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**TRATAMENTO FARMACOLÓGICO PARA OBESIDADE: MECANISMOS DE
AÇÃO, SEGURANÇA E EFICÁCIA TERAPÊUTICA**

**VITÓRIA
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Trabalho de Conclusão de Curso apresentado ao Centro de Educação Física e Desportos da Universidade Federal do Espírito Santo, como requisito parcial para a obtenção do título de bacharel em Educação Física.

Orientadora: Prof. Dr(a) Ana Paula Lima Leopoldo

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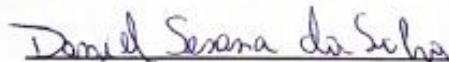
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RESUMO

A obesidade é uma doença crônica e multifatorial associada a alto risco de comorbidades metabólicas e cardiovasculares, como diabetes mellitus tipo 2, dislipidemia e hipertensão arterial. O tratamento farmacológico tem sido destacado como uma estratégia complementar à modificação do estilo de vida, especialmente para indivíduos que não alcançam perda de peso satisfatória através da dieta e exercício físico. Este estudo é uma revisão descritiva e qualitativa da literatura que examina os principais medicamentos atualmente utilizados ou em desenvolvimento para o tratamento da obesidade, incluindo orlistato, anfepramona, sibutramina, mazindol, liraglutida, semaglutida, tirzepatida, retatrutida e bimagrumabe, com o objetivo de identificar seus principais efeitos e eficácia clínica no tratamento e manejo da obesidade. Mecanismos de ação, eficácia clínica, perfis de segurança e eventos adversos foram abordados. Evidências indicam que agonistas de GLP-1 e agonistas de receptores de incretina duplos ou triplos promovem maior redução de peso e melhorias nos parâmetros metabólicos, com perfis de segurança aceitáveis. Terapias inovadoras, como o bimagrumab, mostram-se promissoras na preservação da massa magra durante a perda de peso, e consequentemente na saúde metabólica. Em conclusão, a farmacoterapia representa uma ferramenta importante no manejo da obesidade, devendo ser utilizada sob supervisão médica e integrada com tratamentos multidisciplinares.

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1. INTRODUÇÃO

Reconhecida como uma doença crônica multifatorial e um dos principais problemas de saúde pública mundial, a obesidade se define pelo excesso de adiposidade que pode comprometer a saúde (ABESO, 2026). O Atlas Mundial da Obesidade (2025) projeta que, até o ano de 2030, o sobrepeso e a obesidade afetarão aproximadamente 3 bilhões de adultos em todo o mundo, evidenciando a magnitude e a progressão dessa condição. No que se refere ao continente americano, as estimativas apontam para um crescimento expressivo da prevalência, passando de 67% em 2020 para cerca de 77% até o ano de 2035. No Brasil, a prevalência de obesidade atinge aproximadamente 31% da população adulta, o que corresponde a cerca de um em cada três brasileiros, com projeções que indicam aumento desse percentual nos próximos cinco anos (Tokarnia, 2026).

O aumento contínuo da obesidade pode ser atribuído, principalmente, a alterações nos padrões alimentares e comportamentais, caracterizadas pelo consumo elevado de dietas hipercalóricas e pela inatividade física (Anastácio et al., 2020). No Brasil, uma parcela expressiva da população adulta, estimada entre 40-50%, não atinge as recomendações mínimas de prática de atividade física quanto à frequência e intensidade, fator que contribui diretamente para o agravamento desse cenário (Tokarnia, 2026). A caracterização do excesso de peso é frequentemente realizada por meio do Índice de Massa Corporal (IMC), calculado pelo peso em quilogramas dividido pela altura em metros ao quadrado. A classificação subdivide-se em: Sobrepeso (IMC 25-29,9), Obesidade Grau I (IMC 30-34,9), Obesidade Grau II (IMC 35- 39,9) e Obesidade Grau III (IMC $\geq$ 40,0) (WHO, 2025). A literatura científica destaca que um IMC elevado está diretamente associado a diversas questões de saúde e qualidade de vida, resultando em aumento do risco de mortalidade (Rabacow, 2019). A obesidade está fortemente associada a um estado inflamatório crônico de baixa intensidade, caracterizado por alterações metabólicas persistentes que afetam diferentes sistemas do organismo, o que favorece o desenvolvimento progressivo de diversas comorbidades. Entre essas condições, destacam-se a dislipidemia, a hipertensão arterial sistêmica e o diabetes mellitus tipo 2 (DM2), além de outras complicações relevantes, como as doenças cardiovasculares, hepáticas e alguns tipos de câncer, fatores que contribuem de maneira significativa para o aumento do risco de mortalidade prematura (Moschonis; Trakman, 2023; Ward et al., 2022).

A cultura de inatividade física, associada ao consumo alimentar inadequado, constitui importante determinante da adoção de um estilo de vida sedentário, intensificado pela

tecnologia e pela urbanização. Esse cenário favorece a instalação de desequilíbrio energético, no qual o gasto calórico diário não é suficiente para compensar a ingestão alimentar, contribuindo para o aumento da prevalência da obesidade.

Paralelamente, a crescente disponibilidade de alimentos ultraprocessados, marcados por alta densidade energética, elevados teores de gorduras saturadas, açúcares e sódio e reduzido valor nutricional, contribui de forma expressiva para o consumo calórico excessivo. Em conjunto com a baixa demanda energética diária, esse padrão alimentar favorece um balanço energético positivo persistente, criando condições propícias ao acúmulo de tecido adiposo e ao aumento do risco de obesidade e suas morbidades associadas (Popkin; Adair; Ng, 2012).

A literatura científica aponta o excesso de adiposidade como uma das principais preocupações de saúde pública contemporânea, visto que apresenta elevada prevalência e impacto negativo na qualidade de vida de indivíduos pertencentes a diferentes faixas etárias e contextos socioeconômicos, afetando desde crianças e adolescentes até adultos e idosos (Christinelli et al., 2020). Além disso, seu caráter multifatorial e progressivo reforça a complexidade do seu manejo clínico e preventivo. Estudos recentes propõem uma distinção conceitual entre “obesidade clínica” e “obesidade pré-clínica”, contribuindo para uma compreensão mais precisa das diferentes manifestações da doença.

A obesidade clínica é caracterizada como uma condição crônica e sistêmica, na qual o excesso de adiposidade está diretamente associado a alterações fisiopatológicas, disfunções orgânicas e metabólicas e/ou limitações substanciais nas atividades da vida diária. Destaca-se que, mesmo na ausência de comprometimento funcional ou metabólico objetivamente mensurável, a presença de restrições significativas na mobilidade, no autocuidado e em outras tarefas cotidianas atribuíveis ao excesso de adiposidade já é suficiente para classificar o indivíduo nessa condição. Em contrapartida, a obesidade pré-clínica refere-se à presença de excesso de adiposidade com preservação funcional dos tecidos e órgãos, sem evidências atuais de repercussões clínicas significativas, embora associada a risco aumentado para o desenvolvimento futuro de doenças e agravos à saúde (TLDE, 2025).

Diante disso, estratégias terapêuticas baseadas na modificação do estilo de vida, especialmente por meio da associação entre dieta hipocalórica equilibrada e prática regular de exercício físico, destacam-se como abordagens fundamentais tanto na prevenção quanto no tratamento do excesso de peso e de suas complicações (Christinelli et al., 2020). Essa abordagem integrada não apenas favorece a redução da massa de gordura, como também

contribui para a preservação e/ou aumento da massa muscular, aspecto fundamental para a manutenção do metabolismo ativo. Paralelamente, observa-se ainda melhora significativa em parâmetros metabólicos e fisiológicos, incluindo aumento da sensibilidade à insulina e melhora do perfil lipídico e inflamatório (Ho et al., 2024). Entretanto, nem todos os indivíduos respondem de forma satisfatória ou conseguem manter aderência a essas intervenções ao longo do tempo, seja por fatores biológicos, comportamentais, ambientais ou psicossociais (ABESO, 2026). Diante dessa limitação, torna-se necessário, em alguns casos, recorrer a estratégias terapêuticas adicionais, como o tratamento farmacológico e, em situações mais graves, a indicação cirúrgica, as quais têm como objetivo auxiliar no manejo da doença e na redução dos riscos associados (SBCBM, 2026).

A intervenção farmacológica no tratamento da obesidade tem ganhado destaque, refletindo-se em aumento expressivo no consumo de medicamentos. Segundo dados da ANVISA (2025), o Brasil registrou um crescimento notável de 500% no uso de fármacos, evidenciando a crescente busca por soluções médicas para o manejo do peso corporal. Esses medicamentos atuam por meio de uma gama diversificada de mecanismos de ação, que visam modular processos fisiológicos complexos envolvidos na regulação energética e no metabolismo. Entre os principais mecanismos, destacam-se a inibição da absorção de gordura no trato gastrointestinal, a modulação da saciedade por meio da atuação em centros cerebrais específicos, a regulação neuroendócrina do apetite, a estimulação da termogênese para o aumento do gasto energético, entre outros (Silva; Baiense; Andrade, 2023). Neste contexto, a evolução farmacológica tem permitido o desenvolvimento e a rigorosa testagem de novos compostos. Tais avanços têm resultado na identificação de agentes terapêuticos que não apenas demonstram segurança clínica robusta, mas também exibem efeitos positivos significativos na redução do peso corporal e na melhoria de parâmetros metabólicos associados à obesidade (Santana et al., 2025).

Apesar dos avanços farmacológicos no tratamento da obesidade, a utilização desenfreada e inadequada de medicamentos anorexígenos representa um desafio significativo para a saúde pública. Frequentemente, esses fármacos são empregados sem a devida prescrição médica e, crucialmente, desacompanhados de mudanças substanciais no estilo de vida, como a adoção de uma dieta equilibrada e a prática regular de atividade física (Costa et al., 2022). Essa abordagem sem supervisão compromete a eficácia a longo prazo e eleva consideravelmente o risco do efeito rebote, no qual o paciente recupera o peso perdido, após a interrupção do tratamento. Tal fenômeno não apenas frustra o indivíduo, mas também pode agravar o quadro

de obesidade, o que torna futuras intervenções mais complexas e reforça a necessidade imperativa de uma abordagem multidisciplinar e individualizada no manejo da doença (Sousa et al., 2021).

Entre os fármacos abordados neste estudo, destacam-se a anfepramona e a sibutramina, que exercem predominantemente efeitos centrais no sistema nervoso, atuando na modulação da saciedade por meio da inibição da recaptação de neurotransmissores, o que contribui para a redução da ingestão alimentar (Duarte et al., 2020; Naccarato; Lago, 2014). Outro medicamento amplamente utilizado é o orlistate, cujo mecanismo de ação consiste na inibição da enzima lipase pancreática, promovendo menor digestão e absorção de gorduras da dieta e, consequentemente, menor aporte calórico total (Silva; Santos; Queiroz, 2022). Recentemente, novas classes terapêuticas têm ganhado destaque no tratamento da obesidade, como a liraglutida e a semaglutida, ambas pertencentes aos agonistas do receptor do peptídeo-1 semelhante ao glucagon (GLP-1R), que apresentam ação tanto central quanto periférica, influenciando a saciedade e o controle metabólico (Andersen; Knop; Vilsbøll, 2021a; Del Olmo-García; Merino-Torres, 2018). Além disso, terapias recentes como a tirzepatida, um agonista dual que atua simultaneamente nos receptores GLP-1 e GIP (polipeptídeo insulínico dependente da glicose), potencializam efeitos sobre saciedade, homeostase glicêmica e gasto energético (Le Roux; Mondoh, 2024). Outro agente relevante é o mazindol, um fármaco anorexígeno que atua na inibição da recaptação de neurotransmissores, promovendo redução do apetite e eficácia especialmente em indivíduos com resposta inicial positiva ao tratamento farmacológico (Lucchetta et al., 2017).

Ainda no campo das terapias farmacológicas, pesquisadores tem investigado a retatrutida, um agonista triplo de GLP-1, GIP e glucagon, com potencial para promover melhorias importantes no metabolismo lipídico e glicêmico, além de aumento do gasto energético e redução do apetite (Urva et al., 2022). Adicionalmente, o bimagrumab, um anticorpo monoclonal que atua sobre o receptor tipo II (ActRII), tem demonstrado potencial para promover aumento de massa muscular e, concomitante, redução da gordura corporal (Heymsfield et al., 2021).

Diante desse cenário, o presente estudo tem como objetivo analisar os agentes farmacológicos atualmente utilizados na prática clínica, bem como aqueles ainda em desenvolvimento para o tratamento da obesidade, com enfoque em seus mecanismos de ação, eficácia clínica, perfis de segurança e potencial terapêutico, visando contribuir para a avaliação crítica das evidências disponíveis, para o aperfeiçoamento das estratégias contemporâneas e

futuras de manejo da obesidade em indivíduos com comportamento sedentário. Além disso, busca-se ampliar o conhecimento dos futuros profissionais de Educação Física sobre as abordagens farmacológicas aplicadas a essa condição, favorecendo uma atuação interdisciplinar mais qualificada na prescrição de exercício físico e na promoção de mudanças do estilo de vida.

Ressalta-se que o produto principal deste trabalho é apresentado sob a forma de artigo científico. Assim, o artigo intitulado “Tratamento Farmacológico para Obesidade: Mecanismo de Ação, Segurança e Eficácia Terapêuticas”, publicado em periódico científico, constitui o corpo central deste Trabalho de Conclusão de Curso, reunindo a fundamentação teórica, os procedimentos metodológicos, os resultados e a discussão. Por fim, expõem-se as considerações finais.

2. ARTIGO CIENTÍFICO

Tratamento Farmacológico para Obesidade: Mecanismos de Ação, Segurança e Eficácia Terapêutica

Pharmacological Treatment for Obesity: Mechanisms of Action, Safety and Therapeutic Efficacy

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PHARMACOLOGICAL TREATMENT FOR OBESITY: MECHANISMS OF ACTION, SAFETY AND THERAPEUTIC EFFICACY

TRATAMENTO FARMACOLÓGICO PARA A OBESIDADE: MECANISMOS DE AÇÃO, SEGURANÇA E EFICÁCIA TERAPÊUTICA

TRATAMIENTO FARMACOLÓGICO PARA LA OBESIDAD: MECANISMOS DE ACCIÓN, SEGURIDAD Y EFICACIA TERAPÉUTICA

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ABSTRACT

Obesity is a chronic and multifactorial disease associated with high risk of metabolic and cardiovascular comorbidities, such as type 2 diabetes mellitus, dyslipidemia and arterial hypertension. Pharmacological treatment has been highlighted as a complementary strategy to lifestyle modification, especially for individuals who do not achieve satisfactory weight loss through diet and physical exercise. This study is a descriptive, qualitative literature review that examines the main drugs currently used in development for obesity management, including orlistate, anfepramone, sibutramine, mazindol, liraglutide, semaglutide, tirzepatide, retatrutide and bimagrumab, with the aim of identifying their primary impacts and clinical effectiveness in the treatment and management of obesity. Mechanisms of action, clinical efficacy, safety profiles, and adverse events were addressed. Evidence indicates that GLP-1 agonists and dual or triple incretin receptor agonists promote greater weight reduction and improvements in metabolic parameters, with acceptable safety profiles. Innovative therapies, such as bimagrumab, show promise in preserving lean mass during weight loss, thereby metabolic health. In conclusion, pharmacotherapy represents an important tool in the management of obesity, and should be used under medical supervision and integrated with multidisciplinary strategies such as lifestyle modifications to optimize outcomes, minimize risks, and promote sustained weight loss maintenance.

Keywords: Obesity. Pharmacological Treatment. Anorectics. Emerging Therapies.

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INTRODUCTION

Obesity is a multifactorial chronic disease, characterized by excess adiposity, and is recognized as one of the main global public health problems (BRASIL, 2024). According to projections from the World Atlas of Obesity 2024, by 2035, it is estimated that about 3.3 billion adults worldwide will be overweight or obese, representing approximately 54% of the global adult population (World Obesity Federation, 2025). The global prevalence of obesity more than doubled between 1990 and 2022 (WHO, 2024).

Between 2017 and March 2020, obesity affected 41.9% of adults in the U.S., while severe obesity reached 9.2%, corresponding to more than 100 million and 22 million individuals, respectively (CDC, 2025). In Brazil, data from 2019 indicate that 60.3% of the population was overweight, and obesity affected 25.9% of adults aged 18 years or older (IBGE, 2021). According to the World Atlas of Obesity, projections suggest that by 2030, 50% of the global population will have a high BMI. In addition, it is estimated that by 2025, 31% of the Brazilian adult population will be obese (World Obesity Atlas, 2025).

The scientific literature indicates that the rising prevalence of obesity is strongly related to changes in the population eating and behavioral patterns, especially due to the increased consumption of high-calorie diets, rich in sugars, fats, and ultra-processed foods, coupled with a sedentary behavior (Barros et al., 2013; Fernández Meré; Álvarez Blanco, 2004; Hachem; Brennan, 2016). Although genetic, hormonal, and metabolic factors also contribute to the development of obesity, it is estimated that only about 5% of cases are attributable to these factors (Zilberstein; Ramos; Galvao Neto, 2002).

Obesity is directly linked to the accumulation of abdominal fat which is strongly associated with a chronic inflammatory condition, and confers a high risk for the development of comorbidities, such as dyslipidemia, hypertension, type 2 diabetes mellitus (T2DM), as well as cardiovascular and liver diseases and certain types of cancer, which substantially increases mortality risk (Moschonis; Trakman, 2023; Ward et al., 2022). It is therefore recognized as a major public health concern, affecting children, adolescents, adults and older adults across socioeconomic groups. Studies have shown that the combination of a low-calorie diet and increased physical exercise is an effective strategy for body weight control and improving body-composition improvement. This combined approach enhances fat-mass reduction, increases or maintenance of muscle mass, and contributes to improvements in metabolic parameters as evidenced by Christinelli et al., (2020).



Dietary prescription, although essential for the treatment of obesity, remains one of the main challenges for sustaining the patient engagement throughout the therapeutic process. Researchers point out that across the different phases of dietary re-education, adherence to nutritional plans tends to be compromised by several factors often perceived as restrictions or deprivations. Consequently, lifestyle changes can trigger feelings of discomfort, resistance, or demotivation, especially in the absence of individualized and flexible strategies that consider the patient's dietary reality (Lara Leticia Cardoso de Oliveira, 2023; Santiago; Cyrillo; Cervato-Mancuso, 2023). In this context, the use of pharmacotherapy as a complementary strategy to lifestyle modifications has emerged as an effective therapeutic approach in the management of obesity.

Brazil is among the countries with the highest use of anorectic drugs worldwide (Marquis; Quintilio, 2021). According to ANVISA (2025), the consumption of these medications increased by 500% in Brazil (ANVISA, 2025). These drugs act through various mechanisms, including inhibition of fat absorption, modulation of satiety, neuroendocrine regulation of appetite, stimulation of thermogenesis, and alterations in glucose and lipid metabolism (Silva; Baiense; Andrade, 2023). With advances of biotechnology and pharmacology, new compounds have been developed and tested, demonstrating clinical safety and positive effects (Santana et al., 2025).

Among the drugs discussed in this study, amfepramona and sibutramine stand out, as they have predominantly central actions, and modulate satiety by inhibiting neurotransmitter reuptake (Duarte et al., 2020a; Naccarato; Lago, 2014a). Another drug used is orlistat, which acts by inhibiting the action of pancreatic lipase, thereby reducing total caloric intake (Silva; Santos; Queiroz, 2022a). New therapeutic classes have gained prominence, such as liraglutide and semaglutide, which are glucagon-like peptide-1 receptor agonists (GLP-1R agonists) with both central and peripheral action (Andersen; Knop; Vilsbøll, 2021a; Del Olmo-García; Merino-Torres, 2018a). In addition, more potent drugs have emerged, such as tirzepatide, a dual agonist that simultaneously activates GLP-1 and GIP (glucose-dependent insulinotropic polypeptide) receptors, enhancing effects on satiety, glycemic control, and energy metabolism (Le Roux; Mondoh, 2024a). Mazindol is an anorectic agent that inhibits neurotransmitters reuptake, reducing appetite, and demonstrating efficacy in weight loss, particularly in individuals who exhibit a significant initial response to treatment (Lucchetta et al., 2017a).



Furthermore retatrutide, a triple agonist of GLP-1, GIP and glucagon, that still in the research phase, can bring significant improvements in lipid and glucose metabolism, as well as increased energy expenditure (Urva et al., 2022a). Another innovative agent is bimagrumab, a monoclonal antibody that binds to the activating type II receptor (ActRII), which has shown potential to promote a significant increase in lean mass and a simultaneous reduction in body fat (Heymsfield et al., 2021a). Therefore, the objective of this study is to examine the pharmacological agents currently in clinical use, as well as those under development for the management of obesity. Specifically, it seeks to elucidate their mechanisms of action, clinical efficacy, safety profiles, and therapeutic potential. A critical appraisal of the available evidence aims to advance understanding of both current and emerging strategies for the clinical management of obesity.

METHODOLOGY

This study is a narrative review with descriptive and qualitative approach, aimed at collect and critically analyze the available scientific evidence on the use of drugs in the treatment of obesity, considering its mechanism of action, clinical efficacy, adverse effects, and applicability in the current therapeutic context. The information was obtained from searches carried out in the databases: PubMed, Virtual Health Library (VHL), Google Scholar and SciELO, using inclusion criteria that prioritized regency, scientific relevance and full text availability. The keywords used in the search included: *"Obesity"*, *"Pharmacological Treatment"*, *"Anorectic Drugs"*, *"Sibutramine"*, *"Amfepramone"*, *"Mazindol"*, *"Orlistat"*, *"Semaglutide"*, *"Liraglutide"*, *"Tirzepatide"*, *"Retracted"*, *"Bimagrumab"*. Articles were selected, provided they were available in full text and aligned with the central objective of the study. After applying exclusion criteria, such as duplicity, absence of the full text or thematic inadequacy.

RESULTS AND DISCUSSION

Anorexic drugs, or appetite inhibitors, have been used for decades in the treatment of obesity, primarily due to their action on the central nervous system, thereby promoting satiety and reducing food intake. Despite their initial effectiveness in promoting, these drugs do not directly target the multifactorial pathophysiological mechanism underlying obesity, and are often regarded as a palliative strategy focused on the consequence of the disease rather than its



underlying causes (Londoño-Lemos, 2012). In this context, it is essential to further investigate anorectic agents, to elucidate their mechanisms of action and to assess their risk–benefit profiles across diverse patient population. Scientific research is fundamental in identifying patient subgroups that may benefit from the use of these drugs with improved safety and efficacy.

Some reported adverse effects, such as arterial hypertension, mood disorders, seizures and neuropsychiatric alterations, raise concerns regarding the long-term safety (Costa et al., 2021a; Lucas, 2019; Vargas et al., 2018). In addition, indiscriminate non-prescribed use, frequently motivated by aesthetic purposes, constitutes a concerning phenomenon that underscores the need for health education strategies and stricter regulatory oversight. The efficacy of anorectics agents, when used judiciously, under medical supervision and within evidence-based protocols, may represent a viable therapeutic option in the management of obesity, particularly in cases where behavioral interventions alone does fail to achieve desired outcomes (Costa et al., 2021b).

Orlistate

Orlistat (tetra-hydrolipstatin) is an U.S. Food and Drug Administration (FDA)-approved pharmacological agent for the treatment of obesity. It is a saturated derivative of lipstatin, a natural substance produced by the microorganism *Streptomyces toxytricini*, which acts as a selective, irreversible inhibitor of gastrointestinal lipases (Silva; Santos; Queiroz, 2022b).

According to FDA guidelines, Clinical indications include: (i) individuals with obesity, defined as a body mass index (BMI) ≥ 30 kg/m²; (ii) overweight individuals (BMI ≥ 27 kg/m²) with comorbidities such as hypertension, type 2 diabetes, or dyslipidemia; and (iii) individuals who require pharmacological support for weight loss maintenance and prevention of weight regain following previous interventions (Silva; Santos; Queiroz, 2022c).

Thus, it is considered an anti-obesity drug that acts as a specific, long-acting inhibitor with local action of gastrointestinal lipases, which are essential enzymes for the digestion of dietary fats. Its primary site of action is the lumen of the stomach and small intestine, where it reversibly inhibits gastric and pancreatic lipases through covalent binding to the serine residue at the catalytic site of these enzymes. This interaction prevents the hydrolysis of ingested triglycerides into free fatty acids and monoglycerides, the forms normally absorbed by the intestinal mucosa (Guercioli, 1997). As a result of the enzyme inhibition, triglycerides remain intact and are excreted in the feces, leading to an approximate 30% reduction in dietary fat



absorption when administered at recommended therapeutic dose. This peripheral mechanism of action, which does not require systemic absorption, confers orlistat a distinct pharmacological profile primarily aimed at inhibiting intestinal fat absorption (Hall et al., 2021).

Orlistat is available in oral formulations at doses of 60 mg (over-the-counter) and 120 mg (prescription). The recommended therapeutic dose is 120 mg taken orally, administered three times daily, during or within one hour after meals containing fat (Bansal; Patel; Al Khalili, 2025). Owing to its mechanism of action, orlistat may reduce the absorption of fat-soluble vitamins (A, D, E, and K), therefore, daily supplementation is recommended to prevent nutritional deficiencies (Grunvald et al., 2022a). Commonly reported adverse effects include fecal incontinence, loose stools, rectal pain or discomfort, dental and gingival disorders, lower respiratory tract infections, menstrual irregularities, anxiety, fatigue, urinary tract infections, and abdominal distension (Silva; Santos; Queiroz, 2022d).

According to a randomized, double-blind, placebo-controlled clinical trial conducted in India, the efficacy and safety of orlistat were evaluated in 80 obese patients (BMI > 30). Participants were divided into two groups: one received 120 mg of orlistat three times daily, and the other received a placebo. Treatment with orlistat resulted in gastrointestinal adverse events such as diarrhea (28.5%), oily stools (25.7%), abdominal pain (31.4%), and fecal urgency (34.2%), which were generally mild and self-limited. No significant changes were observed in laboratory parameters such as hemoglobin, leukocytes, creatinine, and hepatic transaminases. The authors concluded that orlistat is effective for weight reduction, has an acceptable safety profile, and is useful as a complement to lifestyle changes such as diet and physical activity (Jain et al., 2011).

The American Gastroenterological Association (AGA) suggests that orlistat should not be used in obese or overweight adults with metabolic comorbidities, due to its limited efficacy in inducing clinically significant weight loss. Studies have shown that although orlistat may promote modest weight reduction, its effects are generally lower than those observed with other more recent pharmacologic therapies and strongly depend on adherence to lifestyle changes. However, patients who attach greater value to the potential benefit of weight loss and less importance on gastrointestinal adverse effects may consider orlistat as a viable therapeutic option (Grunvald et al., 2022b).



Amfepramone

The active ingredient of this drug acts predominantly by stimulating dopaminergic neurons, promoting an increase in the release of dopamine in presynaptic terminals, a mechanism directly associated with its action on the central nervous system (Naccarato; Lago, 2014b; Silva; Silva; Oyama, 2013a).

It is a derivative of β -phenethylamine, with chemical structure similar to that of the neurotransmitters norepinephrine ($C_9H_{13}NO_3$) and dopamine ($C_8H_{11}NO_2$), as well as amphetamines, which confers anorexogenic Properties to the drug. The dopaminergic action of the drug exerts a direct influence on the hypothalamic centers that regulate appetite and satiety, thereby modulating these mechanisms and contributing to reduced food intake. This action is particularly important in clinical contexts where control of hunger and eating behavior is required. From a pharmacokinetic point of view, the compound is rapidly absorbed in the gastrointestinal tract, which favors the early onset of therapeutic effects. After metabolism, elimination occurs mainly by renal route, with urinary excretion (Melo, 2021; Naccarato; Lago, 2014; Purifarma, 2018).

The drug is administered orally, at a dose of 25 mg, three times daily, one hour before meals. The dosage can reach up to 120 mg per day, when prescribed by a doctor, according to individual needs (Purifarma, 2018). However, its use requires caution because studies report several associated adverse effects. Among the most frequently observed events are: cardiac arrhythmias, nervousness, psychomotor agitation, insomnia, tachycardia, and gastrointestinal disorders, such as abdominal pain, nausea, vomiting, diarrhea, dry mouth, chills, palor, excitability, reduced libido, in rarer cases, psychotic manifestations (Purifarma, 2018; Soto-Molina et al., 2015). Given this safety profile, its use should be restricted and carried out exclusively under medical prescription, with strict supervision and continuous monitoring of therapeutic response and potential adverse effects (Naccarato; Lago, 2014c). Acting on the central nervous system, this drug should be used for a short duration, due to the potential serious side effects, high risk of abuse and dependence, as well as the possibility of triggering symptoms and psychiatric syndromes such as psychotic episodes and depressive episodes (Vasques; Martins; Azevedo, 2004). The cardiotoxicity associated with amphetamines and their derivatives may manifest as cardiomyopathy, arrhythmias, or acute myocardial infarction, especially in chronic users. These drugs raise noradrenaline levels and promote vascular



spasms, which can induce coronary vasoconstriction and precipitate ischemic events (Oliveira et al., 2010).

Sibutramine

Sibutramine is a drug indicated mainly for individuals with a body mass index (BMI) equal to or greater than 30 kg/m², or ≥ 27 kg/m², when associated with obesity-related comorbidities such as dyslipidemias, hypertension or type 2 diabetes. Its use is recommended when non-pharmacological interventions, such as a balanced diet and regular physical activity, fail to achieve adequate weight reduction. In Brazil, sibutramine is approved for the treatment of obesity and metabolic syndrome, and is considered a second-line therapeutic option (Nigro et al., 2021).

In this context, sibutramine, whose molecular formula is C₁₇H₂₆ClN, has the following chemical nomenclature: N-dimethyl-1-[1-(4-chlorophenyl)cyclobutyl]-N,3-trimethylbutan-1-amine. It is designated as a crystalline compound of milky-white crystalline compound, with an estimated water solubility of 2.9 mg/mL (Soares et al., 2022). Its absorption occurs in the gastrointestinal tract, while its biotransformation takes place in the liver, via cytochrome P450 isoenzymes. After the formation of the inactive metabolites, their main route of elimination is urinary excretion. The peak plasma concentration is reached approximately 3 to 4 hours after administration with a half-life of 14 to 16 hours (Costa; Duarte, 2017).

The mechanism of action of sibutramine is based on the decreased reuptake of serotonin and norepinephrine in the central nervous system (Cruz, 2020). The drug belongs to the class of norepinephrine and serotonin (5-HT) reuptake inhibitors. Its action consists of blocking presynaptic norepinephrine and 5-HT transporters in the appetite and satiety centers located in the hypothalamus, which promotes reduced hunger by intensifying the anorexigenic effects of these neurotransmitters in the central nervous system (Duarte et al., 2020b).

The usual recommended dose for adults is 15 mg per day, orally. Doses higher than this value are not indicated, as they may cause significant adverse effects (Radaelli; Pedroso; Medeiros, 2016). Among the side effects most observed in clinical studies are: headache, dry mouth, constipation, insomnia, rhinitis, pharyngitis, and increased blood pressure (Soares; Júnior, 2021; Souza et al., 2017). In addition, it may be associated with increased systemic blood pressure and heart rate, changes that require strict monitoring, especially in individuals with elevated cardiovascular risk, as highlighted by Tomas et al., (2023), continuous medical



follow-up is essential to assess the evolving risk-benefit profile and to ensure therapeutic safety during treatment.

Initially developed as an antidepressant, sibutramine did not demonstrate satisfactory clinical efficacy in this use. However, during the preliminary studies, significant weight loss was observed in the participants, which redirected its use to the treatment of obesity (Souza et al., 2017). Subsequent clinical studies indicated that the weight loss promoted by the drug is moderate, especially when associated with dietary restriction and the adoption of healthy lifestyle habits (Nigro et al., 2021).

Evidence indicates that sibutramine can be effective as an auxiliary agent in weight loss and maintenance in obese adolescents, as demonstrated by Franco et al., (2014). The authors conducted a double-blind, crossover clinical trial lasting 12 months, in which participants used sibutramine and placebo at different periods. During the subsequent six months, individuals who initiated sibutramine after placebo continued to lose weight, whereas those who discontinued the drug experienced weight regain. These findings indicate that sibutramine played a key role in maintaining weight loss, especially when adherence to lifestyle changes began to decrease. In summary, sibutramine may represent an effective therapeutic tool in the management of obesity.

Mazindol

Mazindol is a non-amphetamine anorectic agent, structurally classified as a tricyclic derivative. Its pharmacological action is comparable to that of antidepressants, although its clinical use is mainly aimed at appetite control. It acts predominantly on the central nervous system by inhibiting the reuptake of neurotransmitters, especially serotonin and norepinephrine, while promoting partial inhibition of dopaminergic activity (Lucchetta et al., 2017b; Pereira et al., 2012). This neurochemical modulation contributes to increased satiety, decreased appetite and, consequently, reduced food intake. There is also evidence that mazindol blocks gastric secretion, which may intensify its appetite-suppressing effect (Silva; Silva; Oyama, 2013b).

In addition to these mechanisms, it is believed that the drug is involved in the inhibition of glucose absorption and in the increase in locomotor activity, aspects that may additionally contribute to weight reduction (Silva; Silva; Oyama, 2013c). In terms of pharmacokinetics, mazindol has a slow but complete absorption, reaching serum concentrations of approximately 2.19 ng/mL about 8 hours after oral administration (Lucchetta et al., 2017c).



Regarding the safety profile, the most frequently reported adverse events include insomnia, headache, dry mouth, nausea, dizziness, irritability, palpitations, weakness, gastric discomfort, and hyperhidrosis. Due to its action on catecholaminergic pathways, the use of mazindol should be carefully monitored in patients with a history of cardiovascular disease, especially arrhythmias or arterial hypertension (Oliveira et al., 2009).

The effectiveness of mazindol in reducing body weight was demonstrated in a clinical study conducted by Tanaka et al., (2024), at a specialized clinic in Japan. The experimental research involved patients with severe obesity who were treated with the drug and followed longitudinally. The results demonstrated significant weight loss, as well as improvements in key metabolic parameters, such as fasting glucose and lipid profile parameters. Based on these findings, the authors suggest that mazindol may represent a promising therapeutic alternative in the treatment of severe obesity, provided that it is combined with strict medical supervision and multidisciplinary intervention strategies.

The study conducted by Huerta-Cruz et al., (2022) demonstrated that weight loss in the first month of treatment with mazindol and the timing of drug tolerance are good predictors of therapeutic efficacy. Patients who lost ≥ 4 kg in the first month and developed tolerance later (4th to 6th month) had better results. On the other hand, those with < 2 kg loss and early tolerance (up to the 3rd month) showed a poorer therapeutic response. These data reinforce the use of these parameters to adjust treatment early in patients with obesity.

Liraglutide and Semaglutide

The Food and Drug Administration (FDA) approved liraglutide for the treatment of obesity in adults in 2014 and later, in 2020, extended its indication to adolescents aged 12 years and older. Semaglutide was approved for chronic body weight control in adults in 2021, and its indication was expanded to adolescents (≥ 12 years) in 2022 (Chao et al., 2022; Novo Nordisk, 2022a, 2025).

These drugs belong to the class of GLP-1 analogues (GLP-1RAs), widely used in the treatment of type 2 diabetes and obesity. Both were developed based on the structure of GLP-1 (glucagon-like peptide-1), a human hormone that plays a key role in regulating blood glucose and satiety (Andersen; Knop; Vilsbøll, 2021b; Mahapatra; Karuppasamy; Sahoo, 2022). Semaglutide presents more efficient structural modifications than liraglutide to prolong its action. Among these modifications, the replacement of the amino acid in position 8 by α -



aminobutyric acid (Aib) stands out, which confers resistance to degradation by the enzyme dipeptidyl peptidase-4 (DPP-4), as well as the of a C18 fatty acid linked via a hydrophilic spacer, which increases its affinity for plasma albumin. These characteristics give semaglutide a half-life of approximately seven days, allowing once-weekly administration. In contrast, liraglutide, although it also modifies its structure with the replacement of arginine by lysine, has a shorter half-life, between 11 and 13 hours, requiring daily administration (Smith et al., 2019a).

Both semaglutide and liraglutide exert their effects by enhancing glucose-dependent insulin secretion and suppressing glucagon release (Del Olmo-Garcia; Merino-Torres, 2018; Shah; Vella, 2014). They also act in the central nervous system (CNS), where they exert a direct influence on hypothalamic centers that regulate appetite, hunger and satiety (Andraos; Muhar; Smith, 2023; Reddy; Stanwood; Galli, 2014).

Studies have shown that the use of GLP-1RAs is associated with decreased food intake, delayed gastric emptying, and increased secretion of anorexic hormones such as leptin and peptide YY, which play an important role in inducing satiety (Temple, 2022). Thus, in addition to improving glycemic control, semaglutide and liraglutide also act as modulators of eating behavior, being particularly useful in clinical contexts involving obesity and insulin resistance (Goldenberg; Steen, 2019; Knudsen; Lau, 2019; Smith et al., 2019b).

Regarding dosage, liraglutide is administered subcutaneously daily, with doses of up to 1.8 mg/day for the treatment of type 2 diabetes mellitus and 3.0 mg/day for the management of obesity. In turn, semaglutide is administered once weekly, at doses of up to 1.0 mg/week for type 2 diabetes mellitus and up to 2.4 mg/week for obesity management (Novo Nordisk, 2015, 2017, 2022b). Studies have shown that GLP-1 receptor agonists are associated with several adverse effects, particularly gastrointestinal disorders, including nausea, vomiting, diarrhea, constipation, dyspepsia, gastritis and, in rare cases, pancreatitis (Christou et al., 2019).

A randomized, double-blind, controlled clinical trial conducted by Rubino et al., (2022), evaluated the efficacy and safety of semaglutide 2.4 mg given once weekly compared to liraglutide 3.0 mg given daily in overweight or obese adults without type 2 diabetes. The sample consisted of 338 individuals with a body mass index (BMI) ≥ 30 kg/m² or ≥ 27 kg/m² with associated comorbidities. After 68 weeks of intervention, it was observed that the mean body weight reduction was 15.8% in semaglutide group and 6.4% in liraglutide group. It is concluded that weekly semaglutide demonstrated greater efficacy in weight reduction compared to daily



liraglutide, presenting a similar safety profile. These findings indicate once Weekly semaglutide demonstrated superior efficacy in weight reduction compared with once-day liraglutide, while exhibiting a comparable safety profile. Therefore, semaglutide represents a more effective therapeutic option for the treatment of obesity in adults without type 2 diabetes.

Tirzepatide

Tirzepatide is a synthetic molecule composed of 39 amino acids that acts as a agonist of GLP-1 (glucagon-like peptide type 1) and GIP (gastric inhibitor peptide) receptors, thereby enhancing body weight reduction and improving glycemic control. This combined action makes the drug a promising option for the management of obesity (Filho, 2024a; Horvatic, 2025).

The Brazilian Health Regulatory Agency (ANVISA) approved the use of tizerpatide for the treatment of overweight and obesity with comorbidities in Brazil. The decision, published in the Brazillian Official Gazette, expands the indication of the drug, already authorized since September 2023 for the treatment of type 2 diabetes (CFF, 2025; Filho, 2024b).

Regarding its action, GLP-1 is an incretin hormone secreted by the L cells of the small intestine in response to nutrient intake (Le Roux; Mondoh, 2024b). Its biological effects are mediated through activation of G-protein-coupled receptors, leading to increased intracellular cAMP levels and activation of protein kinase A (PKA). Among its main effects, it stimulates insulin secretion, suppresses glucagon release, delays gastric emptying, reduces food intake and modulates inflammatory processes (Jakubowska; Roux; Viljoen, 2024). GLP-1 receptors are also present in several brain regions associated with food reward and emotional regulation (Heppner et al., 2015a; Yapici-Eser et al., 2020). The glucose-dependent insulinotropic polypeptide (GIP) is released by intestinal K cells after meals (Inagaki et al., 1989a). It binds to G-protein-coupled receptors, promoting increase in intracellular cAMP, and calcium concentrations, and activation of the MAPK/ERK signaling pathways. It stimulates insulin secretion under normoglycemic and hyperglycemic conditions, enhances glucagon release, delays gastric emptying and exerts anabolic effects on adipose tissue by promoting lipogenesis and adipogenesis while inhibiting lipolysis (Drucker, 2006; Nicze et al., 2024a).

The drug is usually administered subcutaneously, once weekly at doses ranging from 5 to 15 mg. The substance has a prolonged half-life of approximately five days and demonstrates up to a five fold greater potency in GLP-1 receptor activation (Abdel-Malek; Yang; Miras, 2023). Clinical evidence indicates significantly greater efficacy in promoting weight loss and



glycemic control compared with conventional therapies. While insulin use may be associated with weight gain in certain patients with type 2 diabetes, clinical studies indicate that patients treated with tirzepatide achieved substantially greater mean weight loss and improved metabolic control, reinforcing its superiority as a therapeutic strategy for individuals with type 2 diabetes and concomitant obesity (Małeck et al., 2023; Sinha et al., 2023).

A systematic review evaluated tirzepatide in individuals with obesity without type 2 diabetes and demonstrated significant weight loss, as well as improvements in metabolic and cardiovascular parameters. The adverse events were predominately mild, transient gastrointestinal, suggesting good tolerability. The authors considered it a promising option for obesity treatment, although they recommended further long-term studies (Al Zweihary, 2024). In clinical trials, tirzepatide was shown to reduce appetite and body weight. The most frequently reported adverse events were nausea, vomiting, and diarrhea, usually mild and related to dose escalation. These findings suggest an acceptable safety profile, especially with gradual dose titration (Chavda et al., 2022).

As an example, in the study conducted by Wadden et al., (2023), 972 adults with a BMI ≥ 27 kg/m², without a diagnosis of type 2 diabetes participated in a 12 weeks intensive Lifestyle intervention. Of the participants, 579 who experienced $\geq 5\%$ loss of initial body weight were randomized to receive tirzepatide (10 mg or 15 mg) or placebo for 72 weeks. The tirzepatide-treated group achieved an additional mean weight loss of 18.4%, while the placebo group had a mean weight gain of 2.5%. In addition to significant weight reduction, participants who received tirzepatide showed clinically relevant improvements in cardiometabolic parameters and quality of life.

Evidence presented by Alawaji et al., (2025) reinforced the therapeutic potential of tirzepatide in the context of acute pancreatitis. Its experimental model, pancreatitis was induced by L-arginine, the use of the drug resulted in reduced serum concentrations of lipase and amylase, which are biomarkers of pancreatic injury. Histopathology presented biochemical data with structural changes in disease characteristics, including vacuolar degeneration, periductal fibrosis and lytic necrosis, with preservation of pancreatic architecture. Tirzepatide showed a protective effect, associated with modulation of inflammatory pathways and control of oxidative stress. There was a decrease in the amount of pro-inflammatory cytokines, such as IL-6, accompanied by an increase in anti-inflammatory cytokines, such as IL-4 and IL-10,



suggesting a balance of inflammatory response. In addition, a reduction of reactive oxygen species was observed, which indicated less oxidative damage to the pancreatic tissue.

Retatrutide

A new drug that has been studied is retatrutide, currently in phase III clinical development and not yet approved by the FDA. This stage of development is mainly due to the need to complete large-scale, rigorous phase III clinical trials, expected to continue through 2025 (Abdul-Rahman et al., 2024; Scott; Bloom, 2018).

Retatrutide (RETA; LY3437943) is a 39-amino-acid peptide conjugated to a C20 diacid fatty moiety. It is a recombinant protein engineered to function as a triple agonist of the human GIP, GLP-1, and glucagon (GCG) receptors. This means that it simultaneously activates three key biological pathways involved in the regulation of appetite, glucose metabolism, and adipose tissue homeostasis (Jastreboff et al., 2023; Urva et al., 2022b).

GLP-1, as previously described, has important effects such as stimulation insulin secretion, suppressing glucagon release, delaying gastric emptying and reduction food intake. Its receptors are also distributed in brain areas associated with food reward and emotional regulation (Heppner et al., 2015b; Kappe et al., 2012; Müller et al., 2019). Glucose-dependent insulinotropic polypeptide (GIP) is an incretin hormone secreted after meals (Inagaki et al., 1989b). Its receptors are mainly present in pancreatic β cells, as well as in adipose and nervous tissue. GIP stimulates insulin secretion under and hyperglycemic conditions, contributes to appetite reduction through delayed gastric emptying, and acts synergistically with GLP-1 (Nicze et al., 2024b). However, unlike GLP-1, it also increases glucagon secretion. In adipose tissue, it promotes adipogenesis and inhibits lipolysis (Müller et al., 2018). Glucagon is a hormone produced mainly in pancreatic α cells (Jakubowska; Roux; Viljoen, 2024b). Its release is induced by low levels of glucose, acting mainly in the liver through G-protein-coupled receptors. It promotes glycogenolysis and gluconeogenesis, and inhibits hepatic glycogenesis, thereby increasing blood glucose levels (Christensen et al., 2011). In adipose tissue, it stimulates lipolysis and ketogenesis, while reducing lipogenesis. It also influences brown fat thermogenesis, although its effects in humans still lack robust clinical relevance (Newsome; Ambrey, 2023).

By activating GLP-1 and GIP receptors, retratutide improves glycemic control and contributes to body weight reduction, while concomitant glucagon receptor agonism may



reduce hepatic fat by stimulating fat acids oxidation and reducing hepatic lipogenesis (Boland et al., 2020; Urva et al., 2022c).

The pharmacokinetics of retatrutide demonstrate dose-proportional exposure with a half-life of approximately 6 days, which enables once-weekly subcutaneous administration (Urva et al., 2022).

The phase II clinical study, evaluated 24 weeks of treatment with weekly retatrutide doses ranging from 1, 4, 8 to 12 mg. Doses were escalated over the first 4 to 8 weeks, especially at the highest doses (8 and 12 mg), to minimize gastrointestinal adverse effects. There was a mean body weight reduction of up to 25.9% after 48 weeks at a dose of 12 mg. Reductions in liver fat occurred predominantly during the first 24 weeks, paralleling weight loss. Most common adverse effects were: nausea, diarrhea, vomiting and constipation, with greater intensity at high doses, leading to discontinuation in some cases (Ye; Scherer, 2013).

Encouraging findings with retatrutide have led to the development of a series of phase III clinical trials, collectively termed the TRIUMPH program, designed to evaluate its efficacy and safety across diverse population. TRIUMPH-1 aims to recruit approximately 2,300 participants with obesity or overweight by May 2026. TRIUMPH-2 will include nearly 1,000 individuals with type 2 diabetes and obstructive sleep apnea, also scheduled for completion in 2026. The TRIUMPH-3 will assess weight variation in individuals with obesity and established cardiovascular disease, and is expected to conclude February 2026. TRIUMPH-4 will target those with knee osteoarthritis, with estimated completion in December 2025. In addition to evaluating weight-loss efficacy, these studies will investigate longitudinal changes in body composition during the treatment, given that loss of lean mass may compromise metabolic and functional health and quality of life (Count; Hall; Klein, 2024; Locatelli et al., 2024; Mechanick et al., 2025; Prado et al., 2024).

Bimagrumab

Bimagrumab is a recently investigated, fully human monoclonal antibody. Its mechanism of action involves binding to activin type II receptor (ActRII), thereby blocking endogenous ligands that inhibit skeletal muscle growth. In preclinical animal models, ActRII blockade demonstrated not only anabolic effects on skeletal muscle, but also extramuscular effects, including modulation of brown adipose tissue (BAT) differentiation and activity (Fournier et al., 2012; Rooks et al., 2017). In humans, bimagrumab has been shown to promote



an increases in lean mass accompanied by reductions in adiposity, counteracting the typical loss of muscle mass observed during diet-induced weight loss (Heymsfield et al., 2021b).

A single intravenous dose of bimagrumab in human participants increased lean mass, significantly reduced total body fat mass, and improved insulin sensitivity compared with placebo over a 10-week period in healthy volunteers with insulin resistance who were not dieting (Garito et al., 2018). These observations suggest that bimagrumab may represent a novel therapeutic strategy for obesity and related metabolic disorders. In a randomized phase II clinical trial of Heymsfield et al., (2021c) the effects of bimagrumab in 75 adults with obesity (BMI 28–40 kg/m²) and type 2 diabetes. Participants received monthly intravenous infusions of bimagrumab (10 mg/kg, up to a maximum of 1,200 mg) or placebo for 48 weeks, with both groups receiving standardized dietary counseling and physical activity guidance. The results showed that blockade of activin type II receptors (ActRII) by bimagrumab significantly reduced total body fat, increased lean mass, and improved glycemic control. These findings suggest a novel pharmacological approach for the treatment of obesity associated with type 2 diabetes.

At the American Diabetes Association (ADA) Scientific Sessions in June 2025, results from the BELIEVE study were presented, a randomized, double-blind, phase 2b clinical trial lasting 72 weeks. The study evaluated the efficacy of bimagrumab alone or in combination with semaglutide in 500 adults with obesity. Participants received semaglutide 1.0 or 2.4 mg once-weekly subcutaneous injection and/or intravenous (IV) infusions of bimagrumab 10 or 30 mg at weeks 4, 16, 28, and 40. The combination of bimagrumab and semaglutide resulted in approximately 22.1% total body weight reduction, of which 92.8% corresponded to fat mass, with preservation of lean mass. Common adverse effects of bimagrumab included muscle spasms, diarrhea, and acne, whereas semaglutide was associated with nausea, diarrhea, constipation, and fatigue (Heymsfield, 2025; Jackson, 2025). Despite the promising results of the BELIEVE study, bimagrumab has not yet received FDA approval, however, the observed efficacy suggests potential progression to phase III clinical trials in the coming years.

CONCLUSION

Obesity represents a growing and multifactorial public health, that requires therapeutic strategies beyond related behavioral modifications. Pharmacotherapy, as discussed in this study, constitutes an important tool for achieving and maintaining body weight reduction,



especially in individuals who do not obtain satisfactory results with dietary interventions and physical activity alone.

Currently available drugs and those under exhibit diverse mechanisms of action – from central modulation of satiety to modulation of nutrient absorption and complex hormonal pathways enabling a more personalized and effective therapeutic approach. Recent advances, such as dual and triple incretin receptor agonists, and agents such as bimagrumab, highlight expanding therapeutic potential.

Despite the advances, the use of anti-obesity medications should be guided by clearly defined clinical protocols, including careful risk–benefit assessment and continuous monitoring to prevent complications and optimize outcomes. The integration of pharmacological therapy with multidisciplinary follow-up and sustainable lifestyle modifications is essential to ensure long-term efficacy and patient safety.

REFERENCES

- ABDEL-MALEK, Mariana; YANG, Lisa; MIRAS, Alexander Dimitri. Pharmacotherapy for chronic obesity management: a look into the future. **Internal and Emergency Medicine**, v. 18, n. 4, p. 1019–1030, jun. 2023.
- ABDUL-RAHMAN, Toufik *et al.* The power of three: Retatrutide's role in modern obesity and diabetes therapy. **European Journal of Pharmacology**, v. 985, p. 177095, 15 dez. 2024.
- AL ZWEIHARY, Ali M. Safety and Effectiveness of Tirzepatide Use in Obesity Without Type 2 Diabetes Mellitus. **Cureus**, v. 16, n. 1, p. e51788, jan. 2024.
- ALAWAJI, Razan *et al.* Assessing the therapeutic potential of Tirzepatide in modulating inflammatory responses and mitigating acute pancreatitis. **Animal Models and Experimental Medicine**, v. 8, n. 10, p. 1876–1887, 20 out. 2025.
- ANDERSEN, Andreas; KNOP, Filip Krag; VILSBØLL, Tina. A Pharmacological and Clinical Overview of Oral Semaglutide for the Treatment of Type 2 Diabetes. **Drugs**, v. 81, n. 9, p. 1003–1030, jun. 2021.
- ANDRAOS, John; MUHAR, Harleen; SMITH, Shawn R. Beyond glycemia: Comparing tirzepatide to GLP-1 analogues. **Reviews in Endocrine & Metabolic Disorders**, v. 24, n. 6, p. 1089–1101, dez. 2023.
- ANVISA, Agência Nacional de Vigilância Sanitária. **JIFE Analisa Tráfico na Internet e faz Recomendações ao Brasil**. Brasília, , 2025.

3. CONSIDERAÇÕES FINAIS

A obesidade é um dos principais desafios contemporâneos em saúde pública, caracterizando-se por uma condição crônica, progressiva e multifatorial, que envolve interações complexas entre fatores genéticos, metabólicos, ambientais e comportamentais. Assim, estratégias terapêuticas baseadas exclusivamente em modificações do estilo de vida, mostram-se insuficientes para uma parcela significativa dos indivíduos, especialmente aqueles com obesidade clínica, caracterizada por maior gravidade com morbidades associadas.

Dessa forma, a farmacoterapia emergiu como uma abordagem relevante, no desempenho da promoção de perda de peso corporal, sobretudo, na manutenção a longo prazo. O uso é indicado para indivíduos que não alcançam resultados satisfatórios apenas com intervenções nutricionais e prática de atividade física, contribuindo, assim, para potencializar a redução da adiposidade, bem como para a melhora de parâmetros metabólicos e redução do risco cardiovascular.

Os fármacos atualmente disponíveis, assim como aqueles em desenvolvimento, apresentam mecanismos de ação distintos e complementares, que abrangem desde a modulação de centros hipotalâmicos relacionados à fome e saciedade até a interferência na absorção intestinal de nutrientes e na regulação de vias hormonais complexas, como as mediadas pelas incretinas. Nesse cenário, destacam-se avanços recentes envolvendo agonistas duplos e triplos de receptores de incretinas, que atuam simultaneamente em diferentes alvos metabólicos, potencializando os efeitos terapêuticos.

Entretanto, apesar dos avanços promissores, a utilização de medicamentos antiobesidade deve ser conduzida de forma criteriosa, baseada em protocolos clínicos bem estabelecidos e individualizados. Assim, torna-se imprescindível a realização de uma avaliação detalhada da relação risco-benefício, considerando as características clínicas dos indivíduos, possíveis efeitos adversos, contraindicações e interações medicamentosas. Além disso, o monitoramento contínuo é essencial para assegurar a eficácia do tratamento, prevenir complicações e ajustar a terapêutica conforme necessário.

Por fim, destaca-se que a abordagem da obesidade deve ser necessariamente integrada e multidisciplinar. A associação entre farmacoterapia, intervenções nutricionais, prática regular de atividade física e suporte psicológico constituem a base para resultados sustentáveis e

seguros. Tal integração não apenas potencializa a eficácia e duração do tratamento, mas também contribui para a melhoria da qualidade de vida, com concomitante redução do estigma frequentemente associado à obesidade.

4. REFERÊNCIAS

- ABDEL-MALEK, Mariana; YANG, Lisa; MIRAS, Alexander Dimitri. Pharmacotherapy for chronic obesity management: a look into the future. **Internal and Emergency Medicine**, v. 18, n. 4, p. 1019–1030, jun. 2023.
- ABDUL-RAHMAN, Toufik *et al.* The power of three: Retatrutide's role in modern obesity and diabetes therapy. **European Journal of Pharmacology**, v. 985, p. 177095, 15 dez. 2024.
- AL ZWEIHARY, Ali M. Safety and Effectiveness of Tirzepatide Use in Obesity Without Type 2 Diabetes Mellitus. **Cureus**, v. 16, n. 1, p. e51788, jan. 2024.
- ALAWAJI, Razan *et al.* Assessing the therapeutic potential of Tirzepatide in modulating inflammatory responses and mitigating acute pancreatitis. **Animal Models and Experimental Medicine**, v. 8, n. 10, p. 1876–1887, 20 out. 2025.
- ANDERSEN, Andreas; KNOP, Filip Krag; VILSBØLL, Tina. A Pharmacological and Clinical Overview of Oral Semaglutide for the Treatment of Type 2 Diabetes. **Drugs**, v. 81, n. 9, p. 1003–1030, jun. 2021.
- ANDRAOS, John; MUHAR, Harleen; SMITH, Shawn R. Beyond glycemia: Comparing tirzepatide to GLP-1 analogues. **Reviews in Endocrine & Metabolic Disorders**, v. 24, n. 6, p. 1089–1101, dez. 2023.
- ANASTÁCIO, Carine de Oliveira Avelar *et al.* Perfil nutricional de alimentos ultraprocessados consumidos por crianças no Rio de Janeiro. **Revista de Saúde Pública**, v. 54, p. 89–89, 4 set. 2020
- ANVISA, Agência Nacional de Vigilância Sanitária. **JIFE Analisa Tráfico na Internet e faz Recomendações ao Brasil**. Brasília, , 2025.
- ARTIGO | TIRZEPATIDA: EFICAZ CONTRA DIABETES E OBESIDADE. CRM-PB, [S.d.]**. Disponível em: <<https://crmpb.org.br/noticias/arr-tirzepatida-eficaz-contradiabetes-e-obesidade/>>. Acesso em: 10 ago. 2025
- ASSOCIAÇÃO BRASILEIRA PARA O ESTUDO DA OBESIDADE E SÍNDROME METABÓLICA. **Diretriz Brasileira de Tratamento Farmacológico da Obesidade**. São Paulo: ABESO, 2026. Disponível em: https://abeso.org.br/wp-content/uploads/2026/03/Diretrizes-ABESO_completo_20260320.pdf. Acesso em: 27 abr. 2026.
- BANSAL, Agam B.; PATEL, Preeti; AL KHALILI, Yasir. Orlistat. *In: StatPearls*. Treasure Island (FL): StatPearls Publishing, 2025.
- BARROS, Livia Moreira *et al.* Mudanças na qualidade de vida após a cirurgia bariátrica. **Revista de Enfermagem UFPE on line**, v. 7, n. 5, p. 1365–1375, 7 abr. 2013.
- BOLAND, Michelle L. *et al.* Resolution of NASH and hepatic fibrosis by the GLP-1R/GcgR dual-agonist Cotadutide via modulating mitochondrial function and lipogenesis. **Nature Metabolism**, v. 2, n. 5, p. 413–431, maio 2020.

BRASIL, Ministério da Saúde. **Boletim Epidemiológico**. Secretaria de Vigilância em Saúde e Ambiente, , 16 abr. 2024. Disponível em: <<https://www.gov.br/saude/pt-br/centrais-de-conteudo/publicacoes/boletins/epidemiologicos/edicoes/2024/boletim-epidemiologico-volume-55-no-07.pdf>>

CDC. **Adult Obesity Facts**. Disponível em: <<https://www.cdc.gov/obesity/adult-obesity-facts/index.html>>. Acesso em: 10 ago. 2025.

CFF, Conselho Federal de Farmácia. **Anvisa aprova Mounjaro para tratamento de obesidade e sobrepeso no Brasil**. , 2025.

CHAO, Ariana M. *et al.* Clinical Insight on Semaglutide for Chronic Weight Management in Adults: Patient Selection and Special Considerations. **Drug Design, Development and Therapy**, v. 16, p. 4449–4461, 2022.

CHAVDA, Vivek P. *et al.* Tirzepatide, a New Era of Dual-Targeted Treatment for Diabetes and Obesity: A Mini-Review. **Molecules**, v. 27, n. 13, p. 4315, 5 jul. 2022.

CHRISTENSEN, Mikkel *et al.* The Alpha-Cell as Target for Type 2 Diabetes Therapy. **The Review of Diabetic Studies : RDS**, v. 8, n. 3, p. 369, 10 nov. 2011.

CHRISTINELLI, Heloá Costa Borim *et al.* Eficácia de um programa de reeducação alimentar e prática de exercício físico na obesidade. **Revista Gaúcha de Enfermagem**, v. 41, p. e20190213, 20 nov. 2020.

CHRISTOU, Georgios A. *et al.* Semaglutide as a promising antiobesity drug. **Obesity Reviews: An Official Journal of the International Association for the Study of Obesity**, v. 20, n. 6, p. 805–815, jun. 2019.

CONTE, Caterina; HALL, Kevin D.; KLEIN, Samuel. Is Weight Loss-Induced Muscle Mass Loss Clinically Relevant? **JAMA**, v. 332, n. 1, p. 9–10, 2 jul. 2024.

COSTA, Alciêne Maria de Jesus; DUARTE, Stênio Fernando Pimentel. Principais Medicamentos Utilizados no tratamento da Obesidade e Vias de Ação: Uma Revisão Sistemática. **ID on line. Revista de psicologia**, v. 11, n. 35, p. 199–209, 28 maio 2017.

COSTA, André Falcão da *et al.* Riscos do uso indiscriminado de medicamentos anorexígenos: uma revisão sistemática da literatura / Risks of the indiscriminate use of anorexigenous medicines: a systematic review of the literature. **Brazilian Journal of Development**, v. 8, n. 5, p. 40718–40733, 25 maio 2022.

COSTA, Igor Martins *et al.* Uso de análogos de GLP-1 no tratamento da obesidade: uma revisão narrativa / Use of GLP-1 analogues in treatment of obesity: a narrative review. **Brazilian Journal of Health Review**, v. 4, n. 2, p. 4236–4247, 3 mar. 2021.

CRUZ, Fernanda do Carmo Santa. Perfil de segurança e eficácia da sibutramina e alternativas terapêuticas para o tratamento da obesidade no Brasil. 2020.

DEL OLMO-GARCIA, María Isabel; MERINO-TORRES, Juan Francisco. GLP-1 Receptor Agonists and Cardiovascular Disease in Patients with Type 2 Diabetes. **Journal of Diabetes Research**, v. 2018, p. 4020492, 2018.

Diretriz ABESO 2026: Estamos finalmente tratando a obesidade como doença crônica - Portal Afya. Disponível em: <<https://portal.afya.com.br/endocrinologia/diretriz-abeso-2026-estamos-finalmente-tratando-a-obesidade-como-doenca-cronica>>. Acesso em: 30 abr. 2026.

DRUCKER, Daniel J. The biology of incretin hormones. **Cell Metabolism**, v. 3, n. 3, p. 153–165, 1 mar. 2006.

DUARTE, Ana Paula Neves Bittencourt *et al.* Uso de anfepramona, femproporex, mazindol e sibutramina no Tratamento de pacientes com sobrepeso ou obesidade: análise Farmacológica e clínica. **International Journal of Health Management Review**, v. 6, n. 2, 2020.

ENDOCRINOLOGY, The Lancet Diabetes &. Redefining obesity: advancing care for better lives. **The Lancet Diabetes & Endocrinology**, v. 13, n. 2, p. 75, 1 fev. 2025.

FERNÁNDEZ MERÉ, L. Á.; ÁLVAREZ BLANCO, M. ^a. Obesidad y cirugía bariátrica: implicaciones anestésicas. **Nutrición Hospitalaria**, v. 19, n. 1, p. 34–44, fev. 2004.

FILHO, João Modesto. **TIRZEPATIDA: EFICAZ CONTRA DIABETES E OBESIDADE.** CRM-PB, , 2024.

FOURNIER, Brigitte *et al.* Blockade of the Activin Receptor IIB Activates Functional Brown Adipogenesis and Thermogenesis by Inducing Mitochondrial Oxidative Metabolism. **Molecular and Cellular Biology**, v. 32, n. 14, p. 2871–2879, jul. 2012.

FRANCO, Ruth Rocha; COMINATO, Louise; DAMIANI, Durval. O efeito da sibutramina na perda de peso de adolescentes obesos. **Arquivos Brasileiros de Endocrinologia & Metabologia**, v. 58, p. 243–250, abr. 2014.

GOLDENBERG, Ronald M.; STEEN, Oren. Semaglutide: Review and Place in Therapy for Adults With Type 2 Diabetes. **Canadian Journal of Diabetes**, v. 43, n. 2, p. 136–145, mar. 2019.

GRUNVALD, Eduardo *et al.* AGA Clinical Practice Guideline on Pharmacological Interventions for Adults With Obesity. **Gastroenterology**, v. 163, n. 5, p. 1198–1225, nov. 2022.

GUERCIOLINI, R. Mode of action of orlistat. **International Journal of Obesity and Related Metabolic Disorders: Journal of the International Association for the Study of Obesity**, v. 21 Suppl 3, p. S12-23, jun. 1997.

HACHEM, Aleeya; BRENNAN, Leah. Quality of Life Outcomes of Bariatric Surgery: A Systematic Review. **Obesity Surgery**, v. 26, n. 2, p. 395–409, fev. 2016.

HALL, Michael E. *et al.* Weight-Loss Strategies for Prevention and Treatment of Hypertension: A Scientific Statement From the American Heart Association. **Hypertension (Dallas, Tex.: 1979)**, v. 78, n. 5, p. e38–e50, nov. 2021.

HEPPNER, Kristy M. *et al.* Expression and distribution of glucagon-like peptide-1 receptor mRNA, protein and binding in the male nonhuman primate (Macaca mulatta) brain. **Endocrinology**, v. 156, n. 1, p. 255–267, jan. 2015.

HEYMSFIELD, S. **Resultados de Eficácia e Segurança do Estudo BELIEVE: Redução de Peso e Composição Corporal.** . Resultados do Estudo BELIEVE de Heymsfield S. apresentado em Sessões Científicas da American Diabetes Association **Anais...** . Chicago, 20 jun. 2025.

HEYMSFIELD, Steven *et al.* Effect of Bimagrumb vs Placebo on Body Fat Mass Among Adults With Type 2 Diabetes and Obesity: A Phase 2 Randomized Clinical Trial. **JAMA Network Open**, v. 4, p. e2033457, 13 jan. 2021.

HO, Yiling *et al.* Synergistic Effects of Time-Restricted Feeding and Resistance Training on Body Composition and Metabolic Health: A Systematic Review and Meta-Analysis. **Nutrients**, v. 16, n. 18, p. 3066, 11 set. 2024.

HORVATICH, Guilherme. **Anvisa aprova Mounjaro para tratamento de obesidade e sobrepeso no Brasil.** Disponível em: <<https://site.cff.org.br/noticia/Noticias-gerais/09/06/2025/anvisa-aprova-mounjaro-para-tratamento-de-obesidade-e-sobrepeso-no-brasil>>. Acesso em: 10 ago. 2025.

HUERTA-CRUZ, Juan Carlos *et al.* Combined First Month Body Weight Loss and Development of Tolerance as Predictors of 6-Month Efficacy of Mazindol in Mild and Moderate Obese Subjects. **Journal of Clinical Medicine**, v. 11, n. 11, p. 3211, jan. 2022.

IBGE, Coordenação de Trabalho e (ORG.). **Pesquisa Nacional de Saúde.** Rio de Janeiro, RJ: Ibge, 2021.

INAGAKI, Nobuya *et al.* Gastric Inhibitory Polypeptide: Structure and Chromosomal Localization of the Human Gene. **Molecular Endocrinology**, v. 3, n. 6, p. 1014–1021, 1 jun. 1989.

JACKSON, Vitória. **A combinação Bimagrumb/Semaglutida proporciona perda substancial de massa gorda e preserva a massa magra.** HCP Live, , 2025. Disponível em: <<https://www.hcplive.com/view/believe-bimagrumb-semaglutide-combo-yields-substantial-fat-mass-weight-loss-preserves-lean-mass>>

JAIN, SuyogS *et al.* Evaluation of efficacy and safety of orlistat in obese patients. **Indian Journal of Endocrinology and Metabolism**, v. 15, n. 2, p. 99, 2011.

JAKUBOWSKA, Agnieszka; ROUX, Carel W. le; VILJOEN, Adie. The Road towards Triple Agonists: Glucagon-Like Peptide 1, Glucose-Dependent Insulinotropic Polypeptide and Glucagon Receptor - An Update. **Endocrinology and Metabolism**, v. 39, n. 1, p. 12–22, 14 fev. 2024.

JASTREBOFF, Ania M. *et al.* Triple-Hormone-Receptor Agonist Retatrutide for Obesity - A Phase 2 Trial. **The New England Journal of Medicine**, v. 389, n. 6, p. 514–526, 10 ago. 2023.

KAPPE, Camilla *et al.* GLP-1 secretion by microglial cells and decreased CNS expression in obesity. **Journal of Neuroinflammation**, v. 9, n. 1, p. 276, 23 dez. 2012.

KNUDSEN, Lotte Bjerre; LAU, Jesper. The Discovery and Development of Liraglutide and Semaglutide. **Frontiers in Endocrinology**, v. 10, 12 abr. 2019.

Lara Letíciaa Cardoso De Oliveira. EFEITO REBOTE DAS DIETAS RESTRITIVAS EM MULHERES. 24 nov. 2023.

LE ROUX, Carel; MONDOH, Alvin. Treatment of obesity with medications binding the glucagon-like peptide 1 receptor: what is the current state of play? **Expert Opinion on Pharmacotherapy**, v. 25, n. 2, p. 131–138, 22 jan. 2024.

LOCATELLI, João Carlos *et al.* Incretin-Based Weight Loss Pharmacotherapy: Can Resistance Exercise Optimize Changes in Body Composition? **Diabetes Care**, v. 47, n. 10, p. 1718–1730, 1 out. 2024.

LONDOÑO-LEMO, Milton Enrique. Tratamiento farmacológico contra la obesidad. **Revista Colombiana de Ciencias Químico-Farmacéuticas**, v. 41, n. 2, p. 217–261, 1 jul. 2012.

LUCAS, Bárbara Belmiro. Farmacoterapia da obesidade: uma revisão da literatura. 28 maio 2019.

LUCCHETTA, Rosa Camila *et al.* Systematic review and meta-analysis of the efficacy and safety of amfepramone and mazindol as a monotherapy for the treatment of obese or overweight patients. **Clinics (Sao Paulo, Brazil)**, v. 72, n. 5, p. 317–324, maio 2017.

MAHAPATRA, Manoj Kumar; KARUPPASAMY, Muthukumar; SAHOO, Biswa Mohan. Semaglutide, a glucagon like peptide-1 receptor agonist with cardiovascular benefits for management of type 2 diabetes. **Reviews in Endocrine & Metabolic Disorders**, v. 23, n. 3, p. 521–539, jun. 2022.

MAŁECKI, Maciej T. *et al.* Predictors of $\geq 15\%$ Weight Reduction and Associated Changes in Cardiometabolic Risk Factors With Tirzepatide in Adults With Type 2 Diabetes in SURPASS 1-4. **Diabetes Care**, v. 46, n. 12, p. 2292–2299, 1 dez. 2023.

MARQUES, Danielle de Oliveira; QUINTILIO, Maria Salete Vaceli. FARMACOLOGIA DA OBESIDADE E RISCOS DAS DROGAS PARA EMAGRECER. **Revista Coleta Científica**, v. 5, n. 9, p. 38–49, 12 jul. 2021.

MECHANICK, Jeffrey I. *et al.* Strategies for minimizing muscle loss during use of incretin-mimetic drugs for treatment of obesity. **Obesity Reviews: An Official Journal of the International Association for the Study of Obesity**, v. 26, n. 1, p. e13841, jan. 2025.

MELO, Josylane Vargas Martins. OS EFEITOS DOS ANOREXÍGENOS NO TRATAMENTO DA OBESIDADE. 2021.

MOSCHONIS, George; TRAKMAN, Gina Louise. Overweight and Obesity: The Interplay of Eating Habits and Physical Activity. **Nutrients**, v. 15, n. 13, p. 2896, 27 jun. 2023.

MÜLLER, T. D. *et al.* Anti-Obesity Therapy: from Rainbow Pills to Polyagonists. **Pharmacological Reviews**, v. 70, n. 4, p. 712–746, 1 out. 2018.

MÜLLER, T. D. *et al.* Glucagon-like peptide 1 (GLP-1). **Molecular Metabolism**, v. 30, p. 72–130, 1 dez. 2019.

NACCARATO, Monique Campos; LAGO, Eloi Marcos de Oliveira. USO DOS ANOREXÍGENOS ANFEPRAMONA E SIBUTRAMINA: BENEFÍCIO OU PREJUÍZO À SAÚDE? **Revista Saúde - UNG-Ser - ISSN 1982-3282**, v. 8, n. 1–2, p. 66–72, 29 ago. 2014.

NEWSOME, Philip N.; AMBERY, Phil. Incretins (GLP-1 receptor agonists and dual/triple agonists) and the liver. **Journal of Hepatology**, v. 79, n. 6, p. 1557–1565, 1 dez. 2023.

NICZE, Michał *et al.* Molecular Mechanisms behind Obesity and Their Potential Exploitation in Current and Future Therapy. **International Journal of Molecular Sciences**, v. 25, n. 15, p. 8202, jan. 2024.

NIGRO, Ana Helena Lancellotti *et al.* Medicamentos utilizados no tratamento da obesidade: revisão da Literatura. **International Journal of Health Management Review**, v. 7, n. 3, 2021.

NOVO NORDISK. **WEGOVY (semaglutide) injection, for subcutaneous use Initial.** , 2022.

NOVO NORDISK. **Saxenda liraglutide injection 3mg.** , 2025.

OLIVEIRA, Fernanda Brandão de *et al.* Infarto agudo do miocárdio após uso de anfepramona. **Rev. bras. cardiol. (Impr.)**, p. 362–364, 2010.

OLIVEIRA, Raquel Cordeiro de *et al.* A farmacoterapia no tratamento da obesidade. **RBONE - Revista Brasileira de Obesidade, Nutrição e Emagrecimento**, v. 3, n. 17, 2009.

PEREIRA, Fabíola *et al.* Avaliação de prescrições de anorexígenos em farmácia magistral. v. 93, p. 481–486, 2 dez. 2012.

POPKIN, Barry M.; ADAIR, Linda S.; NG, Shu Wen. NOW AND THEN: The Global Nutrition Transition: The Pandemic of Obesity in Developing Countries. **Nutrition Reviews**, v. 70, n. 1, p. 3–21, jan. 2012.

PRADO, Carla M. *et al.* Muscle matters: the effects of medically induced weight loss on skeletal muscle. **The Lancet. Diabetes & Endocrinology**, v. 12, n. 11, p. 785–787, nov. 2024.

PURIFARMA. **Anfepramona HCL.** , 2018.

RABACOW, Fabiana M.; AZEREDO, Catarina M.; REZENDE, Leandro F. M. Deaths Attributable to High Body Mass in Brazil. *Preventing Chronic Disease*, [s. l.], v. 16, p. 190143, 17 out. 2019. DOI: <http://dx.doi.org/10.5888/pcd16.190143>. Disponível em: https://www.cdc.gov/pcd/issues/2019/19_0143.htm. Acesso em: 28 abr. 2026.

RADAELLI, Maqueli; PEDROSO, Roberto Costa; MEDEIROS, Liciane Fernandes. Farmacoterapia da obesidade: Benefícios e Riscos. **Saúde e Desenvolvimento Humano**, v. 4, n. 1, p. 101–115, 3 maio 2016.

REDDY, India A.; STANWOOD, Gregg D.; GALLI, Aurelio. Moving beyond energy homeostasis: new roles for glucagon-like peptide-1 in food and drug reward. **Neurochemistry International**, v. 73, p. 49–55, jul. 2014.

ROOKS, Daniel S. *et al.* Effect of bimagrumab on thigh muscle volume and composition in men with casting-induced atrophy. **Journal of Cachexia, Sarcopenia and Muscle**, v. 8, n. 5, p. 727–734, out. 2017.

RUBINO, Domenica M. *et al.* Effect of Weekly Subcutaneous Semaglutide vs Daily Liraglutide on Body Weight in Adults With Overweight or Obesity Without Diabetes. **JAMA**, v. 327, n. 2, p. 138–150, 11 jan. 2022.

SANTANA, Gracielle Silva *et al.* Alvos moleculares dos fármacos utilizados na perda de peso dos pacientes com obesidade. **Cuadernos de Educación y Desarrollo**, v. 17, n. 1, p. e7220–e7220, 13 jan. 2025.

SANTIAGO, Luciana Alves Cangerana; CYRILLO, Denise Cavallini; CERVATO-MANCUSO, Ana Maria. A dieta restrita como fator interveniente na adesão ao tratamento para perda de peso. **Revista da Associação Brasileira de Nutrição - RASBRAN**, v. 14, n. 1, p. 1–11, 2023.

SCOTT, R. V.; BLOOM, S. R. Problem or solution: The strange story of glucagon. **Peptides**, Newer peptide-based agents for treatment of patients with Type 2 diabetes. v. 100, p. 36–41, 1 fev. 2018.

SHAH, Meera; VELLA, Adrian. Effects of GLP-1 on appetite and weight. **Reviews in Endocrine & Metabolic Disorders**, v. 15, n. 3, p. 181–187, set. 2014.

SILVA, Antônia Vanessa Ferreira; SANTOS, Laryssa Bispo dos; QUEIROZ, Fellipe José Gomes. Os riscos do uso de medicações para o emagrecimento. **Revista JRG de Estudos Acadêmicos**, v. 5, n. 11, p. 56–66, 25 set. 2022.

SILVA, Luciana Fernandes Oliveira da; SILVA, Francinie Valeska Mendes da; OYAMA, Silvia Maria Ribeiro. Prevalência do uso de medicamentos para emagrecer entre universitárias. **Revista Recien - Revista Científica de Enfermagem**, v. 3, n. 7, p. 19–26, 5 abr. 2013.

SILVA, Thays Alves da; BAIENSE, Alex Sandro Rodrigues; ANDRADE, Leonardo Guimarães de. AUTOMEDICAÇÃO DE ANOREXÍGENOS E SEUS EFEITOS COLATERAIS. **Revista Ibero-Americana de Humanidades, Ciências e Educação**, v. 9, n. 4, p. 1828–1845, 29 abr. 2023.

SINHA, Rachel *et al.* Efficacy and Safety of Tirzepatide in Type 2 Diabetes and Obesity Management. **Journal of Obesity & Metabolic Syndrome**, v. 32, n. 1, p. 25–45, 30 mar. 2023.

SMITH, Nicholas K. *et al.* GLP-1: Molecular mechanisms and outcomes of a complex signaling system. **Neurochemistry International**, v. 128, p. 94–105, set. 2019.

SOARES, Jessyane De Freitas *et al.* Uma revisão de literatura sobre o uso da sibutramina, sua eficácia e os riscos na terapêutica na obesidade. **Research, Society and Development**, v. 11, n. 12, p. e253111234599, 13 set. 2022.

SOARES, Sayra Ferreira; JÚNIOR, Omero Martins Rodrigues. O comparativo da anfepramona e da sibutramina no tratamento da obesidade / The comparison of amphepramone and sibutramine in the treatment of obesity. **Brazilian Journal of Development**, v. 7, n. 11, p. 106917–106927, 22 nov. 2021.

SOUSA, Débora Tahais da Conceição *et al.* Risco do uso indiscriminado de medicamentos para emagrecimento / Risk of indiscriminate use of medicines for slimming. **Brazilian Journal of Health Review**, v. 4, n. 6, p. 28589–28602, 21 dez. 2021.

SOTO-MOLINA, Herman *et al.* Six-month efficacy and safety of amfepramone in obese Mexican patients: a double-blinded, randomized, controlled trial. **International Journal of Clinical Pharmacology and Therapeutics**, v. 53, n. 7, p. 541–549, jul. 2015.

SOUZA, Syliana Sana Silva de *et al.* Sibutramina: falhas e incompletude de documentos na prescrição e dispensação. **Revista de Atenção à Saúde**, v. 15, n. 51, p. 23–33, 15 fev. 2017.

TANAKA, Yoshimitsu *et al.* Changes in Body Weight in Severely Obese Patients Treated with the Anorexiant Mazindol. **Journal of Clinical Medicine**, v. 13, n. 7, p. 1860, 23 mar. 2024.

TEMPLE, Norman J. The Origins of the Obesity Epidemic in the USA-Lessons for Today. **Nutrients**, v. 14, n. 20, p. 4253, 12 out. 2022.

The practical guide: Identification, evaluation, and treatment of overweight and obesity in adults. National Institutes of Health (NIH), National Heart, Lung, and Blood institute (NHLBI), Bethesda, 2000.

TOMAS, Ramon Faria *et al.* O USO DOS ANÁLOGOS DE GLP-1 NO TRATAMENTO DA OBESIDADE: UMA REVISÃO DE LITERATURA. **Revista Ibero-Americana de Humanidades, Ciências e Educação**, v. 9, n. 4, p. 1063–1073, 29 abr. 2023.

TOKARNIA, Mariana. **Um a cada três brasileiros vive com obesidade, mostra relatório global**. Agência Brasil, Rio de Janeiro, 4 mar. 2025. Disponível em: <https://agenciabrasil.ebc.com.br/saude/noticia/2025-03/um-cada-tres-brasileiros-vive-com-obesidade-mostra-relatorio-global>. Acesso em: 30 abr. 2026.

URVA, Shweta *et al.* LY3437943, a novel triple GIP, GLP-1, and glucagon receptor agonist in people with type 2 diabetes: a phase 1b, multicentre, double-blind, placebo-controlled, randomised, multiple-ascending dose trial. **Lancet (London, England)**, v. 400, n. 10366, p. 1869–1881, 26 nov. 2022.

VARGAS, Mariana Alves e *et al.* Análise dos efeitos adversos associados ao uso do anorexígeno sibutramina: revisão sistemática. **Journal of Health & Biological Sciences**, v. 6, n. 3, p. 313–326, 2 jul. 2018.

VASQUES, Fátima; MARTINS, Fernanda Celeste; AZEVEDO, Alexandre Pinto de. Aspectos psiquiátricos do tratamento da obesidade. **Archives of Clinical Psychiatry (São Paulo)**, v. 31, p. 195–198, 2004.

WADDEN, Thomas A. *et al.* Tirzepatide after intensive lifestyle intervention in adults with overweight or obesity: the SURMOUNT-3 phase 3 trial. **Nature Medicine**, v. 29, n. 11, p. 2909–2918, nov. 2023.

WARD, Zachary J. *et al.* Excess mortality associated with elevated body weight in the USA by state and demographic subgroup: A modelling study. **EClinicalMedicine**, v. 48, p. 101429, jun. 2022.

WHO. **Health Emergency appeal.** , 2024. Disponível em: <<https://www.who.int/news-room/events/detail/2024/01/15/default-calendar/who-s-health-emergency-appeal-2024>>

World Obesity Atlas, 2025. , [S.d.]. Disponível em: <https://s3-eu-west-1.amazonaws.com/wof-files/World_Obesity_Atlas_2025_rev1.pdf>. Acesso em: 15 set. 2025

WORLD HEALTH ORGANIZATION. Obesity and overweight. Genebra: WHO, 2025. Disponível em: <https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight>. Acesso em: 28 abr. 2026.

WORLD OBESITY FEDERATION, Atlas Mundial da Obesidade. **Obesity and Overweight.** Londres: Federação Mundial da Obesidade, 2025.

YAPICI-ESER, Hale *et al.* Association between GLP-1 receptor gene polymorphisms with reward learning, anhedonia and depression diagnosis. **Acta Neuropsychiatrica**, v. 32, n. 4, p. 218–225, ago. 2020.

YE, Risheng; SCHERER, Philipp E. Adiponectin, driver or passenger on the road to insulin sensitivity? **Molecular Metabolism**, v. 2, n. 3, p. 133–141, 19 abr. 2013.

ZILBERSTEIN, Bruno; RAMOS, Almino Cardoso; GALVAO NETO, Manoel. O papel da cirurgia no tratamento da obesidade. **RBM - Revista Brasileira de Medicina**, v. 59, n. 4, p. 258–264, 2002.

5. ANEXOS

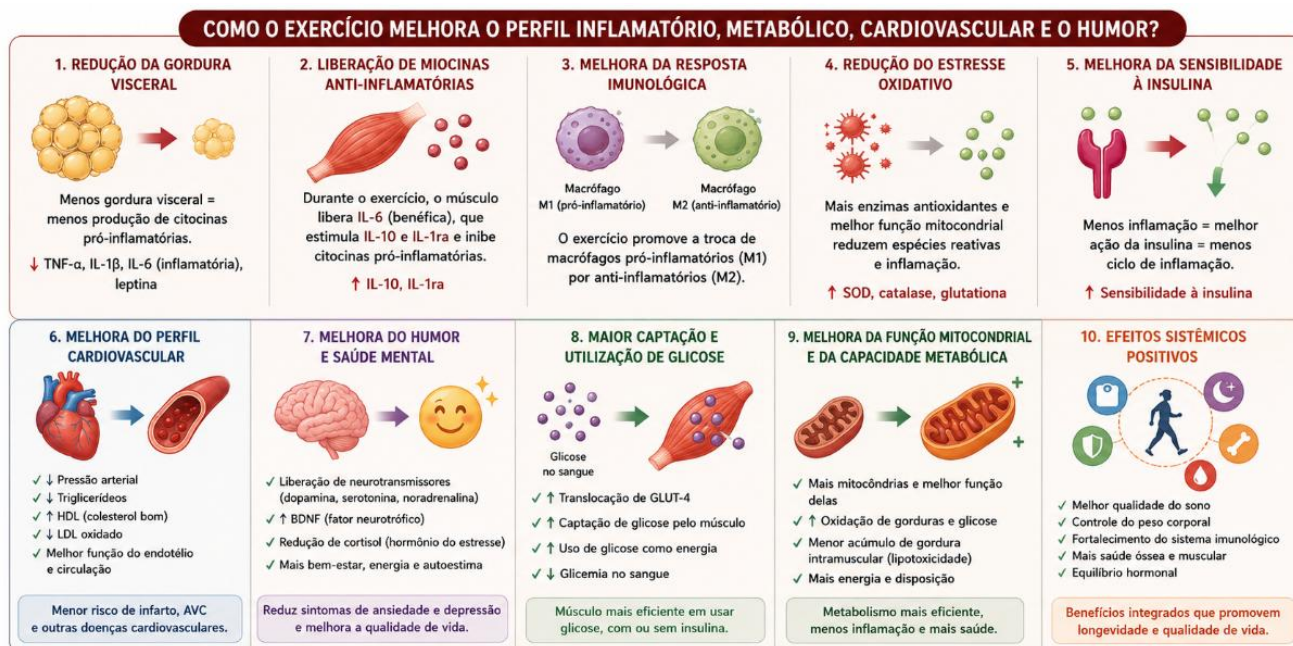


Figura 1 – Principais benefícios fisiológicos promovidos pelo exercício físico no organismo humano. Fonte: Figura produzida com auxílio de inteligência artificial generativa (OpenAI, 2026), a partir da sistematização de evidências provenientes da literatura científica consultada pelos autores.

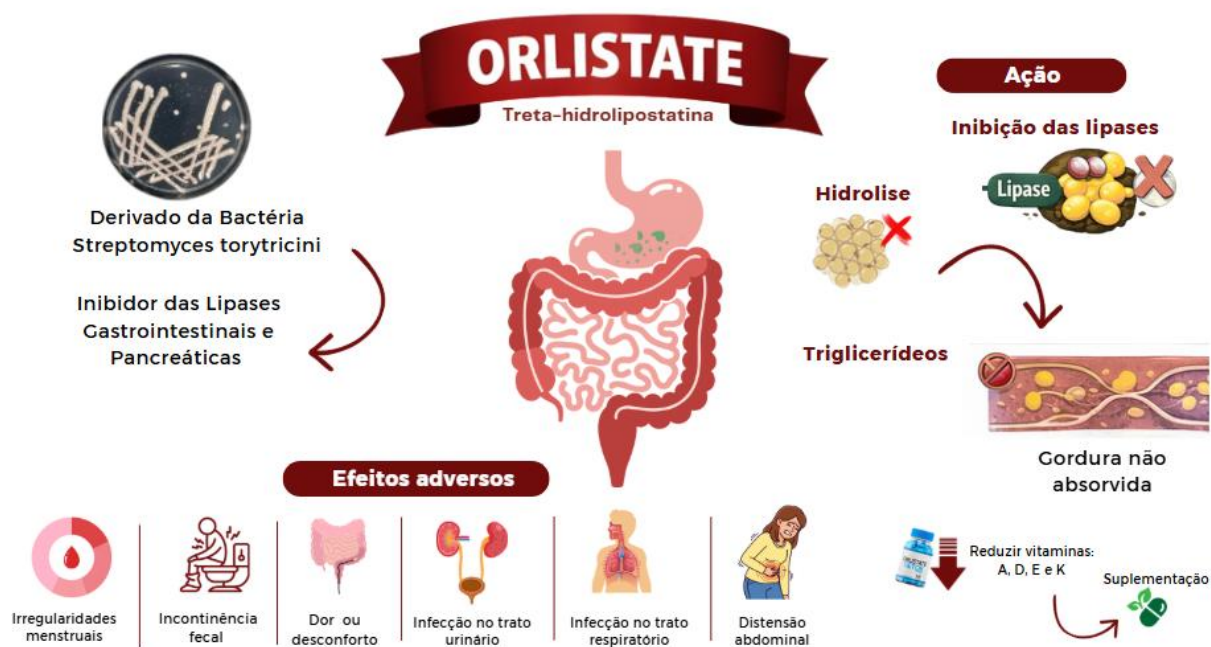


Figura 2 – Orlistate, atuação fisiológica e efeitos colaterais. Fonte: Produzida pelo autor no Canva (Plataforma de design gráfico, 2026), com base nos conhecimentos descritos na literatura científica.



Figura 3 – Anfepramona, atuação fisiológica e efeitos colaterais. Fonte: Produzida pelo autor no Canva (Plataforma de design gráfico, 2026), com base nos conhecimentos descritos na literatura científica.



Figura 4 – Sibutramina, atuação fisiológica e efeitos colaterais. Fonte: Produzida pelo autor no Canva (Plataforma de design gráfico, 2026), com base nos conhecimentos descritos na literatura científica.

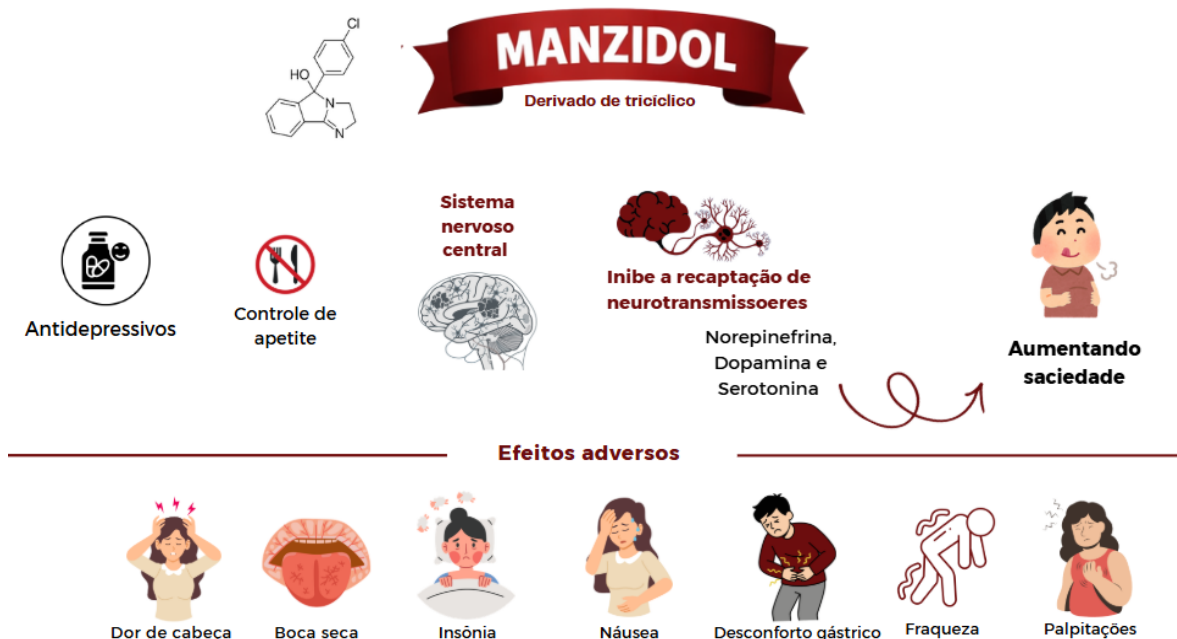


Figura 5 – Manzidol, atuação fisiológica e efeitos colaterais. Fonte: Produzida pelo autor no Canva (Plataforma de design gráfico, 2026), com base nos conhecimentos descritos na literatura científica.

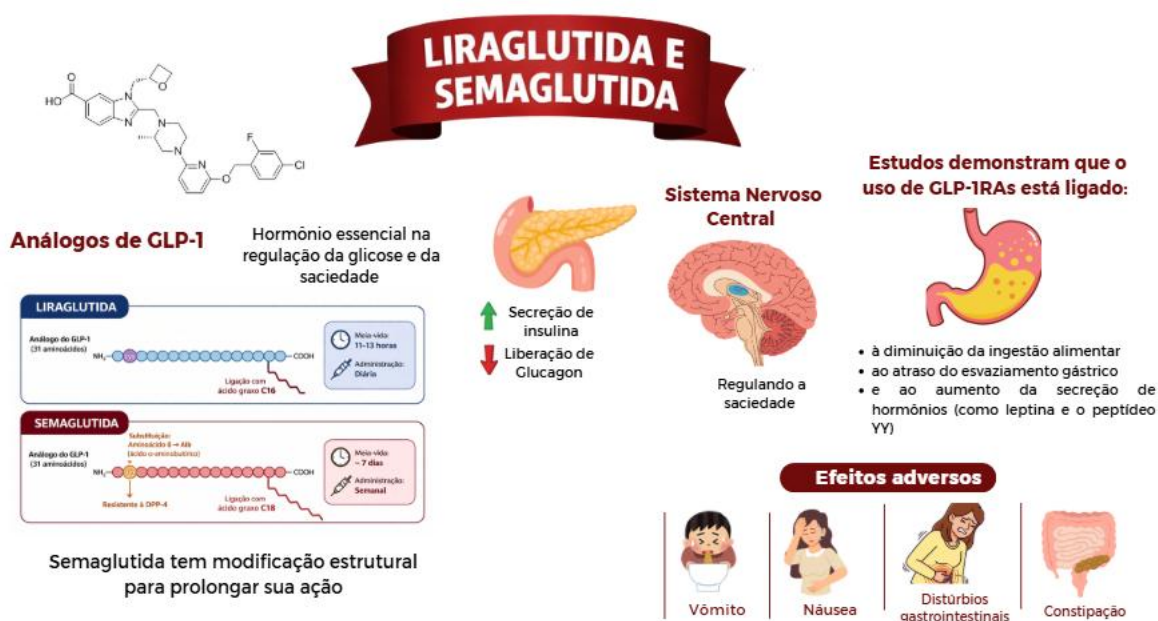


Figura 6 – Liraglutida e Semaglutida, atuação fisiológica e efeitos colaterais. Fonte: Produzida pelo autor no Canva (Plataforma de design gráfico, 2026), com base nos conhecimentos descritos na literatura científica.

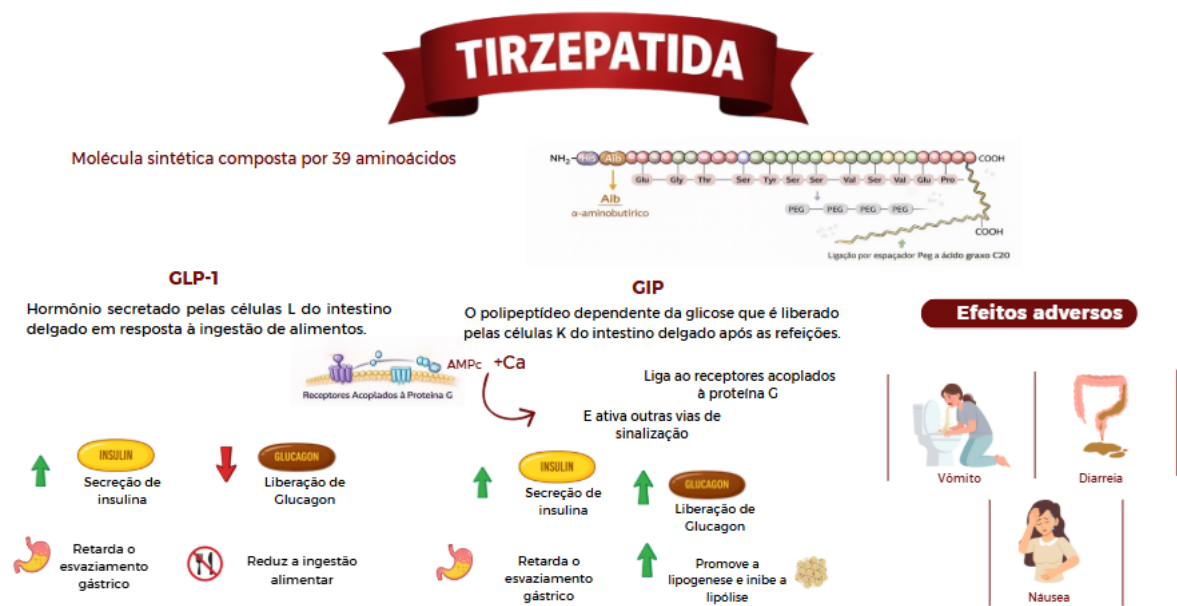


Figura 7 – Tizerpartida, atuação fisiológica e efeitos colaterais. Fonte: Produzida pelo autor no Canva (Plataforma de design gráfico, 2026), com base nos conhecimentos descritos na literatura científica.

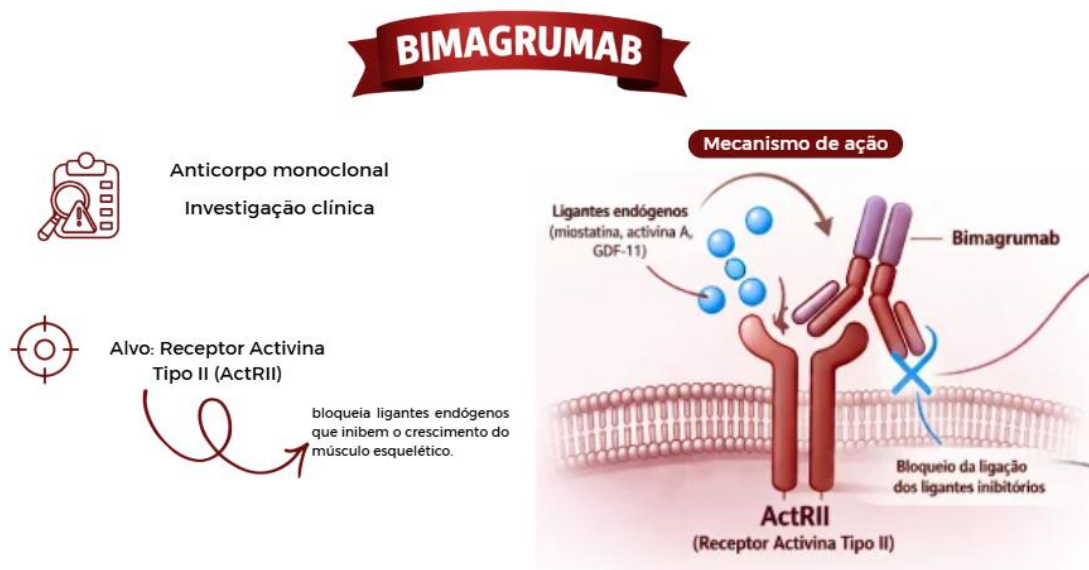


Figura 8 – Bimagrumab, atuação fisiológica e efeitos colaterais. Fonte: Produzida pelo autor no Canva (Plataforma de design gráfico, 2026), com base nos conhecimentos descritos na literatura científica.

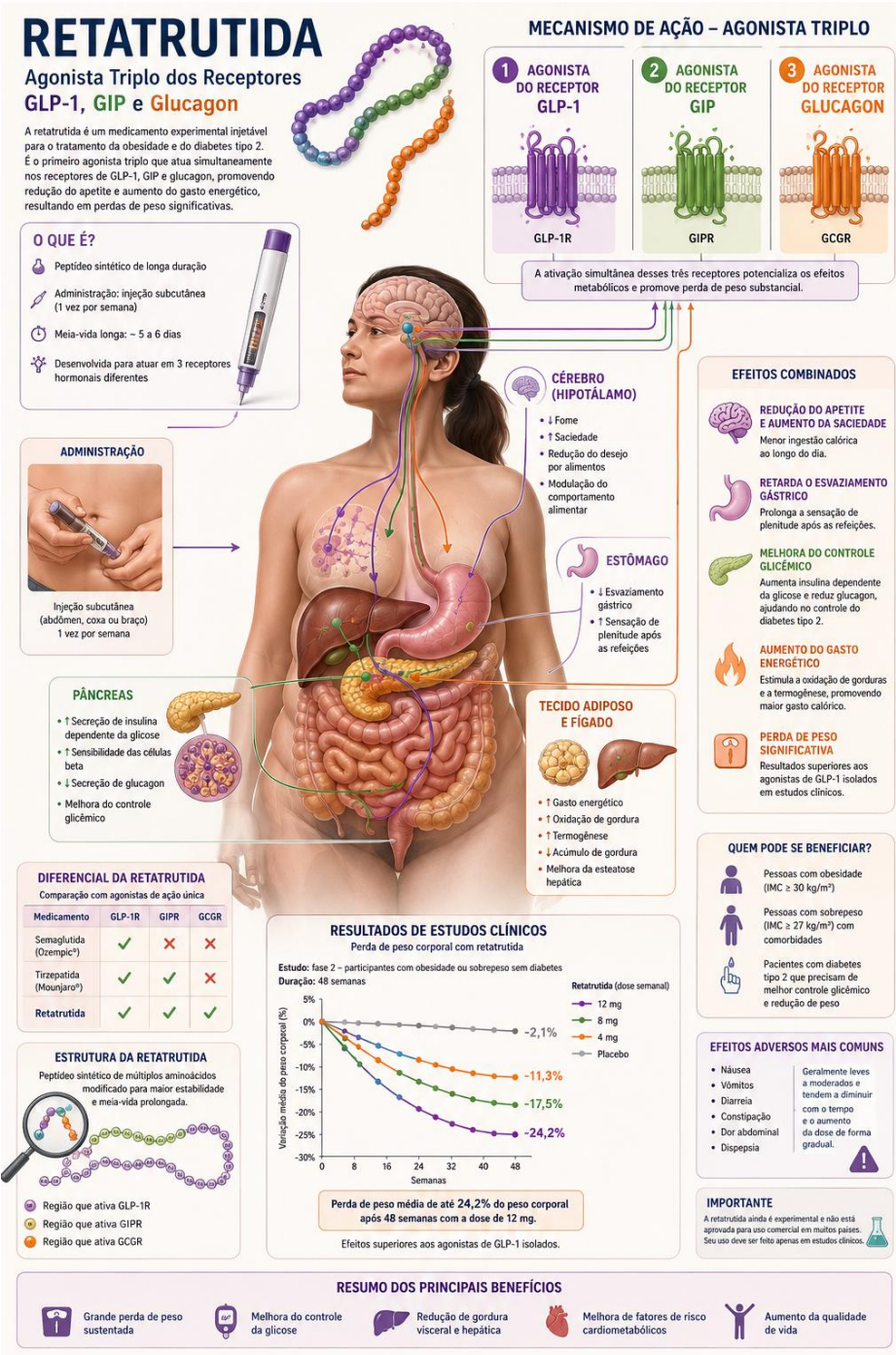


Figura 9 – Mecanismos fisiológicos da Retatrutida no organismo humano e sua estruturação. Fonte: Figura produzida com auxílio de inteligência artificial generativa (OpenAI, 2026), a partir da sistematização de evidências provenientes da literatura científica consultada pelos autores.