Examining the Neuroprotective Effects of Chrysin

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Background

- Over the next 40 years the proportion of older people (>60 years) is estimated to increase from 11% to 22%
  - World Health Organization (WHO)
  - Mental diseases are the most common health problem in this demographic
- Flavonoids (a type of phytochemical) are the largest group of plant secondary metabolites
  - Exhibit a wide range of health benefits including neuroprotective effects

Sources & Chemistry

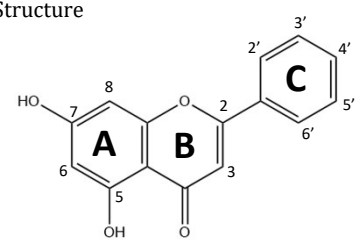
- Main Sources
  - Fruits and vegetables main dietary source
  - Principal constituent of Radix scutellariae
  - Recent studies focused on propolis & honey

Raw Propolis 8 oz. (n.d.). Ebeehoney.com. Retrieved April 28, 2024, from https://ebeehoney.com/products/raw-propolis-8-oz

Radix Scutellariae - Huang Qin | Products | China Nature. (n.d.). China Nature NV. Retrieved April 28, 2024, from https://www.chinanature.be/en/products/radix-scutellariae-huang-qin

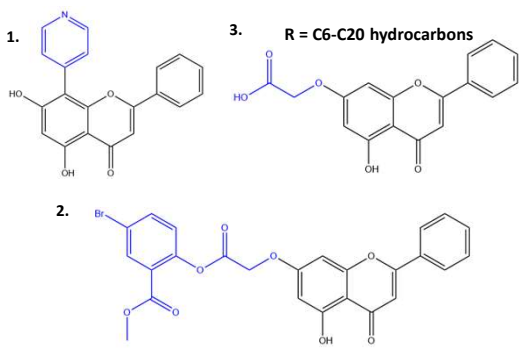
- Chemical Formula
  - 5,7-dihydroxy-2-phenyl-4H-chromen-4-one

    OR
  - 5,7-dihydroxyflavone
- Structure



- Characteristic features of flavones
  - B2-B3 double bond
  - Lack of oxygenation at B-3
  - Other derivatives rise from additions to ring-A
- Unique feature of Chrysin
  - Lacks oxygenation on ring-C

Enhancing Chrysin's Biological Effects



Promising Derivatives for Various Health Applications

1. Addition of a pyridine at A-8
   - Improved anti-inflammatory effect
   - Over 95% inhibition at 10 μM concentration
2. Salicylic acid derivative
   - Improved immunosuppressive activity
   - Comparable to cyclosporin A
3. Long-chain derivative
   - Enhanced antitumor activity
   - Especially in H22 cells *in vitro*

Neuroprotective Effects of Chrysin

Neuroinflammation Reduction

- Reduction in microglia activation
  - Blocks pro-inflammatory cytokine expression
- Inhibits c-Jun N-terminal kinase (JNK) and Nuclear factor-kB (NF-kB)
  - Key Mediators in neuroinflammation

Anti-atherogenic

- Hyperlipidemia has been linked to pathogenesis of neurological diseases
- Reduces hepatic damage and atherosclerotic plaque size

cardiogram. (2022, December 1). High Cholesterol (Hyperlipidemia). Cardiogram. https://cardiogram.com/high-cholesterol/

Anti-depressant

- Alterations in brain neurotrophins and brain Na(+), K(+)-ATPase linked to depression development
- Tested at a 20 mg/kg dose in lab mice
- Upregulated brain-derived neurotrophic factor (BDNF) and nerve growth factor (NGF)

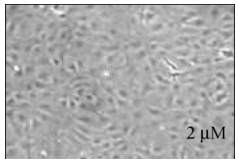
Anti-epileptic

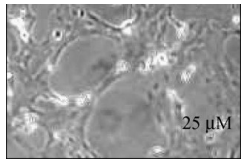
- Administered intracerebroventricularly
- Found to be a ligand for benzodiazepine receptors
  - CNS: competitive mechanism
  - PNS: mixed-type mechanism
- Reduced seizure size and immobility period observed in lab mice

Challenges

- Bioavailability
  - 0.003 – 0.02%
  - Maximum plasma concentration: 12-64 μM
  - Maximum serum concentration: 1 μmol/L
- Toxicity
  - Recommended daily dose: 0.5-3 grams
  - Inhibits de novo DNA synthesis
    - Leads to reduce cell numbers
  - Oxidation of Chrysin can form toxic byproducts

Chrysin Toxicity Visualized in Trout Liver Cells





Toxicity became visible between 2 and 10 μM

Future Direction

Focus on deeper understanding of Chrysin effects on human biochemistry:

- Bioavailability, pharmacokinetics, and pharmacodynamics
- Molecular mechanisms underlying effects
- Clinical and toxicity studies

References

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