gaia HERBS PRO

Protocol for Enhancing and Tapering GLP-1 Receptor Agonist Therapy with Herbal and Dietary Interventions

A Guide for Optimized Patient Care

Featuring an Exclusive Protocol Developed by Dr. Leah Linder, ND

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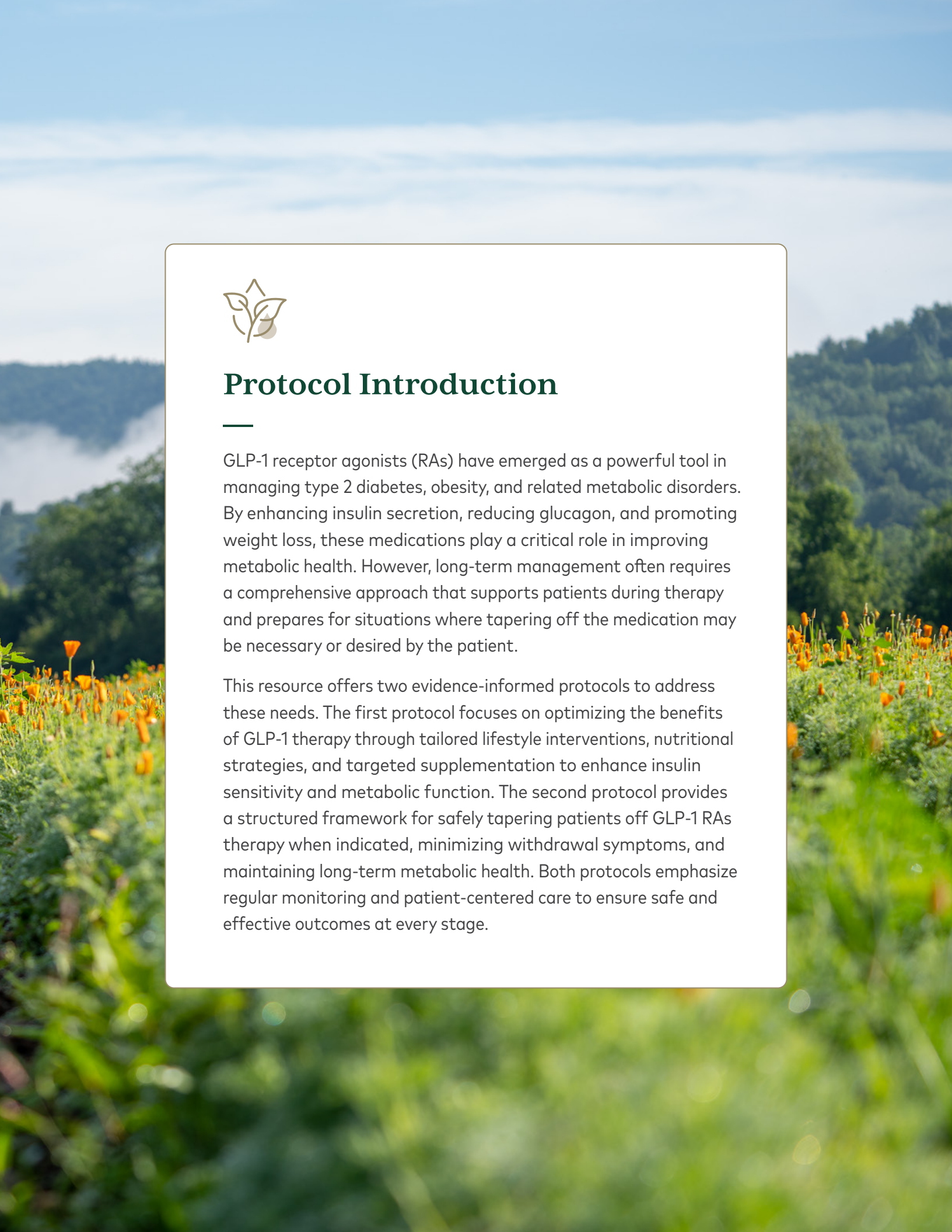


Protocol Introduction

GLP-1 receptor agonists (RAs) have emerged as a powerful tool in managing type 2 diabetes, obesity, and related metabolic disorders. By enhancing insulin secretion, reducing glucagon, and promoting weight loss, these medications play a critical role in improving metabolic health. However, long-term management often requires a comprehensive approach that supports patients during therapy and prepares for situations where tapering off the medication may be necessary or desired by the patient.

This resource offers two evidence-informed protocols to address these needs. The first protocol focuses on optimizing the benefits of GLP-1 therapy through tailored lifestyle interventions, nutritional strategies, and targeted supplementation to enhance insulin sensitivity and metabolic function. The second protocol provides a structured framework for safely tapering patients off GLP-1 RAs therapy when indicated, minimizing withdrawal symptoms, and maintaining long-term metabolic health. Both protocols emphasize regular monitoring and patient-centered care to ensure safe and effective outcomes at every stage.

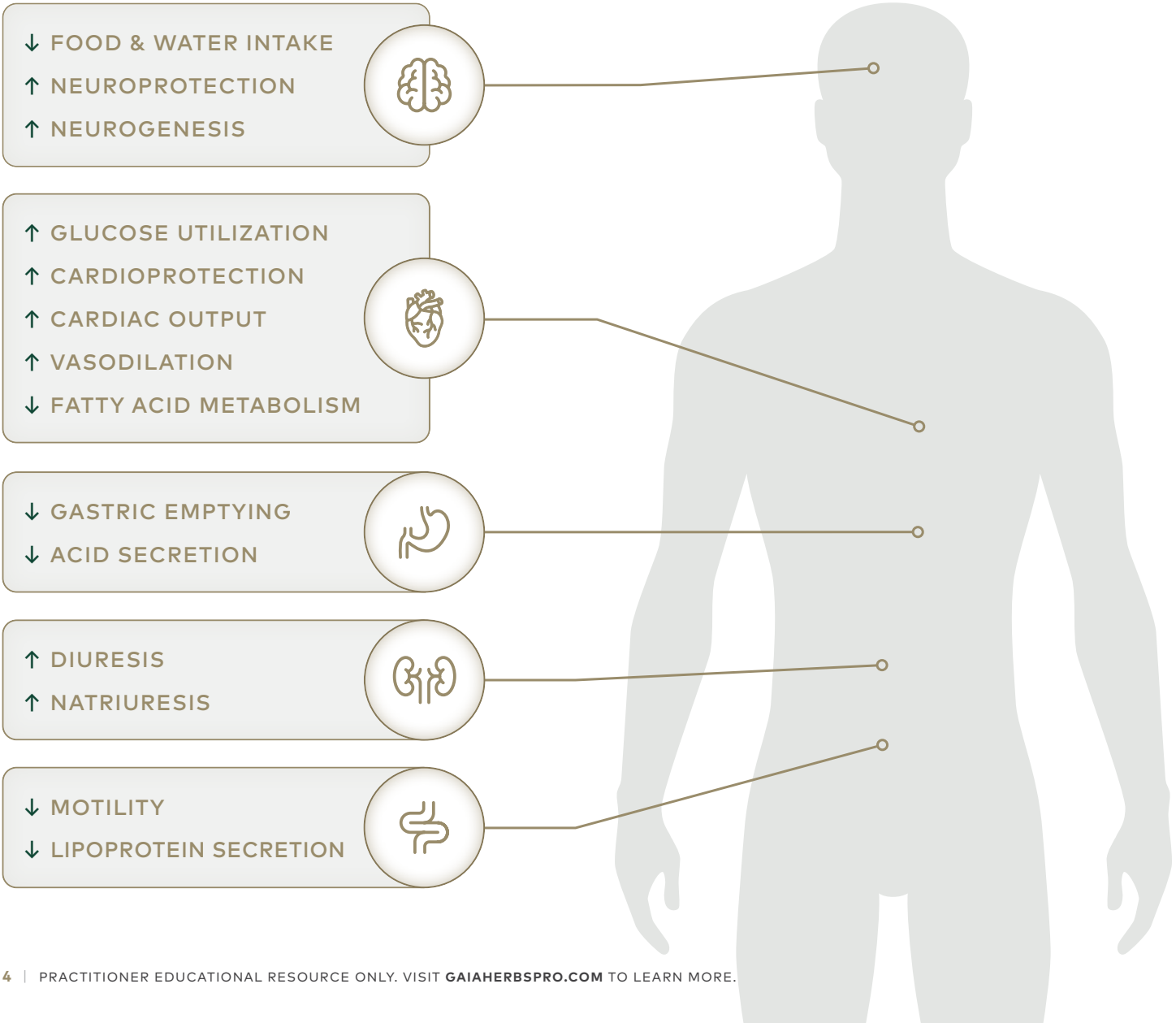
Protocol Overview

Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) are a class of incretin-based therapies that act on multiple physiological pathways to increase insulin secretion and decrease glucagon, thereby controlling glucose levels. They also transiently slow gastric emptying, reduce appetite, and facilitate weight loss along with other metabolic improvements.

Due to these mechanisms, this class of medication has gained wide popularity in treating hyperglycemia in individuals with type 2 diabetes mellitus, as well as a broad spectrum of metabolic disorders, including obesity and cardiovascular disease.

This protocol provides evidence-informed strategies for supporting patients on GLP-1 RAs medications through diet, lifestyle modifications, and targeted herbal supplementation to support healthy insulin sensitivity, blood glucose levels, and balanced metabolic function.*

GLP-1 Effects on the Body



Key Functional Medicine Labs for Managing and Tapering Off GLP-1 RA Medications

Proper monitoring of functional medicine labs is critical not only during GLP-1 RAs therapy but also before and throughout the tapering process. Key markers, including blood glucose levels, insulin sensitivity, lipid panels, inflammatory markers, and liver and kidney function provide essential insights into the patient's metabolic status and organ health. Regular monitoring during GLP-1 RAs therapy ensures that the treatment remains effective and safe, while ongoing assessments during tapering help track progress, address potential imbalances, and minimize the risk of complications. By maintaining a thorough understanding of the patient's functional health at every stage, practitioners can optimize outcomes, adjust treatment strategies as needed, and support long-term metabolic health effectively and safely.

BLOOD GLUCOSE REGULATION AND INSULIN SENSITIVITY

Monitoring glucose and insulin markers is critical for assessing metabolic health, insulin resistance, and glycemic control—particularly relevant for adjusting diet and herbal therapies while on or transitioning from GLP-1 RAs.

- **Fasting Blood Glucose:** Assesses baseline glucose control and detects both hypo- and hyperglycemia risks.
- **Hemoglobin A1c (HbA1c):** Provides a 3-month average of blood glucose levels; track for trend changes, especially during tapering.
- **Fasting Insulin:** Indicates insulin sensitivity and hyperinsulinemia, a key marker for managing tapering as patients may need enhanced insulin sensitivity support.
- **C-Peptide:** Reflects endogenous insulin production and helps differentiate between exogenous insulin needs and pancreatic function.
- **2-Hour Postprandial Glucose** (optional): Offers insight into glucose handling and potential spikes after meals, which GLP-1 agonists often help manage.
- **Advanced Glycation End Products (AGEs) or Glycation Panel** (Optional): If available, AGEs provide insight into long-term glucose exposure and oxidative stress, which is relevant for patients with prolonged hyperglycemia or diabetes.

LIPID PROFILE

GLP 1 RAs provide cardiovascular benefits, thus monitoring lipid levels can help track any changes in lipid metabolism during therapy or tapering.

- **Lipid Panel:** Assesses total cholesterol, LDL, HDL, and triglycerides to monitor cardiovascular risk.
- **Advanced Lipid Panel (Apolipoprotein B, Lipoprotein (a), LDL particle size)(optional):** For patients with higher cardiovascular risk, advanced lipid markers provide detailed insights into particle size and density, which GLP-1 RA therapy can influence.

INFLAMMATORY AND OXIDATIVE STRESS MARKERS

These markers are important for evaluating the body's inflammatory state, which can impact glycemic control and metabolic health, and may fluctuate when patients taper off GLP-1 RAs.

- **High-Sensitivity C-Reactive Protein (hs-CRP):** A marker for systemic inflammation and cardiovascular risk; higher levels are often seen in metabolic syndrome and type 2 diabetes.
- **F2-Isoprostanes:** Reflects oxidative stress levels, useful for assessing the potential oxidative burden that can accompany tapering.
- **Ferritin:** High levels can reflect inflammation, so it's valuable in monitoring systemic inflammation status.

LIVER FUNCTION TESTS

GLP-1 RAs can affect liver enzymes, and liver health is key in glucose and lipid metabolism.

- **ALT, AST, GGT:** Monitors liver enzymes for potential hepatotoxicity, especially in patients with pre-existing liver conditions.
- **Albumin:** Assesses liver function and overall protein status, which may impact metabolic processes.

KIDNEY FUNCTION TESTS

Given the renal excretion of GLP-1 RAs, kidney health is important to monitor for both current users and those tapering off.

- **Creatinine and eGFR (Estimated Glomerular Filtration Rate):** Reflects kidney function and the ability to excrete medications effectively.
- **Blood Urea Nitrogen (BUN):** Assesses kidney health; elevations can indicate altered renal function that may affect medication excretion.

COMPREHENSIVE MICRONUTRIENT PANEL

Nutrient deficiencies can influence glycemic control, inflammation, and energy metabolism. This panel provides a snapshot of essential vitamins and minerals that support glucose metabolism and overall metabolic health.

- **Vitamin D:** Essential for insulin sensitivity; low levels are common in diabetes and metabolic syndrome.
- **Magnesium:** Important for glucose regulation, insulin sensitivity, inflammation regulation, and GI health.
- **B Vitamins (especially B12 and Folate):** Supports mitochondrial function and energy production; deficiencies can impact energy levels and glycemic control.
- **Zinc:** Important for immune health and insulin function, as low levels can contribute to insulin resistance.

GUT HEALTH AND MICROBIOME MARKERS

GLP-1 RAs influence gut motility and hormone balance, so assessing gut health is critical, especially if patients are tapering off.

- **Calprotectin and Secretory IgA:** Markers for intestinal inflammation and immune function; disturbances in these markers can impact glycemic control.
- **Comprehensive Stool Analysis:** To assess microbiome balance, gut inflammation, digestive enzyme levels, and presence of short-chain fatty acids (SCFAs) like butyrate, which are linked to endogenous GLP-1 production.
- **Lactulose-Mannitol Test:** Checks for intestinal permeability, which can exacerbate inflammation and influence glucose regulation.

HORMONE PANEL (OPTIONAL)

Hormonal imbalances can disrupt glucose regulation, impair insulin sensitivity, and hinder weight management. Addressing these imbalances is crucial for optimizing metabolic function and achieving better long-term health outcomes.

- **Comprehensive Thyroid Screening:** Thyroid function plays a critical role in metabolic regulation, and assessing its function ensures that underlying or coexisting thyroid dysfunction is not contributing to treatment challenges or complicating outcomes.
- **Cortisol (Salivary or Urinary Cortisol Panel):** Provides insight into adrenal function and potential stress-related glucose dysregulation.
- **Insulin-like Growth Factor-1 (IGF-1):** Tracks metabolic health, as IGF-1 plays a role in glucose metabolism and may be impacted by GLP-1 RA therapy.

Protocol
Supportive Strategies for Complementing GLP-1 RAs Therapies

MOA OVERVIEW

1 Development of the Need for GLP-1 RAs

- High blood glucose levels due to insulin resistance or type 2 diabetes
- Weight gain or difficulty in weight management

2 Mechanism of GLP-1 RAs

- GLP-1 RAs increase insulin secretion in a glucose-dependent manner
- Inhibit glucagon release, reducing glucose production by the liver
- Slow gastric emptying and promote satiety, aiding in weight loss

3 Effects of GLP-1 RAs on Blood Sugar and Weight

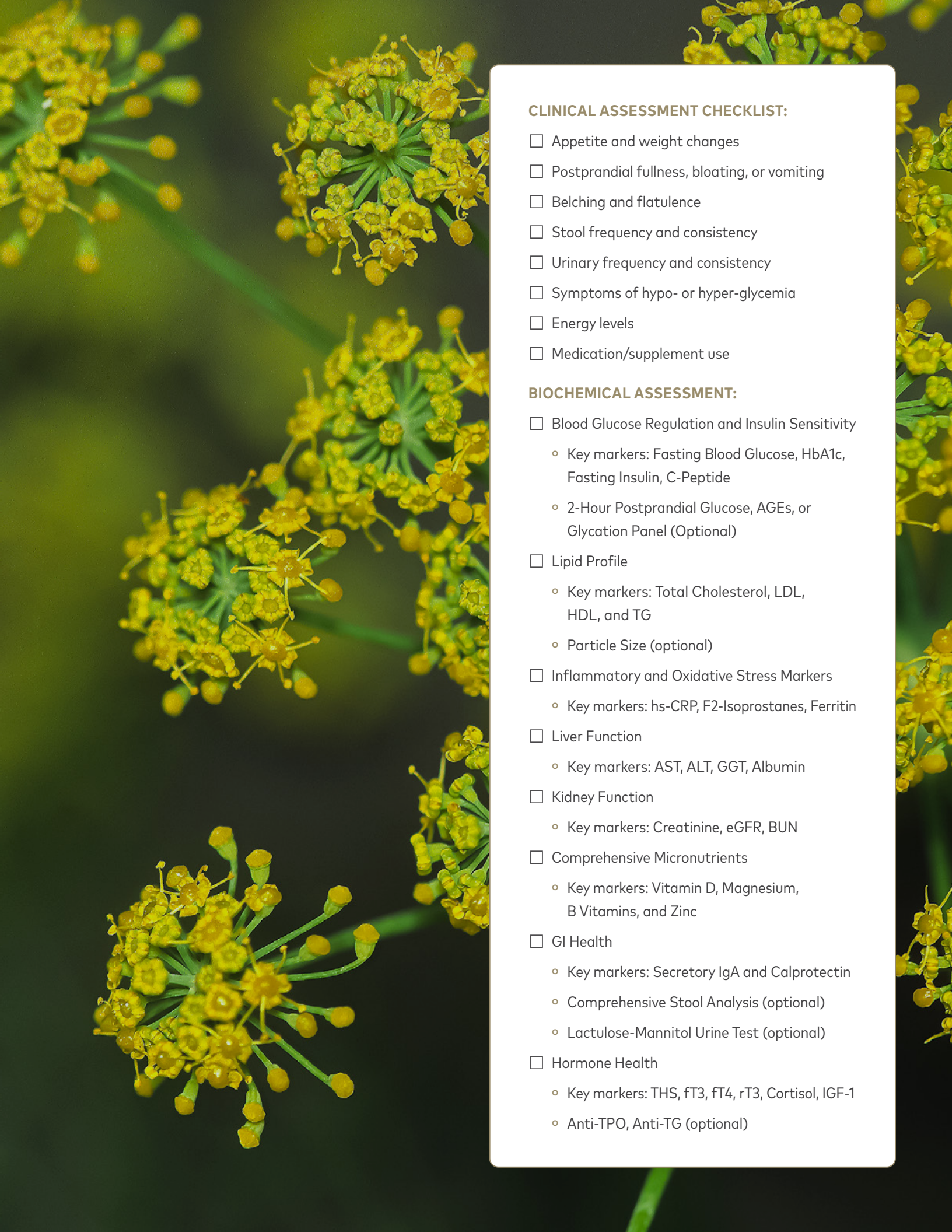
- Lowers postprandial and fasting blood glucose
- Reduces appetite and caloric intake
- Contributes to weight loss and metabolic health

4 Role of Targeted Herbal Supplements

- AMPK Activators: Promote glucose uptake, lipid oxidation, and insulin sensitivity
- GLUT-4 Enhancers: Support glucose uptake into muscle, cardiac, and adipose cells
- Antioxidants: Reduce oxidative stress and inflammation, supporting metabolic health
- Carminatives: Reduce the side effects of GLP-1 RAs and improve patient compliance

5 Enhanced Patient Care and Effectiveness of GLP-1 RAs

- Improved blood glucose control with combined use of GLP-1 RAs and supportive supplements
- Reduced side effects, such as GI symptoms, by managing inflammation and oxidative stress
- Enhanced weight loss and metabolic health outcomes, improving patient adherence



CLINICAL ASSESSMENT CHECKLIST:

- ☐ Appetite and weight changes
- ☐ Postprandial fullness, bloating, or vomiting
- ☐ Belching and flatulence
- ☐ Stool frequency and consistency
- ☐ Urinary frequency and consistency
- ☐ Symptoms of hypo- or hyper-glycemia
- ☐ Energy levels
- ☐ Medication/supplement use

BIOCHEMICAL ASSESSMENT:

- ☐ Blood Glucose Regulation and Insulin Sensitivity
  - Key markers: Fasting Blood Glucose, HbA1c, Fasting Insulin, C-Peptide
  - 2-Hour Postprandial Glucose, AGEs, or Glycation Panel (Optional)
- ☐ Lipid Profile
  - Key markers: Total Cholesterol, LDL, HDL, and TG
  - Particle Size (optional)
- ☐ Inflammatory and Oxidative Stress Markers
  - Key markers: hs-CRP, F2-Isoprostanes, Ferritin
- ☐ Liver Function
  - Key markers: AST, ALT, GGT, Albumin
- ☐ Kidney Function
  - Key markers: Creatinine, eGFR, BUN
- ☐ Comprehensive Micronutrients
  - Key markers: Vitamin D, Magnesium, B Vitamins, and Zinc
- ☐ GI Health
  - Key markers: Secretory IgA and Calprotectin
  - Comprehensive Stool Analysis (optional)
  - Lactulose-Mannitol Urine Test (optional)
- ☐ Hormone Health
  - Key markers: THS, fT3, fT4, rT3, Cortisol, IGF-1
  - Anti-TPO, Anti-TG (optional)

NUTRITIONAL CONSIDERATIONS

- **Macronutrient Balance:** Balanced meals with low-glycemic carbohydrates, lean proteins, and healthy fats stabilize postprandial glucose levels. Additionally, dietary fiber (like leafy greens, oats, and legumes) slow glucose absorption, enhances satiety, and provides valuable fuel to the gut microbiota, which in turn promotes the production of SCFAs which stimulate the endogenous production of GLP-1.
- **Anti-Inflammatory Foods to Enhance GLP-1 Benefits:** Oxidative stress and inflammation can impair GLP-1 function, making it essential to include anti-inflammatory foods in the diet. Nutrient-dense options like berries, dark leafy greens, cruciferous vegetables, and healthy fats from olive oil, nuts, and avocado provide antioxidants, phytonutrients, and fiber. These nutrients support immune function, cellular health, and metabolic balance while reducing inflammation, stabilizing blood sugar levels, and promoting better long-term outcomes for individuals with diabetes or those at risk for metabolic disorders.
- **Reducing Pro-Inflammatory Foods:** Minimizing the intake of refined sugars and processed foods is essential for managing inflammation and promoting overall health. Refined sugars can lead to spikes in blood sugar levels, increasing oxidative stress and triggering pro-inflammatory pathways. Processed foods, often high in trans fats, artificial additives, and refined carbohydrates, further contribute to systemic inflammation by disrupting gut health and suppressing immune function. Chronic inflammation caused by these dietary choices has been linked to insulin resistance, weight gain, cardiovascular disease, and other metabolic disorders. By focusing on whole, nutrient-dense foods and reducing pro-inflammatory options, individuals can support a balanced immune response, enhance metabolic function, and lower the risk of chronic diseases.
- **Micronutrients:** High blood sugar levels and diabetes have been linked to micronutrient deficiencies, including vitamin D, chromium, and magnesium.[4] Focusing on nutrient-dense foods and "eating the rainbow" ensures a diverse intake of essential vitamins and minerals that support glucose metabolism, insulin sensitivity, and overall metabolic health.

LIFESTYLE RECOMMENDATIONS

- **Physical Activity:** Weight Training: Highlight the benefits of weight training, as it helps preserve muscle mass and improves insulin sensitivity, making it an excellent adjunct to GLP-1 RAs medications. Explain that maintaining muscle mass supports metabolic rate, aiding in glycemic control and reinforcing the medication's effects.

  Postprandial Walks: Encourage patients to take short walks after meals, which promotes glucose uptake by the muscles and improves insulin sensitivity. Postprandial walks reduce post-meal blood sugar spikes, complementing the GLP-1 agonist's ability to stabilize blood glucose levels.
- **Mental Well-Being:** Educate patients on the impact of stress on blood glucose levels and encourage stress-reducing practices like meditation, mindfulness, or deep breathing exercises. Stress management helps reduce cortisol, which can otherwise interfere with glucose regulation and counteract some benefits of GLP-1 agonists. Additionally, encourage good sleep habits, as quality sleep improves insulin sensitivity, reduces cravings, and can enhance the overall effectiveness of GLP-1 therapy.
- **Hydration:** Stress the importance of staying well-hydrated, as adequate hydration supports kidney function, helping to excrete any excess glucose. Hydration also improves cellular insulin sensitivity and minimizes blood sugar fluctuations, making it a supportive practice alongside GLP-1 agonist use. Recommend aiming for half of the individual's weight in ounces of fluid per day, with added minerals if necessary, to optimize cellular hydration.

Product Recommendations

AMPK Activator

UPREGULATES ADIPONECTIN, AMPK, AND GLUT4*

This formula combines clinically researched ingredients, including InnoSlim® (*Astragalus membranaceus* and *Panax notoginseng* extracts), Wellemon® whole lemon fruit extract, Japanese knotweed, organic ginger root powder, and bilberry extract, to support healthy metabolic balance and energy production.* Each component works synergistically to enhance AMPK activation, supporting insulin sensitivity, healthy blood sugar metabolism, and mitochondrial function, while promoting antioxidant defenses to combat oxidative stress.*

INGREDIENT	INGREDIENT BREAKDOWN	BACKGROUND MOA
InnoSlim®	***Astragalus membranaceus* and *Panax notoginseng* Root Extracts:** This blend is designed to upregulate adiponectin and activate AMPK, which supports glucose uptake, lipid metabolism, and healthy insulin sensitivity.*	This blend works by upregulating adiponectin, a hormone that activates AMPK, enhancing glucose uptake and lipid oxidation. Activated AMPK promotes GLUT4 translocation to cell membranes, facilitating glucose uptake independently of insulin, supporting healthy blood sugar levels and improving insulin sensitivity.[5]
Wellemon®	**Whole Lemon Fruit Extract:** Rich in bioflavonoids, Wellemon® enhances antioxidant activity and promotes healthy metabolic processes, supporting blood glucose stability.*	Wellemon® provides bioflavonoids, particularly eriocitrin, which enhances antioxidant defenses and supports glucose metabolism. Eriocitrin activates the Nrf2 pathway, enhancing antioxidant enzyme production and reducing oxidative stress in cells, thus supporting metabolic and cardiovascular health.[6]
Japanese Knotweed	***Polygonum cuspidatum* Root Extract with Trans-Resveratrol:** Known for its high resveratrol content, Japanese knotweed activates AMPK and SIRT1, promoting mitochondrial biogenesis, enhancing antioxidant defenses, and supporting cardiovascular health.*	Japanese knotweed, rich in trans-resveratrol, activates AMPK and SIRT1, which are critical for cellular energy regulation and mitochondrial health. This activation supports metabolic balance, reduces oxidative stress, and promotes anti-inflammatory effects by inhibiting pro-inflammatory cytokines, which can aid in glucose and lipid metabolism.[7]
Organic Ginger	***Zingiber officinale* Root Powder:** Ginger promotes antioxidant defenses and supports healthy blood sugar levels through its impact on glucose metabolism.*	Ginger contains gingerols and shogaols, which activate the PI3K/Akt pathway and enhance GLUT4 translocation, supporting glucose uptake and insulin sensitivity.[8] Ginger also activates the Nrf2 pathway, which increases antioxidant defense mechanisms, reducing oxidative stress and supporting healthy blood glucose levels.[9]
Bilberry	***Vaccinium myrtillus* Berry Extract:** Bilberry is a rich source of anthocyanins with antioxidant properties that help reduce oxidative stress and support blood vessel health, complementing the effects of AMPK activation on metabolic health.*	Bilberry contains anthocyanins, which are powerful antioxidants that reduce oxidative stress and inflammation, supporting vascular health. Anthocyanins also enhance insulin sensitivity by modulating inflammatory pathways, complementing AMPK activation's effects on metabolic balance.[10]

AMPK activation and GLP-1 receptor agonists MOA: AMPK (5′ AMP-activated protein kinase) is an enzyme that plays a key role in homeodynamic energy balance throughout the body. AMPK activation and GLP-1 receptor agonists (GLP-1 RAs) both exert substantial metabolic, cardiovascular, and immunoregulatory benefits through distinct yet complementary mechanisms.

Metabolically, AMPK activation enhances glucose uptake via GLUT4 translocation, lowering glucose levels in cells and overall blood glucose concentration.[5] Meanwhile, GLP-1 RAs enhance insulin secretion in a glucose-dependent manner and inhibit glucagon release, modulating blood glucose.[11]

Cardiovascularly, AMPK activation influences energy balance and lipid metabolism by activating pathways such as ACC phosphorylation, leading to reduced fatty acid synthesis, which can lower the risk of atherosclerosis and subsequent heart attack and stroke.[12] GLP-1 RAs act on GLP-1 receptors in the myocardium and endothelial cells, leading to reduced inflammation and oxidative stress and lowering the risk of major cardiovascular events and death.

Immunoregulatory effects from both AMPK activation and GLP-1 RAs foster T regulatory (Treg) cell proliferation, promoting immune tolerance and reducing inflammatory cytokine release through pathways like NF-kB inhibition.[13]

Additionally, AMPK activation brings **additional benefits** by reducing oxidative stress (via Nrf2 upregulation) and mitigating endoplasmic reticulum stress, alongside increasing cellular NAD(+) levels and mitochondrial biogenesis through PGC-1α, and sirtuin 1 (SIRT1) activity.[14] GLP-1 also contributes to improved physical endurance, facilitating skeletal muscle remodeling and metabolic adaptation through pathways such as mTORC1 inhibition and PKA activation.[15] Together, these effects underscore the extensive benefits of AMPK and GLP-1 RA activation across multiple biological pathways and markers, influencing health outcomes on several fronts.

Product Recommendations

Tri-Glycemic

SUPPORTS POSTPRANDIAL GLUCOSE LEVELS*

This formula combines clinically researched ingredients including, BPL-1® heat-treated *Bifidobacterium lactis,* ABAlife® fig fruit extract, bitter melon extract, and organic ginger root extract, to support healthy blood glucose levels and overall metabolic balance.* Each component works to improve glucose metabolism, promote beneficial gut microbiota activity, and enhance cellular resilience, helping to maintain optimal blood sugar and immune health.*

INGREDIENT	INGREDIENT BREAKDOWN	BACKGROUND MOA
Kimchi Postbiotic Extract	Postbiotics from fermented foods like kimchi help support gut microbiota diversity promoting the production of beneficial compounds, including SCFAs, that support healthy immune and metabolic function.*	Kimchi postbiotics contain bioactive compounds produced during fermentation, including short-chain fatty acids (SCFAs) like butyrate, acetate, and propionate, as well as beneficial metabolites. These SCFAs serve as the main source of energy for colonocytes and also play a role in anti-inflammatory activity and glucose regulation. Specifically, SCFAs stimulate the G protein-coupled receptors, GPR41 and GPR43, in the gut, which can enhance the secretion of endogenous GLP-1. Increased GLP-1 promotes insulin secretion, improving postprandial glucose control.[16] Additionally, SCFAs, particularly butyrate, can inhibit the NF-κB pathway, reducing inflammation and oxidative stress, which are key factors in insulin resistance and metabolic disorders.[17]
ABAlife® Fig Fruit Extract	*Ficus carica,* or fig extract, has been studied for its role in supporting healthy blood sugar levels and the endogenous production of GLP-1, which may help maintain glucose balance and support healthy postprandial insulin sensitivity within normal range.*	Fig fruit extract is rich in abscisic acid (ABA), a phytohormone that can enhance glucose uptake and reduce postprandial blood glucose levels by stimulating insulin secretion. ABA binds to the LANCL2 receptor, which activates the PI3K/Akt pathway, leading to the translocation of GLUT4 to the cell membrane. This facilitates glucose uptake in muscle and adipose tissues independently of insulin, which helps reduce blood glucose levels.[18] ABA may also activate PPARγ (Peroxisome proliferator-activated receptor gamma), a nuclear receptor involved in glucose and lipid metabolism, promoting insulin sensitivity and reducing blood glucose levels.[19]
Bitter Melon Extract	*Momordica charantia* Fruit Extract: Known for its traditional use, bitter melon contains compounds that can support healthy glucose levels within normal range.*	Bitter melon contains bioactive compounds, including charantin, vicine, and polypeptide-p, that mimic insulin activity and enhance glucose metabolism. For example, they can activate AMP-activated protein kinase (AMPK), a cellular energy sensor that promotes glucose uptake and fatty acid oxidation. AMPK activation helps reduce blood glucose by enhancing GLUT4 translocation and glucose uptake in muscle cells.[20] Additionally, some compounds in bitter melon inhibit DPP-4 (dipeptidyl peptidase-4), an enzyme that breaks down GLP-1, thus prolonging GLP-1 action. This indirectly supports insulin secretion and reduces postprandial blood sugar spikes.[21]
BPL1®	Heat-treated *Bifidobacterium lactis* (BPL1): This postbiotic strain is researched for its metabolic effects, supporting healthy lipid and glucose metabolism within normal range, and immune health through its influence on supporting healthy GI function.*	Heat-treated BPL1 postbiotic exerts metabolic benefits by influencing the gut microbiota and host metabolism. Although it is non-viable, it still has bioactive properties that impact glucose and lipid metabolism. BPL1 can reinforce the gut barrier, reducing endotoxemia (lipopolysaccharides, or (LPS), entering circulation).[22] Lower LPS levels reduce inflammation, which can improve insulin sensitivity. BPL1 also influences PPARα (peroxisome proliferator-activated receptor alpha), promoting lipid metabolism and reducing inflammation. This receptor activation helps to lower blood glucose and reduce triglycerides, benefiting metabolic health.[23]
Organic Ginger Root Extract	Promotes circulatory warming and alleviates occasional nausea.*	Ginger contains active compounds like gingerols and shogaols, which have antioxidant, anti-inflammatory, and glucose-lowering effects. Ginger's active compounds activate the PI3K/Akt pathway, similar to insulin, promoting the translocation of GLUT4 to the cell membrane in muscle cells, leading to increased glucose uptake and improved blood glucose control.[24] Ginger also activates the Nrf2 (nuclear factor erythroid 2–related factor 2) pathway, which enhances the body's antioxidant defenses. By reducing oxidative stress, Nrf2 activation indirectly supports insulin sensitivity and metabolic resilience.[25] Ginger is also able to reduce levels of pro-inflammatory cytokines like TNF-α and IL-6, which are associated with insulin resistance and chronic inflammation in metabolic disorders.[26]

Product Recommendations

GI-BFF

SUPPORTS OCCASIONAL GAS & BLOATING*

Formulated with a blend of natural ingredients, including Benegut® perilla leaf extract, organic fennel seed, organic cinnamon bark, organic peppermint leaf essential oil, organic chamomile flower extract, and bitter fennel seed extract, this product supports a balanced gut environment and promotes digestive comfort.* Each component is designed to soothe the gastrointestinal tract, reduce occasional bloating, and support a healthy inflammatory response, helping to maintain optimal gut health and comfort.*

INGREDIENT	INGREDIENT BREAKDOWN	BACKGROUND MOA
Benegut®	Perilla leaf extract, rich in polyphenols, is known for its ability to support gastrointestinal health, especially in reducing occasional digestive discomfort, bloating, and gas.*	Perilla leaf extract is rich in polyphenolic compounds like rosmarinic acid, which has anti-inflammatory and antispasmodic effects. Rosmarinic acid can inhibit COX and LOX enzymes, reducing inflammation and providing relief from occasional digestive discomfort.[27] Additionally, it may act on TRPA1 (transient receptor potential ankyrin 1) channels in the gut, promoting smooth muscle relaxation and reducing gas formation.[28]
Organic Fennel Seed	Traditionally used to ease digestion, fennel seed can support smooth muscle relaxation in the gut and reduce occasional gas, helping to maintain digestive comfort.*	Fennel contains anethole, a bioactive compound that supports gut motility and reduces muscle spasms by modulating calcium channels in smooth muscle cells.[29] Anethole also has mild antimicrobial properties that can help maintain a balanced gut microbiota and alleviate occasional digestive issues.[30]
Organic Cinnamon Bark	Known for its antioxidant and anti-inflammatory properties, cinnamon bark can help support a healthy inflammatory response in the gastrointestinal tract and promote digestive wellness.*	Cinnamon contains cinnamaldehyde, which has antioxidant and anti-inflammatory properties. Cinnamaldehyde activates the Nrf2 pathway, enhancing antioxidant defenses and reducing oxidative stress in the gut. It also inhibits inflammatory markers, supporting a healthy gut environment and helping to relieve occasional digestive discomfort.[31]
Organic Peppermint Leaf Essential Oil	Peppermint essential oil provides soothing effects on the digestive tract, relieving occasional indigestion, and supporting smooth muscle relaxation in the intestines.*	Peppermint oil contains menthol, which has antispasmodic effects by acting on calcium channels to relax the smooth muscles of the gastrointestinal tract. Menthol's effect on TRPM8 (transient receptor potential melastatin 8) receptors provides a cooling sensation, which can help soothe occasional indigestion and reduce feelings of discomfort.[32]
Organic Chamomile Flower Extract	Chamomile has calming properties and may help reduce occasional digestive discomfort and support relaxation in the gastrointestinal system.*	Chamomile contains apigenin and bisabolol, compounds known for their calming and anti-inflammatory properties. These compounds act on GABA receptors, supporting relaxation, and may reduce occasional digestive discomfort by decreasing inflammation and promoting smooth muscle relaxation in the gut.[33, 34]

FOR ADDITIONAL SUPPORT (OPTIONAL)

Microbiome Cleanse is an excellent add-on for individuals on GLP-1 RAs, as it supports a balanced gut microbiome essential for optimal metabolic health. This formula combines antimicrobial and anti-inflammatory botanicals like blackwalnut, oregano, and cinnamon bark to help manage harmful bacteria and reduce gut inflammation, and peppermint oil to soothe digestion, enhancing gut comfort and nutrient absorption. Together, these ingredients help maintain a healthy gut environment, potentially boosting the effectiveness of GLP-1 RAs in supporting blood glucose regulation and overall metabolic health.

Magnesium Glycinate 400 mg is a beneficial addition for those on GLP-1 RAs medications, as it supports metabolic health, muscle relaxation, and overall well-being. Magnesium plays a key role in blood glucose regulation, insulin sensitivity, and energy production, complementing the effects of GLP-1 RAs. The glycinate form is highly bioavailable and gentle on the digestive system, making it ideal for maintaining adequate magnesium levels without causing gastrointestinal discomfort. This addition helps promote stable blood sugar, reduces muscle cramps, and supports restful sleep, all of which can enhance the overall effectiveness of a GLP-1 RA health protocol.

Product Protcol

DURATION:

Supplement one product at a time after the patient has been on GLP-1 RAs medications for at least one month. Supplements are added in - one product per week to monitor tolerance- in order of health concern(s):

GI-BFF - Supports those with occasional gas, bloating, and nausea. (i.e., the common side effects of GLP-1 RAs medication)*

AMPK Activator - Metabolism, energy, and antioxidant support*

Tri-Glycemic - Blood sugar support*

Note: Be sure to monitor blood sugar levels regularly, especially when combining with additional anti-diabetic medications.

PRODUCT	MORNING	MIDDAY	EVENING
AMPK Activator (1 cap, with food)	●	●	
Tri-Glycemic (1 cap, with food)	●		
GI-BFF (1 cap 10-15 minutes before meals)	●	●	●

Protocol
Supportive Strategies for GLP-1 Tapering

MOA OVERVIEW

1 Need for Tapering Off GLP-1 Agonists

- Manage Side Effects: Tapering can reduce intolerable side effects like nausea or abdominal discomfort.
- Met Treatment Goals: Gradual discontinuation may follow successful weight loss or glycemic control.
- Cost/Access Issues: High cost, limited access, or desire to decrease dependence on pharmacotherapy might necessitate switching to alternative therapies.

2 Impact of Reduced GLP-1 RAs Activity on the Body

- Challenges with weight management during tapering
- Decreased support for insulin secretion and glucose-dependent insulin modulation
- Reduced appetite regulation and potential for increased food intake
- Faster gastric emptying, which may lead to blood sugar spikes and cravings

3 Potential Challenges During Tapering

- Risk of elevated blood glucose levels without GLP-1 RAs support
- Possible weight gain due to reduced appetite regulation
- Increased susceptibility to blood glucose variability and metabolic fluctuations

4 Role of Targeted Herbal Supplements to Support Tapering

- AMPK Activators (e.g., astragalus, ginseng): Help maintain glucose uptake and lipid oxidation, supporting blood sugar stability and energy balance
- GLP-1 Secretagogues: Act as natural stimulators of GLP-1 secretion, improving glucose balance and appetite regulation as GLP-1 RAs levels are reduced
- Antioxidants: Combat oxidative stress and inflammation, helping to stabilize metabolic health and ease tapering-related side effects

5 Enhanced Support for Patient Care During Tapering

- Improved blood glucose control with adjunctive herbal supplements, supporting smooth glucose transitions off GLP-1 RAs
- Reduction of tapering side effects, such as blood sugar fluctuations and GI discomfort, by managing oxidative stress and inflammation
- Support for weight management and metabolic health, promoting sustainable lifestyle habits and enhancing patient adherence through the tapering process

OVERVIEW OF TOPIC

Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) are a class of incretin-based therapies widely used for their ability to enhance insulin secretion, inhibit glucagon release, slow gastric emptying, reduce appetite, and support weight loss. These mechanisms have made GLP-1 RAs popular for managing hyperglycemia in individuals with type 2 diabetes, as well as for addressing a range of metabolic conditions, including obesity and cardiovascular disease. However, there may be instances where patients wish to discontinue GLP-1 RAs, either due to personal choice, desire to reduce dependence on pharmacotherapy, side effects, or a desire to transition to lifestyle-based or alternative management approaches.

This protocol provides evidence-informed strategies for supporting patients who are tapering off GLP-1 RAs medications. It outlines a comprehensive evidence-informed approach that combines diet, lifestyle modifications, and targeted herbal supplementation to maintain insulin sensitivity, regulate blood glucose levels, and promote balanced metabolic function. By incorporating interventions that support endogenous GLP-1 secretion, decrease inflammatory markers, and enhance gut health, this protocol aims to facilitate a smoother transition off GLP-1 RAs while helping patients maintain metabolic stability and overall health.

CLINICAL ASSESSMENT CHECKLIST:

- ☐ Appetite and weight changes
- ☐ Postprandial fullness, bloating, or vomiting
- ☐ Belching and flatulence
- ☐ Stool frequency and consistency
- ☐ Urinary frequency and consistency
- ☐ Symptoms of hypo- or hyper-glycemia
- ☐ Energy levels or fatigue
- ☐ Medication/supplement use

BIOCHEMICAL ASSESSMENT:

- ☐ Blood Glucose Regulation and Insulin Sensitivity
  - Key markers: Fasting Blood Glucose, HbA1c, Fasting Insulin, C-Peptide
  - 2-Hour Postprandial Glucose, AGEs, or Glycation Panel (optional)
- ☐ Lipid Profile
  - Key markers: Total Cholesterol, LDL, HDL, and TG
  - Particle Size (optional)
- ☐ Inflammatory and Oxidative Stress Markers
  - Key markers: hs-CRP, F2-Isoprostanes, Ferritin
- ☐ Liver Function
  - Key markers: AST, ALT, GGT, Albumin
- ☐ Kidney Function
  - Key markers: Creatinine, eGFR, BUN
- ☐ Comprehensive Micronutrients
  - Key markers: Vitamin D, Magnesium, B Vitamins, and Zinc
- ☐ GI Health
  - Key markers: Secretory IgA and Calprotectin
  - Comprehensive Stool Analysis (optional)
  - Lactulose-Mannitol Urine Test (optional)
- ☐ Thyroid Function
  - Key markers: THS, fT3, fT4, rT3
  - Anti-TPO, Anti-TG (optional)

NUTRITIONAL CONSIDERATIONS

- **Macronutrient Balance:** Encourage patients to continue focusing on balanced meals that include low-glycemic carbohydrates, lean proteins, and healthy fats. As the appetite-regulating effects of GLP-1 RAs decrease, advise patients to prioritize high-fiber foods such as leafy greens, oats, and legumes. These can help manage satiety and slow glucose absorption, supporting more stable blood glucose levels. Explain that dietary fiber fuels the gut microbiota, promoting short-chain fatty acid (SCFA) production, which may help stimulate endogenous GLP-1 secretion to support appetite regulation naturally.
- **Anti-Inflammatory Foods to Support Metabolic Health:** As patients taper off GLP-1 RAs, they may benefit from incorporating foods rich in antioxidants to combat oxidative stress and inflammation. Recommend options like berries, dark leafy greens, and cruciferous vegetables. Healthy fats, such as those from olive oil, nuts, and avocado, also support cellular health and provide sustained energy, which is helpful for adapting to potential changes in hunger and blood glucose regulation.
- **Reducing Pro-Inflammatory Foods:** Advise patients to minimize refined sugars and processed foods, as these can contribute to blood glucose fluctuations and increase inflammation. Educate them on how a stable, anti-inflammatory diet may reduce the risk of blood sugar spikes during the tapering process.
- **Micronutrient Support:** Highlight the importance of certain micronutrients, including vitamin D, chromium, and magnesium, which play key roles in insulin sensitivity and glucose metabolism. Encourage patients to consume foods rich in these nutrients, such as leafy greens, nuts, seeds, and fortified options, and consider recommending supplements if appropriate. Reinforce that sufficient micronutrient levels can support metabolic stability as their body adjusts to lower GLP-1 RAs levels.

LIFESTYLE RECOMMENDATIONS

- **Physical Activity:** Encourage patients to continue or initiate weight training exercises, as preserving muscle mass helps maintain metabolic rate and improves glucose regulation. Explain that weight training also enhances insulin sensitivity and reduces visceral fat, which supports glycemic control—especially valuable when GLP-1 RAs support is decreasing. In addition, brief, gentle walks after meals to assist with glucose uptake into the muscles and reduce post-meal blood sugar spikes, enhance insulin sensitivity, and aid digestion, which can be especially helpful as the body adapts to the absence of GLP-1 RAs effects.
- **Mental Well-Being:** Guide patients in implementing stress management techniques, such as mindfulness practices, deep breathing exercises, or meditation, to help regulate cortisol levels and prevent cortisol-related blood sugar spikes. Highlight the importance of prioritizing sleep hygiene, as quality sleep can improve insulin sensitivity, reduce cravings, and support a smoother transition off GLP-1 RAs.
- **Hydration:** Emphasize the importance of staying hydrated, particularly as hydration supports kidney function in flushing excess glucose and aids in maintaining stable blood sugar levels. Encourage patients to aim for half their body weight in ounces of water daily and add electrolytes if necessary. Proper hydration can also enhance cellular insulin sensitivity and reduce blood sugar fluctuations, supporting their overall metabolic health during the taper.

Product Recommendations

AMPK Activator

UPREGULATES ADIPONECTIN, AMPK, AND GLUT4*

This formula combines clinically researched ingredients, including InnoSlim® (*Astragalus membranaceus* and *Panax notoginseng* extracts), Wellemon® whole lemon fruit extract, Japanese knotweed, organic ginger root powder, and bilberry extract, to support healthy metabolic balance and energy production.* Each component works synergistically to enhance AMPK activation, supporting insulin sensitivity, healthy blood sugar metabolism, and mitochondrial function, while promoting antioxidant defenses to combat oxidative stress.*

INGREDIENT	INGREDIENT BREAKDOWN	BACKGROUND MOA
InnoSlim®	***Astragalus membranaceus* and *Panax notoginseng* Root Extracts:** This blend is designed to upregulate adiponectin and activate AMPK, which supports glucose uptake, lipid metabolism, and healthy insulin sensitivity.*	This blend works by upregulating adiponectin, a hormone that activates AMPK, enhancing glucose uptake and lipid oxidation. Activated AMPK promotes GLUT4 translocation to cell membranes, facilitating glucose uptake independently of insulin, supporting healthy blood sugar levels and improving insulin sensitivity.[5]
Wellemon®	**Whole Lemon Fruit Extract:** Rich in bioflavonoids, Wellemon® enhances antioxidant activity and promotes healthy metabolic processes, supporting blood glucose stability.*	Wellemon® provides bioflavonoids, particularly eriocitrin, which enhances antioxidant defenses and supports glucose metabolism. Eriocitrin activates the Nrf2 pathway, enhancing antioxidant enzyme production and reducing oxidative stress in cells, thus supporting metabolic and cardiovascular health.[6]
Japanese Knotweed	***Polygonum cuspidatum* Root Extract with Trans-Resveratrol:** Known for its high resveratrol content, Japanese knotweed activates AMPK and SIRT1, promoting mitochondrial biogenesis, enhancing antioxidant defenses, and supporting cardiovascular health.*	Japanese knotweed, rich in trans-resveratrol, activates AMPK and SIRT1, which are critical for cellular energy regulation and mitochondrial health. This activation supports metabolic balance, reduces oxidative stress, and promotes anti-inflammatory effects by inhibiting pro-inflammatory cytokines, which can aid in glucose and lipid metabolism.[7]
Organic Ginger	***Zingiber officinale* Root Powder:** Ginger promotes antioxidant defenses and supports healthy blood sugar levels through its impact on glucose metabolism.*	Ginger contains gingerols and shogaols, which activate the PI3K/Akt pathway and enhance GLUT4 translocation, supporting glucose uptake and insulin sensitivity.[8] Ginger also activates the Nrf2 pathway, which increases antioxidant defense mechanisms, reducing oxidative stress and supporting healthy blood glucose levels.[9]
Bilberry	***Vaccinium myrtillus* Berry Extract:** Bilberry is a rich source of anthocyanins with antioxidant properties that help reduce oxidative stress and support blood vessel health, complementing the effects of AMPK activation on metabolic health	Bilberry contains anthocyanins, which are powerful antioxidants that reduce oxidative stress and inflammation, supporting vascular health. Anthocyanins also enhance insulin sensitivity by modulating inflammatory pathways, complementing AMPK activation's effects on metabolic balance.[10]

AMPK activation and GLP-1 receptor agonists MOA: Activating AMPK could provide a supportive metabolic and cardiovascular foundation for individuals tapering off GLP-1 medications.

Metabolically, as GLP-1 RAs are tapered, AMPK activation can help maintain glucose balance by enhancing GLUT4 translocation, which supports glucose uptake and stabilizes blood glucose levels. This mechanism may help counteract potential blood glucose increases as the insulin-modulating effects of GLP-1 RAs decrease.[5]

Cardiovascularly, AMPK's activation of ACC phosphorylation can limit fatty acid synthesis, reducing atherosclerotic risk and potentially mitigating any cardiovascular effects as the heart-protective benefits of GLP-1 RAs taper.[12]

Immunoregulatory, AMPK activation supports T regulatory (Treg) cell proliferation, which may balance inflammation and support immune health, potentially complementing the immunoregulatory properties of GLP-1 RAs.[13]

Moreover, **AMPK offers additional cellular benefits** that may aid in this transition, such as reducing oxidative stress via Nrf2 upregulation, alleviating endoplasmic reticulum stress, and enhancing mitochondrial function through PGC-1α, sirtuin 1 (SIRT1) activity, and increased NAD(+) levels.[14] Together, these effects offer a potentially beneficial foundation for individuals tapering off GLP-1 RAs therapies.

Product Recommendations

Quercetin Synergy 500

MAST CELL SUPPORT*

Formulated with a synergistic blend of quercetin, vitamin C, manganese, bromelain, turmeric, and citrus bioflavonoids, this product supports a balanced inflammatory response, promotes antioxidant defenses, and enhances glucose metabolism.* Quercetin Synergy is designed to assist individuals tapering off GLP-1 RAs medications by naturally supporting GLP-1 secretion, insulin sensitivity, and blood glucose stability.*

INGREDIENT	INGREDIENT BREAKDOWN	BACKGROUND MOA
Quercetin	A powerful flavonoid with anti-inflammatory and antioxidant properties, quercetin supports endogenous GLP-1 secretion, improves glucose utilization, and inhibits DPP-IV enzyme activity, helping to maintain balanced blood sugar levels.*	Quercetin has been shown to directly stimulate endogenous GLP-1 secretion by increasing glucose utilization in GLP-1-secreting cells, leading to higher ATP levels, KATP channel blockade, and GLP-1 exocytosis.[35] Quercetin also inhibits enzymes like DPP-IV, which prolongs the action of GLP-1, supporting steady insulin release and glucose control during the tapering period.[36] Additionally, quercetin reduces pro-inflammatory cytokines (e.g., IL-1β, IL-6, TNF-α), promoting a healthier inflammatory profile.[37]
Vitamin C	Known for its immune-supporting and antioxidant effects, vitamin C enhances quercetin absorption and combats oxidative stress, supporting metabolic health and glucose balance.*	Vitamin C supports antioxidant defenses and reduces oxidative stress, which may become more pronounced during the transition off GLP-1 RAs.[38] It also enhances quercetin's bioavailability, increasing its effectiveness in metabolic regulation.[39]
Manganese	An essential trace mineral, manganese supports antioxidant defenses and plays a role in glucose metabolism and energy production, complementing the metabolic benefits of quercetin.*	Manganese is a cofactor for enzymes like manganese-superoxide dismutase (MnSOD), which helps protect cells from oxidative damage while supporting key metabolic processes such as glucose conversion and insulin signaling.[40] Additionally, manganese may stimulate the secretion of GLP-1 by influencing enzymes involved in GLP-1 production (e.g., glucose-6-phosphate dehydrogenase (G6PD)), modulating ion channels, and supporting mitochondrial function in gut cells, ensuring that cells have the necessary energy to produce and secrete GLP-1, especially after meals.[41]
Bromelain	An enzyme derived from pineapple, bromelain aids in the absorption of quercetin and provides additional anti-inflammatory support, helping to manage inflammation during the tapering process.*	Bromelain facilitates quercetin absorption and offers additional anti-inflammatory support, helping to manage symptoms like bloating or GI discomfort that may arise as GLP-1 RAs are tapered.[42]
Turmeric (Curcumin)	Rich in curcuminoids, turmeric has potent anti-inflammatory and antioxidant effects, supporting a healthy inflammatory response and metabolic stability.*	Curcumin in turmeric activates the Nrf2 pathway, enhancing antioxidant defenses and reducing oxidative damage, supporting cellular health during metabolic transitions. Curcumin also inhibits pro-inflammatory markers, promoting stable metabolic health.[43]
Citrus Bioflavonoids	Derived from citrus fruits, bioflavonoids have antioxidant and anti-inflammatory effects, enhancing overall cellular resilience and metabolic health.*	Citrus bioflavonoids reinforce antioxidant activity and enhance vascular health, supporting glucose control and reducing inflammation, which can assist in stabilizing blood glucose levels as patients taper off GLP-1 RAs medications.[44]

Product Recommendations

Ginger – Turmeric Postbiotic

FROM WHOLE GINGER AND TURMERIC ROOT, FERMENTED WITH CABBAGE

This formula features a potent blend of organic turmeric, ginger, and sauerkraut juice concentrate extract, providing 3 billion postbiotic cells per serving, which is equivalent to the amount of cells found in a 28 g serving of sauerkraut. Designed to support gut health, reduce inflammation, and promote digestive wellness, Ginger-Turmeric Postbiotic offers a natural approach to maintaining a balanced gut microbiome and supporting immune function.*

INGREDIENT	INGREDIENT BREAKDOWN	BACKGROUND MOA
Fermented Extract: Organic Green Cabbage, Organic Carrots, Organic Onions, Organic Ginger, Organic Jalapenos, Organic Turmeric, Organic Cumin Seed, Sea Salt, wild-type lactic acid bacteria from spontaneous fermentation	Turmeric is known for its powerful anti-inflammatory and antioxidant properties, which support a healthy inflammatory response and aid in digestive comfort.*	Turmeric contains curcuminoids, which activate the Nrf2 pathway, enhancing antioxidant defenses and reducing oxidative stress. This action helps modulate the body's inflammatory response, supporting gut health and overall cellular resilience.*
	Ginger promotes digestive health by supporting smooth muscle relaxation in the gastrointestinal tract and providing relief from occasional indigestion	Ginger's active compounds, such as gingerols and shogaols, have anti-inflammatory and digestive benefits. They support smooth muscle relaxation in the gastrointestinal tract, reducing symptoms of bloating and discomfort while promoting a balanced digestive process.[45]
	Fermented sauerkraut juice is rich in postbiotic compounds and beneficial metabolites that support gut microbiota balance, enhancing overall digestive health and immune support.*	Postbiotics from fermented sauerkraut juice provide short-chain fatty acids (SCFAs) and other metabolites that support a balanced gut microbiome. SCFAs, such as butyrate, promote gut health by nourishing colonocytes, reducing inflammation, and enhancing immune function.[46]

FOR ADDITIONAL SUPPORT (OPTIONAL)

Tri-Glycemic - This formula combines clinically researched ingredients including, BPL-1® heat-treated *Bifidobacterium lactis,* ABAlife® fig fruit extract, bitter melon extract, and organic ginger root extract, to support healthy blood glucose levels and overall metabolic balance.* Each component works to improve glucose metabolism, promote beneficial gut microbiota activity, and enhance cellular resilience, helping to maintain optimal blood sugar and immune health.*

Product Protcol

DURATION:

Supplementation is recommended for at least 3 months while tapering off of GLP-1 RAs medication, though they can be continued for a longer duration depending on diet and lifestyle factors, as well as health goals.

AMPK Activator - Metabolism, energy, and antioxidant support*

Quercetin Synergy 500 - Supports a healthy inflammatory response and promotes metabolic balance*

Ginger-Turmeric Postbiotic - Promotes a healthy gut and healthy inflammatory response.*

PRODUCT	MORNING	MIDDAY	EVENING
AMPK Activator (1-2 cap(s) with food)	●	●	
Quercetin Synergy 500 (1 cap, with food)	●		
Ginger-Turmeric Postbiotic (2 caps with food)			●

References

[1] *Drucker DJ, Nauck MA. The incretin system: glucagon-like peptide-1 receptor agonists and dipeptidyl peptidase-4 inhibitors in type 2 diabetes. Lancet. 2006;368(9548):1696-1705. doi:10.1016/S0140-6736(06)69705-5*

[2] *Nauck M. Incretin therapies: highlighting common features and differences in the modes of action of glucagon-like peptide-1 receptor agonists and dipeptidyl peptidase-4 inhibitors. Diabetes Obes Metab. 2016;18(3):203-216. doi:10.1111/dom.12591*

[3] *Dailey MJ, Moran TH. Glucagon-like peptide 1 and appetite. Trends Endocrinol Metab. 2013;24(2):85-91. doi:10.1016/j.tem.2012.11.008*

[4] *Mehri A. Trace Elements in Human Nutrition (II) - An Update. Int J Prev Med. 2020;11:2. Published 2020 Jan 3. doi:10.4103/ijpvm.IJPVM_48_19*

[5] *Zhang BB, Zhou G, Li C. AMPK: an emerging drug target for diabetes and the metabolic syndrome. Cell Metab. 2009;9(5):407-416. doi:10.1016/j.cmet.2009.03.012*

[6] *Yao L, Liu W, Bashir M, Nisar MF, Wan CC. Eriocitrin: A review of pharmacological effects. Biomed Pharmacother. 2022;154:113563. doi:10.1016/j.biopha.2022.113563*

[7] *Theodotou M, Fokianos K, Moniatis D, et al. Effect of resveratrol on non-alcoholic fatty liver disease. Exp Ther Med. 2019;18(1):559-565. doi:10.3892/etm.2019.7607*

[8] *Tajik Kord M, Pourrajab F, Hekmatimoghaddam S. Ginger Extract Increases GLUT-4 Expression Preferentially Through AMPK Than PI3K Signalling Pathways in C2C12 Muscle Cells. Diabetes Metab Syndr Obes. 2020;13:3231-3238. Published 2020 Sep 15. doi:10.2147/DMSO.S260224*

[9] *Hong MK, Hu LL, Zhang YX, et al. 6-Gingerol ameliorates sepsis-induced liver injury through the Nrf2 pathway. Int Immunopharmacol. 2020;80:106196. doi:10.1016/j.intimp.2020.106196*

[10] *Belwal T, Nabavi SF, Nabavi SM, Habtemariam S. Dietary Anthocyanins and Insulin Resistance: When Food Becomes a Medicine. Nutrients. 2017;9(10):1111. Published 2017 Oct 12. doi:10.3390/nu9101111*

[11] *McCoy RG, Herrin J, Swarna KS, et al. Effectiveness of glucose-lowering medications on cardiovascular outcomes in patients with type 2 diabetes at moderate cardiovascular risk. Nat Cardiovasc Res. 2024;3(4):431-440. doi:10.1038/s44161-024-00453-9*

[12] *McCarty MF. AMPK activation--protean potential for boosting healthspan. Age (Dordr). 2014;36(2):641-663. doi:10.1007/s11357-013-9595-y*

[13] *Mazzieri A, Basta G, Calafiore R, Luca G. GLP-1 RAs and SGLT2i: two antidiabetic agents associated with immune and inflammation modulatory properties through the common AMPK pathway. Front Immunol. 2023;14:1163288. Published 2023 Nov 20. doi:10.3389/fimmu.2023.1163288*

[14] *Salminen A, Kaarniranta K. AMP-activated protein kinase (AMPK) controls the aging process via an integrated signaling network. Ageing Res Rev. 2012;11(2):230-241. doi:10.1016/j.arr.2011.12.005*

[15] *Wu L, Zhou M, Li T, et al. GLP-1 regulates exercise endurance and skeletal muscle remodeling via GLP-1R/AMPK pathway. Biochim Biophys Acta Mol Cell Res. 2022;1869(9):119300. doi:10.1016/j.bbamcr.2022.119300*

[16] *Kimura I, Ichimura A, Ohue-Kitano R, Igarashi M. Free Fatty Acid Receptors in Health and Disease. Physiol Rev. 2020;100(1):171-210. doi:10.1152/physrev.00041.2018*

[17] *Yin L, Laevsky G, Giardina C. Butyrate suppression of colonocyte NF-kappa B activation and cellular proteasome activity. J Biol Chem. 2001;276(48):44641-44646. doi:10.1074/jbc.M105170200*

[18] *Derosa G, Maffioli P, D'Angelo A, Preti PS, Tenore G, Novellino E. Abscisic Acid Treatment in Patients with Prediabetes. Nutrients. 2020;12(10):2931. Published 2020 Sep 24. doi:10.3390/nu12102931*

[19] *Guri AJ, Hontecillas R, Bassaganya-Riera J. Abscisic acid synergizes with rosiglitazone to improve glucose tolerance and down-modulate macrophage accumulation in adipose tissue: possible action of the cAMP/PKA/PPAR γ axis. Clin Nutr. 2010;29(5):646-653. doi:10.1016/j.clnu.2010.02.003*

[20] *Iseli TJ, Turner N, Zeng XY, et al. Activation of AMPK by bitter melon triterpenoids involves CaMKKγ. PLoS One. 2013;8(4):e62309. Published 2013 Apr 25. doi:10.1371/journal.pone.0062309*

[21] *Elekofehinti OO, Ariyo EO, Akinjiyan MO, et al. Potential use of bitter melon (Momordica charantia) derived compounds as antidiabetics: In silico and in vivo studies. Pathophysiology. 2018;25(4):327-333. doi:10.1016/j.pathophys.2018.05.003*

[22] *Balaguer F, Enrique M, Llopis S, et al. Lipoteichoic acid from Bifidobacterium animalis subsp. lactis BPL1: a novel postbiotic that reduces fat deposition via IGF-1 pathway. Microb Biotechnol. 2022;15(3):805-816. doi:10.1111/1751-7915.13769*

[23] *Fang H, Rodrigues E-Lacerda R, Barra NG, et al. Postbiotic impact on host metabolism and immunity provides therapeutic potential in metabolic disease. Endocr Rev. Published online September 5, 2024. doi:10.1210/endrev/bnae025*

[24] *Stadlbauer V, Haselgrübler R, Lanzerstorfer P, et al. Biomolecular Characterization of Putative Antidiabetic Herbal Extracts. PLoS One. 2016;11(1):e0148109. Published 2016 Jan 28. doi:10.1371/journal.pone.0148109*

[25] *Peng S, Yao J, Liu Y, Duan D, Zhang X, Fang J. Activation of Nrf2 target enzymes conferring protection against oxidative stress in PC12 cells by ginger principal constituent 6-shogaol. Food Funct. 2015;6(8):2813-2823. doi:10.1039/c5fo00214a*

References Continued

[26] *Velayati A, Vafa MR, Sani'ee N, Darabi Z. Therapeutic effects and mechanisms of action of ginger and its bioactive components on inflammatory response, oxidative stress, the immune system, and organ failure in sepsis: a comprehensive systematic review. Nutr Rev. 2024;82(12):1800-1819. doi:10.1093/nutrit/nuad156*

[27] *Gamaro GD, Suyenaga E, Borsoi M, Lermen J, Pereira P, Ardenghi P. Effect of rosmarinic and caffeic acids on inflammatory and nociception process in rats. ISRN Pharmacol. 2011;2011:451682. doi:10.5402/2011/451682*

[28] *Bassoli A, Borgonovo G, Morini G, De Petrocellis L, Schiano Moriello A, Di Marzo V. Analogues of perillaketone as highly potent agonists of TRPA1 channel. Food Chem. 2013;141(3):2044-2051. doi:10.1016/j.foodchem.2013.05.063*

[29] *Kooti W, Moradi M, Ali-Akbari S, Sharafi-Ahvazi N, Asadi-Samani M, Ashtary-Larky D. Therapeutic and pharmacological potential of Foeniculum vulgare Mill: a review. J Herbmed Pharmacol. 2015;4(1):1-9.*

[30] *Khan RU, Fatima A, Naz S, Ragni M, Tarricone S, Tufarelli V. Perspective, Opportunities and Challenges in Using Fennel (Foeniculum vulgare) in Poultry Health and Production as an Eco-Friendly Alternative to Antibiotics: A Review. Antibiotics (Basel). 2022;11(2):278. Published 2022 Feb 20. doi:10.3390/antibiotics11020278*

[31] *Kim NY, Trinh NT, Ahn SG, Kim SA. Cinnamaldehyde protects against oxidative stress and inhibits the TNFγ induced inflammatory response in human umbilical vein endothelial cells. Int J Mol Med. 2020;46(1):449-457. doi:10.3892/ijmm.2020.4582*

[32] *Hawthorn M, Ferrante J, Luchowski E, Rutledge A, Wei XY, Triggle DJ. The actions of peppermint oil and menthol on calcium channel dependent processes in intestinal, neuronal and cardiac preparations. Aliment Pharmacol Ther. 1988;2(2):101-118. doi:10.1111/j.1365-2036.1988.tb00677.x*

[33] *Yeom JW, Cho CH. Herbal and Natural Supplements for Improving Sleep: A Literature Review. Psychiatry Investig. 2024;21(8):810-821. doi:10.30773/pi.2024.0121*

[34] *Sándor Z, Mottaghipisheh J, Veres K, et al. Evidence Supports Tradition: The in Vitro Effects of Roman Chamomile on Smooth Muscles. Front Pharmacol. 2018;9:323. Published 2018 Apr 6. doi:10.3389/fphar.2018.00323*

[35] *Anghel SA, Badea RA, Chiritoiu G, Patriche DS, Alexandru PR, Pena F. Novel luciferase-based glucagon-like peptide 1 reporter assay reveals naturally occurring secretagogues. Br J Pharmacol. 2022;179(19):4738-4753. doi:10.1111/bph.15896*

[36] *Ansari P, Choudhury ST, Seidel V, et al. Therapeutic Potential of Quercetin in the Management of Type-2 Diabetes Mellitus. Life (Basel). 2022;12(8):1146. Published 2022 Jul 28. doi:10.3390/life12081146*

[37] *Cheng SC, Huang WC, S Pang JH, Wu YH, Cheng CY. Quercetin Inhibits the Production of IL-1γ-Induced Inflammatory Cytokines and Chemokines in ARPE-19 Cells via the MAPK and NF-γB Signaling Pathways. Int J Mol Sci. 2019;20(12):2957. Published 2019 Jun 17. doi:10.3390/ijms20122957*

[38] *Ceriello A, Novials A, Ortega E, et al. Vitamin C further improves the protective effect of GLP-1 on the ischemia-reperfusion-like effect induced by hyperglycemia post-hypoglycemia in type 1 diabetes. Cardiovasc Diabetol. 2013;12:97. Published 2013 Jun 27. doi:10.1186/1475-2840-12-97*

[39] *Guo Y, Mah E, Bruno RS. Quercetin bioavailability is associated with inadequate plasma vitamin C status and greater plasma endotoxin in adults. Nutrition. 2014;30(11-12):1279-1286. doi:10.1016/j.nut.2014.03.032*

[40] *Li L, Yang X. The Essential Element Manganese, Oxidative Stress, and Metabolic Diseases: Links and Interactions. Oxid Med Cell Longev. 2018;2018:7580707. Published 2018 Apr 5. doi:10.1155/2018/7580707*

[41] *Chen P, Bornhorst J, Aschner M. Manganese metabolism in humans. Front Biosci (Landmark Ed). 2018;23(9):1655-1679. Published 2018 Mar 1. doi:10.2741/4665*

[42] *Atuahene D, Costale A, Martello E, et al. A Supplement with Bromelain, Lentinula edodes, and Quercetin: Antioxidant Capacity and Effects on Morphofunctional and Fecal Parameters (Calprotectin, Cortisol, and Intestinal Fermentation Products) in Kennel Dogs [published correction appears in Vet Sci. 2024 Mar 27;11(4):149. doi: 10.3390/vetsci11040149]. Vet Sci. 2023;10(8):486. Published 2023 Jul 27. doi:10.3390/vetsci10080486*

[43] *Ashrafizadeh M, Ahmadi Z, Mohammadinejad R, Farkhondeh T, Samarghandian S. Curcumin Activates the Nrf2 Pathway and Induces Cellular Protection Against Oxidative Injury. Curr Mol Med. 2020;20(2):116-133. doi:10.2174/1566524019666191016150757*

[44] *Mahmoud AM, Hernández Bautista RJ, Sandhu MA, Hussein OE. Beneficial Effects of Citrus Flavonoids on Cardiovascular and Metabolic Health. Oxid Med Cell Longev. 2019;2019:5484138. Published 2019 Mar 10. doi:10.1155/2019/5484138*

[45] *Bode AM, Dong Z. The Amazing and Mighty Ginger. In: Benzie IFF, Wachtel-Galor S, editors. Herbal Medicine: Biomolecular and Clinical Aspects. 2nd edition. Boca Raton (FL): CRC Press/Taylor & Francis; 2011. Chapter 7. Available from: https://www.ncbi.nlm.nih.gov/books/NBK92775/*

[46] *Akhtar M, Chen Y, Ma Z, et al. Gut microbiota-derived short chain fatty acids are potential mediators in gut inflammation. Anim Nutr. 2021;8:350-360. Published 2021 Dec 29. doi:10.1016/j.aninu.2021.11.005*

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