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Network Pharmacology Analysis of Phytochemicals Targeting PCOS - Associated Genes: A Bioinformatics Approach to Therapeutic Intervention

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Abstract

Polycystic ovary syndrome (PCOS) involves dysregulation of miR-200b/ZEB and PI3K pathways. Using network pharmacology with STITCH/STRING databases, we identified 8 phytochemicals targeting key PCOS genes (ESR1, ESR2, PIK3CA, ZEB1, ZEB2) and hsa-miR-200b-3p. Analysis revealed 14 high-confidence interactions (mean score: 0.831). Genistein showed maximal estrogen receptor binding (0.996), while quercetin and curcumin demonstrated dual targeting of reproductive and metabolic pathways. This systems-level approach identifies multi-target phytochemicals restoring the miR-200b feedback loop for improving PCOS reproductive outcomes.

Introduction

Background

- **PCOS** affects 8-13% of reproductive-age women with **hormonal dysregulation and impaired ovarian function**
- Dysregulation of **miR-200b/ZEB** axis and **PI3K signaling** impair follicle development
- **Phytochemicals** offer multi-target therapeutic alternatives

? Research Gap

- ? **Individual phytochemicals** show limited efficacy due to narrow target specificity
- ? **Multi-target mechanisms** of phytochemicals in PCOS remain poorly understood
- ? Integrated understanding of **compound-pathway networks** is lacking

Study Objective

- Identify phytochemicals simultaneously targeting miR-200b/ZEB and PI3K pathways
- Elucidate molecular mechanisms for restoring ovarian homeostasis in PCOS

Materials and methods

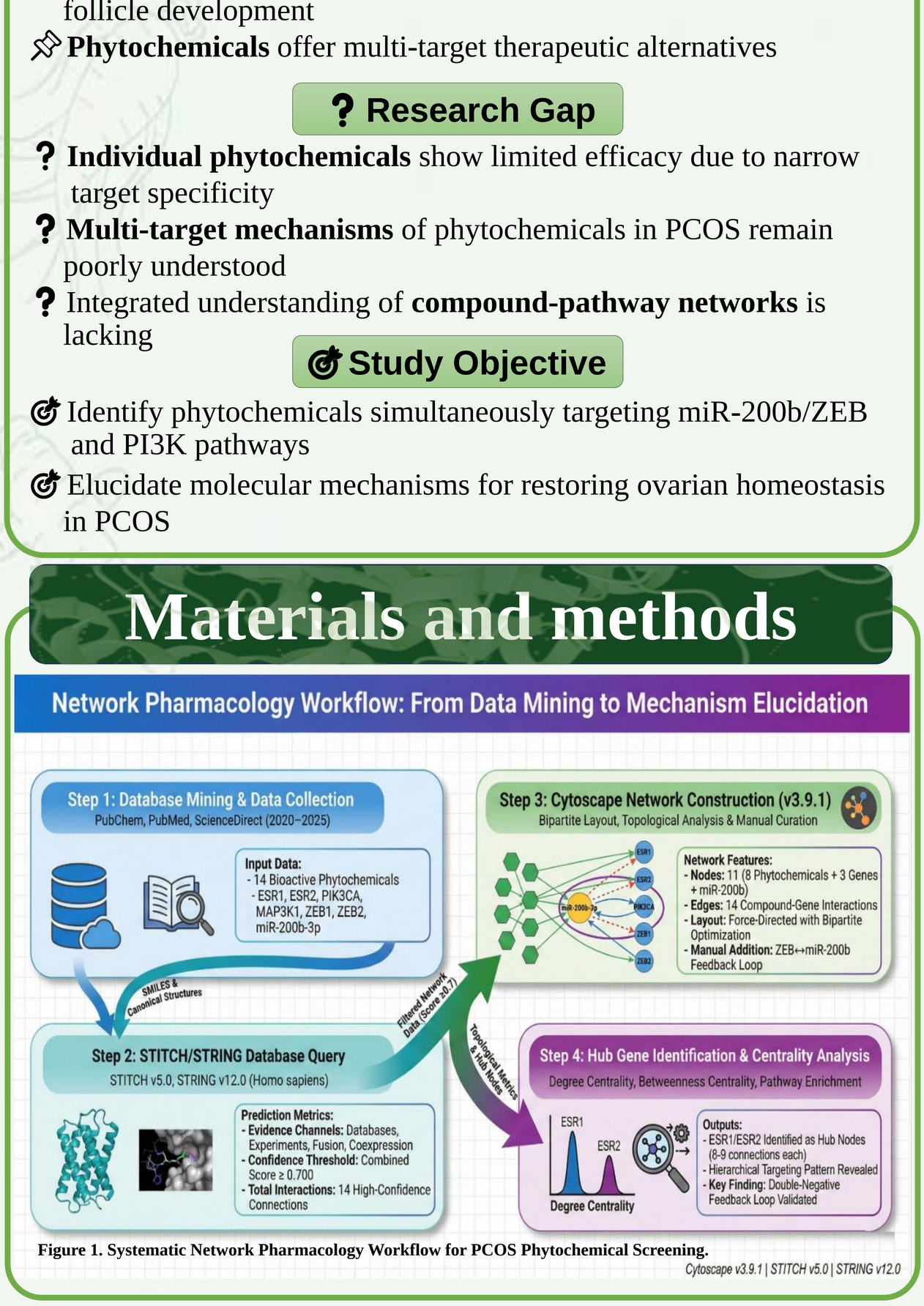


Figure 1. Systematic Network Pharmacology Workflow for PCOS Phytochemical Screening.

Results and discussion

Construction of Phytochemical-Gene Interaction Network

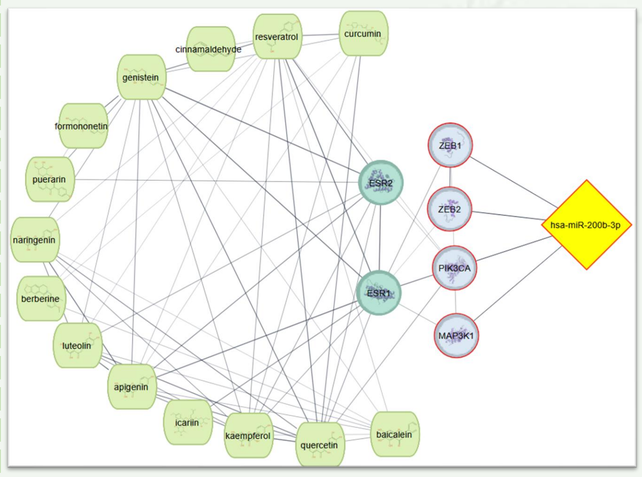


Figure 2. Compound-target interaction network in Cytoscape showing phytochemicals.

Network Construction

- 14 high-confidence compound-gene interactions
- 8 phytochemicals targeting 3 key genes (ESR1, ESR2, PIK3CA) + miR-200b-3p

Key Findings

- **Genistein & Resveratrol:** maximal estrogen receptor binding
- **Quercetin & Kaempferol:** dual targeting of ESR and PI3K pathways
- Phytochemicals activate ESR → suppress ZEB → restore miR-200b feedback loop

Hierarchical Mechanism

- ESR1/ESR2 act as hub nodes
- Multi-target compounds show superior synergistic potential

Quantitative Analysis of Binding Affinities

Phytochemical-Target Binding Affinity Profile

Combined Confidence Scores from STITCH/STRING Database

	ESR1 *(Estrogen Receptor 1)*	***ESR2*** *(Estrogen Receptor 2)*	***PIK3CA*** *(Phosphatidylinositol 3-Kinase)*
Genistein	0.996 ★★★	0.996 ★★★	-
Resveratrol	0.991 ★★★	0.945	-
Quercetin	0.847	0.961	-
Curcumin	-	-	0.841
Kaempferol	0.726	0.743	0.723
Apigenin	0.725	0.736	-
Luteolin	0.700	-	-

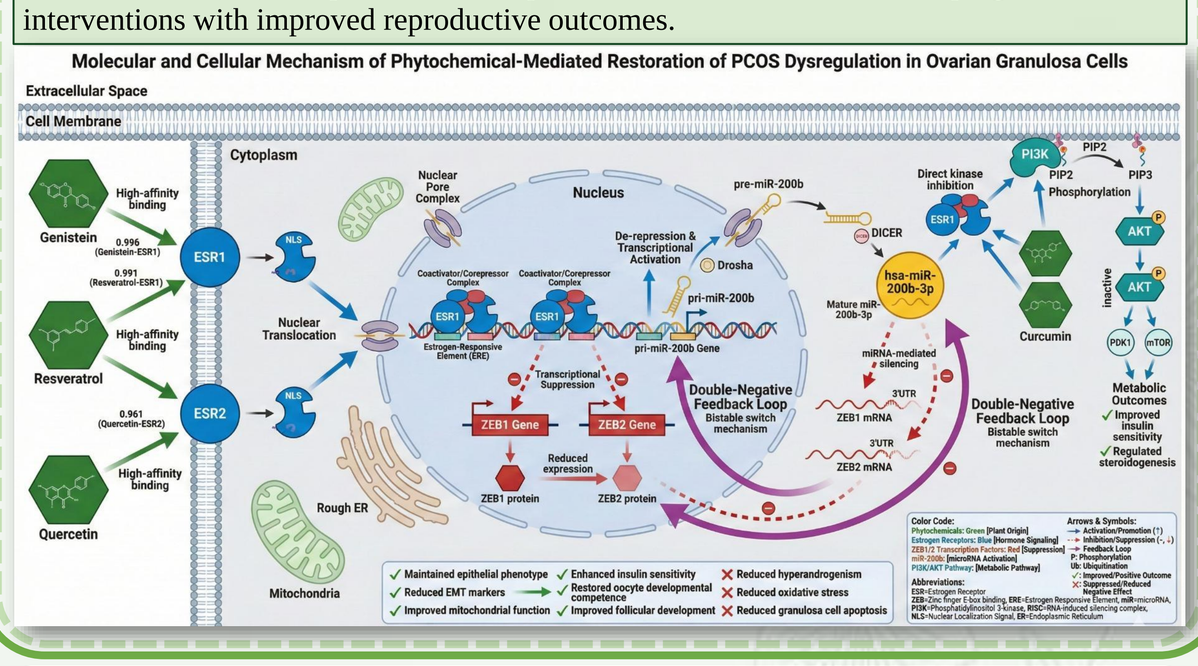
Binding Affinity Scale

- 0.99-1.00: Maximal/Near-maximal binding
- 0.94-0.99: High affinity
- 0.84-0.94: Moderate-high affinity
- 0.70-0.84: Moderate affinity (Confidence threshold)
- — No interaction/Below threshold

- **Maximal estrogen receptor binding**: Genistein (0.996) and Resveratrol (0.991) demonstrate high-affinity phytoestrogenic activity
- **Polypharmacological compounds**: Quercetin and Kaempferol show dual targeting of reproductive (ESR1/ESR2) and metabolic (PIK3CA) pathways
- **Mean network confidence score**: 0.831 ± 0.082 (14 high-confidence interactions, threshold ≥0.700)

Conclusion

Network pharmacology analysis identified 8 bioactive phytochemicals targeting the dysregulated miR-200b/ZEB axis and PI3K pathway in PCOS. Genistein and resveratrol exhibited maximal estrogen receptor binding (score 0.996), while multi-target compounds addressed both reproductive and metabolic dysfunction. This systems-level approach rationalizes herbal therapeutic use and provides a framework for developing novel PCOS interventions with improved reproductive outcomes.



References

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