IMPACT FUSION INTERNATIONAL

Nutri-Mastic

Intact Nutrition™

SGP+

Research, Validation and Commercialization of Technologies

Disclaimer:

1. The following document is a Work-In-Progress (WIP). Hence, there are space holders marked in RED within the paper for additional studies that are under review by the IFUS Scientific Team.

2. This paper is initiated from claims being made by ranchers and dairymen applying SGP+™ as part of their respective Bovine Ration Management.

3. The intention of this paper is to offer plausible scientific reasoning and evidence as to why these respective ranchers and dairymen are observing specific improvements in the respective Herd Performance.

4. This paper also attempts to explain why present scientific thinking, reasoning, and established analytical methods may not be fully actualized or capable of explaining the efficacy of SGP+™ in generating the Herd Performance reported to IFUS by ranchers and dairymen.

5. This paper in a result of the IFUS' Scientific Team's search for raw truth, even if that truth does not support the claims of ranchers and dairymen applying SGP+™ as part of the respective Bovine Ration Management.

6. This paper acknowledges that the IFUS Scientific Team is often faced with the question, "That is well and good in practice and results, but what about the theory?" (i.e., the paper is driven by Herd Performance Results, which at times lack established quantitative measures).

7. However, when costs are reduced by orders of magnitude, odors and flies disappear from pastures, antibiotics are no longer required, infant calf mortality is all but eliminated, herds require less water, meat quality is said to significantly improve, milk bags are said to be huge, and more, then it begs the questions, "How and Why?"

8. To that effect, IFUS has compiled significant evidence that supports the reports from ranchers and dairymen that flies are no longer found on their herds and fly larvae cannot be found in their manure pats.

9. Hence, IFUS concludes that SGP+™ can have a dramatic effect on preventing the New World Screwworm Fly from (1) being attracted to beef and dairy cattle, (2) wanting to feed off the cow, (3) discouraging the fly to lay her eggs into the cow, and (4) preventing the larvae from becoming a mature fly. There is even evidence to suggest that the Humic Substances produced by SGP+™ can affect the New World Screwworm's gestation once its larvae fall to the ground.

Part 1a of 5: Plausible Scientific Evidence of the Efficacy of SGP+™ in Bovine Herd Resistance to the Screwworm Fly and General Fly Population

(Rev.4-30May25-ifus)

CONFIDENTIAL

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Per study after study on bovine health and well-being, it seems that the adage of old holds, whereby "an ounce of prevention is worth a pound of cure."

Hence, IFUS offers what it believes is that ounce of prevention as it offers a cure.

Preface:

The IFUS Scientific Team holds an incredible value for raw scientific truth.

With that, the Team's exploration into natural remedies to mitigate, ameliorate, and/or eradicated the New World Screwworm Fly begins with a study published in 2021: Ficus palmate, Juniperus procera, and Nerium oleander: These plants have been evaluated for their larvicidal effect against the screwworm fly. "Larvicidal Activity of Selected Plant Extracts Against the Screwworm Fly Chrysomya Albiceps," Al-Jameeli M. M. Larvicidal, Biosci Biotech Res Asia 2021;18(3). http://dx.doi.org/10.13005/bbra/2934

The ingredients in IFUS's Proprietary Bovine Ration Management Product / Technology (SGP+™) contains the active ingredients found in *Nerium Oleander* and more. Hence, IFUS offers in this paper plausible scientific evidence as to the efficacy of SGP+™ to remediate, mitigate, and possibly ameliorate fly infestations on beef and dairy herds (and this includes the New World Screwworm Fly).

Furthermore, in the study "Health-Promoting Phytonutrients Are Higher in Grass-Fed Meat and Milk," (van Vliet, Stephan & Provenza, Frederick & Kronberg, Scott. (2021). Frontiers in Sustainable Food Systems. 4. 555426. 10.3389/fsufs.2020.555426.), "Emerging data indicate that when livestock are eating a diverse array of plants on pasture, additional health-promoting phytonutrients—terpenoids, phenols, carotenoids, and anti-oxidants—become concentrated in their meat and milk. Several phytochemicals found in grass-fed meat and milk are in quantities comparable to those found in plant foods known to have anti-inflammatory, anti-carcinogenic, and cardioprotective effects. As meat and milk are often not considered as sources of phytochemicals, their presence has remained largely underappreciated in discussions of nutritional differences between feedlot-fed (grain-fed) and pasture-finished (grass-fed) meat and dairy, which have predominantly centered around the ω-3 fatty acids and conjugated linoleic acid. Grazing livestock on plant-species diverse pastures concentrates a wider variety and higher amounts of phytochemicals in meat and milk compared to grazing monoculture pastures, while phytochemicals are further reduced or absent in meat and milk of grain-fed animals. The co-evolution of plants and herbivores has led to plants/crops being more productive when grazed in accordance with agroecological principles. The increased phytochemical richness of productive vegetation has potential to improve the health of animals and upscale these nutrients to also benefit human health. Several studies have found increased anti-oxidant activity in meat and milk of grass-fed vs. grain-fed animals."

If what we understand about the Screwworm Fly, (specifically the New World Screwworm Fly) is true, then prevention is the single best preventative measure in dealing with the current infestation plaquing beef and dairy. Hence, based on Herd Performance reported by ranchers and dairymen using SGP+™ as part of their respective Ration Management, the Team continually explores how:

1. preventive measures through Bovine Ration Management,

2. can result in improved Bovine Herd Performance,

3. while providing natural ingredients that repel flies, to include the New World Screwworm Fly.

To that end, the IFUS Scientific Team is challenged with exploring:

- Best methods to ameliorate and/or mitigate the New World Screwworm Fly in manner that is timely, cost-effective, safe, environmentally-friendly, naturally, and prudent.

- Ingredients, which are byproducts of a Ration Management alternative, that ameliorates and/or mitigates the New World Screwworm Fly through supporting the overall health and well-being of the herd.

  Where the IFUS Scientific Team acknowledges that short-term radical methods may be required to stem the current/pending infestations, a longer-term solution may be in order…especially one born from "sustainability" and as a by-product of overall cost-effective Herd Performance. Furthermore, if Climate Science is even remotely correct, then the problem with the New World Screwworm Fly becoming an annual event may become a new reality. Even if the New World Screwworm Fly is ameliorated, there remains the challenge of overall fly management as it is said to "wreak $6 billion in losses annually to U.S. cattle production due to decreased weight gain or milk production, veterinary needs and control measures."

Other data tells a similar story:

- "The economic impact of fly problems on beef and dairy herds in the U.S. is significant, with annual losses estimated to be in the billions. Here are some key figures:
    - Horn flies: Estimated cost of over $850 million annually ("Causes, costs and effects of flies in beef cattle," Progressive Cattle, February 24, 2017)
    - Face flies: Contribute to industry losses estimated at $230 million (Understanding the Effects of Flies on Cattle Production, Champion Animal Health, October 7, 2020)
    - House flies: Economic losses due to nuisance or irritation, and the transmission of pathogens, estimated at around $750 million (Understanding the Effects of Flies on Cattle Production, Champion Animal Health, October 7, 2020)

Irrespective of the actual total dollars expended as losses to the beef and cattle industry on fly management, it is a substantial number.

Hence, our IFUS Scientific team is reaching out to the worldwide scientific community comprised of scientists in various fields of expertise. These efforts have uncovered substantial evidence that the ingredients from which SGP+™ is formulated can have a dramatic effect on preventing the New World Screwworm Fly from (1) being attracted to beef and dairy cattle, (2) wanting to bite the cow, (3) discouraging the fly to lay her eggs into the cow, and (4) preventing the larvae from becoming a mature fly.

Furthermore, cattle trials (at the two IFUS Test Ranches operated by private ranchers) have clearly demonstrated the reduction of other fly populations. Many of these flies are attracted to manure, where they lay their eggs. Many are also "biting" flies, that can cause irritations to the hide as well as the eyes, ears, nose, mouths, and rear-ends of the cattle. These reported decreases in "other" biting fly populations (by ranchers and dairymen applying SGP+™ as part of their respective ration management) suggests (1) a decrease in VOC's from the cow and its manure, (2) an increase in natural tannins or other such compounds that repel flies, (3) a reduction in wounds caused by the biting flies and/or from cows lacerating their hides from the irritation caused by these flies, and/or (4) a decrease in blood-born emissions that would otherwise attract the New World Screwworm Fly.

Hence, the IFUS Scientific Team offers in this "Part 1a" White Paper, scientifically plausible justification for the application of a formulation made from natural ingredients to include Chios Mastic Gum, Carob, Ionic Minerals, Sugarcane Bagasse, and Water. "Part 1a" is offered within a narrow context of broader science discussed in, "Part 1 of 5: Plausible Scientific Evidence of the Efficacy of SGP+™ in Bovine Herd Performance through Bovine Ration Management: Lignin, Degraded and Depolymerized Lignin, and Select Synergies from Mastic, Ionic Minerals, and Carob."

- Additionally, a "Part 2" White Paper presently under development with a first draft nearly complete offers further supporting evidence of the efficacy of SGP+™ ("Part 2: Plausible Scientific Evidence of the Efficacy of SGP+™ in Bovine Herd Performance through Bovine Ration Management: The Science Behind Mastic and Carob Individually and Collectively as well as Synergies with Ionic Minerals and Degraded/Depolymerized Lignin.")

Of note is that the research performed to date by the IFUS Scientific Team is in search of explanations as to the Herd Performance Claims being made by ranchers and dairymen who are applying SGP+™ as part of their respective Ration Management Strategy. Furthermore, presently established and standard analytical methods (e.g., Forage Analysis, Manure Analysis, I.V.T.D., etc.) provide intriguing and invaluable clues as to the efficacy of SGP+™…notwithstanding that these valuable analytical and testing methods were not designed to fully illustrate the efficacy of a product / technology like SGP+™.

So, to begin with the IFUS Scientific Team's search for truth, the following thoughts are offered for your consideration.

IFUS Point 1: What we think we know about the "New World" Screwworm Fly vs. the Old World Screwworm Fly.

IFUS Point 1a: The "New World Screwworm (NWS, Cochliomyia hominivorax) is a devastating pest. When NWS fly larvae (maggots) burrow into the flesh of a living animal, they cause serious, often deadly damage to the animal. NWS can infest livestock, pets, wildlife, occasionally birds, and in rare cases, people." ("New World Screwworm, Animal and Plant Health Inspection Service, U.S. DEPARTMENT OF AGRICULTURE, Last Modified: May 07, 2025) (https://www.aphis.usda.gov/sites/default/files/new-world-screwworm-what-you-need-to-know-brochure.pdf)

IFUS Point 1b: "One female can lay 200 – 300 eggs at a time and may lay up to 3,000 eggs during her 10- to 30-day lifespan. Eggs hatch into larvae (maggots) that burrow into the wound to feed on the living flesh. After feeding, larvae drop to the ground, burrow into the soil, and emerge as adult screwworm flies." https://www.cdc.gov/myiasis/about-new-world-screwworm-myiasis/index.html

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IFUS Point 2: What attracts the Screwworm Fly to Beef and Dairy Herds?

IFUS Point 2a: "The New World Screwworm fly is attracted to open wounds or body orifices on cattle and dairy herds, where it lays its eggs. The larvae, which hatch from these eggs, burrow into the skin and feed on the tissue, causing significant damage to the animals. This behavior makes the flies particularly harmful to livestock, as they can lead to severe infections and even death if not treated promptly (1 / 2)."

IFUS Point 2a-1: Ref.(1) Protecting the herd from New World screwworm: A new threat to herds comes from the New World screwworm, which is currently advancing through Central America into southern Mexico. (https://www.beefmagazine.com/livestock-management/protecting-the-herd-from-new-world-screwworm)

IFUS Point 2a-2: Ref. (2) Livestock Health: Beware of New World Screwworm, (https://utbeef.tennessee.edu/livestock-health-beware-of-new-world-screwworm/)

IFUS Point 2b: What specific chemicals are thought to attract the Screwworm Fly?

There is evidence that suggests that, "Screwworm females are attracted to wounds that may be as small as those caused by the feeding of the invasive cattle tick Rhipicephalus (Boophilus) microplus (OIE, World Organisation for Animal Health, 2013), which has periodic outbreaks in Mexico and south Texas (Pérez de León et al., 2012). Feeding by screwworm larvae expands the wound (myiasis) attracting further oviposition and, if not treated, this may cause the death of the animal. It is suggested that the olfactory senses of a Screwworm Fly (like most flies damaging bovine herds) are as highly evolved as any insect encountered on Earth. (Gutierrez AP, et.al., Deconstructing the eradication of new world screwworm in North America: retrospective analysis and climate warming effects. Med Vet Entomol. 2019 Jun;33(2):282-295. doi: 10.1111/mve.12362. Epub 2019 Feb 13. PMID: 30758067; PMCID: PMC6849717.)

Studies illustrate that within 2-seconds of a manure pat leaving the cow, many flies can sense, land, sample, and begin laying larvae within a manure pat.

Furthermore, Paul V. Hickner, et.al. published an article titled, "A new formulation of screwworm fly attractant with reduced hazardous chemicals and transport restrictions," (J. of Medical Entomology, 60(4):631-636 (2023). https://doi.org/10.1093/jme/tjad043). In it, Dr. Hickner states, "Lures are an important component of the screwworm eradication program, where they are used for surveillance, sample collection, and strain evaluation in the field. The first chemical lure, later named swormlure, was developed based on the attractiveness of C. hominivorax to volatile organic compounds (VOCs) produced from decomposing animal tissues. The formulation has changed little over the years and presently contains 10 chemicals, one of which is dimethyl disulfide (DMDS)."

Hence, the IFUS Scientific Team begins with the notion of an olfactory understanding of the Screwworm Fly. The intention is possible remediation of those "Root Causes" to olfactory attraction of the Screwworm Fly to Bovine Herds, but also considers the olfactory repulsion of the fly.

> IFUS Point 2b-1: In addition to the attraction of the New World Screwworm Fly to sulfides, studies offer "The specific chemicals that attract the screwworm fly to bovines include:
>
> - Acetic acid
> - Benzoic acid
> - Butyric acid
> - Valeric acid
> - Phenol

- Indole
- p-Cresol
- Iso-butanol
- Sec-butanol
- Acetone

These chemicals are primarily derived from decomposing or bacteria-inoculated bovine blood (1)."

> IFUS Point 2b-1.1: Ref.(1) "A new formulation of screwworm fly attractant with reduced hazardous chemicals and transport restrictions," Paul V. Hickner, et.al., J. of Medical Entomology, 60(4):631-636 (2023). https://doi.org/10.1093/jme/tjad043

IFUS Point 2b-2: However, there is evidence that suggests that a Screwworm Fly can be attracted to a cow's hide from so much as a Tick bite. (https://www.cattlerange.com/articles/2025/05/ncba-believes-new-world-screwworms-will-enter-the-u-s-by-late-summer/)

It is suggested that the olfactory senses of a New World Screwworm Fly (like most flies damaging bovine herds) are as highly evolved as any insect or bug encountered on Earth.

IFUS Point 2b-2: Paul V. Hickner, et.al, in a study titled, "Physiological and molecular correlates of the screwworm fly attraction to wound and animal odors," (Scientific Reports volume 10, Article number: 20771 (2020) https://doi.org/10.1038/s41598-020-77541-w), states: "Antennal olfactory sensitivity is the outcome from the binding of odorants with the members of three divergent protein families—odorant receptors (ORs), ionotropic receptors (IRs), and gustatory receptors (GRs)—together referred as chemosensory gene families (31). We previously identified 79 ORs, 84 GRs, 88 IRs and 51 odorant binding proteins (OBPs) in the screwworm genome (30). The birth and diversification of these gene families (32), together with the functional characterization of candidate genes—such as those differentially expressed between sexes, or physiological stages of female—offers the potential to isolate and identify chemicals that are highly effective and selective (4). Taken together, this work identifies the olfactory similarities and differences between two screwworm species and provides insight into the molecular phylogeny of chemosensation in the screwworm flies."

IFUS Point 2b-2.1: Ref.(31) Robertson, H. M. Molecular evolution of the major arthropod chemoreceptor gene families. Annu. Rev. Entomol. 64, 227–242 (2019).

IFUS Point 2b-2.2: Ref.(30) Scott, M. J. et al. Genomic analyses of a livestock pest, the New World screwworm, find potential targets for genetic control programs. Commun. Biol. 3, 424. https://doi.org/10.1038/s42003-020-01152-4 (2020).

IFUS Point 2b-2.3: Ref.(32) Benton, R. Multigene family evolution: perspectives from insect chemoreceptors. Trends Ecol. Evol. 30, 590–600 (2015).

IFUS Point 2b-2.4: Ref.(4) Carey, A. F. & Carlson, J. R. Insect olfaction from model systems to disease control. Proc. Natl. Acad. Sci. 108, 12987–12995 (2011).

IFUS Point 2b-3: Hence, we consider the "binding of odorants with the members of three divergent protein families—odorant receptors (ORs), ionotropic receptors (IRs), and gustatory receptors (GRs)." We also note that *D. melanogaster* is being used as a "Baseline Indicator Species."

IFUS Point 2b-3.1: Odorant receptors (ORs): "A total of 55 ORs were expressed in both sexes, with the exception of Or3, which had no read counts in any of the male replicates. Of the 55 ORs expressed in the antennae, 16 (29.1%) were DE, with eight displaying female-biased expression and eight displaying male-biased expression (Fig. 4a). Based on the estimated OR phylogeny, three female-biased and six male-biased ORs were closely related to D. melanogaster ORs (Fig. 5b). Five ORs with male-biased expression (ChomOr13, ChomOr65, ChomOr73, ChomOr74 and ChomOr78) are in a clade with DmelOr67d, the cis-vaccenyl acetate pheromone receptor (34,35) (Fig. 4b,c)."

IFUS Point 2b-3.1a: Ref.(34) Ha, T. S. & Smith, D. P. A pheromone receptor mediates 11-cis-vaccenyl acetate-induced responses in Drosophila. J. Neurosci. 26, 8727–

8733 (2006).

IFUS Point 2b-3.1b: Ref.(35) Kurtovic, A., Widmer, A. & Dickson, B. J. A single class of olfactory neurons mediates behavioural responses to a Drosophila sex pheromone. Nature 446, 542–546 (2007).

IFUS Point 2b-3.2: Ionotropic receptors (IRs): "The estimated IR phylogeny suggests that these are closely related to their namesake in D. melanogaster (Fig. 5b). In D. melanogaster, Ir75a detects several carboxylic acids (acetic, butyric and propionic) (40), while Ir76a detects amines such as pyrrolidine and phenylethylamine (41) (Fig. 5c)."

IFUS Point 2b-3.2a: Ref.(40) Benton, R., Vannice, K. S., Gomez-Diaz, C. & Vosshall, L. B. Variant ionotropic glutamate receptors as chemosensory receptors in Drosophila. Cell 136, 149–162 (2009).

IFUS Point 2b-3.2b: Ref.(41) Silbering, A. F. et al. Complementary function and integrated wiring of the evolutionarily distinct Drosophila olfactory subsystems. J. Neurosci. 31, 13357–13375 (2011).

IFUS Point 2b-3.3: Gustatory receptors (GRs): "None of the 15 GRs expressed in C. hominivorax antennae were DE between sexes. The antennal GRs included three putative CO2 receptors, of which two (ChomGr2 and ChomGr3) were among the most highly expressed GRs, while the third (ChomGr1) was expressed at a much lower level (Fig. S1a,b). All six putative sugar receptors (ChomGr4-Gr9) were expressed in the antennae (Fig. S1a,b). The estimated GR phylogeny suggests ChomGr25 is closely related to DmelGr57a (Fig. S1b), which is associated with bitter taste in D. melanogaster (45). These results are similar to findings in D. melanogaster in which two CO2 receptors and five sugar receptors were expressed in the antennae (46). Function of the remaining five GRs is difficult to predict due to their divergence from D. melanogaster GRs."

IFUS Point 2b-3.3a: Ref.(45) Weiss, L. A., Dahanukar, A., Kwon, J. Y., Banerjee, D. & Carlson, J. R. The molecular and cellular basis of bitter taste in Drosophila. Neuron 69, 258–272 (2011).

IFUS Point 2b-3.3b: Ref.(46) Menuz, K., Larter, N. K., Park, J. & Carlson, J. R. An RNA-seq screen of the Drosophila antenna identifies a transporter necessary for ammonia detection. PLoS Genet 10, e1004810 (2014).

IFUS 2b-4: Hence, the IFUS Scientific Team begins with the notion of olfactory understanding, and possible remediation of those "Root Causes" to olfactory attraction of the Screwworm Fly to Bovine Herds. Additionally, in latter sections, evidence of the impact of active ingredients in SGP+™ on the repulsion as well as larval development prevention of New World Screwworm Fly is offered.

IFUS 2b-5: Based on the highly evolved olfactory capabilities of the new World Screwworm Fly, we begin with open wounds as a first part of attraction and "The Chemicals that cause smell in open wounds include (1):

- Cadaverine and putrescine, released by anaerobic bacteria during tissue putrefaction.
- Volatile organic compounds (VOCs) such as amines, sulfur compounds, and fatty acids.
- Bacterial metabolic processes that produce volatile compounds."

IFUS Point 2b-5.1: Ref.(1) "The screwworm fly, Cochliomyia hominivorax (Coquerel), was successfully eradicated from the United States by the sterile insect technique (SIT). However, recent detection of these flies in the Florida Keys, and increased risk of introductions to the other areas warrant novel tools for management of the flies. Surveillance, a key component of screwworm control programs, utilizes traps baited with rotting liver or a blend of synthetic chemicals such as swormlure-4. **In this work, we evaluated the olfactory physiology of the screwworm fly and compared it with the non-obligate ectoparasitic secondary screwworm flies, C. macellaria, that invade necrotic wound and feed on dead tissue**. These two species occur in geographically overlapping regions. C. macellaria, along with other blowflies such as the exotic C. megacephala, greatly outnumber C. hominivorax in the existing monitoring traps. Olfactory responses to swormlure-4 constituents between sex and mating status (mated vs unmated) in both species were recorded and compared. Overall, responses measured by the antennograms offered insights into the comparative olfactory physiology of the two fly species. We also present detailed analyses of the antennal transcriptome by RNA-Sequencing that reveal significant differences between male and female screwworm flies. The differential expression patterns were confirmed by quantitative PCR. Taken together, this integrated study provides insights into the physiological and molecular correlates of the screwworm's attraction to wounds, and identifies molecular targets that will aid in the development of odorant-based fly management strategies. (Hickner, P.V., Mittapalli, O., Subramoniam, A. et al. Physiological and molecular correlates of the screwworm fly attraction to wound and animal odors. Sci Rep 10, 20771 (2020). https://doi.org/10.1038/s41598-020-77541-w)

IFUS 2b-6: "Biconical, F3, and wind oriented (WOT) traps, and black cloth targets, baited with the odour attractant swormlure-4, were assessed as catching and killing devices for the New World screwworm fly, Cochliomyia hominivorax (Coquerel), in Mexico." (Torr SJ, Hall MJR. Odour-baited targets to control New World screwworm, Cochliomyia hominivorax (Diptera: Calliphoridae): a preliminary study. Bulletin of Entomological Research. 1992;82(3):417-423. doi:10.1017/S0007485300041213)

IFUS 2b-6.1: "Fifteen candidate mixtures in which the ratios of the 10 components found in swormlure-2 (SL-2) were altered and compared with SL-2 for attractiveness to adult Cochliomyia hominivorax (Coquerel)."

IFUS 2b-6.1a: Swormlure 4 MeSH Supplementary Concept Data 2025:

- MeSH Supplementary
- Swormlure 4
- Unique ID
- C077611
- RDF Unique Identifier
- http://id.nlm.nih.gov/mesh/C077611
- Entry Term(s)
- swormlure-4

- Registry Numbers
- 93793-76-1
- CAS Type 1 Name
- Swormlure 4
- Heading Mapped to
  *Butanols
  *Carboxylic Acids
  *Disulfides
- Drug Combinations
  *Indoles
  *Phenols
- screwworm attractant; a mixture of dimethyl disulfide, sec- and iso-butanols, phenol, 4-methylphenol, indole, and acetic, butyric, valeric and benzoic acids
- Source
  - Med Vet Entomol 1992 Apr;6(2):98-102
  - Date of Entry
  - 1992/11/25
  - Revision Date
  - 2000/08/22

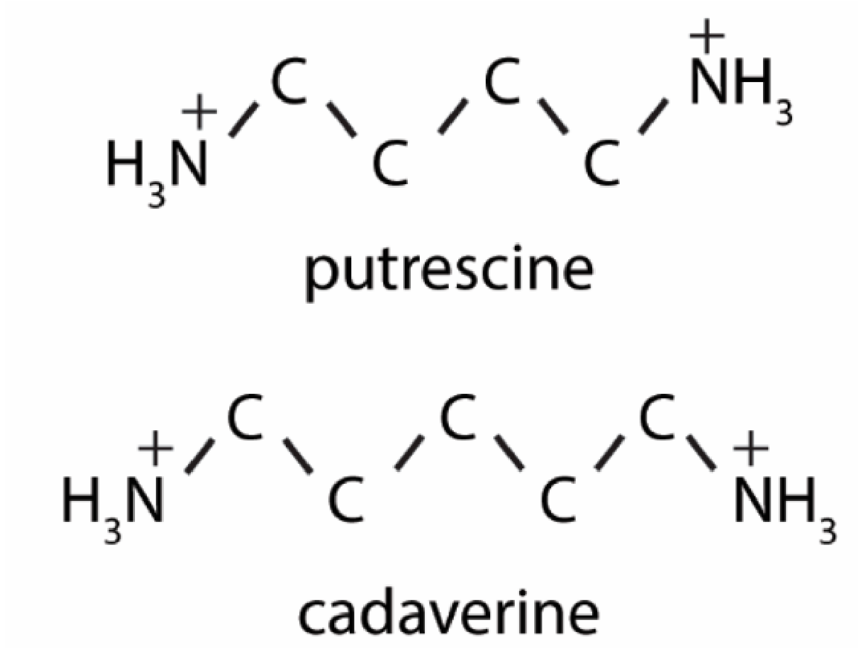
(USE THE INFORMATION ON IFUS 2b-6.1a to further develop following points)

IFUS Point 3: What do we know about the specific chemicals generated from wounds that attract the Screwworm Fly?

IFUS Point 3a-1: "Cadaverine and putrescine, released by anaerobic bacteria during tissue putrefaction."

IFUS Point 3a-1.1: "Putrescine (butane-1,4-diamine) and cadaverine (pentane-1,5-diamine; 1,5-Diaminopentane) are foul-smelling compounds produced when amino acids decompose in decaying animals. They are also found in small amounts in living cells. L. Briege and O. Bocklisch isolated both compounds in 1885, and A.

Ladenburg prepared them soon afterwards.(1)”



“Putrescine is a four-carbon alkane-alpha,omega-diamine. Putrescine is formed by the decarboxylation of ornithine and arginine and is responsible for the foul odour of putrefying flesh. It has a role as a fundamental metabolite and an antioxidant. Cadaverine is a five-carbon, aliphatic diamine synthesized by the decarboxylation of lysine. It is less toxic than histamine and tyramine and can cause adverse effects such as hypotension and bradycardia when consumed via the digestive route.(1)”

“Bacteria use diamines, like cadaverine or putrescine, generated by the decarboxylation of lysine or arginine, to buffer the pH of their environment.(1)”

IFUS Point 3a-1.1a: Ref.(1) TüNDE KOVáCS. Cadaverine, a metabolite of the microbiome, reduces breast cancer aggressiveness through trace amino acid receptors.[J]. ACS Applied Electronic Materials, 2019. DOI:10.1038/s41598-018-37664-7.

IFUS Point 3a-2: Additional volatile organic compounds (VOCs) such as Skatole (also known as 3-methylindole) are produced in dying animal flesh. IFUS wonders if Skatole serves as an attractant to both the Female and the Male New World Screwworm Fly. Swormlore4 contains indoles as part of its formulation.

IFUS Point 3a-2.1: "Skatole or 3-methylindole is an organic compound belonging to the indole family. It occurs naturally in the feces of mammals and birds and is the primary contributor to fecal odor. In low concentrations, it has a flowery smell and is found in several flowers and essential oils, including those of orange blossoms, jasmine, and Ziziphus mauritiana. It has also been identified in certain cannabis varieties. (1)"

IFUS Point 3a-2.1a: Ref.(1)Oswald, Iain W. H.; et.al., (2023-10-12). "Minor, Nonterpenoid Volatile Compounds Drive the Aroma Differences of Exotic Cannabis". ACS Omega. 8 (42): 39203–39216. doi:10.1021/acsomega.3c04496. ISSN 2470-1343. PMC 10601067. PMID 37901519.

IFUS Point 3a-2.2: Biosynthesis, chemical synthesis, and reactions: Skatole is derived from the amino acid tryptophan in the digestive tract of mammals. Tryptophan is converted to indoleacetic acid, which decarboxylates to give the methylindole. (6, 7) Once it is created in the digestive tract of mammals, it is metabolized by cytochrome P450 enzymes in the liver. (8)

IFUS Point 3a-2.2a: Ref. (6) Whitehead, T. R.; et.al., (25 January 2008). "Catabolic pathway for the production of skatole and indoleacetic acid by the acetogen Clostridium drakei, Clostridium scatologenes, and swine manure". Applied and Environmental Microbiology. 74 (6): 1950–3. Bibcode:2008ApEnM..74.1950W. doi:10.1128/AEM.02458-07. PMC 2268313. PMID 18223109.

IFUS Point 3a-2.2b: Ref. (7) Yokoyama, M. T.; Carlson, J. R. (1979). "Microbial metabolites of tryptophan in the intestinal tract with special reference to skatole". The American Journal of Clinical Nutrition. 32 (1): 173–178. doi:10.1093/ajcn/32.1.173. PMID 367144.

IFUS Point 3a-2.2c: Ref. (8) Bilić-Šobot, Diana; et.al., (2016-10-20). "Chestnut wood extract in boar diet reduces intestinal skatole production, a boar taint compound". Agronomy for Sustainable Development. 36 62. Germany: Springer Science+Business Media. doi:10.1007/s13593-016-0399-1.

ISSN 1773-0155. OCLC 8092619612.

IFUS Point 3a-2.3: Skatole can be synthesized via the Fischer indole synthesis. (9) Emil Fischer (1886) "Indole aus Phenylhydrazin" (Indole from phenylhydrazine), Annalen der Chemie, vol. 236, pages 126-151; for Fischer's synthesis of skatole, see page 137. (Fischer was not the first to prepare skatole. It was prepared, via other methods, in 1880 by von Baeyer, and in 1883 by Otto Fischer and German and by Fileti.)

IFUS Point 3a-2.4: It is said to give a violet color upon treatment with potassium ferrocyanide.

IFUS Point 3a-2.5: Skatole, along with the fecal odorant indole, can be neutralized by combining it with other scents, by producing perfumes or air fresheners that lack skatole and indole. In a manner similar to noise-cancelling headphones, the scent produced by the resultant concentrations of skatole and indole relative to other substances in the freshener is thus "in-phase" and perceived as pleasant. (10) Holusha, John (15 July 1990). "Technology; Making Bad Smell Good by Tricking the Nose". The New York Times.

IFUS Point 3a-2.3: Insect studies: Skatole is one of many compounds that are attractive to males of various species of orchid bees, which apparently gather the chemical to synthesize pheromones; it is commonly used as bait for these bees for study.[11] It is also known for being an attractant for the Tasmanian grass grub beetle (Aphodius tasmaniae).[12]

ADDRef.(11)

Add Ref.(12)

IFUS Point 3a-2.3a Skatole has been shown to be an attractant to gravid mosquitoes in both field and laboratory conditions. Because this compound is present in feces, it is found in combined sewage overflows (CSO), as streams and lakes containing CSO water have untreated human and industrial waste. CSO sites are thus of particular interest when studying mosquito-borne diseases such as West Nile virus.[13] Add Ref.(13)

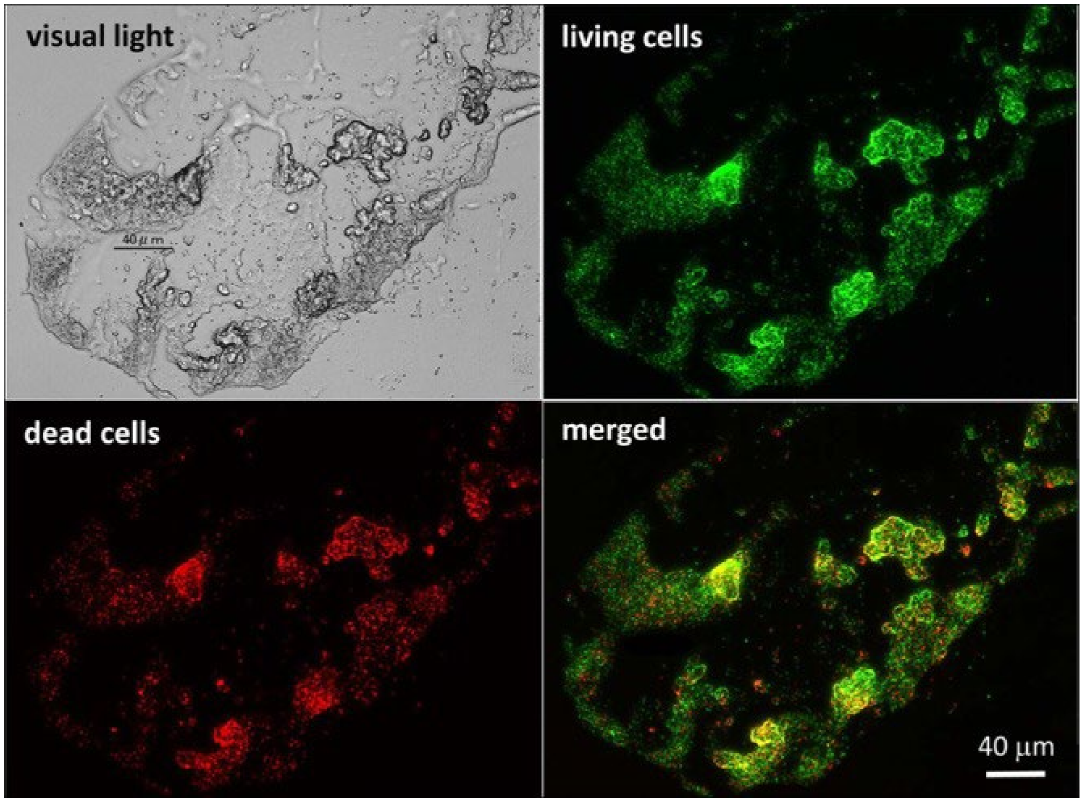
IFUS Point 3a-2.3b: The release of skatole by certain parasitic wasps in the family Bethylidae is used to determine which subfamily the species belongs to. Species of the Epyrinae subfamily release skatole, while those in the Bethylinae subfamily release a different chemical, spiroacetal.[14] Add Ref.(14)

IFUS Point 3a-2.4: Adult Screwworm male flies feed on flowers and live for 2–3 weeks, whereas adult females live approximately 10 days on average, feeding on serous fluids at animal wounds and decomposing animals (Thomas & Mangan, 1989; OIE, World Organisation for Animal Health, 2013). (Gutierrez AP, et.al., Deconstructing the eradication of new world screwworm in North America: retrospective analysis and climate warming effects. Med Vet Entomol. 2019 Jun;33(2):282-295. doi: 10.1111/mve.12362. Epub 2019 Feb 13. PMID: 30758067; PMCID: PMC6849717.

IFUS Point 3a-2.3c(i): Ranchers and dairymen, applying SGP+™ to their respective Ration Management, report that after a month or so of feeding SGP+™ to their herds, flies on cattle and fly larvae in manure pats are no longer found, and there is no smell other than a "fresh earth" smell to their pastures. One might deduce that through the ration mix of SGP+™ to typically cracked corn (85/15), improved digestibility and absorbability (per the plausible evidence presented in the IFUS Part 1 and 2 White Papers) remediates Skatole production. In doing so, the "flower-attractant" properties associated with Skatole are no longer present to attract the male New World Screwworm Fly, and may in fact also have an effect on the female as the males may produce in lower levels of attractant pheromones.

IFUS Point 3a-2.3c(ii): Of note, is a study that states: "In the gallic acid-supplemented cultures, up to 20% of the added indole remained unmetabolized compared to the control (0.32 mM relative to the initial 1.7 mM), indicating that gallic acid inhibits the degradation of indole by B. unamae CK43B." (Kim D, et.al., Induction of biofilm formation in the betaproteobacterium Burkholderia unamae CK43B exposed to exogenous indole and gallic acid. Appl Environ Microbiol. 2013 Aug;79(16):4845-52. doi: 10.1128/AEM.01209-13. Epub 2013 Jun 7. PMID: 23747701; PMCID: PMC3754724.)

(See Fig.4)



IFUS Point 3a-2.3c(iii): Also, other studies discuss the "Reduction of 3-methylindole production and prevention of acute bovine pulmonary edema and emphysema with lasalocid." (Nocerini MR, et.al., Reduction of 3-methylindole production and prevention of acute bovine pulmonary edema and emphysema with lasalocid. J Anim Sci. 1985 Jan;60(1):232-8. doi: 10.2527/jas1985.601232x. PMID: 3972744.)

IFUS Point 3a-2.3c(iii-a): Haydock LAJ, Fenton RK, Sergejewich L, Squires EJ, Caswell JL. Acute interstitial pneumonia and the biology of 3-methylindole in feedlot cattle. Animal Health Research Reviews. 2022;23(1):72-81. doi:10.1017/S1466252322000020

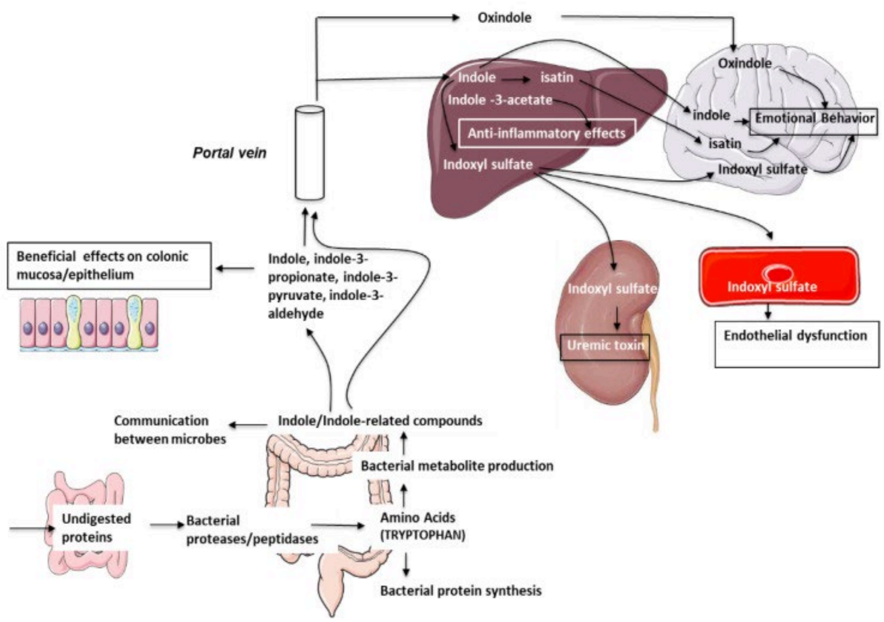
IFUS Point 3a-2.3c(iii-b): Hammond AC, Carlson JR, Breeze RG. Indole toxicity in cattle. Vet Rec. 1980 Oct 11;107(15):344-6. doi: 10.1136/vr.107.15.344. PMID: 7210436.

IFUS Point 3a-2.3c(iv): Later in this White Paper (and more comprehensively in the IFUS Part 1 & 2 White Papers), a broader explanation of the efficacy of Gallic Acid in cell rejuvenation (anti-aging and more) and preventing unwanted cell death is offered. Furthermore, the effect of Gallic Acid as an antimicrobial substance in disease causing bacteria is established. This offers once more plausible evidence that SGP+™, through the creation of Herd Wellness, offers a natural immunity to the effects brought to bear by the New World Screwworm Fly (and broader fly) problem impacting beef and dairy herd.

IFUS Point 3a-2.3c(v): With that said, one finds support for Herd Health and Well-Being as a preventative measure in fly remediation and more in science like: "Production of Indole and Indole-Related Compounds by the Intestinal Microbiota and Consequences for the Host: The Good, the Bad, and the Ugly," Naouel Tennoune, et.al., Microorganisms. 2022 Apr 28;10(5):930. doi: 10.3390/microorganisms10050930, PMCID: PMC9145683 PMID: 35630374

IFUS Point 3a-2.3c(vi): Hence, the roles of natural plant phytochemicals that promote health and well-being in mammals (like Gallic Acid), may in fact hold critical capabilities in providing cost-effective and eco-friendly solutions. This would include the elimination of odors associated with poor health, dying tissue, and more. Hence, this overall improvement in health and well-being might also provide some level of a defense shield through various integrated metabolic processes against pests like flies (to include the New World Screwworm Fly).

Figure 1. (Microorganisms. 2022 Apr 28;10(5):930. doi: 10.3390/microorganisms10050930)



Schematic representation of the effects of indole and indole-related compounds synthesized by the intestinal microbiota on communication between microbes, and effects of bacterial metabolites and co-metabolites on host tissues. A minor portion of undigested or partially digested dietary and endogenous proteins is transferred from the small to the large intestine. There, these nitrogenous compounds are intensively degraded into their amino acid constituents by bacterial proteases and peptidases. The amino acids, including tryptophan, are used for microbial protein synthesis and bacterial metabolism, releasing numerous compounds into the luminal content. Tryptophan metabolism by specific bacterial species releases indole and several indole-related compounds. Several of these compounds are implicated in communication between intestinal microbes. The indolic compounds indole, indole-3-propionate, indole-3-pyruvate, and indole-3-aldehyde have been shown in experimental models to exert beneficial effects on the intestinal mucosa/epithelium in different physiological and pathophysiological situations. Indole and related compounds are then transferred from the lumen to the portal blood and reach the liver. In the liver, indole is partly metabolized into indoxyl sulfate. Although indole and indole-3-acetate have been shown in pre-clinical studies to exert anti-inflammatory effects on liver cells, indoxyl sulfate released from the liver has been clearly identified as a uremic toxin that is deleterious for kidney tubular cells, thus accelerating chronic kidney disease. In addition, indoxyl sulfate exerts deleterious effects on the endothelium, and is thus one element involved in endothelial dysfunction. Emerging experimental data suggest that indole, indoxyl sulfate, isatin, and oxindole are 4 indolic compounds that enter the brain by unknown mechanisms, exerting there, depending on the dose used, either beneficial or deleterious effects on brain activity and emotional behavior.

IFUS Point 3a-2.3c(vii): For more information on the efficacy of Carob, Mastic Gum, and depolymerized lignin from the biome contained in Sugarcane Bagasse, please refer to IFUS Part 1 and Part 2 White Papers. There you will find plausible evidence of the efficacy of the ingredients found within the SGP+™ formulation and their positive impacts on the health, well-being, and overall Herd Performance. There are specific studies published on the positive effects of these active ingredients on bovine liver function and more. And, this includes resistance to fly populations to include the New World Screwworm Fly.

IFUS Point 3a-c: As stated above in IFUS Point 2b, sulfides are used to bate the New World Screwworm Fly. Hence this section will consider the fatty acids that attract the New World Screwworm Fly.

IFUS Point 3a-c.1: ADD THE SCIENCE DISCOVERED TO DATE HERE

IFUS Point 3a-d: Volatile organic compounds (VOCs) such as amines (the diamines Cadaverine and Putrescine), sulfur compounds, and fatty acids. As stated above in IFUS Point 2b, sulfides are used to bate the New World Screwworm Fly. Hence this section will consider the fatty acids that attract the New World Screwworm Fly.

IFUS Point 3a-d.1: ADD THE SCIENCE DISCOVERED TO DATE HERE

IFUS Point 4: How can SGP+™ mitigate or ameliorate the New World Screwworm Fly Infestation problem?

IFUS Point 4a: Plant-originated triterpenes are important insecticidal molecules. The research on insecticidal activity of molecules from Meliaceae plants has always received attention due to the molecules from this family showing a variety of insecticidal activities with diverse mechanisms of action. In this paper, we discuss 102 triterpenoid molecules with insecticidal activity of plants of eight genera (Aglaia, Aphanamixis, Azadirachta, Cabralea, Carapa, Cedrela, Chisocheton, and Chukrasia) in Meliaceae. In total, 19 insecticidal plant species are presented. Among these species, Azadirachta indica A. Juss is the most well-known insecticidal plant and azadirachtin is the active molecule most widely recognized and highly effective botanical insecticide. However, it is noteworthy that six species from Cedrela were reported to show insecticidal activity and deserve future study. In this paper, a total of 102 insecticidal molecules are summarized, including 96 nortriterpenes, 4 tetracyclic triterpenes, and 2 pentacyclic triterpenes. Results showed antifeedant activity, growth inhibition activity, poisonous activity, or other activities. Among them, 43 molecules from 15 plant species showed antifeedant activity against 16 insect species, 49 molecules from 14 plant species exhibited poisonous activity on 10 insect species, and 19 molecules from 11 plant species possessed growth regulatory activity on 12 insect species. Among these molecules, azadirachtins were found to be the most successful botanical insecticides. Still, other molecules possessed more than one type of obvious activity, including 7-deacetylgedunin, salannin, gedunin, azadirone, salannol, azadiradione, and methyl angolensate. Most of these molecules are only in the primary stage of study activity; their mechanism of action and structure–activity relationship warrant further study. (Insecticidal Triterpenes in Meliaceae: Plant Species, Molecules and Activities: Part I (Aphanamixis-Chukrasia), Meihong Lin, et.al., Int J Mol Sci. 2021 Dec 9;22(24):13262. Doi: 10.3390/ijms222413262, PMCID: PMC8704831 PMID: 34948062)

IFUS Point 4a-1: "The most effective natural pesticides derived from triterpenes include:

IFUS Point 4a-1.1: Azadirachtin: The active compound from the neem tree (Azadirachta indica), known for its insecticidal properties. Triterpenes: Various tetracyclic triterpenes possess anti-insect properties and are recognized for their effectiveness in pest control. These compounds are widely recognized for their effectiveness in natural pest control methods. ("Insecticidal Triterpenes in Meliaceae: Plant Species, Molecules and Activities: Part I (Aphanamixis-Chukrasia), Meihong Lin, et.al., Int J Mol Sci. 2021 Dec 9;22(24):13262. Doi: 10.3390/ijms222413262, PMCID: PMC8704831 PMID: 34948062.)

IFUS Point 4b: SGP+™ is a formulation of natural ingredients made from Chios Mastic Gum emulsified with Ionic Minerals in Water, Carob, and degraded & depolymerized Sugarcane Bagasse. The focus of:

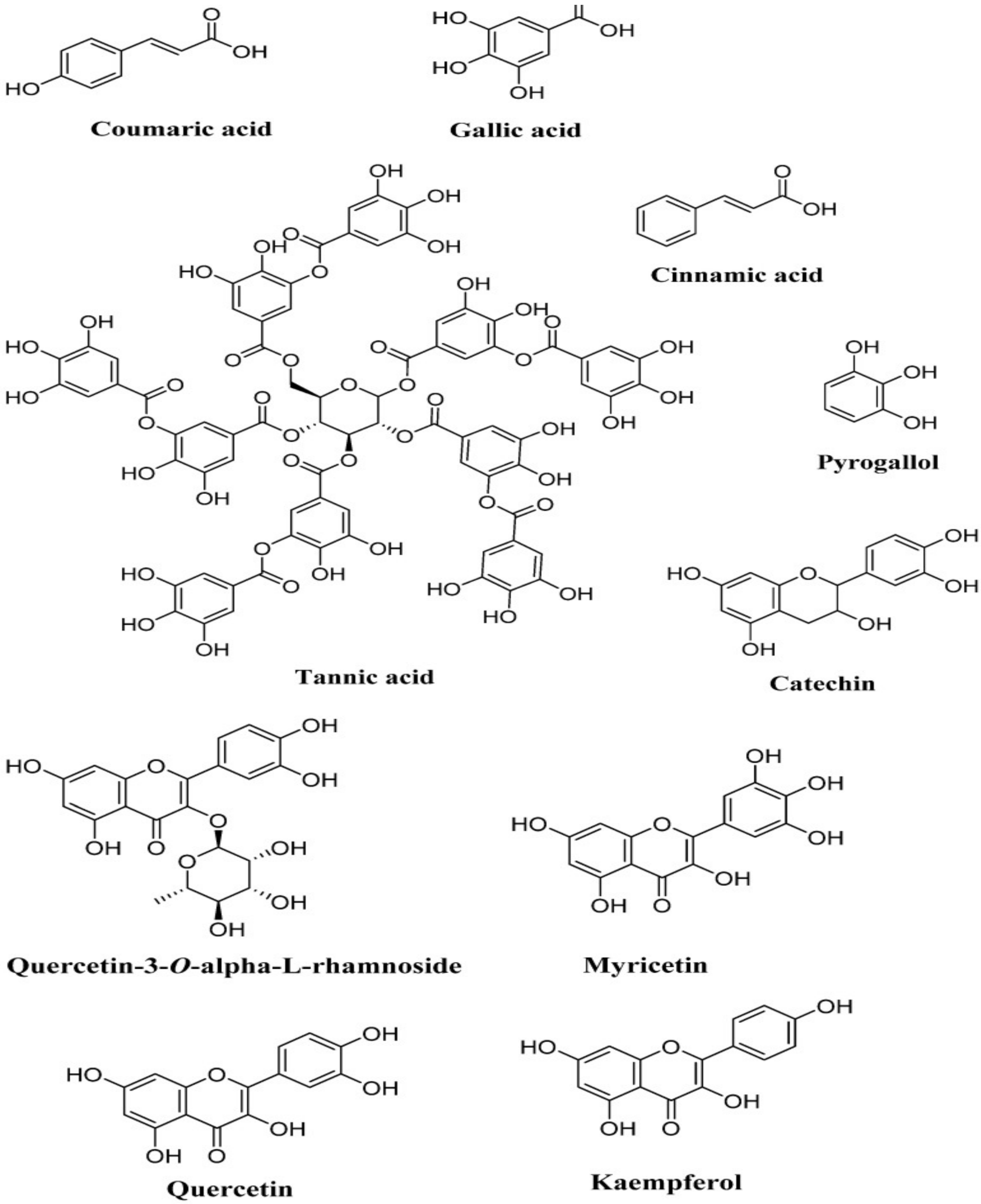
- IFUS Point 4b-1: Carob
- IFUS Point 4b-2: Mastic Gum
- IFUS Point 4b-3: Lignin
- IFUS Point 4b-4: Ionic Minerals

FIX FORMATTING

IFUS Point 4b-1: Carob: "*Ceratonia siliqua* (carob) contains insecticidal triterpenoids. Research has shown that the methanol extracts from the plant exhibit significant insecticidal activity against mosquito larvae and housefly larvae." ("Study of the effect of dryness and storage on Ceratonia siliqua L. stem extracts and evaluation of their insecticidal activity," Esraa A. Elhawary, et.al., Scientific Reports, Volume 15, Article number: 11123 (2025))

IFUS Point 4b-1.1: The content in this thread is to be used in further elucidation of active ingredient in Carob that is presently (or can be) used in fly management (specifically the New World Screwworm Fly). Of specific note continues to be the role of Gallic Acid (as well as the combination of other chemical compounds per Fig. 2 & Table 3 below) in so many aspects of in Bovine Ration Management, Digestion, Absorption, General Metabolism, and Manure…all of which greatly impact beef and dairy herd performance…as well as seemingly reducing or eradicating flies.

IFUS Point 4b-1.2: Figure 2. Demonstrates an example of "Chemical compounds present in C. siliqua L. (Exploring Carob (Ceratonia siliqua L.): A Comprehensive Assessment of Its Characteristics, Ethnomedicinal Uses, Phytochemical Aspects, and Pharmacological Activities" (Widad Dahmani, et.al., Plants (Basel). 2023 Sep 18;12(18):3303. Doi: 10.3390/plants12183303)



One then can find a more comprehensive listing and the sources of "Chemical composition of carob (C. siliqua L.)." in Table 3 below:

Class	Compounds	Part of the Plant	References
Phenols	Resorcinol	Leaves, pods, pulp, seeds	[102]
	Vanillin, fraxidin, 2,4-bis(dimethylbenzyl)-6-butylphenol	Leaves	[102,109]
	Alizarin, hydroquinone, lignan bis(trihydroxyphenyl)methanone	Pods	[110,111]
Phenolic acids	Gallic acid, chlorogenic acid, syringic acid, ferulic acid, coumaric acid, cinnamic acid	Leaves, pods, pulp, seeds	[4,5,89,102,110,111,112,113,114,115,116,117,118,119,120,121,122,123,124,125,126,127,128,129,130]
	4-Hydroxybenzoic acid, caffeic acid, vanillic acid, gentisic acid	Leaves, pods, pulp	[5,89,102,112,113,114,119,121,122,125,126,127,128,129]
	Tannic acid	Leaves, pods, seeds	[4,122]
	Ellagic acid, rosmarinic acid	Pods, pulp, seeds	[111,119,125,126,127]
	Sinapic acid	Pulp, seeds	[111,126]
	Pyrogallol, methyl gallate, benzoic acid, protocatechuic acid	Pods, pulp	[4,5,110,111,119,120,122,128,129]
	Quinic acid	Leaves, pods	[109,120]
	Transferulic acid, *O*-feruloylrutinose, *O*-feruloylrutinose isomer, *p*-coumaroyl-galloylhexose, *O*-*p*-coumaroylrutinose, siliquapyranone	Pods	[110,120,125]
	4-Hydroxy-coumaric acid	Leaves	[112,113]
	5-Caffeoylquinic acid, myristic acid, ascorbic acid	Pulp	[111,126,131]
Flavonoids	Epicatechin, quercetin, kaempferol, luteolin, catechin, apigenin	Leaves, pods, pulp, seeds	[4,5,89,102,110,111,112,113,115,116,118,119,120,121,122,123,124,125,126,127,128,130,131,132]
	Epigallocatechin gallate, rutin, myricetin, naringenin	Leaves, pods, pulp	[4,5,110,111,112,113,114,116,117,118,119,120,121,123,124,125,126,127,128]
	Iso-rhamnetin	Leaves, pods, seeds	[102,110,111,119,125]
	Leucoanthocyanins	Leaves, pulp, seeds	[133]
	Genistein	Leaves, pods	[5,119]
	Quercitrin, catechin tannins	Leaves, pulp	[112,113,115,127,133]
	Anthocyanins	Pods, pulp, seeds	[5,134,135]
	Myricitrin, daidzein, flavonol, morin	Leaves	[102,112,113,114,116]
	Rhamnosides, chrysoeriol, tricetin dimethyl ether, (iso)schaftoside-4′-*O*-glucoside, gallocatechin, chrysoeriol-*O*-deoxyheoxoside, dihydroxyflavanone hexoside, tetrahydroxy flavanone, trihydroxy flavone (apigenin isomer), kampferide, methoxykampferol, dihydroxy flavanone, tricetin dimethyl ether, cirsiliol, flavone glycosides, hydroxytyrosol	Pods	[5,110,119,120,122]
	Crismaritin, catechol, isoquercetrin, flavonols 3′,4′,5,7-OH, 2-hexadecanol scutellarin tetramethyl ether, silybin B, hydroxytyrosol, catechin gallate	Pulp	[4,126,129,131]
	Apigenin flavone, chrysin aglycones	Seeds	[119]

IFUS Point 4b-2: Does *Pistacia lentiscus* (Chios Mastic Gum Trees) have insecticidal properties?

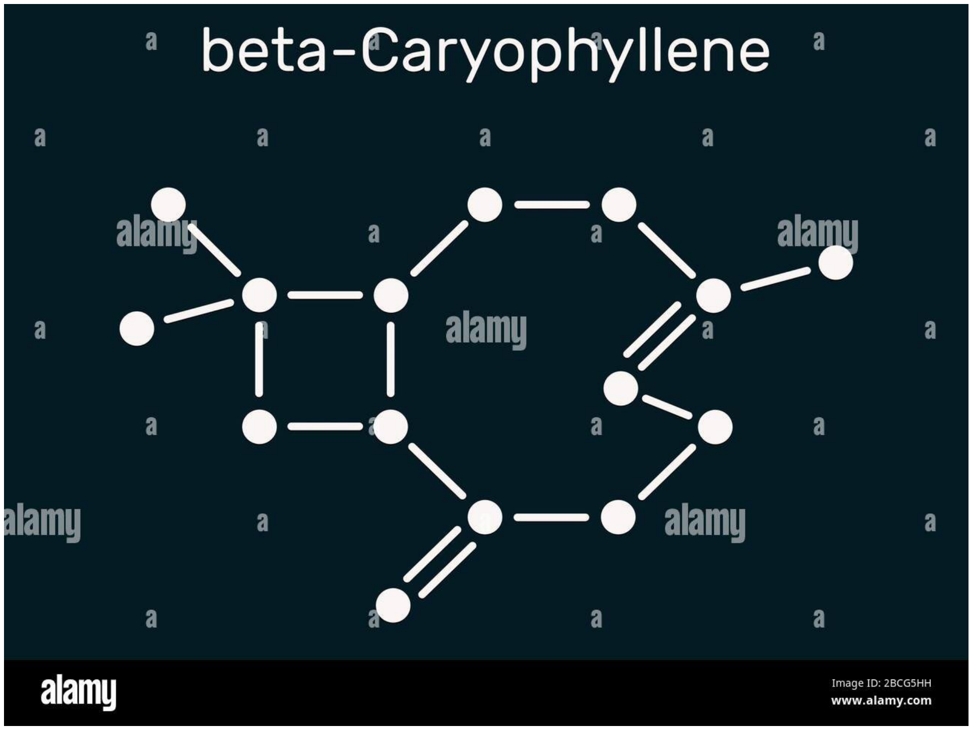
IFUS Point 4b-2.1: "Yes, Pistacia lentiscus has insecticidal properties. Research has shown that the fruit extract of Pistacia lentiscus is toxic to the larvae of the grapevine moth, Lobesia botrana, indicating its potential as an insecticide. Additionally, the essential oil from this plant has been found to exhibit acaricidal effects against red poultry mites, Dermanyssus gallinae, suggesting its effectiveness in controlling certain insect pests (1,2)

IFUS Point 4b-2.1a: Ref. (1) Insecticidal Effect of Pistacia lentiscus (Anacardiaceae) Metabolites against Lobesia botrana (Lepidoptera: Tortricidae), Ioanna Dasenak, et.al, Agronomy 2022, 12(4), 755; https://doi.org/10.3390/agronomy12040755

IFUS Point 4b-2,1b: Ref. (2) Pistacia lentiscus essential oil and its pure active components as acaricides to control Dermanyssus gallinae (Acari: Mesostigmata), Dhouha Alimi, et.al., Veterinary Parasitology, Volume 322, October 2023, 110028, https://doi.org/10.1016/j.vetpar.2023.110028

IFUS Point 4b-2.2: What chemical in *Pistacia lentiscus* repels insects?

IFUS Point 4b-2.2a: B-caryophyllene: "The chemical in Pistacia lentiscus that repels insects is β-caryophyllene, which is the most effective component of its essential oil. This essential oil has shown high repellent activity against various insect pests, making it a potential eco-friendly alternative to chemical repellents." (Pistacia lentiscus essential oil has repellent effect against three major insect pests of pasta, Hind Houria Bougherra, et.al., Industrial Crops and Products, Volume 63, January 2015, Pages 249-255)



IFUS Point 4b-2.2b: What do we know about β-caryophyllene? “Caryophyllene, more formally (−)-β-caryophyllene (BCP), is a natural bicyclic sesquiterpene that occurs widely in nature. Caryophyllene is notable for having a 29yclobutene ring, as well as a trans-double bond in a 9-membered ring, both rarities in nature.” (Sell, Charles S. (2006). “Terpenoids”. Kirk-Othmer Encyclopedia of Chemical Technology. Doi:10.1002/0471238961.2005181602120504.a01.pub2. ISBN 0471238961.)

IFUS Point 4b-2.2c: “It is a constituent of many essential oils, especially clove oil, the oil from the stems and flowers of Syzygium aromaticum (cloves), the essential oil of Cannabis sativa, copaiba, rosemary, and hops. Sell, Charles S. (2006). ‘Terpenoids’.”(Kirk-Othmer Encyclopedia of ChemicalTechnology.doi:10.1002/0471238961.2005181602120504.a01.pub2. ISBN 0471238961.

IFUS Point 4b-2.2d: “Caryophyllene is one of the chemical compounds that contributes to the aroma of black pepper. Jirovetz, L., et.al, (November 2002). “Aroma compound analysis of Piper nigrum and Piper guineense essential oils from Cameroon using solid-phase microextraction–gas chromatography, solid-phase microextraction–gas chromatography–mass spectrometry and olfactometry". Journal of Chromatography A. 976 (1–2): 265–275. Doi:10.1016/S0021-9673(02)00376-X. PMID 12462618.

IFUS Point 4b-2.2e: "B-Caryophyllene has the highest cannabinoid activity compared to the ring opened isomer α-caryophyllene humulene which may modulate CB2 activity." Hashiesh, Hebaallah Mamdouh, et.al., (1 August 2021). "A focused review on CB2 receptor-selective pharmacological properties and therapeutic potential of β-caryophyllene, a dietary cannabinoid". Biomedicine & Pharmacotherapy. 140: 111639. Doi:10.1016/j.biopha.2021.111639. PMID 34091179. S2CID 235362290.

IFUS Point 4b-2.2f: The approximate quantity of caryophyllene in the essential oil of each source is given in square brackets ([ ]):

- Cannabis (Cannabis sativa) [3.8–37.5% of cannabis flower essential oil]
    - Mediavilla, V., et.al., "Essential oil of Cannabis sativa L. strains". International Hemp Association. Retrieved 11 July 2008.
- Black caraway (Carum nigrum) [7.8%]Cloves (Syzygium aromaticum) [1.7–19.5% of clove bud essential oil]
    - Alma, M. Hakki, et.al., (23 May 2007). "Chemical composition and content of essential oil from the bud of cultivated Turkish clove (Syzygium aromaticum L.)". BioResources. 2 (2): 265–269. Doi:10.15376/biores.2.2.265-269.
- Hops (Humulus lupulus)[25] [5.1–14.5%]
    - Bernotienë, G.;, et.al., (2004). "Chemical composition of essential oils of hops (Humulus lupulus L.) growing wild in Auktaitija" (PDF). Chemija. 2. 4: 31–36. Archived from the original (PDF) on March 7, 2023. Retrieved September 6, 2010.
- Basil (Ocimum spp.)[27] [5.3–10.5% O. gratissimum; 4.0–19.8% O. micranthum]

- Vasconcelos Silva, et.al., (August 2, 2004). Cragg, G. M.; Bolzani, V. S.; Rao, G. S. R. S. (eds.). "Composition of essential oils from three Ocimum species obtained by steam and microwave distillation and supercritical CO2 extraction". Arkivoc. 2004 (6): 66–71. Doi:10.3998/ark.5550190.0005.609. hdl:2027/spo.5550190.0005.609.
- Oregano (Origanum vulgare)[4.9–15.7%]
    - Harvala C, Menounos P, Argyriadou N (February 1987). "Essential oil from Origanum dictamnus". Planta Medica. 53 (1): 107–109. doi:10.1055/s-2006-962640. PMID 17268981. S2CID 260278580.
    - Harvala C, Menounos P, Argyriadou N (February 1987). "Essential oil from Origanum dictamnus". Planta Medica. 53 (1): 107–109. doi:10.1055/s-2006-962640. PMID 17268981. S2CID 260278580.
    - Harvala C, Menounos P, Argyriadou N (February 1987). "Essential oil from Origanum dictamnus". Planta Medica. 53 (1): 107–109. doi:10.1055/s-2006-962640. PMID 17268981. S2CID 260278580.
- Black pepper (Piper nigrum) [7.29%]
    - Jirovetz, L., et.al., (November 2002). "Aroma compound analysis of Piper nigrum and Piper guineense essential oils from Cameroon using solid-phase microextraction–gas chromatography, solid-phase microextraction–gas chromatography–mass spectrometry and olfactometry". Journal of Chromatography A. 976 (1–2): 265–275. Doi:10.1016/S0021-9673(02)00376-X. PMID 12462618.
- Lavender (Lavandula angustifolia) [4.62–7.55% of lavender oil]
    - Prashar, A.; (2004). "Cytotoxicity of lavender oil and its major components to human skin cells". Cell Proliferation. 37 (3): 221–229. Doi:10.1111/j.1365-2184.2004.00307.x. PMC 6496511. PMID 15144499.

    - Umezu, T., et.al., (December 2006). “Anticonflict effects of lavender oil and identification of its active constituents”. Pharmacology Biochemistry and Behavior. 85 (4): 713–721. Doi:10.1016/j.pbb.2006.10.026. PMID 17173962. S2CID 21779233.
- Rosemary (Rosmarinus officinalis) [0.1–8.3%]
    - Ormeño, E., et.al., (September 2008). “Production and diversity of volatile terpenes from plants on calcareous and siliceous soils: effect of soil nutrients”. Journal of Chemical Ecology. 34 (9): 1219–1229. Bibcode:2008JCEco..34.1219O. doi:10.1007/s10886-008-9515-2. PMID 18670820. S2CID 28717342.
- True cinnamon (Cinnamomum verum) [6.9–11.1%]
    - Kaul, Pran N, et.al., (1 January 2003). “Volatile constituents of essential oils isolated from different parts of cinnamon (Cinnamomum zeylanicum Blume)”. Journal of the Science of Food and Agriculture. 83 (1): 53–55. Bibcode:2003JSFA...83...53K. doi:10.1002/jsfa.1277.
- Malabathrum (Cinnamomum tamala) [25.3%]
    - Ahmed, Aftab, et.al., (2000). “Essential oil constituents of the spice Cinnamomum tamala (Ham.) Nees & Eberm”. Flavour and Fragrance Journal. 15 (6): 388–390. Doi:10.1002/1099-1026(200011/12)15:6<388::AID-FFJ928>3.0.CO;2-F.
- Ylang-ylang (Cananga odorata) [3.1–10.7%]
- Copaiba oil (Copaifera)
    - Leandro, Lidiam Maia, et.al., (30 March 2012). “Chemistry and Biological Activities of Terpenoids from Copaiba (Copaifera spp.) Oleoresins”. Molecules. 17 (4): 3866–3889. Doi:10.3390/molecules17043866. PMC 6269112. PMID 22466849.
    - Sousa, João Paulo B., et.al., (March 2011). “Validation of a gas chromatographic method to quantify sesquiterpenes in copaiba oils”. Journal

of Pharmaceutical and Biomedical Analysis. 54 (4): 653–659. Doi:10.1016/j.jpba.2010.10.006. PMID 21095089.

IFUS Point 4b-2.2f: Does β-caryophyllene produce an odor? "Caryophyllene is a unique cannabis terpene because it can bind to the CB2 receptors in the body's endocannabinoid system (ECS). Most people describe beta-caryophyllene as having a "woodsy, strong, spicy" odor."

IFUS Point 4b-2.3: Does the new world screwworm fly have CB2 receptors? "Insects lack cannabinoid receptors, which are known to be present in mammals, birds, reptiles, and fish (CB1 and CB2 receptors). This absence is likely linked to the low production of arachidonic acid and endocannabinoid ligands, such as anandamide, in insects (3)." ("What Insects Have Cannabinoid Receptors?" David Grimaldi, https://blog.entomologist.net/what-insects-have-cannabinoid-receptors.html)

IFUS Point 4b-2.3a: "The absence of cannabinoid receptors in insects is believed to be due to the lack of endocannabinoid ligands, which are precursors to the body's endocannabinoids. Insects produce minimal to no arachidonic acid, which is a precursor in the body's manufacturing of its endocannabinoids. The endocannabinoid system (ECS) consists of three parts: endogenous ligands, G-protein coupled receptors (GPCRs), and enzymes to degrade. Non-CB receptors present in insects include 5-hydroxytryptamine (serotonin) receptors (5HT1A/2 A), transient receptor potential vanilloid cation channel receptors (TRPV), and two cannabinoid receptors, CB1 and CB2, expressed in mammals, birds, reptiles, and fish."

IFUS Point 4b-2.3a.1: Of note, beef and dairy "cows have CB2 receptors, which are most highly expressed in immune cells and exert mainly anti-inflammatory effects. (1, 2, 3, 4, 5)" This content will be further explored in the IFUS Part 2 White Paper, specifically for the effect of β-caryophyllene on the overall Bovine Herd Performance. Furthermore, this overall effect may in fact impact the New World Screwworm Fly (as well as other flies) from being attracted through fatty acid metabolism as well as VOC reduction due to reduced inflammation, improved wound prevention and healing, and overall herd health improvements.

IFUS Point 4b-2.3a.1(i): Ref. (1) Silver RJ. The Endocannabinoid System of Animals. Animals (Basel). 2019 Sep 16;9(9):686. doi: 10.3390/ani9090686. PMID: 31527410; PMCID: PMC6770351.

IFUS Point 4b-2.3a.1(ii): Ref. (2) Silver RJ. The Endocannabinoid System of Animals. Animals (Basel). 2019 Sep 16;9(9):686. doi: 10.3390/ani9090686. PMID: 31527410; PMCID: PMC6770351.

IFUS Point 4b-2.3a.1(iii): Ref. (3) Kent-Dennis, C., Klotz, J.L. The endocannabinoid system in bovine tissues: characterization of transcript abundance in the growing Holstein steer. BMC Vet Res 20, 481 (2024). https://doi.org/10.1186/s12917-024-04319-x

IFUS Point 4b-2.3a.1(iv): Ref. (4) Kra, G.; Daddam, J.R.; Moallem, U.; Kamer, H.; Ahmad, M.; Nemirovski, A.; Contreras, G.A.; Tam, J.; Zachut, M. Effects of Environmental Heat Load on Endocannabinoid System Components in Adipose Tissue of High Yielding Dairy Cows. Animals 2022, 12, 795. https://doi.org/10.3390/ani12060795

IFUS Point 4b-2.3a.1(v): Ref. (5) Mackie K. Cannabinoid receptors: where they are and what they do. J Neuroendocrinol. 2008 May;20 Suppl 1:10-4. doi: 10.1111/j.1365-2826.2008.01671.x. PMID: 18426493.

IFUS Point 4b-2.3a.2: Additionally, the beneficial effects of CB2 receptors in beef and dairy cows are established by studies like: "The endocannabinoid system (ECS) is involved in the regulation of energy metabolism, immune function and reproduction in mammals. The ECS is consisted of the endocannabinoid (eCB) ligands, enzymes, and cannabinoid receptors. In mammals, the cannabinoid-1 receptor (CB1/CNR1) is expressed in the central nervous system and in peripheral tissues; and its activation increases anabolic processes. The cannabinoid-2 receptor (CB2/CNR2) is most highly expressed in immune cells, and its activation exerts mainly anti-inflammatory effects." (Maya Zachut, et.al., International Symposium on Ruminant Physiology: The involvement of the endocannabinoid system in metabolic and inflammatory responses in dairy cows during negative energy balance, Journal of Dairy Science, 2025, ISSN 0022-0302, https://doi.org/10.3168/jds.2024-25772. (https://www.sciencedirect.com/science/article/pii/S0022030225000177))

IFUS Point 4b-2.3b: "Odorant binding proteins (OBPs) function to bind odorants and transport them to olfactory receptors. Here, behavioral assays revealed that β-caryophyllene strongly attracted mated, instead of virgin females. (1, 2, 3)"

IFUS Point 4b-2.3b-i: Ref. (1) "Bactrocera dorsalis is a destructive agricultural pest that attacks over 600 plant species. β-Caryophyllene is considered a potential compound for developing novel female attractants due to its attraction to B. dorsalis females. However, the unknown perception mechanism of β-caryophyllene has been the bottleneck of this process. Odorant binding proteins (OBPs) function to bind odorants and transport them to olfactory receptors. Here, behavioral assays revealed that β-caryophyllene strongly attracted mated, instead of virgin females. RT-qPCR confirmed BdorOBP32 up-regulation out of five OBPs in mated females compared to virgin females. Microscale thermophoresis (MST) results showed BdorOBP32 bind β-caryophyllene with relatively high affinity. Subsequently, CRISPR/Cas9 knockout of BdorOBP32 reduced electroantennograms responses and behavioral preferences to β-caryophyllene in mutants. Moreover, molecular docking and behavioral analysis identified a novel female attractant (α-angelica lactone) targeting BdorOBP32. These findings highlight BdorOBP32 plays critical roles in β-caryophyllene perception and offer new insights for developing novel olfactory behavior modulators." ("BdorOBP32 Perceiving β-Caryophyllene: A Molecular Target for Female Attractant Development in Bactrocera dorsalis" Quan Lei, et.al., J Agric Food Chem . 2025 May 7;73(18):11209-11217. doi: 10.1021/acs.jafc.5c00167. Epub 2025 Apr 24., PMID: 40272313)

IFUS Point 4b-2.3b-ii: Ref. (2) "As important components in insect periphery nerve system and key players in insect behaviors, both insect OBPs and ORs represent alternative targets for the identification of compounds with semiochemical activity (or agonist effect) and tools to design strong antagonists to enhance desired behavioral responses of insect pests and reduce the use of insecticides and subsequent resistance." ("Odorant Receptors and Odorant-Binding Proteins as Insect Pest Control Targets: A Comparative Analysis," Herbert Venthur, et.al., Front. Physiol., 23 August 2018 Sec. Invertebrate Physiology Volume 9 - 2018 https://doi.org/10.3389/fphys.2018.01163)

IFUS Point 4b-2.3b-ii1: Ref. (3) The oriental fruit fly Bactrocera dorsalis (Hendel) is a notorious pest of fruit crops. Gravid females locate suitable oviposition sites by detecting host plant volatiles. Here, we demonstrate that 1-octen-3-ol, a volatile from mango, guides the oviposition behavior of female flies. Two odorant receptors (BdorOR7a-6 and BdorOR13a) are identified as key receptors for 1-octen-3-ol perception by qPCR analysis, heterologous expression in Xenopus laevis oocytes and HEK 293 cells followed by in vitro binding assays, as well as CRISPR/Cas9 genome editing in B. dorsalis. Molecular docking and site-directed mutagenesis are used to determine major binding sites for 1-octen-3-ol. Our results demonstrate the potential of 1-octen-3-ol to attract gravid females and molecular mechanism of its perception in B. dorsalis. BdorOR7a-6 and BdorOR13a can therefore be used as molecular targets for the development of female attractants. Furthermore, our site-directed mutagenesis data will facilitate the chemical engineering of 1-octen-3-ol to generate more efficient attractants. "Two odorant receptors regulate 1-octen-3-ol induced oviposition behavior in the oriental fruit fly," Li Xu, et.al., Communications Biology volume 6, Article number: 176 (2023), https://doi.org/10.1038/s42003-023-04551-5

IFUS Point 4b-3.1: Furthermore, there are suggested links to Gallic Acid and Arachidonic acid (AA), a precursor for eicosanoids. Eicosanoids are said to be critical to fly immunity. Hence, this is another possible pathway that warrants further investigation. With that said, it is established that, "Gallic acid can impair the growth of insect larvae without causing significant harm to their parasitoid wasps (1)." This is but one more of a series of studies suggesting Gallic Acid's anti-larval efficacy (and explored in the sections dedicated to Gallic Acid).

IFUS Point 4b-3.1a: Ref. (1) Effect of gallic acid on the larvae of Spodoptera litura and its parasitoid Bracon hebetor, Abhay Punia, et.al., Sci Rep. 2021 Jan 12;11:531. doi: 10.1038/s41598-020-80232-1, PMCID: PMC7803745 PMID: 33436810

IFUS Point 4b-3.2: "Mono- and sesquiterpenes are volatile compounds of which many are used as fragrance chemicals because of their pleasant odours. B-Caryophyllene (1) (Fig. 1) is a sesquiterpene present in natural products e.g. the oil of cloves, cinnamon leaves and copaiba balsam, all of which have been used as natural remedies and as fragrances. The odour of β-caryophyllene, is described as woody and spicy (Verghese, 1994), and β-caryophyllene itself has been commonly used as a fragrance chemical since the 1930s (Opdyke, 1973). Caryophyllene was detected in 33% of 300 analyzed cosmetic products on the Dutch market in the beginning of the 1990s (de Groot et al., 1994). In another study (Rastogi et al., 1998), chemical analyses of 71 deodorants on the European market 1998, revealed that 45% of the analyzed products contained caryophyllene."

- (The fragrance chemical β-caryophyllene—air oxidation and skin sensitization, Maria Sköld, et.al., Food and Chemical Toxicology, Volume 44, Issue 4, April 2006, Pages 538-545, https://doi.org/10.1016/j.fct.2005.08.028)

IFUS Point 4c: Ranchers and visitors to the IFUS Test Ranches continually report that their pastures have no offensive smells. More so, ranchers state that there is a "fresh earth and woodsy, with hints of spice" smell to their pastures. Hence, is this just another bit of coincidental evidence (in the overall long and ever-expanding list of coincidental evidence)?

IFUS Point 4d: We now take a step back or maybe a view from a higher perspective. When considering this one (1) ingredient (β-caryophyllene), one finds (once more) synergies. Not only is β-caryophyllene produced in Mastic Gum (which is a key ingredient in Nutri-Mastic™, which is in turn used to formulate SGP+™), but also produced in:

IFUS Point 4d-1: Carob: "β-caryophyllene is produced in carob as a bioactive compound, particularly identified in female carob moths, which exhibit behavioral attraction to higher concentrations of this compound in host fruits. Additionally, the extraction of volatile organic compounds (VOCs) from carob fruits has been studied, indicating the presence of β-caryophyllene among other compounds. (1, 2)

IFUS Point 4d-1.1: Ref. (1) Identification of Bioactive Plant Volatiles for the Carob Moth by Means of GC-EAD and GC-Orbitrap MS, Seyed Ali Hosseini, et.al., Appl. Sci. 2021, 11(18), 8603; https://doi.org/10.3390/app11188603

IFUS Point 4d-1.2: Ref. (2) HS-SPME-GC/MS Analysis for Revealing Carob's Ripening, Panagiota Fella, et.al., Metabolites. 2022 Jul 15;12(7):656. Doi: 10.3390/metabo12070656

IFUS Point 4d-2: Microbial depolymerization of lignin. "Yes, β-caryophyllene can be naturally produced by microbial depolymerization of lignin from sugarcane bagasse. Recent studies have shown that microbial production of β-caryophyllene has been primarily studied using genetically modified yeast strains, such as Saccharomyces cerevisiae and Escherichia coli, which have demonstrated promising results in terms of production efficiency. This process is considered a sustainable alternative for the production of this terpenoid, which has various applications in the food, cosmetic, and pharmaceutical industries. (1, 2)

IFUS Point 4d-2.1: Ref (1) An Update on Microbial Biosynthesis of β-Caryophyllene, a Sesquiterpene with Multi-Pharmacological Properties, Lidia Tsigoriyna, et.al., Fermentation 2024, 10(1), 60; https://doi.org/10.3390/fermentation10010060

IFUS Point 4d-2.1: Ref (2) Adaptive laboratory evolution of β-caryophyllene producing Saccharomyces cerevisiae, Avinash Godara, et.al., Microbial Cell Factories volume 20, Article number: 106 (2021), https://doi.org/10.1186/s12934-021-01598-z

IFUS Point 4d-3: As evidence of the synergies resulting from the active ingredients in SGP+™, "β-caryophyllene has several potential impacts on bovines:

1. It exhibits analgesic, antitumor, and antioxidant effects, which may be beneficial for bovine health.
2. Research indicates that β-caryophyllene may have immunocytotoxic properties, suggesting potential health benefits without evidence of toxicity.
3. It has been shown to have beneficial effects on obesity and liver diseases, which could be relevant for bovine health.
   3.1. Furthermore, β-caryophyllene (BCP) has shown beneficial effects on bovine digestion through its interaction with cannabinoid receptors and peroxisome proliferator-activated receptors (PPARs), which may aid in conditions like obesity and liver diseases (3).
4. Additionally, studies have evaluated its effects on bovine oocytes, indicating its potential role in reproductive health.

Overall, β-caryophyllene shows promise in enhancing bovine health through various biological properties. (1, 2, 3, 4)"

IFUS Point 4d-2a: Ref. 1 Bovine Viral Diarrhea Virus (BVDV): A Preliminary Study on Antiviral Properties of Some Aromatic and

Medicinal Plants, Silvia Madeddu, et.al, Pathogens. 2021 Mar 29;10(4):403. Doi: 10.3390/pathogens10040403, PMCID: PMC8066157 PMID: 33805453

IFUS Point 4d-2b: Ref. 2 Chapter 37 – Safety and toxicology of the dietary cannabinoid β-caryophyllene, George Laylson da Silva Oliveira, et.al., Neurobiology and Physiology of the Endocannabinoid System, 2023, Pages 481-492

IFUS Point 4d-2c: Ref. 3 Protective Effects of I-β-Caryophyllene (BCP) in Chronic Inflammation, Rosaria Scandiffio, et.al., Nutrients. 2020 Oct 26;12(11):3273. Doi: 10.3390/nu12113273, PMCID: PMC7692661 PMID: 33114564

IFUS Point 4d-2d: Ref. 4: Medical food development by dietetic management of the endocannabinoid system through dietary sources of β-caryophyllene, Victor Chiruta, March 2021, SSRN Electronic Journal 3(3):1-9, DOI:10.1142/S2575900020300039, LicenseCC BY-NC 4.0

IFUS Point 4e-3: Also, as wound prevention and rapid wound healing reduces the VOC's and other odorants produced from wounds, "Beta-caryophyllene enhances wound healing through multiple routes," Koyama S, Purk A, Kaur M, Soini HA, Novotny MV, Davis K, Kao CC, Matsunami H, Mescher A. Beta-caryophyllene enhances wound healing through multiple routes. PLoS One. 2019 Dec 16;14(12):e0216104. doi: 10.1371/journal.pone.0216104. PMID: 31841509; PMCID: PMC6913986.

IFUS Point 4e-4: β-caryophyllene is but one of a long list of bioactive plant-based compounds, that when used and formulated properly, can produce beneficial effects on mammals, plants, and even beneficial insects and bugs. This includes bovines.

IFUS Point 4e-4.1: Hence, based on Herd Performance as reported by the IFUS Test Ranches (owned and operated by private ranchers) as well as other ranchers and dairymen applying SGP+™ as part of their respective Bovine Ration Management, a solution to the Screwworm Fly infestation problem can be found. In this case, by way of improving Herd Performance through improved Bovine Nutrition, which impacts Bovine Digestion and Absorption as well as Bovine Metabolism, odors can be produced by natural plant-based compound that will dramatically affect the New World Screwworm Fly from (1) being attracted to beef and dairy cattle, and (2) wanting to bite the cow. Hence, (3) discouraging the fly to lay her eggs into the cow, and (4) preventing the larvae from becoming a mature fly.

IFUS Point 4e-5: Let's take a moment to deviate as to possible current thinking that would prevent such a solution from being advanced. For the past 100-years, the Ethylene-Cycle-based economy from crude oil has provided for a series of synthetic chemicals. The application of these chemicals has been driven by major shifts from an agrarian-based society to a metropolitan-based society as well as two major economic crashes and two World Wars. The need to feed the masses (no longer capable of feeding itself) as well as the armies gathered for war, required the mass production of food. Science at the time offered alternatives without fully comprehending the impacts of those alternatives.

IFUS Point 4e-5.1: Much of the world has now called upon science to find new eco-friendly solutions to the mass production of healthier food. Hence, solutions like SGP+™ must be considered, especially when considering its proclivity to provide financial remedies to ailing beef and dairy operations.

IFUS Point 4e-5.2: Fly management, control, and/or eradication is a byproduct of SGP+™'s natural ingredients and integrated solutions. Hence, the question that is begged: Is SGP+™ "Snake-Oil" or is it an actual product and technology that when applied with discipline and intelligence provides a long-list of positive Herd Performance outcomes (to include dealing with the New World Screwworm Infestation).

IFUS Point 4e-5.3: Considering just the chemicals synthetically produced, the The Merek Veterinary Manual states: "To protect animals from infestation and also to kill larvae in small wounds that are difficult to detect, animals can be sprayed thoroughly with ronnel or sprayed with or dipped in coumaphos." (https://www.merckvetmanual.com/integumentary-system/flies/obligatory-myiasis-producing-flies-of-animals#Diagnosis_v3279267)

IFUS 4e-5.3a: "Coumaphos is a nonvolatile, fat-soluble phosphorothioate with ectoparasiticide properties: it kills insects and mites. It is well known by a variety of brand names as a dip or wash, used on farm and domestic animals to control ticks, mites, flies and fleas." (Asuntol – Cattle, Goat, Sheep – anti lice, fleas, sucking flies and mite". Vetcontact.com.)

IFUS Point 4e-5.3b: The actual "Preferred IUAPC name" for Coumaphos is: O-(3-Chloro-4-methyl-2-oxo-2H-1-benzopyran-7-yl) O,O-diethyl phosphorothioate.

IFUS Point 4e-5.3c: Anyone who has taken basic Organic Chemistry knows that if a chemical has the term "methyl" followed by "ethyl" (as is the case with Coumaphos), one can end the sentence with "BAD SHIT; i.e., Methyl-Ehtyl-Bad-Shit!" And, if it has Methyl-Di-Ethyl, then one can name it "Methyl-Ethyl-Really-Bad-Shit!" Many of these Methyl-Ethyl and related specific compounds are noted or suspected to produce the trifecta of being (1) carcinogens, (2) teratogens, and (3) mutagens, while some just outright kill mammalian lifeforms. They can do so on contact with skin, inhalation, or other orifices.

FIX THIS AS THERE IS NOW DATA IFUS Point 4e-5.4d: Furthermore, it seems that little or NO data is available that demonstrates the efficacy of these chemicals in mitigating the New World Screwworm infestation. If such information exists, the IFUS Scientific Team has not as of yet uncovered it.

IFUS Point 4f-5: Hence, in consideration of the aforementioned, the IFUS Scientific Team is reaching out to the world to understand how information like that of Table 3 (above) can be used to understand the efficacy of SGP+™ in mitigating the New World Screwworm threat. This includes the fact that when reviewing Table 3, any number of the active ingredients of Carob can also be found in Mastic Gum as well as produced from naturally depolymerized lignin by White Rot Fungi and other naturally occurring microbes that exist within the biome of Sugarcane Bagasse.

IFUS Point 4f-5.1: Furthermore, the metabolic processes prior to and within bovine digestion have been shown to that a two-stage fermentation process of lignin from Sugarcane Bagasse begins *in vitro* and continues *in vivo* (associated with the degradation and depolymerization of S-, G-, and H- lignin by White Rot Fungi and other parts of the natural biome within Sugarcane Bagasse).

IFUS Point 4f-5.2: Furthermore, the science is demonstrating that synergistic products from Mastic Gum, Carob, and naturally depolymerized lignin from Sugarcane Bagasse integrate to produce enhanced Bovine Herd Performance (to include reduced and/or eliminated fly populations). To date, the IFUS test ranches (and other SGP+™ users) are reporting that they are seeing NO FLIES whatsoever, irrespective of species.

IFUS Point 4g: Are there natural products that could prove more effective than chemicals like Coumaphos? Let's us consider yet another natural plant-based active ingredient found in SGP+™. Gallic Acid (GA) is just one ingredient common to Carob and Mastic Gum as well as being produced from naturally depolymerized lignin. Hence, we offer as an example the efficacy of Gallic Acid to mitigate the New World Screwworm Fly problem (as well as other flies).

IFUS Point 4g-1: One of the chemicals produced from wounds in the bovine hide is Cadaverine. We find that: "Gallic acid (GA) does reduce cadaverine levels in the body. It regulates amino acid metabolism by suppressing the synthesis of cadaverine and enhancing its degradation, which ultimately leads to a reduction in cadaverine levels. "The metabolic regulation mechanism of gallic acid on biogenic amines and nitrosamines in reduced-nitrite Chinese fermented sausages: A perspective of metabolomics and metagenomics," Qin Zhou, et.al., Food Chemistry, Volume 456, 30 October 2024, 139900

IFUS Point 4g-1.1: Please note that Gallic Acid is shown in numerous studies to be balanced and regulated in bovine digestion with Ellagic Acid.

IFUS Point 4g-1.2: "Ellagic acid has been shown to have various protective effects, including reducing cell viability and promoting apoptosis in certain cancer cells, which suggests a potential relationship with cell death mechanism." This content is further explained in the IFUS White Paper: "Part 2: Plausible Scientific Evidence of the Efficacy of SGP+™ in Bovine Herd Performance through Bovine Ration Management: The Science Behind Mastic and Carob Individually and Collectively as well as Synergies with Ionic Minerals and Degraded/Depolymerized Lignin."

IFUS Point 4g-2: "Gallic acid has a significant effect on putrescine production. It was found that putrescine formation from agmatine diminished in the presence of gallic acid, indicating that gallic acid can inhibit putrescine synthesis. Additionally, putrescine levels rise within hours after acidification, suggesting a direct relationship between gallic acid and putrescine levels. Therefore, gallic acid may play a role in regulating putrescine production in certain contexts. (1, 2)"

IFUS Point-4g-2a: Ref. (1) The influence of phenolic compounds on the growth of Lactobacillus hilgardii X1B and putrescine formation was assayed at concentrations normally present in wine. Agmatine degradation increased growth and survival of the microorganism and the alkalinity of the media. Bacterial growth was stimulated by phenolic compounds, except for gallic acid and quercetin. Putrescine formation from agmatine diminished in the presence of protocatechuic, vanillic and caffeic acids, and the flavonoids catechin and rutin. The concentration of phenolic compounds decreased after five days of incubation of L hilgardii X1B, except for gallic acid and quercetin. The results indicate that phenolic compounds, besides their already known beneficial properties to human health, seem to be a natural way of diminishing putrescine formation. "Putrescine production from agmatine by Lactobacillus hilgardii: Effect of phenolic compounds," María R. Alberto, et.al., Food Control, Volume 18, Issue 8, August 2007, Pages 898-903, https://doi.org/10.1016/j.foodcont.2006.05.006

IFUS Point-4g-2a: Ref. (2) "Apoptosis is one of the natural biological processes of programmed and controlled destruction of own cells in the multi-cellular organism. This mechanism is needed and affects the proper development, homeostasis, and prevention of excessive, harmful multiplication of body cells. It can be induced by various stimuli and common signalling mediators [69], such as 6-hydroxydopamine or reactive oxygen species (ROS). As reported in [70], GA exhibits dose-dependent anti-apoptotic properties as it prevents the 6-hydroxydopamine-induced apoptosis (through its auto-oxidation) of dopaminergic cells. The cited paper also showed that the compound affects intracellular glutathione levels, ROS production, and Ca^{2+} influx, which independently indicates a protective effect of GA against apoptosis."A Concise Profile of Gallic Acid—From Its Natural Sources through Biological Properties and Chemical Methods of Determination, Dorota Wianowska, et.al., Molecules. 2023 Jan 25;28(3):1186. Doi: 10.3390/molecules28031186, PMCID: PMC9919014 PMID: 36770851

IFUS Point 4g-3: Furthermore, "Gallic acid can impair the growth of insect larvae without causing significant harm to their parasitoid wasps." ("Effect of gallic acid on the larvae of Spodoptera litura and its parasitoid Bracon hebetor," Abhay Punia, et.al., Sci Rep. 2021 Jan 12;11:531. doi: 10.1038/s41598-020-80232-1, PMCID: PMC7803745 PMID: 33436810

IFUS Point 4g-3a: The larvicidal nature of Gallic Acid found in Carob and Mastic and produced depolymerized lignin from Sugarcane Bagasse will be explored in a later topic as it represents another layer of fascinating biochemistry. However, it is worthy to comment that these continued synergies provided by nature to produce and eco-friendly and cost-effective solution to both the greater fly problem as well as the New World Screwworm Fly through enhanced Bovine Herd Performance seems to be at the very least worthy of serious consideration and deeper scientific exploration. Of course, there's nothing like results to prove a point…that is, a lack of flies on the herds and the manure, as well as lack of fly larvae in the manure.

IFUS Point 4g-4: Additionally, "Gallic acid activates hepatic PPAR signaling, which may promote fatty acid degradation and suppress the macrophage response (1). It has been tested for anti-LOX activity using linoleic acid (2). Additionally, gallic acid can inhibit the oxidation of linoleic acid (4)."

IFUS Point 4g-4-1: Ref. (1) Gallic acid acts as an anti-inflammatory agent via PPARγ-mediated immunomodulation and antioxidation in fish gut-liver axis, Xuyang Zhao, et.al., Aquaculture, Volume 578, 15 January 2024, 740142, https://doi.org/10.1016/j.aquaculture.2023.740142

IFUS Point 4g-4-2: Ref. (2) Anti-Lipoxygenase Activity of Leaf Gall Extracts of Terminalia chebula (Gaertn.) Retz. (Combretaceae), Ravi Shankara Birur Eshwarappa, et.al., Pharmacognosy Res. 2016 Jan-Mar;8(1):78–82. doi: 10.4103/0974-8490.171103, PMCID: PMC4753765 PMID:

26941541

IFUS Point 4g-4-3: Ref. (4) Protection of lipids from oxidation by epicatechin, trans-resveratrol, and gallic and caffeic acids in intestinal model systems, Zohar Kerem, et.al., J Agric Food Chem. 2006 Dec 27;54(26):10288-93. doi: 10.1021/jf0621828., PMID: 17177572

IFUS Point 4g-5: Another study shows, "Here we measured inhibition of the oxidation of linoleic acid (LA) in authentic fluid from rat small intestine (RIF) by two dietary polyphenols, a flavonoid, epicatechin (EC), and a stilbene, resveratrol (RV), and by gallic (GA) and caffeic (CA) acids, and their partition coefficients. Both polyphenols inhibited 80%, and CA inhibited 65%, of the production of hexanal. GA was the weakest antioxidant in this assay. Interestingly, measuring peroxides production in RIF showed that only epicatechin inhibited the first stage of oxidation. The oxidizing agent, the antioxidant compound, the solution pH and lipophilicity are known to affect the total antioxidative activity. We suggest that the mechanism of this activity changes in accord with the environment: i.e., RV may act as a free radial scavenger, but here, in protecting lipids in intestinal fluid from oxidation, it acts as a hydrogen atom donor." ("Protection of lipids from oxidation by epicatechin, trans-resveratrol, and gallic and caffeic acids in intestinal model systems," J Agric Food Chem. 2006 Dec 27;54(26):10288-93. doi: 10.1021/jf0621828. PMID: 17177572 DOI: 10.1021/jf0621828)

IFUS Point 4g-6: "If Gallic Acid suppresses linolic acid in a beneficial manner for overall bovine health, the effect of this suppression could reduce the production of Eicosanoids, which are compounds derived from arachidonic acid or other polyunsaturated fatty acids of 20-carbon length. Since insects to include flies possess virtually no arachidonic acid, polyunsaturated fats like linolic acid are key to insect/fly immune systems."

IFUS Point 4g-6.1: "Eicosanoids play crucial roles in mediating insect immunity (1,2,3,4,5). They signal a wide range of cellular immune reactions to infections, invasions, and wounding, including nodulation, cell spreading, hemocyte migration, and releasing prophenoloxidase from oenocytoids

(2) Eicosanoids also work through a common mechanism that involves the inhibition of cyclooxygenases (COXs) (3).

IFUS Point 4g-6.1a: Ref. (1) Eicosanoid-mediated immunity in insects, Yonggyun Kim, et.al., Developmental & Comparative Immunology Volume 83, June 2018, Pages 130-143, https://doi.org/10.1016/j.dci.2017.12.005

IFUS Point 4g-6.1b: Ref (2) Eicosanoid Signaling in Insect Immunology: New Genes and Unresolved Issues, Yonggyun Kim, et.al., Genes (Basel). 2021 Feb 1;12(2):211. doi: 10.3390/genes12020211, PMCID: PMC7912528 PMID: 33535438

IFUS Point 4g-6.1c: Ref (3) Eicosanoids and biogenic monoamines modulate the nodulation process and phenoloxidase activity in flesh flies, Dorrah, M.A., et.al., Int J Trop Insect Sci 44, 711–722 (2024). https://doi.org/10.1007/s42690-024-01196-7

IFUS Point 4g-6.1d: Ref (4) Eicosanoid-mediated immunity in insects, Yonggyun Kim, et.al., Developmental & Comparative Immunology Volume 83, June 2018, Pages 130-143, https://doi.org/10.1016/j.dci.2017.12.005

IFUS Point 4g-6.1e: Ref (5) Role of eicosanoids in insect immunity: new insights and recent advances, Shubhranil Brahma, et.al., Insect Science, 19Aug2014, https://onlinelibrary.wiley.com/doi/abs/10.1111/1744-7917.13434?msockid=268b2f9a74d861970f7a3a6075f16085

IFUS Point 4h-1: Hence, the ingredients from which SGP+™ is formulated, can have a dramatic effect on preventing the New World Screwworm Fly from (1) being attracted to beef and dairy cattle, and (2) wanting to bite the cow. Furthermore, there is additional biochemistry that supports the production of other natural chemicals in and from SGP+™ that (3) discourage the fly to lay her eggs into the cow, and (4) prevent the larvae from becoming a mature fly.

IFUS Point 4h-1a: Add the recently uncovered evidence here to include possible links between Oleane, β-caryophyllene, Ellagic Acid, Gallic Acid, Heme Peroxidases, and Ionic Minerals

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IFUS Point 5: What does the Science Tell Us as to the New World Screwworm Fly Olfactory Response to Attractant VOC Reduction and Repellent VOC Production from Polyphenols, Peroxidases, Tannins, Flavonoids, Flavanols, Furfurals, and more.

IFUS Point 5a: The complexity of SGP+™ in producing Herd Performance Improvement (as reported by ranchers and dairymen applying the formulation as part of their respective ration management), leads the IFUS Scientific Team to further explore the possible implications of polyphenols and peroxidases producing natural tannins, flavonoid, flavanols, and the like, while reducing the furfurals.

IFUS Point 5a-1: These inter-relations between ration fed, digestibility, and absorbability affect the manure and emissions of a variety of VOC's (many of which are said to attract the flies withing seconds from quite some distance away.) Hence, in consideration of the highly refined nature of the olfactory capabilities of the New World Screwworm Fly, a deeper exploration into these components found in the ingredients of SGP+™, plus the science which supports their presence within and/or produced by the formulation and its subsequent digestion and absorption. The question is basic: Do these ingredients and the biochemistry of digestion impact the "binding of odorants with the members of three divergent protein families—odorant receptors (ORs), ionotropic receptors (IRs), and gustatory receptors (GRs)."

Hence, we begin with the phenolics as (1) VOC's that attract the New World Screwworm Fly, and (2) integral parts of bovine metabolism that creates herd health and well-being.

IFUS Point 5a-1-1: "Since the concentration of phenolics is much higher in the intestinal fluid than is ever achieved in plasma or other body tissues, it is suggested that their antioxidant activity could be exerted in the gastrointestinal tract (GIT), breaking the propagation of lipid peroxides oxidation and production of toxic compounds." ("Protection of lipids from oxidation by epicatechin, trans-resveratrol, and gallic and caffeic acids in intestinal model systems," Zohar Kerem, et.al, J Agric Food Chem. 2006 Dec 27;54(26):10288-93. doi: 10.1021/jf0621828. PMID: 17177572 DOI: 10.1021/jf0621828)

IFUS Point 5a-1-2: "Consumption of polyphenols is associated with health promotion through diet, although many are poorly absorbed in animals and humans alike. Lipid peroxides may reach the intestine and initiate deleterious oxidation. Here we measured inhibition of the oxidation of linoleic acid (LA) in authentic fluid from rat small intestine (RIF) by two dietary polyphenols, a flavonoid, epicatechin (EC), and a stilbene, resveratrol (RV), and by gallic (GA) and caffeic (CA) acids, and their partition coefficients. Both polyphenols inhibited 80%, and CA inhibited 65%, of the production of hexanal." (Protection of lipids from oxidation by epicatechin, trans-resveratrol, and gallic and caffeic acids in intestinal model systems, Zohar Kerem, et.al., J Agric Food Chem. 2006 Dec 27;54(26):10288-93. doi: 10.1021/jf0621828., PMID: 17177572)

TO BE CONTIUED

IFUS POINT 6: Does Supporting Biochemistry and Science Exist as to the New World Screwworm Fly Olfactory Response to Attractant VOC Reduction and Repellent VOC Production from Polyphenols, Peroxidases, Tannins, Flavonoids, Flavanols, Furfurals, and more?

IFUS Point 6a: The following study says, "Yes." "In two-choice assays, Orco mutants displayed an impaired response to floral-like and animal host-associated odors, suggesting that OR-mediated olfaction is involved in foraging and host-seeking behaviors in C. hominivorax. These results broaden our understanding of the chemoreception basis of niche occupancy by blowflies." (Paulo DF, et.al., "Disruption of the odorant coreceptor Orco impairs foraging and host finding behaviors in the New World screwworm fly," Sci Rep. 2021 May 31;11(1):11379. doi: 10.1038/s41598-021-90649-x.

PMID: 34059738; PMCID: PMC8167109.)

IFUS Point 6a-1: “Here, we hypothesized that olfactory chemoreception may have played a critical role in the adaptive transition from a necro-saprophagous to an obligate ectoparasitic habit in blowflies. Olfaction is a core chemosensory process in sensory perception, and divergences in olfaction-related genes are known to contribute to premating isolation, speciation and niche adaptation in insects (15,16). We adopted the New World screwworm, Cochliomyia hominivorax (Coquerel 1858), as our research model. The screwworm is the sole obligate ectoparasite among the Cochliomyia genus, which includes four endemic species to the Americas, in addition to nearly all of the closely related blowflies, which are primarily carrion feeders (10,17). Adult screwworms feed on flower nectar while their larvae feed on the live tissues of animals. Gravid female screwworms rely on odors emitted from wounded warm-blooded vertebrates to find suitable hosts for oviposition (4,18,19), and lay their eggs on the dried margins of wounds and bodily orifices of their selected animal hosts. After hatching, the larvae infest and consume the animal living tissues to complete their development.

Adult male flies feed at flowers and live for 2–3 weeks, whereas adult females live approximately 10 days on average, feeding on serous fluids at animal wounds and decomposing animals (Thomas & Mangan, 1989; OIE, World Organisation for Animal Health, 2013). (Gutierrez AP, et.al., Deconstructing the eradication of new world screwworm in North America: retrospective analysis and climate warming effects. Med Vet Entomol. 2019 Jun;33(2):282-295. doi: 10.1111/mve.12362. Epub 2019 Feb 13. PMID: 30758067; PMCID: PMC6849717.

IFUS Point 6a-1.1: Ref.(15) Smadja C, Butlin RK. On the scent of speciation: the chemosensory system and its role in premating isolation. Heredity. 2009;102:77–97. doi: 10.1038/hdy.2008.55. [DOI] [PubMed] [Google Scholar]

IFUS Point 6a-1.2: Ref.(16) Bohbot JD, Pitts RJ. The narrowing olfactory landscape of insect odorant receptors. Front. Ecol. Evol. 2015;3:39. doi: 10.3389/fevo.2015.00039. [DOI] [Google Scholar]

IFUS Point 6a-1.3: Ref.(10) Junqueira ACM, et al. Large-scale mitogenomics enables insights into Schizophora (Diptera) radiation and population diversity. Sci. Rep. 2016;6:21762. doi: 10.1038/srep21762. [DOI] [PMC free article] [PubMed] [Google

Scholar]

IFUS Point 6a-1.4: Ref.(17) Yusseff-Vanegas S, Agnarsson I. Molecular phylogeny of the forensically important genus Cochliomyia (Diptera: Calliphoridae) Zookeys. 2016;609:107. doi: 10.3897/zookeys.609.8638. [DOI] [PMC free article] [PubMed] [Google Scholar]

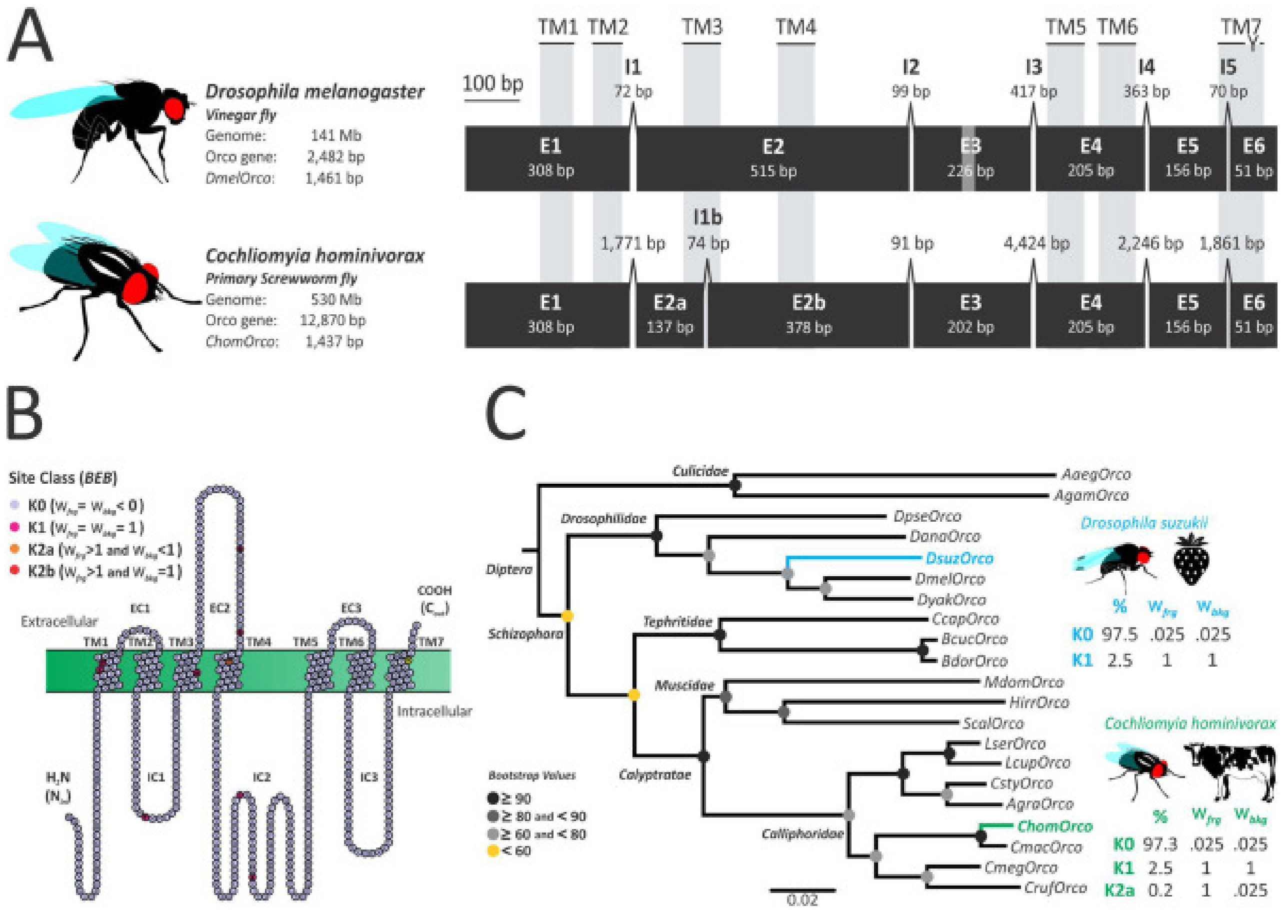
IFUS Point 6a-1.5: Ref.(4) Hall M, Wall R. Myiasis of humans and domestic animals. Adv. Parasitol. 1995;35:257–334. doi: 10.1016/S0065-308X(08)60073-1. [DOI] [PubMed] [Google Scholar]

IFUS Point 6a-1.6: Ref.(18) Tomberlin JK, et al. A review of bacterial interactions with blow flies (Diptera: Calliphoridae) of medical, veterinary, and forensic importance. Ann. Entomol. Soc. Am. 2017;110:19–36. doi: 10.1093/aesa/saw086. [DOI] [Google Scholar]

IFUS Point 6a-1.7: Ref.(19) Zhu JJ, et al. Semiochemicals released from five bacteria identified from animal wounds infested by primary screwworms and their effects on fly behavioral activity. PLoS ONE. 2017;12:e0179090. doi: 10.1371/journal.pone.0179090. [DOI] [PMC free article] [PubMed] [Google Scholar]

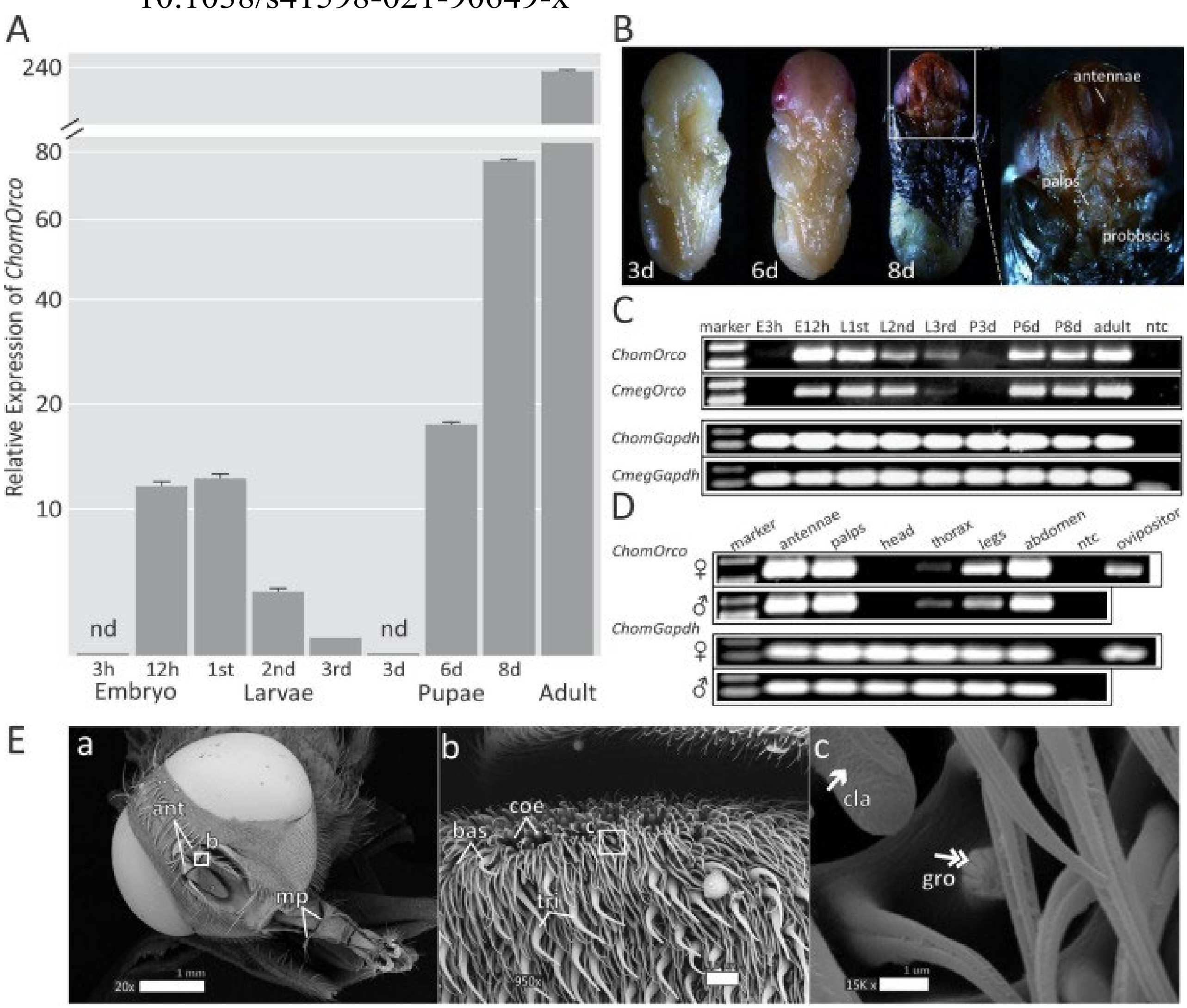
IFUS Point 6a-2: In insects, the sense of odors in complex environments is mediated by several chemosensory genes expressed in porous sensilla attached to olfactory organs, including the antennae and maxillary palps (25). Inside the sensilla, odors are solubilized and shuttled through the inner lymph to receptor sites present in the olfactory sensory neurons (OSNs). Two distinct receptor families, named ionotropic receptor (IR) and odorant receptor (OR), are responsible for recognizing the intercepted signals, resulting in the activation of OSNs and a cascade of neural events leading to a multitude of behavioral responses (16, 25–28). Although the OR and IR gene families include a large number of members (for instance, 60 and 66 genes in Drosophila melanogaster, respectively (29)) the proper function of all divergent ORs is dependent on a common odorant receptor coreceptor, named Orco (27,30,31). A failure to encode Orco results in abnormal behaviors driven by OR-mediated olfaction, while maintaining other chemosensory pathways intact (32–37). In this context, an Orco knockout strain of C. hominivorax would provide a simple system to rapidly differentiate olfactory behaviors mediated by the OR and IR families in this species. In this study, we isolated the Orco orthologue of C. hominivorax (named ChomOrco), characterized its sequence in a phylogenetic context, and assessed its developmental and tissue expression patterns. We next expanded our previous CRISPR/Cas9 genome editing protocols (23) to develop a germline Orco null strain, and evaluated the contribution of OR-mediated olfaction in foraging and host-seeking behaviors in C. hominivorax. The data presented here provides new functional evidence on the chemoreception basis of ecological specialization in the screwworm fly. (See Figures 1 & 2 below)

IFUS Point 6a-2.1: Figure 1 Sci Rep. 2021 May 31;11:11379. doi: 10.1038/s41598-021-90649-x



Screwworm Orco orthologue is highly conserved within diptera. (A) Comparison between the Orco genomic organization in D. melanogaster (DmelOrco) and C. hominivorax (ChomOrco). Exons are represented by numbered black boxes (E1-E6) and introns as connecting lines (I1-I5). The seven transmembrane domains (TM1-TM7), conserved tyrosine residue at TM7 (Y), and nucleotide length variation at E3 (gray strip) are also represented (dipteran's Orco sequence alignment is shown in Supplementary Fig. S1). (B) Predicted protein topology of ChomOrco displaying significant characterized sites by Bayes Empirical Bayes (BEB). (C) Maximum Likelihood (ML) reconstruction of relationships between dipteran Orco sequences (species and accessions used can be found in Supplementary Table S3). Bootstrap support values, estimated from 500 non-parametric replications, are shown at their respective nodes. Normalized non-synonymous (dN) to synonymous (dS) substitution rates (ω) were estimated to test the branches leading to C. hominivorax (in green) and D. suzukii (in blue) species for events of episodic diversification. The number of sites estimated to be evolving under purifying (K0), relaxed (K1), and positive (K2a or K2b) selection is shown for these lineages (foreground branch; ωfrg) in relation to the rest of the tree (background branch; ωbkg).

IFUS Point 6a-2.2: Figure 2: Sci Rep. 2021 May 31;11:11379. doi: 10.1038/s41598-021-90649-x



Expression of Orco is conserved among blowflies and broadly detected in chemosensory-related tissues of C. hominivorax adults. (A) Relative expression of ChomOrco during the screwworm development by qPCR. Measurements are given by the quantification of ChomOrco normalized to GAPDH using the $2^{-\Delta Ct}$ method and presented as fold-change relative to the third instar larvae using the $2^{-\Delta\Delta Ct}$ method. Data are represented as mean ± SD (n = 9). Cycle thresholds above 35 were considered non-detected (nd). (B) Intrapuparial development of C. hominivorax at three (3d), six (6d), and eight days (8d) after pupation. A closer view of the head region (white square) reveals the fully developed sensory structures of the adult form present in the late pupae stage. (C) Semi-quantitative comparison between developmental Orco expression in C. hominivorax (Chom) and C. megacephala (Cmeg) species by RT-PCR. (D) Detection of ChomOrco in adult screwworm female (♀) and male (♂) tissues. For all RT-PCR assays: Amplifications were made in replicates (n = 3), including no template controls (ntc), and GAPDH was amplified as an internal control. Cropped images (delineated by black lines) are from samples run on different gels. Full-length gels are displayed in Supplementary Fig. S2. (E) The main olfactory structures of C. hominivorax viewed under electron microscopy. (panel a) Screwworm female's head highlighting the antennae (ant), and the maxillary palps (mp). (panel b) A closer view of the proximal surface of the third antenna segment reveals a number of tricoide (tri), basiconic (bas), and two morphotypes of coelonic (coe) sensilla (panel c), named grooved (gro) and clavate (cla). These morphotypes are adorned with multi-wall pores (single arrows) and grooves (double arrows), which presumably facilitate the entrance of odor molecules into the antennae.

IFUS Point 6a-2.2a: Ref.(25) Carey AF, Carlson JR. Insect olfaction from model systems to disease control. Proc. Natl. Acad. Sci. USA. 2011;108:12987–12995. doi: 10.1073/pnas.1103472108. [DOI] [PMC free article] [PubMed] [Google Scholar]

IFUS Point 6a-2.2b: Ref.(16) Bohbot JD, Pitts RJ. The narrowing olfactory landscape of insect odorant receptors. Front. Ecol. Evol. 2015;3:39. doi: 10.3389/fevo.2015.00039. [DOI] [Google Scholar]

IFUS Point 6a-2.2c: Ref.(26) Wicher D, Miazzi F. Functional properties of insect olfactory receptors: Ionotropic receptors and odorant receptors. Cell Tissue Res. 2021;383:7–19. doi: 10.1007/s00441-020-03363-x. [DOI] [PMC free article] [PubMed] [Google Scholar]

IFUS Point 6a-2.2d: Ref.(27) Benton R, Sachse S, Michnick SW, Vosshall LB. Atypical membrane topology and heteromeric function of Drosophila odorant receptors in vivo. PLoS Biol. 2006;4:e20. doi: 10.1371/journal.pbio.0040020. [DOI] [PMC free article] [PubMed] [Google Scholar]

IFUS Point 6a-2.2e: Ref.(28) Silbering AF, et al. Complementary function and integrated wiring of the evolutionarily distinct Drosophila olfactory subsystems. J. Neurosci. 2011;31:13357–13375. doi: 10.1523/JNEUROSCI.2360-11.2011. [DOI] [PMC free article] [PubMed] [Google Scholar]

IFUS Point 6a-2.2f: Ref.(29) Gomez-Diaz C, Martin F, Garcia-Fernandez JM, Alcorta E. The two main olfactory receptor families in Drosophila, ORs and IRs: A comparative approach. Front. Cell. Neurosci. 2018;12:253. doi: 10.3389/fncel.2018.00253. [DOI] [PMC free article] [PubMed] [Google Scholar]

IFUS Point 6a-2.2g: Ref.(30) Larsson MC, et al. Or83b encodes a broadly expressed odorant receptor essential for Drosophila olfaction. Neuron. 2004;43:703–714. doi: 10.1016/j.neuron.2004.08.019. [DOI] [PubMed] [Google Scholar]

IFUS Point 6a-2.2h: Ref.(31) Sato K, et al. Insect olfactory receptors are heteromeric ligand-gated ion channels. Nature. 2008;452:1002–1006. doi: 10.1038/nature06850. [DOI] [PubMed] [Google Scholar]

IFUS Point 6a-2.2i: Ref.(32) DeGennaro M, et al. Orco mutant mosquitoes lose strong preference for humans and are not repelled by volatile DEET. Nature. 2013;498:487–491. doi: 10.1038/nature12206. [DOI] [PMC free article] [PubMed] [Google Scholar]

IFUS Point 6a-2.2j: Ref.(33) Koutroumpa FA, et al. Heritable genome editing with CRISPR/Cas9 induces anosmia in a crop pest moth. Sci. Rep. 2016;6:29620. doi: 10.1038/srep29620.

[DOI] [PMC free article] [PubMed] [Google Scholar]

IFUS Point 6a-2.2k: Ref.(34) Yan H, et al. An engineered orco mutation produces aberrant social behavior and defective neural development in ants. Cell. 2017;170:736–747. doi: 10.1016/j.cell.2017.06.051. [DOI] [PMC free article] [PubMed] [Google Scholar]

IFUS Point 6a-2.2l: Ref.(35) Fandino RA, et al. Mutagenesis of odorant coreceptor Orco fully disrupts foraging but not oviposition behaviors in the hawkmoth Manduca sexta. Proc. Natl. Acad. Sci. USA. 2019;116:15677–15685. doi: 10.1073/pnas.1902089116. [DOI] [PMC free article] [PubMed] [Google Scholar]

IFUS Point 6a-2.2m: Ref.(36) Mansourian S, Fandino RA, Riabinina O. Progress in the use of genetic methods to study insect behavior outside Drosophila. Curr. Opin. Insect Sci. 2019;36:45–56. doi: 10.1016/j.cois.2019.08.001. [DOI] [PubMed] [Google Scholar]

IFUS Point 6a-2.2n: Ref.(37) Karageorgi M, et al. Evolution of multiple sensory systems drives novel egg-laying behavior in the fruit pest Drosophila suzukii. Curr. Biol. 2017;27:847–853. doi: 10.1016/j.cub.2017.01.055. [DOI] [PMC free article] [PubMed] [Google Scholar]

IFUS Point 6a-2.3: Of note is Ref.(38). When reviewed, this led to another article, which indicated that, “Chemical analyses of one such attractive oviposition substrate, incubated blood, identified phenol, 4-methylphenol (p-cresol) and indole as major constituents.” (Grabbe, R. & Turner, J. Screwworm attractants: isolation and identification of organic compounds from bacterially inoculated and incubated blood. Folia Entomol. Mex 25, 120–121 (1973).)

IFUS Point 6a-2.3a: This data led to another question, “Does gallic acid prevent the production phenol, 4-methylphenol (p-cresol)?”

IFUS Point 6a-2.3a-i: “Under the optimized conditions, the oxidative coupling of m-cresol with 4-aminoantipyrine (4-AAP) was catalyzed by the GA-NFs dispersed in solution and adsorbed on filter paper to form an antipyrine dye and it was visually and spectrophotometrically recorded. The m-cresol with range of 0.05–0.5 mM was detected in 10 min and 15 min by using the GA-NFs in solution and on filter paper, respectively. We demonstrated that the NFs can be produced from non-protein molecules and GA-NFs can be used as a promising nanocatalyst for a variety of applications." (Dadi, S., Celik, C. & Ocsoy, I. Gallic acid nanoflower immobilized membrane with peroxidase-like activity for m-cresol detection. Sci Rep 10, 16765 (2020). https://doi.org/10.1038/s41598-020-73778-7)

IFUS Point 6a-2.3a-ii: A follow-up question, "Do m-cresol and p-cresol have different smells?" led to this answer:

- Mixed cresols are used as disinfectants, preservatives, and wood preservatives. (1)
- o-Cresol is used as a solvent, disinfectant, and chemical intermediate. (1)
- m-Cresol is used to produce certain herbicides, as a precursor to the pyrethroid insecticides, to produce antioxidants, and to manufacture the explosive, 2,4,6-nitro-m-cresol. (1)
- p-Cresol is used largely in the formulation of antioxidants and in the fragrance and dye industries. (1)
    - (1) Agency for Toxic Substances and Disease Registry (ATSDR). Toxicological Profile for Cresols. Public Health Service, U.S. Department of Health and Human Services, Atlanta, GA. 1990.

IFUS Point 6a-2.3b: One might wonder as to whether Gallic Acid, which has been shown to be contained and/or produced by the ingredients in SGP+™, might in fact be producing at the wound level m-cresol vs. p-cresol. In consideration of the studies performed on the anti-larvicidal nature of Carob, one can might entertain this to the relevance of IFUS Point 6a-3.

IFUS Point 6a-3: In nature, screwworm females are preferentially attracted by odors released from pre-existing screwworm-infested wounds (4,45,46), as these sites are rich in bacterial-derived semiochemicals that act as animal host-finding cues in complex environments (18,19). This blend of odors can be obtained from waste larval rearing media, which is routinely offered to C. hominivorax females to stimulate oviposition in laboratory colonies (47). In order to evaluate the implications of an impaired OR-olfactory pathway for the recognition of its favored oviposition site, the ability of post-mated C. hominivorax female flies (6-to-9-days-old) to find oviposition media was evaluated in an additional set of two-choice trap assays. We observed that wt and heterozygous females display a strong attraction to the odors released from the oviposition device (Fig. 4D), entering the odor traps just a few minutes after the beginning of the trials and very often laying eggs inside before the end.

IFUS Point 6a-3.1: Ref.(4) Hall M, Wall R. Myiasis of humans and domestic animals. Adv. Parasitol. 1995;35:257–334. doi: 10.1016/S0065-308X(08)60073-1. [DOI] [PubMed] [Google Scholar]

IFUS Point 6a-3.2: Ref.(45) Hammack L. Oviposition by screwworm flies (Diptera: Calliphoridae) on contact with host fluids. J. Econ. Entomol. 1991;84:185–190. doi: 10.1093/jee/84.1.185. [DOI] [PubMed] [Google Scholar]

IFUS Point 6a-3.3: Ref.(46) Thomas DB, Mangan RL. Oviposition and wound-visiting behavior of the screwworm fly, Cochliomyia hominivorax (Diptera: Calliphoridae) Ann. Entomol. Soc. Am. 1989;82:526–534. doi: 10.1093/aesa/82.4.526. [DOI] [Google Scholar]

IFUS Point 6a-3.4: Ref.(18) Tomberlin JK, et al. A review of bacterial interactions with blow flies (Diptera: Calliphoridae) of medical, veterinary, and forensic importance. Ann. Entomol. Soc. Am. 2017;110:19–36. doi: 10.1093/aesa/saw086. [DOI] [Google Scholar]

IFUS Point 6a-3.5: Ref.(19) Zhu JJ, et al. Semiochemicals released from five bacteria identified from animal wounds infested by primary screwworms and their effects on fly behavioral activity. PLoS ONE. 2017;12:e0179090. doi: 10.1371/journal.pone.0179090. [DOI] [PMC free article] [PubMed] [Google Scholar]

IFUS Point 6a-3.6: Ref.(47) Chaudhury MF, Zhu JJ, Sagel A, Chen H, Skoda SR. Volatiles from waste larval rearing media attract gravid screwworm flies (Diptera: Calliphoridae) to Oviposit. J. Med. Entomol. 2014;51:591–595. doi: 10.1603/ME13193. [DOI] [PubMed] [Google Scholar]

IFUS Point 6a-4: Screwworm larvae survival depends on proper host selection made by the mothers, which prefer to lay eggs on dry borders of animal wounds and bodily orifices (46). This decision prevents the embryos from drowning in body fluids while ensuring hatching larvae immediate access to a nutrient-rich environment. Newborn larvae might use olfactory cues to guide their way from the oviposition site into the substrate to feed. Once the feeding source is found, this olfactory-based orientation might be gradually replaced by contact chemoreception, such as gustatory, explaining the decrease in ChomOrco expression during subsequent larval stages (Fig. 2A).)Ref.(46) Thomas DB, Mangan RL. Oviposition and wound-visiting behavior of the screwworm fly, Cochliomyia hominivorax (Diptera: Calliphoridae) Ann. Entomol. Soc. Am. 1989;82:526–534. doi: 10.1093/aesa/82.4.526. [DOI] [Google Scholar])

IFUS Point 6a-4.1: Of note is "A similar pattern is observed in other blowflies, such as Lucilia sericata (49) and C. megacephala (Fig. 2C), indicating that the modulation of Orco expression is also evolutionary conserved. Interestingly, food ingestion by D. melanogaster is enhanced in the presence of microorganism-derived odors (50). Thus, a reduction in olfactory input might be related to the lower rates of larval survival observed for the Orco mutant strain developed in this study."

IFUS Point 6a-4.1-i: Ref.(49) Wang X, et al. Molecular characterization and expression pattern of an odorant receptor from the myiasis-causing blowfly, Lucilia sericata (Diptera: Calliphoridae) Parasitol. Res. 2012;110:843–851. doi: 10.1007/s00436-011-2563-5. [DOI] [PubMed] [Google Scholar]

IFUS Point 6a-4.1-ii: Ref.(50) Depetris-Chauvin A, Galagovsky D, Chevalier C, Maniere G, Grosjean Y. Olfactory detection of a bacterial short-chain fatty acid acts as an orexigenic signal in Drosophila melanogaster larvae. Sci. Rep. 2017;7:14230. doi: 10.1038/s41598-017-14589-1. [DOI] [PMC free article] [PubMed] [Google Scholar]

IFUS Point 6a-5: As stated in IFUS Point 5, the complexity of SGP+™ in producing Herd Performance Improvement (as reported by ranchers and dairymen applying the formulation as part of their respective ration management), leads the IFUS Scientific Team to further explore the possible implications of polyphenols and peroxidases producing natural tannins, flavonoid, flavanols, and the like, while reducing the furfurals. In the IFUS Part 1 and Part 2 White Papers, it is suggested that a two-stage fermentation of lignin (Stage 1 *In Vitro* followed by Stage 2 *In Vivo)* produces a shift in aspects of ruminal digestion from the Lower GI to the Upper GI. Per the science offered this "shift" allows byproducts to be produced that may in fact be at the root of fly remediation on the herds and elimination of fly larval activity in the manure pats. Even the absence of beetles in the manure is noted. These observations are again made plausible by a variety of studies on the symbiosis of:

1. what, when, and how ration is prepared and fed to the herd,
2. how and when that ration is digested,
3. how and when the nutrients from that digestion is absorbed,
4. and finally what nutrients and components remain in the manure.

IFUS Point 6a-5a: Add the content from Part 1 and Part 2 White Papers that demonstrate the biochemistry and other science that supports Point 6.

IFUS Point 6a-5a.1: These inter-relations between ration fed, digestibility, and absorbability affect the manure and emissions of a variety of VOC's (many of which are said to attract the flies withing seconds from quite some distance away.) Hence, in consideration of the highly refined nature of the olfactory capabilities of the New World Screwworm Fly, a deeper exploration into

IFUS Point 6a-5a.2: "Since the concentration of phenolics is much higher in the intestinal fluid than is ever achieved in plasma or other body tissues, it is suggested that their antioxidant activity could be exerted in the gastrointestinal tract (GIT), breaking the propagation of lipid peroxides oxidation and production of toxic compounds." ("Protection of lipids from oxidation by epicatechin, trans-resveratrol, and gallic and caffeic acids in intestinal model systems," Zohar Kerem, et.al, J Agric Food Chem. 2006 Dec 27;54(26):10288-93. doi: 10.1021/jf0621828. PMID: 17177572 DOI: 10.1021/jf0621828)

IFUS Point 6a-5a.3: "Consumption of polyphenols is associated with health promotion through diet, although many are poorly absorbed in animals and humans alike. Lipid peroxides may reach the intestine and initiate deleterious oxidation. Here we measured inhibition of the oxidation of linoleic acid (LA) in authentic fluid from rat small intestine (RIF) by two dietary polyphenols, a flavonoid, epicatechin (EC), and a stilbene, resveratrol (RV), and by gallic (GA) and caffeic (CA) acids, and their partition coefficients. Both polyphenols inhibited 80%, and CA inhibited 65%, of the production of hexanal." (Protection of lipids from oxidation by epicatechin, trans-resveratrol, and gallic and caffeic acids in intestinal model systems, Zohar Kerem, et.al., J Agric Food Chem. 2006 Dec 27;54(26):10288-93. doi: 10.1021/jf0621828., PMID: 17177572)

IFUS Point 6a-5a.4: To Be Continued

IFUS Point 7: Are there any specific natural plant-based compounds that repel the New World Screwworm Fly?

IFUS Point 7a: **Ficus palmate, Juniperus procera, and Nerium oleander: These plants have been evaluated for their larvicidal effect against the screwworm fly. "Larvicidal Activity of Selected Plant Extracts Against the Screwworm Fly Chrysomya Albiceps,"** Al-Jameeli M. M. Larvicidal, Biosci Biotech Res Asia 2021;18(3). http://dx.doi.org/10.13005/bbra/2934

IFUS Point 7a-1: Does Nerium oleander produce triterpenes of oleanane? "Yes, Nerium oleander does produce triterpenes of oleanane type. New oleanane-type triterpenes have been isolated from the leaves of Nerium oleander, indicating the presence of these compounds. (1,2,3)"

IFUS Point 7a-1.1: Ref. (1): Three New Triterpenes from Nerium oleander and Biological Activity of the Isolated Compounds, Liwei Fu, et.al., Journal of Natural Products. Vol 68/Issue 2 (https://pubs.acs.org/doi/10.1021/np040072u)

IFUS Point 7a-1.2: Ref. (2): "Triterpenoids from the leaves of Nerium oleander," Sabira B Phytochemistry, Volume 44, Issue 2, January 1997, Pages 329-332, https://doi.org/10.1016/S0031-9422(96)00515-8

IFUS Point 7a-1.3: Ref. (3): Oleanane-, ursane-, lupane-, and taraxasterane-type pentacyclic triterpenes isolated from the medicinal plants Nerium Oleander, Ixeris Chinensis, Sonchus Oleraceus And Phytolacca Americana. Cytotoxicity studies on human cancer cell lines, and mdr cancer reversal and anti-inflammatory activities. Pentacyclic Triterpenes as Promising Agents in Cancer," Bai, L., et.al, Pentacyclic Triterpenes as Promising Agents in Cancer. 89-126.

IFUS Point 7b: In a study published by Rattan, R. S. (2010). (Mechanism of action of insecticidal secondary metabolites of plant origin. Crop. Protection 29, 913-920.), "Secondary metabolites present in plants apparently function as defense (toxic), which inhibits reproduction and other processes. The phytochemical biomolecules could be used for maximizing the effectiveness and specificity in future insecticide design with specific or multiple target sites, while ensuring the economic and ecological sustainability."

IFUS Point 7c: In another study by Ashwani Kumar, et.al, "Major Phytochemicals: Recent Advances in Health Benefits and Extraction Method," (Molecules. 2023 Jan 16;28(2):887. Doi: 10.3390/molecules28020887), "Table 1: Major phytochemicals, their sources, active sites, and the related health benefits" reveals that a "Oleanane" can be found in the "Middle lamella of legumes."

IFUS Point 7c-1: As Carob is a legume and Chios Mastic Gum Trees is a "dioecious evergreen shrub", it was found that:

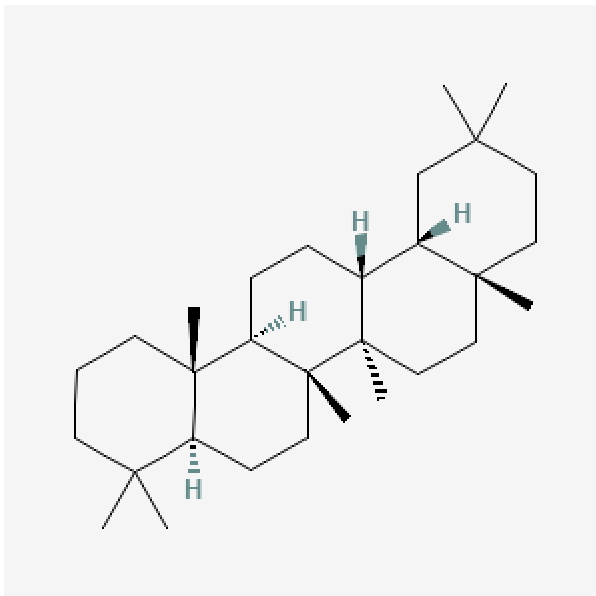
IFUS Point 7c-1-1: "Mastic gum, a resin obtained from the mastic tree, contains triterpenes of oleanane (3).

IFUS Point 7c-1-1a: Ref. 3:

"Oleanane is a pentacyclic triterpenoid, a class of molecules made up of six connected isoprene units. The naming of both the ring structures and individual carbon atoms in oleanane is the same as in steroids. As such, it consists of a A, B, C, D, and E ring, all of which are six-membered rings." International Union of Pure and Applied Chemistry (2014). Nomenclature of Organic

Chemistry: IUPAC Recommendations and Preferred Names 2013. The Royal Society of Chemistry. P. 1538. Doi:10.1039/9781849733069. ISBN 978-0-85404-182-4.

18β-Oleanane



IFUS Point 7c-1-2: "Triterpenes of oleanane from various plants have been found to repel insects (1,2,3,4,5). These compounds exhibit insect growth inhibitory activity and can act as antifeedant inhibitors (1). Some species of Doryphorina leaf beetles produce oleanane triterpene glycosides in their defensive glands (2).

IFUS Point 7c-1-2a: Ref. 1: Ceanothane and oleanane-type triterpenes from Talguenea quinquenervia have insecticidal activity against Cydia pomonella, Tenebrio molitor and Drosophila melanogaster, Soledad Quiroz, et.al., Industrial Crops and Products, Volume 74, 15 November 2015, Pages 759-766

IFUS Point 7c-1-2b: Ref. 2: Recycling plant wax constituents for chemical defense: hemi-biosynthesis of triterpene saponins from beta-amyrin in a leaf beetle, Pascal Laurent, et.al., Naturwissenschaften. 2003

Nov;90(11):524-7. Doi: 10.1007/s00114-003-0471-y. Epub 2003 Oct 14.

IFUS Point 7c-1-2d: Ref. 3: Biotransformation of Oleanane and Ursane Triterpenic Acids, Natalia A Luchnikova, et.al., Molecules. 2020 Nov 25;25(23):5526. Doi: 10.3390/molecules25235526

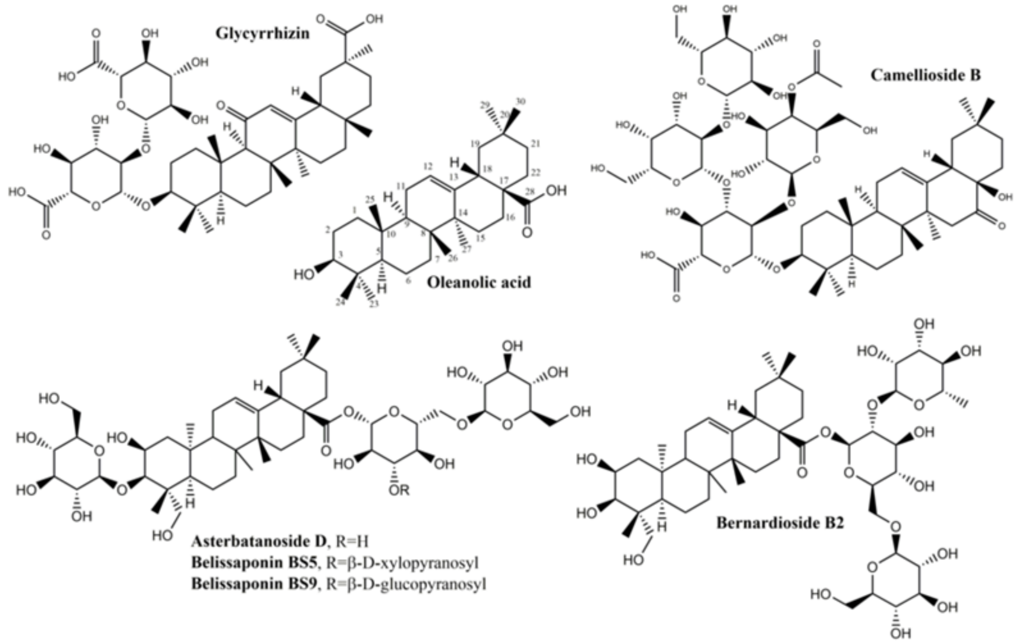
IFUS Point 7c-1-2e: Ref. 4: Insecticidal Triterpenes in Meliaceae: Plant Species, Molecules and Activities: Part I (Aphanamixis-Chukrasia), Meihong Lin, et.al., Int J Mol Sci. 2021 Dec 9;22(24):13262. Doi: 10.3390/ijms222413262

IFUS Point 7c-1-2f: Ref. 5: New biofunctional effects of oleanane-type triterpene saponins, Matsuda, H. et.al., J Nat Med 77, 644–664 (2023). https://doi.org/10.1007/s11418-023-01730-w

IFUS Point 7c-1-3: "Triterpenes of oleanane (1,2,3,4,5) repel insects. These compounds have insect growth inhibitory activity and can inhibit insect feeding. Examples of oleanane-type triterpenes include ceanothane, elatosides, momordins, senegasaponins, camelliasaponins, and escins."

IFUS Point 7d: Natural Ingredients from Plant Based Solutions that Mitigate, Ameliorate, and/or Erradicatic the New World Screwworm Fly

In a study "Insecticidal Triterpenes in Meliaceae: Plant Species, Molecules and Activities: Part I (Aphanamixis-Chukrasia), Meihong Lin, et.al., Int J Mol Sci. 2021 Dec 9;22(24):13262. Doi: 10.3390/ijms222413262, PMCID: PMC8704831 PMID: 34948062



IFUS Point 7d-1: Ref. 1: Ceanothane and oleanane-type triterpenes from Talguenea quinquenervia have insecticidal activity against Cydia pomonella, Tenebrio molitor and Drosophila melanogaster, Soledad Quiroz, et.al., Industrial Crops and Products, Volume 74, 15 November 2015, Pages 759-766

IFUS Point 7d-2: Ref. 2: New biofunctional effects of oleanane-type triterpene saponins, Hisashi Matsuda, et.al., J Nat Med. 2023 Jul 12;77(4):644–664. Doi: 10.1007/s11418-023-01730-w

IFUS Point 7d-3: Ref. 3: Oleanane-type triterpenoids from Sabia limoniacea and their anti-inflammatory activities, Yan Huang, et.al., Bioorganic Chemistry, Volume 151, October 2024, 107683

IFUS Point 7d-4: Ref. 4: Insecticidal Triterpenes in Meliaceae: Plant Species, Molecules and Activities: Part I (Aphanamixis-Chukrasia), Meihong Lin, et.al., Int J Mol Sci. 2021 Dec 9;22(24):13262. Doi: 10.3390/ijms222413262

IFUS Point 7d-5: Ref. 5: Triterpenes from Maytenus gonoclada and their attractive effects on Tenebrio molitor, Fernando C. Silva, et.al., Chem Nat Compd 49, 571–574

(2013)., https://doi.org/10.1007/s10600-013-0676-z

IFUS Point 7e: B-caryophyllene affects odorant receptors (ORs) of flies? β-caryophyllene affects odorant receptors (ORs) of flies (1,2,3,5). It has a significant effect on the choice of first instar larvae1. It strongly attracts mated females (2). However, its isomer α-Caryophyllene shows repellent effects (3).

IFUS Point 7e-1: Ref (1) Stage-specific expression of an odorant receptor underlies olfactory behavioral plasticity in Spodoptera littoralis larvae, Santosh V Revadi, et.al., BMC Biol. 2021 Oct 28;19:231. doi: 10.1186/s12915-021-01159-1, PMCID: PMC8555055 PMID: 34706739

IFUS Point 7e-2: Ref (2) BdorOBP32 Perceiving β-Caryophyllene: A Molecular Target for Female Attractant Development in Bactrocera dorsalis, Quan Lei, et.al., J Agric Food Chem. 2025 May 7;73(18):11209-11217. doi: 10.1021/acs.jafc.5c00167. Epub 2025 Apr 24., PMID: 40272313 DOI: 10.1021/acs.jafc.5c00167

IFUS Point 7e-3: Ref (3): Molecular basis of peripheral olfactory sensing during oviposition in the behavior of the parasitic wasp Anastatus japonicus, Yinliang Wang, et.al., Insect Biochemistry and Molecular Biology, Volume 89, October 2017, Pages 58-70, https://doi.org/10.1016/j.ibmb.2017.09.001

Ifus Point 7e-4: Ref. (5): Two odorant receptors regulate 1-octen-3-ol induced oviposition behavior in the oriental fruit fly, Li Xu, et.al., Commun Biol 6, 176 (2023). https://doi.org/10.1038/s42003-023-04551-5

IFUS Point 7f: "B-caryophyllene affects gustatory receptors (GRs) in flies. β-caryophyllene affects gustatory receptors (GRs) in flies (1,2,5). GRs are members of a large G-protein coupled receptor family and are phylogenetically different from taste receptors in most other animals2. β-caryophyllene is a natural bicyclic sesquiterpene found in cannabis and non-cannabis plants (3.4)."

IFUs Point 7f-1: Ref (1) Recent Advancements in Studies on Chemosensory Mechanisms Underlying Detection of Semiochemicals in Dacini Fruit Flies of Economic Importance (Diptera: Tephritidae), Hajime Ono, et.al., Insects. 2021 Jan

26;12(2):106. doi: 10.3390/insects12020106, PMCID: PMC7911962 PMID: 33530622

IFUS Point 7f-2: Ref (2) Molecular and Cellular Designs of Insect Taste Receptor System, Front Cell Neurosci. 2010 Jun 18;4:20. doi: 10.3389/fncel.2010.00020, PMCID: PMC2896210 PMID: 20617187

IFUS Point 7f-3: Ref (5) Multiple gustatory receptors required for the caffeine response in Drosophila, Youngseok Lee, et.al., Proc Natl Acad Sci U S A. 2009 Feb 25;106(11):4495–4500. doi: 10.1073/pnas.0811744106, PMCID: PMC2657413 PMID: 19246397

IFUS Point 7f-4: Ref (3) A focused review on CB2 receptor-selective pharmacological properties and therapeutic potential of β-caryophyllene, a dietary cannabinoid, Hebaallah Mamdouh Hashiesh, et.al., Biomed Pharmacother. 2021 Aug:140:111639. doi: 10.1016/j.biopha.2021.111639. PMID: 34091179 DOI: 10.1016/j.biopha.2021.111639

IFUS Point 7f-5: Ref (4) β-Caryophyllene: A Sesquiterpene with Countless Biological Properties, Fabrizio Francomano, et.al., Applied Sciences, December 20199(24), DOI:10.3390/app9245420

IFUS Point 7g: Plant-originated triterpenes affect odorant receptors (ORs) of flies (1,2,3,4,5). The study confirmed the attractive effects of four plant volatiles to flies and identified candidate ORs for perception of these volatiles1. Multiple functional receptors in insects' olfactory system include ORs, odorant-degrading enzymes (ODEs), and odorant-binding proteins (OBPs) (2). Research has investigated the impact of plant odors on fly perception and behavior (3). ORs from flies have been deorphanized, and fundamental molecular properties of odorant-OR interactions have been uncovered (4,5).

IFUS Point 7g-1: Ref. (1) Odorant receptor 75 is essential for attractive response to plant volatile p-anisaldehyde in Western flower thrips, Xuan-Pu Luan, et.al., Pesticide Biochemistry and Physiology, Volume 211, June 2025, 106421, https://doi.org/10.1016/j.pestbp.2025.106421

IFUS Point 7g-2: Ref. (2) Olfactory receptors in Bactrocera species for sustainable fruit fly management: A review and future perspectives, Saleem Jaffar, et.al., Royal Entomology Society, Physiological Entomology, Volume49, Issue2, June 2024, Pages 67-90, 24, First Published, January 2024 https://doi.org/10.1111/phen.12428

IFUS Point 7g-3: Insect Odorscapes: From Plant Volatiles to Natural Olfactory Scenes, Lucie Conchou, et.al., Front Physiol. 2019 Aug 2;10:972. doi: 10.3389/fphys.2019.00972, PMCID: PMC6688386 PMID: 31427985

IFUS Point 7g-4: Odorant Reception in Insects: Roles of Receptors, Binding Proteins, and Degrading Enzymes, Walter S. Leal, Annual Review of Entomology Volume 58, 2013, Vol. 58:373-391 (Volume publication date January 2013) https://doi.org/10.1146/annurev-ento-120811-153635

IFUS Point 7g-5: Engineered odorant receptors illuminate structural principles of odor discrimination, Claire A de March, et.al., xiv [Preprint]. 2023 Nov 17:2023.11.16.567230. doi: 10.1101/2023.11.16.567230. PMID: 38014344 PMCID: PMC10680712

IFUS Point 7h: Do Plant-originated triterpenes affect Gustatory receptors (GRs) of flies? "Plant-originated triterpenes affect gustatory receptors (GRs) of flies (1,2,3,4,5). GRs are members of a large G-protein coupled receptor family and are phylogenetically different from taste receptors of most other animals (1,5). They contribute to deciphering a host plant's metabolic code in insects (2)."

IFUS Point 7h-1: Ref. (1) Molecular and Cellular Designs of Insect Taste Receptor System, Kunio Isono, et.al., Front Cell Neurosci. 2010 Jun 18;4:20. doi: 10.3389/fncel.2010.00020, PMCID: PMC2896210 PMID: 20617187

IFUS Point 7h-2: Ref. (2) Contact chemosensation of phytochemicals by insect herbivores, Stefan Pentzold, et.al., Nat Prod Rep. 2017 May 9;34(5):478–483. doi: 10.1039/c7np00002b, PMCID: PMC5436039 PMID: 28485430

IFUS Point 7h-3: Ref. (3): Insect olfactory neurons: receptors, development, and function, Hua Yan, Current Opinion in Insect,

Science, Volume 67, February 2025, 101288, https://doi.org/10.1016/j.cois.2024.101288

IFUS Point 7h-4: Ref. (4) An Odorant-Binding Protein Required for Suppression of Sweet Taste by Bitter Chemicals, Yong Taek Jeong, et.al., Neuron, Volume 79, Issue 4, 725 - 737

IFUS Point 7h-5: Ref. (5) Molecular and cellular designs of insect taste receptor system, Front. Cell. Neurosci., 17 June 2010, Sec. Cellular Neurophysiology, Volume 4 - 2010 | https://doi.org/10.3389/fncel.2010.00020

Add the scientific linkages and synergies to the NEXT SECTION

IFUS Point 7g: Mastic Gum: It has triterpenes of oleanane, euphane, lupine-type. Alpha-tocopherol, polyphenols, verbenone, alpha-terpineol, and linalool were also identified in the resin. "Anti-inflammatory activity of Chios mastic gum is…" Nutrition Journal, US National Library of Medicine.

References

"The effect of mastic gum on Helicobacter pylori…" Phytomedicine, Elsevier, Academia.

"In Vitro and In Vivo Activities of Chios Mastic Gum…" Antimicrobial Agents and Chemotherapy, American Society for Microbiology, US National Library of Medicine.

"Is Chios mastic gum effective in the treatment…" Journal of Ethnopharmacology, Academia.

"Chios mastic gum decreases renin levels and…" Biomedicine & Pharmacotherapy, US National Library of Medicine.

"Comparison of the Effect of Xylitol Gum- and Mastic…" Journal of Dentistry, Tehran University of Medical Sciences.

"Chios mastic treatment of patients with active Crohn's…" World Journal of Gastroenterology, US National Library of Medicine.

"Herbal and plant therapy in patients with inflammatory…" Annals of Gastroenterology, US National Library of Medicine.

“Anti-inflammatory activity of Chios mastic gum is…” Nutrition Journal, US National Library of Medicine.

“Current knowledge on alleviating Helicobacter pylori…” Integrative Medicine Research, US National Library of Medicine.

IFUS Point 7h: Develop this added section and link/cite articles with direct link to depolymerized lignin from Sugarcane Bagasse

Depolymerized lignin can produce various products, including triterpenes. The depolymerization of lignin involves methods such as thermochemical, mechanical, chemical catalysis, and biological treatment, which can yield a range of value-added products, including aromatic compounds and phenolic molecules. While the specific presence of triterpenes is not explicitly mentioned, the depolymerization process is significant for converting lignin into biofuels and other valuable chemicals.

Ref. 1: N.L. Radhika, Sarita Sachdeva, Manoj Kumar, Lignin depolymerization and biotransformation to industrially important chemicals/biofuels, Fuel,Volume 312, 2022, 122935, ISSN 0016-2361, https://doi.org/10.1016/j.fuel.2021.122935. (https://www.sciencedirect.com/science/article/pii/S0016236121027964)

Ref. 2: Depolymerization of lignin: Recent progress towards value-added chemicals and biohydrogen production, Hina Ramzan, Muhammad Usman, Faiqa Nadeem, Muhammad Shahzaib, Muneeb Ur Rahman, Reeta Rani Singhania, Farzana Jabeen, Anil Kumar Patel, Chunyao Qing, Shengyong Liu, Grzegorz Piechota, Nadeem Tahir, Bioresource Technology, Volume 386, 2023,129492, ISSN 0960-8524, https://doi.org/10.1016/j.biortech.2023.129492.

Draw the overlays and synergies from the science above. Are New World Screwworm Flies repelled by strong, spicy aromas?

Yes, strong, spicy aromas can repel flies. Flies are known to dislike scents such as peppermint, lavender, and eucalyptus. These natural repellents can create an unwelcoming environment for flies, making them effective in keeping them away.

Ranchers and visitors to the IFUS Test Ranches continually report that their pastures have no offensive smells. More so, ranchers state that there is a "fresh earth" smell to their pastures. Is it just coincidental,

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IFUS Point 8: Summary and Conclusions

Concluding Statement 1: There is significant data that has been reviewed that must be added to this White Paper to draw plausible and definitive conclusions. However, even with the data presented at this time, one can find several biochemical pathways that provide plausible evidence that illustrates how SGP+™ is producing the results reported by ranchers and dairymen applying the product as part of a Ration Management Technology.

Concluding Statement 2: In the study (van Vliet, Stephan & Provenza, Frederick & Kronberg, Scott. (2021). "Health-Promoting Phytonutrients Are Higher in Grass-Fed Meat and Milk," Frontiers in Sustainable Food Systems. 4. 555426. 10.3389/fsufs.2020.555426.), "Emerging data indicate that when livestock are eating a diverse array of plants on pasture, additional health-promoting phytonutrients—terpenoids, phenols, carotenoids, and anti-oxidants—become concentrated in their meat and milk. Several phytochemicals found in grass-fed meat and milk are in quantities comparable to those found in plant foods known to have anti-inflammatory, anti-carcinogenic, and cardioprotective effects. As meat and milk are often not considered as sources of phytochemicals, their presence has remained largely underappreciated in discussions of nutritional differences between feedlot-fed (grain-fed) and pasture-finished (grass-fed) meat and dairy, which have predominantly centered around the ω-3 fatty acids and conjugated linoleic acid. Grazing livestock on plant-species diverse pastures concentrates a wider variety and higher amounts of phytochemicals in meat and milk compared to grazing monoculture pastures, while phytochemicals are further reduced or absent in meat and milk of grain-fed animals. The co-evolution of plants and herbivores has led to plants/crops being more productive when grazed in accordance with agroecological principles. The increased phytochemical richness of productive vegetation has potential to improve the health of animals and upscale these nutrients to also benefit human health. Several studies have found increased anti-oxidant activity in meat and milk of grass-fed vs. grain-fed animals."

> Conclusion 2a: Based on the aforementioned studies, one could postulate that the plant-based phytonutrients (like those provided by the ingredients in SGP+™) and the byproducts from those phytonutrients would be found not only in the meat and milk of beef and dairy cows, but their hides as well. This would include plant-based compounds or those derived from plant-based compounds that would have dramatic effect on preventing the New World Screwworm Fly from (1) being attracted to beef and dairy cattle, (2) wanting to bite the cow, (3) discouraging the fly to lay her eggs into the cow, and (4) preventing the larvae from becoming a mature fly.

Concluding Statement 3: TO BE CONTINUED.