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Trenbolone: Pharmacology, Mechanisms, Toxicity, and Translational Challenges

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Abstract

Background: Trenbolone is a potent synthetic anabolic steroid with marked androgen-receptor activity and distinctive pharmacological properties. Although it has been extensively investigated in experimental models, its potential therapeutic applications and safety profile in humans remain poorly characterized. This review summarizes the available preclinical and clinical evidence concerning the pharmacological properties, anabolic mechanisms, tissue effects, neurobehavioral actions, and potential adverse effects of trenbolone.

Methods: The available experimental and clinical literature on trenbolone was reviewed.

Results: Preclinical studies consistently demonstrate that trenbolone is a highly potent anabolic-androgenic agent capable of increasing skeletal muscle mass, promoting lean-tissue accretion, reducing adiposity, and preserving bone mineral density and mechanical strength in several animal models. Its anabolic effects appear to involve complex regulation of protein turnover, including suppression of protein degradation, modulation of glucocorticoid-mediated catabolism, growth-factor signaling, IGF-related pathways, satellite-cell activity, myostatin/SMAD signaling, and Wnt5a expression.

Trenbolone is not aromatized to estrogen and is resistant to 5α-reductase metabolism, characteristics that distinguish its tissue pharmacology from testosterone and may contribute to differences in prostate, bone, adipose, and skeletal-muscle responses. Some studies suggest that trenbolone can produce favorable anabolic and skeletal effects with less prostate enlargement than supraphysiological testosterone under specific experimental conditions.

Additional animal studies have reported improvements in adiposity, insulin sensitivity, lipid metabolism, and myocardial responses to ischemia-reperfusion. However, these effects occur alongside substantial androgenic and endocrine activity, including suppression of endogenous reproductive function and, at higher exposures, prostate enlargement and other androgen-dependent effects. Genotoxicity studies have generally found no convincing evidence of DNA damage or tumor initiation under the conditions tested. Neurological findings are mixed, with cellular toxicity observed at supraphysiological concentrations but limited behavioral or cognitive impairment in some animal models.

Human evidence remains sparse and consists predominantly of case reports and uncontrolled exposure histories, frequently involving high doses and concomitant use of multiple anabolic steroids or other performance-enhancing substances. Reported complications include reproductive and endocrine suppression, psychiatric and behavioral disturbances, cardiovascular events, metabolic abnormalities, pancreatitis, and renal injury. Although these reports provide important safety signals, attribution specifically to trenbolone is often uncertain because of polypharmacy, supraphysiological exposure, and other confounding factors.

Conclusion: The preclinical literature establishes a strong biological basis for trenbolone's potent anabolic and androgenic effects and identifies potentially important actions on skeletal muscle, bone, adipose tissue, and metabolic pathways. Nevertheless, the substantial endocrine activity and emerging clinical safety signals highlight that trenbolone cannot be regarded as a purely anabolic or inherently safe compound.

Keywords: Trenbolone; Pharmacological Effects; Safety

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Pharmacological Properties and Preclinical Evidence of Trenbolone

In 2001, Nasrollah T. Shahidi from the United States reviewed the clinical applications of anabolic-androgenic steroids and emphasized that these agents had been used clinically, with reported benefits in a variety of disorders, including sarcopenia, cachexia associated with chronic diseases and HIV infection, chronic obstructive pulmonary disease, severe burn injuries, and alcoholic hepatitis.

Anabolic-androgenic steroids had also been used in the treatment of bone marrow failure syndromes, constitutional growth retardation in children, and hereditary angioedema.

Reported adverse effects included virilization in females and children, behavioral changes such as aggression, hepatotoxicity, and alterations in blood lipid levels and coagulation factors [1].

The 1976 study by Neumann characterized trenbolone acetate as a potent anabolic-androgenic steroid with pharmacological activity broadly similar to 19-nortestosterone derivatives.

Neumann study reported that approximately threefold greater androgenic activity than testosterone propionate, alongside substantial anabolic and antigonadotropic effects. Trenbolone acetate was reported to be non-estrogenic and only weakly progestational, distinguishing its activity profile from some other steroidal agents.

The study also highlights its strong virilizing and reproductive-axis effects, emphasizing that anabolic activity is accompanied by significant androgenic properties [2].

The 1978 experimental study in rats by Brian G. Vernon and Peter J. Buttery provided important preclinical evidence that trenbolone acetate produces a net anabolic effect through modulation of whole-body and muscle protein turnover, particularly by reducing protein catabolism rather than solely stimulating protein synthesis [3].

During the same year, Brian G. Vernon and Peter J. Buttery published another study which showed that trenbolone acetate increased growth rate in female rats and produced a significant increase in total carcass nitrogen, indicating enhanced lean tissue accretion rather than water retention.

The treatment also tended to reduce carcass fat content, supporting a favorable anabolic effect on body composition.

Interestingly, trenbolone reduced the fractional synthetic rates of skeletal muscle and uterine proteins, indicating that increased growth was not simply due to stimulation of protein synthesis.

The authors suggested that trenbolone may promote net protein deposition through alterations in protein turnover and reduced protein degradation [4].

The 1981 study by van Logten and colleagues evaluated the physiological, metabolic, endocrine, reproductive, and toxicological effects of trenbolone alongside endogenous hormones and other growth-promoting agents.

The authors concluded that trenbolone can exert endocrine and reproductive effects, but, unlike DES, there was no evidence of mutagenicity [5].

The 1982 study by Santidrian and Thompson demonstrated that trenbolone acetate alters myofibrillar protein turnover, as assessed by urinary 3-methylhistidine excretion, with responses strongly dependent on the sex and adrenal status of the rats.

Trenbolone increased growth and reduced myofibrillar protein breakdown in adrenalectomized female rats, whereas in adrenalectomized males it increased 3-methylhistidine output without significantly improving growth.

These findings support the anabolic action of trenbolone through modulation of muscle protein degradation, potentially involving antagonism of catabolic effects mediated by glucocorticoids and estrogens [6].

The 1983 study by Ballard and Francis used cultured rat L6 myoblasts to examine how growth factors, glucocorticoids, and anabolic agents regulate intracellular protein breakdown. Insulin, fetal bovine serum, and bovine colostrum inhibited protein degradation, whereas dexamethasone stimulated it, demonstrating opposing anabolic and catabolic influences.

Trenbolone, diethylstilboestrol, and testosterone did not directly alter intracellular protein breakdown or prevent the catabolic action of glucocorticoids in this in-vitro model.

The findings therefore suggested that trenbolone's anabolic effects are unlikely to result from a direct inhibition of muscle protein degradation. Instead, the authors proposed an indirect mechanism involving modulation of growth-factor/somatomedin activity, providing an early mechanistic perspective on trenbolone's anabolic actions [7].

The 1983 study by Thomas and Rodway demonstrated that trenbolone acetate exerts anti-glucocorticoid effects on adrenal function in growing female rats, reducing the afternoon peak of plasma corticosterone and the corticosterone response to ACTH.

Trenbolone also reduced hepatic tyrosine aminotransferase activity, while not altering the induction of this enzyme by exogenous corticosterone, suggesting that its effects were not due to impaired hepatic responsiveness to glucocorticoids.

Despite these endocrine changes, trenbolone-treated rats showed significantly greater growth than controls.

The study suggested that trenbolone's anabolic activity may be partly related to suppression or antagonism of glucocorticoid-mediated catabolic processes, although the precise mechanism linking reduced adrenal activity to enhanced growth remained unresolved [8].

The 1988 study by Richold from England evaluated the genotoxic and cancer-initiating potential of 17β-hydroxytrenbolone and its cattle-specific metabolite, 17α-hydroxytrenbolone, using an extensive battery of in vitro and in vivo assays.

17β-Hydroxytrenbolone was consistently negative in bacterial mutation, cytogenetic, micronucleus, DNA-repair, mammalian-cell mutation, and animal genotoxicity assays, with only equivocal responses in the mouse lymphoma assay at highly cytotoxic concentrations. 17α-Hydroxytrenbolone was similarly negative in most assays, although a weak positive response occurred in the mouse lymphoma assay, again mainly at highly toxic concentrations.

Neither compound demonstrated evidence of DNA damage or tumor initiation in vivo in the tests performed.

The authors concluded that both trenbolone forms lack genotoxic activity and do not act as cancer initiators, supporting a low genotoxic

hazard under the experimental conditions studied [9].

The 1989 study by Thompson from the United States and his research team reported a two-week study in young female rats which showed that trenbolone promoted faster growth, increased protein deposition, and reduced body fat.

Trenbolone-treated rats also developed larger semi-membranous muscles with approximately 60% more DNA, suggesting enhanced muscle-cell activity.

Although trenbolone did not directly stimulate satellite-cell proliferation in culture, satellite cells from treated animals showed greater proliferative responses to FGF and IGF-I.

Serum from trenbolone-treated rats likewise enhanced satellite-cell proliferation, indicating that systemic factors may contribute to its anabolic effects.

The authors suggested that trenbolone-induced skeletal muscle hypertrophy may involve increased satellite-cell proliferation and differentiation through enhanced responsiveness to growth factors such as IGF-I and FGF [10].

Taken together, the preclinical literature from 1976 to 1989 establishes trenbolone as a potent anabolic steroid with marked effects on protein metabolism, growth, body composition, and endocrine function.

Across animal and cellular models, its anabolic activity was consistently associated with increased lean-tissue accretion, enhanced growth, reduced body fat, and alterations in muscle protein turnover. Importantly, several studies suggested that these effects may result not simply from increased protein synthesis, but from reduced protein degradation and modulation of glucocorticoid-, growth-factor-, and IGF-related pathways [2-10].

At the same time, these studies demonstrate that trenbolone is pharmacologically active well beyond skeletal muscle, producing substantial androgenic, anti-gonadotropic, reproductive, and adrenal effects.

The findings therefore do not support viewing trenbolone as a purely anabolic compound; rather, its anabolic effects occur within a broader and complex endocrine pharmacology [2, 5, 8].

The available genotoxicity studies were generally reassuring, with no convincing evidence of DNA damage or tumor initiation under the experimental conditions examined [5, 9]. However, the absence of genotoxicity in these models should not be interpreted as evidence of overall safety in humans.

Thus, the preclinical evidence provides a strong biological rationale for trenbolone's anabolic potency but cannot adequately define its efficacy, dose-response relationship, long-term toxicity, or risk-benefit profile in humans. The apparent disconnect between substantial pharmacological activity and the limited systematic human evidence underscores the need for well-designed human studies.

Such investigations should carefully evaluate both therapeutic or performance-related effects and potential adverse consequences, with particular attention to long-term endocrine, cardiovascular, reproductive, metabolic, and psychological outcomes.

Ultimately, animal and in-vitro evidence can establish biological plausibility, but only appropriately designed human research can determine the clinical significance and safety profile of trenbolone exposure in humans.

Trenbolone: Pharmacological Properties, Tissue Selectivity, and Therapeutic Potential

In 2005, Alexius Freyberger from Germany and colleagues reported that trenbolone demonstrated clear androgenic activity in castrated rats, increasing androgen-sensitive tissue weights at higher doses. These findings confirm its potent androgen-receptor-mediated effects and support its classification as an anabolic-androgenic steroid with dose-dependent biological activity [11].

In 2010, Joshua F. Yarrow from the United States and his research tea, reviewed the pharmacological properties of 17β-hydroxyestra-4, 9, 11-trien-3-one (trenbolone; 17β-TBOH), a synthetic anabolic steroid with a high affinity for the Androgen Receptor (AR).

They proposed that trenbolone may exhibit tissue-selective anabolic effects resembling some of the properties sought with Selective Androgen Receptor Modulators (SARMs). Trenbolone has been reported to promote skeletal muscle growth, support bone mass, and reduce adiposity. Its anabolic effects may also involve modulation of endogenous growth-factor signaling and antagonism of glucocorticoid-mediated actions.

Compared with testosterone, trenbolone appears to produce less growth of certain androgen-sensitive tissues, including the prostate and accessory sex organs. This difference is related, at least in part, to its metabolism: unlike testosterone, trenbolone is not a substrate for 5α-reductase and is not aromatized to estrogenic metabolites. In contrast, testosterone undergoes tissue-specific conversion to the more potent androgen Dihydrotestosterone (DHT) through 5α-reductase and to 17β-estradiol through aromatase [12].

Structurally, trenbolone is a 19-nor anabolic-androgenic steroid and belongs to the broader group of nandrolone-derived steroids. The absence of the C19 methyl group is a characteristic structural feature of this group and contributes to its distinctive anabolic-androgenic profile. Trenbolone is recognized as a highly potent anabolic steroid, although its anabolic and androgenic effects depend on the experimental model, dose, tissue, and route of administration [1, 13].

Trenbolone is also distinguished from testosterone and nandrolone by its metabolism. Trenbolone acetate, an esterified form of trenbolone, is hydrolyzed to 17β-trenbolone (17β-hydroxyestra-4, 9, 11-trien-3-one), the biologically active compound.

Trenbolone exhibits potent androgen-receptor agonist activity and has been reported to possess greater androgen-receptor activity than DHT in certain experimental systems. Unlike testosterone and nandrolone, trenbolone is not a substrate for 5α-reductase and does not undergo aromatization to estrogens. These metabolic characteristics contribute to its distinctive tissue-selective pharmacological profile [1, 12, 14].

In 2011, Joshua F Yarrow and his research team investigated the tissue-selective anabolic effects of trenbolone in an experimental rat model, with particular attention to its effects on skeletal muscle, bone, adiposity, hemoglobin, and the prostate.

Three-month-old male F344 rats either orchiectomized or left intact, received graded doses of trenbolone enanthate, supraphysiological testosterone enanthate, or vehicle for 29 days. In both intact and orchiectomized animals, all doses of trenbolone

enanthate and supraphysiological testosterone enanthate increased the mass of the androgen-sensitive levator ani/bulbocavernosus muscle by approximately 35-40% compared with sham-treated animals ($P \leq 0.001$). Both treatments also provided dose-dependent partial protection against orchiectomy-associated losses in total and trabecular bone mineral density ($P < 0.05$) and reduced visceral fat accumulation ($P < 0.05$).

Importantly, the lowest doses of trenbolone enanthate did not increase prostate volume, while hemoglobin concentrations remained comparable to those observed in sham-treated animals in both orchiectomized and intact rats. In contrast, supraphysiological testosterone enanthate and high-dose trenbolone enanthate increased prostate volume by 84% and 68%, respectively ($P < 0.01$). These findings suggested that, in this experimental model, trenbolone enanthate could promote anabolic effects in skeletal muscle and provide partial protection against bone loss while producing less prostate enlargement and fewer changes in hemoglobin at lower doses than supraphysiological testosterone.

The findings of Yarrow and his research team were particularly important because they provided preclinical evidence for the possibility of achieving a degree of tissue selectivity with a potent anabolic-androgenic steroid. This study provided a mechanistic and experimental basis for further investigation into compounds capable of promoting anabolic effects while minimizing undesirable effects in androgen-sensitive tissues.

Therefore, the authors emphasized the need for further preclinical studies to investigate the potential of trenbolone as an option for testosterone replacement therapy [15].

The 2012 study by Sean C McCoy from the United States and his research team demonstrates that trenbolone enanthate may offer a beneficial alternative to testosterone therapy for preventing androgen-deficiency-related bone loss.

In skeletally mature orchiectomized rats, both trenbolone enanthate and testosterone enanthate completely prevented reductions in trabecular bone mineral density at the distal femur. Notably, trenbolone also increased femoral neck strength by 28%, whereas testosterone produced no significant improvement in bone strength.

Unlike testosterone, which nearly doubled prostate mass, trenbolone maintained prostate mass at levels comparable to sham-operated animals.

Both treatments similarly increased hemoglobin concentrations and levator ani/bulbocavernosus muscle mass. These findings suggest that trenbolone can preserve bone quantity while providing additional benefits for bone mechanical strength. The markedly lower prostate response to trenbolone enanthate is particularly relevant given the potential adverse effects associated with testosterone therapy [16].

The 2012 study by Joshua F Yarrow and his research team demonstrates that trenbolone exerts significant androgenic effects on adiponectin regulation and visceral adipose tissue.

In gonadectomized rats, androgen deficiency increased circulating total adiponectin, whereas testosterone enanthate markedly reduced adiponectin concentrations. Trenbolone enanthate similarly prevented the gonadectomy-induced rise in adiponectin and reduced adiponectin protein expression in visceral fat.

The reduction in total adiponectin was dose-dependent, with higher trenbolone doses producing greater suppression. Importantly, trenbolone maintained or increased High-Molecular-Weight (HMW) adiponectin, suggesting differential regulation of adiponectin forms. Both testosterone and trenbolone also reduced visceral fat mass, supporting their lipolytic and body-composition effects.

The inverse relationship between androgen levels and total adiponectin indicates that androgen signaling is an important regulator of adipokine metabolism. Overall, these findings provide preclinical evidence that trenbolone modulates adipose tissue and adiponectin independently of aromatization or 5α-reduction [17].

The 2014 study by Fan Ye from the United States and his research team demonstrates that trenbolone produces strong anabolic and myotrophic effects in skeletal muscle without requiring conversion by 5α-reductase or aromatase.

Both testosterone and trenbolone suppressed muscle-wasting genes and increased anabolic growth factors such as IGF-1 and mechano-growth factor.

Trenbolone showed greater suppression of atrogin-1 and uniquely reduced glucocorticoid receptor expression, suggesting enhanced anti-catabolic activity.

Both androgens increased muscle mass and markers of muscle regeneration, confirming their capacity to promote skeletal muscle growth.

The authors concluded that trenbolone may regulate muscle maintenance through distinct molecular pathways from testosterone, supporting its preclinical anabolic potential [18].

The 2014 study by Darren T Beck from the United States and his research team provides important preclinical evidence that trenbolone can maintain skeletal health through androgenic mechanisms independent of aromatization.

In skeletally mature orchiectomized rats, both testosterone enanthate and trenbolone enanthate prevented cancellous bone loss and suppressed the high bone turnover associated with androgen deficiency.

Both androgens also improved femoral neck shear strength compared with untreated orchiectomized animals. Aromatase inhibition with anastrozole did not diminish the bone-protective effects of trenbolone, indicating that its skeletal actions do not require conversion to estrogen. Similarly, trenbolone produced strong anabolic effects on levator ani/bulbocavernosus muscle and prevented the increase in visceral adiposity caused by orchiectomy.

These muscle and adipose effects were also unaffected by aromatase inhibition. Overall, the findings demonstrate that trenbolone directly promotes bone, muscle, and favorable body-composition outcomes through non-aromatizable androgenic pathways [19].

In 2015, Daniel G Donner from Australia and his research team reported that six-week trenbolone treatment in male rats produced marked anabolic effects, characterized by a 37% reduction in fat mass and an 11% increase in lean mass. Trenbolone also substantially improved serum lipid profiles, reducing triglycerides, HDL, and LDL, alongside improved insulin sensitivity and overall cardio-metabolic risk factors.

Despite these metabolic benefits, trenbolone caused pronounced

prostate enlargement, with prostate mass increasing by approximately 149% and histology indicating benign hyperplasia.

The treatment also suppressed circulating sex hormones, confirming significant endocrine effects associated with trenbolone exposure.

No adverse effects were detected on cardiac function, myocardial susceptibility to ischemia-reperfusion injury, or liver histology and enzyme activity during the six-week treatment period [20].

In 2016, Daniel G Donner from Australia and his research team reported that in a rat model of testosterone deficiency with obesity-related metabolic syndrome, trenbolone produced significant metabolic and cardiovascular benefits.

Trenbolone reduced subcutaneous and visceral fat accumulation, hypercholesterolemia, hypertriglyceridaemia, and hyperinsulinemia, indicating improved metabolic function. It also reduced myocardial injury following ischemia-reperfusion, suggesting potential cardioprotective effects in this experimental model.

Compared with testosterone replacement, trenbolone produced broader protection against metabolic abnormalities and myocardial damage.

Importantly, trenbolone was associated with less cardiac fibrosis and prostate hyperplasia than testosterone, although adverse androgenic effects remained evident [21].

During the same year, Daniel G Donner from Australia and his research team published a study which investigated the effects of visceral adiposity and testosterone deficiency on femoral bone health in male Wistar rats, with particular emphasis on the potential therapeutic role of trenbolone. A high-fat/high-sugar diet induced visceral obesity and was associated with reduced femoral bone mineral area, content, stiffness, and strength.

Testosterone deficiency caused by orchiectomy further aggravated reductions in bone mineral density and mechanical strength. Both testosterone and trenbolone treatment restored bone mineral area, content, density, and energy to failure.

However, trenbolone uniquely reduced visceral adiposity and produced greater improvements in femoral stiffness and strength. These findings suggest that visceral adiposity and androgen deficiency independently contribute to osteoporosis, altered bone geometry, and compromised bone strength.

The study provided preclinical evidence that trenbolone may exert beneficial skeletal effects beyond those achieved with testosterone replacement. Therefore, trenbolone may represent a potentially more effective androgenic candidate for preserving bone health in testosterone-deficient males with visceral obesity [22].

The studies reviewed provide substantial preclinical evidence that trenbolone is a highly potent anabolic-androgenic steroid with pronounced androgen-receptor-mediated activity.

Across experimental animal models, trenbolone consistently demonstrated anabolic effects involving skeletal muscle, bone, adipose tissue, and metabolic regulation. Its pharmacological profile is distinguished from that of testosterone by its high androgen-receptor activity and by its resistance to 5α-reductase metabolism and aromatization to estrogenic metabolites. These characteristics appear to contribute to differences in tissue responses compared with testosterone.

The available studies demonstrate that trenbolone can increase skeletal muscle mass, reduce visceral adiposity, preserve bone mineral density, and improve aspects of bone strength and metabolic function in androgen-deficient and metabolically compromised animal models. Several investigations also reported potentially favorable effects on glucose metabolism, lipid profiles, insulin sensitivity, and myocardial responses to ischemia–reperfusion injury. Importantly, some studies suggested that trenbolone may produce anabolic effects in skeletal muscle and bone with less prostate enlargement than testosterone at certain doses and under specific experimental conditions.

However, these findings should be interpreted cautiously. The evidence also demonstrates that trenbolone is not free from significant androgenic and endocrine effects. Higher doses and prolonged exposure were associated with prostate enlargement, suppression of endogenous sex hormones, and other androgen-dependent changes. Differences between studies further indicate that the effects of trenbolone are influenced by dose, duration of treatment, route of administration, experimental model, and the tissue examined. Overall, the preclinical literature establishes a strong pharmacological basis for further scientific investigation of trenbolone while simultaneously highlighting important safety concerns.

The findings suggest potential therapeutic applications, particularly in conditions associated with androgen deficiency, muscle loss, bone loss, and metabolic dysfunction. Consequently, carefully designed human studies are required to determine whether the beneficial effects observed in experimental models can be reproduced in humans and whether they can be achieved without unacceptable adverse effects.

The transition from promising preclinical evidence to clinical application therefore requires rigorous assessment of pharmacokinetics, pharmacodynamics, endocrine effects, cardiovascular and metabolic safety, reproductive effects, prostate health, and long-term outcomes.

Molecular Mechanisms Underlying the Myotrophic Effects of Trenbolone

The 2017 experimental study by V J Dalbo and his research team from the United States and Australia in orchiectomized adult rats showed that both testosterone and trenbolone markedly increased skeletal muscle fiber cross-sectional area compared with androgen deprivation.

Both androgens also substantially increased satellite cell numbers, indicating enhanced muscle regenerative capacity without increasing myonuclei per fiber.

Interestingly, testosterone and trenbolone increased myostatin protein levels, while also altering SMAD2/3 signaling and several genes involved in myostatin regulation.

Trenbolone therefore demonstrated a strong myotrophic effect comparable to testosterone despite its distinct pharmacological properties [23].

The 2018 study by Petey W Mumford from the United States, investigated the relationship between aging, androgen signaling, Wnt signaling, and skeletal muscle loss in male Fischer 344 rats.

They found that Androgen Receptor (AR) and Wnt5 protein

levels in the gastrocnemius muscle progressively declined with age and were associated with reduced muscle mass.

In vitro experiments showed that recombinant Wnt5a increased the size of C2C12-derived myotubes, suggesting a role in maintaining muscle fiber size.

In orchiectomized rats, both testosterone enanthate and trenbolone enanthate increased Wnt5a protein expression in androgen-sensitive skeletal muscle. Importantly, trenbolone, a non-aromatizable androgen, produced this effect, indicating that Wnt5a regulation does not require aromatization to estrogen.

The authors suggested that androgen signaling can positively regulate Wnt5a expression in skeletal muscle.

Age-related reductions in AR signaling may therefore contribute to diminished Wnt5a activity and progressive muscle loss. These results provide preclinical evidence for an androgen-AR-Wnt5a pathway that may be relevant to understanding the effects of trenbolone on skeletal muscle [24].

The studies reviewed here provide further preclinical evidence that trenbolone exerts pronounced effects on skeletal muscle through androgen-dependent molecular and cellular mechanisms. In orchiectomized animal models, trenbolone increased skeletal muscle fiber cross-sectional area and enhanced satellite-cell numbers, demonstrating its capacity to counteract the muscle loss associated with androgen deficiency. These effects were comparable in several respects to those produced by testosterone, despite the distinct pharmacological characteristics of trenbolone.

The findings also indicate that trenbolone influences multiple regulatory pathways involved in skeletal muscle growth and maintenance. In particular, trenbolone altered myostatin protein expression, SMAD2/3 signaling, and genes associated with myostatin regulation, suggesting that its anabolic effects may involve complex interactions between androgen signaling and pathways controlling muscle protein synthesis, regeneration, and inhibition of muscle growth. The increase in satellite-cell numbers further supports the possibility that trenbolone promotes not only muscle hypertrophy but also aspects of skeletal muscle regenerative activity.

The 2018 findings provide additional insight by identifying a potential relationship between androgen receptor signaling and the Wnt5a pathway. Age-related reductions in androgen receptor and Wnt5a expression were associated with skeletal muscle loss, whereas testosterone and trenbolone increased Wnt5a expression in androgen-sensitive skeletal muscle. Importantly, trenbolone produced this effect without requiring aromatization to estrogen, supporting the concept that androgen-receptor signaling can directly influence Wnt5a-mediated regulation of skeletal muscle.

Taken together, these findings suggest that trenbolone's myotrophic activity extends beyond a simple increase in androgen-receptor stimulation and may involve coordinated regulation of satellite cells, myostatin/SMAD signaling, Wnt5a, and other pathways involved in muscle growth and maintenance.

Nevertheless, these mechanisms have been demonstrated primarily in experimental models, and their relevance to human skeletal muscle physiology remains uncertain.

Further human studies are therefore necessary to determine whether the molecular and cellular effects observed in animals translate into clinically meaningful benefits and to establish the safety, dose-response relationships, and long-term consequences of trenbolone exposure in humans.

Neurotoxic Potential and Behavioral Effects of Trenbolone

The 2019 study by Sofia Zelleroth from Sweden and her research team examined the neurotoxic effects of several anabolic-androgenic steroids, including trenbolone, in primary rat cortical cell cultures. Supraphysiological concentrations of trenbolone produced cellular toxicity after both single and repeated exposure, characterized by impaired mitochondrial function and increased LDH release. Repeated trenbolone exposure also promoted apoptosis, indicating potential neuronal cell injury at high concentrations. The study provided preclinical evidence that excessive trenbolone exposure may adversely affect brain cells through androgen-receptor-dependent pathways [25].

The 2024 study by Sofia Zelleroth and her research team reported the treatment of male Wistar rats with nandrolone decanoate, testosterone decanoate, or trenbolone decanoate to evaluate their somatic and behavioral effects.

Trenbolone decanoate did not significantly impair recognition memory or alter behavioral responses or corticosterone levels under the experimental conditions. Among the steroids examined, nandrolone decanoate produced the most pronounced effects, including impaired recognition memory and alterations in several organs. These findings suggest that trenbolone may have a comparatively limited impact on cognitive and behavioral function at the tested dose and exposure duration [26].

The studies reviewed here provide important but limited preclinical evidence regarding the effects of trenbolone on the nervous system and behavioral function.

The 2019 study demonstrated that supraphysiological concentrations of trenbolone can produce cellular toxicity in primary rat cortical cells, including impaired mitochondrial function, increased LDH release, and apoptosis following repeated exposure. These findings raise concerns about the potential vulnerability of neural tissue to excessive or prolonged exposure to trenbolone and suggest that its effects on neuronal cells may involve androgen-receptor-mediated mechanisms.

However, the findings from the 2024 animal study provide a contrasting perspective. Under the experimental conditions examined, trenbolone decanoate did not significantly impair recognition memory, produce major behavioral abnormalities, or alter corticosterone concentrations in male rats. Compared with the other anabolic-androgenic steroids investigated, nandrolone decanoate produced more pronounced cognitive and systemic effects.

These results suggest that the neurobehavioral consequences of trenbolone may depend substantially on dose, duration of exposure, steroid formulation, experimental model, and the biological system being evaluated.

Taken together, the available evidence does not support a simple conclusion that trenbolone is either uniformly neurotoxic or completely devoid of neurological effects. Rather, the findings indicate a potential exposure-dependent risk that warrants further investigation. The cellular toxicity observed at high concentrations

is particularly relevant because it demonstrates that trenbolone can adversely affect neuronal cells under certain experimental conditions, while the absence of significant cognitive or behavioral impairment in an animal model suggests that these cellular findings cannot automatically be extrapolated to whole-organism effects.

An important limitation of the current evidence is the absence of adequate human data. The concentrations and exposure conditions used in experimental studies may not directly correspond to human exposure, and differences in metabolism, pharmacokinetics, androgen-receptor distribution, and brain physiology may substantially influence neurological responses. Consequently, further research is required to determine whether the neurobiological effects observed in preclinical models have clinical relevance.

Overall, the existing preclinical evidence provides a basis for continued investigation but remains insufficient to establish the long-term neurological safety of trenbolone in humans. Well-designed human studies, supported by appropriate neuroendocrine, cognitive, and neurological assessments, are therefore necessary to clarify the potential risks and benefits of trenbolone exposure.

Clinical Safety Profile and Potential Adverse Effects of Trenbolone

The use of trenbolone and other anabolic steroids has been widely reported among elite bodybuilders. Dorian Yates, a former professional bodybuilder, has stated that he used trenbolone and other anabolic steroids for more than a decade. Apart from loss of testicular function and the need for testosterone replacement therapy, he reported that he did not experience prominent mental or psychiatric adverse effects from trenbolone and described using doses of up to 200 mg per week to avoid renal injury [27-29].

Such individual experiences, however, should not be interpreted as evidence of safety, particularly because long-term anabolic steroids use is frequently associated with the concomitant use of multiple anabolic agents and other performance-enhancing substances.

Clinical case reports involving athletes who used high doses of trenbolone, usually in combination with other anabolic steroids, have provided important information concerning its potential adverse effects. These reports have described abnormalities involving the cardiovascular, metabolic, pancreatic, psychiatric, and renal systems, although the contribution of trenbolone itself is often difficult to distinguish from that of other concurrently administered substances [30-37].

In 1994, Jensen and colleagues from Denmark reported the case of a 26-year-old bodybuilder who had used trenbolone and stanozolol for 10 weeks. After approximately one month of use, serum Creatine Kinase (CK), including the CK-MB isoenzyme, increased to approximately five to ten times the normal level.

Despite these biochemical abnormalities, the patient did not develop cardiac symptoms, and electrocardiography was normal. Three weeks after discontinuation of trenbolone and stanozolol, CK and CK-MB levels returned to normal, suggesting a reversible association with the anabolic-steroid exposure [30].

Matthew J. Geraci and colleagues in the United States reported the case of a 33-year-old bodybuilder without significant previous medical history who developed new-onset diabetes while using supraphysiological doses of bovine growth hormone, trenbolone acetate, and testosterone.

The authors emphasized, however, that growth hormone itself can increase cellular insulin resistance and reduce glucose uptake, potentially contributing substantially to the development of diabetes in this setting [31]. Thus, this case illustrates the difficulty of attributing metabolic complications specifically to trenbolone when several potent anabolic and growth-promoting agents are used simultaneously.

In 2019, Vidhya Lakshmi Kumar from the United States and her research team reported the case of a 24-year-old bodybuilder who developed recurrent acute pancreatitis in association with the use of trenbolone together with other anabolic steroids [32]. Although the clinical course raised concern about a possible relationship between the anabolic-steroid regimen and pancreatitis, the concomitant use of multiple agents limits the ability to establish trenbolone as the sole causative factor.

Also in 2019, Sabrina Lehmann from Germany and her research team reported the death of a 34-year-old bodybuilder approximately three hours after a gym workout.

The individual had reportedly used multiple anabolic-androgenic steroids, including stanozolol, metandienone, trenbolone, boldenone, drostanolone, and testosterone, together with clenbuterol.

Autopsy examination demonstrated left ventricular hypertrophy and marked narrowing of the right coronary artery, with a residual vascular lumen of approximately 3 mm. The authors attributed the death to the use of multiple performance-enhancing substances in the context of significant cardiovascular pathology [33].

In 2020, Mohamed Adil Shah Khoodoruth and Adeel Ahmad Khan from Qatar reported the case of a 33-year-old bodybuilder who developed aggression, hostility, destructive impulses, and persecutory delusions while using testosterone propionate, testosterone cypionate, and trenbolone acetate at doses reported to reach 200 mg daily.

The patient also had testicular atrophy and below-normal plasma testosterone concentrations. The case illustrates both the potential psychiatric consequences of supraphysiological androgen exposure and the profound suppression of endogenous gonadal function that may accompany prolonged anabolic steroid use [34].

In the same year, Pascal Kintz from France and his research team reported the case of a 59-year-old former weightlifter who developed cardiac insufficiency and subsequently died despite treatment with quinidine. Toxicological investigation identified combined exposure to several anabolic steroids, including testosterone, testosterone propionate, testosterone decanoate, boldenone, trenbolone, and metandienone. The authors attributed the fatal outcome to the combined anabolic-steroid exposure [35].

In 2025, Nisrine N. Makarem and Mohammad El Jammal from Beirut reported the case of a 35-year-old bodybuilder who developed an acute myocardial infarction following a six-week anabolic-steroid cycle containing testosterone enanthate, trenbolone acetate, and nandrolone. Coronary angiography demonstrated an approximately 80% stenotic lesion in the mid-segment of the obtuse marginal artery [36].

Although the case provides further evidence of serious cardiovascular events occurring during anabolic-steroid use, the simultaneous administration of several steroids makes it difficult to

determine the independent contribution of trenbolone.

In 2026, Kaitlyn C. Lizardo from the United States and colleagues reported a 41-year-old man who developed severe hypercalcemia, with a serum calcium concentration of 15 mg/dL, together with acute kidney injury and a creatinine concentration of 6.02 mg/dL. The clinical presentation was attributed to trenbolone exposure [37]. This report raises the possibility of clinically important renal and metabolic toxicity associated with trenbolone, although additional evidence is required to establish a causal relationship.

Preclinical Experimental Evidence Also Suggests that Trenbolone Does Not Necessarily Reproduce All of the Physiological Feedback Effects of Endogenous Testosterone

In 2011, Geary et al. investigated the effects of trenbolone acetate in combination with LHRH immunization in young bulls. LHRH immunization markedly reduced serum testosterone concentrations, scrotal circumference, and testicular weight, demonstrating profound suppression of reproductive function. In contrast, trenbolone alone produced only a tendency toward reduced circulating testosterone concentrations and did not significantly affect testicular weight or pituitary FSH stores.

Both LHRH immunization and castration altered pituitary LH and FSH stores, whereas trenbolone had relatively limited effects on these parameters. Notably, trenbolone did not restore the normal negative-feedback regulation of gonadotropin synthesis.

The authors therefore concluded that trenbolone possesses androgenic activity but does not fully reproduce the physiological feedback effects of endogenous testosterone on the hypothalamic-pituitary-gonadal axis [38].

Taken together, the available evidence indicates that trenbolone exposure can be associated with potentially serious adverse effects involving reproductive, cardiovascular, metabolic, psychiatric, pancreatic, and renal systems. Nevertheless, most clinical reports involve supraphysiological doses and/or combinations of several anabolic steroids and other performance-enhancing substances.

Consequently, these reports provide important signals of potential toxicity but often cannot establish trenbolone as the sole causal agent. The preclinical evidence further suggests that trenbolone's androgenic activity does not necessarily translate into normal physiological feedback regulation of the hypothalamic-pituitary-gonadal axis.

The evidence reviewed here provides an important transition from preclinical findings to the limited clinical experience available in humans. Reports involving bodybuilders and other individuals exposed to trenbolone indicate that its use, particularly at supraphysiological doses and in combination with multiple anabolic-androgenic steroids, may be associated with potentially serious adverse effects involving the cardiovascular, metabolic, pancreatic, psychiatric, renal, and reproductive systems.

Individual accounts of prolonged trenbolone use without prominent psychiatric symptoms cannot be regarded as evidence of safety. Such experiences are subject to substantial limitations, including differences in dose, duration of exposure, individual susceptibility, concurrent use of other anabolic agents, and the absence of systematic clinical monitoring. Similarly, clinical case reports provide important signals of potential toxicity but generally cannot establish a direct causal relationship between trenbolone and a particular adverse event when several substances are administered simultaneously.

The reported clinical cases nevertheless illustrate a broad range of potentially serious complications. These include biochemical evidence of muscle or cardiac injury, metabolic disturbances, acute pancreatitis, severe psychiatric and behavioral changes, cardiovascular disease and myocardial infarction, cardiac insufficiency, and acute kidney injury associated with severe hypercalcemia.

The recent reports of myocardial infarction and severe hypercalcemia with acute kidney injury further demonstrate the continuing emergence of clinically important safety signals associated with anabolic-steroid exposure.

At the same time, attribution of these outcomes specifically to trenbolone remains challenging. Most reported individuals had used combinations of anabolic steroids and, in some cases, other performance-enhancing substances. Consequently, the available clinical literature should be interpreted as evidence of potential risk rather than definitive proof that trenbolone independently causes each reported complication. This distinction is particularly important when evaluating rare but severe outcomes such as myocardial infarction, cardiac failure, pancreatitis, and acute kidney injury.

The reproductive findings provide an additional indication that trenbolone should not be considered a simple pharmacological substitute for endogenous testosterone. Preclinical evidence suggests that although trenbolone possesses strong androgenic activity, it does not necessarily reproduce the normal negative-feedback regulation of the hypothalamic-pituitary-gonadal axis. Its ability to exert androgenic effects while producing a different pattern of endocrine feedback highlights the distinction between pharmacological androgen-receptor activation and physiological testosterone replacement.

Overall, the human evidence surrounding trenbolone is characterized by significant safety signals but substantial uncertainty regarding causality, dose-response relationships, long-term consequences, and individual susceptibility. The predominance of case reports and uncontrolled exposures makes it impossible to determine the true incidence or magnitude of trenbolone-associated adverse effects. At the same time, the severity of several reported outcomes makes the absence of systematic clinical investigation an important knowledge gap.

Taken together with the available preclinical evidence, these observations that trenbolone has demonstrated considerable pharmacological and anabolic activity in experimental models, but its potential clinical benefits and risks in humans remain insufficiently characterized.

Carefully designed human studies are therefore needed to establish its pharmacokinetic and pharmacodynamic properties, endocrine effects, cardiovascular and metabolic safety, renal and neurological consequences, reproductive effects, and long-term risk–benefit profile. Until such evidence becomes available, findings from animal studies and individual clinical reports should be interpreted cautiously and should not be considered sufficient evidence of therapeutic safety or efficacy in humans.

Conclusion

The preclinical literature establishes a strong biological basis for trenbolone's potent anabolic and androgenic effects and identifies potentially important actions on skeletal muscle, bone, adipose tissue, and metabolic pathways. Nevertheless, the substantial endocrine activity and emerging clinical safety signals highlight that trenbolone cannot be regarded as a purely anabolic or inherently safe compound.

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