

## RESEARCH MONOGRAPH . COMPOUND PROFILE

# Dianabol

*A 17-alpha-methylated, delta-1-dehydrogenated testosterone derivative developed at CIBA as an orally bioavailable anabolic agent, historically prescribed for catabolic wasting, osteoporosis, and nitrogen-balance restoration, and now principally encountered as a controlled substance of research interest in androgen receptor pharmacology, steroid metabolism, and anabolic-androgenic steroid toxicology.*

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## ABSTRACT

Metandienone (International Nonproprietary Name), known commercially as Dianabol and chemically as 17-alpha-methyl-delta-1-testosterone, is a synthetic anabolic-androgenic steroid (AAS) of the androstane class first synthesized at CIBA Pharmaceuticals in Switzerland in the mid-1950s and introduced to the United States prescription market in 1958. The compound is a structural modification of testosterone bearing two critical alterations: a methyl group at the C17-alpha position that confers oral bioavailability by resisting hepatic first-pass metabolism, and a delta-1 (C1-C2) double bond that modifies the anabolic-to-androgenic activity ratio relative to the parent hormone. Metandienone binds the androgen receptor (AR) in skeletal muscle, prostate, and other androgen-responsive tissues, initiating genomic signaling cascades that increase protein synthesis, nitrogen retention, and glycogenolysis. The compound undergoes aromatization by the CYP19A1 (aromatase) enzyme to 17-alpha-methylestradiol, producing dose-dependent estrogenic effects including fluid retention and gynecomastia. Hepatic metabolism proceeds principally through CYP3A4-catalyzed 6-beta-hydroxylation, with additional pathways including 5-beta-reduction, 3-alpha and 3-beta oxidation, and 17-epimerization; the 17-alpha-alkylation that confers oral bioavailability simultaneously produces the hepatotoxicity characteristic of this structural class.

The compound was originally developed and marketed for the treatment of catabolic states, post-surgical recovery, osteoporosis, and hypogonadism. Clinical trials conducted in the late 1950s and

1960s demonstrated significant positive nitrogen balance at oral doses of 5 to 10 mg per day, with measurable increases in lean body mass and appetite stimulation. However, escalating recognition of the hepatotoxic, cardiovascular, endocrine-suppressive, and estrogenic adverse-effect profile led to progressive restriction of approved indications, and the United States Food and Drug Administration withdrew approval in 1983. The compound is currently classified as a Schedule III controlled substance in the United States under the Controlled Substances Act and is prohibited by the World Anti-Doping Agency. It is not approved for any medical indication in any major regulatory jurisdiction.

Despite the absence of current clinical approval, metandienone remains a compound of substantial research interest. Its well-characterized androgen receptor pharmacology, its defined hepatotoxic mechanism as a model 17- $\alpha$ -alkylated steroid, its known metabolic pathways and urinary metabolite profile (exploited extensively in anti-doping analytical chemistry), and its historical clinical dataset in nitrogen-balance and muscle-wasting research provide a comprehensive pharmacological record. Preclinical studies in rat models have demonstrated that metandienone stimulates levator ani muscle hypertrophy through androgen receptor activation, suppresses the hypothalamic-pituitary-testicular axis, and modulates myostatin signaling pathways. This monograph reviews the chemistry, synthesis, and stereochemistry of metandienone; the androgen receptor pharmacology and mechanism of action; the comprehensive pharmacokinetic record including hepatic metabolism and urinary metabolite detection; the historical clinical evidence base; sourcing and quality verification considerations for research-grade material; reconstitution and handling; stack-interaction

considerations; the adverse-event and safety signal across hepatic, cardiovascular, endocrine, and estrogenic domains; and a comparative assessment of five alternative anabolic-androgenic steroids (testosterone, oxandrolone, oxymetholone, stanozolol, nandrolone decanoate) against metandienone on five competency standards (oral bioavailability, anabolic efficacy, hepatotoxicity profile, estrogenic burden, and overall risk-benefit in research contexts).

# 1. Compound Identification

## 1.1 Names, synonyms, and registry identifiers

**International Nonproprietary Name:** Metandienone.

**British Approved Name:** Methandienone.

**United States Adopted Name (historical):** Methandrostenolone.

**Marketed name:** Dianabol (CIBA Pharmaceuticals; United States, 1958 to 1983). The Dianabol trade name is the canonical identifier in the historical clinical literature, the sports pharmacology literature, and the anti-doping analytical chemistry literature. Generic versions were marketed in various jurisdictions under names including Danabol, Naposim, Averbol, and Metanabol [1].

**Chemical Abstracts Service registry number:** 72-63-9 (free base). No salt form is in common pharmaceutical or research use; the compound is administered and supplied as the free steroid.

**PubChem Compound Identifier:** CID 6300.

**International Union of Pure and Applied Chemistry name:** (8S,9S,10S,13S,14S,17S)-17-hydroxy-10,13,17-trimethyl-7,8,9,11,12,14,15,16-octahydro-6H-cyclopenta[a]phenanthren-3-one. Alternative systematic names in common use include 17-beta-hydroxy-17-alpha-methylandrosta-1,4-dien-3-one and 17-alpha-methyl-delta-1-testosterone.

**United States patent:** US 2,900,398 (CIBA; inventors of record: Wettstein, Hunger, Meystre, Ehmann) [2].

## 1.2 Structural class and chemistry

Metandienone is a synthetic androstane steroid. It is a derivative of testosterone bearing two structural modifications: (a) a methyl group at the C17-alpha position (17-alpha-alkylation), which confers resistance to hepatic first-pass oxidation and enables oral bioavailability; and (b) a double bond between the C1 and C2 positions (delta-1-dehydrogenation), which modifies the anabolic-to-androgenic dissociation

ratio relative to testosterone and methyltestosterone [3]. The compound is therefore the 17- $\alpha$ -methylated derivative of boldenone ( $\Delta^1$ -testosterone) and the  $\Delta^1$  analogue of methyltestosterone (17- $\alpha$ -methyltestosterone).

**Molecular formula:** C<sub>20</sub>H<sub>28</sub>O<sub>2</sub>.

**Exact mass:** 300.2089 g/mol (monoisotopic).

**Molecular weight:** 300.44 g/mol.

**Physical properties:** White to off-white crystalline powder. Melting point approximately 165 to 166 degrees Celsius. Specific optical rotation +9.3 degrees. Soluble in ethanol, methanol, chloroform, and dimethyl sulfoxide; sparingly soluble in water. The compound is a neutral steroid with no ionizable functional groups at physiological pH.

**Stereochemistry:** Metandienone contains five stereocenters at carbons 8, 9, 10, 13, and 17 of the steroid nucleus. The absolute configuration is (8S,9S,10S,13S,14S,17S), corresponding to the natural trans-anti-trans ring junction geometry of the androstane skeleton. The 17- $\beta$ -hydroxyl group and the 17- $\alpha$ -methyl group are in the axial and equatorial orientations, respectively, when the D-ring adopts the envelope conformation. The compound is supplied as a single stereoisomer; epimerization at C17 (producing the 17- $\alpha$ -hydroxy epimer) is a known metabolic pathway but does not occur appreciably in the solid state or in solution under standard storage conditions.

## 1.3 Synthesis

The original CIBA synthesis of metandienone proceeds from testosterone or from methyltestosterone through a two-step modification. From testosterone, the route involves (a) 17- $\alpha$ -methylation by treatment with methyllithium or methylmagnesium bromide in ether or tetrahydrofuran to introduce the C17- $\alpha$ -methyl group, producing methyltestosterone; followed by (b) microbiological or chemical dehydrogenation at the C1-C2 bond to introduce the  $\Delta^1$  double bond [2, 3]. The chemical dehydrogenation is typically accomplished with 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ) or selenium dioxide in dioxane. Alternatively, from boldenone ( $\Delta^1$ -testosterone, which carries the C1-C2 double bond but lacks the C17- $\alpha$  methyl), 17- $\alpha$ -methylation produces metandienone directly. Industrial synthesis optimizes these steps for yield (typically 50 to 70 percent overall from commercially available starting material) and for stereochemical integrity

at C17. The product is purified by recrystallization from acetone, ethanol, or ethyl acetate, and characterized by nuclear magnetic resonance spectroscopy, melting point, infrared spectroscopy, and high-performance liquid chromatography. Analytical reference standards for anti-doping applications are prepared by certified reference material suppliers (Cerilliant, Sigma-Aldrich, National Measurement Institute Australia) under accredited conditions [4].

## 2. Abstract

Metandienone (Dianabol) is a synthetic 17- $\alpha$ -alkylated, delta-1-dehydrogenated testosterone derivative that was the first widely marketed oral anabolic-androgenic steroid. Developed at CIBA Pharmaceuticals and released to the United States prescription market in 1958, the compound was originally indicated for catabolic wasting states, post-surgical nitrogen-balance restoration, osteoporosis, and pituitary-deficient dwarfism [1, 5]. Its mechanism of action is androgen receptor (AR) agonism: metandienone binds the AR in skeletal muscle, bone, and other androgen-responsive tissues, translocates to the nucleus, and initiates transcription of genes governing protein synthesis, nitrogen retention, and glycogenolysis. The compound also undergoes aromatization by CYP19A1 to 17- $\alpha$ -methylestradiol, producing estrogenic effects at the estrogen receptor including fluid retention and gynecomastia [6].

The pharmacokinetic profile is dominated by oral absorption (time to peak plasma concentration approximately 1 to 2 hours), hepatic metabolism principally through CYP3A4-mediated 6- $\beta$ -hydroxylation, and a plasma elimination half-life of approximately 3 to 6 hours [7, 8]. The 17- $\alpha$ -alkylation that enables oral bioavailability is simultaneously the structural basis for the dose-dependent hepatotoxicity that limits the therapeutic index: intrahepatic cholestasis, elevated serum transaminases, and rare cases of peliosis hepatis and hepatocellular carcinoma have been associated with chronic administration of metandienone and other 17- $\alpha$ -alkylated steroids [9, 10].

Clinical trials conducted in the 1960s demonstrated positive nitrogen balance and lean-mass gains at oral doses of 5 to 10 mg per day in hospitalized patients with wasting conditions [5, 11]. However, dose-dependent hepatotoxicity, suppression of the hypothalamic-pituitary-testicular (HPT) axis with consequent hypogonadism, unfavorable lipoprotein alterations (suppression of high-density lipoprotein cholesterol by 20 to 70 percent, elevation of low-density lipoprotein cholesterol), and estrogenic side effects progressively narrowed the therapeutic window. The FDA withdrew approval in 1983. The compound is currently classified as a Schedule III controlled substance in the United States under the Anabolic Steroids Control Act of 1990, and is prohibited at all times by the World Anti-Doping Agency under the category S1 (anabolic agents) [12].

In contemporary research, metandienone serves as a model 17- $\alpha$ -alkylated steroid for studies of androgen receptor pharmacology, steroid hepatotoxicity mechanisms, hypothalamic-pituitary-gonadal axis suppression, anti-doping analytical method development, and anabolic-androgenic steroid metabolism. Its metabolite profile is among the most comprehensively characterized of any synthetic steroid, with over 20 identified urinary metabolites exploited for detection windows extending to 19 days after a single 5 mg oral dose [4, 13].

## 3. Discovery and Development History

### 3.1 Origin

The synthesis of metandienone is attributed to the pharmaceutical chemistry group at CIBA AG (Basel, Switzerland) in the mid-1950s. The inventors of record on United States Patent 2,900,398 are Albert Wettstein, Charles Hunger, Charles Meystre, and Ludwig Ehmann [2]. The compound was part of a systematic program to develop orally bioavailable anabolic steroids that would separate the anabolic (nitrogen-retaining, muscle-building) properties of testosterone from its androgenic (virilizing) properties. The key structural innovation was the combination of 17-alpha-methylation (already established for methyltestosterone, synthesized by CIBA in 1935) with delta-1-dehydrogenation, which animal assays in the castrated-rat levator-ani/ventral-prostate model indicated would shift the anabolic-to-androgenic ratio in favor of anabolic activity [3, 14].

### 3.2 Clinical introduction and early medical use

CIBA introduced metandienone to the United States market in 1958 under the trade name Dianabol. Approved indications included the treatment of conditions in which a positive nitrogen balance and anabolic effect were desired: post-surgical recovery, chronic illness-associated wasting, severe burns, fracture healing, osteoporosis, and pituitary-deficient dwarfism [1, 5]. Recommended oral doses were 5 mg per day in adults, with some clinicians prescribing up to 10 to 15 mg per day for severely catabolic patients. Clinical reports from the late 1950s and 1960s documented significant positive nitrogen balance, weight gain, appetite stimulation, and increased serum protein levels in hospitalized patients receiving metandienone [5, 11, 15].

### 3.3 Association with athletic performance

The introduction of metandienone into competitive athletics is attributed to Dr. John Bosley Ziegler, a physician associated with the York Barbell Club and the United States Olympic weightlifting program. Following the 1954 World Weightlifting Championships in Vienna, where Soviet athletes reportedly demon-

strated the performance-enhancing effects of exogenous testosterone, Ziegler began collaborating with CIBA to evaluate anabolic steroids for athletic application [16]. CIBA provided Ziegler with metandienone for administration to weightlifters training at York Barbell beginning in approximately 1959. The subsequent rapid diffusion of metandienone use through competitive weightlifting, bodybuilding, and other strength sports in the 1960s and 1970s was a principal driver of the broader anabolic steroid abuse phenomenon in athletics [16, 17].

### 3.4 Regulatory restriction and market withdrawal

Recognition of the hepatotoxic, cardiovascular, and endocrine adverse effects of metandienone at supraphysiological doses led to progressive regulatory action. In 1970, the FDA reclassified metandienone as "probably effective" (rather than definitively effective) for its marketed indications, a designation that initiated a re-evaluation process. In 1983, CIBA voluntarily withdrew Dianabol from the United States market; the FDA subsequently removed the compound from the list of approved drugs [1]. The Anabolic Steroids Control Act of 1990 classified metandienone and other AAS as Schedule III controlled substances in the United States, establishing criminal penalties for non-medical possession and distribution [12]. The compound is prohibited by the World Anti-Doping Agency and by all major sports governing bodies.

### 3.5 Current status

Metandienone is not approved for any medical indication in any major regulatory jurisdiction (United States, European Union, United Kingdom, Japan, Australia). It continues to be manufactured clandestinely for the illicit performance-enhancement market and is available as a research-grade chemical from analytical reference suppliers. The compound's principal contemporary significance is as a model AAS for pharmacological, toxicological, and anti-doping research [4, 13].

## 4. Mechanism of Action

Metandienone is an agonist of the androgen receptor. Its principal pharmacological activities are mediated through genomic signaling at the AR, with secondary estrogenic activity mediated through aromatase-catalyzed conversion to 17-alpha-methylestradiol. These activities operate in concert to produce the anabolic, androgenic, and estrogenic effects observed clinically and in preclinical models.

### 4.1 Androgen receptor agonism

The androgen receptor is a nuclear receptor transcription factor of the steroid receptor superfamily encoded by the AR gene on the X chromosome. In the absence of ligand, the AR resides in the cytoplasm in a complex with heat-shock proteins (HSP90, HSP70, HSP56). Ligand binding induces conformational change, dissociation from the chaperone complex, nuclear translocation, homodimerization, and binding to androgen response elements (AREs) in the promoter regions of target genes. Co-activator recruitment to the AR-ARE complex initiates transcription of genes governing protein synthesis, nitrogen retention, erythropoiesis, bone mineral density, and secondary sexual characteristics [18].

Metandienone binds the AR ligand-binding domain with moderate to high affinity. Studies using rat skeletal muscle and prostate cytosol preparations have characterized the relative binding affinity (RBA) of metandienone for the AR as approximately 10 to 30 percent of that of dihydrotestosterone (DHT) and approximately 30 to 60 percent of that of testosterone, depending on the tissue source and assay conditions [19, 20]. The lower RBA relative to DHT is offset by the higher effective molar concentration achieved through oral dosing and by the compound's resistance to 5-alpha-reductase metabolism (the delta-1 double bond prevents 5-alpha-reduction), which preserves the parent compound in tissues where testosterone would be converted to the more potent DHT.

The downstream genomic consequences of AR activation by metandienone in skeletal muscle include upregulation of ribosomal protein synthesis, increased amino acid transport, positive nitrogen balance (reduced urinary nitrogen excretion by approximately 30 percent at therapeutic doses), enhanced glycogenolysis,

and stimulation of insulin-like growth factor 1 (IGF-1) expression [5, 21]. In bone, AR activation stimulates osteoblast differentiation and inhibits osteoclast activity, the basis for the historical osteoporosis indication.

## 4.2 Aromatization and estrogenic activity

Metandienone is a substrate for the aromatase enzyme (CYP19A1), which catalyzes the oxidative removal of the C19 angular methyl group and aromatization of the A-ring. The aromatization product is 17-alpha-methylestradiol, an estrogenic steroid that binds the estrogen receptor (ER-alpha and ER-beta) and initiates estrogenic signaling [6, 22]. The rate of aromatization of metandienone is moderate relative to testosterone; however, because the 17-alpha-methylestradiol metabolite is resistant to hepatic conjugation (owing to the 17-alpha-methyl group), its effective estrogenic potency at steady state may exceed that predicted from aromatization rate alone.

The estrogenic consequences of metandienone administration include dose-dependent fluid retention (mediated through estrogen-stimulated release of hypothalamic arginine vasopressin, which increases renal water reabsorption), gynecomastia (proliferation of glandular breast tissue in males), and contribution to the unfavorable lipoprotein profile. These effects are preventable or manageable through co-administration of aromatase inhibitors (anastrozole, letrozole) or selective estrogen receptor modulators (tamoxifen, raloxifene), a pharmacological strategy that is well characterized in the endocrine literature but has limited clinical application given the absence of an approved indication for metandienone [6, 22].

## 4.3 Non-genomic signaling

In addition to the classical genomic pathway, metandienone and other androgens activate rapid, non-genomic signaling cascades through membrane-associated AR or through AR-independent mechanisms. These include activation of the phosphatidylinositol 3-kinase/Akt pathway, mitogen-activated protein kinase (MAPK/ERK) signaling, and intracellular calcium mobilization. The non-genomic signaling contributes to the rapid (minutes to hours) effects of androgens on muscle cell proliferation and differentiation that precede the slower genomic transcriptional response [18].

## 4.4 Hypothalamic-pituitary-testicular axis suppression

Exogenous androgen administration, including metandienone, suppresses the hypothalamic-pituitary-testicular (HPT) axis through negative feedback. Metandienone and its estrogenic metabolite 17-alpha-methylestradiol act at the hypothalamus to suppress gonadotropin-releasing hormone (GnRH) pulsatility and at the anterior pituitary to reduce luteinizing hormone (LH) and follicle-stimulating hormone (FSH) secretion. The consequent reduction in endogenous testosterone production, spermatogenesis, and testicular volume is dose-dependent and is the basis for the hypogonadal state observed during and after metandienone administration [23, 24]. Preclinical studies in the rat training model have confirmed that metandienone treatment significantly suppresses serum LH and testosterone concentrations and reduces testicular weight [24].

## 4.5 Myostatin pathway modulation

A 2011 study by Fragkaki et al. in intact rats performing treadmill exercise training characterized the effects of metandienone on the myostatin signaling cascade. In gastrocnemius muscle, mRNA expression of myostatin (MSTN), Smad7, and MyoD was reduced by training alone but was not further modulated by metandienone treatment, suggesting that the anabolic effect of metandienone in trained animals operates through AR-mediated pathways independent of myostatin suppression [24]. In contrast, levator ani muscle (a highly androgen-sensitive tissue) showed significant mass increases with metandienone treatment that were further augmented by concurrent training, confirming the tissue-selective anabolic response.

## 5. Pharmacokinetics and Routes of Administration

### 5.1 Absorption

Metandienone is rapidly and substantially absorbed from the gastrointestinal tract after oral administration. The 17- $\alpha$ -methyl group confers resistance to hepatic first-pass oxidation at the C17 position, enabling oral bioavailability. Published estimates of oral bioavailability range from approximately 50 to 70 percent, with the remainder undergoing first-pass hepatic metabolism principally through CYP3A4-mediated 6- $\beta$ -hydroxylation [7, 8]. Time to peak plasma concentration is approximately 1 to 2 hours after oral administration. The compound is typically administered as uncoated tablets or capsules; enteric coating is not required owing to stability in gastric acid.

### 5.2 Distribution

Metandienone distributes extensively into tissues. The volume of distribution has not been precisely determined in human pharmacokinetic studies but is estimated to be moderate to large, consistent with other lipophilic steroid hormones. Plasma protein binding is moderate; the compound binds to sex hormone-binding globulin (SHBG) with lower affinity than testosterone or DHT, reflecting the structural modifications at C1-C2 and C17, and binds to albumin at concentrations consistent with non-specific lipophilic partitioning [19]. The compound crosses the blood-brain barrier; central nervous system effects including mood alteration, increased aggression, and libido changes are well documented in clinical and observational reports.

### 5.3 Metabolism

Hepatic metabolism of metandienone is extensive and proceeds through multiple pathways [7, 8, 13]:

(a) 6-beta-hydroxylation: The principal metabolic pathway, catalyzed predominantly by CYP3A4. The 6-beta-hydroxymetandienone metabolite is further conjugated (glucuronidation, sulfation) and excreted in urine.

(b) 5-beta-reduction: Reduction of the delta-4 double bond by 5-beta-reductase produces 5-beta-dihydrometandienone and downstream reduced metabolites.

(c) 3-alpha and 3-beta oxidation/reduction: Interconversion of the 3-keto group with 3-alpha-hydroxy and 3-beta-hydroxy metabolites.

(d) 17-epimerization: Epimerization at C17 produces the 17-alpha-hydroxy (17-epi) metabolite, which is pharmacologically inactive.

(e) Conjugation: Phase II metabolism produces glucuronide and sulfate conjugates of the hydroxylated and reduced metabolites, which are excreted in urine.

The delta-1 double bond is resistant to 5-alpha-reductase, which means that unlike testosterone, metandienone is not converted to a more potent 5-alpha-reduced metabolite in androgen-target tissues. This resistance is a consequence of the conjugated diene system (delta-1,4-dien-3-one) and contributes to the tissue-selectivity profile of the compound relative to testosterone [3].

## 5.4 Elimination

The plasma elimination half-life of metandienone is approximately 3 to 6 hours after oral administration [7, 8]. Elimination is predominantly hepatic (metabolic), with the conjugated metabolites excreted in urine (approximately 60 to 70 percent of the administered dose) and in feces via biliary excretion (approximately 20 to 30 percent). Less than 5 percent of the administered dose is excreted unchanged in urine.

For anti-doping purposes, the urinary detection window for the principal metabolites (6-beta-hydroxymetandienone, epimetandienone) is approximately 3 to 5 days after a single oral dose. A long-term metabolite, 18-nor-17-beta-hydroxymethyl-17-alpha-methylandrosta-1,4,13-trien-3-one, discovered through advances in liquid chromatography-tandem mass spectrometry, extends the detection window to approximately 19 days after a single 5 mg oral dose [4, 13].

## 5.5 Routes of administration

The principal route of administration is oral. Metandienone was historically supplied as 5 mg tablets (Dianabol, CIBA) and is currently encountered in the illicit market as 5 mg, 10 mg, 25 mg, and 50 mg tablets or capsules of variable quality. Injectable preparations of metandienone are uncommon; the compound is not formulated as an ester for intramuscular depot injection (unlike testosterone, nandrolone, and boldenone, which are commonly esterified). Sublingual and transdermal administration have been explored in research settings but are not standard [1].

## 5.6 Special populations

Formal pharmacokinetic studies in special populations (pediatric, geriatric, hepatic impairment, renal impairment) were not conducted to contemporary regulatory standards before market withdrawal. Historical clinical use in pediatric patients for pituitary-deficient dwarfism employed body-weight-adjusted doses (approximately 0.04 to 0.1 mg/kg/day). Hepatic impairment would be expected to substantially prolong elimination and increase exposure to both the parent compound and hepatotoxic metabolites. Renal impairment would be expected to have minimal effect on parent-compound pharmacokinetics but may delay elimination of conjugated urinary metabolites.

## 6. Preclinical Pharmacology

### 6.1 Anabolic activity in the castrated-rat bioassay

The castrated-rat levator-ani/ventral-prostate bioassay is the standard preclinical assay for anabolic-androgenic dissociation. Metandienone produces dose-dependent increases in levator ani muscle weight (the anabolic endpoint) at oral doses lower than those required to produce equivalent increases in ventral prostate weight (the androgenic endpoint), confirming the anabolic-favoring dissociation designed into the molecule [14, 25]. The anabolic-to-androgenic ratio in the castrated-rat bioassay is reported as approximately 90 to 210 : 40 to 60 (relative to methyltestosterone = 100 : 100), though published values vary across laboratories and assay conditions.

### 6.2 Muscle hypertrophy in training models

Fragkaki et al. (2011) characterized the effects of metandienone (0.17 mg/day, oral gavage, 8 weeks) in intact male Wistar rats performing treadmill exercise training [24]. Metandienone treatment significantly increased levator ani muscle mass compared to vehicle-treated controls. The combination of metandienone and exercise training produced levator ani hypertrophy greater than either intervention alone. Gastrocnemius muscle mass increased with training but was not further augmented by metandienone, consistent with tissue-selective androgen sensitivity.

### 6.3 Hypothalamic-pituitary-testicular axis effects

In the same rat training model, metandienone treatment significantly suppressed serum LH and serum testosterone concentrations and reduced absolute and relative testicular weight, confirming the suppressive effect on the HPT axis in intact animals [24]. These findings are consistent with the clinical observation of hypogonadism during and after metandienone administration in humans.

## 6.4 Hepatotoxicity models

The 17- $\alpha$ -alkylated steroids, including metandienone, produce dose- and duration-dependent hepatotoxicity in animal models. The principal mechanism is intrahepatic cholestasis: the 17- $\alpha$ -alkyl group interferes with bile acid transport at the canalicular membrane, reducing bile flow and producing intracellular accumulation of cytotoxic bile acids [9, 10]. In rat models, metandienone administration at supraphysiological doses produces elevated serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST), histological evidence of centrilobular cholestasis, and in chronic dosing, peliosis hepatis (blood-filled hepatic cysts). These findings parallel the clinical hepatotoxicity observed in humans.

## 6.5 Cardiovascular effects in animal models

Chronic metandienone administration in animal models produces cardiac hypertrophy (increased left ventricular mass relative to body weight), myocardial fibrosis, and impaired diastolic function. The mechanism is multifactorial: direct AR-mediated cardiac myocyte hypertrophy, indirect effects of volume overload from estrogen-mediated fluid retention, and contribution from the atherogenic lipoprotein profile [26].

## 7. Clinical Evidence Base

### 7.1 Nitrogen balance and catabolic wasting

The principal clinical evidence for metandienone efficacy derives from studies conducted in the late 1950s and 1960s in patients with catabolic wasting states. Metandienone at 5 to 10 mg per day produced significant positive nitrogen balance (reduction in urinary nitrogen excretion by approximately 30 percent), weight gain (approximately 2 to 5 kg over 4 to 8 weeks of treatment), and increased serum protein levels in hospitalized patients recovering from surgery, severe burns, chronic infections, and debilitating illness [5, 11, 15]. Appetite stimulation was a consistent reported effect.

### 7.2 Osteoporosis

The FDA in 1970 rated metandienone as "probably effective" for the treatment of osteoporosis. Clinical studies in postmenopausal women and in corticosteroid-induced osteoporosis demonstrated modest increases in calcium retention and bone mineral density at oral doses of 2.5 to 5 mg per day, but the virilizing adverse effects (hirsutism, voice deepening, acne) at these doses limited acceptability, and the compound was not established as a first-line therapy [1, 5].

### 7.3 Performance and body composition in healthy subjects

Hervey et al. (1981) conducted a double-blind, placebo-controlled, crossover trial of metandienone (100 mg/day for 6 weeks) in healthy men undergoing standardized athletic training [27]. Metandienone treatment produced significant increases in body weight (approximately 3.3 kg), lean body mass (approximately 2.3 kg), and potassium retention (indicating cellular mass gain) compared to placebo. Fat mass was unchanged. These findings provided controlled evidence that metandienone produces genuine lean-tissue accretion in trained individuals, though the supra-physiological dose used in this study substantially exceeds the historical therapeutic dose range.

## 7.4 Lipid and metabolic effects

Clinical monitoring during metandienone administration has consistently demonstrated unfavorable changes in serum lipoproteins. Thompson et al. (1989) reported that oral AAS administration (including metandienone) produced reductions in HDL cholesterol of 20 to 70 percent and increases in LDL cholesterol of approximately 30 to 50 percent within 2 to 9 weeks of initiation, with effects reversible over approximately 3 to 5 months after discontinuation [28, 29]. Effect on blood lipids and liver function tests was examined in a controlled clinical study published in the British Medical Journal, confirming dose-dependent hepatic enzyme elevation and lipoprotein disturbance at therapeutic and supraphysiological doses [30].

## 7.5 Limitations of the clinical evidence

The clinical evidence base for metandienone is historically significant but methodologically limited by contemporary standards. Most efficacy studies were conducted before modern randomized controlled trial methodology was established; sample sizes were small; blinding was incomplete; and outcomes were frequently assessed by non-validated instruments. The withdrawal of regulatory approval in 1983 precluded further properly designed clinical trials. The compound's current Schedule III status and WADA prohibition further limit the feasibility of new clinical research.

## 8. Sourcing and Quality Verification

Pharmaceutical-grade metandienone is no longer manufactured by any regulated pharmaceutical company. The compound is available from two principal sources for research applications:

**Certified reference material suppliers:** Analytical reference standards of metandienone and its principal metabolites are supplied by Cerilliant (a Sigma-Aldrich subsidiary), the National Measurement Institute Australia (NMI), the United States Pharmacopeia (USP), and other certified reference material producers at greater than 99 percent purity by HPLC [4]. These materials are intended for use as analytical standards in anti-doping laboratories and forensic chemistry; they are supplied in milligram quantities at analytical-standard pricing (typically \$50 to \$200 per 10 to 100 mg).

**Research chemical suppliers:** Research-grade metandienone is available from multiple suppliers (Cayman Chemical, Toronto Research Chemicals, MedChemExpress, LGC Standards, others) at greater than 98 percent purity by HPLC. Supply is in milligram to gram quantities as the free steroid.

**Illicit market:** Metandienone circulates widely in the illicit performance-enhancement market as tablets or capsules labeled at 5 to 50 mg per unit. Quality control in this market is inconsistent; published analyses of illicit AAS products have demonstrated frequent under-dosing, over-dosing, mislabeling, contamination with other AAS, and presence of pharmaceutical excipients not declared on the label [31, 32]. Illicit-market material is not suitable for controlled research.

Investigators should confirm compound identity and purity on every research-grade lot through:

- High-performance liquid chromatography area-percent purity (target greater than 98 percent)
- Mass spectrometry confirmation of molecular weight (expected  $[M+H]^+ = 301.22$ )
- Melting point determination (expected 165 to 166 degrees Celsius)
- Nuclear magnetic resonance spectroscopy ( $^1H$  and  $^{13}C$ ) for structural confirmation

- Residual solvent analysis by gas chromatography

Third-party analytical confirmation is especially important for metandienone research given the prevalence of counterfeit and mislabeled material in non-pharmaceutical supply chains.

## 9. Reconstitution and Handling

Metandienone is supplied as a crystalline powder and is stable in the solid state at room temperature. For research applications, the following handling guidelines apply:

**Storage:** Room temperature (15 to 25 degrees Celsius) in a desiccated container protected from light. The compound is stable under these conditions for at least 24 months. Refrigerated storage (2 to 8 degrees Celsius) is acceptable but not required for the solid.

**Stock solutions:** Metandienone is freely soluble in ethanol (approximately 50 mg/mL), methanol (approximately 50 mg/mL), dimethyl sulfoxide (approximately 100 mg/mL), and chloroform. Aqueous solubility is limited (less than 1 mg/mL); for aqueous-compatible applications, the compound is dissolved in a water-miscible organic cosolvent (ethanol, dimethyl sulfoxide, polyethylene glycol 400) and diluted into aqueous buffer at final cosolvent concentrations not exceeding 0.1 to 1 percent volume-to-volume. Stock solutions in dimethyl sulfoxide are stable at minus 20 degrees Celsius for at least 6 months.

**In vivo research formulations:** For oral gavage in rodent studies, metandienone is typically dissolved in corn oil, sesame oil, or a vehicle consisting of 10 percent ethanol, 40 percent polyethylene glycol 400, and 50 percent saline. Doses in the published rat literature range from 0.1 to 5 mg/kg/day by oral gavage [24].

**Handling precautions:** Metandienone is a potent androgen. Standard laboratory personal protective equipment (gloves, laboratory coat, eye protection) should be used during handling of the solid and stock solutions. Avoid inhalation of dust and skin contact.

# 10. Stack Interactions and Combinations

The term "stack" in the anabolic steroid pharmacology literature refers to the concurrent administration of multiple AAS or the combination of AAS with ancillary agents. Although no approved medical application exists for metandienone combinations, the research and clinical toxicology literature documents several pharmacologically relevant interactions:

**Aromatase inhibitors (anastrozole, letrozole, exemestane):** Co-administration reduces the conversion of metandienone to 17-alpha-methylestradiol and mitigates estrogenic effects (fluid retention, gynecomastia). The interaction is well characterized at the enzyme level; anastrozole at 1 mg/day effectively suppresses aromatization in the presence of AAS [6].

**Selective estrogen receptor modulators (tamoxifen, raloxifene):** Co-administration blocks estrogenic signaling at the receptor level without reducing aromatization. Tamoxifen at 20 mg/day prevents gynecomastia in the setting of aromatizable AAS exposure [22].

**Other 17-alpha-alkylated oral AAS (oxymetholone, stanozolol, oxandrolone):** Concurrent administration produces additive or synergistic hepatotoxicity. The combination of multiple 17-alpha-alkylated steroids substantially increases the risk of intrahepatic cholestasis and should be avoided in any research context [9, 10].

**Injectable AAS (testosterone, nandrolone decanoate, boldenone undecylenate):** Concurrent administration produces additive androgen receptor activation and additive HPT axis suppression. The combination of an oral 17-alpha-alkylated steroid with an injectable ester is a common pattern in the illicit performance-enhancement literature; the injectable component does not add to the hepatotoxic risk (non-17-alpha-alkylated steroids do not produce cholestatic hepatotoxicity).

**CYP3A4 inhibitors (ketoconazole, itraconazole, ritonavir, grapefruit juice):** Strong CYP3A4 inhibitors may reduce 6-beta-hydroxylation of metandienone, increasing parent-compound exposure and potentially increasing both anabolic ef-

fect and hepatotoxic risk [7, 8]. One published report demonstrated that 6',7'-dihydroxybergamottin (a grapefruit juice constituent and CYP3A4 inhibitor) increased the oral bioavailability of metandienone in an in vitro model [33].

**CYP3A4 inducers (rifampin, carbamazepine, phenytoin, St. John's wort):** Induction of CYP3A4 increases 6-beta-hydroxylation and reduces metandienone exposure, potentially compromising efficacy in dose-response research.

**Hepatotoxic agents (acetaminophen at high doses, ethanol, isoniazid, methotrexate):** Concurrent exposure to other hepatotoxic agents increases the risk of clinically significant liver injury in the setting of metandienone administration.

**Human chorionic gonadotropin (hCG) and selective estrogen receptor modulators for HPT axis recovery:** Following discontinuation of metandienone (and other AAS), the suppressed HPT axis may require weeks to months for recovery of endogenous testosterone production. hCG (which directly stimulates testicular Leydig cells) and tamoxifen or clomiphene (which block estrogen negative feedback at the hypothalamus and pituitary) are used in the clinical endocrinology literature to facilitate HPT axis recovery, though formal clinical trials specific to post-metandienone recovery are lacking [23].

# 11. Adverse Events and Safety Signal

## 11.1 Hepatotoxicity

Hepatotoxicity is the principal safety concern with metandienone and all 17-alpha-alkylated AAS. The adverse-event spectrum includes [9, 10, 30]:

- Elevated serum transaminases (ALT, AST): Dose-dependent, typically mild (1.5 to 3 times the upper limit of normal) at therapeutic doses (5 to 10 mg/day), more pronounced at supraphysiological doses. Onset within 2 to 4 weeks of initiation; reversible on discontinuation.
- Intrahepatic cholestasis: The characteristic hepatic lesion. Manifests as conjugated hyperbilirubinemia, jaundice, pruritus, and elevated alkaline phosphatase. Onset typically within 1 to 6 months of continuous administration.
- Peliosis hepatis: Blood-filled hepatic cysts, reported principally with chronic (months to years) administration of 17-alpha-alkylated steroids. Potentially life-threatening if cysts rupture.
- Hepatocellular carcinoma and hepatic adenoma: Rare, reported with chronic (years) administration. Causal attribution is complicated by confounding factors in case reports.

## 11.2 Cardiovascular adverse effects

Metandienone produces a well-characterized atherogenic lipoprotein profile [28, 29]:

- HDL cholesterol suppression: 20 to 70 percent reduction, dose-dependent, onset within 2 to 9 weeks. The mechanism involves hepatic lipase upregulation by androgens, which accelerates HDL catabolism.
- LDL cholesterol elevation: Approximately 30 to 50 percent increase, contributing to a pro-atherogenic ratio.
- Blood pressure elevation: Reported in some studies, likely multifactorial (fluid retention from estrogenic activity, direct vascular AR-mediated effects, sympathetic activation).

- Left ventricular hypertrophy: Documented in echocardiographic studies of chronic AAS users; direct AR-mediated cardiac myocyte hypertrophy and volume overload contribute [26].
- Thrombotic events: Increased erythropoiesis (polycythemia) and altered coagulation factor expression increase the risk of venous and arterial thrombosis.

### 11.3 Endocrine adverse effects

- HPT axis suppression: Dose-dependent suppression of LH, FSH, and endogenous testosterone. Chronic administration produces hypogonadism with testicular atrophy, oligospermia or azospermia, and reduced libido on discontinuation [23, 24].
- Estrogenic effects: Gynecomastia (dose-dependent, reported in approximately 10 to 30 percent of users at supraphysiological doses), fluid retention, and increased adiposity in estrogen-sensitive depots [6, 22].

### 11.4 Androgenic adverse effects

- Acne vulgaris (dose-dependent, commonly on the back and shoulders)
- Androgenic alopecia (male-pattern hair loss in genetically predisposed individuals)
- Virilization in female subjects (hirsutism, voice deepening, clitoral enlargement, menstrual irregularity)
- Premature epiphyseal closure in adolescent subjects (via estrogen-mediated effects on growth plates)

### 11.5 Psychological adverse effects

- Mood alteration, irritability, increased aggression ("roid rage" in colloquial terminology)
- Dependence and withdrawal syndrome: AAS dependence meeting DSM criteria has been documented; withdrawal features include depression, fatigue, reduced libido, and insomnia [34]
- Mania and psychotic symptoms at high doses (rare)

## 11.6 Other adverse effects

- Acneiform dermatitis and seborrhea
- Tendon weakening (increased muscle strength without proportional tendon adaptation)
- Altered glucose tolerance (insulin resistance, particularly at supraphysiological doses)
- Prostate hypertrophy (at chronic supraphysiological doses)

## 12. Comparative Assessment

This section presents a structured comparative assessment of five alternative anabolic-androgenic steroids against metandienone, evaluated on five competency standards: oral bioavailability, anabolic efficacy, hepatotoxicity profile, estrogenic burden, and overall risk-benefit in research contexts. The five comparators were selected as the principal AAS with substantial clinical or research pharmacology records and with relevance to the historical and contemporary applications of metandienone.

### 12.1 Testosterone (injectable esters: enanthate, cypionate, propionate)

**Mechanism:** Endogenous androgen; full AR agonist. Converted to DHT by 5-alpha-reductase in target tissues and to estradiol by aromatase.

**Oral bioavailability:** Native testosterone has negligible oral bioavailability owing to extensive hepatic first-pass metabolism. Exogenous testosterone is therefore administered as intramuscular depot injections of ester prodrugs (enanthate, cypionate, undecanoate) or as transdermal preparations. Oral testosterone undecanoate (Jatenzo, approved 2019) achieves oral bioavailability through lymphatic absorption but requires twice-daily dosing with food. Metandienone has substantially superior oral bioavailability in the conventional tablet formulation.

**Anabolic efficacy:** Testosterone is the reference standard for anabolic-androgenic potency (anabolic:androgenic ratio = 100:100 by convention). At equivalent androgen-receptor occupancy, testosterone and metandienone produce comparable anabolic effects; the practical difference is the route of administration and the contribution of 5-alpha-reduced and aromatized metabolites.

**Hepatotoxicity profile:** Non-17-alpha-alkylated. Injectable testosterone esters do not produce cholestatic hepatotoxicity and have a substantially more favorable hepatic safety profile than metandienone. This is the principal safety advantage of testosterone over metandienone and all 17-alpha-alkylated oral steroids [9, 10].

**Estrogenic burden:** Testosterone aromatizes to estradiol. Estrogenic effects (fluid retention, gynecomastia) are dose-dependent and comparable in magnitude to metandienone at equipotent androgenic doses; however, estradiol (from testosterone) is more efficiently hepatically conjugated than 17-alpha-methylestradiol (from metandienone), potentially reducing the steady-state estrogenic load.

**Overall risk-benefit in research:** Testosterone is the reference AAS for clinical and research applications, with a comprehensive pharmacokinetic database, multiple approved formulations, and a safety profile superior to metandienone for hepatic endpoints. The requirement for injection or specialized oral formulations is the principal operational disadvantage. For research requiring an oral AAS, metandienone provides convenience that testosterone does not match in conventional formulations.

## 12.2 Oxandrolone (Anavar)

**Mechanism:** Synthetic DHT derivative; AR agonist. The 2-oxa modification (replacement of the C2 carbon with oxygen) in the A-ring increases anabolic selectivity and reduces androgenic potency. Does not undergo aromatization.

**Oral bioavailability:** High. Oxandrolone is 17-alpha-alkylated but carries the 2-oxa modification that partially mitigates hepatotoxic potential. Oral bioavailability is comparable to metandienone.

**Anabolic efficacy:** The anabolic-to-androgenic ratio in the castrated-rat bioassay is approximately 322 to 630 : 24, substantially more anabolic-selective than metandienone [35]. Clinical studies in burn patients, HIV wasting, and corticosteroid-induced catabolism have demonstrated significant lean-mass gains at 10 to 20 mg/day with minimal androgenic adverse effects.

**Hepatotoxicity profile:** As a 17-alpha-alkylated steroid, oxandrolone carries hepatotoxic potential. However, clinical studies at approved doses (5 to 20 mg/day) have demonstrated a lower incidence and severity of hepatic enzyme elevation than metandienone at comparable or lower milligram doses, likely reflecting the 2-oxa modification and the lower required dose for equivalent anabolic effect [36].

**Estrogenic burden:** Oxandrolone does not aromatize. Estrogenic effects (fluid retention, gynecomastia) are absent. This is a significant advantage over metandienone for applications where estrogenic effects confound outcome assessment.

**Overall risk-benefit in research:** Oxandrolone has a more favorable safety profile than metandienone (lower hepatotoxicity, no estrogenic effects, reduced androgenic burden) and retains FDA approval (Oxandrin) for adjunctive therapy in weight-recovery programs. It is the preferred oral AAS for clinical research in catabolic states. Metandienone has higher absolute anabolic potency per milligram but a substantially less favorable safety profile.

## 12.3 Oxymetholone (Anadrol)

**Mechanism:** Synthetic DHT derivative; AR agonist. 17-alpha-alkylated. Does not aromatize directly but produces estrogenic effects through an incompletely characterized mechanism (possibly direct ER activation by the parent compound or a metabolite) [37].

**Oral bioavailability:** High. 17-alpha-alkylated; comparable to metandienone.

**Anabolic efficacy:** The most potent oral AAS by milligram dose. Clinical doses of 50 to 150 mg/day produce rapid and substantial lean-mass gains. Anabolic efficacy exceeds metandienone on a milligram-per-milligram basis [37].

**Hepatotoxicity profile:** As a 17-alpha-alkylated steroid, oxymetholone produces dose-dependent hepatotoxicity comparable to or greater than metandienone. Cases of peliosis hepatis and hepatocellular carcinoma have been reported with chronic use. The compound retains FDA approval (Anadrol-50) for the treatment of acquired aplastic anemia, but hepatic monitoring is mandatory during therapy [9].

**Estrogenic burden:** Despite being a DHT derivative (which cannot aromatize), oxymetholone produces significant estrogenic effects including fluid retention and gynecomastia. The mechanism is debated; direct activation of the estrogen receptor by oxymetholone or by its 2-hydroxymethylene metabolite has been proposed. The estrogenic burden is comparable to or greater than metandienone [37].

**Overall risk-benefit in research:** Oxymetholone is more potent than metandienone but carries equal or greater hepatotoxic and estrogenic risk. Its principal advantage is FDA-approved status for aplastic anemia, providing a regulatory pathway for clinical research. For anabolic research endpoints, oxymetholone offers greater potency at the cost of a narrower therapeutic index.

## 12.4 Stanozolol (Winstrol)

**Mechanism:** Synthetic DHT derivative with a pyrazole ring fused to the A-ring; AR agonist. 17-alpha-alkylated. Does not aromatize.

**Oral bioavailability:** High. 17-alpha-alkylated; comparable to metandienone. Also available as an aqueous injectable suspension (Winstrol Depot), providing an alternative route.

**Anabolic efficacy:** The anabolic-to-androgenic ratio in the castrated-rat bioassay is approximately 320:30, substantially more anabolic-selective than metandienone [25]. Clinical experience at 2 to 6 mg/day demonstrated efficacy in hereditary angioedema prophylaxis (the current principal medical application) and modest lean-mass effects.

**Hepatotoxicity profile:** As a 17-alpha-alkylated steroid, stanozolol produces cholestatic hepatotoxicity comparable to metandienone at comparable hepatic exposure. Published cases of severe cholestasis, peliosis hepatis, and hepatic failure have been associated with stanozolol use [9, 10].

**Estrogenic burden:** Stanozolol does not aromatize and does not produce clinically significant estrogenic effects. Fluid retention is minimal. This is a significant advantage over metandienone for lean-mass preservation research.

**Overall risk-benefit in research:** Stanozolol has a more favorable anabolic-to-androgenic ratio and zero estrogenic burden compared to metandienone, but equivalent hepatotoxic potential as a 17-alpha-alkylated steroid. It retains limited clinical approval (hereditary angioedema prophylaxis in some jurisdictions). The absence of estrogenic effects makes it preferable to metandienone for research where estrogenic confounding is undesirable; the hepatotoxic risk is equivalent.

## 12.5 Nandrolone decanoate (Deca-Durabolin)

**Mechanism:** Synthetic 19-nortestosterone derivative; AR agonist. Non-17-alpha-alkylated; administered as the decanoate ester by intramuscular injection. Converted by 5-alpha-reductase to 5-alpha-dihydronandrolone, which has lower AR affinity than nandrolone itself (the reverse of the testosterone-to-DHT conversion), conferring tissue-selective anabolic activity [38].

**Oral bioavailability:** Negligible. Nandrolone decanoate requires intramuscular injection. This is an operational disadvantage relative to metandienone.

**Anabolic efficacy:** The anabolic-to-androgenic ratio of nandrolone is approximately 125:37, more anabolic-selective than testosterone but less dramatically dissociated than oxandrolone or stanozolol [38]. Clinical studies in HIV wasting, chronic renal failure, and osteoporosis have demonstrated significant lean-mass gains and bone mineral density increases at 100 to 200 mg every 2 weeks.

**Hepatotoxicity profile:** Non-17-alpha-alkylated. Nandrolone decanoate does not produce cholestatic hepatotoxicity. The hepatic safety profile is substantially superior to metandienone and all 17-alpha-alkylated oral steroids [9, 10].

**Estrogenic burden:** Nandrolone aromatizes to estradiol at a rate substantially lower than testosterone (approximately 20 percent of the testosterone aromatization rate). Estrogenic effects are minimal at therapeutic doses. Nandrolone also has progestogenic activity at the progesterone receptor, which can produce gynecomastia through a non-estrogenic mechanism at high doses.

**Overall risk-benefit in research:** Nandrolone decanoate has a substantially more favorable hepatic safety profile and lower estrogenic burden than metandienone. Its principal disadvantages are the requirement for intramuscular injection and the progestogenic activity. For research applications where hepatic safety is a priority and oral dosing is not required, nandrolone decanoate is preferred over metandienone.

## 12.6 Comparator summary

The five comparators occupy distinct positions in the AAS pharmacology space. **Testosterone** is the reference standard with no hepatotoxic risk from the injectable formulation but requiring injection. **Oxandrolone** is the safest oral AAS with current FDA approval, offering low hepatotoxicity and no estrogenic effects at the cost of lower absolute potency. **Oxymetholone** is the most potent oral AAS but carries hepatotoxic and estrogenic risk equal to or exceeding metandienone. **Stanozolol** provides a non-aromatizing oral alternative with favorable anabolic selectivity but equivalent hepatotoxic risk. **Nandrolone decanoate** provides the most favorable safety profile overall but requires injection.

Metandienone occupies the position of the first and most historically characterized oral AAS. Its advantages include oral bioavailability, well-documented pharmacokinetics, a comprehensive urinary metabolite profile valuable for analytical chemistry research, and a historical clinical evidence base that, despite methodological limitations, provides foundational data on nitrogen balance and anabolic efficacy in humans. Its disadvantages include the hepatotoxicity inherent to 17-alpha-alkylation, the estrogenic burden from aromatization to 17-alpha-methylestradiol, and the absence of current regulatory approval in any jurisdiction. For contemporary clinical research in catabolic or muscle-wasting conditions, oxandrolone (FDA-approved, lower hepatotoxicity, no estrogenic effects) and nandrolone decanoate (non-hepatotoxic, injectable) are generally preferred. Metandienone retains its principal research value as a model compound for AAS pharmacology, steroid hepatotoxicity, anti-doping method development, and androgen receptor biology studies.

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