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Research advances of *Nitraria* genus: from extreme environmental adaptation to the exploitation of multifunctional bioactive components

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Abstract

Nitraria is typical halophytic shrubs that adapt to high salinity, drought, and ultraviolet radiation. It accumulates abundant structurally varied secondary metabolites endowed with notable pharmacological and nutritional properties, rendering it a valuable reservoir of natural bioactive substances. As the secondary metabolites of *Nitraria*, anthocyanins, alkaloids, and polysaccharides confer strong stress resistance and diverse bioactivities, along with prominent pharmacological and nutritional values, making this genus an ideal reservoir of natural bioactive compounds. This review systematically summarizes recent progress in *Nitraria* research, including genomic/transcriptomic characteristics, chemical constituents, pharmacological activities, stress-responsive mechanisms, and molecular regulatory mechanisms. Studies have advanced from genome size estimation to organelle genome assembly and phylogenomic analyses, laying a foundation for understanding its environmental adaptation and specialized metabolism. However, current research still lacks sufficient exploration of alkaloid and polysaccharide synthesis, epigenetic regulation, and clinical translation. Future work should integrate multi-omics, functional genomics, structure–activity analysis, and clinical translation to support the utilization of *Nitraria*. In summary, *Nitraria* is not only a valuable model for investigating plant adaptation to extreme environments but also a valuable resource for natural product discovery, drug development, and functional food applications.

Keywords: *Nitraria*, Phytochemical constituents, Pharmacological activities, Anthocyanin biosynthesis, Molecular mechanism

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Introduction

The genus *Nitraria* L. comprises typical halophytic shrubs widely distributed in arid, semi-arid, and saline habitats across Eurasia and Australia. *Nitraria tangutorum* (*N. tangutorum*) and *Nitraria sibirica* (*N. sibirica*) are endemic to the Qinghai-Xizang Plateau. They act as key dominant plants to prevent wind erosion, fix sand, and improve saline-alkali land in desert areas[1]. *Nitraria* fruit is rich in nutrients with a unique taste and has a long history of traditional application. Morpho-physiological traits including succulent leaves and well-developed root systems represent typical evolutionary adaptations enabling survival under extreme habitats characterized by high salinity, drought, and intense ultraviolet radiation[2,3]. Succulent degeneration of leaves, wax or trichome coverage, and highly-developed root systems constitute the hallmark morphological and physiological features underlying its adaptation to high-salt, drought, and nutrient-impoverished environments. Classics such as *Bencao Gangmu* and *Bencao Shiyi* record that its fruit can tonify the spleen and stomach, soothe the nerves, and aid sleep. They are also used for relieving exterior syndromes and soothing the nerves in Mongolian and Uyghur medicine. It has also been widely used in folk medicine abroad. Its fruit is processed into jams and drinks in Central Asia, while branches and leaves are used to treat inflammation and joint pain in North Africa and Southern Europe. Modern development is relatively mature, with products such as *Nitraria* fruit juice, wine, and fermented drinks, as well as health products and cosmetics containing *Nitraria* polysaccharides and flavonoids. Its medicinal potential and ecological restoration value are attracting increasing international attention.

In recent years, with growing recognition of the value of distinctive plant resources, studies on *Nitraria* have progressed from basic ecological surveys and preliminary phytochemical analyses to systematic, in-depth mechanistic research. *Nitraria* contains anthocyanins[4–6], flavonoids[7–9], alkaloids[10–12], polysaccharides[13–15], and phenolic acids[11,12,16,17]. These bioactive constituents underpin its diverse pharmacological activities, such as antioxidant[18,19], anti-inflammatory[13,18,20], antimicrobial[21–23], hypoglycemic[10,24], hypolipidemic[15,25,26], and neuroprotective effects[4]. Notably, the biosynthesis, accumulation, and regulation of these secondary metabolites are closely linked to its adaptation to extreme environments.

Despite recent progress, *Nitraria* research still has obvious imbalances and bottlenecks. Studies on characteristic bioactive components mostly focus on phytochemistry and preliminary pharmacological validation, with few systematic investigations into biosynthesis mechanisms, regulatory networks, and structure–activity relationships. Four scientific questions need addressing: First, how to identify the complete biosynthetic pathways and key rate-limiting enzyme genes for characteristic bioactive components? Second, which transcription factors and epigenetic modifications form the core regulatory network of the metabolic pathways? Third, how do extreme environmental signals coordinately regulate

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stress resistance and specific metabolite accumulation in *Nitraria*? Fourth, what are the structure–activity relationships between bioactive components and their biological activities? Focusing on the chemical structures, pharmacological activities, and molecular mechanisms of *Nitraria* components, this review summarizes recent advances in relevant fields, analyzes research limitations, and outlines a mechanism-driven blueprint for future studies, aiming to provide a theoretical foundation and technical pathway for sustainable, in-depth exploitation of *Nitraria* resources.

From genomic landscapes to transcriptional dynamic responses

Genomic characteristics and evolutionary insights

Genomic research on *Nitraria* has advanced from preliminary exploration to fine-scale mapping. The chloroplast genomes of *N. tangutorum* and *N. roborowskii* are 159,383 and 159,397 bp in length[27]. Phylogenomic analyses reveal that *N. tangutorum* and *N. roborowskii* form a monophyletic clade positioned at the base of the order Sapindales[27]. Sequencing of the complete plastid genome (159,369 bp) of *Nitraria sphaerocarpa* (*N. sphaerocarpa*) has laid the groundwork for phylogenetic and plastid genetic studies of the genus[28]. A breakthrough came with the release of the chromosome-level high-quality reference genome of *N. sibirica*[29]. Integrating PacBio HiFi and chromosome conformation capture (Hi-C), the genome assembly totalled 456.66 Mb, consisting of 170 contigs with an N50 value of 9.07 Mb[29]. Phylogenomic analyses indicate that *Nitraria* underwent the shared ancestral γ hexaploidy event during evolution, with no recent lineage-specific whole-genome duplication detected[29]. This may be associated with its relatively stable diploid status and specialized niche-adaptation strategies. In-depth genome mining identified 63 Calmodulin-like (CML) genes; *NtSl03G1136* and *NtSl01G1645* were verified to enhance salt tolerance in transgenic poplar by alleviating H_2O_2 accumulation[30]. These high-quality genomic resources offer critical support for genome-wide mining of gene families related to stress resistance and secondary metabolism, as well as comparative genomic and evolutionary biological studies (Fig. 1).

Transcriptomic dissection of development and stress responses

Transcriptomics has become a core tool for unraveling the dynamic regulatory mechanisms underlying biological processes in *Nitraria* (Fig. 1). In the context of developmental and metabolic regulation, RNA-Seq of three key fruit coloring stages (green, yellow, and red) in *N. tangutorum* established a transcript library containing 69,306 unigenes[31]. Differential expression analysis indicated that the transition from green to red is accompanied by extensive differential gene expression, with the anthocyanin biosynthesis pathway significantly activated. qRT-PCR analysis revealed that core structural genes directly contribute to fruit color phenotypic variations by activating specific metabolic pathways at the transcriptional level[31]. Integrated metabolomic and transcriptomic analyses comparing the fruits of *N. tangutorum*, *N. sibirica*, and *N. roborowskii* revealed that while the three species share the basic framework of flavonoid metabolism, interspecific differences in flavor and color are primarily driven by differential gene expression in the anthocyanin pathways. Key structural genes governing metabolic flux were identified as critical determinants[32].

In the stress response, multiple transcriptomic studies have delineated the complex transcriptional regulatory networks of *Nitraria* under salt, drought, and alkali stresses, with three synergistic core regulatory modules: (1) Ion homeostasis regulation: Salt stress induces the plasma membrane-localized Na^+/H^+ antiporter *SOS1*, vacuolar Na^+/H^+ antiporter 1/2/6, and vacuolar H^+-ATPase that provide proton motive force for secondary transport[33–35], while high-affinity potassium transporter genes are upregulated to maintain optimal intracellular K^+/Na^+ ratio[36]. (2) Osmoprotectant and reactive ROS scavenging: Stress upregulates the key proline synthesis gene *P5CS*, soluble sugar metabolism genes, and antioxidant enzymes, including superoxide dismutase (SOD), peroxidase (POD),

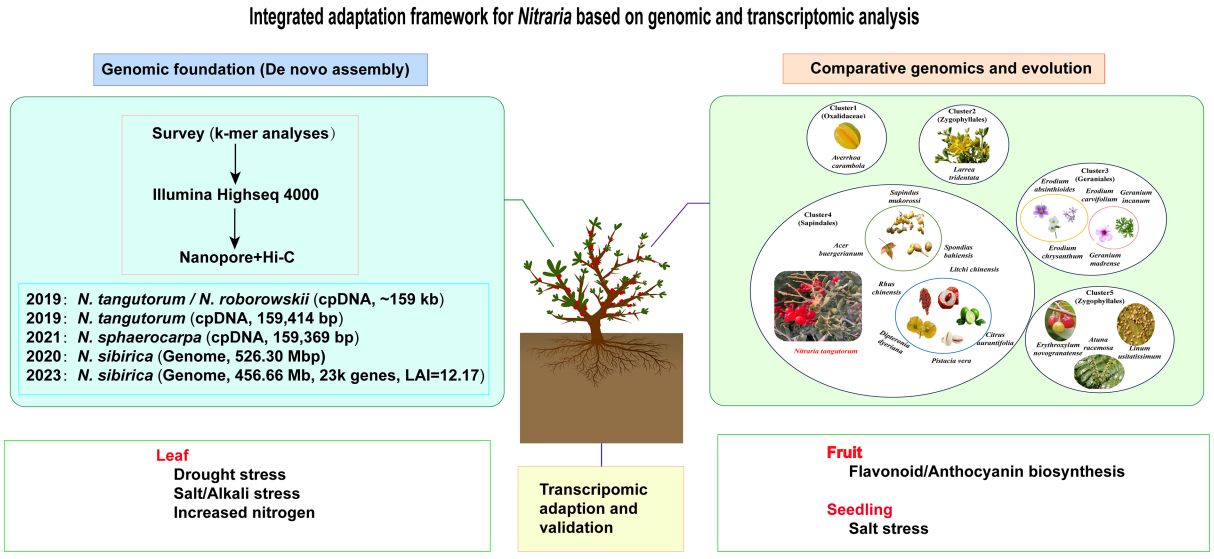

Fig. 1 Genome and transcriptome-based studies on adaptive evolution in *Nitraria*. This study employed multi-platform sequencing technologies to assemble the complete chloroplast genomes and whole-genome sequences of *N. tangutorum* and *N. sibirica*. Combined with transcriptomic profiling, it elucidates the molecular regulatory mechanisms underlying abiotic stress tolerance and the biosynthesis of bioactive compounds in the fruit of these species.

catalase (CAT), and ascorbate peroxidase (APX), which are broadly upregulated[37,38], synergistically promoting osmolyte accumulation and mitigating oxidative stress. (3) Signal perception and transcriptional cascades: Stress signals are amplified via plant hormone signaling pathways, activating AP2/ERF, WRKY, bHLH, NAC, and MYB transcription factors[39–42]. These factors form an upstream regulatory network that modulates downstream functional genes, orchestrating ion transport, osmolyte synthesis, and antioxidant defense.

For instance, PacBio full-length transcriptome sequencing of *N. sibirica* under salt stress identified salt-tolerant candidate genes including *AMYB2*, *CML38*, and *H*$^+$*-PPase*[33]. Under drought stress, downregulation of nitrate reductase (NR) in *N. tangutorum* inhibits glutamine synthesis, while upregulated protochlorophyllide reductase promotes chlorophyll a synthesis and chlorophyll b-to-a conversion, facilitating adaptation to stressful light environments[43]. Alkali stress induces cell membrane damage, increased electrolyte leakage, and excessive ROS accumulation in *N. tangutorum* seedlings[42]. Exogenous abscisic acid (ABA) promotes *NtFLS*, *NtF3H*, and *NtANR* transcription, activating flavonoid biosynthetic pathways[42]. From a systems biology perspective, these studies dissect the molecular mechanisms by which *Nitraria* regulates stress resistance and secondary metabolism via multi-level gene expression modulation, providing a basis for mining bioactive component synthesis regulatory targets.

Despite breakthroughs in genomic and transcriptomic research on *Nitraria*, significant limitations persist. High-quality genomes are only available for a few species (e.g., *N. sibirica*), while genomes of Qinghai-Xizang Plateau endemics (*N. tangutorum* and *N. roborowskii*) are uncharacterized, restricting interspecific comparative studies on stress resistance and metabolism. Most transcriptomic studies focus on single stresses or single developmental stages, lacking dynamic transcriptional regulatory data under combined stresses and across the full life cycle, which is disconnected from the complexity of natural habitats. Furthermore, functional prediction of key secondary metabolism biosynthetic genes in genome annotations relies on homologous alignment with scarce direct functional validation, leaving gene-metabolite associations speculative.

Structural diversity of chemical constituents and analytical methodology

Flavonoids

Anthocyanins

Anthocyanins are water-soluble, characteristic bioactive pigments, widely distributed in the fruit of *Nitraria* species. To date, more than 20 monomeric anthocyanins have been identified (Table 1), among which cyanidin derivatives are the predominant components, accompanied by minor pelargonidin, delphinidin, peonidin, and malvidin derivatives. All anthocyanins are glycosylated at the C3 position with glucose, diglucose, rutinoside and other sugar moieties (Fig. 2). Among them, cyanidin 3-(2''-[6'''-coumaroyl]-glucosyl)-glucoside (C3G) is the predominant monomer, accounting for 87.06% of the total anthocyanin content[4,5,44], and its isolation and purification have been successfully achieved[44].

A signature structural feature of anthocyanins in *Nitraria* is the high proportion of acylation. In the fruit of *N. tangutorum*, acylated anthocyanins account for up to 65.7% of the total anthocyanin content[47], with coumaric acid, caffeic acid, and ferulic acid as the main acyl donors. Such acylation modifications not only enrich fruit coloration through bathochromic shifts but also significantly enhance the stability of anthocyanins against light, heat, and pH changes, as well as improve their bioavailability. This is consistent with the adaptive evolutionary characteristics of plant secondary metabolites in the extreme habitats of the Qinghai-Xizang Plateau.

Extraction technologies for anthocyanins have evolved from traditional solvent maceration to green physical-assisted methods. The yields of total anthocyanins by conventional water extraction, 70% ethanol maceration, and acidic ethanol maceration are 1.60 ± 0.13 mg cyanidin-3-glucoside equivalent (CGE)/L dry weight (DW)[48], 704.50 ± 3.28 mg/g (DW)[4], and 45.83 mg/100 g fresh weight (FW)[47], respectively. Ultrasound-assisted extraction, subcritical water extraction, and microwave-ultrasound synergistic enzymatic hydrolysis significantly improve extraction efficiency, with yields reaching 346.27 ± 2.42 mg/g FW[5] and 1.075 mg/g DW[6], while better preserving the native structures and biological activities of anthocyanins.

Other flavonoids

Flavonoids in *Nitraria* are mainly composed of flavonols and their glycosides, with isorhamnetin and its derivatives (e.g., 3-*O*-rutinoside, 3-*O*-glucoside) as the characteristic flavonoid constituents of this genus[47]. More than 20 monomeric compounds have been isolated and purified, including isorhamnetin-3-*O*-4-rhamnosyl-galactosyl robinin, isorhamnetin-3-robinin, and tangutoside[8,49–51].

The composition and content of flavonoids show remarkable species and tissue-specificity. The ethyl acetate extract of *N. tangutorum* fruit contains 40.61 ± 1.23 mg rutin equivalent (RE)/g DW of total flavonoids[48], which can be increased to 60.00 mg quercetin equivalent (QE)/g DW after further ethyl acetate partitioning of the methanol extract[8]. Seeds of *N. tangutorum* are flavonoid-enriched tissues, containing three quercetin derivatives, three kaempferol derivatives, and eight isorhamnetin derivatives; rutin is the most abundant flavonoid in the fruit, reaching 1,298.48 ± 82.10 μg/g[47]. For *N. schoberi*, tissue-specific distribution is distinct: luteolin-7-*O*-glucoside (252.40 μg/mL) and isorhamnetin-3-*O*-rhamnoside (278.01 μg/mL) are dominant in 70% ethanol leaf extracts, while isorhamnetin aglycone reaches 1.46 μg/mL in stems[52]. Isorhamnetin-3-*O*-robinin is the main component in chloroform leaf extracts, whereas quercetin-O-hexoside (9.54%), isorhamnetin-3-*O*-glucoside (19.27%), and isorhamnetin-3-*O*-rutinoside (19.71%) are predominant in methanol extracts, with isorhamnetin glucuronide and isorhamnetin aglycone accounting for 17.21% and 13.75%, respectively[53]. Notably, *N. tangutorum* (NT), *N. sibirica* (NS), and *N. roborowskii* (NR) share similar flavonoid profiles but differ significantly in content: kaempferol-3-*O*-rutinoside and quercetin are most abundant in NS; rutin, dioscin, and vitexin are highest in NT; and all these components are lowest in NR[32].

Phenolic acids

Phenolic acids in *Nitraria* are dominated by phenylpropanoic and benzoic acids. Common constituents including gallic acid, protocatechuic acid, chlorogenic acid, caffeic acid, and ferulic acid have been identified[54,55] (Table 2). Nineteen structurally diverse phenolic acid derivatives have also been isolated from leaves and fruit, such as caffeoylmalic acid, depsides, *trans*-coumaric acid, tangutoside A, *trans*-ferulic acid-4-*O*-*β*-D-glucoside, and glucosyl syringic acid[56,57].

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Table 1. Anthocyanins isolated from the fruits of *Nitraria*.

No.	Compound	MS^+ (m/z)	MS/MS (m/z)	Molecular formula	Core structure	Key distinguishing structural features		Species	Ref.
						3'	5'		
1	Cyanidin-3-*O*-diglucoside	611.16	287.05	$C_{27}H_{31}O_{16}^+$	Cyanidin	Di-Glu	OH	*N. sibirica*	[1,5,45,46]
2	Cyanidin-3-*O*-sambubioside	581.15	287.05	$C_{26}H_{29}O_{15}^+$	Cyanidin	Samb	OH	*N. sibirica*/*N. tangutorum*	[4,5,45]
3	Pelargonidin-3-*O*-diglucoside	595.17	271.06	$C_{27}H_{31}O_{15}^+$	Pelargonidin	Di-Glu	OH	*N. sibirica*/*N. tangutorum*	[1,5,46]
4	Peonidin-3-*O*-diglucoside	625.18	301.07	$C_{28}H_{33}O_{16}^+$	Peonidin	Diglucoside	OH	*N. sibirica*/*N. tangutorum*	[1,5,46]
5	Cyanidin-3-[2''-(6'''-transcaffeoyl)-glucosyl]-glucoside	773.19	287.05	$C_{36}H_{37}O_{19}^+$	Cyanidin	*Trans*-caffeoyl-Di-Glu	OH	*N. sibirica*/*N. tangutorum*	[5,46]
6	Cyanidin-3-[2″-(6‴-transcoumaroyl)-glucosyl]-glucoside	757.20	287.05	$C_{36}H_{37}O_{18}^+$	Cyanidin	*Trans*-coumaroyl-Di-Glu	OH	*N. sibirica*/*N. tangutorum*	[1,4,5,44–46]
7	Pelargonidin-3-*O*-(caffeoyl)-diglucoside	757.20	271.06	$C_{36}H_{37}O_{18}^+$	Pelargonidin	Caffeoyl-Di-Glu	OH	*N. sibirica*/*N. tangutorum*	[1,4,5,45]
8	Pelargonidin-3-[3-[2''-(6'''-transcoumaroyl)-glucosyl]-glucoside	741.20	271.06	$C_{36}H_{37}O_{17}^+$	Pelargonidin	Transcoumaroyl-Di-Glu	OH	*N. sibirica*/*N. tangutorum*	[5,45,46]
9	Cyanidin-3-*O*-[2-*O*-(*β*-D-glycopyranosyl)-*β*-D-glucopyranoside]	611.16	287.05	$C_{27}H_{31}O_{16}^+$	Cyanidin	*β*-D-glycopyranosyl-*β*-D-glucopyranoside	OH	*N. tangutorum*	[1,4]
10	Cyanidin-3-[2″-(6‴-cis-caffeoyl)-glucosyl]-glucoside	773.19	287.05	$C_{36}H_{37}O_{19}^+$	Cyanidin	Cis-caffeoyl-Di-Glu	OH	*N. tangutorum*	[4]
11	Cyanidin-3-[2″-(6‴-ferulyl)-glucosyl]-glucoside	787.21	287.05	$C_{37}H_{39}O_{19}^+$	Cyanidin	Ferulyl-Di-Glu	OH	*N. tangutorum*	[1,4]
12	Pelargonidin-3-[2″-(6‴-ferulyl)-glucosyl]-glucoside	771.21	271.06	$C_{37}H_{39}O_{18}^+$	Pelargonidin	Ferulyl-Di-Glu	OH	*N. tangutorum*	[4]
13	Pelargonidin-3-[2″-(6‴-cis-coumaroyl)-glucosyl]-glucoside	741.20	271.06	$C_{36}H_{37}O_{17}^+$	Pelargonidin	*Cis*-coumaroyl-Di-Glu	OH	*N. tangutorum*	[1]
14	Cyanidin-3-*O*-hexose	449.11	287.05	$C_{21}H_{21}O_{11}^+$	Cyanidin	Hex	OH	*N. tangutorum*	[1]
15	Cyanidin-3-*O*-(cis-*p*-coumaroyl)-diglucoside	757.20	287.05	$C_{36}H_{37}O_{18}^+$	Cyanidin	*Cis*-*p*-coumaroyl-Di-Glu	OH	*N. tangutorum*	[1,46]
16	Delphinidin-3-*O*-(cis-*p*-coumaroyl)-glucoside	611.16	303.08	$C_{30}H_{27}O_{14}^+$	Delphinidin	*Cis*-*p*-coumaroyl-Di-Glu	OH	*N. tangutorum*	[1]
17	Cyanidin-3-*O*-(*p*-coumaroyl)-glucoside	595.17	287.05	$C_{30}H_{27}O_{13}^+$	Cyanidin	*p*-coumaroyl-Glu	OH	*N. tangutorum*	[1,45]
18	Malvidin-3-*O*-glucoside	493.13	331.10	$C_{23}H_{25}O_{12}^+$	Malvidin	Glu	OH	*N. tangutorum*	[45]
19	Delphinidin-3-*O*-(6″-*O*-coumaroyl)-glucoside,5-*O*-glucoside	773.19	303.08	$C_{36}H_{37}O_{19}^+$	Delphinidin	Coumaroyl-Glu	Glu	*N. tangutorum*	[4,45]
20	Delphinidin-3-*O*-(cis-p-coumaroyl)-glucoside-5-*O*-glucoside	773.19	303.08	$C_{36}H_{37}O_{19}^+$	Delphinidin	*cis*-*p*-coumaroyl-Glu	Glu	*N. tangutorum*	[1,45]
21	Delphinidin-3-*O*-(trans-p-coumaroyl)-glucoside-5-*O*-glucoside	773.19	303.08	$C_{36}H_{37}O_{19}^+$	Delphinidin	*Trans*-*p*-coumaroyl-Glu	Glu	*N. tangutorum*	[1]
22	Delphinidin-3-*O*-(caffeoyl)-diglucoside	773.19	303.08	$C_{36}H_{37}O_{19}^+$	Delphinidin	Caffeoyl-Di-Glu	OH	*N. tangutorum*	[46]
23	Peonidin-3-*O*-(6″-*O*-coumaroyl)-glucoside, 5-*O*-glucoside	771.21	301.07	$C_{37}H_{39}O_{18}^+$	Peonidin	Coumaroyl-Glu	Glu	*N. tangutorum*	[45]
24	Malvidin-3-*O*-(6″-*O*-acetyl)-glucoside	535.15	331.10	$C_{25}H_{27}O_{13}^+$	Malvidin	Acetyl-Glu	OH	*N. tangutorum*	[45]
25	Petunidin-3-*O*-(6″-*O*-coumaroyl)-glucoside	625.17	317.07	$C_{31}H_{29}O_{14}^+$	Petunidin	Coumaroyl-Glu	OH	*N. tangutorum*	[45]
26	Peonidin-3-*O*-(6″-*O*-coumaroyl)-glucoside	609.16	301.07	$C_{30}H_{27}O_{14}^+$	Peonidin	Coumaroyl-Glu	OH	*N. tangutorum*	[45]
27	Malvidin-3-*O*-(6"-*O*-coumaroyl)-glucoside, 5-*O*-glucoside	801.24	331.10	$C_{38}H_{39}O_{19}^+$	Malvidin	Coumaroy-Glu	Glu	*N. tangutorum*	[45]
28	Malvidin-3-*O*-(cis-6"-*O*-coumaroyl)-glucoside	639.20	331.10	$C_{31}H_{31}O_{14}^+$	Malvidin	Cis-coumaroy-Glu	OH	*N. tangutorum*	[45]
29	Malvidin-3-*O*-(trans-6"-*O*-coumaroyl)-glucoside	639.20	331.10	$C_{31}H_{31}O_{14}^+$	Malvidin	*Trans*-coumaroy-Glu	OH	*N. tangutorum*	[45]
30	Delphinidin-3-rutinoside	611.16	303.08	$C_{27}H_{31}O_{16}^+$	Delphinidin	Rut	OH	*N. tangutorum*	[46]

Note: Di-Glu, diglucoside; Samb, sambubioside; Glu, glucoside; Hex, hexoside; Rut, rutinoside.

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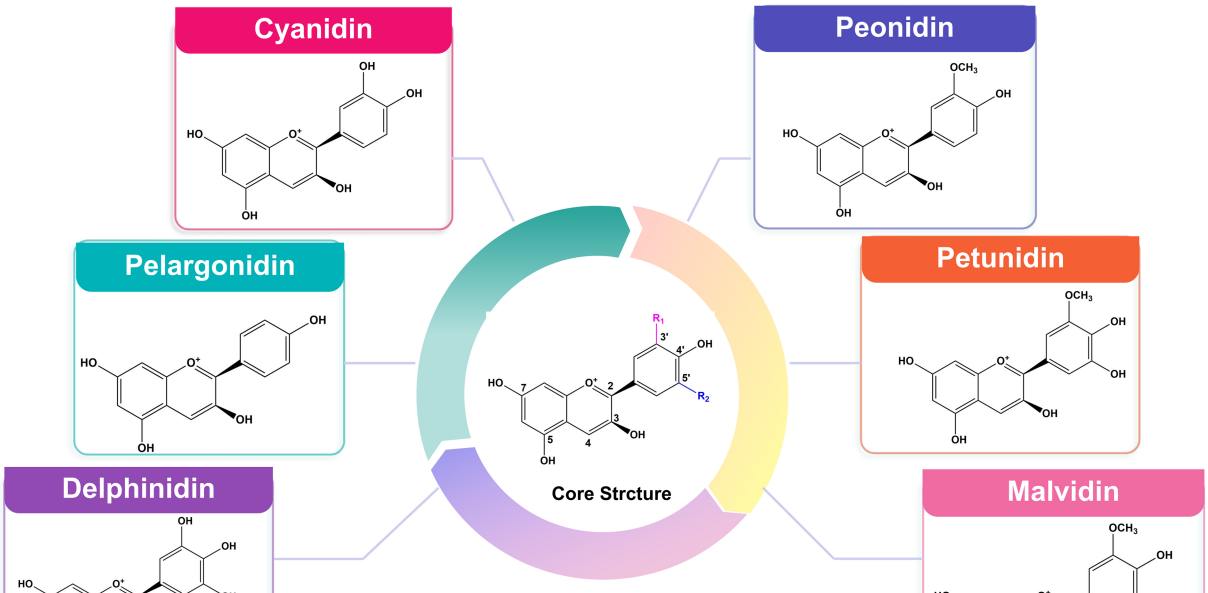

Six basic structures of anthocyanins

Name	Substitution pattern		Molecular weight
	R1	R2	
Cyanidin	OH	H	287.24
Pelargonidin	H	H	271.24
Delphinidin	OH	OH	303.24
Peonidin	OCH_3	H	301.27
Petunidin	OCH_3	OH	317.27
Malvidin	OCH_3	OCH_3	331.30

Fig. 2 Core skeleton and six basic structural classes of anthocyanidins. This figure illustrates the positively charged flavylium core skeleton of anthocyanidins, as well as the six fundamental anthocyanidin monomers derived from substitutions on the B-ring. A supplementary table lists their respective substituent groups and molecular weight characteristics.

Table 2. Summary of partial identified main bioactive constituents in *Nitraria*.

No.	Compound	$[M-H]^-$	Molecular formula	Categories	Species	Ref.
1	Isorhamnetin	315.05	$C_{16}H_{12}O_7$	Flavonoid	*N. retusa*	[8]
2	Isorhamnetin 3-*O*-glucoside	477.10	$C_{22}H_{22}O_{12}$	Flavonoid	*N. retusa*	[8,49]
3	Isorhamnetin 3-*O*-rutinoside	623.16	$C_{28}H_{32}O_{16}$	Flavonoid	*N. sibirica/N. tangutorum*	[8,12,49]
4	Kaempferol 3-*O*-neohesperidoside	593.15	$C_{27}H_{30}O_{15}$	Flavonoid	*N. tangutorum*	[12]
5	Kaempferol 7-*O*-rutinoside	593.15	$C_{27}H_{30}O_{15}$	Flavonoid	*N. tangutorum*	[12]
6	Quercetin 3-*O*-rutinoside	609.15	$C_{27}H_{30}O_{16}$	Flavonoid	*N. sibirica/N. tangutorum*	[12,56]
7	Quercetin-3-*O*-(2G-rhamnosyl-rutinoside)	755.20	$C_{33}H_{40}O_{20}$	Flavonoid	*N. sibirica/N. tangutorum*	[12,56]
8	Glucosyl-4-hydroxycinnamic acid	325.06	$C_{15}H_{18}O_8$	Phenolic acid	*N. sibirica*	[58]
9	Gallic acid	169.02	$C_7H_6O_5$	Phenolic acid	*N. retusa*	[54,55]
10	Ferulic acid hexoside	355.10	$C_{16}H_{20}O_9$	Phenolic acid	*N. tangutorum*	[12]
11	Caffeic acid derivative	259.03	NA	Phenolic acid	*N. tangutorum*	[12]
12	Ellagic acid	301.00	$C_{14}H_6O_8$	Phenolic acid	*N. retusa*	[54,55]
13	Flazin	307.07	$C_{17}H_{12}N_2O_4$	Alkaloid	*N. sibirica/N. tangutorum*	[12,56,58]
14	N-(fructofuranosyl-2-*O*-glucoside)-tryptophan	526.99	$C_{23}H_{32}N_2O_{12}$	Alkaloid	*N. sibirica*	[58]
15	Tangutorid E	301.11	$C_{16}H_{18}N_2O_4$	Alkaloid	*N. sibirica/N. tangutorum*	[12,58]
16	Tangutorid C	345.07	$C_{17}H_{18}N_2O_6$	Alkaloid	*N. sibirica*	[58]
17	Tangutorid D	345.07	$C_{17}H_{18}N_2O_6$	Alkaloid	*N. sibirica*	[58]
18	β-carboline derivative	347.12	$C_{17}H_{20}N_2O_6$	Alkaloid	*N. tangutorum*	[12]
19	Tryptophan hexoside	365.13	$C_{17}H_{22}N_2O_7$	Alkaloid	*N. tangutorum*	[12]
20	Asparagine hexoside (I)	293.12	$C_{10}H_{18}N_2O_8$	Alkaloid	*N. tangutorum*	[12]
21	Tryptophan fructoside	365.13	$C_{17}H_{22}N_2O_7$	Alkaloid	*N. tangutorum*	[12]

Phenolic acid contents also exhibit species-, tissue-, and extraction-dependent specificity. The hydroalcoholic extract of *N. sibirica* fruit contains 23.60 ± 0.03 mg gallic acid equivalent (GAE)/g dry extract[59]. The total phenolic acid content was higher in leaves than that in fruit, flowers, and stems of *N. schoberi*. The water extraction-alcohol precipitation obtained the maximum phenolic acid level of 46.97 mg GAE/g DW, which was higher than those extracted by methanol and acetone[16]. After ethyl acetate partitioning, the

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methanol extract of *N. tangutorum* contains up to 170.00 mg GAE/g DW[8]. Extraction techniques strongly affect phenolic acid recovery: ultrasound-assisted extraction yields 23.98 ± 0.33 mg GAE/g dry residue[60].

The accumulation of flavonoids and phenolic acids is further modulated by environments and exogenous treatments. Drought stress promotes flavonoid biosynthesis by activating hormone signaling pathways[7]. High-altitude significantly enhances the accumulation of flavonoids such as kaempferol-3-*O*-rhamnogalactoside-7-*O*-glucoside and rutin[9]. Combined treatment with NaCl and salicylic acid (SA) increases total phenolic acids to 62.20 mg GAE/g[61]. Fermentation of *N. sibirica* fruit with probiotics including *Lactobacillus acidophilus*, *Lactiplantibacillus plantarum*, and *Streptococcus thermophilus* reshapes the phenolic acid profile and enriches sinapic acid, caffeic acid, and other phenolic acids[62].

Alkaloids

Nitraria species are alkaloid-enriched halophytic shrubs. More than 20 structurally unique monomeric alkaloids have been isolated and identified (Table 2), with β-carboline and quinazoline skeletons as the core structural types. Several novel alkaloids with unprecedented structures have been discovered, including spirocyclic β-carbolines (komavine, acetylkomavine[63], and N-allylisonitrarine[64]) and tangutorid-type alkaloids[10,65], making *Nitraria* a valuable natural resource for the discovery of drug lead compounds.

A mature technical system has been established for the extraction and purification of alkaloids. Extraction mainly relies on organic solvent maceration combined with acid-base treatment, while direct maceration with chloroform or ethanol gives low alkaloid yields (1.23%[66] and 3.83 mg/g [equivalent to 0.383%][67]). HPD-450 macroporous resin enriches total alkaloids by up to 18.08%[67]. Silica gel column chromatography, macroporous resin adsorption, and HPLC enable efficient isolation of monomeric alkaloids.

Alkaloid composition and distribution show strong species- and tissue-specificity. Leaves of *N. sibirica* contain 16 alkaloids, while fruits contain 12 alkaloids (including the newly reported N-[fructofuranosyl-2-*O*-glucoside]-tryptophan)[58]. Eight β-carboline alkaloids and four tryptophan derivatives have been identified in *N. tangutorum* fruit[12]. Fruits of *N. roborowskii* possess the most diverse alkaloid profile, including ten β-carbolines, nine cyclopeptides, three indoles, and five pyrroles[11].

Polysaccharides

Polysaccharides of *Nitraria* are homogeneous heteropolysaccharides with molecular weights ranging from 14.40 to 67.45 kDa. Their monosaccharide composition is dominated by glucose, galactose, arabinose, rhamnose, mannose, xylose, and galacturonic acid[11,13,20,68]. The molar ratios of monosaccharides and glycosidic linkage patterns vary significantly across species, tissues, and extraction methods, which are the key factors determining their structural and biological activities. Fruit polysaccharides of *N. sibirica* are rich in galacturonic acid, displaying typical pectic polysaccharide characteristics, while leaf polysaccharides differ distinctly in monosaccharide composition[15,20]. Polysaccharides of *N. tangutorum* are dominated by glucose (26.73%) and galactose (38.08%)[13]. Leaf polysaccharides of *N. sibirica* are rich in rhamnose (33.70%) and galactose (18.10%)[20]. The neutral fraction NSP-1 of *N. sibirica* is dominated by mannose, whereas acidic fractions NSP-2 and NSP-3 feature rhamnose[14].

Extraction and fractionation technologies for polysaccharides are increasingly mature. Traditional hot water extraction yields 3.59% (DW)[13], while ultrasound-assisted and cellulase-assisted extraction improve extraction efficiency, with yields reaching 14.11% ± 1.23% (DW)[69]. Fractionation is commonly performed using Sephadex column chromatography, DEAE-52, and AB-8, enabling efficient separation, which lays a foundation for structural elucidation and activity studies.

Analytical technology platform for bioactive constituents

Characterization of the complex bioactive constituents in *Nitraria* highly depends on modern hyphenated chromatographic mass spectrometry and spectroscopic techniques, with an integrated system established from high-throughput screening to precise structural identification. UPLC-HRMS is the core technique for rapid profiling and quantification of constituents. Coupling with Q-TOF or Orbitrap enables high-throughput identification, relative quantification, and preliminary structural elucidation of trace components in complex extracts.^{1}H-NMR,^{13}C-NMR, HSQC, and HMBC represent standard methods for identifying planar structures and absolute configurations, and are indispensable for clarifying the fine structures of characteristic bioactive constituents in *Nitraria*. Synergistic application of modern separation and analytical techniques is crucial for expanding the chemical database of *Nitraria* and dissecting its bioactive constituent structures.

Notable imbalances exist in *Nitraria* phytochemical studies: anthocyanins and flavonoids' structural identification is relatively comprehensive, but the complete biosynthetic pathways of alkaloids and the fine structures of polysaccharides remain unclear. Most constituent distribution studies focus on fruit and leaves, while bioactive constituents in other tissues lack systematic exploration. Structure–activity relationship studies are mostly limited to *in vitro* experiments, lacking systematic validation of structural stability, *in vivo* metabolic transformation products, and their activities, which restricts their application and translation in functional food and pharmaceutical fields.

Pharmacological activities and potential mechanisms

Antioxidant and anti-inflammatory activities

The antioxidant activity of *Nitraria* species is predominantly concentrated in polar fractions enriched with polyphenols, flavonoids, and polysaccharides. In *in vitro* assays, these crude extracts possess strong scavenging effects against DPPH· and ABTS radicals, and can effectively reduce ferric ions and inhibit lipid peroxidation, with clear dose–effect relationships between activity and constituent content. The aqueous extract of *N. schoberi* fruit shows a total antioxidant capacity of 49.65 ± 2.33 μg ascorbic acid equivalent (AAE)/mg extract[21]. The ethanol extract of *N. schoberi* yields a total antioxidant status (TAS) value as high as 45.82 mg GAE/g DW[16]. Ethyl acetate extracts of *N. retusa* leaves display an IC_{50} as low as 16.40 ± 4.40 μg/mL for DPPH· radical scavenging[55]. The chloroform extract of *N. schoberi* leaves affords the strongest protection against hydroxyl radical-induced DNA damage and the highest antioxidant potency (0.95 mmol·L^{-1} Trolox equivalent)[70]. Online HPLC-DPPH· screening confirms that C3G acts as the core antioxidant constituent[4].

The antioxidant action of *Nitraria* depends on both direct chemical quenching and long-term modulation by activating the

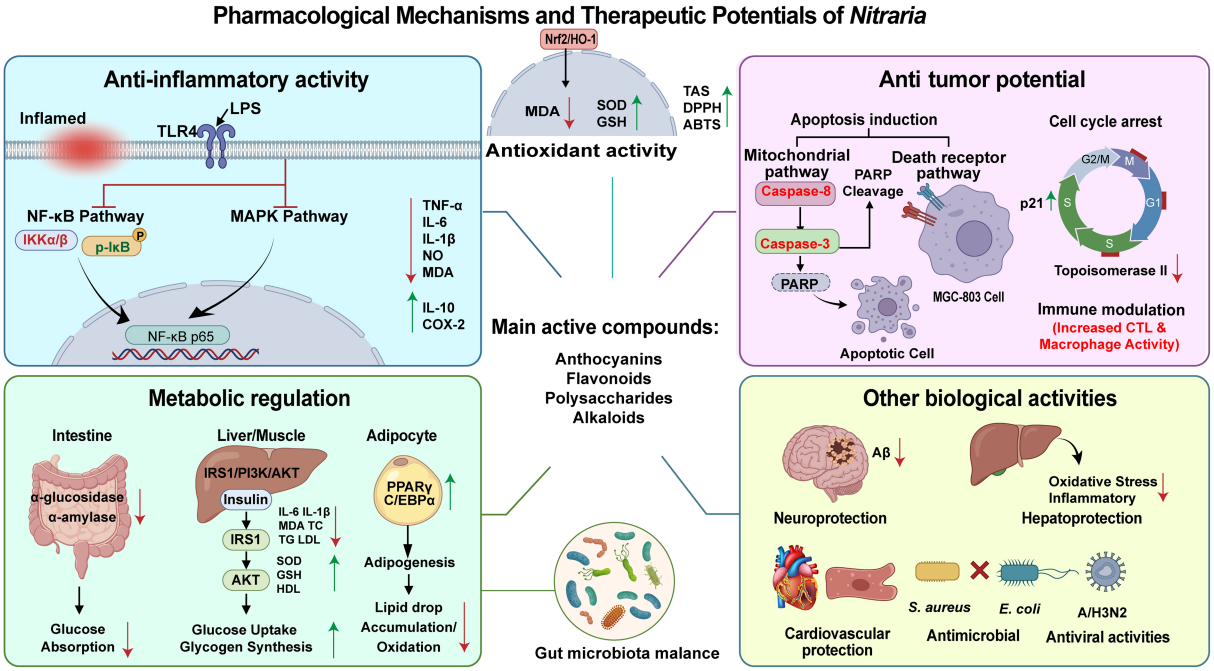

Fig. 3 Multitarget pharmacological regulatory mechanisms of bioactive constituents in *Nitraria*. This figure depicts the multi-target pharmacological pathways of key bioactive components from *Nitraria*, including anthocyanins and flavonoids, covering their mechanisms of anti-inflammation, antioxidant activity, anti-tumor effects, regulation of glucose and lipid metabolism, and antimicrobial and antiviral activities.

endogenous cellular antioxidant defense system (Fig. 3). In animal model experiments, *N. tangutorum* anthocyanin crude extracts significantly increase total superoxide dismutase (T-SOD) and glutathione (GSH) levels in hyperlipidemic rats[71]. Its chloroform extract activates the intracellular nuclear factor erythroid 2-related factor 2 (Nrf2)/Heme oxygenase-1 (HO-1) signaling axis, a key regulator of antioxidant enzyme expression[48]. The ethyl acetate fraction suppresses oxidative stress injury and protects renal function by scavenging radicals and restoring GSH, melatonin (MT), and other antioxidant molecules[56,72]. Fruit polysaccharide NTP markedly reduces malondialdehyde (MDA) elevation and protects lung tissue from lipopolysaccharide (LPS)-induced oxidative damage[13].

The anti-inflammatory activity of *Nitraria* is mediated by multi-targeted inhibition of inflammatory signaling pathways (Fig. 3). Crude extracts (chloroform fraction[48], anthocyanins[1], and polysaccharides[20]) effectively suppress excessive nitric oxide (NO) release in LPS-stimulated RAW 264.7 cells, downregulate pro-inflammatory cytokines including TNF-α, IL-1β, and IL-6, and upregulate the anti-inflammatory cytokine IL-10 (Fig. 3). The central mechanism involves blockade of aberrant activation of nuclear factor-κB (NF-κB) and mitogen-activated protein kinase (MAPK) cascades, thereby alleviating inflammation-mediated tissue injury[1,48]. In animal model experiments, polysaccharide NTP from *N. tangutorum* fruit reverses LPS-induced upregulation of toll-like receptor 4 (TLR4), phosphorylated inhibitor of nuclear factor kappa-B kinase α/β (IKKα/β) and phosphorylated NF-κB, and restores p-IκBα expression, conferring anti-inflammatory protection in mouse lung tissue via inhibition of the TLR4/IKK/NF-κB pathway[13]. High-dose *N. tangutorum* fruit extract (NTFE, 20.00 g/kg) promotes biosynthesis of antimicrobial non-ribosomal peptides in Hu sheep and downregulates LPS-associated inflammatory pathways[73]. Polysaccharide NRLP from *N. schoberi* leaves relieves carrageenan-induced mouse paw edema by inhibiting histamine release, reducing prostaglandin biosynthesis, and attenuating cyclooxygenase-2 (COX-2) upregulation[20]. Aqueous and methanol extracts of *N. schoberi* fruit also clearly inhibit carrageenan-induced rat paw edema[18].

Studies on antioxidant and anti-inflammatory effects of *Nitraria* are mainly based on crude extracts, with sufficient evidence from *in vitro* assays and animal models. Only a few bioactivities have been traced to definite monomers, including C3G, glucosylsorbitol, and isoimperatorin A. Flavonoids and polysaccharides exert anti-inflammatory effects via targeted inhibition of the NF-κB/MAPK signaling pathway. Currently, *in vivo* verification of the anti-inflammatory activity of single isolated monomers remains absent, and relevant pharmacological evidence is mostly limited to crude extracts. There is an obvious translational gap between identified active constituents and clinical application.

Antitumor potential

The antitumor activity of *Nitraria* is characterized by selective cytotoxicity, anti-proliferation, and multi-pathway induction of tumor cell apoptosis. Its active components exert targeted inhibition on various tumor cell lines (Fig. 3). The ethyl acetate extract from *N. retusa* leaves exhibits excellent anti-genotoxic potential against K562 cells[51] and shows potent anti-proliferative effects on human colorectal Caco2 cells[55]. Additionally, the ethanol extract of *N. sibirica* inhibits A549, MCF7, and cervical HeLa cancer cells[67], polysaccharide NSP-3 suppresses MCF7 cells[14], and the n-hexane subfraction of *N. schoberi* acts strongly against MCF7 and HepG-2 cells[23]. Monomeric compounds isorhamnetin and isorhamnetin-3-*O*-rutinoside isolated from *N. retusa* exhibited stronger anti-proliferative activity against Caco2 cells than quercetin. Acylation further potentiated the anti-proliferative effect of isorhamnetin-3-*O*-glucoside[8].

Apoptosis is a key mechanism restraining tumor cell survival, proliferation, and invasion. Bioactive constituents from *Nitraria* trigger targeted regulation by activating caspase cascades and PARP

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cleavage (Fig. 3). *N. schoberi* leaf crude extract induces apoptosis in K562 cells via the mitochondrial apoptotic pathway, characterized by PARP cleavage and activation of caspase-3 and caspase-8[74]. Flavonoids in its leaf methanol crude extract induce apoptosis in TK6 cells through caspase-3 activation, and the extract (800.00 μg/mL) induces 11% apoptosis in 4T1 cells[75]. The ethyl acetate fraction and its major component, isorhamnetin-3-*O*-robinobioside, exert significant anti-proliferative effects on human TK6 lymphoblasts via DNA fragmentation, PARP cleavage, and enhanced caspase-3 activity[76]. *Nitraria* aqueous decoction inhibits MGC-803 cells, inducing nuclear pyknosis and apoptotic body formation[77]. Additionally, the chloroform extract (the major compounds are β-sitosterol and palmitic acid), ethyl acetate, and methanol extracts of *N. schoberi* leaves sensitize glioblastoma (GBM) to temozolomide-induced apoptosis, enhancing chemotherapy[19, 53].

Certain characteristic constituents of *Nitraria* block tumor cell proliferation via cell cycle arrest. Monomer Tangutorine from *N. tangutorum* upregulates p21 expression, inhibits topoisomerase II activity, disrupts DNA replication, and arrests human colon HT-29 cancer cells at specific phases[78]. Regarding tumor invasion and metastasis, chloroform and methanol extracts of *N. schoberi* leaves at 100 μg/mL reduce invasion of U87 cells by 51.70% and 74.50%, respectively[53].

Nitraria also exerts indirect antitumor effects by regulating host immune function. Co-administration of Nitraria flavone and 5-fluorouracil achieves tumor inhibition rates of 50.73% (Hepatoma) and 47.22% (U14 cervical cancer) via immune regulation, while elevating serum hemolysin levels and phagocytic indices[79]. The methanol extract and chloroform extract inhibit tumor volume in tumor-bearing mice by 95.19% and 84.52%, markedly restore splenic lymphocyte proliferation, enhance CTL activity to 54.64% and 46.98%, and boost host macrophage lysosomal activity by 255.37% and 145.96%[80,81]. In animal model experiments, the methanol extract of *N. schoberi* leaves inhibits 4T1 tumors in mice by 56.25%, and Nr-MeOH at 100.00 mg/kg increases macrophage lysosomal activity by 223.07% in tumor-bearing mice[75]. *Nitraria* thus suppresses tumors by remodeling host immune surveillance.

There are significant hierarchical differences in antitumor evidence of *Nitraria* species. Crude extracts present anti-proliferative and pro-apoptotic effects in various tumor cell lines and animal models. A few monomers, including isorhamnetin-3-*O*-robinobioside and nitrarine, exert bioactivities via the caspase pathway, cell cycle arrest, and immunomodulation. Nevertheless, all relevant antitumor studies are restricted to *in vitro* cellular and animal experiments, lacking monomer target verification, structure–activity relationship analysis, and clinical data, leading to a prominent translational gap.

Intervention in metabolic diseases

Nitraria exerts multi-target, multi-pathway regulatory effects on glycolipid metabolic disorders, representing promising natural agents for metabolic diseases (Fig. 3). Hypoglycemic activity is achieved mainly through three routes: inhibition of carbohydrate-digesting enzymes, improvement of insulin sensitivity, and protection of pancreatic β-cells. Polysaccharides NTB-Z, NTB-C[11], and NTB-40[11] from *N. tangutorum*, and NRK-C from *N. roborowskii*[12] all potently inhibit sucrase and maltase.

For improving insulin sensitivity and preserving β-cells, active constituents from *Nitraria* maintain glucose homeostasis chiefly via regulation of the insulin receptor substrate 1 (IRS1)/Phosphatidylinositol 3-kinase (PI3K)/Protein kinase B (AKT) pathway. In animal model experiments, NTB-40 markedly ameliorates high-fat diet–streptozotocin (STZ)-induced diabetic mice by stabilizing glycolipid metabolism, mitigating inflammation and oxidative stress mediated by IL-6 and IL-1β, modulating IRS1/PI3K/AKT signaling, reducing hepatic gluconeogenesis, promoting glycogen synthesis, and peripheral glucose uptake, thereby alleviating insulin resistance (IR)[24]. Currently, abundant studies have focused on the lipid-lowering activities of monomers isolated from *Nitraria*. Multiple *in vitro* and animal model investigations have explored their lipid-regulating mechanisms and potency. Furthermore, depside compounds and cyclo (tyr-tyr) from *N. tangutorum* fruit effectively improve insulin resistance[10]. Benzyl-*O*-β-d-glucopyranoside and (3S,5R,6R,7E,9S)-megastigmane-7-ene-3-hydroxy-5,6-epoxy-9-*O*-β-d-glucopyranoside from *N. sibirica* leaves inhibit protein tyrosine phosphatase 1B (PTP1B), a negative regulator of insulin signaling[57]. However, research on lipid-lowering constituents of *Nitraria* remains confined to *in vitro* cell experiments and animal model validations, with no successful translation into clinical application so far.

Hypolipidemic and anti-obesity activities are achieved mainly by regulating lipid metabolic pathways, suppressing adipogenesis, promoting fatty acid oxidation, and reshaping gut microbiota to improve dyslipidemia. *N. schoberi* ethanol extract (NRE)[82], fruit polysaccharide NRFP[15], *N. sibirica* leaves ethanol extract (NSL-EPE)[83], and *N. roborowskii* fruit extract[25] significantly reduce TG and LDL-C in model animals. *N. tangutorum* fruit anthocyanins ameliorate non-alcoholic fatty liver disease by attenuating hepatic oxidative stress (lowering MDA, restoring SOD, and elevating GSH-Px) and regulating lipid metabolism (reducing serum total protein [ST], alanine transaminase [ALT], total cholesterol [TC], triglyceride [TG], and low-density lipoprotein [LDL], and elevating high-density lipoprotein [HDL])[83]. Lipidomic analysis confirms that *N. roborowskii* fruit extract modulates glycerophospholipid and glycerolipid metabolism to lower lipids[25]. NRE[82] reduces lipid droplet formation and intracellular TG deposition, suppressing differentiation of 3T3-L1 preadipocytes. Monomeric compounds luteolin-7-*O*-glucoside, isorhamnetin-3-*O*-rutinoside, and isorhamnetin also possess the same efficacy[52]. Moreover, *Nitraria* downregulates core adipogenic transcription factors including PPARγ and C/EBPα in 3T3-L1 cells, reducing lipid accumulation, while upregulating lipolytic and fatty acid oxidation genes such as ATGL and HADH to maintain lipid homeostasis[82,84].

Nitraria extracts also remodel gut microbiota to regulate host energy metabolism and physiological homeostasis (Fig. 3). FNT increases the relative abundance of beneficial rumen bacteria, including *Lachnospira*, *Rhodocyclaceae*, and candidate *Arthrobacter* in Hu sheep, improving ruminal microecological balance[85]. NTFE elevates the ruminal acetate/propionate ratio, promotes enrichment of fiber-degrading bacteria, inhibits methanogenic archaea, downregulates LPS biosynthesis, and alleviates inflammation-associated metabolic disorders[73]. Notably, preliminary human clinical trials (RCT, randomized controlled trial) confirm that continuous administration of NRE is safe in overweight/obese subjects, effectively lowering serum TG and improving waist–hip ratio, providing early clinical evidence for its application[26].

Research on glycolipid regulation has established relatively sufficient evidence. Polysaccharide and alkaloid extracts relieve insulin resistance and regulate lipid metabolism in animal models. Cyclic dipeptides and lignan glycosides can regulate IRS1/PI3K/AKT and PTP1B pathways. Only one small-sample RCT has verified the lipid-regulating effect of relevant extracts so far. Studies on monomer

lipid-lowering effects remain restricted to *in vitro* tests and animal experiments. Unclear long-term safety, dose-response patterns, and applicable groups impede further clinical transformation.

Other biological activities

Owing to its structurally diverse bioactive constituents, *Nitraria* exhibits multi-target, multi-functional biological profiles (Fig. 3). Its potential in neuroprotection, cardiovascular protection, hepatoprotection, antimicrobial, and antiviral effects has been increasingly validated. For neuroprotection, constituents reduce Aβ deposition and alleviate cerebral ischemia-reperfusion injury, offering new strategies for neurodegenerative and cerebrovascular diseases[4,86,87]. For cardiovascular protection, extracts counteract doxorubicin-induced cardiomyocyte damage, improve cardiac function, and exert mild hypotensive effects[17,45,66], supporting adjunctive therapy for cardiovascular disorders. Hepatoprotective activity is achieved by suppressing hepatic oxidative stress and inflammation, mitigating chemical and metabolic liver injury[72]. Antimicrobial activity is observed against pathogenic bacteria including *Escherichia coli*, as well as fungi such as *Aspergillus niger*[22,23,55]. Antiviral potential has been confirmed against influenza A/H3N2 virus[88].

In conclusion, pharmacological studies on *Nitraria* present distinct evidence stratification. Antioxidant and anti-inflammatory research is mostly based on crude extracts with few valid monomer data. Antitumor monomers have definite effects without systematic *in vitro* and *in vivo* validation. Glycolipid modulation has been verified via extracts, monomers, and preliminary human trials. Most biological effects are derived from integrated functions of crude extracts. Insufficient research on monomer targets, structure–activity rules, synergistic effects, and unified evaluation standards form a persistent barrier between basic research and clinical practice. Further studies shall confirm core active components, explore their action mechanisms, complete pharmacological verification and safety assessment, and accelerate targeted exploitation of the medicinal potentials of *Nitraria*.

Molecular regulatory mechanisms from stress perception to secondary metabolism

Synergistic molecular regulation of multiple pathways in stress resistance

The adaptation of *Nitraria* species to extreme habitats depends on the synergistic effect of three core pathways: ion homeostasis, osmotic adjustment, and oxidative stress defense (Fig. 4). The regulatory mechanisms have been elucidated from physiological phenotypes to functional gene validation, with key gene functions confirmed by heterologous transgenic experiments, providing critical evidence for interpreting halophyte stress-resistant molecular mechanisms.

Ion homeostasis and compartmentalization are the core of *Nitraria* salt tolerance. The core regulatory mechanism involves the coordinated action of ion transporters on the plasma membrane and tonoplast to extrude and compartmentalize Na^+, maintain intracellular K^+ homeostasis, and keep the K^+/Na^+ ratio within a suitable range (the K^+/Na^+ ratio remains above 1.5 under salt stress)[89]. *SOS1* (Na^+/H^+ antiporter) and *NHX1* are the core proteins for Na^+ transport: the former mediates Na^+ efflux, and the latter enables Na^+ sequestration into vacuoles. The energy for this process is directly driven by the transmembrane proton gradient established by tonoplast H^+-ATPase and H^+-PPase, which upregulated the expression of *NsVHA*, *NsVP1*, and *NsNHX1* genes[35]. *NtSOS2* can restore the salt-sensitive phenotype of the *Arabidopsis SOS2-1* mutant, increasing the survival rate to 62.38% under 150 mmol·L^{-1} NaCl stress,

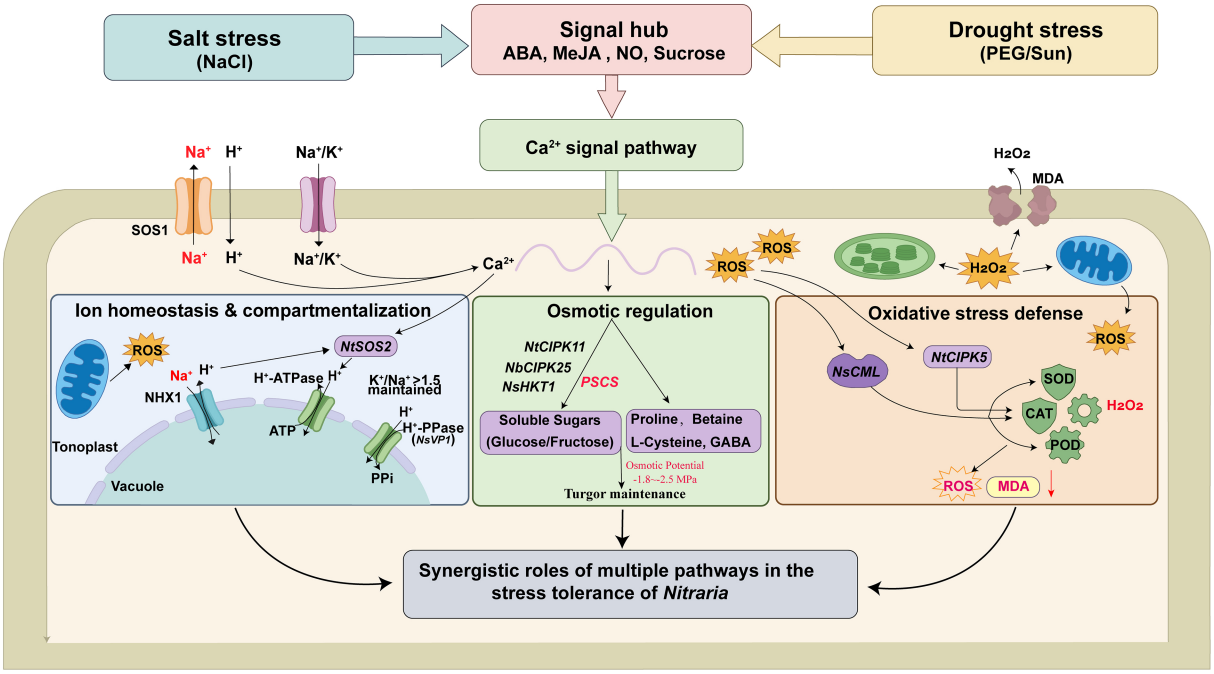

Fig. 4 Synergistic multi-pathway defense mechanisms of *Nitraria* under salt and drought stress. This figure dissects the molecular mechanisms by which *Nitraria* copes with salt and drought stresses via synergistic interactions among three major pathways: ion homeostasis, osmotic adjustment, and antioxidative defense.

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confirming the central role of the SOS signaling pathway[90]. Furthermore, *NsSRO1a* enhances the drought resistance of plants by regulating ROS metabolism under drought stress[91].

Osmotic adjustment relies on stress-induced accumulation of osmolytes. Under drought and salt stress, *Nitraria* rapidly accumulates soluble sugars, proline, and glycine betaine, lowering cellular osmotic potential to sustain turgor and the structural stability of biological macromolecules. Under 20% PEG stress, proline and soluble sugars in leaves of *N. sibirica* increase 4.70- and 2.90-fold. This process is regulated by genes including *NtCIPK11*[92] and *NsHKT1*[93], which promote osmolyte synthesis by activating the expression of key enzymes in proline biosynthesis (*P5CS*) and soluble sugar metabolism[38]. Root metabolites (e.g., L-cysteine, 4-aminobutyric acid) assist osmotic balance by modulating carbon-nitrogen metabolism[93].

Oxidative stress defense eliminates stress-induced ROS via activating the antioxidant enzyme system and non-enzymatic antioxidant synthesis, avoiding membrane lipid peroxidation (Fig. 4). Under 200 mmol·L^{-1} NaCl stress, *N. tangutorum* upregulates its antioxidant defense, with SOD and CAT activities significantly elevated, while exogenous H_2O_2 pretreatment further enhances antioxidant capacity and reduces oxidative stress[37]. *NsCML* genes are key regulators, enhancing antioxidant enzyme activity through calcium signaling to achieve efficient ROS scavenging[30].

Plant hormones and signaling molecules act as a central hub integrating the above three pathways (Fig. 4). Exogenous application of ABA (15 μM), methyl jasmonate (MeJA) (50 μM), and sodium nitroprusside (SNP) (50 μM) increases the survival rate of *Nitraria* under salt and alkali stress by 30%–50%[42,47]. Under drought stress, sucrose (40.00 g/L) promotes adventitious root formation in *N. tangutorum* by coordinately regulating hormone crosstalk and activating the H_2O_2 signaling pathway[94]. Current molecular studies have limitations: The focus is on single-gene functional validation with insufficient dissection of synergistic regulatory networks and pathway crosstalk. Tissue-specific expression patterns have not been systematically clarified, and molecular regulatory mechanisms under extreme combined stresses are scarce. In addition, fine transcriptional regulatory mechanisms such as promoter regulatory elements and transcription factor characteristics of stress-resistant genes remain to be deeply elucidated.

Molecular regulatory network of secondary metabolite biosynthesis

The biosynthesis and regulation of secondary metabolites in *Nitraria*, including anthocyanins, flavonoids, alkaloids, and polysaccharides, are co-mediated by nuclear gene transcriptional regulation, environmental signal induction, and plant hormone signaling. Among them, the flavonoid and anthocyanin pathways are relatively well-studied, while the alkaloid and polysaccharide biosynthesis pathways remain preliminary, representing the core bottleneck in current molecular regulation research of *Nitraria*.

Precise transcriptional regulation of flavonoid biosynthesis

Anthocyanin and flavonoid biosynthesis in *Nitraria* fruit follows the classical phenylpropanoid-flavonoid pathway (Fig. 5). Its molecular regulation core relies on the spatiotemporal control of structural genes and upstream activation by transcription factors, which jointly determine the directional accumulation and fruit coloration. Phenylalanine ammonia-lyase (*PAL*), chalcone synthase (*CHS*),

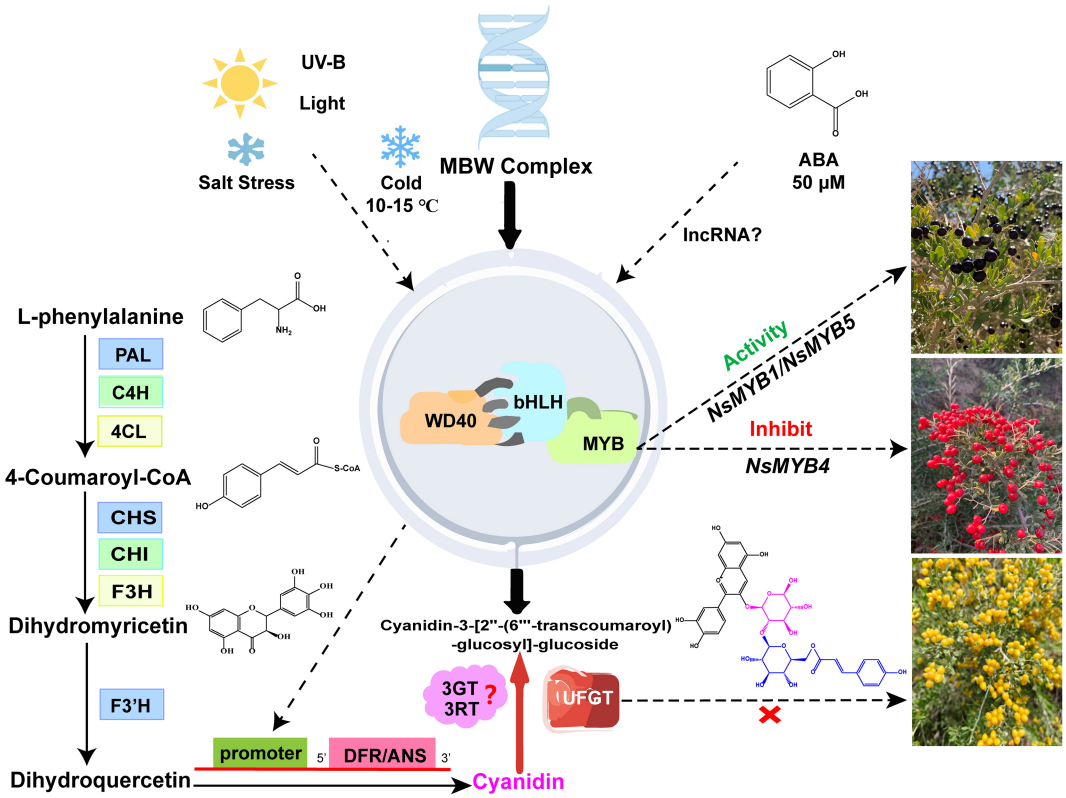

Fig. 5 Anthocyanin biosynthetic pathway and molecular regulatory network in *Nitraria* fruit. This figure defines the core biosynthetic pathway of anthocyanins in *Nitraria* fruits starting from L-phenylalanine and reveals the molecular basis underlying the formation of distinct fruit phenotypes modulated by environmental and endogenous signaling cues.

anthocyanidin synthase (*ANS*), and UDP-glucose: flavonoid 3-*O*-glucosyltransferase (*UFGT*) are core structural genes, with *UFGT* being the key rate-limiting enzyme for anthocyanin biosynthesis in *N. tangutorum* fruit[9,95]. UFGT enzyme activity in red fruit of *N. tangutorum* is 5-fold higher than in yellow mutants, and UFGT downregulation is associated with the loss of anthocyanin glycosylation in yellow fruit[95].

R2R3-MYB transcription factors are core upstream regulators, forming MBW complexes with bHLH and WD40 proteins to bind structural gene promoters and activate transcription (Fig. 5). *NsMYB1*[5] and *NsMYB5*[96] of *N. sibirica* are functional activators: their heterologous expression in tobacco increases petal anthocyanin content by 6.9- and 5.4-fold, respectively, and significantly upregulates structural genes, including *PAL*, *CHS*, *DFR*, and *UFGT*. In contrast, the MYB repressor *NsMYB4* inhibits tobacco anthocyanin accumulation. Furthermore, the regulatory network and hierarchical feedback mechanisms among MYB activators and repressors, their target genes, and bHLH transcription factors remain unclear.

Environmental and hormonal signals regulate transcription factors and structural genes to induce secondary metabolite accumulation, representing an important molecular basis for coupling stress resistance and secondary metabolism in *Nitraria* (Fig. 5). High altitude, low temperature, and strong UV-B significantly increased *N. tangutorum* fruit anthocyanin content by inducing MYB and bHLH expression and activating downstream structural genes[9]. Exogenous ABA and SNP promoted the accumulation of flavonoids and anthocyanins in *N. tangutorum* seedlings under alkali stress[42]. These signals positively regulate flavonoid biosynthesis by inducing MYB expression and promoting MBW, reflecting the synergistic evolutionary strategy of *Nitraria* for stress defense and bioactive component accumulation in extreme environments.

Research status of alkaloids, polysaccharides, and epigenetics

Studies on the molecules of secondary metabolism in *Nitraria* exhibit a prominent research imbalance. Flavonoid and anthocyanin biosynthetic pathways have been systematically studied, while alkaloid and polysaccharide biosynthesis remain hypothetical. Meanwhile, protein post-translational modifications, non-coding RNA-mediated regulation, and hierarchical feedback networks remain poorly elucidated, and the mechanisms of environmental stress-directed metabolite accumulation and interspecific differences in metabolic regulation need further exploration.

β-carboline and quinazoline alkaloids are characteristic bioactive constituents of *Nitraria*. The biosynthetic pathways and regulatory mechanisms remain unclear. Preliminary hypotheses have only been proposed via phytochemical analysis and isotopic tracing, indicating their skeletons are potentially formed by enzymatic or non-enzymatic condensation and cyclization of precursor skeletons with tryptamine to generate the β-carboline parent nucleus[97]. Novel alkaloids LI-III[97] have revised traditional biosynthetic theories, while related key enzymes and genes lack functional verification. *Nitraria* polysaccharides are homogeneous heteropolysaccharides, whose biosynthesis relies on the synergistic action of glycosyltransferases, polysaccharide polymerases, and modifying enzymes. Current studies merely confirm their monosaccharide components and glycosidic linkages, and the core enzymes, transcription factors, and signaling pathways governing polysaccharide synthesis remain uncharacterized.

Epigenetic modifications such as DNA methylation, histone modification, and non-coding RNAs regulate gene expression, plant environmental adaptation, and metabolic plasticity. Epigenetic research on *Nitraria* remains preliminary without systematic regulatory mechanisms. Salt stress reduces histone H3 lysine 9 dimethylation (H3K9me2) levels by 38% in *N. sibirica,* which was presumed to regulate salt-responsive genes[98], while its target genes and regulatory pathways are unconfirmed. The stress response patterns and major regulatory patterns of other core epigenetic modifications remain undefined. In terms of non-coding RNA regulation, only a small number of long non-coding RNAs (lncRNAs) and microRNAs (miRNAs) have been screened, lacking functional verification. Their targets, molecular mechanisms, and regulatory networks related to stress signaling and secondary metabolism also remain unclear.

Correlation mechanism between stress response and bioactive substance accumulation

Stress adaptation and secondary metabolism in *Nitraria* are tightly interconnected. Salinity, drought, and intense ultraviolet radiation can activate stress-related genes such as *SOS*, *NHX*, and *P5CS,* which maintain ion homeostasis and osmotic adjustment to improve stress tolerance. These stresses also stimulate signals such as ABA and H_2O_2 to regulate transcription factors, further activating biosynthetic pathways of secondary metabolites. Harsh environmental conditions serve not only as survival pressure but also as regulatory triggers for secondary metabolism, coordinating stress defense and metabolic processes to promote bioactive compound accumulation. This synergistic mode enables *Nitraria* to adapt to extreme habitats and endows the plants with strong stress resistance and high medicinal potential. Overall, stress responses are closely coupled with metabolite synthesis, and stress signals function as key inducers driving secondary metabolism.

Discussion

Nitraria is a distinctive medicinal halophyte with great research value in extreme plateau habitats, and its research direction is highly consistent with the scope of medicinal plant biology journals. *Nitraria* regulates physiological metabolism via endogenous hormones, resists salt and drought stress via stress-tolerance genes, and modulates secondary metabolism via MYB/bHLH transcription factors, accumulating bioactive medicinal components. These compounds are not only the basis for its adaptation to extreme environments but also the core material basis for exerting medicinal effects.

Current research has elucidated anthocyanin biosynthetic pathways and core genes, and verified *in vitro* pharmacological activities of flavonoids. Nevertheless, notable research gaps remain. The biosynthesis and regulatory genes of alkaloids and polysaccharides lack systematic analysis, while epigenetic regulatory mechanisms are limited. The correlation between stress signals and the targeted accumulation of medicinal components also remains poorly defined. Most pharmacological investigations adopt crude extracts, with scarce studies on compound targets and structure–activity relationships, hindering further exploitation of *Nitraria* resources. Further exploration of the association between stress adaptation and active ingredient synthesis, complementation of molecular regulatory mechanisms, and excavation of the medicinal potential of characteristic metabolites will enrich metabolic regulation theories of plateau medicinal plants and provide a theoretical basis for germplasm utilization and natural drug development.

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Future research directions and perspectives

Given the limitations of existing research and the high resource value of *Nitraria*, future research should focus on five priority areas: First, relying on high-throughput sequencing technology to complete the chromosome-level genome assembly and pan-genome construction of *Nitraria* species endemic to the Qinghai-Xizang Plateau, clarifying the genetic basis of stress tolerance and metabolism. Second, clarifying the fine structures of alkaloids and polysaccharides, and elucidating the structure–activity relationship through *in vitro* synthesis and modification, while tracking their *in vivo* metabolic rules by combining metabolomics and pharmacokinetics. Third, conducting large-scale and long-term cohort clinical trials to verify the efficacy of *Nitraria* extracts in the treatment of metabolic disorders and inflammatory diseases, and improving safety evaluation to support the application of functional foods and drugs. Fourth, cloning and verifying the key enzymes involved in the synthesis of alkaloids and polysaccharides, deciphering the synergistic regulatory mechanism between epigenetic modification and transcription factors, and clarifying the molecular connection among stress resistance, epigenetics, transcription, and metabolism. Fifth, optimizing green extraction processes, developing formulation technologies including microcapsules and nanocarriers, and designing gut microbiota-regulating composite functional foods to promote the efficient and sustainable industrial utilization of *Nitraria* resources.

Conclusions

As representative halophytic shrubs dominating the extreme habitats of the Qinghai-Xizang Plateau, *Nitraria* presents a tight coupling between ecological adaptability and resource value. To address the four core scientific questions proposed in the introduction, this review systematically summarizes the current research progress: Regarding the synthesis of active components, the key rate-limiting enzyme (UFGT) and core pathways in anthocyanin biosynthesis have been elucidated, whereas the complete synthetic pathways of alkaloids and polysaccharides still need further investigation. In terms of regulatory mechanisms, the MYB transcription factor-mediated regulatory network for flavonoids has been initially established, yet the epigenetic regulatory system still needs improvement. Regarding the association between stress and metabolism, it has been confirmed that adverse environmental signals can synchronously regulate the activation of stress response and secondary metabolism through ABA signaling. Currently, research on structure–activity relationships is still based on crude extracts, and the molecular mechanism underlying the correlation between the structure of monomeric compounds and their pharmacological effects remains to be further explored.

The stress-responsive gene pool at the genomic level and the dynamic response network at the transcriptomic level collectively drive the structural specialization of secondary metabolites, among which highly acylated anthocyanins and structurally novel β-carboline alkaloids are typical characteristic components. These metabolites endow *Nitraria* with diverse pharmacological activities, making it a high-quality resource for functional foods and pharmaceutical intermediates. However, current research still has limitations, including incomplete genome sequencing coverage, insufficient characterization of chemical structures, and simplistic pharmacological evaluation models. Future research should focus on integrating multi-omics technologies, further exploring molecular regulatory mechanisms, and promoting the efficient transformation of basic research into industrial applications, thereby providing theoretical and technical support for the sustainable utilization of plant resources in extreme environments.

Author contributions

The authors confirm their contributions to the paper as follows: study conception and design, methodology, visualization: Chen H, Bao X, Zong Y; draft manuscript preparation: Chen H, Chen Y, Bao X, Zong Y; writing – review and editing: Luo Q, Bao X, Zong Y; supervision, project administration: Bao X, Zong Y; funding acquisition: Bao X. All authors reviewed the results and approved the final version of the manuscript.

Data availability

Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

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Conflict of interest

The authors declare that they have no conflict of interest.

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References

[1] Sang J, Zhang Y, Sang J, Li CQ. 2019. Anthocyanins from *Nitraria tangutorun*: qualitative and quantitative analyses, antioxidant and anti-inflammatory activities and their stabilities as affected by some phenolic acids. *Journal of Food Measurement and Characterization* 13:421–430

[2] Li X, Liu H, Li C, Li Y. 2024. A systematic review on the morphology structure, propagation characteristics, resistance physiology and exploitation and utilization of *Nitraria tangutorum* Bobrov. *PeerJ* 12:e17830

[3] Ren S, Lv G, Teng D. 2021. Anatomical structure of *Nitraria* spp. leaves from different habitats in Southern Xinjiang, China. *Human and Ecological Risk Assessment: an International Journal* 27:790–803

[4] Chen S, Zhou H, Zhang G, Dong Q, Wang Z, et al. 2021. Characterization, antioxidant, and neuroprotective effects of anthocyanins from *Nitraria tangutorum* Bobr. fruit. *Food Chemistry* 353:129435

[5] Bao X, Zong Y, Hu N, Li S, Liu B, et al. 2022. Functional R2R3-MYB transcription factor *NsMYB1*, regulating anthocyanin biosynthesis, was relative to the fruit color differentiation in *Nitraria sibirica* Pall. *BMC Plant Biology* 22:186

[6] Ren L, Dong Q, Liu Z, Wang Y, Tan N, et al. 2024. Optimization of subcritical water extraction, UPLC-triple-TOF-MS/MS analysis, antioxidant and α-glucosidase inhibitory activities of anthocyanins from *Nitraria sibirica* Pall. fruits. *Food Chemistry* 23:101626

[7] Chang Y, Lv G, He X. 2024. Growth adaptation of *Nitraria sibirica* in drought: Hormone-mediated flavonoid accumulation, altered

metabolic pathways, and decreased network complexity. *Environmental and Experimental Botany* 221:105720

[8] Hadj Salem J, Chevalot I, Harscoat-Schiavo C, Paris C, Fick M, et al. 2011. Biological activities of flavonoids from *Nitraria retusa* (Forssk.) Asch. and their acylated derivatives. *Food Chemistry* 124:486−494

[9] Zhao Q, Zhang J, Li Y, Yang Z, Wang Q, et al. 2024. Integrated metabolomic and transcriptomic analysis of *Nitraria* berries indicate the role of flavonoids in adaptation to high altitude. *Metabolites* 14:591

[10] Yue H, Li J, Wu L, Wang F, Li Z, et al. 2025. Tentative characterization of three novel coumaroyl glucoside β-carboline alkaloids and discovery of hypoglycemic compounds from *Nitraria tangutorum* Bobr. fruit. *Food Chemistry* 481:143923

[11] Wu D, Jiang S, Wang G, Wang L, Wu L, et al. 2024. Characterization of alkaloids and phenolics in *Nitraria roborowskii* Kom. fruit by UHPLC-triple-TOF-MS/MS and its sucrase and maltase inhibitory effects. *Food Chemistry* 447:138743

[12] Jiang S, Chen C, Dong Q, Shao Y, Zhao X, et al. 2021. Alkaloids and phenolics identification in fruit of *Nitraria tangutorum* Bobr. by UPLC-Q-TOF-MS/MS and their a-glucosidase inhibitory effects *in vivo* and *in vitro*. *Food Chemistry* 364:130412

[13] Meng J, Deng K, Hu N, Wang H. 2021. *Nitraria tangutorum* Bobr.-derived polysaccharides protect against LPS-induced lung injury. *International Journal of Biological Macromolecules* 186:71−78

[14] Abuduwaili A, Mutailifu P, Nuerxiati R, Gao Y, Aisa HA, et al. 2021. Structure and biological activity of polysaccharides from *Nitraria sibirica* pall fruit. *Food Bioscience* 40:100903

[15] Rjeibi I, Feriani A, Hentati F, Hfaiedh N, Michaud P, et al. 2019. Structural characterization of water-soluble polysaccharides from *Nitraria retusa* fruits and their antioxidant and hypolipidemic activities. *International Journal of Biological Macromolecules* 129:422−432

[16] Zar Kalai F, Dakhlaoui S, Hammami M, Mkadmini K, Ksouri R, et al. 2022. Phenolic compounds and biological activities of different organs from aerial part of *Nitraria retusa* (Forssk.) Asch.: effects of solvents. *International Journal of Food Properties* 25:1524−1538

[17] Turghun C, Bakri M, Abdulla R, Ma Q, Aisa HA. 2020. Comprehensive characterisation of phenolics from *Nitraria sibirica* leaf extracts by UHPLC-quadrupole-orbitrap-MS and evaluation of their anti-hypertensive activity. *Journal of Ethnopharmacology* 261:113019

[18] Almasarwah SY, Oran SA, Darwish RM. 2023. Efficacy of *Nitraria retusa* L. fruits aqueous and methanol extracts as antioxidant and anti-inflammatory activities on carrageenan-induced paw edema in rats. *Tropical Journal of Natural Product Research* 7:2725−2729

[19] Boubaker J, Lahmar A, Salek A, Kriffa M, Chekir-Ghedira L. 2025. Cytotoxic effect of antioxidant products from *Nitraria retusa* leaves in combination with temozolomide on glioblastoma cell growth. *Research Square* Preprint

[20] Rjeibi I, Hentati F, Feriani A, Hfaiedh N, Delattre C, et al. 2019. Novel antioxidant, anti-α-amylase, anti-inflammatory and antinociceptive water-soluble polysaccharides from the aerial part of *Nitraria retusa*. *Foods* 9:28

[21] Mariem C, Sameh M, Nadhem S, Soumaya Z, Najiba Z, et al. 2014. Antioxidant and antimicrobial properties of the extracts from *Nitraria retusa* fruits and their applications to meat product preservation. *Industrial Crops and Products* 55:295−303

[22] Chen GL, Qi J, Zhan G, Jun R, Ren L. 2015. Antioxidant and antimicrobial activities of extracts from fruits of *Nitraria sibirica* Pall. *in vitro*. *Acta Horticulturae* 1106:137−142

[23] Mohamed AA, Ali SI, Darwesh OM, El-Hallouty SM, Sameeh MY. 2015. Chemical compositions, potential cytotoxic and antimicrobial activities of *Nitraria retusa* methanolic extract sub-fractions. *International Journal of Toxicology and Pharmacology Research* 7:204−212

[24] Jiang S, Wang L, Jia W, Wu D, Wu L, et al. 2023. Hypoglycemic effect of *Nitraria tangutorum* fruit by inhibiting glycosidase and regulating IRS1/PI3K/AKT signalling pathway and its active ingredient identification by UPLC-MS. *Food & Function* 14:7869−7881

[25] Jia QQ, Yang ZF, Wang Q, Zhao Q, Jia YJ, et al. 2023. Chemical profiling of *Nitraria roborowskii* Kom. by UPLC-Q-Orbitrap-MS and their hypolipidemic effects *in vivo*. *Chemistry & Biodiversity* 20:e202300683

[26] Laouani A, Nasrallah H, Sassi A, Ferdousi F, Kalai FZ, et al. 2024. Antiobesity and hypolipidemic potential of *Nitraria retusa* extract in overweight/obese women: a randomized, double-blind, placebo-controlled pilot study. *Nutrients* 16:317

[27] Dong Q, Hu N, Suo Y, Chi X, Wang H. 2019. The complete chloroplast genome sequences of two species from Nitraria. *Mitochondrial DNA Part B* 4:1229−1230

[28] Song F, Feng Y. 2021. The complete chloroplast genome of the desert shrub *Nitraria sphaerocarpa* (Nitrariaceae) and phylogenetic analysis. *Mitochondrial DNA Part B* 6:1901−1903

[29] Ma X, Ru D, Morales-Briones DF, Mei F, Wu J, et al. 2023. Genome sequence and salinity adaptation of the desert shrub *Nitraria sibirica* (Nitrariaceae, Sapindales). *DNA Research* 30:dsad011

[30] Wu X, Zhu J, Zhu L, Tang Y, Hao Z, et al. 2023. Genome-wide analyses of calmodulin and calmodulin-like proteins in the halophyte *Nitraria sibirica* reveal their involvement in response to salinity, drought and cold stress. *International Journal of Biological Macromolecules* 253:127442

[31] Wang J, Dang Z, Zhang H, Zheng L, Borjigin T, et al. 2016. Gene transcript profiles in the desert plant *Nitraria tangutorum* during fruit development and ripening. *Molecular Genetics and Genomics* 291:383−398

[32] Li Y, Wang S, Zhao Q, Wang Q, Yang Z, et al. 2025. Integrating metabolomics and transcriptomics comprehensively reveals the global metabolic differences in three species of *Nitraria* berries. *Scientific Reports* 15:15507

[33] Li H, Tang X, Yang X, Zhang H. 2021. Comprehensive transcriptome and metabolome profiling reveal metabolic mechanisms of *Nitraria sibirica* Pall. to salt stress. *Scientific Reports* 11:12878

[34] Tang X, Wang R, Yang X, Zhu J, Liu Z. et al. 2014. Isolation and expression analysis of a vacuolar membrane Na^+/H^+ antiporter gene *NtNHX1* from Nitraria tangutorum. *Scientia Silvae Sinicae* 50:38−44 (in Chinese)

[35] Tang X, Zhang H, Shabala S, Li H, Yang X, et al. 2021. Tissue tolerance mechanisms conferring salinity tolerance in a halophytic perennial species *Nitraria sibirica* Pall. *Tree Physiology* 41:1264−1277

[36] Lu L, Wang Y, Chen Y, Zhu L, Wu X, et al. 2025. Salt stimulates carbon fixation in the halophyte *Nitraria sibirica* to enhance growth. *Forestry Research* 5:e004

[37] Zhang N, Cahaeraduqin S, Du J, Pan Y, Wang R, et al. 2024. Effects of exogenous H_2O_2 on ROS metabolism in *Nitraria tangutorum* Bobr. leaves under salt stress. *Journal of Northeast Agricultural University (English Edition)* 31:20−27

[38] Zheng L, Dang Z, Li H, Zhang H, Wu S, et al. 2014. Isolation and characterization of a Δ1-pyrroline-5-carboxylate synthetase (*NtP5CS*) from *Nitraria tangutorum* Bobr. and functional comparison with its *Arabidopsis* homologue. *Molecular Biology Reports* 41:563−572

[39] Didi DA, Su S, Sam FE, Tiika RJ, Zhang X. 2022. Effect of plant growth regulators on osmotic regulatory substances and antioxidant enzyme activity of *Nitraria tangutorum*. *Plants* 11:2559

[40] Li X, Liu H, He C, Li Y. 2025. Physiological mechanisms of exogenous ABA in alleviating drought stress in *Nitraria tangutorum*. *Plants* 14:2643

[41] Gao Z, Gao S, Li P, Zhang Y, Ma B, et al. 2021. Exogenous methyl jasmonate promotes salt stress-induced growth inhibition and prioritizes defense response of *Nitraria tangutorum* Bobr. *Physiologia Plantarum* 172:162−175

[42] Zhang J, Cheng K, Liu X, Dai Z, Zheng L, et al. 2023. Exogenous abscisic acid and sodium nitroprusside regulate flavonoid biosynthesis and photosynthesis of *Nitraria tangutorum* Bobr in alkali stress. *Frontiers in Plant Science* 14:1118984

[43] Liu C, Duan N, Chen X, Li H, Zhao X, et al. 2022. Metabolic pathways involved in the drought stress response of *Nitraria tangutorum* as revealed by transcriptome analysis. *Forests* 13:509

[44] Wang YM, Yu CH, Zhao XJ, Zhao JQ. 2020. A rapid high-performance liquid chromatography separation of a new anthocyanin from *Nitraria tangutorum*. *Journal of Asian Natural Products Research* 22:503−507

[45] Zhang M, Ma J, Bi H, Song J, Yang H, et al. 2017. Characterization and cardioprotective activity of anthocyanins from *Nitraria tangutorum* Bobr. by-products. *Food & Function* 8:2771−2782

[46] Zheng J, Li H, Ding C, Suo Y, Wang L, et al. 2011. Anthocyanins composition and antioxidant activity of two major wild *Nitraria tangutorun* Bobr. variations from Qinghai–Tibet Plateau. *Food Research International* 44:2041−2046

[47] Gao Z, Wang YC, Chang YX. 2016. Determination of flavonoids and anthocyanins in *Nitraria tangutorum* by high performance liquid chromatography coupled with tandem mass spectrometry. *Protein & Peptide Letters* 23:424−432

[48] Zou Q, Feng J, Li T, Cheng G, Wang W, et al. 2022. Antioxidation and anti-inflammatory actions of the extract of *Nitraria Tangutorum* Bobr. fruits reduce the severity of ulcerative colitis in a dextran sulphate sodium-induced mice model. *Journal of Functional Foods* 91:105005

[49] Halim AF, Saad HEA, Hashish NE. 1995. Flavonol glycosides from *Nitraria retusa*. *Phytochemistry* 40:349−351

[50] Jiang S, Zhang Y, Zhao X, Shao Y, Wei W, et al. 2021. A new flavonol acylglycoside from the fruits of *Nitraria tangutorum* Bobr. *Natural Product Research* 35:3652−3657

[51] Boubaker J, Ben Sghaier M, Skandrani I, Ghedira K, Chekir-Ghedira L. 2012. Isorhamnetin 3-O-robinobioside from *Nitraria retusa* leaves enhance antioxidant and antigenotoxic activity in human chronic myelogenous leukemia cell line K562. *BMC Complementary and Alternative Medicine* 12:135

[52] Kalai FZ, Boulaaba M, Ksouri R, Isoda H. 2021. Identification of main phenolic compounds of *Nitraria retusa* leaf and stem extracts and evaluation of their anti-adipogenic activity in 3T3-L1 cells. *Research Square* Preprint

[53] Boubaker J, Lahmar A, Salek A, Selmi M, Kriffa M, et al. 2025. Antitumoral effect of Nitraria retusa bioactive compounds on two glioblastoma cell lines. *Human Cell* 39:23

[54] Jia Q, Zhang S, Zhang H, Yang X, Cui X, et al. 2020. A comparative study on polyphenolic composition of berries from the Tibetan Plateau by UPLC-Q-Orbitrap MS system. *Chemistry & Biodiversity* 17:e2000033

[55] Khowdiary MM, Alatawi Z, Alhowiti A, Amin MA, Daghistani H, et al. 2024. Phytochemical analysis and multifaceted biomedical activities of *Nitraria retusa* extract as natural product-based therapies. *Life* 14:1629

[56] Song Q, Zhao H, Fu Z, Chen D, Lu Y. 2018. Antioxidant and anticomplement compounds isolated from *Nitraria sibirica* fruit by high-speed counter-current chromatography. *Pharmacognosy Magazine* 14:541−547

[57] Turghun C, Bakri M, Liu GY, Bobakulov K, Aisa HA. 2021. Phenolic glycosides from *Nitraria sibirica* leaves and their *in vitro* biological activities. *Natural Product Research* 35:1388−1392

[58] Song Q, Xia X, Ji C, Chen D, Lu Y. 2019. Optimized flash extraction and UPLC-MS analysis on antioxidant compositions of *Nitraria sibirica* fruit. *Journal of Pharmaceutical and Biomedical Analysis* 172:379−387

[59] Senejoux F, Girard C, Aisa HA, Bakri M, Kerram P, et al. 2012. Vasorelaxant and hypotensive effects of a hydroalcoholic extract from the fruits of *Nitraria sibirica* Pall. (Nitrariaceae). *Journal of Ethnopharmacology* 141:629−634

[60] Kalai FZ, Mkadmini K, Hammami M, Isoda H, Ksouri R. 2022. Intensification of phenolic compounds extraction from *Nitraria retusa* leaves by ultrasound-assisted system using box–behnken design and evaluation of biological activities. *Biological and Chemical Research* 9:19−34

[61] Rafiee D, Ebrahimi MA, Qavami N, Zarinpanjeh N. 2023. The effect of NaCl and salicylic acid on total phenolic and flavonoid contents in suspension culture of Nitraria schoberi. *Journal of Medicinal plants and By-products* 12:397−404

[62] Yang IF, Liub C. 2024. Combined microbial fermentation converts bioactive compounds in *Nitraria tangutorum* Bobrov fruit and displays its antidiabetic potential. *JSM Biotechnology and Biomedical Engineering* 9:1093

[63] Tulyaganov TS, Nazarov OM, Levkovich MG, Abdullaev ND. 2001. Alkaloids of the *Nitraria* genus. komavine and acetylkomavine. *Chemistry of Natural Compounds* 37:61−64

[64] Tulyaganov TS, Nazarov OM. 2000. Alkaloids of *Nitraria schoberi*. N-methylnitrarine. *Chemistry of Natural Compounds* 36:393−395

[65] Zhao JQ, Wang YM, Yang YL, Zeng Y, Wang QL, et al. 2017. Isolation and identification of antioxidant and α-glucosidase inhibitory compounds from fruit juice of *Nitraria tangutorum*. *Food Chemistry* 227:93−101

[66] Bakri M, Yi Y, Chen LD, Aisa HA, Wang MH. 2014. Alkaloids of *Nitraria sibirica* Pall. decrease hypertension and albuminuria in angiotensin II-salt hypertension. *Chinese Journal of Natural Medicines* 12:266−272

[67] Turghun C, Bakri M, Abudulla R, Sun G, Aisa HA. 2018. UHPLC-MS^n -assisted characterization of bioactive alkaloids extracted from *Nitraria sibirica* leaves and enriched using response surface method and adsorption on macroporous resin. *Industrial Crops and Products* 125:529−536

[68] Zhao B, Liu J, Chen X, Zhang J, Wang J. 2018. Purification, structure and anti-oxidation of polysaccharides from the fruit of *Nitraria tangutorum* Bobr. *RSC Advances* 8:11731−11743

[69] Abuduwaili A, Zhang X, Yi Y, Yang B, Wali A, et al. 2026. A comparative study on the structural properties of polysaccharides from *Nitraria sibirica* fruits with different extraction methods and their antioxidant and prebiotic activities. *Chemistry & Biodiversity* 23:e02596

[70] Boubaker J, Skandrani I, Bouhlel I, Ben sghaier M, Neffati A, et al. 2010. Mutagenic, antimutagenic and antioxidant potency of leaf extracts from *Nitraria retusa*. *Food and Chemical Toxicology* 48:2283−2290

[71] Ma T, Hu N, Ding C, Zhang Q, Li W, et al. 2016. *In vitro* and *in vivo* biological activities of anthocyanins from *Nitraria tangutorun* Bobr. fruits. *Food Chemistry* 194:296−303

[72] Chaâbane M, Koubaa M, Soudani N, Elwej A, Grati M, et al. 2017. *Nitraria retusa* fruit prevents penconazole-induced kidney injury in adult rats through modulation of oxidative stress and histopathological changes. *Pharmaceutical Biology* 55:1061−1073

[73] Du X, Cheng X, Feng M, Liang Y, Wang Y, et al. 2025. *Nitraria tangutorum* fruit extract modulates rumen fermentation and microbiota in Hu sheep. *Journal of Agriculture and Food Research* 24:102282

[74] Boubaker J, Bhouri W, Ben Sghaier M, Bouhlel I, Skandrani I, et al. 2011. Leaf extracts from *Nitraria retusa* promote cell population growth of human cancer cells by inducing apoptosis. *Cancer Cell International* 11:37−45

[75] Boubaker J, Lahmar A, Ben Toumia I, Ghedira K, Chekir-Ghedira L. 2024. Antitumoral potency of isorhamnetin and its derivates carbohydrate in methanol extract from *Nitraria retusa* leaves. *Research Square* Preprint

[76] Boubaker J, Wissem B, Mohammed BS, Ines B, Mounira K, et al. 2012. Flavonoids products from *Nitraria retusa* leaves promote lymphoblastoid cells apoptosis. *Nutrition and Cancer* 64:1095−1102

[77] Wang Y, Xie Q, Ding X, Sun X, Luo S, et al. 2018. 白刺对胃癌 MGC-803 细胞的抑制作用 [Study of Inhibitory Action of BaiCi on Gastric Cancer MGC-803 Cells]. *西部中医药 [Western Journal of Traditional Chinese Medicine]* 31:14−18 (in Chinese)

[78] Liu BPL, Chong EYY, Cheung FWK, Duan JA, Che CT, et al. 2005. Tangutorine induces p21 expression and abnormal mitosis in human colon cancer HT-29 cells. *Biochemical Pharmacology* 70:287−299

[79] Yu F, Wei K, Lian X. 2003. Effect and mechanism of nitrary flavone on Hep, U_ (14) tumor of mice. *Chinese Pharmacological Bulletin* 19:886−888

[80] Boubaker J, Chaabane F, Bedoui A, Aloui R, Ben Ahmed B, et al. 2015. Antitumoral potency of methanolic extract from *Nitraria retusa* leaves via its immunomodulatory effect. *Cancer Cell International* 15:82

[81] Boubaker J, Ben Toumia I, Sassi A, Bzouich-Mokded I, Ghoul Mazgar S, et al. 2018. Antitumoral potency by immunomodulation of chloroform extract from leaves of *Nitraria retusa*, Tunisian medicinal plant, via its major compounds β-sitosterol and palmitic acid in BALB/c mice bearing induced tumor. *Nutrition and Cancer* 70:650−662

[82] Zar Kalai F, Han J, Ksouri R, El Omri A, Abdelly C, et al. 2013. Antiobesity effects of an edible halophyte *Nitraria retusa* forssk in 3T3-L1 preadipocyte differentiation and in C57B6J/L mice fed a high fat diet-induced obesity. *Evidence-Based Complementary and Alternative Medicine* 2013:368658

[83] Li B, Liu K, Zhang J, Li C. 2019. Anthocyanins from the fruits of *Nitraria tangutorun* Bobr. improve nonalcoholic fatty liver injury induced by high-fat diet in mice. *Food Science* 40:217−223

[84] Zar Kalai F, Han J, Ksouri R, Abdelly C, Isoda H. 2014. Oral administration of *Nitraria retusa* ethanolic extract enhances hepatic lipid

metabolism in db/db mice model 'BKS. Cg-Dock7^{m}+/+ Lepr$^{db/}$J' through the modulation of lipogenesis-lipolysis balance. *Food and Chemical Toxicology* 72:247–256

[85] Du X, Cheng X, Dong Q, Zhou J, Degen AA, et al. 2022. Dietary supplementation of fruit from *Nitraria tangutorum* improved immunity and abundance of beneficial ruminal bacteria in Hu sheep. *Animals* 12:3211

[86] Iida A, Usui T, Zar Kalai F, Han J, Isoda H, et al. 2015. Protective effects of *Nitraria retusa* extract and its constituent isorhamnetin against amyloid β-induced cytotoxicity and amyloid β aggregation. *Bioscience, Biotechnology, and Biochemistry* 79:1548–1551

[87] Wang H, Zhou J, Bi H, Yang X, Chen W, et al. 2021. Bioactive ingredients from *Nitraria tangutorun* Bobr. protect against cerebral ischemia/reperfusion injury through attenuation of oxidative stress and the inflammatory response. *Journal of Medicinal Food* 24:686–696

[88] Kurskaya O, Prokopyeva E, Bi H, Sobolev I, Murashkina T, et al. 2022. Anti-influenza activity of medicinal material extracts from Qinghai–Tibet plateau. *Viruses* 14:360

[89] Mei X, Dai T, Shen Y. 2023. Adaptive strategy of *Nitraria sibirica* to transient salt, alkali and osmotic stresses via the alteration of Na^+/K^+ fluxes around root tips. *Journal of Forestry Research* 34:425–432

[90] Zhu L, Li M, Huo J, Lian Z, Liu Y, et al. 2021. Overexpression of *NtSOS2* from halophyte plant *N. tangutorum* enhances tolerance to salt stress in Arabidopsis. *Frontiers in Plant Science* 12:716855

[91] Duan R, Zhang H, Zhao Y, Zhang H, Li R, et al. 2025. Analysis of *SRO* gene family in *Nitraria sibirica* Pall. and the function of *NsSRO1a* in improving plant drought tolerance. *Tree Physiology* 45:tpaf050

[92] Lu L, Chen X, Wang P, Lu Y, Zhang J, et al. 2021. *CIPK11*: a calcineurin B-like protein-interacting protein kinase from *Nitraria tangutorum*, confers tolerance to salt and drought in *Arabidopsis*. *BMC Plant Biology* 21:123

[93] Zhang H, Qi C, Li C, Huang D, Mao H, et al. 2024. Overexpression of high affinity K^+ transporter from *Nitraria sibirica* enhanced salt tolerance of transgenic plants. *Plant Science* 342:112052

[94] Qi D, Xiao H, Liu H, Zheng L, Wang Y. 2025. Sucrose enhances adventitious root formation in *Nitraria tangutorum* under drought stress via hormonal homeostasis and hydrogen peroxide signaling. *Physiologia Plantarum* 177:e70521

[95] Zhang H, Hu A, Wu H, Zhu J, Zhang J, et al. 2023. Integrated metabolome and transcriptome analysis unveils novel pathway involved in the fruit coloration of *Nitraria tangutorum* Bobr. *BMC Plant Biology* 23:65

[96] Bao X, Zong Y, Hu N, Liu B, Wang H. 2023. 西伯利亚白刺 *NsMYB5* 调控果实花青素生物合成 [*NsMYB5* regulates anthocyanin biosynthesis in fruits of *Nitraria sibirica*]. *西北农业学报 [Acta Agriculturae Boreali-occidentalis Sinica]* 8:1215–1222 (in Chinese)

[97] Gravel E, Harfouche A, Salame R, Leblanc K, Maciuk A, et al. 2013. Spontaneous formation of nitrarine and polycyclic skeletons related to *Nitraria* indolic alkaloids under non-enzymic conditions. *Chemistry – A European Journal* 19:14515–14520

[98] Granot G, Grafi G. 2014. Epigenetic information can reveal phylogenetic relationships within Zygophyllales. *Plant Systematics and Evolution* 300:1819–1824