Essential Oil from Lemon Peels Inhibit Key Enzymes Linked to Neurodegenerative Conditions and Pro-oxidant Induced Lipid Peroxidation

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Abstract: This study sought to investigate the effects of essential oil from lemon (Citrus limon) peels on acetylcholinesterase (AChE) and butyrylcholinesterase (BChE) activities in vitro. The essential oil was extracted by hydrodistillation, dried with anhydrous Na2SO4 and characterized using gas chromatography. Antioxidant properties of the oil and inhibition of pro-oxidant-induced lipid peroxidation in rats brain homogenate were also assessed. The essential oil inhibited AChE and BChE activities in a concentration-dependent manner. GC analysis revealed the presence of sabinene, limonene, α-pinene, β-pinene, neral, geranial, 1,8-cineole, linalool, borneol, α-terpinol, terpinen-4-ol, linalyl acetate and β-caryophyllene. Furthermore, the essential oil exhibited antioxidant activities as typified by ferric reducing property, Fe²⁺-chelation and radicals [DPPH, ABTS, OH, NO] scavenging abilities. The inhibition of AChE and BChE activities, inhibition of pro-oxidant induced lipid peroxidation and antioxidant activities could be possible mechanisms for the use of the essential oil in the management and prevention of oxidative stress-induced neurodegeneration.

Key words: lemon peels, essential oil, acetylcholinesterase, butyrylcholinesterase, neurodegeneration

1 Introduction

Citrus peels are by-products of the citrus industry and are majorly considered as waste products in many countries. Large amount of peels are generated from the juice production process due to the fact that peels are about 65% of the total weight of the fruits. While the developed countries have an efficient means of handling this waste, they are a major environmental menace in many developing countries. However, these peels have been shown to be excellent sources of bioactive compounds which possess medicinal potentials. Citrus peels are in use in Chinese medicine and African folklore in the management of degenerative conditions, though there is dearth of information on the scientific basis for the use of the peels. Much of the bioactivity of citrus peels have been linked to the phenolic content, which are more concentrated in the peels that in the juices and seeds. However, there are a lot of other bioactive constituents, such as essential oils, which also contribute to their observed medicinal uses. Essential oils can be obtained in significant quantities from the peels of citrus fruits and they contain numerous compounds rich in polyphenols and terpene hydrocarbons.

Recent trends in the management of neurodegenerative conditions, especially Alzheimer’s disease is to increase brain acetylcholine levels with the use of cholinesterase inhibitors. This is because in Alzheimer’s disease conditions there is elevated cholinesterase activities which serve to break down the neurotransmitters acetylcholine and butyrylcholine thereby giving rise to the symptoms observed in AD. However, due to the side effects associated with the use of synthetic cholinesterase inhibitors, attention is been given to natural sources of cholinesterase inhibitors. Some sea weeds, citrus juices, vegetables and herbs have been shown to be sources of cholinesterase inhibitors. In addition, the use of foods rich in antioxidants have been proposed to be beneficial in the prevention and management of neurodegenerative conditions because the high oxygen consumption of the brain cells and neurons especially, attack by reactive oxygen species.

Lemon (Citrus limon) is grown in many parts of the world for juice production and like the other citrus fruits, the peels are considered as waste. While, the juice have...
been shown to possess anticholinesterase and antioxidative properties, there is dearth of information on the medicinal potentials of the peels, especially the essential oils, which are a major component of the peels and can be extracted in significant amount. This study, therefore investigated the anticholinesterase and antioxidative potentials of essential oils from Lemon peels.

2 Materials and Methods

2.1 Materials

2.1.1 Sample collection

Lemon (*Citrus limon*) peels were collected from the Akure (South west, Nigeria) main market. The peels were dried to a moisture content of 12% and ground to fine powder using Waring Commercial heavy Duty Blender (Model 37BL18; 240CB6). Authentication of the samples was carried out at the Department of Crop, Soil and Pest management (CSP), Federal University of Technology, Akure, Nigeria.

2.1.2 Essential oil isolation

100 g of the ground orange peel powder was subjected to hydrodistillation for 3 h in an all glass Clevenger – type apparatus according to the method recommended by the European Pharmacopoeia 15. The extracted oil sample was passed over anhydrous sodium sulphate and stored in sealed vials at 4°C for further analysis 16–18.

2.1.3 Chemicals and reagents

Chemicals and reagents used such as thiobarbituric acid (TBA), 1,10-phenanthroline, deoxyribose, gallic acid, Folin–Ciocalteau’s reagent were procured from Sigma-Aldrich, Chemie GmbH (Steinheim, Germany), dinitrophenyl hydrazine (DNPH) from ACROS Organics (New Jersey, USA), hydrogen peroxide, methanol, acetic acid, thiourea, Copper sulphate, sulfuric acid, sodium carbonate, aluminum chloride, potassium acetate, sodium dodecyl sulphate, iron (II) sulfate, potassium ferricyanide and ferric chloride were sourced from BDH Chemicals Ltd., (Poole, England). Except stated otherwise, all other chemicals and reagents were of analytical grades and the water was glass distilled.

2.2 Methods

2.2.1 Determination of total phenol content

The total phenol content was determined according to the method of Singleton et al. 10. Briefly, appropriate dilutions of the essential oil was oxidized with 2.5 mL 10% Folin–Ciocalteau’s reagent (v/v) and neutralized by 2.0 mL of 7.5% sodium carbonate. The reaction mixture was incubated for 40 min at 45°C and the absorbance was measured at 765 nm in the spectrophotometer. The total phenol content was subsequently calculated as gallic acid equivalent.

2.2.2 Determination of total flavonoid content

The total flavonoid content of the essential oil was determined using a slightly modified method reported by Meda et al. 20. Briefly, 0.5 mL of appropriately diluted sample was mixed with 0.5 mL methanol, 50 μL 10% AlCl3, 50 μL 1 M potassium acetate and 1.4 mL water and allowed to incubate at room temperature for 30 min. The absorbance of the reaction mixture was subsequently measured at 415 nm and the total flavonoid content calculated as quercetin equivalent.

2.2.3 GC analysis

The analytical GC was carried out by Hewlett-Packard 5890 gas chromatograph Hewlett-Packard Corp., Palo Alto, CA equipped with Flame Ionization Detectors (FID) with DB-5 column (30 m length, 0.25 mm column id., 0.25 μm film thickness). The following conditions were applied: Injection temperature: 290°C, Injection volume: 1.0 μL. Injection mode: Split (1:50). Temperature program: 50°C for 4 min, rising at 3°C/min to 240°C, then rising at 15°C/min to 300°C, held at 300°C for 3 min. FID(290°C): H2 flow: 50 mL/min; air flow: 400 mL/min.

2.2.4 Acetylcholinesterase (AChE) and butyrylcholinesterase (BChE) inhibition assay

Inhibition of acetylcholinesterase (AChE) was assessed by a modified colorimetric method 21. The AChE activity was determined in a reaction mixture containing 200 μL of brain AChE solution (EC 3.1.1.7) in 0.1 M phosphate buffer, pH 8.0, 100 μL of a solution of 5,5′-dithio-bis(2-nitrobenzolic) acid (DTNB 3.3 mM in 0.1M phosphate buffered solution, pH 7.0, containing NaHCO3 6 mM), essential oil (0 –100 μL) and 500 μL of phosphate buffer, pH 8.0. After incubation for 20 min at 25°C, acetylthiocholine iodide (100 μL of 0.05 mM water solution) was added as the substrate, and AChE activity was determined by UV spectrophotometry from the absorbance changes at 412 nm for 3.0 min at 25°C. 100 μL of butyrylthiocholine iodide was used as a substrate to assay butyrylcholinesterase enzyme, while all the other reagents and conditions were the same. Prestigmine was used as positive control at concentrations in the range of therapeutic doses. The AChE and BChE inhibitory activity was expressed as percentage inhibition.

2.2.5 Lipid peroxidation assay

2.2.5.1 Handling and use of animals

Approval was obtained from the relevant Departmental ethics committee responsible for the use of laboratory animals. The handling and the use of the animals were in accordance with NIH Guide for the care and use of laboratory animals. Male Wistar rats weighing 80 g – 130 g used for this experiment were purchased from the breeding colony of the Department of Biochemistry, University of Ilorin, Nigeria. The rats were maintained at 25°C on a 12 h light/dark cycle with free access to food and water. They were acclimatized under these conditions for two weeks.
prior to the commencement of the experiments.

**2.2.5.2 Preparation of Brain Homogenates**

The rats were decapitated under mild diethyl ether anaesthesia and the brain was rapidly isolated and placed on ice and weighed. This tissue was subsequently homogenized in cold saline (1/10 w/v) with about 10-up-and-down strokes at approximately 1200 rev/min in a Teflon glass homogenizer. The homogenate was centrifuged for 10 min at 3000 xg to yield a pellet that was discarded, and a low-speed supernatant (S1) was kept for lipid peroxidation assay.\(^{22}\)

**2.2.5.3 Lipid Peroxidation and Thiobarbituric Acid Reactions**

The lipid peroxidation assay was carried out using the modified method of Ohkawa et al.\(^{23}\). Briefly, 100 \(\mu\)L S1 fraction was mixed with a reaction mixture containing 30 \(\mu\)L of 0.1 M pH 7.4 Tris-HCl buffer, essential oil (0 - 100 \(\mu\)L) and 30 \(\mu\)L of 250 \(\mu\)M freshly prepared FeSO\(_4\) (the procedure was also carried out using 15 mM quinolinic acid). The volume was made up to 300 \(\mu\)L by water before incubation at 37°C for 1 h. The colour reaction was developed by adding 300 \(\mu\)L of 8.1% SDS (Sodium dodecyl sulphate) to the reaction mixture containing S1, which was subsequently followed as percentage of the control.

**2.2.6 Determination of DPPH* scavenging ability**

The free radical scavenging ability of the oil extract against DPPH free radical was evaluated as described by Gyanfi et al.\(^{24}\). Briefly, an appropriate dilution of the extract (1 mL) was mixed with 1 mL 0.4 mM DPPH radicals in methanolic solution. The mixture was left in the dark for 30 min, and the absorbance was taken at 516 nm. The control was carried out by using 2 mL DPPH solution without the test samples. The DPPH free radical scavenging ability was subsequently as percentage of the control.

**2.2.7 Determination of ABTS* scavenging ability**

The total antioxidant capacity was determined based on 2,2-azinobis (3-ethylbenzothiazole-6-sulfonate radical (ABTS\(^{+}\)) scavenging ability of the extract according to the method described by Re et al.\(^{25}\). ABTS\(^{+}\) was generated by reacting ABTS aqueous solution (7 mM) with \(K_{3}S_{2}O_{8}\) (2.45 mM, final concentration) in the dark for 16 h and adjusting the absorbance at 734 nm to 0.700 with ethanol. 0.2 \(\mu\)L of appropriate dilution of the extract was added to 2.0 mL ABTS\(^{+}\) solution and the absorbance was measured at 734 nm after 15 min. The trolox equivalent antioxidant capacity (TEAC) was subsequently calculated using trolox as the standard.

**2.2.8 Determination of Reducing Power**

The reducing property of the extract was determined by assessing the ability of the extract to reduce FeCl\(_3\) solution as described by Oyaiizu\(^{26}\). A 2.5 mL aliquot was mixed with 2.5 mL of 200 mM sodium phosphate buffer (pH 6.6) and 2.5 mL of 1% potassium ferricyanide. The mixture was incubated at 50°C for 20 min and then 2.5 mL of 10% trichloroacetic acid was added. This mixture was centrifuged at 801 \(\times\) g for 10 min. 5 mL of the supernatant was mixed with an equal volume of water and 1 mL of 0.1% ferric chloride. The absorbance was measured at 700 nm and ferric reducing power was subsequently calculated using ascorbic acid equivalent.

**2.2.9 Nitric oxide scavenging activity**

Nitric oxide scavenging assay was performed using Griess reagent method by method reported by Susanta et al.\(^{27}\). Briefly, 0.3 mL of sodium nitroprusside (5 mM) was added to 1 mL each of various concentrations of the extract. The test tubes were then incubated at 37°C for 150 min. After 150 min, 0.5 mL of Griess reagent (equal volume of 1% sulphanilamide on 5% ortho-phosphoric acid and 0.01% naphthyl ethylenediamine in distilled water, used after 12 hrs of preparation) was added. The absorbance was measured at 546 nm.

**2.2.10 Determination of Fe\(^{2+}\) chelating ability**

The Fe\(^{2+}\) chelating ability of the oil extract was determined using a modified method of Minotti and Aust\(^{28}\), with a slight modification by Puntel et al.\(^{29}\). Freshly prepared 500 \(\mu\)M FeSO\(_4\) (150 \(\mu\)L) was added to a reaction mixture containing 168 \(\mu\)L of 0.1 M Tris-HCl (pH 7.4), 218 \(\mu\)L saline and the (0 – 25 \(\mu\)L). The reaction mixture was incubated for 5 min, before the addition of 13 \(\mu\)L of 0.25% 1, 10-phenanthroline (w/v). The absorbance was subsequently measured at 510 nm in a spectrophotometer. The Fe\(^{2+}\) chelating ability was subsequently calculated.

**2.2.11 Fenton’s reaction (Inhibition of Degradation of deoxyribose)**

The ability of the essential oil to prevent Fe\(^{2+}\)/H\(_{2}\)O\(_{2}\)-induced decomposition of deoxyribose was carried out using the method of Halliwell and Gutteridge\(^{30}\). Briefly, appropriate dilution of the essential oil was added to a reaction mixture containing 120 mL 20 mM deoxyribose, 400 \(\mu\)L 0.1 M phosphate buffer, 40 \(\mu\)L 20 mM hydrogen peroxide and 40 \(\mu\)L 500 \(\mu\)M FeSO\(_4\), and the volume was made up to 800 \(\mu\)L with distilled water. The reaction mixture was incubated at 37°C for 30 min, and the reaction was then stopped by the addition of 0.5 mL of 2.8% trichloroacetic acid (TCA), this was followed by the addition of 0.4 mL of 0.6% thiobarbituric acid (TBA) solution. The tubes were subsequently incubated in boiling water for 20 min. The absorbance was measured at 532 nm in spectrophotometer. The percentage (%) OH radical scavenging ability was subsequently calculated.

**2.2.12 Data Analysis**

The results of the three replicates were pooled and expressed as mean ± standard deviation (S.D.). Student’s
3 Results and Discussion

3.1 Phenolic Distribution and chemical constituents

The results of the total phenol and flavonoid distribution in the lemon peel essential oil are presented in Table 1. The total phenolic content reported as gallic acid equivalent was 7.42 mg/100 g, while the total flavonoid content reported as quercetin equivalent was 3.56 mg/100 g. The GC analysis as presented in Table 2 revealed the presence of sabinene (4.18%), limonene (53.08%), α-pinene (3.82%), β-pinene (9.53%), myrcene (3.33%) neral (4.70%), geranial (3.34%), 1,8-cineole (3.38%), linalool (3.70%), borneol (5.58%), α-terpineol (0.25%), terpinen-4-ol (0.23%), linalyl acetate (1.48%) and β-caryophyllene (1.49%).

3.2 Anticholinesterase activity

The effects of the essential oil on acetylcholinesterase and butyrylcholinesterase activities are presented in Fig. 1 and 2. The EC₅₀ values for the dose-dependent inhibition of AChE and BChE activities by the essential oil were 164.35 μL/L and 169.32 μL/L respectively. The EC₅₀ values for prostigmine inhibition of AChE and BChE activities were 45.82 μL/L and 44.38 μL/L respectively. The dose-dependent inhibition of acetylcholinesterase (AChE) and butyrylcholinesterase (BChE) activity by the lemon peel essential oil is of immense importance in the management of neurodegenerative conditions as this increases communication between nerve cells. More so, the butyrylcholinesterase (BChE) inhibition by the essential oil is also beneficial as BChE increases the neurotoxicity of certain plaques thereby making the brain more susceptible to Alzheimer's disease. The anticholinesterase activity of the essential oil could be linked to the phenolic content, as some phenolic rich plant extracts have been shown to inhibit cholinesterases. The anticholinesterase property of the essential oil was lower than that of prostigmine as shown in Fig. 1 and 2, however the side effects experienced with synthetic cholinesterase inhibitors are not expected to be experi-

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Chemical composition of lemon peel essential oil.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parameter (unit)</td>
<td>Value</td>
</tr>
<tr>
<td>Composant</td>
<td>RT %</td>
</tr>
<tr>
<td>sabinene</td>
<td>7.068</td>
</tr>
<tr>
<td>limonene</td>
<td>8.940</td>
</tr>
<tr>
<td>α-pinene</td>
<td>9.758</td>
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<tr>
<td>β-pinene</td>
<td>11.325</td>
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<tr>
<td>benzyl alcohol</td>
<td>11.672</td>
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<tr>
<td>cis ocimene</td>
<td>12.902</td>
</tr>
<tr>
<td>myrcene</td>
<td>13.022</td>
</tr>
<tr>
<td>alo ocimene</td>
<td>13.132</td>
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<tr>
<td>pinene-2-ol</td>
<td>13.789</td>
</tr>
<tr>
<td>α-thujene</td>
<td>14.228</td>
</tr>
<tr>
<td>gamma terpinene</td>
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</tr>
<tr>
<td>neral</td>
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<tr>
<td>geranial</td>
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<tr>
<td>isoaartemisia</td>
<td>16.409</td>
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<tr>
<td>1,8-cineole</td>
<td>16.924</td>
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<tr>
<td>linalool</td>
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<tr>
<td>borneol</td>
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<tr>
<td>α-terpineol</td>
<td>18.643</td>
</tr>
<tr>
<td>terpinen-4-ol</td>
<td>18.847</td>
</tr>
<tr>
<td>thymyl methyl ether</td>
<td>19.704</td>
</tr>
<tr>
<td>ascaridole</td>
<td>20.068</td>
</tr>
<tr>
<td>ethyl cinnamate</td>
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</tr>
<tr>
<td>borneol acetate</td>
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<tr>
<td>β-bisabolene</td>
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<tr>
<td>linalyl acetate</td>
<td>22.068</td>
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<tr>
<td>β-caryophyllene</td>
<td>22.281</td>
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<tr>
<td>β-Elemene</td>
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<tr>
<td>germacrene D</td>
<td>23.883</td>
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<tr>
<td>bicyclogermacrene</td>
<td>24.321</td>
</tr>
<tr>
<td>viridiflorol</td>
<td>29.492</td>
</tr>
<tr>
<td>torreyol</td>
<td>29.663</td>
</tr>
<tr>
<td>tetra decanoic acid</td>
<td>29.962</td>
</tr>
</tbody>
</table>

RT: retention time

Table 1 | The total phenolic content reported as gallic acid equivalent, total flavonoid content reported as quercetin equivalent, trolox equivalent antioxidant capacity and ferric reducing antioxidant property reported as ascorbic acid equivalent.

<table>
<thead>
<tr>
<th>Parameter (unit)</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total phenol (gallic acid equivalent) (mg/100g)</td>
<td>7.42 ± 0.34</td>
</tr>
<tr>
<td>Total flavonoid (quercetin equivalent) (mg/100g)</td>
<td>3.56 ± 0.27</td>
</tr>
<tr>
<td>Trolox equivalent antioxidant capacity (mmol/g)</td>
<td>3.64 ± 0.31</td>
</tr>
<tr>
<td>Ferric reducing antioxidant property (ascorbic acid equivalent) (mg/100g)</td>
<td>27.09 ± 0.93</td>
</tr>
</tbody>
</table>

Values represent means of triplicate readings

376

Anticholinesterase properties of lemon peel essential oil

enced with the use of natural compounds\textsuperscript{8,9}. The anticholinesterase activity of the essential oil could also be linked to the presence of some constituents identified by GC analysis such as borneol, β-pinene and 1,8-cineole, which have been reported to possess anticholinesterase properties\textsuperscript{32,36}. The synergistic action of the volatile compounds identified in the oils, majorly classified as monoterpensoids and phenylpropanoids could contribute to their cholinesterase inhibitory ability\textsuperscript{37,38}. Furthermore, Mukherjee et al.\textsuperscript{13} attributed the anticholinesterase activity of phenylpropanoids to hydrophobic interactions between their hydrocarbon skeleton and the hydrophobic active site of AChE.

3.3 Lipid preoxidation Inhibition

The incubation of rat’s brain homogenates in presence of Fe\textsuperscript{2+} and quinolinic acid caused a significant increase ($p < 0.05$) in the malondialdehyde (MDA) content as shown in Figs. 3 and 4. The increase in malondialdehyde content when rat’s brain homogenates were incubated in the presence of Fe\textsuperscript{2+} is through decomposition of hydrogen peroxide to produce OH\textsuperscript{*}\textsuperscript{39}. However, the essential oil inhibited Fe\textsuperscript{2+} induced MDA production in a dose-dependent manner with EC\textsubscript{50} values of 90.68 µL/L which could be attributed to the ability of the oil to chelate Fe\textsuperscript{2+} or scavenge OH\textsuperscript{*}\textsuperscript{39}. Reactive oxygen species-induced malondialdehyde (MDA) production in the brain has been linked to the development of Alzheimer’s disease since there is a huge amount of brain phospholipids which are easily attacked by free radicals\textsuperscript{11,40,41}. The incidence of neurodegenerative conditions have been linked to increased levels of iron in the brain through increased iron transportation across the blood-brain barrier\textsuperscript{42}. Iron then causes harmful effects in the brain by decomposing hydrogen peroxide to produce hydroxyl radicals (OH\textsuperscript{*}). Therefore, the OH\textsuperscript{*} scavenging ability of the essential oil could be a possible mechanism by
which they protect the brain from lipid peroxidation\textsuperscript{39, 43}. Similarly, the incubation of rat’s brain homogenates in the presence of quinolinic acid caused a significant increase in the MDA content due to increased lipid peroxidation brought about by the ability of quinolinic acid to form complexes which induce excess free radical formation\textsuperscript{44}. Quinolinic acid has been implicated in many neurodegenerative conditions including Alzheimer’s disease and Parkinson’s disease\textsuperscript{45–47}. The essential oil inhibited quinolinic acid-induced MDA production in a dose-dependent manner with EC\textsubscript{50} value of 89.95 $\mu$L/L. The inhibition of quinolinic acid induced-lipid peroxidation by the essential oils as well as the NO* scavenging ability could be beneficial in the management of neurodegenerative conditions because quinolinic acid has been linked to AD development through the production of NO* in the brain\textsuperscript{48}. Two of the lemon essential oil compounds, limonene and linalool have been shown to inhibit MDA production when fed to female rats given an overdose of 7,12-dimethylbenz (a) anthracene (DMBA)\textsuperscript{49}.

3.4 Antioxidant activity

Antioxidants have been proposed to be beneficial in the management of neurodegenerative conditions as the role of free radicals in such conditions have been well established since brain cells consume a high amount of oxygen\textsuperscript{14}. The radical scavenging ability of the essential oil used in this study is exhibited by their DPPH, ABTS, OH and NO radical scavenging activities. The ABTS* scavenging ability presented as trolox equivalent antioxidant capacity of the essential oil was 3.64 mmol/TEAC g and the ferric reducing ability presented as ascorbic acid equivalent was 27.09 mg/100g. Furthermore, the lemon peel essential oil scavenged DPPH*, OH* and NO* in dose-dependent manner and the EC\textsubscript{50} values were 205.93 $\mu$L/L (DPPH*), 191.62 $\mu$L/L (OH*) and 340.24 $\mu$L/L (NO*) (Figs. 5A, 5B, 5C). The radical scavenging abilities of the essential oil could be linked to the presence of phenolic monoterpenes\textsuperscript{50}. Although, Aazza \textit{et al.}\textsuperscript{51} showed that some of the essential oil components of lemon peels as revealed by this study such as $\alpha$-pinene, $\beta$-pinene, limonene, linalool, 1,8-cineole, linalyl acetate and borneol had less than 50% DPPH* scavenging ability, the...
observed radical scavenging ability of the essential oils used in this study could be a result of synergistic effect of the volatile constituents.

Figure 5D showed that the essential oil had a dose-dependent Fe$^{2+}$ chelating ability with EC$_{50}$ value of 133.5 μL/L. Iron plays an important role in the generation of hydroxyl radicals and also in the development of neurodegenerative conditions as it accumulates in the brain of patients with Alzheimer’s disease. The ferric reducing antioxidant property and Fe$^{2+}$ chelating ability of the citrus peel essential oil could therefore be beneficial in the management/prevention of neurodegenerative conditions. The ferric reducing ability of the essential oil could be attributed to constituents such as α-pinene, limonene, linalool, 1,8-cineole and linalyl acetate, which have been shown to have reductive potential. The Fe$^{2+}$ chelating ability of the essential oil could be attributed to the presence of functional groups such as –OH in linalool and borneol, –O– in 1,8-cineole and –C=O– in linalyl acetate in a favourable structure–function configuration. The EC$_{50}$ values revealed that the essential oil had significantly higher Fe$^{2+}$ chelating ability than OH$^*$ scavenging ability. The higher Fe$^{2+}$ chelating ability of the essential oil could be of therapeutic importance in the protective ability of the essential oil against oxidative stress, due to the high reactivity of OH$^*$.

4 Conclusion

The inhibition of cholinesterases and Fe$^{2+}$ and quinolinic acid-induced MDA production as well as radicals (DPPH$, \cdot$, ABTS$, \cdot$, OH$^*$ and NO$^*$) scavenging abilities are possible mechanisms by which lemon peel essential oil could be used in the management and/or prevent neurodegenerative conditions. However, further in vivo experiments and clinical trials are recommended.

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Anticholinesterase properties of lemon peel essential oil


