FOOD and HEALTH

FOOD and HEALTH
E-ISSN 2602-2834

Food Health 9(4), 293-303 (2023) • https://doi.org/10.3153/FH23026 Research Article

Antioxidant and 3-hydroxy-3-methylglutaryl Coenzyme A reductase inhibitory activities of some plant samples

Elmas Irmak ÇİL ARSLAN, Özlem SAÇAN

Cite this article as:
Çil Arslan, E.I., Saçan, Ö. (2023). Antioxidant and 3-hydroxy-3-methylglutaryl Coenzyme A reductase inhibitory activities of some plant samples. *Food and Health,* 9(4), 293-303. https://doi.org/10.3153/FH23026

Istanbul University-Cerrahpaşa, Faculty of Engineering, Department of Chemistry, Istanbul, Türkiye.

ORCID IDs of the authors:
E.I.C.A. 0000-0001-7888-5118
Ö.S. 0000-0001-6503-4613

Submitted: 08.02.2023
Revision requested: 20.04.2023
Last revision received: 04.05.2023
Accepted: 14.06.2023
Published online: 27.07.2023

Correspondence:
Özlem SAÇAN
E-mail: osacan@iuc.edu.tr

Available online at
http://jfhs.scientificwebjournals.com

ABSTRACT

The antioxidant activity capacities of some plants, and their inhibitory effects on the HMG-CoA reductase enzyme, the rate-determining enzyme of cholesterol synthesis, were investigated in our study. Antioxidant activity capacity and inhibitory effect of the HMG-CoA reductase enzyme were detected in all plant extracts used in our research. From the results obtained, it was determined that both antioxidant activity and % inhibition values of HMG-CoA reductase enzyme increased as the plant extracts concentration increased. The strongest ABTS and DPPH radical scavenging activities were exhibited by pomegranate fruit extract (IC_{50}= 1.07 ±0.04 mg/mL and IC_{50}= 0.39 ±0.01 mg/mL, respectively). At the same time, lemon had the strongest DMPD radical scavenging activity (IC_{50}= 9×10^{-4} ±6×10^{-5} mg/mL). The best HMG-CoA reductase inhibitory activity was observed in persimmon fruit extract (IC_{50}= 0.71 ±0.18 µg/mL). The inhibitory power of this extract was much higher than that of the enzyme's standard inhibitor, Atorvastatin (IC_{50}= 1.76 ±0.12 µg/mL). The extracts' potent antioxidant and inhibitory properties can be attributed to the rich phytochemical composition of plant extracts. Thus, it may be a potential source of new bioactive compounds effective against oxidative stress, hypercholesterolemia and cardiovascular complications.

Keywords: Antioxidant activity, Enzyme, HMG-CoA reductase, Inhibition, Plants

Introduction

Free radicals are metabolic by-products continuously produced via normal metabolic processes of the biological system. These molecules are highly reactive and unstable, thus detrimental to organisms' general well-being. In humans, the excessive production of these molecules, coupled with compromised antioxidant-oxidant balance, present severe health challenges such as cardiovascular dysfunction, premature ageing, neurological disorders and mutagenesis (Aruoma, 1994; Bagchi and Puri, 1998; Floyd, 1999; Njie-Mbye et al., 2013) these lead modification and destruction of biologically important macromolecules such as lipids, proteins, DNA and carbohydrates. The biological system is armed with an antioxidant defence mechanism that helps eliminate the toxic effect of free radicals. This antioxidant defence system involves the activity of antioxidant enzymes (i.e., superoxide dismutase, catalase, glutathione peroxidase and glutathione reductase) that works synergistically with the non-enzymatic antioxidant systems that include vitamins (vitamin A, C and E), antioxidant minerals (i.e. copper, zinc and selenium), appropriate biological levels of uric acid and bilirubin, plant-based antioxidants (such as polyphenols) etc. Some of these antioxidant molecules can unilaterally capture or detoxify free radicals, thus essential for healthy living.

Cholesterol is a lipid synthesised by all animal cells via the mevalonate pathway (Brown and Goldstein, 1997; Espenshade and Hughes, 2007). It is an indispensable component of the cell membrane and an important precursor of steroid hormones, bile and vitamin D (Yeagle, 1991; Hanukoglu, 1992; Haines, 2001; Payne and Hales, 2004). Despite the biological significance of cholesterol, its elevated level in human blood has health consequences such as the increased risk of atherosclerosis, heart attack, stroke, and peripheral artery disease (Lewington et al., 2007; Brunzell et al., 2008). Various studies have shown that lowering blood cholesterol levels can reduce the risk of coronary heart disease, regress existing atherosclerotic lesions in peripheral arteries, and reduce the risk of stroke risk and cardiovascular disease (Grundy et al., 2019). Thus, regulating both intake and biosynthesis of cholesterol is essential for normal well-being. The regulation of cholesterol levels in patients usually involves the use of statins. These group of compounds are known to be excellent inhibitors of hydroxy methylglutaryl-CoA (HMG-CoA) reductase (an important enzyme of the mevalonate pathway), thereby having the ability to slow down the biosynthesis of mevalonate and accumulation of cholesterol, and its accompanying defects (Nicholls, 2008; Kizer et al., 2010). Despite the proven effects of HMG-CoA reductase in reducing blood cholesterol levels and risk cardiovascular disease, they are suggested to cause liver damage, neuropathy, pancreatic dysfunction, muscle pain/damage, bleeding stroke, an increased risk of diabetes mellitus and sexual dysfunction (Golomb and Evans, 2008; Bellosta and Corsini, 2012; Naci et al., 2013; Collins et al., 2016; Lehrer and Rheinstein, 2020). Therefore, finding alternative food-based sources capable of HMG-CoA reductase inhibition is of medical significance.

Plants are outstanding sources of phytoactive compounds, thus, exhibit remarkable antioxidant activities (Magaji et al., 2022). Reports have shown that flavonoids and polyphenols can prevent the oxidation of haemoglobin to methaemoglobin through the scavenging of nitrites, thereby preventing anaemia (Frei et al., 1988; Choi et al., 1988; Kang et al., 1996). Moreover, plant-based chemicals such as carotenoids, flavonoids, glycosides, polyphenols, saponins, and terpenes act as inhibitors of enzymes while also exhibiting regenerative, wound healing, anti-inflammatory, and antitumor activity. A diet rich in these phytochemicals positively correlates with lower degenerative and pathological diseases and improved well-being (Willcox et al., 2004; Mahato and Sharma, 2019). In the present study, the antioxidant activity and HMG-CoA reductase inhibitory effects of 80% ethyl alcohol extract of some plant extracts were investigated.

Materials and Methods

Plant Samples

Quince (*Cydenia vulgaris*), apple (*Malus domestica*), grapefruit (*Citrus paradise*), lemon (*Citrus limon*), pomegranate (*Punica granatum*), persimmon (*Diospyros kaki*), radish (*Raphanus sativus*) and onion (*Allium cepa*) were bought from local market, washed and rinsed with distilled water, then dried in the shade. Individual extracts were prepared with 80% ethyl alcohol using the dried plant parts.

Preparation of Ethyl Alcohol Extracts

Five grams of the dried plant sample was placed in a 250 mL Erlenmeyer flask containing 50 mL of 80% ethyl alcohol; the flask was closed with a parafilm. The mixture was stirred continuously in a dark cupboard at room temperature for 7 days. The solvent used for extraction was removed from the resulting filtrate under reduced pressure using a rotary evaporator. The amount of extract obtained was weighed and recorded.

ABTS Radical Scavenging Activity

2,2'-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid) (ABTS) radical scavenging activity was performed according to the method of Arnao et al. (2001). ABTS was dissolved in distilled water to make a 7.4 mM, adding 1 mL of 2.6 mM potassium persulfate. The solution was kept away from light at room temperature for 12 to 16 hours. To 1 mL of the resulting solution, 60 mL of methyl alcohol was added to obtain the freshly prepared ABTS radical cation solution required for each experiment. Plant extracts (150 µL) were added to 2850 µL of ABTS radical cation, then kept in the dark for 2 hours before taking absorbance reading at a wavelength of 734 nm. Butylated hydroxyanisole (BHA) was used as a standard ABTS radical scavenger. % ABTS radical scavenging activity was calculated as follows:

ABTS radical scavenging activity (%) =
$[(A_0-A_1) / A_0] \times 100$

A_0=Control absorbance value.

A_1=Absorbance value of sample and standard.

DMPD Radical Scavenging Activity

The basis of DMPD radical scavenging activity is that in acidic pH, DMPD forms a stable-coloured radical cation in a suitable oxidant solution. The DMPD extreme shows a maximum absorbance value of 505 nm. Antioxidants that transfer H atoms to the DMPD extreme lead to decolourising the radical solution.

$DMPD_{(colourless)} + Oxidant\ (Fe^{3+}) + H^+ \longrightarrow DMPD^{\cdot+}_{(purple)}$

$DMPD^{\cdot+}_{(purple)} + AOH \longrightarrow DMPD^{+}_{(colourless)} + AO$

DMPD radical scavenging activity was performed according to the method of Fogliano et al. (1999). A 209 mg DMPD radical was dissolved in 10 mL of bidistilled water. A 1 mL of this solution was taken and added to 100 mL of Na-acetate buffer (0.1 M, pH: 5.3). A coloured DMPD radical cation was obtained by adding 0.2 mL of 0.05 M $FeCl_3$ to the solution. In the radical scavenging assay, 1 mL of the radical solution was added to 0.5 mL of extract solutions. After 10 minutes, absorbance was taken using a spectrophotometer at 505 nm against the buffer solution. Epicatechin was used as a standard. DMPD radical scavenging activity was calculated as follows:

Percentage DMPD radical scavenging activity =
$[(A_0-A_1) / A_0] \times 100$

A_0: DMPD initial absorbance

A_1: Absorbance of the sample

DPPH Radical Scavenging Activity

1,1′-diphenyl-2-picrylhydrazil (DPPH) radical scavenging activity was determined according to the method developed by Brand-Williams et al. (1995). A 20 mg/L solution of DPPH in methyl alcohol was prepared daily. To 1.5 mL of the DPPH solution, 0.75 mL of various concentrations of plant extracts (0.001–5 mg/mL) were added. The absorbance value was read after 5 minutes against the blank at 517 nm using a spectrophotometer. A 0.75 mL methyl alcohol and 1.5 mL DPPH solution were used as control. Rutin (0.0001-1.0 mg/mL) was used as a standard percentage of DPPH radical scavenging activity and was calculated using the following formula:

DPPH radical scavenging activity (%) =
$[(A_0-A_1) / A_0] \times 100$

A_0: Absorbance of control

A_1: Absorbance of sample and standard material

HMG-CoA Reductase Inhibition Assay

The inhibitory activity of the HMG-CoA reductase was assayed using the procedure outlined in the CS1090 kit of Sigma Aldrich. Briefly, 910 µL of buffer was placed into a test tube and added 5 µL of the inhibitors (0.01-10.00 µg/mL). The solutions were thoroughly mixed before adding 20 µL of NADPH, and 60 µL of HMG-CoA, then allowed to stand for 5 minutes at room temperature. After that, 5 µL of HMG-CoA reductase was added to the mixture, gently mixed, and allowed to stand for another 5 minutes. The absorbance of samples was read spectrophotometrically at 340 nm against corresponding reagent blanks. Atorvastatin was used as the standard inhibitor of HMG-CoA reductase.

Percentage enzyme inhibition was calculated as follows:

% Inhibition = $(A_0 – A_1 / A_0) \times 100$

A_0: Absorbance of control

A_1: Absorbance of sample and standard material

For enzyme inhibitor activities, the results are given as half maximal inhibitory concentrations (IC_{50} values) calculated regression prepared from the concentrations of samples. Using regression analysis data, half maximum inhibition/scavenging concentration (IC_{50}) was calculated from enzyme inhibition % activities and antioxidant activities % (for ABTS, DMPD, and DPPH radical scavenging). Lower IC_{50} values

indicate higher inhibitory potential and antioxidant activities of the tested plant extract.

Results and Discussion

Plants are natural sources of biologically active compounds (such as vitamins and polyphenols) with diverse biochemical and therapeutic activities (Proteggente et al., 2002; Rufino et al., 2010; Rinaldo et al., 2014; Afam et al., 2021). Among the therapeutic benefit of fruits and vegetables is their strong antioxidant activities (Wang et al., 1996; Karadeniz et al., 2005; Almeida et al., 2011; Dandare et al., 2017; Magaji et al., 2022). Quince has been reported to contain high levels of ascorbic acid (Gheisari and Abhari, 2014; Mir et al., 2016). Phytochemical analysis reveals that apples contain the appreciable level of vitamin C, phenols and flavonoids (that include anthocyanins, catechin, chlorogenic acid, hydroxycinnamic acids, phloridzin, procyanidins and quercetin) (Siqueira et al. 2013; Djenidi et al., 2020; Asale et al., 2021; Vasile et al., 2021). Citrus, including grapefruit and lemon, were reported to be exclusively rich in vitamin C and α-tocopherol, in addition to phytochemicals like flavonoids, condensed tannins, limonoids, gallic acid, protocatechuic acid, p-hydroxybenzoic acid, vanillic acid, caffeic acid, p-coumaric acid, salicylic acid, ferulic acid, anisic acid, triterpenes and sinapic acid (Garcia-Closas et al., 2004; Gorinstein et al., 2004; Uckoo et al., 2012; Agudelo et al., 2017; Makni et al., 2018; Alrasheid et al., 2019; Djenidi et al., 2020). In different varieties of pomegranate, phenolic compounds (ellagic acid, gallic acid, chlorogenic acid, caffeic acid, vanillic acid, ferulic acids trans-2- hydrocinnamic acid, quercetin) and flavonoids (catechin, rutin, quercetin and phloridzin) were identified (Hmid et al., 2017; Djenidi et al., 2020; Tekin and Kucukbay et al., 2020). Phytochemical analysis by Lee et al. (2012), Murathan (2020) and Aydin (2021) reported the presence of tartaric acid, malic acid, lactic acid, gallic acid, citric acid, catechins, phenols, flavonoids and ascorbic acid in persimmon fruit. Radish fruits are rich in flavonoids (such as myricetin, catechin, epicatechin, and quercetin), phenols (e.g. quercetin, o-coumaric acid, tyrosol, sinapic acid, vanillic acid, vinyl guaiacol), glycosides, terpenes and fatty acids (Beevi et al., 2010; Xiao et al., 2012; Baenas et al., 2014; Goyeneche et al., 2015; Park et al., 2016; Selyutina and Gapontseva, 2016; Chihoub et al., 2019). Onion, on the other hand, contains high levels of organosulfur and phenolic compounds such as onions, cycloalliin, isoalliin, methiin, quercetin and rutin (Alagarsamy et al., 2018; Zhao et al., 2021). These phytochemicals are responsible for fruits and vegetables' antioxidant activities and therapeutic benefits.

The antioxidant activities of plants investigated in the present study are presented in Table 1. Persimmon and quince exhibited minor ABTS radical scavenging activity (with IC_{50} values of 17.80 ±1.12 and 9.47 ±0.83 mg/mL, respectively), while apple IC_{50} = 6.32 ±0.09 mg/mL), lemon (IC_{50}= 4.96 ±0.20 mg/mL), onion (IC_{50}= 3.73 ± 0.08 mg/mL), grapefruit (IC_{50}= 3.63 ±0.11 mg/mL) and radish (IC_{50}= 2.90 ±0.05 mg/mL) had moderate ABTS radical scavenging activity. The strongest ABTS radical scavenging action was exhibited by pomegranate (IC_{50}= 1.07 ±0.04 mg/mL). The ABTS radical scavenging activities of the plants above were far below that of BHA (IC_{50}= 0.07 ±3.0×10^{-3}), used as a standard. Analysis of DMPD radical scavenging activity revealed that lemon had the strongest DMPD radical scavenging activity (IC_{50}= 9×10^{-4} ±6×10^{-5} mg/mL), followed by grapefruit, onion and pomegranate respectively (IC_{50}= 0.04 ±1x10^{-3}, 0.06 ±6×10^{-3}, 0.08 ±6×10^{-3} mg/mL). The minor scavenging activities were found in quince (IC_{50}= 1.15 ±0.03 mg/mL), apple (IC_{50}= 1.20 ±0.06 mg/mL), radish (IC_{50} = 1.25 ±0.04 mg/mL) and persimmon (IC_{50}= 1.70 ±0.02 mg/mL). Despite the excellent DMPD radical scavenging activity exhibited by lemon in the present study, its action was still below that of the standard used, i.e. epicatechin (IC_{50}= 6.6×10-5 ±4.8×10^{-5} mg/mL). As observed in the present study, pomegranate (IC_{50} = 0.39 ±0.01 mg/mL) and grapefruit (IC_{50} = 0.99 ±0.05 mg/mL) exhibited strong DPPH radical scavenging activities, though not beyond that of rutin (IC_{50}= 0.24 ±0.01 mg/mL) which used as standard. Lemon, apple, onion, persimmon, and radish (IC_{50} values of 1.97 ±0.08, 2.24 ±0.15, 2.45 ±0.17, 3.42 ±0. 42, 4.74 ±0.04 mg/mL, respectively) had moderate scavenging activities, while quince (IC_{50}= 9.02 ±0.17 mg/mL) had the minor scavenging activity.

The outcomes of the present finding agree with previous reports that indicated antioxidant and free radical scavenging activity of reported quince, apple, grapefruit, lemon, pomegranate, persimmon, radish and onion. Quince has been shown to contain high levels of phytochemicals. The fruit exhibit promising antioxidant activity such as reducing power, ferric reducing antioxidant power (FRAP) and DPPH radical scavenging activity in the range of 70.9-89.5%, 1.40-1.68 µM and 79.91-82.61%, respectively (Mir et al., 2016). Similarly, Muzykiewicz et al. (2018) reported that ripe and unripe quince fruit have DPPH, FRAP, and ABTS radical scavenging activity. At 60 minutes extraction time, 70% ethanol of the unripe fruit had DPPH and ABTS radical scavenging activity of 29.43 ±0.31 % and 9.10±0.16 %, respectively, as against 15.78 ±0.59 % and 7.19±0.44 % of the ripe fruit. DPPH radical scavenging activity of the unripe and ripe fruits are 1.51 and 0.81 mg Trolox/g, respectively. Asale et al. (2021) reported that apple juice had DPPH radical scavenging

activity and iron-reducing power of up to 86.20 ±2.28 µg/mL and 1.93 ± 0.66 mg/mL, respectively. The highest total antioxidant activity observed was 0.46 ±0.08 mg BHT equivalent/g. More so, a study by Siqueira et al. (2013) have shown that apple has both strong DPPH radical and ferric-reducing antioxidant power (FRAP), thus exhibiting excellent antiradical effects.

Citruses such as grapes and lemons are rich in ascorbic acid (Makni et al., 2018; Alrasheid et al., 2019) and thus are excellent antioxidant sources. Studies have shown that grapefruit had both DPPH and ABTS radical scavenging activity. Depending on the variety, DPPH scavenging activity ranged from 35.25 ±0.15% to 46.08 ±0.10 %, while ABTS radical scavenging activity was between 0.61 ±0.06% to 0.92 ±0.08 (Sicari et al., 2018). In another study by Agudelo et al. (2017), grapes exhibited a DPPH scavenging activity ranging from 5.61 ±0.07 to 8.61 ±0.10 mg/mL, while the ferric reducing power of the fruit was between 1.67 ±0.01 to 3.10 ±0.30 mg/mL. The highest lipid peroxidation inhibition as β-carotene bleaching and TBARS formation inhibition are 19.2 ±0.70 mg/mL and 4.17 ±0.06 mg/mL (Agudelo et al., 2017). Conversely, Lemon had a DPPH radical quenching ability of IC_{50}= 434.50 ±5.9 µg/ml and a reducing power of around 0.15 µg/mL (Makni et al., 2018). A report by Oikeh et al. (2015) showed that Grape and lemon juice have DPPH scavenging activity (24.0 ±0.10 and 5.25 ±0.40 mg/mL, respectively) and FRAP 364.2 ±10.25 and 122.75 ±3.25 µmol/L Fe(II)/g respectively). Ripe fruit of pomegranate has been shown to have antioxidant activities by a testing method such as DPPH radical scavenging activity, ABTS scavenging activity and FRAP of 319.2 ±4.2, 778.8 ±2.4 and 525.3 ±15.8 µmol Trolox/g dry mass, respectively (Magangana et al., 2021). Comparative antioxidant analysis between astringent, non-astringent and wild types of persimmons by Aydin (2021) indicated that the wild type had higher antioxidant potential than the other types. The ABTS, CUPRAC, DPPH, and FRAP activities were 112.95 ± 1.48, 550.24 ± 1.30, 232.56 ± 3.08 and 542.69 ± 1.84 µmol Trolox/g, respectively. Research into the antioxidant potentials of radishes revealed that some varieties of the fruit could have superoxide radical scavenging activity of up to 68.87% at 1000 µg/mL and a DPPH activity of about 20.78% (Park et al., 2016). Onion is an essential source of bioactive and antioxidant compounds as a vegetable. The antioxidant activities of this vegetable are reported not to be drastically influenced by heating or cooking (Moreno-Ortega et al., 2020). FRAP and DPPH radical scavenging activities were 12.40 ±0.12 mg Trolox/g dry mass and 8.00 ± 0.23 mg Trolox/g dry mass before heating. After heating for 10 minutes at 80ºC, the FRAP and DPPH radical scavenging activities were reduced to 10.57 ±0.34 and 6.50 ±0.37 mg Trolox/g dry mass (Ren et al., 2017).

In general, the antioxidant activities exhibited by fruits and the vegetable investigated in the present study can be attributed to the phytochemical component such as ascorbic acid, tocopherol, quercetin, and rutin, among other vitamins and polyphenols present in the plant extracts.

Table 1: Antioxidant activities of ethyl alcohol extracts from various plants.

Plant/Standard Inhibitor	ABTS (IC_{50}; mg/mL)*	DMPD (IC_{50}; mg/mL)*	DPPH (IC_{50}; mg/mL)*
Quince	9.47 ±0.83	1.15 ±0.03	9.02 ±0.17
Apple	6.32 ±0.09	1.20 ±0.06	2.24 ±0.15
Grapefruit	3.63 ±0.11	0.04 ±1x10^{-3}	0.99 ±0.05
Lemon	4.96 ±0.20	9×10^{-4} ±6×10^{-5}	1.97 ±0.08
Pomegranate	1.07 ±0.04	0.08 ±6×10^{-3}	0.39 ±0.01
Persimmon	17.80 ±1.12	1.70 ±0.02	3.42 ±0. 42
Radish	2.90 ±0.05	1.25 ±0.04	4.74 ±0.04
Onion	3.73 ±0.08	0.06 ±6×10^{-3}	2.45 ±0.17
BHA	0.07 ±3.0×10^{-3}	-	-
Epicatechin	-	6.6×10^{-5} ±4.8×10^{-5}	-
Rutin	-	-	0.24 ±0.01

* Mean ± SD of triplicate values

As seen in Table 2, the HMG-CoA reductase inhibitory activity of persimmon (IC_{50}= 0.71 ±0.18 µg/mL) was higher than that of Atorvastatin (IC_{50}= 1.76 ±0.12 µg/mL) which is a standard inhibitor of the enzyme. The inhibitory action of radish (IC_{50}= 1.81 ±0.56 µg/mL) was close to that of the standard inhibitor. More so, lemon (IC_{50}= 5.31 ±0.80 µg/mL) and apple (IC_{50}= 12.42 ±2.53 µg/mL) also had intense inhibitory action on the enzyme. In contrast, onion, quince, pomegranate and grapefruit, respectively (IC_{50}= 62.92 ±2.94, 79.36 ±3.94, 329.98 ±163.14 and 13741.89 ±3485.70 µg/mL) exhibited lower HMG-CoA reductase inhibitory activity. Statins are reported to be excellent inhibitors of HMG-CoA reductase. They help down-regulate cholesterol biosynthesis (Collins et al., 2016). Plant-based statins (such as lovastatin, pravastatin, and simvastatin) derived from sterols during the fermentation process play a significant role in cholesterol biosynthesis via HMG-CoA reductase inhibition, thus reducing the risk of cardiovascular diseases and infarction (Furberg et al., 1994; Byington et al., 1995; Pedersen et al., 1998; Furberg, 1999). The HMG-CoA reductase inhibitory activity of fruits and vegetables observed in the present study is likely due to the rich phytochemical composition of the plant, which is in the form of polyphenols, sterols, vitamins, and fatty acids.

Table 2: HMG-CoA reductase inhibition activity of ethyl alcohol extracts prepared from various plants

Plant/Standard Inhibitor	Concentration (µg/mL)	Inhibition (%)*	IC_{50} Values (µg/mL)*
Quince	1.00	19.85 ±4.9	79.36 ±3.94
	10.00	35.95 ±0.78	
	100.00	55.60 ±1.17	
Apple	0.10	20.94 ±4.87	12.42 ±2.53
	1.00	30.41 ±8.03	
	10.00	45.91 ±4.00	
Grapefruit	1000.00	12.35 ±4.64	13741.89 ±3485.70
	5000.00	17.82 ±0.48	
	10000.00	42.73 ±7.58	
Lemon	0.10	6.35 ±1.69	5.31 ±0.80
	1.00	29.68 ±3.54	
	10.00	76.84 ±6.83	
Pomegranate	10.00	34.30 ±1.18	329.98 ±163.14
	100.00	47.56 ±11.85	
	1000.00	70.17 ±0.58	
Persimmon	0.01	36.87 ±1.65	0.71 ±0.18
	0.10	42.64 ±1.02	
	1.00	54.60 ±3.27	
Radish	0.10	37.95 ±2.55	1.81 ±0.56
	1.00	47.57 ±6.74	
	5.00	82.95 ±4.10	
Onion	50.00	45.50 ±1.44	62.92 ±2.94
	75.00	51.67 ±3.45	
	100.00	72.93 ±4.81	
Atorvastatin	0.50	4.81 ±0.64	1.76 ±0.12
	1.00	30.37 ±8.91	
	2.50	72.59 ±2.79	

* Mean ± SD of triplicate values

Conclusion

In conclusion, the fruits and vegetable extracts examined in the present study showed strong antioxidant activity. The plants also exhibited promising HMG-CoA reductase inhibition activity, especially persimmon and radish fruit. These potent antioxidant and inhibitory properties can be attributed to the rich phytochemical composition of plant extracts. Thus, it can be a potential source of new bioactive compounds effective against oxidative stress, hypercholesterolemia and cardiovascular complications.

Compliance with Ethical Standards

Conflict of interests: The author(s) declares that for this article, they have no actual, potential, or perceived conflict of interest.

Ethics committee approval: Authors declare that this study includes no experiments with human or animal subjects.

Funding disclosure: The Scientific Research Project Coordination Unit of Istanbul University-Cerrahpaşa supported this work. Project No. 28070

Acknowledgments: -

Disclosure: -

References

Afam, I.O.J., Henry S., Thakhani T., Adewale O.O., Henry O.U., Tonna A.A. (2021). Antioxidant-rich natural fruit and vegetable products and human health. *International Journal of Food Properties*, 24(1), 41-67. https://doi.org/10.1080/10942912.2020.1866597

Agudelo, C., Barros, L., Santos-Buelga, C., Martinez-Navarrete, N., Ferreira, I.C.F.R. (2017). Phytochemical content and antioxidant activity of grapefruit (Star Ruby): A comparison between fresh freeze-dried fruits and different powder formulations. *LWT - Food Science and Technology*, 80, 106-112. https://doi.org/10.1016/j.lwt.2017.02.006

Alagarsamy, S., Chellappan, P., Jesuraj, M.T., Mohan, M.S.G., Balakrishnan, R. (2018). Phytochemical analysis and antioxidant potential of the crude extract of *Allium oschaninii* scape. *Oriental Pharmacy and Experimental Medicine*, 18, 309-316. https://doi.org/10.1007/s13596-018-0339-5

Almeida, M.M.B., de Sousa, P.H.M., Arriaga, A.M.C., do Prado, G.M., de Carvalho Magalhaes, C.E., Maia, G.A., de Lemos, T.L.G. (2011). Bioactive compounds and antioxidant activity of fresh exotic fruits from northeastern Brazil. *Food Research International*, 44(7), 2155–2159. https://doi.org/10.1016/j.foodres.2011.03.051

Alrasheid, A.A., Mohamed, A.A., Mohieldin, E.G., Eldein, K.I., Yassin, L.F., Widdatallh, M.O., Alnour, M.I., Eltilib, S.H., Ahmed, S.A., Ayoub, S.M.H. (2019). Phytochemical investigation and assessment of antimicrobial, anti-inflammatory and antioxidant activities of Sudanese *Citrus paradisi* peel extract. *Pharmacognosy and Phytotherapy*, 11(1), 1-8. https://doi.org/10.5897/JPP2018.0531

Arnao, M.B., Cano, M., Acosta, M. (2001). The hydrophilic and lipophilic contribution to total antioxidant activity. *Food Chemistry*, 73, 239-244. https://doi.org/10.1016/S0308-8146(00)00324-1

Aruoma, O.I. (1994). Nutrition and health aspects of free radicals and antioxidants. *Food and Chemical Toxicology*, 32, 671–683. https://doi.org/10.1016/0278-6915(94)90011-6

Asale, Y., Dessalegn, E., Assefa, D., Abdisa, M. (2021). Phytochemicals and antioxidant activity of different apple cultivars grown in South Ethiopia: Case of the wolayta zone. *International Journal of Food Properties,* 24(1), 354-363. https://doi.org/10.1080/10942912.2021.1885440

Aydin, E. (2021). Attributes of total phenolic content, antioxidant capacity and in-vitro simulated bioaccessibility of astringent, non-astringent and wild (rootstock) persimmons. *Gida*, 46(3), 669-680. https://doi.org/10.15237/gida.GD21032

Baenas, N., Garcia-Viguera, C., Moreno, D.A. (2014). Biotic elicitors effectively increase the glucosinolates content in Brassicaceae sprouts. *Journal of Agricultural and Food Chemistry*, 62, 1881–1889. https://doi.org/10.1021/jf404876z

Bagchi, K., Puri, S. (1998). Free radicals and antioxidants in health and diseases. *Eastern Mediterranean Health Journal*, 4, 350–360. https://doi.org/10.26719/1998.4.2.350

Beevi, S.S., Narasu, M.L., Gowda, B.B. (2010). Polyphenolics profile, antioxidant and radical scavenging activity of leaves and stem of *Raphanus sativus* L. *Plant Foods for Human Nutrition*, 65, 8–17.
https://doi.org/10.1007/s11130-009-0148-6

Bellosta, S., Corsini, A. (2012). Statin drug interactions and related adverse reactions. *Expert Opinion on Drug Safety*, 11(6), 933–946.
https://doi.org/10.1517/14740338.2012.712959

Brand-Williams, W., Cuvelier, M.E., Berset, C. (1995). Use of a free radical method to evaluate antioxidant activity. *LWT-Food Science and Technology*, 28(1), 25-30.
https://doi.org/10.1016/S0023-6438(95)80008-5

Brown, M.S., Goldstein, J.L. (1997). The SREBP pathway: regulation of cholesterol metabolism by proteolysis of a membrane-bound transcription factor. *Cell*, 89(3), 331–340.
https://doi.org/10.1016/S0092-8674(00)80213-5

Brunzell, J.D., Davidson, M., Furberg, C.D., Goldberg, R.B., Howard, B.V., Stein J.H., Witztum, J.L. (2008). Lipoprotein management in patients with cardiometabolic risk: Consensus statement from the American Diabetes Association and the American College of Cardiology Foundation. *Diabetes Care,* 31(4), 811–822.
https://doi.org/10.2337/dc08-9018

Byington, R.P., Jukema, J.W., Salonen, J.T., Pitt, B., Bruschke, A.V., Hoen, H., Furberg, C.D., Mancini, J. (1995). Reduction in cardiovascular events during pravastatin therapy: Pooled analysis of clinical events of the Pravastatin Atherosclerosis Intervention Program. *Circulation,* 92(9), 2419–2425.
https://doi.org/10.1161/01.CIR.92.9.2419

Chihoub, W., Dias, M.I., Barros, L., Calhelha, R.C., Alves, M.J., Harzallah-Skhiri, F., Ferreira, I.C.F.R. (2019). Valorisation of the green waste parts from turnip, radish and wild cardoon: Nutritional value, phenolic profile and bioactivity evaluation. *Food Research International*, 126, 108651.
https://doi.org/10.1016/j.foodres.2019.108651

Choi, J.S., Park, S.H., Choi, J.H. (1989). Nitrite scavenging effect by flavonoids and its structure-effect relationship. *Archives of Pharmacal Research*, 12(1), 26–33.
https://doi.org/10.1007/BF02855742

Collins, R., Reith, C., Emberson, J., Armitage, J., Baigent, C., Blackwell, L., et al. (2016). Interpretation of the evidence for the efficacy and safety of statin therapy. *Lancet*, 388(10059), 2532–2561.
https://doi.org/10.1016/S0140-6736(16)31357-5

de Almeida Siqueira, E.M., Rosa, F.R., Fustinoni, A.M., de Sant'Ana, L.P., Arruda, S.F. (2013). Brazilian savanna fruits contain higher bioactive compounds content and higher antioxidant activity relative to the conventional red delicious apple. *PLoS ONE*, 8(8), e72826.
https://doi.org/10.1371/journal.pone.0072826

Dandare, S.U., Mainasara, B.B., Magaji, U.F., Dandare, A., A.Lailaba A., Sadiq, M.E. (2017). In vitro antioxidant activity of *Chrysophyllum albidum* fruit. *Nigerian Journal of Basic and Applied Science*, 25(1), 17-22.
https://doi.org/10.4314/njbas.v25i1.3

Djenidi, H., Khennouf, S., Bouaziz, A. (2020). Antioxidant activity and phenolic content of commonly consumed fruits and vegetables in Algeria. *Progress in Nutrition*, 22(1), 224-235.
https://doi.org/10.23751/pn.v22i1.7701

Espenshade, P.J., Hughes, A.L. (2007). Regulation of sterol synthesis in eukaryotes. *Annual Review of Genetics*, 41, 401–427.
https://doi.org/10.1146/annurev.genet.41.110306.130315

Floyd, R.A. (1999). Neuroinflammatory processes are important in neurodegenerative diseases: An hypothesis to explain the increased formation of reactive oxygen and nitrogen species as major factors involved in neurodegenerative disease development. *Free Radical Biology and Medicine*, 26(9–10),1346–1355.
https://doi.org/10.1016/S0891-5849(98)00293-7

Fogliano, V., Verde, V., Randazzo, G., Ritieni, A. (1999). Method for measuring antioxidant activity and its application to monitoring the antioxidant capacity of wines. *Journal of Agricultural and Food Chemistry*, 47, 1035-1040.
https://doi.org/10.1021/jf980496s

Frei, B., Stocker, R., Ames, B.N. (1988). Antioxidant defences and lipid peroxidation in human blood plasma. *Proceedings of the National Academy of Sciences*, 85, 9748–9752.
https://doi.org/10.1073/pnas.85.24.9748

Furberg, C.D., Adams, H.P., Applegate, W.B., Byington, R.P., Espeland, M.A., Hartwell, T., Hunninghake, D.B., Lefkowitz, D.S., Probstfield, J., Riley, W.A., Young, B. (1994). Effect of lovastatin on early carotid atherosclerosis and cardiovascular events. Asymptomatic Carotid Artery Progression Study (ACAPS) Research Group. *Circulation*, 90, 1679–1687.
https://doi.org/10.1161/01.CIR.90.4.1679

Furberg, C.D. (1999). Natural statins and stroke risk. *Circulation*, 99(2), 185–188.
https://doi.org/10.1161/01.CIR.99.2.185

Garcia-Closas, R., Berenguer, A., Tormo, M.J., Sanchez, M.J., Quiros, J.R., Navarro, C. (2004). Dietary sources of vitamin C, vitamin E and specific carotenoids in Spain. *British Journal of Nutrition,* 91, 1005–1011.
https://doi.org/10.1079/BJN20041130

Gheisari, H.R., Abhari, K.H. (2014). Drying method effects on the antioxidant activity of quince (*Cydonia oblonga* Miller) tea. *Acta Scientiarum Polonorum. Technologia Alimentaria*, 13(2), 129-134.
https://doi.org/10.17306/J.AFS.2014.2.2

Golomb, B.A., Evans, M.A. (2008). Statin adverse effects: A review of the literature and evidence for a mitochondrial mechanism. *American Journal of Cardiovascular Drugs*, 8 (6), 373–418.
https://doi.org/10.2165/0129784-200808060-00004

Gorinstein, S., Cvikrová, M., Machackova, I., Haruenkit, R., Park, Y.S., Jung, S.T., Yamamoto, K., Ayala, A.L.M., Katrich, E., Trakhtenberg, S. (2004). Characterization of antioxidant compounds in Jaffa sweeties and white grapefruits. *Food Chemistry*, 84(4), 503–510.
https://doi.org/10.1016/S0308-8146(03)00127-4

Goyeneche, R., Roura, S., Ponce, A., Vega-G´alvez, A., Quispe-Fuentes, I., Uribe, E., Di Scala, K. (2015). Chemical characterization and antioxidant capacity of red radish (*Raphanus sativus* L.) leaves and roots. *Journal of Functional Foods*, 16, 256–264.
https://doi.org/10.1016/j.jff.2015.04.049

Grundy, S.M., Stone, N.J., Bailey, A.L., Beam, C., Birtcher, K.K., Blumenthal, R.S., et al. (2019). 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the management of blood cholesterol: A report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation*, 139(25), e1082–e1143.
https://doi.org/10.1161/CIR.0000000000000698

Haines, T.H. (2001). Do sterols reduce proton and sodium leaks through lipid bilayers? *Progress in Lipid Research*, 40(4), 299–324.
https://doi.org/10.1016/S0163-7827(01)00009-1

Hanukoglu, I. (1992). Steroidogenic enzymes: Structure, function, and role in regulation of steroid hormone biosynthesis. *The Journal of Steroid Biochemistry and Molecular Biology*, 43(8), 779–804.
https://doi.org/10.1016/0960-0760(92)90307-5

Hmid, I., Elothmani, D., Hanine, H., Oukabli, A., Mehinagic, E. (2017). Comparative study of phenolic compounds and their antioxidant attributes of eighteen pomegranate (*Punica granatum* L.) cultivars grown in Morocco. *Arabian Journal of Chemistry*, 10, S2675–S2684.
https://doi.org/10.1016/j.arabjc.2013.10.011

Kang, Y.H., Park, Y.K., Lee, G.D. (1996). The nitrite scavenging and electron donating ability of phenolic compounds. *Korean Journal of Food Science and Technology*, 28(2), 232–239.

Karadeniz, F., Burdurlu, H.S., Koca, N., Soyer, Y. (2005). Antioxidant activity of selected fruits and vegetables grown in Turkey. *Turkish Journal of Agriculture Forestry*, 29, 297-303.

Kizer, J.R., Madias, C., Wilner, B., Vaughan, C.J., Mushlin, A.I., Trushin, P., Jr Gotto, A.M., Pasternak, R. (2010). Relation of different measures of low-density lipoprotein cholesterol to risk of coronary artery disease and death in a meta-regression analysis of large-scale trials of statin therapy. *The American Journal of Cardiology,* 105(9), 1289–1296.
https://doi.org/10.1016/j.amjcard.2009.12.051

Lee, J.H., Lee, Y.B., Seo, W.D., Kang, S.T., Lim, J.W., Cho, K.M. (2012). Comparative studies of antioxidant activities and nutritional constituents of Persimmon juice (*Diospyros kaki* L. cv. Gapjubaekmok). *Preventive Nutrition and Food Science*, 17(2), 141–151.
https://doi.org/10.3746/pnf.2012.17.2.141

Lehrer, S., Rheinstein, P. (2020). Statins combined with niacin reduce the risk of peripheral neuropathy. *International Journal of Functional Nutrition*, 1(1), 3. https://doi.org/10.3892/ijfn.2020.3

Lewington, S., Whitlock, G., Clarke, R., Sherliker, P., Emberson, J., Halsey, J., Qizilbash, N., Peto, R., Collins, R. (2007). Blood cholesterol and vascular mortality by age, sex, and blood pressure: A meta-analysis of individual data from 61 prospective studies with 55,000 vascular deaths. *Lancet*, 370(9602), 1829–1839. https://doi.org/10.1016/S0140-6736(07)61778-4

Magaji, U.F., Sacan, O., Yanardag, R. (2022). Antilipase, antiacetylcholinesterase and antioxidant activities of *Moringa oleifera* extracts. *Romanian Biotechnological Letters, 27*(1), 3208-3214.

Magangana, T.P., Makunga, N.P., la Grange, C., Stander, M.A., Fawole, O.A., Opara, U.L. (2021). Blanching pretreatment promotes high yields, bioactive compounds, antioxidants, enzyme inactivation and antibacterial activity of 'wonderful' pomegranate peel extracts at three different harvest maturities. *Antioxidants*, 10, 1119. https://doi.org/10.3390/antiox10071119

Mahato, D., Sharma, H.P. (2019). Phytochemical profiling and antioxidant activity of *Leea macrophylla* Roxb. ex Hornem.-in vitro study. *Journal of Traditional Knowledge*, 18(3), 493-499.

Makni, M., Jemai, R., Kriaa, W., Chtourou, Y., Fetoui, H. (2018). *Citrus limon* from Tunisia: Phytochemical and physicochemical properties and biological activities. *BioMed Research International*, 2018, 6251546. https://doi.org/10.1155/2018/6251546

Mir, S.A., Wani, S.M., Wani, T.A., Ahmad, M., Gani, A., Masoodi, F.A., Nazir, A. (2016). Comparative evaluation of the proximate composition and antioxidant properties of processed products of quince (*Cydonia oblonga* Miller). *International Food Research Journal*, 23(2), 816-821.

Moreno-Ortega, A., Pereira-Caro, G., Luis O.J., Manuel M.R.J., Moreno-Rojas, R., Perez-Aparicio, J., Manuel M.R.J. (2020). Changes in the antioxidant activity and metabolite profile of three onion varieties during the elaboration of 'black onion'. *Food Chemistry*, 311, 125958. https://doi.org/10.1016/j.foodchem.2019.125958

Murathan, Z.T. (2020). Phytochemical screening and antioxidant activity of *Diospyros lotus* L. fruits grown in Turkey. *Acta Scientiarum Polonorum Hortorum Cultus*, 19(2), 49–55. https://doi.org/10.24326/asphc.2020.2.5

Muzykiewicz, A., Zielonka-Brzezicka, J., Klimowicz, A. (2018). Quince (*Cydonia oblonga* Mill.) as a useful source of antioxidants–antioxidant activity evaluation. *Herba Polonica*, 64(4), 23-33. https://doi.org/10.2478/hepo-2018-0020

Naci, H., Brugts, J., Ades, T. (2013). Comparative tolerability and harms of individual statins: A study-level network meta-analysis of 246 955 participants from 135 randomized, controlled trials. *Circulation: Cardiovascular Quality and Outcomes*, 6(4), 390–399. https://doi.org/10.1161/CIRCOUTCOMES.111.000071

Nicholls, S.J. (2008). Rosuvastatin and progression of atherosclerosis. *Expert Review of Cardiovascular Therapy*, 6(7), 925–933. https://doi.org/10.1586/14779072.6.7.925

Njie-Mbye, Y.F., Kulkarni-Chitnis M., Opere C.A., Barrett A., Ohia S.E. (2013). Lipid peroxidation: Pathophysiological and pharmacological implications in the eye. *Frontiers in Physiology*, 4, 366. https://doi.org/10.3389/fphys.2013.00366

Oikeh, E.I., Omoregie, E.S., Oviasogie, F.E., Oriakhi, K. (2015). Phytochemical, antimicrobial, and antioxidant activities of different citrus juice concentrates. *Food Science and Nutrition*, 4(1), 103–109. https://doi.org/10.1002/fsn3.268

Park, C., Baskar, T., Park, S.Y., Kim, S.J., Valan, A.M., Al-Dhabi, N., Kim, J., Park, S. (2016). Metabolic profiling and antioxidant assay of metabolites from three radish cultivars *(Raphanus sativus). Molecules*, 21(2), 157. https://doi.org/10.3390/molecules21020157

Payne, A.H., Hales, D.B. (2004). Overview of steroidogenic enzymes in the pathway from cholesterol to active steroid hormones. *Endocrine Reviews*, 25(6), 947–970. https://doi.org/10.1210/er.2003-0030

Pedersen, T.R., Kjekshus, J., Pyörälä, K., Olsson, A.G., Cook, T.J., Musliner, T.A., Tobert, J.A., Haghfelt, T.

(1998). Effect of simvastatin on ischemic signs and symptoms in the Scandinavian simvastatin survival study (4S). *The American Journal of Cardiology*, 81, 333–335. https://doi.org/10.1016/S0002-9149(97)00904-1

Proteggente, A.R., Pannala, A.S., Paganga, G., Van Buren, L., Wagner, E., Wiseman, S., Van De Put, F., Dacombe, C., Rice-Evans, C.A. (2002). The antioxidant activity of regularly consumed fruit and vegetables reflects their phenolic and vitamin C composition. *Free Radical Research*, 36(2), 217-233. https://doi.org/10.1080/10715760290006484

Ren, F., Perussello, C.A., Zhang, Z., Gaffney, M.T., Kerry, J.P., Tiwari, B.K. (2017). Enhancement of phytochemical content and drying efficiency of onions (*Allium cepa* L.) through blanching. *Journal of the Science of Food and Agriculture,* 98(4), 1300-1309. https://doi.org/10.1002/jsfa.8594

Rinaldo, D., Fils-Lycaon, B., Mbéguié-A-Mbéguié, D. (2014). Antioxidant activity of tropical fruits as related to their polyphenol, vitamin C and carotenoid contents: A review. *Acta Horticulturae,* 1040, 261–268. https://doi.org/10.17660/ActaHortic.2014.1040.36

Rufino, M.S.M., Alves, R.E., Brito, E.S., Perez-Jimenez, J., Saura-Calixto, F., Mancini-Filho, J. (2010). Bioactive compounds and antioxidant capacities of 18 non-traditional tropical fruits from Brazil. *Food Chemistry*, 121(4), 996–1002. https://doi.org/10.1016/j.foodchem.2010.01.037

Selyutina, G., Gapontseva, O. (2016). Component composition of radish root essential oil. *Ukrainian Food Journal*, 5, 653-666. https://doi.org/10.24263/2304-974X-2016-5-4-5

Sicari, V., Pellicano, T. M., Giuffre, A. M., Zappia, C., Capocasale, M., Poiana, M. (2018). Physical chemical properties and antioxidant capacities of grapefruit juice (*Citrus paradisi*) extracted from two different varieties. *International Food Research Journal*, 25(5), 1978-1984.

Tekin, Z., Kucukbay, F. (2020). Evaluation of phytochemical contents and antioxidant activity of pomegranate flower. *Journal of The Turkish Chemical Soceity Chemistry A*, 7(1), 37–42. https://doi.org/10.18596/jotcsa.628615

Uckoo, R.M., Jayaprakasha, G.K., Balasubramaniam, V.M., Patil, B.S. (2012). Grapefruit (*Citrus paradisi* Macfad) phytochemicals composition is modulated by household processing techniques. *Journal of Food Science*, 17(9), 141-151. https://doi.org/10.1111/j.1750-3841.2012.02865.x

Vasile, M., Bunea, A., Ioan, C.R., Ioan, B.C., Socaci, S., Viorel, M. (2021). Phytochemical content and antioxidant activity of *Malus domestica* Borkh peel extracts. *Molecules*, 26(24), 7636. https://doi.org/10.3390/molecules26247636

Wang, H., Cao, G., Prior, R.L. (1996). Total antioxidant capacity of fruits. *Journal of Agricultural and Food Chemistry*, 44(3), 701-705. https://doi.org/10.1021/jf950579y

Willcox, J.K., Ash, S.K., Catignani, G.L. (2004). Antioxidants and prevention of chronic diseases. *Critical Reviews in Food Science and Nutrition*, 44(4), 275–295. https://doi.org/10.1080/10408690490468489

Xiao, Z., Lester, G. E., Luo, Y., Wang, Q. (2012). Assessment of vitamin and carotenoid concentrations of emerging food products: Edible microgreens. *Journal of Agricultural and Food Chemistry*, 60(31), 7644–7651. https://doi.org/10.1021/jf300459b

Yeagle, P.L. (1991). Modulation of membrane function by cholesterol. *Biochimie*, 73(10), 1303–1310. https://doi.org/10.1016/0300-9084(91)90093-G

Zhao, X.X., Lin, F.J., Li, H., Li, H.B., Wu, D.T., Geng, F., Ma, W., Wang, Y., Miao, B.H., Gan, R.Y. (2021). Recent advances in bioactive compounds, health functions, and safety concerns of onion (*Allium cepa* L.). *Frontiers in Nutrition*, 8, 669805. https://doi.org/10.3389/fnut.2021.669805