Protocatechuic Acid; A Natural Green Chemical Fertilizer.

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Title: Protocatechuic Acid; A Natural Green Chemical Fertilizer.

Eligibility criteria is met for the **Small business Award.**

Focus Area 3: Design of greener chemicals. Protocatechuic acid (PCA) is a green chemical reagent, presently categorized as biocide by EPA. PCA is found in small amounts everywhere in nature; soil, water ways, all plants, fruit and vegetables. PCA is common to the human diet. The bacteria in the human bowel manufacture a small amount daily.

Fertilizer Environmental Problems are Well Known: Many fertilizers have accompanying toxicity. The most common yet most hazardous fertilizer is anhydrous ammonia. Nitrogen and phosphorus runoff from agricultural fields are some of the largest sources of pollution to coastal "dead zones" across the United States.

Nitrogen fertilizers containing nitrates can contaminate groundwater because nitrates are highly soluble in water. At high levels, nitrates can poison humans, particularly children. Lower levels of nitrates can also be deadly to amphibians.

Plants absorb the fertilizers through the soil, and thereby enter the food chain. In addition, fertilization may lead to water, soil and air pollution. The amount of nitrate may increase in drinking water and rivers as a result of high levels of nitrogen fertilizer use.

Today there is an urgent need to find new ways to satisfy the current and growing food demand and maintain crop protection and food safety. One of the most promising ways is to replace chemical fertilizers with biofertilizers. That is exactly what PCA would do.

Most recent Milestones are the critical discoveries resulting in a US patents application using protocatechuic acid (PCA) as a natural fertilizer. The work is original and novel as evidenced by the US patent application.

Application No. 16/890,911 title: FERTILIZER COMPOSITIONS AND PLANTS CONTAINING PROTOCATECHUIC ACID, AND USES THEREOF. 2021

It is known that phenolic acids in plants enhance resistance to disease and predators while protecting plants against herbivores and plant-associated microorganisms. The science supporting this and an US patent application demonstrated that PCA, a phenolic acid used as a fertilizer at time of planting increased the phenolic acid of PCA in the grown lettuce plant 6 and 7 times (not 6 or 7%).

The US Component: The inventor is an US citizen. All the research was performed at independent contract laboratories in USA. The assembly of the commercial fertilizer is in all independent contact USA GMP facilities.

Abstract:

PCA is a small molecule, a phenolic acid, and a biocide by EPA designation. This Green Chemistry application proposes using PCA as a fertilizer for plants, fruits and vegetables. This

use of PCA is intended to replace any and all fertilizers that have known toxicity; i.e. anhydrous ammonia, and those with nitrogen and phosphorous. PCA is safe by every measure. PCA is a natural chemical found throughout the environment; soil, plants, trees, rivers and lakes, fruits and vegetables. It is common to the human diet. It has been designated at Generally Recognized As Safe (G.R.A.S.) by FDA as a food flavoring. PCA is non-toxic, non-allergenic and non-mutagenic.

The implementation is eminent, awaiting EPA approval. The raw material is available in 1000-kilogram quantities accompanied by a Certificate of Analysis. There are multiple government certified manufacturing facilities in USA. Distribution channels are in place. There is a known ready market waiting for purchase.

The quantitative benefit to the environment is the replacement or minimizing of existing fertilizers. The amount spared by the use of this alternative natural reagent is large, but not easily calculated. A PCA substitute would eliminate the use of toxins; i.e. anhydrous ammonia, and those with nitrogen and phosphorous.

The experimental evidence supporting the US patent application assessed the natural amount of PCA in the control soil which was minimal as naturally utilized by soil bacteria. The experimental method added PCA to the lettuce seeds in three ways: i.e. by preliminary soaking, raw crystals sparsely sprinkled in the planting bed, and 1% PCA in water spray on the seeds in the planting trough.

After maturity, the lettuce was analyzed for amount and the effect of PCA. There was 6 and 7 times more PCA in the treated lettuce compared to the controls. The experimental leaves were larger. The treated lettuce did not brown on cutting or bruising. Therefore, the treated lettuce had potential longer shelf live. The increased PCA in the plant carries an increased nutritional value as the literature documents the many health and wellness benefits of PCA. Plus, the increased phenolic acids within a plant increases the potential to resist predators and contamination during growth.

The PCA fertilizer leaves the soil and goes to animal and human consumption of the plant. The amounts of PCA discharged into the environment would be miniscule, not concentrated, widely distributed and add little PCA to the already abundant PCA in nature. PCA being native to the environment will not add any foreign pollution. There will no need to mitigate as required with the present toxins of nitrogen and phosphorous.

PCA's potential toxicity to the waste water has been cited, as by Das, et al. This is not likely. The amounts (5-25mM) in vitro supporting their contention, ironically is the same amount shown as beneficial in vivo mammalian studies. PCA at 25 mM in water on an infected mammalian wound resulted in accelerated healing. The use of PCA will not produce any fumes, carbon dioxide nor require any extra use of energy.

Scope of the program

The use of protocatechuic acid (PCA) as a fertilizer should be a safe and effective utilization not otherwise present with existing fertilizers with toxic properties.

Dose Explanation: The dosage terminology requires some clarification. PCA in aqueous delivery vehicle of 0.25-1% may be considered the delivery dose. This would be when preliminary coating of seeds and or the spray application to the seeds in the soil. Either way upon evaporation of the water the raw crystals remain. This is same result as when the raw crystals are applied to the seeds in the planting trough. Either way the resultant dose is 100% raw crystals in small amounts delivered sparsely to the soil.

Fate of the This Fertilizer: The natural amount of PCA in the soil is miniscule as it is naturally metabolized by the soil's bacteria. The additional amount of PCA as a fertilizer is miniscule. The 1% PCA spray in water would be localized to the seeds themselves and the seeds in the planting trough. The entire field would not be sprayed with this reagent and method. The amount may be estimated as follows. 1% PCA in 1 liter is 10 grams. (1 gallon = 3.7 liters) A gallon of water would have 37 grams. A gallon of 1% PCA delivered as prescribed may cover an acre of field in the trough or on the seeds. The PCA leaves the field as it moves into the plant which will be widely distributed.

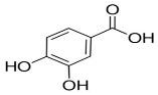
Distribution: The PCA fertilizer leaves the soil, and enters the plant, fruit or vegetable. Upon harvesting the PCA enhanced produce is distributed to many various and diverse markets. Subsequent sale to the consumer cause further disperses the PCA throughout the environment.

Upon ingestion of a PCA enhanced produce, the human pharmacokinetics and pharmacodynamics are well known. PCA is readily absorbed into the blood stream in 30 minutes. Its peak concentration is 2 hours, during which time it is further metabolized to various multiple benign chemicals common to the human body. The duration is 6 hours leaving only small amount of PCA to be eliminated in the urine or feces.

Therefore, the dispersion of the original dose of PCA fertilizer even if used in large amounts at a given geographical location would result in miniscule amounts discharged widely beyond the original or any subsequent geographical environment.

This method of fertilization with PCA eliminates introduction of hazardous substances and hazards to public health that may exist with toxic reagents presently in use; triclosan or quaternary ammoniums.

Chemical Nature: PCA is a small molecule, a benzoic acid with chemical name of 2,4 di-hydroxybenzaldehyde. The CAS number is 99 50 3.



PCA exists throughout nature and the addition of miniscule amounts by the known amounts, distribution and biological fate will not be a pollutant, but only add small amount to the existing PCA ecological presence.

Realized Benefits and Drawbacks

Benefits: The benefits are clear and many for the use of PCA as a fertilizer. The protection and enhancement of the plant due to the increased phenolic acid. The absence of any potential adverse impact upon the environment due to its geographical dispersion and subsequent degradation by human consumption of the produce.

The health benefits of PCA are well known should PCA be in produce.

PCA is a known powerful anti-oxidant which is common to health and wellness. 10X more powerful than vitamin E.

PCA is known anti-inflammatory. Inflammation is common denominator of all disease.

As show in the US patents, PCA is an anti-bacterial, biofilm destroying and anti-viral for encoated virus; i.e. SARS-CoV-2 when applied to an article of hard or cloth surface.

Drawbacks: The draw backs as fertilizer are not apparent. The chemical is non-hazardous, readily available, and cost effective, has ease of application and is biodegradable.

Safety: PCA has been recognized as safe for ingestion by FDA as a food flavoring additive. PCA has an existing FDA G.R.A.S. designation as Generally Recognized As Safe. http://www.ift.org/~/media/Food%20Technology/pdf/2009/06/0609feat_GRAS24text.pdf

PCA is Common to the Human Diet: You can and do eat it. In fact, you consume it every day in your diet. PCA is ingested daily in various amounts and foods. The following is a list and amounts of PCA in common foods.
http://phenol-explorer.eu/contents/polyphenol/412

The bacteria in the human bowl produce a small amount daily.

The potential inflammability is nil with the dry crystalline residue. The same with water.

Pilot Plant Exists: The reagent PCA is available from many international sources. There are many US GMP plants available for manufacture into a commercial product. The following are used at the present time; Samson Pharma, City of Commerce, CA and QYK Brands, Garden Grove, CA.

Manufacture: PCA is presently biochemically manufactured, thereby eliminating the trace metals found in previous production by extraction from plant material. Certificate of Analysis accompanies each production which is subsequently verified by independent laboratory for percentage and purity.

EPA application was initiated in Jan 2020; but is still under review.

Technology Comparisons: PCA is not found in other fertilizers. PCA is native to the environment. It is safe by any measure. PCA is non-toxic, non-allergenic and non-mutagenic. Although prices are rising due to shipping costs plus world-wide inflation the cost of goods for PCA is relatively low, such to be commercially viable and competitive with the existing market.

Performance: This has been established in vivo proof of principle pilot studies supporting an US patent application.

The broad application is assured by societal and humanitarian unmet need, the product availability and the small amounts of PCA released over time into the environment following produce production, distribution and consumption.

Planned Commercialization: Commercialization awaits an EPA application that was submitted 23 months prior to this writing. The reagent is available in 1000-kilogram quantities. The manufacturing facilities are in place.

Technology was launched under emergency in a non-related use as sanitizer spray due to its antimicrobial properties.

The Commercial Products: PCA is delivered as a raw crystal to the user. It has a 2-year shelf life. It would be combined with fresh water at the farm site. There is safety in its use concerning amount as PCA solubility in water is limited at 1.24%. The raw crystals are easily controlled in amount via normal application methods.

Science and Innovation: The application is original, and determined novel as evidence by the US patent application.

Human Metabolism: The pharmacokinetics and pharmacodynamics are known; already in the medical literature.

Reference

1. Das, R., Hamid, S. & Annuar, M. Highly Efficient and Stable Novel NanoBiohybrid Catalyst to Avert 3,4-Dihydroxybenzoic Acid Pollutant in Water. *Sci Rep* **6,** 33572 (2016). https://doi.org/10.1038/srep33572