FULVIC MINERAL COMPLEX: ORGANIC ACIDS AND BENEFITS

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The following text is compiled from data and articles on the benefits to humans or animals of the 13 organic acids found in Fulvic Mineral Complex *(listed in order of occurrence)*; please see referenced articles for more information.

GALLIC / CAFFEIC / FUMARIC / SHIKIMIC / CINNAMIC / FERULIC / BENZOIC / PROTOCATECHUIC / ACETIC / MALIC / PHENYLACETIC / SUCCINIC / LACTIC

GALLIC ACID

Gallic acid, an antioxidant, is an anti-inflammatory agent. Gallic acid, the major bioactive compound of Toona sinensis, inhibited inflammation in vivo (Hsiang et al., 2013), and, in vitro, the inhibition of inflammation by gallic acid was attributed to gallic acid's potential ability to scavenge free radicals, among other potential attributes that work against inflammation (Kroes, Van Den Berg, Quarles van Ufford, Van Dijk, & Labadie, 1992).

Exhibiting neuroprotective effects, gallic acid prevented oxidative stress-related injury in neurodegenerative diseases (Lu, Nie, Belton, Tang, & Zhao, 2006). Gallic acid inhibits pro-inflammatory gene expression in rheumatoid arthritis (Yoon et al., 2013).

Gallic acid is cytotoxic to cancer cells, and, by nature of its composition, can selectively target the cancer cells it has distinguished from normal cells (Inoue et al., 1995).

Gallic acid has been shown to induce cancer cell death in different cancer cell lines, and, in addition, it has inhibited tumor growth in vivo. (Ji et al., 2009, p. 7596; Kawada et al., 2001, p. 847). (Cell death is a necessary part of life; in cancer, cell death becomes non-functioning…) The mechanism by which gallic acid contributes to cancer cell death is via protein regulation, upregulating a protein that programs cell death and downregulating a protein that inhibits cell death (Liang et al., 2014).

CAFFEIC ACID

Caffeic acid can act as an effective anti-inflammatory drug, having specific immunopharmacological activity by modulating inflammatory gene expression (Yang et al., 2013, p. 4).

Caffeic acid may be helpful in the prevention or mitigation of chronic disease of the heart muscle and could provide anti-inflammatory, antioxidant and anticoagulant effects in the cardiac tissue of diabetic subjects (Chao, Hsu, & Yin, 2009, p. 7).

Caffeic acid significantly decreased microscopic lesion scores and inflammation in the colon, and therefore may help prevent colitis (Ye et al., 2007).

The anticancer properties of caffeic acid may have an effect against breast cancer, contributing to the reduction of breast cancer tumor growth (Rosendahl et al., 2015, p. 1877).

Preventing the proliferation of fibrosarcoma cells, caffeic acid led to increased levels of reactive oxygen species (which suppress tumors at higher levels) and also led to the reprogramming of cancer cells that resulted in cancer cell death and lower levels of cancer cell replication. Caffeic acid has potent anticancer properties (Rajendra Prasad, Karthikeyan, Karthikeyan, & Reddy, 2011).

FUMARIC ACID

Somewhat low doses of orally administered fumaric acid protect from inflammatory responses, possibly due to its modulating actions inside the intestinal tract, and suggesting that fumaric acid is an anti-inflammatory agent (Shakya, Singh, Chatterjee, & Kumar, 2014, p. 176).

The esters of fumaric acid have a beneficial effect on and are licensed in Europe for the treatment of psoriasis; they have been used for this in Europe since 1959. The 2009 German evidence-based guidelines for psoriasis treatment recommended fumaric acid esters as a first-line treatment for moderate to severe manifestations of a common form of psoriasis, and they have become the most prescribed treatment for psoriasis (Balak, 2015).

Fumaric acid esters are also effective in the treatment of multiple sclerosis, suggesting that fumaric acid esters demonstrate immunomodulatory and also neuroprotective mechanisms (Moharregh-Khiabani, Linker, Gold, & Stangel, 2009). The beneficial effects of the esters of fumaric acid are evidence to be through an antioxidative mode of action (Gold, Linker, & Stangel, 2012).

Fumaric acid had a marked effect on the production of cancer of the liver; all test subjects that were given fumaric acid and a known carcinogen exhibited no tissue cancer in the liver, whereas the many control group subjects did develop liver carcinomas (Akao & Kuroda, 1990; Kuroda, Terao, & Akao, 1987).

SHIKIMIC ACID

Shikimic acid (and its derivatives) have anticoagulant, anti-inflammatory, antioxidant and anticancer effects (Tang et al., 2009; Xing et al., 2012; Chang et al., 2003; Aghil et al., 1992), amongst other effects (Chen, Hou, Li, Zu, & Yang, 2014, p.1).

The pretreatment of liver cells with shikimic acid led to the reversal of oxidative damage in liver cells by action of mechanisms that supported cellular defense mechanisms and antioxidant activity, amongst other important supportive actions (Mannaa et al., 2014).

Shikimic acid is a component of the production of the popular antiviral drug called oseltamivir, or, Tamiflu (Estévez & Estévez, 2012). Tamiflu is the only oral drug sanctioned for influenza treatment (Borah, 2015, p. 1675).

Shikimic acid lessened neurologic deficit, decreased brain swelling, increased cerebral blood flow and imparted other benefits to subjects with middle cerebral artery thrombosis and indicating a protection of cerebral function (Ma et al., 1999, pp. 702-704).

Shikimic acid has an antibacterial effect against Staphylococcus aureus, showing that Shikimic acid has potential as an antibacterial agent (Bai et al., 2015). A derivative of shikimic acid also supported the immune system against E. coli, and is proposed as a potential medicine (Davies et al., 1994).

Shikimic acid is also an effective analgesic (Lin, Lan, Wei, Liao, & Wei, 2008; Zhang, 1989).

CINNAMIC ACID

Cinnamic acid derivatives show high antioxidant potential and are indicated as potential therapies for diseases related to the oxidative degradation of lipids (Sharma, 2011, p. 410), mostly due their ability to scavenge free radicals well (Sova, 2012).

One study resulted in the highest level of antioxidant capacity against damage caused by a pesticide via the prevention and reduction of oxidative stress (Mousa, Khudier, Mohammad, Sabbar, & Ahmed, 2013). Cinnamic acid prevented damage from this mutagen by stopping its ability to mutate genes and also by stopping the mutation of genes after the genes have been damaged to an extent (Mousa, Khudiar, Muhsin, Sabbar, & Ahmed, 2014, p. 7).

Forms of cinnamic acid have neuroprotective effects against oxidative damage, even at low levels of application (Chavarria et al., 2015).

Trans-cinnamic acid is a bacteriostat (Sharma, 2011, p. 409)—or, a substance that prevents bacteria from proliferating—but is also an antibacterial—as in, it can also kill bacteria (Narasimhan, Belsare, Pharande, Mourya, & Dhake, 2004).

Derivatives of cinnamic acid have also been reported to have antiviral and antifungal properties (Sova, 2012). Also, cinnamic acid and its derivatives have shown promise as potential treatments for anxiety, hyperglycemia, diabetes, liver protection and lowering cholesterol levels as well as against parasites and tuberculosis, amongst other uses (Sharma, 2011).

FERULIC ACID

Ferulic acid and a few derivatives have been proven effective as antioxidants, antimicrobials, antiinflammatories, liver protectants, neuroprotectants, anticancer agents, antidiabetic agents and promoters of reduced cholesterol levels in the blood... (Brenelli de Paiva, Goldbeck, Dantas dos Santos, & Marcio Squina, 2013, p. 405)

As an antioxidant, ferulic acid can prevent induced liver toxicity, mainly by preventing oxidative stress injury to the liver (Wang, Sheng, Ji, & Wang, 2014, p. 545).

Ferulic acid supplementation is emerging as a therapeutic response to Alzheimer's disease, reducing oxidative damage as a free radical scavenger and protein build-up in the brain as an amyloid inhibitor (Mancuso et al., 2007; Sgarbossa, Giacomazza, & Di Carlo, 2015).

In Type II diabetic adult subjects, ferulic acid (known for its antidiabetic property) improved insulin sensitivity and liver-based formation of glycogen from sugar, among other functions that help to maintain sugar homeostasis (Narasimhan, Chinnaiyan, & Karundevi, 2015). Ferulic acid has specific protective effects against the (effects of) diabetes-related kidney damage (Sun et al., 2016, p. 14; Fujitaa et al., 2008; Choi et al., 2011).

Ferulic acid has neuroprotective effects, reducing the size of the area of dead brain tissue (due to a lack of blood supply or oxygen to the brain) and increasing neurological scores, in part due to its ability to suppress superoxide radicals (Cheng et al., 2008).

Sperm vitality and motility is enhanced with ferulic acid, which is beneficial for both fertile and infertile people, and it is recommended as a potential cure for infertility related to reduced sperm motility (one of the major causes of infertility) (Zheng & Zhang, 1997).

BENZOIC ACID

A form of benzoic acid interferes with cell-to-cell interaction processes and therefore inhibiting the invasion of non-small cell lung cancer cells (Shibata et al., 2000).

Benzoic acid derivatives have antioxidant capacity against free radicals (Velika & Kron, 2012).

One inventor has demonstrated that benzoic acid derivatives selectively target cancer cells and destroy tumor tissue, causing complete cell death in tumor tissue (U.S. Patent No. US 7183269 B2, 2007).

Benzoic acid derivatives have an effect in alleviating pain and other adverse effects of sickle cell anemia, seemingly having anti-sickling properties (Pierre, Moses, & Peter, 2015, p. 3).

Benzoic acid derivatives inhibit an influenza enzyme that is key to the ability of influenza to infect the host (Atigadda et al., 1999).

PROTOCATECHUIC ACID

Protocatechuic acid could be protective against cancer growth and is recommended as a potential cancer chemopreventive (Tanaka, Tanaka, & Tanaka, 2011). The chemopreventive action of protocatechuic may in part be due to its inhibition of cancer cell proliferation, tumor growth and biomarker manifestation (Tanaka, Kojima, Suzui, & H, 1993; Tanaka, Kojima, Kawamori, & Mori, 1995; Tseng et al., 1998).

Protocatechuic acid induces antioxidant or detoxifying gene expression, helping reinforce internal defenses against oxidation (Varì et al., 2011).

As an antioxidant, protocatechuic acid helps protect nerve cells from oxidative damage and had neuroprotective properties that indicate its potential in the treatment of neurodegenerative diseases (Guan, Bao, Jiang, & An, 2006; Guan, Ge, Liu, & Cui, 2009; Guan et al., 2011).

Protocatechuic acid can selectively induce liver lining cancer cell death (Yip, Chan, Pang, Tam, & Wong, 2006). As a potent anticancer agent, protocatechuic acid can also halt invasion, retard growth and cause programmed cell death in breast, lung, liver, cervix and prostate cancers (Yin, Lin, Wu, Tsao, & Hsu, 2009).

Protocatechuic acid effectively promotes the growth of joint cartilage cells, which generally have poor regenerative capacity and which will, if left to degenerate, develop into osteoarthritis (Luo et al., 2015, p. 1865). Protocatechuic acid has analgesic and anti-inflammatory effects in arthritis and other join-related diseases (Lende et al., 2011).

ACETIC ACID

In the first report of successful local chemical treatment for prostate cancer, direct injection of acetic acid successfully obliterated prostate cancer tumors, suggesting such a therapy for use in early prostate cancer and in nonoperative, localized cases of advanced prostate cancer (Bhullar et al., 2013).

The performance of form of acetic acid against inflammation is comparable, if not better than, nonsteroidal anti-inflammatory drugs (NSAIDs) like Ibuprofen (Khedr, Shehata, & Mohamed, 2014). Acetic acid derivatives were found to have a longer activity time than indomethacin, a typical drug with anti-fever, anti-inflammatory and analgesic actions (Sharma & Ray, 2008) and were also free of the gastrointestinal toxicity that is common to NSAIDs (Sharma & Ray, 2007).

Acetic acid completely eradicates antibiotic-tolerant bacteria that are resistant to traditional treatments and the mature biofilms that such bacteria produce on prosthetics, making it the one of the only effective, nontoxic measures of treating biofilms involved in chronic infections, with the added benefit of contributing to wound-healing promotion (Bjarnsholt et al., 2015, pp. 364-371).

Acetic acid is ideal for use in treating burn wounds in patients who live in parts of the world with limited resources; it is effective at low dilutions and does not become less active with evaporation, in addition to having good antibacterial activity against a range of bacteria (Fraise, Wilkinson, Bradley, Oppenheim, & Moiemen, 2013).

Acetic acid, which has been used for over 6000 years for the treatment of burn wounds and as an antiseptic, showed comparable and, in some cases, greater bactericidal properties, with an effect on a wide range of bacteria and even at low concentrations (Ryssel et al., 2009).

Test scores indicating the amount of glucose in the blood (after a meal) and insulin response scores were significantly reduced when starchy meals were supplemented with acetic acid (given as vinegar), probably via the mechanism of a delayed gastric emptying rate (Liljeberg & Björck, 1998). Vinegar abated high blood sugar following a meal by twenty percent when compared to the placebo control (Johnston, Steplewska, Long, Harris, & Ryals, 2010).

MALIC ACID

Malic acid has a critical role in ATP production, and may be deficient in fibromyalgia; fibromyalgia symptoms may be caused by a process that results in a deficiency in malic acid and other substances that are necessary for ATP synthesis (Abraham & Flechas, 1992). Significant reductions in all major pain and tenderness measurements were recorded in a trial of a tablet that was eighty percent malic acid for the treatment of fibromyalgia (Russell, Michalek, Flechas, & Abraham, 1995).

Malic acid contributed to the prevention or breaking up of clots in the blood vessels and/or heart in vitro (Zhang, Zhaio, & Bian, 2013), contributed to a significant anti-blood clot effect in vivo and contributed to a significant reduction in recovery time (Zhang, Zhao, & Bian, 2014).

Malic acid contributed to a protective effect on the heart during a heart attack (Khazanov, Kiseliova, Vasiliev, & Chernyschova, 2008). The protective effect of malic acid against the injury resulting from a heart attack may be due to its anti-inflammatory properties, its direct benefits to the heart muscle cells and/or its antiplatelet aggregation (“blood thinning”) activity (Tang et al., 2013, pp. 4-9).

PHENYLACETIC ACID

Phenylacetic acid was (produced, in this case, by a bacterial strain that was isolated from Korean fermented soybean cooking paste and was) proven to have strong antimicrobial properties that countered bacteria and yeast like Staphylococcus aureus, Escherichia coli, and Candida albicans (Kim et al., 2004).

A form of phenylacetic acid was shown to have more powerful effects against inflammation, pain and fever than aspirin and ibuprofen, and was also shown to have a low chance of causing ulcers in the stomach or gut (Atkinson & Leach, 1976). Diclofenac, first synthesized in 1973, is a currently and commonly used (often as an over-the-counter) nonsteroidal anti-inflammatory drug (NSAID)--used to reduce inflammation and pain--that is derived from phenylacetic acid. In a study done at one clinic, giving craniotomy patients a dose of diclofenac before surgery significantly lowered pain scores and additional pain-killing/inflammation-reducing drug requirements at all periods of the study, including in the five days following the operations, when difficult-to-treat headaches are otherwise common (Molnár et al., 2015).

Phenylacetic acid and its derivatives, commonly under study as anticancer agents, scavenge free radicals in addition to promoting cell differentiation, since cancer leads to poor differentiation (Glód & Grieb, 2005, p. 266).

SUCCINIC ACID

Succinic acid could inhibit cell death in the heart after a lack of blood flow and oxygen to the heart by increasing the protein expression in heart muscle cells (Tang et al., 2014).

Succinic acid contributed to the prevention or breaking up of clots in the blood vessels and/or heart in vitro (Zhang, Zhaio, & Bian, 2013), contributed to a significant anti-blood clot effect in vivo and contributed to a significant reduction in recovery time (Zhang, Zhao, & Bian, 2014).

In cases of women with chronically inflamed uteri who were experiencing an upsurge in pain and inflammation, succinic acid derivatives reduced levels of inflammatory protein-signalers (secreted by immune system cells) in the blood and related affective anxiety disorder symptoms (Volchegorskii, Pravdin, & Uzlova, 2014).

A form of succinic acid, known by its trade name cytoflavin, is often used in treatment of stroke and other diseases related to the brain and its blood vessels (Awake Brain: Quality Nootropics, 2016). Cytoflavin effectively treated the side effects of mild brain injury and brain concussion, reducing pain, pain-killing and sedative drug use, anxiety, depression and abnormal physical weakness and improving tested neurocognitive performance, sleep quality, attention and information processing (Skoromets & Pugacheva, 2010). Cytoflavin, tested clinically during the acute phase of cranial stroke, resulted in higher social and functional activities scores, better short- and long-term memories and better overall health (Shestakov, Kosenkova, Kichigina, Larikova, & Starikova, 2011). Cytoflavin in cases of spinal disease resulted in faster pain relief, improved emotional states and the restoration of previously imbalanced nerve sensitivity (Stetsura, Sholomov, Schukovsky, Salina, & Likhacheva, 2015).

A succinic acid derivative, when used as part of treatment for acute gastrointestinal infections led to a more immediate cessation of associated symptoms, like vomiting and diarrhea (Tikhonova, Liapina, & Shul'diakov, 2013).

Many clinical trials have tested derivatives of succinic acid in addition to the common treatment for chronic viral hepatitis, resulting in boosted antioxidant activity, better scores on treatment measurement indices and higher levels of efficacy of treatment (Stel'makh, Radchenko, & Kozlov, 2011).

In elderly cases of type II diabetes, succinic acid derivatives had a moderating effect on blood sugar levels, alleviated shaking, relieved diabetes-caused nerve damage symptoms and improved the overall quality of life (Odin, Belikova, & Pushkova, 2002).

A derivative of succinic acid has been found to be an inhibitor against several strains of the human immunodeficiency virus (HIV), interfering with the virus propagation, in vitro (Chang et al., 1991).

LACTIC ACID

Lactic acid-producing bacteria (Lactobacillus species) have the ability to lower cholesterol levels in the blood (Buck & Gilliland, 1994).

Lactic acid bacteria may reduce risk of cancer, preventing cancer from flourishing, possibly by mechanism of the related reduction in enzymes that convert procarcinogens into carcinogens (Fernandes & Shahani, 1990).

A type of lactic acid-producing bacteria, when administered over eight weeks to human test subjects infected with H. pylori, a bacterium that lives in the digestive tract and often leads to ulcers, resulted in significant overall improvement. Thus, it was concluded that this lactic acid bacterium had a diminishing effect on H. pylori, in addition to reducing inflammation of the stomach lining (Sakamotoa et al., 2000).

A strain of lactic acid-producing bacteria has an enhancing effect on the body's cellular immune response and is suggested a potentially useful, immune boosting dietary supplement (Sheih, Chiang, Wang, Liao, & Gill, 2001). This same strain was more specifically discovered to confer the immune-supporting benefits of inhibiting or preventing pathogen growth (Jones & Versalovic, 2009, p. 5; Spinler et al., 2008) and is also a promising therapy for both infantile colic (Savino, Pelle, Palumeri,

Oggero, & Miniero, 2007) and infantile-childhood eczema (Abrahamsson et al., 2007; Gromert & Axelsson, 2009; Forsberg, Abrahamsson, Björkstén, & Jenmalm, 2013).

REFERENCES

Abraham, G. E., & Flechas, J. D. (1992). Management of fibromyalgia: Rationale for the use of magnesium and malic acid. *Journal of Nutritional Medicine*, *3*(1), 49-59. http://dx.doi.org/10.3109/13590849208997961

Abrahamsson, T.R., Jakobsson, T., Böttcher, M.F., Fredrikson, M., Jenmalm, M.C., & Björkstén, B. (2007). Probiotics in prevention of IgE-associated eczema: A double-blind, randomized, placebo-controlled trial. *Journal of Allergy and Clinical Immunology*, *119*(5), 1174-1180.

Aghil, O., Bibby, M.C., Carrington, S.J., Double, J., Douglas, K.T., & Phillips, R.M. (1992). Synthesis and cytotoxicity of shikimate analogues. *Anti-cancer Drug Design*, *7*(1), 67-82.

Akao, M., & Kuroda, K. (1990). Inhibitory effect of fumaric acid on hepatocarcinogenesis by thioacetamide in mice. *Chemical and Pharmaceutical Bulletin*, *38*(7), 2012-2014.

Atigadda, V.R., Brouillette, W.J., Duarte, F., Ali, S.M., Babu, Y.S., & Bantia, S. (1999). Potent inhibition of influenza sialidase by a benzoic acid containing a 2-pyrrolidinone substituent. *Journal of Medicinal Chemistry*, *42*(13), 2332-2343.

Atkinson, D., & Leach, E.C. (1976). Anti-inflammatory and related properties of 2-(2,4-dichlorophenoxy)phenylacetic acid (fenclofenac). *Agents and Actions*, *6*(5), 657-665.

Awake Brain: Quality Nootropics. (2016). *Cytoflavin Instructions and Dosage* [Fact sheet]. Retrieved March 3, 2016, from http://awakebrain.com/cytoflavin-use

Bai, J., Wu, Y., Liu, X., Zhong, K., Huang, Y., & Gao, H. (2015). Antibacterial activity of shikimic acid from pine needles of Cedrus deodara against Staphylococcus aureus through damage to cell membrane. *International Journal of Molecular Sciences*, *13*(16), 27145-27155. Retrieved from http://www.pubfacts.com/detail/26580596/Antibacterial-Activity-of-Shikimic-Acid-from-Pine-Needles-of-Cedrus-deodara-against-Staphylococcus-a

Balak, D. (2015). Fumaric acid esters in the management of psoriasis. *Psoriasis: Targets and Therapy*, *5*, 9-23. http://dx.doi.org/10.2147/PTT.S51490

Bhullar, J.S., Subhas, G., Chaudhary, S., Silberberg, B., Tilak, J., & Decker, M. (2013). Intratumoral acetic acid injection eradicates human prostate cancer tumors in a murine model. *World Journal of Urology*, *31*(2), 331-337. http://dx.doi.org/10.1007/s00345-012-0994-y

Bjarnsholt, T., Alhede, M., Jensen, P. &., Nielsen, A. K., Johansen, H. K., & Homøe, P. (2015). Antibiofilm properties of acetic acid. *Advances in Wound Care*, *4*(7), 363-372. http://dx.doi.org/10.1089/wound.2014.0554

Borah, J.C. (2015). Shikimic acid: A highly prospective molecule in pharmaceutical industry. *Current Science*, *109*(9), 1672-1679. Retrieved from http://www.currentscience.ac.in/Volumes/109/09/1672.pdf

Brenelli de Paiva, L., Goldbeck, R., Dantas dos Santos, W., & Marcio Squina, F. (2013). Ferulic acid and derivatives: Molecules with potential application in the pharmaceutical field. *Brazilian Journal of Pharmaceutical Sciences*, *49*(3), 395-411. Retrieved from http://www.scielo.br/pdf/bjps/v49n3/v49n3a02.pdf

Buck, L.M., & Gilliland, S.E. (1994). Comparisons of freshly isolated strains of Lactobacillus acidophilus of human intestinal origin for ability to assimilate cholesterol during growth. *Journal of Dairy Science*, *77*(10), 2925-2933.

Chang, R.S., Ding, L., Chen, G.Q., Pan, Q.C., Zhao, Z.L., & Smith, K.M. (1991). Dehydroandrographolide succinic acid monoester as an inhibitor against the human immunodeficiency virus. *Proceedings of the Society for Experimental Biology and Medicine. Society for Experimental Biology and Medicine*, *97*(1), 59-66.

Chang, Y.-C., Almy, E. A., Blamer, G. A., Gray, J. I., Frost, J. W., & Strasburg, G. M. (2003). Antioxidant activity of 3-dehydroshikimic acid in liposomes, emulsions, and bulk oil. *Journal of Agricultural and Food Chemistry*, *51*(9), 2753-2757. http://dx.doi.org/10.1021/jf025970f

Chao, P.-C., Hsu, C.-C., & Yin, M.-C. (2009). Anti-inflammatory and anti-coagulatory activities of caffeic acid and ellagic acid in cardiac tissue of diabetic mice. *Nutrition and Metabolism*, *6*(33), 1-8. http://dx.doi.org/10.1186/1743-7075-6-33

Chavarria, D., Silva, T., Martins, D., Bravo, J., Summavielle, T., & Garridoc, J. (2015). Exploring cinnamic acid scaffold: Development of promising neuroprotective lipophilic antioxidants. *Medicinal Chemistry Communications*, (6), 1043-1053. http://dx.doi.org/10.1039/c5md00018a

Chen, F., Hou, K., Li, S., Zu, Y., & Yang, L. (2014). Extraction and chromatographic determination of shikimic acid in Chinese conifer needles with 1-Benzyl-3-methylimidazolium bromide ionic liquid aqueous solutions. *Journal of Analytical Methods in Chemistry*, 1-12. http://dx.doi.org/10.1155/2014/256473

Cheng, C.-Y., Ho, T.-Y., Lee, E. J., Su, S.-Y., Tang, N.-Y., & Hsieh, C.-L. (2008). Ferulic acid reduces cerebral infarct through its antioxidative and anti-inflammatory effects following transient focal cerebral ischemia in rats. *The American Journal of Chinese Medicine: An International Journal of Comparative Medicine East and West*, *36*(6), 1105. http://dx.doi.org/10.1142/s0192415x08006570

Choi, R., Kim, B. H., Naowaboot, J., Lee, M. Y., Hyun, M. R., & Cho, E. J. (2011). Effects of ferulic acid on diabetic nephropathy in a rat model of type 2 diabetes. *Experimental and Molecular Medicine*, *43*, 676-683. http://dx.doi.org/10.3858/emm.2011.43.12.078

Davies, G.M., Barrett-Bee, K.J., Jude, D.A., Lehan, M., Nichols, W.W., & Pinder, P.E. (1994). (6S)-6-fluoroshikimic acid, an antibacterial agent acting on the aromatic biosynthetic pathway. *Antimicrobial Agents and Chemotherapy*, *38*(2), 403-406. Retrieved from http://www.ncbi.nlm.nih.gov/pmc/articles/PMC284469/

Estévez, A.M., & Estévez, R.J. (2012). A short overview on the medicinal chemistry of (-)-shikimic acid. *Mini Reviews in Medicinal Chemistry*, *12*(14), 1443-1454.

Fernandes, C.F., & Shahani, K.M. (1990). Anticarcinogenic and immunological properties of dietary lactobacilli. *Journal of Food Protection*, *53*(8), 704-710.

Forsberg, A., Abrahamsson, T.R., Björkstén, B., & Jenmalm, M.C. (2013). Pre- and post-natal Lactobacillus reuteri supplementation decreases allergen responsiveness in infancy. *Clinical and Experimental Allergy: journal of the British Society for Allergy and Clinical Immunology*, *43*(4), 434-442. http://dx.doi.org/10.1111/cea.12082

Fraise, A.P., Wilkinson, M., Bradley, C.R., Oppenheim, B., & Moiemen, N. (2013). The antibacterial activity and stability of acetic acid. *Journal of Hospital Infection*, *84*(4), 329-331. http://dx.doi.org/10.1016/j.jhin.2013.05.001

Fujitaa, A., Sasakia, H., Doia, A., Okamotoa, K., Matsunoa, S., & Furutaa, H. (2008). Ferulic acid prevents pathological and functional abnormalities of the kidney in Otsuka Long-Evans Tokushima fatty diabetic rats. *Diabetes Research and Clinical Practice*, *79*(1), 11-17. http://dx.doi.org/10.1016/j.diabres.2007.08.009

Glód, B.K., & Grieb, P. (2005). Estimation of antioxidative properties of phenylacetic acids using ion-exclusion chromatography. *Acta Chromatographica*, *15*, 258-268. Retrieved from http://www.us.edu.pl/uniwersytet/jednostki/wydzialy/chemia/acta/ac15/zrodla/17_AC15.pdf

Gold, R., Linker, R.A., & Stangel, M. (2012). Fumaric acid and its esters: An emerging treatment for multiple sclerosis with antioxidative mechanism of action. *Clinical Immunology*, *142*(1), 44-48. http://dx.doi.org/10.1016/j.clim.2011.02.017

Gromert, N., & Axelsson, I. (2009). Lactobacillus reuteri effect on atopic eczema in childhood. *Journal of Pediatric Gastroenterology and Nutrition*, *48*(3), 148-149.

Guan, S., Bao, Y.-M., Jiang, B., & An, L.-J. (2006). Protective effect of protocatechuic acid from Alpinia oxyphylla on hydrogen peroxide-induced oxidative PC12 cell death. *European Journal of Pharmacology*, *538*(1-3), 73-79. http://dx.doi.org/10.1016/j.ejphar.2006.03.065

Guan, S., Ge, D., Liu, T.-Q., & Cui, Z.-F. (2009). Protocatechuic acid promotes cell proliferation and reduces basal apoptosis in cultured neural stem cells. *Toxicology in Vitro*, *23*(2), 201-208. http://dx.doi.org/10.1016/j.tiv.2008.11.008

Guan, S., Zhang, X.L., Ge, D., Liu, T.Q., Ma, X.H., & Cui, Z.F. (2011). Protocatechuic acid promotes the neuronal differentiation and facilitates survival of phenotypes differentiated from cultured neural stem and progenitor cells. *European Journal of Pharmacology*, *670*(2-3), 471-478. http://dx.doi.org/10.1016/j.ejphar.2011.09.020

Hsiang, C.Y., Hseu, Y.C., Chang, Y.C., Kumar, K.J., Ho, T.Y., & Yang, H.L. (2013). Toona sinensis and its major bioactive compound gallic acid inhibit LPS-induced inflammation in nuclear factor-κB transgenic mice as evaluated by in vivo bioluminescence imaging. *Food Chemistry*, *136*(2), 426-434. http://dx.doi.org/10.1016/j.foodchem.2012.08.009

Inoue, M., Suzuki, R., Sakaguchi, N., Li, Z., Takeda, T., & Ogihara, Y. (1995). Selective induction of cell death in cancer cells by gallic acid. *Biological and Pharmaceutical Bulletin*, *18*(11), 1526-1530. http://dx.doi.org/10.1248/bpb.18.1526

Ji, B.C., Hsu, W.H., Yang, J.S., Hsia, T.C., Lu, C.C., & Chiang, J.H. (2009). Gallic acid induces apoptosis via caspase-3 and mitochondrion-dependent pathways in vitro and suppresses lung xenograft tumor growth in vivo. *Journal of Agricultural and Food Chemistry*, *57*(16), 7596-7604. http://dx.doi.org/10.1021/jf901308p

Johnston, C.S., Steplewska, I., Long, C.A., Harris, L.N., & Ryals, R.H. (2010). Examination of the antiglycemic properties of vinegar in healthy adults. *Annals of Nutrition and Metabolism*, *56*(1), 74-79. http://dx.doi.org/10.1159/000272133

Jones, S.E., & Versalovic, J. (2009). Probiotic Lactobacillus reuteribiofilms produce antimicrobial and anti-inflammatory factors. *BioMed Central Microbiology*, *9*(35), 1-9. http://dx.doi.org/10.1186/1471-2180-9-35

Kawada, M., Ohno, Y., Ri, Y., Ikoma, T., Yuugetu, H., & Asai, T. (2001). Anti-tumor effect of gallic acid on LL-2 lung cancer cells transplanted in mice. *Anti-Cancer Drugs*, *12*(10), 847-852.

Khazanov, V.A., Kiseliova, A.A., Vasiliev, K.Y., & Chernyschova, G.A. (2008). Cardioprotective effects of trimetazidine and a combination of succinic and malic acids in acute myocardial ischemia. *Bulletin of Experimental Biology and Medicine*, *146*(2), 218-222.

Khedr, M.A., Shehata, T.M., & Mohamed, M.E. (2014). Repositioning of 2,4-dichlorophenoxy acetic acid as a potential anti-inflammatory agent: In silico and pharmaceutical formulation study. *European Journal of Pharmaceutical Sciences*, *65*, 130-138. http://dx.doi.org/10.1016/j.ejps.2014.09.014

Kim, Y., Cho, J.Y., Kuk, J.H., Moon, J.H., Cho, J., & Kim, Y.C. (2004). Identification and antimicrobial activity of phenylacetic acid produced by Bacillus licheniformis isolated from fermented soybean, chungkookjang. *Current Microbiology*, *48*(4), 312-317.

Kreutz, W. (2007). *U.S. Patent No. US 7183269 B2; Synergistic compositions for the selective control of tumor tissue.* Washington, DC: U.S. Patent and Trademark Office. Retrieved from https://www.google.com/patents/US7183269

Kroes, B.H., Van Den Berg, A.J., Quarles van Ufford, H.C., Van Dijk, H., & Labadie, R.P. (1992). Anti-inflammatory activity of gallic acid. *Planta Medica*, *58*(6), 499-504.

Kuroda, K., Terao, K., & Akao, M. (1987). Inhibitory effect of fumaric acid on hepatocarcinogenesis by thioacetamide in rats. *Journal of the National Cancer Institute*, *79*(5), 1047-1051.

Lende, A.B., Kshirsagar, A.D., Deshpande, A.D., Muley, M.M., Patil, R.R., & Bafna, P.A. (2011). Anti-inflammatory and analgesic activity of protocatechuic acid in rats and mice. *Inflammopharmacology*, *19*(5), 255-263. http://dx.doi.org/10.1007/s10787-011-0086-4

Liang, W., Li, X., Li, Y., Li, C., Gao, B., & Gan, H. (2014). Gallic acid induces apoptosis and inhibits cell migration by upregulating miR-518b in SW1353 human chondrosarcoma cells. *International Journal of Oncology*, *44*(1), 91-98. http://dx.doi.org/10.3892/ijo.2013.215

Liljeberg, H., & Björck, I. (1998). Delayed gastric emptying rate may explain improved glycaemia in healthy subjects to a starchy meal with added vinegar. *European Journal of Clinical Nutrition*, *52*(5), 368-371.

Lin, J., Lan, Q.X., Wei, Y.F., Liao, L.Y., & Wei, G.F. (2008). An experimental study of the extraction procedure of medicinal components from star anise and its analgesic function. *Journal of Youjiang Medical College for Nationalities*, *2*, 195-196.

Lu, Z., Nie, G., Belton, P.S., Tang, H., & Zhao, B. (2006). Structure-activity relationship analysis of antioxidant ability and neuroprotective effect of gallic acid derivatives. *Neurochemistry International*, *48*(4), 263-274.

Luo, L.-K., Wei, Q.-J., Liu, L., Lin, X., Lin, C.-W., & Zheng, L. (2015). Protocatechuic acid benefits proliferation and phenotypic maintenance of rabbit articular chondrocytes: An in vitro study. *Experimental and Therapeutic Medicine*, *9*(5), 1865-1870. http://dx.doi.org/10.3892/etm.2015.2326

Ma, Y., Xu, Q.P., Sun, J.N., Bai, L.M., Guo, Y.J., & Niu, J.Z. (1999). Antagonistic effects of shikimic acid against focal cerebral ischemia injury in rats subjected to middle cerebral artery thrombosis. *Acta Pharmacologica Sinica*, *20*(8), 701-704. Retrieved from http://www.chinaphar.com/1671-4083/20/701.pdf

Mancuso, C., Scapagini, G., Currò, D., Giuffrida, S. A.M., De Marco, C., & Butterfield, D.A. (2007). Mitochondrial dysfunction, free radical generation and cellular stress response in neurodegenerative disorders. *Frontiers in Bioscience: A Journal and Virtual Library*, *1*(12), 1107-1123.

Mannaa, K., Khana, A., Dasa, D.K., Kesha, S.B., Dasa, U., & Ghosh, S. (2014). Protective effect of coconut water concentrate and its active component shikimic acid against hydroperoxide mediated oxidative stress through suppression of NF-κB and activation of Nrf2 pathway. *Journal of Ethnopharmacology*, *155*(1), 132-146. http://dx.doi.org/10.1016/j.jep.2014.04.046

Moharregh-Khiabani, D., Linker, R.A., Gold, R., & Stangel, M. (2009). Fumaric acid and its esters: An emerging treatment for multiple sclerosis. *Current Neuropharmacology*, *7*(1), 60-64. http://dx.doi.org/10.2174/157015909787602788

Molnár, C., Simon, &., Kazup, &., Gál, J., Molnár, L., & Novák, L. (2015). A single preoperative dose of diclofenac reduces the intensity of acute postcraniotomy headache and decreases analgesic requirements over five postoperative days in adults: A single center, randomized, blinded trial. *Journal of Neurological Sciences*, *353*(1-2), 70-73. http://dx.doi.org/10.1016/j.jns.2015.04.005

Mousa, N.K., Khudiar, S.H., Muhsin, E.A., Sabbar, S.S., & Ahmed, I.A. (2014). Cinnamic acid activity towards Trichlorfon pesticide and liver function enzymes in rat. *Magazine of Biology for University of Al-Kufa*, *6*(1), 1-10. Retrieved from http://www.iqjb.net/wp-content/uploads/2013/12/5.pdf

Mousa, N.K., Khudier, S.H., Mohammad, A.N., Sabbar, S.S., & Ahmed, I.A. (2013). Antioxidant activity of cinnamic acid against trichlorfon in mice. *Iraqi Journal of Life Technologies*, *12*(2), 54-62.

Narasimhan, A., Chinnaiyan, M., & Karundevi, B. (2015). Ferulic acid exerts its antidiabetic effect by modulating insulin-signalling molecules in the liver of high-fat diet and fructose-induced type-2 diabetic adult male rat. *Applied Physiology, Nutrition and Metabolism*, *40*(8), 769-781. http://dx.doi.org/10.1139/apnm-2015-0002

Narasimhan, B., Belsare, D., Pharande, D., Mourya, V., & Dhake, A. (2004). Esters, amides and substituted derivatives of cinnamic acid: Synthesis, antimicrobial activity and QSAR investigations. *European Journal of Medicinal Chemistry*, *39*(10), 827-834.

Odin, V.I., Belikova, T.V., & Pushkova, E.S. (2002). Diabetes mellitus in the elderly: Succinic acid compounds in treating diabetic neuropathies. *Advances in Gerontology*, *9*, 83-87.

Pierre, L. L., Moses, N. M., & Peter, C. M. (2015). Structure activity relationship (SAR) of some benzoic acid derivatives from plant origin that exhibit anti-sickling properties in vitro. *Natural Products Chemistry & Research*, *3*(3), 1-4. http://dx.doi.org/10.4172/2329-6836.1000176

Rajendra Prasad, N., Karthikeyan, A., Karthikeyan, S., & Reddy, B.V. (2011). Inhibitory effect of caffeic acid on cancer cell proliferation by oxidative mechanism in human HT-1080 fibrosarcoma cell line. *Molecular and Cellular Biochemistry Journal*, *349*(1), 11-19. http://dx.doi.org/10.1007/s11010-010-0655-7

Rosendahl, A.H., Perks, C.M., Zeng, L., Markkula, A., Simonsson, M., & Rose, C. (2015). Caffeine and caffeic acid inhibit growth and modify estrogen receptor and insulin-like growth factor I receptor levels in human breast cancer. *Clinical Cancer Research: An Official Journal of the American Association for Cancer Research*, *21*(8), 1877-1887. http://dx.doi.org/10.1158/1078-0432.CCR-14-1748

Russell, I.J., Michalek, J.E., Flechas, J.D., & Abraham, G.E. (1995). Treatment of fibromyalgia syndrome with Super Malic: A randomized, double blind, placebo controlled, crossover pilot study. *The Journal of Rheumatology*, *22*(5), 953-958.

Ryssel, H., Kloeters, O., Germann, G., Schäfer, T., Wiedemann, G., & Oehlbauer, M. (2009). The antimicrobial effect of acetic acid--an alternative to common local antiseptics? *Burns: Journal of the International Society for Burn Injuries*, *35*(5), 695-700. http://dx.doi.org/10.1016/j.burns.2008.11.009

Sakamotoa, I., Igarashib, M., Kimurac, K., Takagib, A., Miwab, T., & Koga, Y. (2000). Suppressive effect of Lactobacillus gasseri OLL 2716 (LG21) on Helicobacter pylori infection in humans. *Journal of Antimicrobial Chemotherapy*, *47*(5), 709-710.

Savino, F., Pelle, E., Palumeri, E., Oggero, R., & Miniero, R. (2007). Lactobacillus reuteri versus simethicone in the treatment of infantile colic: A prospective randomized study. *Pediatrics*, *119*(1), 124-130.

Sgarbossa, A., Giacomazza, D., & Di Carlo, M. (2015). Ferulic acid: A hope for Alzheimer's disease therapy from plants. *Nutrients*, *7*(7), 5764-5782. http://dx.doi.org/10.3390/nu7075246

Shakya, A., Singh, G. K., Chatterjee, S. S., & Kumar, V. (2014). Role of fumaric acid in anti-inflammatory and analgesic activities of a Fumaria indica extracts. *Journal of Intercultural Ethnopharmacology*, *3*(4), 173-178. http://dx.doi.org/10.5455/jice.20140912021115

Sharma, M., & Ray, S.M. (2007). Aromatic amide derivatives of 5,6-dimethoxy-2,3-dihydro-1H-inden(-1-yl)acetic acid as anti-inflammatory agents free of ulcerogenic liability. *Bioorganic and Medicinal Chemistry Letters*, *17*(24), 6790-6796.

Sharma, M., & Ray, S.M. (2008). Synthesis and biological evaluation of amide derivatives of (5,6-dimethoxy-2,3-dihydro-1H-inden-1-yl)acetic acid as anti-inflammatory agents with reduced gastrointestinal ulcerogenecity. *European Journal of Medicinal Chemistry*, *43*(10), 2092-2102.

Sharma, P. (2011). Cinnamic acid derivatives: A new chapter of various pharmacological activities. *Journal of Chemical and Pharmaceutical Research*, *3*(2), 403-423. Retrieved from http://jocpr.com/vol3-iss2-2011/JCPR-2011-3-2-403-423.pdf

Sheih, Y.H., Chiang, B.L., Wang, L.H., Liao, C.K., & Gill, H.S. (2001). Systemic immunity-enhancing effects in healthy subjects following dietary consumption of the lactic acid bacterium Lactobacillus rhamnosus HN001. *Journal of the American College of Nutrition*, *20*(2), 149-156.

Shestakov, V.V., Kosenkova, N.V., Kichigina, E.V., Larikova, T.N., & Starikova, N.L. (2011). Clinical efficacy of cytoflavin in the combined treatment of patients during acute phase of ischemic stroke. *Klinicheskaia Meditsina*, *89*(1), 38-40.

Shibata, J., Murakami, K., Wierzba, K., Aoyagi, Y., Hashimoto, A., & Sano, M. (2000). Anticancer effect of 4-[3,5-bis(trimethylsilyl)benzamido] benzoic acid (TAC-101) against A549 non-small cell lung cancer cell line is related to its anti-invasive activity. *Anticancer Research*, *20*(5A), 3169-3176.

Skoromets, A.A., & Pugacheva, E.L. (2010). Efficacy of the complex drug cytoflavin in the treatment of consequences of mild brain injury. *Zhurnal Nevrologii I Psikhiatrii Imeni S.S. Korsakova*, *110*(3), 31-36.

Sova, M. (2012). Antioxidant and antimicrobial activities of cinnamic acid derivatives. *Mini Reviews in Medicinal Chemistry*, *12*(8), 749-767.

Spinler, J. K., Taweechotipatr, M., Rognerud, C. L., Ou, C. N., Tumwasorn, S., & Versalovic, J. (2008). Human-derived probiotic Lactobacillus reuteri demonstrate antimicrobial activities targeting diverse enteric bacterial pathogens. *Anaerobe*, *14*(3), 166-171. http://dx.doi.org/10.1016/j.anaerobe.2008.02.001

Stel'makh, V.V., Radchenko, V.G., & Kozlov, V.K. (2011). Metabolic correctors based on succinic acid as pathogenic therapy in chronic virus hepatitis. *Terapevticheskii? Arkhiv*, *83*(2), 67-71.

Stetsura, Y.A., Sholomov, I.I., Schukovsky, N.V., Salina, E.A., & Likhacheva, E.B. (2015). The effect of the succinic acid preparation on the dynamics of neurological and emotional disturbances in patients with dorsopathy. *Zhurnal Nevrologii I Psikhiatrii Imeni S.S. Korsakova*, *115*(3), 45-48.

Sun, G.D., Li, C.Y., Cui, W.P., Guo, Q.Y., Dong, C.Q., & Zou, H.B. (2016). Review of herbal Traditional Chinese Medicine for the treatment of diabetic nephropathy. *Journal of Diabetes Research*, 1-18. http://dx.doi.org/10.1155/2016/5749857

Tanaka, T., Kojima, T., Kawamori, T., & Mori, H. (1995). Chemoprevention of digestive organs carcinogenesis by natural product protocatechuic acid. *Cancer*, *75*(6), 1433-1439. Retrieved from http://onlinelibrary.wiley.com/doi/10.1002/1097-0142(19950315)75:6%2B%3C1433::AID-CNCR2820751507%3E3.0.CO;2-4/pdf

Tanaka, T., Kojima, T., Suzui, M., & H. (1993). Chemoprevention of colon carcinogenesis by the natural product of a simple phenolic compound protocatechuic acid: Suppressing effects on tumor development and biomarkers expression of colon tumorigenesis. *Cancer Research*, *53*(17), 3908-3913. Retrieved from http://cancerres.aacrjournals.org/content/53/17/3908.long

Tanaka, T., Tanaka, T., & Tanaka, M. (2011). Potential cancer chemopreventive activity of protocatechuic acid. *Journal of Experimental & Clinical Medicine*, *3*(1), 27-33. http://dx.doi.org/10.1016/j.jecm.2010.12.005

Tang, L., Xiang, H., Sun, Y., Qiu, L., Chen, D., & Deng, C. (2009). Monopalmityloxy shikimic acid: Enzymatic synthesis and anticoagulation activity evaluation. *Applied Biochemistry and Biotechnology*, *158*(2), 408-415. http://dx.doi.org/10.1007/s12010-008-8440-8

Tang, X., Liu, J., Dong, W., Li, P., Li, L., & Lin, C. (2013). The cardioprotective effects of citric acid and L-malic acid on myocardial ischemia/reperfusion injury. *Evidence-Based Complementary and Alternative Medicine*, *820695*, 1-11. http://dx.doi.org/10.1155/2013/820695

Tang, X.L., Liu, J.X., Li, P., Dong, W., Li, L., & Zheng, Y.Q. (2014). Protective effect of succinic acid on primary cardiomyocyte hypoxia/reoxygenation injury. *China Journal of Chinese Materia Medica*, *38*(21), 3742-3746.

Tikhonova, E.O., Liapina, E.P., & Shul'diakov, A.A. (2013). Efficacy of pathogenetic therapy in patients with acute gastrointestinal infections using succinic acid derivatives (reamberin). *Eksperimental'naia I Klinicheskaia Farmakologiia*, *76*(1), 11-13.

Tseng, T.-H., Hsu, J.-D., Lo, M.-H., Chu, C.-Y., Chou, F.-P., & Huang, C.-L. (1998). Inhibitory effect of Hibiscus protocatechuic acid on tumor promotion in mouse skin. *Cancer Letters*, *126*(2), 199-207. http://dx.doi.org/10.1016/S0304-3835(98)00010-X

Varì, R., D'Archivio, M., Filesi, C., Carotenuto, S., Scazzocchio, B., & Santangelo, C. (2011). Protocatechuic acid induces antioxidant/detoxifying enzyme expression through JNK-mediated Nrf2 activation in murine macrophages. *The Journal of Nutritional Biochemistry*, *22*(5), 409-417. http://dx.doi.org/10.1016/j.jnutbio.2010.03.008

Velika, B., & Kron, I. (2012). Antioxidant properties of benzoic acid derivatives against superoxide radical. *Free Radicals and Antioxidants*, *2*(4), 62-67. http://dx.doi.org/10.5530/ax.2012.4.11

Volchegorskii, I.A., Pravdin, E.V., & Uzlova, T.V. (2014). Effects of 3-hydroxypyridine derivatives and succinic acid on endometrial leukocyte infiltration, cytokinemia and related affective symptoms during exacerbation of the chronic inflammation of the uterus and adnexa. *Bulletin of Experimental Biology and Medicine*, *156*(3), 347-352. http://dx.doi.org/10.1007/s10517-014-2346-y

Wang, J.-M., Sheng, Y.-C., Ji, L.-L., & Wang, Z.-T. (2014). Ferulic acid prevents liver injury and increases the anti-tumor effect of diosbulbin B in vivo. *Journal of Zhejiang University*, *15*(6), 540-547. http://dx.doi.org/10.1631/jzus.B1300250

Xing, J., Sun, J., You, H., Lv, J., Sun, J., & Dong, Y. (2012). Anti-inflammatory effect of 3,4-oxo-isopropylidene-shikimic acid on acetic acid-induced colitis in rats. *Inflammation*, *35*(6), 1872-1879. http://dx.doi.org/10.1007/s10753-012-9509-7

Yang, W. S., Jeong, D., Yi, Y.-S., Park, J. G., Seo, H., & Moh, S. H. (2013). IRAK1/4-Targeted anti-inflammatory action of caffeic acid. *Mediators of Inflammation*, 1-13. http://dx.doi.org/10.1155/2013/518183

Ye, Z., Henderson, A., Liu, Z., Lee, K., Lee, S.-O., & Wannemuehler, M. J. (2007). Anti-inflammatory effect of caffeic acid, rutin and hypoxoside in C3H mouse model of colitis. *The Federation of American Societies for Experimental Biology Journal*, *21:550*(11).

Yin, M.-C., Lin, C.-C., Wu, H.-C., Tsao, S.-M., & Hsu, C.-K. (2009). Apoptotic effects of protocatechuic acid in human breast, lung, liver, cervix, and prostate cancer cells: Potential mechanisms of action. *Journal of Agricultural and Food Chemistry*, *57*(14), 6468-6473. http://dx.doi.org/10.1021/jf9004466

Yip, E., Chan, A., Pang, H., Tam, Y.K., & Wong, Y.H. (2006). Protocatechuic acid induces cell death in HepG2 hepatocellular carcinoma cells through a c-Jun N-terminal kinase-dependent mechanism. *Cell Biology and Toxicology*, *22*(4), 293-302.

Yoon, C.H., Chung, S.J., Lee, S.W., Park, Y.B., Lee, S.K., & Park, M.C. (2013). Gallic acid, a natural polyphenolic acid, induces apoptosis and inhibits proinflammatory gene expressions in rheumatoid arthritis fibroblast-like synoviocytes. *Join, Bone, Spine: Revue du Rhumatisme Journal*, *80*(3), 274-279. http://dx.doi.org/10.1016/j.jbspin.2012.08.010

Zhang, J. (1989). Studies on the chemical constituents of the stems and leaves of Illicium dunnianum. *China Journal of Chinese Materia Medica*.

Zhang, Q.C., Zhaio, Y., & Bian, H.M. (2013). Antiplatelet activity of a novel formula composed of malic acid, succinic acid and citric acid from Cornus officinalis fruit. *Phytotherapy Research*, *27*(12), 1894-1896. http://dx.doi.org/10.1002/ptr.4934

Zhang, Q.C., Zhao, Y., & Bian, H.M. (2014). Anti-thrombotic effect of a novel formula from corni fructus with malic acid, succinic acid and citric acid. *Phytotherapy Research*, *28*(5), 722-727. http://dx.doi.org/10.1002/ptr.5052

Zheng, R.L., & Zhang, H. (1997). Effects of ferulic acid on fertile and asthenozoospermic infertile human sperm motility, viability, lipid peroxidation, and cyclic nucleotides. *Free Radical Biology and Medicine*, *22*(4), 581-586.