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Original Research Article

Network pharmacology integrated molecular docking demonstrates the therapeutic mode of Panax ginseng against ovarian cancer

Xiao-Fei Sun[1], Salam Pradeep Singh[2]*
[1]Chinese Medicine Pharmacy, Beijing Jishuitan Hospital, 31 Xinjiekou East Street, Xicheng District, Beijing, 100035, China
[2]Suchee Bioinformatics Institute, Imphal West, Pin-795001, Manipur, India

For correspondence: **Email: salampradeep@gmail.com; **Tel:** +91-8486268935*

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Abstract

Purpose: *To investigate the mode of action of the active ingredients of Panax ginseng against ovarian cancer protein targets elucidated using a network pharmacology approach and molecular docking study.*
Methods: *An integrated protein-protein interactions (PPI) network targeting ovarian cancer and P. ginseng was constructed using a network pharmacology approach and molecular docking was carried out for the active constituents of P. ginseng against the target protein of P. ginseng.*
Results: *Ninety-six compounds were used for the molecular docking simulation against five different proteins from a PPI network of proteins linked to ovarian cancer. The protein-ligand interaction showed strong molecular interaction at the active site of the proteins ($p < 0.05$).*
Conclusion: *Ginsenosides and their derivatives present in P. ginseng successfully inhibit several key enzymes and proteins associated with ovarian cancer, which may act as potential therapeutic targets for the disease.*

Keywords: *Ginseng, Ovarian cancer, Network pharmacology, Docking, Ginsenosides*

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INTRODUCTION

Panax ginseng is the most common and popular herb among ginseng and has a broad range of therapeutic and pharmacological purposes [1]. Ginsengs are among the most valued herbs in ancient China, Japan, and Korea and are regarded as multipurpose herbs that can be used to treat different diseases [2]. The ginsengs were believed to be used by the Emperors of China and were thought to be discovered in the hilly regions of Manchuria in China [3]. In recent times, ginseng was also discovered and thought to be cultivated in mountainous and hilly areas. The herbal preparations of ginseng have become the most popular and best-selling herbal medicines in China in recent times and are used to treat a wide range of medical conditions [5].

In ancient times, herbs and medicinal plants played an important role in human health and provided various benefits in the treatment of a wide range of diseases and disorders [6]. Moreover, they are often used in customary

rituals and traditions because of their healing properties [7]. However, the effective dosage of these herbs is also important, and ancient herbal practitioners are aware of their toxicity dose and lethal doses [8]. In general, there are mainly two varieties of ginseng that can be cultivated i.e., red ginseng and white ginseng. The red ginseng variety which is of Korean origin is mostly cultivated in the European region while the white variety is of Chinese origin [9].

Several countries have commercially started the cultivation of Asian ginseng (*Panax ginseng* C.A. Meyer) and it is grown in more than 40 countries [10]. Modern analytical methods have identified about 110 chemical substances derived from ginseng species and their metabolites. The chemical entities isolated from various ginseng species were classified into different groups based on their structural similarities and possess specific bioactivities against various diseases [11]. To date, approximately 40 types of ginsenosides have been isolated from different parts of *P. ginseng* and their chemical structures were analyzed using infrared spectroscopy and mass spectrometry [11]. Ginseng is also considered one of the most widely used herbal formulations available in the Chinese market and is reported to have a broad range of therapeutic and pharmacological applications [12].

Ovarian, cancer is a type of gynecologic malignancy with abnormal cells in the ovary that may spread to the surrounding areas [13]. It is one of the most serious types of cancer with a cure rate of 30 % and a very high mortality rate due to chemoresistance. The major cause of ovarian carcinoma is linked to genetic and epigenetic factors and multiple studies have proposed that oxidative stress is involved in the progression and development of ovarian carcinoma [14-16]. One of the most important players involved in chemoresistance onset and cancer progression is the Nuclear Factor Erythroid 2-Related Factor 2 (NFE2L2 or NRF2) [17].

In this study, the mode of action of various constituents of *P. ginseng* against ovarian cancer was elucidated using a network pharmacology approach and molecular docking study. To date, very few reports are available on the therapeutic potential of *P. ginseng* against ovarian cancer and its mechanism of action thus more exploration is required using computational tools and techniques before starting experimental research to save cost and time. Furthermore, molecular docking approaches will help in determining the potential action of active compounds that interact with possible protein targets in humans in the treatment of ovarian cancer.

METHODS

Chemical compounds of *Panax ginseng*

A search was carried out in the Traditional Chinese Medicine Systems Pharmacology Database and Analysis Platform (TCMSP, http://tcmspw.com/index.php) to retrieve the major chemical compounds present in *P. ginseng*. All compounds associated with *P. ginseng* were optimized using MM2 force fields in Chemoffice 2010 (Perkin Elmer, USA) and converted to Sybyl mol2 format. The protein targets linked to the bioactive compounds were extracted, and their PDB IDs and UniProt IDs were retrieved.

Target proteins of *Panax ginseng*

The potential protein targets of *P. ginseng* were determined using the Genecards database and proteins were extracted. This was followed by constructing a protein-protein interactions (PPI) network using Cytoscape (Cytoscape 3.9, USA).

Target proteins of ovarian cancer

The target proteins of *P. ginseng* associated with various types of diseases were identified using SuperPred (http://prediction.charite.de) and the protein associated with ovarian cancer was selected for further analysis. The 3D structures of these proteins were retrieved from the Protein Databank.

Construction of interactions networks

The core targets of ovarian cancer and the bioactive compounds present in *P. ginseng* were used to construct the PPI network. Furthermore, a herb–component network was constructed using the data from the TMCH database and established the interaction between *P. ginseng* and its active compounds. The component–target–pathway network was also constructed using Cytoscape version 3.9 (http://www.cytoscape.org/).

Molecular docking study

Molecular docking simulation was carried out using MVD 7.0 (Molexus IVS, Denmark) for the targeted proteins associated with ovarian cancer. In all cases, initially, the potential ligand-binding site and its active site were predicted. First, 3D X-ray structures of the target were retrieved and the structures were prepared using Protein

Preparation Tool. Potential ligand binding sites or the active site residues of the protein were predicted using the Cavity Detection tool and bond flexibility and side chain flexibility of the protein for the active site search space were set with 1.0 tolerance and 0.90 strength. The root mean squared deviation (RMSD) threshold was set at 2.00 A for multiple cluster poses and the algorithm was set with a maximum of 1,000 iterations and a simplex evolution size of 50. For each compound at least 50 docking engine runs were performed for better accuracy of the docking simulation. The most accurate and stable poses were carried forward for ligand-protein interaction energy analysis.

Statistical analysis

All statistical analyses were carried out using Molegro Data Modeller 2.0 (Molexus IVS, Denmark) and MS Excel 2010 (Microsoft, Inc, USA). All results are expressed as mean ± standard deviation (SD). A *p*-value of < 0.05 was considered statistically significant.

RESULTS

Active constituents of *P. ginseng*

The details of the exclusive and active ingredients present in *P. ginseng* (95 compounds) were retrieved from the Traditional Chinese Medicine Systems Pharmacology Database and Analysis Platform (TCMSP). Furthermore, other pharmacokinetic parameters required in the drug discovery processes such as oral bioavailability (OB), drug-likeness (DL) Caco-2, blood-brain barrier (BBB), and fractional negative accessible surface area (FASA) were also observed.

Target proteins of *Panax ginseng*

The network of protein targets of *P. ginseng* retrieved from the STICH database and their protein description are presented in Figure 1. It is observed that *P. ginseng* is associated with 8 major proteins viz. CYP2E1, GSTA2, HMOX1, IL6, MLANA, SERPINE1, TYR and VEGFA.

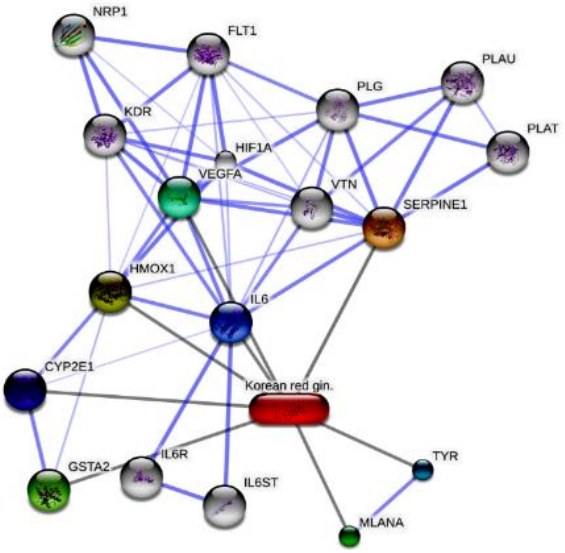

Figure 1: PPI Network of *P. ginseng* and its target protein viz. cytochrome P450 (CYP2E), fms-related tyrosine kinase 1 (FLT1), glutathione S-transferase alpha 2 (GSTA2), heme oxygenase decycling 1 (HMOX-1), hypoxia-inducible factor 1 (HIF1A), interleukin 6 receptor (IL6R), interleukin 6 signal transducer (IL6ST), kinase insert domain receptor (KDR), melan-A (MLANA), neuropilin 1 (NRP1), plasminogen activator tissue (PLAT), plasminogen activator urokinase (PLAU), plasminogen (PLG), serpin peptidase inhibitor clade E (SERPINE1), tyrosinase (TYR); Interleukin 6 (IL6), vascular endothelial growth factor A (VEGFA), vitronectin (VTN)

Target proteins of ovarian cancer

The target proteins of ovarian cancer were determined using the Genecards database and the target hit with a score of 60 above was taken for constructing the protein-protein interaction network (Figure 2). The highest target protein score was BRCA2 (BRCA2 DNA Repair Associated) with a relevance score of 421.66 abu. The target proteins of *P. ginseng* such as IL6 (63.41), SERPINE1 (33.28), and VEGFA (65.53) had good relevance score. Target proteins such as TYR, HMOX1, CYP2E1, MLANA, and GSTA2 scored 22.46, 22.26, 20, 14.4 and 5 abu respectively.

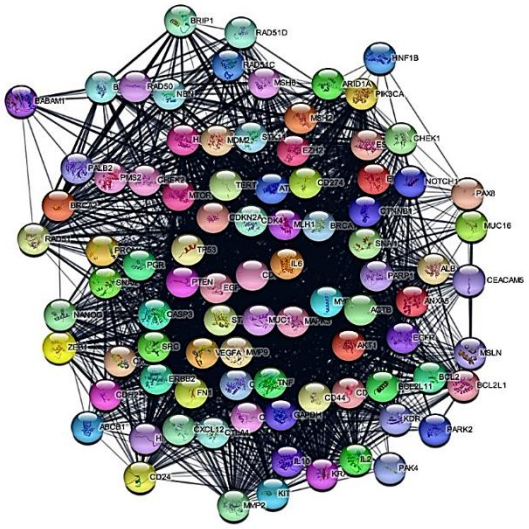

Figure 2: Target Proteins of ovarian cancer obtained from the Gene cards database and network constructed using Cytoscape

Target proteins of ovarian cancer linked with *P. ginseng*

The protein targets of ovarian cancer linked with *P. ginseng* were established from the above two networks and are presented in Table 1.

Molecular docking study

Molecular docking was carried out against six ovarian cancer target proteins and the active sites were set for 3V2A (X:-27.10, Y: 18.03, Z: 7.63), 4VCN (X: 4.08, Y: 22.02, Z: 21.56), 4V24 (X: 23.52, Y: 3.71, Z:-9.19), 6E43 (X: 68.08, Y: 17.00, Z: 49.47), 6TIW (X: 222.97, Y: 171.58, Z: 281.28) and 1ALU (X: 11.21, Y: -14.58, Z: 2.05). In all the cases, the binding site was placed within a restricted space sphere of 15 Å with a grid resolution of 0.30 Å. The results of the molecular docking score are presented in Table 2 (PDB ID: 3V2A), Table 3 (4VCN), Table 4 (PDB ID: 4V24), Table 5 (PDB ID: 6E43), Table 6 (PDB ID: 6TIW) and Table 7 (PDB ID: 1ALU).

In several of the cases, analogs and derivatives of ginsenoside docked at the active site of the targeted protein associated with ovarian cancer with favorable docking scores and interaction energy in terms of total energy, MolDock score, interaction energy, and rank score. The particulars regarding in-depth molecular interaction analysis which depicts the intra-molecular interaction energy, intra-molecular interaction distances, and interaction among the protein-ligand atoms show that the interaction between the atoms of these compounds and the enzyme and their interaction distance and energy are also major factors in the favorable binding of the top docking hits which are mostly derivatives and analogs of ginsenosides. The protein-ligand interaction analysis which showed strong molecular interaction of the active compounds of *P. ginseng* at the active site of the targeted proteins are presented in Figure 3, Figure 4, and Figure 5.

Table 1: Target Proteins of ovarian cancer linked with *P. ginseng*

Protein Name	Gene name	UniProt	PDB ID
Sphingosine kinase 1	SPKH1	Q9NYA1	4V24
Kinesin-like protein 1	KIF13A	P52732	6TIW
Vascular endothelial growth factor receptor 2	VEGFA	P35968	3V2A
Cyclin-dependent kinase 2/cyclin A	CDK2	P24941	4VCN
Indoleamine 2,3-dioxygenase	INDO1	P14902	6E43
Interleukin 6	IL6	P05231	1ALU

Table 2: Molecular docking score of *P. ginseng* compounds docked against VEGFA (PDB ID: 3V2A)

Ligand	MolDock Score	Rerank Score	Interaction	HBond	LE1	LE3	Total Score
20(R)-ginsenoside Rg2	-132.29	-100.76	-130.27	-1.53	-4.90	-3.73	-373.49
MOL002312	-116.16	-93.28	-133.46	-12.38	-2.70	-2.17	-360.15
20(S)-Ginsenoside-Rh1	-115.84	-95.62	-132.45	-7.10	-3.62	-2.99	-357.62
Folinic acid	-134.39	-84.77	-122.21	-6.38	-3.95	-2.49	-354.19
Suchilactone	-115.12	-91.94	-132.49	-7.14	-2.09	-1.67	-350.44
Trifolirhizin	-114.84	-82.62	-130.61	-17.32	-2.55	-1.84	-349.77
Notoginsenoside R6	-128.07	-70.94	-132.03	-12.23	-1.91	-1.06	-346.24
20(S)-ginsenoside-Rg2	-119.67	-75.23	-135.22	-7.30	-2.18	-1.37	-340.96
Ramalic acid	-116.00	-88.78	-110.38	-4.88	-4.64	-3.55	-328.24
Ginsenoside-Rh1	-107.36	-75.88	-121.52	-14.93	-2.39	-1.69	-323.76

Table 3: Molecular docking score of *P. ginseng* compounds docked against CDK2 (PDB ID: 4VCN)

Ligand	MolDock Score	Rerank Score	Interaction	HBond	LE1	LE3	Total
MOL002312	-155.7	-125.6	-170.5	-16.0	-3.6	-2.9	-474.4
Notoginsenoside R2	-152.9	-110.4	-151.8	-7.5	-2.8	-2.0	-427.4
Ginsenoside La	-166.6	-62.1	-174.9	-14.1	-2.5	-0.9	-421.1
alpha-Guttiferin	-138.8	-116.3	-150.8	-6.1	-4.2	-3.5	-419.8
Ginsenoside La	-134.0	-107.4	-160.8	-8.8	-2.4	-2.0	-415.4
Trifolirhizin	-136.6	-107.9	-154.8	-7.8	-4.3	-3.4	-414.7
20(S)-ginsenoside-Rg2	-145.7	-85.7	-164.0	-10.3	-2.6	-1.6	-409.9
Ginsenoside rh2	-130.5	-108.2	-153.1	-4.4	-3.0	-2.5	-401.7
Folinic acid	-129.6	-107.3	-145.4	-7.4	-3.8	-3.2	-396.7
MOL005337	-134.7	-35.4	-196.8	-16.8	-2.0	-0.5	-386.4

Table 4: Molecular docking score of *P. ginseng* compounds docked against SPKH1 (PDB ID: 4V24)

Ligand	MolDock Score	Rerank Score	Interaction	HBond	LE1	LE3	Total
Ginsenosiderf	-175.30	-143.22	-181.49	-10.71	-5.16	-4.21	-520.09
MOL002312	-165.49	-122.52	-184.76	-7.56	-3.85	-2.85	-487.03
Suchilactone	-155.30	-128.21	-162.12	-4.83	-5.75	-4.75	-460.96
Folinic acid	-162.75	-61.92	-206.22	-11.82	-2.91	-1.11	-446.71
7alpha-L-Rhamnosyl-6-methoxylutcolin	-137.73	-114.42	-166.53	-12.22	-4.17	-3.47	-438.53
alpha-Guttiferin	-146.55	-119.69	-159.72	-2.92	-4.44	-3.63	-436.94
Trifolirhizin	-137.26	-115.75	-156.30	-9.55	-4.29	-3.62	-426.77
Sanchinoside C1	-159.86	-33.90	-202.48	-11.13	-2.85	-0.61	-410.82
Pandamine	-145.97	-83.92	-172.76	-1.85	-3.65	-2.10	-410.25
Notoginsenoside R2	-173.00	-29.76	-181.91	-21.01	-3.20	-0.55	-409.43

Table 5: Molecular docking score of *P. ginseng* compounds docked against INDO1 (PDB ID: 6E43)

Ligand	MolDock Score	Rerank Score	Interaction	HBond	LE1	LE3	Total
MOL002312	-196.47	-154.74	-214.56	-14.34	-4.57	-3.60	-588.29
Ginsenoside Re	-181.17	-73.24	-246.81	-12.77	-2.74	-1.11	-517.83
Ginsenosiderf	-190.44	-81.80	-216.27	-20.31	-3.40	-1.46	-513.69
Ginsenoside-Rg3	-185.83	-75.46	-226.46	-7.18	-3.38	-1.37	-499.67
Folinic acid	-155.70	-134.41	-174.35	-10.65	-4.58	-3.95	-483.65
Darutoside	-165.49	-111.55	-189.71	-9.12	-4.04	-2.72	-482.64
Ginsenoside-Rh4	-164.71	-115.74	-187.62	-5.18	-3.74	-2.63	-479.62
Ginsenoside Rg5	-154.89	-94.26	-202.81	-8.30	-2.87	-1.75	-464.87
7alpha-L-Rhamnosyl-6-methoxylutcolin	-140.72	-132.40	-168.46	-10.71	-4.26	-4.01	-460.57
20(R)-ginsenoside Rg2	-160.51	-71.19	-195.60	-14.82	-2.92	-1.29	-446.34

Table 6: Molecular docking score of *P. ginseng* compounds docked against KIF13A (PDB ID: 6TIW)

Ligand	MolDock Score	Rerank Score	Interaction	HBond	LE1	LE3	Total
20(S)-ginsenoside-Rg2	-166.05	-132.90	-167.42	-6.12	-4.88	-3.91	-481.28
Ginsenoside-Rg3	-158.43	-128.71	-157.82	-2.08	-5.87	-4.77	-457.69
Trifolirhizin	-144.32	-114.51	-161.61	-10.07	-4.51	-3.58	-438.60
MOL002312	-149.67	-109.05	-155.27	-15.03	-3.48	-2.54	-435.03
alpha-Guttiferin	-142.47	-118.73	-161.70	-2.99	-4.32	-3.60	-433.81
Folinic acid	-162.06	-66.57	-186.24	-13.31	-2.95	-1.21	-432.34
7alpha-L-Rhamnosyl-6-methoxylutcolin	-136.98	-111.86	-162.95	-7.44	-4.15	-3.39	-426.77
Suchilactone	-141.15	-83.76	-163.61	-10.68	-2.57	-1.52	-403.29
Ramalic acid	-133.12	-110.13	-137.66	0.00	-5.32	-4.41	-390.64
Ginsenoside La	-126.39	-64.58	-166.42	-13.24	-2.30	-1.17	-374.10

Table 7: Molecular docking score of *P. ginseng* compounds docked against IL6 (PDB ID: 1ALU)

Ligand	MolDock Score	Rerank Score	Interaction	HBond	LE1	LE3	Total
MOL002312	-93.44	-88.15	-130.49	-1.82	-2.17	-2.05	-318.12
Ginsenoside-Rg3	-91.92	-76.28	-113.16	-4.50	-1.67	-1.39	-288.92
20(R)-ginsenoside Rg2	-78.91	-69.53	-108.98	-6.97	-1.43	-1.26	-267.08
Ginsenoside-Rg3_qt	-93.98	-68.75	-91.77	-0.45	-2.85	-2.08	-259.87
Suchilactone	-77.97	-66.10	-93.14	-0.84	-2.89	-2.45	-243.39
Ginsenoside Rg5	-71.29	-65.75	-108.99	-7.35	-1.32	-1.22	-255.92
Ginsenosiderf	-67.08	-65.72	-101.42	-8.14	-1.20	-1.17	-244.72
Dianthramine	-76.71	-64.91	-90.92	-6.13	-3.65	-3.09	-245.42
Ginsenoside La	-74.20	-64.55	-117.45	-3.95	-1.35	-1.17	-262.67
Malonyl ginsenoside Rd_qt	-88.24	-64.25	-88.33	-5.00	-2.67	-1.95	-250.45

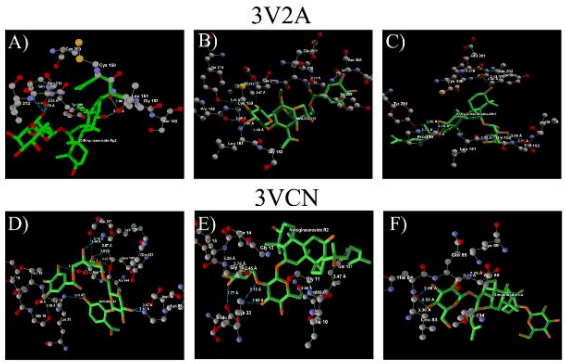

Figure 3: Molecular interaction analysis of top three docking hits at the active site of 3V2A viz. (A) 20(R)-ginsenoside Rg2 (B) MOL002312 and (C) 20(S)-Ginsenoside and the top three docking hits at the active site of 4VCN viz. (D) MOL002312 Rg2 (E) Notoginsenoside R2 and (F) Ginsenoside La revealing hydrogen bond interaction

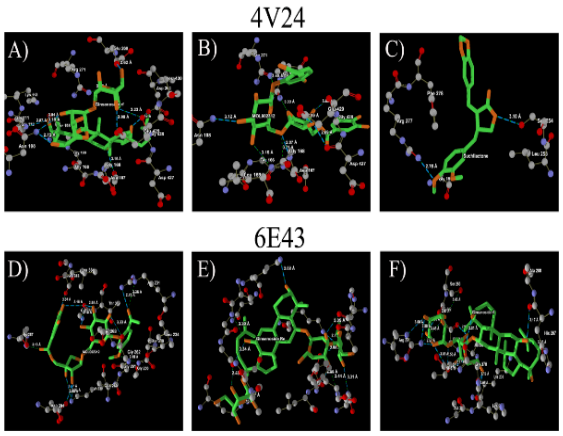

Figure 4: Molecular interaction analysis of top three docking hits at the active site of 4V24 viz. (A) Ginsenosiderf (B) MOL002312 and (C) Suchilactone and the top three docking hits at the active site of 6E43 viz. (D) MOL002312 Rg2 (E) Ginsenoside Re and (F) Ginsenosiderf revealing hydrogen bond interaction

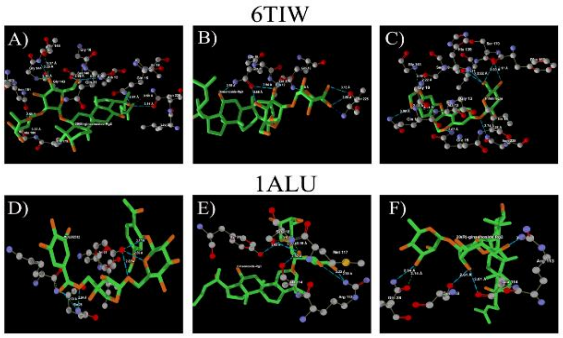

Figure 5: Molecular interaction analysis of top three docking hits at the active site of 6TIW viz. A) 20(S)-ginsenoside-Rg2 **(**B) Ginsenoside-Rg3 and (C) Trifolirhizin and the top three docking hits at the active site of 1ALU viz. (D) MOL002312 (E) Ginsenoside-Rg3 and (F) 20(R)-ginsenoside Rg2 revealing hydrogen bond interaction

DISCUSSION

In this investigation, the biological mechanism of *P. ginseng* against ovarian cancer was studied by constructing a network pharmacology map. A total of 96 bioactive substances present in *P. ginseng* were screened against six protein targets linked to ovarian cancer. Among the 96 exclusive constituents, ginsenosides and their derivatives were found to be the major active constituents which comprise a total of 40 compounds. In fact, ginsenosides are known for their pharmacological properties including anti-inflammatory, anti-cancer, vasorelaxant, and anti-oxidant activities [18]. Molecular docking studies showed that MOL002312, 20(R)-ginsenoside Rg2, 20(S)-Ginsenoside-Rh1, notoginsenoside R2, notoginsenoside R6, suchilactone, ginsenosiderf, ginsenoside Re, ginsenosiderf, folinic acid, and trifolirhizin were docked at the active sites of the six different target proteins (PDB ID: 3V2A, 4VCN, 4V24, 6E43, 6TIW, and 1ALU). MOL002312 docked with five different proteins viz. 3V2A, 4VCN,

4V24, 6E43, and 1ALU. Similarly, 20(S)-ginsenoside-Rh1, ginsenosiderf, and 20(R)-ginsenoside Rg2 were docked with three different proteins. In molecular docking, its computational algorithms are used to predict the most stable and optimum pose of a ligand compared to another one when bound thereby forming a stable complex [19].

In the present study, derivatives of ginsenosides were found to be promising candidates that docked at the protein targets, thereby revealing the strong binding affinity and potent activity of ginsenosides. The H-bond energy also revealed the existence of strong hydrogen bonding interactions with top docking hits at the active sites of ovarian cancer-targeted proteins. The H-bond score is the hydrogen bonding energy between the protein and the ligand calculated using modified piecewise linear potential (PLP) [20]. Thus, these compounds may play important roles in the treatment of ovarian cancer. In fact, these compounds have antibacterial, anti-inflammatory, and antitumor activities, in addition to other pharmacological properties as reported previously [21]. The analogs or derivatives of ginsenosides are known to possess different pharmacological mechanisms because of their variation in chemical structures. In the past few years, much effort and research has focused on the individual ginsenosides to study their specific mechanism of action against a wide range of diseases instead of focusing on the whole root of *P. ginseng* [22]. The potential medical applications of ginsenosides and their mechanism of action has led many researchers to emphasize special focus on Rb1, Rg1, Rg3, Re, Rd, and Rh1 ginsenosides derivatives [23].

Molecular docking simulations were performed using MVD 7.0. which uses a differential evolution algorithm. The docking engine algorithm considers the sum of the intermolecular interaction energy between the ligand and the protein and the intramolecular interaction energy of the ligand. The scoring function employs the modified PLP with new hydrogen bonding and electrostatic terms yielding a better docking score accuracy [24]. Furthermore, ovarian cancer is considered a serious cancer type with a high incidence of chemoresistance and an increased fatality rate. Therefore, the chemo-prevention of ovarian cancer through the application of natural compounds such as genocides of *P. ginseng* is crucial and requires a new generation of anti-cancer treatments because synthetic methods are facing problems with many side effects and resistance. It was also reported in a mouse model study that the inhibition of ovarian cancer growth with the combination of ginsenoside Rh2 and a platinum drug (CDDP) could stop the progression of human ovarian cancer (HRA) cells [25]. Thus, ginseng treatment inhibits the growth of ovarian tumors. However, this study has certain limitations because only computational *in vivo* and network pharmacology approaches were used. Second, the study requires experimental screening and bioassay analysis of the compounds against their protein target.

CONCLUSION

A PPI map of *P. ginseng* and ovarian cancer has been constructed and six proteins associated with *P. ginseng* and ovarian cancer are predicted. Furthermore, molecular docking carried out against these six proteins using 96 active ingredients or compounds present in *P. ginseng* reveals that ginsenosides and their derivatives successfully inhibited these proteins with favourable docking scores and binding affinity. Thus, this study provides new insights into the mechanism of action of ginsenosides and their derivatives against ovarian cancer. Hence, ginsenosides such as 20(S)-ginsenoside-Rg2, Ginsenoside Re, Ginsenoside rf, MOL002312 and 20(R)-ginsenoside Rg2 might be potent candidate for the treatment of ovarian cancer.

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Ethical approval

None provided.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Conflict of Interest

No conflict of interest associated with this work.

Contribution of Authors

We declare that this work was done by the authors named in this article, and all liabilities pertaining to claims relating to the content of this

article will be borne by the authors. Xiao-Fei Sun, Salam Pradeep Singh performed all the experiments. The whole study was designed by Xiao-Fei Sun and Salam Pradeep Singh.

REFERENCES

1. *Yang Y, Ju Z, Yang Y, Zhang Y, Yang L, Wang Z. Phytochemical analysis of Panax species: a review. J Ginseng Res 2021; 45(1): 1-21.*
2. *Chen W, Balan P, Popovich DG. Comparison of ginsenoside components of various tissues of New Zealand forest-grown Asian ginseng (Panax Ginseng) and American ginseng (Panax Quinque folium L.). Biomolecules 2020; 10(3): 372.*
3. *Nair R, Sellaturay S, Sriprasad S. The history of ginseng in the management of erectile dysfunction in ancient China (3500-2600 BCE). Indian J Urol 2012; 28(1): 15-20.*
4. *Jin Y, Cui R, Zhao L, Fan J, Li B. Mechanisms of Panax ginseng action as an antidepressant. Cell Prolif 2019; 52(6): e12696.*
5. *Ratan ZA, Haidere MF, Hong YH, Park SH, Lee JO, Lee J, Cho JY. Pharmacological potential of ginseng and its major component ginsenosides. J Ginseng Res 2021; 45(2): 199-210.*
6. *Wang CZ, Anderson S, DU W, He TC, Yuan CS. Red ginseng and cancer treatment. Chin J Nat Med 2016; 14(1): 7-16.*
7. *Zhang H, Abid S, Ahn JC, Mathiyalagan R, Kim YJ, Yang DC, Wang Y. Characteristics of Panax ginseng Cultivars in Korea and China. Molecules 2020; 25(11): 2635.*
8. *Liu H, Lu X, Hu Y, Fan X. Chemical constituents of Panax ginseng and Panaxnotoginseng explain why they differ in therapeutic efficacy. Pharmacol Res 2020; 161: 105263.*
9. *Mancuso C, Santangelo R. Panax ginseng and Panaxquinquefolius: From pharmacology to toxicology. Food ChemToxicol 2017; 107(Pt A): 362-372.*
10. *Guo M, Shao S, Wang D, Zhao D, Wang M. Recent progress in polysaccharides from Panax ginseng C. A. Meyer. Food Funct 2021; 12(2): 494-518.*
11. *Lee JW, Ji SH, Lee YS, Choi DJ, Choi BR, Kim GS, Baek NI, Lee DY. Mass spectrometry-based profiling and imaging of various ginsenosides from panax ginseng roots at different Ages. Int J Mol Sci 2017; 18(6): 1114.*
12. *Lee IS, Kang KS, Kim SY. Panax ginseng Pharmacopuncture: Current Status of the Research and Future Challenges. Biomolecules 2019; 10(1): 33.*
13. *Penny SM. Ovarian Cancer: An Overview. Radiol Technol 2020; 91(6): 561-575.*
14. *Ding DN, Xie LZ, Shen Y. Insights into the role of oxidative stress in ovarian cancer. Oxid Med Cell Longev 2021; 2021: 8388258.*
15. *Calaf GM, Urzua U, Termini L, Aguayo F. Oxidative stress in female cancers. Oncotarget 2018; 9(34): 23824-23842.*
16. *Stewart C, Ralyea C, Lockwood S. Ovarian Cancer: An integrated review. SeminOncolNurs 2019; 35(2): 151-156.*
17. *Kossaï M, Leary A, Scoazec JY, Genestie C. Ovarian cancer: A heterogeneous disease. Pathobiol 2018; 85(1-2): 41-49.*
18. *Kim JH. Pharmacological and medical applications of Panax ginseng and ginsenosides: a review for use in cardiovascular diseases. J Ginseng Res 2018; 42(3): 264-269.*
19. *Torres PHM, Sodero ACR, Jofily P, Silva-Jr FP. Key topics in molecular docking for drug design. Int J Mol Sci 2019; 20(18): 4574.*
20. *Chen D, Oezguen N, Urvil P, Ferguson C, Dann SM, Savidge TC. Regulation of protein-ligand binding affinity by hydrogen bond pairing. Sci Adv 2016; 2(3): e1501240.*
21. *Maela MP, van der Walt H, Serepa-Dlamini MH. The antibacterial, antitumor activities, and bioactive constituents' identification of Alectra sessiliflora bacterial endophytes. Front Microbiol 2022; 13: 870821*
22. *Ratan ZA, Haidere MF, Hong YH, Park SH, Lee JO, Lee J, Cho JY. Pharmacological potential of ginseng and its major component ginsenosides. J Ginseng Res 2021; 45(2): 199-210.*
23. *Mohanan P, Subramaniyam S, Mathiyalagan R, Yang DC. Molecular signaling of ginsenosides Rb1, Rg1, and Rg3 and their mode of actions. J Ginseng Res 2018; 42(2): 123-132.*
24. *Thomsen R, Christensen MH. MolDock: a new technique for high-accuracy molecular docking. J Med Chem 2006; 49(11): 3315-3321.*
25. *Nakata H, Kikuchi Y, Tode T, Hirata J, Kita T, Ishii K, Kudoh K, Nagata I, Shinomiya N. Inhibitory effects of ginsenoside Rh2 on tumor growth in nude mice bearing human ovarian cancer cells. Jpn J Cancer Res 1998; 89(7): 733-740.*