

# Unlocking the Bioactive Potential of Elderberry Extract: A Comprehensive BioMAP Analysis and Comparative Bioactivity Profiling of FENO-SAMBUCUS<sup>TM</sup>

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Abstract: The scientific exploration of bioactive compounds, particularly from plant-based sources, serves as a cornerstone for advancing research in their health-promoting properties. Eevia Health Plc undertook a rigorous investigation into the bioactivity of their standardized organic certified Elderberry Extract, FENO-SAMBUCUS<sup>TM</sup>, utilizing the BioMAP analysis by Eurofins. BioMAP is a methodological framework that simulates various human disease models to decode the bioactivity of test agents across a spectrum of biological contexts in primary human cells. The comprehensive analysis revealed significant antiproliferative, anti-inflammatory, and immunomodulatory activities, bringing to light the extract's potential in a myriad of health and wellness applications. Notably, a comparative bioactivity analysis highlighted a mathematical similarity with ODN2006, a known immunomodulatory agent, paving the way for further exploration into the extract's potential in immune health supplements and therapeutic applications. In the study, the assumably strongest competitor to the FENO-SAMBUCUS™ was tested in the same way and on the same primary cells from the same human donors. An overlay of the test results revealed similarities and differences in the bioactivity of each test agent. This investigation not only substantiates the traditional and empirically derived uses of elderberry extracts but also provides a robust scientific foundation for its application in health-enhancing supplements and further clinical research.

**Keywords:** Elderberry Extract; BioMAP Analysis; Bioactivity Profiling; FENO-SAMBUCUS<sup>TM</sup>; Bioactive Potential, Immunomodulatory Activities, Anti-inflammatory Compounds, Antiproliferative Effects, Cardiovascular Health, Tissue Remodeling, Hemostasis

## 1. Introduction

The exploration of bioactive compounds from plant-based sources has burgeoned into a pivotal domain within scientific research, particularly concerning the investigation of health-promoting properties inherent within such compounds. Eevia Health Plc, situated in the heart of the Fenno-Scandinavian Forest, close to the Arctic Circle in Northern Finland, engages in rigorous scientific endeavors to elucidate the bioactive potential harbored within compounds extracted from selected arctic and North-European plants and fruits. Standardized organically certified extracts are manufactured from raw materials, such as bilberries, lingonberries, tart cherries, elderberries, pine

bark and chaga mushrooms. Science has shown that these organic extracts may harbor potent, healthpromoting properties. This research on these botanical extracts extends beyond mere extraction, delving into an exhaustive understanding of the intricacies of their bioactivities and substantiation of their application within dietary supplement formulations, all grounded in scientific precision and rigorous scrutiny.

Central to Eevia Health's scientific methodology is the BioMAP assay platform operated by Eurofins, an extensive biomarker framework simulating various human disease models and biological responses to decode the bioactivity of test agents across diverse biological contexts. The Eurofins BioMAP Assay Platform features a wide collection of biological assays. From cell-based viability assays to immunofluorescence staining and gene expression profiling, this platform is very complete; It truly is the Swiss Army knife of biomedical research assay.

This assay provides scientific substantiation for the applications in health and wellness domains and acts as a pivotal step towards illuminating the bioactive potential of different natural ingredients and guiding subsequent, robust human clinical studies. With the help of the BioMAP Assay Platform, the researchers at Eevia Health can delve deeper into the mechanisms underlying the bioactivities and identify potential therapeutic targets within their natural botanical extracts.

Certified organic FENO-SAMBUCUS<sup>™</sup> is a spray-dried extract from the organic European elderberry fruit (*Sambucus Nigra* L.) which Eevia Health offers in different standardized concentrations of the bioactive anthocyanin. The top concentration contains not less than 30% anthocyanins, but also 17%, 14%, and 7% standardized concentrations are offered. In this study, the 14% concentration of anthocyanins was used, as this concentration is widely used in leading elderberry consumer brands in the world. However, Eevia Health is currently in the process of investigating the bio efficacy of its 30% variant.

The FENO-SAMBUCUS<sup>™</sup> extracts are sustainably manufactured utilizing Eevia Health's green chemistry platform, in combination with their proprietary purification process named PURE-RES<sup>™</sup>. Contrary to most known competing elderberry products that employ more conventional filtration systems, such as ceramic filtration, which typically excludes molecules based on size, the PURE-RES<sup>™</sup> purification technology fundamentally operates based on the affinity of polyphenol molecules for specific polarities. Hence, it retains a wide range of polyphenols and effectively concentrates larger nutrients, like Proanthocyanidins (PAC) as well as anthocyanins. It significantly reduces the content of sugar and organic acids compared to competing technologies, and ensures the retention of important bioactive molecules, making Eevia Health's FENO-SAMBUCUS<sup>™</sup> the most comprehensively structured extract in the market today.

In the study, the assumably strongest competitor to the FENO-SAMBUCUS<sup>™</sup> was tested in the same way and on the same primary cells from the same human donors. An overlay of the test results revealed similarities and differences in the bioactivity of each test agent. The results are discussed in

#### 2. Methodology

#### 2.1. BioMAP Analysis

The BioMAP analysis, developed by Eurofins, utilizes a network of human primary cell-based systems to evaluate the bioactivity of test agents in a diverse array of biological contexts, simulating various disease models and biological responses. Through this comprehensive approach, the analysis provides detailed insights into the safety, efficacy, and functional characteristics of test agents, such as Eevia Health's FENO-SAMBUCUS<sup>™</sup>, by means of fifty biomarkers, and one hundred and fifty protein markers in primary human cells and comparisons against a substantial reference database of known bioactive agents.

#### 2.2. Objectives and Scope of Analysis

The principal objective of employing the BioMAP analysis in Eevia Health's research program is to meticulously characterize the bioactivity of FENO-SAMBUCUS<sup>™</sup> 14% anthocyanins Elderberry Extract. This encompasses a broad assessment across multiple biological and disease relevance

categories, such as inflammation, immunomodulation, tissue remodeling, and hemostasis, providing a robust, detailed, and versatile bioactivity profile that serves as a basis for further investigations and applications.

## 2.3. Analytical Procedure

The analysis is executed across different concentrations of FENO-SAMBUCUS<sup>™</sup> to discern its bioactivity profile in twelve disease-related systems. Specific concentrations (100000 ng/ml, 33000 ng/ml, 11000 ng/ml, and 3700 ng/ml) were analyzed to evaluate its antiproliferative activity on distinct human primary cells, including:

- Coronary artery smooth muscle cells
- Peripheral blood mononuclear and B cells
- Endothelial and epithelial cells (venular and bronchial respectively)
- Fibroblasts (dermal and lung)

Moreover, the impact on biomarker activities is scrutinized, elucidating the extract's influence across several biological and disease classifications, such as:

- Inflammation-related activities
- Immunomodulatory activities
- Tissue remodeling activities
- Hemostasis-related activities

## 2.4. Data Analysis and Comparative Bioactivity Profiling

To deeper explore into the potential applications and mechanistic actions of FENO-SAMBUCUS<sup>™</sup>, the bioactivity data derived from the BioMAP analysis is subjected to comparative bioactivity profiling. This involves a meticulous comparison of FENO-SAMBUCUS<sup>™</sup> with agents from the BioMAP reference database of over 4,500 drug molecules and compounds to unravel similarities and divergences in their bioactivity profiles. Statistical methods like Pearson's correlation coefficients are used to quantify the significance of the resemblances and differences.

# 2.5. Ensuring Data Validity and Relevance

Through a stringent data validation process, the BioMAP analysis ensures that the resultant bioactivity profile of FENO-SAMBUCUS<sup>™</sup> is not only accurate but also relevant, providing a solid scientific foundation upon which its potential health benefits and applications can be explored, communicated, and utilized in dietary supplement product development activities.

## 3. Results

## 3.1. Overview of the BioMAP Profile of FENO-SAMBUCUS™

Eevia Health's Organic Certified Elderberry Extract FENO-SAMBUCUS<sup>™</sup>, identified as the test agent FS14, demonstrated compelling bioactivity across a spectrum of biomarker readouts in the BioMAP analysis, with a profile across the twelve (12) systems shown in Figure 1.



**Figure 1.** BioMAP profile of FENO-SAMBUCUS<sup>TM</sup> in the Diversity PLUS Panel. The X-axis lists the quantitative proteinbased biomarker readouts measured in each system. The Y-axis represents a log-transformed ratio of the biomarker readouts for the drug-treated sample (n = 1) over vehicle controls ( $n \ge 6$ ). The grey region around the Y-axis represents the 95% significance envelope generated from historical vehicle controls. Biomarker activities are annotated when 2 or more consecutive concentrations change in the same direction relative to vehicle controls, are outside of the significance envelope, and have at least one concentration with an effect size > 20% (|log10 ratio| > 0.1). Biomarker key activities are described as modulated if these activities increase in some systems but decrease in others. Cytotoxicity is indicated on the profile plot by a thin black arrow above the X-axis, and antiproliferative effects are indicated by a thick grey arrow. Cytotoxicity and antiproliferative arrows only require one concentration to meet the indicated threshold for profile annotation.

The systems showed 24 annotated readouts of significant and relevant bioactivity. No cytotoxicity was observed at the tested concentrations. The extract showcased a profile that warrants deeper exploration in the context of dietary supplement formulation.

## 3.1.1. Antiproliferative Activity

In the BioMAP analysis, FENO-SAMBUCUS<sup>™</sup> was observed to exert antiproliferative effects on several human primary cells at varying concentrations (100000 ng/ml, 33000 ng/ml, 11000 ng/ml, and 3700 ng/ml)., namely:

- Coronary artery smooth muscle cells
- Endothelial cells
- Fibroblasts

This suggests a potential utility in managing conditions where the proliferation of these cells may be detrimental, such as in certain cardiovascular conditions.

## 3.1.2. Impact on Biomarker Activities

Biological and Disease Relevance Categories were meticulously analyzed, revealing the following detailed activities:

Biological and Disease Relevance Category	Decreased activity	Increased activity
Inflammation-related activities	VCAM-1, IP-10, ITAC, MIG, Eot3, MCP-1	IL8
Immunomodulatory activities	M-CSF, slL-10, slL-2	sIL-6
Tissue remodeling activities	uPAR, MMP1, Col-I, Col-III, Col-IV, tPA	
Hemostasis-related activities		TF

## Table 1. Biological and disease relevance activity impact of FENO-SAMBUCUS Elderberry extract.

FENO-SAMBUCUS<sup>™</sup> mediated changes in key biomarker activities, providing insights into its bioactivity across several biological and disease classifications. Notable impacts were observed in the following activities:

• Inflammation-related activities: FENO-SAMBUCUS<sup>™</sup> demonstrated a capacity to modulate inflammation, evidenced by decreased Eotaxin 3, VCAM-1, MCP-1, I-TAC, MIG, IP-10, and an increase in IL-8.

• **Immunomodulatory activities:** The extract showcased immunomodulatory properties, with a decrease in sIL-10, M-CSF, sIL-2, and an increase in sIL-6, suggesting potential applications in modulating immune responses in the body.

• **Tissue remodeling activities:** A decrease in Collagen I, Collagen IV, tPA, MMP-1, Collagen III, and uPAR indicates the extract's potential role in influencing tissue remodeling processes.

• **Hemostasis-related activities:** An increase in TF (Tissue Factor) points toward the extract's possible influence on hemostasis-related activities.

#### 3.2. Comparative Bioactivity Analysis: FENO-SAMBUCUS<sup>™</sup> and ODN2006

In a meticulous exploration of mathematically analogous compound profiles from the BioMAP Reference Database, FENO-SAMBUCUS<sup>TM</sup>, at a concentration of 100000 ng/ml, demonstrated a notable similarity to ODN2006 (1  $\mu$ M). The relevance of the similarity was reflected by Pearson's correlation coefficient, r=0.734. Importantly, this coefficient surpasses our predetermined threshold (r≥0.7), underscoring a mechanistically relevant similarity between the two compounds. The overlay of the profile of the two test agents are shown in Figure 2.



**Figure 2.** Top Database Search Result for FENO-SAMBUCUS<sup>TM</sup> (100000 ng/ml) is ODN2006 (1  $\mu$ M). Overlay of the top similarity match from an unsupervised search of the BioMAP Reference Database of > 4,500 agents with EEV\_(1) FS14. Common biomarker readouts are annotated when the readout for both profiles is outside of the significance envelope with an effect size > 20% (|log10 ratio| > 0.1) in the same direction. Similarity search results are filtered and ranked as described in Appendix A. Profiles are identified as having mechanistically relevant similarity if the Pearson's correlation coefficient is  $\geq$  0.7. Additional information can be found in Appendix A.

ODN2006, a Class B-type cytosine-phosphate-guanine oligodeoxynucleotide (CpG-ODN), is distinguished as a highly specific ligand for Toll-like receptor-9 (TLR9, CD289), an immune pattern-recognition receptor (PRR) that identifies CpG motifs within bacterial DNA. ODN2006 mimics the immunostimulatory effects of bacterial DNA, presenting a spectrum of applications such as vaccine adjuvants, anti-allergic agents, and stimulants for immune tolerance and autoimmunity-related biology.

Ten common activities were annotated within several systems: BT (sIL-2, sIL-6), BF4T (Eotaxin 3), BE3C (I-TAC), HDF3CGF (VCAM-1, IP-10, I-TAC, M-CSF, Prolif 72), and IMphg (sIL-10), providing a substantial basis for further exploration and comparison of the bioactive profiles of FENO-SAMBUCUS<sup>™</sup> and ODN2006.

TLR9 is an immune pattern-recognition receptor (PRR) that recognizes CpG motifs within bacterial DNA. Synthetic ODN such as. ODN2006 mimics the immunostimulatory effects of bacterial DNA that can be used as vaccine adjuvants and anti-allergic agents as well as stimulants for immune tolerance and autoimmunity-related biology. The human TLR9 is primarily expressed on B cells and plasmacytoid dendritic cells (pDC) where its activation strongly stimulates B cell activation and triggers IFNG secretion from pDCs. There were nine activities common to both profiles.

## 3.3. Comparative Bioactivity Analysis: FENO-SAMBUCUS™ and COMPETITOR PRODUCT

A sample of the assumably strongest COMPETITOR PRODUCT named in the study as NW14 was acquired. The COMPETITOR PRODUCT is also an elderberry extract with 14% anthocyanins manufactured using ceramic filtration, which is a filtration approach that excludes molecules based on size and not based on chemical class. Hence, although the concentration of anthocyanins is the same in both test agents, FENO-SAMBUCUS<sup>TM</sup> will contain more of other phenolic compounds such as proanthocyanidins (PACs), while the COMPETITOR PRODUCT will contain more sugars, organic acids, and non-soluble fibers and much less of large molecules such as PACs. The COMPETITOR PRODUCT was applied in the BioMAP test system in the same manner as Eevia Health's FS14 extract.

The results from both test agents were then compared at multiple concentrations. The comparison between FENO-SAMBUCUS<sup>™</sup> and the COMPETITOR PRODUCT at a concentration of 100000 ng/ml, demonstrated both similarities and differences.



Figure 2. Overlay of FENO-SAMBUCUS™ and COMPETITOR PRODUCT at 100000 ng/ml

There are nine differentiating activities that are annotated within the following systems: 3C (IL-8), BT (sTNF  $\alpha$ ), HDF3CGF (MCP-1, ICAM-1, Collagen I, Collagen III), KF3CT (MCP-1), MyoF (TIMP-1), and IMphg (IL-1 $\alpha$ ).

There are 23 common activities within the following systems: 3C (Prolif), LPS (TF), SAg (IL-8, Pcyto), BT (sIL-2, sIL-6), BE3C (I-TAC), CASM3C (TM, Prolif), HDF3CGF (VCAM-1, IP-10, I-TAC, MIG, M-CSF, Prolif 72), KF3CT (IP-10, IL-8, MIG), MyoF (Collagen I, Collagen IV), and IMphg (CD69, IL-8, sIL-10).

Common biomarker readouts are annotated when the readout for both profiles is outside of the significance envelope with an effect size > 20% (|log10 ratio | > 0.1) in the same direction.

# 4. Discussion

#### 4.1. Interpretation of the Antiproliferative Activity

The notable antiproliferative activity of FENO-SAMBUCUS<sup>TM</sup>, demonstrated across several human primary cells, unveils a realm of potential applications, particularly in cardiovascular health. The inhibition of proliferation in coronary artery smooth muscle cells, endothelial cells, and fibroblasts might suggest utility in managing conditions like atherosclerosis, where uncontrolled cellular proliferation can contribute to vessel constriction and subsequent cardiovascular challenges.

#### 4.2. Bioactivity and Biomarker Modulation

## 4.2.1. Inflammation and Immunomodulation

The anti-inflammatory and immunomodulatory capacities of FENO-SAMBUCUS<sup>™</sup> are particularly striking and align with existing clinical findings on elderberry extracts. The modulation

of inflammatory and immunomodulatory markers, such as VCAM-1, MCP-1, and various interleukins, parallels the findings of previous studies that have explored the potential health benefits of elderberry and its extracts. Particularly noteworthy is the modulation of soluble interleukin-6 (sIL-6), a cytokine with a dual role in inflammation, potentially indicating a sophisticated immune-modulating effect by FENO-SAMBUCUS<sup>TM</sup>. Elevated sIL-6 expression can be associated with both pro-inflammatory and anti-inflammatory responses, making it a key focus in understanding the nuanced immunomodulatory capacities of elderberry extract, especially in the contexts of immune response balancing and managing inflammation in various health conditions.

For example, a randomized, double-blind, placebo-controlled study by Tiralongo et al. (2016)<sup>1</sup> found that air travelers using elderberry extract 10 days before and up to 4–5 days after traveling experienced a lower duration and reduced severity of cold symptoms, which can be associated with its immunomodulatory properties. Furthermore, a study by Hawkins et al. (2019)<sup>2</sup> reported that elderberry supplementation can reduce upper respiratory symptoms, and another by Zakay-Rones et al. (2004)<sup>3</sup> declared that elderberry extract seems to offer an efficient, safe and cost-effective treatment for influenza.

TLR9 activity is an essential component of the immune system's defense mechanism against various bacterial and viral pathogens. As a pattern-recognition receptor (PRR), TLR9 plays a crucial role in the recognition and response to unmethylated CpG DNA motifs present in pathogen genomes. Upon activation, TLR9 initiates intracellular signaling cascades leading to the production of pro-inflammatory cytokines, chemokines, and type I interferons, all critical for mounting an effective immune response.

It is interesting that the elderberry extract can modulate TLR8 activity which influences innate immunity responses. There are potential immunomodulatory properties by activating TLR9 signaling pathways. Further work may shed light on the intricate workings of our immune system and pave the way for novel interventions that leverage TLR activity for improved health outcomes.

The capability of elderberry extract to modulate inflammation and immune response has been substantiated in this study, suggesting its relevant application in dietary supplements aimed at supporting immune health and managing inflammation. The exploration of FENO-SAMBUCUS<sup>™</sup> in a similar context, especially given its bioactivity profile and its impact on sIL-6 expression, could offer novel insights and applications in managing immune-related health conditions.

#### 4.2.2. Tissue Remodeling and Hemostasis

Exploring FENO-SAMBUCUS<sup>TM</sup>'s impact on tissue remodeling and hemostasis biomarkers, its implications for tissue repair and vascular health become evident. The modulation of collagens, MMP-1, and TF implies potential applications in sustaining tissue integrity and influencing blood coagulation processes, which could be pivotal in wound healing and vascular health management.

The traditional use of elderberry leaves for wound and burn treatments provides a historical context for its potential in supporting tissue repair and integrity<sup>4</sup>. Moreover, in vitro studies have indicated that elderberry extracts can be effective in preventing free-radical-induced cell damage and have positive effects on skin cell health (Wójciak M. et al., 2023)<sup>5</sup>.

A study by Tiboc Schnell et al. (2021)<sup>6</sup> further underscores the potential role of elderberry, specifically *Sambucus nigra* L., in managing inflammation and influencing tissue remodeling. This study investigated the effects of *Sambucus nigra* L. extract in a rat model of lipopolysaccharide-induced subacute rhinosinusitis and found that it mitigated inflammation, reduced oxidative stress, and influenced tissue remodeling in the nasal and sinus mucosa. This was reflected in reduced levels of pro-inflammatory cytokines, diminished lipid peroxidation, and modulation of Matrix Metalloproteinases (MMPs) and their inhibitors (TIMPs), which are crucial in tissue remodeling processes. Notably, this study suggests that *Sambucus nigra* L. extract not only attenuates localized inflammatory responses but also exerts protective effects against systemic inflammatory responses, providing a compelling argument for further exploration of elderberry extracts like FENO-SAMBUCUS<sup>™</sup> in the context of tissue remodeling and hemostasis.

Thus, the bioactivity profile of FENO-SAMBUCUS<sup>™</sup>, enriched by historical, in vitro, and animal model insights, lends itself to further exploration in tissue remodeling, repair, and hemostasis.

### 4.3. Comparative Insights: FENO-SAMBUCUS™ vs. ODN2006

The mathematical similarity in the bioactivity profiles of FENO-SAMBUCUS<sup>™</sup> and ODN2006, substantiated by a Pearson's correlation coefficient of 0.734, illuminates intriguing possibilities in immune modulation and therapeutic applications. The notable similarity justifies the exploration of FENO-SAMBUCUS<sup>™</sup> in contexts where ODN2006 has found applicability, such as immune stimulation and as a potential adjuvant.

ODN2006, known for its role as a specific ligand for TLR9 and its subsequent immunostimulatory effects, has been explored in various pharmaceutical applications, including vaccine adjuvants and immunotherapeutic agents in the context of cancer. For instance, PF-3512676 (CPG 7909), a TLR9 agonist developed by Pfizer, has been thoroughly investigated in numerous clinical trials as an immunotherapeutic agent and vaccine adjuvant across various cancers, including non-small cell lung cancer and melanoma<sup>7</sup>. Another noteworthy example includes SD-101, developed by Dynavax Technologies (now TriSalus Life Science), which has been studied for its potential in treating various types of cancer, such as melanoma, by enhancing the immunogenicity of other therapeutic agents<sup>8</sup>.

Thus, the comparative analysis with FENO-SAMBUCUS<sup>™</sup> not only provides a deeper insight into the potential mechanistic similarities and divergences between the two but also sets a stage for exploring the extract in similar therapeutic and supplementary contexts.

Moreover, the alignment in the bioactivity profiles between FENO-SAMBUCUS<sup>™</sup> and ODN2006, particularly in immunomodulation, opens a promising avenue for exploring the potential use of Elderberry Extract in immune health supplements. This parallel not only highlights the feasibility of FENO-SAMBUCUS<sup>™</sup> as a viable option in managing immune responses and related health conditions but also introduces a prospect of offering a natural alternative or supplement to synthetic agents like ODN2006.

## 4.4. Comparative Insights: FENO-SAMBUCUS™ vs. COMPETITOR PRODUCT

The overlay comparison between the FENO-SAMBUCUS<sup>™</sup> and the COMPETITOR PRODUCT showed both similarities and differences. These traits is subject to further study. For instance, there was a clear difference in the strength of response on the sIL-6 biomarker, also known as soluble Interleukin-6. This is a crucial component in the field of immunology and inflammation research. It serves as an indicator for the activation of a specific signaling pathway that leads to the production and release of pro-inflammatory cytokines such as IL-6. Elevated levels of sIL-6 have been associated with various acute and chronic inflammatory conditions, making it a valuable diagnostic tool in clinical settings. Further investigation into the precise mechanisms involved in this interaction between the two elderberry extracts and sIL-6 is warranted to fully understand the difference in response and its implications for the therapeutic potential in managing inflammation-related disorders.

## 5. Conclusion

Eevia Health Plc has critically investigated the bioactivity of Elderberry Extract, FENO-SAMBUCUS<sup>™</sup>, through the lens of the BioMAP assay platform, uncovering significant activities across various biological and disease-associated categories, thereby underlining its substantial potential in health-enhancing applications. The extract demonstrated notable antiproliferative, antiinflammatory, and immunomodulatory activities, which not only align with but also scientifically validate its traditional and empirically derived uses. A comparative bioactivity analysis with ODN2006, yielding a Pearson's correlation coefficient of 0.734, indicates potential mechanistic and therapeutic parallels, particularly in the realm of immunomodulation. This research not only reconfirms the bioactive potential of elderberry extracts but also accentuates the indispensable role of scientific validation in converting traditional and empirical knowledge into viable applications, such as dietary supplement formulation.

Eevia Health plans to leverage these findings in our research and clinical development program, with a focus on crafting scientifically substantiated, bioactive botanical extracts and steering the journey from traditional empirical wisdom to the development of practical applications, including effective dietary supplements with documented health benefits. Future research, guided by these findings, may explore the clinical applications and mechanistic investigations of FENO-SAMBUCUS<sup>TM</sup>, propelling a refined, integrated approach to botanical extract research and application in the health and wellness sector.

**Supplementary Materials:** For additional information on Eevia Health's BioMAP report, please contact the authors.

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**Conflicts of Interest:** François-Karl Brouillette conducted his contributions under a mandate provided by Eevia Health. Stein Ulve and Petri Lackman are employees of Eevia Health Plc., Finland.

## Abbreviations

BioMAP ODN2006	Biological Matrices Analysis Platform Specific oligodeoxynucleotide
CpG-ODN	Cytosine-phosphate-guanine oligodeoxynucleotide
TLR9	Toll-like receptor-9
PRR	Pattern-recognition receptor
sIL-6	Soluble Interleukin-6
MCP-1	Monocyte chemoattractant protein-1
VCAM-1	Vascular cell adhesion molecule-1
MMP-1	Matrix metalloproteinase-1
TF	Tissue Factor
tPA	Tissue Plasminogen Activator
M-CSF	Macrophage Colony-Stimulating Factor
MIG	Monokine Induced by Gamma interferon
IP-10	Interferon Gamma-Induced Protein 10
I-TAC	Interferon-Inducible T-cell Alpha Chemoattractant
IL-8	Interleukin-8
sIL-10	Soluble Interleukin-10
sIL-2	Soluble Interleukin-2
uPAR	Urokinase Plasminogen Activator Receptor

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