NUTRITION NEEDS IN THE ERA OF ANTI-OBESITY MEDICATIONS

MGP Ingredients

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Executive Summary

Anti-obesity medications, such as glucagon-like peptide-1 (GLP-1) receptor agonists have transformed obesity treatment with an estimated 1 in 8 adults using the medications and millions more eligible. However, the rapid weight loss accompanying these medications presents health and nutrition challenges for individuals and targeted dietary strategies are needed to overcome these challenges. This white paper reviews the key nutritional concerns for individuals taking anti-obesity medications and discusses opportunities for dietary protein and fiber to help meet nutritional and health needs.

Key health & nutrition concerns:

- Muscle mass loss from rapid weight loss
- Nutrient gaps due to reduced intake
- Gastrointestinal side effects from reduced intake and motility
- Post-medication weight maintenance

Opportunity areas:

- Protein supplements and foods to maintain muscle mass and help manage appetite
- Dietary fiber to minimize GI side effects, manage appetite and improve glycemic response
- The combination of plant protein and dietary fiber to help individuals maintain weight loss for the long-term

The Rise of Anti-Obesity Medications

In 2010, the first GLP-1 receptor agonist was approved for use to treat type 2 diabetes (T2D). Commonly known as Victoza® (liraglutide), a once-daily injection was shown to help control long-term blood glucose levels in individuals with T2D. Interestingly, approximately 54% of individuals taking Victoza also lost ~5% of their body weight (1), triggering a new wave of research and development on GLP-1 agonists as anti-obesity medications. Before this time, weight loss medications were few, mostly ineffective, and riddled with undesirable side effects. Some (e.g., phentermine) had been removed from the market due to harmful effects on the heart. However, the stunning and significant weight loss results with GLP-1 receptor agonists ushered in a new era of anti-obesity medications.

GLP-1 receptor agonists include semaglutide (Ozempic®, Wegovy®, Rybelsus®), tirzepatide (Mounjaro®, Zepbound®), dulaglutide (Trulicity®), and liraglutide (Victoza®, Saxenda®), among others. Clinical trials have demonstrated that individuals using these medications can achieve weight loss ranging from 8% to 21% of their initial body weight (2). Given their effectiveness, the demand for these medications has surged, with recent data showing a 700% increase in patients prescribed a GLP-1 receptor agonist between 2019 and 2023 (3) (Figure 1). It is currently estimated that 1 in 8 US adults have used a GLP-1 receptor agonist (4).

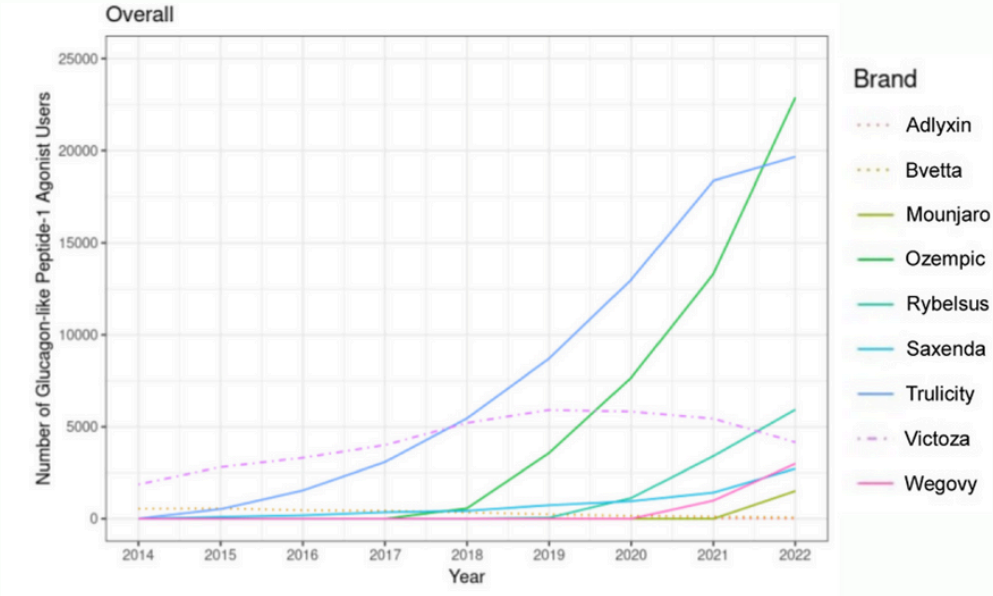


Figure 1. Increase over time in GLP-1 receptor agonist users. From (5)

Despite their rapid adoption and growth trajectory, GLP-1 receptor agonists are still only used by a fraction of those who may benefit from them. In the US, an estimated 42% of the population meet the criteria for obesity and thus could be prescribed these medications. Additionally, new oral versions of these medications are anticipated by 2026, which may make it easier to access these medications in the future. As the market expands, so too does the need for nutritional strategies to help maintain good health while taking these medications.

How GLP-1 Receptor Agonists Work

GLP-1 receptor agonists work by mimicking the natural GLP-1 hormone, which is secreted by the intestines in response to food intake. These medications bind to GLP-1 receptors throughout the body, triggering several physiological effects that contribute to both glycemic control and weight loss.

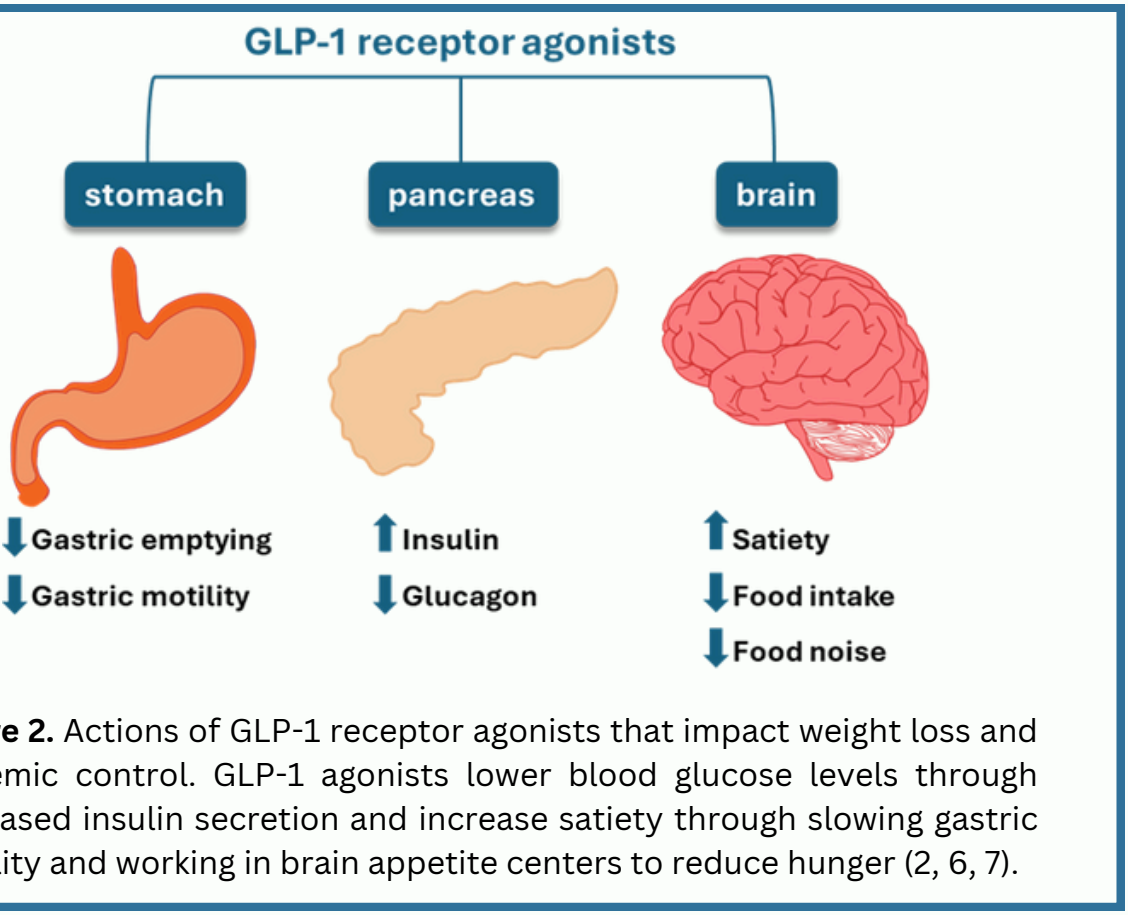


Figure 2. Actions of GLP-1 receptor agonists that impact weight loss and glycemic control. GLP-1 agonists lower blood glucose levels through increased insulin secretion and increase satiety through slowing gastric motility and working in brain appetite centers to reduce hunger (2, 6, 7).

Beyond these metabolic effects, emerging research suggests that GLP-1 agonists may alter taste perception and food preferences, further reinforcing their impact on appetite regulation. For example, Khan and Doty (8) reported that GLP-1 receptor activation may suppress the perception of all five basic taste qualities, leading to a decreased desire for foods high in fat, salt, and sugar. Similarly, functional magnetic resonance imaging (fMRI) studies have shown reduced neuronal responses to food-related stimuli in brain regions associated with appetite and reward, potentially explaining the reduced cravings for highly palatable foods, commonly referred to as “food noise.” (9). Other appetite-related receptors similar to GLP-1 receptors are being investigated for weight loss, including gastric inhibitory peptide (GIP), amylin, and glucagon receptors.

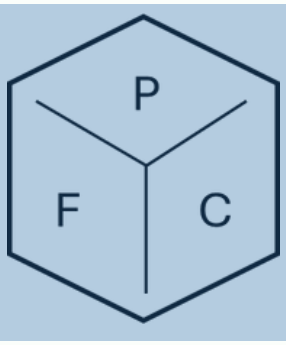
Nutritional Implications of Anti-Obesity Medication Use

As demand for anti-obesity medications grow and they become more accessible, health care professionals and food manufacturers must consider how to design diets and foods that support the individuals using these medications. While these nutritional needs have not been well investigated, plenty of anecdotal reports exist and much has been learned from other weight management interventions, including very low-calorie diets and bariatric surgery.

LOSS OF LEAN MUSCLE MASS

Studies suggest that 11 – 50% of total weight loss may be muscle mass, depending on rate and extent of weight reduction (10). Loss of muscle mass can lead to weakness, fatigue, and a reduction in metabolic rate. Dietary protein can help mitigate the loss of muscle mass, however, with reduced appetite and food intake, consuming adequate protein is challenging.





NUTRIENT INSUFFICIENCY

With reduced food intake there is also greater risk of nutrient insufficiencies, particularly for nutrients that most Americans don't get enough of, including dietary fiber, vitamin D, iron, calcium, and potassium.

GASTROINTESTINAL DISCOMFORT

40% to 70% of individuals taking anti-obesity medications, particularly GLP-1 receptor agonists, experience gastrointestinal (GI) discomfort in the form of nausea, vomiting, diarrhea or constipation (11). While the effects typically resolve over time, as many as 6% of individuals discontinue using GLP-1 receptor agonists due to GI side effects.





DISCONTINUED USE

50% - 75% of patients stop taking anti-obesity medications after one year (12). While the primary reason is due to the high cost, some stop because they reach the desired amount of weight loss or do not adapt to the side effects. However, discontinuing medication will result in a return of appetite and weight regain without dietary management and physical activity to maintain satiety and weight loss.

Emerging data suggests anti-obesity medications may alter the gut microbiota, however, studies so far have been small and have not considered how dietary factors and weight loss may interact with the anti-obesity medications and gut microbiota (13).

Nutritional Strategies to Support Health While Taking Anti-Obesity Medications

Preservation of lean muscle mass with adequate protein

Prioritizing protein intake at meals and snacks is essential to help preserve muscle mass during rapid weight loss. This is particularly critical for older adults who are already losing muscle mass due to age and may therefore be at higher risk of weakness, falls or fractures. It is recommended that individuals undergoing rapid weight loss consume at least 60 – 75 g protein per day (14). This can be challenging due to reductions in appetite, but spreading the intake across the day can help ensure these protein needs are met. Most Americans consume the least amount of protein at breakfast so focusing on increasing protein intake at breakfast can help get a head start on the protein needs for the day. Ideally, 15 g to 25 g of protein at each meal would ensure that protein needs are met (14).

While animal-based proteins tend to outperform plant-based proteins for anabolic properties, other trade-offs may need to be considered when choosing protein sources (15). Plant proteins have been associated with a reduced risk of T2D while animal proteins tend to be associated with an increased risk of T2D (16). Considering T2D is a common comorbidity with obesity and many individuals on these anti-obesity medications also have T2D, the inclusion of more plant-based proteins in the diet may be more desirable. Wheat protein has also been shown to stimulate muscle protein synthesis similar to milk protein, although higher doses may be required in older adults to achieve anabolic effects similar to animal protein (17). Alternatively, the combination of wheat protein with pulse proteins or fortification with limiting amino acids, such as methionine or lysine, may improve the anabolic effects (15).

Opportunity areas for Arise® Wheat Protein Isolates

- Incorporation of wheat protein isolates into more carbohydrate-based breakfast foods, such as breads and cereals, may provide increased protein at the breakfast meal, enabling higher protein intake throughout the day to help preserve muscle mass.
- Use of wheat protein isolates in meal replacement foods may also help increase protein intake.
- Inclusion of wheat protein isolates, particularly in place of refined carbohydrates, may provide additional benefits to metabolic health (lower glycemic response and improved insulin response) and develop good habits for a time when anti-obesity medications may be discontinued.
- The combination of wheat protein isolate with pulse proteins or enrichment with essential amino acids (e.g., methionine or lysine) may improve anabolic properties, but would need to be investigated.



Ensure adequate fiber intake to help alleviate GI side effects

According to the Dietary Guidelines for Americans, adequate intake of fiber is around 22 – 34 g/day depending on age and sex, yet the average American consumes only 10 – 15 g/d. For those with decreased food intake from anti-obesity medications, intake is likely to be even less. This, coupled with the inhibitory effects of GLP-1 receptor agonists on gut motility, may explain the prevalence of GI side effects, such as constipation, with these medications.

Insoluble fibers can accelerate transit time in the gut which could help alleviate problems with constipation resulting from the use of anti-obesity medications. Additionally, slowly fermented fibers, such as resistant starches, are less likely to create additional unwanted GI side effects of gas and bloating while still stimulating the growth of beneficial microbes in gut (18).

Dietary fiber can also help contribute to better glycemic control and heart health, which are common co-morbidities with obesity. Dietary fiber intake, particularly grain fibers, are associated with lower risk of T2D and cardiovascular disease (19-22). This is likely due to their negligible impact on glycemic response, as well as their positive impact on cardiovascular risk factors, such cholesterol and blood pressure (19, 23).

Opportunities for Fibersym® Resistant Starch

- Clinical evidence demonstrates Fibersym is well tolerated with little impact on GI discomfort, suggesting it is an ideal fiber to help individuals on anti-obesity medications meet their fiber needs without further contributing to GI side effects (24, 25).
- Fibersym has also been shown to support a lean gut microbial phenotype (24, 26) and support the growth of Bifidobacteria, which have been linked with a healthy body weight and improvements in cardiometabolic risk factors (25, 27).
- Inclusion of Fibersym in the place of fully digestible starches improves glycemic and insulinemic responses which will help further stabilize glycemic control while taking anti-obesity medications.
- As a low-calorie, functional source of fiber, Fibersym can help support the goals of satiety and appetite control.



Nutritional Strategies to Support Health While Transitioning Off Anti-Obesity Medications

Individuals who choose to stop taking anti-obesity medications will need continued dietary management to maintain their weight loss. Without medications, appetite will return, which can increase intake and increase the likelihood of weight regain (2). Additionally, the benefits of glycemic control offered by some of these medications will be eliminated and better management of blood glucose may be necessary for some individuals.

Protein + Fiber for Appetite Management



Protein and fiber play complementary roles in appetite regulation, which will be of particular importance to individuals trying to manage hunger after discontinuing anti-obesity medications (28). The satiety-enhancing effects of protein have been well established likely due to its effects on hormonal appetite regulation and slower gastric emptying (29, 30). Consuming 20 – 30 g of protein can stimulate satiety hormones including peptide YY (PYY) and GLP-1 (31), with plant proteins showing similar effects as animal proteins despite varying amino acid profiles (32, 33). Protein has also been shown to increase diet-induced thermogenesis, contributing to greater energy burning after a meal, supporting long-term weight maintenance (34). Studies of weight maintenance after weight loss have shown higher protein intake to help maintain body weight and preserve muscle mass while decreasing fat mass (35, 36).

Dietary fiber has also been shown to impact appetite by delaying gastric emptying, and enhancing gut hormone signaling, including PYY and GLP-1 (37, 38). Fermentable fibers, such as resistant starches, can stimulate the formation of short-chain fatty acids in the gut, which may enhance satiety while also improving metabolic and intestinal health (39). Additionally, the low caloric value of resistant starch can help maintain an appropriate energy balance for weight maintenance. Resistant starch may also contribute to weight maintenance by lowering body fat and improving body composition (25, 26), both important for long-term success.



Together, protein and fiber can help regulate hunger, reduce energy intake, and support weight maintenance after the use of anti-obesity medications.

Protein + Fiber for Glycemic Control & Metabolic Health

Protein and dietary fiber are also valuable dietary components for maintenance of healthy blood glucose levels after transitioning off anti-obesity medications. Protein does not contribute to postprandial glycemia and can further reduce postprandial glucose spikes by enhancing insulin secretion (40). Additionally, in individuals with T2D, diets high in plant protein have been shown to provide greater improvements in glycemic control compared to diets with more animal protein (41).

Similarly, dietary fiber reduces postprandial glycemia by slowing carbohydrate digestion and absorption and enhancing insulin sensitivity (19). Dietary fiber can also have favorable impacts on markers of long-term glycemic control, such as fasting glucose and hemoglobin A1c (HbA1c) (42). Resistant starch type 4 has been shown to significantly lower glucose and insulin responses (43-45), and SCFAs produced by fermentation may also contribute to improvements in insulin sensitivity (46).

Plant-based diets, naturally higher in plant proteins and dietary fiber, have also been associated with lower risk of cardiovascular disease and improvements in cardiometabolic health markers (47, 48).

Overall, the combination of protein and fiber can help individuals transitioning off of anti-obesity medications to better regulate glucose, improve insulin sensitivity, and sustain metabolic improvements over time.

Opportunities for Fibersym® resistant starch and Arise® wheat protein isolate

- Arise, as a plant protein, can be used in foods to help with glycemic control and appetite suppression as individuals transition off of anti-obesity medications
- Fibersym, as a low calorie resistant starch, can be used alone or in combination with Arise to help manage weight, appetite, and glycemic control after discontinuing anti-obesity medications.
- The use of foods with Arise or Fibersym throughout the weight loss journey (during and after weight loss) will better help individuals successfully transition through the discontinuation phase without having to dramatically change their diet or foods.







Conclusion

The increasing use of anti-obesity medications presents both challenges and opportunities for nutrition and food science innovation. While these medications are highly effective, they also pose risks for loss of muscle mass, GI side effects and nutrient inadequacies. Dietary strategies that focus on protein for muscle mass preservation and dietary fiber for metabolic health and GI comfort are needed to ensure positive long-term outcomes and to support individuals' nutritional needs both during and after medication use.





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