive oxygen species [2,12]. Another antioxidant component was superoxide dismutase (SOD) which is located in cell compartments such as chloroplasts and mitochondria that are also play a role in catalyzing the dismutation of O2- to less reactive compound such as O2 and H2O2.[13–15] Research described that papaya leaves have the highest chlorophyll content among green leafy vegetables such as cassava leaves, pegagan, spinach, grass-jelly, water spinach and basil.[16]

Papaya leaves have been shown to contain many components that can increase the total antioxidant level in blood. A study using chlorophyll in papaya leaves gives effects on superoxide dismutase and glucose level of diabetic rats.[17] The component of papaya leaves such as quercetin, tannin, and alkaloid carpaine could lower both cholesterol and triglycerides levels.[18,19] Another study using papaya leaves extract could significantly decrease LDL cholesterol and increase HDL cholesterol in serum significantly.[20]

However, papaya leaves have a bitter taste caused by saponin compound which according to research acts both as an antidiabetic and antidyslipid [21,22]. Several food processes are made in order to increase acceptance, one of them is in jelly form. It has been shown in a preliminary study that papaya leaves jelly was satisfying. Foodstuffs were incorporated into the product to reduce bitterness and improve the taste. The product developed was composed of papaya leaves juice, jelly, stevia powder, and skim milk. This article is aimed to investigate the effect of papaya leaves jelly on lipid profile in prediabetic women.

METHODS

This research was conducted at Sendangmulyo, Tandang (Tembalang Sub-district) and Semarang City Government office in Pandanaran Building Semarang, Indonesia from March to June 2016 using a pretest-posttest controlled group design. The sample size was calculated using unpaired numerical analytical formulas with standard deviations based on chlorophyll study [23]. The treatment group was provided with papaya leaves jelly while the control group received jelly with green dye.

Subjects were recruited from residential areas and offices in Semarang with inclusion criteria that were overweight according Asia Pacific criteria (Body Mass Index above 23 kg/m2),[24] women aged 35-50 years, waist circumference above 80 cm, not consuming alcohol, non-smoking, not taking anti-hyperglycemic or anti-hypertensive drugs, and not being pregnant or breastfeeding. Eligible subjects were those with fasting blood sugar above 90 mg/dl and willing to comply with research procedures and providing informed consent was recruited.

Food intake data were obtained using 3 times repeated of 24 hours recall consist of 2 weekdays and 1 day at weekend, while physical activity data used International Physical Activity Questionnaire (IPAQ) with 3 times data retrieval. Lipid profile (triglycerides, total cholesterol, LDL cholesterol and HDL cholesterol) was measured using fasting blood samples, collected by a qualified phlebotomist, and measured using Cholesterol Oxidase Para Aminophenazone (CHOD-PAP).

Anthropometric data of body weight was measured using digital weight scales with 0.1 precision and height was measured using a microtoise with 1 mm accuracy. Compliance data was obtained from filling out the checklist form filled by the researcher through direct observation while the subject consuming the products.

The safe dose to lower lipid profile were based on Panam Parikh study which gave daily spirulina supplementation by 8 grams containing 60.8 mg of chlorophyll for 60 days [23]. According to the laboratory test, 8.1 grams of papaya leaves jelly contain 7.4% chlorophyll. The dose given to the subjects was 24.6 grams, contains of 182.4 mg of chlorophyll for 20 days.

The analysis was conducted using SPSS. A normality test using Saphiro-Wilk was conducted. Differences in triglyceride, LDL, HDL, and total cholesterol before and after intervention were compared using paired t-tests, while differences between groups were analyzed using independent t-test. Significance was tested using alpha < 0.05 two tailed. This research was approved under Ethical clearance number 149/EC/FK-RSDK/2016.

RESULTS

Characteristics of The Subjects

Total subjects of 221 women were screened with a final number of 26 women were recruited, 13 in each group. The characteristics comparison before intervention between the treatment and the control group were shown in table 1. Statistical analysis showed that the characteristics between both groups were no different (p>0.05).

Lipid Profile

Not all subjects were in prediabetic stage despite they were prone for this condition related to their body mass index. Among all lipid profile, triglyceride in treatment group was the only parameter that reduced significanty (table 2) with 18.23 mg/dl reduction (table 3). However, triglyceride level as well as other parameters were not different (p>0.05) when it compares with the control group (tabel 3).

Table 1. Characteristics of Subjects Before Intervention, Data of Nutritional Adequacy and Physical Activity During Treatment

Characteristic/ Variable	Treatment (n=13)	Control (n=13)	p-value
	mean±SD	mean±SD	
Age (years)	43.46±4.29	43.69±3.49	0.88[a]
BMI (kg/m^2)	28.09±3.17	29.09±2.78	0.41[a]
Waist circumference (cm)	89.43±5.58	89.41±7.23	0.71[b]
Food intake			
Energy intake (%)	75.60±22.27	74.41±15.94	0.87[a]
Carbohydrate intake (%)	47.46±31.78	68.31±24.10	0.07[a]
Fat intake (%)	71.70±62.66	84.48±32.60	0.52[a]
Protein intake (%)	52.47±38.09	62.77±21.40	0.52[b]
Fiber intake (%)	25.40±14.31	26.43±20.90	0.48[b]
Sodium intake (%)	24.35±20.26	12.60±16.29	0.02[b*]
Potassium intake (%)	23.74±8.15	18.58±6.85	0.09[a]
Calcium intake (%)	23.61±12.84	18.15±8.51	0.24[b]
Magnesium intake (%)	49.59±12.82	55.88±25.32	0.70[b]
Vitamin C (%)	75.95±87.19	33.12±24.53	0.08[b]
Physical activity (MET-minute)	3822.44±2051.96	4278.03±5445.17	0.34[b]

[a] Independent t-test; [*] significantly different; [b] Mann-Whitney test

Table 2. Difference of lipid profile between the control and treatment group in diabetic women

Variable	Treatment (n=13)			Control (n=13)		
	Before (mean±SD)	After (mean±SD)	p-value	Before (mean±SD)	After (mean±SD)	p-value
FBG (mg/dl)	101.62±10.03	107.15±12.82	0.056[b]	98.08±9.67	96.08±11.54	0.427[a]
Triglyceride (mg/dl)	128.00±49.87	109.77±39.78	0.049[a*]	89.69±32.20	80.00±21.93	0.113[a]
LDL (mg/dl)	140.92±30.95	143.92±30.69	0.482[a]	147.31±16.67	150.92±21.76	0.462[a]
HDL (mg/dl)	40.62±9.57	40.46±7.57	0.943[a]	37.31±4.59	38.00±5.56	0.668[a]
Total Cholesterol (mg/dl)	207.31±39.59	205.54±38.66	0.701[a]	200.69±23.73	205.15±25.88	0.207[a]

[a] Paired t test; [b] Wilcoxon; *significant

Table 3. Difference of lipid profile change between groups

Variable	Treatment (Mean±SD)	Control (Mean±SD)	Sig (p)
ΔFBG (mg/dl)	5.53±10.76	-2.00±8.77	0.057[b]
ΔTriglyceride (mg/dl)	-18.23±30.07	-9.69±20.43	0.407[a]
ΔLDL (mg/dl)	3.00±14.90	3.61±17.15	0.923[a]
ΔHDL (mg/dl)	-0.15±7.53	0.69±5.67	0.749[a]
ΔTotal Cholesterol (mg/dl)	-1.76±16.20	4.46±12.04	0.277[a]

[a] Independent t test; [b] Mann-Whitney

Despite the number was insignificant, fasting blood glucose and LDL apparently increased, while HDL lowered (tabel 3).

DISCUSSION

According to the CDC, approximately 90% of subjects with pre-diabetes were not realized they have it. Furthermore, nearly 3 out of 4 subjects with this condition will develop type 2 diabetes within 5 years. However, in some cases it can be treated through diet and lifestyle modification.[25] Green leafy vegetables not only as a part of diet with abundant source of vitamins and minerals, but also as medicinal plants that have bioactive components to be used as pharmaceuticals. Among them, carica papaya is not only cultivated for its pleasant fruit, but also its leaf for their bioactive properties.[26] Hypoglycemic agent[17] as well as anti-hyperlipidemic agent[27] are shown to be the strength of this leaves.

Characteristic subjects by age, BMI, and waist circumference in both groups showed no difference (p>0.05). There was no difference in nutritional intake and physical activity of the subjects in both groups during intervention except sodium intake with mean intake in the treatment group was higher than the control one. Several subjects in the treatment group consume high-sodium food such as salted fish, instant noodles, light snacks with flavorings and artificial preservatives. Nutrition education about balanced nutrition had been conducted in both groups as an effort in controlling intake.

There was a significant decrease in triglyceride levels but not in LDL, HDL, and total

cholesterol after intervention in the treatment group which may be affected by the papaya leaves content in jelly. Papaya leaves contain several antioxidant compounds that potentially balanced the state of oxidative stress. Previous studies showed that chlorophyll has high bioactivity such as antioxidant, catalyzer, which prevent lipid oxidation [28,29].

Chlorophyll has an ability to scavenge DPPH free radical that produced by lipid autoxidation process and act as a chain breaker by donating its electron to free radical and becoming stable [30]. Saponin and steroid play a role as antihyperlipidemic by inhibiting intestinal lipid absorption via resin-like action and inhibition of lipase activity [10,11,31]. Papaya leaves also contain flavonoid names kaempferol and quercetin. Saponin and flavonoid could enhance antioxidative system activity and increase the activity of lipoprotein lipase (LPL) that reduce free fatty acid and hence decrease triglyceride levels [32].

There was a reduction in total cholesterol in the treatment group by 1.76 mg/dl, while total cholesterol in the control group increased 4.46 mg/dl. The decrease of total cholesterol in the treatment group due to chlorophyll in papaya leaves. Chlorophyll could stimulate heart function in lowering total cholesterol by enhancing activity and amount of LDL receptor, increase bile acids excretion, decrease renin levels, and widen blood vessel [33].

The decrease of total cholesterol in the treatment group also due to papaya leaves contain active components, such as saponin, flavonoid quercetin, tannin, and alkaloid carpaine.[34] Saponin inhibits bile acid reabsorption in small intestine then excreted to feces. To compensate that mechanism, cholesterol serum converted by the heart into bile acid so there will be a decrease in cholesterol levels in the blood.[35] Flavonoid quercetin as antioxidant flavonoid protects LDL cholesterol so it is not oxidized by free radical. Besides, as antioxidant, flavonoid could potentially decrease total cholesterol by increase bile acid excretion.[36] Tannins on papaya leaves decrease cholesterol absorption in the small intestine and increase bile acid excretion by the same mechanism as saponins [37]. Alkaloid carpaine on papaya leaves inhibit lipase enzyme, thus inhibiting fat breakdown into smaller molecules. This process results a decrease in the amount of fat that can be absorbed by intestine so that the total cholesterol levels lowered [38].

There was no significant reduction in LDL, HDL, and total cholesterol in the treatment group. This might due to the baseline condition of LDL cholesterol which still in borderline high, while HDL was particularly in control group is in desirable category although the difference was not significant in both groups.[39] According to the chinese guideline, the recommendation of lipid lowering target is a reduction of minimum 40% and above.[40] The overweight subjects also not likekly represent a higher level of lipid profile. Furthermore, several subjects were in desirable level of total cholesterol.[41]

There was no difference in triglyceride, LDL, HDL, and total cholesterol changes between both groups. This case happened because jelly products that were consumed by both of the groups equally contain fiber, skim milk, and stevia sweeteners that also affect lowering triglyceride, LDL, HDL, and total cholesterol.

CONCLUSION

The consumption of papaya leaves jelly for 20 days can reduce triglyceride levels significantly, but there was no significant reduction on LDL, HDL, and total cholesterol levels in treatment group. Future study needs to be conducted to investigate the effectiveness of papaya leaves among prediabetes subjects on lowering LDL, HDL, and total cholesterol. A comprehensive approach is needed to promote a healthy lifestyle including physically active and diet modification include an adequate green leavy vegetables to maintain a normal nutrition status thus avoid in developing diabetes.

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REFERENCES

1. Badan Penelitian dan Pengembangan Kesehatan RI. Hasil Riset Kesehatan Dasar (RISKESDAS). 2013.
2. Tuso P. Prediabetes and lifestyle modification: time to prevent a preventable disease. Perm J. 2014;18(3):88–93.
3. Care D, Suppl SS. 2. Classification and diagnosis of diabetes: Standards of medical care in diabetesd2019. Diabetes Care. 2019;42(January):S13–28.
4. Punthakee Z, Goldenberg R, Katz P. Definition, Classification and Diagnosis of Diabetes, Prediabetes and Metabolic Syndrome. Can J Diabetes. 2018;42:10–5.
5. Nawale RB, Mourya VK, Bhise SB. Non-enzymatic glycation of proteins : A cause for complications in diabetes. Indian J Biochem Biophys. 2006;43:337–44.
6. Singh VP, Bali A, Singh N, Jaggi AS. Advanced Glycation End Products and Diabetic Complications. Korean J Physiol Pharmacol. 2014;18:1–14.

7. Bisht S, Sisodia SS. Diabetes, dyslipidemia, antioxidant and status of oxidative stress. Int J Res Ayurveda Pharm. 2010;1(1):33–42.
8. Salami R, Feizi A, Amini M, Iraj B. The profile of hypertension and dyslipidemia in prediabetic subjects; results of the Isfahan Diabetes Prevention program: A large population-based study. Adv Biomed Res. 2015;4(1).
9. Lalitha P, V AP, K PB. Lipid patterns in Prediabetic and diabetic patients in Rural tertiary care centre. Int J Biol Med Res. 2013;3(1):3181–4.
10. Adeneye AA, Adeyemi OO, Agbaje EO. Anti-obesity and antihyperlipidaemic effect of Hunteria umbellata seed extract in experimental hyperlipidaemia. J Ethnopharmacol. 2010;130(2):307–14.
11. Gepts W, Lecompte PM. The Pancreatic Islets in Diabetes. Am J Med. 1981;70(1):105–15.
12. Hsu C-Y, Chao P-Y, Hu S-P, Yang C-M. The Antioxidant and Free Radical Scavenging Activities of Chlorophylls and Pheophytins. Food Nutr Sci. 2013;04(08):1–8.
13. Leonowicz G, Trzebuniak KF, Zimak-Piekarczyk P, Ślesak I, Mysliwa-Kurdziel B. The activity of superoxide dismutases (SODs) at the early stages of wheat deetiolation. PLoS One. 2018;13(3).
14. European Food Safety Authority. Scientific Opinion on the substantiation of health claims related to superoxide dismutase (SOD) and protection of DNA, proteins and lipids from oxidative damage, protection of the skin from photo-oxidative (UV-induced) damage (ID 2305, 3161), reduction of. EFSA J. 2010;8(10).
15. Lanfer-Marquez UM, Barros RMC, Sinnecker P. Antioxidant activity of chlorophylls and their derivatives. Food Res Int. 2005;38(8–9):885–91.
16. Setiari N, Nurchayati Y. Eksplorasi Kandungan Klorofil pada beberapa Sayuran Hijau sebagai Alternatif Bahan Dasar Food Supplement. BIOMA. 2009;11(1):6–10.
17. Nissa C, Kartasurya MI, Rahmawati B. Effects of Chlorophyll in Papaya Leaves on Superoxide Dismutation and Blood Glucose Level of Diabetic Rats. Makara J Heal Res. 2015;19(2):75–80.
18. Juárez-Rojop IE, Tovilla-Zárate CA, Aguilar-Domínguez DE, Fuente LFR de la, Lobato-García CE, Blé-Castillo JL, et al. Phytochemical screening and hypoglycemic activity of carica papaya leaf in streptozotocin-induced diabetic rats. Brazilian J Pharmacogn. 2014;24(3):341–7.
19. Otsuki N, Dang NH, Kumagai E, Kondo A, Iwata S, Morimoto C. Aqueous extract of Carica papaya leaves exhibits anti-tumor activity and immunomodulatory effects. J Ethnopharmacol. 2010;127(3):760–7.
20. Zetina-Esquivel AM, Tovilla-Zárate CA, Guzmán-Garcia C, Rodríguez-Hernández A, Castell-Rodríguez AE, Ble-Castillo JL, et al. Effect of Carica Papaya Leaf Extract on Serum Lipids and Liver Metabolic Parameters of Rats Fed a High Cholesterol Diet. Health (Irvine Calif). 2015;7(9):1196–205.
21. Ayoola PB, Adeyeye A. Phytochemical and Nutrient Evaluation of Carica Papaya (Pawpaw) Leaves. IJRRAS. 2010;5(3):325–8.
22. Alli Smith Y, Adanlawo IG. Tissue lipid profile of rats administered saponin extract from the root of bitter kola. Adv Biochem. 2013;1(1):1–4.
23. Parikh P, Mani U, Iyer U. Role of Spirulina in the Control of Glycemia and Lipidemia in Type 2 Diabetes Mellitus. J Med Food. 2001;4(4):193–9.
24. Pan W-H, Yeh W-T. How to define obesity? Evidence-based multiple action points for public awareness, screening, and treatment: an extension of Asian-Pacific recommendations. Asia Pac J Clin Nutr. 2008;17(3):370–4.
25. Dugan J, Cantillep A, Newberry K, Shubrook J. A call to action on prediabetes. J Am Acad Physician Assist. 2018;31(10):26–30.
26. Juárez-Rojop IE, Díaz-Zagoya JC, Ble-Castillo JL, Miranda-Osorio PH, Castell-Rodríguez AE, Tovilla-Zárate CA, et al. Hypoglycemic effect of Carica papaya leaves in streptozotocin-induced diabetic rats. BMC Complement Altern Med. 2012;12(236):3–11.
27. Sheneni VD, Shaibu IE, Okpe JM, Omada AA. In-vivo biological effect of Carica papaya leaf extracts on P-407 induced hyperlipidemic Wistar rats. MOJ Food Process Technol. 2018;6(4):409–12.
28. Ferruzzi MG, Böhm V, Courtney PD, Schwartz SJ. Antioxidant and antimutagenic activity of dietary chlorophyll derivatives determined by radical scavenging and bacterial reverse mutagenesis assays. J Food Sci. 2002;67(7):2589–95.
29. Kusmita L. The Influence of Strong and Weak Acid Upon Aggregation and Pheophytinization of Chlorophyll A and B. Indo J Chem. 2009;9(1):70–6.
30. Horton R, Moran LA, Ochs RS, Rawn DJ, Scrimgeour KG. Principles of Biochemistry. 2002. 491 p.
31. Hamden K, Jaouadi B, Zaraî N, Rebai T, Carreau S, Elfeki A. Inhibitory effects of

estrogens on digestive enzymes, insulin deficiency, and pancreas toxicity in diabetic rats. J Physiol Biochem. 2011;67(1):121–8.
32. Komolafe K, Olaleye MT, Akindahunsi AA. Lipid-Lowering Effect of Parkia Biglobosa Leaf Saponins in Triton-X 1339- Induced Hyperlipidemic Rats. Res J Pharm Biol Chem Sci. 2013;4(1):576–85.
33. Karimah F. Pengaruh Pemberian Klorofil dari Tanaman Alfalfa (Medicago Sativa) terhadap Kadar Kolesterol Total Tikus Putih (Rattus Norvegicus) Strain Wistar. Surakarta : Universitas Sebelas Maret; 2010.
34. Ekananda N. Bay Leaf in Dyslipidemia Therapy. Artik Rev J Major. 2015;4(4):64–9.
35. Ismoyojati Y, Ismoyowati, Suswoyo I. Kadar Kolesterol dan Trigliserida dalam Darah Itik Rambin Jantan yang Diberi Tepung Daun Salam (Syzygium poluanthum) dalam Ransum. J Ilm Peternak. 2014;2(146–154).
36. Carvajal-Zarrabal O, Waliszewski SM, Barradas-Dermitz DM, Orta-Flores Z, Hayward-Jones PM, Nolasco-Hipólito C, et al. The consumption of Hibiscus sabdariffa dried calyx ethanolic extract reduced lipid profile in rats. Plant Foods Hum Nutr. 2005;60(4):153–9.
37. Tebib K, Besançon P, Rouanet JM. Dietary grape seed tannins affect lipoproteins, lipoprotein lipases and tissue lipids in rats fed hypercholesterolemic diets. J Nutr. 1994;124(12):2451–7.
38. Rahayu S, Tjitraresmi A. Review Artikel: Tanaman Pepaya (Carica papaya L.) dan Manfaatnya Dalam Pengobatan. Farmaka. 2016;14(1):1–17.
39. Lee Y, Siddiqui WJ. Cholesterol levels. StatPearls Publishing LLC.; 2020. 1–17 p.
40. Wu N-Q, Li J-J. Clinical considerations of lipid target and goal in dyslipidemia control. Chronic Dis Transl Med. 2016;2(1):3–6.
41. Magalhães MEC. New cholesterol targets of SBC Guidelines on Dyslipidemia. Int J Cardiovasc Sci. 2017;30(6):466–8.