THE SHIKIMATE PATHWAY, THE MICROBIOME, AND DISEASE:

HEALTH EFFECTS OF GMOS ON HUMANS

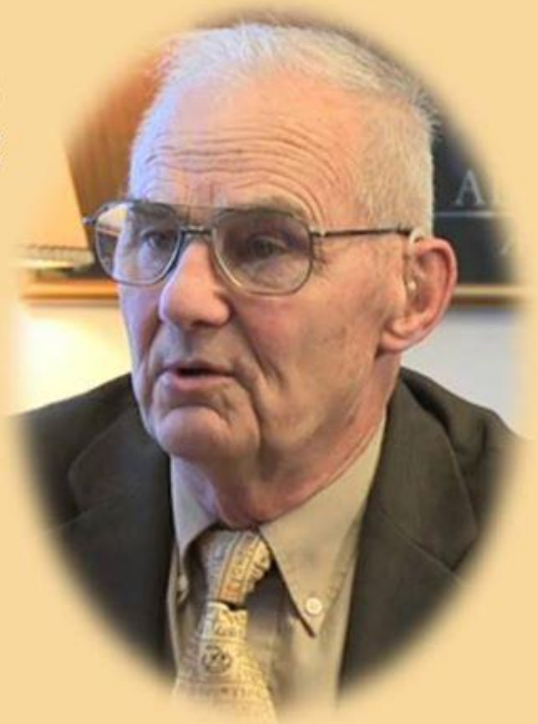
Jeanne D'Brant, DACBN, DC, CTN, RH (AHG)

Associate Professor of Biology & Allied Health, State University of NY

THE TRUTH ABOUT GENETIC ENGINEERING

AN INFECTIOUS-TYPE DISEASE

"Genetic engineering as we currently practice it is really an infectious-type disease. In fact, Dr. Patrick Brown of the University of California said it is much more like a virus infection than a breeding program."



Dr. Don Huber, Professor Emeritus, Plant Pathology, Purdue University

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SAFE FOR HUMAN CONSUMPTION?

Fact: Glyphosate disables the Shikimate pathway

Human cells lack the Shikimate pathway, which is found in plants and bacteria

Biotech industry: knocking out the Shikimate pathway therefore is not of consequence to human health

Fact: The human microbiome contains trillions of bacteria which play crucial roles in maintaining our ecology

Fact: The human microbiome is severely impacted by use of glyphosate and its adjuvants

“ONLY” IN BACTERIA

The Shikimate Pathway is found in all of the three biological domains of life: Bacteria, Archaea, and Eukarya.

Bacteria include Enterococcus, Firmicutes, Bifidobacteria and others found in the human gut.

Archaea are the most ancient life forms known, one-celled organisms which thrive in extreme environments.

Eukaryotes include algae, yeasts, plants, fungi; all animals including insects, crustaceans, birds, reptiles, amphibians, and fish and all mammals.

The life forms on planet Earth which possess the SHIKIMATE pathway:

all Prokaryotes—essentially every single-celled organism on earth including bacteria and archaea

all Eukaryotes except mammals (rodents, bats, moles, primates, cats, dogs, bears, seals, etc.)

every other life form on the planet is **directly** harmed and altered biochemically through damage to the ancient Shikimate molecular chain.

AMERICAN ACADEMY OF ENVIRONMENTAL MEDICINE

- Genetically modified foods present serious health risks to humans including altered gastrointestinal function, immune disorders, infertility, accelerated aging, and insulin dysregulation.

- AAEM urges all doctors to recommend GM-free diet for their patients

- Since GMOs were introduced in 1996, the percentage of Americans with three or more chronic illnesses went from 7% to 13% and we have witnessed an unprecedented rise in autism, food allergies, digestive disorders, and reproductive issues. GM foods are believed to be contributory to the diabetes and obesity problems in the population, now seen at epidemic levels.

Some of the issues:

Glyphosate adversely impacts neurotransmitter production, with serious adverse consequences.

Level II genetic engineering has created “silencers” which knock out unintended genes. Self-propagating GMO pollution will outlast nuclear waste and affect the health of future generations.

Genetic modification introduces genes across species in unprecedented ways, with unknown consequences.

GM foods contain formaldehyde, a known carcinogen, and promote ammonia production.

GM foods create novel, pro-inflammatory proteins. Inflammation underlies every chronic disease process currently known.

GM crops contain higher levels of pesticides and most are engineered to be pesticide tolerant, which has created “superweeds” with herbicide resistance, requiring more and deadlier pesticide application, a positive feedback system which perpetuates itself.

GM PROTEINS AND BIOTECH

GE creates novel proteins which have been shown to be pro-inflammatory. Genes contain the “recipes” for creating amino acids which join together to form proteins, altered genes create unknown proteins which are not identical to the naturally produced protein.

The biotech industry assumes that there are no other effects produced by genetic alteration, a very arguable supposition. Research on GM peas in Australia was halted when mice fed GM peas developed allergies and asthmatic reactions to the pea proteins and cross-reactivity to egg white protein fed to them concurrently. This research also noted that the assembly of the GM proteins (post-translational modification) showed subtle but concrete differences in the attachment of sugar units to the proteins (a biochemical process called glycosylation).

Related issues include biotech industry procedures to evaluate digestive stability of GM proteins using artificially low Ph and pepsin-enriched media, (which cause the proteins to break down rapidly) and then arguing that GM proteins do not appear in feces of animals which consume them. Chowdhury, et. al., found that rapid degradation of GM proteins does not in fact occur in vivo and thus the engineered proteins are found in feces of animals who consume them and in the soil where the feces fall.

INDUSTRY TESTING

Amazingly, **the biotech testing process does not use its own GH proteins**!!! Citing the difficulty of extracting Gm proteins from GM plants, the industry conducts its tests of the effects of its altered proteins with substituted "surrogate" proteins produced by bacteria! These surrogate proteins will not evidence the allergenicity or toxicity of the actual proteins to which humans are exposed. Further, the process of prokaryotic bacterial glycosylation is different than in eukaryotic plants, it has only been discovered recently that bacteria are able to glycosylate.

Careful analysis of the opinions of the EFSA's (European Food Safety Authority) panel on GMOs reveals that their conclusions about the safety of a particular engineered protein such as the CP4 EPSAPS protein (which confers tolerance to glyphosate) or the PAT protein (which confers resistance to glucosinate ammonium) are based upon historical approvals for other proteins by "nationally competent authorities" and are not referenced. Many of the currently approved GM crops are have not been considered specifically for the allergenicity and safety, but refer to prior statements and approvals that include evaluations which have raised the spectre of concerns, ignored potential allergenicity and quote uncited sources.

OTHER CONCERNS

GM crops have been found to contain seriously depleted levels of mineral micronutrients . Minerals, or metals, are required for catalytic enzyme activities in the human body.

Glyphosate has strong antibiotic activities, especially against Lactobacilli, Bifidobacteria, and Enterococcus faecalis in the gut.

GM genes enter the digestive tracts of humans and animals via foods and soil where GE grains have been excreted as well as via consumption of GM crops.

Genetically engineered “promiscuous” genes spread throughout the gene pool.

PROMISCUOUS GENES

GE genes escape from GE crops to their wild relatives via reproductive exchange and by pollen. The GE pollen floats on the wind and coats the bodies of pollinating insects (who utilize the Shikimate pathway). Cross-pollination of nearby species occurs through proximity and foraging animals such as deer, which carry plant seeds in their fur, expanding the potential for gene transfer. Gene escape from cultivated crops has been documented for corn, canola, quinoa, cotton, rice, sorghum, beets, melon, and others. Multiple ecosystems are affected.

CONSEQUENCES OF GENE ESCAPE

Traits that enhance survival, such as those for disease, pest, and herbicide resistance, will potentially create new invasive weeds. Plants engineered to survive environmental changes such as drought, temperature and salinity will increase the survival of wild plants, which will affect the ecological balance of their predators and commensals, such as fungi, viruses, insects, worms and bacteria. These are affected not only by the increased resistance of the mutated plants but also by harm to their Shikimate mechanism, which produces tyrosine, melanin, and other important neurochemicals.

THE WEB OF LIFE

Genetic modification is based on an obsolete scientific theory

Genetic modification is based on a theory called the Central Dogma, which asserts that one gene will express one protein. However, scientists working with the United States National Human Genome Research Institute discovered that this is not how the genome expresses, that genes operate in a complex network in ways that are not fully understood. This finding undermines the entire basis for genetic engineering.

Traits are controlled by multiple genes.

Gene expression is a complex choreography involving promoter regions, operons, controller, inducer and repressor loci, and enzymes, mutually interdependent and interrelated, whose expression is modified by epigenetic factors from the environment, our foods and our lifestyle behaviors.

The gene “silencers” introduced in GM engineering are able to conform to multiple genes in addition to the intended ones, effectively silencing expression of our genome in unintended ways.

SILENCERS

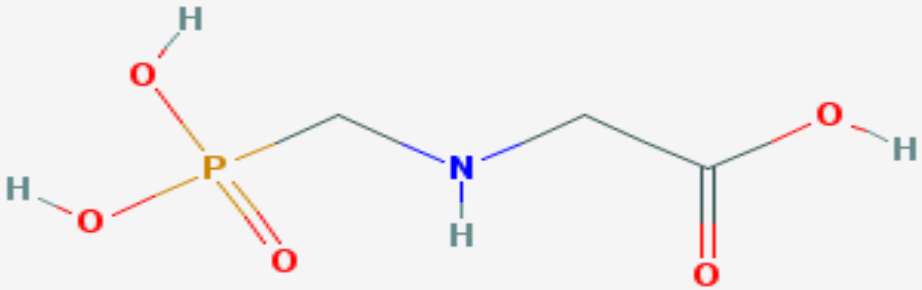
- Some types of GE wheat use “level II” gene silencing mechanisms designed to alter wheat’s carbohydrate content, according to Australian research. (Heinemann)

- These silencers also match well with at least a dozen other human genes, probably silencing their expression. The dozen matches “were extensive and identical” and consumption of these double-stranded RNA silencers appeared to affect glycogen storage in humans, leading to obesity.

WHAT IS GLYPHOSATE?

- Active ingredient in Round Up
- “N-phosphonomethyl glycine” $C_3H_8NO_5P$
- An endocrine communication molecule disruptor, along with neonicotinoid insecticides (bee colony collapse disorder)
- Has antibiotic actions, especially to important gut bacteria such as Lactobacilli and Bifidobacteria.
- Downregulates the manufacture of the essential aromatic amino acids phenylalanine, tryptophan, and tyrosine.

MOLECULAR STRUCTURE



Chemical Names: Glyphosate; N-(Phosphonomethyl)glycine; 1071-83-6; Glyphosphate; Glycine, N-(phosphonomethyl)-; Roundup More...

Molecular Formula: $C_3H_8NO_5P$

WHAT IS THE SHIKIMATE PATHWAY?

FROM WIKI:

The **shikimate pathway** (shikimic acid pathway) is a seven step metabolic route used by bacteria, fungi, algae, parasites and plants for the biosynthesis of aromatic amino acids (phenylalanine, tyrosine, and tryptophan). *This pathway is not found in animals*, (incorrect!) hence the products of this pathway represent essential amino acids that must be obtained from the animal's diet. However, this pathway is found with microbes that live within animals in the gut microbiome.

- The first enzyme involved is the shikimate kinase, an enzyme that catalyzes the ATP-dependent phosphorylation of shikimate to form shikimate 3-phosphate. Shikimate 3-phosphate is then coupled with phosphoenol pyruvate to give 5-enolpyruvylshikimate-3-phosphate via the enzyme 5-enolpyruvylshikimate-3-phosphate (EPSP) synthase.

GOOD AND BAD GUT BACTERIA

Growth of Lactobacilli and Bifidobacteria holds other, pathogenic bacteria in check. When their numbers decline from eating GM foods, opportunists and pathogens thrive.

All bacteria produce waste, but the metabolic products of pathogens are inflammatory, producing cytokines (messages) which promote general inflammation in the body and underlie specific diseases such as cardiovascular, dementias, bipolar disorders, schizophrenia, autism, and many others.

GUT MICROBIOTA

Gut flora are of a complex community of microorganisms colonizing the digestive tracts and other sites in animals. The **gut microbiome** refers to the genomes of the gut microorganisms.

Gut microbes are of benefit to their host by harvesting the molecular energy from the fermentation (anaerobic metabolism) of undigested carbohydrates and subsequent absorption of short-chain fatty acids. Important among these FAs are the butyrates, metabolized by the epithelium in the colon; propionates metabolized by the liver; and acetates processed by muscle tissue. Intestinal bacteria are known to manufacture B vitamins and vitamin K and are important for metabolism and recirculation of bile acids, sterols and environmental chemicals, or xenobiotics.

Humans have on average about 100 trillion organisms in the intestinal tract, ten times the number of cells in the body.[The metabolic actions of this bacterial population function as an organ, unrecognized by western medicine. The gut flora community contain about one hundred times the amount of genes found in the human genome.

THE MICROBIOME IN HUMAN HEALTH

- Our flora outnumber our cells by at least a 10 to 1 ratio
- Flora are found in all body fluids and organs

  Gut flora synthesize vitamins and create anti-inflammatory compounds
- They maintain intestinal permeability
- Bacteria in the gut digestion energy substrates for us, stimulate cell growth, repressing the growth of pathogenic and opportunistic bacteria, and train the immune system to respond only to pathogens via complex processing involving the Peyer's Patches and other MALT tissues. Peyer's patches are loci of immune surveillance which contain specialized white blood cells which sample bacterial populations entering our digestive systems, primarily from foods, and deliver these sample to other immune cells for identification.

COOPERATION AND MYSTERY

While between 300 and 1000 different species are known to live in the gut, 500 species are seen most commonly. 99% of the bacteria are members of about 30 or 40 known species. Other organisms such as archaea, protozoa, and fungi are found in the gut flora, and their activities are still a mystery.

Research suggests that the connection between our cells and our gut is not just commensal (coexistence without harm to either), but of mutual benefit. Flora perform a plethora of useful functions, including fermentation of unused energy substrates, immune system training, containing growth of pathogens and opportunists, regulating gut development, and producing beneficial vitamins such as biotin and vitamin K, and manufacturing hormones which affect fat storage in the host. In mutuality, the flora are allowed to thrive in a nutrient-rich, protected environment. Imbalance of flora can lead to overcolonization by species capable of disease production via infection, increased cancer risk, or decreased immune function.

COMPOSITION OF THE MICROBIOME

The makeup of microbiota depends upon factors such as diet, immune status, and colonization history. Some organisms are better able to complement specific metabolic enzymes than others. *Bacteroides* will alter the break down of carbs depending on other foods in the diet. The four most dominant bacterial phyla in the gut are Firmicutes, Bacteroidetes, Actinobacteria, and Proteobacteria. Most bacteria are *Bacteroides*, *Clostridium*, *Ruminococcus*, *Peptococcus*, *Peptostreptococcus*, and *Bifidobacterium*. *Escherichia* and *Lactobacilli* are found to a lesser extent. *Bacteroides* alone make up about 30% of all human gut bacteria, indicating their importance to human functioning. Other studies have yielded different species and conclusions are still evolving.

Fungi currently recognized include *Candida*, *Saccharomyces*, Penicillium and *Aspergillus*.

Archaea, the most ancient of organisms, are important in the breakdown of the bacterial products of fermentation.

Diversity of microbiota in fecal samples is much more pronounced in adults than children, although interpersonal variance is higher in children than in adults. The maturation of the gut flora into an adult-like community happens within the first three years of life, raising concerns about disruption of this natural colonization process via antibiotic administration and consumption of GM soy formula. *Bifidobacteria longum* dominate in breast fed babies, and are found to decline in proportion to increasing age. Analysis of kinship of the microbiome across nations has shown that despite cultural influence, sharing a common environment is a strong determinant of individual microbiome composition. This familial effect is not genetic and is consistent across populations.

GUT FLORA AND DIET

Gut flora preponderance is associated with foods consumed, diet being the main determinant of gut flora composition. *Prevotella*, *Bacteroides* and *Ruminococcus* are three main classifications. *Prevotella* is found in higher concentrations in those who consume the grain-based agrarian diet and simple sugars, while *Bacteroides* is associated with consumption of animal proteins, and saturated fats.

The composition of the gut microbiome depends on geographic origin. There are variations in Prevotella concentration, urease gene levels, and genes for glutamate synthesis and degradation of other amino acids and vitamin biosynthesis. U.S. microbiota population reflects increased fat consumption compared to Amerindian or Malawian populations subsisting on corn. Other studies have shown a large difference in the composition of microbiota between European and rural African children. The greater diversity and of gut flora in Africans probably reflects the ingestion of tough-to-degrade plant polysaccharides and has been associated with reduced incidence of non-infectious colonic disease such as cancer. Gatherer/hunter populations had different gut flora composition based upon their consumption of diverse plant foods and wild meats with different amino acid and fat composition.

ACQUISITION OF GUT FLORA IN HUMAN INFANTS

During birth and rapidly thereafter, bacteria from the mother and the environment colonize the newborn's gut. Immediately after vaginal delivery, babies may have bacterial strains derived from the mothers' vaginal flora, including fecal flora, in their upper GI tracts. Those born by caesarean section have less exposure to their mother's microflora, and show increased colonization from the hospital environment, nursing staff, other infants, etc. The initial inoculum of C-section babies is usually dominated by *Staphyloccocus*, *Corynebacterium* and *Propionibacterium* species. The primary gut flora post caesarean delivery may be disturbed for up to six months, while vaginally-delivered babies require one month or less to develop well-established intestinal flora. After birth, oral, skin and environmental, bacteria are freely transferred from mother to infant via breastfeeding, kissing, and touch.

FUNCTIONS OF FLORA

Carbohydrate fermentation and absorption

- Rats raised in sterility and lacking in gut flora require 30% more calories to maintain their weight than normals.
- Bacteria ferment carbs to SCFAs via saccharolytic fermentation., with products such as propionic acid, butyric acid and acetic acid These are utilized by host cells as a important source of useful energy and are involve d in the absorption of essential dietary minerals including iron, calcium, and magnesium. Gases and organic acids produced by saccharolytic fermentation include acetic acid (used by muscle), propionic acid (aids in hepatic production of energy, or ATP) and butyric acid for gut epithelia , known to be cancer-preventative. Gut bacteria also facilitate the absorption and storage of lipids and produce and aid the absorption of necessary vitamins.
- In proteolytic fermentation, proteinaceous enzymes, dead host and bacterial cells, collagen and elastin proteins from the diet, can produce toxins and carcinogens in addition to SCFAs. Thus, a diet lower in certain types of proteins reduces exposure to harmful toxins.
- Beneficial flora increase the gut's absorption of water, damaging bacterial levels, stimulate growth of human gut enterocytes.

GROWTH AND COMPETITIVE INHIBITION

- SCFAs increase growth of intestinal epithelial cells controlling their proliferation and differentiation. They also stimulate the lymphatic tissue in the gut. Bacteria change the expression of cell surface proteins such as sodium/glucose transporters in gut epithelia and help to prevent injury to the gut mucosa during digestion.

- Gut flora provide competitive inhibition in regards to less desirable bacteria, both invaders and pathogenic bacteria which normally reside in the gut in controlled numbers. This is called the "barrier effect." Harmful yeasts and bacterial species such as *Clostridium* are held in check due to competition from helpful gut flora adhering to the gut lining. Disruption of this mechanism by antibacterial GMO activity leads to gut balance disruption and increased rate of infection.

- Gut flora prevent the growth of pathogens by competing for nutrients and attachment sites on the epithelium. Indigenous gut flora also produce bacteriocins, which are proteinaceous toxins that inhibit growth of bacterial strains, and kill harmful microbes.

- The fermentation process produces lactic acid and FAs which acidify the pH of the colon, preventing the proliferation of harmful species of bacteria and facilitating that of helpful species. Lower pH also appears to enhance the excretion of carcinogens.

YIN YANG

- Beneficial Enterococcus bacteria antagonize pathogenic Clostridia. Enterococci are extremely vulnerable to glyphosate.
- When there are less Enterococci, Clostridia and Salmonella thrive.
- There are multiple strains of Clostridia and Salmonella, the pathogenic strains are known to have the most resistance to glyphosate.

PSEUDOMONAS AND FORMALDEHYDE

- Pseudomonas are opportunistic pathogens, which create the blue-green color and characteristic odor of burn infections. Pseudomonas are capable of breaking down glyphosate to make amino acids for their own growth. In so doing, they create formaldehyde, a carcinogen and neurotoxin. Low levels of formaldehyde are associated with misfolding of the tau proteins in neurons, forming protein-aggregate tangles similar to those seen in dementia stricken-brains.

MOLECULAR BASIS FOR THE HERBICIDE RESISTANCE OF ROUNDUP READY CROPS

Todd Funke,Huijong Han, Martha L. Healy-Fried, Markus Fischer, Ernst Schönbrunn
Edited by Brian W. Matthews, University of Oregon, Eugene, OR, (received for review May 3, 2006)

Abstract

The engineering of transgenic crops resistant to the broad-spectrum herbicide glyphosate has greatly improved agricultural efficiency worldwide. Glyphosate-based herbicides, such as Roundup, target the shikimate pathway enzyme 5-enolpyruvylshikimate 3-phosphate (EPSP) synthase, *the functionality of which is absolutely required for the survival of plants.* Roundup Ready plants carry the gene coding for a glyphosate-insensitive form of this enzyme, obtained from *Agrobacterium* sp. strain CP4. Once incorporated into the plant genome, the gene product, CP4 EPSP synthase, confers crop resistance to glyphosate. Although widely used, the molecular basis for this glyphosate-resistance has remained obscure. We generated a synthetic gene coding for CP4 EPSP synthase and characterized the enzyme using kinetics and crystallography. The CP4 enzyme has unexpected kinetic and structural properties that render it unique among the known EPSP synthases. Glyphosate binds to the CP4 EPSP synthase in a condensed, noninhibitory conformation.

INTERACTION OF THE HERBICIDE GLYPHOSATE WITH ITS TARGET ENZYME 5-ENOLPYRUVYLSHIKIMATE 3-PHOSPHATE SYNTHASE IN ATOMIC DETAIL

Ernst Schönbrunn, Susanne Eschenburg, Wendy A. Shuttleworth, John V. Schloss, Nikolaus Amrhein‖,
Jeremy N. S. Evans, and Wolfgang Kabsch§

Edited by Gregory A. Petsko, Brandeis University, Waltham, MA, and approved December 13, 2000 (received for review August 25, 2000)

Abstract

Biosynthesis of aromatic amino acids in plants, many bacteria, and microbes relies on the enzyme 5-enolpyruvylshikimate 3-phosphate (EPSP) synthase, a prime target for drugs and herbicides. We have identified the interaction of EPSP synthase with one of its two substrates (shikimate 3-phosphate) and with the widely used herbicide glyphosate by x-ray crystallography.

The two-domain enzyme closes on ligand binding, thereby forming the active site in the interdomain cleft. Glyphosate appears to occupy the binding site of the second substrate of EPSP synthase (phosphoenol pyruvate), mimicking an intermediate state of the ternary enzyme·substrates complex. The elucidation of the active site of EPSP synthase and especially of the binding pattern of glyphosate provides a valuable roadmap for engineering new herbicides and herbicide-resistant crops, as well as new antibiotic and antiparasitic drugs.

ACTIONS OF GLYPHOSATE

- The active ingredient in glyphosate derives from the amino acid glycine. Once it is absorbed by the plant, it binds and blocks the enzyme EPSPS (enolpyruvylshikimate-3-phosphate), This enzyme, found at the beginning of the chemical pathway, converts simple carbohydrates into aromatic (ring form) amino acids, hormones, vitamins and other essential plant metabolites. Glyphosate prevents EPSPS from entering into the chloroplast, which causes a deficiency in the manufacture of amino acids (phenylalanine, tyrosine, tryptophan) and ultimately death of the plant by starvation.
- The glyphosate molecule is not particularly water soluble so adjuvants are added for easier spraying and to ensure rapid uptake so that the herbicide is not washed off by rain after spraying.

PHENYLALANINE

Phenylalanine is a precursor to:

- Tyrosine
- Dopamine
- Norepinephrine
- Epinephrine
- Melanin

- Essential amino acids include: arginine (conditionally), phenylalanine (sufficient levels to create tyrosine also), methionine (enough to make cysteine as well), histidine, isoleucine, leucine, lysine, threonine, valine, tryptophan.

ALKALOIDS AND TYROSINE

- Natural Products
- 2013, pp 405-460
- Date: 15 May 2013
- **Alkaloids Derived from Tyrosine: Modified Benzyltetrahydroisoquinoline Alkaloids**
- Dr. Feroz Khan, Tabish Qidwai, Rakesh K. Shukla, Vikrant Gupta

  Secondary metabolites are produced by plants in response to biotic or abiotic interactions with their environment and confer protection through a variety of antimicrobial, pesticidal, and pharmacological properties. Alkaloids are a class of plant secondary metabolites that traditionally have been classified as basic compounds derived from amino acids that contain one or more heterocyclic nitrogen atom. About 20 % of plant species accumulate alkaloids, which are mostly derived from amino acids, e.g., phenylalanine, tyrosine, tryptophan, and lysine. The alkaloids are popular for their medicinal importance. The pharmaceutically important representatives of secondary metabolites are mostly alkaloids derived from tyrosine. In this chapter, we summarized the prior information, basic knowledge about the alkaloids, origin, physicochemical properties, uses, classification, biosynthetic reactions, and distribution of tyrosine-derived alkaloids especially opium alkaloids and their biosynthetic pathways in plants. We have also reviewed different web resources related to alkaloids and secondary metabolic pathway databases such as KEGG.

- PAs, isoquinoline alkaloids, including opium alkaloids, papaverine, pseudomorphine, and berberine are all secondary metabolite alkaloids derived from tyrosine!

PHENYLALANINE

Is converted to tyrosine in the Shikimate pathway in plants and bacteria.

Tyrosine is made from phenylalanine-rich foods in humans and other mammals, including:

- Soy protein isolate, potassium type, crude protein basis Tyrosine: 2008mg
- Egg, white, raw, fresh Tyrosine: 1904mg
- Cheese, cottage, lowfat, 1% milkfat Tyrosine: 1833mg
- Seaweed, spirulina, dried Tyrosine: 1782mg
- Fish, Salmon, Chum, raw (Alaska Native) Tyrosine: 1774mg
- Quail, breast, meat only, raw Tyrosine: 1704mg
- Game meat, buffalo, water, raw Tyrosine: 1653mg
- Egg, white, dried Tyrosine: 1651mg
- Game meat, buffalo, water, cooked, roasted Tyrosine: 1645mg
- Pumpkin leaves, raw Tyrosine: 1642mg
- Crustaceans, shrimp, mixed species, canned Tyrosine: 1620mg
- Turkey, all classes, light meat, raw Tyrosine: 1619mg
- Game meat, moose, cooked, roasted Tyrosine: 1608mg
- Pork, Leg sirloin tip roast, boneless, separable lean and fat, raw [Leg sirloin tip roast, URMIS #3647, Vastas lateralis\Rectus Femoris] Tyrosine: 1606mg
- Mustard greens, cooked, boiled, drained, with salt Tyrosine: 1587mg

TYROSINE IS A PRECURSOR TO:

L-dopa and dopamine

Catecholamines –epinephrine and norepinephrine

Coumaric acid

Melanin

In Papaver somniferum, plant alkaloids convert tyrosine to morphine and mescaline

COUMARIC ACID

- Coumaric acid is a hydroxycinnamic acid, an organic compound that is a hydroxy derivative of cinnamic acid. It can be found in a wide variety of edible plants such as peanuts, garlic, carrots, tomatoes, wine, vinegar, barley, and commercial breads which contain flaxseed.
- *p*-Coumaric acid has antioxidant properties and may reduce the risk of gastric cancer by blocking the formation of nitrosamines.
- **Biological Effects**
- *p*-Coumaric acid is found in honey, but not in the substitute high-fructose corn syrup that honey bee keepers have fed to their colonies. The absence of coumaric acid may be a contributor to Colony Collapse Disorder because *p*-coumaric acid has been found to help honey bees detoxify pesticides.
- Br J Nutr. 2007 Mar;97(3):458-63.
- **p-Coumaric acid, a common dietary phenol, inhibits platelet activity in vitro and in vivo.**
- Luceri C[1], Giannini L, Lodovici M, Antonucci E, Abbate R, Masini E, Dolara P.

Abstract

- p-Coumaric acid is a ubiquitous plant metabolite with antioxidant and anti-inflammatory properties. The antiplatelet activity of this compound was analyzed both ex vivo and in vitro. 4-CA, administered to rabbits for 2 weeks at the dose of 5 mg/kg, mixed with food, inhibited ADP-induced platelet aggregation without affecting blood coagulation. This effect was associated with a marked increase in plasma antioxidant activity, measured as ferric reducing ability of plasma, and with the reduction of thromboxane B2 production. The antiplatelet effect was confirmed by in vitro experiments on human blood....4CA was able to modify platelet function, and 4CA interfered with the arachadonic acid cascade, reducing thromboxane B2 production and lipopolysaccharide-induced prostaglandin E2 generation . **The data show that 4CA is an antioxidant compound with good antiplatelet activity at doses that can be obtained with dietary intervention, suggesting possible applications for primary prevention of vascular disease.**

TYROSINE DYSREGULATION

Phenylalanine levels in GMO foods are reduced, therefore synthesis of its downstream metabolites: tyrosine, dopamine, norepinephrine, epinephrine and melanin are affected.

Tyrosine synthesis impairment in GMO foods has affects upon the absorption of UV light, a biochemical process with esoteric qualities.

Thyroid hormones T3 and T4 are derivatives of tyrosine, which serves as another link between tyrosine dysregulation and obesity.

DOPAMINE

Deficient dopamine is associated with decreased ability to feel pleasure. The affect is dulled, flattened, there is low drive and motivation, with difficulty in completing even interesting tasks. Concentration is impaired, and cravings for stimulants appear, leading to addictions. The individual fatigues easily, is lethargic and has difficulty getting out of bed.

Tyrosine deficiency is documented to reduce dopamine levels.

Other factors which may be synergistic:

*deficiencies of vitamins B3, B6, D3, and C,

*magnesium, iron and zinc deficiencies

*adrenal exhaustion

*lead, cadmium and other heavy metal exposure

*chronic opioid, alcohol and marijuana use

*low estrogen or HGH levels

*sleep loss

*under-methylation

*hypothyroidism

*chronic stress

FAR REACHING EFFECTS OF MELANIN

- a hormone synthesized from tyrosine via phenylalanine
- found in most living organisms--animals, plants, fungi and bacteria—except arachnids
- found in skin cells called melanocytes, it colors skin, hair, irises, feathers and scales,

  the stria vascularis of inner ear, medulla and zona reticularis of adrenal glands, and two important areas of the brain-the substantia nigra (produces dopamine) and the locus ceruleus
- is an absorber of light and dissipates UVb radiation
- melanin functions in cephalopod protection (think “squid ink”) is protective against chemical stresses, temperature damage, heavy metals,
- a major immune defense mechanism in invertebrates involves encapsulating invading microbes with melanin, which generates free radicals to destroy them.
- some fungi use melanin for photosynthesis to capture gamma rays
- the black, melanin-rich feathers of birds are less vulnerable to bacterial attack
- melanin plays a major role in light absorption in the retina of birds
- it is involved in the browning of fruits such as bananas

MELANIN, CONT'D

- nicotine has a higher affinity for melanin-containing tissue
- melanin granules (melanosomes) protect DNA against ionizing radiation (UV rays)
- melanin is an antioxidant believed to be cell-protective via its sequestering of toxic metal ions, including iron
- has a role in melanoma development
- has a role in solar heat absorption for body temp, especially for cold-blooded animals
- minimizes the amount of light entering the eye, its deficiency associated with cataracts
- provides for the absorption of scattered light within the eye, creating keener sight and sharpness of vision

TYROSINE

- Has a key role in cell signal transduction, because its OH group can receive high energy PO4 groups via important enzymes called receptor protein kinases
- **Receptor tyrosine kinases** are the cell membrane receptors for many growth factors, hormones, and cellular signaling molecules (cytokines). There are 90 unique genes coding tyrosine kinases in humans, 58 of which encode receptor tyrosine kinase proteins. RTK proteins are key regulators of normal cellular functions and have a critical role in the onset and progression of many cancers.
- When the OH groups receive the PO4 group (the process of phosphorylation), the target proteins then behave differently due to their altered energy levels.

TYROSINE AND PHOTOSYNTHESIS

- Tyrosine interacts critically with chlorophyll and manganese clusters in Photosystem II of photosynthesis.
- These interactions add an electron to oxidized chlorophyll and donate a proton from an OH group for other important uses.

- **This is an antioxidant activity performed upon one of the most critical molecules found in plant tissue, the primary creator of food sources in the food chain**

TRYPTOPHAN

- Derived from phenylalanine, tryptophan is a precursor to serotonin and melatonin
- Tryptophan has profound effects upon mood disorders, depression, carbohydrate craving, dysglycemias, and obesity via serotonin
- The nitrogen in tryptophan is physically involved with complex protein folding and may play a role in prion disease
- Tryptophan depletion is associated with depression, low self-esteem, aggression, impulsivity, obsessive thoughts, compulsive eating disorders and weight gain

GLYPHOSATE IS ONLY ONE OF THE PROBLEMS….

Surfactants are added to Round up formulas to

According to research at the Institute of Biology in Caen, France, the four different formulas of RoundUp produced by Monsanto are highly toxic to human cell lines at concentrations far below their recommended agricultural use.

POEA AND AMPA

Adjuvants are considered to be inert ingredients, not measured in the environment and protected as trade secrets by manufacturers.

POEA (polyethoxylated tallow amine) is known to be a prominent adjuvant used in Roundup to improve solubility and penetration.

AMPA (aminomethylphosphoric acid) is the major metabolite of glyphosate. AMPA and glyphosate are major contaminants found rivers, affecting amphibians, oxygen-producing algae, and bacteria.

AMPA V. POEA V. GLYPHOSATE

- Alarming finding: toxicities of RoundUp formulas are not proportional to glyphosate concentration, other (unknown) substances are also responsible for cell-killing power

- **AMPA and POEA kill cells in two ways:**

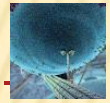
  mitochondrial poisoning

  plasma membrane damage

.

THE MITOCHONDRIA

Powering the Cell: Mitochondria



XVIVO Scientific Animation

Mitochondria

THE PLASMA MEMBRANE

- animhttps://www.youtube.com/watch?v=lQLZAMWqSdkation

Fluid Mosaic Model

AMPA

- AMPA alone destroys cell membranes
- Glyphosate 3 -8 X more toxic to mitochondria than AMPA
- Because cell membrane damage is more destructive to cellular function, AMPA has more toxic effects than glyphosate, considered to be a worse toxin

POEA

- The worst of the three studied toxins in its killing effects upon human cells
- POEA so potent that damage is seen on the plasma membrane and the mitochondria at 1 ppm (part per million)

ROUNDUP FORMULAS

- The most damaging formula: is RoundUp400 which kills 100% of human cells at 20 ppm.
- All RoundUp ***formulas*** are more toxic than the single ingredients alone, causing cellular death more quickly.
- The surfactants are synergistic with glyphosate in their dangerous effects upon human cell lines.

GLYPHOSATE

- begins toxicity at 10,000 ppm
- affects mitochondria
- linked to spontaneous abortion, multiple myeloma, and non-Hodgkin's lymphoma, many others
- glyphosate alone inhibits DNA transcription in the eggs of sea urchins, causes developmental delays in live young. It is heavily linked to the global demise of amphibians and is considerably more toxic to frogs than it is to plants.

- but studying the effects of glyphosate alone is not enough!

DECREASED DETOX

- Detoxification is an essential process for life, accomplished in humans through activities of the liver, white blood cells other tissues.
- Cells impacted by glyphosate have shown decreased levels of methionine.
- Methionine is the essential sulfur-containing amino acid found in eggs, fish, beef, poultry and game, with lesser amounts found in seeds, nuts, and legumes. It is necessary to prevent homocysteinuria and blood vessel damage and protects the liver against steatohepatitis, or fatty degeneration. Its deficiency is associated with hepatic fibrosis, upregulation of proinflammatory genes, increased lipid peroxidation and cell membrane damage, decreased detoxification in the liver especially of estrogens and xenoestrogens, toxic metals, and other environmental chemicals.
- Methionine is necessary for biosynthesis of carnitine, taurine and cysteine.

GLYCINE

Glycine, another essential amino acid, is also found in decreased levels in GM plants. Among its functions:

* a glucogenic amino acid, regulating blood sugar
* DNA and RNA strand synthesis
* anti-aging–30+ % of collagen is glycine
* boosts creatine levels for maintaining/adding muscle mass
* important roles in wound healing and tissue repair
* regulates bile acid synthesis for fat metabolism
*has important neurotransmitter inhibitory function in bipolar disorders and seizures
*influences states of schizophrenia (via its metabolite, serine)
*improves memory loss
*inhibits angiogenesis in neoplasms
*reduces prostate hyperplasia

PAL AND AMMONIA

- Phenylalanine ammonia lyase (PAL) is an enzyme which catalyses the conversion of the amino acid phenylalanine to a substance called trans-cinnamate, releasing ammonia in the process. Some of glyphosate's growth-retardant effects upon plants work through this PAL mechanism. Increased ammonia levels are highly associated with the autistic brain. It causes destruction of both neurons and their support cells, astrocytes, which process ammonia to remove it from the CNS.
- Depression, poor cognition and sleep disorders are associated with elevated ammonia levels in the brain

AUTISM AND GLYPHOSATE

Features of autism:

- Disturbances in microbiota with increased short chain fatty acids and ammonia in the gut
- SCFAs and ammonia are byproducts of anaerobic fermentation, inferring anaerobic overgrowth with species such as Clostridia, Bacteriodetes, and Desulfovibrio.
- Autistic children show elevations of Clostridia in their feces

GLUTEN INTOLERANCE

- Increased anaerobic fermentation in the gut leads to altered amines, (nitrogen-containing groups), phenols (alcohols), hydrogen sulfide and ammonia by-products which are toxic to the colon and create inflammation, leading to leaky guy syndrome and food intolerances.
- Excess circulatory ammonia by-products are associated with liver disorders.

HEPATIC FUNCTION

- Glyphosate's induction of the PAL pathway is postulated to have a blocking action on the urea pathway, impairing the liver in its detoxification of ammonia through this urea pathway, a critical hepatic function. The increased metabolism of phenylalanine via the PAL pathway and the faulty degradation of tyrosine are related to the metabolite p-Cresol which is associated with the sulfate deficiencies of autism spectrum disorder and to *Clostridium difficile* activity.

TRYPTOPHAN

- A damaged gut barrier cannot allow for transfer of micronutrients across its compromised lining.
- Glyphosate is thought to directly affect the synthesis of tryptophan, an essential amino acid. The depletion of tryptophan results in decreased serotonin and melatonin production in the brain. Serotonin is an important neurotransmitter whose depletion leads to overeating, especially of carbohydrates. Thus, increased obesity is associated with impaired tryptophan metabolism, and diabetes and many cancers are associated with obesity.
- Via hepatic activities, tryptophan metabolism creates NAD+, an essential co-factor in in DNA repair and ATP (cellular energy) synthesis.
- Reduced tryptophan levels at the blood brain barrier results in improper signaling, weight gain, and unresponsiveness to SSRI anti-depressants.

ENDOTOXINS

- Endotoxins are lipopolysaccharides produced by certain gram negative bacteria. Glyphosate shifts gut bacterial populations towards endotoxin producers.
- In large quantities, they produce severe diarrhea, hemorrhage and shock.
- Smaller amounts are associated with altered WBC and immune function, and altered resistance to infection.
- Fecal transfer of bacteria from obese humans to germ-free mice resulted in fat mice within 16 weeks. This effect is compounded if a high-fat diet is introduced, and a high carb diet is worse.

OBESITY IN GMO SOUTH AFRICA

- South Africa, which has freely adopted GMO crops, has the highest rate of obesity in all of the African continent. This may be due GMOs or to other factors, and needs further investigation.

MS AND MYELIN SHEATH ATTACK

- The myelin sheath is composed of phosphorus-rich fatty acids which insulate nerves and allow for nerve signal conduction rates hundreds of times faster than unmyelinated nerves.

- Attack and destruction of the myelin sheath is associated with LPS (lipopolysaccharide) release from inflamed gut mucosa.

C. DIFF

- C. diff infections are hospital and assisted living nightmares. The bacteria causes colitis, inflammatory bowel disease, and severe diarrhea which can lead to death. P-Cresol formed by anaerobic metabolism of tyrosine by C. diff bacteria is known to be highly toxic to the CNS, cardiovascular system, pulmonary, renal, and hepatic systems.
- Recent studies have shown that C. diff infections were nearly absent in IBD patients prior to 2003. While antibiotic use is associated with C. diff infections, the link between glyphosate and C. diff is largely ignored.

SOY FORMULAS AND AUTISM

- Formula-fed babies have more C. diff in their feces than breast-fed babies. The autistic population has, in general, experienced less breast-feeding.
- Autism is associated with inflammation of the gut mucosa, an immunopathology of infiltration by intestinal epithelial lymphocytes into the gut lining. This infiltration of WBCs—both eosinophils and lymphocytes, is a direct response to the impaired barrier function.
- Autism is also characterized by impaired sulfate metabolism and a significantly reduced level of free sulfate in the bloodstream (one third of normal level) as well as excess production of NO. There elevated levels of phenols, produced by Clostridia and other bacteria. The elevated urinary levels of toxic phenol, the decreased ability to sulfate, and the genetic defect in the gene encoding for the enzyme phenol sulfotransferase can all be contained with a framework of glyphosate-induced damage to the gut bacteria and resulting effects upon the blood stream.

MINERAL DEFICIENCIES

- Plants exposed to glyphosate on their root systems have been shown to create mineral deficient seeds; lacking calcium, magnesium, iron and manganese.
- Minerals are co-factors for catalytic enzyme function.
- The industrialized diet already lacks minerals and trace minerals due to farming practices, and the under-consumption of plant foods in the SAD (Standard American Diet) exacerbates the mineral deficiencies of the population

CYP ENZYMES

- Cytochrome p450 enzymes are a special class of enzymes of major importance in detoxification of drugs and environmental chemicals.
- CYP enzymes are an essential part of microbial biology and function in fundamental biochemical processes of oxidation and reduction, *redox,* the transfer of electrons and chemical bonding. These are the fundamental atomic-level particle interactions of life itself. Glyphosate has been shown to disrupt the activities of multiple CYP enzymes.
- Among the many devastating effects may be the disruption of vitamin D3 activation in the liver.

- Glyphosate's alteration of CYP function has been correlated with under activation of Vitamin D in the liver. With CYP1B expression disrupted by glyphosate, retinoic acid levels rise, leading to faulty bile synthesis and impaired fat metabolism. The dramatic rise in "fatty liver" syndrome in the past years correlates with increases use of GM crops. Human CYP7B1 mutations are also implicated in spastic paraplegia and movement disorders associated with demyelination of the spinal cord.

GLYPHOSATE AND CHOLESTEROL

- Bile acids are poorly secreted in the presence of glyphosate, and CYP7A1 mutations are associated with high cholesterol content in the liver as well as elevated serum LDL. CYP enzyme disruption occurs when glyphosate from GM foods reach the liver via high concentrations in the portal vein.
- Cholesterol is an important constituent of all cell membranes, which are the “brain” of the cell, a major site of molecular cross-talk or interaction, where receptors bind to ligands and information crosses from outside the cell to its interior on the way to the nucleus to affect DNA transcription and gene encoding.

Cholesterol is the mother molecule of all steroid hormones, including the estrogens and androgens.

SUMMARY OF IMPAIRED CYP FUNCTION

Effects include compromise of:

- cholesterol regulation & steroid hormone synthesis
- cell membrane synthesis, receptor binding and nuclear penetration
- normal cell metabolic function
- vitamin D3 genesis
- detox of xenobiotics
- regulation of retinoic acid synthesis

OTHER PATHOLOGIES

- Lysosomal disorders: lysosomes are key players in phagocytosis, pinocytosis (cell drinking), and the processes of importing and exporting crucial materials from the cell (endo and exo cytosis). Lysosome disorder is a significant feature of dementias, Parkinson's, CV disease and cardiac failure.
- Abnormal blood clotting and eNOS (nitric oxide synthase) dysfunction have also been reported.

DEPRESSION AND SLEEP DISORDERS

Features:

- lower serum tryptophan
- increased gut permeability
- increased inflammatory markers (Il-6, IL-8)
- increased rates of suicides and violent behaviors
- impaired melatonin production

ZINC DEFICIENCY

- Vitamin D3 synthesis by hepatic CYP3 enzymes is known to be impaired by glyphosate
- Zinc deficiency leads to impaired immunity
- Zinc deficiency common in general population, especially the elderly
- Studies show zinc supplementation is ineffective in dementia patients unless vit A and vit D are simultaneously supplemented
- Thus, vit D deficiency may exacerbate zinc deficiency, leading to compromised immunity, falling hair, brittle nails, anosmia and loss of taste.

GLYPHOSATE EFFECTS

- Research show glyphosate induces increased inflammatory cytokine production.
- Early studies indicate glyphosate disrupts endocrine signaling with sequelae of tissue overgrowth in the breasts.
- Rats studies show LT glyphosate ingestion is associated with massive mammary tumors.
- Breast cancer risk is known to be associated with polymorphisms of the CYP gene CYP1A2 and the enzyme SULT1A1, which lead to altered expression of both estrogen and testosterone and other risk factors for breast ca. Glyphosate's disruption of sulfate bioavailabilty via altering SULT1A1 and altering CYP1A1 gets compounded by glyphosate's depletion of tryptophan (leading to obesity) and diminished sulfate synthesis (impairing detox).
- Obese post menopausal women are at far greater risk for breast cancer than lean premenopausal women.
- Subcutaneous fat expresses aromatase in breast tissue and general body adipose tissue.

Belize: Herbs of the Rainforest

16 CE hours available from NYCC, ACBN eligible

Join Dr. Jeanne D'Brant in a profound exploration of the natural wonders of the Central American rainforest. Gain hands-on experience of the profound healing power of rainforest medicinal and a new appreciation of the exquisite splendor of the flora and fauna of Belize. Tour the extensive rainforest medicinal trails at Ix Chel Farm and Barton Creek.

Itinerary 8 days
Cost: $3,450 All Inclusive

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- **7 nights luxury hotels, including break fast, lunch and dinner**
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- **riverboat and motor coach excursions**
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CONTACT

- Jeanne D'Brant, DACBN, DC, CTN, RH (AHG)
- website: http://drjeanne.org
- Facebook: Talisman Cultural Tours
- Email: drjeanne@optonline.net