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Emerging Muscle Growth-Promoting Agents: Mechanisms of Action, Therapeutic Potential, Misuse in Sport, and Associated Health Complications – A Narrative Review

Konrad Gawin
Central Clinical Hospital of the Medical University of Łódź
Ul. Pomorska 251, 92-213 Łódź, Poland
https://orcid.org/0009-0007-2242-4356
konrad.gawin1@icloud.com

Wiktoria Zawiślak
Dr Karol Jonscher Municipal Medical Center,
Ul. Milionowa 14, 93-113 Łódź
https://orcid.org/0009-0009-2028-8885
zawislak.wiktoria@gmail.com

Maria Dąbrowska
J. Struś Multispecialist Municipal Hospital in Poznań
ul. Szwajcarska 3, 61-285 Poznań
https://orcid.org/0009-0005-6115-0701
marysia-dabrowska1@wp.pl

Corresponding author:
Konrad Gawin, konrad.gawin1@icloud.com

Abstract
The development of novel muscle growth-promoting agents has significantly expanded the possibilities of pharmacological intervention in skeletal muscle disorders. Selective androgen receptor modulators (SARMs), myostatin and activin pathway inhibitors, growth hormone secretagogues, and follistatin-based therapies represent promising approaches for treating conditions associated with muscle loss, including sarcopenia, cachexia, and neuromuscular

diseases. However, their increasing misuse for performance enhancement has raised important concerns regarding safety, regulation, and anti-doping control. This narrative review summarizes current knowledge regarding the mechanisms of action, therapeutic potential, adverse effects, and misuse of emerging anabolic agents. Although these compounds can promote increases in lean body mass, evidence demonstrating consistent improvements in muscle strength and physical performance remains limited. Furthermore, potential risks involving endocrine dysfunction, metabolic disturbances, cardiovascular complications, hepatotoxicity, and long-term safety remain insufficiently characterized. Continued research is required to determine their clinical value while preventing inappropriate use in sport.

Aim

The aim of this review was to summarize current evidence regarding emerging pharmacological and genetic strategies for enhancing skeletal muscle growth, with particular focus on mechanisms of action, therapeutic applications, safety concerns, and misuse in sport.

Materials and Methods

A narrative review of the current scientific literature was conducted, including clinical trials, preclinical studies, systematic reviews, and relevant reports concerning SARMs, myostatin/activin inhibitors, growth hormone secretagogues, follistatin-based therapies, and gene-based approaches.

Results

Emerging anabolic agents demonstrate promising effects on muscle mass regulation through different molecular pathways. However, clinical benefits remain inconsistent, particularly regarding improvements in muscle function. Safety concerns and potential misuse represent major challenges requiring further investigation and regulatory oversight.

Conclusions

Novel muscle growth-promoting therapies provide promising opportunities for treating muscle-wasting conditions; however, their clinical implementation requires robust evidence from long-term studies. Future strategies should prioritize functional outcomes, individualized treatment approaches, and effective measures to limit misuse in sport.

Keywords: skeletal muscle hypertrophy, selective androgen receptor modulators (SARMs), myostatin inhibitors, growth hormone secretagogues, ghrelin receptor agonists, follistatin-based therapy, adverse effects

Introduction

Skeletal muscle plays a fundamental role in human health by contributing to locomotion, metabolic regulation, physical performance, and overall quality of life. The maintenance and development of muscle mass are regulated by a complex interaction of mechanical stimuli, nutritional factors, endocrine signaling, and molecular pathways that control protein synthesis and degradation. While physiological muscle hypertrophy is primarily achieved through resistance exercise and adequate protein intake, pharmacological strategies designed to enhance muscle growth have attracted increasing scientific and clinical interest.(McGlory et al. 2019)[1] Over the past decade, substantial advances in molecular biology and pharmacology have led to the development of novel compounds capable of stimulating skeletal muscle hypertrophy through mechanisms distinct from those of traditional anabolic-androgenic steroids (AAS). These include selective androgen receptor modulators (SARMs), myostatin and activin signaling inhibitors, follistatin-based therapies, growth hormone secretagogues, and other emerging anabolic agents. (Fonseca et al. 2020)[2]Many of these compounds were originally developed to treat muscle wasting associated with aging, cancer cachexia, neuromuscular disorders, chronic illness, and prolonged immobilization. Although several agents have

demonstrated promising anabolic effects in preclinical and early clinical studies, few have received regulatory approval, and their long-term efficacy and safety remain incompletely understood.(Cruz-Jentoft et al. 2019)[3], (Chakraborty et al. 2025)[4]

The increasing accessibility of these compounds through online markets and the growing interest in performance enhancement have contributed to their widespread misuse among recreational athletes, bodybuilders, and competitive sports participants. Unlike conventional anabolic steroids, many emerging muscle growth-promoting agents are marketed as safer alternatives despite the limited availability of robust clinical evidence supporting such claims. Their use has been associated with a variety of adverse outcomes, including endocrine dysfunction, hepatotoxicity, cardiovascular complications, psychiatric disturbances, metabolic abnormalities, and suppression of the hypothalamic–pituitary–gonadal axis. Furthermore, the rapid emergence of new compounds presents significant challenges for anti-doping authorities and healthcare professionals due to limited toxicological data and difficulties in laboratory detection.(Sagoe et al. 2015)[5], (Pope et al. 2014)[6].

Recent progress in understanding skeletal muscle regulatory pathways has also highlighted the therapeutic potential of targeting signaling molecules such as myostatin, activin receptors, insulin-like growth factor-1 (IGF-1), and androgen receptors. However, the distinction between legitimate therapeutic use and non-medical performance enhancement has become increasingly blurred, raising important clinical, ethical, and regulatory concerns.(Wackerhage et al. 2019)[7]

Given the expanding number of novel anabolic compounds and the growing body of evidence regarding their biological effects, a comprehensive synthesis of current knowledge is warranted. Therefore, the aim of this narrative review is to summarize the mechanisms of action, therapeutic potential, patterns of misuse in sport, and the adverse health effects associated with emerging muscle growth-promoting agents. Additionally, this review discusses current challenges in anti-doping efforts and identifies gaps in the existing literature that should be addressed by future research.

Selective Androgen Receptor Modulators (SARMs)

Selective androgen receptor modulators (SARMs) constitute a class of non-steroidal compounds designed to selectively bind to androgen receptors in a tissue-specific manner, with the aim of promoting anabolic effects in skeletal muscle and bone while minimizing androgenic activity in other tissues such as the prostate, skin, and liver. The development of SARMs was originally driven by the need for safer alternatives to anabolic-androgenic steroids (AAS), particularly for the treatment of conditions associated with muscle wasting, osteoporosis, and age-related sarcopenia.(Narayanan et al. 2008)[8]

Unlike traditional AAS, SARMs exhibit partial agonist activity at the androgen receptor and demonstrate selective modulation of downstream gene transcription depending on the tissue context. This selectivity is thought to arise from differences in coactivator and corepressor recruitment, as well as tissue-specific receptor conformations. Preclinical studies have shown that SARMs can increase lean body mass and improve muscle strength in animal models without producing the full spectrum of androgenic side effects observed with testosterone or synthetic anabolic steroids.(Narayanan et al. 2018)[9]

Among the most widely studied SARMs are enobosarm (ostarine, MK-2866), ligandrol (LGD-4033), RAD-140 (testolone), S-23, and YK-11. These compounds differ in their receptor affinity, anabolic potency, and pharmacokinetic profiles. For example, ligandrol and RAD-140 have demonstrated strong anabolic effects in preclinical models, while enobosarm has progressed furthest in clinical trials for cancer cachexia and age-related muscle wasting. (Wen et al. 2025) [10]

Despite initial optimism, clinical trials evaluating SARMs in humans have yielded mixed results. While some studies have demonstrated modest increases in lean body mass,

improvements in functional outcomes such as muscle strength and physical performance have often been inconsistent or limited. Additionally, dose-dependent adverse effects, including suppression of endogenous testosterone production, have been observed even in short-term administration. (Basaria et al. 2013)[11]

A significant concern regarding SARMs is their potential for endocrine disruption. Suppression of the hypothalamic–pituitary–gonadal axis has been documented, leading to reduced luteinizing hormone and follicle-stimulating hormone levels, decreased testosterone production, and symptoms consistent with hypogonadism following discontinuation. Recovery of hormonal function may be delayed or incomplete in some users, particularly after prolonged exposure or high-dose misuse.(Thevis et al. 2018)[12]

Hepatotoxicity has also been reported in association with several SARMs, particularly those obtained from unregulated online markets. Elevations in liver enzymes, cholestatic injury patterns, and cases of acute liver injury have been documented. The risk appears to be higher in products contaminated with undeclared substances or when SARMs are used in supraphysiological doses beyond those investigated in clinical trials. From a cardiovascular perspective, SARMs may negatively affect lipid profiles by reducing high-density lipoprotein (HDL) cholesterol and potentially increasing low-density lipoprotein (LDL) cholesterol. These alterations, combined with possible increases in hematocrit and blood pressure, raise concerns about long-term cardiovascular risk, especially in individuals engaging in chronic misuse for performance enhancement. (Koller et al. 2021)[13]

The increasing availability of SARMs through online marketplaces has contributed to their widespread use among athletes and recreational bodybuilders. Despite being classified as investigational compounds, SARMs are frequently marketed as “research chemicals” and falsely advertised as safe alternatives to anabolic steroids. Analytical studies have demonstrated that many commercially available products are mislabeled, contaminated, or contain different dosages than declared.From an anti-doping perspective, SARMs represent a significant challenge due to their structural diversity, rapid emergence of new analogues, and low-dose potency. The World Anti-Doping Agency has included multiple SARMs on its Prohibited List under the category of non-approved substances. Advanced analytical techniques, including mass spectrometry and metabolite profiling, are required for their detection, but continuous development of novel derivatives complicates enforcement efforts. (Wagoner et al, 2017) [14]

In conclusion, SARMs represent a rapidly evolving class of compounds with significant anabolic potential but also considerable safety concerns. While initial research suggested a favorable therapeutic profile, accumulating evidence highlights meaningful risks involving endocrine, hepatic, and cardiovascular systems. Their widespread non-medical use underscores the need for continued regulatory oversight, improved detection methods, and further long-term clinical studies to clarify their safety and efficacy profiles.

Myostatin and Activin Pathway Inhibitors

Myostatin (growth differentiation factor 8, GDF-8) is a key negative regulator of skeletal muscle growth belonging to the transforming growth factor-β (TGF-β) superfamily. Under physiological conditions, myostatin inhibits muscle hypertrophy by suppressing satellite cell activation and reducing protein synthesis while simultaneously promoting catabolic signaling pathways. The activin signaling system, particularly activin A and related ligands (e.g., GDF-11), shares overlapping receptors with myostatin, mainly activin type II receptors (ActRIIA and ActRIIB), and collectively contributes to the regulation of muscle mass. Pharmacological inhibition of this pathway has therefore emerged as a promising strategy to counteract muscle wasting conditions such as sarcopenia, cachexia, and neuromuscular disorders. Recent advances have led to the development of monoclonal antibodies, ligand traps, and receptor

decoys designed to block myostatin/activin signaling and enhance skeletal muscle anabolism.(Rodriguez et al.2014)[15]

Among the most studied therapeutic approaches are monoclonal antibodies targeting either myostatin itself or its signaling receptors. Bimagrumab, a fully human monoclonal antibody directed against activin type II receptors, blocks the binding of myostatin and activin A, thereby inhibiting downstream Smad2/3 signaling pathways responsible for muscle protein degradation. Preclinical and early clinical studies have demonstrated that such receptor blockade can increase lean body mass and skeletal muscle volume in humans, particularly in populations with sarcopenia or muscle wasting disorders. Similar strategies include trevogrumab and garetosmab, which target myostatin and activin A respectively, reflecting a shift toward more selective modulation of this pathway rather than complete systemic inhibition. These agents are currently being investigated in clinical trials, including combination therapies with metabolic drugs such as GLP-1 receptor agonists, with the aim of improving body composition by reducing fat mass while preserving or increasing lean mass.(Rooks et al. 2017)[16]

Another important subgroup of myostatin pathway inhibitors includes ligand-neutralizing antibodies and engineered fusion proteins that bind circulating myostatin or related ligands before receptor activation occurs. Apitegromab is a notable example, functioning by selectively binding the inactive precursor forms of myostatin (promyostatin and latent myostatin), thereby preventing its activation. Other investigational agents, such as taldefgrobep alfa, act as soluble decoy receptors or ligand traps that sequester myostatin and activin molecules in circulation. These strategies aim to reduce off-target effects associated with receptor-level inhibition while maintaining anabolic efficacy. Although early results in animal models and phase I/II clinical trials suggest improvements in lean mass, the translation into meaningful functional outcomes such as muscle strength and physical performance remains inconsistent, which represents a major limitation of this therapeutic class.(Crawford et al. 2024)[17](Dagbay et al 2020)(18)

Gene-based and advanced biologic strategies are also being explored to achieve long-term suppression of myostatin signaling. Experimental approaches include adeno-associated virus (AAV)-mediated delivery of follistatin, a natural inhibitor of myostatin and activins, which has demonstrated potent muscle hypertrophy effects in preclinical models. Additionally, RNA-based technologies such as small interfering RNA (siRNA) targeting myostatin mRNA have shown the ability to significantly reduce myostatin expression for extended periods following a single administration. These emerging modalities offer the potential for sustained anabolic effects but raise important concerns regarding safety, immune response, and irreversible physiological alterations. Moreover, the long-term consequences of chronic myostatin suppression on tendon integrity, cardiac muscle function, and metabolic homeostasis remain insufficiently understood, highlighting the need for cautious translational development.(Al-Zaidy et al. 2015)[19]

Despite promising anabolic effects, the clinical development of myostatin and activin pathway inhibitors has been challenging. Many compounds have demonstrated increases in lean body mass without corresponding improvements in muscle strength or functional capacity, suggesting that muscle quality may not parallel muscle quantity. Additionally, variability in trial outcomes has been observed depending on patient population, disease state, and baseline muscle mass. Some trials have also reported adverse effects such as mild gastrointestinal symptoms, fatigue, and musculoskeletal complaints, although overall safety profiles have generally been acceptable in short-term studies. Importantly, the lack of long-term data limits definitive conclusions regarding cardiovascular safety, endocrine effects, and potential compensatory biological adaptations that may reduce efficacy over time.(Suh et al. 2020)[20]

From a sports and performance-enhancement perspective, myostatin and activin pathway inhibitors have gained attention as potential doping agents due to their strong anabolic potential

and 24246theoretical ability to increase muscle mass without the androgenic side effects associated with anabolic steroids. However, their misuse is currently limited by high cost, restricted availability, and the requirement for parenteral administration in most cases. Nevertheless, their classification as non-approved substances by the World Anti-Doping Agency underscores their relevance in anti-doping control frameworks. Ongoing research efforts are focused on improving detection methods and understanding pharmacokinetic signatures to prevent illicit use. Overall, while inhibition of the myostatin–activin axis represents one of the most promising frontiers in muscle biology, significant gaps remain between experimental efficacy and clinically meaningful outcomes, as well as between therapeutic use and potential misuse in sport.

Growth Hormone Secretagogues and Ghrelin Receptor Agonists

Growth hormone secretagogues (GHSs) comprise a heterogeneous group of peptide and non-peptide compounds that stimulate endogenous growth hormone (GH) secretion through activation of the growth hormone secretagogue receptor type 1a (GHSR1a), a G protein-coupled receptor predominantly expressed in the hypothalamus and anterior pituitary. The endogenous ligand for this receptor is ghrelin, a 28-amino acid peptide primarily synthesized by X/A-like cells of the stomach following acylation by ghrelin O-acyltransferase (GOAT). Activation of GHSR1a stimulates pulsatile GH secretion, enhances appetite, and modulates multiple physiological processes, including glucose metabolism, gastrointestinal motility, inflammation, cardiovascular function, and energy homeostasis. Unlike recombinant human growth hormone (rhGH), which directly elevates circulating GH concentrations, growth hormone secretagogues amplify endogenous hormone release while largely preserving physiological feedback mechanisms mediated by somatostatin and insulin-like growth factor-1 (IGF-1). Consequently, these agents have attracted considerable interest as potentially safer anabolic therapies for muscle wasting disorders while simultaneously becoming compounds of concern in sports medicine due to their misuse for performance enhancement. Recent structural studies of GHSR1a have substantially improved the understanding of ligand binding and receptor activation, facilitating the development of novel agonists with improved selectivity and pharmacokinetic properties.(Abizaid et al. 2020)[21], (Price et al. 2021)[22], (Liu et al. 2021)[23].

Growth hormone secretagogues are generally classified into peptide and non-peptide agonists. Peptide secretagogues include GHRP-2, GHRP-6, hexarelin, ipamorelin, and pralmorelin, whereas non-peptide compounds include ibutamoren (MK-677), anamorelin, capromorelin, and macimorelin. Although all activate GHSR1a, their pharmacodynamic characteristics differ considerably. Peptide agonists typically induce rapid, pulsatile GH release following parenteral administration, whereas orally active non-peptide agonists produce a more sustained stimulation of GH and IGF-1 secretion due to their longer half-lives. Among these compounds, ibutamoren has been the most extensively investigated as an oral ghrelin mimetic capable of increasing circulating GH and IGF-1 concentrations for prolonged periods without suppressing endogenous pituitary function. Anamorelin, another orally active ghrelin receptor agonist, has primarily been developed for cancer cachexia because of its combined anabolic and orexigenic properties. In contrast, macimorelin has gained regulatory approval as a diagnostic agent for adult growth hormone deficiency rather than as an anabolic therapy, reflecting the diversity of clinical applications within this pharmacological class.(Sigalos et al. 2023)[24],[25]

The anabolic effects of growth hormone secretagogues are mediated primarily through stimulation of the GH–IGF-1 axis. Increased GH secretion promotes hepatic synthesis of IGF-1, which subsequently activates intracellular signaling pathways such as phosphatidylinositol-3 kinase (PI3K)/Akt and mammalian target of rapamycin (mTOR), resulting in enhanced protein synthesis, reduced proteolysis, and increased satellite cell activity. Nevertheless,

accumulating evidence indicates that improvements in muscle mass are generally modest compared with those achieved using supraphysiological doses of recombinant GH or anabolic-androgenic steroids. Clinical studies evaluating ibutamoren in older adults have consistently demonstrated increases in lean body mass and serum IGF-1 concentrations; however, improvements in muscle strength, physical performance, or functional capacity have been considerably less pronounced. Similar observations have been reported for anamorelin in patients with cancer cachexia, where increases in body weight and lean body mass were not consistently accompanied by clinically meaningful gains in handgrip strength or physical function. These findings suggest that stimulation of anabolic signaling alone may be insufficient to restore muscle quality in complex catabolic conditions and emphasize the importance of combining pharmacological interventions with resistance exercise and nutritional support.(Nass et al 2018)[26], (Temel et al 2016)[27].

Although growth hormone secretagogues generally demonstrate a more physiological endocrine profile than exogenous GH administration, their safety remains an important consideration. The most frequently reported adverse effects include increased appetite, peripheral edema, transient fluid retention, fatigue, headache, and mild arthralgia. Because activation of GHSR1a also influences glucose metabolism, prolonged administration—particularly of ibutamoren—may impair insulin sensitivity, increase fasting glucose concentrations, and promote insulin resistance in susceptible individuals. Furthermore, chronic elevation of circulating IGF-1 theoretically raises concerns regarding long-term cardiovascular risk and the stimulation of latent neoplastic processes, although convincing clinical evidence supporting these outcomes remains limited. Early trials involving elderly populations also raised concerns regarding fluid overload and congestive heart failure in selected high-risk patients, highlighting the importance of careful patient selection and long-term safety monitoring. At present, no growth hormone secretagogue has demonstrated sufficient long-term efficacy and safety to justify widespread use for the treatment of sarcopenia or age-related muscle loss.(Aguiar-Oliveira et al. 2019)[28], (Adunsky et al 2021)[29],[30]

The growing popularity of growth hormone secretagogues in recreational sport represents a significant challenge for anti-doping organizations. Compounds such as ibutamoren, ipamorelin, GHRP-2, GHRP-6, and hexarelin are marketed through unregulated online vendors as agents capable of increasing muscle mass, accelerating recovery, improving sleep quality, and promoting fat loss despite the absence of robust clinical evidence supporting these claims in healthy individuals. Their appeal stems largely from oral availability in the case of ibutamoren, preservation of endogenous GH secretion, and the misconception that they are safer than recombinant GH or anabolic steroids. However, these substances remain prohibited in competitive sport because they enhance endogenous GH signaling and may confer an unfair performance advantage. Continuous advances in analytical mass spectrometry and biomarker-based detection have improved the identification of these compounds and their metabolites, although newly synthesized analogues continue to present substantial analytical challenges. Future research should focus on establishing long-term safety profiles, determining clinically meaningful functional outcomes, and identifying patient populations that may genuinely benefit from GHSR agonist therapy while minimizing the risk of misuse in sport.

Follistatin-Based Therapies and Gene Therapy

Follistatin is an endogenous glycoprotein encoded by the **FST gene** and represents one of the most important extracellular regulators of skeletal muscle growth through modulation of the transforming growth factor-β (TGF-β) superfamily signaling pathway. Unlike selective inhibitors targeting only myostatin (growth differentiation factor-8, GDF-8), follistatin interacts with multiple ligands, including myostatin, activin A, activin B, and related members of the TGF-β family. By binding these ligands, follistatin prevents their interaction with activin type

II receptors (ActRIIA and ActRIIB), resulting in reduced Smad2/3 signaling and attenuation of pathways associated with muscle growth inhibition and fibrosis. Experimental studies have demonstrated that increased follistatin expression produces significant skeletal muscle hypertrophy, primarily through enhanced myofiber growth and activation of anabolic signaling pathways. The physiological importance of this mechanism is supported by animal models showing that follistatin overexpression can induce muscle enlargement comparable to that observed following genetic inhibition of myostatin. (Barbé et al. 2017)[31], (Iskenderian et al 2018)[32]

Several isoforms of follistatin exist due to alternative splicing of the FST gene, with follistatin-344 (FS344) and its circulating derivative follistatin-315 (FS315) being the most relevant in therapeutic research. The biological effects of follistatin depend strongly on its ability to bind different ligands and its tissue distribution. FS288 demonstrates high affinity for activin and is predominantly associated with extracellular matrix binding, whereas FS315 exhibits greater systemic circulation and reduced interaction with non-muscle tissues. This distinction has encouraged the development of muscle-targeted follistatin strategies aimed at maximizing anabolic effects while minimizing unwanted systemic consequences, particularly alterations in reproductive hormone regulation through activin inhibition. Early preclinical investigations using recombinant follistatin proteins demonstrated increased muscle mass; however, systemic administration remains challenging due to protein stability, pharmacokinetics, and the potential for broad endocrine effects. Consequently, current research has increasingly focused on gene delivery approaches capable of achieving sustained and localized follistatin expression. (Al-Zaidy et al 2015)[33]

Gene therapy represents one of the most promising approaches for exploiting follistatin biology in the treatment of muscle-wasting disorders. Adeno-associated virus (AAV)-based vectors have been extensively investigated as delivery platforms because of their ability to induce long-lasting transgene expression with relatively low pathogenicity. AAV-mediated delivery of the FS344 isoform has demonstrated substantial increases in muscle size and strength in animal models, including non-human primates. In a landmark preclinical study, intramuscular administration of an AAV1-FS344 vector resulted in durable increases in skeletal muscle mass and functional strength without major abnormalities in examined organs, supporting further clinical investigation. More recent advances in AAV vector engineering, including improved muscle tropism and reduced immunogenicity, have further increased the potential of gene-based follistatin therapies. However, translation from experimental models to humans remains complex due to differences in immune response, vector distribution, and long-term regulation of transgene expression. (Kota et al 2009)[34]

The clinical development of follistatin gene therapy has primarily focused on rare neuromuscular disorders characterized by progressive muscle loss rather than healthy individuals seeking performance enhancement. One of the first human studies evaluated intramuscular delivery of follistatin gene therapy in patients with Becker muscular dystrophy. This approach demonstrated acceptable short-term safety and provided preliminary evidence of improved functional outcomes, although larger controlled trials are required to determine therapeutic efficacy. Beyond muscular dystrophies, follistatin-based strategies are being investigated as potential interventions for sarcopenia, cachexia, and age-related decline in muscle function. Nevertheless, clinical translation has been slower than initially anticipated because increasing muscle size does not necessarily correspond to improved muscle quality, neuromuscular coordination, or functional performance. Similar limitations have been observed with other myostatin pathway inhibitors, where increases in lean body mass were not consistently accompanied by proportional improvements in strength. (Mendell et al 2014)[35]

Despite significant therapeutic potential, follistatin-based therapies present several unresolved safety challenges. Because follistatin regulates multiple members of the TGF-β superfamily,

excessive or prolonged inhibition may affect processes beyond skeletal muscle, including reproductive function, immune regulation, fibrosis, and tissue repair. In addition, long-term expression achieved through gene therapy raises concerns regarding dose control, reversibility, and immune reactions against viral vectors or transgene products. Current AAV-based approaches are limited by pre-existing neutralizing antibodies, potential inflammatory responses, and difficulties in achieving repeat administration. Reviews of muscle-directed AAV gene therapy emphasize that immune-mediated complications remain one of the major barriers to widespread clinical application. (Kumar et al 2023)[36]

From a sports medicine perspective, follistatin-based interventions represent a potential future category of performance-enhancing agents due to their ability to remove endogenous limitations on muscle growth. However, current evidence does not support the use of commercially marketed follistatin peptides or unregulated gene-based products for muscle enhancement in healthy athletes. Most evidence demonstrating significant anabolic effects comes from experimental gene transfer models rather than approved human therapies. The possibility of misuse has attracted attention from anti-doping organizations because manipulation of myostatin–follistatin signaling represents a form of potential gene doping. Future advances in molecular detection methods will be necessary to identify illicit use, particularly as gene therapy technologies become more accessible. Overall, follistatin-based therapies remain one of the most scientifically promising approaches for enhancing skeletal muscle growth, but their transition from experimental biology to safe clinical application requires further investigation regarding efficacy, long-term safety, and ethical considerations. (Wetzlich et al. 2023)[37]

Adverse Effects and Safety Concerns of Emerging Muscle Growth-Promoting Agents

The development of novel pharmacological agents capable of enhancing skeletal muscle growth has generated considerable interest in both clinical medicine and sports performance. Compounds such as selective androgen receptor modulators (SARMs), myostatin and activin pathway inhibitors, growth hormone secretagogues, and gene-based anabolic therapies were initially investigated as potential treatments for muscle wasting disorders, including sarcopenia, cancer cachexia, and neuromuscular diseases. However, the increasing non-medical use of these compounds among athletes and recreational users has raised substantial concerns regarding their long-term safety. Unlike conventional anabolic-androgenic steroids, many emerging muscle-enhancing agents lack extensive clinical experience, and their safety profiles are often based on short-term trials, small study populations, or preclinical models. Recent systematic reviews emphasize that the available evidence is insufficient to establish long-term cardiovascular, endocrine, metabolic, and oncological safety, particularly among healthy individuals using these substances for performance enhancement rather than medical indications. (Vignali et al. 2023)[38]

One of the most significant safety concerns relates to endocrine disruption, particularly among compounds affecting androgen receptor signaling or the growth hormone axis. Although SARMs were designed to selectively activate androgen receptors in skeletal muscle while reducing androgenic effects in reproductive tissues, clinical and post-marketing data indicate that these compounds can still suppress the hypothalamic–pituitary–gonadal axis. Reported consequences include reductions in endogenous testosterone production, decreased luteinizing hormone and follicle-stimulating hormone concentrations, and symptoms associated with hypogonadism after discontinuation. Similarly, growth hormone secretagogues and ghrelin receptor agonists, including ibutamoren, increase endogenous GH and insulin-like growth factor-1 (IGF-1) concentrations, which may interfere with glucose metabolism and insulin sensitivity during prolonged exposure. Although these agents generally preserve physiological feedback mechanisms better than exogenous hormone administration, available studies remain

limited in duration, preventing definitive conclusions regarding their long-term endocrine safety. (Basaria et al. 2013)[39], (Dalton et al 2013)[40]

Hepatic and metabolic complications represent another important area of concern, particularly for orally administered anabolic compounds. SARMs have been repeatedly associated with drug-induced liver injury (DILI), with recent analyses identifying cases of hepatocellular and cholestatic liver damage, jaundice, and elevated liver enzymes among users. A major challenge in assessing hepatotoxicity is the unregulated nature of the commercial market, where products marketed as SARMs frequently contain undeclared substances, incorrect dosages, or additional anabolic agents. This lack of quality control makes it difficult to determine whether adverse effects result from the pharmacological activity of SARMs themselves or from contamination and adulteration. In addition to hepatic risks, anabolic compounds may negatively influence lipid metabolism by reducing high-density lipoprotein cholesterol and increasing cardiovascular risk factors. Recent reviews have highlighted potential interactions between androgen receptor activation and cardiovascular disease pathways, including endothelial dysfunction, lipid abnormalities, and adverse cardiac remodeling. (Leciejewska et al 2023)[41](Mohamed et al 2023)[42]

Agents targeting the myostatin–activin pathway and follistatin-based therapies introduce a different category of safety challenges due to their involvement in broad biological processes beyond skeletal muscle regulation. Although inhibition of myostatin or activin signaling can induce substantial increases in muscle mass, these pathways participate in tissue repair, fibrosis regulation, immune modulation, and metabolic control. Consequently, excessive or prolonged suppression may theoretically interfere with physiological adaptation and organ homeostasis. Clinical trials involving activin receptor inhibitors, such as bimagrumab, have demonstrated increases in lean body mass; however, improvements in functional strength have often been modest, suggesting that increased muscle quantity does not necessarily translate into improved muscle quality. Moreover, the long-term consequences of chronic manipulation of TGF-β family signaling remain unclear. Similar concerns apply to follistatin-based gene therapies, where persistent transgene expression creates additional challenges related to dose control, reversibility, immune responses, and potential off-target effects. These limitations represent major barriers preventing widespread clinical application despite promising experimental results.(Sartori et al 2014)[43]

Gene therapy and advanced molecular approaches represent the most innovative but also the least characterized category of muscle-enhancing interventions. Adeno-associated virus (AAV)-mediated delivery of anabolic genes, including follistatin or other regulators of muscle growth, has demonstrated remarkable effects in animal models, including increased muscle size and strength. However, translation into humans requires careful consideration of immunogenicity, vector distribution, durability of expression, and the possibility of irreversible biological changes. Previous clinical experience with AAV-based therapies has shown that immune responses against viral vectors or transgene products may limit efficacy and create safety concerns. Furthermore, gene-based enhancement of skeletal muscle raises ethical and regulatory issues because of its potential application as a form of gene doping in sport. Current anti-doping strategies must therefore evolve alongside biotechnology developments to detect not only conventional pharmacological agents but also molecular modifications affecting muscle growth pathways. (Aguti et al. 2018)[44], (Bulaklak et al. 2017)[45], (Kumar et al. 2023)[46].

The misuse of emerging anabolic agents represents a growing challenge for sports medicine, clinicians, and regulatory authorities. A common misconception among users is that novel compounds are inherently safer because they are described as “selective,” “natural,” or “research-based.” However, selectivity in molecular targeting does not eliminate systemic effects, particularly when compounds are used at supraphysiological doses or without medical

supervision. Current evidence indicates that many emerging muscle growth-promoting agents may provide measurable anabolic effects, but these benefits are accompanied by uncertain long-term risks. Future research should prioritize large-scale, long-duration clinical studies evaluating cardiovascular outcomes, endocrine recovery, metabolic consequences, and organ-specific toxicity. Until such evidence becomes available, the therapeutic use of these compounds should remain restricted to controlled clinical investigations, while their non-medical use for performance enhancement should be considered a significant public health and safety concern.

Misuse in Sport and Anti-Doping Perspective

The continuous development of pharmacological agents capable of enhancing skeletal muscle growth has significantly altered the landscape of performance-enhancing substances in modern sport. While traditional anabolic-androgenic steroids remain among the most frequently detected doping agents, recent years have witnessed a substantial increase in the emergence of novel compounds targeting specific molecular pathways involved in skeletal muscle hypertrophy. Selective androgen receptor modulators (SARMs), myostatin and activin pathway inhibitors, growth hormone secretagogues, ghrelin receptor agonists, and gene-based therapies have attracted considerable attention because of their potential anabolic effects combined with the perception of improved safety and reduced detectability. Many of these compounds remain investigational drugs or have never received regulatory approval for clinical use. Nevertheless, they are widely marketed through online platforms and underground laboratories as performance-enhancing agents despite the absence of robust evidence supporting their efficacy or long-term safety. The rapid expansion of these substances has created an important challenge for anti-doping authorities, which must continuously adapt analytical methodologies to detect newly emerging compounds and their metabolites. Recent anti-doping surveillance demonstrates that the number of newly identified performance-enhancing molecules continues to increase annually, reflecting the dynamic interaction between pharmaceutical innovation and illicit drug misuse in sport. (Thomas et al. 2023)[47], (Thevis et al. 2026)[48]

One of the principal reasons for the growing popularity of these compounds among athletes is the misconception that selective molecular targeting results in minimal adverse effects while simultaneously reducing the likelihood of detection. SARMs are frequently promoted as "safe anabolic alternatives" to testosterone, whereas ghrelin receptor agonists and growth hormone secretagogues are advertised as physiological stimulators of endogenous hormone production rather than exogenous hormone administration. Similarly, inhibitors of the myostatin–activin pathway are often presented as revolutionary anabolic therapies capable of increasing muscle mass without the endocrine disturbances associated with anabolic steroids. However, these marketing claims are largely unsupported by high-quality clinical evidence. Studies investigating products purchased through the internet have repeatedly demonstrated that many preparations contain undeclared pharmacologically active ingredients, incorrect dosages, multiple prohibited substances, or entirely different compounds than those listed on product labels. Such findings substantially increase the risk of adverse health effects and inadvertent anti-doping rule violations, particularly among athletes who mistakenly believe they are consuming legal nutritional supplements rather than prohibited pharmacological agents. (Barrios et al. 2025)[49], (Ingle et al 2026)[50]

The rapid appearance of novel anabolic compounds also presents considerable analytical challenges for anti-doping laboratories. Unlike conventional anabolic steroids, whose metabolic profiles have been extensively characterized over several decades, many emerging compounds possess unique chemical structures, limited pharmacokinetic data, and previously unknown metabolic pathways. Consequently, analytical methods must be continuously updated to identify parent compounds, long-term metabolites, and indirect biomarkers capable of

extending detection windows. High-resolution liquid chromatography coupled with tandem mass spectrometry has become the cornerstone of modern anti-doping analysis, allowing laboratories to detect extremely low concentrations of prohibited substances and to identify newly synthesized analogues before they become widely available on the illicit market. Recent advances have also incorporated metabolomics, isotope ratio mass spectrometry, biomarker profiling, and artificial intelligence-assisted data interpretation, enabling more sensitive and comprehensive detection strategies. Nevertheless, pharmaceutical innovation frequently outpaces analytical development, resulting in a continuous "cat-and-mouse" relationship between manufacturers of performance-enhancing drugs and anti-doping scientists. (Thomas et al. 2025)[51]

Among emerging forms of doping, gene and cell doping represent perhaps the greatest future challenge for sports integrity. Gene doping refers to the non-therapeutic use of nucleic acids, gene editing technologies, genetically modified cells, or vectors capable of altering gene expression to enhance athletic performance. Advances in molecular medicine, particularly CRISPR/Cas9 genome editing, adeno-associated viral (AAV) vectors, messenger RNA technologies, and RNA interference therapeutics, have substantially expanded the number of potential molecular targets that could theoretically be exploited for performance enhancement. Experimental manipulation of genes regulating erythropoiesis, angiogenesis, mitochondrial biogenesis, muscle hypertrophy, and tissue regeneration—including follistatin, myostatin, insulin-like growth factor-1 (IGF-1), vascular endothelial growth factor (VEGF), and erythropoietin (EPO)—has demonstrated remarkable physiological effects in experimental models. Although no confirmed cases of gene doping have been reported in elite sport, anti-doping organizations consider this threat sufficiently significant to invest considerable resources into developing molecular detection strategies. Current research focuses on identifying transgene-derived nucleic acids, vector-specific DNA sequences, abnormal protein expression profiles, circulating extracellular vesicles, and transcriptomic signatures capable of distinguishing therapeutic interventions from illicit genetic enhancement. (Thevis et al 2025)[52]

The regulatory framework governing these substances has evolved in parallel with scientific progress. According to the current prohibited list of the World Anti-Doping Agency, all non-approved pharmacological substances without regulatory authorization are prohibited at all times under category S0. SARMs are specifically classified as "other anabolic agents" within category S1, while growth hormone, growth hormone secretagogues, growth factors, peptide mimetics, and agents affecting the TGF-β signaling pathway—including compounds interfering with activin receptor signaling—are prohibited under categories S2 and S4. Gene and cell doping remain prohibited under category M3 regardless of whether performance enhancement has been conclusively demonstrated. Importantly, WADA regulations prohibit substances not only because of proven ergogenic effects but also when they pose potential health risks or violate the spirit of sport. Consequently, investigational drugs that have never completed clinical development may still be prohibited despite limited human efficacy data. This precautionary regulatory approach has become increasingly important as pharmaceutical pipelines continue to generate novel biologically active molecules with potential applications beyond their intended therapeutic indications. (National Center for Biotechnology Information, 2025), (Thomas et al. 2025)[51]

An additional challenge in anti-doping practice is the increasing prevalence of inadvertent doping associated with contaminated dietary supplements. Surveys conducted across multiple countries consistently demonstrate that a substantial proportion of commercially available sports supplements contain undeclared substances prohibited by WADA, including anabolic agents, stimulants, selective androgen receptor modulators, growth hormone secretagogues, and metabolic modulators. In many cases, contamination results from inadequate manufacturing

practices or intentional adulteration designed to enhance the perceived effectiveness of products marketed for muscle building, fat loss, or athletic performance. Under the principle of strict liability established in the World Anti-Doping Code, athletes remain fully responsible for any prohibited substance detected in their biological samples, irrespective of intent or product labeling. Consequently, the use of non-certified dietary supplements represents a significant risk for both elite and recreational athletes, emphasizing the need for education, certified supplement programs, and rigorous quality control throughout the nutritional supplement industry. (Barrios et al. 2025)[49]

The future of anti-doping science will increasingly depend on integrating molecular biology, bioinformatics, artificial intelligence, and personalized biomarker profiling into routine doping control. Rather than relying exclusively on direct identification of prohibited substances, emerging strategies focus on detecting biological fingerprints left by pharmacological or genetic manipulation. Longitudinal monitoring through the Athlete Biological Passport, multi-omics technologies, digital analytical platforms, and machine learning algorithms may substantially improve the ability to identify novel performance-enhancing interventions before conventional analytical methods become available. Simultaneously, continued collaboration among academic researchers, pharmaceutical companies, anti-doping laboratories, and regulatory agencies will be essential for maintaining the integrity of competitive sport. As innovative anabolic therapies continue to emerge from translational medicine, balancing legitimate therapeutic development with effective prevention of misuse will remain one of the central challenges facing sports medicine and anti-doping science in the coming decade.

Future Directions

The rapid expansion of knowledge regarding the molecular regulation of skeletal muscle has fundamentally transformed the development of anabolic therapies. Future research is expected to move beyond the traditional concept of increasing muscle mass toward interventions that improve overall muscle quality, contractile performance, metabolic function, and long-term physical capacity. Clinical experience accumulated over the past decade has demonstrated that increases in lean body mass alone do not necessarily translate into meaningful improvements in muscle strength, mobility, or quality of life. Consequently, future therapeutic strategies will likely focus on identifying molecular targets capable of simultaneously promoting muscle hypertrophy, enhancing neuromuscular function, improving mitochondrial efficiency, and reducing fibrosis and chronic inflammation. Recent reviews emphasize that skeletal muscle should be considered a complex endocrine and metabolic organ rather than merely a contractile tissue, suggesting that future pharmacological interventions must address multiple biological pathways simultaneously rather than targeting a single anabolic mechanism. (Joshi et al. 2025)[54], (Liu et al. 2025)[55]

One of the most promising directions involves combination therapies targeting complementary signaling pathways responsible for muscle homeostasis. Early clinical studies have shown that inhibition of the myostatin–activin axis consistently increases lean body mass; however, improvements in functional performance remain modest. This discrepancy has shifted attention toward combining myostatin inhibitors with resistance exercise, nutritional interventions, selective androgen receptor modulators, incretin-based therapies, or agents improving mitochondrial function. Recent experimental studies have also investigated the simultaneous modulation of anabolic pathways such as PI3K/Akt/mTOR together with suppression of catabolic regulators including FoxO transcription factors, ubiquitin–proteasome signaling, and inflammatory cytokines. Such multimodal approaches may better reproduce the physiological adaptations observed during exercise and reduce the compensatory mechanisms that often limit the efficacy of single-target therapies. Future clinical trials are therefore expected to evaluate

integrated pharmacological strategies rather than isolated anabolic compounds. (Wetzlich et al. 2026)[56], (Huang et al. 2025)[57]

Gene therapy is likely to become one of the most transformative areas of muscle-enhancing medicine during the next decade. Continued improvements in adeno-associated viral (AAV) vectors, tissue-specific promoters, lipid nanoparticle delivery systems, messenger RNA therapeutics, antisense oligonucleotides, and CRISPR/Cas-based genome editing have substantially expanded the possibilities for long-term regulation of muscle growth. Experimental approaches targeting follistatin, insulin-like growth factor-1 (IGF-1), dystrophin restoration, or myostatin suppression have demonstrated encouraging results in preclinical models, while several gene-based therapies are currently undergoing clinical evaluation for inherited neuromuscular disorders. Nevertheless, major translational challenges remain, including vector immunogenicity, durability of transgene expression, off-target genetic modifications, dose optimization, and long-term safety. Future advances will likely focus on developing reversible and tightly regulated gene expression systems capable of minimizing adverse effects while preserving therapeutic efficacy. These innovations may ultimately extend beyond rare genetic diseases and become applicable to more common conditions such as sarcopenia, frailty, and cancer cachexia. Joshi et al. 2025)[54] (Wetzlich et al. 2026)[56], (Huang et al. 2025)[57]

Another rapidly evolving field is precision medicine, which aims to individualize anabolic therapy according to each patient's molecular and physiological characteristics. Growing evidence indicates that substantial variability exists in treatment response depending on age, sex, genetic background, inflammatory status, endocrine profile, nutritional state, and disease etiology. Advances in genomics, transcriptomics, proteomics, metabolomics, and artificial intelligence are expected to facilitate the identification of biomarkers capable of predicting therapeutic response and adverse effects before treatment initiation. Personalized medicine may also improve patient selection for specific interventions, allowing clinicians to distinguish individuals who are most likely to benefit from selective androgen receptor modulators, myostatin inhibitors, growth hormone secretagogues, or gene-based therapies. Furthermore, digital health technologies, wearable sensors, and remote physiological monitoring may enable continuous assessment of muscle function and treatment response, providing more clinically relevant outcome measures than lean body mass alone. (Liu et al. 2025)[58]

Despite remarkable scientific progress, several critical challenges must be addressed before emerging anabolic therapies can be widely implemented in clinical practice. Long-term randomized clinical trials remain scarce, particularly those evaluating cardiovascular safety, endocrine recovery, oncological risk, and durability of functional improvements. Regulatory agencies increasingly emphasize that future drug development should prioritize clinically meaningful outcomes—including muscle strength, mobility, independence, and quality of life—rather than isolated changes in muscle volume. Simultaneously, continued collaboration between molecular biologists, clinicians, pharmaceutical companies, sports medicine specialists, and anti-doping organizations will be essential to balance legitimate therapeutic innovation with the prevention of misuse in sport. As increasingly sophisticated anabolic compounds and gene-based technologies become available, the distinction between therapeutic intervention and performance enhancement may become progressively less clear. Therefore, future research should not only focus on improving efficacy but also on establishing robust safety profiles, ethical frameworks, and analytical tools capable of detecting illicit applications while supporting the development of effective treatments for patients suffering from muscle-wasting disorders. (Samali et al 2025)[59]

Discussion

The present narrative review demonstrates that the field of pharmacological muscle enhancement has undergone rapid development over the past decade, driven by advances in molecular biology, endocrinology, and translational medicine. Novel anabolic agents—including selective androgen receptor modulators (SARMs), myostatin and activin pathway inhibitors, growth hormone secretagogues, and follistatin-based gene therapies—represent fundamentally different therapeutic approaches compared with conventional anabolic-androgenic steroids. Although these compounds target distinct molecular pathways, a common finding across the available literature is that improvements in lean body mass do not consistently translate into clinically meaningful improvements in muscle strength, physical performance, or quality of life.

This discrepancy between structural and functional outcomes remains one of the greatest challenges in the development of anabolic therapies. Most clinical studies have used lean body mass as the primary endpoint because it is relatively easy to quantify using imaging techniques such as dual-energy X-ray absorptiometry or MRI. However, accumulating evidence suggests that muscle quantity alone is an insufficient surrogate for functional recovery. Muscle quality, neuromuscular coordination, mitochondrial function, fibrosis, and metabolic capacity appear to contribute equally, if not more, to physical performance than absolute muscle size. Consequently, future clinical trials should prioritize clinically relevant outcomes such as muscle strength, mobility, exercise tolerance, falls, independence in activities of daily living, and patient-reported quality of life rather than relying predominantly on changes in body composition.

Another important observation emerging from this review is that no currently available pharmacological strategy provides an ideal balance between efficacy and safety. SARMs were developed to overcome the androgenic adverse effects associated with anabolic steroids, yet clinical experience has demonstrated persistent endocrine suppression, hepatotoxicity, and unfavorable lipid alterations in some users. Similarly, inhibition of the myostatin–activin pathway consistently increases lean body mass but has produced variable improvements in physical function across different patient populations. Growth hormone secretagogues preserve physiological endocrine feedback more effectively than recombinant growth hormone but remain associated with glucose dysregulation, fluid retention, and uncertain long-term cardiovascular safety. Gene-based interventions, particularly follistatin therapies, offer perhaps the greatest anabolic potential but simultaneously introduce unique concerns regarding irreversible genetic modification, immune responses, dose regulation, and ethical acceptability.

These findings highlight an important principle in skeletal muscle therapeutics: successful manipulation of a single anabolic signaling pathway is unlikely to fully restore muscle function in complex catabolic disorders. Muscle homeostasis is regulated through highly interconnected endocrine, inflammatory, metabolic, neural, and mechanical mechanisms. Therefore, pharmacological interventions targeting only one molecular pathway may trigger compensatory biological responses that limit therapeutic efficacy. This concept explains why several compounds demonstrating remarkable anabolic effects in experimental models have shown only modest functional benefits in clinical trials. Future therapeutic strategies will likely require multimodal approaches combining pharmacological treatment with resistance exercise, nutritional optimization, rehabilitation, and management of underlying disease processes.

The review also emphasizes the growing importance of precision medicine in anabolic therapy. Considerable heterogeneity exists among patients with muscle-wasting disorders regarding age, sex, hormonal milieu, inflammatory status, nutritional deficiencies, genetic background, and disease etiology. These factors substantially influence both therapeutic efficacy and susceptibility to adverse effects. Advances in genomics, transcriptomics, proteomics,

metabolomics, and artificial intelligence may facilitate identification of biomarkers capable of predicting treatment response before therapy is initiated. Such personalized approaches could improve patient selection, reduce unnecessary drug exposure, and optimize the benefit-risk ratio of emerging anabolic interventions. Likewise, digital health technologies and wearable physiological monitoring may provide continuous assessment of muscle performance in real-world settings, allowing clinicians to evaluate outcomes beyond static measurements of lean body mass.

An equally important aspect discussed throughout this review is the increasing divergence between therapeutic innovation and non-medical misuse. Many of the compounds currently under clinical investigation have rapidly become available through unregulated online markets long before sufficient evidence regarding efficacy and safety has been established. The perception that selective or investigational agents are inherently safer than conventional anabolic steroids is not supported by current evidence. Instead, products marketed as research chemicals frequently contain inaccurate dosages, undisclosed pharmacologically active substances, or contaminants, substantially increasing health risks. This problem extends beyond elite sport and increasingly affects recreational athletes and individuals seeking cosmetic body composition improvements.

From the perspective of sports medicine, the rapid emergence of novel anabolic agents presents substantial challenges for anti-doping authorities. Pharmaceutical innovation frequently progresses faster than the development of analytical detection methods, creating a continuous cycle in which newly synthesized compounds appear before validated laboratory assays become available. Emerging technologies such as metabolomics, transcriptomic profiling, biomarker-based detection, and artificial intelligence-assisted interpretation are expected to become increasingly important components of future anti-doping programs. Gene and cell doping represent particularly complex future threats because conventional analytical strategies may prove insufficient for detecting molecular modifications rather than administered substances.

Several limitations within the current body of evidence should also be acknowledged. Most available studies involve relatively small sample sizes, short follow-up periods, and heterogeneous patient populations with varying disease severity. Many clinical trials have focused on surrogate biomarkers instead of long-term functional outcomes, making direct comparisons between therapeutic approaches difficult. Furthermore, evidence regarding healthy individuals remains extremely limited because ethical considerations preclude large-scale randomized studies evaluating performance enhancement. Consequently, much of the available knowledge regarding misuse is derived from case reports, observational studies, and anti-doping investigations rather than controlled clinical research. These limitations should be considered when interpreting both therapeutic efficacy and safety.

Overall, the available evidence suggests that emerging muscle growth-promoting agents hold considerable promise for the treatment of sarcopenia, cachexia, neuromuscular disorders, and other muscle-wasting conditions. Nevertheless, substantial scientific, clinical, ethical, and regulatory challenges remain before these therapies can be safely integrated into routine clinical practice. Future research should prioritize large randomized controlled trials with extended follow-up, standardized functional outcome measures, comprehensive safety assessment, and direct comparisons between pharmacological and multimodal therapeutic strategies. At the same time, continued collaboration between clinicians, molecular biologists, pharmaceutical developers, and anti-doping organizations will be essential to maximize therapeutic benefits while minimizing the risks associated with misuse and performance enhancement.

Conclusion

Emerging muscle growth-promoting agents represent a rapidly developing field with significant therapeutic potential for the treatment of muscle-wasting disorders. Compounds targeting

androgen receptors, myostatin–activin signaling, the growth hormone axis, and genetic regulators of muscle growth have demonstrated promising anabolic effects; however, their ability to produce meaningful improvements in muscle function remains limited and requires further investigation.

Despite advances in molecular targeting, current evidence indicates that increases in muscle mass do not necessarily translate into improved strength, physical performance, or quality of life. Moreover, concerns regarding endocrine disruption, cardiovascular and metabolic effects, hepatotoxicity, immune responses, and long-term safety remain major barriers to widespread clinical application. The misuse of these compounds in sport further highlights the need for strict regulation, improved detection strategies, and increased awareness of their potential risks.

Future research should focus on personalized, multimodal approaches that combine pharmacological interventions with exercise, nutritional strategies, and rehabilitation. Long-term clinical trials and advanced monitoring methods are essential to determine the true therapeutic value and safety profile of these emerging therapies. Balancing innovation in muscle medicine with ethical considerations and prevention of misuse will remain a key challenge in the development of future anabolic treatments.

Author's contribution

Conceptualization: Konrad Gawin, Wiktoria Zawiślak
Methodology: Konrad Gawin, Wiktoria Zawiślak,
Software: Konrad Gawin, Wiktoria Zawiślak,
Check: Konrad Gawin, Wiktoria Zawiślak,
Formal analysis: Konrad Gawin, Wiktoria Zawiślak,
Investigation: Konrad Gawin, Wiktoria Zawiślak,
Resources: Konrad Gawin, Wiktoria Zawiślak,
Data curation: Konrad Gawin, Wiktoria Zawiślak,
Writing- rough preparation: Konrad Gawin, Wiktoria Zawiślak,
Writing- review and editing: Konrad Gawin, Wiktoria Zawiślak,
Visualization: Konrad Gawin, Wiktoria Zawiślak,
Supervison: Konrad Gawin, Wiktoria Zawiślak,
Project administration Konrad Gawin, Wiktoria Zawiślak

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