Protocatechuic Acid (PCA)

- Protective Role of Protocatechuic Acid in Glioma: Modulation of Cell Growth, Migration, and Pyroptosis via NLRP3/Caspase-1/GSDMD Axis
- Retraction to "Protocatechuic acid attenuates cerebral aneurysm formation and progression by inhibiting TNF-alpha/Nrf-2/NF-kB-mediated inflammatory mechanisms in experimental rats"
- Decoding the key compounds and mechanism of Shashen Maidong decoction in the treatment of lung cancer
- A Traditional Chinese Medicine Plant Extract Prevents Alcohol-Induced Osteopenia
- Protocatechuic acid as an inhibitor of the JNK/CXCL1/CXCR2 pathway relieves neuropathic pain in CCI rats
- Protocatechuic acid attenuates cerebral aneurysm formation and progression by inhibiting TNF-alpha/Nrf-2/NF-kB-mediated inflammatory mechanisms in experimental rats
- Protocatechuic Acid Suppresses Microglia Activation and Facilitates M1 to M2 Phenotype Switching in Intracerebral Hemorrhage Mice
- Protocatechuic acid attenuates brain edema and blood-brain barrier disruption after intracerebral hemorrhage in mice by promoting Nrf2/HO-1 pathway

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Protocatechuic Acid (PCA) is a natural phenolic compound found in many plants, fruits, and vegetables. It belongs to the family of hydroxybenzoic acids and acts as a potent antioxidant.

Chemical Structure

- 3,4-dihydroxybenzoic acid
- Benzene ring with two hydroxyl groups (-OH) and one carboxylic acid group (-COOH)

Properties

Property	Effect
Antioxidant	Neutralizes free radicals and reduces oxidative stress
Anti-inflammatory	Lowers inflammation in tissues
Antimicrobial	Inhibits certain bacteria and fungi
Anticancer potential	May inhibit cancer cell growth (under investigation)
Neuroprotective	Protects nerve cells from oxidative and toxic damage

Natural Sources

- Green tea
- Olives and olive oil
- Berries (e.g., blueberries, blackberries)
- Nuts
- Hibiscus flowers

Medical and Research Interest

Protocatechuic Acid is being researched for its potential protective role against:

- Cancer development
- Cardiovascular diseases
- Diabetes
- Neurodegenerative diseases (such as Alzheimer's disease)

> **Note:** Current evidence is mostly based on in vitro (cell culture) and animal studies; clinical trials in humans are limited.

A study aimed to investigate whether pyroptosis can be activated by PCA in glioma cells.

Different concentrations of PCA were used to treat glioma cell lines U87 and U251 for varying durations.Cell proliferation was quantified using the Cell Counting Kit-8 (CCK-8) assay. The Transwell chamber assay was employed to evaluate cell invasion, while cell migration was assessed via the scratch assay. Pyroptosis levels were determined through immunofluorescence staining. Additionally, the protein and mRNA expression levels of nucleotide-binding and oligomerization domain-like receptor thermal protein domain-associated protein 3 (NLRP3), cysteinyl aspartate-specific proteinase (caspase-1), and gasdermin D (GSDMD) were analyzed using Western blotting and quantitative reverse-transcription polymerase chain reaction (qRT-PCR).

Intervention with PCA resulted in a significant suppression of viability, invasion, and migration of glioma cells in a dose-dependent manner ($p < 0.05$). Additionally, the GSDMD positivity rate, as well as the protein and mRNA expression levels of NLRP3, caspase-1, and GSDMD, showed significant increases in glioma cells ($p < 0.05$). Further intervention with NLRP3-specific inhibitor MCC950 reversed the effects of PCA and resulted in a significant increase in cell viability and number of invading cells ($p < 0.01$), a significant decrease in GSDMD positivity ($p < 0.01$), and a significant decrease in the protein and mRNA expression levels of NLRP3, caspase-1, and GSDMD in glioma cells ($p < 0.01$).

PCA mediates pyroptosis in glioma cells by regulating the NLRP3/caspase-1/GSDMD signaling pathway [1)]

This study provides promising preliminary evidence that PCA induces pyroptosis in glioma cells via activation of the NLRP3/caspase-1/GSDMD pathway, inhibiting their proliferation, invasion, and migration. However, translational and mechanistic gaps remain, particularly the need for in vivo studies, dose optimization, and validation across more glioma models.

Overall, the research is well-conceived, methodologically solid for an in vitro study, and lays important groundwork for future preclinical investigations.

1)

Zhang W, Cai Y, Zheng H. Protective Role of Protocatechuic Acid in Glioma: Modulation of Cell Growth, Migration, and Pyroptosis via NLRP3/Caspase-1/GSDMD Axis. Discov Med. 2025 Apr;37(195):659-668. doi: 10.24976/Discov.Med.202537195.57. PMID: 40287802.