ABSTRACT

Oxidative stress-induced neurodegenerative diseases have become more prevalent lately due to the stressful environment and lifestyle. Growing empirical scientific evidences which support the use of plant-derived antioxidants in the control of neurodegenerative disorders has been validated in the present investigation. *Loranthus parasiticus* (L.) Merr, a Chinese traditional folk medicine which has been used in treating brain diseases was selected for the present study. Therefore, *L. parasiticus* was hypothesized to exhibit antioxidative and neuroprotective properties in NG108-15 neuroprotection model. *Loranthus parasiticus* aqueous fraction (LPAF) which showed the highest antioxidative and neuroprotective activities against H$_2$O$_2$ among the tested extract and fractions was subjected to a bioassay-guided fractionation and isolation approach to identify the most potent neuroprotective compound. (+)-Catechin was found to be the most potent neuroprotective compound and its underlying mechanisms were evaluated subsequently. (+)-Catechin significantly reduced reactive oxygen species production, phosphatidylserine externalization, mitochondrial membrane potential depolarization, sub-G$_1$ apoptotic fraction induction, and increased the percentage of cell viability following H$_2$O$_2$-induced oxidative stress insult. Moreover, (+)-catechin increased the H$_2$O$_2$-induced reduction of SOD and GPx activities. (+)-Catechin also upregulated Bcl-2 and downregulated Bax, resulting in a decreased ratio of Bax/Bcl-2. Interestingly, oxidative stress-induced overexpression of chemokine CCL21 was significantly attenuated by (+)-catechin, indicating a novel role of (+)-catechin in neuroprotection context via the regulation of neuronal chemokine CCL21. Collectively, the present findings have proven our hypothesis and support the use of *L. parasiticus* in managing oxidative stress related neurodegenerative diseases.
ABSTRAK

ACKNOWLEDGEMENTS

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On a special note I would like to thank also to all my friends for their caring and support to make this thesis a success.

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Outside the lab, despite the geographical distance, my family members are always nearby. I thank my family members and relatives for their continually courage, love, and support over my researching life.

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<thead>
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<th>Abbreviation</th>
<th>Full Form</th>
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<tbody>
<tr>
<td>ATCC</td>
<td>American type culture collection</td>
</tr>
<tr>
<td>AIF</td>
<td>Apoptosis-inducing factor</td>
</tr>
<tr>
<td>APAF</td>
<td>Apoptosis protease activating factor</td>
</tr>
<tr>
<td>BH</td>
<td>Bcl-2 homology</td>
</tr>
<tr>
<td>BHT</td>
<td>Butylated hydroxytoluene</td>
</tr>
<tr>
<td>BD</td>
<td>Becton Dickinson</td>
</tr>
<tr>
<td>CD</td>
<td>Cluster of differentiation</td>
</tr>
<tr>
<td>CDK</td>
<td>Cyclin-dependent kinase</td>
</tr>
<tr>
<td>DAPI</td>
<td>4',6-diamidino-2-phenylindole</td>
</tr>
<tr>
<td>DCH-DA</td>
<td>2,7 dichlorofluorescein diacetate</td>
</tr>
<tr>
<td>DMEM</td>
<td>Dulbecco’s modified Eagle’s medium</td>
</tr>
<tr>
<td>DMSO</td>
<td>Dimethyl sulfoxide</td>
</tr>
<tr>
<td>DPPH</td>
<td>2,2-diphenyl-1-picrylhydrazyl</td>
</tr>
<tr>
<td>DTNB</td>
<td>5',5'-dithio-bis(2-nitrobenzoic acid)</td>
</tr>
<tr>
<td>EDTA</td>
<td>Ethylenediaminetetraacetic acid</td>
</tr>
<tr>
<td>EGCG</td>
<td>(−)-epigallocatechin-3-gallate</td>
</tr>
<tr>
<td>FACS</td>
<td>Fluorescent activated cell sorting</td>
</tr>
<tr>
<td>FADD</td>
<td>Fas-associated protein with death domain</td>
</tr>
<tr>
<td>FeCl₃</td>
<td>Ferric chloride</td>
</tr>
<tr>
<td>FeSO₄</td>
<td>Ferrous sulfate</td>
</tr>
<tr>
<td>FITC</td>
<td>Fluorescein isothiocyanate</td>
</tr>
<tr>
<td>FBS</td>
<td>Fetal bovine serum</td>
</tr>
<tr>
<td>GAE/gDW</td>
<td>Gallic acid equivalent per gram of dry weight</td>
</tr>
<tr>
<td>GPCR</td>
<td>G-protein coupled receptor</td>
</tr>
<tr>
<td>Acronym</td>
<td>Definition</td>
</tr>
<tr>
<td>---------</td>
<td>------------</td>
</tr>
<tr>
<td>GPx</td>
<td>Glutathione peroxidase</td>
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<td>GR</td>
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<td>GSH</td>
<td>Glutathione</td>
</tr>
<tr>
<td>GSSG</td>
<td>Oxidized glutathione</td>
</tr>
<tr>
<td>GST</td>
<td>Glutathione-S-transferase</td>
</tr>
<tr>
<td>HAT</td>
<td>Hypoxanthine-aminopterin-thymidine</td>
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<td>HMBS</td>
<td>Hydroxymethylbilane synthase</td>
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<tr>
<td>HNE</td>
<td>4-hydroxy-2-nonenal</td>
</tr>
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<td><em>Loranthus parasiticus</em> aqueous fraction</td>
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<td><em>Loranthus parasiticus</em> ethanol extract</td>
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<td>3-(4,5-domethylthiazol-2-yl)-2,5-diphenyltetrazolim</td>
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<td>NADPH</td>
<td>Nicotinamide adenine dinucleotide phosphate</td>
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<td>NG108-15</td>
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<td>Nuclear magnetic resonance</td>
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