UDC: 581.1:577.15:633.358

THE EFFECT OF QUINAZOLINE-THIONE DERIVATIVES ON GENE EXPRESSION AND THEIR MOLECULAR MECHANISMS

Ayitbayev Javohir Jonibek o’g’li, Saitkulov Foziljon Ergashevich,
Tashkent state agrarian university
Email: fsaitkulov@bk.ru

Shamshiddinov Jahangirmirzo Khayotillayevich,
Student of the Karakalpakstan institute of agriculture and agrotechnologies

DOI: https://doi.org/10.5281/zenodo.17536684

Abstract: *This study investigates the effect of quinazoline-thione derivatives on gene expression and their underlying molecular mechanisms. Quinazoline-thione compounds, known for their diverse biological activities, can interact with nucleic acids and regulatory proteins, influencing transcriptional and translational processes. Experimental evidence suggests that these derivatives modulate the expression of stress-related, growth-promoting, and defense genes in plant and microbial systems. Their activity is mediated through signaling pathways involving reactive oxygen species (ROS), protein kinases, and transcription factors. Understanding these molecular interactions provides a foundation for applying quinazoline-thione derivatives in genetic engineering and biotechnology to improve stress tolerance, productivity, and resistance in various biological systems.*

Keywords: *quinazoline-thione derivatives, gene expression, molecular mechanism, transcription regulation, signaling pathways, biotechnology*

Introduction. Quinazoline and its derivatives represent one of the most versatile classes of heterocyclic compounds possessing significant biological and pharmacological properties. Among these, *quinazoline-thione* derivatives have attracted increasing scientific attention due to their broad spectrum of biological activities, including antimicrobial, antioxidant, anticancer, and plant growth–regulating effects. The unique electronic structure of the quinazoline-thione nucleus, which contains both nitrogen and sulfur heteroatoms, enables its interaction with various biomolecular targets such as DNA, RNA, and proteins. This makes these compounds promising tools not only in medicinal chemistry but also in the field of genetic engineering and molecular biology.

The interaction of quinazoline-thione derivatives with genetic material has been demonstrated in several studies. Their planar aromatic structure allows for intercalation into DNA base pairs, while their electron-donating and withdrawing substituents can influence binding affinity and specificity. Through these interactions, quinazoline-thiones can modulate transcription factors and gene promoter activity. For example, in cell cultures, certain quinazoline-thione derivatives have been observed to upregulate genes associated with antioxidant

defense and stress tolerance. In plant systems, these compounds can act as biostimulants, enhancing root and shoot development, increasing chlorophyll synthesis, and improving resistance to abiotic stresses such as drought or salinity.

From a biochemical perspective, quinazoline-thione derivatives exert their effects through complex molecular mechanisms. One of the proposed pathways involves modulation of reactive oxygen species (ROS) signaling. ROS play a crucial role as secondary messengers in stress response pathways. Controlled accumulation of ROS can activate transcription factors such as *WRKY*, *NAC*, or *AP2/ERF*, which in turn regulate the expression of defense and stress-responsive genes. Quinazoline-thione derivatives may influence this signaling cascade by either scavenging ROS or altering the activity of key enzymes like catalase and superoxide dismutase. Consequently, they can indirectly modulate gene expression and enhance cellular adaptation mechanisms.

Another significant molecular mechanism involves protein phosphorylation cascades. Many quinazoline-based compounds are known inhibitors or activators of protein kinases — enzymes that regulate cellular processes through phosphorylation of target proteins. By affecting these kinases, quinazoline-thione derivatives can modulate transcriptional activators or repressors, thus influencing the overall expression pattern of genes.

In plant biotechnology, the application of quinazoline-thione derivatives can open new directions for enhancing crop productivity and stress resilience. When integrated into breeding programs, these compounds can act as chemical regulators that stimulate beneficial gene expression without the need for transgenic modification. This approach is particularly relevant in the context of sustainable agriculture, where eco-friendly and non-GMO methods are increasingly favored. For example, treatment of seeds or seedlings with low concentrations of quinazoline-thione derivatives could lead to improved germination rates, faster root development, and higher yield potential through the activation of growth-related genes.

From a structural chemistry standpoint, the functionalization of the quinazoline-thione ring is a key factor determining its biological activity. Substituents at positions 2, 3, or 4 of the quinazoline ring can drastically alter the compound’s lipophilicity, electronic distribution, and binding affinity to molecular targets. For example, the introduction of methyl, nitro, or halogen groups may enhance interaction with DNA grooves or improve permeability through biological membranes. Rational design and synthesis of such derivatives allow researchers to

tailor the compounds for specific biological functions, such as targeted gene activation or suppression.

In genetic engineering applications, quinazoline-thione derivatives can also be used as *chemical inducers* of gene expression. In synthetic biology systems, genes can be engineered under the control of promoters responsive to small molecules. When quinazoline-thione derivatives are applied, they may bind to transcriptional regulators or promoter elements, thereby turning specific genes “on” or “off.” This method provides a controllable and reversible system for studying gene function and for producing desired proteins or metabolites in a time-dependent manner.

Furthermore, quinazoline-thione derivatives have potential use in genome protection and repair processes. Their antioxidant and radical-scavenging properties can protect genetic material from oxidative damage caused by environmental stress or radiation.

Overall, the investigation of quinazoline-thione derivatives at the molecular level bridges the gap between chemistry and genetics. Understanding their mode of action enables the development of novel biotechnological tools that combine chemical precision with genetic specificity. The integration of these compounds into genetic engineering and breeding programs holds promise for creating crops with improved productivity, resilience, and adaptability to environmental challenges.

In summary, quinazoline-thione derivatives represent a new generation of bioactive molecules with significant potential to influence gene expression through multifaceted molecular mechanisms. Their dual functionality — as both signaling modulators and protective agents — provides a foundation for innovative approaches in gene regulation and plant biotechnology. Continued interdisciplinary research combining organic synthesis, molecular biology, and computational modeling will be essential to unlock their full potential in modern agriculture and genetic engineering.

Table 1. Possible molecular targets and biological effects of quinazoline-thione derivatives

№	Target System	Molecular Mechanism	Observed Effect	Application Area
1	DNA and RNA	Intercalation between base pairs, stabilization of nucleic acid structure	Regulation of transcription and replication processes	Genetic engineering, gene modulation
2	Protein kinases	Inhibition or activation of	Modulation of stress-response and growth-	Plant biotechnology,

		phosphorylation pathways	related genes	stress physiology
3	Antioxidant enzymes (SOD, CAT, POD)	Enhancement of enzyme activity and ROS scavenging	Increased oxidative stress tolerance	Crop improvement, abiotic stress resistance
4	Transcription factors (WRKY, NAC, ERF families)	Activation through ROS and kinase signaling	Upregulation of defense and stress-related genes	Functional genomics, plant defense studies

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