

Review

Injectables Pharmacotherapies for Obesity: Mechanisms, Efficacy, and Aesthetic Implications

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Abstract: Obesity remains a complex global health issue, necessitating multifaceted treatment approaches. Injectable pharmacotherapies have emerged as effective strategies to manage obesity by targeting metabolic pathways that regulate appetite, energy expenditure, and fat distribution. This review explores the mechanisms, clinical efficacy, and safety profiles of key injectable agents, including GLP-1 and GIP receptor agonists and lipolytic compounds. Additionally, it highlights the aesthetic challenges following significant weight loss, such as skin laxity, and discusses the role of biostimulators and non-invasive technologies in mitigating these effects. Despite the therapeutic promise of injectable agents, their widespread application is hindered by adverse effects, high costs, and accessibility issues. This paper underscores the need for integrative treatment models that combine pharmacological interventions with aesthetic and behavioral therapies to optimize patient outcomes. Future research should focus on refining personalized protocols and expanding the accessibility of these treatments to diverse populations.

Keywords: overweight; injectable agents; weight loss; clinical pharmacology; metabolic modulation; aesthetic implication



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1. Introduction

Overweight, encompassing both obesity and excess weight, is a complex, long-term condition that has become a highly prevalent public health issue, representing one of the most significant challenges to human health and well-being in the 21st century [1]. It is characterized by increased body fat storage, particularly intra-abdominal fat accumulation, and is associated with a higher risk of metabolic and cardiovascular diseases [2]. According to the World Health Organization (WHO), more than 1.9 billion adults are overweight, with over 650 million classified as obese, reflecting an alarming growth trend in recent decades [3]. In addition to direct health impacts, obesity poses a significant burden on healthcare systems and the global economy [4].

The pathophysiology of obesity is complex and multifactorial, involving a wide range of factors such as environmental, sociocultural, physiological, medical, behavioral, genetic, and epigenetic contributors that drive its onset and long-term persistence [5]. Key biological mechanisms include hypothalamic–pituitary axis dysregulation, insulin resistance, low-grade chronic inflammation, and hormonal alterations that modulate appetite and energy storage [6]. These complexities make therapeutic approaches challenging, necessitating strategies that go beyond traditional interventions like diet and physical exercise.

Given the limitations of conservative interventions, pharmacological treatments have emerged as effective alternatives, particularly for patients with grade II or higher obesity [7]. In recent years, the development of injectable agents has shown promising results, offering benefits such as improved adherence, sustained weight reduction, and better control of associated comorbidities. These agents target specific molecular pathways, including GLP-1, GIP, and beta-3 adrenergic receptors, and promote localized lipolysis through lipolytic compounds, thereby expanding the therapeutic arsenal [6]. However, their application extends beyond metabolic benefits, influencing aesthetic outcomes and patient quality of life [8,9].

Individuals with obesity have aesthetic challenges, especially in the context of pharmacological interventions aimed at weight reduction or improvement of metabolism. This is because such therapies, even though successful in reducing adiposity, eventually lead to changes in skin elasticity and soft tissue integrity as well as volume redistribution, which can result in sagging skin, stretch marks, or localized fat deposits that remain resistant to further weight reduction efforts. These issues demand, at the very minimum, a multidisciplinary approach whereby pharmacological management is combined with aesthetic procedures comprising dermal fillers, bio-stimulators, and skin-tightening technologies aimed at restoring symmetry and enhancing overall skin quality. Such combined interventions not only improve the physical aspect but also take into consideration the psychological aspect and body confidence [10,11].

This review delves into the pharmacological properties, clinical efficacy, and safety profiles of the leading injectable therapies for obesity, while addressing the aesthetic and psychosocial implications associated with rapid weight loss. By exploring the intersection between metabolic modulation and aesthetic interventions, this study aims to provide a comprehensive perspective on the evolving landscape of obesity treatment.

2. Materials and Methods

This study provides a narrative review of the literature. A search was conducted for studies published within the last 15 years in English, Portuguese, or Spanish on PubMed, focusing on intervention studies (clinical trials) available in full text that address the use of injectable pharmacological agents for overweight management. They must also have discussed the subject, namely, the use of pharmacological agents in overweight management.

The use of standard descriptors and Boolean operators for a systematic search (e.g., “name of the active ingredient” AND (“injectable” OR “injectable drugs”) AND (obesity OR “localized fat” OR “metabolic accelerators” OR “weight loss”)) produced scant results when applied using time and study type filters. This seems to indicate avoid of knowledge with their usage in this context, especially very rigorous studies like clinical trials.

PubMed was searched using targeted keywords for all the pharmacological actives described throughout this work, applying filters for time, language, availability of free full articles, and study type. The agents searched included liraglutide, semaglutide, tirzepatide, phosphatidylcholine, sodium deoxycholate, caffeine, taurine, L-carnitine, chromium picolinate, inositol, choline, N-acetyl, L-tyrosine, 5-HTP, L-theanine, phenylalanine, vitamin B12, L-arginine, ornithine, methionine, and beta-hydroxy-beta-methylbutyrate (HMB).

Titles and abstracts were screened for relevance to the scope of the study. Selected studies, including those prior to 2009 when more recent data were unavailable, were used to examine the mechanism of action, clinical efficacy, and safety profiles of injectable agents.

3. Pathophysiology of Obesity

Obesity is a complex biological-behavioral-environmental multivariate condition. It results from the interaction of many pathways, the main ultimate determinant being an energy imbalance where chronic caloric intake is greater than energy expenditure for an extended period, resulting in fat storage in adipose tissue. The situation has been aggravated by decreased calorie expenditure due to a sedentary lifestyle [12].

Nature and nurture factors contribute substantially. Some genes like the fat mass and obesity-associated (FTO) gene are linked to the regulation of appetite, the expenditure of energy, and the storage of fats in the body. Epigenetic changes caused by environmental factors, such as lifestyle and stress, can change gene function and imprint on metabolism [13]. Neuroendocrine control underlies the pathophysiology of obesity. In most obese patients, there is dysfunction at the hypothalamic level. Most of the time, this involves the phenomenon of leptin resistance, or the inability of the hormone produced by adipose tissues to inhibit hunger; levels of ghrelin, the so-called “hunger hormone”, are also usually elevated [12,13]. Chronic hyperinsulinemia, through modulation of appetite and promotion of fat storage, also disturb control of the appetite center.

Fat itself helps things along, letting out helpers like TNF- α and IL-6, which add to a kind of slow inflammation that harms metabolism [14,15]. Also, an increase in both how many and how big fat cells are (adipocyte hyperplasia and hypertrophy) marks obesity.

Hormonal imbalances are also applicable. Insulin resistance, which is common in obesity, reduces the uptake of glucose and therefore promotes the storage of fat [14]. Cortisol, related to chronic stress, mobilizes visceral fat depositions, and deregulations of thyroid hormones can reduce the basal metabolic rate.

The composition of the gut microbiota is yet another vital factor. Dysbiosis (imbalance in the intestinal bacteria) affects metabolic actions, energy derivation from food, and the storage of fats [16]. Changes in short-chain fatty acid production may influence the regulation of appetite for energy balance.

Behavioral and psychological factors continue to play a part in obesity. For example, poor dietary habits include ultra-processed foods and eating because of stress or depression; these lead to overeating. Inadequate sleep worsens the effect by also disturbing the functioning of hormones such as leptin and ghrelin that are responsible for stimulating one's appetite [17].

Obesity is also heavily influenced by environmental and sociocultural factors. High-calorie food availability; urbanization, which diminishes physical activities; and economic factors that do not allow access to more healthy choices all lead to increasing weight. Developmental programming effects, like those from maternal obesity and malnutrition during pregnancy, create vulnerability to obesity at a later age. Exposure to endocrine disruptors, like BPA compounds, interfere with metabolic homeostasis [18].

The last point is that mitochondrial dysfunction and cellular mechanisms cause reasons for obesity. The poor lipid metabolism and extra oxidative stress build up in wrong places, so they disrupt cellular function [13,18]. These linked factors show how complex obesity is, needing many ways to manage it. For example, that would be through food, exercise, medicine, or help with behavior.

4. Injectable Medications for Weight Loss

Injectable agents for weight loss have specific mechanisms of action, making them essential tools in obesity management. The main groups include GLP-1 receptor agonists, GIP receptor antagonists, lipolytic compounds used in mesotherapy, and metabolic accelerators and optimizers. These drugs target distinct metabolic and hormonal pathways, offering an integrated therapeutic approach for obese patients [12].

The distinct mechanisms of action of these drug groups highlight the complexity and efficacy of available therapeutic approaches for obesity management, emphasizing their importance in clinical practice (Table 1).

Table 1. Overview of drug classes, 2025.

Drug Class	Medication Name	Brand Name	Dosage	Administration Interval	Manufacturer	Country of Origin
GLP-1 Receptor Agonists	Liraglutide	Saxenda®	0.6 mg to 3 mg per day, subcutaneous	Daily	Novo Nordisk	Denmark
GLP-1 Receptor Agonists	Mazdutide *	-	3.0 mg to 10 mg per week, subcutaneous	Weekly	Innovent Biologics	China
GLP-1 Receptor Agonists	Semaglutide	Wegovy®	0.25 mg to 2.4 mg per week, subcutaneous	Weekly	Novo Nordisk	Denmark
GLP-1 Receptor Agonists	Survodutide *	-	0.3 mg to 4.8 mg per week, subcutaneous	Weekly	Boehringer Ingelheim	Germany
GLP-1 and GIP Receptor Agonists	Tirzepatide	Mounjaro®	5 mg to 15 mg per week, subcutaneous	Weekly	Eli Lilly	United States

* Investigational drugs still undergoing clinical trials. **Source:** Own elaboration.

4.1. GLP-1 Receptor Agonists

GLP-1 receptor agonists, such as liraglutide and semaglutide, mimic the action of the incretin hormone GLP-1, modulating appetite and glycemic metabolism. These drugs act on the central nervous system by activating anorexigenic neurons in the hypothalamic arcuate nucleus, promoting satiety and reducing appetite [13].

Additionally, they delay gastric emptying, prolonging postprandial satiety, and increase glucose-dependent insulin secretion while suppressing glucagon secretion, reducing hepatic gluconeogenesis. Liraglutide, administered subcutaneously in daily doses up to 3 mg, and semaglutide, administered weekly in doses up to 2.4 mg, have shown significant efficacy in weight reduction and metabolic control [6,15].

The adverse effects of injectable metabolic agents vary depending on their mechanisms of action, the dosages used, and the individual susceptibility of the patient. Among GLP-1 receptor agonists, liraglutide generally causes gastrointestinal symptoms such as nausea, vomiting, diarrhea, and constipation, as well as injection site reactions such as erythema and pruritus [19]. It has rarely been associated with pancreatitis, and preclinical studies have identified a potential risk of thyroid neoplasms. Semaglutide has a similar adverse effect profile, with nausea and vomiting being common, especially during the initiation or adjustment of treatment. In rarer cases, generalized weakness and hypoglycemia were observed, particularly when used with other hypoglycemic agents such as insulin [20].

To mitigate the gastrointestinal adverse effects associated with GLP-1 receptor agonists, several strategies can be adopted, the most effective of which are gradual dosage adjustment, division of prescribed doses, and use of medications that help control nausea and vomiting. Patient education on the importance of slow dose titration is also essential to reduce discomfort. In addition, the use of symptomatic treatments, such as antiemetics, can improve patient adherence to treatment [16,21].

Emerging GLP-1 receptor agonists such as mazdutide and survodutide, currently in Phase 3 clinical trials, mimic the action of oxyntomodulin, a proglucagon-derived peptide that promotes weight loss by increasing energy expenditure and reducing food intake. Both mazdutide and survodutide are designed to activate these receptors with different balances of glucagon and GLP-1 activity, showing potential for effective weight management in clinical settings [15].

Mazdutide is effective for weight loss in both diabetic and non-diabetic patients. Additionally, the drug demonstrates effectiveness in reducing blood pressure, total cholesterol, triglycerides, LDL, and HDL. In patients with type 2 diabetes mellitus, mazdutide is associated with lower HbA1c levels and fasting plasma glucose. However, its use is linked to mild to moderate gastrointestinal side effects [22]. The use of survodutide was associated with significant reduction in systolic and diastolic blood pressure, plasma triglycerides, and weight loss. The most common adverse effects of survodutide were gastrointestinal disorders [23].

Metabolic agents used in therapeutic protocols generally have a well-established safety profile, with toxicity varying based on dosage, administration route, and the individual susceptibility of the patient. Among GLP-1 receptor agonists such as liraglutide, semaglutide, and tirzepatide, studies demonstrate overall safety when used at therapeutic doses with appropriate monitoring [24]. However, these compounds are contraindicated in individuals with a history of medullary thyroid carcinoma or multiple endocrine neoplasia type 2, due to preclinical findings suggesting risks associated with these specific conditions [6,15].

4.2. GIP Receptor Agonists

GIP receptor agonists enhance the action of gastric inhibitory peptide (GIP), an incretin that stimulates lipogenesis and energy storage. By inhibiting this pathway, these agents reduce visceral fat deposition and promote efficient energy utilization [14]. Tirzepatide, a dual GLP-1 and GIP agonist administered weekly in doses ranging from 5 mg to 15 mg, has demonstrated synergistic effects, enhanced weight loss, and improved glycemic profiles [15]. Tirzepatide is often associated with gastrointestinal disturbances, including nausea, diarrhea, and flatulence. It also carries a risk of pancreatitis in predisposed patients and hypoglycemia when combined with other antidiabetic medications [25].

GIP and GLP-1 regulate food intake by acting on the brain's satiety center and stimulating insulin secretion in pancreatic β -cells. However, they differ in glucagon regulation: GIP increases its production during hypoglycemia, while GLP-1 reduces it during hyperglycemia. Additionally, GIP stimulates lipogenesis, whereas GLP-1 promotes lipolysis, supporting healthy adipocytes and adiponectin secretion. Together, these incretins contribute to metabolic homeostasis, preventing glycemic fluctuations, dyslipidemia, and reducing cardiovascular risk in individuals with type 2 diabetes and obesity [15].

4.3. Mesotherapy Compounds

Compounds used in mesotherapy, including phosphatidylcholine and sodium deoxycholate, promote localized lipolysis. Phosphatidylcholine destabilizes adipocyte cell membranes, facilitating the emulsification and release of triglycerides, while sodium deoxycholate acts as a detergent, solubilizing lipids and inducing adipocyte apoptosis [26]. These compounds are administered at concentrations of 2–5% for phosphatidylcholine and approximately 1% for deoxycholate in small volumes of 0.2–0.5 mL per injection site at intervals of 15 to 30 days. Despite their widespread use in aesthetic treatments, robust studies validating the long-term efficacy of mesotherapy are still limited [26]. In addition to adipocytolytic agents, other pharmacological classes are used to enhance lipolysis, such as β 3-adrenergic receptor agonists, which increase intracellular cAMP levels and activate

lipolytic enzymes including protein kinase A and hormone-sensitive lipase [27]. Furthermore, α 2-adrenergic receptor antagonists, such as yohimbine, are employed to counteract lipolysis inhibition and facilitate fat mobilization in resistant adipose tissue [28,29]. Compounds that inhibit lipogenesis and stimulate fatty acid β -oxidation also contribute to therapeutic outcomes; L-carnitine, for instance, acts as a cofactor in the mitochondrial transport of long-chain fatty acids, promoting their oxidation and reducing lipid accumulation [30]. The synergistic combination of these compounds optimizes the efficacy of mesotherapy protocols in aesthetic practice [26].

Although certain adrenergic modulators have demonstrated lipolytic potential through α 2-adrenergic antagonism and β -adrenergic agonism, respectively, their use—particularly via injectable routes—may be associated with significant adverse effects. Agents that act as α 2-adrenergic antagonists can induce systemic sympathomimetic reactions such as tachycardia, hypertension, anxiety, tremors, dizziness, and gastrointestinal discomfort due to central nervous system stimulation and peripheral vasoconstriction [28,29]. Additionally, in individuals sensitive to adrenergic stimulation, even low doses may trigger palpitations or panic-like symptoms. These potential systemic effects raise concerns regarding the safety profile of these agents, especially in aesthetic applications where their use is off-label and lacks standardized dosing protocols. Therefore, caution is required when incorporating these compounds into mesotherapy protocols, and thorough patient screening and risk-benefit assessment are essential [27].

The injectable use of α 2-adrenergic antagonists presents safety concerns due to their systemic sympathomimetic effects, including tachycardia, hypertension, and anxiety. Toxicologically, excessive doses may lead to central nervous system overstimulation, cardiovascular instability, and gastrointestinal disturbances. Caution is required, as clinical safety data for injectable forms remain limited and off-label. These effects are supported by studies indicating that α 2-adrenoceptor blockade enhances sympathetic nervous activity, which may provoke adverse systemic reactions, particularly in individuals sensitive to adrenergic stimulation [28,29].

Regarding the safety of the technique, mesotherapy is a safe procedure with mild and temporary side effects, such as nausea, fatigue, numbness, sweating, headache, ecchymosis, bleeding, pain, and local reactions at the injection site [31,32].

4.4. Metabolic Accelerators and Optimizers

Injectable metabolic accelerators for weight loss can be classified based on their predominant mechanisms of action, such as thermogenesis stimulators, lipolysis modulators, and metabolic optimizers. Each class plays a distinct role in the treatment of metabolic conditions such as obesity, metabolic syndrome, and body weight control [33].

Thermogenesis stimulators include compounds such as caffeine and taurine. Caffeine acts as an adenosine receptor antagonist, increasing the release of catecholamines and stimulating thermogenesis, leading to increased basal energy expenditure and the use of fat as an energy substrate. At high doses, caffeine inhibits the phosphodiesterase enzyme, leading to an increase in intracellular cyclic AMP (cAMP), prolonging the effects of catecholamines, and amplifying lipolysis. The recommended dose is 50 mg to 100 mg, administered intramuscularly weekly [34]. Taurine, on the other hand, modulates calcium ion transport and facilitates bile synthesis, promoting lipid metabolism and reducing visceral fat. Additionally, it has antioxidant properties that optimize mitochondrial function, with a dosage of 200 mg intramuscularly per week [35].

Injectable metabolic accelerators, while effective in managing metabolic conditions, may cause adverse effects in some patients, depending on the active compound, dosage, and individual sensitivity. Among thermogenesis stimulators, caffeine is associated with insomnia, tachycardia, tremors, anxiety, increased blood pressure, and gastrointestinal disturbances due to its action as an adenosine antagonist and stimulation of the sympathetic nervous system [34]. Taurine, generally well-tolerated, may cause nausea or abdominal discomfort at high doses [36].

Lipolysis modulators include L-carnitine, chromium picolinate, inositol, and choline. L-carnitine plays a crucial role in transporting fatty acids to the mitochondria, where they are oxidized and converted into energy, reducing fat deposits and increasing energy availability [37]. The usual dose is 200 mg to 600 mg intramuscularly, administered two to three times per week. Chromium picolinate improves insulin signaling, promoting glucose uptake by cells and reducing lipogenesis, with a dose of 100 mcg intramuscularly per week [38]. Inositol acts as a precursor to signaling molecules in lipid metabolism, aiding in the reduction of visceral fat and glucose metabolism, with a dosage of 100 mg to 200 mg weekly [39]. Choline, essential in the formation of acetylcholine and lipid metabolism, functions as a lipotropic agent, reducing liver fat at doses of 200 mg to 500 mg intramuscularly per week [40].

Lipolysis modulators also present varying safety profiles. L-carnitine can cause a fish-like body odor, nausea, vomiting, muscle cramps, and diarrhea, especially at higher doses [37]. Chromium picolinate, rarely, can cause liver or kidney toxicity, along with symptoms such as rashes, headaches, and dizziness [38]. Inositol is generally well-tolerated, but high doses may cause diarrhea, nausea, and fatigue [41]. Choline, essential for lipid metabolism, may result in strong body odor, nausea, excessive sweating, and, in some cases, hypotension [40].

The adverse effects of metabolic accelerators depend on various factors and can be minimized with dose adjustments and regular patient monitoring. It is essential that the prescription and use of these agents are carried out under professional supervision, considering each patient's preexisting health conditions and medical history.

Metabolic optimizers include agents such as vitamin B12, L-arginine, ornithine, methionine, and HMB. Vitamin B12, essential for energy metabolism and neurological function, increases mitochondrial energy production and corrects metabolic deficiencies associated with obesity when administered at doses of 2500 mcg intramuscularly weekly [42]. L-arginine, a precursor to nitric oxide, enhances vasodilation and nutrient delivery to tissues, increasing fatty acid oxidation at doses of 200 mg to 600 mg [36]. Ornithine participates in the urea cycle, promoting ammonia removal and assisting in muscle regeneration and fatigue reduction, with a dosage of 200 mg weekly [43]. Methionine acts as a methyl donor, supporting liver metabolism and reducing visceral fat at doses of 100 mg intramuscularly per week [40]. HMB, derived from leucine metabolism, reduces muscle protein breakdown and stimulates protein synthesis, helping preserve lean mass, with doses of 2 g to 3 g intramuscularly per week [44].

Regarding safety and the emergence of adverse events, vitamin B12 may cause rashes, itching, diarrhea, and, in rare cases, severe allergic reactions [42]. L-arginine may cause gastrointestinal disturbances, including nausea, diarrhea, and abdominal cramps, as well as hypotension at high doses [43]. Ornithine is generally well-tolerated but may occasionally cause abdominal discomfort in some individuals [45]. Methionine, at high doses, may elevate homocysteine levels, increase cardiovascular risks, and cause liver toxicity, nausea, and vomiting [46]. Finally, HMB is considered safe but may cause mild gastrointestinal disturbances in some cases [44].

4.5. Appetite Regulators

Appetite regulators include compounds such as N-acetyl, L-tyrosine, 5-HTP, L-theanine, and phenylalanine. N-acetyl is involved in the synthesis of neurotransmitters related to energy metabolism and appetite modulation, serving as an essential precursor in neuroendocrine regulation, with doses ranging from 20 mg to 50 mg intramuscularly per week [40]. L-tyrosine, a direct precursor to dopamine, norepinephrine, and epinephrine, enhances sympathetic activity and increases basal energy expenditure, with a similar dosage [47]. 5-HTP, a precursor to serotonin, reduces food cravings and regulates caloric intake, with doses of 4 mg to 20 mg intramuscularly per week [40]. L-theanine acts on GABA receptors, reducing anxiety and controlling emotional eating associated with highly caloric foods, with doses of 10 mg to 20 mg per week [48]. Phenylalanine, a precursor to dopamine and norepinephrine, helps control appetite and modulate mood, contributing to reduced caloric intake at doses of 50 mg per week [47].

Appetite regulators also present specific adverse effects. N-acetyl is associated with headaches, insomnia, irritability, and gastric discomfort [49]. L-tyrosine can cause anxiety, hypertension, insomnia, and palpitations, especially at higher doses [41]. 5-HTP, a serotonin precursor, may cause nausea, diarrhea, abdominal bloating, and, in rare cases, serotonin syndrome, especially when combined with antidepressants [50]. L-theanine has minimal adverse effects, rarely causing mild drowsiness or gastric discomfort [48]. Phenylalanine, a precursor to catecholamines, may cause hypertension, tachycardia, insomnia, anxiety, and irritability [47].

These injectable agents have distinct pharmacological profiles that, when grouped into classes, provide an integrated view of their therapeutic applications. Their specific properties allow for personalized protocols, optimizing results in the management of obesity and related metabolic conditions. It is essential that their use be supervised by qualified professionals, considering the individual needs of patients and potential adverse effects (Table 2).

Lipid modulators, such as L-carnitine, inositol, choline, and chromium picolinate, exhibit high tolerability and safety when used at appropriate doses. Studies suggest that L-carnitine is particularly effective in optimizing energy metabolism, while chromium picolinate aids in glucose control, making both agents suitable for integrated protocols [37,38].

Appetite regulators, including 5-HTP, L-tyrosine, phenylalanine, and L-theanine, have a high safety profile when administered alone or in carefully adjusted combinations. These agents play crucial roles in controlling food intake and modulating neurotransmitters, making them widely used in weight loss strategies [48].

Metabolic optimizers, such as vitamin B12, L-arginine, ornithine, and HMB, also demonstrate high safety in studies, even with prolonged use. Vitamin B12 is essential for metabolic and neurological function, while HMB supports the preservation of lean mass, making it a valuable resource in protocols aimed at optimizing body composition [42,43].

Available data indicate that these metabolic agents are safe for clinical use when administered according to individualized protocols and under professional supervision. Regular monitoring and personal adjustments are essential to maximize therapeutic effectiveness and minimize potential risks.

Table 2. Pharmacological details of active ingredients.

Active Ingredient	Classification	Dosage	Mechanism of Action
5-HTP	Appetite Regulator	4 mg to 20 mg/day	Precursor of serotonin; reduces food cravings
Caffeine	Thermogenesis Stimulant	50 mg to 100 mg/day	Adenosine antagonist; increases thermogenesis
Choline	Lipolysis Modulator	200 mg to 500 mg/day	Involved in lipid metabolism and reduces liver fat
Chromium Picolinate	Lipolysis Modulator	100 mcg/day	Improves insulin signaling
Inositol	Lipolysis Modulator	100 mg to 200 mg/day	Supports lipid metabolism and reduces visceral fat
L-Arginine	Metabolic Optimizer	200 mg to 600 mg/day	Precursor of nitric oxide; improves vasodilation
L-Carnitine	Lipolysis Modulator	200 mg to 600 mg, 2–3 times/day	Transports fatty acids to the mitochondria
L-Theanine	Appetite Regulator	10 mg to 20 mg/day	Modulates GABA receptors; reduces food-related anxiety
L-Tyrosine	Appetite Regulator	20 mg to 50 mg/day	Precursor of dopamine; increases energy expenditure
Methionine	Metabolic Optimizer	100 mg/day	Methyl group donor; reduces visceral fat
N-Acetyl	Appetite Regulator	20 mg to 50 mg/day	Modulates neurotransmitters for appetite control
Ornithine	Metabolic Optimizer	200 mg/day	Involved in the urea cycle; reduces ammonia
Phenylalanine	Appetite Regulator	50 mg/day	Precursor of dopamine; controls appetite and mood
Taurine	Thermogenesis Stimulant	200 mg/day	Promotes lipid metabolism and antioxidant function
Vitamin B12	Metabolic Optimizer	2500 mcg/day	Improves energy metabolism and neurological function
Yohimbine	Thermogenesis Stimulant	5 mg to 10 mg/day	α 2-Adrenergic receptor antagonists

Source: Own elaboration.

5. Common Drug Interactions

Drug interactions involving pharmaceutical agents and metabolic accelerators are determined by their mechanisms of action, shared metabolic pathways, and physiological effects. These interactions may enhance or antagonize therapeutic outcomes and, in some cases, increase the risk of adverse effects (Table 3).

GLP-1 receptor agonists, such as liraglutide, semaglutide, and tirzepatide, have a significant risk of interacting with drugs that slow gastric emptying or alter intestinal transit. These agents slow gastric emptying, potentially altering the absorption of orally administered drugs and reducing the effectiveness of agents like orlistat, whose action depends on the presence of lipids in the gastrointestinal tract. Additionally, combining GLP-1 agonists with metabolic accelerators that stimulate the sympathetic nervous system, such as caffeine, can exacerbate nausea or gastrointestinal discomfort, commonly observed at the beginning of GLP-1 treatment [6].

Table 3. Drug interactions and clinical recommendations.

Drug/Class	Potential Interactions	Clinical Recommendations
5-HTP (Appetite Regulator)	Risk of serotonin syndrome with antidepressants; interaction with thermogenics may cause insomnia	Avoid patients taking antidepressants; monitor insomnia
Chromium Picolinate (Lipid Modulator)	Mild interactions; potential synergy with metabolic modulators	Assess synergistic impacts; maintain adequate supplementation
HMB (Metabolic Optimizer)	Generally safe; minimal metabolic interactions with accelerators	General monitoring; considered safe for therapeutic combinations
L-Arginine (Metabolic Optimizer)	Hypotension in combination with antihypertensives; interaction with thermogenics may exacerbate cardiovascular effects	Monitor hypotension; carefully adjust in combined protocols
L-Carnitine (Lipid Modulator)	Potential increase in ammonia with combined use; exacerbation of gastrointestinal disorders with thermogenics	Monitor ammonia levels; adjust doses of synergistic agents
Liraglutide (GLP-1 Agonist)	Risk of reduced absorption of oral medications; potential nausea enhancement with thermogenics	Monitor gastrointestinal symptoms and adjust oral medication doses
Semaglutide (GLP-1 Agonist)	Risk of interaction with hypoglycemics; enhancement of gastrointestinal symptoms with caffeine	Avoid combinations with potent hypoglycemics; start with low doses
Tirzepatide (GLP-1 and GIP Agonist)	Risk of pancreatitis; interaction with hypoglycemics can cause hypoglycemia	Monitor blood glucose and signs of pancreatitis; avoid aggressive combinations

Source: Own elaboration.

Lipid metabolism modulators, such as L-carnitine, choline, and inositol, generally have a low potential for direct interactions. However, their simultaneous use with metabolic accelerators may enhance the efficiency of energy metabolism. Elevated fatty acid oxidation, however, can increase ammonia levels in patients with impaired liver or kidney function, requiring careful monitoring. Co-administration with thermogenic agents, such as caffeine, should be evaluated cautiously, as it may exacerbate gastrointestinal effects like nausea and abdominal discomfort [37]. The concomitant use of appetite regulators, such as 5-HTP, L-tyrosine, and phenylalanine, with metabolic accelerators that stimulate the central nervous system can lead to sympathetic hyperactivity, causing insomnia, anxiety, and, in rare cases, serotonin syndrome. This interaction is particularly significant in patients already using antidepressants due to the risk of serotonin overload [50].

Finally, metabolic optimizers, such as vitamin B12 and HMB, have a low risk of significant interactions. However, high doses of L-arginine combined with metabolic accelerators may cause hypotension, especially in sensitive individuals or those taking antihypertensive medications. This combination requires monitoring, as it may impair tissue perfusion in critical areas [43].

6. Injectable Weight Loss Agents and Aesthetic Dysfunctions: Strategies to Combat Skin Laxity with Biostimulators and Technologies

The use of injectable agents in obesity treatment has emerged as an effective tool for weight reduction and improvement of metabolic parameters. Key medications include GLP-1 and GIP receptor agonists, lipolysis modulators, and thermogenesis stimulators [24,51].

While these interventions promote fat loss and subsequent aesthetic enhancement, they often result in aesthetic dysfunctions such as excessive skin laxity, affecting both the face and body [5].

Rapid weight loss induced by agents like semaglutide and tirzepatide is associated with a significant reduction in subcutaneous adipose tissue volume, leading to tissue laxity. This phenomenon arises due to the loss of mechanical support provided by fat, highlighting the need for complementary interventions to address this aesthetic condition [6]. Beyond physical impacts, postweight loss skin laxity can generate significant psychosocial consequences, often overlooked by healthcare professionals. The focus on fat reduction tends to neglect the emotional discomfort and body dissatisfaction that accompany residual skin laxity. Patients report decreased self-esteem, insecurity regarding appearance, and difficulties maintaining motivation to continue treatment, underscoring the importance of comprehensive and multidisciplinary care [51].

The psychosocial effects of skin laxity are even more pronounced in the face, as changes in facial contour directly affect the patient's aesthetic perception and identity. Facial fat loss accentuates nasolabial folds, deepens tear troughs, and causes cheek ptosis, resulting in an aged appearance. Dissatisfaction with these effects can lead to anxiety and depression, negatively impacting quality of life and social interactions [52]. The neglect of this aspect by professionals focusing solely on body weight loss reinforces the need for approaches that integrate facial and body treatments. Addressing skin laxity through body harmonization involves not only fat reduction but also collagen stimulation to prevent and treat cutaneous laxity [53]. This integrated approach highlights the importance of treating obesity while implementing protocols that improve skin quality, promoting patient self-esteem and overall well-being.

Collagen biostimulators, such as poly-L-lactic acid (PLLA) and calcium hydroxyapatite (CaHA), play a crucial role in tissue restructuring for patients undergoing weight loss therapies. These agents promote a controlled inflammatory response that stimulates the synthesis of type I and III collagen, restoring skin firmness and elasticity [54]. Studies show that PLLA, when injected into deep dermal layers, induces neocollagenesis for up to 18 months post-procedure. PLLA acts through indirect biostimulation: its microparticles, upon injection, trigger a mild inflammatory response that leads to new collagen production over time, providing gradual and natural improvement in skin texture and firmness [55].

Widely used in facial rejuvenation, PLLA stimulates endogenous collagen production, resulting in significant improvements in skin firmness and elasticity. Its efficacy and safety have been demonstrated in recent studies [54]. Additionally, PLLA effectively restores facial volume lost due to aging, addressing static wrinkles, particularly in the mid and lower face. The gradual and natural volumization achieved with PLLA enhances facial contours and overall appearance. Complementing PLLA, calcium hydroxyapatite not only stimulates collagen production but also acts as an immediate dermal filler. Its microparticles provide structural support while promoting tissue regeneration and continuous collagen synthesis. This dual mechanism yields both immediate and progressive results, making it ideal for treating areas like the cheeks, jawline, and temples, which are prone to laxity following fat loss [56].

In addition to biostimulators, technologies such as fractional radiofrequency, high-intensity focused ultrasound (HIFU), and CO₂ laser are employed to induce collagen fiber contraction and stimulate neocollagenesis. Acting synergistically with biostimulators, these technologies enhance results and improve skin firmness [57]. Fractional radiofrequency heats the deep skin layers to temperatures between 40 and 45 °C, causing partial denaturation of existing collagen fibers and initiating a repair process that leads to the synthesis of new fibers [58].

High-intensity focused ultrasound (HIFU) penetrates various skin depths (1.5 mm to 4.5 mm), creating thermal coagulation points in the superficial muscular aponeurotic system (SMAS). This non-surgical lifting effect is particularly effective for the neck, submental area, and jawline [59]. Fractional CO₂ laser, by removing superficial skin layers while stimulating deeper collagen production, addresses laxity associated with wrinkles and scars, contributing to comprehensive facial revitalization [60]. Although there are no specific studies published in indexed journals combining weight-loss medications with strategies to combat skin laxity, these approaches have demonstrated clinical efficacy in minimizing laxity associated with weight loss. The combination of these therapies provides a robust solution for treating skin laxity, particularly in patients who have experienced significant weight loss, with minimal adverse effects reported.

7. Discussion

Overweight is a complex condition that requires multifaceted approaches to its successful management. It is strongly linked to some very serious metabolic, cardiovascular, and psychosocial comorbidities and complications and, arguably, represents one of the greatest contemporary global public health challenges, if not burdens, on healthcare systems. This has further opened newer frontiers whereby the use of injectable medications and metabolic stimulators in weight loss is gaining ground over the traditional dietary, physical, and behavioral methods [48].

Injectable products have considerable advantages over oral products, especially in pharmacokinetics and end results in the patient. The increased bioavailability and faster onset of action with injectables will be particularly useful for localized fat reduction and injections of compounds like GLP-1 agonists. They will greatly benefit patients with gastrointestinal disorders or those with impaired absorption, providing an alternative for those who need quick or precise results. Improvements in compliance occurred because injectables had to be used, and systemic side effects, as seen with oral medications, could be diminished with long-acting injectable forms. Although these need to be administered by professionals and hence are costlier, the efficiency and dependability of injectable treatments underline their role in modern approaches to weight loss [61].

Liraglutide and semaglutide are some of the most common preparations of GLP-1 receptor agonists that are currently used to treat obesity. The compounds mimic the effects of naturally occurring incretins primarily by increasing satiety as well as the additional main mechanisms of action which are the major factors leading to their effects, namely, slowing down stomach emptying, hence regulating food consumption [62,63]. These agents provide substantial aid, particularly in type 2 diabetes, in which they help to control glycemia without an associated risk for hypoglycemia by inducing glucose-dependent release of insulin. Data from recent clinical trials prove the superior effects of semaglutide since most participants recorded an excess of 15% loss of body weight in a duration of 68 weeks. These effects are superior to the outcomes identified in most interventions that are non-pharmacological. Thus, the findings from the studies make GLP-1 receptor agonists become the preferred cornerstones for treating obesity pharmacologically [62].

The benefits of GLP-1 receptor agonists may be lost after discontinuation, leading to increased HbA1c levels and weight gain. Treatment efficacy tends to stabilize after the first year, but continued use is necessary for long-term maintenance. Treatment failures may occur after 42 to 50 months, especially in patients with higher HbA1c levels or in men, highlighting the need for continued monitoring. After discontinuation, careful management is essential to prevent rebound effects, manifested by increased HbA1c and weight gain, depending on the dose used. This highlights the importance of continued treatment or close monitoring to prevent loss of the benefits achieved during drug use [64].

The GLP-1 agonists are restricted by adverse reactions, such as nausea, vomiting, and diarrhea. Severe adversities can lead to pancreatitis and cholelithiasis, which need continuous medical monitoring and risk-benefit analysis with caution [19]. Moreover, their subcutaneous route of administration and high cost may limit their access, particularly in developing countries [65].

Injectable metabolic stimulants, such as L-carnitine, inositol, choline, and taurine, represent another critical therapeutic group targeting key metabolic processes, including fatty acid oxidation, lipolysis, and mitochondrial function [36]. L-carnitine plays a pivotal role in transporting fatty acids into the mitochondrial matrix for β -oxidation, facilitating energy production. Inositol has been associated with enhanced insulin sensitivity and the mobilization of stored fats, while choline contributes to lipid emulsification and supports liver health. Additionally, choline's antioxidant properties extend its influence to lipid metabolism regulation and cardiovascular function [64]. Despite their generally recognized safety, metabolic stimulants can cause gastrointestinal discomfort and localized reactions at the injection site, particularly at high doses. However, the current body of evidence regarding the efficacy of these compounds remains limited, underscoring the urgent need for further research to establish standardized treatment protocols and investigate their interactions with other pharmacological therapies.

Injectable agents are effective for weight loss, but they also raise a very pertinent issue of aesthetic sequelae, such as increased skin laxity after significant fat reduction, for which there needs to be comprehensive personalized care [66]. In addition to aesthetic considerations, leading to surface laxity of skin, mainly on the face, there are psychological considerations as well. Therefore, it is imperative to promote treatment that enhances tissue reorganization and thus psychologically helps the patient. Aesthetic interventions have proven to be effective in improving the quality and firmness of skin, adapting flabbiness to what postweight-loss management should be [67]. The integration of biostimulators with non-invasive technologies offers a promising strategy for addressing deep skin concerns. Biostimulators can be integrated with non-invasive technologies in the treatment regimen for deep skin concerns. These can elicit collagen production and the natural contours of the face, therefore improving skin elasticity as well as overall appearance. Personalized treatment programs will optimize results and improve patient satisfaction as well as long-term adherence to aesthetic management plans. Therefore, multidisciplinary and patient-oriented approaches are effective in the management of the consequences following massive weight loss [53].

Injectable weight loss medications offer several advantages, including improved bioavailability, rapid onset of action, and effective weight reduction. However, they also come with notable limitations that must be critically considered. Despite providing improved bioavailability and onset of action and the achievement of the desired effect, available evidence is plagued by small sample sizes, short follow-up duration, and heterogeneity in clinical outcomes.

A key challenge is the lack of comprehensive head-to-head studies comparing these medications in terms of safety, efficacy, and convenience. GLP-1 receptor agonists, such as semaglutide and liraglutide, demonstrate superior weight loss efficacy and metabolic benefits but are often associated with gastrointestinal side effects and high costs, which may hinder adherence. In contrast, metabolic stimulators like L-carnitine and inositol target lipid metabolism and generally have a favorable safety profile, yet their clinical effectiveness remains less substantiated by robust trials. Additionally, the frequency of administration varies. Some injectables require daily dosing, while others, like semaglutide, allow for weekly applications, which can enhance patient compliance. Despite these differences, the absence of standardized comparative data prevents a clear ranking of these treatments,

emphasizing the need for well-structured studies that assess long-term outcomes, patient preference, and risk-benefit ratios.

Beyond efficacy and administration convenience, common challenges include high costs and frequent dosing schedules, which can impact adherence. Another crucial consideration is the potential interaction between injectable agents and other medications. For instance, while L-arginine is a promising metabolic stimulant, when combined with antihypertensive drugs, it may significantly lower blood pressure, requiring careful administration. These challenges further highlight the necessity of a multidisciplinary approach to obesity management, wherein physicians, pharmacists, and nutritionists collaborate to enhance treatment safety and efficacy while addressing the needs and preferences of a patient.

Injectable medicines for fat loss are usually seen as safe when given in recommended amounts and checked regularly. Substances such as GLP-1 receptor agonists show a good safety record; however, they are not good for patients who have had medullary thyroid cancer or multiple endocrine neoplasia type 2 because there may be a risk of tumors based on early tests in animals. These safety points show how important it is to check patients carefully and understand the risks before starting treatment [68]. Like metabolic agents, low-to-moderate risks of toxicity are associated with the inappropriate use or excessive dosages of L-carnitine and choline. Prolonged misuse of these compounds can cause metabolic imbalances or hepatic overload. This necessitates the use of treatment programs that are unique to each user. Individualized treatment protocols, provided that they are used under the constant supervision of people with appropriate qualifications, will help curb attendant risks as the therapeutic potentials of these agents would be maximized in weight management strategies.

The future of injectable medication for managing obesity will depend on the development of therapeutic options that are both effective and safe. As an example of such innovation, emerging dual agonists that target GLP-1 and GIP receptors appear to be more efficacious than their traditional single-target GLP-1 counterparts, representing a potential advantage for greater weight loss and improved metabolic control. These developments indicate a rather marked move to more meaningful and effective treatment approaches [69]. Moreover, the use of biomarkers and artificial intelligence in the treatment of obesity will lead us into a new era of personalized medicine. These technologies would permit interventions that are extremely precise and individualized, maximizing the outcomes by adjusting the treatment to the metabolic and physiological uniqueness of each patient. New biological and metabolizable agents that target the oxidation of fats while maintaining the mass of lean tissue are also in the process of being established, which may open the therapeutic possibilities further. The innovations in nanotechnology and the controlled-release systems open up a way to increase the potency as well as accuracy of the injectable formulations. Such technologies would ensure the therapeutic effectiveness by target delivery and sustained release; hence, inefficacy and side effects will be minimized. These are some of the changes that create a new era for the management of obesity, capable of changing it with better results for the patients.

Optimal effects of injectable weight loss medications can be achieved via lifestyle modification. A healthy balanced diet, routine physical activity, and behavioral interventions can work in synergy to maximize results and help the individual sustain weight in the long term. Such modifications act in pharmacological synergy with injections, ensuring results are both effective and sustainable [70].

New injectable drugs for treating obesity seem to provide not just metabolic gains but also mental well-being, which are key parts of a complete and varied care method. These mental boosts, like better self-confidence and quality of life, show more the complete

promise of such treatments. However, big issues remain, mainly about safety, how well they work, and if patients follow guidelines, which still need more study and creativity. The success of these treatments in making a positive health impact across the globe will need a joint push in proving their worthiness with evidence and filling the rifts existing in the clinical know-how. Also, the role of professional education in facilitating proper treatment and better results for patients cannot be overlooked. Finally, wide access through affordability and fair dispersal will greatly be needed to bring these new inventions to a larger community and promote the function of injectable agents in full-fledged obesity control.

8. Conclusions

Pharmacotherapy for weight loss not only restores glycemic control and reduces cardiometabolic risk factors—sometimes independently of weight reduction—but also mitigates the metabolic adaptation that limits further weight loss. This process occurs gradually and represents a unique yet underrecognized challenge in obesity therapy and, by extension, in medicine. While no single pharmacotherapy currently offers both complete efficacy and safety in promoting weight loss and improving metabolism, the combination of injectable therapies has emerged as a promising strategy. These therapies provide benefits for weight reduction and metabolic health, although long-term success will depend on ease of administration, affordability, and the minimization of side effects. Following significant weight loss, patients may experience undesirable aesthetic outcomes, such as skin laxity, which often require complementary treatments. Collagen biostimulators, microfocused ultrasound, and fractional radiofrequency have demonstrated efficacy in improving skin quality and restoring firmness. Injectable agents, such as GLP-1 and GIP receptor agonists, have shown effectiveness in managing weight and enhancing metabolic parameters. However, the future of obesity treatment lies in the development of personalized therapies that address weight loss, metabolic optimization, and aesthetic outcomes in a comprehensive manner. This integrated approach not only enhances clinical outcomes but also improves self-esteem, significantly contributing to the patient's overall well-being and quality of life.

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