Propyl gallate

Propyl gallate is used to protect oils and fats in products from oxidation; it is used in foods, cosmetics, hair products, adhesives, biodiesel, and lubricants.

https://pubmed.ncbi.nlm.nih.gov/38927877/

Generation of Hydrogen Peroxide in Cancer Cells: Advancing Therapeutic Approaches for Cancer Treatment 2024

4.1.4. **Propyl Gallate**

Propyl gallate (PG), chemically known as propyl-3,4,5-trihydroxybenzoate, is widely present in processed food and cosmetics, hair products, and lubricants [82 – 85]. This versatile compound boasts various biological properties, including potential antitumor effects. PG alone demonstrated antioxidative and cytoprotective properties against cellular damage and gained a pro-oxidative property in combination with copper (II) [86].

https://pubmed.ncbi.nlm.nih.gov/33865947/

Enhanced cell death effects of MAP kinase inhibitors in propyl gallate-treated lung cancer cells are related to increased ROS levels and GSH depletion 2021

Propyl gallate (PG) has an anti-growth effect in lung cancer cells. The present study investigated the effects of mitogen-activated protein kinase (MAPK; MEK, JNK, and p38) inhibitors on PG-treated Calu-6 and A549 lung cancer cells in relation to cell death as well as reactive oxygen species (ROS) and glutathione (GSH) levels. PG induced cell death in both Calu-6 and A549 lung cancer cells at 24 h, which was accompanied by loss of mitochondrial membrane potential (MMP; ΔΨm). All of the tested MAPK inhibitors increased cell death in both PG-treated lung cancer cell lines. In particular, MEK inhibitor strongly enhanced cell death and MMP (ΔΨm) loss in PG-treated Calu-6 cells and p38 inhibitor had the same effects in A549 cells as well. PG increased ROS levels and caused GSH depletion in both cell lines at 24 h. MAPK inhibitors increased O2•- levels and GSH depletion in PG-treated Calu-6 cells, and JNK and p38 inhibitors increased ROS levels and GSH depletion in PG-treated A549 cells. In conclusion, MAPK inhibitors increased cell death in PG-treated Calu-6 and A549 lung cancer cells. Enhanced cell death and GSH depletion in Calu-6 cells caused by the MEK inhibitor were related to increased O2•- levels, and the effects of the p38 inhibitor in A549 cells were correlated with increased general ROS levels.

https://pubmed.ncbi.nlm.nih.gov/38373208/

Propyl gallate induces human pulmonary fibroblast cell death through the regulation of Bax and caspase-3 2024

Propyl gallate (PG) has been found to exert an inhibitory effect on the growth of different cell types, including lung cancer cells. However, little is known about the cytotoxicological effects of PG specifically on normal primary lung cells. The current study examined the cellular effects and cell death resulting from PG treatment in human pulmonary fibroblast (HPF) cells. DNA flow cytometry results demonstrated that PG (100-1,600 μM) had a significant impact on the cell cycle, leading to G1 phase arrest. Notably, 1,600 μM PG slightly increased the number of sub-G1 cells. Additionally, PG (400-1,600 μM) resulted in the initiation of cell death, a process that coincided with a loss of mitochondrial membrane potential (MMP; ΔΨm). This loss of MMP (ΔΨm) was evaluated using a FACS cytometer. In PG-treated HPF cells, inhibitors targeting pan-caspase, caspase-3, caspase-8, and caspase-9 showed no significant impact on the quantity of annexin V-positive and MMP (ΔΨm) loss cells. The administration of siRNA targeting Bax or caspase-3 demonstrated a significant attenuation of PG-induced cell death in HPF cells. However, the use of siRNAs targeting p53, Bcl-2, or caspase-8 did not exhibit any notable effect on cell death. Furthermore, none of the tested MAPK inhibitors, including MEK, c-Jun N-terminal kinase (JNK), and p38, showed any impact on PG-induced cell death or the loss of MMP (ΔΨm) in HPF cells. In conclusion, PG induces G1 phase arrest of the cell cycle and cell death in HPF cells through apoptosis and/or necrosis. The observed HPF cell death is mediated by the modulation of Bax and caspase-3. These findings offer insights into the cytotoxic and molecular effects of PG on normal HPF cells.

https://pubmed.ncbi.nlm.nih.gov/38438412/

Propyl gallate induces cell death in human pulmonary fibroblast through increasing reactive oxygen species levels and depleting glutathione 2024

Propyl gallate (PG) exhibits an anti-growth effect on various cell types. The present study investigated the impact of PG on the levels of reactive oxygen species (ROS) and glutathione (GSH) in primary human pulmonary fibroblast (HPF) cells. Moreover, the effects of N-acetyl cysteine (NAC, an antioxidant), L-buthionine sulfoximine (BSO, a GSH synthesis inhibitor), and small interfering RNA (siRNAs) against various antioxidant genes on ROS and GSH levels and cell death were examined in PG-treated HPF cells. PG (100-800 μM) increased the levels of total ROS and $O_2^{\cdot-}$ at early time points of 30-180 min and 24 h, whereas PG (800-1600 μM) increased GSH-depleted cell number at 24 h and reduced GSH levels at 30-180 min. PG downregulated the activity of superoxide dismutase (SOD) and upregulated the activity of catalase in HPF cells. Treatment with 800 μM PG increased the number of apoptotic cells and cells that lost mitochondrial membrane potential (MMP; $\Delta\Psi_m$). NAC treatment attenuated HPF cell death and MMP ($\Delta\Psi_m$) loss induced by PG, accompanied by a decrease in GSH depletion, whereas BSO exacerbated the cell death and MMP ($\Delta\Psi_m$) loss without altering ROS and GSH depletion levels. Furthermore, siRNA against SOD1, SOD2, or catalase attenuated cell death in PG-treated HPF cells, whereas siRNA against GSH peroxidase enhanced cell death. In conclusion, **PG induced cell death in HPF cells by increasing ROS levels and depleting GSH**. NAC was found to decrease HPF cell death induced by PG, while BSO enhanced cell death. The findings shed light on how manipulating the antioxidant system influence the cytotoxic effects of PG in HPF cells.

https://pubmed.ncbi.nlm.nih.gov/33125113/

Propyl gallate reduces the growth of lung cancer cells through caspase-dependent apoptosis and G1 phase arrest of the cell cycle 2020

Propyl gallate (3,4,5-trihydroxybenzoic acid propyl ester; PG) is a synthetic phenolic antioxidant which exerts many effects on tissue and cell functions. In the present study, Calu-6 and A549 lung cancer cells were used to examine the molecular mechanism of the anti-growth effects of PG in relation to apoptosis and cell cycle arrest. PG inhibited the growth of both lung cancer cell types in a dose-dependent manner with an IC50 of 800 μM at 24 h based on MTT assays. Furthermore, PG upregulated the activities of caspase-3 and caspase-8 in Calu-6 cells. In conclusion, PG treatment inhibited the growth of lung cancer cells, especially Calu-6 cells via caspase-dependent apoptosis as well as G1 phase arrest of the cell cycl

https://pubmed.ncbi.nlm.nih.gov/35889456/

The Anti-Apoptotic Effects of Caspase Inhibitors in Propyl Gallate-Treated Lung Cancer Cells Are Related to Changes in Reactive Oxygen Species and Glutathione Levels 2022

Propyl gallate [3,4,5-trihydroxybenzoic acid propyl ester; PG] exhibits an anti-growth effect in various cells. In this study, the anti-apoptotic effects of various caspase inhibitors were evaluated in PG-treated Calu-6 and A549 lung cancer cells in relation to reactive oxygen species (ROS) and glutathione (GSH) levels. Treatment with 800 μM PG inhibited the proliferation and induced the cell death of both Calu-6 and A549 cells at 24 h. Each inhibitor of pan-caspase, caspase-3, caspase-8, and caspase-9 reduced the number of dead and sub-G1 cells in both PG-treated cells at 24 h. PG increased ROS levels, including $O_2^{\cdot-}$, in both lung cancer cell lines at 24 h. Generally, caspase inhibitors appeared to decrease ROS levels in PG-treated lung cancer cells at 24 h and somewhat reduced $O_2^{\cdot-}$ levels. PG augmented the number of GSH-depleted Calu-6 and A549 cells at 24 h. Caspase inhibitors did not affect the level of GSH depletion in PG-treated A549 cells but differently and partially altered the depletion level in PG-treated Calu-6 cells. In conclusion, PG exhibits an anti-proliferative effect in Calu-6 and A549 lung cancer cells and induced their cell death. PG-induced lung cancer death was accompanied by increases in ROS levels and GSH depletion. Therefore,

the anti-apoptotic effects of caspase inhibitors were, at least in part, related to changes in ROS and GSH levels.

https://pubmed.ncbi.nlm.nih.gov/27375080/
Propyl gallate sensitizes human lung cancer cells to cisplatin-induced apoptosis by targeting heme oxygenase-1 for TRC8-mediated degradation 2016
Collectively, our data provide the potential application of PG in combination chemotherapy to enhance drug sensitivity in lung cancer by targeting HO-1.

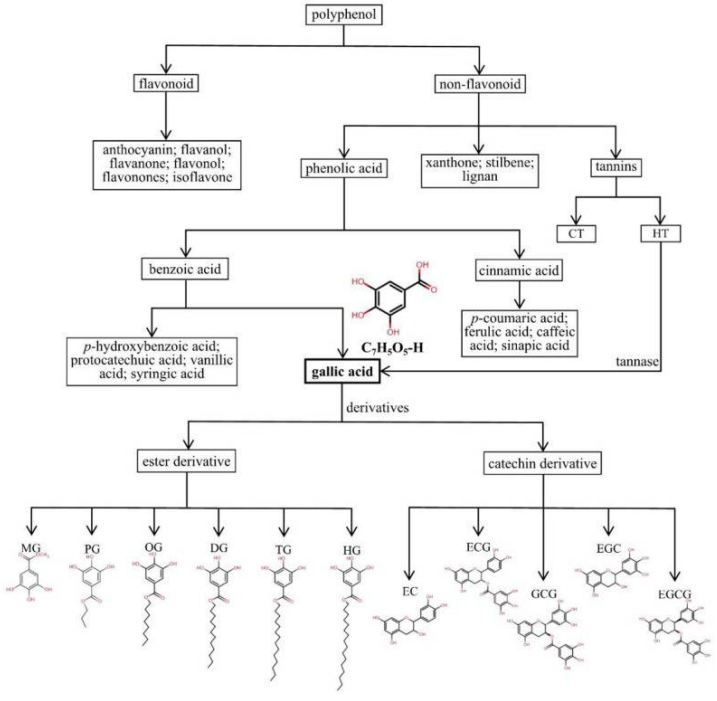
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10878342/
Propyl gallate induces human pulmonary fibroblast cell death through the regulation of Bax and caspase-3 2024
Propyl gallate (PG) has been found to exert an inhibitory effect on the growth of different cell types, including lung cancer cells. However, little is known about the cytotoxicological effects of PG specifically on normal primary lung cells. The current study examined the cellular effects and cell death resulting from PG treatment in human pulmonary fibroblast (HPF) cells. DNA flow cytometry results demonstrated that PG (100–1,600 μM) had a significant impact on the cell cycle, leading to G1 phase arrest. Notably, 1,600 μM PG slightly increased the number of sub-G1 cells. Additionally, PG (400–1,600 μM) resulted in the initiation of cell death, a process that coincided with a loss of mitochondrial membrane potential (MMP; ΔΨm).
The observed HPF cell death is mediated by the modulation of Bax and caspase-3. These findings offer insights into the cytotoxic and molecular effects of PG on normal HPF cells.
Interestingly, the antioxidative and cytoprotective properties of PG may switch to pro-oxidative and cytotoxic properties in the presence of Cu(II) [8].

https://pubmed.ncbi.nlm.nih.gov/9607607/
DNA strand break induction and enhanced cytotoxicity of propyl gallate in the presence of copper(II) 1998
The synergistic interaction between PG and Cu(II) is probably caused by a redox reaction between both compounds, whereby reactive species such as ROS are formed, which are responsible for the observed genotoxic and cytotoxic effects. Our results demonstrate that the antioxidative and cytoprotective properties of propyl gallate may change to prooxidative, cytotoxic and genotoxic properties in the presence of Cu(II).

https://www.sciencedirect.com/science/article/abs/pii/S0308814622031818
Pharmacokinetic and toxicological overview of propyl gallate food additive 2023
The EFSA has evaluated the use of PG in food industry. It establishes an acceptable daily intake (ADI) of 0.5 mg/kg bw per day. Based on exposure assessment, it can be concluded that at the current level of use, PG is not of safety concern.

https://analyticalsciencejournals.onlinelibrary.wiley.com/doi/10.1002/jat.4231
Propyl gallate decreases the proliferation of Calu-6 and A549 lung cancer cells via affecting reactive oxygen species and glutathione levels 2021
In this study, Calu-6 and A549 lung cancer cells were used to examine the anti-proliferative effect of PG in relation to reactive oxygen species (ROS) and glutathione (GSH) levels. PG (100–1,600 μM) dose-dependently inhibited the proliferation of Calu-6 and A549 cells at 24 h, and PG at 800–1,600 μM strongly induced cell death in both cell lines. PG (800–1,600 μM) increased cellular metabolism in Calu-6 but not A549 cells at 4 h. PG either increased or decreased ROS levels, including $O_2^{\cdot -}$ and $^{\cdot}OH$, depending on the incubation doses and times of 1 or 24 h.
In conclusion, PG dose-dependently decreased the proliferation of Calu-6 and A549 lung cancer cells, which was related to changes in ROS levels and the depletion of GSH.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7525003/
Impact of Gallic Acid on Gut Health: Focus on the Gut Microbiome, Immune Response, and Mechanisms of Action 2020
The GA derivatives include two types: ester and catechin derivatives. The most common ester derivatives of GA are alkyl esters, which are composed mainly of methyl gallate (MG), propyl gallate (PG), octyl gallate (OG), dodecyl gallate (DG), tetradecyl gallate (TG), and hexadecyl gallate (HG), and some of the main catechin derivatives are epicatechin (EC), epicatechin gallate (ECG), epigallocatechin (EGC), gallocatechin gallate (GCG), and epigallocatechin gallate (EGCG) (42–45).
Owing to the properties of potent antioxidants scavenging of reactive oxygen species, several GA derivatives, such as DG, PG, OG, TG, and HG, are widely used in the food manufacturing, pharmaceutical, and cosmetic industries (43, 45, 50).



It has been widely claimed that polyphenols are good source of natural health products and are beneficial for human health (51–55). Oliver et al. found that polyphenols have high instability to light, heat, and pH due to the existence of multiple hydroxyl groups (56).
Moreover, polyphenols are quickly absorbed in the GIT, with rapid metabolism within the human gut and a high elimination rate *in vivo*, resulting in low and inconsistent oral bioavailability (59–61).

https://pubmed.ncbi.nlm.nih.gov/24160552/
Geno- and cytotoxicity of propyl gallate food additive 2014
Synthetic phenolic food additives, such as propyl 3,4,5-trihydroxybenzoate (propyl galate; PG), have been used as an antioxidant in the food industry to prevent oils from spoiling. Their toxicity is one of the challengeable issues resulting from the widespread usage of them in food-related industrials. In this study, we investigated the anticell proliferation effects of PG on A549 lung cancer cells. The result showed that PG dose and time dependently decreased the growth of A549 cells with an half-maximal inhibitory concentration of approximately 1 × 10(-3) and 5 × 10(-4)M of PG at 48 and 72 hours, respectively.