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The Role of Pharmaceutical Science in Mitigating the Adverse Effects of Steroids on Animals

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Abstract

Pharmaceutical science plays a crucial role in mitigating the adverse effects of steroids in animals, as steroids, beneficial for their anti-inflammatory and immunosuppressive properties, can cause significant side effects. Steroids are frequently used in veterinary medicine to treat various ailments, including immune-mediated illnesses, inflammatory disorders, and allergies. Additionally, anabolic steroids are used to promote growth in food animals, although this practice is controversial due to potential health risks to humans and is banned in the European Union. The use of steroids, while beneficial in certain cases, leads to a range of adverse effects, such as HPA axis inhibition, metabolic abnormalities, and behavioral changes. Anabolic steroids, in particular, can cause liver and kidney damage, heart issues, and cognitive deficits. To address these issues, pharmaceutical research focuses on developing safer steroid formulations by modifying their chemical structures, such as creating selective androgen receptor modulators (SARMs), and optimizing administration routes to minimize systemic exposure. The chapter also focuses on understanding the pharmacokinetics and pharmacodynamics of steroids, as well as developing precise analytical methods to detect steroid abuse. The goal is to provide safer and more effective steroid treatments for animals and balancing their advantages with potential risks. The chapter also details the different types of steroids, such as mineralocorticoids and glucocorticoids, and their applications in animals. The mechanisms of steroid action are described, including their interaction with intracellular receptors and their impact on gene expression. The chapter underscores the need for careful regulation and monitoring of steroid use, considering the wide range of laws and restrictions across different nations.

Keywords: Pharmaceutical Science, Steroids, Adverse Effects, Veterinary Medicine, Anabolic Steroids, Glucocorticoids

Introduction

Because of their strong anti-inflammatory and immunosuppressive properties, steroids are often employed in veterinary medicine. They are used to treat a number of ailments, such as immune-mediated illnesses, inflammatory disorders, and allergies. In several nations, anabolic steroids are especially utilized to encourage the development of animals raised for food (Williams, 2018). The necessity to boost meat output to satisfy the demands of an expanding world population is what motivates this approach. However, the European Union has strictly prohibited the use of anabolic steroids in animals raised for food due

to worries about the possible health dangers to humans. Although there are certain advantages to using steroids, it's important to understand that steroid treatment has drawbacks. In cases of severe illness, steroids can save lives (Wanner, 2004a). They are used, for instance, to treat autoimmune hemolytic anemia, a disorder that, if ignored, can harm an infant's brain. Additionally, they are helpful in treating infantile spasms and hypoglycemia, which can have long-term neurological effects. Anabolic steroids are used to increase muscle development and feed efficiency in animals in addition to their medicinal uses. Increased meat output and financial gains for farmers may result from this (Shafiq Ur Rehman et al., 2024). Even at physiological dosages, long-term steroid usage can have a variety of negative consequences, such as,

1) Inhibiting the HPA axis including Moon faces, buffalo hump, central trunk obesity, hirsutism, acne, skin atrophy, and growth inhibition are examples of physical alterations, 2) Immunosuppression including metabolic abnormalities such as muscular atrophy, decreased bone mineral density, osteoporosis, and hyperglycemia; and ocular consequences such as glaucoma and cataracts, 3) Behavioral alterations, including mental disorders, increased hunger, and sleeplessness (Pofi et al., 2023). Serious health hazards, +including liver and kidney damage, heart muscle degeneration, blood clotting issues, and an elevated chance of muscle and tendon rupture, are linked to anabolic steroids in particular. Additionally, they may cause brain shrinkage and cognitive deficits in the developing brain (Pofi et al., 2023). In order to address the negative effects of steroids on animals, pharmaceutical research is essential. In order to maximize the therapeutic effects of steroids and reduce their unwanted side effects, their chemical structure must be altered. For example, scientists are creating selective androgen receptor modulators (SARMs), which target particular tissues without having the negative side effects of conventional anabolic steroids maximizing administration routes. Steroids can be delivered directly to the target region by topical administration, including oral inhalation, which minimizes adverse effects and systemic exposure (Pilla & Suchodolski, 2020). Fig. 1 shows the molecular structure of corticosteroid.

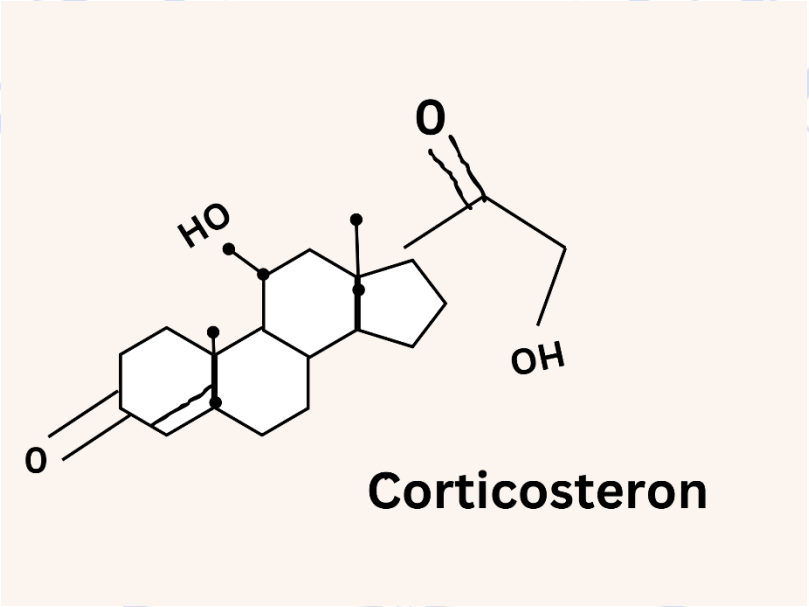

Fig. 1: The molecular structure of Corticosterone

Types of Steroids and Their Applications in Animals

Aldosterone, a mineralocorticoid, gets its name from its role in preserving electrolyte balance. Nevertheless, a wider variety of actions in non-classic target cellular areas are also triggered by mineralocorticoids, including some effects on wound healing following damage. Furthermore, in the absence of tissue damage, a persistent and unwarranted rise in aldosterone production (in relation to intravascular volume and dietary salt consumption) triggers a wound-healing response. In order to avoid undesirable cardiac remodeling and fibrosis, anti-aldosterone medication therapy (such as spironolactone) may be advised (Pofi R et al., 2020). By inhibiting PLA2, reducing the manufacture of interleukins and many other proinflammatory cytokines, suppressing cell-mediated immunity, reducing the synthesis of complement, and lowering leukocyte production and activity, glucocorticoids restrict almost every aspect of the inflammatory process. This makes glucocorticoids the most effective anti-inflammatory medications so far (Nuñez et al., 2020).

Additionally, they are the most often used anti-inflammatory medications. However, there is a significant chance of negative consequences due to the wide range of their pharmacologic and physiological actions. The immune system, stress response, and the metabolism of fats, proteins, and carbohydrates are all significantly impacted by glucocorticoids. Fluid and electrolyte

balance are impacted by natural glucocorticoids since they also exhibit some mineralocorticoid action (Neethi Raj et al., 2018). Despite the fact that corticosteroids can be quite successful in reducing or avoiding inflammation, the same receptor mediates both their pharmacologic and physiological modes of action. This clarifies the underlying connection between their pharmacologic and physiological effects as well as the potential harm that supraphysiologic exposure to corticoids may cause to a number of metabolic, hormonal, and immunologic processes (Matthews et al., 2008). Like hydrocortisone (cortisol), all therapeutic corticosteroids have a 21-carbon steroid structure. Changes to this skeleton change the compound's duration of action and protein-binding affinity, as well as the degree of anti-inflammatory efficacy and metabolic effects. Glucocorticoid and anti-inflammatory action are increased when an extra double bond is added between cortisol's C-1 and C-2 in all synthetic corticosteroids. Prednisolone is about four to five times more selective than cortisol, for example, and this one change has no effect on mineralocorticoid activity, leading to an increased glucocorticoid/mineralocorticoid potency ratio (Liverani et al., 2012). As with 9-alpha-fluorocortisol (fludrocortisone) and isoflupredone, further fluorination at the C-9 position increases the activity of both glucocorticoids and mineralocorticoids. Fludrocortisone (given as fludrocortisone acetate) has a mineralocorticoid impact that is 125 times stronger than cortisol, while its glucocorticoid effect is only 10 times more. Because of its mineralocorticoid selectivity, it is utilized in small animal therapy to treat adrenocortical insufficiency (Liverani et al., 2012).

Although it lacks selectivity for mineralocorticoid effects and raises the risk of severe hypokalemia, isoflupredone is used as an anti-inflammatory medication in cattle. A fluorinated derivative that has been substituted at position C-16 by an OH radical or a CH3 group, such as triamcinolone, dexamethasone, or betamethasone, has a strong anti-inflammatory glucocorticoid effect but almost no mineralocorticoid effect (Li et al., 2001). These fluorocorticosteroids get a new ability due to this last replacement on C-16, which allows them to induce parturition in a variety of animals, including cattle. When given to cattle after 255 days of gestation, the short-acting formulations of dexamethasone and flumethasone can cause parturition; nevertheless, forced calving is often linked to a high rate of side effects, such as retained placenta (Koziol-White et al., 2020).

Esters are used to deliver several corticoids. The degree of water/lipid solubility and the compound's in vivo distribution are both regulated by the esterification of the alcohol at C-21. Water-insoluble medications (such methylprednisolone acetate) that may be given intramuscularly, subcutaneously, or intra-articularly as long-acting formulations are produced by esterification with a monoacid, such as acetic acid. Diacetate, terbutate, and pivalate are further water-insoluble esters (Huizenga et al., 1998a). On the other hand, when the same corticoid is esterified by a diacid like succinic acid, a hydrosoluble ester can be produced since the second acid function (as in the case of methylprednisolone sodium succinate) permits the formation of a salt. Moreover, phosphate esters dissolve in water. Life-threatening illnesses like heaves or hypersensitivity reactions are frequently treated with intravenous or intramuscular solutions of free steroids or hydrosoluble esters. Although esters can also be taken orally, the free active component is absorbed after hydrolysis by pancreatic esterase in the digestive tract lumen. As a result, a formulation may be short-acting when taken orally but long-acting when given parenterally (Huizenga et al., 2022).

Understanding the Mechanisms of Steroid Action

Growth, development, metabolism, immunological response, and behavior are only a few of the physiological processes that are significantly influenced by steroid hormones (Huang et al., 2006). They work by engaging with particular intracellular receptors, which eventually results in changes to the expression of certain genes. This complex process is essential for preserving homeostasis, but it also explains why using steroids, whether legal or illegal, may have negative side effects. The sources emphasize how common steroids are in veterinary medicine, especially because of their strong immunosuppressive and anti-inflammatory properties. Animals with a variety of inflammatory and immune-mediated disorders are frequently treated with corticosteroids, a family of steroid hormones generated by the adrenal cortex(Hafezi-Moghadam et al., 2002). Their effectiveness comes from their capacity to control the synthesis and function of cytokines, which are important inflammatory mediators. By efficiently inhibiting the production of pro-inflammatory cytokines, chemokines, and adhesion molecules, corticosteroids reduce the inflammatory cascade. Their anti-inflammatory properties are further enhanced by the fact that they counteract the actions of known pro-inflammatory mediators, including interleukin-1 and tumor necrosis factor. By successfully lowering vascular permeability, vasodilation, and the inflow of inflammatory cells, this multifaceted strategy eventually lessens the swelling and redness brought on by inflammation (Gong et al., 2016). But there is a cost associated with corticosteroids' strong effects. The hypothalamic-pituitary-adrenal (HPA) axis' delicate balance can be upset by prolonged or high-dose usage, which can decrease the body's natural production of cortisol. Wide-ranging effects may result from this suppression, including the possibility of adrenal insufficiency, a potentially fatal illness marked by the body's incapacity to produce a sufficient stress response (Falhammar et al., 2007). Fig. 2 shows glucocorticoid mode of action.

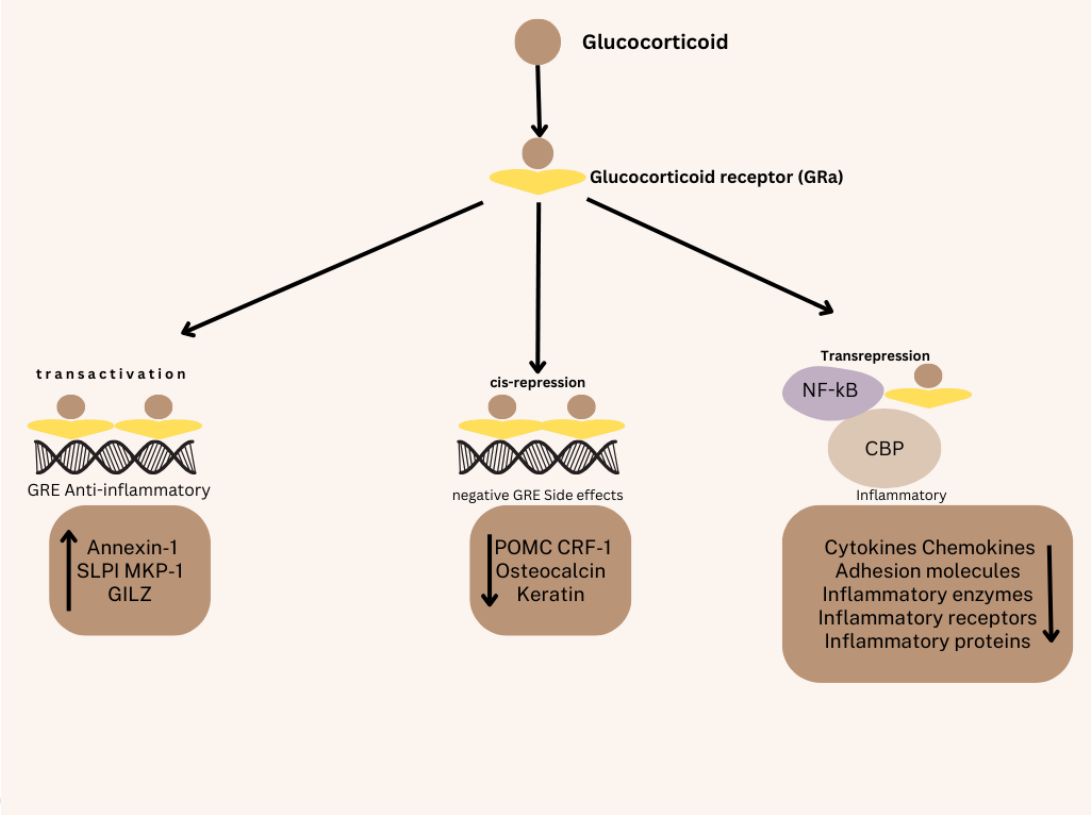

Fig. 2: Glucocorticoids regulate gene expression in several ways.

Glucocorticoids enter the cell to bind to glucocorticoid receptors (GR) in the cytoplasm that translocate to the nucleus. GR homodimers bind to glucocorticoid-response elements (GRE) in the promoter region of steroid-sensitive genes, which may encode anti-inflammatory proteins. Less commonly, GR homodimers interact with negative GREs to suppress genes. Nuclear GR also interact with co-activator molecules, such as CREB-binding protein (CBP), which is activated by pro-inflammatory transcription factors, such as nuclear factor-kB (NF-kB), thus switching off the inflammatory genes that are activated by these transcription factors.

Abbreviations: CRF, corticotrophin releasing factor; GILZ, glucocorticoid-induced leucine zipper protein; IkB-a, inhibitor of NF-kB; MKP-1, mitogen-activated kinase phosphatase-1; POMC, proopiomelanocortin; SLPI, secretory leukoprotease inhibitor.

A Comprehensive Overview of Steroid Use in Veterinary Medicine

The vast class of organic molecules known as steroids has a similar chemical structure. Because of their strong anti-inflammatory and immunosuppressive properties, as well as their capacity to support muscle development and repair, they are frequently utilized in veterinary therapy. The adrenal cortex naturally produces a family of steroid hormones called corticosteroids, which are frequently utilized to treat a range of inflammatory and immune-mediated diseases in animals. Although their usage is frequently restricted because of worries about possible negative consequences, synthetic steroids, particularly anabolic steroids, are also utilized. Treating joint pain is one of the most significant uses of corticosteroids in veterinary medicine (Falhammar et al., 2007). For many years, they have been utilized to treat ailments including osteoarthritis and rheumatoid arthritis in animals. By regulating the synthesis and activity of cytokines, which are important mediators of inflammation, corticosteroids reduce inflammation. They successfully slow down the inflammatory cascade by inhibiting the production of adhesion molecules, chemokines, and pro-inflammatory cytokines (El-Maouche et al., 2015). They further enhance their anti-inflammatory capabilities by counteracting the actions of known pro-inflammatory mediators, such as interleukin-1 and tumor necrosis factor. By successfully lowering vascular permeability, vasodilation, and the inflow of inflammatory cells, this multifaceted strategy eventually lessens the swelling and redness brought on by inflammation. Even while corticosteroids can significantly reduce pain and enhance joint function, there is a chance that using them could have negative side effects, especially if used often or in large doses (Earl Gray et al., 2006).

The hypothalamic-pituitary-adrenal (HPA) axis is suppressed when corticosteroid usage occurs, which is one of the strongest side effects. Suppression of the HPA axis, a complex mechanism that controls the body's reaction to stress, can result in a number of negative consequences, including adrenal insufficiency. The following are other possible adverse effects of corticosteroids:
Articular cartilage toxicity, weakened immune system, higher chance of infection, high blood sugar, especially in people with diabetes (Capper et al., 2021).
In veterinary medicine, anabolic steroids—synthetic forms of testosterone—are occasionally used to encourage muscle development and repair. However, because of their potential for abuse and negative consequences, their usage is frequently contentious. Animals using anabolic steroids may have a variety of adverse consequences, such as, damage to the kidneys and liver,cardiovascular diseases, reproductive dysfunction and behavioral abnormalities like impatience and hostility,
cognitive deficits and brain shrinkage, especially in young animals (Camozzi et al., 2018).

Understanding Steroid-Induced Adverse Effects

Strong medications known as corticosteroids have a significant impact on a number of physiological functions, such as metabolism, inflammation, immunological response, and even behavior. Their contact with certain intracellular receptors mediates these actions, which eventually result in changes in gene expression. Although corticosteroids are useful therapeutic drugs in both human and veterinary medicine because of these qualities, using them frequently results in a range of negative side effects, from minor to serious (Buttgereit et al., 1999).It is essential to comprehend the processes behind these side effects in order to create plans to lessen their impacts and guarantee the prudent and safe usage of corticosteroids. The dosage and length of therapy are two important variables that affect how severe steroid-induced side effects are. There is a higher chance of experiencing negative effects with higher dosages and longer exposure times. The method of administration also matters since systemic administration raises the risk of systemic adverse effects more than local or topical treatment (Anawalt, 2019). The particular corticosteroid used is another important factor. The adverse impact profiles of various corticosteroids vary due to their potencies, durations of action, and mineralocorticoid activity. For example, triamcinolone and other corticosteroids are linked to an increased risk of subcutaneous fat atrophy and skin hypopigmentation. Chronic corticosteroid usage raises serious concerns because it suppresses the hypothalamic-pituitary-adrenal (HPA) axis (Abercrombie et al., 2003).
Adrenal insufficiency, a potentially fatal illness marked by a failure to release enough cortisol in reaction to stress, can result from this suppression. Additional noteworthy side effects include immunosuppression, muscular atrophy, decreased bone mineral density and osteoporosis, metabolic abnormalities such hyperglycemia, and a variety of behavioral and physical changes. The negative consequences of using anabolic steroids in animals go beyond those of corticosteroids (Abdelkarim et al., 2024). These substances have the potential to harm organs, such as the liver and kidneys, and have a detrimental effect on cardiovascular health. Additionally, anabolic steroids have the potential to seriously alter the reproductive system, which can result in infertility in both men and women. Because anabolic steroid exposure during important developmental stages can cause brain shrinkage, cognitive deficits, and behavioral abnormalities, their effects on the growing nervous system, especially the brain, are also a serious issue (Abdelkarim et al., 2024). Regulatory agencies, researchers, and doctors must work together to address the complex problem of steroids' negative consequences.

The Adverse Effects of Prescribed GCs

There is no question about the therapeutic advantages of GCs. However, therapy is linked to serious side effects, particularly when taken in reverse circadian regimens (greater dosages in the evening compared to the morning), at high doses, and for longer periods of time (>2 weeks) (“Erratum,” 2007).These include, a higher risk of infection, hypertension, adrenal suppression, musculoskeletal disorders (osteoporosis, osteonecrosis, myopathy, sarcopenia), metabolic effects (dyslipidemia, glucose intolerance or diabetes mellitus (DM), and an increased overall mortality rate (Williams, 2018). The intensity and scope of this adverse effect profile frequently make it difficult for patients who benefit clinically from GC therapy as well as treating doctors to accept the potentially serious side-effect profile (Williams, 2018). Here, an overview of the current management approaches is provided that have been employed and a summary of the available data describing the negative consequences of GC treatment. An increased risk of death has been linked to some of the negative effects of long-term GC usage. While few studies have particularly examined cardiovascular mortality, the majority of published research has mostly examined all-cause mortality (Wanner, 2004a). Most, but not all, studies have linked GCs to a higher risk of all-cause death. For cardiovascular-specific mortality, similar discrepancies have been reported (Shafiq Ur Rehman et al., 2024). Prednisolone (or similar) at 7.5 mg was shown to be a "safe" threshold dosage below which mortality was not elevated, and the majority of the trials showed a clear correlation between GC dose and death. True causal correlations cannot be shown in this observational research, and there are significant methodological considerations when examining links between GC exposure and mortality. First, it is difficult

to understand the intricate connections between the result and the treatment indication, which might alter over time. It is also necessary to take into account the confounder of the particular illness indication of GC treatment. This is significant since GCs are frequently provided to patients who are nearing the end of their lives and have severe disease severity. In situations when anti-inflammatory or immunosuppressive effects are required, corticosteroids are a crucial and life-saving treatment. Many processes in the body are impacted by corticosteroids. The steroid molecule diffuses across cell membranes and attaches itself to glucocorticoid receptors, changing the receptor's conformation to provide an impact. The receptor glucocorticoid complex can enter the nucleus of the cell, where it dimerizes and attaches itself to glucocorticoid receptors (Pofi et al., 2023). (Fig. 3).

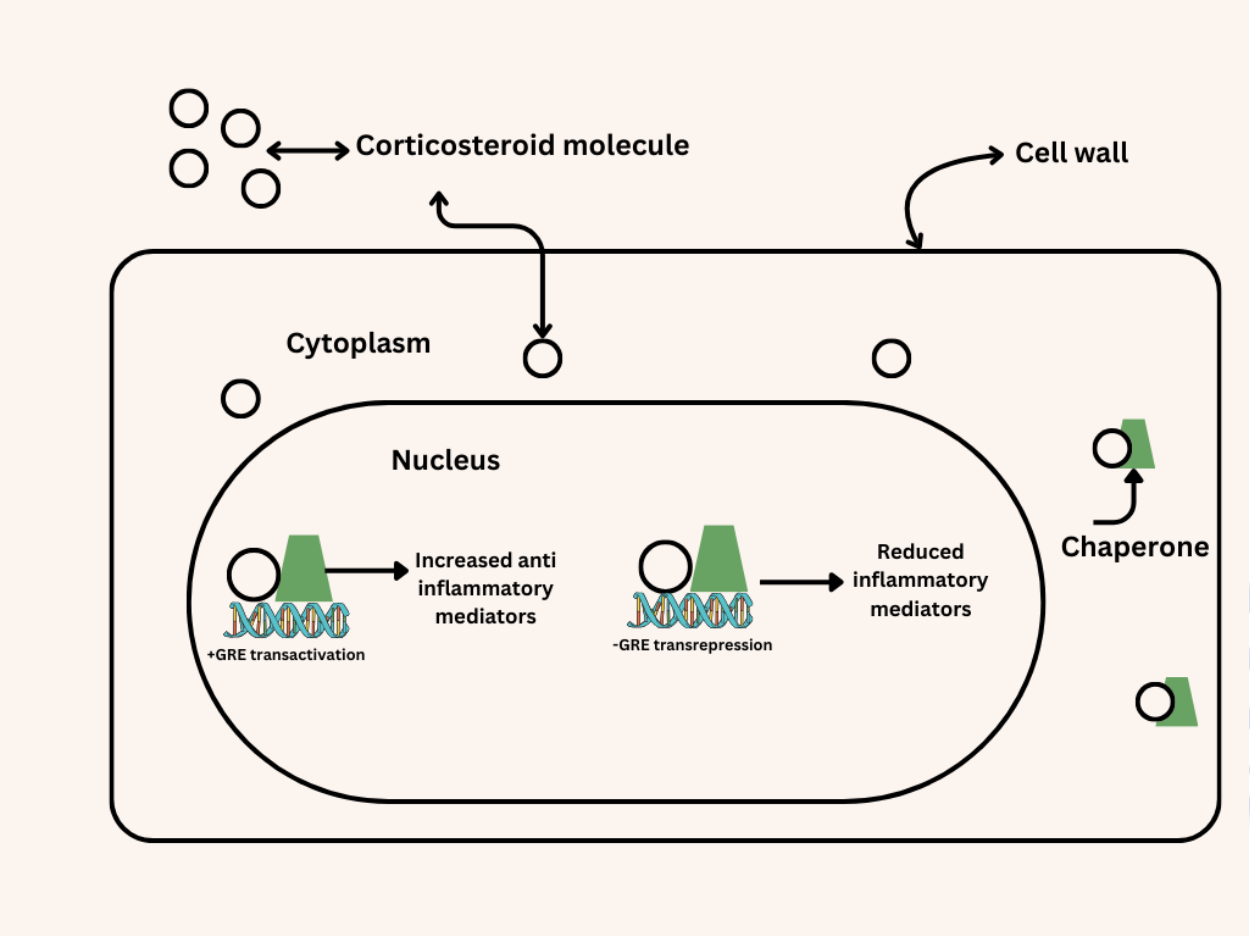

Fig. 3: The mechanism of action of corticosteroids at the cellular level. Corticosteroid molecules diffuse across the cell wall into the cytoplasm, where they bind to their receptors, forming a complex with chaperone proteins. This complex translocates to the nucleus, where it interacts with glucocorticoid response elements (GRE) on the DNA. Through GRE transactivation, corticosteroids increase the production of anti-inflammatory mediators, while GRE trans repression decreases the production of inflammatory mediators, ultimately reducing inflammation.

The Role of Pharmaceutical Science in Minimizing Risks

According to the sources, further study is required to minimize the negative effects of steroid treatment while preserving or improving its positive advantages. Creating safer and more precise steroid formulations is one strategy. This entails altering the chemical makeup of current steroids to increase their selectivity for target tissues, perhaps lowering the dosage needed and the possibility of off-target effects. For instance, the creation of selective androgen receptor modulators (SARMs) aims to minimize the unwanted androgenic side effects, such prostate enlargement and virilization, while maximizing the anabolic advantages of androgens for muscle growth and repair. Optimizing dosing schedules to reduce adverse effects is an additional tactic ("Reversible Steroid Dementia in Patients without Steroid Psychosis," 1984). This entails adjusting the dosage and frequency of administration according to the species, age, weight, and ailment of the patient. Furthermore, because early

corticosteroid administration corresponds with the body's normal cortisol cycle, it can lessen the chance of hypothalamic-pituitary-adrenal axis suppression (Wanner, 2004b).
It's also critical to employ adjuvant therapy to mitigate the negative effects of steroids. Bisphosphonates and calcium supplements, for instance, can help reduce the risk of osteoporosis linked to long-term corticosteroid usage. Novel approaches to medication distribution provide a viable way to increase effectiveness and lower toxicity. Side effects can be minimized and systemic exposure can be decreased by directing medication delivery to certain tissues. Corticosteroids, for example, can be used topically or inhaled orally to transport the medication directly to the site of inflammation, lowering the possibility of systemic side effects. Furthermore, the application of nanoparticles or other innovative delivery methods can enhance tissue penetration, medication stability, and bioavailability, which may result in safer and more effective treatments (Starkman, 2013).

Regulation and Monitoring of Steroid Use

Anabolic steroid usage as growth promoters in animals raised for food is a controversial topic with vastly differing laws across the world. Since 1988, the use of hormonal growth accelerators in cattle has been strictly prohibited by the European Union (EU) (Williams, 2018). Growing worries about the possible negative health consequences of steroid residues in meat products led to the enactment of this prohibition, which is detailed in Council Directive 96/22/EC. Additionally, the EU forbids importing meat from animals that have had these treatments. As a result, imports of meat from nations including the US, Canada, Argentina, and Australia—where the use of certain steroids in animals is legal—have been subject to limitations. On the other hand, non-EU nations have taken a different tack, with some permitting the legitimate use of steroids in cattle production. The Food and Drug Administration (FDA) in the United States, for instance, has approved the use of certain steroid hormone formulations in sheep and cattle (Wanner, 2004a).
According to the FDA, these compounds are safe for human consumption as long as they are used below the recommended levels. In a similar vein, Canada allows the restricted use of steroid hormones in the development of cattle. Brazil has banned the use of testosterone, zeranol, and trenbolone acetate in cattle and sheep since 1991, whereas Argentina permits their use. With the implementation of more stringent rules by the Ministry of Agriculture (MOA), China's laws governing the use of steroids in animals raised for food have changed throughout time(Pofi et al., 2023). However, because veterinary medication residue limits are updated slowly, worries about abuse persist despite efforts to conform to international standards. To protect consumer safety, strict rules are in place in Japan, including residue limitations for veterinary medications, including anabolic testosterone. However, in many Asian nations, it might be difficult to keep an eye on anabolic steroid abuse, especially in small-scale farming operations. Although the use of several growth boosters in cattle has been authorized in South Africa, the country, like many others in Africa, struggles to adequately monitor and enforce laws because of resource limitations (Priya et al., 2024).

Future Directions: Advancing Research and Development

Although there are certain situations in which using steroids in animals might be advantageous, further research and development is required to solve current issues and reduce possible hazards (Pope et al., 2014). To fully evaluate the long-term effects of steroid exposure in animals, especially with regard to chronic low-dose exposure, further study is desperately needed. Research should look at the possible impacts on the immunological, neurological, and endocrine systems, among other physiological systems. This study will help provide evidence-based recommendations for the use of steroids and advance a more sophisticated understanding of the hazards connected to their use. Creating Specific and Sensitive Detection Techniques: (Lone, 1997). To successfully monitor and manage the illegal use of steroids in animals raised for food, testing techniques must be continuously improved. It is crucial to create very sensitive and specific techniques that can identify a greater variety of steroid molecules, including new synthetic variants. Investigating cutting-edge technologies like biosensors, metabolomics-based methods, and high-resolution mass spectrometry may be part of this (Daughton & Ruhoy, 2013). Improved detection capabilities will bolster regulatory efforts to guarantee consumer safety and preserve fair competition within the meat business. Research should focus on creating safer substitutes for traditional steroid treatments in animals. This could entail looking into: Innovative drug delivery methods: These might precisely transport steroids to the site of action, lowering the chance of side effects and systemic exposure (Manson et al., 2009).

Selective androgen receptor modulators (SARMs) by specifically activating androgen receptors in target tissues, these substances may be able to distinguish between positive anabolic benefits and unfavorable androgenic side effects. NSAIDs, or non-steroidal anti-inflammatory drugs: In certain situations, NSAIDs may provide efficient anti-inflammatory and pain relief without the hormonal side effects of steroids. Approaches involving gene therapy: These have the potential to modify

inflammatory responses over the long term and may lessen the requirement for frequent steroid treatment. Encouraging Conscientious Use: To promote appropriate and prudent steroid usage in animals, cooperation between researchers, veterinarians, regulatory bodies, and the cattle sector is essential (Malkawi et al., 2018). This partnership might concentrate on: o Creating precise, fact-based guidelines: To reduce the possibility of residues in food items, they should include suggested doses, treatment durations, and withdrawal periods for certain steroids.

Conclusion

Pharmaceutical science is vital in reducing the negative impacts of steroids on animals, aiming to balance therapeutic advantages with potential risks. The development of safer steroid formulations is a key area of focus. This involves modifying chemical structures to enhance tissue selectivity and minimize off-target effects, through the creation of selective androgen receptor modulators (SARMs). Optimizing how steroids are administered, such as through topical or inhaled methods, is also important to reduce systemic exposure and adverse effects. A thorough understanding of how steroids move through the body (pharmacokinetics) and how they interact with it (pharmacodynamics) is essential. This, along with the development of precise analytical methods for detecting steroid abuse, is crucial for ensuring safer steroid use. The overarching goal is to promote the responsible and ethical use of steroids in animals, protecting both animal health and consumer safety. This involves improvements in formulations, precise monitoring, and ongoing research. There is a necessity for international collaboration and adherence to stringent regulations, considering the varying legal frameworks and concerns about steroid use in different countries. Future research should focus on alternative therapies, such as exploring non-steroidal anti-inflammatory drugs (NSAIDs) and gene therapy, and enhancing detection methods.

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