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Title: The Dose-Dependent Effect of *Rheum Palmatum* on Neuronal Viability

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ABSTRACT

This study examines the neuroprotective effects of *Rheum palmatum* root extract on neuronal viability. In vitro experiments showed that the extract preserved 96% cell viability at 0.2% concentration but dropped to 89% at 2%, indicating a dose-dependent effect. The findings suggest potential therapeutic benefits at optimal doses, while higher concentrations may be toxic. Further studies are needed to explore its role in neurodegenerative disease treatment.

Keywords:
Rheum palmatum,
neuroprotection,
neurodegenerative disease.

INTRODUCTION

1. *Rheum Palmatum*

Rheum palmatum, commonly known as Chinese rhubarb, is a perennial plant belonging to the Polygonaceae family. This plant is notable for its broad leaves and red stem, making a lasting impression (Choi & Hwang, 2005). It grows in most parts of Asia, especially in the high-altitude regions of the Himalayas, Tibet, and China.

Rheum palmatum has been used in traditional Chinese medicine for centuries as an anti-bloating, anti-inflammatory, and liver disease treatment, securing a significant place in modern medicine as well (Yang et al., 2017). Its roots exhibit a mustard-yellow color when fresh and range from light yellow to dark brown when dried.

These roots possess pharmacological effects due to their active compounds, particularly anthraquinone derivatives (emodin and aloe-emodin), phenolic compounds, and tannins (Guo et al., 2011). Structurally, the plant is also notable. It is a long-lived herbaceous plant with thick stems that can grow up to 1 to 2 meters and broad, lobed leaves supported by thick, hairy stalks that can expand up to 60 cm (Choi & Hwang, 2005). Its flowers are small, usually pale green or red, and arranged in racemes.

2. Pharmacological Properties and Chemical Components

The extract obtained from dried *Rheum palmatum* roots is of great pharmacological interest due to its rich chemical composition (Tang et al., 2014). The primary bioactive components include anthraquinone derivatives (emodin, aloe-emodin,

rhein, chrysophanol, and physcion), tannins, and flavonoids (Yang et al., 2017). These compounds are responsible for various medicinal effects:

- **Anthraquinones:** Emodin and aloe-emodin exhibit anti-inflammatory, antioxidant, and anticancer properties. Emodin regulates mitochondrial functions and controls cell apoptosis (Guo et al., 2011).
- **Rhein:** Plays a crucial role in neurodegenerative diseases by exhibiting anti-inflammatory effects and reducing amyloid-beta accumulation (Liu et al., 2013).
- **Tannins:** Prevent free radical damage due to their antioxidant properties (Choi & Hwang, 2005).
- **Flavonoids:** Regulate cellular stress mechanisms and offer vascular protective effects (Yang et al., 2017).

These chemical components contribute to the plant's antimicrobial, hepatoprotective, antitumorigenic, and neuroprotective effects. Traditionally used for liver diseases, inflammation, and immune system disorders, the extract has gained significant interest in oncology (Guo et al., 2011). Experiments on lung and ovarian cancer suggest promising effects of rhubarb root extract in these areas (Liu et al., 2013).

3. Neurons and Nervous System Functions

Neurons, the fundamental units of the nervous system, play a crucial role in the functionality of both the brain and body. These cells receive, process, and transmit information through electrical and chemical signals (Bear et al., 2020). A typical neuron is divided into three main parts: soma (cell body), dendrites, and axon.

3.1. Structure Of A Neuron

The cell body contains the nucleus and other organelles, regulating essential metabolic processes. Dendrites are branched structures that receive signals from other neurons and transmit them to the soma. The axon is a long extension that facilitates signal transmission to other neurons or effector cells (Purves et al., 2018).

Neurons communicate through specialized connections called synapses. Electrical signals travel to the axon terminals, where they are converted into chemical signals and transmitted to the receptors of another neuron. Neurotransmitters such as dopamine, glutamate, and GABA regulate this process and form the basis of neurological functions (Kandel et al., 2021).

The transmission capacity and sensitivity of neurons directly affect central nervous system functions. Complex processes such as learning, memory, sensory perception, and motor control rely on the flawless operation of neurons (Bear et al., 2020). However, neurodegenerative diseases like Alzheimer's and Parkinson's can damage nerve cells, disrupting neuron-to-neuron communication mechanisms (Selkoe & Hardy, 2016).

4. Basic Mechanisms of Neuronal Transmission

Neurotransmission is a complex process involving electrical and chemical mechanisms. Electrical transmission occurs through action potentials, where ion channels regulate the flow of sodium and potassium ions, altering the neuron's membrane potential. This process is faster in myelinated axons, allowing rapid signal propagation.

Chemical transmission, on the other hand, involves neurotransmitter release at synapses, where they bind to receptors on the receiving neuron to transmit signals. Key neurotransmitters, such as dopamine, serotonin, and glutamate, play crucial roles in motor control, mood regulation, and learning. Disruptions in these systems are linked

to neurological disorders like Alzheimer's and Parkinson's disease, making the understanding of neurotransmission vital for developing treatments for these conditions.

5. Effect of *Rheum palmatum* Root Extract on Neurons

Rheum palmatum root extract, rich in anthraquinone derivatives like emodin, rhein, and aloe-emodin, has shown promising effects in treating neurological disorders. It helps protect neurons, prevent degeneration, and improve function (Guo et al., 2011). In vitro studies indicate that the extract reduces oxidative stress and suppresses inflammation (Liu et al., 2013).

Emodin, in particular, prevents apoptosis, supports neurotransmission, and enhances mitochondrial function (Purves et al., 2018). In vivo studies confirm its positive impact on cognitive functions and its protective effects against toxins (Yang et al., 2017). The extract reduces inflammation, oxidative damage, and amyloid beta accumulation in neurodegenerative models (Selkoe & Hardy, 2016). Further clinical research is needed to fully assess its effects on human health.

6. Molecular Mechanisms of Action

The effects of *Rheum palmatum* root extract on neurons have been investigated at the cellular and molecular levels. The extract's biologically active components, particularly anthraquinones and flavonoids, have been shown to reduce oxidative stress in nerve cells, playing a key role in maintaining neuronal health (Zhou et al., 2021).

Molecularly, the extract increases the expression of antioxidant enzymes, such as superoxide dismutase and catalase, reducing oxidative damage (Wang et al., 2020). It inhibits the production of reactive oxygen species (ROS), supporting mitochondrial function, energy production, and neuronal survival (Li et al., 2019).

Additionally, the extract regulates cell membrane permeability, influencing ion channel function and improving neurotransmission (Chen et al., 2022). *Rheum palmatum* extract also enhances synaptic plasticity, contributing to cognitive functions like learning and memory (Zhang et al., 2020). It reduces neuroinflammation, protecting nerve cells from damage, and its effects are linked to the regulation of gene expression through pathways like NF-κB, MAPK, and Nrf2 (Xu et al., 2018). These molecular mechanisms help prevent apoptosis, strengthen synaptic connections, and protect against neurodegeneration, forming a foundation for potential therapeutic uses in neurological diseases (Liu et al., 2021).

7. Effect of *Rheum palmatum* Root Extract on Neurological Diseases

Research on *Rheum palmatum* root extract shows promising neuroprotective effects, particularly in neurodegenerative disorders like Alzheimer's and Parkinson's. The bioactive compounds in the extract protect nerve cells from oxidative stress and inflammation, potentially preventing neurodegeneration (Zhou et al., 2021; Li et al., 2019).

8. Alzheimer's Disease

Alzheimer's disease is a neurodegenerative disorder characterized by beta-amyloid plaques and tau protein abnormalities, leading to cognitive decline (Huang & Mucke, 2012). Traditional treatments provide symptomatic relief but have limited effects on disease progression (Yiannopoulou & Papageorgiou, 2020).

Rheum palmatum root extract, with compounds like emodin and aloe-emodin, shows antioxidant and anti-inflammatory properties. It reduces oxidative stress, inhibits glial cell activation, and prevents beta-amyloid accumulation (Chen et al., 2022). Animal studies suggest the extract improves learning and memory, slowing neurodegeneration (Wang et al., 2020), activating Nrf2 and MAPK pathways to boost antioxidant responses (Xu et al., 2018).

6. Parkinson's Disease

Parkinson's disease is characterized by the degeneration of dopaminergic neurons and α-synuclein accumulation, leading to motor and cognitive impairments (Poewe et al., 2017). Current treatments provide symptom relief but do not halt progression (Kalia & Lang, 2015). *Rheum palmatum* root extract shows promise, with emodin binding to α-synuclein, monoamine oxidase B, and catechol-O-methyltransferase, inhibiting α-synuclein aggregation and protecting dopaminergic neurons (Zhang et al., 2020; Li et al., 2019). It also supports mitochondrial function and enhances neuronal survival by inhibiting ROS production (Chen et al., 2022).

METHOD

1. Problem Definition

The aim of this study is to determine the possibility of usage of the bioactive compounds in the *Rheum Palmatum* extract in the treatment of neurodegenerative diseases. This study, evaluates the impact of bioactive compounds in the *rheum palmatum* extract on neuron viability and proves its neuroprotective properties.

2. Hypothesis

The bioactive compounds in *Rheum Palmatum* keep the neuron viability stable and demonstrate neuroprotective properties.

3. Materials and Methods

3.1. Materials

- Rheum palmatum (Rhubarb Root)
- 96% Ethanol
- Soxhlet Apparatus
- HT22 Mouse Hippocampal Neuronal Cells
- Dulbecco's Modified Eagle Medium (DMEM)
- Fetal Bovine Serum (FBS)
- Penicillin-Streptomycin (1%)
- Carbon Dioxide (CO_2) Incubator
- 96-Well Plates
- Dimethyl Sulfoxide (DMSO)
- MTT Assay Kit
- DMSO (for MTT Assay)
- Spectrophotometer
- DCFH-DA Fluorescent Dye
- SPSS Software

3.2. Method

Rheum palmatum roots were obtained, ground into a fine powder, and extracted using Soxhlet extraction with 96% ethanol for 6 hours. The extract was then concentrated by removing ethanol and stored at -20°C.

HT22 mouse hippocampal neuronal cells were cultured in DMEM containing 10% fetal bovine serum (FBS) and 1% penicillin-streptomycin and incubated at 37°C with 5% CO_2. Cells were seeded into 96-well plates at a density of 1×10^4 cells/mL and incubated for 24 hours for adhesion.

The extract was prepared at 0.2% and 2% concentrations using DMSO (ensuring a final concentration below 0.1%) and applied to the cells, with control groups receiving only the culture medium or 0.1% DMSO. After 24 hours of incubation, cell viability was assessed using the MTT assay, where formazan crystals were dissolved in DMSO and absorbance was measured at 570 nm.

Oxidative stress was analyzed by measuring reactive oxygen species (ROS) levels with DCF-DA fluorescent dye, while antioxidant activity was

assessed by determining superoxide dismutase (SOD) and catalase (CAT) enzyme activities. Statistical analysis was performed using SPSS, with significance set at $p<0.05$.

FINDINGS

1. Effect of Rhubarb Root Extract on Cell Viability

In the control group, cell viability was measured at 94%. When 0.2% rhubarb root extract was applied, viability increased to 96%, whereas 2% rhubarb root extract led to a decrease in viability to 89%. These results visually presented in the above graph demonstrate that different concentrations of rhubarb extract influence cell viability.

2. Dose-Dependent Impact on Cell Viability

The increase in viability at 0.2% concentration suggests that low doses of rhubarb extract may promote cellular health. However, the decline at 2% concentration indicates that higher doses may have cytotoxic effects.

3. Possible Reasons for the Observed Effects

- **Cellular Support at Low Doses:** The slight increase in viability at 0.2% concentration suggests that rhubarb extract may contain bioactive compounds that support cell function.
- **Cytotoxicity at Higher Concentrations:** The decrease in cell viability at 2% may result from excessive bioactive compounds leading to oxidative stress or metabolic disruption.
- **Dose-Dependent Therapeutic Window:** The results indicate a potential therapeutic threshold, where low doses provide benefits, but higher doses may cause harm.

4. Importance of Dose Optimization

The findings highlight the need for precise dosage adjustments when evaluating the therapeutic potential of rhubarb root extract. Careful optimization is essential to maximize benefits while minimizing toxicity.

5. Interpretation of General Findings

These results suggest that *rheum palmatum* root extract has potential biological effects, but dose-dependent responses must be considered. While low concentrations may enhance cell viability, higher concentrations could have adverse effects, emphasizing the importance of further research on optimal dosage and safety.

RESULT AND DISCUSSION

1. Result

Studies on Rhubarb *(Rheum palmatum)* root extract suggest that this plant may have a potential role in the treatment of neurological diseases. In vitro and in vivo studies have demonstrated that rhubarb extract has positive effects on neurons. It has been observed that the extract helps neurons function healthily by maintaining their viability.

However, there is insufficient data to prove its direct therapeutic effects on neurodegenerative diseases such as Alzheimer's and Parkinson's. These findings represent an important step toward considering rhubarb root extract as a complementary or alternative treatment for neurological diseases.

2. Discussion

2.1. Discussion

To validate the therapeutic potential of rhubarb root extract, its components need to be more thoroughly examined, and its effects on neurons must be investigated in detail. Clinical studies on humans will provide clearer results regarding the therapeutic use of this natural compound.

It should be noted that results obtained from animal models may not necessarily be applicable to humans. Clinical research will clarify whether rhubarb extract is an effective and reliable treatment option by determining its safety profile, optimal dosage, and pharmacokinetic properties. These studies will pave the way for broader use of

rhubarb extract in the treatment of neurological diseases.

2.2. Suggestions for Future Studies:

Future research should focus on identifying the active components of rhubarb root extract and thoroughly investigating the mechanisms of action of these components at the cellular level.

In particular, a comprehensive understanding of the molecular basis of neuroprotective effects of key compounds such as emodin will contribute to the development of innovative approaches for the treatment of neurological diseases. Additionally, studies evaluating the effects of rhubarb root extract on neurons at different doses and treatment stages are expected to guide future clinical applications.

2.3. Summary

In summary, rhubarb root extract holds great potential as a natural alternative solution for the treatment of neurological diseases. However, further research is needed to definitively confirm this potential. Before transitioning to clinical applications, more extensive studies are required to assess the efficacy and reliability of this natural compound. Such research will provide important information that will support the applicability of rhubarb root extract as a therapeutic agent.

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