Bölüm
9

DOĞAL KAYNAKLI BİTKİSEL TOKSİNLER VE BESIN TOKSİKOLOJİSİNDEKİ ÖNEMİ

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GİRİŞ

Sağlıklı ve uzun bir yaşam için en temel koşul yeterli ve dengeli beslenme yanı sıra güvenli besin tüketimidir. Besin güvenliğini bozan etmenler arasında besin değerini azaltan işlemler, kimyasal kirleticiler, doğal kaynaklı besin toksinleri ve mikrobiyal toksinler yer almaktadır. Bu etkenler arasında en masum gibi görüneni ancak sürekli maruz kalındığından belki de en tehlikeli olanı doğal kaynaklı bitkisel toksinlerdir. Çünkü bitkisel ürünlerin hayvansal gıdalara kıyasla daha zararsız olduğuna inanılmaktadır. İnsanlar yaşamları boyunca farkında olmadan bu etkenlere sürekli maruz kalmaktadır. Vücudumuzun bu kirletici ve toksik maddeleri zararsız hale getiren immün sistemi ve antitoksik dönüşümü sağlayan metabolizması aşıldığında veya yetersiz kaldığında mutajenik, genotoksik, organotoksik ve enzim inhibe edici zararlı etkiler ortaya çıkabilmektedir.

İnsan sağlığını tehlikeye sokabilen doğal kaynaklı toksinler veya biyojenik aminler meyve, sebze ve tahıl ürünlerinde doğal olarak bulunmaları yanında gıdaların işlenmesi ve bozulması sonucunda da meydana gelebilirler. Bazıları da vücudumuzda sentezlenebilmektedir. Sağlıklı beslenmede yer alması gereken güvenilir besinler, raf ömrü süresince fiziksel, kimyasal ve biyolojik riskleri taşımayan, toksik madde içermeyen besinler olarak tanımlanmaktadır. Günümüzde alınan tüm sıkı önlemlere rağmen tarımda kullanılan kimyasallar, veteriner hekimlikte kullanılan ilaçlar ve gıda katkı maddeleri halk sağlığını ciddi şekilde tehdit etmeye devam etmektedir. Ayrıca üretim ve işleme aşamalarında kaliteli üretim uygulamalarına uyulmaması da toksik madde içeriğini arttırabilmektedir. Bu nedenle besinlerin üreticiden tüketiciye ulaşana kadar ki her aşamasında besin güvenliğine azami dikkat gösterilmesi gerekmektedir (1,2). Bu hususta besin kirliliği ve üretim veya saklama koşullarından kaynaklı toksik maddelerden insan sağlığının korunmasındaki başlıca koşul olmalıdır.

Klasik yaklaşımda beslenme yoluyla alınan gıdaların içeriğindeki temel besin öğelerinin belli oranlarda karbonhidrat, yağ, protein, vitamin ve mineral içermesi önerilmektedir. Ancak besinlerde, zararlı kimyasalların (besin öğesi olmayan) veya besin kaynaklı toksik maddelerin hangi oranda müsaade edilebileceği konusu halen tartışma konusudur. Besinlerin bileşiminde zararlı bileşikler olarak Maillard reaksiyon ürünlerin (akrilamid, furfural ve türevleri), fitotoksinlerin ve mikotoksinler gibi doğal besin toksinleri, kimyasal kirleticiler ve mikrobiyal toksinler bulunabilir. Her besin maddesi bu kimyasal kirleticilerin bir veya birden fazlasını farklı miktarlarda bün-

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KAYNAKLAR

1. Siruguri V. Journey from food toxins to food safety: Transition over a century in service of nation. *Indian J Med Res*. 2018;148(5):488-995. doi:10.4103/ijmr.IJMR_1692_18
2. Thompson LA, Darwish WS. Environmental Chemical Contaminants in Food: Review of a Global Problem. *J Toxicol*. 2019;1(2019):2345283. doi:10.1155/2019/2345283
3. Lahiani A, Yavin E, Lazarovici P. The Molecular Basis of Toxins' Interactions with Intracellular Signaling via Discrete Portals. *Toxins (Basel)*. 2017;9(3):E107. doi:10.3390/toxins9030107
4. Cuciureanu R. The current aspects of food quality. *Rev Med Chir Soc Med Nat Iasi*. 103(1-2):42-48. http://www.ncbi.nlm.nih.gov/pubmed/10756884. Accessed October 8, 2019.
5. Burkina V, Rasmussen MK, Pilipenko N, Zamaratskaia G. Comparison of xenobiotic-metabolising human, porcine, rodent, and piscine cytochrome P450. *Toxicology*. 2017;375:10-27. doi:10.1016/j.tox.2016.11.014
6. Brewer CT, Chen T. Hepatotoxicity of Herbal Supplements Mediated by Modulation of Cytochrome P450. *Int J Mol Sci*. 2017;18(11). doi:10.3390/ijms18112353
7. Dolan LC, Matulka RA, Burdock GA. Naturally occurring food toxins. *Toxins (Basel)*. 2010;2(9):2289-2332. doi:10.3390/toxins2092289
8. Bardócz S. Polyamines in food and their consequences for food quality and human health. *Trends Food Sci Technol*. 1995;6(10):341-346. doi:10.1016/S0924-2244(00)89169-4
9. RICE SL, EITENMILLER RR, KOEHLER PE. Biologically Active Amines in Food: A Review. *J Milk Food Technol*. 1976;39(5):353-358. doi:10.4315/0022-2747-39.5.353
10. Kalač P. Health effects and occurrence of dietary polyamines: A review for the period 2005-mid 2013. *Food Chem*. 2014;161:27-39. doi:10.1016/j.foodchem.2014.03.102
11. Santos S. Biogenic amines: their importance in foods. *Int J Food Microbiol*. 1996;29(2-3):213-231. http://www.ncbi.nlm.nih.gov/pubmed/8796424. Accessed October 9, 2019.
12. Ruiz-Capillas C, Herrero AM. Impact of biogenic amines on food quality and safety. *Foods*. 2019;8(2). doi:10.3390/foods8020062
13. Stratton JE, Hutkins RW, Taylor SL. Biogenic amines in cheese and other fermented foods: A review. *J Food Prot*. 1991;54(6):460-470. doi:10.4315/0362-028X-54.6.460
14. Shalaby AR. Significance of biogenic amines to food safety and human health. *Food Res Int*. 1996;29(7):675-690. doi:10.1016/S0963-9969(96)00066-X
15. Taylor SL. Histamine food poisoning: toxicology and clinical aspects. *Crit Rev Toxicol*. 1986;17(2):91-128. doi:10.3109/10408448609023767
16. Naila A, Flint S, Fletcher G, Bremer P, Meerdink G. Control of biogenic amines in food - existing and emerging approaches. *J Food Sci*. 2010. doi:10.1111/j.1750-3841.2010.01774.x
17. Doeun D, Davaatseren M, Chung MS. Biogenic amines in foods. *Food Sci Biotechnol*. 2017. doi:10.1007/s10068-017-0239-3
18. Kumar J, Das S, Teoh SL. Dietary Acrylamide and the Risks of Developing Cancer: Facts to Ponder. *Front Nutr*. 2018;5:14. doi:10.3389/fnut.2018.00014
19. Tamanna N, Mahmood N. Food Processing and Maillard Reaction Products: Effect on Human Health and Nutrition. *Int J Food Sci*. 2015;2015(526762):1-6. doi:10.1155/2015/526762
20. Glatt H, Schneider H, Liu Y. V79-hCYP2E1-hSULT1A1, a cell line for the sensitive detection of genotoxic effects induced by carbohydrate pyrolysis products and other food-borne chemicals. *Mutat Res*. 2005;580(1-2):41-52. doi:10.1016/j.mrgentox.2004.11.005
21. Lee YC, Shlyankevich M, Jeong HK, Douglas JS, Surh YJ. Bioactivation of 5-hydroxymethyl-2-furaldehyde to an electrophilic and mutagenic allylic sulfuric acid ester. *Biochem Biophys Res Commun*. 1995;209(3):996-1002. doi:10.1006/bbrc.1995.1596
22. Monien BH, Engst W, Barknowitz G, Seidel A, Glatt H. Mutagenicity of 5-hydroxymethylfurfural in V79 cells expressing human SULT1A1: identification and mass spectrometric quantification of DNA adducts formed. *Chem Res Toxicol*. 2012;25(7):1484-1492. doi:10.1021/tx300150n
23. Zhao L, Chen J, Su J, et al. In vitro antioxidant and antiproliferative activities of 5-hydroxymethylfurfural. *J Agric Food Chem*. 2013;61(44):10604-10611. doi:10.1021/jf403098y
24. Yamada P, Nemoto M, Shigemori H, Yokota S, Isoda H. Isolation of 5-(hydroxymethyl)furfural from Lycium chinense and its inhibitory effect on the chemical mediator release by basophilic cells. *Planta Med*. 2011;77(5):434-440. doi:10.1055/s-0030-1250402
25. Kitts DD, Chen X-M, Jing H. Demonstration of antioxidant and anti-inflammatory bioactivities from sugar-amino acid maillard reaction products. *J Agric Food Chem*. 2012;60(27):6718-6727. doi:10.1021/jf2044636
26. Lin S-M, Wu J-Y, Su C, Ferng S, Lo C-Y, Chiou RY-Y. Identification and mode of action of 5-hydroxymethyl-2-furfural (5-hmf) and 1-methyl-1,2,3,4-tetrahydro-β-carboline-3-carboxylic acid (MTCA) as potent xanthine oxidase inhibitors in vinegars. *J Agric Food Chem*. 2012;60(39):9856-9862. doi:10.1021/jf302711e
27. Li MM, Wu LY, Zhao T, et al. The protective role of 5-HMF against hypoxic injury. *Cell Stress Chaperones*. 2011;16(3):267-273. doi:10.1007/s12192-010-0238-2
28. Moretti A, Logrieco AF, Susca A. Mycotoxins: An Underhand Food Problem. *Methods Mol Biol*. 2017;1542:3-12. doi:10.1007/978-1-4939-6707-0_1
29. Pulido OM, Gill S. Food and Toxicologic Pathology: An Overview. In: Haschek W, Rousseaux C WM, ed. *Haschek and Rousseaux's Handbook of Toxicologic Pathology*. 3rd ed. Elsevier Inc.; 2013:1051-1076. doi:10.1016/B978-0-12-415759-0.00035-2
30. Deshpande SS. Food Additives. In: *Handbook of Food Toxicology*. Marcel Dekker; 2002:219-284.
31. CARROLL KK. Erucic acid as the factor in rape oil affecting adrenal cholesterol in the rat. *J Biol Chem*. 1953;200(1):287-292. http://www.ncbi.nlm.nih.gov/pubmed/13034784. Accessed October 8, 2019.

32. Chien KR, Bellary A, Nicar M, Mukherjee A, Buja LM. Induction of a reversible cardiac lipidosis by a dietary long-chain fatty acid (erucic acid). Relationship to lipid accumulation in border zones of myocardial infarcts. *Am J Pathol*. 1983;112(1):68-77. http://www.ncbi.nlm.nih.gov/pubmed/6859230. Accessed October 8, 2019.
33. Ratanasethkul C, Riddell C, Salmon RE, O'Neil JB. Pathological changes in chickens, ducks and turkeys fed high levels of rapeseed oil. *Can J Comp Med Rev Can Med Comp*. 1976;40(4):360-369. http://www.ncbi.nlm.nih.gov/pubmed/1000400. Accessed October 8, 2019.
34. Matson FH. Potential toxicity of food lipids. In: *Toxicants Occurring Naturally in Foods, (2nd Ed.),Committee on Food Protection, Food and Nutrition Board, National Research Council, National Academy of Sciences: Washington, DC, USA*. National Academies Press; 1973:189-209. doi:10.17226/21278
35. Mori H, Tanaka T HI. Toxicants in Food: Naturally Occurring. In: *Ioannides C, (Editor), Nutrition and Chemical Toxicity, Wiley-VCH -.* ; 1998:1-27. https://www.wiley-vch.de/en/areas-interest/natural-sciences/life-sciences-11ls/cell-molecular-biology-11ls3/biochemistry-11ls36/nutrition-and-chemical-toxicity-978-0-471-97453-6. Accessed October 8, 2019.
36. McMillan DC, Jollow DJ. Favism: divicine hemotoxicity in the rat. *Toxicol Sci*. 1999;51(2):310-316. doi:10.1093/toxsci/51.2.310
37. Bicakci Z. A hemolysis trigger in glucose-6-phosphate dehydrogenase enzyme deficiency. Vicia sativa (Vetch). *Saudi Med J*. 2009;30(2):292-294. http://www.ncbi.nlm.nih.gov/pubmed/19198723. Accessed October 8, 2019.
38. Arese P, Mannuzzu L, Turrini F. Pathophysiology of favism. *Folia Haematol Int Mag Klin Morphol Blutforsch*. 1989;116(5):745-752. http://www.ncbi.nlm.nih.gov/pubmed/2481620. Accessed October 8, 2019.
39. Hegazy MI, Marquardt RR. Metabolism of vicine and convicine in rat tissues: absorption and excretion patterns and sites of hydrolysis. *J Sci Food Agric*. 1984;35(2):139-146. http://www.ncbi.nlm.nih.gov/pubmed/6708462. Accessed October 8, 2019.
40. Frohlich AA, Marquardt RR. Turnover and hydrolysis of vicine and convicine in avian tissues and digesta. *J Sci Food Agric*. 1983;34(2):153-163. doi:10.1002/jsfa.2740340207
41. Arbid MSS, Marquardt RR. Effects of intraperitoneally injected vicine and convicine on the rat: Induction of favism-like signs. *J Sci Food Agric*. 1986;37(6):539-547. doi:10.1002/jsfa.2740370606
42. Albano E, Tomasi A, Mannuzzu L, Arese P. Detection of a free radical intermediate from divicine of vicia faba. *Biochem Pharmacol*. 1984;33(10):1701-1704. doi:10.1016/0006-2952(84)90299-5
43. RR. M. Convicine and their role aglycnes-divine and isouramil. In: *P. Cheeke P. Toxicants of Plant Origin*. CRC Press; 1989:614-623.
44. Jones JMJ. *Food Safety*. St. Paul, MN, USA: Eagan Press; 1995.
45. Shibamoto T, Bjeldanes LF. Natural Toxins in Plant Foodstuffs. In: *Introduction to Food Toxicology*. Elsevier; 1993:67-96. doi:10.1016/b978-0-08-092577-6.50010-1
46. Stanley T. Omaye. Toxicity of Nutrients. In: Omaye ST, ed. *Food and Nutritional Toxicology*. Boca Raton, FL, USA: CRC Press; 2004:205-213.
47. Banwell JG, Boldt DH, Meyers J, Weber FL. Phytohemagglutinin derived from red kidney bean (Phaseolus vulgaris): a cause for intestinal malabsorption associated with bacterial overgrowth in the rat. *Gastroenterology*. 1983;84(3):506-515. http://www.ncbi.nlm.nih.gov/pubmed/6822324. Accessed October 8, 2019.
48. Zhang Z, Zhao Z. Correlations between phytohemagglutinin response and leukocyte profile, and bactericidal capacity in a wild rodent. *Integr Zool*. 2015;10(3):302-310. doi:10.1111/1749-4877.12133
49. Jönsson T, Olsson S, Ahrén B, Bøg-Hansen TC, Dole A, Lindeberg S. Agrarian diet and diseases of affluence – Do evolutionary novel dietary lectins cause leptin resistance? *BMC Endocr Disord*. 2005;5(1):10. doi:10.1186/1472-6823-5-10
50. Livingston JN, Purvis BJ. Effects of wheat germ agglutinin on insulin binding and insulin sensitivity of fat cells. *Am J Physiol*. 1980;238(3):E267-75. doi:10.1152/ajpendo.1980.238.3.E267
51. Banwell JG, Howard R, Kabir I, Costerton JW. Bacterial overgrowth by indigenous microflora in the phytohemagglutinin-fed rat. *Can J Microbiol*. 1988;34(8):1009-1013. doi:10.1139/m88-177
52. Dobbins JW, Laurenson JP, Gorelick FS, Banwell JG. Phytohemagglutinin from red kidney bean (Phaseolus vulgaris) inhibits sodium and chloride absorption in the rabbit ileum. *Gastroenterology*. 1986;90(6):1907-1913. doi:10.1016/0016-5085(86)90260-X
53. (FDA) USF and DA. Phytohaemagglutinin. In: *Bad Bug Book. Foodborne Pathogenic Microorganisms and Natural Toxins Handbook*. ; 2001:202-205. http://www.cfsan.fda.gov/~mow/intro.html. Accessed October 8, 2019.
54. Buhler R. Eating raw, undercooked dry beans can be unpleasant | Archives | hpj.com. *High Plains J*. 2004;Nov 15. https://www.hpj.com/archives/eating-raw-undercooked-dry-beans-can-be-unpleasant/article_81f7455b-8b53-5014-87fb-34e79dfb236c.html. Accessed October 8, 2019.
55. Randel RD, Chase CC, Wyse SJ. Effects of gossypol and cottonseed products on reproduction of mammals. *J Anim Sci*. 1992;70(5):1628-1638. doi:10.2527/1992.7051628x
56. Coutinho EM. Gossypol: a contraceptive for men. *Contraception*. 2002;65(4):259-263. doi:10.1016/S0010-7824(02)00294-9
57. Förstermann U, Alheid U, Frölich JC, Mülsch A. Mechanisms of action of lipoxygenase and cytochrome P-450-mono-oxygenase inhibitors in blocking endothelium-dependent vasodilatation. *Br J Pharmacol*. 1988;93(3):569-578. doi:10.1111/j.1476-5381.1988.tb10312.x
58. Wei J, Kitada S, Rega MF, et al. Apogossypol derivatives as pan-active inhibitors of antiapoptotic B-cell lymphoma/leukemia-2 (Bcl-2) family proteins. *J Med Chem*. 2009;52(14):4511-4523. doi:10.1021/jm900472s
59. Wei J, Kitada S, Rega MF, et al. Apogossypol derivatives as antagonists of antiapoptotic Bcl-2 family proteins. *Mol Cancer Ther*. 2009;8(4):904-913. doi:10.1158/1535-7163.MCT-08-1050

60. GREER MA. Goitrogenic substances in food. *Am J Clin Nutr*. 5(4):440-444. doi:10.1093/ajcn/5.4.440
61. Herr I, Büchler MW. Dietary constituents of broccoli and other cruciferous vegetables: implications for prevention and therapy of cancer. *Cancer Treat Rev*. 2010;36(5):377-383. doi:10.1016/j.ctrv.2010.01.002
62. Oberleas D, ed. Natural sulfur compounds. In: *Toxicants Occurring Naturally in Foods*. 2nd ed. National Academies Press; 1973:210-234. doi:10.17226/21278
63. Oberleas D. Cyanogenetic Glycosides. In: Conn E, ed. *Toxicants Occurring Naturally in Foods*. 2nd ed. Washington, D.C.: National Academies Press; 1973:299-308. doi:10.17226/21278
64. Wentworth JM, Agostini M, Love J, Schwabe JW, Chatterjee VK. St John's wort, a herbal antidepressant, activates the steroid X receptor. *J Endocrinol*. 2000;166(3):R11-6. doi:10.1677/joe.0.166r011
65. Karioti A, Bilia AR. Hypericins as potential leads for new therapeutics. *Int J Mol Sci*. 2010;11(2):562-594. doi:10.3390/ijms11020562
66. de los Reyes GC, Koda RT. Determining hyperforin and hypericin content in eight brands of St. John's wort. *Am J Health Syst Pharm*. 2002;59(6):545-547. doi:10.1093/ajhp/59.6.545
67. Hammerness P, Basch E, Ulbricht C, et al. St. John's wort: A systematic review of adverse effects and drug interactions for the consultation psychiatrist. *Psychosomatics*. 2003;44(4):271-282. doi:10.1176/appi.psy.44.4.271
68. Hallström H, Thuvander A. Toxicological evaluation of myristicin. *Nat Toxins*. 1997;5(5):186-192. doi:10.1002/nt.3
69. Deshpande SS. Toxicants and antinutrients in plant foods. In: Deshpande SS, ed. *Handbook of Food Toxicology*. Marcel Dekker; 2002:331-372.
70. TRUITT EB, DURITZ G, EBERSBERGER EM. Evidence of monoamine oxidase inhibition by myristicin and nutmeg. *Proc Soc Exp Biol Med*. 1963;112:647-650. doi:10.3181/00379727-112-28128
71. Prakash AS, Pereira TN, Reilly PEB, Seawright AA. Pyrrolizidine alkaloids in human diet. *Mutat Res - Genet Toxicol Environ Mutagen*. 1999;443(1-2):53-67. doi:10.1016/S1383-5742(99)00010-1
72. Culvenor CCJ. Estimated intakes of pyrrolizid1ne alkaloids by humans. A comparison with dose rates causing tumors in rats. *J Toxicol Environ Health*. 1983;11(4-6):625-635. doi:10.1080/15287398309530372
73. Panter K. Natural toxins of plant origin. In: Dabrowski, WM; Sikorski Z, ed. *Toxins in Food*. Washington, D.C.: CRC Press LLC; 2005:11=63. www.crcpress.com. Accessed October 8, 2019.
74. McGuffin M. *Botanical Safety Handbook - Google Kitaplar*. 1st ed. (McGuffin, M.; Hobbs, C; Upton RG, ed.). Boca Raton, FL, USA: CRC Press; 1997. https://books.google.com.tr/books?id=PWp0mkyFuYsC&printsec=frontcover&hl=tr#v=onepage&q&f=false. Accessed October 8, 2019.
75. Homburger F, Boger E. The carcinogenicity of essential oils, flavors, and spices: a review. *Cancer Res*. 1968;28(11):2372-2374. http://www.ncbi.nlm.nih.gov/pubmed/4881506. Accessed October 8, 2019.
76. Ueda A, Aoyama K, Manda F, Ueda T, Kawahara Y. Delayed-type allergenicity of triforine (Saprol). *Contact Dermatitis*. 1994;31(3):140-145. doi:10.1111/j.1600-0536.1994.tb01952.x
77. Services. USD of H and H. *14th Report on Carcinogens*.; 2016. https://ntp.niehs.nih.gov/whatwestudy/assessments/cancer/roc/index.html?utm_source=direct&utm_medium=prod&utm_campaign=ntpgolinks&utm_term=roc#toc1. Accessed October 8, 2019.
78. Wislocki PG, Miller EC, Miller JA, McCoy EC, Rosenkranz HS. Carcinogenic and Mutagenic Activities of Safrole, 1′ -Hydroxysafrole, and Some Known or Possible Metabolites. *Cancer Res*. 1977;37(6):1883-1891.
79. Iqbal, I; Maqbool B. Acute Cyanide Poisoning - Nishtar Medical Journal. *Nishtar Med J*. 2009;1(2):26-28. https://www.yumpu.com/en/document/view/36516784/acute-cyanide-poisoning-nishtar-medical-journal. Accessed October 8, 2019.
80. Vetter J. Plant cyanogenic glycosides. *Toxicon*. 2000;38(1):11-36. doi:10.1016/S0041-0101(99)00128-2
81. Cigolini D, Ricci G, Zannoni M, et al. Hydroxocobalamin treatment of acute cyanide poisoning from apricot kernels. *Emerg Med J*. 2011;28(9):804-805. doi:10.1136/emj.03.2011.3932rep
82. Suchard JR, Wallace KL, Gerkin RD. Acute cyanide toxicity caused by apricot kernel ingestion. *Ann Emerg Med*. 1998;32(6):742-744. doi:10.1016/s0196-0644(98)70077-0
83. Food SC on. *Opinion of the Scientific Committee on Food on Thujone*.; 2003. http://europa.eu.int/comm/food/fs/sc/scf/index_en.html. Accessed October 8, 2019.
84. Galli CL, Galli G, Tragni E, Caruso D, Fiecchi A. Quantitative analysis of alpha, beta-thujone, pulegone, safrole, coumarin and beta-asarone in alcoholic beverages by selected-ion monitoring. *J Appl Toxicol*. 1984;4(5):273-276. doi:10.1002/jat.2550040514
85. Ben Farhat M, Jordán MJ, Chaouech-Hamada R, Landoulsi A, Sotomayor JA. Variations in essential oil, phenolic compounds, and antioxidant activity of tunisian cultivated Salvia officinalis L. *J Agric Food Chem*. 2009;57(21):10349-10356. doi:10.1021/jf901877x
86. Patočka J, Plucar B. Pharmacology and toxicology of absinthe. *J Appl Biomed*. 2003;1(4):199-205. doi:10.32725/jab.2003.036
87. Millet Y, Jouglard J, Steinmetz MD, Tognetti P, Joanny P, Arditti J. Toxicity of some essential plant oils. Clinical and experimental study. *Clin Toxicol*. 1981;18(12):1485-1498. doi:10.3109/15563658108990357
88. de los Reyes GC, Koda RT. Poison on Line — Acute Renal Failure Caused by Oil of Wormwood Purchased through the Internet. *Am J Heal Pharm*. 2002;59(6):545-547. doi:10.1056/NEJM199709183371205
89. Bonkovsky HL, Cable EE, Cable JW, et al. Porphyrogenic properties of the terpenes camphor, pinene, and thujone (with a note on historic implications for absinthe and the illness of Vincent van Gogh). *Biochem Pharmacol*. 1992;43(11):2359-2368. doi:10.1016/0006-2952(92)90314-9
90. Höld KM, Sirisoma NS, Casida JE. Detoxification of alpha- and beta-Thujones (the active ingredients of absinthe): site specificity and species differences in cytochrome P450 oxidation in vitro and in vivo. *Chem Res Toxicol*. 2001;14(5):589-595. doi:10.1021/tx000242c