

JUVENILE PHYTOHORMONES & BIOLOGICAL ACTIVITIES

By

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1. **Abscisic acid (ABA)** a sesquiterpene terpenoid derived from C₄₀ carotenoids.
2. **Auxins:** of which they are five major Auxins: Indole-3-Acetic Acid (IAA) is the most abundant, Indole-3-Butyric Acid (IBA), Indole-3-Propionic Acid (IPA), 2-Phenylacetic Acid (PAA), with an indole ring structure derived from the amino acid, tryptophan.
3. **Brassinosteroids** derivative from 5 α -cholestan.
4. **Cytokinins** derived from adenine include: Kinetin, Zeatin, 6-isopentenyladenine, and benzyl adenine.
5. **Gibberellins** (the largest group of plant hormones) terpenoids related to sterols.
6. **Jasmonates:** Jasmonic acid (JA) – Methyl jasmonate (MeJA) – *cis*-jasmonone and derived from the fatty acid α -linolenic acid.
7. **Polyamines**
8. **Salicylates** are synthesized from the amino acid phenylalanine.
9. **Strigolactones** are a group of sesquiterpene lactones (terpenoids) and are synthesized from a carotenoid precursor.
10. **Systemin**

Plant Growth Hormones PGH	Plant Immune Hormones PIH	Plant Stress Hormones PSH
<ul style="list-style-type: none"> • Auxins • Brassinosteroids • Cytokinins • Gibberellins • Strigolactones • Polyamines 	<ul style="list-style-type: none"> • Abscisic Acid • Auxins • Brassinosteroids • Cytokinins • Jasmonates • Salicylates • Strigolactones • Systemin 	<ul style="list-style-type: none"> • Abscisic Acid • Brassinosteroids • Jamonates • Salicylates • Strigolactones • Systemin

JUVENILE PHYTOHORMONES & THEIR BIOLOGICAL ACTIVITIES

Having over 1,057 biological activities in the human body.

Abscisic Acid (ABA) (C₁₅H₂₀O₄) 110 activities.

<p>Activate adenylate cyclase (AC) that catalyze the conversion of adenosine triphosphate (ATP) to 3',5'-cyclic AMP (cAMP) and pyrophosphate.</p> <p>Activate chemokinesis</p> <p>Activate PPAR-γ</p> <p>Acts as a human cytokine</p> <p>Akt/mTORC₂ activator</p> <p>Antiadipogenic</p> <p>Antiaging</p> <p>Anti-alcoholism</p> <p>Anti-Alzheimerian</p> <p>Antiangiogenic</p> <p>Anti-atherosclerotic</p> <p>Anticancer: breast, colon, gastric, leukemia, liver, oral tongue squamous cell carcinoma, pancreatic, prostate and skin.</p> <p>Anti-colitis including ulcerative colitis</p> <p>Anti-Crohn's disease</p> <p>Antidepressant by RA inhibition</p> <p>Antidiabetic</p> <p>Anti-epileptic</p> <p>Anti-Huntington's disease</p> <p>Antihyperglycemic</p> <p>Antihypertensive</p> <p>Antihypertriglyceridemic</p> <p>Anti-hypoxic</p> <p>Anti-IBD</p> <p>Antiinflammatory (potent)</p> <p>Anti-ischemic</p> <p>Anti-metabolic syndrome</p> <p>Antimetastatic</p> <p>Anti-mood disorders</p> <p>Anti-neuroinflammatory</p> <p>Anti-neuropathy</p>	<p>Increase NO and eNOS</p> <p>Increases bone morphogenetic protein-7</p> <p>Increases liver detoxifying enzymes</p> <p>Increases NMDAR hypofunction, a novel mechanism of NMDA receptor potentiation.</p> <p>Increases WBCs</p> <p>Induces differentiation of tumor cells or reverts cancerous cells cycle to normal cells.</p> <p>Inhibitor of the MEP pathway against broad-spectrum microbial infections: anti-H-pylori, antimalarial, and antiprotozoal.</p> <p>Inhibits the growth and induces the differentiation of cancer cells.</p> <p>Innate immune responses regulator</p> <p>Insulinemic</p> <p>LANCL₂ agonist</p> <p>Lipid peroxidation inhibitor</p> <p>LPS inhibitor</p> <p>Melatonin agonist</p> <p>Modulator of PPAR-γ: regulates fatty acid storage and glucose metabolism.</p> <p>Morphogenic</p> <p>Neuroprotective</p> <p>Neutralize hCG</p> <p>NF-κB inhibitor</p> <p>NMDA receptor potentiator</p> <p>Osteogenic</p> <p>Peripheral immune response regulator</p> <p>PGE₂ inhibitor</p> <p>PON1 gene regulator</p> <p>Pro-inflammatory cytokines modulator</p> <p>Pro-insulin</p> <p>Promotes digestion</p> <p>Promotes somatic cell fitness</p>
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<p>Antiobesity</p> <p>Antiosteoporotic</p> <p>Anti-Parkinson</p> <p>Antiproliferative</p> <p>Antiprostaglandin</p> <p>Anti-Schizophrenic</p> <p>Anti-stroke</p> <p>Antitumor</p> <p>Apoptotic</p> <p>Assist in the removal of toxins from fat cells</p> <p>Autocrine microglial activation</p> <p>Autocrine/paracrine mobilization and activation of MSC function.</p> <p>Cardioprotective</p> <p>Control synaptic plasticity and learning memory function.</p> <p>COX-2 inhibitor</p> <p>CRH regulator</p> <p>Cytotoxic</p> <p>Decrease extreme hypercholesterolemia</p> <p>Decrease intracellular Na⁺ and K⁺</p> <p>Decrease stress by cortisol inhibition</p> <p>Enhanced GLP-1 transcription, glucose homeostasis.</p> <p>Glycemic control</p> <p>Granulocyte activation</p> <p>Hypolipidemic</p> <p>Hypotensive</p> <p>Immunomodulator</p> <p>Increase cAMP</p> <p>Increase Cyclic ADP-ribose</p> <p>Increase GLP-1</p> <p>Increase intracellular Ca²⁺ concentration thereby increases apoptosis.</p>	<p>RARα antagonist, reduce protein expression of (mtP53, Ki-67, Cyclin D1 and mRNA expression of mtP53, hTERT.</p> <p>Reduce elevated fibrinogens</p> <p>Regenerative by activating cyclic ADP-ribose-mediated expansion and stimulation of MSC cells, contribute to tissue repair.</p> <p>Regulate cell cycle arrest</p> <p>Regulate metabolic pathways involved with glucose transporters, hexokinase, pyruvate kinase M2, lactate dehydrogenase A, pyruvate dehydrogenase kinase, fatty acid synthase and glutaminase beneficial for chemotherapy resistance.</p> <p>Retinoic acid (RA) inhibitor</p> <p>Reverse insulin resistance</p> <p>ROS inhibitor</p> <p>Stimulate insulin release through pancreatic cells and also increase sensitivity of fat cells to insulin, which makes it a potent weapon against metabolic syndrome and diabetes type 2.</p> <p>Stimulate hemopoietic stem cells progenitors</p> <p>Stimulate pancreatic β-cells</p> <p>Stimulates ATP</p> <p>Stimulates endocrine glands secretions of enzymes and hormones.</p> <p>Stimulates phagocytosis</p> <p>Suppress aortic vascular VCAM-1 and MCP-1 expression and plasma MCP-1 concentrations.</p> <p>Target glucose homeostasis</p> <p>TNF-α inhibitor</p> <p>Triggers NO</p> <p>Upregulates ApoE deficiency</p> <p>Upregulates glucose transporter Glut4</p> <p>UV-B inhibitor</p> <p>Vasculoprotective</p> <p>Vasodilator</p>
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AUXINS

1. **Indole-3-Acetic Acid (IAA)** (C₁₀H₉NO₂)
2. **Indole-3-Butyric Acid (IBA)** (C₁₂H₁₃NO₂)
3. **Indole-3-propionic acid (IPA)** (C₁₁H₁₁NO₂)

4. **2-Phenylacetic Acid (PAA)** (C₈H₈O₂)
5. **4-Chloroindole-3-Acetic Acid (4-Cl-IAA)** (C₁₀H₈ClNO₂) unknown human biological activities.

Auxins having a total of 94 activities.

Indole-3-Acetic Acid (IAA) 46 activities.

5-hydroxy indole acetic acid, is the final excretion product of serotonin and normalized serum serotonin level. This could potentially play an *adjuvant* role in the treatment of depression.

A non-steroidal antiinflammatory drugs (NSAIDs).

Anti-ALS

Anti-Alzheimerian

Anti-arthritis

Antiasthmatic

Anticancer: bladder, breast, colon, gastric, kidney, leukemia, liver, melanoma, and prostate.

Antidementia

Antidepressant

Antidiabetic

Anti-IBD

Antiinflammatory

Anti-Lupus

Antimetastatic

Anti-migraine

Anti-MS

Anti-myalgia

Antineurodegenerative

Anti-Parkinsonian

Antiproliferative

Antithrombosis

Anti-thyroiditis

Antitumor

Apoptotic

Auxin is a sort of a "**Molecular Glue**" that improves the ability of transport inhibitor response (TIR1) to bind to its peptide target. In the absence of auxin, TIR1 does not bind to its target as tightly. TIR1 that are known to be involved in the proliferation of cancer.

Auxins and ethanolamine synergistically elevated the stimulation of DNA synthesis in hepatocytes

IAA is a **Ubiquitin Ligase agonist**, promoting protein-protein interaction rather than disrupting the interaction. **Dysfunctions of this system** can disrupt cellular homeostasis and lead to a host of disorders.

IAA plays an essential role in the coordination of many growth factors and behavioral processes.

IAA **regulate homeostasis, cell cycle, and DNA repair** pathways.

Immunotoxins for leukemia

Inhibits multidrug resistance protein 4 (MRP4) and breast cancer resistance protein (BCRP).

Potent anticancer properties

Regulates gene expression by promoting Skp, Cullin, F-box-protein containing complex (SCF) ubiquitin-ligase-catalyzed degradation of the Aux/IAA transcription repressors. SCF-mediated proteolytic control of cellular processes.

Removes any substances that increase estrogen, especially of interest are the polychlorinated biphenyls (PCBs) plasticizers that mimics estrogen and well-known to disrupt the endocrine system. IAA helps in the detoxification from xenoestrogens.

Specific indole-producing bacteria can reduce intestinal inflammation.

Stimulates cell growth and provides better resistance to disease.

Stimulates or inhibits the expression of specific genes. Auxin induces Transcription by targeting for degradation members of the Aux/IAA family of transcriptional repressor proteins.

Stimulation of enzymes - Indoles, which are found in auxins, stimulates enzymes that make estrogen less effective and could reduce the risk for breast cancers. Indoles, detoxifies excess xenoestrogens.

The SYNERGISTIC ACTIVITY of "IAA with BRs and CKs" plays an important role in the **prevention of organ death and abortion**.

Treatment with IAA induces reactive oxygen species (ROS) which increases flavonoid antioxidant activity.

<p>inhibitors have been shown to be effective in reducing kynurenic acid production, with associated changes in neurotransmitter release and pro-cognitive effects.</p> <p>A protective effect against chromium III (Cr-III)-induced carcinogenesis by direct *OH scavenging ability, and H₂O₂, which thereby reduces the formation of the damaged DNA product, 8-hydroxydeoxyguanosine (8-OH-dG). An effective radical scavenger.</p> <p>Activates PXR regulates intestinal barrier function through TLR4.</p> <p>Antagonizes toxin-induced mitochondrial damage in the brains triggered by the electron transport inhibitors such as doxorubicin and antimycin A, and the proton potential dissipater carbonylcyanide-p-trifluoromethoxyphenylhydrazone (FCCP).</p> <p>Antiasphyxia</p> <p>Antidysbiosis</p> <p>Antidystonia</p> <p>Antiepileptic</p> <p>Antiischemic</p> <p>Antineurodegenerative</p> <p>Antiviral agent against HCV being a dimerization inhibitor of core, the capsid protein of the virus.</p> <p>A potent neuroprotective effect against deposition of amyloid β-protein and against a variety of oxidotoxins. Amyloid-β and concomitant oxidative stress are major pathogenic events in Alzheimer's disease (AD).</p> <p>Cytokines modulator: activator of the antiinflammatory cytokines and inhibitor of pro-inflammatory cytokines.</p>	<p>Increases neurotransmitters levels in the brain.</p> <p>Increases the activity of mitochondrial Complex I – generator of half the number of free radicals produced by the mitochondria – and Complex IV, activities that tend to diminish through the course of aging.</p> <p>Inhibitor of mucosal myeloperoxidase (MPO) enzyme activity.</p> <p>IPA is an even more potent scavenger of hydroxyl radicals than melatonin, the most potent scavenger of hydroxyl radicals that is synthesized by human enzymes.</p> <p>IPA on longevity increases the size, fertility and 300% longer lifespan than their untreated peers.</p> <p>Keeps peace with the aryl hydrocarbon receptor (AhR) signaling, modulates the mucosal microbiota.</p> <p>Maintains host-microbe homeostasis at mucosal surface.</p> <p>Neuroprotective</p> <p>NF-kB inhibitor</p> <p>Reduces DNA damage and lipid peroxidation in neurons.</p> <p>Regulate intestinal barrier function through PXR. PXR is a physiologic regulator of intestinal permeability indispensable in all intestinal inflammatory conditions and diseases.</p> <p>Reverts age-dependent decline in mitochondrial proton motive force and energetic capacity.</p> <p>Specific indole-producing bacteria can reduce intestinal inflammation.</p> <p>TNF-α inhibitor</p>
<p>BRASSINOSTEROIDS (BRs)</p> <p><i>are The Master Regulators of both Phytohormones as well as for Humans Steroidal Hormones Dysfunction. In fact, BRs are the Biochemical Exemplification of Phytosociology analogous to Human Physiology “Steroidal – Similarities.” With reported 114 known biological activities so far known having human health benefits.</i></p>	
<p>5αR inhibitor</p> <p>Activates the Innate Immune System.</p> <p>Adaptogen Polycrest: Preparation for a new activity in response to environmental stimuli (such as, fighting, fleeing, mating). Preparation for a new phase of life (for example, puberty, caring for offspring, menopause, andropause).</p>	<p>DNA repair</p> <p>Dopaminergic neurons protector.</p> <p>Effective for reducing plaque formation in arteriosclerosis or/and restores and repairs the reticulo endothelial system. Temporal arteritis.</p> <p>Endocrine-Immunomodulation</p>

<p>Alter human P450 activity, which is involved in the synthesis of toxic chemicals in humans and plants, involved in that chemical's metabolism and elimination when it is ingested and seen as a noxious foreign compound.</p> <p>Analgesic</p> <p>Androgen modulator</p> <p>Anesthetic</p> <p>Anti-acne</p> <p>Anti-acne vulgaris</p> <p>Anti-androgenic alopecia (AGA)</p> <p>Antiangiogenic</p> <p>Anti-autoimmune</p> <p>Anti-benign prostatic hyperplasia (BPH)</p> <p>Antibiotic</p> <p>Anticancer (breast, cervical, leukemias, lung, melanoma, osteosarcoma, and prostate).</p> <p>Anticancer for hormones positive malignancies.</p> <p>Anti-CFS and anti-CFIDS, anti-mononucleosis.</p> <p>Anti-congenital adrenal hyperplasia.</p> <p>Antidiabetic</p> <p>Antiecdysteroid</p> <p>Antifungal</p> <p>Antigenotoxic</p> <p>Antiherpetic</p> <p>Anti-Hidradenitis suppurative causing abscesses or subcutaneous boil-like infections.</p> <p>Anti-hirsutism</p> <p>Anti-hyperandrogenemia</p> <p>Antihyperglycemic</p> <p>Anti-hyperhidrosis (excessive sweating)</p> <p>Anti-hypernatremia</p> <p>Anti-hypersexuality</p> <p>Antihypertensive</p> <p>Antiinfertility females and males</p> <p>Antiinflammatory like that of no other steroids and is not an immunosuppressant but rather an immuno-regulator. Excellent for Lupus, Celiac disease, and Ulcerative Colitis.</p>	<p>Enhance the function of liver microsomes – crucial for the safe detoxification of xenobiotics.</p> <p>Enhanced the level of ascorbic acid, and carotenoids concentration.</p> <p>Fungicidal</p> <p>H₂O₂ inhibitor</p> <p>Helps in maintaining Homeostasis</p> <p>HMG-CoA reductase (or natural "Statins"). Reduces Total Cholesterol and low density lipoproteins (LDL) while improving high-density lipoproteins (HDL), also reduce C-Reactive Protein and Fibrinogens.</p> <p>Hypocholesterolemic</p> <p>Immunomodulator</p> <p>Immunomodulator normalizing an over-reactive antibody by improving B-cells antigen response.</p> <p>Improves ascorbate peroxidase (APOX) and dehydroascorbate reductase (DHAR).</p> <p>Improves cognitive function.</p> <p>Increase detoxifying enzymes: catalase (CAT), superoxide dismutase (SOD) and glutathione reductase (GR).</p> <p>Increase HDL</p> <p>Increase hexokinase activity in all tissues studied, thus reducing blood glucose level, increases hemoglobin and high density lipoprotein (HDL).</p> <p>Increase insulin secretion by pancreatic β cells.</p> <p>Increase metabolism (the breakdown or synthesis of biological molecules).</p> <p>Increases all liver detoxifying enzymes.</p> <p>Increases in 5' adenosine monophosphate-activated protein kinase (AMP) concentration in cellular energy homeostasis.</p> <p>Increases the level of glutathione and phytochelatin enzyme synthase in the chelation of toxic metal stress.</p> <p>Induced apoptosis (Programmed Death Cell)</p> <p>Inhibit interleukin 6 (IL-6), which is primarily responsible for the triggering off the autoimmune reaction. Thyroid function can resume normal activity when the autoimmune responses are triggered off.</p> <p>Inhibits cancer cell growth</p>
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Antimetastatic	Inhibits oxidative stress and damage
Antimicrobial	Insulinemic
Anti-MS	Keratolytic (anti-wart or anti-corn)
Antimycotic	Mitogen-activated protein (MAP) kinase modulator.
Antineurodegenerative	Modulator of testosterone, dehydroepiandrosterone sulfate (DHEAS), dehydroepiandrosterone (DHEA), androstenedione, and androstanediol.
Antineurotoxic	Musculotropic: promoting growth, repair, and maintenance of the musculoskeletal system.
Antioxidant	Neuronal
Anti-Parkinson	Neuroprotective
Anti-Polycystic ovarian syndrome (PCOS)	Potent corrector of adrenal steroidal dysfunction.
Antiproliferative	Prevent neuronal apoptosis.
Antipyretic	Prostaglandin inhibitor, COX-1 and COX-2 inhibitor, Phospholipase A ₂ production inhibitor and Anti-leukotrienes.
Antirheumatic	Protect the translational machinery and heat-shock protein synthesis.
Antiseborrheic	Protects dopaminergic cells
Antitumor	Protein Kinases and enzymes modulator
Antitumor adrenal and ovarian	Reduce CRP
Antiviral against: Junin virus (JV) (Arenaviridae); measles virus (MV) (Paramixoviridae), herpes simplex type 1 and 2 (HSV-1 and HSV-2).	Reduce hemoglobin A1c
Apoptotic	Reduce the activities of peroxidase (POD), and polyphenol oxidase (PPO).
Auto-immune reactions immunomodulator BSKs (brassinosteroid signaling kinases). <i>Insensitive-Suppressor-Inhibitor-Regulator.</i>	Regulates elevated Leptin but only as an <i>adjuvant</i> (Phosphorylation of reductase).
BRs for <i>electrolytes homeostasis especially in hypernatremia.</i>	<i>Regulator of steroidal hormone dysfunctions.</i>
Carcinomic gene disruptor-nuclear receptor interactions.	ROS inhibitor
Cell expansion in the presence of a potentially growth-limiting cell wall.	Specific immunoprecipitation and purification of receptor-protein complexes.
Chemopreventive	Stimulates the synthesis of pathogenesis-related proteins in bacterial, fungal, and viral infections by increasing the salicylates level in immune response.
Chemotherapeutic	Stimulation or inhibition regulator of growth and development. <i>Bipolar/Biphasic.</i> For genetic disorders especially related to dwarfism or growth problems.
Control of the Reproductive Cycle and Fertility. The SYNERGY “Auxins Indole-3-acetic acid-Brassinosteroids-Cytokinin” plays an important role in Preventing Organ Death and Abortion and miscarriages.	The ultimate androgen regulator
Cytopathic (CPE)	Toxic metals detoxification
Cytotoxic	
Decrease elevated fibrinogens	
Decrease LDL	
Decrease the anti-apoptotic protein Bcl-2	

<p>Detoxifies pesticides and herbicides-insecticides. BRs had a positive effect on the activation of glutathione S-transferase (GST), peroxidase (POD), and glutathione reductase (GR).</p>	<p>Very effective in correcting chronic allergies-related causes by increasing immune competence, liver, and adrenals dysfunctions.</p>
<p>CYTOKININS (CKs) Kinetin (C₁₀H₉N₅O) – Zeatin (C₁₀H₁₃N₅O) and others, 64 activities.</p>	
<p>Adenosine (A_{2A})-receptor signaling antagonist</p> <p>AChE inhibitors, zeatin is the most potent AChE inhibitor in AD.</p> <p>Activate caspase-3 and selectively induces apoptosis in cancer cells through the classical mitochondria dependent apoptosis pathway, leaving unscathed healthy cells.</p> <p>Alleviate diabetic symptoms and complications, including fasting serum glucose, without affecting insulin levels.</p> <p>Anti-Huntington's disease (HD)</p> <p>Anti-alcoholism withdrawals</p> <p>Anti-Alzheimerian</p> <p>Anticancer activities against: colon, basal cells, bladder, breast, colon, leukemia, liver, melanoma, and multiple myelomas.</p> <p>Anticancer: induction of p21^{sup}.WAF-1 protein, the natural cyclin-dependent kinases inhibitor, by CKs activity in breast cancer cell line MCF-7-molecular mechanism of the effect.</p> <p>Anticarcinogenic</p> <p>Anticholinesterase</p> <p>Antidementia</p> <p>Antidiabetic type I and II</p> <p>Anti-dyskinesia</p> <p>Antifungal</p> <p>Anti-gout</p> <p>Anti-graft rejection</p> <p>Anti-hyperpigmentation</p> <p>Anti-ischemic</p> <p>Anti-multiple sclerosis (MS)</p> <p>Antineoplastic</p> <p>Antineurodegenerative</p> <p>Antioxidant protects against free radicals that improves the skin's natural moisture barrier and visibly reduces wrinkles.</p>	<p>Control the cell cycle both at the G1/S which prevent any mistakes and G2/M transitions involved in the cellular response to DNA damage.</p> <p>Control the defense status of specific organs and thus contribute to the regulation of optimal defenses against bacterial infection.</p> <p>Cytotoxic</p> <p>DNA and cellular repair</p> <p>Dopamine D₂ receptor agonist</p> <p>ERK, JNK and p38 MAPKs signaling pathways inhibitor.</p> <p>Immunomodulator</p> <p>Improve human digestion system utilizing nutrients 20 to 30% better absorption. Thus, correct nutritional deficiencies.</p> <p>Influences on the cellular DNA repair mechanisms.</p> <p>Inhibit lipofuscin</p> <p>Inhibitors of Trypanosoma brucei phosphoglycerate kinase.</p> <p>Kinetin have been shown to reduce wrinkles and improve skin texture, reduce telangiectasia, and mottled hyperpigmentation skin.</p> <p>Kinetin decreased hexokinase activity significantly in the liver and kidney, but not significantly in other tissues, and significantly reduced serum cholesterol level.</p> <p>Kinetin riboside preferentially induces apoptosis by modulating Bcl-2 family proteins and caspase-3 in cancer cells.</p> <p>Kinetin's are potent anti-senescence agents highly correlated with their ability to influence membrane by its lipid peroxidation inhibition.</p> <p>Neuroprotective</p> <p>Platelet aggregation inhibitor</p> <p>Plays a prominent role in the regulation of cell cycle – mitosis – endoreplication and cell proliferation.</p> <p>Prevent β-amyloid protein formation of plaque in the brain.</p> <p>Regenerative</p>

<p>Antiparasitic against <i>Trypanosoma brucei</i> known as sleeping sickness.</p> <p>Anti-Parkinson's disease (PD)</p> <p>Anti-polycystic kidney disease (PKD)</p> <p>Antiproliferative effect of CKs is attributed to the inhibition of cyclin-dependent kinase (CDK) activity.</p> <p>Antipsoriatic</p> <p>Anti-restenosis prevents the restriction of blood flow in coronary artery blockage.</p> <p>Anti-rheumatoid arthritis (RA)</p> <p>Antisenescence</p> <p>Anti-systemic lupus erythematosus (SLE)</p> <p>Anti-thrombosis</p> <p>Antitumor</p> <p>Cardioprotective</p> <p>CDK1 inhibitor responsible for DNA repair by CKs.</p> <p>CDK2 inhibitor responsible for its anticancer, antiproliferative and antitumor activities by CKs.</p> <p>CKs are expert's selective cyclin dependent kinase (CDK) inhibitors CDK1 and CDK2 that play an essential role in the maintenance of normal cell cycle, tissue homeostasis, and in tumor suppression.</p>	<p>Stimulating RNA and protein synthesis</p> <p>The SYNERGY "IAA-BRs-CKs" plays an important role in preventing organ death and abortion.</p> <p><i>trans</i>-Zeatin was shown to attenuates ultraviolet (UV) induced down-regulation of aquaporin-3 in cultured human skin keratinocytes expose anti-photoaging and anti-hyperpigmentation. <i>trans</i>-Zeatin inhibits UVB-induced MMP-1 expression, which may be mediated by inhibition of ERK, JNK and p38 MAPKs signaling pathways in HSFs. <i>trans</i>-Zeatin is a potential agent for the management of skin photoaging hyperpigmentation prevention.</p> <p>UV inhibitor for the treatment of skin photoaging.</p> <p><i>When CKs is present the DNA is replicated perfectly every time.</i></p> <p>Zeatin antiaging activities in the prevention of cell enlargement, reduction of intracellular debris, prevention of actin polymerization, and enhancement of cellular ability to decompose hydrogen peroxide H₂O₂ and to cope with ethanol and oxidative stresses.</p>
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FLORIGEN 9 activities.

The elusive identity of florigen. Scientists never before knew that a phytohormone could be a complex mixture of protein and RNA. More recently, generated genetic and biochemical data suggest that florigen is a phytohormone and protein complex encoded by the gene belonging to the phosphatidylethanolamine-binding protein (PEBP).

A family that are highly conserved throughout nature and have no significant sequence homology with other proteins of known structure or function. A variety of biological roles have previously been described for members of this family, including ***lipid binding, roles as odorant*** effector molecules or ***opioids, interaction with the cell-signaling machinery***, regulation of flowering plant stem architecture, and ***a function as a precursor protein of a bioactive brain neuropeptide***. The structure also suggests that ligand binding may lead to coordinated release of the N-terminal region of the protein to form the hippocampal ***neurostimulatory peptide***, which is known to be active in the development of the hippocampus. These studies are consistent with a primary biological role for human PEBP as a transducer of signals from the interior membrane surface (Banfield et al., 1998). Florigen can stimulate ***alpha wave brain activity***, inducing a relaxed mental state, and increasing REM sleep. Could potentially be beneficial for sleep apnea and fibromyalgia.

GIBBERELLINS

The largest group of phytohormones and terpenoids related to sterols. 136 fully characterized gibberellins that have been so far isolated from all sources. Only about 15 of the GA's have biological activity the rest are likely breakdown products of, or precursors to, the active ones. The most bioactive GAs is GA₁, GA₃, GA₄, and GA₇. With 54 activities.

<p>A <i>metabolically stable</i> and <i>potent P2Y₂ agonist</i>.</p> <p>Androgenic</p> <p>Antiaging by its regenerative capacity on various aspect of aging increasing cell renewal and tissue growth.</p> <p>Anti-allergies</p> <p>Antiallopecic</p> <p>Antiangiogenic</p> <p>Anti-arteriosclerotic</p> <p>Antiarthritic</p> <p>Anti-asthmatic</p> <p>Anticancer (acute myeloid leukemia, skin melanoma).</p> <p>Anti-COPD</p> <p>Anti-Cystic Fibrosis (CF) by inhibiting sodium absorption, restore chloride conductance, and rehydrate the CF airway surface. Also, increase mucociliary clearance.</p> <p>Antidiabetic</p> <p>Anti-dry eyes</p> <p>Antihyperglycemic</p> <p>Anti-infertility males: caused a significant increase in semen ejaculate volume (EV), sperm concentration (SCon), total sperm out-put (TSO) and sperm motility (%). Increase live sperm and decrease abnormal sperm. In males induce testicular steroidogenesis markers: 3β-hydroxysteroid dehydrogenase (3β-HSD), 17β-hydroxysteroid dehydrogenase (17β-HSD), increase tissue testosterone (T) content, increase steroidogenic acute regulatory protein (StAR) and androgen binding protein (ABP).</p> <p>Antiinflammatory activity thru the modulation of pro-inflammatory cytokines: interleukins: IL-1β, IL-18, TNF-α, and nitric oxide (NO).</p> <p>Anti-neurodegenerative</p> <p>Anti-osteopenic/morphogenic</p> <p>Anti-osteoporotic</p> <p>Antitumor</p> <p>Apoptotic</p> <p>Chemoattractant for phagocytes</p> <p>Decrease platelet counts</p>	<p>GA₃ increases cytosolic serum calcium concentration, thus induction of apoptosis and able of osteogenic activity.</p> <p>Hypoglycemic mild</p> <p>In males increases the secretion of testosterone and in females increases estradiol secretion.</p> <p>Increase cellular α-amylase expression and can be useful for therapeutic application in human's salivary gland regeneration and as well improving carbohydrates digestion.</p> <p>Increase human hair growth for the treatment of alopecia.</p> <p>Increase uric acid antioxidant activity</p> <p>Increases adenosine triphosphate (ATP) cellular energy.</p> <p>Increases libido</p> <p>Increases the number of RBC, WBC, and Neutrophil.</p> <p>Modulator of P2Y₂ receptor signaling expressed in the kidney: collecting duct, in the modulation of water transport for the maintenance of water homeostasis.</p> <p>Neuroantiinflammatory</p> <p>Neuronal</p> <p>Neuroprotective</p> <p>P2Y₁ receptor is a putative target for melanoma therapy (White et al., 2005).</p> <p>P2Y₂ as a morphogen receptor that potentiates neurotrophin signaling in neuronal development and regeneration.</p> <p>P2Y₂ receptor agonist promote mucociliary clearance expectorant and as well mucosal hydration, potential for the treatment of Allergies, Asthma, Bronchiectasis, Bronchitis, Chronic Obstructive Pulmonary Diseases (COPDs), Cystic Fibrosis (CF), Dry eyes, stimulate subretinal fluid reabsorption in conditions that result in Retinal detachment or Retinal edema and increase neurones in the brain. Wound healing and rejuvenation, renewal, repair, and maintenance of healthy skin mucosal hydration and regenerate connective tissues.</p> <p>Purinergic signaling has been implicated in many biological processes, adenosine triphosphate (ATP) and other extracellular nucleotides may have therapeutic potential in the treatment of some</p>
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<p>Direct androgenic-like action on testes in male and stimulates completion of spermatogenesis.</p> <p>GA₃ and JA in the prevention or treatment for arteriosclerotic disease GAs increase the expression of P2Y purinergic receptors are a family of <i>newly characterized plasma membrane molecules</i> involved in several and yet only partially known cellular functions such as vascular reactivity, apoptosis, and cytokine secretion.</p> <p>GA₃ and JA on human skin keratinocytes increases cell growth, stimulates cell turnover, and increase the expression of mucin-1, mucin-2, mucin-3A, mucin-3B, mucin-4, mucin-5B, mucin-5AC, mucin-6, mucin-7, mucin-11, mucin-13, mucin-15, mucin-17, mucin-19, or mucin-20 genes thus, promotes the secretion of mucus within the reproductive tract of a female mammal for the treatment of vaginal atrophy.</p> <p>GA₃ decrease in alanine aminotransferase (ALT) and aspartate aminotransferase (AST) liver enzymes. But increases Alkaline phosphatase (ALP) and acid phosphatase (AcP) enzymes activities.</p> <p>GA₃ delay senescence</p> <p>GA₃ effect on α-amylase is probably through encouraging tissue lipogenesis.</p> <p>GA₃ increase hexokinase activity in liver thus decreasing glucose.</p>	<p>cancer by signaling through P2Y purinoceptor 2 (P2Y₂). Different P2Y₂ receptor subtypes have been identified in a variety of different cancer types, in both primary samples of human cancer tissue and cell lines. <i>In vivo</i> studies of the use of ATP suggest that it can decrease the rate of cancer cells growth, and the first clinical trials have been undertaken. Thus, agents acting at P2Y₂ receptors may provide a therapeutic target in the treatment of cancer (White & Burnstock, 2006).</p> <p>Reduce elevated creatinine level having a renoprotective effect.</p> <p>Repairs and protects connective tissues integrity</p> <p>Stimulates RNA and protein synthesis</p> <p>Stimulation, of Tissue Excitation and Toxins Elimination.</p> <p>The novel and superior polypharmacological synergistic – interactions – activities of three juvenile hormones: ABA, GAs, and JA are effective, Purinergic Signaling System Receptors Modulators (agonists/antagonists).</p> <p>Wound healing and a potent antiinflammatory attributed to its polymorphonuclear leukocyte infiltration inhibition.</p>
JASMONATES	
<p>Jasmonic acid (JA) – <i>methyl-jasmonate</i> (MeJA) – <i>cis-jasmone</i> derived from the fatty acid α-linolenic acid. With 54 activities.</p>	
<p>A most important characteristic of jasmonates is their ability to selectively only target and kill cancer cells, while leaving unscathed healthy normal cells. Having a wide-broad spectrum anticancer activities against a multitude of cancers include: brain, bladder, breast, cervical, colon, endometrial, esophageal, gastric, leukemia's, liver, lung, lymphoma, melanoma, pancreas, multiple myeloma, pancreas, prostate and sarcoma cancers. The role of jasmonates, having a profound effect in the multifactorial targets for the prevention of cancer's development is undeniable. Furthermore, is the real potential of MeJA in the treatment of oncological malignancies?</p> <p>Antiangiogenic</p> <p>Antianxiety</p>	<p>JA has been shown to upregulate collagens, hyaluronic acid and fibrillin. A safe and effective phytohormone for cosmetic use in the treatment for reducing the appearance wrinkles, reduce photoaging, improves texture, and pores of the facial skin.</p> <p>Jasmonates are involved in an apoptotic response.</p> <p>Kills prostate cancer cells <i>via</i> the inactivation of the 5-lipoxygenase enzyme.</p> <p>Lipids peroxidation inhibitor</p> <p>MeJA – JA and cis-jasmone complex can target all multifactorial cause of cancers, causing a catastrophic cancer cellular failure and subsequent cell apoptosis (except when inducing redifferentiation).</p>

Antibacterial and **antifungal** properties. MeJA causes induction of a **protease inhibitor** that accumulates at low concentrations in response to wounding or pathogenic attacks bacterial or fungal. MeJA as a chemical **elicitor of immune defense mechanisms** rather than a direct antimicrobial effect.

Anticancer to both **blood** and **solid tumors** seem to be responsive to the jasmonate compound, known also as MeJA.

Antiinflammatory

Anti-insomnia

Antiproliferative

Antitumor

Antiviral activity against human papillomavirus (HPV).

Apoptotic

Chemopreventive

Chemotherapeutic

cis-Jasmone and MeJA can cross brain blood barrier (BBB) and were shown to increase significantly the sleeping time of mice induced by pentobarbital, suggesting that these fragrant phytohormones **potentiates the GABA_A receptor response**. Both phytohormones having a **tranquillizing effect on the brain** and could potentially be beneficial in the treatment of anxieties-related insomnia.

cis-Jasmone antiinflammatory activities *via* cytokines modulation. *cis*-Jasmone impairs interferon (IFN)- γ , and tumor necrosis factor alpha (TNF- α) induced inflammatory chemokine production by inhibiting the activation of signal transducers and activators of transcription 1 (STAT1) for the treatment of atopic dermatitis (AD), and Crohn's disease.

cis-Jasmone or MeJA antiproliferative and apoptotic effects against lung and advanced prostate cancers. By increasing the expression of Bax, p21, and caspase-3 activity.

Cytotoxic MeJA induced apoptosis in many cancer cell lines. MeJA is more effective in killing human transformed cell lines than its non-methylated form JA and caused the highest level of cytotoxicity.

Cytotoxic to **neuroblastoma cancer cells** leaving unscathed normal neurons. Jasmonates are **5-LOX inhibitors**, which are also

MeJA acts as a broad-spectrum hexokinase-detaching anticancer agent, taking advantage of the distinct energy metabolism of cancer cells.

MeJA antiglycation activity: against advanced glycation end-products (AGE).

MeJA **decreased insulin-like growth factor-1 receptor (IGF1R) phosphorylation**, however, it enhanced protein kinase B (PKB), also known as Akt phosphorylation and abolished the anti-apoptotic effect of IGF1 and could potentially be beneficial in the treatment of endometrial cancer.

MeJA **enhances memory performance** through **inhibition of oxidative stress** and **anticholinesterase** activity.

MeJA enhances the **antioxidant activity** and flavonoid content in both plants and humans and its **antiproliferative effects** on human cancers A549 (lung) and HL-60 (leukemia) cell lines and **induce apoptosis**. MeJA ameliorate the oxidative stress induced by all kinds of biotic and abiotic stress.

MeJA is a potent 5-LOX and Leukotriene B₄ receptor antagonist for the prevention of human pancreatic cancer.

MeJA is a potent Malondialdehyde (MDA) inhibitor thus, reducing oxidative stress and having antimutagenic activities. MDA inhibition offers a protective effect on the corneas of patients suffering from keratoconus and bullous keratopathy, and was shown effective against osteoarthritis.

MeJA is a scavenger of reactive oxygen species (ROS) and hydrogen peroxide (H₂O₂) by enhancing the antioxidant defense system, from secondary metabolite and assist in the detoxification of the toxic metal arsenic (As). It enhanced the enzymatic activities and gene expression of important antioxidants: ascorbate peroxidase (APX), catalase (CAT), peroxidase (POD) and superoxide dismutase (SOD), secondary metabolites: cinnamyl alcohol dehydrogenase (CAD), phenylalanine ammonialyase (PAL), and polyphenol peroxidase (PPO). Furthermore, is the induction of lipoxygenase gene suggest that MeJA plays an **effective role in the regulation of multiple transcriptional pathways**, which are involved in oxidative stress responses.

MeJA plays an effective role in the regulation of **multiple transcriptional pathways**, which are involved in oxidative stress responses.

<p>overexpressed in brain among many cancers including: Barret's adenocarcinoma, bladder, brain, breast MDA-MB-231 cells, colon, colorectal, esophagus, gastric, glioma cells, hepatocellular carcinoma (HCC), mesothelioma, neuroblastoma, oral carcinoma pancreas, PC-3 prostate cells, and canine osteosarcoma.</p> <p>Enhanced phenylalanine ammonia-lyase (PAL) activity and -1,3-glucanase activity that inhibits fungal growth.</p> <p>GA₃ and JA are beneficial hormones for the prevention and treatment of atherosclerotic plaque. They increase the expression of P2Y purinergic receptors a family of newly characterized plasma membrane molecules involved in several and yet only partially known cellular functions such as vascular reactivity, apoptosis, and cytokine secretion.</p> <p>GA₃ and JA on human skin keratinocytes increases cell growth, stimulates cell turnover, and promotes the secretion of mucus within the reproductive tract of a female mammal.</p> <p>In one study on canine malignant histiocytoma, MeJA resulted in the highest inhibition of cancer cell growth (82.2%), followed by doxorubicin (80.7%) and JA (36.5%).</p> <p>Increases anthocyanin accumulation in the stems and leaves.</p> <p>Increases the amount of paclitaxel (Taxol) produced. MeJA is probably the most potent anticancer and antileukemia agent known to man.</p> <p>Increases the concentration of anthocyanins (cyanidin 3-galactosides), 6-methoxypodophyllotoxin antiviral-HPV. Chlorogenic acid, ellagic acid, flavanols and flavonols, myricetin, phloridzin, various quercetin(s) and resveratrol-stilbene-viniferin.</p> <p>Interferon (IFN)-γ, and tumor necrosis factor alpha (TNF-α) inhibitor.</p>	<p>MeJA reduces decay and enhances antioxidant capacity.</p> <p>MeJA regulates antioxidant defense and suppresses arsenic (As) and cadmium uptake.</p> <p>MeJA was shown to increase the hypoglycemic efficacy of plants with antidiabetic activity by increasing its flavonoids content like that of quercetin glycosides and rutin.</p> <p>Mitochondriotoxic only to cancerous cells</p> <p>Potent antioxidant increasing the levels of superoxide dismutase (SOD), glutathione reductase (GR), catalase (CAT) and peroxidase (Px) activities.</p> <p>Potentiate the GABA_A receptor response having tranquilizing and antianxiety effects for the treatment of insomnia.</p> <p>Promotes the production of defense proteins that are used to fend off invading organisms. Improves systemic acquired resistance.</p> <p>Reduce decay and tissue necrosis</p> <p>Stimulate proliferation of fibroblasts, or keratinocytes and/or stimulate the production of collagen by fibroblasts.</p> <p>Stimulates wound response and protects against dehydration.</p> <p>The ability of jasmonates to suppress replication of mammalian cancer cell lines is of clinical importance.</p> <p>The gene CYP71A2 encoding the cytochrome P450s is induced by MeJA.</p> <p>The potentiating effect of MeJA can be added also to conventional X-ray and cisplatin therapies to increase their cytotoxic effect while lowering the effective dose required and thus reducing conventional chemotherapy undesired side effects.</p> <p>Topical desquamating (skin peeling) agent, antidermatitic.</p>
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POLYAMINES (PAs)
with a mind, boggling total of **378** biological activities.

PAs are NO LONGER CONSIDERED PHYTOHORMONES, although they can be considered as *PLANT GROWTH REGULATORS* or one of the several kinds of metabolites required for essential development of plant's as well human processes and this is the reason I kept them part of the phytohormones.

PAs GENERAL FUNCTIONS 32 functions.

<p>Activating protein synthesis systems</p> <p>Antiallergic activity</p> <p>Antioxidant activity reducing reactive oxygen species (ROS).</p> <p>Blocking calcium ion channels</p> <p>Cell growth and proliferation</p> <p>Chelating agents</p> <p>Directly involved in regulation of programmed cell death.</p> <p>DNA replication and stabilization</p> <p>Enhance the permeability of the blood–brain barrier (BBB).</p> <p>Environmental stressful stimuli from fungi PAs can control cellular signal transduction, as well as to modulate protein-protein interactions.</p> <p>Essential for cellular and tissue growth and regeneration.</p> <p>Essential for the growth, maintenance, of normal cells function.</p> <p>Gene's transcription and translation regulation.</p> <p>Hypothermic and hypotensive</p> <p>It promotes various nucleic-acid biosynthesis</p> <p>Mediating the action of hormones and other growth factors.</p> <p>Membrane stability</p> <p>Modulating pro-inflammatory cytokines</p> <p>Modulating the immune response</p> <p>Modulation of chromatin structure</p> <p>Ornithine decarboxylase (ODC) is exquisitely regulated by PAs.</p>	<p>PAs accumulation may function as part of a homeostatic mechanism to keep intracellular pH at a constant value.</p> <p>Play a role in the regulation of DNA replication and cell division, and are implicated in the control of senescence and morphogenesis.</p> <p>Precursors of several classes of alkaloids</p> <p>Receptor-ligand interactions</p> <p>Regulation of apoptosis</p> <p>Regulation of ion channels: glutamate receptor ion, potassium channels (Kir), and mainly spermine regulates conductance in connexin 40 contribute to the ion selectivity of this gap junction channel, including N-methyl-D-aspartate (NMDA) and α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) receptors and kainate receptors.</p> <p>Signal transduction</p> <p>Stabilizing cell membranes or enhancing membrane permeability to compounds.</p> <p>Stabilizing cellular macromolecules and aiding the dissipation of excess energy in stress response.</p> <p>They are theranostic agents: combination of two words: therapeutic and diagnostic tests. Sometimes used interchangeably referred to as Theragnostics. Use of radionuclide-labeled agents that specifically permit to diagnose a disease in individuals and then use identical or closely related agents for the treatment of such diseases. Or rather, is it a therapeutic agent whose administration and dosing is guided by diagnostic metrics. Probably, theranostic encompasses both concepts and many additional ones.</p> <p>The interaction of PAs with ion channels is of central importance for neurotransmittance.</p>
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The only proven inherited human disease associated with the dysregulation of PAs metabolism is Snyder-Robinson syndrome (SRS) that occurs exclusively in males linked to intellectual disability. Other characteristics associated with this condition starts very early childhood a marfanoid habitus, skeletal defects like, kyphoscoliosis, osteoporosis, and facial dysmorphic lack of asymmetry as well as hypotonia (floppiness), movement disorders, often with difficulty walking and unsteady gait, seizures, abnormalities of the genitalia and kidneys.

PAs SPECIFIC BIOLOGICAL ACTIVITIES

DIAMINES

General Biological activities include: 7 activities

- Blocking calcium ion channels
- Mediating the action of hormones and other growth factors.
- Modulating pro-inflammatory cytokines.
- Modulating the immune response

<ul style="list-style-type: none"> • Play a major role in humans as cytoprotective molecules • Regulation of apoptosis • Stabilizing cellular macromolecules and aiding the dissipation of excess energy in stress response. 	
1,3-Diaminopropane 16 activities	Cadaverine 8 activities.
<p><i>Adjuvant</i> for cholinesterase and thrombosis inhibitors.</p> <p>Antibacterial activity against Mycobacterium tuberculosis.</p> <p>Anticancer</p> <p>Antimicrobial by increasing hypersusceptibility to antibiotics.</p> <p>Antiparasitic with antitrypanosomal activity</p> <p>Anti-priapism a urologic emergency</p> <p>Antiproliferative and antitumor</p> <p>Anti-renal lithiasis specific for cystinuria stones</p> <p>Chelator for toxic metals</p> <p>Increases penicillin production</p> <p>Involved in polyamine oxidase (PAO) a key element for oxidative burst to induce programmed cell death (apoptosis).</p> <p>Ornithine decarboxylase (ODC) potent inhibitor, shown to be effective against bladder, cervical hyperplasia, and neuroblastoma cancers.</p> <p>Potent antifungal activity</p> <p>Synergistic to conventional antibiotics and chemotherapy.</p> <p>UV light inhibitor with radioprotective activity</p> <p>Vasoactive intestinal peptide (VIP) neuromodulator for the treatment of achalasia, Crohn's disease, cystic fibrosis (CF), derangement of smooth muscle activity, Hirschsprung's disease, inflammatory bowel disease (IBD), and intestinal ischemia.</p>	<p>A necessary precursor in the biosynthesis of quinolizidine alkaloids.</p> <p><i>Adjuvant</i> sensitizing agent for both antibiotic and chemotherapy resistance.</p> <p>Cadaverine and putrescine are associated with oral malodor of halitosis.</p> <p>Can serve as electrostatic bridges between negative phosphate charges on nucleic acids and other negatively charged polymers.</p> <p>Electrostatically disrupt the pili-pili interactions, which mediate microcolony formation of cholera toxin. Interfered with autoagglutination and biofilm formation.</p> <p>Helps in the conjugation of drugs against luciferase-transduced tumor cells improves therapeutic efficacy for loco-regional treatment of peritoneal carcinomatosis.</p> <p>Increase the expression levels of lysyl oxidases, which protect against aortic aneurysm progression in Marfan syndrome.</p> <p>Quorum sensing (QS) play a potential signal mediating role in both the colonization and virulence gene expression within the human host.</p>
Putrescine with 8 activities.	
<p>Antidepressant-like effects mediated through its interaction with the PA-site of NMDA receptors.</p> <p>Anti-osteoclastogenic and anti-migration activities activity by inhibiting the migration of preosteoclasts <i>via</i> Ca²⁺- protein tyrosine kinase 2 (PTK₂)-proto-oncogene tyrosine-protein kinase (Src)-nuclear factor of activated T-cells, cytoplasmic 1 (NFATc1) signaling pathways suggested to be beneficial in the treatment of bone disorders such as osteoporosis.</p>	<p>Neuroprotection by the conversion of putrescine into GABA, which then activates presynaptic GABA_B receptors.</p> <p>Play a role in the modulation of depression</p> <p>Putrescine has been shown to play a pivotal role in normal hair cycle follicle development.</p> <p>Sedating effects in epilepsy and decrease neurological insults.</p>

<p>It is present in the human reproductive system; secretion called seminal plasma or semen. A nutritional regulator of fertility. Promote sperm motility. It is involved in ovarian follicle development and ovulation in females, and for the synthesis of steroidogenesis in the ovary. Play a role in embryo implantation and important for placenta formation and function. Furthermore, help in intrauterine growth of embryo and fetus.</p>	<p>Topical application of putrescine, a transglutaminase inhibitor (prevent hypertrophic scar formation) mediated by cross-linking of fucoprotein in the extracellular wound matrix and supports a role in this process in the generation of incisional wound strength.</p>
TRIAMINES	
Homospermidine 14 activities.	Norspermidine 18 activities.
<p>A unique precursor of pyrrolizidine alkaloids</p> <p>Anticancer</p> <p>Anti-chlorella viruses</p> <p>Antimalarial</p> <p>Antineoplastic</p> <p>Antiparasitic against Plasmodium falciparum.</p> <p>Anti-Plasmodium, anti-Trypanosoma and anti-Leishmania.</p> <p>Antiproliferative</p> <p>Antisenescence activity on the skin</p> <p>Antitumor activity is by inhibition of cell growth through the induction of apoptosis in human liver hepatoma cells.</p> <p>Apoptotic in B16 melanoma cells</p> <p>Improves brain cognitive functions</p> <p>Mediates the effective drug delivery via the polyamines transporter (PAT), and helped the proper cytotoxic goods of chemotherapy.</p> <p>Potent antitumor suppressing pulmonary metastasis.</p>	<p>A novel therapeutic use for norspermidine is that it both prevent the formation of new bacterial biofilms and collapse the structure of existing biofilms. It can lead to biofilm disassembly. It disassembles large and resistant microbial aggregate. Inhibits planktonic growth and biofilm formation in an exopolysaccharide-independent manner.</p> <p>Antiangiogenic</p> <p>Antibacterial against Gram-negative: Acinetobacter baumannii, Klebsiella pneumoniae, and Pseudomonas aeruginosa. In Gram-positive: Bacillus subtilis, Vancomycin-resistant Enterococcus faecium, methicillin-resistant Staphylococcus aureus (MRSA), Staphylococcus epidermidis, and Streptococcus mutans.</p> <p>Anticancer and antitumor activities against L1210 leukemia, Lewis lung 3LL carcinoma, liver, and EL4 lymphoma, and pancreatic cancers.</p> <p>Antimetastatic</p> <p>Antimigration</p> <p>Antineoplastic</p> <p>Cytotoxic trinuclear Pd(II) complex of norspermidine (Pd(3)NSpd(2)) may be regarded as a potential new metal-based drug against breast cancer, coupling a significant efficiency with a low toxicity.</p> <p>High affinity PAs transport inhibitors</p> <p>In Maize – Zea Mays (germinating seeds) the amount of norspermidine is 6- to 15-fold greater than that of its common counterpart (spermidine) in the three genotypes.</p> <p>Increase the levels of specific low molecular weight sphingomyelins especially in the membranous myelin sheath that surrounds some nerve cell axons, which could potentially be beneficial for multiple sclerosis (MS).</p> <p>Iron-chelating properties</p>

	<p>Norspermidine treatment triggers a transcriptional response similar to that observed when cytosolic misfolded proteins accumulate. It reduced the levels of polyubiquitinated proteins and <i>in vitro</i> inhibited the ubiquitination reaction, probably interfering with E₃ enzymes. This toxic effect can be explained if norspermidine were denaturing proteins or disturbing the Ubiquitin Proteasome System (UPS). It interacts with the E₂-E₃ enzyme complex and thus preventing the correct degradation of misfolded or denaturated proteins by these enzymes. These misfolded proteins could then form insoluble toxic aggregates, which in turn would trigger a Heat Shock response.</p> <p>Norspermidine was shown effective at the inhibition of spermidine transport determined in T-47D human breast cancer cells.</p> <p>Selective immunosuppressive on IgM production was associated with the inhibition of cell growth, because DNA and RNA syntheses measured by 3H-TdR and 3H-UR incorporation were also similarly reduced.</p> <p>Tackle multidrug resistant bacterial infections</p> <p>Trypanothione reductase inhibitor with antiparasitic activities against sleeping sickness, Chagas' disease, Leishmania and trypanosomes.</p> <p>Vermifuge</p>
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Spermidine/Hypusine 51 activities.

<p>A carbonic anhydrase (CA) inhibitor used for the treatment of edema (diuretics), epilepsy, gastric, and duodenal ulcers, glaucoma, hypokalemic periodic paralysis, mountain sickness, neurological disorders, osteoporosis, primary periodic paralysis, and pseudo tumor cerebri.</p> <p>A potent antiinflammatory, by NF-kB inhibition on the production nitric oxide (NO), by inhibition of the pro-inflammatory cytokines, for the treatment of rheumatoid arthritis (RA) or systemic lupus erythematosus (SLE) and other inflammatory diseases.</p> <p>A potent stimulator of human hair growth promotes hair shaft elongation and prolonged hair growth anagen phase. Spermidine also upregulated expression of the epithelial stem cell-associated keratins K15 and K19. Spermidine is a potent stimulator of human hair growth and a previously unknown modulator of human epithelial stem cell biology. It prevented apoptosis, in hair bulb regression, by preserving the expression of anti-apoptotic molecules such as Bcl-2, MAP-kinases and their phosphorylated forms.</p>	<p>Hypusine modification of the eukaryotic initiation factor 5A is emerging as a crucial regulator in cancer, infections, and inflammation. Hypusine modification in eIF-5A is crucial for homeostasis in mammals and a valuable and safe target for therapeutic intervention in cancer. eIF-5A is an ancient and poorly understood protein, eIF5A, may be critical for cytokines release and signaling.</p> <p>Immunomodulator</p> <p>Inducer of AUTOPHAGY and spermidine is considered the most antisenescence of all PAs. Enhanced autophagy is crucial for PAs-induced suppression of necrosis and enhanced longevity. Both resveratrol and spermidine can induce autophagy in cytoplasts (enucleated cells). SIRT1 activity is required for resveratrol-induced autophagy but not for spermidine-mediated autophagy induction. Autophagy is mostly if not always a cytoprotective event.</p> <p>It is present in the human reproductive system; secretion called seminal plasma or semen. A nutritional regulator of fertility. Promote sperm motility. It is involved in ovarian follicle</p>
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<p>Antiaging, increases lifespan and resistance to stress, and decreases the occurrence of age-related pathology and loss of locomotor ability.</p> <p>Antiangiogenic agents through copper chelation.</p> <p>Anticancer contrary to popular belief when used as a complex of balanced PAs and not that of isolated analogs.</p> <p>Antidiabetic: either inhibition of mTOR or activation of AMPK by spermidine will play two crucial roles, first being the activation of autophagy and secondly the reduction of endoplasmic reticulum stress, which will reduce pancreatic β-cell death by apoptosis and thus can be a novel therapeutic candidate in the treatment of insulin resistance in type 2 diabetes and preserving pancreatic β-cell mass. Recently it was demonstrated the interaction of spermidine and mTOR signaling in the synthesis of antizyme (AZ). Spermidine still increased hydrogen peroxide resistance in autophagy-deficient individuals.</p> <p>Antifungal against <i>Candida albicans</i></p> <p>Antiglycation attenuates advanced glycation end products (AGE). Furthermore, it inhibits lipofuscin and oxidative stress, all known has noxious substances.</p> <p>Anti-neurodegenerative increases learning and cognitive memory. Rescue the motor dysfunction. A positive modulation of the NMDA receptor/channel through activation of the glycine and spermidine sites can synergistically compensate deficiency of hippocampal NMDA and muscarinic receptor-mediated neurotransmission involved in working memory function. Spermidine is crucial for olfactory memory formation. It suppresses age-dependent memory impairment by preventing adverse increase of presynaptic active zone size and release.</p> <p>Anti-osteoclastogenic and anti-migration activities activity by inhibiting the migration of preosteoclasts via Ca^{2+}- protein tyrosine kinase 2 (PTK₂)-proto-oncogene tyrosine-protein kinase (Src)-nuclear factor of activated T-cells, cytoplasmic 1 (NFATc1) signaling pathways suggested to be beneficial in the treatment of bone disorders such as osteoporosis.</p> <p>Anti-pancreatitis by decreasing N¹-acetyltransferase (SSAT). Elevated levels of RNA transcripts of SAT1 in the bloodstream have been associated with a higher risk of suicide.</p> <p>Antiparasitic activity: antimalarial – antiplasmodial against <i>Plasmodium falciparum</i> and <i>Trypanosoma</i></p>	<p>development and ovulation in females, and for the synthesis of steroidogenesis in the ovary. Play a role in embryo implantation and important for placenta formation and function. Furthermore, help in intrauterine growth of embryo and fetus.</p> <p>Lipid peroxidation inhibitor and involved in lipid metabolism and induces changes in lipid composition it may be of benefit in demyelinating diseases, such as multiple sclerosis (MS).</p> <p>PA–hypusine axis as a new tumor suppressor network regulating apoptosis.</p> <p>Prevents Immunosenescence modulating the relationship between inflammaging and immunosenescence. Adaptation/remodeling process leading to increased inflammation and on the other to decreased immune response (immune-paralysis) mastered by the innate immune system lack of response.</p> <p>Prevents necrosis</p> <p>Prevents telomere erosion: increasing telomere length and telomerase activity as well.</p> <p>Pro-inflammatory cytokines modulator</p> <p>Promote liver regeneration and function decreasing xenobiotic insults. Helps in the stimulation of liver detoxification enzymes.</p> <p>Protects against α-synuclein neurotoxicity. Spermidine rescued α-synuclein-induced loss of dopaminergic neurons, for the treatment of Parkinson disease (PD),</p> <p>Reduces age-related oxidative protein damage</p> <p>Selective Hypotensive</p> <p>Spermidine and spermine are required for the maintenance of pancreatic integrity and liver regeneration.</p> <p>Spermidine and spermine as novel regulators of the expression of the arginine vasopressin gene.</p> <p>Spermidine in human dermal fibroblasts (HDFs), inhibits matrix metalloproteinase-2 (MMP-2) activity and expression. Furthermore, it inhibits histone acetyltransferase (HAT), phospho-extracellular-signal related kinase (p-ERK), phospho-c-jun N-terminal kinase (p-JNK), and nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB) for the treatment of limiting metastasis. Furthermore, spermidine increases the expression levels of histone deacetylase 1 (HDAC1), sirtuin 1 (SIRT1), phospho-p38 (p-p38) and all together spermidine</p>
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<p>brucei that cause African trypanosomiasis also known as sleeping sickness.</p>	<p>is an attractive compound for the treatment of cancer and related inflammation.</p>
<p>Antiproliferative</p>	<p>Spermidine induces mitophagy through ataxia telangiectasia mutated (ATM)-dependent activation of the PINK1/Parkin pathway for the regulation of human fibroblasts: connective tissue that produces collagen and other fibers.</p>
<p>Antiviral inhibiting the replication enzymes of hepatitis C virus (HCV). It was found that spermine and spermidine activate HCV RNA-dependent RNA polymerase (NS5B protein).</p>	<p>Spermidine is a histone deacetylase (HDAC) inhibitor that has a long history of uses in neurology and psychiatry as a mood stabilizer and anti-epileptic.</p>
<p>Beclin 1 is central to initiating autophagy its deficit suggests that the process is indeed blocked in the pathophysiology of schizophrenia.</p>	<p>Spermidine is an acetylase inhibitor that stimulates autophagy independent of SIRT1 in human.</p>
<p>Cardioprotective thru inhibition of cell adhesion through suppression of lymphocyte function-associated antigen 1 (LFA-1) for vascular integrity health. It increases the availability of arginine for nitric oxide (NO) synthesis.</p>	<p>Spermine is regarded as being the most potent feedback inhibitor of ornithine decarboxylase (ODC). Second is spermidine and putrescine is the least, effective in supporting various other biological processes.</p>
<p>Chelator of toxic metals</p>	<p>Spermidine natural acetylation enhances the activity of some transcription factors such as the tumor suppressor p53. Histone deacetylase inhibitors equipped with estrogen receptor modulation activity. The anticancer activity that is selectively more potent against MCF-7 (ERα positive breast cancer) compared to MDA-MB-231 (triple negative breast cancer), DU145 (prostate cancer) or Vero (noncancerous cell line), has been showed by spermidine acetylation.</p>
<p>Cytoprotective: spermidine increases overexpression of Pep4p, which extend chronological lifespan specifically through the protein's anti-necrotic function. This function, which is triggered by histone hypoacetylation, was dependent on PAs biosynthesis and was exerted <i>via</i> enhanced intracellular levels of putrescine, spermidine, and its precursor S-adenosyl-methionine.</p>	<p>Spermidine's ability to keep gut integrity helps to reduce the incidence of indigestion and is an intestinal antiinflammatory activities good for the treatment of inflammatory bowel diseases (IBD), diverticulosis, Dysbiosis, Crohn's disease (CD) and ulcerative colitis (UC). The gene locus encoding protein-tyrosine phosphatase non-receptor type 2 (PTPN2) has been associated with IBD. Spermidine reduce elevated IFN-γ signaling and a faulty mucosal barrier. It increases both protein-tyrosine phosphatase (TCPTP), levels and enzymatic activity in the protection of epithelial barrier function during periods of inflammation, acting as a negative regulator of the proinflammatory cytokine IFN-γ.</p>
<p>Cytostatic agent that inhibit the proliferation of certain tumor cells.</p>	<p>Spermine and spermidine activate HCV RNA-dependent RNA polymerase (NS5B protein). Effectively inhibit the helicase reaction catalyzed by another enzyme of HCV replication - helicase/NTPase (NS3 protein). Inhibition effects on the replication of the HCV genome in an infected cell.</p>
<p>Decreased the incidence of age-related kidney glomerular atrophy.</p>	
<p>DNA stability, cell growth, proliferation, and apoptosis.</p>	
<p>Enhanced cardiac autophagy, mitophagy and mitochondrial respiration, and it also improved the mechano-elastical properties of cardiomyocytes <i>in vivo</i>, coinciding with increased titin phosphorylation, and suppressed subclinical inflammation.</p>	
<p>Essential for epidermal keratinocyte function for the regeneration of hair, nail, and skin.</p>	
<p>Eukaryotic initiation factor 5A (eIF-5A) is the only known protein to contain the unusual amino acid hypusine [N (ϵ)- (4-amino-2-hydroxybutyl)-lysine], which is synthesized on eIF5A at a specific lysine residue from the PA spermidine by two catalytic steps. eIF5A is the only protein to contain the unique amino acid hypusine.</p>	
<p>Hypusine modification is absolutely required for eIF5A action in cytokine signaling, it is proposed that this modification could serve as a new drug</p>	

target for pancreatic islet β -cell protection in the setting of diabetic inflammation.	Trigger epigenetic deacetylation of histone H3 through inhibition of histone acetyltransferases (HAT), suppressing oxidative stress and necrosis.
TETRAAMINES	
Homospermine 7 activities.	Norspermine 23 activities.
<p><i>Play a key role in DNA delivery</i> and in determining the transfection efficiency.</p> <p>Enter cells, reduced cellular putrescine and spermidine pools, while exerting only a small effect on the spermine pool.</p> <p>Antidiarrheal include: idiopathic ulcerative colitis (IUC) or Crohn colitis, short-gut syndrome, chronic pancreatitis, ischemic bowel disease, enteroenteric fistulae, inflammatory bowel diseases (IBD), refractory AIDS-related diarrhea and other viral caused diarrhea and other gastrointestinal tract disorders known to cause diarrhea.</p> <p>Antimicrobial activity against Gram-positive <i>Staphylococcus aureus</i>.</p> <p>Anti-trypanosomal</p> <p>Homospermine penetrates the N-methyl-D-aspartate (NMDA) receptors channel pore and exhibits neuroprotective effects against excitatory toxicity in focal cerebral ischemia and suppressed intracellular calcium influx.</p> <p>N^1, N^{14}-<i>bis</i>(ethyl)homospermine on the growth, PAs levels, and survival of U-87 MG and SF-126 human brain tumor cells was examined in tissue culture.</p>	<p>N^1-acetylspermine, <i>sym</i>-norspermine, and <i>sym</i>-norspermidine, are excellent substrates for SSAT.</p> <p>Acetyl-coA a statin for lipid and carbohydrates metabolism.</p> <p>Androgen modulator</p> <p>Anti-asthma</p> <p>Anti-baldness</p> <p>Anticancer by p65</p> <p>Antidiabetic</p> <p>Antihypoxic</p> <p>Antiinflammatory by NF-kB inhibition</p> <p>Antiischemic</p> <p>Anti-keratosis follicularis spinulosa decalvans (alopecia of the eyelashes and eyebrows).</p> <p>Antiproliferative</p> <p>Cytokines modulation</p> <p>N^1, N^{14}-<i>bis</i>(ethyl)norspermine (BENSPM) in athymic (nude) mouse xenografts of two human pancreatic ductal adenocarcinoma cell lines. BENSPM was found to exert greater antitumor activity in vivo than either N^1, N^{14}-<i>bis</i>(ethyl)homospermine BEHSPM or other conventional agents, largely because higher doses could be given due to its lower toxicity to mice. BENSPM shows greater activity than any other agent we have thus far tested against pancreatic-cancer models. BENSPM exhibits promising anticancer effects, which render it suitable for further optimization to develop a new metal-based chemotherapeutic drug for breast and prostate cancers treatment.</p> <p>Norspermine can functionally substitute for thermospermine.</p> <p>Norspermine exerts antitumor activity against two human melanoma xenografts. It also potentiates the apoptotic activity of the pure antiestrogen ICI 182780 in breast cancer cells</p> <p>Norspermine model for lipoplex formation with respect to gene delivery (lipofection), a key first step in gene therapy. The observed self-assembly phenomena are discussed with respect to DNA charge neutralization and DNA bending with loss of</p>

	<p>ethidium cation intercalation sites, ultimately leading to DNA condensation.</p> <p>Norspermine, thermospermine and spermine are natural proton pump inhibitors (PPI) for the treatment of gastric and duodenum ulcers and gastro esophageal reflux disease (GERD), Zollinger-Ellison syndrome, including all digestive tube disorders.</p> <p>Oxidoreductase activity (acts as hydrogen or electron acceptor and becomes reduced).</p> <p>Regeneration of new tissue</p> <p>Skin moisturizer</p> <p>Toxins detoxification</p> <p>$\alpha 9\beta 1$-integrin involved in vascular endothelial growth factor (VEGF).</p>
Spermine 40 activities.	
<p>A carbonic anhydrase (CA) inhibitor used for the treatment of edema (diuretics), epilepsy, gastric, and duodenal ulcers, glaucoma, hypokalemic periodic paralysis, mountain sickness, neurological disorders, osteoporosis, primary periodic paralysis, and pseudo tumor cerebri.</p> <p>A synergistic effect by spermine and antibiotics ruled out the hypothesis of spermine serving as an efflux pump inhibitor in this organism. This interesting finding of the effect of spermine on antibiotic susceptibility provides the basis for a new potential approach against drug-resistant pathogens by use of existing beta-lactam antibiotics.</p> <p>Antiglycation by attenuating advanced glycation end products (AGE).</p> <p>Anti-osteoclastogenic and anti-migration activities activity by inhibiting the migration of preosteoclasts via Ca^{2+}- protein tyrosine kinase 2 (PTK₂)-proto-oncogene tyrosine-protein kinase (Src)-nuclear factor of activated T-cells, cytoplasmic 1 (NFATc1) signaling pathways suggested to be beneficial in the treatment of bone disorders such as osteoporosis.</p> <p>Because spermine decrease CD11a/CD18, this could serve as an antiinflammatory to reduce elevated pro-inflammatory cytokines TNFα and IL-1β levels. Since cell adhesion is critical for the genesis and maintenance of tissue structure its integrity and function for the treatment of spondyloarthritis (SpA) or rheumatoid arthritis (RA).</p>	<p>Spermine cross talking with growth phytohormones, and influence the skin, hair growth, male and female fertility, fat deposits, pancreatic and hepatic integrity, and regenerative growth in mammals.</p> <p>Spermine deficiency was shown to be a cause of deafness and sterility. Spermine-related defect in the functioning of cardiac Kir channels could account for arrhythmias leading to sudden death. The effect of the absence of spermine on glutamate receptor ion channels in the brain may account for the neurological symptoms and could contribute to the lack of fertility and normal growth, but more direct effects on repressing gene expression.</p> <p>Spermine inhibit nitrite production without causing cytotoxicity and inhibitor of inducible nitric oxide (iNOS). Both spermine and spermidine inhibits the secretion of pro-inflammatory cytokines TNF-α and monocyte chemoattractant protein-1 (MCP-1), and that SPM/SPD are efficient immunomodulators and antiinflammatory agents. However, SPM was shown to be more effective than what was observed with SPD alone and when the two were added simultaneously the effect was significantly more potent by additive and synergistic activities.</p> <p>Spermine is a natural antioxidant and antiinflammatory inhibiting the cytochrome C reduction initiated by FMLP- or PMA-stimulated human granulocytes. It inhibits the Fe(III)/xanthine oxidase stimulated lipid peroxidation of brain phospholipid liposomes. Also inhibits the generation of the transport of superoxide radicals from stimulated granulocytes, and inhibits the</p>

<p>Cyclin E protein is fully recovered by spermine, which helps to control the cell cycle. It can prevent cell lineage-specific abnormalities, such as impaired maturation due to increased cell proliferation and apoptosis or accelerated senescence. The anti-senescent activity of spermine effect could result from inhibition of RNase activity.</p> <p>Enhancement and inhibition of DNA transcriptional activity by spermine was shown. Uptake of spermine by the liver mitochondria and its influence on the transport of phosphate has been demonstrated. A preservative activity by this class of agent.</p> <p>Essential for epidermal keratinocyte function for the regeneration of hair, nail, and skin.</p> <p>Exogenous spermine supplementation augmented DNA methyltransferase activity (DNA MTase) in Jurkat and HT-29 cells and inhibited PAs deficiency-induced global alteration in DNA methylation status <i>in vitro</i>, that typically acts to repress gene transcription. In addition, increased spermine intake was associated with a decreased incidence of colon tumors in BALB/c mice. Spermine seems to play important roles in inhibiting age-associated and PAs-deficient induced abnormal gene methylation as well as pathological changes including prevention of tumorigenesis.</p> <p>Increase cytosolic adenosine diphosphate (ADP) and epinephrine-induced platelet aggregation. Spermine arrests or inhibits thrombin-, epinephrine-, arachidonate-, or ristocetin-induced platelet aggregation. Spermine unique ability for reducing elevated fibrinogen levels is by inhibiting both platelet aggregation and glycoprotein IIb/IIIa activation. Spermine antithrombotic effect. Spermine is a selective and reversible GP IIb/IIIa antagonist that was shown to play a pivotal role in its ability for modulating platelet's activity more than just being a strict inhibitor.</p> <p>Inhibit or suppress stress at a cellular level, acting as stress-suppressing, stress-reducing, and stress-preventing agents by increasing cell division rate or by preventing degradation of cell functions. Keeping the cell membranes taut and strong helps in the fight against wrinkles and sagging skin by increasing collagen and elastin.</p> <p>It is present in the human reproductive system; secretion called seminal plasma or semen. A nutritional regulator of fertility. Promote sperm</p>	<p>Haber-Weiss reaction by forming an unreactive chelate with Fe.</p> <p>Spermine is a powerful regulator of erythrocyte cation channel cytosolic Ca²⁺ activity and, thus, cell survival and modulator of apoptosis.</p> <p>Spermine is found in high concentrations in the epidermis. Spermine is an important epidermal antioxidant that can penetrate the stratum corneum of the skin and considered to have potent antioxidant that is 20-30 times stronger than vitamin E delay's cell aging. Production of spermine increases when the skin is exposed to UV rays, it is a damage sensing molecule actively up taken by skin cells, and a free radical scavenger and a sugar radical scavenger and an antiinflammatory.</p> <p>Spermine is found in large concentrations in semen to stabilize and protect the DNA of the sperm cells. Protection of replicating DNA against oxidative damage by singlet oxygen is crucial for cell survival.</p> <p>Spermine is involved in cell growth. Since it interacts with the double helix, it can stabilize the DNA molecule. Recent evidence of the antimutagenic and anticarcinogenic capacity of spermine has focused attention on the mechanism(s) by which such agents can protect cells from induced damages. Spermine has a remarkable stabilizing effect on mitochondria, functions.</p> <p>Spermine is regarded as being the most potent feedback inhibitor of ornithine decarboxylase (ODC). Second is spermidine and putrescine is the least, effective in supporting various other biological processes.</p> <p>Spermine modulates differently the activity of alkaline phosphatase in jejunum and ileum in 14-day-old rat, which had received spermine orally for 3 days, once daily, an increase of alkaline phosphatase activity in the jejunum and a decrease of this activity in the ileum was observed.</p> <p>Spermine oxidase as an important positive regulator of muscle gene expression and fiber size, and elucidate p21-mediated repression of spermine oxidase as a key step in the pathogenesis of skeletal muscle atrophy. Spermine oxidase maintains basal skeletal muscle gene expression and fiber size it is strongly repressed by conditions that cause skeletal muscle atrophy.</p>
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motility. It is involved in ovarian follicle development and ovulation in females, and for the synthesis of steroidogenesis in the ovary. Play a role in embryo implantation and important for placenta formation and function. Furthermore, help in intrauterine growth of embryo and fetus.

Modulate various ion channels and receptors in the brain, exert neuroprotective, antidepressant, and other effects *in vivo* such as increasing longevity. It works on the regulation of the astroglial network under both normal and pathological conditions.

Norspermine, thermospermine and spermine are natural proton pump inhibitors (PPI) for the treatment of gastric and duodenum ulcers and gastro esophageal reflux disease (GERD), Zollinger-Ellison syndrome, including all digestive tube disorders.

Promote liver regeneration and function decreasing xenobiotic insults. Helps in the stimulation of liver detoxification enzymes.

Regulate the innate immune response by downregulating the synthesis of potentially injurious pro-inflammatory cytokines. Spermine was shown to effectively inhibited the synthesis of the proinflammatory cytokines tumor necrosis factor (TNF), interleukin-1 (IL-1), IL-6, macrophage inflammatory proteins 1-alpha (MIP-1 α), and MIP-1 β chemokines. Furthermore, inhibit inducible nitric oxide synthase (iNOS) and nitrotyrosine, and to decrease serum concentrations of pro-inflammatory mediators, thus improving nitrate and interferon- γ levels while enhancing the concentration of IL-10 an antiinflammatory cytokine thus harmonizing both the pro-inflammatory and antiinflammatory cytokines homeostasis.

Spermine and spermidine activate HCV RNA-dependent RNA polymerase (NS5B protein). Effectively inhibit the helicase reaction catalyzed by another enzyme of HCV replication - helicase/NTPase (NS3 protein). Inhibition effects on the replication of the HCV genome in an infected cell.

Spermine and spermidine are required for the maintenance of **pancreatic integrity** and **liver regeneration**.

Spermine and spermidine as novel regulators of the expression of the arginine vasopressin gene.

Spermine antiangiogenic and antiinflammatory activities is caused by a of decrease lymphocyte function-associated antigen 1 (LFA-1)–CD11a/CD18) expression on human lymphocyte

Spermine reduced total phosphatase activity by 135%–175%. An antisenescence function for spermine is also indicated by phosphatase reduced activity. Spermine, exhibit antisenescence properties. Metabolic interactions between PAs, particularly spermine and its role in stress response with cell oxidative balance and transport/biosynthesis of amino acids as a strategy to cope with oxidative damage produced during senescence.

Spermine stimulates nicotinamide adenine dinucleotide phosphate (NADPH)–dependent activity of the mixed-function oxidase (MFO) system several-fold. Stereospecific (different effect on 6 beta- and 16 alpha-testosterone hydroxylation).

Spermine suppresses sensitivity of cervical carcinoma cells to lymphokine-activated killer (LAK) lymphocytes from more than half of normal individuals. Spermine may be an important immunosuppressive agent in natural immunity against cervical cancer.

Spermine was shown to be a better antioxidant than spermidine. Spermine also inhibited SNP-, Fe²⁺/EDTA- and free Fe²⁺-induced TBARS production, but had a modest effect. Spermidine, in turn, also discretely inhibited SNP-, Fe²⁺/EDTA- and free Fe²⁺-induced TBARS production. Spermine is antioxidant with free radical scavenger properties and are definite lipid peroxidation inhibitor.

Spermine, can significantly decrease the capacity of *Neisseria gonorrhoeae* Gram-negative bacteria to form a biofilm, as well as for Gram-negative *Bacillus subtilis* biofilm.

Spermine, with positive charges, on the strongly inwardly rectifying muscarinic K⁺ (KACH) channel. Spermine (300 nM to 3 microM) **restored the relaxation of KACH currents**, which had been lost in the inside-out configuration **slowing down the heart rate**. The order of potency of PAs in reducing open probability (Po) at +40 mV was spermine > or = spermidine > putrescine > ornithine; arginine had no significant effect. Because **submillimolar concentrations of spermine** and **spermidine** are available in the cytosol of most cells, these PAs may be the unrecognized or unidentified intracellular gating factors for strong inward rectifiers such as KACH and IK1 channels

Stimulate NADPH provides the reducing equivalents for biosynthetic reactions and the oxidation-reduction involved in protecting against

<p>and adhesion capacity of human peripheral-blood mononuclear cells (PBMCs) to HUVECs.</p> <p>Spermine confers protection against lethal sepsis partly by attenuating surrogate inflammatory markers seen in sepsis- and high-mobility group box 1 (HMGB1)-induced inflammatory responses. Spermine, inhibits endotoxin-induced cytokine release. The protective effects were associated with a significant reduction in peritoneal and serum levels of several surrogate markers of sepsis for example, interleukin-6 (IL-6), keratinocyte-derived chemokine (KC), monocytes chemoattractant protein-1 (MCP-1), macrophage inflammatory protein-2 (MIP-2), tissue inhibitor of metalloproteinase-1 (ti-MP-1), soluble tumor necrosis factor-alpha receptor I (sTNF-α-Ri), and soluble tumor necrosis factor-alpha receptor II (sTNF-α-RII) during a late stage of sepsis.</p>	<p>the toxicity of reactive oxygen species (ROS), thus spermine increases the regeneration of glutathione (GSH). NADPH is also used for anabolic pathways, such as lipid synthesis, cholesterol synthesis, and fatty acid chain elongation.</p> <p>Norspermine thermospermine and spermine are the most effective at inhibiting on H⁺, K⁺-ATPase K⁺-ATPase activity on the gastric mucosa for its reported anti-ulcerogenic healing properties.</p>
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Thermospermine 3 activities.

Thermospermine is not a minor PA in the plant kingdom. It plays a role in the modulation of auxin signaling for plants' growth development. ACL5 gene is expressed specifically during xylem formation from procambial cells to differentiating xylem vessels. Loss-of-function mutants of ACL5 display over proliferation of xylem vessels along with severe dwarfism, suggesting that **thermospermine plays a role in the repression** of xylem differentiation. Studies of suppressor mutants of ACL5 that recover the wild-type phenotype in the absence of thermospermine suggest that **thermospermine acts on the translation of specific mRNAs containing upstream open reading frames (uORFs)**. **Thermospermine is a novel type of plant growth regulator** and may also serve **in the control of wood biomass production**.

Not a lot is known about thermospermine functions in the human body and its biological activities are just now surfacing.

It is an effective anti-ulcerogenic activity by anti-H⁺/K⁺-ATPase activity. The proton is the acidifying agent, secreted by the H⁺/K⁺-ATPase pump in the gastric fluid. Among the tetraamines tested, linear tetraamines have stronger anti-ulcerogenic activity in both restraint stress-induced gastric ulceration and ulceration in pylorus-ligated rats. **Norspermine thermospermine and spermine were the most effective** H⁺/K⁺-ATPase inhibitors on the activity on the gastric mucosa. The H⁺/K⁺-ATPase pump or proton pump is a magnesium-dependent enzyme which causes the exchange of a proton against a potassium ion through a membrane. This pump is present throughout the colon, the kidney, but especially in the stomach where it is most active. In the stomach, this pump causes the secretion of protons into the gastric fluid, which increases hydrochloric acid (HCl). It generates a gradient of pH of more than 6 units: whereas the blood pH is alkaline 7.3 that of the gastric, fluid is about 1. The principal stimulant of the H⁺/K⁺-ATPase pump is dietary food ingestion, which acts by the release of histamine, gastrin, and acetylcholine, which is activated, *via* the cAMP or calcium, protein kinases (PKs) which, themselves, activate the H⁺/K⁺-ATPase. Gastrin is secreted by the pyloric antrum under the influence of vagal stimulation and food consumption. Gastrin stimulates secretion by the gastric mucosa of protons, pepsin, and the intrinsic factor. Gastrin stimulates pancreatic secretion, and inhibits the electrolyte and water reabsorption by the intestine, which increase peristalsis and can cause diarrhea. Furthermore, gastrin relaxes the Oddi sphincter and slows down gastric emptying.

In other words, norspermine, thermospermine and spermine are natural proton pump inhibitors (PPI) for the treatment of gastric and duodenum ulcers and gastro esophageal reflux disease (GERD), Zollinger-Ellison syndrome, including all digestive tube disorders. And unlike the synthetic irreversible PPI, which includes: omeprazole, lansoprazole, pantoprazole, rabeprazole, and esomeprazole the S-isomer of omeprazole, PAs do not cause the same side effects. Firstly, PAs are reversible PPI and do not cause the risks associated with the development of certain bacteria by overtly decreasing essential HCl. They

are superior due to their antibiofilms disassembly – antibacterial and prebiotic activities in addition to being endogenous in the human body. Secondly, they never will cause osteoporosis aggravation like what has been shown and reported with the prescribing of synthetic PPI. In fact, spermine has been shown to possess anti-osteoclast and anti-migration activities by inhibiting the migration of preosteoclasts, which prevents osteoporosis. Thirdly, many PAs are pro-inflammatory cytokine's modulators – potent antiinflammatory in addition to decreasing necrotic tissues and essential for tissue's and cellular regeneration. How incredible is all this? Agmatine is also an effective anti-ulcerogenic agent who has been shown to possess antibacterial activity against H. Pylori, antiinflammatory, sedative for stress induce ulcers, etc....

AGMATINE (AGM) 118 activities.

A clonidine displacing substance (CDS). Mild reductions in heart rate and mild hypotensive effect by activating both central and peripheral control systems *via* modulation of several of its molecular targets including: **activates imidazoline receptors** subtypes, **norepinephrine (noradrenaline)** release and **NO production**.

A **neuromodulator** and **co-transmitter**, in the mediation of both the CNS and peripheral nervous systems.

Abrogate the acute restraint stress (ARS) in the hippocampus.

Activates adenylate cyclase (AC), which is effective for the treatment of angina, antidepressant by modulating neurotransmitters serotonergic (inhibitor) or dopaminergic (stimulator), antiglaucoma reduce intraocular pressure, antispasmodic, antiasthma, bronchodilator, cerebral vasodilatation and increase brain blood circulation, anti-eczema, antihypertension, antiobesity, and antipsoriatic.

Activates S-adenosylmethionine decarboxylase (AdoMetDC) and an ornithine decarboxylase (ODC) inhibitor.

Advanced glycation end product (AGE) inhibitor

AGM is a precursor for PAs synthesis, **competitive inhibitor of PAs transport**, and an **inducer of spermidine/spermine acetyltransferase (SSAT)**, and **inducer of antizyme**.

AGM is a specific **inhibitor of the key enzyme diamine oxidase (DAO)** for GABA formation in PAs degradation pathway.

Alcohol withdrawal. A *n*-methyl-d-aspartate receptor (NMDAR) modulator, to reverse its intoxicating side effects.

Analgesic **adjuvant** for alleviating pain and improving quality of life in spinal discs-degenerative associated radiculopathy.

Anti-adipose, anti-cellulite, anti-lipolysis

Governing ruler of PAs homeostasis and its **indirect role on autophagy homeostasis** by keeping in check the correct level of spermidine responsible for inducing autophagy. This is the beauty of phytochemistry with human chemistry and their interactions.

Growth hormone (GR) agonist

Hypoglycemic effects of AGM are the result of simultaneous modulation of several molecular mechanisms involved in blood glucose regulation.

Hypotensive (mild)

Improves athletic exercise: endurance, performance, and recovery.

Improves cognition at an oral dose of 1.6-6.4mg/kg: 150lb person the dose could be 217-435mg and never to exceed 6.4mg/kg of the total of bodyweight. AGM increases activity in the prefrontal cortex areas of the brain associated with working memory, attention span, executive functioning, and long term potentiation (memory storage and recall), by increasing activity in the hippocampus.

Improves gastro esophageal reflux disease (GERD).

Improves post-traumatic stress disorder (PTSD).

Increase total catecholamines from the adrenal glands: epinephrine, norepinephrine, dopamine, and serotonin having an antidepressive effect, in addition to AGM increasing GABA which has GABAergic effect typically having a relaxing, antianxiety, and anti-convulsive effects.

Increased of arginine and phosphorus are associated with a decreased risk of infection post-operative stress and is used to synthesize the antimicrobial molecule AGM under conditions of active infection.

Increases brain-derived neurotrophic factor (BDNF).

<p>Anti-Alzheimer, anti-dementia</p> <p>Anti-anorexic nervosa</p> <p>Antianxiety</p> <p>Antiasthemic by its antiviral activity and increasing adenosine triphosphate (ATP) cellular energy currency.</p> <p>Anticancer especially for intestinal cancers and <i>adjuvant</i> synergistic with chemotherapy for leukemia.</p> <p>Anti-cerebral edema</p> <p>Anti-chronic fatigue syndrome (CFS)</p> <p>Anti-constipation</p> <p>Anticonvulsant</p> <p>Antidepressant activity. In the brain, prefrontal cortex, responsible for working memory, attention span, and executive functioning, AGM increases serotonin, norepinephrine/noradrenaline by modulating α2-adrenergic receptor, and increases dopamine levels. The regulation of 5-HT1A/1B and α2 receptors, and activation adenylate cyclase (AC) in the frontal cortex is one of the important mechanisms by which AGM exert an antidepressant-like action. The antidepressant-like effect may also be dependent on its ability to maintain the pro-/anti-oxidative homeostasis in the hippocampus. A selective serotonin reuptake inhibitors involve in the modulation of imidazoline receptors by AGM. Furthermore, AGM is one of the modulator for neurohormones in the brain keeping them in balance.</p> <p>Antidiabetic effect increasing insulin secretion, sensitivity, and release by AGM is produced by two mechanisms, stimulation of adrenal gland to enhance β-endorphin secretion immunoreactivity in a way parallel to the reduction of plasma glucose in sham-operated high fructose fed diet and a direct activation of peripheral I2-imidazoline receptor in tissues, for its insulinotropic activity. It was also shown to increase pancreatic β-cells. These studies strongly suggest that AGM may be beneficial as an <i>adjuvant</i> for the treatment of diabetes type 2, and having a direct effect for glucose homeostasis.</p> <p>Anti-diabetic ketoacidosis</p> <p>Antifibrosis (liver)</p> <p>Antihyperglycemic short term</p> <p>Antihypertensive <i>adjuvant</i> effect by the activation of I1-imidazoline receptor in the medulla oblongata</p>	<p>Increases β-endorphins through the activation of imidazoline receptor I(2)R, which is mainly induced by the I(2A) subtype located in adrenal glands, and increase adenosine triphosphate (ATP) production, both of which are known to increase cellular energy in the muscles and endorphins happy chemical in the brain and pain relievers.</p> <p>Induces the release of some peptide hormones</p> <p>Inhibit nitric oxide synthase (NOS) enzymes, which modulate elevated levels of nitric oxide (NO).</p> <p>Inhibit the effects on caffeine-induced locomotor activity ONLY in males.</p> <p>Inhibition of protein arginine ADP-ribosylation could be beneficial in the treatment of restenosis and has been implicated in some forms of cancer and neuroprotective effect.</p> <p>Inhibits the thermal hyperalgesia</p> <p>Insulinotropic</p> <p>Ion channels. Including: ATP-sensitive K+ channels, voltage-gated Ca²⁺ channels, and acid-sensing ion channels (ASICs).</p> <p>Lipid peroxidation inhibitor</p> <p>MAO inhibitor</p> <p>Matrix metalloproteases (MMPs). Indirect down-regulation of the enzymes MMP 2 and 9.</p> <p>Membrane transporters. AGM specific-selective uptake sites, organic cation transporters (mostly OCT2 subtype), extraneuronal monoamine transporters (ENT), PAs transporters, and mitochondrial AGM specific-selective transport system.</p> <p>Modulates N-methyl-D-aspartate (NMDA) receptor activation.</p> <p>Narcotic true alternative capable of real analgesia</p> <p>Nephroprotective: preventing renal dysfunction</p> <p>Nerve cell's protector by ways of attenuating AGEs formation preventing nerve cell's damage. Cuts down on production of destructive enzymes (called metalloproteases) that can lead to nerve damage. It decreases pain-inducing activities, by preventing some mineral salts from getting into your neurons. Improves cell's communication by increasing neurotransmitter function. Modulates the production of nitric oxide (NO) and thus enhances the ability of nerves to sustain insults.</p> <p>Neuronal by increasing neurogenesis. Regulates neuronal stem cell differentiation.</p>
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<p>is NOT by itself sufficient for rebellious hypertension multi-causes.</p> <p>Anti-hypometabolic syndrome</p> <p>Antihypoxic, increases oxygen level</p> <p>Anti-ischemic by inhibition of nitric oxide (NO) elevation, seen in hypoxic-ischemic brain injury (Feng et al., 2002).</p> <p>Anti-ischemic</p> <p>Anti-metabolic syndrome</p> <p>Antineoplastic</p> <p>Antineurodegenerative</p> <p>Anti-neurodegenerative</p> <p>Antineuropathy at a dose of 1,300-2,670 mg once or three times daily. Adult effective average dose is 1,000 mg 3 times daily. High dose are very sedative cautions should be exercised operating or driving any machinery.</p> <p>Anti-neurotoxic</p> <p>Antinociceptive <i>adjuvant</i> potentiates morphine-induced spinal but not supraspinal analgesia.</p> <p>Antiobesity</p> <p>Anti-obsessive compulsive disorder (OCD) all types.</p> <p>Antioxidant activity against free radicals, H₂O₂, LPS-induced reactive oxygen species (ROS) accumulation involving Heme oxygenase 1 (HO-1) expression induced by the nuclear factor-erythroid 2-related factor (2Nrf2) via PI3K/Akt pathway activation. Nrf2 is a powerful protein that is latent within each cell in the body, unable to move or operate until it is released by an Nrf2 activator. Once released it migrates into the cell nucleus and bonds to the DNA at the location of the Antioxidant Response Element (ARE), which is the master regulator of the total antioxidant system that is available in all human cells.</p> <p>Antioxidant</p> <p>Antiproliferative activity due to its regulatory effects on intracellular PAs levels.</p> <p>Anti-radiculopathy for spinal disks degeneration</p> <p>Anti-renal hypertension</p> <p>Antisciatica</p> <p>Antisciatica: adult dose 1,000-2,000 mg 3 times daily depending on severity and response.</p>	<p>Neuroprotective</p> <p>Neurotransmitter receptors and receptor ionophores. Nicotinic, imidazoline I1 and I2, α2-adrenergic, glutamate NMDAr, and serotonin 5-HT2A and 5HT-3 receptors. Binds to α2-adrenergic receptor and imidazoline receptor binding sites, and blocks NMDA receptors and other cation ligand-gated channels.</p> <p>Nootropic</p> <p>Opioids/morphine addiction, including the psychoactive plant called Kratom – Psychotria viridis from the Mitragyna Speciosa tree, which contains an alkaloid 7-hydroxymitragynine stronger than morphine that exhibits opiate-like analgesia and addiction. Kratom's popularity has surged since the crack-down on opiates by the DEA; it also costs a lot less than traditional opiates. The recommended dose for AGM is 2 grams before each dose tapered, three times daily. Reduce daily opiate by half a milligram every day. Smoothest and most effortless taper imaginable, and clear of withdrawal symptoms so effectively. No anxieties or depressions were observed, and in my professional experience, this needs to be a part of the protocol used in every rapid detox. AGM is a much superior agent to the drugs Suboxone and Methadone, which also produce terrible withdrawal symptoms when tapering down.</p> <p>Orexigenic (appetite stimulant) effect of AGM is coupled to increased neuropeptide Y (NPY) activity mediated by stimulation of α₂-adrenoceptors (causing sedation and analgesia) within the hypothalamic paraventricular nucleus (PVN). This signifies the importance of AGM or α₂-adrenoceptor modulators in the development of novel therapeutic agents for the treatment of behavioral eating-related disorders especially when having severe appetite loss as seen in anorexia nervosa, or muscle wasting due to cystic fibrosis (CF), geriatric decreasing appetite, cancer, or AIDS.</p> <p>Potentiate the effect of opioid analgesia (positive action), and inhibit tolerance to and substance dependence or relapse on opioids/morphine (negative actions) chronic users. A biphasic opioid function modulator (BOFM). The main mechanisms of AGM action are related to inhibition of the adaptation of opioid receptor signal transduction induced by chronic opioid/morphine treatment or addiction.</p>
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<p>Anti-sepsis</p> <p>Anti-traumatic brain injury (TBI)</p> <p>Antitumor</p> <p>Antiulcerogenic</p> <p>Antiviral action by preventing virus attachment to the cell surface: herpes simplex virus (HSV-1), human cytomegalovirus (CMV), Epstein barr virus (EBV), human papillomavirus HPV types 6, 16, 31, and 45, and respiratory syncytial virus (RSV).</p> <p>Anxiolytic</p> <p>Apoptosis modulator</p> <p>Attenuate short-term social memory and locomotor activity impairments, neuroprotective against the loss of dopaminergic neurons.</p> <p><i>Biphasic apoptosis</i> and <i>anti-apoptosis</i> activities: having a selective apoptosis activity for cancer cells only, while leaving unscathed healthy cells. Having a neuroprotective effect against neurotoxins and having anti-apoptotic activity on brain neurons thus, improving cognitive function as well as learning memory.</p> <p>Calcium Ca²⁺ channels blocker (CCB), antihypertensive.</p> <p>Cardioprotective by interacting with endothelial cells being a vasodilator. These cells form a thin layer along blood vessel walls. As AGM molecules pass through blood vessels, they attach to receptors on endothelial cell membranes. In response, endothelial cells make nitric oxide (NO), a gas that helps to dilates blood vessels.</p> <p>Causes a 3-fold increase in the nicotinamide adenine dinucleotide phosphate (NADPH) oxidase activity of neuronal nitric oxide synthase (nNOS) and leads to oxidative inactivation of the enzyme, which is been proven effective in the prevention of morphine tolerance. NADPH is also used for anabolic pathways, such as lipid and cholesterol synthesis, and fatty acid chain elongation. It protects against the toxicity of reactive oxygen species (ROS), allowing the regeneration of glutathione (GSH), an important antioxidant that is used in metabolic and biochemical reactions for DNA synthesis and repair, protein synthesis, prostaglandin synthesis, amino acid transport, and enzyme activation.</p> <p>Chemopreventive</p> <p>Chemotherapeutic</p>	<p>Prevents parietal cells destruction during the formation of gastric acid for the treatment of gastroesophageal reflux disease (GERD).</p> <p>Pro-inflammatory cytokines modulator inhibits: IL-1β, IL-6, NF-kB, and TNF-α.</p> <p>Protect the retinal ganglion cells from apoptosis and this has been noted with topical application of AGM in a reduction of cell apoptosis from 55.44% down to 18.65%, associated with a reduction in positive ocular hypotensive for the treatment of glaucoma. This protective effect also extends to ischemic ocular injury and potentially all retinal disorders.</p> <p>Protects the brain from neurotoxins and strokes (ischemia). AGM is a novel neurotransmitter that is created and destroyed in the brain neurons at the site of which it is also stored. The mechanism of action allows AGM to regulate neurotransmission, indirectly modulating NMDA receptor activity and prevents glutamate-induced excitotoxicity. Neurotransmitter regulation improves significantly in NMDA receptors that play many crucial roles in memory and increased learning capacity. AGM modulates all crucial memory receptors.</p> <p>Reduce body weight gain by elevating the synthesis and levels of cAMP, thereby mimicking the effects of caloric restriction with respect to metabolic reprogramming. It improves tissue and systemic levels of carnitine and short chain acylcarnitine, increased β-oxidation but diminished incomplete fatty acids oxidation, decreased fat but increased protein mass, and increased hepatic ureagenesis, and gluconeogenesis but decreased glycolysis.</p> <p>Reduce elevated cortisol levels, by reducing the hyperactivation of the hypothalamic-pituitary-adrenal axis (HPAA).</p> <p>Regulate hypometabolic syndrome in CFS and prevents metabolic syndrome including antiobesity.</p> <p>Regulation of hepatic fatty acid oxidation (FAO) and ketogenesis by AGM for the treatment of CFS or any caused of asthenia.</p> <p>Regulator of mitochondria cell death (apoptosis).</p> <p>Sedative effect</p> <p>Speeds up wound healing, serve in the coordination of the early and repair phase pathways of arginine in inflammation.</p> <p>Stimulate gluconeogenesis</p>
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<p>Control of ureagenesis (urea cycle) waste removal of nitrogen.</p> <p>Cytokines modulator</p> <p>Enhance glomerular filtration rate (GFR) and to exert nephroprotective effects by preventing kidney atrophy.</p> <p>Enhance signaling through the Cannabinoid (CB1) receptor.</p> <p>For the treatment of dopamine deficiency: Attention-deficit/hyperactivity disorder (ADHD), Autism, Drug addiction, Obsessive-compulsive disorder (OCD), Parkinson disease (PD), Restless leg syndrome (RLS), Schizophrenia, and Tourette syndrome (TS).</p> <p>Free radical scavenger, especially H₂O₂</p> <p>Gastroprotective due to its alkalinity, where it protects parietal cells of the stomach lining against the back up of stomach acid for the treatment of gastro esophageal reflux disease (GERD).</p>	<p>Stimulates hepatic fatty acid oxidation (FAO) a possible mechanism for up-regulation of ureagenesis in the removal of toxic nitrogen. Increased O₂ uptake and urea synthesis even without addition of exogenous fatty acid.</p> <p>Suppression of MicroRNA let-7a expression by AGM regulates neural stem cell (NSC) differentiation.</p> <p>Synergistic with all illicit drugs potentiating their effects.</p> <p>Synergistic with the antidepressant and smoking cessation drug Bupropion also known as Wellbutrin and Zyban.</p> <p>α2A receptor agonist binds with a high affinity to both imidazoline and α2-adrenergic receptors of all subclasses. AGM with morphine produces antinociceptive enhancement via an α2-adrenergic receptor-mediated mechanism and AGM–morphine combinatorial synergistic potentiating effect an effective therapeutic strategy for medical treatment of pain.</p>
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SALICYLATES
are divided into two groups, **acetylated** and **nonacetylated**.
synthesized from the amino acid phenylalanine with 97 activities.
Salicylic Acid (SA)
Methyl Salicylate (MSA)

<p>Aldose-reductase-inhibitor (ARI)</p> <p>Ameliorate hepatic steatosis by inhibition of the hepatokine fetuin-A through the modulation of AMPK-NF-κB pathway (Jung et al., 2013).</p> <p>AMP-activated protein kinase: a key regulator of energy balance with many roles in human disease. AMPK activators have both antitumor and antiinflammatory activities. AMPK may be involved in viral infection: downregulation of AMPK during hepatitis C virus infection appears to be essential for efficient viral replication.</p> <p>AMPK activator</p> <p>Analgesic</p> <p>Analgesic, non-steroidal antiinflammatory (NSAID) a Cyclooxygenase 2 (COX-2) inhibitor.</p> <p>Angiogenesis inhibitor: prevents by 35% breast, colon, pancreas, and prostate cancers. Antineoplastic. Suppress the proliferation in lymphoblastic leukemia, and melanoma in human cancer cells induces apoptosis.</p> <p>Anti; acne, dandruff, psoriasis, calluses, corns, keratosis pilaris and wart's.</p>	<p>Directly activates adenosine monophosphate-activated protein kinase (AMPK) a central regulator of cell growth and metabolism and this action play a role in the anticancer effects of SA.</p> <p>Egr1 inhibitor</p> <p>Endorphins Stimulator</p> <p>Fungicide</p> <p>High glucose has been shown to alters tendon homeostasis through downregulation of the AMPK/Egr1 pathway and the expression of downstream tendon-related genes in tenocytes. AMPK activation with SA reduced the expression of early growth response transcription factor 1 (Egr1), transcription factor scleraxis (Scx), transforming growth factor beta 1 (TGF-β1), collagens: Col1a1, Col1a2, and biglycan (BGN) could be of benefits for the treatment of diabetic tendinopathy.</p> <p>IL-1β and IL-8 inhibitors</p> <p>Immune reporter's response signaling pathways.</p>
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Antiangiogenic	Increases cell metabolism rate to take advantage of new complete more advantageous nutrient and environmental conditions.
Anti-arteriosclerotic destabilizing plaque that builds up in the arteries.	
Antiarthritic	Insectifuge
Antibacterial	Insulinemic
Anticancer (breast, colon, epithelial, leukemia, melanoma, pancreas, and prostate), antidementia.	Keratolytic
Anticancer: breast, lymphoblastic leukemia, melanoma, and prostate, cancer cells.	Melanin inhibitor
Antidermatotic	Mild antibiotic
Antidiabetic: antihyperglycemic, hypoglycemic, and insulinemic. Activation of AMPK altering the energy status of the cell, provides beneficial outcomes in fighting against metabolic disorders such as insulin resistance and type 2 diabetes. SA reverse many of the metabolic defects associated with insulin resistance.	Mild antibiotic.
Antieczemic	Mild anti-clotting
Antifungal	Mild diuretic
Antifungal	mTORC1 inhibitor
Antihyperglycemic	NSAIDs (nonsteroidal anti-inflammatory drugs), SA inhibit the enzymes COX-1 and COX-2. It also inhibits pro-inflammatory cytokines.
Antihyperpigmentation	Pesticide
Antiichthyosic	Potent epidermal growth factor receptor (EGF-r) tyrosine kinase inhibitor.
Anti-ischemic	Potentiate NADPH oxidase-mediated reactive oxygen generation in some cancer cells to promote apoptosis.
Antimicrobial	Prevents heart attack. Reduces the risk of ischemic stroke and indirectly lowers the risk of dementia that complicates vascular disease.
Antineoplastic	Prostaglandin inhibitor.
Antineuralgic	Reduce the risk of pregnancy complications in women with pre-eclampsia and in those with antiphospholipid antibody syndrome (APS, Hughes syndrome).
Antioncycchomycotic	Release of natural endorphins.
Antioxidant	SA and Jasmonic acid: RNA silencing mechanisms systemic response, as they can block virus replication.
Antiperiodic	SA can be listed among antioxidants and phytochemicals.
Antipodagric	SA is capable of penetrating and breaking down fats and lipids, causing moderate chemical burns of the skin at very high concentrations.
Antiproliferative	SA paradoxical effect. Uricosuric (remove excess uric acid) in large amount and in low dosage increase uric acid either way they be both beneficial or not beneficial this is dose dependent and the state of health of an individual.
Antiproliferative.	
Antipsoriatic	
Antipyretic	
Antipyretic.	
Antirheumatic	
Antiseborrheic	
Antisenescence	

<p>Antiseptic</p> <p>Antitumor</p> <p>Antitympanitic</p> <p>Antiviral</p> <p>Antiwart</p> <p>Apoptotic</p> <p>Apoptotic.</p> <p>BGN inhibitor</p> <p>Cancer-preventive</p> <p>Carbonic anhydrase (CA) isozymes I and II inhibitors.</p> <p>Cardioprotective</p> <p>c-Myc inhibitor</p> <p>Col1a1 and Col1a2 inhibitors</p> <p>Comedolytic</p> <p>Cosmetic application by inhibiting the heat shock protein 47 expression. Retards senescence (regulatory role) by preventing photoaging of the skin being anti-melasma for the treatment of hyperpigmentation.</p> <p>Dermatitogenic</p> <p>Desmolytic</p>	<p>Sa possess mild diuretic properties.</p> <p>SA regulates c-Myc level at both transcriptional and post-transcription levels. Inhibition of c-Myc may be an important pathway by which SA exerts an anticancer activity, decreasing the occurrence of cancer in epithelial tissues.</p> <p>Scx inhibitor</p> <p>Suppresses growth in PI3K-mutant breast cancer by activating AMPK and inhibiting mammalian target of rapamycin complex 1 (mTORC1) signaling.</p> <p>TGF-β1 inhibitor</p> <p>The mild anti-clotting effect of natural salicylates provides cardioprotective benefits; reduce the production of platelet aggregating factor thromboxane A2. Antithrombotic.</p> <p>Thermogenic</p> <p>Tineacide</p> <p>TNF-α inhibitor</p> <p>Triggers systemic immune response.</p> <p>Trypsin inhibitor</p> <p>Uricosuric</p> <p>Works as a keratolytic agent by causing the cells of the epidermis to shed more readily, preventing pores from clogging up, and allowing room for new cell growth regeneration.</p>
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STRIGOLACTONES
are a group of sesquiterpene lactones (terpenoids) and are synthesized from a carotenoid precursor, with 47 activities.

<p>Activates stress response mediated by both P38 and JNK1/2 MAPK.</p> <p>Allelochemical</p> <p>Anthelmintic</p> <p>Anti-Alzheimerian</p> <p>Antiatherosclerosis</p> <p>Antibiotic</p> <p>Anticancer: breast, cervical, colon, epidermal (oral), leukemia, liver, lung, melanoma, osteosarcoma, and prostate.</p> <p>Antidysplastic</p> <p>Antiinflammatory</p> <p>Antimalarial</p>	<p>Increases ATP</p> <p>Increases CA²⁺ permeability</p> <p>Induce apoptosis</p> <p>Induce G2/m cell cycle arrest</p> <p>Irreversible mammospheres dissociation and cell apoptotic.</p> <p>Mediate fast synaptic transmission</p> <p>Neuronal</p> <p>Neuroprotective</p> <p>PDGF inhibitor</p> <p>Phosphorus homeostasis</p> <p>PI3K/AKT activation inhibitor</p> <p>Potent inhibitors of self-renewal</p>
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<p>Antimetastatic</p> <p>Antimicrobial</p> <p>Antineoplastic</p> <p>Antineurotoxic</p> <p>Antiparasitic</p> <p>Antiproliferative</p> <p>Antitumor</p> <p>Chemopreventive</p> <p>Cytokines modulator</p> <p>Cytotoxic: against human oral epidermoid (KB), cervical epithelioid (Hela), and liver (hepa59T/VGH) carcinoma cells.</p> <p>Enhance the absorption of essential nutrients.</p> <p>Favors endophytic growth, increase genome instability.</p>	<p>Potent synergy with BRCA1-proficient cells</p> <p>Prebiotics</p> <p>Prevents restenosis</p> <p>Pro-cognitive effects by modulating the α-7-nachr activation and desensitization.</p> <p>Protects synapses from $\alpha\beta$-induced damage.</p> <p>Regulates nitrogen level</p> <p>Selective DNA repair inhibitor</p> <p>Selective inducer of DNA damage</p> <p>Stimulate NADH concentration</p> <p>Stress and survival signaling pathways modulator.</p> <p>Synergistic with chemotherapy</p> <p>Synergistic with PARP inhibitors</p> <p>VSMC inhibitor</p>
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SYSTEMIN with 21 investigational potential activities.

<p>Anti-adipocyte</p> <p>Antibacterial</p> <p>Anti-chloasma</p> <p>Antifungal</p> <p>Anti-hyperpigmentation</p> <p>Antihypertensive</p> <p>Antiinflammatory</p> <p>Antiobesity</p> <p>Antisenescence</p> <p>Antiviral Hep C and HIV</p> <p>Antiwrinkle</p>	<p>Atrial natriuretic peptides (ANP) modulator.</p> <p>Cardioprotective</p> <p>Congestive Heart Failure (CHF).</p> <p>Diuretic</p> <p>Hypotensive</p> <p>Immunomodulator</p> <p>Increases collagen and elastin.</p> <p>Increases connective tissue</p> <p>Protease inhibitor</p> <p>Vasodilator</p>
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PLANT STEM CELLS (PSC®): Meristem, the botanical term, refers to specialized cells responsible for plant growth and regeneration in both plants and humans. PSC® have already demonstrated to possess a significant potential in the prevention and treatment of human diseases, being potent rejuvenator in the reversal of the aging process by **increasing somatic cells fitness** with the synergistic activity of the phytohormone abscisic acid (ABA). With 16 activities.

<p>Cell cycle regulation and increasing cell mitosis</p> <p>Epigenetic</p> <p>Increase sexual reproduction</p> <p>Increases the activity of human lymphocytes</p> <p>Interrupts defective genes and inhibit DNA mistranslated information.</p> <p>Intervene with genetic toxicity</p>	<p>Not only prevents and limits but also heals cytological injuries caused by toxins.</p> <p>Prevents collagen and elastin loss</p> <p>Reduces inflammation</p> <p>Regulates master genes</p> <p>Rejuvenators of dying cells</p> <p>Repairs and prevents tissues necrosis</p>
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They assist in the rejuvenation of dying cells and tissues.	Restores the reticulo-endothelial system (RES)
Modulates signaling cascades and their pathways	Stimulate human stem cell renewal by 80%
Table created by Dominique Richard © 2017.	