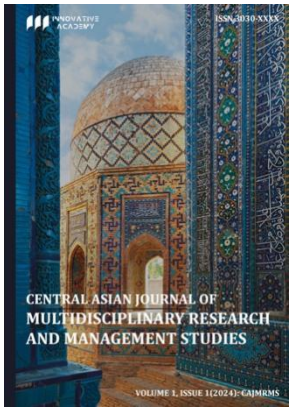

GLYCYRRHETINIC ACID AND ITS DERIVATIVES: CHEMICAL PROPERTIES, STRUCTURAL FEATURES AND BIOLOGICAL SIGNIFICANCE

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ABSTRACT

Glycyrrhetinic acid is a pentacyclic triterpenoid compound obtained through the hydrolysis of glycyrrhizin, the major bioactive component of licorice (Glycyrrhiza glabra). Due to its unique chemical structure and diverse functional groups, glycyrrhetinic acid and its derivatives have attracted considerable attention in pharmaceutical, biochemical, and medicinal chemistry research. This review analyzes the chemical properties, structural characteristics, synthesis pathways, and biological significance of glycyrrhetinic acid derivatives. Particular emphasis is placed on the relationship between molecular structure and biological activity, including anti-inflammatory, antioxidant, antiviral, hepatoprotective, and anticancer effects. The chemical modification of glycyrrhetinic acid has resulted in numerous derivatives with improved pharmacological properties and enhanced therapeutic potential. Understanding the chemical behavior of glycyrrhetinic acid provides important perspectives for the development of new bioactive molecules.

1. Introduction. Natural products have played an essential role in the discovery and development of therapeutic agents. Among plant-derived bioactive compounds, triterpenoids represent an important class of molecules characterized by complex carbon skeletons and a wide range of biological activities. Glycyrrhetinic acid (GA) is one of the most significant pentacyclic triterpenoids derived from licorice root (Glycyrrhiza glabra).

Licorice has been used traditionally for centuries due to its medicinal properties. The main active compound of licorice extract is glycyrrhizin, a glycoside composed of glycyrrhetinic acid linked with glucuronic acid residues. During metabolic processes or chemical hydrolysis, glycyrrhizin is converted into glycyrrhetinic acid, which demonstrates stronger biological activity.

Chemically, glycyrrhetinic acid belongs to the oleanane-type pentacyclic triterpenoid family. Its molecular formula is $C_{30}H_{46}O_4$, with a molecular weight of approximately 470.68 g/mol. The structure contains a carboxylic acid group, hydroxyl group, ketone group, and hydrophobic pentacyclic ring system. These functional groups determine its chemical reactivity and interaction with biological targets.

The modification of glycyrrhetinic acid has become an important research direction because the natural molecule has limited water solubility and bioavailability. Various derivatives, including esters, amides, salts, and heterocyclic modifications, have been synthesized to improve pharmacological characteristics.

The aim of this article is to analyze the chemical properties of glycyrrhetinic acid and its derivatives, including structural features, chemical reactions, synthesis approaches, and biological relevance.

2. Materials and Methods.

2.1. Literature Analysis. Scientific information regarding glycyrrhetinic acid and its derivatives was collected from biochemical, pharmaceutical, and organic chemistry research sources. The analysis focused on molecular structure, chemical characteristics, synthetic modifications, and biological applications.

2.2. Structural and Chemical Evaluation. The chemical structure of glycyrrhetinic acid was evaluated according to:

functional group composition;
molecular formula;
oxidation characteristics;
esterification and derivatization reactions;
relationship between structure and biological activity.

2.3. Comparative Analysis of Derivatives. Different classes of glycyrrhetinic acid derivatives were compared according to:

chemical modification type;
physicochemical properties;
biological activity;
potential pharmaceutical applications.

3. Results

3.1. Chemical Structure of Glycyrrhetinic Acid. Glycyrrhetinic acid is characterized by a pentacyclic triterpenoid skeleton derived from the oleanane structure. The molecule consists of five fused rings containing 30 carbon atoms.

Important structural elements include:

C-3 hydroxyl group;
C-11 ketone group;
C-30 carboxylic acid group;
double bond in the triterpenoid framework.

These functional groups are responsible for chemical transformation reactions and biological interactions.

The presence of oxygen-containing groups increases polarity compared with simple hydrocarbons; however, the large hydrophobic skeleton makes glycyrrhetinic acid poorly soluble in water.

3.2. Physical and Chemical Properties

Glycyrrhetinic acid appears as a white crystalline powder. It is practically insoluble in water but soluble in organic solvents such as ethanol, chloroform, and dimethyl sulfoxide.

Important physicochemical properties include:

Molecular formula: $C_{30}H_{46}O_4$
Molecular weight: 470.68 g/mol
Chemical class: pentacyclic triterpenoid
Functional groups: hydroxyl, carbonyl, carboxyl groups

The acidic nature of glycyrrhetinic acid is mainly determined by the carboxylic group. This allows formation of salts with alkaline substances.

3.3. Chemical Reactivity of Glycyrrhetinic Acid

Esterification. One of the most common chemical modifications is esterification of the carboxyl group. Esters of glycyrrhetinic acid demonstrate altered solubility and improved pharmacological properties.

Examples include:

methyl glycyrrhetinate;

acetate derivatives;

aromatic ester derivatives.

Esterification can reduce acidity and modify membrane permeability.

Acylation. The hydroxyl group at position C-3 can undergo acylation reactions. Acyl derivatives often show improved stability and biological activity.

Oxidation and Reduction. The carbonyl and hydroxyl groups allow oxidation–reduction reactions. Such modifications may influence molecular conformation and receptor interactions.

3.4. Glycyrrhetinic Acid Derivatives

3.4.1. Glycyrrhetinic Acid Salts. Salt formation improves water solubility and pharmaceutical usability. Sodium and potassium salts are commonly studied because of their increased bioavailability.

3.4.2. Ester Derivatives

Esterification produces molecules with modified lipophilicity.

Advantages:

improved absorption;

increased chemical stability;

controlled biological activity.

3.4.3. Amide Derivatives

Amide formation at the carboxyl group produces compounds with different pharmacological characteristics. These derivatives are investigated as potential anti-inflammatory and anticancer agents.

3.4.4. Heterocyclic Derivatives

Introduction of heterocyclic fragments can enhance interaction with biological targets. Nitrogen-containing derivatives often demonstrate increased activity.

3.5. Biological Properties Related to Chemical Structure

Anti-inflammatory Activity. Glycyrrhetinic acid inhibits enzymes involved in inflammatory pathways. One important mechanism is inhibition of 11β-hydroxysteroid dehydrogenase type 2, which influences corticosteroid metabolism.

Structural modifications can enhance anti-inflammatory effects.

Antioxidant Activity. The presence of oxygen-containing functional groups contributes to antioxidant behavior. Glycyrrhetinic acid derivatives may reduce oxidative stress by regulating reactive oxygen species.

Antiviral Properties. Some glycyrrhetinic acid derivatives demonstrate antiviral activity by affecting viral replication processes and cellular signaling pathways.

Hepatoprotective Effects. Licorice-derived compounds are widely studied for liver protection. Glycyrrhetinic acid contributes to membrane stabilization and reduction of inflammatory damage.

Anticancer Potential. Modified derivatives have shown potential cytotoxic effects against several cancer cell lines. The activity depends strongly on structural modifications of the triterpenoid framework.

4. Discussion. The chemical properties of glycyrrhetinic acid are closely connected with its molecular structure. The pentacyclic triterpenoid skeleton provides rigidity and hydrophobic interactions, while oxygen-containing groups determine chemical reactivity.

A major limitation of natural glycyrrhetinic acid is its poor water solubility. This affects absorption and pharmaceutical application. Therefore, chemical modification remains a key strategy for improving its properties.

Ester derivatives demonstrate enhanced lipophilicity, allowing better membrane penetration. However, excessive hydrophobicity may decrease biological availability. Therefore, balanced structural optimization is required.

Amide derivatives represent another important research direction because they may provide improved stability compared with esters. Additionally, introduction of nitrogen-containing groups may increase interaction with enzymes and receptors.

The structure–activity relationship of glycyrrhetinic acid demonstrates that small chemical changes can significantly influence biological effects. Modification at C-3 and C-30 positions is especially important because these sites participate in molecular interactions.

Future research should focus on:

improving solubility;

developing targeted delivery systems;

designing multifunctional derivatives;

studying molecular mechanisms of action.

5. Conclusion. Glycyrrhetinic acid is an important pentacyclic triterpenoid compound with significant chemical and biological value. Its unique molecular structure containing hydroxyl, carbonyl, and carboxyl groups allows various chemical modifications.

The derivatives of glycyrrhetinic acid demonstrate improved physicochemical and pharmacological properties compared with the parent compound. Esterification, amide formation, and heterocyclic modification represent effective strategies for developing new bioactive molecules.

Due to its anti-inflammatory, antioxidant, antiviral, hepatoprotective, and anticancer potential, glycyrrhetinic acid remains an important target in pharmaceutical chemistry and natural product research.

References:

1. Asl, M. N., Hosseinzadeh, H. (2008). Review of pharmacological effects of Glycyrrhiza sp. and its bioactive compounds.

2. Fiore, C., Eisenhut, M., Ragazzi, E., et al. (2005). Antiviral effects of glycyrrhizin and its derivatives.

3. Tang, Z. H., Li, T., Tong, Y. G., et al. (2015). Glycyrrhetinic acid and its derivatives: biological activities and therapeutic potential.

4. Isbrucker, R. A., Burdock, G. A. (2006). Risk and safety assessment on the consumption of licorice root.