

# Clinical Research & References

1. "Nonalcoholic Fatty Liver Disease (NAFLD) & NASH - NIDDK." National Institute of Diabetes and Digestive and Kidney Diseases, National Institute of Diabetes and Digestive and Kidney Diseases, <https://www.niddk.nih.gov/health-information/liver-disease/nafl-d-nash>. Accessed 16 May 2023.
2. "Nonalcoholic Steatohepatitis (NASH)." Stanford Health Care, <https://stanfordhealthcare.org/medical-conditions/liver-kidneys-and-urinary-system/nonalcoholic-steatohepatitis-nash.html>. Accessed 16 May 2023.
3. "Risk factors for NAFLD - Non-Alcoholic Fatty Liver Disease." NCBI, <https://www.ncbi.nlm.nih.gov/books/NBK384735/>. Accessed 16 May 2023.
4. Vassilatou, Evangelina. "Nonalcoholic fatty liver disease and polycystic ovary syndrome." NCBI, <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4093689/>. Accessed 16 May 2023.
5. "Nonalcoholic Fatty Liver Disease and Insulin Resistance: New Insights and Potential New Treatments." NCBI, 14 April 2017, <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5409726/>. Accessed 16 May 2023.
6. Ratziu V, Giral P, Jacqueminet S, Charlotte F, Hartemann-Heurtier A, Serfaty L, Podevin P, Lacorte JM, Bernhardt C, Bruckert E, Grimaldi A, Poynard T; LIDO Study Group. Rosiglitazone for nonalcoholic steatohepatitis: one-year results of the randomized placebo-controlled Fatty Liver Improvement with Rosiglitazone Therapy (FLIRT) Trial. *Gastroenterology*. 2008 Jul;135(1):100-10. doi: 10.1053/j.gastro.2008.03.078. Epub 2008 Apr 8. PMID: 18503774.
7. Belfort R, Harrison SA, Brown K, Darland C, Finch J, Hardies J, Balas B, Gastaldelli A, Tio F, Pulcini J, Berria R, Ma JZ, Dwivedi S, Havranek R, Fincke C, DeFronzo R, Bannayan GA, Schenker S, Cusi K. A placebo-controlled trial of pioglitazone in subjects with nonalcoholic steatohepatitis. *N Engl J Med*. 2006 Nov 30;355(22):2297-307. doi: 10.1056/NEJMoa060326. PMID: 17135584.
8. Sanyal AJ, Chalasani N, Kowdley KV, McCullough A, Diehl AM, Bass NM, Neuschwander-Tetri BA, Lavine JE, Tonascia J, Unalp A, Van Natta M, Clark J, Brunt EM, Kleiner DE, Hoofnagle JH, Robuck PR; NASH CRN. Pioglitazone, vitamin E, or placebo for nonalcoholic steatohepatitis. *N Engl J Med*. 2010 May 6;362(18):1675-85. doi: 10.1056/NEJMoa0907929. Epub 2010 Apr 28. PMID: 20427778; PMCID: PMC2928471.
9. Lin HZ, Yang SQ, Chuckaree C, Kuhajda F, Ronnet G, Diehl AM. Metformin reverses fatty liver disease in obese, leptin-deficient mice. *Nat Med*. 2000 Sep;6(9):998-1003. doi: 10.1038/79697. PMID: 10973319.
10. Haukeland JW, Konopski Z, Eggesbø HB, von Volkman HL, Raschpichler G, Bjørø K, Haaland T, Løberg EM, Birkeland K. Metformin in patients with non-alcoholic fatty liver disease: a randomized, controlled trial. *Scand J Gastroenterol*. 2009;44(7):853-60. doi: 10.1080/00365520902845268. PMID: 19811343.
11. Lavine JE, Schwimmer JB, Van Natta ML, Molleston JP, Murray KF, Rosenthal P, Abrams SH, Scheimann AO, Sanyal AJ, Chalasani N, Tonascia J, Unalp A, Clark JM, Brunt EM, Kleiner DE, Hoofnagle JH, Robuck PR; Nonalcoholic Steatohepatitis Clinical Research Network. Effect of vitamin E or metformin for treatment of nonalcoholic fatty liver disease in children and adolescents: the TONIC randomized controlled trial. *JAMA*. 2011 Apr 27;305(16):1659-68. doi: 10.1001/jama.2011.520. PMID: 21521847; PMCID: PMC3110082.
12. Gómez-Domínguez E, Gisbert JP, Moreno-Monteagudo JA, García-Buey L, Moreno-Otero R. A pilot study of atorvastatin treatment in dyslipidemic, non-alcoholic fatty liver patients. *Aliment Pharmacol Ther*. 2006 Jun 1;23(11):1643-7. doi: 10.1111/j.1365-2036.2006.02926.x. PMID: 16696815.
13. Foster T, Budoff MJ, Saab S, Ahmadi N, Gordon C, Guerci AD. Atorvastatin and antioxidants for the treatment of nonalcoholic fatty liver disease: the St Francis Heart Study randomized clinical trial. *Am J Gastroenterol*. 2011 Jan;106(1):71-7. doi: 10.1038/ajg.2010.299. Epub 2010 Sep 14. PMID: 20842109.
14. Nelson A, Torres DM, Morgan AE, Fincke C, Harrison SA. A pilot study using simvastatin in the treatment of nonalcoholic steatohepatitis: A randomized placebo-controlled trial. *J Clin Gastroenterol*. 2009 Nov-Dec;43(10):990-4. doi: 10.1097/MCG.0b013e31819c392e. PMID: 19448566.
15. Zein CO, Lopez R, Fu X, Kirwan JP, Yerian LM, McCullough AJ, Hazen SL, Feldstein AE. Pentoxifylline decreases oxidized lipid products in nonalcoholic steatohepatitis: new evidence on the potential therapeutic mechanism. *Hepatology*. 2012 Oct;56(4):1291-9. doi: 10.1002/hep.25778. PMID: 22505276; PMCID: PMC3430813.
16. Adams LA, Zein CO, Angulo P, Lindor KD. A pilot trial of pentoxifylline in nonalcoholic steatohepatitis. *Am J Gastroenterol*. 2004 Dec;99(12):2365-8. doi: 10.1111/j.1572-0241.2004.40064.x. PMID: 15571584.
17. Satapathy SK, Sakhuja P, Malhotra V, Sharma BC, Sarin SK. Beneficial effects of pentoxifylline on hepatic steatosis, fibrosis and necroinflammation in patients with non-alcoholic steatohepatitis. *J Gastroenterol Hepatol*. 2007 May;22(5):634-8. doi: 10.1111/j.1440-1746.2006.04756.x. PMID: 17444848.
18. Van Wagner LB, Koppe SW, Brunt EM, Gottstein J, Gardikiotes K, Green RM, Rinella ME. Pentoxifylline for the treatment of non-alcoholic steatohepatitis: a randomized controlled trial. *Ann Hepatol*. 2011 Jul-Sep;10(3):277-86. PMID: 21677329.
19. Zein CO, Yerian LM, Gogate P, Lopez R, Kirwan JP, Feldstein AE, McCullough AJ. Pentoxifylline improves nonalcoholic steatohepatitis: a randomized placebo-controlled trial. *Hepatology*. 2011 Nov;54(5):1610-9. doi: 10.1002/hep.24544. Epub 2011 Aug 24. PMID: 21748765; PMCID: PMC3205292.

20. Ratziu V, de Ledinghen V, Oberti F, Mathurin P, Wartelle-Bladou C, Renou C, Sogni P, Maynard M, Larrey D, Serfaty L, Bonnefont-Rousselot D, Bastard JP, Rivière M, Spénard J; FRESGUN. A randomized controlled trial of high-dose ursodeoxycholic acid for nonalcoholic steatohepatitis. *J Hepatol*. 2011 May;54(5):1011-9. doi: 10.1016/j.jhep.2010.08.030. Epub 2010 Oct 31. PMID: 21145828.
21. Dufour JF, Oneta CM, Gonvers JJ, Bihl F, Cerny A, Cereda JM, Zala JF, Helbling B, Steuerwald M, Zimmermann A; Swiss Association for the Study of the Liver. Randomized placebo-controlled trial of ursodeoxycholic acid with vitamin e in nonalcoholic steatohepatitis. *Clin Gastroenterol Hepatol*. 2006 Dec;4(12):1537-43. doi: 10.1016/j.cgh.2006.09.025. PMID: 17162245.
22. Kudo H, Yata Y, Takahara T, Kawai K, Nakayama Y, Kanayama M, Oya T, Morita S, Sasahara M, Mann DA, Sugiyama T. Telmisartan attenuates progression of steatohepatitis in mice: role of hepatic macrophage infiltration and effects on adipose tissue. *Liver Int*. 2009 Aug;29(7):988-96. doi: 10.1111/j.1478-3231.2009.02006.x. Epub 2009 Apr 6. PMID: 19386026.
23. Georgescu EF, Ionescu R, Niculescu M, Mogoanta L, Vancica L. Angiotensin-receptor blockers as therapy for mild-to-moderate hypertension-associated non-alcoholic steatohepatitis. *World J Gastroenterol*. 2009 Feb 28;15(8):942-54. doi: 10.3748/wjg.15.942. PMID: 19248193; PMCID: PMC2653406.
24. Kaji K, Yoshiji H, Kitade M, Ikenaka Y, Noguchi R, Shirai Y, Aihara Y, Namisaki T, Yoshii J, Yanase K, Tsujimoto T, Kawaratani H, Fukui H. Combination treatment of nonalcoholic steatohepatitis in rats. *Am J Physiol Gastrointest Liver Physiol*. 2011 Jun;300(6):G1094-104. doi: 10.1152/ajpgi.00365.2010. Epub 2011 Mar 3. PMID: 21372165.
25. Torres DM, Jones FJ, Shaw JC, Williams CD, Ward JA, Harrison SA. Rosiglitazone versus rosiglitazone and metformin versus rosiglitazone and losartan in the treatment of nonalcoholic steatohepatitis in humans: a 12-month randomized, prospective, open-label trial. *Hepatology*. 2011 Nov;54(5):1631-9. doi: 10.1002/hep.24558. PMID: 21748770.
26. Froese, DS, Fowler, B, Baumgartner, MR. Vitamin B<sub>12</sub>, folate, and the methionine remethylation cycle—biochemistry, pathways, and regulation. *J Inherit Metab Dis*. 2019; 42: 673–685. <https://doi.org/10.1002/jimd.12009>
27. Talari HR, Molaqanbari MR, Mokfi M, Taghizadeh M, Bahmani F, Tabatabaei SMH, Sharifi N. The effects of vitamin B12 supplementation on metabolic profile of patients with non-alcoholic fatty liver disease: a randomized controlled trial. *Sci Rep*. 2022 Aug 18;12(1):14047. doi: 10.1038/s41598-022-18195-8. PMID: 35982162; PMCID: PMC9388548.
28. Tripathi M, Singh BK, Zhou J, Tikno K, Widjaja A, Sandireddy R, Arul K, Abdul Ghani SAB, Bee GGB, Wong KA, Pei HJ, Shekeran SC, Sinha RA, Singh MK, Cook SA, Suzuki A, Lim TR, Cheah CC, Wang J, Xiao RP, Zhang X, Chow PKH, Yen PM. Vitamin B<sub>12</sub> and folate decrease inflammation and fibrosis in NASH by preventing syntaxin 17 homocysteinylation. *J Hepatol*. 2022 Nov;77(5):1246-1255. doi: 10.1016/j.jhep.2022.06.033. Epub 2022 Jul 9. PMID: 35820507.
29. Talari HR, Molaqanbari MR, Mokfi M, Taghizadeh M, Bahmani F, Tabatabaei SMH, Sharifi N. The effects of vitamin B12 supplementation on metabolic profile of patients with non-alcoholic fatty liver disease: a randomized controlled trial. *Sci Rep*. 2022 Aug 18;12(1):14047. doi: 10.1038/s41598-022-18195-8. PMID: 35982162; PMCID: PMC9388548.
30. Pathikkal A, Puthusseri B, Divya P, Rudrappa S, Chauhan VS. Folate derivatives, 5-methyltetrahydrofolate and 10-formyltetrahydrofolate, protect BEAS-2B cells from high glucose-induced oxidative stress and inflammation. *In Vitro Cell Dev Biol Anim*. 2022 May;58(5):419-428. doi: 10.1007/s11626-022-00691-w. Epub 2022 Jun 9. PMID: 35678985; PMCID: PMC9179225.
31. Liu Z, Zeng Y, Shen S, Wen Y, Xu C. Association between folate and non-alcoholic fatty liver disease among US adults: a nationwide cross-sectional analysis. *Chin Med J (Engl)*. 2023 Jan 20;136(2):233-235. doi: 10.1097/CM9.0000000000002516. PMID: 36804281; PMCID: PMC10106170.
32. Cordero P, Gomez-Uriz AM, Campion J, Milagro FI, Martinez JA. Dietary supplementation with methyl donors reduces fatty liver and modifies the fatty acid synthase DNA methylation profile in rats fed an obesogenic diet. *Genes Nutr*. 2013 Jan;8(1):105-13. doi: 10.1007/s12263-012-0300-z. Epub 2012 May 31. PMID: 22648174; PMCID: PMC3534997.
33. Schmidl D, Howorka K, Szegedi S, Stjepanek K, Puchner S, Bata A, Scheschy U, Aschinger G, Werkmeister RM, Schmetterer L, Garhofer G. A pilot study to assess the effect of a three-month vitamin supplementation containing L-methylfolate on systemic homocysteine plasma concentrations and retinal blood flow in patients with diabetes. *Mol Vis*. 2020 Apr 24;26:326-333. PMID: 32355442; PMCID: PMC7190578.
34. Jain, R., Manning, S., & Cutler, A. (2020). Good, better, best: Clinical scenarios for the use of L-methylfolate in patients with MDD. *CNS Spectrums*, 25(6), 750-764. doi:10.1017/S1092852919001469
35. Stracquadanio M, Ciotta L, Palumbo MA. Effects of myo-inositol, gymnemic acid, and L-methylfolate in polycystic ovary syndrome patients. *Gynecol Endocrinol*. 2018 Jun;34(6):495-501. doi: 10.1080/09513590.2017.1418852. Epub 2017 Dec 21. PMID: 29265900.
36. "Vitamin E - Health Professional Fact Sheet." NIH Office of Dietary Supplements, 26 March 2021, <https://ods.od.nih.gov/factsheets/VitaminE-HealthProfessional/>. Accessed 16 May 2023.
37. Asbaghi, O., Nazarian, B., Yousefi, M. et al. Effect of vitamin E intake on glycemic control and insulin resistance in diabetic patients: an updated systematic review and meta-analysis of randomized controlled trials. *Nutr J* 22, 10 (2023). <https://doi.org/10.1186/s12937-023-00840-1>
38. Pacana T, Sanyal AJ. Vitamin E and nonalcoholic fatty liver disease. *Curr Opin Clin Nutr Metab Care*. 2012 Nov;15(6):641-8. doi: 10.1097/MCO.0b013e328357f747. PMID: 23075940; PMCID: PMC4984672.

39. Eliades M, Spyrou E. Vitamin D: a new player in non-alcoholic fatty liver disease? *World J Gastroenterol*. 2015 Feb 14;21(6):1718-27. doi: 10.3748/wjg.v21.i6.1718. PMID: 25684936; PMCID: PMC4323447.
40. Sung CC, Liao MT, Lu KC, Wu CC. Role of vitamin D in insulin resistance. *J Biomed Biotechnol*. 2012;2012:634195. doi: 10.1155/2012/634195. Epub 2012 Sep 3. PMID: 22988423; PMCID: PMC3440067.
41. Markotić A, Kelava T, Markotić H, Silovski H, Mrzljak A. Vitamin D in liver cancer: novel insights and future perspectives. *Croat Med J*. 2022 Apr 30;63(2):187-196. doi: 10.3325/cmj.2022.63.187. PMID: 35505652; PMCID: PMC9086812.
42. Hariri M, Zohdi S. Effect of Vitamin D on Non-Alcoholic Fatty Liver Disease: A Systematic Review of Randomized Controlled Clinical Trials. *Int J Prev Med*. 2019 Jan 15;10:14. doi: 10.4103/ijpvm.IJPVM\_499\_17. PMID: 30774848; PMCID: PMC6360993.
43. Kooshki F, Moradi F, Karimi A, Niazkar HR, Khoshbaten M, Maleki V, Pourghassem Gargari B. Chromium picolinate balances the metabolic and clinical markers in nonalcoholic fatty liver disease: a randomized, double-blind, placebo-controlled trial. *Eur J Gastroenterol Hepatol*. 2021 Oct 1;33(10):1298-1306. doi: 10.1097/MEG.0000000000001830. PMID: 32804855.
44. Havel PJ. A scientific review: the role of chromium in insulin resistance. *Diabetes Educ*. 2004;Suppl:2-14. PMID: 15208835.
45. "Effects of Different Chromium Compounds on Hematology and Inflammatory Cytokines in Rats Fed High-Fat Diet." *Frontiers*, 15 January 2021, <https://www.frontiersin.org/articles/10.3389/fimmu.2021.614000/full>. Accessed 16 May 2023.
46. Chen WY, Chen CJ, Liu CH, Mao FC. Chromium attenuates high-fat diet-induced nonalcoholic fatty liver disease in KK/HIJ mice. *Biochem Biophys Res Commun*. 2010 Jul 2;397(3):459-64. doi: 10.1016/j.bbrc.2010.05.129. Epub 2010 May 27. PMID: 20513351.
47. Hosui A, Kimura E, Abe S, Tanimoto T, Onishi K, Kusumoto Y, Sueyoshi Y, Matsumoto K, Hirao M, Yamada T, Hiramatsu N. Long-Term Zinc Supplementation Improves Liver Function and Decreases the Risk of Developing Hepatocellular Carcinoma. *Nutrients*. 2018 Dec 10;10(12):1955. doi: 10.3390/nu10121955. PMID: 30544767; PMCID: PMC6316561.
48. Kim J, Lee S. Effect of zinc supplementation on insulin resistance and metabolic risk factors in obese Korean women. *Nutr Res Pract*. 2012 Jun;6(3):221-5. doi: 10.4162/nrp.2012.6.3.221. Epub 2012 Jun 30. PMID: 22808346; PMCID: PMC3395787.
49. Kirkil G, Hamdi Muz M, Seçkin D, Sahin K, Kūçūk O. Antioxidant effect of zinc picolinate in patients with chronic obstructive pulmonary disease. *Respir Med*. 2008 Jun;102(6):840-4. doi: 10.1016/j.rmed.2008.01.010. Epub 2008 Mar 4. PMID: 18295467.
50. Lee DE, Lee SJ, Kim SJ, Lee HS, Kwon OS. Curcumin Ameliorates Nonalcoholic Fatty Liver Disease through Inhibition of O-GlcNAcylation. *Nutrients*. 2019 Nov 8;11(11):2702. doi: 10.3390/nu1112702. PMID: 31717261; PMCID: PMC6893521.
51. Saadati, S., Sadeghi, A., Mansour, A. *et al.* Curcumin and inflammation in non-alcoholic fatty liver disease: a randomized, placebo controlled clinical trial. *BMC Gastroenterol* 19, 133 (2019). <https://doi.org/10.1186/s12876-019-1055-4>
52. Gupta N, Verma K, Nalla S, Kulshreshtha A, Lall R, Prasad S. Free Radicals as a Double-Edged Sword: The Cancer Preventive and Therapeutic Roles of Curcumin. *Molecules*. 2020 Nov 18;25(22):5390. doi: 10.3390/molecules25225390. PMID: 33217990; PMCID: PMC7698794.
53. Zhang DW, Fu M, Gao SH, Liu JL. Curcumin and diabetes: a systematic review. *Evid Based Complement Alternat Med*. 2013;2013:636053. doi: 10.1155/2013/636053. Epub 2013 Nov 24. PMID: 24348712; PMCID: PMC3857752.
54. Rahmani AH, Alsahli MA, Aly SM, Khan MA, Aldebasi YH. Role of Curcumin in Disease Prevention and Treatment. *Adv Biomed Res*. 2018 Feb 28;7:38. doi: 10.4103/abr.abr\_147\_16. PMID: 29629341; PMCID: PMC5852989.
55. Gillissen A, Schmidt HH. Silymarin as Supportive Treatment in Liver Diseases: A Narrative Review. *Adv Ther*. 2020 Apr;37(4):1279-1301. doi: 10.1007/s12325-020-01251-y. Epub 2020 Feb 17. PMID: 32065376; PMCID: PMC7140758.
56. Beckerman, James. "Milk Thistle: Benefits and Side Effects." *WebMD*, 9 June 2021, <https://www.webmd.com/digestive-disorders/milk-thistle-benefits-and-side-effects>. Accessed 16 May 2023.
57. Gobalakrishnan S, Asirvatham SS, Janarthanam V. Effect of Silybin on Lipid Profile in Hypercholesterolaemic Rats. *J Clin Diagn Res*. 2016 Apr;10(4):FF01-5. doi: 10.7860/JCDR/2016/16393.7566. Epub 2016 Apr 1. PMID: 27190826; PMCID: PMC4866124.
58. Kwon DY, Jung YS, Kim SJ, Kim YS, Choi DW, Kim YC. Alterations in sulfur amino acid metabolism in mice treated with silymarin: a novel mechanism of its action involved in enhancement of the antioxidant defense in liver. *Planta Med*. 2013 Aug;79(12):997-1002. doi: 10.1055/s-0032-1328704. Epub 2013 Jun 27. PMID: 23807810.
59. Mirzaei E, Sabetian G, Masjedi M, Heidari R, Mirjalili M, Dehghanian A, Vazin A. The effect of silymarin on liver enzymes and antioxidant status in trauma patients in the intensive care unit: a randomized double blinded placebo-controlled clinical trial. *Clin Exp Hepatol*. 2021 Jun;7(2):149-155. doi: 10.5114/ceh.2021.107067. Epub 2021 Jun 22. PMID: 34295981; PMCID: PMC8284169.
60. Al Zorzour RH, Ahmad M, Asmawi MZ, Kaur G, Saeed MAA, Al-Mansoub MA, Saghir SAM, Usman NS, Al-Dulaimi DW, Yam MF. Phyllanthus Niruri Standardized Extract Alleviates the Progression of Non-Alcoholic Fatty Liver Disease and Decreases Atherosclerotic Risk in Sprague-Dawley Rats. *Nutrients*. 2017 Jul 18;9(7):766. doi: 10.3390/nu9070766. PMID: 28718838; PMCID: PMC5537880.

61. Ranilla LG, Kwon YI, Apostolidis E, Shetty K. Phenolic compounds, antioxidant activity and in vitro inhibitory potential against key enzymes relevant for hyperglycemia and hypertension of commonly used medicinal plants, herbs and spices in Latin America. *Bioresour Technol*. 2010 Jun;101(12):4676-89. doi: 10.1016/j.biortech.2010.01.093. Epub 2010 Feb 25. PMID: 20185303.
62. Ballester P, Cerdá B, Arcusa R, Marhuenda J, Yamedjeu K, Zafrilla P. Effect of Ginger on Inflammatory Diseases. *Molecules*. 2022 Oct 25;27(21):7223. doi: 10.3390/molecules27217223. PMID: 36364048; PMCID: PMC9654013.
63. Ballester P, Cerdá B, Arcusa R, Marhuenda J, Yamedjeu K, Zafrilla P. Effect of Ginger on Inflammatory Diseases. *Molecules*. 2022 Oct 25;27(21):7223. doi: 10.3390/molecules27217223. PMID: 36364048; PMCID: PMC9654013.
64. Bianca Fuhrman and others, Ginger Extract Consumption Reduces Plasma Cholesterol, Inhibits LDL Oxidation and Attenuates Development of Atherosclerosis in Atherosclerotic, Apolipoprotein E-Deficient Mice, *The Journal of Nutrition*, Volume 130, Issue 5, May 2000, Pages 1124–1131, <https://doi.org/10.1093/jn/130.5.1124>
65. Alizadeh-Navaei R, Roozbeh F, Saravi M, Pouramir M, Jalali F, Moghadamnia AA. Investigation of the effect of ginger on the lipid levels. A double blind controlled clinical trial. *Saudi Med J*. 2008 Sep;29(9):1280-4. PMID: 18813412.
66. Alsahli MA, Almatroodi SA, Almatroudi A, Khan AA, Anwar S, Almutary AG, Alrumaihi F, Rahmani AH. 6-Gingerol, a Major Ingredient of Ginger Attenuates *Diethylnitrosamine*-Induced Liver Injury in Rats through the Modulation of Oxidative Stress and Anti-Inflammatory Activity. *Mediators Inflamm*. 2021 Jan 19;2021:6661937. doi: 10.1155/2021/6661937. PMID: 33531877; PMCID: PMC7837795.
67. "Dandelion - Western New York Urology Associates, LLC." WNY Urology Associates, <https://www.wnyurology.com/content.aspx?chunkid=21667>. Accessed 16 May 2023.
68. Pflugstgraf IO, Taulescu M, Pop RM, Orăsan R, Vlase L, Uifalean A, Todea D, Alexescu T, Toma C, Pârvu AE. Protective Effects of *Taraxacum officinale* L. (Dandelion) Root Extract in Experimental Acute on Chronic Liver Failure. *Antioxidants (Basel)*. 2021 Mar 24;10(4):504. doi: 10.3390/antiox10040504. PMID: 33804908; PMCID: PMC8063808.
69. Cai L, Wan D, Yi F, Luan L. Purification, Preliminary Characterization and Hepatoprotective Effects of Polysaccharides from Dandelion Root. *Molecules*. 2017 Aug 25;22(9):1409. doi: 10.3390/molecules22091409. PMID: 28841174; PMCID: PMC6151742.
70. Davaatseren M, Hur HJ, Yang HJ, Hwang JT, Park JH, Kim HJ, Kim MJ, Kwon DY, Sung MJ. *Taraxacum officinale* (dandelion) leaf extract alleviates high-fat diet-induced nonalcoholic fatty liver. *Food Chem Toxicol*. 2013 Aug;58:30-6. doi: 10.1016/j.fct.2013.04.023. Epub 2013 Apr 18. PMID: 23603008.
71. Khoshbaten M, Aliasgarzadeh A, Masnadi K, Tarzamani MK, Farhang S, Babaei H, Kiani J, Zaare M, Najafipour F. N-acetylcysteine improves liver function in patients with non-alcoholic Fatty liver disease. *Hepat Mon*. 2010 Winter;10(1):12-6. Epub 2010 Mar 1. PMID: 22308119; PMCID: PMC3270338
72. Khoshbaten M, Aliasgarzadeh A, Masnadi K, Tarzamani MK, Farhang S, Babaei H, Kiani J, Zaare M, Najafipour F. N-acetylcysteine improves liver function in patients with non-alcoholic Fatty liver disease. *Hepat Mon*. 2010 Winter;10(1):12-6. Epub 2010 Mar 1. PMID: 22308119; PMCID: PMC3270338.
73. Jain SK, Velusamy T, Croad JL, Rains JL, Bull R. L-cysteine supplementation lowers blood glucose, glycated hemoglobin, CRP, MCP-1, and oxidative stress and inhibits NF-kappaB activation in the livers of Zucker diabetic rats. *Free Radic Biol Med*. 2009 Jun 15;46(12):1633-8. doi: 10.1016/j.freeradbiomed.2009.03.014. Epub 2009 Mar 26. PMID: 19328229; PMCID: PMC3568688.
74. De Oliveira CP, Simplicio FI, de Lima VM, Yuahasi K, Lopasso FP, Alves VA, Abdalla DS, Carrilho FJ, Laurindo FR, de Oliveira MG. Oral administration of S-nitroso-N-acetylcysteine prevents the onset of non alcoholic fatty liver disease in rats. *World J Gastroenterol*. 2006 Mar 28;12(12):1905-11. doi: 10.3748/wjg.v12.i12.1905. PMID: 16609997; PMCID: PMC4087516.
75. Dlodla PV, Nkambule BB, Mazibuko-Mbeje SE, Nyambuya TM, Marcheggiani F, Cirilli I, Ziqubu K, Shabalala SC, Johnson R, Louw J, Damiani E, Tiano L. N-Acetyl Cysteine Targets Hepatic Lipid Accumulation to Curb Oxidative Stress and Inflammation in NAFLD: A Comprehensive Analysis of the Literature. *Antioxidants (Basel)*. 2020 Dec 16;9(12):1283. doi: 10.3390/antiox9121283. PMID: 33339155; PMCID: PMC7765616.
76. Ardekani, A., Tabrizi, R., Maleki, E., Bagheri Lankarani, K., Heydari, S. T., Moradinazar, M., & Akbari, M. (2023). Effects of coenzyme Q10 supplementation on lipid profiles and liver enzymes of nonalcoholic fatty liver disease (NAFLD) patients: A systematic review and meta-analysis of randomized controlled trials. *Food Science & Nutrition*, 00, 1–9. <https://doi.org/10.1002/fsn3.3315>
77. Jane L Tarry-Adkins and others, Coenzyme Q<sub>10</sub> prevents hepatic fibrosis, inflammation, and oxidative stress in a male rat model of poor maternal nutrition and accelerated postnatal growth, *The American Journal of Clinical Nutrition*, Volume 103, Issue 2, February 2016, Pages 579–588, <https://doi.org/10.3945/ajcn.115.119834>
78. Yoo JY, Yum KS. Effect of Coenzyme Q<sub>10</sub> on Insulin Resistance in Korean Patients with Prediabetes: A Pilot Single-Center, Randomized, Double-Blind, Placebo-Controlled Study. *Biomed Res Int*. 2018 Jul 29;2018:1613247. doi: 10.1155/2018/1613247. PMID: 30151373; PMCID: PMC6087610.
79. "How Does BioPerine® Increase Absorption of Nutrients?" Superfood Science Supplements, 8 June 2021, <https://www.superfoodscience.com/blogs/health-blog/bioperine-nutrient-absorption>. Accessed 16 May 2023.
80. Derosa G, Maffioli P, Sahebkar A. Piperine and Its Role in Chronic Diseases. *Adv Exp Med Biol*. 2016;928:173-184. doi: 10.1007/978-3-319-41334-1\_8. PMID: 27671817.

81. Mohammadi M, Najafi H, Mohamadi Yarijani Z, Vaezi G, Hojati V. Piperine pretreatment attenuates renal ischemia-reperfusion induced liver injury. *Heliyon*. 2019 Aug 13;5(8):e02180. doi: 10.1016/j.heliyon.2019.e02180. PMID: 31463384; PMCID: PMC6706586.
82. Sabina, E. P., Harris Souriyani, A. D., Jackline, D., & Rasool, M. K. (2010, December 20). Piperine, an active ingredient of black pepper attenuates acetaminophen-induced hepatotoxicity in mice. [https://pdf.sciencedirectassets.com/280158/1-s2.0-S1995764511X00020/1-s2.0-S1995764511600114/main.pdf?X-Amz-Security-Token=IQoJb3JpZ2luX2VjEj%2F%2F%2F%2F%2F%2F%2F%2F%2F%2FwEaCXVzLWVhc3QtMSJGMEQICFQ0E8smRv7A0Lc9oXKh2OR16NjPFUNVv6rWGYIHXRuAiAmGZQbSgHTgORrI](https://pdf.sciencedirectassets.com/280158/1-s2.0-S1995764511X00020/1-s2.0-S1995764511600114/main.pdf?X-Amz-Security-Token=IQoJb3JpZ2luX2VjEj%2F%2F%2F%2F%2F%2F%2F%2F%2F%2F%2FwEaCXVzLWVhc3QtMSJGMEQICFQ0E8smRv7A0Lc9oXKh2OR16NjPFUNVv6rWGYIHXRuAiAmGZQbSgHTgORrI)
83. Tang X, Wei R, Deng A, Lei T. Protective Effects of Ethanolic Extracts from Artichoke, an Edible Herbal Medicine, against Acute Alcohol-Induced Liver Injury in Mice. *Nutrients*. 2017 Sep 11;9(9):1000. doi: 10.3390/nu9091000. PMID: 28891983; PMCID: PMC5622760.
84. Richter, Amy, and Miho Hatanaka. "Top 8 Health Benefits of Artichokes and Artichoke Extract." Healthline, <https://www.healthline.com/nutrition/artichoke-benefits>. Accessed 16 May 2023.
85. Crane, Michael. "Bergamot Polyphenols Tackle Liver Conditions Linked to Metabolic Syndrome." *Nutritional Outlook*, 3 June 2016, <https://www.nutritionaloutlook.com/view/bergamot-polyphenols-tackle-liver-conditions-linked-metabolic-syndrome>. Accessed 16 May 2023.
86. Musolino V, Gliozzi M, Bombardelli E, Nucera S, Carresi C, Maiuolo J, Mollace R, Paone S, Bosco F, Scarano F, Scicchitano M, Macri R, Ruga S, Zito MC, Palma E, Gratteri S, Ragusa M, Volterrani M, Fini M, Mollace V. The synergistic effect of *Citrus bergamia* and *Cynara cardunculus* extracts on vascular inflammation and oxidative stress in non-alcoholic fatty liver disease. *J Tradit Complement Med*. 2020 Feb 8;10(3):268-274. doi: 10.1016/j.jtcme.2020.02.004. PMID: 32670822; PMCID: PMC7340872.
87. Ferro Y, Montalcini T, Mazza E, Foti D, Angotti E, Gliozzi M, Nucera S, Paone S, Bombardelli E, Aversa I, Musolino V, Mollace V, Pujia A. Randomized Clinical Trial: Bergamot Citrus and Wild Cardoon Reduce Liver Steatosis and Body Weight in Non-diabetic Individuals Aged Over 50 Years. *Front Endocrinol (Lausanne)*. 2020 Aug 11;11:494. doi: 10.3389/fendo.2020.00494. PMID: 32849284; PMCID: PMC7431622.

## Ingredient Glossary

- **BergaCynFF®** (*Citrus bergamia*) and *Cynara cardunculus* (artichokes), - Patented and clinically shown ingredient demonstrates the micronization and co-grinding of both ingredients leads to a better absorption and tissue distribution of orally given compounds\*.
- (Bergamont (*Citrus bergamia*))** - nutraceutical containing bioactive components of bergamont that are clinically shown to support a reduction of liver fat.\*
- Cynara cardunculus* (artichokes)** - Artichoke has been used for centuries because of its choleric (bile stimulating) properties that assist with fat metabolism. Clinically demonstrated to lead to regeneration on injured liver cells and support a reduction in abnormally stored liver fat.\*
- **B12 (methylcobalamin)** - Supports a reduction of hepatic (liver) fat accumulation, aids in reversal of liver inflammation and fibrosis.\*
  - **L-Methylfolate** - helps repair DNA, assists the detoxification process in the body and aids in lowering liver enzymes.\*
  - **Vitamin E** - Vitamin E is a potent antioxidant useful for the management of NAFLD. Helps improve several biochemical and histological derangements of NAFLD.\*
  - **Vitamin D** - Essential vitamin that has anti-inflammatory and anti-fibrotic effects to help with liver disease.\*
  - **Zinc Picolinate** - Bioavailable form of Zinc that is involved in the glucose, lipid,

and protein metabolism and antioxidant processes in biological pathways to assist with liver function.\*

- **Coenzyme Q10 (Ubiquinone)** - CoQ10 supplementation improves glycaemic control and reduces liver inflammation in patients with non-alcoholic fatty liver disease.\*
- **Organic Turmeric** -Turmeric aids in protecting the liver against damage caused by free radicals, toxins, and alcohol and supports healthy liver detoxification. By clearing out excess cholesterol, turmeric aids to reduce fatty deposits in the liver and may help to reduce liver inflammation.\*
- **Organic Milk Thistle** - Active ingredient Silymarin acts as a strong antioxidant by reducing free radical production which are clinically shown to help with liver detoxification and aid with liver cirrhosis.\*
- **Organic Chanca Piedra Extract** - A well known clinically studied herb that supports an improvement in liver function and decreased serum levels of glucose and insulin concentrations.\*
- **Organic Ginger Root Extract** - Ginger supplementation is a new therapeutic strategy for NAFLD by improving the body's antioxidant activity, and reducing levels of inflammation and insulin resistance.\*
- **Dandelion Root** - A well known clinically studied herb that supports an improvement in liver functions by inhibiting the pancreatic lipase, decreasing the lipogenesis and reducing the inflammation in the liver.\*
- **L-Cysteine** - Strong antioxidant that is valued for its ability to increase glutathione levels in the body. It helps to promote proper liver detoxification.\*
- **Chromium Picolinate** - Plays a key role in the regulation of glucose and lipid metabolism and may improve insulin sensitivity.\*
- **BioPerine®** - A patented extract ingredient used to enhance nutrient absorption, stabilize blood sugar levels and help support drug bioavailability.\*