Lead induced inflammation, learning deficit and memory loss in mice: Neuroprotective efficacy of *Curcuma longa*

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Lead induced inflammation, learning deficit and memory loss in mice: Neuroprotective efficacy of Curcuma longa

Overview

@ Lead toxicity
@ Mechanism of lead (Pb) induced neurotoxicity
@ Lead induced neurodegeneration and related Alzheimers’ disease
@ Medicinal plants and its property
@ Experimental design
@ Results
@ Discussion/Conclusion
Humans are often exposed to lead from water, food contamination and air pollution.
Physiological effects of Lead

@ Lead (Pb) is a systemic toxicant that can affect to all organ systems, primarily the central nervous system.

Effects on adults:
- Brain disease
- Anemia
- Colic
- Non-specific symptoms
- Memory impairment
- Sperm abnormalities
- Kidney disease
- Possible gout
- Spontaneous abortion
- Possible non-specific symptoms
- Possible memory impairment

Effects on children:
- Death
- Coma
- Convulsions
- Brain disease
- Kidney disease
- Frank anemia
- Colic
- Decreased capacity to transport oxygen
- Increased risk of hypertension in adulthood
- Body can’t maintain adequate calcium levels
- Developmental toxicity
  - Decreased IQ level
  - Decreased hearing
  - Decreased growth
  - Impaired nerve function
  - Trans-placental transfer

*Non-specific symptoms may include headache, fatigue, sleep disturbance, anorexia, constipation, joint pain, muscle pain, and decreased libido.
Mechanism of Lead induced neurotoxicity

Reactive oxygen species, ROS/ Reactive nitrogen species, RNS

Oxidative stress

Inflammation

Neuronal and supporting cell

Apoptosis

Nurodegeneration

Learning deficit & Memory loss
Fate of neuron stem cells after lead exposure

Lead ion (Pb2+)

Cortex

Hippocampus

Learning & Memory loss

Occupational lead exposure can increase the risk of Alzheimer's disease by 3-4 times.

@ Inflammation is a general marker of tissue damage in any disease, and may be neuronal cell death and tissue damage in AD.

Tangpong et al., 2006
The cause of Alzheimer's Disease is not fully understood. It is believed there may be genetic (hereditary) factors involved, with a breakdown of proteins resulting in the formation of protein deposits (senile plaques) within the brain.

Environmental factors and infection may also have an influence on the progress of the disease, but the extent of this is not fully known.
Chemotherapeutic drugs, Doxorubicin

ROS/RNS

Microglia

TNF-α

MT-NOS

iNOS

O$_2^-$

OONO$^-$

MnSOD

nitration/inactivation

Apoptosis

Learning deficit, Memory loss

Chemotherapeutic drugs, Doxorubicin

Tangpong et al., Neurobiol Dis. 2006; Tangpong et al., J Neurochem. 2007;
Inhibitors of neuroinflammatory: A new model of neuroprotective action

Inhibitors:
- Anti-TNFα, Volproate,
- Phytoestrogen
- Natural products
Medicinal plants in local area

- **T. laurifolia**
  - Antioxidant
  - Anti-inflammatory
  - Anti-cancer

- **Garcinia mangostana**

- **Curcuma longa**
Medicinal plants extraction method

Pressurized Hot Water Extraction (PHWE)
(Temperature 120 °C, 15 ponds, 30 min)

Filtration

Color/Oder

Concentration

Freezing (Lyophilizer)
Curcumin (Curcuma longa)

Medical properties of curcumin;
1. Anti-inflammatory and antioxidant
2. Anti-cancer
3. Diuretic and Renoprotective activity
4. Anti-hypercholesterolemia
5. Neuroprotective property
6. Reduced cholinergic dysfunction

(Yadav et al., 2011)

Active compound: Polyphenolic compound
Experimental design

Male IRC Mice

- Forced Swimming Test
- Water Maze Swimming Test
- Depression, Learning deficit, and Memory loss

Plasma, RBC

Brain

Inflammation markers @ TNF-α, COX-2 and iNOS

Lipid peroxidation (Malonaldehyde, MDA)

AChE activity and expression

ChAT expression
**RESULTS**

Table 1: Pb-treated group showed significantly less body weight compared with that of control groups

<table>
<thead>
<tr>
<th>Group</th>
<th>Initial Body Weight (g)</th>
<th>Final Body Weight (g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium acetate</td>
<td>29.53 ± 0.35</td>
<td>37.16 ± 1.01</td>
</tr>
<tr>
<td>Pb (1% in drinking water)</td>
<td>30.01 ± 0.37</td>
<td>32.80 ± 0.58&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Cur (200mg/kgBW/day)</td>
<td>30.22 ± 0.38</td>
<td>37.50 ± 0.80&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Pb (1%) + Cur(100mg/kgBW/day)</td>
<td>30.78 ± 0.37</td>
<td>36.50 ± 0.71&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>Pb (1%) + Cur(200mg/kgBW/day)</td>
<td>30.25 ± 0.46</td>
<td>38.69 ± 0.58&lt;sup&gt;d&lt;/sup&gt;</td>
</tr>
<tr>
<td>Pb +VitE(100mg/kgBW/day)</td>
<td>30.97 ± 0.42</td>
<td>37.13 ± 1.38&lt;sup&gt;e&lt;/sup&gt;</td>
</tr>
<tr>
<td>Vehicle control</td>
<td>30.32 ± 0.44</td>
<td>37.66 ± 0.89</td>
</tr>
</tbody>
</table>
Figure 1: Curcumin inhibited Pb induced inflammatory, TNF-\(\alpha\), COX-2 and iNOS, expression.
Table 2: Curcumin protect lead (Pb) induced oxidative stress in blood and brain of mice

<table>
<thead>
<tr>
<th>Group</th>
<th>Plasma MDA (nM)</th>
<th>RBC MDA (µM/gHb)</th>
<th>Brain MDA (nM/g protein)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium acetate</td>
<td>91.43±3.42</td>
<td>3.72 ± 0.18</td>
<td>37.67 ± 3.43</td>
</tr>
<tr>
<td>Pb (1%)</td>
<td>178.74±4.54(^a)</td>
<td>6.98 ± 0.44(^a)</td>
<td>50.8 ± 2.71(^a)</td>
</tr>
<tr>
<td>Cur (200mg/kgBW)</td>
<td>87.83±2.12(^b)</td>
<td>3.89 ± 0.11(^b)</td>
<td>38.88 ± 1.46(^b)</td>
</tr>
<tr>
<td>Pb + Cur 100mg/kgBW</td>
<td>125.78±3.21(^c)</td>
<td>4.14 ± 0.94(^c)</td>
<td>42.08 ± 0.62(^c)</td>
</tr>
<tr>
<td>Pb + Cur 200mg/kgBW</td>
<td>103.94±5.76(^d)</td>
<td>3.65 ± 0.2(^d)</td>
<td>39.02 ± 1.93(^d)</td>
</tr>
<tr>
<td>Pb + VitE100mg/kgBW</td>
<td>102.42±4.69(^e)</td>
<td>4.15 ± 0.2(^e)</td>
<td>38.76 ± 1.18(^e)</td>
</tr>
<tr>
<td>Vehicle Control</td>
<td>94.19±3.49</td>
<td>3.65 0.12</td>
<td>37.67 ± 1.43</td>
</tr>
</tbody>
</table>
Figure 2: The protective effect of Curcumin against Pb induced AChE activity in mouse model.
Figure 4: Curcumin prevented Pb reduced AChE and ChAT expression

Neuronal cell apoptosis
Figure 3: Curcumin attenuated Pb induced memory loss and learning deficit and depressant-like effect in the Force swimming test (FST).

<table>
<thead>
<tr>
<th>Condition</th>
<th>Latency Time (s)</th>
<th>Immobility Time (s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium acetate</td>
<td>60</td>
<td>40</td>
</tr>
<tr>
<td>Pb alone</td>
<td>80</td>
<td>60</td>
</tr>
<tr>
<td>Pb + Cur 200mg/kgBW</td>
<td>100</td>
<td>80</td>
</tr>
<tr>
<td>Pb + Cur 100mg/kgBW</td>
<td>120</td>
<td>100</td>
</tr>
<tr>
<td>Pb + VitE 100mg/kgBW</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vehicle Control</td>
<td>140</td>
<td>120</td>
</tr>
</tbody>
</table>
@ Curcumin significantly alleviates Pb induced neurotoxicity,

@ Curcumin suppress inflammation, oxidative damage of circulation system and brain tissue,

@ Curcumin can alteration in neurotransmitter and expression of enzymes AChE and ChAT with a reduction learning deficit and memory loss
Herbal Products

Curcuma longa

Nano-emulsion Skin care products

Curcumin anti-doxy capsule

Curcumin Soap
Free radical biology of medicine/Toxicology/ Neurodegeneration/Metabolic syndrome-DM/
Natural products/Innovation for Health