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Review Article

Advances in Omics Studies, Biological and Clinical Potentialities of *Cistanches* Herba (*Rou Cong Rong*)

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Abstract

Cistanches herba, known as *Rou Cong Rong* in Chinese, is a precious nourishing traditional Chinese medicine. *Cistanches* herba contains many bioactive compounds, the most important of which are phenylethanoid glycosides and polysaccharides. The rapid development of sequencing technology opens a new perspective for the research and application of *Cistanches* herba, and enables people to study the synthesis and action mechanism of their active components from the genome level. However, the absence of genomic and transcriptome analysis of *Cistanche* herba has hindered its development in planting, pharmacodynamics, and clinical studies. In this paper, we summarized the research on the omics of *Cistanche* herba for the first time and update the latest research progress on the biological functions and clinical applications of key compounds. In conclusion, this review eventually provided a new perspective for the further study of the pharmacodynamics and industrial development of novel active compounds in *Cistanche* herba.

Keywords: *Cistanche* herba; Omics; Biological activities; Clinical application; Phenylethanoid glycosides

Aabbreviations: 4CL: 4-Coumarate-CoA Ligase; 5-HT: Hydroxytryptamine; ACT: Acteoside; AD: Alzheimer's Disease; AKT: Protein Kinase B; ALD: alcoholic liver disease; ARE: antioxidant response element; BDNF: brain-derived neurotrophic factor; BM-DCs: Murine Marrow-Derived Dendritic Cells; *C. deserticola*: *Cistanches deserticola*; *C. salsa*: *Cistanches salsa*; *C. sinensis*: *Cistanches sinensis*; *C. tubulosa*: *Cistanches tubulosa*; CASP-1: Cysteinyl Aspartate Specific Proteinase 1; CCR: Cinnamoyl-CoA Reductase; CDAE: Alditol Extract from *C. deserticola*; CDHE, Ethanol Extract of *C. deserticola*; CDPs: *C. deserticola* Polysaccharides; Cp: Chloroplasts; CRJG: Congrongjing Granules; CTE: *C. tubulosa* Aqueous Extract; CTPG: PhGs of *C.tubulosa*; CYP73A: Cytochrome P450 Family 73; CYP8B1: Cytochrome P450 Family 8 Subfamily B Member 1; ECH, Echinacoside; ERK: Extracellular Regulated protein Kinases; F5H: Ferulate-5-Hydroxylase; FASN, recombinant Fatty Acid Synthase; FGF15: Fibroblast Growth Factor 15; FXR: Farnesoid X Receptor; GO: Gene Ontology; HCC: Hepatocellular Carcinoma; HCT: shikimate o-Hydroxycinnamoyl Transferase; HMGB1: High Mobility Group box-1 Protein; HO-1: Heme Oxygenase-1; IL-1β: Interleukin-1β; IL-6: Interleukin-1β; JAK2: Janus Tyrosine Kinase 2; KEGG: Kyoto Encyclopedia of Genes and Genomes; MAPK: Mitogen-Activated Protein Kinases; MCAO: Middle Cerebral Artery Occlusion; MEK: Mitogen-activated Extracellular signal-regulated Kinase; Mit: Mitochondria; mTOR: Mammalian Target of Rapamycin; NF-κB: Nuclear Factor Kappa-B; NLRP3: Nucleotide-Binding Oligomerization domain 3; Nrf2: Erythroid 2-Related Factor 2; PAL: Phenylalanine

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Ammonialyas; PD: Parkinson's Disease; PhGs: Phenylethanoid Glycosides; PI3K: Phosphoinositide 3-Kinase; PMOP: Postmenopausal Osteoporosis; ROS: Reactive Oxygen Species; rRNA: Ribosomal RNA; SCF: Stem Cell Factor; SREBP-1c: sterol Regulatory Element Binding Protein-1c; STAT3: Signal Transducer and Activator of Transcription 3; TGR5: Takeda G Protein-Coupled Receptor 5; Th17: T Helper Cell 17; TLR4: Toll-Like Receptor 4; TNF-α: Tumor Necrosis Factor-α; TrkB: Tyrosine Kinase B; tRNA: Transfer RNA; VD: Vascular Dementia; WPCD: Polysaccharides of *C. deserticola*

Introduction

Cistanches herba is a kind of traditional Chinese medicine with high medicinal value in history, known as "desert ginseng". There are four species of *Cistanches* herba in China, which are *Cistanche deserticola*, *Cistanche salsa*, *Cistanche tubulosa*, and *Cistanche sinensis*. *C. deserticola* and *C. tubulosa* [1]. *C. deserticola* and *C. tubulosa* are the most commonly used and are recorded in the Chinese Pharmacopoeia. *C. deserticola* has been recognized as "Homologous medicine and Food" in China since 2018. More than 200 compounds have been identified from *Cistanche* herba, including phenylethanoid glycosides (PhGs), polysaccharides, essential oils, iridoid and lignans [2]. Among them, PhGs and polysaccharides have been proven to have a series of biological activities, including anti-oxidative, anti-inflammatory, anti-tumor, and neuroprotective properties [3]. To put it briefly, *Cistanche* herba has a high value of further development, and its biological activities in clinical are increasingly studied.

In recent years, scientists have made in-depth studies on the morphological recognition, composition analysis, structure identification. However, few studies have been conducted on the genome structure, functional genomics, and proteomics of *Cistanche* herba. Therefore, this article reviews the omics studies of *Cistanche* herba, biological functions and clinical applications of important compounds in *Cistanche* herba, in order to discover new potential research directions and industrial development opportunities for *Cistanche* herba.

Genome Structure of Important Organelles

The structure of the nuclear genome in *Cistanche* herba has not been reported, but many scientists have studied organelle genomes [4]. Plastids are unique organelles of green plants, which develop into chloroplasts, chromoplasts, and leucoplasts after maturity [5]. The *Cistanche* herba plastid genomes all showed the conserved quadripartite structure (Table 1). With a total length of 102,657 bp, *C. deserticola* possesses the largest plastome among the three *Cistanche* herba. The plastid genomes of *C. tubulosa*, *C. salsa* and *C. sinensis* are 94,123 bp, 101,776 bp and 87,707 bp, respectively [6]. It is worth noting that the LSC region of *C. deserticola* is the longest (48,350 bp) and the SSC region of *C. sinensis* is the longest (11,865 bp) [6].

Chloroplasts (Cp) are the places where plants perform photosynthesis and have attracted more attention than other plastids because of their important role in plant physiological development [7]. The chloroplasts genome of *C. deserticola* is 109,495 bp in length, consisting of one LSC (48,352 bp), one SSC (398 bp), and two IRs (30,352 bp) [8]. It contained 27 protein-coding genes, four rRNA genes, and 29 tRNA genes. Additionally, genes required for photosynthesis suffer from gene loss and pseudogenization, except for *psb*M [8]. As for the other *Cistanche* herba, the chloroplasts genome size was 111,710 bp in *C. salsa*, 111,500 bp in *C. sinensis*, and 75,375 bp in *C. tubulosa* [9]. Almost all genes related to photosynthesis were pseudogenized or lost, with the most severe loss occurring in *C. tubulosa* [9]. This suggests that *Cistanche* herba cannot photosynthesize independently, and its photosynthesis-related genes or protein products may come from the host *Haloxylon ammodendron*. Mitochondria (Mit) are essential for various metabolic processes, such as cellular respiration and ATP synthesis [10]. The mitochondria genome of *C. tubulosa* was significantly larger than other species (3,978,341 bp). The mitogenomic lengths of the *C. deserticola* and *C. salsa* were 1,860,774 bp and 1,708,661 bp, respectively [11]. It is worth mentioning that *C. tubulosa* has a higher number of genes than *C. deserticola* and *C. salsa* [11].

Gene Expression Profiles

For non-model organisms without reference gene sequences, transcriptome data can be used to discover gene expression profiles and biological characteristics of species on a larger scale [12]. At present, the nuclear genome data of *Cistanche* herba have not been published, but their gene expression profiles are crucial to elucidate its parasitic mechanism, compound synthesis pathway, and environmental adaptation.

Li Y *et al.* performed deep transcriptome sequencing in fleshy stem of *C. deserticola* using Illumina HiSeq2000 platform [13]. Using trinity assembler, they obtained 95,787 transcript sequences ranging from 200 bp to 15,698 bp, having an average length of 950 bases and the N50 length of 1,519 bases. 30098 identified actively expressed transcripts were annotated to a wide range of GO categories and KEGG pathways, such as terpenoid backbone biosynthesis, phenylpropanoid biosynthesis, and carotenoid biosynthesis, indicating that active metabolic processes were underway in the *C. deserticola* stem tissue [13]. A recent study by Hou *et al.* performed the full-length transcriptome sequencing and gene expression profiling of *C. tubulosa* using PacBio combined with BGISEQ-500 RNA-seq technology [14]. A total of 237,772 unique transcripts were obtained, ranging from 199 bp to 31,857 bp. Among the unique transcripts, 188,135 (79.12%) transcripts were annotated [14]. It is worth mentioning that 1080 transcripts were annotated for 22 enzymes related to PhGs biosynthesis [14].

Synthesis of Important Compounds

Traditional natural extraction or artificial chemical synthesis methods are difficult to meet the needs of scientific research and new drug development. Genomic and transcriptomic studies could be used to identify key enzyme coding genes of specific metabolic pathways and optimize these pathways by improving the expression of key enzymes encoding genes to obtain the required components [15]. Based on *de novo* transcriptome of *C. deserticola*, PhGs has two different biosynthesis pathways and 17 enzyme genes [13,14]. The possible post-caffeic acid/ferulic acid reaction process was published for the first time, in which the caffeic/ferulic acid would be first oxidized into phenylpyruvate derivate, then the carboxyl group was removed by decarboxylases, and finally, aldehyde group was converted back into alcohol group by dehydrogenase [13,14]. Another is based on phenylalanine metabolism pathway, in which the phenylalanine

to phenylethanol was achieved by a known 'Enrlich pathway', then phenylethanol is converted to phenylethanol aglycone by monooxygenase or methyltransferase, and further phenylethyl alcohol glycoside is synthesized [13]. The complete picture of lignin biosynthesis pathways in *C. deserticola* was also presented by Li YL *et al.* [13], in which the lignin monomers are biosynthesized from phenylalanine through a series of enzymatic reactions, including hydroxylation, methylation, reduction, and oxidative polymerization process [16,17]. Phenylalanine Ammonialyas (*PAL*) is the first key enzyme in this pathway to convert phenylalanine to cinnamic acid by non-oxidative deamination [18,19]. 4-Coumarate-CoA Ligase (*4CL*) and trans-Cinnamate 4-Monooxygenase (*CYP73A*) subsequently convert cinnamic acid to coumaroyl-CoA. Finally, key enzymes Cinnamoyl-CoA Reductase (*CCR*), shikimate o-Hydroxycinnamoyl Transferase (*HCT*), and Ferulate-5-Hydroxylase (*F5H*) regulate the synthesis of different types of lignin by coumaroyl-CoA [20,21].

Biological Activities

Neuroprotection effects: AD is an irreversible and progressive neurodegenerative disorder whose pathogenesis is complex and not completely clear, including oxidative stress, mitochondrial abnormalities and neuroinflammation [22]. *In vitro* experiments, PhGs of *Cistanche* herba could reduce oxidative stress, scour free radicals, inhibit neural cell apoptosis, and promote neural cell growth and repair [23-25]. *C. Tubulosa* aqueous Extract (CTE) could improve memory loss in AD-like rats [24]. Specifically, Echinacoside (ECH), and Acteoside (ACT), the major components of CTE [26], could significantly improve the learning and memory ability of AD animal models, and the mechanism is related to inhibiting neural cell apoptosis and reducing oxidative stress [23,27-30]. Additionally, PhGs of *Cistanche* herba could regulate brain energy metabolism by regulating insulin signaling [31], and ACT is preferable to total phenylethanoid glycosides in anti-AD [32].

The typical neuropathological features of PD are degeneration of dopaminergic neurons in the substantia nigra [33], accompanied by chronic neuroinflammation [34]. Neurotoxic substances produced by activated microglia are key molecules that mediate the occurrence. ECH of *Cistanche* herba could significantly inhibit the activation of microglia cells induced by inhibiting the inflammatory signaling pathway NLRP3/CASP-1/IL-1β [35]. Additionally, ECH showed neuroprotective effects on PD pathological mice via regulating the IL-6/JAK2/STAT3 pathway to inhibit the activation of microglia [36]. ACT effectively alleviated rotational behavior in PD rats, and its anti-PD mechanism is related to the regeneration of tyrosine hydroxylase-immunoreactive neurons in the substantia nigra and the activation of the Nrf2/ARE signaling pathway [37-39].

PhGs from *C. tubulosa* could regulate neuroinflammation via microglial M1-M2 polarization and alleviate ischemic stroke caused by Middle Cerebral Artery Occlusion (MCAO) [40]. PhGs from *C. deserticola* could improve the stroke through enhancing endogenous neural stem cells proliferation via activating Wnt/β-catenin signaling pathway [41]. Therefore, *Cistanche tubulosa* and *C. deserticola* could be a candidate therapeutic agent or supplements for treating neuroinflammation related to ischemic stroke. Specifically, ACT could alleviate ischemic stroke by inhibiting microglial HMGB1/TLR4/NLRP3 signaling pathway *in vivo* [42]. Vascular Dementia (VD) is a severe cognitive disorder mainly caused by ischemic stroke. PhGs of *Cistanche* herba exerts its learning and memory-promoting effects in rat models of VD by weakening the accumulation of toxic proteins (Aβ and p-tau) and promoting neuronal cytoskeleton regeneration [43]. ECH could exert anti-VD activity by upregulating the expression of brain-derived neurotrophic factor (BDNF) and tyrosine kinase B (TrkB) in the hippocampus of VD rats and alleviating the ischemic injury of neurons [44].

Gastrointestinal Tract Protection Effects

Cistanche herba extract could significantly improve the constipation of *yang* deficiency constipation rats and its mechanism may be related to the regulation of gastrointestinal hormone levels [45]. It could effectively improve the water holding capacity of feces, which is conducive to increasing the excretion of mice [46]. Furthermore, *C. deserticola* extract could improve defecation via SCF/C-kit signaling pathway [47]. In addition, CTE could regulate the composition of intestinal microbiota in rats [48] and restore their disordered intestinal microbiota [49]. Moreover, CTE could restore the growth of lactic acid bacteria and then regulate the structure of intestinal microbiota in mice with intestinal diseases [50]. Polysaccharide, as the main active ingredient of CTE [51], also played intestinal regulatory function mainly by maintaining the balance of intestinal microbiota composition, improving its metabolic function, or synergistic interaction with intestinal microbiota mediated drugs [52]. Additionally, alditol extract from *C. Aeserticola* (CDAE) attenuate functional constipation by regulating bile acid metabolism. It could increase the expression of CYP8B1, FGF15, TGR5, and FXR, thereby modulating bile acid synthesis and enterohepatic circulation [53].

Anti-Osteoporosis Effects

Osteoporosis is a chronic disease characterized by deterioration of the bone structure and low bone mineral density [54]. Many studies have demonstrated that *C. deserticola* extract have significant anti-osteoporosis activity [55-57]. Ethanol extract of *C. Deserticola* (CDHE) improves bone loss in Postmenopausal Osteoporosis (PMOP) mainly through regulating lipid metabolism pathways *in vivo* [58]. ECH and ACT from *C. tubulosa* have shown significant anti-osteoporosis activities in the rat model of osteoporosis combined with AD [59]. ECH and ACT could significantly improve the bone quality and total bone mineral density of the femur in rats and promote bone formation and inhibit bone resorption [60]. ACT from *Cistanche* may exert osteoprotective effects by activating the PI3K/AKT/mTOR signaling pathway to alleviate Dex-induced osteoporosis [61]. In addition, Cistanoside A is able to promote bone formation and prevent bone resorption by interfering with NF-κB and PI3K/Akt pathways [62]. Moreover, total glycosides and polysaccharides from *C. deserticola* could promote osteogenesis formation and improve bone microstructure damage in mice by activating the Wnt/β-catenin signaling pathway [63].

Anti-Depressant Effects

The decoction of *C. deserticola* and *C. tubulosa* could improve spatial learning and memory in mice models of depression, and the mechanism may be related to the 'gut-brain' axis [64]. *C. Deserticola* Polysaccharides (CDPs) showed significant effects on improving abnormal behaviors of depressed rats by maintaining Th17/Treg balance and modulating gut immunity [65]. CTE could significantly improve depression-like behaviors in rats by regulating the structure of intestinal microbiota and restoring the levels of Hydroxytryptamine (5-HT) and BDNF through the 'gut-brain' axis [48]. Caffeic acid is the main degradation product of CTE in depression model rats [66], which could pro-

duce antidepressant effects [67]. These metabolites have good intestinal absorption and bioavailability and are more likely to be absorbed into the blood [68,69]. In addition, ECH could exert antidepressant effects by activating the AMPAR-Akt/ERK-mTOR signaling pathway, in which mTOR is a key signaling target for rapid antidepressant effects [70].

Anti-Tumor Effects

Previous studies have demonstrated that PhGs of *Cistanche* herba exhibit antitumor effects on a variety of tumor cells through different signaling pathways. PhGs of *C. tubulosa* induced apoptosis in Hepatocellular Carcinoma (HCC) cells through both the mitochondria-dependent and MAPK signaling pathways *in vitro* [71]. In addition, PhGs of *C. tubulosa* could inhibit the growth of B16-F10 cells and esophageal cancer ECA-109 cells both *in vitro* and *in vivo* via mitochondria-dependent pathway [72,73]. PhGs of *C. deserticola* could significantly inhibit the mitochondrial respiration and glycolysis functions of HepG2 cells, increase the level of ROS, and inhibit cell proliferation [74]. ECH exerted antiproliferative and proapoptotic functions on HepG2 cells via decreasing TREM2 expression and inactivating the AKT pathway as well as miR-503-3p/TGF-β1/Smad axis [75,76]. Moreover, ECH could not only inhibit the growth of pancreatic cancer SW1990 cells by promoting ROS generation and MAPK signaling pathway [77], but also promote pyroptosis of non-small cell lung cancer cells through Raf/MEK/ERK signaling pathway [78].

Anti-Oxidant Effects

ECH could significantly attenuate ethanol-induced oxidative stress by enhancing the levels of antioxidants and reducing the level of ROS via SREBP-1c/FASN pathway [79]. ECH could also ameliorate oxidative stress and alcohol-induced liver injury by increasing the activity of erythroid 2-related factor 2 (Nrf2), which is promising for the treatment of Alcoholic Liver Disease (ALD) [80]. Additionally, Cistanoside could markedly attenuate the harmful effects of hypoxia-induced oxidative stress by affecting antioxidant enzyme activities in testes and GC-1 cells [81]. Moreover, *Cistanche* polysaccharide is also an effective antioxidant, and its phenolic hydroxyl structure could directly bind to free radicals and the activate antioxidant defense system [82]. The polysaccharide of *C. deserticola* could induce melanogenesis in melanocytes and reduce oxidative stress via activating NRF2/HO-1 pathway, which could be used as a new drug for the treatment of decolorization disease [83].

Immune Regulation Effects

PhGs of *C. Tubulosa* (CTPG) had an immune enhancement function, which could not only significantly increase the numbers of $CD4^+$ and $CD8^+$ T cells but also enhance the activation state of $CD4^+$ T cells [71]. Moreover, CTPG could inhibit the apoptosis of splenocytes induced by cisplatin, which is characterized by the increased numbers of T cells and the decreased numbers of MDSCs and Tregs [71]. Polysaccharides of *C. deserticola* (WPCD) could modulate immune responses *in vitro* and *in vivo*. WPCD significantly promoted the maturation and function of murine Marrow-Derived Cendritic Cells (BM-DCs) through up-regulating the expression levels of MHC-II and allogenic T cell proliferation, as indicated by *in vitro* experiments [84]. Moreover, WPCD could enhance immunogenicity through a balanced Th1-/Th2-type response and an effective T-cell response, which could be used as a polysaccharide adjuvant on seasonal influenza vaccines [85].

Clinical Application

Digestive System

The clinical treatment of *Cistanche* herba on the digestive system is limited to constipation. *Congrong tongbian* decoction (Chinese herba preparation in hospital) has good therapeutic effects on *yang*-deficiency constipation, which refers to the patients with dry stool but difficult defecation, accompanied by cold and waist and knee soreness. After seven days of treatment, the defecation time of patients with constipation significantly shortened, and the defecation effect was strengthened with the increase in dose [86]. *Cistanche* herba decoction (Chinese native medicine preparation made by the hospital) could not only improve constipation caused by hemodialysis but also have long-lasting effects and no adverse reactions [87]. Moreover, *Cistanche* decoction (Chinese native medicine preparation made by the hospital) could effectively improve the constipation symptoms of Parkinson's patients, and the efficacy is better than that of the western medicine group [88].

Nervous System

Cistanche herba is clinically used for the treatment of mild AD. After agents treatment of *C. deserticola* (3222002216000), the cognitive status of mild AD patients has been significantly improved, and the mechanism is mainly related to the reduction of t-tau, TNF-α, and IL-1β in cerebrospinal fluid and delayed hippocampal atrophy [89]. *Cistanche* total glycoside capsules (Z20080047) also had good therapeutic effects on AD. After 12 weeks of treatment, the cognitive function of AD patients was significantly improved and the adverse reactions were less than those of the western medicine group [90]. *Cistanche* herba is usually combined with western medicine in the treatment of PD. *Congrongjing* Granules (CRJG) (Chinese native medicine preparation made by the hospital) could reduce the side effects of western medicine and improve the quality of life in patients with PD, and its efficacy and safety are better [91]. Moreover, *Cistanche* herba (Chinese native medicine preparation made by the hospital) combined with acupuncture and moxibustion could not only improve the motor ability of early PD patients [92], but also improve the non-motor symptoms of PD patients [93]. Additionally, the other two medicines of *Cistanche* could effectively improve life quality of PD patients, *Cistanche Shujing* granule (Chinese native medicine preparation made by the hospital) and *Cistanche Yizhi* (Z20194044) capsule could significantly relieve the depressive symptoms of PD patients [94,95].

Other Diseases

C. deserticola has two-way regulation of bone formation and bone resorption, and could effectively resist osteoporosis. After six months of *C. deserticola* treatment (Chinese native medicine preparation made by the hospital) in patients with primary osteoporosis, the achieved effects are significant, such as improved serum alkaline phosphatase, calcium, and phosphorus metabolism, increased bone density [96]. Additionally, CTE (Chinese native medicine preparation made by the hospital) is helpful to prevent motor organ dysfunction. After 12 weeks of CTE treatment, the stride length and gait speed of patients with locomotive syndrome increased, and no obvious adverse reactions were observed [97]. Moreover, CTE could effectively relieve tinnitus symptoms caused by chronic nephritis. After three months of treatment, the tinnitus symptoms of adult patients with chronic glomerulonephritis were significantly relieved [97].

Table 1: Characteristics of the four *Cistanche* herba organelle genomes.

		C. deserticola	*C. tubulosa*	*C. salsa*	*C. sinensis*	References
Total size (bp)	Plastomes	102,657	94,123	101,776	87,707	[6]
	Cp genome	109,495	75,375	111,710	111,500	[8,9]
	Mit genome	1,860,774	3,978,341	1,708,661	-	[11]
LSC (bp)	Plastomes	48,350	31,017	46,579	26,435	[6]
	Cp genome	48,352	32,470	50,497	52,005	[8,9]
	Mit genome	-	-	-	-	[11]
IRs (bp)	Plastomes	45,507	54,559	46,729	49,407	[6]
	Cp genome	30,352	6,593	30,389	27,458	[8,9]
	Mit genome	-	-	-	-	[11]
SSC (bp)	Plastomes	8,800	8,547	8,468	11,865	[6]
	Cp genome	398	29,719	435	4,579	[8,9]
	Mit genome	-	-	-	-	[11]
GC content (%)	Plastomes	37.95	36.53	37.26	36.95	[6]
	Cp genome	36.27	34.95	36.11	36.75	[8,9]
	Mit genome	44.59	44.57	44.52	-	[11]
Total number of genes	Plastomes	89	72	89	68	[6]
	Cp genome	60	53	61	60	[8,9]
	Mit genome	82	126	75	-	[11]
Total number of protein coding genes	Plastomes	27	22	20	23	[6]
	Cp genome	21	20	21	21	[8,9]
	Mit genome	37	65	41	-	[11]
tRNA	Plastomes	30	26	30	22	[6]
	Cp genome	29	25	28	28	[8,9]
	Mit genome	39	58	31	-	[11]
rRNA	Plastomes	4	4	4	4	[6]
	Cp genome	4	4	4	4	[8,9]
	Mit genome	5	4	3	-	[11]

Cp: Chloroplast; Mit: Mitochondrial; LSC: Large Single-Copy region; SSC: Single-Copy region; IRs: Inverted Repeats; C. deserticola: Cistanches Deserticola; C. salsa: Cistanches salsa; C. sinensis: Cistanches sinensis; C. tubulosa: Cistanches tubulosa; rRNA: Ribosomal RNA; tRNA: Transfer RNA

Conclusions

This article summarized the progress in omics research including the organelle genome and transcriptome of *Cistanche* herba for the first time. We found significant differences in the genomic structure of important organelles of different *Cistanche* herba (Table 1), suggesting that genomic data could solve the long-controversial problem of *Cistanche* herba identification in the future. In addition, the synthesis pathway, biological function and clinical application of PhGs, an important compound of *Cistanche* herba, were reviewed. Future studies should focus on overcoming the technical problems of assembling genome with high heterozygosity, high repeat sequences and high GC content to construct high-quality nuclear genome profiles of *Cistanche* herba, so as to solve the difficult situation of qualitative characterization of transcriptome. Moreover, researchers should integrate the multi-omics data of *Cistanche* herba to elucidate the total synthesis pathways of its important compounds (taking PhGs as an example) and further explore new active compounds. In conclusion, this article provides a new insight for further pharmacological research and clinical application of *Cistanche* herba, and provides a high-level theoretical basis for its industrial transformation.

Author Statements

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Authors Contributions

Huang J were responsible for study concept and design. Zou R and Huang J were responsible for drafting the manuscript. Huang WQ and Xu J participated in the review & editing. All authors have accepted responsibility for the entire content of this manuscript and approved its submission.

Consent to Publish

The Author confirms that the work described has not been published before.

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