WHAT GOES INTO CARBON TECHNOLOGY:

Fulvic and Humic Acid Research

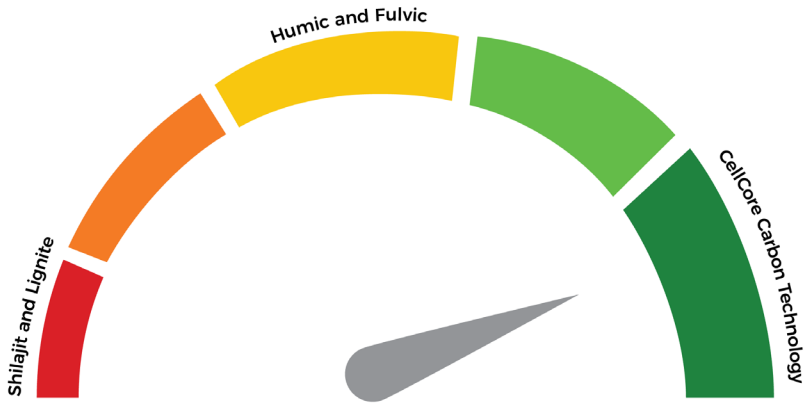
What Is Carbon Technology?

Carbon Technology is a new category of binders and drivers.

Unlike traditional binders (such as activated charcoal, bentonite clay, or diatomaceous earth), Carbon Technology can travel systemically and target chemical toxins, environmental toxins, heavy metals, radiation, retroviruses, and viruses that may be hidden deep within cells and tissues.

Definitions:

- **Fulvic acid:** Fulvic acids are a family of organic acids, natural compounds, and humus components. They are extracts of humic acids, with differences being seen in the functional groups, acidity, degree of polymerization, molecular weight, and color.
- **Humic acid:** Humic acids are a complex mixture of many different organic acids that exist naturally, formed through the natural decay of plant and animal materials and microorganisms' biological activities. They're long-chain molecules that are high in weight and dark brown in color.
- **Humic water:** Humic waters are a natural extract of humic substances (mainly humic and hymatomelanic acids).
- **Shilajit:** Low concentrations of fulvic and humic acids.
- **Potassium humate:** The potassium salt of humic acid.
- **Oxihumate:** Humic acid from coal.
- **Humate:** A salt of humic acid.
- **Oxifulvic acid:** Coal-derived fulvic acid.
- **Ammonium humate:** Humic acid ammonium salt.
- **Synthetic humic acid:** Artificial humic acids (A-HA) made from biomass in a hydrothermal process.
- **Carbohydrate-derived fulvic acid:** A heat-stable, low molecular weight, water-soluble, cationic, colloidal material with proposed therapeutic properties.
- **Humic substances:** Humic substances are components of the natural organic matter in soil, water, and geological organic deposits such as lake sediments, peats, brown coals, and shales. Humic substances in soils and sediments can be divided into three main fractions: humic acids, fulvic acids, and humin.



QUALITY AND EFFECTIVENESS SCALE

Is Fulvic and Humic Acid Toxic?

No, fulvic and humic acids are not toxic. They naturally contain trace amounts of organic heavy metals, not inorganic or toxic heavy metals. The research below demonstrates the safe consumption limits for humic and fulvic acids.

1. No general or organ toxicity was observed in Wistar rats following 90 days of continuous exposure, and a no observed adverse effect level (NOAEL) was determined at 2000 mg/kg bw/day, the highest tested dose. 75 kg / 165 lbs. = 150-gram dose per day (150,000 mg).

   Murbach, Timothy S et al. "A toxicological evaluation of a fulvic and humic acids preparation." Toxicology reports, vol. 7, 1242-1254. 14 Sep. 2020, doi:10.1016/j.toxrep.2020.08.030 Web

2. A 60-day subchronic study was conducted. The acute toxicity test showed that no mortality or toxic effect was observed following oral administration of the maximum dose of 5,000 mg/kg BW/day to mice or rats. 75 kg / 165 lbs. = 375-gram dose per day (375,000 mg)

   Chongshan Dai, Xilong Xiao, Yonglei Yuan, Gaurav Sharma, Shusheng Tang. "A Comprehensive Toxicological Assessment of Fulvic Acid." Evidence-Based Complementary and Alternative Medicine, vol. 2020, Article ID 8899244, 11 pages, 2020. Web

*For reference from the second study, that is equivalent to an adult consuming 5 bottles of HM-ET binder per day for 60 days with no toxic effects.

Absorption and Utilization of Nutrients

1. This study looked at 48 pigs given humic acid to determine its effects on growth performance, blood characteristics, and meat quality. The 48 pigs were split into three groups: A control group, a group given 5% humic acid in feed, and a third given 10% humic acid in feed. The group fed 10% humic acid in feed showed the highest average weight gain, highest lymphocyte count, highest fat marbling score, and had the lowest backfat thickness. This study suggests that humic acid might be utilized as a feed additive in the pigs' diet. **It could improve growth performance, relative lymphocyte counts, and meat quality.**

   Q.Wang et al. "Effects of supplemental humic substances on growth performance, blood characteristics and meat quality in finishing pigs." Livestock Science, Volume 117, Issues 2–3, September 2008, Pages 270-274. Web

TAKEAWAY: Humic and fulvic acid might be utilized as a feed additive in pigs' diets to improve growth performance, relative lymphocyte counts, and meat quality.

2. This study aimed to see if adding fulvic acid to silymarin (milk thistle) would help improve absorption and solubility. The study's results showed that as the concentration of fulvic acid was increased from .2% to 2%, an overall increase in solubility, dissolution profiles, and permeation was observed in the physical mixture and kneading as compared to the control. **This shows that fulvic acid is a promising carrier in silymarin supplement formulations to enhance the supplements' benefits.**

   Javed, Shamama & Kohli, Kanchan & Ahsan, Waquar. "Solubility and Dissolution Enhancement of Silymarin with Fulvic Acid Carrier." International Journal of Drug Development & Research. 8. 9-14. (2016). Web

TAKEAWAY: Fulvic acid exhibited good activity against lipid peroxidation and free radical scavenging in vivo. Adding fulvic acid to silymarin (milk thistle) improves absorption and solubility, enhancing its benefits.

3. This study aimed to determine the influence of humic substances on mineral content changes of calcium, magnesium, copper, and zinc in the meat of broiler chickens. **The results showed that supplements in the feed significantly increased the Ca and Zn content in the breast and thigh muscles of broilers chicks.** This is related to the ability of humic substances to form chelated bonds with elements. In conclusion, the humic substances can be considered a good feed supplement, which can positively affect the nutritional value of chicken meat.

   Skalicka, Magdalena & Nad, Pavel & Bujnak, Lukas & M, Hudák. (2019). "Effect of humic substances on the mineral composition of chicken meat." Animal Husbandry, Dairy and Veterinary Science. 3. 10.15761/AHDVS.1000168. Web

TAKEAWAY: Humic substances added to chicken feed increase Ca and Zn content in the meat.

4. In this study, researchers looked at the modes of actions, beneficial applications, and biological activities of humic acid in poultry health, nutrition, and production. Researchers found that **humic acid helped promote growth and improve nutrient absorptions by improving broiler chickens' gut flora**.

   Arif, Muhammad & Alagawany, Mahmoud & El-Hack, M & Saeed, Muhammad & Arain, Muhammad & Elnesr, Shaaban. (2019). "Humic acid as a feed additive in poultry diets: a review." Iranian Journal of Veterinary Research. 20. 167-172. Web

TAKEAWAY: Humic acid as a feed additive helped promote growth and improve nutrient absorption by improving broiler chickens' gut flora.

5. Researchers found that when they added worm leachate as a source of **humic substance in broiler chickens' drinking water, it had beneficial effects on the growth performance, ileal digestibility of energy, retention of nutrients, and nitrogen retention**. The best results were observed when the worm leachate was mixed at 20% to 30% in the drinking water.

   Gomez-Rosales, S, and M de L Angeles. "Addition of a worm leachate as the source of humic substances in the drinking water of broiler chickens." Asian-Australasian Journal of Animal Sciences, vol. 28, 2 (2015): 215-22. doi:10.5713/ajas.14.0321. Web

TAKEAWAY: Worm leachate as a humic substance source in broiler chickens' drinking water had beneficial effects on the growth performance, ileal digestibility of energy, retention of nutrients, and nitrogen retention.

6. This study study looked at how soil application of humic acid on garden thyme affected the composition of the essential oils and nutrient uptake, and overall plant growth. **Humic acid positively influenced uptake of nutrients N, P, K, Mg, and Fe. It also improved the overall essential oil content.**

   Noroozisharaf, A., Kaviani, M. "Effect of soil application of humic acid on nutrients uptake, essential oil and chemical compositions of garden thyme (Thymus vulgaris L.) under greenhouse conditions." Physiol Mol Biol Plants, 24, 423–431 (2018). https://doi.org/10.1007/s12298-018-0510-y. Web

TAKEAWAY: Humic acid applied to garden thyme positively influenced uptake of nutrients N, P, K, Mg, and Fe. It also improved the overall essential oil content.

7. This study shows that the supplementation of 30 ppm **humic acid** into the diet of Isa Brown layers may **increase the eggshell strength** without affecting egg production and feed efficiency compared to control counterparts.

   Ozturk, Ergin & Coskun, Isa & Ocak, Naime & Erener, Guray. "Effects of dietary humic substances on egg production and eggshell quality of hens after peak laying period." African Journal of Biotechnology. Vol. 8 (6), pp. 1155-1159. (2009). Web

TAKEAWAY: Humic acid added to the diet of layer chickens may increase the eggshell strength and quality.

8. The use of humic substances compared to no use, feeding a diet containing humic substances at 1.5 g kg^{-1} increased the weight gain, feed efficiency, carcass weight without affecting feed consumption, and decreased the total cholesterol level of blood in broilers. Feeding the chickens humic substances at 1.0 g kg^{-1} decreased the feed consumption, lightness of breast meat, and the protein content of both thigh and breast meats. Also the total cholesterol, HDL levels, and LDL level decreased.

   Ozturk, Ergin et al. "Performance, carcass, gastrointestinal tract and meat quality traits, and selected blood parameters of broilers fed diets supplemented with humic substances." Journal of the Science of Food and Agriculture, vol. 92,1 (2012): 59-65. doi:10.1002/jsfa.4541 Web

TAKEAWAY: Adding humic substances to chicken broiler feed enhances weight gain and meat quality.

9. This study found that the use of humic substances with soluble Fe-humic substance complexes, either naturally present in the soil or exogenously supplied to the plants, can promote Fe acquisition in a complex way by providing a readily available iron form in the rhizosphere and by directly affecting plant physiology. Furthermore, the possibility of using Fe-humic substances of different sources, size, and solubility may be considered an environmentally friendly tool for Fe fertilization of crops.

   Zanin, L. et al. "Humic Substances Contribute to Plant Iron Nutrition Acting as Chelators and Biostimulants." Frontiers in Plant Science, (2019). 10.doi:10.3389/fpls.2019.00675 Web

TAKEAWAY: Humic substances with soluble Fe humic substance complexes can promote Fe acquisition by providing a readily available iron form in the rhizosphere and by directly affecting plant physiology, an environmentally friendly way for Fe fertilization of crops.

10. This study found that the type of humic acid used as a fertilizer helped with plant growth and nutrient increase of strawberry plants. It looked at different humic acid concentrations to determine an ideal concentration for growth and nutrient density of nitrogen, potassium, and phosphorus. The research found that at 10 ppm, potassium and phosphorus were the highest, and at 20 ppm, nitrogen was the highest.

    Ameri. S, Atefe & Tehranifar, Ali. "Effect of Humic Acid on Nutrient Uptake and Physiological Characteristic Fragaria ananassa var: Camarosa." Acta Horticulturae. 6. 77-79. (2013). 10.17660/ActaHortic.2014.1049.54. Web

TAKEAWAY: Humic acid fertilizer helped with growth and nutrient absorption of strawberry plants.

11. This study looked at humic acid added to two different types of Alfisol (high organic matter) and an Oxisol (low organic matter) and how it improved teak seed growth and nutrient absorption. It was observed that the **humic acid added to the soil helped improve teak plant growth significantly over control and nutrient absorption of N, P, K, Mg, Ca, Zn, Fe, and Cu, while Mn was decreased**.

J. A. Fagbenro & A. A. Agboola. "Effect of different levels of humic acid on the growth and nutrient uptake of teak seedlings." Journal of Plant Nutrition, 16:8, 1465-1483, (1993). DOI: 10.1080/01904169309364627 Web

TAKEAWAY: Humic acid added to the soil helped improve teak plant growth and nutrient absorption of N, P, K, Mg, Ca, Zn, Fe, and Cu. Mn was decreased.

12. Humic acid was studied to see if it might benefit plant growth by improving nutrient uptake and hormonal effects of gerbera flowers. Different humic acid levels (0, 100, 500, and 1000 mg/L) were applied to a nutrient solution. Root growth increased at 1000 mg/L humic acid incorporated into the solution. **Nutrient contents of leaves and scapes, including nitrogen, phosphorus, potassium, calcium, magnesium, iron, and zinc, were significantly enhanced by humic acid.** However, high levels of HA decreased some nutrient contents. It was found that 500 mg/L of humic acid increased the number of harvested flowers per plant (52%). The highest humic acid levels of 1000 mg/L extended the vase life of harvested flowers by 2—3.66 days and could prevent and delay bent-neck incidence. Researchers believe this was probably due to Ca accumulation in the scapes and the hormone-like humic acid activity.

Nikbakht, A. et al. "Effect of Humic Acid on Plant Growth, Nutrient Uptake, and Postharvest Life of Gerbera." Journal of Plant Nutrition, 31(12), 2155–2167. (2008). doi:10.1080/01904160802462819 Web

TAKEAWAY: Root growth of gerbera flowers increased significantly when humic acid was applied to the nutrient solution. Nutrient contents of leaves and scapes — including nitrogen, phosphorus, potassium, calcium, magnesium, iron, and zinc — were also significantly enhanced.

13. Incorporating fulvic acid at 1000 mg/L provided superior root growth with respect to the control. This study experimented with using fulvic acid to increase potassium levels in tobacco plants to stimulate better plant growth. The study's results suggested that fulvic acid acts similarly to the plant hormone auxin in tobacco, influencing the expression of key genes encoding for transporters and enzymes involved in K uptake and starch metabolism, improving plant growth.

Priya B. N. V.et al. "Fulvic Acid (FA) for Enhanced Nutrient Uptake and Growth: Insights from Biochemical and Genomic Studies." Journal of Crop Improvement, 28:6, 740-757, (2014) DOI: 10.1080/15427528.2014.923084 Web

TAKEAWAY: Superior tobacco plant and root growth and increased K uptake resulted from incorporating fulvic acid in fertilizer.

14. Fulvic acid was shown to increase copper's absorption and simultaneously reduce its toxicity in porcine oviductal epithelial cells.

Sanmanee, Natdhera, and Mayuva Areekijseree. "The effects of fulvic acid on copper bioavailability to porcine oviductal epithelial cells." Biological Trace Element Research, vol. 135, 1-3 (2010): 162-73. doi:10.1007/s12011-009-8508-5 Web

TAKEAWAY: The study suggests that fulvic acid has a strong effect and significant influence on the living surface of porcine oviductal epithelial cells, modifying the effect of copper toxicity.

15. This study looked at how iron and zinc levels affected overall plant growth. When plants were given humic acid with zinc and iron, it resulted in healthy plant growth and rich chlorophyll. **Researchers concluded that humic acid helped iron and zinc to be utilized more effectively by the plants.**

Y. Chen, C.E. Clapp & H. Magen. "Mechanisms of plant growth stimulation by humic substances: The role of organo-iron complexes." Soil Science and Plant Nutrition, 50:7, 1089-1095, (2004) Web

TAKEAWAY: Humic acid helped iron and zinc with utilization by plants, providing evidence that improved Fe, and possibly Zn nutrition, is a major mechanism of plant growth stimulation by humic substances.

16. This study found that **humic acid stimulated nitrogen uptake** (+15% in shoots and +108% in roots) — it was found to increase similarly to growth. Sulfate content (+76% in shoots and +137% in roots) was also strongly stimulated, leading to higher sulfate accumulation. Microscopic analysis showed an **increase in chloroplast number per cell**. In conclusion, humic acid could be used as a supplementary tool to improve winter rapeseed (*Brassica napus*) nitrogen use efficiency because of its ability to promote plant growth and nutrient uptake.

Jannin, L., Arkoun, M., Ourry, A. et al. "Microarray analysis of humic acid effects on Brassica napus growth: Involvement of N, C and S metabolisms." Plant Soil. 359, 297–319 (2012). Web

TAKEAWAY: Humic acid promotes plant growth and nutrient uptake. It stimulated nitrogen uptake, resulting in an increased number of chloroplasts per cell — it could be used as a supplementary tool to improve nitrogen use efficiency.

17. There were observed effects of administering humic substances on pheasants' health, feed conversion, production parameters, egg quality, and hatchability. **The supplement of humic substances at the 0.5% concentration in the feed mixture significantly influenced the hatchability percentage of pheasant chicks**. 72.9% hatchability was achieved in the group without adding humic substances. However, 83.4% hatchability was achieved in the experimental group when humic substances were added.

Sopoliga, Igor et al. "Effect of humic substances on the production parameters of pheasant hens." Acta Fytotechnica et Zootechnica. 19. 11-14. 10.15414/afz.2016.19.01.11-14. 2016. Web

TAKEAWAY: A supplement of humic substances in the feed mixture significantly influenced the hatchability percentage of pheasant chicks.

18. This study showed that adding natural humic substances to broiler chicken diets yields better performance results than adding sodium humate. The feed conversion ratio was significantly better in the humic substance group and worse in the sodium humate group compared to the control group. At the end of the experiment, on day 42 of chickens age, significantly higher European Efficiency Index values were observed in the **humic substance group due to more intensive growth and better feed conversion** than the control and sodium humate groups.

Hreško Šamudovská, Alena & Demeterová, Mária. "Effect of Diet Supplemented with Natural Humic Compounds and Sodium Humate on Performance and Selected Metabolic Variables in Broiler Chickens." Acta Veterinaria Brno. 79. (2010) Web

TAKEAWAY: Broiler chickens fed a diet with added humic substances had more intensive growth and better feed conversion compared to salt-based supplementation.

19. This study looked at 120 Hy Line Brown hens supplemented with humic substances during the first 60 days of their molting stage. The birds were divided into four groups, each with 30 hens. The first and second groups were supplemented with 0.1 and 0.2% HS, respectively. The third group was supplemented with 0.25 mg/kg levamisole hydrochloride. The fourth group received no supplementation. Researchers found that **humic substance supplementation improved egg quality in terms of increased shell thickness and albumin at days 30 and 60 post-molt.**

Sanmiguel, Angélica & Rondon Barragan, Iang. "Supplementation with humic substances in laying hens during molt." CES Veterinary Medicine and Y Zootechnics. 9. 169-178. (2014). Web

TAKEAWAY: Hens supplemented with humic substances had improved egg quality in terms of increased shell thickness and albumin.

20. This study evaluated how humic acids, formed during the breakdown of organic wastes by earthworms (vermicomposting), affected plant growth. Two types of humic substances were used in the study, both extracted from vermicompost from pig manure. One source was humic acid, and the other was humates. They looked at how adding those two compared at different concentrations and with growing different plants. **The incorporation of both types of vermicompost-derived humic acids into either soilless plant growth media increased tomato and cucumber plants' growth significantly in terms of plant heights, leaf areas, shoot and root dry weights.** Plant growth tended to be increased by treatments of the plants with 50-500 mg/kg humic acids but often significantly decreased when the concentrations of humic acids derived in the container medium exceeded 500-1,000 mg/kg.

Atiyeh, R M et al. “The influence of humic acids derived from earthworm-processed organic wastes on plant growth.” Bioresource Technology, vol. 84,1 (2002): 7-14. Web

TAKEAWAY: Humic acids incorporated into either type of soilless plant growth media increased the growth of tomato and cucumber plants significantly in terms of plant heights, leaf areas, shoot, and root dry weights.

Anti-Inflammatory

1. **Fulvic acid can reduce tumor necrosis factor-alpha** (TNF-α) expression after exposure to the endotoxin lipopolysaccharide (LPS) in differentiated human monocytes.

   Junek, R et al. "Bimodal effect of humic acids on the LPS-induced TNF-alpha release from differentiated U937 cells." Phytomedicine: International Journal of Phytotherapy and Phytopharmacology, vol. 16, 5 (2009): 470-6. doi:10.1016/j.] Web

TAKEAWAY: Fulvic acid can reduce tumor necrosis factor-alpha (TNF-α).

2. **Fulvic acid reduced cyclooxygenase 2 (COX2) and prostaglandin E2 (PGE2) secretion** after homocysteine stimulation in primary human monocytes.

   Chien, Shao-Ju et al. "Fulvic acid attenuates homocysteine-induced cyclooxygenase-2 expression in human monocytes." BMC Complementary and Alternative Medicine, vol. 15 61. 13 Mar. 2015, doi:10.1186/s12906-015-0583-x Web

TAKEAWAY: Fulvic acid reduces cyclooxygenase 2 (COX2) and prostaglandin E2 (PGE2) secretion.

3. **Fulvic Acid is shown to reduce** B-hexosaminidase and **histamine release** in immunoglobulin-E-sensitized **mast cells** and basophil cells. Fulvic acid also decreases TNF-α, interleukin-4 (IL-4), and IL-13 from mast cells.

   Yamada P, Isoda H, Han JK, Talorete TP, Abe Y. "Inhibitory effect of fulvic acid extracted from Canadian sphagnum peat on chemical mediator release by RBL-2H3 and KU812 cells." Biosci Biotechnol Biochem., 2007 May; 71(5):1294-305. Web

TAKEAWAY: Fulvic acid reduces histamine release from mast cells.

4. This study looked at how potassium humate derived from brown coal inhibits the activation and/or release of blood products associated with inflammation. **At 40 µg/ml, potassium humate significantly inhibited the release of inflammatory cytokines** TNF-α, IL-1β, IL-6 and IL-10. Complement activation with potassium humate was found to inhibit the activation of both the alternative and classical pathways without affecting red blood cell membrane stability.

   Jansen van Rensburg, C.E., Naude, P.J. "Potassium Humate Inhibits Complement Activation and the Production of Inflammatory Cytokines." In Vitro. Inflammation, 32, 270–276 (2009). https://doi.org/10.1007/s10753-009-9130-6 Web

TAKEAWAY: Potassium humate has anti-inflammatory potential, partially due to the inhibition of pro-inflammatory cytokines.

5. This study found that humic acid inhibited the expression of adhesion molecules from lipopolysaccharide-induced human umbilical vein endothelial cells through the inhibition of nuclear factor-kappa B activation.

   Rung-Jiun Gau et. al. "Humic Acid Suppresses the LPS-Induced Expression of Cell-Surface Adhesion Proteins through the Inhibition of NF-κB Activation." Toxicology and Applied Pharmacology, 166, 59–67 (2000) Web

TAKEAWAY: Humic acid can inhibit the expression of adhesion molecules through inhibiting NF-κB activation. Humic acid may also suppress the immune or inflammatory reaction of HUVECs responsible for endotoxin.

6. This study looked at the anti-inflammatory ability of fulvic acid to act as a ROS scavenger. Fulvic acid was found to decrease $O_2^{\cdot-}$, HOCl, H_2O_2, $OH^{\cdot}$, $ONOO^-$ and $^1O_2$, respectively. **Researchers concluded that fulvic acid could be a good candidate for use in pharmaceutical or food industries as an accessible source of natural antioxidants** and improve food quality by retarding lipid oxidation.

   Noemí Cárdenas Rodríguez et al. "Antioxidant activity of fulvic acid: A living matter-derived bioactive compound." Journal of Food, Agriculture & Environment, Vol.9 (3&4): 123-127. 2011. Web

TAKEAWAY: Fulvic acid could be used in pharmaceutical or food industries as a source of natural antioxidants and for improving food quality by retarding lipid oxidation.

7. In this rat study, researchers evaluated how taking fulvic acid would help prevent heart damage and decrease inflammation in a chemically induced heart attack. They gave rats isoprenaline for two days, which "induces morphological and functional alterations in the heart leading to myocardial necrosis. It also produces excessive production of free radicals resulting from oxidative metabolism of catecholamines." Before giving the rats isoprenaline, they gave some of the rats 100mg/kg, 200mg/kg, or 300mg/kg of fulvic acid for 28 days. They found that the higher the dose of fulvic acid, the less adverse effects of the isoprenaline. **The rats treated with 300mg/kg of fulvic significantly restored Malondialdehyde, Glutathione Reductase, Superoxide Dismutase, and Catalase levels.** "These findings are again correlated with biochemical, hemodynamic, and electrocardiographic modification by different doses of **fulvic acid, which further assure its ability as a potential cardioprotective agent**."

   T. S. Shikalgar & N. S. Naikwade. "Evaluation of Cardioprotective Activity of Fulvic Acid Against Isoproterenol Induced Oxidative Damage in Rat Myocardium." Int. Res. J. Pharm. 2018, 9(1), Web

TAKEAWAY: Rats treated with fulvic acid significantly restored Malondialdehyde, Glutathione Reductase, Superoxide Dismutase, and Catalase levels. These findings further assure its ability as a potential cardioprotective agent.

8. These studies demonstrate that the interaction of humic acid with plants activates antioxidative enzymatic function, thus controlling the ROS content and modifying genes encoding rice tonoplast intrinsic proteins expression, thus improving the growth of the rice plants.

   Andrés Calderín García et al. "Vermicompost humic acids as an ecological pathway to protect rice plants against oxidative stress." Ecological Engineering, Volume 47, October 2012, 203-208. Web

TAKEAWAY: Humic acid provides plants with antioxidants, protecting against ROS and oxidative stress.

9. This study evaluated the safety and anti-inflammatory and wound-healing characteristics of fulvic acid in rats. **Topically-applied fulvic acid at pH 1.98 effectively enhanced the healing rate of wounds infected with *Staphylococcus aureus*.** Fulvic acid topically also inhibits carrageenan-induced inflammation in rats, similarly to indomethacin but with no systemic toxicity. Researchers concluded that **fulvic acid is a safe compound with anti-inflammatory and wound-healing properties** and merits further evaluation in treating patients suffering from similar conditions.

   Riaz Sabi, Pieter Vrey, and Constance E. Jansen van Rensburg. "Carbohydrate-Derived Fulvic Acid (CHD-FA) Inhibits Carrageenan-Induced Inflammation and Enhances Wound Healing: Efficacy and Toxicity Study in Rats." Drugs Development Research, 73: 18–23 (2012). Web

TAKEAWAY: Fulvic acid applied topically enhances wound healing and provides anti-inflammatory benefits.

Arthritis

1. When this study looked at osteoarthritis after 21 days, histopathologic scores of destructive damages and synovitis were reduced in the shilajit group and showed a significant difference compared to the control group. The present study shows that **aqueous extract of shilajit decreased degenerative cartilage changes in knee osteoarthritis**. Also, it **reduced inflammatory reactions in the synovial membrane**.

   Azizi, S., Kheirandiah, R., Azari, O. et al. "Potential pharmaceutic effect of Shilajit (mumie) on experimental osteoarthritis in rat." Comp Clin Pathol, 27, 755–764 (2018). Web

TAKEAWAY: Shilajit decreased degenerative cartilage changes and reduced inflammatory reactions in the synovial membrane in knee osteoarthritis.

2. This study aimed to establish potassium humate's safety and efficacy in a pilot study in patients suffering from knee osteoarthritis. "Screening included clinical assessment, radiographic assessment, laboratory tests and the disease-specific questionnaire, WOMAC™ (Western Ontario and McMaster Universities Osteoarthritis Index questionnaire), and the RAND 36-Item Health Survey." The study monitored blood and biochemical markers, and all stayed within normal ranges. **The potassium humate lowered inflammation markers, including lower CRP levels. Those who were in the potassium humate group all had lower WOMAC scores for pain levels.**

   Van Rensburg, Constance et al. "Potassium Humate Reduces Inflammation and Clinically Improves the Outcomes of Patients with Osteoarthritis of the Knee." The Open Conference Proceedings Journal. 1. (2010). 69-74. 10.2174/2210289201001010069. Web

TAKEAWAY: Potassium humate lowered pain, reduced inflammation, and improved clinical outcome in patients with knee osteoarthritis.

Brain

1. This study found that fulvic acid strongly interferes with tau aggregation, and interestingly an increase in neurites outgrowth has been observed in neural cell cultures. It **shows that fulvic acid has potential protective activity cognitive impairment that can come from Alzheimer's disease.**

   Guzmán-Martinez, Leonardo et al. "Tau oligomers as potential targets for Alzheimer's diagnosis and novel drugs." Frontiers in Neurology, vol. 4 167. 28 Oct. 2013, Web

TAKEAWAY: Fulvic acid prevents tau aggregation. In this context, fulvic acid provides potential protective activity in cognitive impairment from Alzheimer's disease.

2. This study provides evidence showing that **the aggregation process of tau protein, which forms paired helical filaments in vitro, is inhibited by fulvic acid,** affecting the length of fibrils and their morphology. Additionally, **fulvic acid can disassemble pre-formed paired helical filaments**. Fulvic acid is an active compound against pre-formed fibrils, affecting the whole structure by diminishing the length of paired helical filaments and probably acting at the hydrophobic level. Thus, fulvic acid is likely to provide new insights into developing potential treatments for Alzheimer's disease.

   Cornejo, Alberto et al. "Fulvic acid inhibits aggregation and promotes disassembly of tau fibrils associated with Alzheimer's disease." Journal of Alzheimer's Disease: JAD, vol. 27,1 (2011): 143-53. Web

TAKEAWAY: Fulvic acid inhibits tau protein aggregation, likely providing new insights and potential for developing Alzheimer's disease treatments.

Cancer

1. "Humic acid 100 g/mL had a cytotoxic effect on human breast adenocarcinoma MCF-7 cell line at both 24 and 48 h. The effective dose of humic acid simultaneously (24 and 48 h) was 50 µg/mL. The results of this study shed light on the development of alternative therapeutic approaches in the **treatment of cancer by evaluating the cytotoxic effect of humic acid**."

   Aykac, A. et al. "The Cytotoxic Effects of Humic Acid on Human Breast Cancer Cells." Proceedings, 2018, 2, 1565. Web

TAKEAWAY: Humic acid had a cytotoxic effect on human breast adenocarcinoma MCF-7 cell line, which may lead to alternative therapeutic approaches in treatment.

2. This study aimed to evaluate how fulvic acid affects apoptosis in liver cells. It was found that **fulvic-acid significantly upregulated the apoptotic genes at mRNA levels** compared to the non-treated control group.

   Aydin, S et al. "Effects of Fulvic Acid on Different Cancer Cell Lines." Proceedings, 2017, 1, 1031. Web

TAKEAWAY: Fulvic acid inhibited the proliferation of the liver cancer cell lines (Hep3B, HT29, and PC3) used in this study, with Hep3B cells being most sensitive. Additionally, fulvic acid significantly upregulated the apoptotic genes at mRNA levels.

3. A high serum resistin level has recently been found in patients with numerous cancers, including colorectal cancer. Hence, resistin may play a role in colorectal cancer development. Co-treating cells with both fulvic acid and resistin revealed that fulvic acid significantly attenuated the resistin-increased NF- B activation and ICAM-1/VCAM-1 expression and the consequent adhesion of HCT-116 cells to human umbilical vein endothelial cells (HUVECs). These results demonstrate the role of resistin in promoting HCT-116 cell adhesion to HUVECs and **indicate that fulvic acid might be a potential candidate for inhibiting the endothelial adhesion of colorectal cancer in response to resistin.**

   Huang, W.-S et al. "Fulvic Acid Attenuates Resistin-Induced Adhesion of HCT-116 Colorectal Cancer Cells to Endothelial Cells." Int. J. Mol. Sci., 2015, 16, 29370-29382. Web

TAKEAWAY: Fulvic acid might be a potential candidate for inhibiting endothelial adhesion of colorectal cancer in response to resistin (resistin increases the adhesion of this endothelial adhesion).

4. This study showed that fulvic acid has anti-cancer properties by increasing apoptosis and nitric acid and reactive oxygen species production. There was a significant decrease in the colony formation, confirming the anti-proliferative property of the fulvic acid. The TUNEL assay and DNA fragmentation assay showed increased DNA damage and apoptosis from increasing the concentration of fulvic acid. **The study demonstrated that fulvic acid might be useful in liver cancer and related disorders.**

   Kishor Pant et al. "Anti-Proliferative and Anticancer Properties of Fulvic Acid on Hepatic Cancer Cells." Journal of Clinical and Experimental Hepatology, Volume 5, Supplement 2, June 2015, Page S2. Web

TAKEAWAY: Fulvic acid has anti-cancer properties — it increases apoptosis via the production of nitric acid and ROS. Fulvic acid also demonstrated anti-proliferative, apoptotic, and DNA-damaging properties. The study indicates that fulvic acid may be useful in liver cancer and related disorders.

5. Fulvic acid augmented MCA-102 fibrosarcoma cell apoptosis. However, a nitric oxide (NO) inhibitor NG-monomethyl-L-arginine (NMMA) slightly inhibited the fulvic acid-mediated MCA-102 fibrosarcoma cell apoptosis, which was accompanied by low levels of NO. In the present study, we found that fulvic acid induces NO and iNOS generation in RAW 264.7 cells by inducing NF-κB activation. However, NO did not significantly stimulate MCA-102 fibrosarcoma cell apoptosis in the current study. Additionally, fulvic acid enhanced cell death in various human cancer cells such as Hep3B, LNCaP, and HL60. Taken together, **fulvic acid most likely stimulates immune-modulating molecules such as NO and induces cancer cell apoptosis.**

   Jayasooriya, Rajapaksha Gedara Prasad Tharanga et al. "Fulvic acid promotes extracellular anti-cancer mediators from RAW 264.7 cells, causing cancer cell death in vitro." International Immunopharmacology, vol. 36 (2016): 241-248. Web

TAKEAWAY: Fulvic acid most likely stimulates immune-modulating molecules, such as NO, and induces cancer cell apoptosis.

6. Humic acid was studied to see if it stimulated apoptosis of cultured human promyelocytic leukemia HL-60 cells. The data showed that humic acid stimulated apoptosis in HL-60 cells, mainly associated with cytochrome C release from the mitochondria. The apoptosis in the HL-60 cells was accompanied by caspase-3 activation and the specific proteolytic cleavage of poly (ADP-ribose) polymerase (PARP), a significant component of the apoptotic cell death mechanism. **Researchers concluded that humic acid has antiproliferative action and growth inhibition on HL-60 cells through induction of apoptosis**, which may have anti-cancer properties, making it potentially useful for the development of future treatments.

   Yang, Hsin-Ling et al. "Humic acid induces apoptosis in human promyelocytic leukemia HL-60 cells." Life Sciences, vol. 75,15 (2004): 1817-31. doi:10.1016/j.lfs.2004.02.033 Web

TAKEAWAY: Humic acid exerts antiproliferative action and growth inhibition on HL-60 (human promyelocytic leukemia) cells through apoptosis induction — this may have anti-cancer properties that are potentially useful for developing new leukemia drugs and treatments.

Detoxification

1. It has been widely shown that humic acid can effectively interact with pesticides, through sorption or covalent bond formation, and thus affect their mobility and transformation in soil and sediments.

   Chianese, Simeone & Fenti, Angelo & Iovino, Pasquale & Musmarra, Dino & Salvestrini, Stefano "Sorption of Organic Pollutants by Humic Acids: A Review." Molecules (Basel, Switzerland). 25. 10.3390/molecules25040918. (2020). Web

TAKEAWAY: Humic acids show a strong ability to sorb or covalently bond pesticides.

2. This study looked at how **water-soluble pesticides were bound by humic acid**. Interactions may include hydrogen bonding and dipole-dipole interaction, meaning that the positive end of a polar molecule will attract the other molecule's negative end, influencing its position.

   Azadeh Shirzadi et al. "Application of Saturation Transfer Double Difference NMR to Elucidate the Mechanistic Interactions of Pesticides with Humic Acid." Environmental Science & Technology, 2008, 42 (4), 1084-1090. Web

TAKEAWAY: Humic acids can bind water-soluble pesticides.

3. This study indicates that dietary humic substances may improve pigs' growth performance and reduce ammonia emissions from manure.

   F. Ji, J. J. McGlone and S. W. Kim. "Effects of dietary humic substances on pig growth performance, carcass characteristics, and ammonia emission." J. Anim. Sci. 2006. 84:2482–2490. Web

TAKEAWAY: Humic substances fed to pigs may improve growth performance and reduce ammonia emissions in their manure.

4. In this study, researchers looked at toxic chromium forms (which are the oxidized forms Cr2O7(2-) or CrO4(2-) and how they bind to humic acid. These forms are carcinogenic, damaging the kidneys, liver, and blood cells. In the environment, it is a contaminant widely found in groundwater and soil, caused by various industries, including electroplating, chrome tannery processing, wood preserving, and pigment production. Thermodynamic analysis showed that multi-intermolecular forces, including hydrogen bonding, hydrophobic, and electrostatic forces, were involved in the binding process at pH 6.5. The spectral data also indicated that Cr2O7(2-) affected the aromatic ring structures in humic acid. Furthermore, the molecular modeling analysis revealed that a lot of reactive groups and binding cavities in humic acid play a key role in its binding with Cr2O7(2-). This shows that humic acid is a viable way to bind the toxic forms of chromium from the body and environment.

   Gu, Y.-L. et al. "Study on the binding interaction of chromium(VI) with humic acid using UV–vis, fluorescence spectroscopy and molecular modeling." Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy, 136, 1702–1709. (2015). Web

TAKEAWAY: Humic acid binds toxic forms of chromium in the body and the environment.

5. This study looked at wheat treated with chromium — one group was treated with fulvic acid and chromium. The results showed that when the wheat was harvested after four months of growing, the fulvic acid group had increased plant biomass, photosynthetic pigments, and antioxidant enzymes. Chromium uptake decreased in fulvic acid-treated plants, and it showed accumulation in plant chromium treatments alone. The use of **fulvic acid as a soil amendment is a viable way to decrease metal concentration in plants**.

   Ali, S., Bharwana, S.A., Rizwan, M. et al. "Fulvic acid mediates chromium (Cr) tolerance in wheat (Triticum aestivum L.) through lowering of Cr uptake and improved antioxidant defense system." Environ Sci Pollut Res, 22, 10601–10609 (2015). Web

TAKEAWAY: Fulvic acid added to soil decreases metal concentrations in plants.

6. This study looked at two separate sources and two concentrations of fulvic acid and how they prevent absorption of lead in Vicia faba plants. It was found that the higher the concentration of fulvic acid was better at decreasing lead absorption in the Vicia faba plants, showing that **fulvic acid works well at binding lead to prevent absorption**.

   Shahid, M., Dumat, C., Silvestre, J., & Pinelli, E. "Effect of fulvic acids on lead-induced oxidative stress to metal sensitive Vicia faba L. plant." Biology and Fertility of Soils, 48(6), 689–697. (2012). Web

TAKEAWAY: Fulvic acid binds to lead and prevents its absorption by plants.

7. This study looked at how humic acid affected bacterial diversity in animals fed a diet of glyphosate sprayed grains or drank water with glyphosate residues in it. The author's summarized: "supplementation of humic acids in feed not only substantially reduces mycotoxicosis and improves the performance, carcass, gastrointestinal tract, and meat quality traits, but also neutralizes the antimicrobial effect of glyphosate and reduces its accumulation in animal products. Moreover, the use of humic acids in environmental clean-up also serves to promote microbial diversity in ecosystems."

   Shehata, A. A., Et al. "Neutralization of the antimicrobial effect of glyphosate by humic acid in vitro." Chemosphere, vol. 104, June 2014, 258-261. Web

TAKEAWAY: Humic acid neutralizes the antimicrobial effect of glyphosate and reduces mycotoxicosis and glyphosate accumulation in animal products.

8. This study looked at glyphosate residue in different broiler chickens' organs to study the possibility of its neutralization using humic acid. Researchers found that **humic acid-supplemented feed led to a significant decrease in glyphosate content** — by 53% in the liver, 28% in the spleen, 44% in the lung, 50% in the gastrointestinal tract, 16% in the heart, and 63% in muscles in a compared to control group. Researchers conclude that it "will help to overcome the negative effect of glyphosate residues on gastrointestinal microbiota and protect consumers from glyphosate residues in chicken meat."

   Awad A. Shehata, et al. "Distribution of Glyphosate in Chicken Organs and its Reduction by Humic Acid Supplementation." J. Poult. Sci., 51: 333-337, 2014 Web

TAKEAWAY: Humic acid added to feed decreases glyphosate content in chickens' bodies, protecting against glyphosate poisoning and microbiome disruption in consumers of those chickens.

9. This study looked at the effects of humic acids on the acute toxicities of organophosphate pesticide chlorpyrifos (CPF) and organochlorine pesticide 4,4-dichlorodiphenyltrichloroethane (DDT). They were assessed using freshwater (*Cerio-daphnia dubia*) and saltwater crustaceans (*Americamysis bahia*). Due to the salinity of saltwater affecting the binding of pesticides to humic acid, there was not much of a mortality rate improvement in the saltwater crustaceans. However, it was found that **as the humic acid concentrations increased, toxicity levels of pesticides decreased, and mortality rates decreased in freshwater crustaceans.**

   Laurent, C. ME´Zin, and Robert C. Hale. "Effect of Humic Acids onToxicity of DDT and CHlorpyrifos to fFreshwater and Estuarine Invertebrate." Environmental Toxicology and Chemistry, Vol. 23, No. 3, pp. 583–590, 2004 Web

TAKEAWAY: Humic acid decreases the toxicity levels of pesticides, and, therefore, the mortality rate in freshwater crustaceans.

10. This study looked at how humic acid binds to xenobiotics in soil and if microbes in the soil cause a breakdown of humic acid and a release of xenobiotics back into the soil. **They found that most xenobiotics in the study were covalently bound to the humic acid,** and only a small amount that was not covalently bound was very slowly released from the microbial activity. However, these were able to be mineralized or reincorporated back into humus and did not pose any harm to the soil.

    Jean-Marc Bollag. "Decontaminating soil with enzymes." Environ. Sci. Technol. 1992, 26, 10, 1876–1881. Web

TAKEAWAY: Humic acid covalently bonds xenobiotics in the soil, rendering them harmless.

11. The article looked at glyphosate's binding ability with humic and fulvic acid in both sandy soil and clay soil. After 80 days, 40% of glyphosate was bound to humic and fulvic acid in sandy soil vs. clay soil — only 10% of glyphosate was bound. The researchers said absorption of glyphosate was lower in clay soil because the humic and fulvic acids became attached to the metal ions and other clay particles in clay soil. Additional observations were that **humic acid and fulvic acids bound to glyphosate better at lower pH vs. higher pH.**

    Christian N. Albers et al. "The influence of organic matter on sorption and fate of glyphosate in soil – Comparing different soils and humic substances." Environmental Pollution, Volume 157, Issue 10, October 2009, 2865-2870. Web

TAKEAWAY: Humic and fulvic acids effectively bind glyphosate in soil, and this binding ability improves at lower pH vs. higher pH.

12. This study looked at the uptake and elimination of perfluorooctane sulfonate (PFOS) in carp that were given fulvic acid or not given fulvic acid (the control group). When the tissue was analyzed, the **fulvic acid group had much less accumulation of PFOS than the control**.

    Liwen Qiang et al. "Facilitated bioaccumulation of perfluorooctane sulfonate in common carp (Cyprinus carpio) by graphene oxide and remission mechanism of fulvic acid." Environ Sci Technol. 2016 Nov 1; 50(21):11627-11636. Web

TAKEAWAY: Humic and fulvic acids help effectively bind PFOS in soil, and this binding ability improves at lower pH vs. higher pH.

13. This study aimed to look at the effects of pH and metal and humic substances ratio on humic substances complexing capacity and the stability and solubility of metal humic substances complexes in solution. They used four humic substances with different properties and studied their interaction with Cu(II), Zn(II), and Fe(II) at different pH and metal humic substances ratios. The selected humic substances were a humic acid and a whole humic extract (containing the humic and fulvic acids) extracted from black peat, and a fulvic acid and a whole humic extract extracted from a compost of grape solid wastes. This study looked at different types of humic substances with different molecular weights, binding functional groups, and pH effect on solubility and stability of how well or how poorly metals with humic substances are absorbed by plants. This study found that the order of solubility was Zn–HS > Fe–HS > Cu–HS. They found that the order of solubility is inversely related to the order of stability described above, at least in the case of the unfractionated humic substances studied. The solubility of the various metal and humic substance complexes increased in line with a more basic pH. The lower the humic substance's molecular weight, the higher the solubility, and therefore, metal-humic substances are more stable at lower pH and higher molecular weight.

    Jose M. Garcia-Mina. "Stability, solubility and maximum metal binding capacity in metal–humic complexes involving humic substances extracted from peat and organic compost." Organic Geochemistry, 37, (2006). 1960–1972 Web

TAKEAWAY: The solubility of the different metal and humic substances complexes increased in a more basic pH. Lower molecular weight humic substances have high solubility. Therefore, metal-humic substances are more stable at lower pH and higher molecular weight.

14. This study looked at how the pH of fulvic and humic acid played a role in how well they could bind onto radioactive cobalt 60. They found that **both fulvic and humic acid bind better to cobalt 60 when the pH is lower vs. higher pH**.

    Lipeng Zhang et al. "Impact of environmental conditions on the sorption behavior of 60Co(II) on illite." Journal of Radioanalytical and Nuclear Chemistry, vol. 295, pages 1473–1485, (2013) Web

TAKEAWAY: Both fulvic and humic acid bind better to cobalt 60 at lower pH.

15. This study looked at the adsorption of cadmium and copper ions on bare γ-Al^2O_3 particles and γ-Al^2O_3 particles pre-equilibrated with humic acid, ι-carrageenan, or polyacrylic acid (PAA) in 0.55M NaCl solution (similar to natural seawater). The adsorption of those organic substances on alumina particles was studied simultaneously. Researchers found that the interaction of copper ions with alumina particles was enhanced in the presence of humic acid A and was not significantly changed in the presence of PAA or ι-carrageenan compared to the interaction with the bare alumina surface.

    Marta Plavsˇic´, Bozˇena Cosovic´. "Voltammetric study of the role of organic acids on the sorption of Cd and Cu ions by alumina particles." Colloids and Surfaces Physicochemical and Engineering Aspects, 151(1-2), June 1999, 189–20. Web

TAKEAWAY: The interaction of copper ions with alumina particles was enhanced in the presence of humic acid A and was not significantly changed in the presence of PAA or ι-carrageenan.

16. Fulvic acid promoted Cu (II) absorption in concentrations greater than 5 mg C/L, and its promotive ability was more significant at lower pH. The effect of fulvic acid on Pb (II) sorption was similar to that of Cu (II). So at **higher concentrations and lower pH, fulvic acid could better absorb CU (II) and PB (II).**

    Hsin, wu et al. "Effect of fulvic acid on the sorption of Cu and Pb onto gamma-Al2O3." Water Research. 37 (2003). 743-52. Web

TAKEAWAY: Fulvic acid absorbs CU (II) and PB (II) better at higher concentrations and lower pH.

17. This study found that humic acid combined with silicon dioxide had a 10x higher binding ability with heavy metals Pb^{2+}, Cd^{2+}, Cu^{2+}, Zn^{2+}, and Mg^{2+} (from an aqueous solution), compared to unmodified silica. This demonstrates that **humic acid helped to improve the binding capability of silica to heavy metals**.

Panagiota Stathi, Yiannis Deligiannakis. "Humic acid-inspired hybrid materials as heavy metal absorbents." Journal of Colloid and Interface Science, 351 (2010) 239–247. Web.

TAKEAWAY: When silica is combined with humic acid, its ability to bind with heavy metals improves.

18. Soil-derived fulvic acid (SFA) increases Ni^{II} sorption at lower pH and decreases sorption at higher pH.

Strathmann, T. J., & Myneni, S. C. B. "Effect of Soil Fulvic Acid on Nickel(II) Sorption and Bonding at the Aqueous-Boehmite (γ-AlOOH) Interface." Environmental Science & Technology, 39(11), (2005). 4027–4034. Web

TAKEAWAY: Fulvic acid increases nickel(II) sorption and bonding, raising it at lower pH and decreasing it at higher pH.

19. In this study, polyaniline (PANI), a widely studied conducting polymer useful as a heavy metal binder, was combined with humic acid to see how it was able to bind mercury and chromium from water. Various factors affecting uptake behavior, such as aqueous pH, adsorbent concentration, ionic strength, and competing anions, were also studied. **It was found that the combination of PANI and humic acid was much more effective at binding mercury and chromium than PANI alone. It was concluded to be a viable solution for binding heavy metals from various waters.**

Li, Q., Sun et al. "Characteristics of equilibrium, kinetics studies for adsorption of Hg(II) and Cr(VI) by polyaniline/humic acid composite." Desalination, 266(1-3), (2011) 188–194. Web

TAKEAWAY: Polyaniline (PANI) combined with humic acid is much more effective at binding mercury and chromium, demonstrating the combination is a viable solution for binding heavy metals in water.

20. Scientists found that when three different tropical organisms swam in water with fulvic acid, their aluminum toxicity levels were up to six times lower than control groups.

Trenfield, Melanie A et al. "Dissolved organic carbon reduces the toxicity of aluminum to three tropical freshwater organisms." Environmental Toxicology and Chemistry, vol. 31,2 (2012): 427-36. doi:10.1002/etc.1704 Web

TAKEAWAY: When three different tropical organisms swam in water with added fulvic acid, aluminum toxicity levels in those organisms were up to six times lower.

21. This study looked at three different types of humic substances' ability to reduce cadmium and zinc's toxic effects on the green alga *Pseudokirchneriella subcapitata*. Two sources of humic acids from soil and peat significantly reduced cadmium and zinc's toxic effects on the green alga. The source coming from Suwannee River fulvic acids was found not to have the same binding capabilities as the other humic acid sources did at lowering cadmium and zinc. **This shows that the source of humic substances matters, pH matters, and other environmental differences can play a part in how effective humic substances are at binding heavy metals.**

Brahim Koukal et al. "Influence of humic substances on the toxic effects of cadmium and zinc to the green alga Pseudokirchneriella subcapitata." Chemosphere, Volume 53, Issue 8, December 2003, Pages 953-961. Web

TAKEAWAY: Regarding how effective humic substances are at binding heavy metals — the source of humic substances matters, the pH matters, and other environmental differences can play a part.

22. Humic substances — due to their polyelectrolyte nature — interact substantially with and commonly adsorb human-made organic chemicals. Additionally, the ascertained presence of a great variety of chemically reactive functional groups in the molecular structure of humic substances renders them able to chemically bind various organic compounds, including pesticides, petrol (gasoline), plastic derivatives, surfactants, and detergents. Due to their functional groups and hydrophilic and hydrophobic sites, fulvic acid (FA) and humic acid (HA) fractions of humic substances may interact with toxic organic chemicals by various physical and chemical mechanisms, including adsorption, partitioning, solubilization, hydrolysis, photosensitization, and others. In particular; chemical bonds of various strength and stability are suggested to form between humic substances and toxic organic chemicals, ranging from weak, partially reversible, physical associations to strong, irreversible covalent bonds. All these processes will have evident implications in the fate of toxic organic chemicals in the environment, affecting their degradation and detoxification processes, residue persistence and monitoring, mobilization and transport phenomena, phytotoxicity and bioavailability in soils, waters, and sediments, and bioaccumulation in organisms. **Humic acid and fulvic acid may interact with pesticides, petrol (gasoline), plastic derivatives, surfactants, and detergents in several modes, including adsorption, partitioning and solubilization, catalysis in hydrolysis and dealkylation, and photosensitization.**

Senesi, N., & Chen, Y. "Interactions of Toxic Organic Chemicals with Humic Substances." Toxic Organic Chemicals in Porous Media, (1989). 37–90. doi:10.1007/978-3-642-74468-6_3 Web

TAKEAWAY: Fulvic and humic acid fractions of humic substances may interact with toxic organic chemicals (pesticides, petrol (gasoline), plastic derivatives, surfactants, and detergents) by various mechanisms, including adsorption, partitioning and solubilization, catalysis in hydrolysis and dealkylation, and photosensitization.

23. This study looked at DDT adsorption in marine sediment, clay, and humic acid suspended in seawater. Humic acid was found to have a greater adsorbing capacity than clay or sediment. Removal of the humic fraction from sediment reduced the adsorption capacity to less than 60% of the original sediment sample. **It was concluded that suspended humic acids may be important agents that could adsorb pollutants like DDT before reaching the marine environment.**

    Richard H. Pierce Jr., Charles E.Olney, George T. Felbeck Jr. "pp'-DDT adsorption to suspended particulate matter in sea water." Geochimica et Cosmochimica Acta, Volume 38, Issue 7, July 1974, Pages 1061-1073 Web

TAKEAWAY: Humic acid in sediment may play an important role in absorbing pollutants like DDT before reaching the marine environment.

24. A greenhouse experiment was conducted to evaluate the effects of humic acid on corn receiving 0 to 50 mg kg−1 aluminum and 0 to 350 mg kg−1 humic acid. Plants given 50 units of aluminum showed aluminum toxicity symptoms, chlorosis, and necrosis. **Researchers found that the higher the concentration of humic acid added to the aluminum treated plants, and the more the aluminum was chelated by the humic acid, the healthier the corn was.** Another observation was that the less the aluminum reacted with phosphorus, the less insoluble the aluminum phosphate formed was, making the corn healthier.

    Tan K. H.; Binger, A. "Effect of Humic Acid on Aluminum Toxicity in Corn." Soil Science: January 1986, p. 20-25. Web

TAKEAWAY: The higher the concentration of humic acid added to aluminum-treated plants, the more the aluminum was chelated by the humic acid, and the healthier the plant was.

25. Plants were harvested after four months of treatment with or without fulvic acid. The wheat treated with fulvic acid showed increased plant biomass, photosynthetic pigments, and antioxidant enzymes. Simultaneously, it decreased chromium uptake and accumulation in plants compared to the control only treated with chromium. **Researchers concluded that adding the fulvic acid contributed to decreased chromium levels in wheat plants and could be used as an amendment when aiming for decreased metal concentration in plants.**

    Shafaqat Ali et al. "Fulvic acid mediates chromium (Cr) tolerance in wheat (Triticum aestivum L.) through lowering of Cr uptake and improved antioxidant defense system." Environmental Science and Pollution Research, 22(14), 10601–10609.doi:10.1007/s11356-015-4271-7 Web

TAKEAWAY: Adding fulvic acid to wheat plants contributed to lower chromium levels and improved antioxidant defense, concluding that fulvic acid could be added to decrease metal concentration in plants.

26. This study looked at how fulvic acid in the karst aquifer helped to support the microbes in the soil to speed up the breakdown of sulfates and nitrates in groundwater. The researchers found that the fulvic **acid acts as an electron donor** for sulfate-reducing microorganisms and denitrifiers in the porous rock matrix in the soil, helping to speed up the breakdown.

F. Einsiedl et al. "Rapid biotic molecular transformation of fulvic acids in a karst aquifer." Geochimica et Cosmochimica Acta, 71 (2007) 5474–5482, Web

TAKEAWAY: Adding fulvic acid to wheat plants contributed to lower chromium levels and improved antioxidant defense, concluding that fulvic acid could be added to decrease metal concentration in plants. Fulvic acid acts as an electron donor for microbes.

27. This study found that using humic acid had positive effects on chelating lead and had many antioxidant properties, which had lower side effects than other heavy metal chelators.

Klára Krempaská, Ladislav Vaško, Janka Vašková. "Humic Acids as Therapeutic Compounds in Lead Intoxication." *Curr Clin Pharmacol*. 2016;11(3):159-167. doi: 10.2174/1574884711666160813233225. Web

TAKEAWAY: Humic acid chelates lead, has antioxidant properties, and has less side effects than other heavy metal chelators.

28. This study looked at humic acid from manure compost, and humic acid from peat that had acid soil of 3.4 pH added or alkaline soil of 7.7 pH added. It looked at how the different soils could bind to heavy metals (lead, iron, zinc, and copper) in the soil and how it could hold on to the heavy metals. **They found that the soils treated with humic acid were 95% resistant to microbial breakdown and heavy metals' mobilization. This means that the humic acid formed stable binding to heavy metals.** The acidic soil bound zinc and iron tighter than the more alkaline soil. Copper and iron availability increased in the more acidic humic acid soil due to the soluble organic matter's complexation. The more alkaline soil only showed a slight increase in the release of zinc, lead, and copper availability.

Rafael Clemente, M. Pilar Bernal. "Fractionation of heavy metals and distribution of organic carbon in two contaminated soils amended with humic acids." Chemosphere, 64 (2006) 1264–1273 Web

TAKEAWAY: Humic acid-treated soils were 95% resistant to microbial breakdown and mobilization of the heavy metals, meaning that humic acid formed stable binding to the heavy metals. Acidic soil bound zinc and iron tighter than the more alkaline soil.

29. This study found that **humic acid has amphiphilic properties (the ability to be hydrophilic and hydrophobic at the same time)**. **Amphiphilic** ability allows humic acid to be a great binder to a lot of different chemicals and toxins. Researchers found that when it was added to water, there was a "strong association between metal ions and solid humic acid, which makes it possible to use an inexpensive commercial grade for the decontamination of polluted water. **A continuous elution process through a column packed with humic acid allows for the removal of both heavy metals and organic xenobiotics from an aqueous solution.**"

von Wandruszka, R. "Humic acids: Their detergent qualities and potential uses in pollution remediation." Geochem Trans 1, 10 (2000). https://doi.org/10.1186/1467-4866-1-10. Web

TAKEAWAY: Humic acid has amphiphilic properties — it is hydrophilic and hydrophobic at the same time — allowing great binding of a lot of different chemicals and toxins. It removes both heavy metals and organic xenobiotics from an aqueous solution.

30. Researchers found that "**some microorganisms found in soils and sediments can use humic substances as an electron acceptor for the anaerobic oxidation of organic compounds and hydrogen.** This electron transport yields energy to support growth. Microbial humic reduction also enhances the capacity for microorganisms to reduce other, less accessible electron acceptors, such as insoluble Fe(III) oxides, because humic substances can shuttle electrons between the humic-reducing microorganisms and the Fe(III) oxide." The finding that bacteria can donate electrons to humic acids has important implications for the mechanisms by which microorganisms oxidize both natural and contaminant organics in anaerobic soils and sediments. It suggests a biological source of electrons for humic acid helps with the breakdown of heavy metals and other toxins.

Lovley, D., Coates, J., Blunt-Harris, E. et al. "Humic substances as electron acceptors for microbial respiration." Nature, 382, 445–448 (1996). https://doi.org/10.1038/382445a0 Web

TAKEAWAY: Some microbes found in soils and sediments can donate electrons to humic acids (use humic substances as electron acceptors) for the anaerobic oxidation of organic compounds and hydrogen, yielding energy to support growth.

31. This study looks at how humic acids can act as electron shuttles and facilitate biogeochemical cycles, thereby influencing the change of nutrients and environmental pollutants. Researchers investigated how "humic acid-metal (HA-M) complexes (HA-Fe, HA-Cu, and HA-Al) were organized and categorized. The electron shuttle capacities of HA-M complexes were experimentally evaluated through microbial Fe(III) reduction, biocurrent generation, and microbial reduction." **The results show that humic acid's electron shuttle capacities were enhanced after complexation with Fe, but HA-Cu and HA-Al complexes have fewer electrons that can be reversibly transferred compared to humic, so they are not as redox-active.** The extracellular electron transfer activity of the HA-M complexes were in the order HA-Fe > HA-Cu > HA-Al. These findings have important effects on biogeochemical redox processes, given the ubiquitous nature of both HAs and various metals in the environment.

Zhou, Shungui et al. "Influence of Humic Acid Complexation with Metal Ions on Extracellular Electron Transfer Activity." Scientific Reports, vol. 5 17067. 23 Nov. 2015, doi:10.1038/srep17067. Web

TAKEAWAY: Humic acids can act as electron shuttles. These shuttle capabilities were enhanced when complexed with Fe, but less so when humic acids are complexed with Cu and Al.

32. This study compared humic acid and Biochar (a charcoal-like substance made by burning organic material from agricultural and forestry wastes) and how they compare when binding to five different pesticides in soil: 2,4-D, MCPA, metolachlor, carbaryl, and carbofuran. Researchers found that humic acid bound better to 2,4-D, MCPA, and Metolachlor, and Biochar bound better to carbaryl and carbofuran. **Researchers attributed the significant difference in binding abilities to pH. Humic acid is more acid, and Biochar is more alkaline.**

Ćwieląg-Piasecka, I., Medyńska-Juraszek, A., Jerzykiewicz, M. et al. "Humic acid and biochar as specific sorbents of pesticides." J Soils Sediments, 18, 2692–2702 (2018). https://doi.org/10.1007/s11368-018-1976-5 Web

TAKEAWAY: Humic acids compared with a charcoal-like substance: The difference in binding abilities is attributed to pH, with the lower pH humic acid being superior in binding to the more alkaline charcoal-like substance.

33. This study looked at humic acid from four different sources to see which was best at binding to glyphosate. Source one was from peat, source two from volcanic soil, source three from coal, and source four from lignite. This was also found to be the order of best to worse sources of glyphosate binding. Researchers found that the different sources had different properties that made them better or worse glyphosate binders. The bigger the molecular dimensions of humic acid was found to be, the best for binding glyphosate. The smallest molecular dimension had the least ability to bind glyphosate. **Source and size will have different abilities to bind glyphosate.**

A. Piccolo, G. Celano, and P. Conte. "Adsorption of Glyphosate by Humic Substances." J. Agric. Food Chem. 1996, 44, 2442–2446. Web

TAKEAWAY: Bigger molecular dimensions of humic acid are the best for binding glyphosate, and smaller molecular dimensions have the least ability to bind glyphosate. Source and size will have different abilities to bind glyphosate.

34. This review discusses previous and current observations of the interaction between Al^{3+} and river fulvic acid at pH of 4.0, seeing if it binds with an ionic or covalent bond. Researchers found that "binding to soluble river fulvic acids is relatively high, indicating that these stable, biological decay products are important in sequestering and maintaining Al^{3+} ion in the soluble (bio-available) state in natural waters for long periods." This study found that Al^{3+} bound to the river fulvic acid at pH 4.0, and because of the functional binding groups present, it **binds more prominently with ionic bonds than covalent bonds.**

Kelly M Elkins and Donald J Nelson. "Spectroscopic approaches to the study of the interaction of aluminum with humic substances." Coordination Chemistry Reviews, Volume 228, Issue 2, 3 June 2002, 205-225 Web

TAKEAWAY: This study found that Al^{3+} bound to the river fulvic acid at pH 4.0. Because of the functional binding groups present, it binds more prominently with ionic bonds than covalent bonds.

35. This study looked at a synthetic form of polyacrylic acid and natural humic acid from lake sediment. Binding Samarium (Sm) and Europium (Eu) to the synthetic and natural forms of humic acids varied with different molecular sizes and kinetics. In general, the elements bound faster to the synthetic form of humic acid, more than likely because of the homogeneity and monofunctional of its molecular makeup. Researchers found that they bound faster to the small molecular weight structures than the larger weight forms of synthetic and natural humic acid. **Molecular size plays a part in how well certain things are bound to humic acids.**

Clark, S. B., & Choppin, G. R. "A Comparison of the Dissociation Kinetics of Rare Earth Element Complexes with Synthetic Polyelectrolytes and Humic Acid." ACS Symposium Series, Vol. 651 1996, 207–219. doi:10.1021/bk-1996-0651.ch013. Web

TAKEAWAY: Molecular size plays a noteworthy part in how well certain things bind to humic acids.

36. This study looked at humic acid added to aflatoxin-contaminated feed fed to broiler chickens. They found that when humic acid in the form of oxihumate was given to the broiler chickens with the contaminated feed, the humic acid bound to the aflatoxins and neutralized the toxic effects. All performance parameters were improved. Liver weight and aflatoxin residues were a lot less than control, showing that humic acid helps to bind toxins, reduces liver burden, and prevents toxin build-up in the liver. Humic acid groups showed an enhanced humoral immune system, which is typically lowered when exposed to aflatoxins. **In conclusion, adding humic acid to aflatoxin-contaminated chicken feed reduces a lot of the adverse effects and grows healthier chickens.**

Arafat, Rana & Khan, Sohail & Saima. "Evaluation of Humic Acid as an Aflatoxin Binder in Broiler Chickens." Annals of Animal Science. 2016, 17. 10.1515/aoas-2016-0050. Web

TAKEAWAY: Humic acid (as oxihumate) was given to the broiler chickens along with the aflatoxin-contaminated feed. Humic acid bound the aflatoxins and neutralized their toxic effects, improving all the chickens' performance parameters, resulting in healthier chickens.

37. This study looked to find a cost-effective way and ecofriendly way to remove cadmium from soil. They added humic acid to a silty loam, clay loam, and sandy loam. The Clay loam was found to work best with humic acid for cadmium removal. The optimal level of humic substance concentration was found to be (3150 mg C/L), solution pH (6.0), washing time (2 h), and a washing solution/soil ratio. **From this study, researchers concluded that humic acid is "superior to many washing agents in terms of washing effectiveness, safety, benefits to soil, and low cost. Leonardite-derived humic substances have the potential to become the washing agent of choice for the remediation of soils contaminated with Cd and other heavy metals."**

Fande, Meng et al. "Humic substances as a washing agent for Cd-contaminated soils." Chemosphere, Volume 181, August 2017, 461-467 Web

TAKEAWAY: Humic acid is "superior to many washing agents" and has the potential to become the washing agent of choice for the remediation of soils contaminated with Cd and other heavy metals.

38. Fulvic acid and other humic substances can actively participate in oxidation-reduction reactions with transition metal ions and biological systems in terrestrial and aquatic environments. **They can act either as electron donors or electron acceptors, depending on environmental conditions.**

N. Senesi, Y. Chen, M. Schnitzer. "The role of free radicals in the oxidation and reduction of fulvic acid." Soil Biology and Biochemistry, vol. 9, no. 6, 1977. Pages 397-403. Web

TAKEAWAY: Fulvic acid and other humic substances can act either as electron donors or electron acceptors, depending on environmental conditions.

Immune System

1. This study indicated that sheep red blood cells antibodies titer and IgG of pigs fed with probiotic and the fulvic acid + probiotics diets had a more significant response than the control fed pigs. Not only for the lactobacilli, but other strains of probiotic organisms also attenuated the cytokine response. The study results showed that fulvic acid and fulvic acid + probiotics combination groups in performance and immune capacity aspects were better than the antibiotics group. The fulvic acid + probiotics group had better energy, and the ash and phosphorus digestibility were better than the antibiotics group. Thus, **fulvic acid and fulvic acid + probiotics combination show great potential to be antibiotics substitution.**

   Lien, N. "Effects of Fulvic Acid and Probiotic on Growth Performance, Nutrient Digestibility, Blood Parameters and Immunity of Pigs." Journal of Animal Science Advances 2 (2012): 711-721. Web

TAKEAWAY: Fulvic acid combined with probiotics fed to pigs improved their immune capacity, showing potential as a substitute for antibiotics.

2. Soil tested for microbial activity after the addition of 300 ppm humate to it showed a 400 to 5000x increase in microbe activity. Humic acids can inhibit bacterial and fungal growth, thus decreasing levels of mycotoxins in feed. Stress management, immune system, anti-inflammatory activity, antiviral properties, and prevention of intestinal diseases (mainly diarrhea in humans and animals) are described as its beneficial effects.

   K.M.S, Islam & A, Schumacher & Gropp, Jürgen. "Humic Acid Substances in Animal Agriculture." Pakistan Journal of Nutrition. 4. (2005). Web

TAKEAWAY: Humic acid in feed improved gut health for better nutrient use, improved the health status by working against pathogens by developing immunity, and enhanced broilers' growth by increasing protein digestion and trace element utilization.

3. **This study showed that fulvic acid helped decrease the histamine release and allergy response** to beta-hexosaminidase release in human leukemia basophilic (KU812) cells. "Fulvic acid affected the expression of genes that were involved in the following pathways: signal transduction, cytokine–cytokine receptor interaction, immune response, cell adhesion molecules, and IgE receptor beta subunit response."

   Motojima, Hideko et al. "Microarray analysis of immediate-type allergy in KU812 cells in response to fulvic acid." Cytotechnology, vol. 63,2 (2011): 181-90. doi:10.1007/s10616-010-9333-6 Web

TAKEAWAY: Fulvic acid decreased the histamine release and the expression of various genes related to the allergy responses.

4. Oxifulvic acid showed useful antibacterial properties and is effective against various pathologic germs, including *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, and against yeasts like *Candida albicans*. The **antimicrobial properties**, together with its **anti-inflammatory properties**, suggest that oxifulvic acid, applied topically, might be an **effective and safe treatment for skin infections**.

   C. E. J. van Rensburg, A. van Straten, J. Dekker," An in vitro investigation of the antimicrobial activity of oxifulvic acid." Journal of Antimicrobial Chemotherapy, Volume 46, Issue 5, November 2000, 853–854. Web

TAKEAWAY: Oxifulvic acid demonstrated antibacterial properties against Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa, Klebsiella pneumoniae, and yeasts like Candida albicans.

5. This study found that oxihumate inhibited HIV-1 infection of MT-2 cells with an IC(50) of 12.5 µg/ml. Treatment of free and cell-attached HIV with oxihumate irreversibly reduced infectivity, while the susceptibility of target cells to the virus was not impaired by treatment before infection. The HIV particles' infectivity was inhibited by interference with CD4 binding and the V3 loop-mediated step of virus entry. **No viral resistance to oxihumate developed over 12 weeks in vitro. Researchers concluded that oxihumate has potential as a treatment for HIV infected people.**

   van Rensburg, C E J et al. "Investigation of the anti-HIV properties of oxihumate." Chemotherapy, vol. 48, 3 (2002): 138-43. Web

TAKEAWAY: Oxihumate holds promise for the treatment of HIV-infected patients.

6. This study looked at ammonium humate's effectiveness **in treating humate-sensitive viruses like herpes virus type 1 and type 2, influenzae A virus, and Coxsackie-virus A9. Researchers found the herpes viruses and the antiviral activity could be proven in vitro and in vivo.** The explanation — the Phenol body's antiviral properties polymerizates a common structure principle for substances of the humic acid type.

   Klöcking R, Spößig M, Wutzler P, Thiel K-D, Helbig B. "Antiviral wirksame Huminsäuren und huminähnliche Polymere." Z Physiother. 1983; 35:95–101. Web

TAKEAWAY: Ammonium humate showed antiviral activity against herpes viruses in vitro and in vivo.

7. Researchers found that oral administration of humus extract in freshwater fish prevents infection with the fish pathogen *Aeromonas salmonicida*. Fish mortality and development of skin lesions such as hemorrhages and ulcers were significantly suppressed in carp treated with 10%, 5%, or 1% humus extract adsorbed on dry feeding pellets. The median surviving days was also greater in fish treated vs. untreated fish.

Kodama, Hiroshi et al. "Protection against atypical Aeromonas salmonicida infection in carp (Cyprinus carpio L.) by oral administration of humus extract." The Journal of Veterinary Medical Science, vol. 69,4 (2007): 405-8. Web

TAKEAWAY: Humus extract given orally to freshwater fish prevents infection with Aeromonas salmonicida.

8. The benefits of oxihumate on lymphocytes was studied *in vitro* and *ex vivo*. There have been impressive results with **oxihumates regulating lymphocytes from HIV-infected patients.** Researchers found that oxihumates stimulated increased production of IL-2 and improved the expression of the IL-2 receptor. They also found that IL-10 production was stimulated to decrease output. **Researchers in this study concluded that oxihumates show promising benefits for immunocompromised patients.**

Jooné, Gisela Käthe et al. "Investigation of the immunostimulatory properties of oxihumate." Zeitschrift fur Naturforschung. C, Journal of Biosciences, vol. 58,3-4 (2003): 263-7. doi:10.1515/znc-2003-3-421. Web

TAKEAWAY: Oxihumate shows promising benefits for immunocompromised patients.

9. This research looked for broad-spectrum agents that would help protect from viruses. The researchers looked into the anti-viral properties of pomegranate juice and fulvic acid. "Pomegranate juice was previously reported to inactivate HIV and further shown by our group to inactivate influenza, herpesviruses, and poxviruses. A **formulation consisting of fulvic acid, a complex mixture of compounds was previously reported to render vaccinia virus, HIV, and SARS virus non-infectious."** The fulvic acid and pomegranate juice's mechanism of action is thought to block the virus's entry by interacting with the sugar or lipid layer. Or, the surface glycoproteins of enveloped viruses render the virus non-infectious by inhibiting entry into the cells. To test the benefits of fulvic acid further, researchers gave mice intranasally a usually highly lethal dose of influenza A/HK/x31(H3N2 that had been treated with fulvic acid for 5 minutes. **The mice given the fulvic acid-treated virus didn't show any signs of disease**. In contrast, the control group treated with the virus showed excessive weight loss from decreased water consumption and a 75% mortality rate.

Kotwal, Girish J. "Genetic diversity-independent neutralization of pandemic viruses (e.g. HIV), potentially pandemic (e.g. H5N1 strain of influenza) and carcinogenic (e.g. HBV and HCV) viruses and possible agents of bioterrorism (variola) by enveloped virus neutralizing compounds (EVNCs)." Vaccine, vol. 26,24 (2008): 3055-8. Web

TAKEAWAY: A fulvic acid formulation was previously reported to render vaccinia virus, HIV, and SARS virus non-infectious. Mice given a lethal dose of influenza intranasally were treated with fulvic acid for 5 minutes. The mice didn't show any signs of disease, while the control group had a 75% mortality rate.

10. This study found that fulvic acid can activate isolated murine macrophages from the peritoneal cavity. Nitric oxide and reactive oxygen species important for killing bacteria and intracellular signaling increase in fulvic acid-treated peritoneal macrophages.

Igor A. Schepetkin et al. "Characterization and Biological Activities of Humic Substances from Mumie." Journal of Agricultural and Food Chemistry, 2003, 51(18), 5245-5254. Web

TAKEAWAY: Humus extract given orally to freshwater fish prevents infection with Aeromonas salmonicida.

11. This study looked at fulvic acid's impact on the health of a juvenile loach, a type of freshwater fish. It was found that **fulvic acid helped to improve growth performance, intestinal antioxidant ability, and immunity and changed intestinal microflora composition**. Researchers also concluded that fulvic acid could be used as a substitute for antibiotic treatment of the juvenile loach.

Y. Gao, J. He, Z. He et al., "Effects of fulvic acid on growth performance and intestinal health of juvenile loach Paramisgurnus dabryanus (Sauvage)." Fish & Shellfish Immunology, vol. 62, pp. 47–56, 2017. Web

TAKEAWAY: Fulvic acid helped improve growth performance, intestinal antioxidant ability, immunity, and changed intestinal microflora composition in a studied freshwater fish species.

12. Researchers in this study found humic substances led to improved growth, vitality, and faster wound healing of fish. There was also a significant decrease in pathogenic bacteria, fungi, and parasites in the fish. Humic substances led to reduced multifactorial fish diseases, and humic substances **helped to detoxify heavy metals and organic pollutants**.

Meinelt, Thomas et al. "Humic substances." Environmental Science and Pollution Research. 15. 17-22. (2008). Web

TAKEAWAY: Humic substances led to improved growth, better vitality, and faster wound healing of fish. Pathogenic bacteria, fungi, parasites, and multifactorial fish diseases significantly decreased. Humic substances also helped to detoxify heavy metals and organic pollutants.

13. This study found that synthetic humic acid-like polymers that were most effective against herpesvirus 1. Researchers looked at nine different synthetic humic acid-like polymers in this study. Of the nine different types, caffeic acid was found to be the most effective synthetic polymer. Researchers concluded that the caffeic acid polymer's effectiveness for binding viruses was because it has a C=C double bond side chain and a surplus of hydroxylic groups.

B Helbig*, R Klockinq and P Wutzler. "Anti-herpes simplex virus type 1 activity of humic acid-like polymers and their o-diphenolic starting compounds." Antiviral Chemistry & Chemotherapy, 1997 8(3): 265-273. Web

TAKEAWAY: Synthetic humic acid-like polymers inhibit herpes simplex virus type 1 replication and viral activity.

14. This study examined the fungicidal activity of humic acid. It compared humic acid from two different sources, one from an empty fruit bunch of oil palm compost, and the other source was a commercial-grade humic acid. Researchers found that the most effective humic acid source was the empty fruit bunch of oil palm compost humic acid. It inhibited the most mycelial growth and conidial germination of the fungus *C. cucurbitarum* at the highest 1000 mg L-1 of humic acid concentration. **Researchers concluded that the efficacy of humic acid at controlling fungal growth is dependent on the concentration of humic acid, origin of the humic acid, and the structure and properties of the humic acid.**

    Siddiqui, Yasmeen et al. "In vitro Fungicidal Activity of Humic Acid Fraction from Oil Palm Compost." International Journal of Agriculture and Biology. 1560-8530. (2009). Web

TAKEAWAY: Humic acid can be effective at controlling fungal growth, depending on the concentration, origin, and the structure and properties of the humic acid.

15. This study looked at the effect of humic acid and fulvic acid on growth promotion, immune response, and thyroid function of rats. **Based on the results of this study, fulvic and humic acid did not affect weight gain or feed intake of the rats.** They also studied the deviation in the antibody titer against ovalbumin challenge. The conclusion was drawn that **both humic acid and fulvic acid stimulated rats' immune response (250% and 318%**, respectively, over the control value) at 0.4% of supplementation. The spleen saw an increase in the B- dependent areas, which is the marginal lymphoid cell zone. This also indicates that **Humic and fulvic acid are potent humoral immune stimulants**, and they also increase the persistence of antibodies in the system. Humic acid showed no adverse effect on thyroid function. Fulvic acid showed an increase in TSH and lower conversion of T4 to T3, showing a mild hypothyroid effect. The researchers hypothesized that it might be because the form of iodine available for the rats was in a not well-absorbed form and may have affected thyroid hormone levels.

    Vucskits, A. V. et al. "Effect of fulvic and humic acids on performance, immune response and thyroid function in rats." Journal of Animal Physiology and Animal Nutrition, 94(6), 721–728. (2010). Web

TAKEAWAY: Humic acid and fulvic acid stimulated the immune response of rats, are potent humoral immune stimulants, and increase the persistence of antibodies in the system.

16. The data from this study showed that **humic acid could induce apoptosis and inhibited hepatitis B viral-induced autophagosome formation and proliferation in hepatoma cells**.

    Kishor Pant et al. "Humic acid inhibits HBV-induced autophagosome formation and induces apoptosis in HBV-transfected Hep G2 cells." Scientific Reports, volume 6, Article number: 34496 (2016). Web

TAKEAWAY: Humic acid showed anti-viral activity and an inhibitory effect on viral RNA polymerase's endonuclease activity.

17. This research found that oxidative polymer of protocatechuic acid and humic acid inhibit the in vitro replication of influenza virus H1N1 in Madin-Darby canine kidney cells at concentrations of no cytotoxicity. Although these two compounds show structural resemblance, they exhibit different actions of anti-flu. The oxidative polymer of protocatechuic acid inhibitory effect is higher when added at the viral adsorption stage compared with the post-adsorption. It also inhibits hemagglutination and low pH-induced cell-cell fusion. Humic acid shows lower inhibition of hemagglutination and no inhibition on acid-induced cell-cell fusion. **Humic acid exhibits a distinguished inhibitory effect on the endonuclease activity of viral RNA polymerase**. Humic acid showed a plaque reduction assay if added at the stage of adsorption or after the virus entered the host cells.

Lu, F.-J., Tseng, S.-N., Li, M.-L., & Shih, S.-R. "In vitro anti-influenza virus activity of synthetic humate analogues derived from protocatechuic acid." Archives of Virology, 147(2), 273–284. (2002). Web

TAKEAWAY: Humic acid showed anti-influenza virus activity and an inhibitory effect on the endonuclease activity of viral RNA polymerase.

18. In this study, a synthesized humic acid-like compound was made to see how well it affected HIV infectivity. Researchers found that the synthetic humic acid compound could inhibit HIV infectivity by binding V3 loop-specific antibodies and inhibiting viral entry into the cells.

Josef Schneider et al. "Inhibition of HIV-1 in Cell Culture by Synthetic Humate Analogues Derived from Hydroquinone: Mechanism of Inhibition." Virology, Volume 218, Issue 2, 15 April 1996, Pages 389-395. Web

TAKEAWAY: Fulvic and humic acid interfere with HIV infectivity, causing appreciable reductions in virus absorption and recovery efficiencies.

19. This study aimed to evaluate the antifungal activity of fulvic acid against *Candida albicans*. The *Candida albicans* was grown planktonically and as biofilms. **Fulvic acid was shown to be fungicidal, acting through disruption of the cell membrane activity.** Resistance mechanisms, including matrix, efflux, and stress, had a limited role in the fulvic acid activity. So, based on the promising in vitro spectrum of activity and minimal biofilm resistance, fulvic acid shows to be a potential treatment for *Candida albicans*.

Sherry, Leighann et al. "Carbohydrate Derived Fulvic Acid: An in vitro Investigation of a Novel Membrane Active Antiseptic Agent Against Candida albicans Biofilms." Frontiers in Microbiology, vol. 3 116. 29 Mar. 2012, doi:10.3389/fmicb.2012.00116. Web

TAKEAWAY: Fulvic acid showed fungicidal activity, acting through disruption of the cell membrane of Candida albicans.

20. The data gathered in the study showed that **humic acid induced apoptosis and inhibited Hepatitis B Virus** induced autophagosome formation and proliferation in hepatoma cells.

Pant, K., Yadav, A., Gupta, P. et al. "Humic acid inhibits HBV-induced autophagosome formation and induces apoptosis in HBV-transfected Hep G2 cells." Sci Rep, 6, 34496 (2016). https://doi.org/10.1038/srep34496. Web

TAKEAWAY: Humic acid induced apoptosis and inhibited Hepatitis B Virus-induced autophagosome formation and proliferation in hepatoma cells.

Microbiome

1. The goal of the study was to look at the effects of humic acids on innate microbial communities of the colon. 14 people in this study took humic acid for 45 days. Stool samples were taken throughout the study to look at microbiome changes along the way. The sum concentration of colonic microbiota increased from 20% at day 10 to 30% by day 31 and remained stable until day 45 (32%) of humic acid supplementation. The increase in the concentrations in each person was due to growth of preexisting groups. The individual microbial profile of the patients remained unchanged and bacterial diversity remained stable. **Humic acids have a profound effect on a healthy colonic microbiome and may be potentially to control the innate colonic microbiome.**

Swidsinski, Alexander et al. "Impact of humic acids on the colonic microbiome in healthy volunteers." World Journal of Gastroenterology, vol. 23,5 (2017): 885-890. Web

TAKEAWAY: Humic acids have a profound effect on a healthy colonic microbiome and may have potential in controlling the innate colonic microbiome.

Mitochondria

1. Humic acid was shown to stimulate Hþ-ATPase and ion transporter activity in the root plasma membrane. The results showed that the root application of a purified humic acid causes a significant increase in shoot growth that is associated with an enhancement in root H^+-ATPase activity, an increase in nitrate shoot concentration, and a decrease in roots. These effects were associated with significant increases in the shoot concentration in cucumbers.

   Verónica Mora et al. "Action of humic acid on promotion of cucumber shoot growth involves nitrate-related changes associated with the root-to-shoot distribution of cytokinins, polyamines and mineral nutrients." Journal of Plant Physiology, Volume 167, Issue 8, 15 May 2010, Pages 633-642 Web

TAKEAWAY: Humic acid caused a significant increase in shoot growth, an increase in nitrate shoot concentration, and a decrease in roots.

2. Fulvic and humic acids were shown to stimulate cellular respiration in rat liver mitochondria, and also increased the efficiency of the process of oxidative phosphorylation.

   Visser SA. "Effect of humic substances on mitochondrial respiration and oxidative phosphorylation." Sci Total Environ. 1987 Apr; 62:347-54. Web

TAKEAWAY: Fulvic and humic acids stimulated cellular respiration in rat liver mitochondria. They also increased the efficiency of oxidative phosphorylation.

3. In a mouse study, they were forced to swim daily for 7 days and received either the placebo or 30 mg shilajit/kg orally per day for the last 4 days. Swimming caused an 82% decrease in muscle ATP levels, while **shilajit treatment almost doubled the ATP in muscle of mice forced to swim.** Smaller effects of shilajit were observed with respect to ATP in the brain and blood. When mice were treated with a combination of shilajit and CoQ10, muscle ATP levels were 2.44 times higher than untreated animals forced to swim. The primary biochemical function of CoQ10 is to synthesize ATP in the mitochondria. **The results support the contention that shilajit can relieve fatigue and increasing energy and endurance.**

   Stohs, S. J. "Safety and Efficacy of Shilajit (Mumie, Moomiyo)." Phytotherapy Research, 28(4), 475–479. (2013). Web

TAKEAWAY: Shilajit treatment in mice significantly increased muscle ATP levels. Similar, but smaller, effects were observed in the brain and blood. Therefore, shilajit may relieve fatigue and increase energy and endurance.

Other

1. Under conditions of uncontrolled diabetes, with the adverse effects of **hyperglycemia on vascular endothelial cells, it was shown that adding humic water may correct it**. With the use of humic water in this study, they were able to show a significant decrease in inflammatory cytokines, such as TNFα and IL-6, and also lead to the enhancement of cell proliferation.

   Szot, K., Góralczyk, K., Michalska, M. et al. "The effects of humic water on endothelial cells under hyperglycemic conditions: inflammation-associated parameters." Environ Geochem Health, 41, 1577–1582 (2019). Web

TAKEAWAY: Hyperglycemia in diabetes is responsible for endothelium damage and increases surface inflammation of the vascular lining. Humic water, in the proper volume, reduces inflammatory cytokines secreted by endothelial cells, and thus, reduces inflammation. This leads to enhanced cell proliferation. It appears that the adverse effects of hyperglycemia on vascular endothelial cells may be corrected by addition of humic water.

2. **Humic acid was shown to help alleviate the adverse effects of lead toxicity to the thyroid gland tissue and thyroid hormones.** Laying hens fed lead did not have altered triiodothyronine or thyroxine concentrations. However, it caused a 167% increase in thyroid-stimulating hormone concentration. Humic acid supplementation returned the high TSH levels of hens exposed to lead to normal values. The histopathological findings were less severe when humic acid was added to the diet.

   Sahin A et al. "The Effect of Humic Acid Substances on the Thyroid Function and Structure in Lead Poisoning." Rev. Bras. Cienc. Avic., vol.18 no.4 Campinas Oct./Dec. 2016. Web

TAKEAWAY: Humic acid alleviated the adverse effects of lead poisoning on thyroid gland tissue and thyroid hormones.

Skin

1. Oxifulvic acid possesses anti-inflammatory properties and may be of **clinical benefit in the treatment of inflammatory skin conditions in humans**.

   Van Rensburg, C. E. J., Malfeld, S. C. K., & Dekker, J. "Topical application of oxifulvic acid suppresses the cutaneous immune response in mice." Drug Development Research, (2001), 53(1), 29–32. Web

TAKEAWAY: Topically applied oxifulvic acid (coal-derived fulvic acid) has anti-inflammatory properties and may be of clinical benefit in the treatment of human inflammatory skin conditions.

2. High-pressure liquid chromatography (HPLC) analysis revealed that aqueous peat extracts contain up to 18 fractions of water-soluble compounds of fulvic, ulmic, and humic acids. These compounds have been found to have a stimulatory response on the contractile activity of smooth muscles. In vitro diffusion studies showed that the permeability of these substances across human full-thickness skin (thickness: 200 μm^{-1}) is highly selective and the resulting stimulatory activity is dependent on the permeated fraction. **This shows that fulvic and humic acid has great potential to be used in future topical application.**

   Beer, André M et al. "Evaluation of the permeation of peat substances through human skin in vitro." International Journal of Pharmaceutics, vol. 253,1-2 (2003): 169-75. doi:10.1016/s0378-5173(02)00706-8. Web

TAKEAWAY: Fulvic and humic acid is permeable across human full-thickness skin, so has great potential to be used in topical applications.

3. In this rodent study, researchers found that **therapeutic bathing in humic acids extracted from peat resulted in significant reduction of intra-abdominal gynecological adhesions**.

   Mesrogli, M et al. "Erfolgreiche Adhäsionsprophylaxe durch Anwendung von Moor und Huminsäuren [Successful prevention of adhesions using peat and humic acids]." Zentralblatt fur Gynakologie vol. 113,10 (1991): 583-90. Web

TAKEAWAY: Bathing in humic acids resulted in significant reduction of intra-abdominal gynecological adhesions.

4. This study was looking at how humate impacted the structural makeup of collagen. The results suggest that the humate reacts with collagen in vitro and makes it resistant to mechanical and chemical alterations without denaturing them. In vitro incubation with humic substances raises the breaking point of the tail tendon of the rat by about 75%. The chemical resistance of the collagen fibers in tail tendon collagen is also increased by in vitro incubation. **Researchers believe that humates benefits on collagen is because it has numerous phenolic OH-groups, which can raise both the number of stable covalent intermolecular cross-links and, therefore, makes collagen stronger.**

Riede, U.N., Jonas, I., Kirn, B. et al. "Collagen stabilization induced by natural humic substances." Arch Orthop Trauma Surg, 111, 259–264 (1992). https://doi.org/10.1007/BF00571520. Web

TAKEAWAY: Humates shows benefits on collagen because of its numerous phenolic OH-groups, which can raise both the number of stable covalent intermolecular cross-links, strengthening collagen.

5. The goal of this rat study was the evaluation of the effect of the humic acid on the healing of wounds in the mouth. The animals were divided into 4 groups as baseline, saline control (0.09%), chlorhexidine gluconate (0.05%), and humic acid (80 mg/kg) and were treated with these materials for 7 days. The result of this study showed that humic acid enhanced the rate of healing of oral wounds better than the other groups. **These results show that humic acid can be used as an alternative to current treatment methods for oral wounds.**

   Çalışır, Metin et al. "Humic Acid Enhances Wound Healing in the Rat Palate." Evidence-based Complementary and Alternative Medicine: eCAM vol. 2018 1783513. 1 Aug. 2018, doi:10.1155/2018/1783513. Web

TAKEAWAY: Humic acid can be used as an alternative to current treatment methods for healing oral wounds.

6. This study was to evaluate the efficacy and safety of carbohydrate-derived fulvic acid in the treatment of eczema. **Researchers found significant improvements with the carbohydrate-derived fulvic acid in some aspects of eczema** and should be looked into further as a possible treatment for eczema.

   Gandy J, Snyman, van Rensburg. "Randomized, parallel-group, double-blind, controlled study to evaluate the efficacy and safety of carbohydrate-derived fulvic acid in topical treatment of eczema." Clin Cosmet Investig Dermatol. 2011;4:145-148. Web

TAKEAWAY: Significant improvements in eczema occurred from topical treatment with carbohydrate-derived fulvic acid.

7. The goal of this study was to test to see if certain dosages of carbohydrate-derived fulvic acid are safe for use. It was found that after atopic people were treated for 3 days with daily oral dosages of up to 40 mL of a 3.8% solution of a carbohydrate-derived fulvic acid. There was a significant decrease in wheal formation in the skin prick test, confirming that **carbohydrate-derived fulvic acid acts as an inhibitor of the immediate hypersensitivity reaction and that the product is systemically available**. It was concluded that this product was safe at these dosages.

   Gandy, Justin John et al. "Phase 1 clinical study of the acute and subacute safety and proof-of-concept efficacy of carbohydrate-derived fulvic acid." Clinical Pharmacology: Advances and Applications, vol. 4 (2012): 7-11. doi:10.2147/CPAA.S25784. Web

TAKEAWAY: Carbohydrate-derived fulvic acid, an anti-inflammatory agent, acts as an inhibitor of the immediate hypersensitivity reaction to an allergen as illustrated by a skin prick test.

8. Carbohydrate-derived fulvic acid is a promising topical remedy for drug-resistant wound infections. **It accelerated the healing process of wounds infected with methicillin-resistant *Staph. aureus* and multidrug-resistant *P. aeruginosa*** in rats, which is linked to both its antimicrobial and anti-inflammatory properties.

   Zhao, Yanan et al. "Carbohydrate-derived fulvic acid is a highly promising topical agent to enhance healing of wounds infected with drug-resistant pathogens." The Journal of Trauma and Acute Care Surgery, vol. 79,4 Suppl 2 (2015): S121-9. Web

TAKEAWAY: Fulvic acid showed strong activity against a variety of bacterial and fungal pathogens. Treatment with fulvic acid improved and accelerated wound healing, making fulvic acid a promising topical remedy for drug-resistant wound infections. It accelerated the healing process of wounds infected with methicillin-resistant S. aureus and multidrug-resistant P. aeruginosa in rats, which is linked to both its antimicrobial and anti-inflammatory properties.

9. The objectives of this study were to evaluate the safety and anti-inflammatory and wound healing properties of carbohydrate-derived fulvic acid in rats. Carbohydrate-derived fulvic acid effectively reduced carrageenan-induced paw edema in rats, which was comparable to 10 mg/kg p.o. indomethacin. **It showed an increase in the healing of wounds infected with *Staphylococcus aureus*. No signs of toxicity were observed in rats during the 6-day acute and 6-month chronic treatment with carbohydrate-derived fulvic acid.** Carbohydrate-derived fulvic acid is a safe compound with anti-inflammatory and wound-healing properties and merits further evaluation for future treatment.

   Sabi, R., Vrey, P., & van Rensburg, C. E. J. "Carbohydrate-derived Fulvic acid (CHD-FA) inhibits Carrageenan-induced inflammation and enhances wound healing: efficacy and Toxicity study in rats." Drug Development Research, 73(1), 18–23 (2011). Web

TAKEAWAY: Assessing anti-inflammatory and wound healing properties of carbohydrate-derived fulvic acid in rats revealed an increase in the healing of wounds infected with Staphylococcus aureus with no signs of toxicity.

10. Humic substances are effective in the suppression of delayed type hypersensitivity, rat paw edema, a graft versus-host reaction and contact hypersensitivity in rats. They **reduce the C-reactive protein levels of patients suffering from osteoarthritis of the knee and the wheel and flare reaction of patients suffering from hay fever**. They have also been described as cardioprotective and pro-angiogenic. Toxicity studies have indicated that potassium humate is safe in humans up to a daily dosage of 1 g/kg, whereas fulvic acid is safe in humans up to a daily dosage of 1.8 g per adult. The antiinflammatory action of potassium humate can be contributed to the inhibition of the release of inflammatory-related cytokines, an adhesion molecule, oxidants and components of the complement system.

    van Rensburg, C. E. J. Phytother. Res. "The Antiinflammatory Properties of Humic Substances: A Mini Review." Phytotherapy Research, Vol. 29,6, June 2015 p. 791-795 DOI: 10.1002/ptr.5319. Web

TAKEAWAY: Humic substances are effective suppressors of delayed type hypersensitivity, rat paw edema, a graft versus-host reaction, and contact hypersensitivity in rats. They reduce the C-reactive protein levels of patients suffering from knee osteoarthritis and the wheel and flare reaction of patients suffering from hay fever.

11. In this study **carbohydrate-derived fulvic acid was shown to possess broad-spectrum antibacterial activity, as well as being able to down-regulate inflammation and breakdown biofilms**. The properties of carbohydrate-derived fulvic acid could be used as an alternative topical treatment strategy for oral biofilm diseases.

    Sherry, Leighann et al. "Investigating the biological properties of carbohydrate derived fulvic acid (CHD-FA) as a potential novel therapy for the management of oral biofilm infections." BMC Oral Health, vol. 13,47. 24 Sep. 2013, doi:10.1186/1472-6831-13-47. Web

TAKEAWAY: Carbohydrate-derived fulvic acid possesses broad-spectrum antibacterial activity, downregulates inflammation, and breaks down biofilms.