Some of the main components of *Litchi chinensis* seed extracts based on LC-MS and their bioactivities.

Name	Class	Bioactivity	Host/Cell	References
Nicotinamide	Alkaloids	Ameliorating acne	Clinical Trial	[1]
		Preventing cancers	(Multi)	[2, 3]
Stachydrine	Alkaloids	Improving cardiovascular disorders, preventing cancers, neuroprotective and anti-inflammatory effects	(Multi)	[4]
L-Isoleucine	Amino acid derivatives	Immunoregulation	Piglets	[5]
		Regulating glucose metabolism	Mice	[6]
		Antiobesity and hypolipidemic effect	Mice	[7]
Arginine	Amino acid derivatives	Improving cardiovascular disorders	(Multi)	[8]
		Decreasing oxidative stress	Clinical Trial	[9]
Citric acid	Carboxylic acids and derivatives	Cardioprotection	Rats	[10]
Scopolin	Coumarins and derivatives	Improving hepatic steatosis	Mice	[11]
Epicatechin	Flavonoids	Anticancer and improving diabetes	(Multi)	[12]
		Hepatoprotive activity	Mice	[13]
		Cardiovascular protective effect	(Multi)	[14]
Rutin	Flavonoids	Hepatoprotive activity	Mice	[15]
		Protecting intestine	Mice	[16]
		Antioxidant and antiinflammatory activities	Mice	[17]

Name	Class	Bioactivity	Host/Cell	References
Morin	Flavonoids	Improving diabetes, antioxidant and antiinflammatory activities	(Multi)	[18]
		Anticancer activity	(Multi)	[19]
Phloretin	Flavonoids	Anticancer activity	(Multi)	[20]
Quercetin	Flavonoids	Attenuating muscle damage and pain, accelerating recovery	Clinical Trial	[21]
		Improving metabolic diseases	(Multi)	[22]
		Preventing prostate cancer	Rats	[23]
		Antimicrobial, antioxidant, antiinflammatory and liver-protective activities	(Multi)	[24]
		Neuroprotective effects	(Multi)	[25]
		Anticancer activity	(Multi)	[26]
Luteolin	Flavonoids	Anticancer activity	(Multi)	[27]
		Neuroprotective effects	(Multi)	[28]
		Cardioprotection	(Multi)	[29]
Naringin	Flavonoids	Neuroprotective effects	(Multi)	[30]
		Hepatoprotive activity	(Multi)	[31]
Naringenin	Flavonoids	Improving diabetes	(Multi)	[32]
		Neuroprotective effects	(Multi)	[33]
		Cardioprotection	Rats	[34]
Kaempferol	Flavonoids	Protecting intestine	Mice	[35]
		Inhibiting lipid accumulation	Zebrafish	[36]

Name	Class	Bioactivity	Host/Cell	References
Malic acid	Hydroxy acids and derivatives	Cardioprotection	Rats	[10]
Geniposide	Iridoids	Improving diabetes, antioxidant and antiinflammatory activities	(Multi)	[37]
Schizandrin A	Phenylpropanoids	Anticancer activity	Human breast cancer cell line MDA-MB-231	[38]
			Human colorectal cancer cell lines DLD1, RKO, SW480, SW620	[39]
		Antiinflammatory activity	Mice	[40]
		Hepatoprotive activity	Mice	[41]
Shikimic Acid	Organic acids and derivatives	Antiinflammatory activity	Murine macrophage cell line RAW 264.7	[42]
Quinic acid	Organooxygen compounds	Neuroprotective effects	Rats	[43]
5-Hydroxymethylfurfural	Organooxygen compounds	Cardioprotection	Rats	[44]
Protocatechuic acid	Phenolic acids	Anti-inflammatory, antioxidant, anti-hyperglycemia activities	(Multi)	[45]
Gallic acid	Phenols	Antimicrobial activity	-	[46]
		Anticancer activity	Human non-small cell lung cancer cells	[47]
		Cardioprotection	Rats	[48]
		Antiinflammatory activity	Rats	[49]

Name	Class	Bioactivity	Host/Cell	References
		Antiinflammatory activity	Human hepatoma cell line HepG2, murine hepatoma cell line Hepa 1-6, murine macrophage cell line RAW 264	[50]
Protocatechualdehyde	Phenols	Cardioprotection	Rat embryonic ventricular H9c2 cardiomyocytes	[51]
Vanillin	Phenols	Antioxidant and antiinflammatory activities	(Multi)	[52]
		Improving obesity	Mice	[53]
Bengenin	Phenylpropanoids	Antiinflammatory activity	Mice	[54]
Isofraxidin	Phenylpropanoids	Antiinflammatory activity	Mice	[55]
Cryptochlorogenic acid	Phenylpropanoids	Antioxidant and antiinflammatory activities	RAW 264.7 murine macrophage cells	[56]
Chlorogenic acid	Phenylpropanoids	Improving diabetes mellitus	(Multi)	[57]
		Antiinflammatory activity	(Multi)	[58]
		Hepatoprotive activity	Mice	[59]
		Protecting intestine	Rats	[60]
Procyanidin A2	Procyanidins	Improving atherosclerosis	Mice	[61]
		Improving diabetes	Mice	[62]
Procyanidin B2	Procyanidins	Protecting intestine	Mice	[63]
		Improving hepatic steatosis	Mice	[64]
Ginkgolide B	Terpenoids	Neuroprotective effects	(Multi)	[65]
		Antioxidant and antiinflammatory activities	(Multi)	[66]

References

1. F. M. Walocko, A. E. Eber, J. E. Keri, M. A. Al-Harbi and K. Nouri, The role of nicotinamide in acne treatment, *Dermatol Ther*, 2017, **30**.
2. A. Buque, N. Bloy, G. Kroemer and L. Galluzzi, Possible mechanisms of cancer prevention by nicotinamide, *Br J Pharmacol*, 2021, **178**, 2034-2040.
3. I. P. Nikas, S. A. Paschou and H. S. Ryu, The Role of Nicotinamide in Cancer Chemoprevention and Therapy, *Biomolecules*, 2020, **10**.
4. F. Cheng, Y. Zhou, M. Wang, C. Guo, Z. Cao, R. Zhang and C. Peng, A review of pharmacological and pharmacokinetic properties of stachydrine, *Pharmacol Res*, 2020, **155**, 104755.
5. X. Mao, C. Gu, M. Ren, D. Chen, B. Yu, J. He, J. Yu, P. Zheng, J. Luo, Y. Luo, J. Wang, G. Tian and Q. Yang, l-Isoleucine Administration Alleviates Rotavirus Infection and Immune Response in the Weaned Piglet Model, *Front Immunol*, 2018, **9**, 1654.
6. O. Ikehara, N. Kawasaki, K. Maezono, M. Komatsu and A. Konishi, Acute and chronic treatment of L-isoleucine ameliorates glucose metabolism in glucose-intolerant and diabetic mice, *Biol Pharm Bull*, 2008, **31**, 469-472.
7. J. Nishimura, T. Masaki, M. Arakawa, M. Seike and H. Yoshimatsu, Isoleucine prevents the accumulation of tissue triglycerides and upregulates the expression of PPARalpha and uncoupling protein in diet-induced obese mice, *J Nutr*, 2010, **140**, 496-500.
8. J. Gambardella, W. Khondkar, M. B. Morelli, X. Wang, G. Santulli and V. Trimarco, Arginine and Endothelial Function, *Biomedicines*, 2020, **8**.

9. C. R. Morris, L. A. S. Brown, M. Reynolds, C. D. Dampier, P. A. Lane, A. Watt, P. Kumari, F. Harris, S. Manoranjithan, R. D. Mendis, J. Figueroa and S. Shiva, Impact of arginine therapy on mitochondrial function in children with sickle cell disease during vaso-occlusive pain, *Blood*, 2020, **136**, 1402-1406.

10. X. Tang, J. Liu, W. Dong, P. Li, L. Li, C. Lin, Y. Zheng, J. Hou and D. Li, The cardioprotective effects of citric Acid and L-malic Acid on myocardial ischemia/reperfusion injury, *Evid Based Complement Alternat Med*, 2013, **2013**, 820695.

11. A. Yoo, V. P. Narayan, E. Y. Hong, W. K. Whang and T. Park, Scopolin ameliorates high-fat diet induced hepatic steatosis in mice: potential involvement of SIRT1-mediated signaling cascades in the liver, *Sci Rep*, 2017, **7**, 2251.

12. L. A. Abdulkhaleq, M. A. Assi, M. H. M. Noor, R. Abdullah, M. Z. Saad and Y. H. Taufiq-Yap, Therapeutic uses of epicatechin in diabetes and cancer, *Vet World*, 2017, **10**, 869-872.

13. H. Wu, Y. Xie, Y. Xu, Z. Hu, X. Wan, H. Huang and D. Huang, Protective effect of Epicatechin on APAP-induced acute liver injury of mice through anti-inflammation and apoptosis inhibition, *Nat Prod Res*, 2020, **34**, 855-858.

14. I. Bernatova, Biological activities of (-)-epicatechin and (-)-epicatechin-containing foods: Focus on cardiovascular and neuropsychological health, *Biotechnol Adv*, 2018, **36**, 666-681.

15. S. Li, J. Li, R. Pan, J. Cheng, Q. Cui, J. Chen and Z. Yuan, Sodium rutin extends lifespan and health span in mice including positive impacts on liver health, *Br*

J Pharmacol, 2021, DOI: 10.1111/bph.15410.

16. L. S. Fideles, J. A. L. de Miranda, C. D. S. Martins, M. L. L. Barbosa, H. B. Pimenta, P. V. S. Pimentel, C. S. Teixeira, M. A. S. Scafuri, S. O. Facanha, J. E. F. Barreto, P. M. M. Carvalho, A. G. Scafuri, J. L. Araujo, J. A. Rocha, I. G. P. Vieira, N. Ricardo, M. da Silva Campelo, M. Ribeiro, G. A. de Castro Brito and G. S. Cerqueira, Role of Rutin in 5-Fluorouracil-Induced Intestinal Mucositis: Prevention of Histological Damage and Reduction of Inflammation and Oxidative Stress, *Molecules*, 2020, **25**.

17. J. Q. Ma, C. M. Liu and W. Yang, Protective effect of rutin against carbon tetrachloride-induced oxidative stress, inflammation and apoptosis in mouse kidney associated with the ceramide, MAPKs, p53 and calpain activities, *Chem Biol Interact*, 2018, **286**, 26-33.

18. A. Caselli, P. Cirri, A. Santi and P. Paoli, Morin: A Promising Natural Drug, *Curr Med Chem*, 2016, **23**, 774-791.

19. S. Solairaja, M. Q. Andrabi, N. R. Dunna and S. Venkatabalasubramanian, Overview of Morin and Its Complementary Role as an Adjuvant for Anticancer Agents, *Nutr Cancer*, 2021, **73**, 927-942.

20. B. Y. Choi, Biochemical Basis of Anti-Cancer-Effects of Phloretin-A Natural Dihydrochalcone, *Molecules*, 2019, **24**.

21. I. Bazzucchi, F. Patrizio, R. Ceci, G. Duranti, S. Sabatini, P. Sgro, L. Di Luigi and M. Sacchetti, Quercetin Supplementation Improves Neuromuscular Function Recovery from Muscle Damage, *Nutrients*, 2020, **12**.

22. H. Yi, H. Peng, X. Wu, X. Xu, T. Kuang, J. Zhang, L. Du and G. Fan, The Therapeutic Effects and Mechanisms of Quercetin on Metabolic Diseases: Pharmacological Data and Clinical Evidence, *Oxid Med Cell Longev*, 2021, **2021**, 6678662.

23. G. Sharmila, F. A. Bhat, R. Arunkumar, P. Elumalai, P. Raja Singh, K. Senthilkumar and J. Arunakaran, Chemopreventive effect of quercetin, a natural dietary flavonoid on prostate cancer in in vivo model, *Clin Nutr*, 2014, **33**, 718-726.

24. G. E. Batiha, A. M. Beshbishy, M. Ikram, Z. S. Mulla, M. E. A. El-Hack, A. E. Taha, A. M. Algammal and Y. H. A. Elewa, The Pharmacological Activity, Biochemical Properties, and Pharmacokinetics of the Major Natural Polyphenolic Flavonoid: Quercetin, *Foods*, 2020, **9**.

25. L. Alvarez-Arellano, M. Salazar-Garcia and J. C. Corona, Neuroprotective Effects of Quercetin in Pediatric Neurological Diseases, *Molecules*, 2020, **25**.

26. X. Zang, M. Cheng, X. Zhang and X. Chen, Quercetin nanoformulations: a promising strategy for tumor therapy, *Food Funct*, 2021, **12**, 6664-6681.

27. M. Imran, A. Rauf, T. Abu-Izneid, M. Nadeem, M. A. Shariati, I. A. Khan, A. Imran, I. E. Orhan, M. Rizwan, M. Atif, T. A. Gondal and M. S. Mubarak, Luteolin, a flavonoid, as an anticancer agent: A review, *Biomed Pharmacother*, 2019, **112**, 108612.

28. D. Kempuraj, R. Thangavel, D. D. Kempuraj, M. E. Ahmed, G. P. Selvakumar, S. P. Raikwar, S. A. Zaheer, S. S. Iyer, R. Govindarajan, P. N. Chandrasekaran and A. Zaheer, Neuroprotective effects of flavone luteolin in neuroinflammation and neurotrauma, *Biofactors*, 2021, **47**, 190-197.

29. Y. Luo, P. Shang and D. Li, Luteolin: A Flavonoid that Has Multiple Cardio-Protective Effects and Its Molecular Mechanisms, *Front Pharmacol*, 2017, **8**, 692.

30. S. Ahmed, H. Khan, M. Aschner, M. M. Hasan and S. T. S. Hassan, Therapeutic potential of naringin in neurological disorders, *Food Chem Toxicol*, 2019, **132**, 110646.

31. K. Shirani, B. S. Yousefsani, M. Shirani and G. Karimi, Protective effects of naringin against drugs and chemical toxins induced hepatotoxicity: A review, *Phytother Res*, 2020, **34**, 1734-1744.

32. D. J. Den Hartogh and E. Tsiani, Antidiabetic Properties of Naringenin: A Citrus Fruit Polyphenol, *Biomolecules*, 2019, **9**.

33. Z. Nouri, S. Fakhri, F. F. El-Senduny, N. Sanadgol, G. E. Abd-ElGhani, M. H. Farzaei and J. T. Chen, On the Neuroprotective Effects of Naringenin: Pharmacological Targets, Signaling Pathways, Molecular Mechanisms, and Clinical Perspective, *Biomolecules*, 2019, **9**.

34. L. M. Yu, X. Dong, X. D. Xue, J. Zhang, Z. Li, H. J. Wu, Z. L. Yang, Y. Yang and H. S. Wang, Naringenin improves mitochondrial function and reduces cardiac damage following ischemia-reperfusion injury: the role of the AMPK-SIRT3 signaling pathway, *Food Funct*, 2019, **10**, 2752-2765.

35. Y. Qu, X. Li, F. Xu, S. Zhao, X. Wu, Y. Wang and J. Xie, Kaempferol Alleviates Murine Experimental Colitis by Restoring Gut Microbiota and Inhibiting the LPS-TLR4-NF-kappaB Axis, *Front Immunol*, 2021, **12**, 679897.

36. Y. J. Lee, H. S. Choi, M. J. Seo, H. J. Jeon, K. J. Kim and B. Y. Lee, Kaempferol suppresses lipid accumulation by inhibiting early adipogenesis in 3T3-L1 cells and zebrafish, *Food Funct*, 2015, **6**, 2824-2833.

37. Y. X. Zhou, R. Q. Zhang, K. Rahman, Z. X. Cao, H. Zhang and C. Peng, Diverse Pharmacological Activities and Potential Medicinal Benefits of Geniposide, *Evid Based Complement Alternat Med*, 2019, **2019**, 4925682.

38. H. Yan and M. Guo, Schizandrin A inhibits cellular phenotypes of breast cancer cells by repressing miR-155, *IUBMB Life*, 2020, **72**, 1640-1648.

39. B. C. Chen, S. L. Tu, B. A. Zheng, Q. J. Dong, Z. A. Wan and Q. Q. Dai, Schizandrin A exhibits potent anticancer activity in colorectal cancer cells by inhibiting heat shock factor 1, *Biosci Rep*, 2020, **40**.

40. L. Cui, W. Zhu, Z. Yang, X. Song, C. Xu, Z. Cui and L. Xiang, Evidence of anti-inflammatory activity of Schizandrin A in animal models of acute inflammation, *Naunyn Schmiedebergs Arch Pharmacol*, 2020, **393**, 2221-2229.

41. M. J. Jeong, S. R. Kim and U. J. Jung, Schizandrin A supplementation improves nonalcoholic fatty liver disease in mice fed a high-fat and high-cholesterol diet, *Nutr Res*, 2019, **64**, 64-71.

42. T. K. Rabelo, A. G. Guimaraes, M. A. Oliveira, J. Gasparotto, M. R. Serafini, A. A. de Souza Araujo, L. J. Quintans-Junior, J. C. F. Moreira and D. P. Gelain, Shikimic acid inhibits LPS-induced cellular pro-inflammatory cytokines and attenuates mechanical hyperalgesia in mice, *Int Immunopharmacol*, 2016, **39**, 97-105.

43. L. Liu, Y. Liu, J. Zhao, X. Xing, C. Zhang and H. Meng, Neuroprotective Effects of D-(-)-Quinic Acid on Aluminum Chloride-Induced Dementia in Rats, *Evid*

Based Complement Alternat Med, 2020, **2020**, 5602597.

44. G. Wolkart, A. Schrammel, C. N. Koyani, S. Scherubel, K. Zorn-Pauly, E. Malle, B. Pelzmann, M. Andra, A. Ortner and B. Mayer, Cardioprotective effects of 5-hydroxymethylfurfural mediated by inhibition of L-type Ca(2+) currents, *Br J Pharmacol*, 2017, **174**, 3640-3653.

45. A. K. Khan, R. Rashid, N. Fatima, S. Mahmood, S. Mir, S. Khan, N. Jabeen and G. Murtaza, Pharmacological Activities of Protocatechuic Acid, *Acta Pol Pharm*, 2015, **72**, 643-650.

46. Q. Wang, W. F. Leong, R. J. Elias and R. V. Tikekar, UV-C irradiated gallic acid exhibits enhanced antimicrobial activity via generation of reactive oxidative species and quinone, *Food Chem*, 2019, **287**, 303-312.

47. T. Zhang, L. Ma, P. Wu, W. Li, T. Li, R. Gu, X. Dan, Z. Li, X. Fan and Z. Xiao, Gallic acid has anticancer activity and enhances the anticancer effects of cisplatin in nonsmall cell lung cancer A549 cells via the JAK/STAT3 signaling pathway, *Oncol Rep*, 2019, **41**, 1779-1788.

48. D. H. Priscilla and P. S. Prince, Cardioprotective effect of gallic acid on cardiac troponin-T, cardiac marker enzymes, lipid peroxidation products and antioxidants in experimentally induced myocardial infarction in Wistar rats, *Chem Biol Interact*, 2009, **179**, 118-124.

49. A. Shree, J. Islam, A. Vafa, S. Mohammad Afzal and S. Sultana, Gallic acid prevents 1, 2-Dimethylhydrazine induced colon inflammation, toxicity, mucin depletion, and goblet cell disintegration, *Environ Toxicol*, 2020, **35**, 652-664.

50. M. Tanaka, A. Sato, Y. Kishimoto, H. Mabashi-Asazuma, K. Kondo and K. Iida, Gallic Acid Inhibits Lipid Accumulation via AMPK Pathway and Suppresses Apoptosis and Macrophage-Mediated Inflammation in Hepatocytes, *Nutrients*, 2020, **12**.

51. Y. J. Wan, Y. H. Wang, Q. Guo, Y. Jiang, P. F. Tu and K. W. Zeng, Protocatechualdehyde protects oxygen-glucose deprivation/reoxygenation-induced myocardial injury via inhibiting PERK/ATF6alpha/IRE1alpha pathway, *Eur J Pharmacol*, 2021, **891**, 173723.

52. C. S. M. Bezerra-Filho, J. N. Barboza, M. T. S. Souza, P. Sabry, N. S. M. Ismail and D. P. de Sousa, Therapeutic Potential of Vanillin and its Main Metabolites to Regulate the Inflammatory Response and Oxidative Stress, *Mini Rev Med Chem*, 2019, **19**, 1681-1693.

53. J. Guo, X. Han, J. Zhan, Y. You and W. Huang, Vanillin Alleviates High Fat Diet-Induced Obesity and Improves the Gut Microbiota Composition, *Front Microbiol*, 2018, **9**, 2733.

54. X. J. Gao, M. Y. Guo, Z. C. Zhang, T. C. Wang, Y. G. Cao and N. S. Zhang, Bergenin Plays an Anti-Inflammatory Role via the Modulation of MAPK and NF-kappaB Signaling Pathways in a Mouse Model of LPS-Induced Mastitis, *Inflammation*, 2015, **38**, 1142-1150.

55. X. Niu, W. Xing, W. Li, T. Fan, H. Hu and Y. Li, Isofraxidin exhibited anti-inflammatory effects in vivo and inhibited TNF-alpha production in LPS-induced mouse peritoneal macrophages in vitro via the MAPK pathway, *Int Immunopharmacol*, 2012, **14**, 164-171.

56. X. L. Zhao, L. Yu, S. D. Zhang, K. Ping, H. Y. Ni, X. Y. Qin, C. J. Zhao, W. Wang, T. Efferth and Y. J. Fu, Cryptochlorogenic acid attenuates LPS-induced

inflammatory response and oxidative stress via upregulation of the Nrf2/HO-1 signaling pathway in RAW 264.7 macrophages, *Int Immunopharmacol*, 2020, **83**, 106436.

57. Y. Yan, X. Zhou, K. Guo, F. Zhou and H. Yang, Use of Chlorogenic Acid against Diabetes Mellitus and Its Complications, *J Immunol Res*, 2020, **2020**, 9680508.

58. D. Bagdas, Z. Gul, J. A. Meade, B. Cam, N. Cinkilic and M. S. Gurun, Pharmacologic Overview of Chlorogenic Acid and its Metabolites in Chronic Pain and Inflammation, *Curr Neuropharmacol*, 2020, **18**, 216-228.

59. A. Shi, T. Li, Y. Zheng, Y. Song, H. Wang, N. Wang, L. Dong and H. Shi, Chlorogenic Acid Improves NAFLD by Regulating gut Microbiota and GLP-1, *Front Pharmacol*, 2021, **12**, 693048.

60. M. G. Xie, Y. Q. Fei, Y. Wang, W. Y. Wang and Z. Wang, Chlorogenic Acid Alleviates Colon Mucosal Damage Induced by a High-Fat Diet via Gut Microflora Adjustment to Increase Short-Chain Fatty Acid Accumulation in Rats, *Oxid Med Cell Longev*, 2021, **2021**, 3456542.

61. S. Yang, Y. Zhang, W. Li, B. You, J. Yu, X. Huang and R. Yang, Gut Microbiota Composition Affects Procyanidin A2-Attenuated Atherosclerosis in ApoE(-/-) Mice by Modulating the Bioavailability of Its Microbial Metabolites, *J Agric Food Chem*, 2021, **69**, 6989-6999.

62. A. Ahangarpour, G. Afshari, S. A. Mard, A. Khodadadi and M. Hashemitabar, Preventive effects of procyanidin A2 on glucose homeostasis, pancreatic and duodenal homebox 1, and glucose transporter 2 gene expression disturbance induced by bisphenol A in male mice, *J Physiol Pharmacol*, 2016, **67**, 243-252.

63. X. Zhu, X. Tian, M. Yang, Y. Yu, Y. Zhou, Y. Gao, L. Zhang, Z. Li, Y. Xiao, R. E. Moses, X. Li and B. Zhang, Procyanidin B2 Promotes Intestinal Injury Repair and Attenuates Colitis-Associated Tumorigenesis via Suppression of Oxidative Stress in Mice, *Antioxid Redox Signal*, 2021, **35**, 75-92.

64. H. Su, Y. Li, D. Hu, L. Xie, H. Ke, X. Zheng and W. Chen, Procyanidin B2 ameliorates free fatty acids-induced hepatic steatosis through regulating TFEB-mediated lysosomal pathway and redox state, *Free Radic Biol Med*, 2018, **126**, 269-286.

65. K. M. Maclennan, C. L. Darlington and P. F. Smith, The CNS effects of Ginkgo biloba extracts and ginkgolide B, *Prog Neurobiol*, 2002, **67**, 235-257.

66. S. H. Xia and D. C. Fang, Pharmacological action and mechanisms of ginkgolide B, *Chin Med J (Engl)*, 2007, **120**, 922-928.