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BIOACTIVE STEROIDS FOR THE TREATMENT OF OVARIAN CANCER CURRENT AND FUTURISTIC REVIEW

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ABSTRACT

Ovarian cancer represents a significant challenge in women's health, characterized by high mortality rates and limited treatment options. In recent years, there has been growing interest in exploring the potential of bioactive steroids as novel therapeutic agents for ovarian cancer. This review provides a comprehensive analysis of the current state and future prospects of bioactive steroids in the management of ovarian cancer. We begin by outlining the biological mechanisms through which steroids influence cancer progression, highlighting their dual role as both promoters and inhibitors of tumorigenesis. Subsequently, we discuss preclinical studies demonstrating the anticancer effects of various bioactive steroids, including their modulation of steroid hormone receptors, inhibition of cell proliferation, induction of apoptosis, and suppression of angiogenesis and metastasis. Furthermore, we examine the findings from clinical trials evaluating the safety and efficacy of bioactive steroids, such as dehydroepiandrosterone (DHEA), in ovarian cancer patients, along with the challenges and limitations encountered. Looking ahead, we explore potential strategies to enhance the therapeutic efficacy of bioactive steroids,including combination therapies and novel drug delivery approaches. Emerging trends in steroid-based immunotherapy and hormone receptor-targeted therapies are also discussed. Overall, this review underscores the promising role of bioactive steroids as a valuable addition to the armamentarium of ovarian cancer therapeutics, urging further research efforts to optimize their clinical utility.

INTRODUCTION: Ovarian cancer is a complex and heterogeneous disease that poses significant challenges to both patients and healthcare providers.As the fifth most common cause of cancer-related deaths among women,it account sfor a substantial burden of morbidity and mortality worldwide.

Epidemiology: Ovarian cancer incidence rates vary globally, with higher rates observed in developed countries compared to developing nations. Age is a significant risk factor, with the majority of cases occurring in postmenopausal women. Additionally, a family history of ovarian or breast cancer, as well as certain genetic mutations. (e.g., BRCA1 and BRCA2), pre dispose individuals to an increased risk of developing ovarian cancer. (La Vecchia, 2017)

Classification: Ovarian cancer encompasses a spectrum of histological subtypes, including epithelial tumors (serous, endometrioid, mucinous, and clear cell), germ cell tumors, and sex cord-stromal tumors. Epithelial ovarian cancer (EOC) is the most common subtype, accounting for approximately 90%ofcases, while germ cell and sex cord- stromal tumors are less common and often affect women.

Current Treatment Modalities: The standard treatment for ovarian cancer typically involves a combination of surgery and chemotherapy.

Surgical intervention aims to achieve optimal cytoreduction, i.e., the removal of visible tumor masses, followed by adjuvant chemotherapy to eradicate any remaining cancer ells. Platinum-based chemotherapy regimens,such as carboplatin andpaclitaxel,are the cornerstone of treatment for ovarian cancer and have significantly improved survival outcomes over the past few decades. Despite advances in treatment, ovarian cancer remains challenging to manage due to high rates of recurrence and the development of resistance to conventional therapies. Approximately 70% of patients with advanced-stage disease experience disease recurrence following initial treatment, highlighting the need for more effective therapeutic approaches. (Coleridge *et al*., 2021)

Emphasis on the Need for More Effective Therapies:

The high recurrence rates and emergence of drug resistance underscore the urgency to develop novel treatment strategies for ovarian cancer. Immunotherapy, targeted therapies, and novel drug delivery systems are among the innovative approaches being explored to overcome these challenges and improve patient outcomes.Additionally, identifying predictive biomarkers and understanding the molecular mechanisms driving ovariancancer progression are critical for developing personalized and more effective treatment regimens. (Akter *et al.*, 2022)

Role of Steroids in Cancer Therapy: Steroids play intricate roles in cancer therapy,exerting diverse effects on tumorigenesis and tumor progression. Understanding the underlying biological mechanisms is crucial for exploiting their potential as therapeutic agents. Here's a detailed explanation of the role of steroids in cancer therapy: Biological Mechanisms:

Steroid Hormone Receptors: Steroids, including estrogen, progesterone, and androgens, exert their effects primarily through binding to specific intracellular receptors, known as steroid hormone receptors. Upon ligand binding, these receptors undergo conformational changes, Translocate to the nucleus, and act as transcription factors, regulating the expression of target genes involved in cell proliferation, survival, and differentiation. (Thomas, 2012)

Cell Signaling Pathways: Steroids modulate various signaling pathways implicated in cancer progression. For instance, estrogen and androgens can activate the PI3K/Akt/mTOR pathway, which promotes cell growth and survival by regulating protein synthesis, metabolism, and apoptosis inhibition. Progesterone can activate the MAPK/ERK pathway, leading to cell proliferation and differentiation. Steroids can also activate the NF-κB pathway, which regulates genes involved in inflammation, immune response, and cell survival, thus contributing to tumorigenesis. (Miricescu *et al*., 2020)

PI3K/Akt/mTORPathway:

Activation by Estrogen and Androgens: Estrogen and androgens can activate the phosphatidylinositol 3-kinase (PI3K)/protein kinase B (Akt)/mammalian target of rapamycin (mTOR) pathway, a key signaling cascade involved in regulating cell growth, survival, and metabolism.

Mechanism: Upon ligand binding, estrogen receptors (ER) and androgen receptors (AR) can activate PI3K, leading to the phosphorylation and activation ofAkt.ActivatedAkt subsequently phosphorylates and inhibits various downstream targets,including the tuberous sclerosis complex (TSC) and glycogen synthase kinase 3 (GSK3), resulting in the activation of mTOR complex 1 (mTORC1). mTORC1 regulates protein synthesis, lipid metabolism, and cell growth by phosphorylating substrates such as p70S6 kinase and 4E-BP1.

Effect on Cancer Progression: Activation of the PI3K/Akt/mTOR pathway promotes cell proliferation, survival, and metastasis, contributing to tumorigenesis and tumor progression. Dysregulation of this pathway is commonly observed in various cancer types and is associated with resistance to chemotherapy and targeted therapies. (Paplomata and O'Regan, 2014)

Growth Factor Binding to Receptor: The pathway begins when growth factors bind to their respective receptors on the cell membrane. Receptor Dimerization: Binding of

growth factors induces dimerization(pairing)of receptor subunits,leading to activation. PI3K Activation: Dimerized receptors activate PI3K(Phosphoinositide3-kinase),an enzyme that phosphorylates lipids in the cell membrane. PIP3 Production:Activated PI3K catalyzes the production of phosphatidyl inositol-3,4,5-trisphosphate(PIP3) from phosphatidylinositol-4,5- bisphosphate (PIP2). AktActivation: PIP3 recruits Akt (ProteinkinaseB) to the cell membrane, where it is activated by phosphorylation.mTORC2Activation: Activated Akt phosphorylates and activatesmTORC2 (mTOR Complex 2), aprotein complex involvedincellgrowth and survival. AktPhosphorylation: mTORC2 further phosphorylates Akt,enhancing its activity. mTORC1 Activation: Akt phosphorylates and inhibits TSC2 (Tuberous Sclerosis Complex 2), leading to activation of mTORC1 (mTOR Complex 1). Cell Growth and Proliferation: Activated mTORC1 promotes cellgrowth,protein synthesis,and cell proliferation by phosphorylating downstream targets. Feedback Inhibition: Negative feedback mechanisms regulate the pathway to prevent excessive cellgrowth and proliferation. This may involve the inhibition of upstream components such as receptor signaling oractivation of pathways leading to apoptosisor cell cycle arrest. This pathway plays a crucial role in regulating various cellular processes such as growth, proliferation, metabolism, and survival. Dysregulation of the PI3K/Akt/mTOR pathway is associated with various diseases, including cancer, diabetes, and neurological disorders. PI3K/Akt/mTOR pathway, leading to regulation of cell growth, survival, protein synthesis, metabolism, and inhibition of apoptosis. It also modulates the NF-κBpathway,impacting inflammation, immune response, and cellsurvival. The Progesterone branch activates the MAPK/ERK pathway, regulating cell proliferation and differentiation. Similar to the Estrogen/Androgens branch, it also modulates the NF-κB pathway. The Steroids branch directly activates the NF-κB pathway, influencing inflammation, immune response, and cell survival. Overall, the flowchart demonstrates how different types of steroids impact various cellular processes through specific signaling pathways, ultimately contributing to factors associated with cancer progression.

Ligand and Receptor Activation: External ligands (such as growth factors or hormones) bind to receptors on the surface of plant cells. These receptors are represented by the "RTK (Receptor Tyrosine Kinase)" component. Upon ligand binding, the receptors undergo a conformational change, leading to their activation.

2. Activation of Ras: The activated receptors (RTKs) then stimulate the activity of Ras proteins, which are GTPases found in the plant cell. This activation involves a switch from the inactive GDP-bound state to the active GTP-bound state.

3. Activation of Raf: The active form of Ras (Ras-GTP) further activates downstream signaling proteins, including Raf kinase.

Raf kinase is a crucial component in the MAPK/ERK pathway and acts as an intermediate signaling molecule.

4. Activation of MEK: Raf kinase phosphorylates and activates MEK (Mitogen-Activated Protein Kinase Kinase), another key kinase in the pathway.

5. Activation of ERK: MEK, in turn, phosphorylates and activates ERK (Extracellular signal-Regulated Kinase), which is the final kinase in the cascade. ERK activation is critical for transmitting the signal from the cell membrane to the nucleus.

6. Translocation to the Nucleus: Activated ERK molecules translocate from the cytoplasm to the nucleus, where they exert their effects on gene expression.

7. Phosphorylation of Transcription Factors: Within the nucleus, ERK phosphorylates transcription factors (TF), such as Elk-1 and c-Fos, which regulate gene expression.

8. Gene Expression Regulation: The phosphorylated transcription factors bind to specific regulatory regions of target genes,

initiating or enhancing their expression. These target genes are involved in various cellular processes, including cell proliferation, differentiation, and survival.

NF-κB Pathway: Activation by Steroids: Steroids, including glucocorticoids, can activate the nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB) pathway, a critical regulator of inflammation, immune response, and cell survival.

Mechanism: Steroids can activate NF-κB signaling through various mechanisms, including: Direct binding to glucocorticoid receptors (GR) and subsequent regulation of NF-κB activity. Modulation of upstream signaling pathways involved in NF-κB activation, such as the MAPK pathway and the IκB kinase (IKK) complex. Effect on Cancer Progression: Activation of the NF-κB pathway promotes the expression of genes involved in inflammation, immune evasion, and cell survival, thereby creating a pro-tumorigenic microenvironment. Dysregulated NF-κB signaling is implicated in the pathogenesis of various cancers and is associated with: Tumor progression, Metastasis, Resistance to therapy

NF-κB Pathway – Stepwise Mechanism

1. Signal Received: This step represents the initiation of thepathway by an external signal, such as a cytokine or stress stimulus.

2. TNF-α Binding to Receptor (TNF_Receptor): Tumor Necrosis Factor-alpha (TNF-α) binds to its receptor, initiating the activation of the NF-κB pathway.

3. Recruitment of IKK Complex (IKK_Complex): The TNF-α receptor recruits the IKK (IκB kinase) complex to the cell membrane.

4. Phosphorylation of IκB (IκB): The IKK complex phosphorylates IκB (Inhibitor of κB), marking it for degradation.

5. Degradation by Proteasome (Proteasome): Phosphorylated IκB is degraded by the proteasome, freeing NF-κB.

6. Release of NF-κB (NFkB_Translocation)

NF-κB is released from its inhibitory complex and becomes active.

7. Translocation to Nucleus (Nucleus): Activated NF-κB translocates from the cytoplasm into the nucleus.

8. Activation of Gene Transcription (Gene Transcription)- Inside the nucleus, NF-κB binds to specific DNA sequences, activating the transcription of target genes.

9. Transcription (mRNA Synthesis): The activated genes are transcribed into messenger RNA (mRNA).

10. Translation (Protein_Synthesis) The mRNA is translated into proteins by the cellular machinery.

11. Protein Production (Protein Production) The newly synthesized proteins carry out various cellular functions, including: Immune response, Cell survival, Inflammation regulation. Immune Modulation by Steroids Glucocorticoids, such as dexamethasone, are potent immunosuppressive agents that inhibit the production of pro-inflammatory cytokines (e.g., interleukin-1, interleukin-6, tumor necrosis factor-alpha**)** and suppress the function of immune effector cells, including T cells, B cells, and dendritic cells**.** By dampening immunosurveillance and promoting immune evasion, steroids create a permissive microenvironment for tumor growth and metastasis**.**

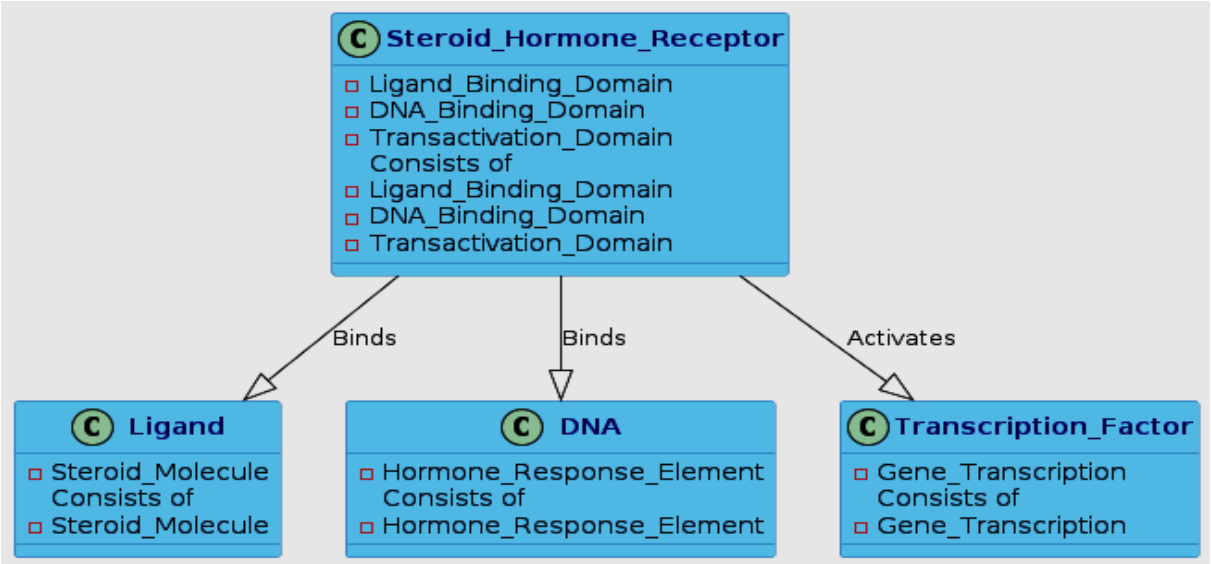
2.2. Dual Role of Steroids

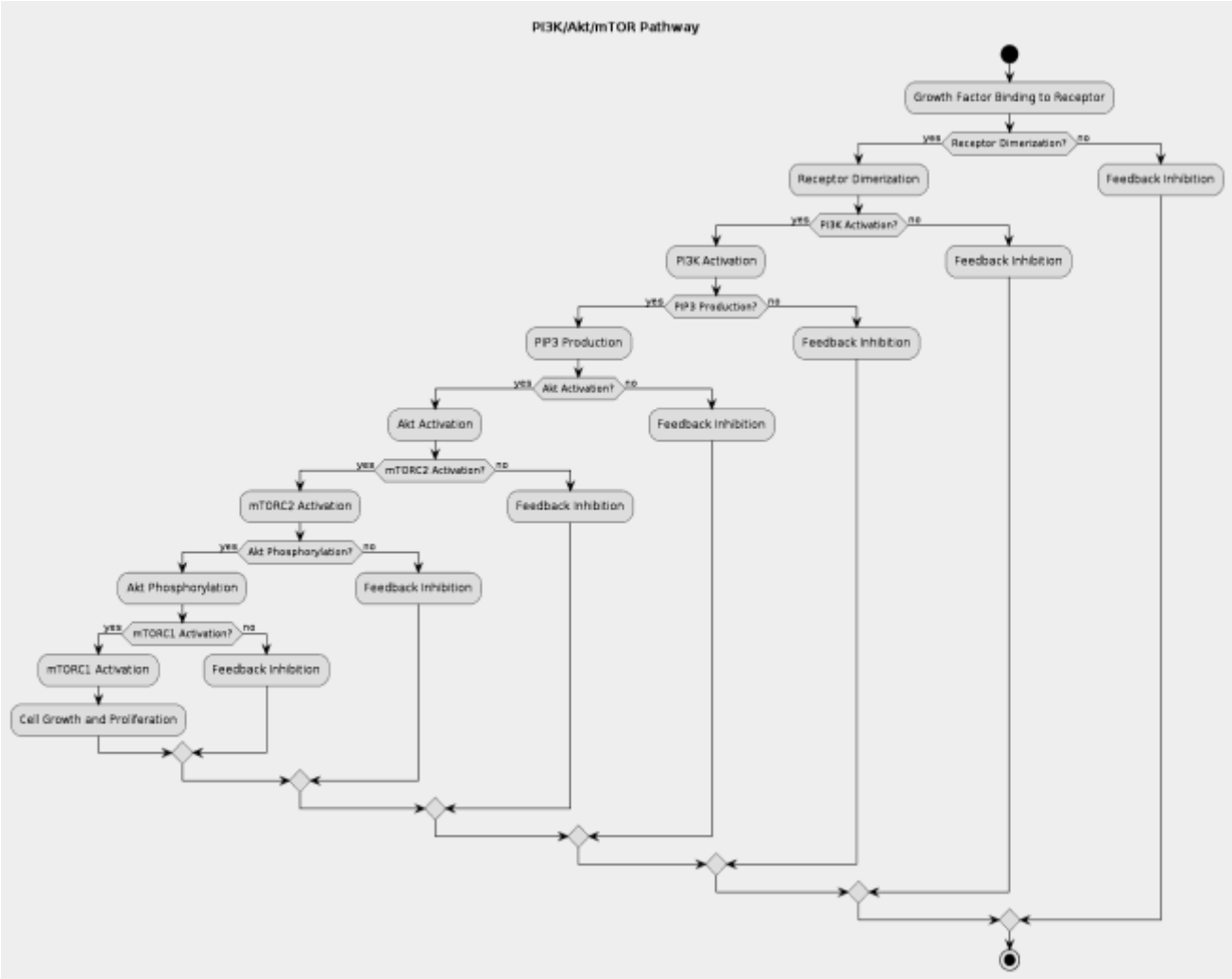
2.2.1. Promoters of Tumorigenesis- Steroids can promote cancer development and progression by stimulating cell proliferation, survival, and metastasis**.**

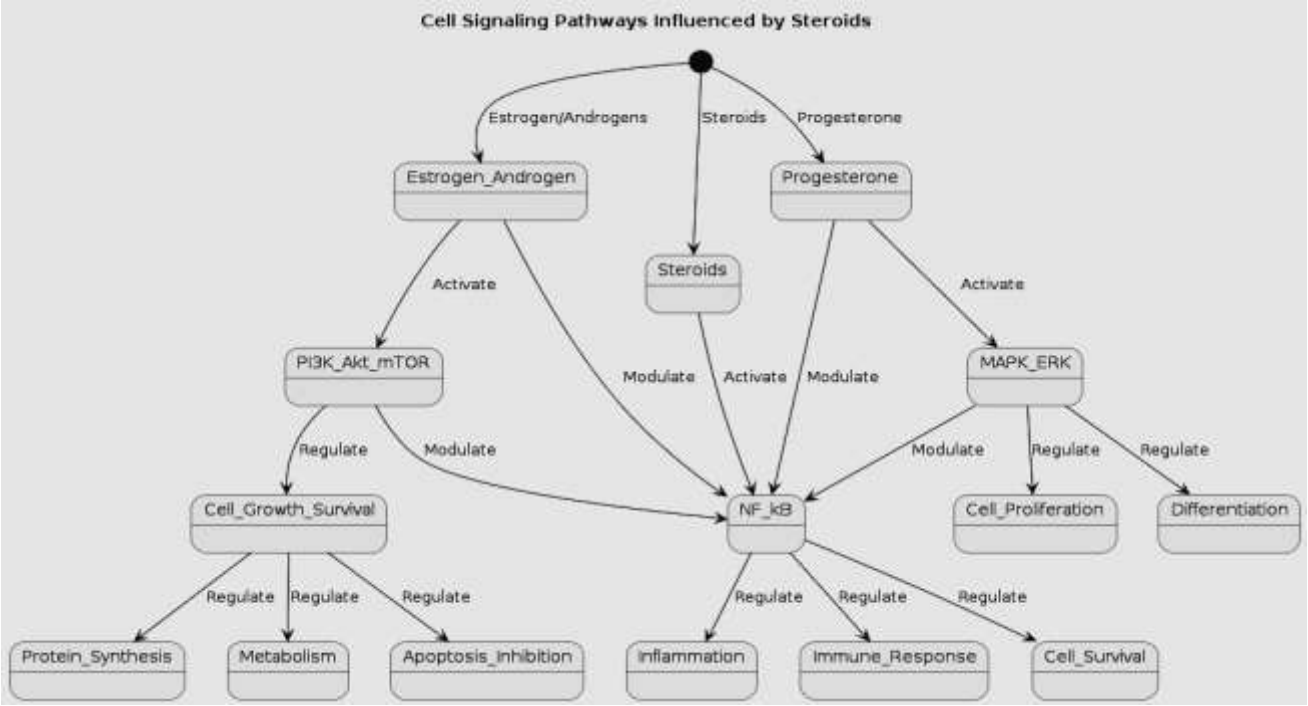
Estrogen and **progesterone** are implicated in the pathogenesis of hormone-sensitive cancers (e.g., breast and endometrial cancers). Estrogen promotes proliferation by upregulating genes like cyclin D1 and inhibiting apoptosis. Androgens stimulate prostate cancer growth through androgen receptor signaling.

2.2.2. Inhibitors of Tumorigenesis- Conversely, steroids can exhibit anticancer effects**:** Glucocorticoids like dexamethasone are used to treat hematological malignancies **(**lymphomas, leukemias**)** due to their pro-apoptotic and anti-inflammatory effects.

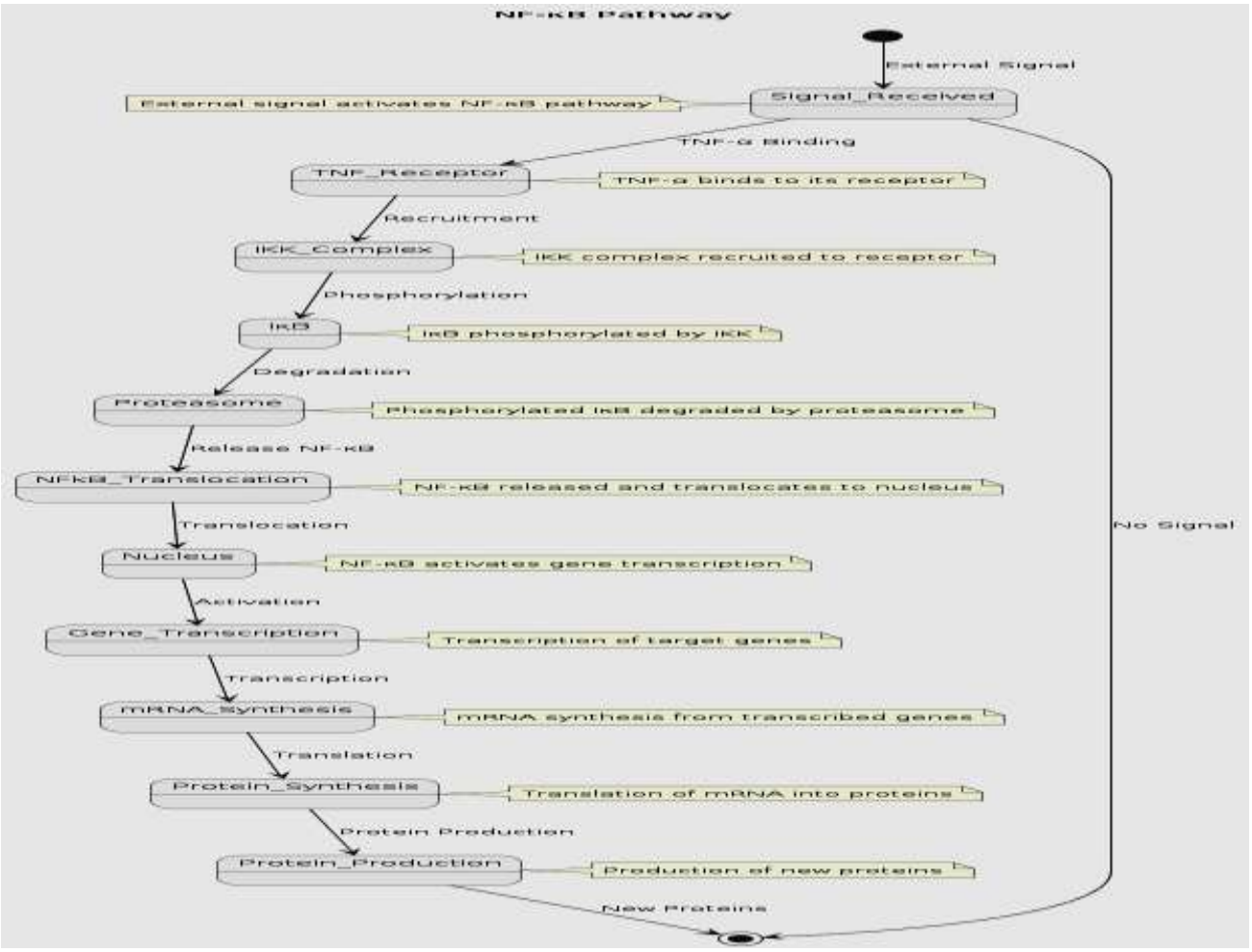
Androgen Deprivation Therapy (ADT) is standard for prostate cancer, targeting androgen dependence for tumor growth and survival.







MAPK/ERK Pathway



2.2.3. Context-Dependent Effects

The effects of steroids on cancer progression are highly **context-dependent**, influenced by:

- **Tumor histology**
- **Hormone receptor status**
- **Genetic alterations**

For example:

- Estrogen receptor-positive breast cancers respond to **hormone therapy**, while receptor-negative ones may not.
- Prostate cancers responsive to androgens benefit from ADT; resistant ones require alternative strategies. *(Kim et al., 2013)*

3. Bioactive Steroids and Ovarian Cancer: Preclinical Studies

3.1. Dehydroepiandrosterone (DHEA)

3.1.1. Study Details:

In vitro studies show DHEA **inhibits proliferation** of ovarian cancer cells by interfering with the **cell cycle** and inducing **apoptosis**.

Animal studies confirm reduced tumor growth and metastasis.

3.1.2.Mechanisms:DHEA:

- Modulates **estrogen and androgen receptors**
- Alters signaling pathways related to **growth and survival**
- Inhibits enzymes in steroid hormone biosynthesis, changing **tumor hormone levels** *(GÜNDOĞAN et al., 2021)*

3.2. Progesterone

3.2.1. Study Details:

Progesterone inhibits ovarian cancer cell proliferation, induces **apoptosis**, and suppresses **angiogenesis** in animal models.

3.2.2. Mechanisms:

- Binds to **progesterone receptors (PR)**
- Activates pathways regulating **cell cycle, apoptosis, and angiogenesis**
- Modulates gene expression related to **inflammation and immunity** *(Wu et al., 2023)*

3.3. Estrogen Receptor Modulators

3.3.1. Study Details:

Agents like **tamoxifen** and **fulvestrant** inhibit ovarian cancer cell proliferation and promote apoptosis.

Tamoxifen reduces tumor growth in animal models.

3.3.2. Mechanisms:

These drugs:

- Act as **estrogen receptor antagonists or SERMs**
- Block estrogen-dependent growth
- Modulate other pathways like **PI3K/Akt/mTOR** *(Smith et al., 2014)*

3.4. Mechanisms of Action

3.4.1. Modulation of Steroid Hormone Receptors:

Bioactive steroids bind to **ER, PR, AR**, altering downstream signaling affecting **growth, survival, and differentiation**.

3.4.2. Inhibition of Cell Proliferation:

Steroids like DHEA **and** progesterone disrupt the cell cycle by affecting cyclins, CDKs**,** and inhibitors**.**

3.4.3. Induction of Apoptosis:

Trigger both:

- Intrinsic apoptosis (mitochondrial pathway)
- Extrinsic apoptosis (death receptor pathway) *(Gómora et al., 2018)*

3.4.4. Suppression of Angiogenesis and Metastasis:

- Inhibit VEGF, angiopoietins
- Reduce cell migration, invasion, ECM adhesion

4. Current State of Bioactive Steroids in Clinical Trials

4.1. Clinical Trials Evaluating DHEA in Ovarian Cancer

4.1.1. DHEA Monotherapy:

Used for patients with advanced/recurrent ovarian cancer with limited treatment options.

4.1.2. Combination Therapies:

Combining DHEA with chemotherapy/targeted therapies to enhance efficacy and reduce resistance.

(Corr et al., 2020)

4.2. Analysis of Outcomes

4.2.1. Response Rates:

Some studies show promising responses; others do not. Influencing factors:

- Tumor type
- Molecular subtype
- Treatment history

4.2.2. Progression-Free Survival (PFS): Mixed outcomes—some trials report improvement**, others** no significant benefit**.**

4.2.3. Overall Survival (OS): Assessment is **challenging** due to:

- Long disease course
- Multiple therapy lines Longer follow-up is needed. *(Villaruz and Socinski, 2013)*

4.2.4. Adverse Effects: Generally well-tolerated. Reported side effects:

- Acne, hirsutism, GI symptoms
- Hormonal effects (e.g., mood changes, menstrual irregularities) Serious events are rare and usually manageable.

4.3. Limitations of Current Trials:

4.3.1. Small Sample Sizes: Many clinical trials evaluating DHEA in ovarian cancer patients have limited sample sizes, which may compromise statistical power and the ability to detect meaningful treatment effects. Small cohorts also increase the risk of selection bias and limit the generalizability of findings.

4.3.2. Heterogeneity of Patient Populations: Variability in patient characteristics—such as age, performance status, tumor histology, and genetic mutations—across different trials can confound the interpretation of results. Subgroup analyses may be necessary to identify patient populations most likely to benefit from DHEA therapy.

4.3.3. Lack of Standardization: Differences in DHEA dosage, treatment duration, and administration schedules among clinical trials make it challenging to compare outcomes and establish optimal treatment protocols. Standardization of treatment regimens is essential to ensure consistency and reproducibility of results. *(Roes and Wittes, 2023)*

4.3.4. Short Follow-Up Periods: Some trials have relatively short follow-up durations, limiting the assessment of long-term outcomes such as overall survival (OS). Ovarian cancer is characterized by prolonged survival even in the setting of recurrence, necessitating extended follow-up to accurately capture late treatment effects and survival trends.

5. Future Directions and Challenges:

5.1. Enhancing Therapeutic Efficacy

5.1.1. Combination Therapies

Synergistic Effects:

Research suggests that combining bioactive steroids with conventional chemotherapeutic agents or targeted therapies can enhance their anticancer effects. For instance, preclinical studies have demonstrated synergistic interactions between steroids like DHEA and agents like paclitaxel or carboplatin, resulting in improved tumor growth inhibition and increased apoptosis in ovarian cancer cells.

Mechanisms of Synergy:

The synergistic effect of combination therapy may arise from complementary mechanisms of action, such as simultaneous targeting of multiple signaling pathways involved in cancer cell survival, proliferation, and metastasis. Additionally, steroids may sensitize cancer cells to chemotherapy or overcome resistance mechanisms, thereby enhancing treatment efficacy.

Clinical Trials:

Clinical trials exploring the efficacy and safety of combination regimens incorporating bioactive steroids are underway. These trials aim to assess the impact on treatment response rates, progression-free survival, and overall survival. Early-phase trials have shown promising results, warranting further investigation in larger, randomized controlled trials. *(Zhang et al., 2016)*

5.1.2. Targeted Delivery Systems

Enhanced Tumor Targeting:

Conventional routes of steroid administration may result in systemic exposure and off-target effects. Researchers are developing targeted delivery systems—such as nanoparticles or liposomes—to encapsulate steroids and deliver them specifically to tumor sites.

Improved Bioavailability: Targeted delivery systems can improve pharmacokinetics by prolonging circulation time and enhancing accumulation in tumor tissues. By optimizing drug release kinetics and uptake mechanisms, these platforms can increase intracellular delivery and therapeutic effects while minimizing systemic toxicity. *(Butler et al., 2024)*

Challenges and Considerations: Designing delivery systems involves addressing challenges like drug loading efficiency, stability, and biocompatibility. Achieving specific uptake by cancer cells while avoiding healthy tissues requires precise engineering.

5.2. Challenges

5.2.1. Dosage and Administration Optimization

Individualized Treatment: Due to patient heterogeneity in ovarian cancer, dosage and administration routes should consider individual factors like age, weight, comorbidities, and genetic background.

Clinical Pharmacokinetics: Dose-finding studies and PK/PD analysis are essential to identify regimens that achieve therapeutic concentrations while minimizing toxicity. Considerations include metabolism, distribution, and elimination. *(Hoffmann et al., 2022)*

5.2.2. Identification of Predictive Biomarkers

Personalized Medicine: Identifying biomarkers such as hormone receptor expression (e.g., ER, AR), genetic mutations (e.g., BRCA1/2), and molecular signatures can guide treatment.

Validation Studies: Biomarker validation requires standardized assays and prospective clinical trials to evaluate predictive value in treatment selection. *(Rodrigues-Ferreira and Nahmias, 2022)*

5.3. Overcoming Resistance Mechanisms

5.3.1. Tumor Adaptation: Resistance mechanisms may involve altered hormone receptor signaling, alternative survival pathways, and tumor microenvironment remodeling.

5.3.2. Combination Strategies: Combining steroids with agents targeting complementary pathways (e.g., PI3K/AKT/mTOR inhibitors, checkpoint inhibitors) or modifying the tumor microenvironment (e.g., angiogenesis inhibitors) may overcome resistance. *(Wu et al., 2021)*

5.4. Preclinical Model Validation

5.4.1. Translational Relevance: Models such as patient-derived xenografts (PDX) and organoids better replicate human disease and help identify biomarkers.

5.4.2.Clinical Correlation: Translating preclinical findings into clinical practice requires rigorous validation and collaboration between researchers and clinicians. *(Spagnol et al., 2023)*

6. Novel Approaches and Emerging Trends:

6.1. Development of Novel Steroid Derivatives:

Structural modification of steroid compounds aims to enhance pharmacokinetics, bioavailability, and specificity. Prodrugs and nanotechnology-based delivery systems support targeted delivery and reduced toxicity. *(Ke, 2018)*

6.2. Targeted Delivery Systems: Ligand-targeted liposomes and nanoparticles enhance specificity by binding to tumor-specific receptors. Gene therapy approaches using tumor-specific promoters further localize drug activation. *(Li et al., 2023)*

6.3. Steroid-Based Immunotherapy: Despite traditional immunosuppressive roles, steroids may enhance tumor immune responses, particularly when combined with checkpoint inhibitors or cancer vaccines. Clinical trials are evaluating their safety and efficacy.

6.4. Hormone Receptor-Targeted Therapies: Therapies targeting ER, PR, or AR pathways (e.g., SERMs, aromatase inhibitors) show promise. Combination approaches and biomarker-guided trials aim to personalize therapy and overcome resistance. *(Tan et al., 2021)*

Table2: Summarizing the current state of bioactive steroids in clinical trials for the treatment of ovarian cancer, along with some futuristic perspectives:

Bioactive Steroid	ClinicalTrial Phase	Mechanism ofAction	Current Status	Futuristic Perspectives
Dexamethasone	Phase III	Glucocorticoid receptor agonist	Undergoing clinical trials for efficacy and safety	Potential combination therapy with immunotherapy
Prednisone	PhaseII	Glucocorticoid receptor agonist t	Investigating efficacy in combination therapies	Nanoparticle delivery systems for targeted therapy
Progesterone	PhaseII	Progesterone receptor agonist	Assessing efficacy in hormone-sensitive tumors	Development of personalized hormone receptor blockers
Testosterone	PhaseI	Androgen receptor agonist	Investigating impact on androgen-sensitive tumors	Targeted delivery systems to minimize sideeffects
Estradiol	PhaseI	Estrogen receptor agonist	Assessing safety and efficacy in hormone-positive tumors	Combination with anti-angiogenic agents for enhanced efficacy
Dehydroepiandrosterone(DHEA)	PhaseII	Androgen precursor	Investigating potential benefits in hormone-sensitive tumors	Combination therapy with PARP inhibitors for synergistic effect
Hydrocortisone	PhaseI	Glucocorticoid receptor agonist	Safety and tolerability assessment	Integration with precision medicine for individualized dosing
Medroxyprogesteroneacetate	PhaseII	Progesterone receptoragonist	Investigating efficacy in hormone-sensitive tumors	Combination with targeted therapies for enhanced response
Fludrocortisone	PhaseI/II	Mineralocorticoid receptor agonist	Safety and efficacy assessment combination therapies	Exploration of immune-modulating effects for immunotherapy
Mifepristone	PhaseI	Progesterone receptorantagonist	Assessing safety and	Potential use in combination with

			preliminary efficacy	chemotherapy or targeted therapy
Anastrozole	PhaseII	Aromataseinhibitor	Investigating efficacy in hormone-positive tumors	Integration with precision medicine for optimized dosing
Finasteride	PhaseI/II	5-alpha-reductaseinhibitor	Safety and efficacy assessment in hormone-sensitive tumors	Combination with immune checkpoint inhibitors for enhanced response

CONCLUSION

In conclusion, the exploration of bioactive steroids as a therapeutic strategy for ovarian cancer presents a compelling narrative of promise and potential. Through preclinical investigations, we have witnessed the profound effects of these compounds in inhibiting tumor growth, inducing apoptosis, and impeding metastasis. These findings underscore the multifaceted roles of steroids in cancer biology and highlight their therapeutic relevance in ovarian cancer management. While early clinical trials have shown encouraging safety profiles and preliminary efficacy, the journey toward. Clinical translation is multifaceted. Challenges such as dose optimization, route of administration, and identification of suitable patient cohorts remain pertinent. Moreover, the intricate interplay between steroids and the tumor microenvironment necessitates a deeper understanding to overcome potential resistance mechanisms and enhance treatment outcomes. As we gaze into the future, there is an imperative for concerted research endeavors to unlock the full therapeutic potential of bioactive steroids in ovarian cancer. This entails the development of novel steroid derivatives with improved pharmacokinetic properties, innovative combination therapies, and the exploration of targeted delivery systems for enhanced efficacy and reduced toxicity. Furthermore, the pursuit of personalized medicine in ovarian cancer hinges on the elucidation of predictive biomarkers that can stratify patients for optimal treatment Selection and response monitoring. By harnessing the power of collaborative research initiatives and leveraging technological advancements, we can propel the field forward and usher in a new era of precision oncology. In essence, the journey towards harnessing bioactive steroids as a cornerstone of ovarian cancer therapy is one imbued with promise, perseverance, and the potential to transform patient outcomes. Through sustained interdisciplinary efforts and unwavering dedication, we can transcend the confines of current therapeutic paradigms and pave the way towards a brighter future for individuals battling this formidable disease.

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