

Below is a detailed breakdown of harms, mechanisms of action, and scientific references for compounds commonly found in UPFs:

1. Aspartame

- **Harm to Human Health:** Linked to potential neurotoxicity, cancer, and metabolic disturbances.
- **Mechanism of Action:** Metabolized into methanol, formaldehyde, and formic acid, which can interfere with DNA and cellular processes at high concentrations.
- **Scientific Reference:** Magnuson BA, et al. "Aspartame: A safety evaluation based on current use levels, regulations, and toxicological and epidemiological studies." *Crit Rev Toxicol.* 2007;37(8):629-727. [DOI](#)

2. Stevia-Derived Compounds

- **Harm to Human Health:** May affect gut microbiota and insulin sensitivity at high doses.
- **Mechanism of Action:** Alteration of gut bacterial composition, potentially affecting metabolic pathways.
- **Scientific Reference:** Nikiforov AI, Eapen AK. "A 90-day dietary study of rebaudioside A in Sprag

3. Carboxymethylcellulose (CMC)

- **Harm to Human Health:** Causes gut microbiota disruption, inflammation, and increased intestinal permeability.
- **Mechanism of Action:** Interferes with the intestinal mucus layer, leading to a "leaky gut" and immune activation.
- **Scientific Reference:** Chassaing B, et al. "Dietary emulsifiers directly alter the gut microbiota composition and induce intestinal inflammation." *Nature.* 2015;519(7541):92-96. [DOI](#)

4. Nitrates and Nitrites

- **Harm to Human Health:** Can form carcinogenic nitrosamines, linked to increased cancer risk.
- **Mechanism of Action:** React with amines under acidic conditions (e.g., in the stomach), producing nitrosamines that damage DNA.

- **Scientific Reference:** Aune D, et al. "Dietary nitrate, nitrite, and the risk of colorectal cancer: A systematic review and meta-analysis of prospective studies." *Nutr Rev.* 2021;79(1):7-20. [DOI](#)

5. Acrolein

- **Harm to Human Health:** Linked to respiratory irritation, oxidative stress, and carcinogenesis.
- **Mechanism of Action:** Generated during high-temperature cooking, causing oxidative damage and inflammation at cellular levels.
- **Scientific Reference:** Stevens JF, Maier CS. "Acrolein: Sources, metabolism, and biomolecular interactions relevant to human health and disease." *Mol Nutr Food Res.* 2008;52(1):7-25. [DOI](#)

6. Acrylamide

- **Harm to Human Health:** Probable human carcinogen; also linked to neurotoxicity.
- **Mechanism of Action:** Forms during the Maillard reaction in high-temperature cooking; interacts with DNA and proteins, causing mutations.
- **Scientific Reference:** Friedman M. "Chemistry, biochemistry, and safety of acrylamide. A review." *J Agric Food Chem.* 2003;51(16):4504-4526. [DOI](#)

7. Furans

- **Harm to Human Health:** Possible human carcinogen; liver toxicity in animal studies.
- **Mechanism of Action:** Forms during heat processing of canned/jarred foods; induces DNA damage and oxidative stress.
- **Scientific Reference:** Goldsmith MR, et al. "Furan in heat-processed foods: Formation, exposure, toxicity, and risk assessment." *Toxicol Res (Camb).* 2017;6(5):764-779. [DOI](#)

8. Heterocyclic Amines (HCAs)

- **Harm to Human Health: Strongly associated with increased cancer risk.**
- **Mechanism of Action:** Formed during high-temperature cooking of meat; HCAs damage DNA, initiating carcinogenesis.
- **Scientific Reference:** Sugimura T. "Nutrition and dietary carcinogens." *Carcinogenesis.* 2000;21(3):387-395. [DOI](#)

9. Polycyclic Aromatic Hydrocarbons (PAHs)

- **Harm to Human Health:** Known carcinogens; can cause lung and gastrointestinal cancers.
- **Mechanism of Action:** Produced by incomplete combustion during grilling or smoking foods; PAHs bind to DNA, leading to mutations.
- **Scientific Reference:** Boström CE, et al. "Cancer risk assessment, indicators, and guidelines for polycyclic aromatic hydrocarbons in the ambient air." *Environ Health Perspect.* 2002;110(Suppl 3):451-488. [DOI](#)

10. Bisphenol A (BPA)

- **Harm to Human Health:** Endocrine disruptor linked to reproductive health issues and cancer.
- **Mechanism of Action:** Mimics estrogen, disrupting hormonal balance and cellular signaling pathways.
- **Scientific Reference:** Rochester JR. "Bisphenol A and human health: A review of the literature." *Reprod Toxicol*. 2013;42:132-155. [DOI](#)

11. Di(2-ethylhexyl) Phthalate (DEHP)

- **Harm to Human Health:** Causes endocrine disruption and reproductive toxicity.
- **Mechanism of Action:** Leaches from packaging materials into food, disrupting hormonal pathways.
- **Scientific Reference:** Hauser R, Calafat AM. "Phthalates and human health." *Occup Environ Med*. 2005;62(11):806-818. [DOI](#)

12. Titanium Dioxide (TiO₂)

- **Harm to Human Health:** Potentially carcinogenic; linked to inflammation and immune dysregulation.
- **Mechanism of Action:** TiO₂ nanoparticles cause oxidative stress, inflammation, and DNA damage.
- **Scientific Reference:** Bettini S, et al. "Food-grade TiO₂ impairs intestinal and systemic immune homeostasis, initiates preneoplastic lesions, and promotes aberrant crypt development in the rat colon." *Sci Rep*. 2017;7:40373. [DOI](#)

13. Advanced Glycation End Products (AGEs)

- **Harm to Human Health:** Associated with increased oxidative stress, chronic inflammation, and heightened risks of diabetes, cardiovascular diseases, and neurodegenerative conditions.
- **Mechanism of Action:** AGEs bind to receptors (RAGEs), triggering inflammatory signaling and oxidative stress, which damage tissues and exacerbate chronic diseases.
- **Scientific Reference:** Uribarri J, et al. "Advanced glycation end products in foods and a practical guide to their reduction in the diet." *J Am Diet Assoc*. 2010;110(6):911–916. [DOI](#)

14. FD&C Red No. 40

- **Harm to Human Health:** Linked to hyperactivity in children and potential allergic reactions.
- **Mechanism of Action:** Synthetic dye metabolites interfere with neurological pathways or act as allergens.
- **Scientific Reference:** Stevens LJ, et al. "Dietary sensitivities and ADHD symptoms: Thirty-five years of research." *Clin Pediatr (Phila)*. 2010;49(4):279–293. [DOI](#)

15. FD&C Yellow No. 6—~~Twilight Yellow~~ (Sunset Yellow)

- **Harm to Human Health:** May provoke allergic reactions, urticaria, and hyperactivity.
- **Mechanism of Action:** Functions as a histamine releaser and acts on neurological pathways.
- **Scientific Reference:** Bateman B, et al. "The effects of a double blind, placebo controlled, artificial food colourings and benzoate preservative challenge on hyperactivity in a general population sample of preschool children." *Arch Dis Child*. 2004;89(6):506–511. [DOI](#)

16. Industrial Trans-Fatty Acids- Hydrogenated oils, Mono and diglycerides, DATEM

- **Harm to Human Health:** Strongly linked to cardiovascular disease, systemic inflammation, and increased LDL cholesterol levels.
- **Mechanism of Action:** Disrupt lipid metabolism and cellular membrane integrity, triggering inflammatory pathways.
- **Scientific Reference:** Mozaffarian D, et al. "Trans fatty acids and cardiovascular disease." *N Engl J Med*. 2006;354(15):1601–1613. [DOI](#)

Need to update section below with specific emulsifiers - most problematic one is carrageenan

17. Emulsifiers (e.g., Xanthan Gum, Carrageenan)

- **Harm to Human Health:** Associated with gut microbiota disturbances, increased intestinal permeability, and inflammation.
- **Mechanism of Action:** Weakens the intestinal mucus barrier, causing immune activation and systemic inflammation.
- **Scientific References:** Chassaing B, et al. "Dietary emulsifiers impact the mouse gut microbiota promoting colitis and metabolic syndrome." *Nature*. 2015;519(7541):92–96. [DOI](#)
- Sellem L, et.al. Food additive emulsifiers and cancer risk: Results from the French prospective NutriNet-Santé cohort. *PLoS Med*. 2024 Feb 13;21(2):e1004338. doi: 10.1371/journal.pmed.1004338. PMID: 38349899; PMCID: PMC10863884.

18. Microbial Transglutaminase

- **Harm to Human Health:** Linked to autoimmune disorders such as celiac disease due to increased gluten immunogenicity.
- **Mechanism of Action:** Modifies gluten peptides, making them more immunogenic and capable of triggering immune responses.
- **Scientific Reference:** Elli L, et al. "Transglutaminase 2 in gluten intolerance: is it a target for novel therapies?" *Mol Nutr Food Res*. 2009;53(9):1010–1023. [DOI](#)

19. **FD&C Blue No. 1**

- **Harm to Human Health:** Linked to hyperactivity, immune system disruption, and an increased risk of kidney tumors. Some research suggests it is a potential neurotoxin. Potential allergic reactions.
- **Mechanism of Action:** Synthetic dye metabolites interfere with neurological pathways or act as allergens.
- **Scientific Reference:** Rambler RM, Rinehart E, Boehmler W, Gait P, Moore J, Schlenker M, Kashyap R. A Review of the Association of Blue Food Coloring With Attention Deficit Hyperactivity Disorder Symptoms in Children. *Cureus*. 2022 Sep 16;14(9):e29241. doi: 10.7759/cureus.29241. PMID: 36262950; PMCID: PMC9573786.

20. **FD&C Blue No. 2**

- **Harm to Human Health:** Linked to hyperactivity, immune system disruption, and an increased risk of kidney tumors. Some research suggests it is a potential neurotoxin. Potential allergic reactions.
- **Mechanism of Action:** Synthetic dye metabolites interfere with neurological pathways or act as allergens.
- **Scientific Reference:** Rambler RM, Rinehart E, Boehmler W, Gait P, Moore J, Schlenker M, Kashyap R. A Review of the Association of Blue Food Coloring With Attention Deficit Hyperactivity Disorder Symptoms in Children. *Cureus*. 2022 Sep 16;14(9):e29241. doi: 10.7759/cureus.29241. PMID: 36262950; PMCID: PMC9573786.

21. **FD&C Green No. 3**

- **Harm to Human Health:** Linked to hyperactivity in children and potential allergic reactions.
- **Mechanism of Action:** Synthetic dye metabolites interfere with neurological pathways or act as allergens.
- **Scientific Reference:** Stevens LJ, et al. "Dietary sensitivities and ADHD symptoms: Thirty-five years of research." *Clin Pediatr (Phila)*. 2010;49(4):279–293. [DOI](#)

22. **FD&C Red No. 3**

- **Harm to Human Health:** Linked to cancer, hyperactivity in children, and potential allergic reactions.
- **Mechanism of Action:** Synthetic dye metabolites interfere with neurological pathways or act as allergens.
- **Scientific Reference:** Stevens LJ, et al. "Dietary sensitivities and ADHD symptoms: Thirty-five years of research." *Clin Pediatr (Phila)*. 2010;49(4):279–293. [DOI](#)

23. FD&C Yellow No.5

- **Harm to Human Health:** Linked to hyperactivity in children and potential allergic reactions.
- **Mechanism of Action:** Synthetic dye metabolites interfere with neurological pathways or act as allergens.
- **Scientific Reference:** Stevens LJ, et al. "Dietary sensitivities and ADHD symptoms: Thirty-five years of research." *Clin Pediatr (Phila)*. 2010;49(4):279–293. [DOI](#)

24. FD&C Orange B

- **Harm to Human Health:** Linked to hyperactivity in children and potential allergic reactions.
- **Mechanism of Action:** Synthetic dye metabolites interfere with neurological pathways or act as allergens.
- **Scientific Reference:** Stevens LJ, et al. "Dietary sensitivities and ADHD symptoms: Thirty-five years of research." *Clin Pediatr (Phila)*. 2010;49(4):279–293. [DOI](#)

25. Butylated hydroxytoluene (BHT)

- **Harm to Human Health:** Linked to endocrine disruption and cancer.
- **Mechanism of Action:**
- **Scientific Reference:** Thompson JA, et.al. A metabolite of butylated hydroxytoluene with potent tumor-promoting activity in mouse lung. *Carcinogenesis*. 1989 Apr;10(4):773-5. doi: 10.1093/carcin/10.4.773. PMID: 2702725.

26. Parabens

- **Harm to Human Health:** Linked to endocrine-disruption, breast cancer and reproductive problems.

- **Mechanism of Action:**

Scientific Reference: Hager E, Chen J, Zhao L. Minireview: Parabens Exposure and Breast Cancer. *Int J Environ Res Public Health*. 2022 Feb 8;19(3):1873. doi: 10.3390/ijerph19031873. PMID: 35162895; PMCID: PMC8834979.

27. Acesulfame Potassium (Ace K)

- **Harm to Human Health:** Linked to cancer.
- **Mechanism of Action:** The principal mechanism of health concern for parabens is their weak estrogenic or endocrine-disrupting activity.
- **Scientific Reference:** Debras C, Chazelas E, Srour B, Druetne-Pecollo N, Esseddik Y, Szabo de Edelenyi F, Agaësse C, De Sa A, Lutchia R, Gigandet S, Huybrechts I, Julia C, Kesse-Guyot E, Allès B, Andreeva VA, Galan P, Hercberg S, Deschasaux-Tanguy M, Touvier M. Artificial sweeteners and cancer risk: Results from the NutriNet-Santé population-based cohort study. *PLoS Med*. 2022 Mar 24;19(3):e1003950. doi: 10.1371/journal.pmed.1003950. PMID: 35324894; PMCID: PMC8946744.

28. Azodicarbonamide

- **Harm to Human Health:** Linked to cancer.
- **Mechanism of Action:** Semicarbazide and urethane can form in azodicarbonamide during baking. It is not approved for use in either Australia or the European Union.
- **Scientific Reference:** Becalski A, Lau BP, Lewis D, Seaman SW. Semicarbazide formation in azodicarbonamide-treated flour: a model study. J Agric Food Chem. 2004 Sep 8;52(18):5730-4. doi: 10.1021/jf0495385. PMID: 15373416.

29. Caramel Color (type III and IV)

- **Harm to Human Health:** Linked to cancer.
- **Mechanism of Action:** Created by heating ammonia and sulfites under high pressure – a process that produces 4-methylimidazole (4-MEI), a potential carcinogen.
- **Scientific Reference:** Smith TJ, Wolfson JA, Jiao D, Crupain MJ, Rangan U, Sapkota A, Bleich SN, Nachman KE. Caramel color in soft drinks and exposure to 4-methylimidazole: a

quantitative risk assessment. PLoS One. 2015 Feb 18;10(2):e0118138. doi: 10.1371/journal.pone.0118138. PMID: 25693062; PMCID: PMC4333292.

30. Dimethylpolysiloxane

- **Harm to Human Health:** There's a lack of large-scale epidemiological studies that have investigated the links between exposure to emulsifiers and cancer risk. May be preserved with formaldehyde.

- **Mechanism of Action:**

Scientific Reference: Sellem L, Srour B, Javaux G, Chazelas E, Chassaing B, Viennois E, Debras C, Druesne-Pecollo N, Esseddik Y, Szabo de Edelenyi F, Arnault N, Agaësse C, De Sa A, Lutchia R, Huybrechts I, Scalbert A, Pierre F, Coumoul X, Julia C, Kesse-Guyot E, Allès B, Galan P, Hercberg S, Deschasaux-Tanguy M, Touvier M. Food additive emulsifiers and cancer risk: Results from the French prospective NutriNet-Santé cohort. PLoS Med. 2024 Feb 13;21(2):e1004338. doi: 10.1371/journal.pmed.1004338. PMID: 38349899; PMCID: PMC10863884.

31. Propyl Gallate

- **Harm to Human Health:** Linked to cancer.

- **Mechanism of Action:**

Scientific Reference: Esazadeh K, Ezzati Nazhad Dolatabadi J, Andishmand H, Mohammadzadeh-Aghdash H, Mahmoudpour M, Naemi Kermanshahi M, Roosta Y. Cytotoxic and genotoxic effects of tert-butylhydroquinone, butylated hydroxyanisole and propyl gallate as synthetic food antioxidants. Food Sci Nutr. 2024 Aug 7;12(10):7004-7016. doi: 10.1002/fsn3.4373. PMID: 39479655; PMCID: PMC11521724.

32. TBHQ (tert-butylhydroquinone)

- **Harm to Human Health:** Linked to cancer, immune system damage, and may trigger food allergies.

- **Mechanism of Action:** Can cause T cells to release proteins that trigger food allergies. These proteins can cause allergies to foods like milk, eggs, nuts, wheat, and shellfish

Scientific Reference:

- Esazadeh K, Ezzati Nazhad Dolatabadi J, Andishmand H, Mohammadzadeh-Aghdash H, Mahmoudpour M, Naemi Kermanshahi M, Roosta Y. Cytotoxic and genotoxic effects of tert-butylhydroquinone, butylated hydroxyanisole and propyl gallate as synthetic food antioxidants. Food Sci Nutr. 2024 Aug 7;12(10):7004-7016. doi: 10.1002/fsn3.4373. PMID: 39479655; PMCID: PMC11521724.
- Naidenko, O.V.; Andrews, D.Q.; Temkin, A.M.; Stoiber, T.; Uche, U.I.; Evans, S.; Perrone-Gray, S. Investigating Molecular Mechanisms of Immunotoxicity and the Utility of ToxCast for Immunotoxicity Screening of Chemicals Added to Food. Int. J. Environ. Res. Public Health 2021, 18, 3332. <https://doi.org/10.3390/ijerph18073332>
- Rockwell CE, Zhang M, Fields PE, Klaassen CD. Th2 skewing by activation of Nrf2 in CD4(+) T cells. J Immunol. 2012 Feb 15;188(4):1630-7. doi: 10.4049/jimmunol.1101712. Epub 2012 Jan 16. PMID: 22250088; PMCID: PMC3273574.

33. **Sucralose**

- **Harm to Human Health:** Linked to leukemia and other blood cancers.
- **Mechanism of Action:**

Scientific Reference:

- Debras C, Chazelas E, Srour B, Druesne-Pecollo N, Esseddik Y, Szabo de Edelenyi F, Agaësse C, De Sa A, Lutchia R, Gigandet S, Huybrechts I, Julia C, Kesse-Guyot E, Allès B, Andreeva VA, Galan P, Hercberg S, Deschasaux-Tanguy M, Touvier M. Artificial sweeteners and cancer risk: Results from the NutriNet-Santé population-based cohort study. PLoS Med. 2022 Mar 24;19(3):e1003950. doi: 10.1371/journal.pmed.1003950. PMID: 35324894; PMCID: PMC8946744.
- M, Soffritti et al. "Sucralose administered in feed, beginning prenatally through lifespan, induces hematopoietic neoplasias in male swiss mice." International journal of occupational and environmental health vol. 22,1 (2016): 7-17. doi:10.1080/10773525.2015.1106075