



Article

Comparative Analysis of Polysaccharides from Chicory Roots and Aerial Parts Reveals Comparable Cytoprotective Effects Associated with MAPK/NF- κ B Signaling

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Abstract

Chicory (*Cichorium intybus* L.) is a widely used nutritional and medicinal plant, whose roots are an important commercial source of inulin, while the aerial parts are often discarded during industrial processing. This study systematically compared chicory polysaccharides (CPs) extracted from aerial parts (CP-A) and roots (CP-R) with respect to their compositional features and cytoprotective effects in an oxygen–glucose deprivation/reperfusion (OGD/R)-induced H9c2 cell injury model. CP-A and CP-R differed in molecular weight distribution and monosaccharide composition, with CP-R exhibiting a higher molecular weight and fructose content. Despite these differences, both fractions significantly improved cell viability and reduced oxidative and biochemical injury markers. Integrated proteomic and transcriptomic analyses indicated that CP-A and CP-R were associated with the modulation of stress-responsive signaling networks, prominently involving oxidative stress-linked MAPK/NF- κ B pathways. These findings demonstrate comparable cytoprotective activities of polysaccharide-rich fractions from roots and aerial parts and support the valorization of chicory aerial biomass as a potential source of functional ingredients for cardiovascular health.

Keywords: chicory polysaccharides; root and aerial parts; compositional features; antioxidant activity; OGD/R-induced injury; H9c2 cells

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1. Introduction

Chicory (*Cichorium intybus* L.) is a widely cultivated medicinal and edible plant that has attracted increasing attention in food science and nutrition [1]. With a long history of traditional use, contemporary studies have demonstrated a broad spectrum of bioactivities, including antioxidant, anti-inflammatory, antitumor, hepatoprotective, and metabolic regulatory effects. The root of chicory is well known as a commercial source of inulin, a prebiotic dietary fiber extensively used in the food industry to promote gut health and regulate lipid and glucose metabolism [2]. Among its phytochemicals, chicory

polysaccharides (CPs) have emerged as key bioactive components, contributing to free radical scavenging, immune modulation, and regulation of oxidative stress-related signaling pathways [3]. Growing interest in CPs has led to the identification of additional biological activities, thereby expanding their potential applications in functional food and health-related industries. For instance, CPs have been shown to exert anti-anxiety effects by modulating gut microbiota composition in a chronic sleep deprivation-induced anxiety model [4]. Moreover, their incorporation into fermented milk products as natural additives enhances antioxidant capacity and improves texture and flavor balance, highlighting their potential as functional food ingredients and nutritional supplements [5]. More recently, polysaccharides isolated from *C. intybus* var. *foliosum* were found to contain a high proportion of inulin [6], further suggesting that chicory is a rich yet underexplored source of bioactive polysaccharides with broad nutritional potential.

Despite growing interest in CPs, most studies have focused on the root, which has traditionally served as the principal industrial raw material and a major source of inulin and other polysaccharides used in food processing and pharmacological research [7]. In contrast, the aerial parts of chicory are typically treated as agricultural by-products and discarded during processing, contributing to both resource waste and potential environmental burden [8]. Nevertheless, accumulating evidence indicates that the aerial parts also possess considerable nutritional and pharmacological potential. Chicory leaves are rich in phenolic compounds that contribute to a broad spectrum of biological activities [8–10]. Consistent with this composition, leaf extracts have demonstrated hepatoprotective, hypolipidemic, and hypoglycemic effects [10], as well as pronounced anti-inflammatory and antimicrobial activities [9]. In addition, recent studies have reported that chicory leaf extract provides photoprotective and anti-inflammatory benefits in UV-B-exposed three-dimensional human skin equivalents [8], further supporting its potential as a functional ingredient for health-related applications. Beyond phenolic compounds, several studies have shown that chicory leaves contain substantial amounts of polysaccharides—sometimes even exceeding those found in the root [11,12]. Nevertheless, research on leaf-derived polysaccharides remains limited, largely confined to preliminary comparisons of total polysaccharide content among different plant parts, without systematic evaluation of their structural characteristics or biological activities [11,12]. Consequently, it remains unclear whether polysaccharides derived from aerial parts share compositional or functional similarities with those from the root. These considerations give rise to two key scientific questions: Are the compositional features of aerial-derived polysaccharides comparable to those of root-derived counterparts? Do they exhibit similar biological activities? Addressing these questions is essential for evaluating whether aerial tissues could serve as alternative or complementary sources of bioactive polysaccharides for dietary fiber extraction and functional ingredient development. However, systematic comparative studies of root- and aerial-derived CPs remain scarce. This gap limits both comprehensive understanding and broader industrial application.

Oxidative stress is a key pathological driver in various chronic diseases, particularly cardiovascular disorders [13,14]. Therefore, evaluating the antioxidant and cytoprotective potential of CPs is of considerable importance. In the present study, we conducted a comprehensive comparative analysis of polysaccharides derived from chicory aerial parts (CP-A) and roots (CP-R) (Figure 1). Their chemical characteristics—including molecular weight distribution and monosaccharide composition—were characterized. Their biological activities were then assessed using an oxygen–glucose deprivation/reoxygenation OGD/R-induced H9c2 cell injury model to simulate myocardial ischemia–reperfusion (I/R) injury in vitro [15]. To further elucidate the molecular basis of their effects, integrated proteomic and transcriptomic analyses were performed. This study provides, to our knowledge, the first systematic comparison of CPs derived from root and aerial parts,

revealing compositional divergence alongside functional convergence. The findings fill an important knowledge gap and provide a theoretical basis for the rational utilization of CPs in functional food development.

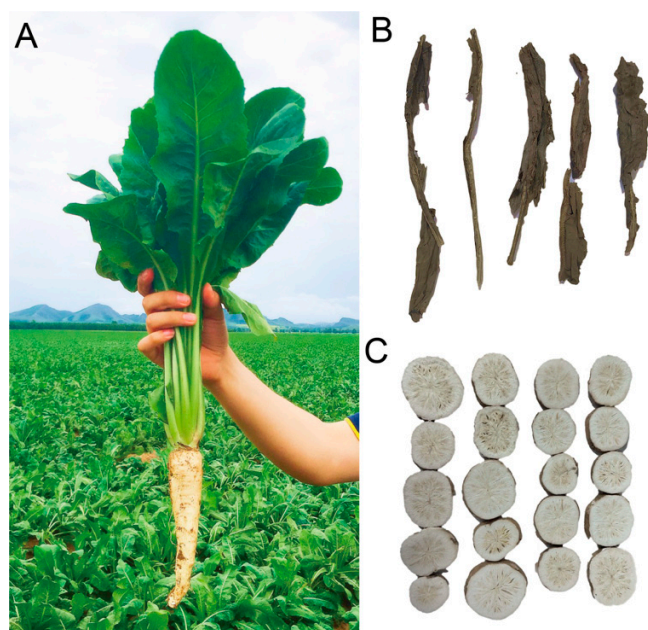


Figure 1. Morphological features and raw materials of chicory (*Cichorium intybus* L.). (A) Fresh whole chicory plant harvested from the cultivation field, showing the aerial parts and roots. (B) Dried aerial parts of chicory used for the preparation of CP-A. (C) Dried chicory roots used for the preparation of CP-R.

2. Results

2.1. Preparation of CP-A and CP-R

Extraction of CPs or inulin from roots or root pulp has been extensively optimized under various thermal, temporal, and solvent conditions. Previous studies have demonstrated that extraction efficiency and chemical composition are strongly influenced by these parameters [16–18]. In this study, aiming to compare bioactive CPs from different plant parts and to evaluate the feasibility of using aerial tissues as alternative resources, a hot-water extraction method was adopted. This approach offers a balance between industrial feasibility and preservation of polysaccharide integrity. Following a modified procedure from a previous report [17], polysaccharides were obtained under optimized aqueous conditions, yielding 14.8% for CP-A and 15.3% for CP-R, with the aerial fraction showing a slightly lower yield.

2.2. Comparison of Molecular Weight

Molecular weight distribution and homogeneity are important physicochemical parameters closely associated with polysaccharide bioactivity [19,20]. The molecular weight distribution of CPs was determined by gel permeation chromatography (GPC), as shown in Figure 2 and Table 1. The retention times for CP-A and CP-R were 19.306 and 17.216 min, respectively, suggesting that CP-R possessed a higher average molecular weight. According to calibration with polyethylene glycol (PEG) standards, CP-R exhibited a number-average molecular weight (M_n) of 2732 Da and a weight-average molecular weight (M_w) of 3588 Da, whereas CP-A showed lower values (M_n = 299 Da, M_w = 403 Da). The narrower peak observed for CP-R indicates greater homogeneity, while the broader, left-shifted peak of CP-A reflects a more heterogeneous molecular profile.

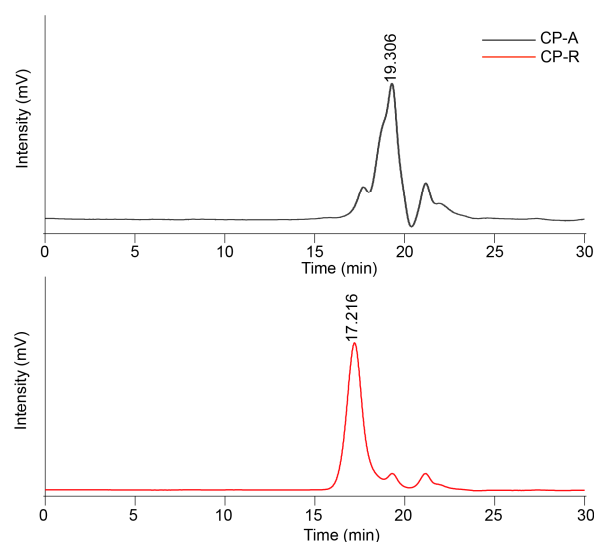


Figure 2. Comparison for molecular weight of CP-A and CP-R.

Table 1. Molecular weight distribution of CP-A and CP-R.

Sample	CP-A	CP-R
Retention Times (min)	19.306	17.216
Number Average Molecular Weight (Da)	299	2732
Weight Average Molecular Weight (Da)	403	3588

2.3. Comparison of Monosaccharide Compositions

Because CPs contain abundant fructose, which is sensitive to thermal degradation during strong acid hydrolysis, two hydrolysis strategies were employed to ensure accurate determination of monosaccharide composition [21]. The low-temperature method preserved fructose integrity, while the conventional TFA hydrolysis provided a complete compositional profile. As shown in Table 2, fructose (Fru) was the predominant monosaccharide in both polysaccharide fractions, accounting for 53.7% of total sugars in CP-A and 91.4% in CP-R. Under conventional hydrolysis (Figure 3), glucose (Glc) emerged as the major neutral sugar in both fractions, contributing to over half of the total monosaccharides (53.4% in CP-A and 54.2% in CP-R). Arabinose (Ara) and galactose (Gal) were also present in notable quantities, while rhamnose (Rha), xylose (Xyl), and mannose (Man) were detected as minor components. These results are consistent with CP-R being enriched in inulin-type fructans, consistent with its established role as a storage polysaccharide in roots. In contrast, the relatively lower fructose proportion and slightly higher presence of Gal, Man, and Xyl in CP-A indicate structural heterogeneity. Notwithstanding slight compositional variations, both fractions possess broadly analogous sugar profiles. The key variation is observed in the relative abundance of Fru.

Table 2. Monosaccharide composition of CP-R and CP-A.

Sample	CP-A	CP-R
Fru (%)	53.7 ¹	91.4 ¹
Ara (%)	16.9 ²	26.7 ²
Gal (%)	18.2 ²	13.8 ²
Glc (%)	53.4 ²	54.2 ²
Man (%)	2.1 ²	0 ²
Rha (%)	5.4 ²	5.2 ²
Xyl (%)	4.0 ²	0 ²

¹ determined by low-temperature method, ² determined by conventional TFA hydrolysis.

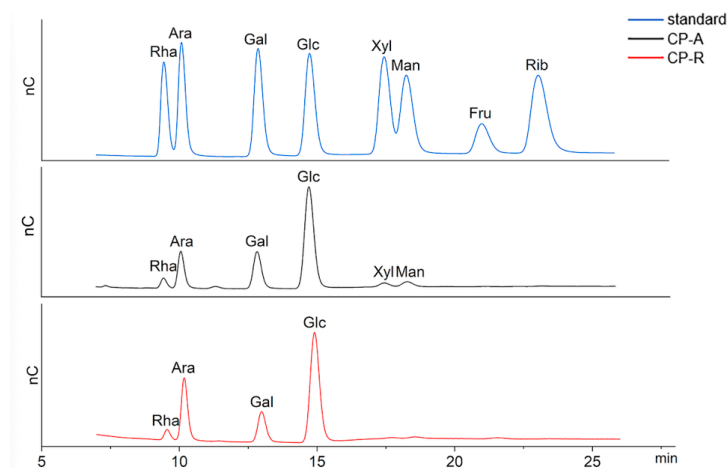


Figure 3. Comparison of the monosaccharide composition of CP-R and CP-A.

2.4. Comparison of Functional Groups by FT-IR Analysis

To further compare the chemical features of CP-A and CP-R at the functional group level, FT-IR spectroscopy was performed in the range of 4000–500 cm^{-1} (Figure 4). Both fractions exhibited typical spectral characteristics of polysaccharides. Broad absorption bands at approximately 3251 cm^{-1} (CP-A) and 3290 cm^{-1} (CP-R) were attributed to O–H stretching vibrations, reflecting abundant hydroxyl groups. Weak bands near 2900 cm^{-1} corresponded to C–H stretching vibrations. Notably, CP-A displayed a more pronounced absorption band at 1592 cm^{-1} , which was less evident in CP-R. This band is generally assigned to asymmetric stretching vibrations of carboxylate groups (COO^-) or to associated bound water, and may indicate the presence of minor acidic polysaccharides or uronic acid-related structures in CP-A. In contrast, CP-R, characterized by fructose-rich fructans, showed a comparatively weaker signal in this region. Strong absorptions in the 1200–1000 cm^{-1} region, particularly at 1043 cm^{-1} (CP-A) and 1024 cm^{-1} (CP-R), were characteristic of C–O–C and C–O–H stretching vibrations associated with glycosidic linkages and ring structures of polysaccharides. Additionally, the signal near 932 cm^{-1} observed in CP-R is consistent with furanose ring vibrations, supporting the presence of fructofuranosyl units typical of inulin-type fructans [22].

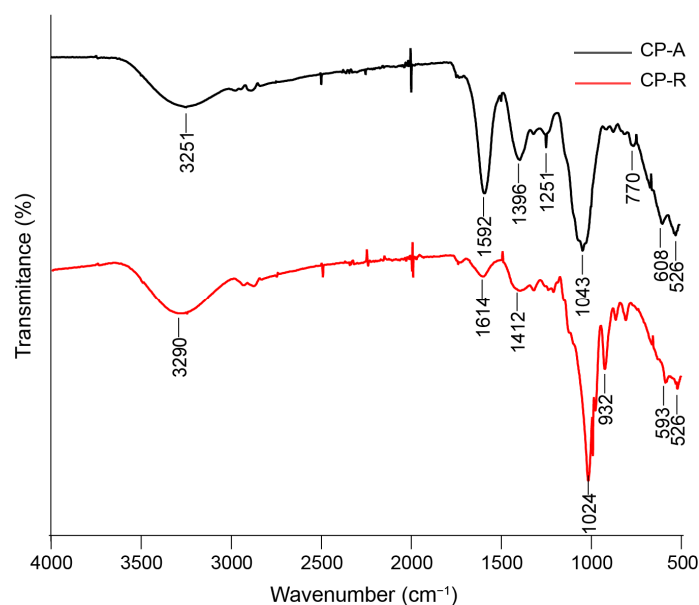


Figure 4. Comparison of FT-IR of CP-R and CP-A.

2.5. CP-A and CP-R Exhibit Comparable Protective Effects Against OGD/R-Induced Injury in H9c2 Cells

As shown in Figure 5A,B, neither CP-A nor CP-R displayed cytotoxicity within the tested range (0–1000 µg/mL), maintaining >95% cell viability. Exposure to OGD/R significantly reduced viability compared with the Control group (Figure 5C), confirming successful model establishment [15]. Treatment with either CP-A or CP-R dose-dependently improved cell survival. Moreover, OGD/R markedly elevated cardiac injury biomarkers CK-MB and cTnT, as well as the oxidative DNA damage marker 8-OHdG (Figure 5D–F). Administration of high-dose CP-A or CP-R (100 µg/mL) significantly lowered CK-MB and cTnT levels ($p < 0.01$) and reduced 8-OHdG accumulation ($p < 0.0001$). These data demonstrate that CP-A and CP-R mitigate OGD/R-induced injury in H9c2 cells, accompanied by attenuation of oxidative stress-associated damage. Given that excessive oxidative stress is a major upstream trigger of stress-responsive signaling cascades during ischemia–reperfusion injury, these findings prompted further investigation into the downstream molecular pathways potentially involved in CP-mediated cytoprotection.

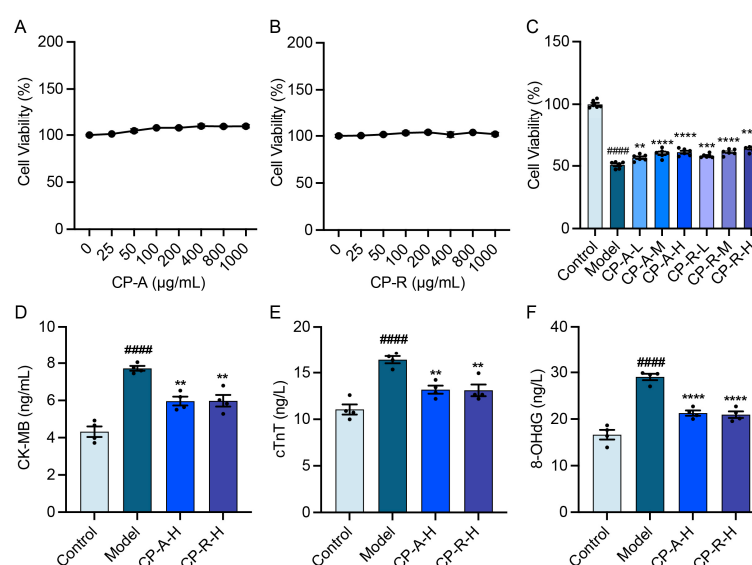


Figure 5. Effects of CP-A and CP-R on H9c2 cell viability and injury biomarkers under OGD/R conditions. (A,B) Effects of CP-A and CP-R on H9c2 cell viability after 24 h of treatment at different concentrations (0–1000 µg/mL). (C) Effects of OGD/R intervention and different concentrations of CP-A (CP-A-L, 25 µg/mL; CP-A-M, 50 µg/mL; CP-A-H, 100 µg/mL) and CP-R (CP-R-L, 25 µg/mL; CP-R-M, 50 µg/mL; CP-R-H, 100 µg/mL) on H9c2 cell viability. Cell viability was determined using the CCK-8 assay. (D–F) Effects of OGD/R intervention and high-dose CP-A (CP-A-H, 100 µg/mL) or CP-R (CP-R-H, 100 µg/mL) on (D) creatine kinase-MB (CK-MB), (E) cardiac troponin T (cTnT), and (F) 8-hydroxydeoxyguanosine (8-OHdG) levels in H9c2 cells. Data are expressed as mean ± SEM ($n = 3$). #### $p < 0.0001$ vs. Control group; ** $p < 0.01$, *** $p < 0.001$, and **** $p < 0.0001$ vs. Model group (one-way ANOVA followed by Tukey’s HSD post hoc test).

2.6. Proteomic Profiling Reveals Shared Pathways Modulated by CP-A and CP-R

Proteomic profiling was performed to investigate stress-responsive molecular networks associated with CP treatment in OGD/R-injured H9c2 cells. Compared with the Control group, OGD/R exposure resulted in 843 differentially expressed proteins (362 downregulated and 481 upregulated; FDR < 0.05 and $|\log_2FC| > 0.585$; Figure 6A, Dataset S1), indicating substantial proteomic remodeling under ischemia–reperfusion conditions. CP-A and CP-R treatment markedly altered the OGD/R-associated proteomic profile (Figure 6B,C). Specifically, CP-A affected 613 proteins (383 downregulated and 230

upregulated), whereas CP-R influenced 518 proteins (277 downregulated and 241 upregulated) under the same statistical thresholds. Intersection analysis identified 156 overlapping differentially expressed proteins across Model vs. Control, CP-A vs. Model, and CP-R vs. Model comparisons (Figure 6D), indicating partially shared regulatory patterns between the two fractions. GO enrichment analysis highlighted oxidoreductase activity, oxidoreductase complex, flavin adenine dinucleotide binding, and cellular response to oxygen levels (Figure 6E). Collectively implicating redox regulation and oxygen-sensitive metabolic adaptation. Enrichment of PML bodies and actin-binding functions further suggests coordinated modulation of nuclear stress signaling and cytoskeletal organization. KEGG pathway analysis revealed significant enrichment in protein export and endoplasmic reticulum protein processing pathways (Figure 6F), processes closely linked to ER stress and redox homeostasis. Together, these findings suggest that CP-A and CP-R were associated with overlapping redox-responsive and stress-adaptive proteomic signatures, consistent with their attenuation of oxidative injury in OGD/R-treated cells.

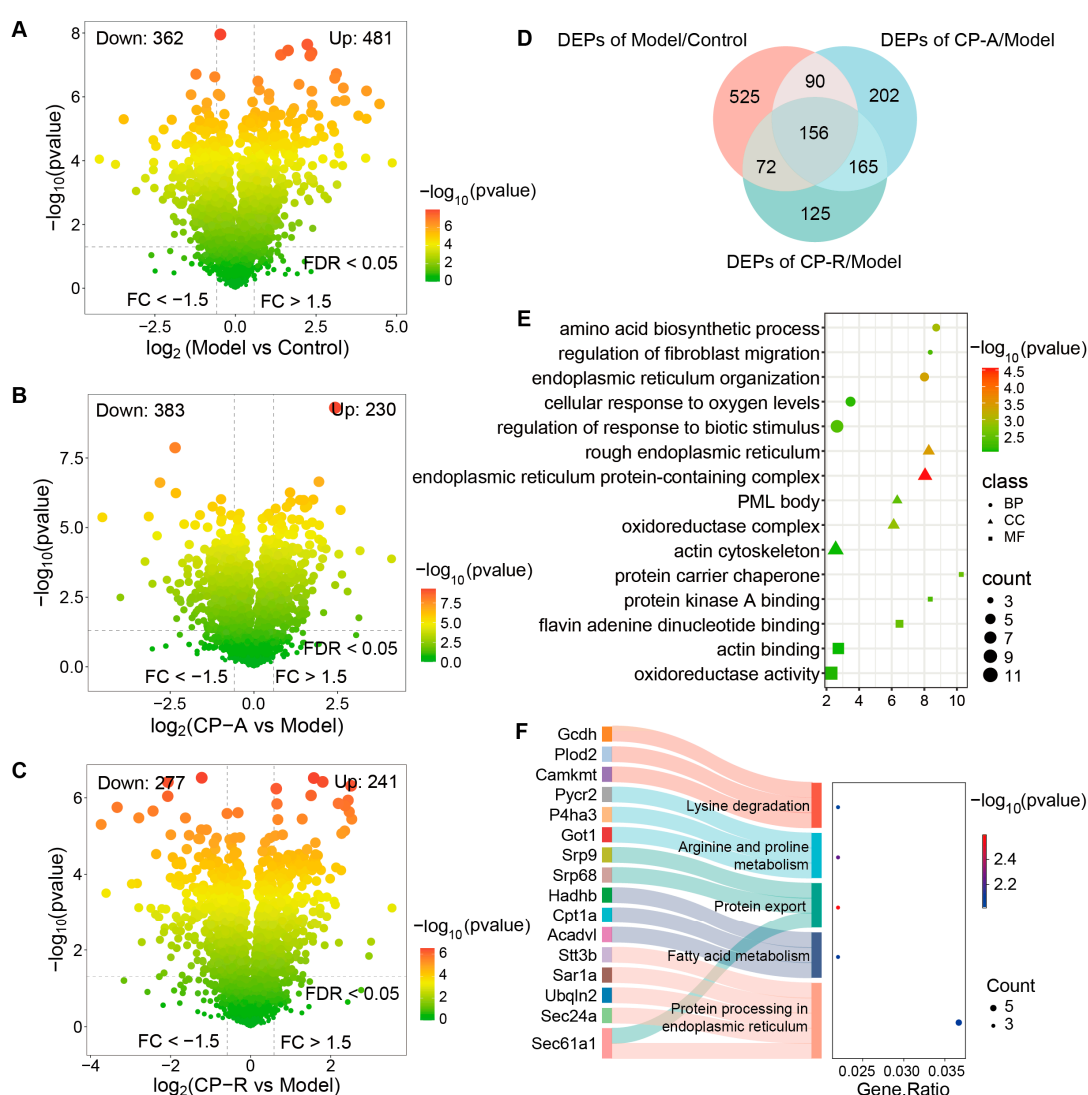


Figure 6. Proteomic profiling and functional enrichment analysis of DEPs in Control, Model, CP-A-treated, and CP-R-treated groups. **(A)** Volcano plot of DEPs in the Model and Control comparison (FDR < 0.05 and $|\log_2\text{FC}| > 0.585$). **(B)** Volcano plot of DEPs in the CP-A and Model comparison (FDR < 0.05 and $|\log_2\text{FC}| > 0.585$). **(C)** Volcano plot of DEPs in the CP-R and Model comparison (FDR < 0.05 and $|\log_2\text{FC}| > 0.585$). **(D)** Venn diagram showing the common DEPs (156) identified across comparisons. **(E)** GO enrichment analysis of the 156 intersecting DEPs, categorized into BP, CC, and MF. **(F)** KEGG pathway enrichment analysis of the 156 intersecting DEPs.

2.7. Transcriptomic Analysis Reveals MAPK-Centered Regulatory Networks in CP-A and CP-R Treatment

Transcriptomic profiling was performed to investigate transcriptional changes associated with CP treatment under OGD/R conditions. As shown in Figure 7A,B (FDR < 0.05 and $|\log_2FC| > 0.585$; Dataset S2), both CP-A and CP-R significantly altered gene expression compared with the model group, with numerous genes up- or downregulated. KEGG pathway enrichment analysis (Figure 7C,D) indicated predominant involvement of pathways related to oxidative stress, inflammation, and survival signaling. Among these, MAPK signaling was consistently enriched in both treatment groups. Gene set enrichment analysis (GSEA) further demonstrated significant negative enrichment of MAPK-related gene sets in CP-A- and CP-R-treated cells compared with the model group (Figure 7E,F). Together, these results indicate that CP-A and CP-R modulate overlapping stress-responsive transcriptional programs, including pathways linking redox imbalance and inflammatory activation.

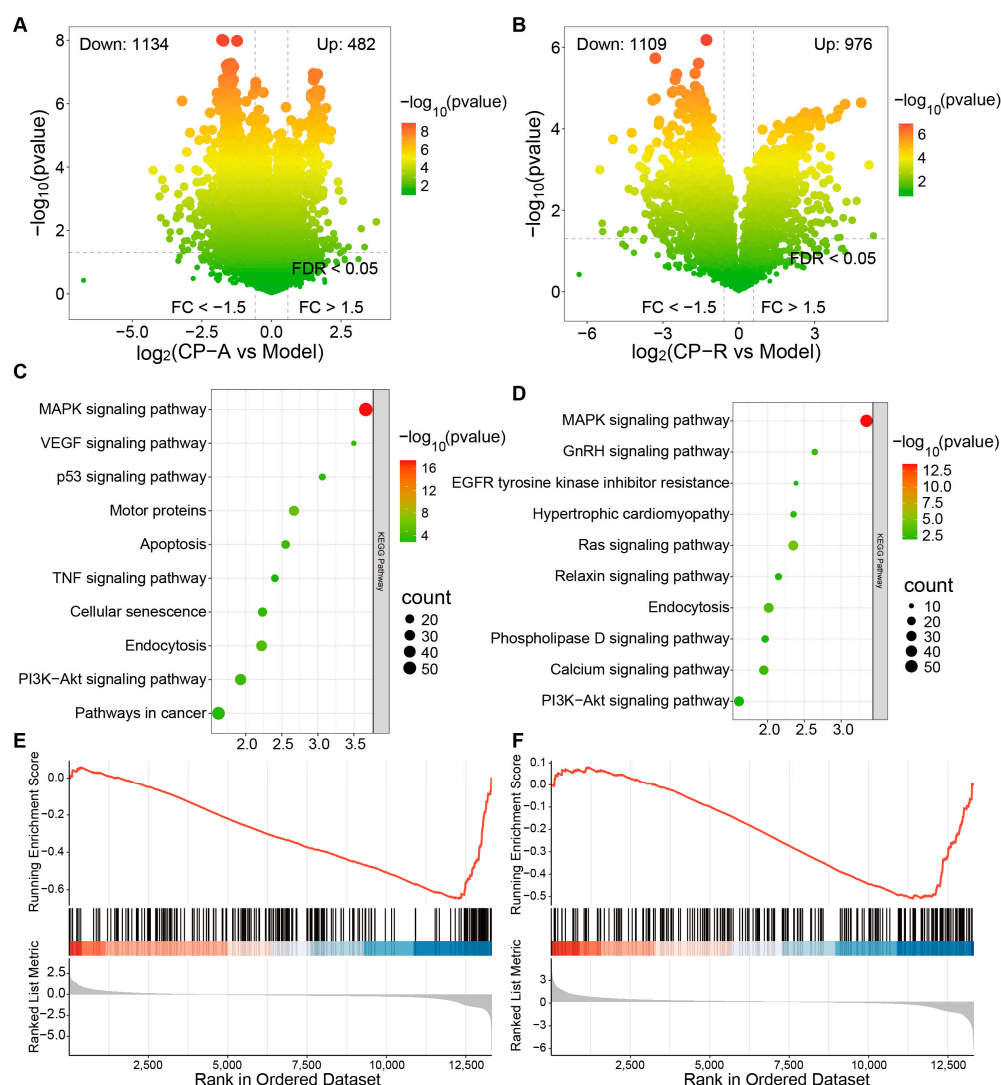


Figure 7. Transcriptomic profiling and pathway enrichment analysis of CP-A and CP-R treatment in OGD/R-injured H9c2 cells. (A) Volcano plot of DEGs in the CP-A vs. Model comparison (FDR < 0.05 and $|\log_2FC| > 0.585$). (B) Volcano plot of DEGs in the CP-R vs. Model comparison (FDR < 0.05 and $|\log_2FC| > 0.585$). (C) KEGG pathway enrichment analysis of significantly enriched pathways in the CP-A vs. Model comparison. (D) KEGG pathway enrichment analysis of significantly enriched pathways in the CP-R vs. Model comparison. (E) GSEA demonstrating significant negative enrichment of the MAPK signaling pathway in the CP-A vs. Model comparison. (F) GSEA

demonstrating significant negative enrichment of the MAPK signaling pathway in the CP-R vs. Model comparison.

2.8. Shared Downregulated Genes Suggest Convergent Modulation of MAPK-Related Signaling

Comparison of downregulated transcripts revealed 290 genes commonly suppressed by CP-A and CP-R (Figure 8A), suggesting a high degree of convergence in their regulatory profiles. GO enrichment (Figure 8B) linked these genes to protein phosphorylation, MAPK cascade regulation, and oxidative stress response, with CC terms enriched in plasma membrane complexes and cytoskeletal components. Cytoscape visualization (Figure 8C) indicated that the MAPK signaling pathway represented a major enriched node, functionally related to Ras, cGMP–PKG, and calcium signaling pathways involved in cellular stress responses. These findings support an association between CP treatment and altered transcriptional regulation of MAPK-centered stress signaling networks.

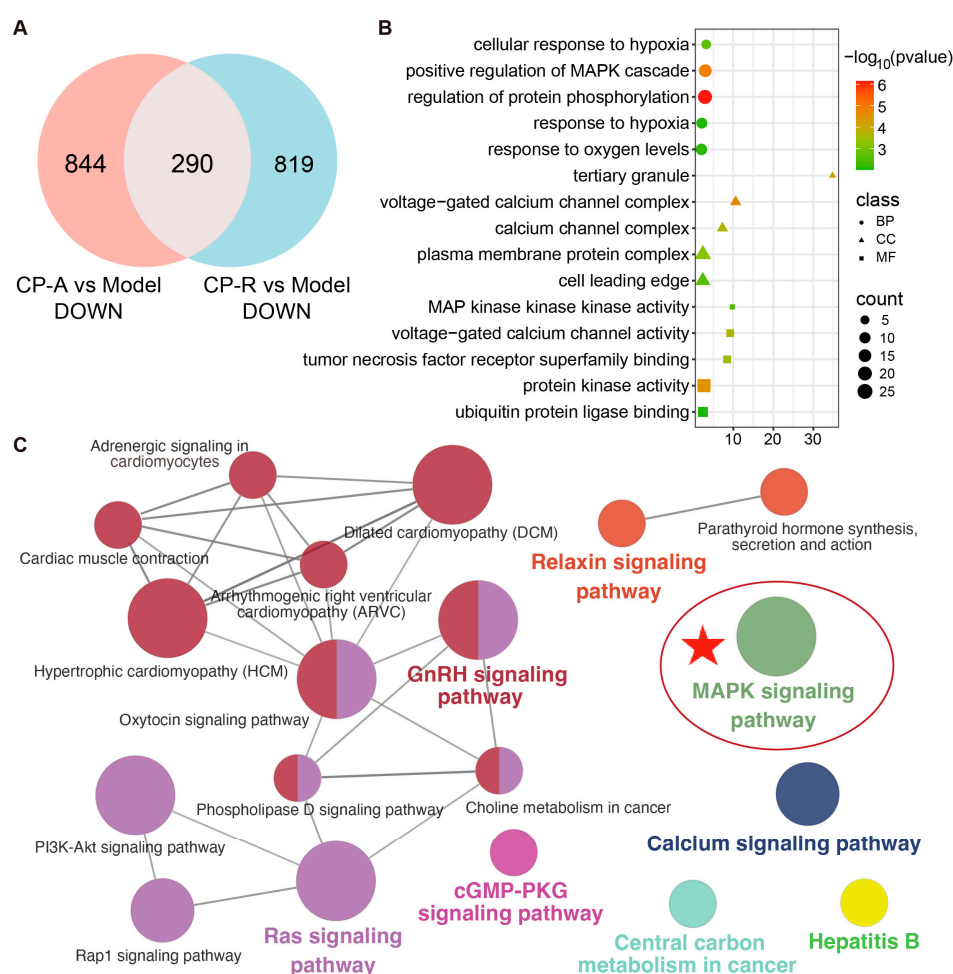


Figure 8. Common downregulated genes and integrated functional enrichment analysis shared by CP-A and CP-R treatments. (A) Venn diagram illustrating the overlap of downregulated DEGs between the CP-A vs. Model and CP-R vs. Model comparisons. (B) GO enrichment analysis of the 290 intersecting genes, showing significantly enriched terms in the BP, CC, and MF categories. (C) Cytoscape visualization of enriched KEGG pathway networks derived from the shared downregulated genes. The MAPK signaling pathway emerged as a central enriched node within stress-related signaling networks, which is marked by a star.

2.9. CP-A and CP-R Attenuate MAPK/NF- κ B Signaling Activation in OGD/R-Injured H9c2 Cells

Given the recurrent enrichment of MAPK-related pathways across multi-omics analyses, we further evaluated key signaling components by Western blot. OGD/R markedly increased phosphorylation of NF- κ B p65 and p38 MAPK and elevated MyD88 and CEBPB expression, consistent with activation of inflammatory and stress-related signaling (Figure 9A). Treatment with CP-A or CP-R significantly reduced phosphorylation ratios (p-p65/p65, p-p38/p38; Figure 9B,D) and downregulated MyD88 and CEBPB expression (Figure 9C,E). The magnitude of inhibition was comparable between treatments, suggesting comparable regulatory effects. Collectively, these results suggest that both root- and aerial-derived CPs are associated with attenuation of redox-sensitive MAPK/NF- κ B signaling under OGD/R conditions, consistent with their modulation of stress-responsive networks identified in omics analyses.

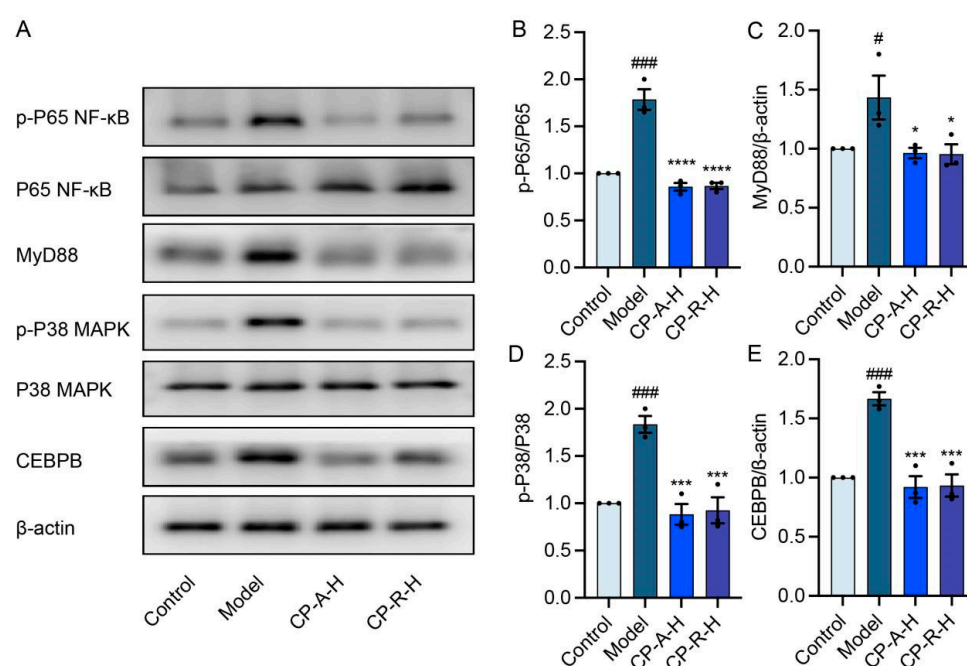


Figure 9. Validation of MAPK/NF- κ B pathway modulation by CP-A and CP-R in H9c2 cells. (A) Expression of p-P65 NF- κ B, P65 NF- κ B, MyD88, p-P38 MAPK, P38 MAPK, and CEBPB proteins detected by Western blot. (B–E) Quantitative analysis of p-P65/P65, MyD88/β-actin, p-P38/P38, and CEBPB/β-actin protein expression levels. Data are presented as means ± SEM ($n = 3$). # $p < 0.05$, ### $p < 0.001$ vs. Control group; * $p < 0.05$, *** $p < 0.001$, **** $p < 0.0001$ vs. Model group (one-way ANOVA, Tukey's HSD post hoc test).

3. Discussion

Plant-derived polysaccharides have attracted increasing interest as functional food ingredients owing to their antioxidant and anti-inflammatory properties [23]. Chicory is widely used in the food industry, particularly as a source of inulin. However, the biological activities of polysaccharides derived from different plant parts have not been systematically compared in cardiomyocyte-relevant models. In this study, we compared polysaccharide-enriched fractions from chicory aerial parts (CP-A) and roots (CP-R). Compositional characterization was integrated with multi-omics-based mechanistic analysis in an OGD/R-induced H9c2 injury model. Despite clear compositional differences, the two fractions exhibited broadly comparable cytoprotective effects.

From a compositional standpoint, CP-A displayed a lower apparent average molecular weight than CP-R, suggesting enrichment of lower-degree polysaccharides in the

aerial fraction [24]. As molecular weights were estimated by GPC using PEG standards, the values reported here represent apparent molecular weights based on calibration curves rather than absolute molecular masses. Fructans constitute a structurally heterogeneous family of β -(2 $\rightarrow$ 1)-linked fructose polymers with variable degrees of polymerization, ranging from short-chain fructooligosaccharides to higher-molecular-weight inulin-type polymers [25]. Therefore, the lower apparent molecular weight of CP-A reflects differences in polymerization degree within fructan-type carbohydrates, rather than the absence of polymeric structures. FT-IR analysis further supported compositional divergence between the two fractions. CP-A exhibited a stronger absorption band near 1590 cm^{-1} , whereas CP-R showed characteristic furanose-associated signals consistent with inulin-type fructans. Monosaccharide analysis also revealed clear differences: fructose predominated in CP-R, while CP-A exhibited a more heterogeneous sugar profile. These results demonstrate distinct carbohydrate compositions between aerial- and root-derived fractions. Such tissue-specific variation is consistent with reported polysaccharides isolated from *Aconitum carmichaelii*, *Camellia oleifera* and *Stemona tuberosa* [26–28].

Notwithstanding these compositional differences described above, CP-A and CP-R conferred comparable protection against OGD/R-induced injury in H9c2 cells. Both fractions improved cell viability and attenuated elevations in CK-MB, cTnT, and 8-OHdG, indicating attenuation of oxidative stress-associated damage. These findings suggest that cytoprotective activity is not restricted to root-derived inulin-type fructans but is also retained in aerial-derived polysaccharide fractions. This observation aligns with previous reports demonstrating the anti-inflammatory and antioxidant effects of chicory extracts via modulation of MAPK/NF- κ B signaling in LPS-stimulated macrophages and hepatocyte injury models [29]. Similar redox-regulating effects have also been described for polysaccharides from *Dendrobium officinale* and *Glycyrrhiza uralensis* [30,31].

To further clarify the central mechanism underlying these protective effects, we reorganized the multi-omics interpretation around a redox-sensitive inflammatory signaling axis centered on MAPK and NF- κ B pathways. It showed that MAPK/NF- κ B signaling was prioritized as the central mechanistic framework based on consistent enrichment across transcriptomic and proteomic datasets, including convergent KEGG enrichment, GSEA results, and shared downregulated gene clusters. Given that ischemia–reperfusion injury is characterized by excessive reactive oxygen species generation and secondary inflammatory activation, the recurrent enrichment of MAPK/NF- κ B pathways likely reflects coordinated modulation of redox-driven inflammatory cascades rather than isolated pathway activation [32,33]. Western blot validation further supported this convergence, demonstrating reduced phosphorylation of p38 MAPK and NF- κ B p65, along with decreased expression of MyD88 and CEBPB [32–35]. The concurrent downregulation of MyD88 and CEBPB is consistent with a MYD88–MAPK/NF- κ B–CEBPB-linked regulatory cascade connecting upstream innate immune signaling with downstream inflammatory transcriptional responses. Collectively, these results suggest that CP-A and CP-R are associated with attenuation of redox-linked stress signaling and partial restoration of cellular homeostasis in cardiomyocyte-like cells. Rather than implying selective molecular targeting, the present data support a broader convergence on redox-sensitive stress signaling networks under OGD/R conditions. Further mechanistic studies will be required to define direct molecular targets.

From an application perspective, the comparable cytoprotective effects of CP-A and CP-R support the sustainable utilization of chicory aerial biomass, which is traditionally discarded during industrial processing. These findings provide experimental evidence for the valorization of the whole chicory plant as a source of bioactive polysaccharides for potential functional food and nutraceutical applications. Several limitations should be acknowledged. First, the structural characterization was limited to molecular weight

distribution, monosaccharide composition, and FT-IR analysis, without detailed elucidation of glycosidic linkages or branching patterns. Second, although CP-R was enriched in inulin-type fructans, direct comparison with a commercial inulin standard was not performed, and co-extracted compounds were not independently quantified, leaving the relative contribution of individual carbohydrate fractions to be clarified. In addition, although integrated omics analyses and protein-level validation consistently indicated modulation of redox-sensitive MAPK/NF- κ B signaling, pathway-specific inhibition or genetic perturbation experiments were beyond the scope of the present study. Therefore, the mechanistic conclusions should be interpreted as associative rather than causally definitive. Third, the present findings are derived from an in vitro H9c2 cell model and do not address the in vivo pharmacokinetics, systemic exposure or therapeutic efficacy. Accordingly, the findings should be interpreted as mechanistic and exploratory observations derived from a controlled in vitro model, rather than evidence of therapeutic efficacy in vivo. While emerging evidence suggests that certain polysaccharide fractions may reach systemic circulation [36], the physiological relevance of such mechanisms for chicory-derived fractions remains unclear. Finally, although aerial biomass represents a promising and underutilized resource, additional purification steps may be required for leaf-derived fractions, potentially affecting industrial scalability. Further studies incorporating advanced structural elucidation, in vivo validation, and techno-economic assessment will be necessary to clarify structure–activity relationships and translational feasibility.

4. Materials and Methods

4.1. Materials

The roots and aerial parts of *Cichorium intybus* L. used in this study were obtained from Fengning Pingan High-Tech Industrial Co., Ltd. (Chengde, China). Monosaccharide standards, including arabinose (Ara), galactose (Gal), glucose (Glc), mannose (Man), fructose (Fru), rhamnose (Rha), ribose (Rib), and Xylose (Xyl) were purchased from Shanghai Yuanye Biotechnology Co., Ltd. (Shanghai, China). Other analytical-grade reagents, including dimethyl sulfoxide (DMSO), Dithiothreitol (DTT), Iodoacetamide (IAA), and Triton X-100, were obtained from Sigma-Aldrich (St. Louis, MO, USA). Trypsin (Promega, Madison, WI, USA), Pierce™ Quantitative Colorimetric Peptide Assay Kit (Thermo Fisher Scientific, Waltham, MA, USA), and C18 desalting columns (Thermo Fisher Scientific) were used for LC-MS/MS.

4.2. Preparation of Chicory Polysaccharides (CPs)

Powdered samples (30 g) of chicory aerial parts and roots were extracted with 200 mL of distilled water under reflux for two successive 2 h cycles. The combined aqueous extracts were concentrated under reduced pressure and precipitated overnight with 70% ethanol at 4 °C. The precipitates were collected by centrifugation at 4000 rpm for 10 min, washed repeatedly with ethanol, and subsequently freeze-dried at −80 °C to obtain polysaccharide fractions from the aerial parts (CP-A) and roots (CP-R). No dialysis step was applied.

4.3. Molecular Weight Distribution Analysis

Each polysaccharide sample (5 mg) was dissolved in 1 mL of distilled water and allowed to stand for 1 h to ensure complete dissolution. The solution was filtered through a 0.22 μ m membrane before analysis. Gel permeation chromatography (GPC) was performed on a Waters E2695 system (Waters Corp., Milford, MA, USA) equipped with a refractive index detector. Separation was achieved using an Agilent PL aquagel-OH MIXED-M column (Santa Clara, CA, USA, 7.5 $\times$ 300 mm, 8 μ m) at 40 °C, with distilled

water as the mobile phase at a flow rate of 1.0 mL/min. Linear polyethylene glycol (PEG) standards were used to construct a calibration curve, and molecular weights were calculated based on retention times. The reported values represent apparent molecular weights derived from PEG calibration.

4.4. Monosaccharide Composition Analysis

Monosaccharide composition of CPs was determined using two hydrolysis methods: a low-temperature hydrolysis for thermolabile fructose and a conventional acid hydrolysis for overall monosaccharide profiling. For low-temperature hydrolysis, approximately 5 mg of each sample was mixed with 1 mL of 2 M trifluoroacetic acid (TFA) and incubated at 60 °C for 1 h. The hydrolysates were then evaporated to dryness under a gentle nitrogen stream. For conventional hydrolysis, samples were treated with 2 M TFA at 121 °C for 2 h and then dried under nitrogen. The residues were rinsed with methanol, evaporated again to remove residual acid, and reconstituted in ultrapure water. Monosaccharides were separated using a Dionex™ CarboPac™ PA20 column (150 × 3.0 mm, 10 µm; Thermo Fisher Scientific, Waltham, MA, USA) on a Thermo ICS 5000+ ion chromatography system equipped with an electrochemical detector. Individual monosaccharides were identified and quantified by comparing their retention times with those of standard sugars.

4.5. Fourier Transform Infrared (FT-IR) Spectroscopy Analysis

The functional groups of CP-A and CP-R were analyzed by FT-IR spectroscopy. Briefly, each sample was dried, ground, and thoroughly mixed with spectroscopic-grade KBr powder and pressed into pellets. The FT-IR spectra were recorded using an FT-IR spectrometer (Bruker, Ettlingen, Germany) over the range of 4000–500 cm⁻¹ at a resolution of 4 cm⁻¹.

4.6. Cell Culture

H9c2 rat cardiomyocytes were cultured in Dulbecco's modified Eagle's medium (DMEM; MeilunBio, MA0581, Dalian, China) supplemented with 10% fetal bovine serum (FBS; Mengma Biotechnology Co., Ltd., MN212103, Tianjin, China) and 1% penicillin–streptomycin (MeilunBio, MA0110, Dalian, China). The cells were maintained at 37 °C in a humidified atmosphere containing 5% CO₂.

4.7. Establishment of Oxygen–Glucose Deprivation/Reperfusion (OGD/R) Model and CPs Treatment

When H9c2 cells reached approximately 80–90% confluence, they were seeded into 96-well or 6-well plates and treated with different concentrations (25, 50, and 100 µg/mL) of CP-A and CP-R for 24 h. The culture medium was then replaced with glucose-free DMEM to induce oxygen–glucose deprivation (OGD). Cells were subsequently incubated in an anaerobic chamber (95% N₂, 5% CO₂) at 37 °C for 2 h. Following OGD, the cells were returned to normoxic conditions (95% air, 5% CO₂), the medium was changed back to complete normal culture medium, and they were incubated for an additional 24 h to simulate reperfusion. The concentration range of CP-A and CP-R (25–100 µg/mL) was selected based on preliminary dose–response experiments evaluating cell viability under non-OGD conditions to exclude potential cytotoxicity. Within this range, no significant cytotoxic effects were observed, and protective trends were detectable under OGD/R stress. The selected concentrations are consistent with those commonly used in in vitro studies of plant-derived polysaccharides [19,20].

4.8. Cell Viability Assay

Cell viability was assessed using the Cell Counting Kit-8 (CCK-8; MeilunBio, MA0218, Dalian, China). After 24 h of OGD/R treatment, 10 μ L of CCK-8 reagent was added to each well and incubated at 37 °C for 1 h. Absorbance was measured at 450 nm using a microplate reader (BioTek Instruments, Winooski, VT, USA).

4.9. Measurement of Cardiac Injury Biomarkers

After treatment, the cell supernatant and lysates were collected for biochemical analysis. The levels of creatine kinase–myocardial band (CK-MB), cardiac troponin T (cTnT), and 8-hydroxy-2'-deoxyguanosine (8-OHdG) were determined using commercial assay kits (Nanjing Jiancheng Bioengineering Institute, Nanjing, China; CK-MB: H197-1-2, cTnT: H149-4-2, 8-OHdG: H165-1-2) according to the manufacturer's protocols.

4.10. Transcriptomic Analysis

Samples from the Model group, CP-A-treated group, and CP-R-treated group were collected for transcriptomic sequencing. DEGs were identified from pairwise comparisons between CP-A and the Model group, and between CP-R and the Model group. Genes with an adjusted p -value (FDR) < 0.05 and $|\log_2FC| > 0.585$ were defined as DEGs. For KEGG enrichment analysis, p -values were adjusted using the Benjamini–Hochberg (BH) method, and FDR < 0.05 was considered statistically significant. Volcano plots were generated to visualize DEG distributions in each comparison. KEGG pathway enrichment and GSEA were performed for each comparison. To identify shared inhibitory events, downregulated DEGs common to both comparisons were extracted for intersection analysis. GO functional annotation was then performed on the intersecting gene set. Biological process network visualization and enrichment analysis were conducted in Cytoscape 3.8.0 to identify key biological processes jointly modulated by CP-A and CP-R.

4.11. Proteomic Analysis

Samples from the Control, Model, CP-A, and CP-R groups were collected for proteomic analysis. Pairwise comparisons were performed between Model vs. Control, CP-A vs. Model, and CP-R vs. Model groups. Proteins with an adjusted p -value (FDR) < 0.05 and $|\log_2FC| > 0.585$ were considered statistically significant. DEPs were identified and visualized using volcano plots. KEGG Pathways enrichment analyses were conducted for each comparison. KEGG enrichment p -values were adjusted for multiple testing using the BH method, and FDR < 0.05 was considered statistically significant. The DEPs shared among all three comparisons were extracted to obtain the intersecting protein set, which was further subjected to GO functional enrichment analysis, including BP, CC, and MF categories, to characterize common protein networks.

4.12. Western Blot Analysis

Total cellular proteins were extracted using RIPA lysis buffer (Applygen, C1053, Beijing, China) containing protease and phosphatase inhibitors (Beyotime Biotechnology, P1045, Shanghai, China). Protein concentrations were determined using a bicinchoninic acid (BCA) assay kit (Beyotime Biotechnology, P0012S, Shanghai, China). Equal amounts of protein were separated by SDS-PAGE and transferred to PVDF membranes. The membranes were blocked and incubated overnight at 4 °C with the following primary antibodies: phospho-NF- κ B p65 (Ser536) (Zen BioScience, Chengdu, China, 310013, 1:1000), NF- κ B p65 (Zen BioScience, 250021, 1:1000), MyD88 (Proteintech, Wuhan, China, 67969-1-Ig, 1:1000), phospho-p38 MAPK (Thr180/Tyr182) (Zen BioScience, 310091, 1:1000), p38 MAPK (Zen BioScience, R25239, 1:1000), and CEBPB (Zen BioScience, R380893, 1:1000). After

incubation with HRP-conjugated secondary antibodies, immunoreactive bands were visualized using an enhanced chemiluminescence (ECL) kit (MeilunBio, MA0186, Dalian, China) and imaged with a Syngene GeneGnome XRQ detection system (Cambridge, UK). Band intensities were quantified using GeneTools software version 4.3.14 (Syngene, Cambridge, UK).

4.13. Statistical Analysis

All experiments were performed in triplicate, and results are expressed as mean $\pm$ standard error of the mean (SEM). Statistical analyses were conducted using SPSS software (version 27.0; IBM, Armonk, NY, USA). One-way analysis of variance (ANOVA) followed by the least significant difference (LSD) test was used to determine significance among groups. Data were first assessed for normality using the Shapiro–Wilk test and for homogeneity of variance using Levene’s test. When assumptions were met, one-way ANOVA followed by the least significant difference (LSD) post hoc test was applied. LSD was selected due to the limited number of group comparisons and the exploratory nature of the study. For non-omics experimental data, a p -value < 0.05 was considered statistically significant. Graphs were generated using GraphPad Prism 9.0 (GraphPad Software, San Diego, CA, USA) and OriginPro 2023 (OriginLab Corp., Northampton, MA, USA).

5. Conclusions

In this study, polysaccharide-enriched fractions from chicory aerial parts and roots were systematically compared with respect to their compositional characteristics and biological functions. Despite differences in molecular weight distribution and monosaccharide composition, CP-A and CP-R exhibited comparable antioxidant and cytoprotective effects in an OGD/R-induced H9c2 injury model. Integrated proteomic and transcriptomic analyses revealed overlapping regulation of oxidative stress-responsive and inflammation-related signaling networks, particularly MAPK- and NF- κ B-associated pathways. These results indicate that polysaccharide fractions derived from chicory aerial biomass—traditionally discarded during industrial processing—display bioactivities comparable to those of root-derived fractions. This work supports the comprehensive utilization of the entire chicory plant as a potential source of functional food and nutraceutical ingredients, while underscoring the need for further *in vivo* validation and detailed structural characterization to clarify bioavailability, structure–activity relationships, and translational potential.

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References

1. Perović, J.; Tumbas Šaponjac, V.; Kojić, J.; Krulj, J.; Moreno, D.A.; García-Viguera, C.; Bodroža-Solarov, M.; Ilić, N. Chicory (*Cichorium intybus* L.) as a Food Ingredient—Nutritional Composition, Bioactivity, Safety, and Health Claims: A Review. *Food Chem.* **2021**, *336*, 127676. <https://doi.org/10.1016/j.foodchem.2020.127676>.
2. Janda, K.; Gutowska, I.; Geszke-Moritz, M.; Jakubczyk, K. The Common Chicory (*Cichorium intybus* L.) as a Source of Extracts with Health-Promoting Properties—A Review. *Molecules* **2021**, *26*, 1814. <https://doi.org/10.3390/molecules26061814>.
3. Birsa, M.L.; Sarbu, L.G. Health Benefits of Key Constituents in *Cichorium intybus* L. *Nutrients* **2023**, *15*, 1322. <https://doi.org/10.3390/nu15061322>.
4. Zhao, Y.; Zhang, Y.; Luo, Y.; Chen, F.; Qiang, M.; Liu, M.; Pan, R.; Chang, Q.; Wang, N.; Usmani, M.W.; et al. Anxiolytic Effects of *Cichorium intybus* L. Oligo-Polysaccharides by Modulating Gut Microbiota, Neuronal Signaling Pathways, and Neuroinflammation in Chronic Sleep Deprivation-Stressed Mice. *Foods* **2025**, *14*, 1859. <https://doi.org/10.3390/foods14111859>.
5. Ning, C.; Li, H.; Xu, Y.; Jia, L.; Wang, J.; Li, W.; Tan, C.; Guo, C.; Wang, S.; Liu, X.; et al. Optimization of Compound Enzyme–Ultrasound Extraction of Chicory Polysaccharides and Their Effects on the Quality of Fermented Milk. *Food Chem. X* **2025**, *31*, 103086. <https://doi.org/10.1016/j.fochx.2025.103086>.
6. Duda, Ł.; Budryn, G.; Olszewska, M.A.; Rutkowska, M.; Kruczkowska, W.; Grabowska, K.; Kołat, D.; Jaśkiewicz, A.; Pasieka, Z.W.; Kłosiński, K.K. Evaluation of Inulin and Polyphenol Content and the Cytotoxicity of *Cichorium Intybus* L. Var. *Foliosum* Root Extracts Obtained by Pectinase- and Pressure-Assisted Extraction. *Nutrients* **2025**, *17*, 1040. <https://doi.org/10.3390/nu17061040>.
7. Akram, H.; Zafar, H.; Abbasi, B.H. The Chicory Root (*Cichorium intybus* var. *sativum*) Frontier: Pioneering Biotechnological Advancements. *Phytochem. Rev.* **2025**, *24*, 5659–5683. <https://doi.org/10.1007/s11101-025-10085-x>.
8. Teichenné, J.; Mariné-Casadó, R.; Alcaide-Hidalgo, J.M.; Tchoumtchoua, J.; Leonard, K.; Escoté, X. Photoprotective and Anti-Inflammatory Potential of Polyphenol-Rich Extracts from Agricultural by-Products of Chicory Leaves, Red Onion Peel, Vineyard Pruning, and Olive Pruning in UV-B-Exposed 3D Human Skin Equivalents. *J. Agric. Food Res.* **2025**, *23*, 102201. <https://doi.org/10.1016/j.jafr.2025.102201>.
9. Al-haliem, S.M.; Mohammed, M.J.; Abedelmaksoud, T.G.; Hesarinejad, M.A.; Baioumy, A.A. Chicory (*Cichorium intybus*) Leaves Extract: Phenolic Composition, Antibacterial Activity, and Antioxidant Capacity Assessment. *Food Sci. Nutr.* **2025**, *13*, e70550. <https://doi.org/10.1002/fsn3.70550>.
10. Krepkova, L.V.; Babenko, A.N.; Lemyaseva, S.V.; Saybel, O.L.; Sherwin, C.M.; Enioutina, E.Y. Modulation of Hepatic Functions by Chicory (*Cichorium intybus* L.) Extract: Preclinical Study in Rats. *Pharmaceuticals* **2023**, *16*, 1471. <https://doi.org/10.3390/ph16101471>.
11. Jurgobnski, A.; Milala, J.; Jubsiewicz, J.; Zdubnczyk, Z. Composition of Chicory Root, Peel, Seed and Leaf Ethanol Extracts and Biological Properties of Their Non-Inulin Fractions. *Food Technol. Biotechnol.* **2011**, *49*, 40–47.
12. Shad, M.A.; Nawaz, H.; Rehman, T.; Ikram, N. Determination of Some Biochemicals, Phytochemicals and Antioxidant Properties of Different Parts of *Cichorium intybus* L.: A Comparative Study. *J. Anim. Plant Sci.* **2013**, *23*, 1060–1066.
13. Leyane, T.S.; Jere, S.W.; Houreld, N.N. Oxidative Stress in Ageing and Chronic Degenerative Pathologies: Molecular Mechanisms Involved in Counteracting Oxidative Stress and Chronic Inflammation. *Int. J. Mol. Sci.* **2022**, *23*, 7273. <https://doi.org/10.3390/ijms23137273>.

14. Zhang, Z.; Guo, J. Deciphering Oxidative Stress in Cardiovascular Disease Progression: A Blueprint for Mechanistic Understanding and Therapeutic Innovation. *Antioxidants* **2025**, *14*, 38. <https://doi.org/10.3390/antiox14010038>.
15. Zhao, H.; Zhang, S.; Zhang, Y.; Ma, A.; Han, M.; Zhang, J.; Qiu, W.; Xiao, W.; Wang, J.; Liu, D. Rosmarinic Acid Suppresses Keap1/Nrf2 Signaling Pathway via Targeting USP15 to Attenuate Myocardial Ischemia/Reperfusion Injury. *J. Agric. Food Chem.* **2025**, *73*, 31348–31360. <https://doi.org/10.1021/acs.jafc.5c09909>.
16. Singh, M.; Rani, H.; Chopra, H.K. Extraction, Optimization, Purification and Characterization of Inulin from Chicory Roots Using Conventional and Greener Extraction Techniques. *Int. J. Biol. Macromol.* **2025**, *306*, 141385. <https://doi.org/10.1016/j.ijbiomac.2025.141385>.
17. Guo, X.; Wang, Z.; Pi, F.; Pan, R.; Zhao, Z.; Yu, S. Sequential Extraction and Physicochemical Characterization of Polysaccharides from Chicory (*Cichorium intybus*) Root Pulp. *Food Hydrocoll.* **2018**, *77*, 277–285. <https://doi.org/10.1016/j.foodhyd.2017.10.004>.
18. Ramasamy, U.S.; Gruppen, H.; Schols, H.A. Structural and Water-Holding Characteristics of Untreated and Ensiled Chicory Root Pulp. *J. Agric. Food Chem.* **2013**, *61*, 6077–6085. <https://doi.org/10.1021/jf401621h>.
19. Zou, X.; Cai, J.; Xiao, J.; Zhang, M.; Jia, X.; Dong, L.; Hu, K.; Yi, Y.; Zhang, R.; Huang, F. Purification, Characterization and Bioactivity of Different Molecular-Weight Fractions of Polysaccharide Extracted from Litchi Pulp. *Foods* **2023**, *12*, 194. <https://doi.org/10.3390/foods12010194>.
20. Zeng, W.; Chen, L.; Xiao, Z.; Li, Y.; Ma, J.; Ding, J.; Yang, J. Comparative Study on the Structural Properties and Bioactivities of Three Different Molecular Weights of *Lycium barbarum* Polysaccharides. *Molecules* **2023**, *28*, 701. <https://doi.org/10.3390/molecules28020701>.
21. Xuan, H.-D.; Shen, S.-N.; Fu, C.-J.; Zhou, J.; Chen, R.-X.; Zhang, J.-Z.; Liu, X.-X.; Li, F.-Q.; Zhao, Y.-F.; Zhang, D.; et al. Enhancing the Anti-Inflammatory Efficacy of Polysaccharides through Processing Techniques: A Case Study on *Atractylodes macrocephala*. *Nat. Prod. Res.* **2025**, 1–9. <https://doi.org/10.1080/14786419.2025.2548615>.
22. Zhang, X.; Hu, P.; Zhang, X.; Li, X. Chemical structure elucidation of an inulin-type fructan isolated from *Lobelia chinensis* Lour with anti-obesity activity on diet-induced mice. *Carbohydr. Polym.* **2020**, *240*, 116357. <https://doi.org/10.1016/j.carbpol.2020.116357>.
23. Wang, X.-F.; Chen, X.; Tang, Y.; Wu, J.-M.; Qin, D.-L.; Yu, L.; Yu, C.-L.; Zhou, X.-G.; Wu, A.-G. The Therapeutic Potential of Plant Polysaccharides in Metabolic Diseases. *Pharmaceuticals* **2022**, *15*, 1329. <https://doi.org/10.3390/ph15111329>.
24. Liu, W.; Jiang, J.; Tang, Z.; Yang, Z.; Qin, J. De Novo Transcriptome Sequencing Analysis Revealed the Expression Patterns of Genes in Different Organs and the Molecular Basis of Polysaccharide Synthesis in *Bletilla striata*. *Genes* **2025**, *16*, 558. <https://doi.org/10.3390/genes16050558>.
25. Apolinário, A.-C.; de Lima Damasceno, B.-P.-G.; de Macêdo Beltrão, N.-E.; Pessoa, A.; Converti, A.; da Silva, J.-A. Inulin-type fructans: A review on different aspects of biochemical and pharmaceutical technology. *Carbohydr. Polym.* **2014**, *101*, 368–378.
26. Fu, Y.-P.; Li, C.-Y.; Zou, Y.-F.; Peng, X.; Paulsen, B.S.; Wangenstein, H.; Inngjerdingen, K.T. Bioactive Polysaccharides in Different Plant Parts of *Aconitum carmichaelii*. *J. Sci. Food Agric.* **2024**, *104*, 746–758. <https://doi.org/10.1002/jsfa.12967>.
27. Feng, S.; Tang, M.; Jiang, Z.; Ruan, Y.; Liu, L.; Kong, Q.; Xiang, Z.; Chen, T.; Zhou, L.; Yang, H.; et al. Optimization of Extraction Process, Structure Characterization, and Antioxidant Activity of Polysaccharides from Different Parts of *Camellia oleifera* Abel. *Foods* **2022**, *11*, 3185. <https://doi.org/10.3390/foods11203185>.
28. Qiu, X.; Ou, Y.; Lu, S.; Liang, Y.; Zhang, Y.; Li, M.; Li, G.; Ma, H.; Wu, Y.; He, Z.; et al. Study of the Structure and Bioactivity of Polysaccharides from Different Parts of *Stemona tuberosa* Lour. *Molecules* **2024**, *29*, 1347. <https://doi.org/10.3390/molecules29061347>.
29. Bayazid, A.B.; Park, S.H.; Kim, J.G.; Lim, B.O. Green Chicory Leaf Extract Exerts Anti-Inflammatory Effects through Suppressing LPS-Induced MAPK/NF-κB Activation and Hepatoprotective Activity in Vitro. *Food Agric. Immunol.* **2020**, *31*, 513–532. <https://doi.org/10.1080/09540105.2020.1742667>.
30. Zhang, J.; Guo, Y.; Si, J.; Sun, X.; Sun, G.; Liu, J. A Polysaccharide of *Dendrobium officinale* Ameliorates H₂O₂-Induced Apoptosis in H9c2 Cardiomyocytes via PI3K/AKT and MAPK Pathways. *Int. J. Biol. Macromol.* **2017**, *104*, 1–10. <https://doi.org/10.1016/j.ijbiomac.2017.05.169>.
31. Niu, P.; Zhang, X.; Zhang, G.; Jing, R.; Qiao, Y.; Zhou, X.; Bai, M.; Peng, L. A Polysaccharide from *Glycyrrhiza uralensis* Attenuates Myocardial Fibrosis via Modulating the MAPK/PI3K/AKT Signaling Pathway. *Int. J. Biol. Macromol.* **2025**, *286*, 138207. <https://doi.org/10.1016/j.ijbiomac.2024.138207>.
32. Wang, X.; Liu, R.; Liu, D. The Role of the MAPK Signaling Pathway in Cardiovascular Disease: Pathophysiological Mechanisms and Clinical Therapy. *Int. J. Mol. Sci.* **2025**, *26*, 2667. <https://doi.org/10.3390/ijms26062667>.

33. Ghiasi, M. Investigating the NF- κ B Signaling Pathway in Heart Failure: Exploring Potential Therapeutic Approaches. *Heliyon* **2024**, *10*, e40812. <https://doi.org/10.1016/j.heliyon.2024.e40812>.
34. Oh, Y.J.; Jin, S.E.; Shin, H.-K.; Ha, H. Daeshiho-Tang Attenuates Inflammatory Response and Oxidative Stress in LPS-Stimulated Macrophages by Regulating TLR4/MyD88, NF- κ B, MAPK, and Nrf2/HO-1 Pathways. *Sci. Rep.* **2023**, *13*, 18891. <https://doi.org/10.1038/s41598-023-46033-y>.
35. Tian, Z.; Wu, X.; Zhang, B.; Li, W.; Wang, C. Transcription Factor CEBPB Mediates Intracranial Aneurysm Rupture by Inflammatory and Immune Response. *CNS Neurosci. Ther.* **2024**, *30*, e14603. <https://doi.org/10.1111/cns.14603>.
36. Liao, W.; Cao, D.; Wang, Y.; Du, Z.; Yao, J.; Dou, P.; Zheng, Y.; Wang, Z.; Chen, X.; Wang, P.; et al. 1,3-and 1,4-linked polysaccharides uptake in intestinal cells relies on clathrin/dynamin 1/Rab5-dependent endocytosis. *Nat. Commun.* **2026**, *17*, 1831. <https://doi.org/10.1038/s41467-026-68542-w>.

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