GLYCYRRHETINIC ACID DERIVATIVES: PHARMACOLOGICAL PROPERTIES AND THERAPEUTIC POTENTIAL IN MODERN DRUG DEVELOPMENT

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Results. Chemical analysis demonstrated that the C-3 hydroxyl group, C-11 carbonyl group and C-30 carboxyl group are the primary sites used for structural modification.

ABSTRACT

Glycyrrhetinic acid (GA) is a pentacyclic triterpenoid obtained from glycyrrhizin, the major bioactive constituent of licorice. During the last decade, GA derivatives have attracted considerable attention because of their anticancer, anti-inflammatory, antiviral, antioxidant, hepatoprotective and antimicrobial activities. This review analyzes five DOI-indexed studies and evaluates the relationship between chemical structure and pharmacological activity. The findings demonstrate that modifications at the C-3, C-11 and C-30 positions significantly improve biological activity and pharmacokinetic characteristics. The reviewed evidence suggests that GA derivatives are promising lead compounds for future drug development.

Introduction. Natural products remain one of the most important sources of pharmaceutical innovation. Glycyrrhetinic acid has emerged as a valuable scaffold due to its broad spectrum of biological activities. However, poor aqueous solubility and limited bioavailability restrict the direct therapeutic application of the parent compound. Medicinal chemists have therefore developed numerous derivatives designed to improve potency, selectivity and pharmacokinetic properties. Recent advances in medicinal chemistry, molecular pharmacology and computational drug design have accelerated the discovery of novel GA derivatives with improved therapeutic profiles. This review summarizes current evidence regarding the pharmacological properties of these compounds and discusses their significance for modern drug discovery.

Materials and Methods. Five peer-reviewed publications with verified DOI identifiers were selected from international scientific databases. Studies were included if they investigated the synthesis, pharmacological activity, mechanism of action, or structure–activity relationship of glycyrrhetinic acid derivatives. Data extracted from each article included chemical modifications, biological targets, experimental models, therapeutic outcomes and proposed mechanisms of action. Comparative analysis was then performed to identify common trends and future research directions.

Results. Chemical analysis demonstrated that the C-3 hydroxyl group, C-11 carbonyl group and C-30 carboxyl group are the primary sites used for structural modification. Researchers introduced amides, esters, heterocyclic fragments and aromatic substituents to enhance biological activity. Anticancer activity was the most extensively investigated pharmacological property. Several derivatives demonstrated stronger cytotoxic effects than native glycyrrhetinic acid against breast, lung, liver and colon cancer cell lines. Anti-inflammatory effects were associated with suppression of NF-κB signaling, reduction of cytokine production and inhibition of oxidative stress. Novel derivatives also exhibited antiviral activity and promising antioxidant effects. Structure–activity relationship analysis indicated that multi-site modification frequently resulted in superior pharmacological performance.

Discussion. The reviewed evidence confirms that glycyrrhetinic acid represents a versatile pharmacological scaffold. Anticancer activity appears to be mediated through apoptosis induction, mitochondrial dysfunction, activation of caspases and inhibition of pro-survival signaling pathways. Anti-inflammatory activity is largely associated with modulation of NF-κB, TNF-α and interleukin signaling. The incorporation of heterocyclic fragments and aromatic substituents has produced derivatives with enhanced antiviral and antitumor activities. Although preclinical results are encouraging, additional in vivo and clinical investigations are necessary. Future studies should focus on pharmacokinetics, toxicity evaluation, targeted delivery systems and formulation development.

Conclusion. Glycyrrhetinic acid derivatives possess considerable therapeutic potential and represent promising candidates for future pharmaceutical development. Structural modifications significantly improve biological activity and may overcome the limitations of the parent molecule. The accumulated evidence supports further investigation of these compounds as anticancer, anti-inflammatory and antiviral agents.

This study investigated the pharmacological properties of glycyrrhetinic acid derivatives and demonstrated the importance of rational structural modification. The authors reported improvements in biological activity, selectivity and molecular interactions with therapeutic targets. Experimental findings highlighted the value of glycyrrhetinic acid as a platform for medicinal chemistry optimization. Mechanistic studies suggested involvement of apoptosis-related pathways, inflammatory mediators and oxidative stress regulation. The results contribute to understanding the structure–activity relationships that govern pharmacological performance [1].

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Structure–Activity Relationship (SAR).

SAR analysis indicates that modifications at C-3 often improve anticancer activity, whereas alterations at C-30 may enhance bioavailability and target affinity. Introduction of heterocyclic moieties frequently improves antiviral activity. Multi-target interactions appear to be responsible for the broad pharmacological profile of many derivatives. These observations provide guidance for future medicinal chemistry programs focused on optimization of glycyrrhetinic acid-based therapeutics.

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