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Evaluating The Effect Of Silicon Pollutants On Human Gene Using In Silico System Biology Approaches.

[1]Ritika Tripathi, [2]Prekshe Garg, [3]Prachi Shrivastav

[1]M.Sc. Scholar, [2]Reserch Scholar, [3]Associate Professor

Amity Institute of Biotechnology, Amity University Uttar Pardesh, Lucknow, India

ABSTRACT

Silicon exposure, a common nanomaterial found in rocks and plants, can transform into asbestos-like compounds, leading to various health risks, including autoimmune diseases like rheumatoid arthritis, cancer, chronic kidney disease, and lupus. The most significant health risk is the incurable lung disease silicosis, which damages interstitial lung tissue. This study aims to evaluate the molecular mechanisms by which silicon exposure may alter gene expression and obstruct biological pathways using system biology methodologies. Transcriptomics is used to pinpoint genes expressed differentially in human cells exposed to varying concentrations of silicon pollution. Silicosis samples were retrieved from GEO dataset (GSE30215) to analyse differentially expressed genes using GEO2R. The list of genes playing a key role in silicosis were also retrieved from various databases like NCBI, OMIM, Gene Card, Mala Card etc. Network analysis helps identify significant regulatory nodes influenced by silicon exposure, highlighting the importance of understanding the potential impact of silicon pollution on human DNA and health. Therefore, protein-protein interaction network analysis was carried out of the identified genes using STRING and the Cytohubba plugin of Cytoscape to identify the priority hub gene based on 12 vital parameters. The “TP53” Gene was identified as the priority gene affected in Silicosis. The lists of 25 phytocompounds were created and phytochemicals were screened based on Lipinski’s Rule of 5 using ADMETLab 3.0. To determine the ideal binding energy for drug development, molecular docking was employed. Molecular docking studies revealed the therapeutic potential of phytocompound Oleanolic acid obtained from Olea europaea as an effective drug against silicosis.

Keywords: Silicon Exposure, Network Analysis, Silicosis, Molecular docking, TP53, Oleanolic acid

1. INTRODUCTION:

Nanomaterials like silica, titanium oxide, and carbon nanotubes are increasingly used in products such as cosmetics and food, though their safety is still under investigation. Due to their structure and size, they may pose health risks similar to asbestos. Silicon, the tenth most abundant element in the universe and second most in Earth's crust, is rare in living organisms and largely unabsorbable by higher animals. It primarily exists in phytoliths and the structures of marine microorganisms[1,2,3,4].

The biological and medical relevance of silicon and its various forms, highlighting its interactions with biochemicals and potential in biomaterials research. While silicon is widely used in orthopaedics, exposure to crystalline silica—especially in industrial settings—poses serious health risks, including silicosis, an untreatable and potentially fatal lung disease. Early detection and monitoring are crucial, and there is a growing need for sensitive technologies to predict and prevent silicosis before symptoms appear[5,6,7,8,9,10].

Peripheral blood gene expression analysis has been shown to be an effective, less invasive method for detecting organ damage and toxic exposure, outperforming traditional markers in animal studies. Recent research explored its potential to identify early lung injury from silica exposure in rats, suggesting it could aid in diagnosing pre-clinical silicosis and developing early biomarkers[11,12,13,14].

Silicon pollutants from glass and semiconductor industries pose serious health risks, primarily through inhalation. Long-term exposure to silicon dust can cause oxidative stress, DNA damage, and inflammation, leading to genotoxic effects and increased cancer risk, particularly lung cancer[15,16,17,18,19]. Silicon nanoparticles may directly interact with DNA, causing mutations and epigenetic changes that affect gene expression. These pollutants are also linked to chronic respiratory diseases like silicosis and COPD[20,21,22,23].

2. REVIEW OF LITERATURE:

Silicon, mainly found as silicon dioxide and silicates, is vital in semiconductor manufacturing. However, its production and disposal can release harmful compounds into the environment. Occupational exposure to silicon pollution is linked to respiratory diseases like silicosis, and recent studies suggest potential DNA damage and long-term health effects[24].

2.1 Mechanism of silicon pollutant exposure:

Humans can be exposed to silicon through inhalation, ingestion, or skin contact, with inhalation being most common in industrial settings. Breathing in fine silicon dioxide dust can lead to lung inflammation and fibrosis. Once inside the body, silicon particles may trigger molecular interactions that disrupt gene production[25,26].

2.2 Cellular uptake and distribution:

Alveolar macrophages help clear inhaled silicon particles via the mucociliary escalator or lymphatic system. However, excessive or prolonged exposure can overwhelm this process, leading to persistent inflammation and cellular damage. Silicon particles may also reach other organs through circulation. A key mechanism of damage is oxidative stress, caused by an imbalance in reactive oxygen species (ROS), leading to DNA, protein, and lipid damage [27,28].

2.3 Genotoxic effect:

Silicon-containing chemical contaminants cause genotoxic effects primarily through oxidative stress. Reactive oxygen species (ROS) generated by silicon particles can lead to DNA strand breaks, base alterations, and cross-linking, resulting in mutations that may cause cancer and disrupt normal cell functions. Studies have shown that silicon dioxide nanoparticles can induce DNA damage in human lung cells, evidenced by increased levels of 8-OHdG, a marker of oxidative DNA damage[29,30].

2.4 Epigenetic Modifications:

Silicon contaminants can cause epigenetic changes—heritable alterations in gene expression without changing the DNA sequence. These include DNA methylation, histone modifications, and non-coding RNA regulation. Exposure to silicon dioxide has been linked to changes in DNA methylation in lung cells, potentially disrupting genes involved in cell cycle regulation, apoptosis, and inflammation[31,32].

2.5 Impact on specific genes:

Exposure to silicon pollutants activates genes involved in inflammation (IL-6, TNF-α), oxidative stress (SOD2, GPX1), and DNA repair (XRCC1, OGG1)[33]. Silicon particles stimulate immune cells, leading to chronic inflammation, tissue damage, and increased cancer risk. Persistent oxidative stress overwhelms cellular defenses, while impaired DNA repair leads to mutations and genomic instability, contributing to disease development[34].

2.6 Short-Term and Long-Term Effects on Health:

Long-term exposure to silicon pollutants, particularly inhaling silicon dioxide, can lead to serious health issues such as silicosis, lung cancer, and chronic respiratory diseases. Recent studies also link silicon exposure to cardiovascular problems due to inflammation and endothelial dysfunction. Additionally, genetic and epigenetic changes caused by silicon may affect multiple organ systems, potentially leading to various disorders[35,36].

2.7 Approaches that are both preventative and therapeutic:

Exposure to silicon pollutants poses health risks, especially in industrial settings, making preventive measures like PPE, ventilation, and safety protocols essential[37]. Antioxidant therapies, such as N-acetylcysteine (NAC), may help reduce oxidative stress, though more clinical trials are needed[38]. Emerging treatments include gene therapy targeting DNA repair and anti-inflammatory responses, as well as epigenetic drugs that reverse harmful genetic changes caused by silicon exposure[39,40].

3. TOOLS AND METHODOLOGY:

3.1 Tools And Databases Used:

3.1.1 NCBI:

(https://www.ncbi.nlm.nih.gov)

The National Center for Biotechnology Information (NCBI), part of the NIH, provides key resources for genetic and biomedical research, including databases like GenBank for nucleotide sequences and PubMed for scientific literature. It supports bioinformatics through tools for accessing genetic data, protein structures, and clinical tests. The NCBI Taxonomy database allows users to explore taxonomic information and links various Entrez domains for integrated biological research[41].

3.1.2 GEO DATASETS:

(https://www.ncbi.nlm.nih.gov/geo/)

The Gene Expression Omnibus (GEO) database, managed by NCBI under NIH, is a public resource that stores high-throughput gene expression and genomics data. It supports researchers in genomics and bioinformatics by providing accessible experimental data for analysis and hypothesis generation[42,56].

3.1.3 OMIM:

(https://www.omim.org)

OMIM (Online Mendelian Inheritance in Man) is a comprehensive, daily-updated database of human genes and genetic disorders, emphasizing genotype-phenotype relationships. It aids geneticists, physicians, and researchers in diagnosing and understanding genetic diseases and developing treatments. Unlike primary databases, OMIM provides expert-reviewed summaries of relevant biological literature and plays a key role in identifying and classifying genetic phenotypes[43].

3.1.4 GENECARDS:

(https://www.genecards.org)

GeneCards is a comprehensive, gene-centric database that integrates genomic, proteomic, transcriptomic, genetic, and functional data from multiple sources. It helps researchers understand gene functions, interactions, and disease associations, supporting advancements in genomics and personalized medicine. Its growing popularity has expanded its scope to include diseases and pathways, raising both opportunities and challenges[44].

3.1.5 MALACARDS:

(https://www.malacards.org)

MalaCards is a comprehensive database of human diseases, offering detailed information on symptoms, genes, pathways, and drug interactions. It compiles data from patient records, clinical trials, and research publications to support medical genetics research and drug discovery. Part of LifeMap Sciences' GeneCards Suite, it integrates content from GeneCards and Gene Analytics [45].

3.1.6 DisGeNET:

(https://www.disgenet.org)

DisGeNET is a versatile platform that explores gene-disease associations by integrating data from scientific literature, curated databases, and animal models. It supports biomedical research, drug development, and precision medicine by aiding in the understanding of genetic factors in diseases. Its GDA and VDA datasets, derived from text mining, include information from 400,000 publications [46].

3.1.6 CYTOSCAPE:

(https://cytoscape.org)

CytoHubba is a Cytoscape plugin used to identify hub genes and key nodes in biological networks. It employs eleven topological analysis methods, including Degree, MCC, and various shortest path-based centralities, to evaluate node importance. MCC has shown higher accuracy compared to other methods, making CytoHubba useful for identifying potential biomarkers and therapeutic targets[47].

3.1.7 STRING NETWORK:

STRING (Search Tool for Retrieval of Interacting Genes/Proteins) is a comprehensive database that provides information on predicted and experimentally validated protein-protein interactions. It integrates data from various sources like high-throughput experiments, computational predictions, and text mining. Researchers can use STRING to explore protein functions, interaction networks, and biological pathways through its interactive online interface [48].

3.1.8 CYTOHUBBA:

CytoHubba is a Cytoscape plugin used to identify hub genes and key nodes in biological networks. It applies 11 topological analysis methods—including Degree, MCC, and various centralities—to assess node significance, aiding in the discovery of potential biomarkers or therapeutic targets. MCC, a newer method, offers higher accuracy than the others [49].

3.1.9 ADMETLAB 3.0 :

(https://admetlab3.scbdd.com)

ADMETlab 3.0 is a web-based tool designed to predict the ADMET (Absorption, Distribution, Metabolism, Excretion, and Toxicity) properties of small molecules. It plays a crucial role in drug discovery by enabling early evaluation of pharmacokinetic and toxicological profiles, saving time and resources. The platform is supported by numerous in silico models built from extensive experimental data [50].

3.1.10 PubChem :

(https://pubchem.ncbi.nlm.nih.gov)

PubChem is a free public database providing extensive chemical information. It includes three interrelated databases: Substance (submitted chemical data), Compound (extracted structures), and BioAssay (biological activity results). It also features PubChem3D for 3D structures and PubChemRDF for data sharing and integration [51].

3.1.11 SWISS-MODEL :

(https://swissmodel.expasy.org)

SWISS-MODEL is a web-based tool for automated homology modeling of protein 3D structures, aiding in functional analysis, protein interactions, and drug binding site prediction through template-based modeling. It includes stages like template selection, alignment, model building, and evaluation. PubChem is a public database providing extensive chemical and biological activity data, consisting of Substance, Compound, and BioAssay databases. It also includes PubChem3D for 3D structures and PubChemRDF for data integration and sharing[52].

3.1.12 SEAMDOCK :

(https://bioserv.rpbs.univ-paris-diderot.fr/services/SeamDock/)

SeamDock is a web-based molecular docking platform designed to predict how small compounds bind to target proteins. It uses advanced algorithms to assess binding affinity and orientation, aiding virtual screening for potential drug candidates. SeamDock supports both global and local docking and simplifies the process by requiring only a web browser and minimal technical skills [53].

3.1.13 SWISDOCK :

(htpp://www.swissdock.ch)

SwissDock is a web-based tool for protein-ligand docking that predicts how small molecules bind to protein targets using the EADock DSS engine. It supports both blind and targeted docking, ranking binding poses by estimated free energy. SwissDock is valuable for drug discovery, helping researchers understand and optimize interactions between drug candidates and proteins[54].

3.2 METHODOLOGY:

3.2.1 Sample Analysis:

Silicosis in humans has been minimally studied using transcriptome sequencing. Data from GEO (Accession ID: GSE30215) was analyzed via GEO2R, comparing A549 lung epithelial cells treated with crystalline silica for 24 hours to untreated controls. The analysis identified silica-induced pulmonary toxicity and differentially expressed genes, filtered using a p-value < 0.05 and log fold change criteria, highlighting both upregulated and downregulated genes [55].

3.2.2 Gene Identification:

A total of 703 silicosis-related genes were collected from databases like NCBI, DisGeNET, GeneCards, MalaCards, and OMIM. After removing duplicates, 33 unique genes remained. These were analyzed using network biology methods to identify primary targets associated with silicosis[42].

3.2.3 Identification Of Target Gene:

A total of 343 genes were imported into Cytoscape to construct a protein-protein interaction (PPI) network using the STRING plugin with a confidence score of 0.90. The top 10 hub genes were identified using the CytoHubba plugin based on twelve parameters, including MCC, Degree, Betweenness, and Closeness. This analysis led to the identification of a key target gene and its related protein sequence[47].

3.2.4 Protein Modeling:

The priority hub gene was discovered via the analysis of the networks that were formed by the string plugin. The Swiss Model tool was used in order to build the three-dimensional protein structure of the hub gene[52]. Following the completion of the model, the PDB format file of the protein structure was downloaded, stored for future study, and exploited for further inquiry. This was accomplished by copying its stringbd sequence into the Swissmodel website.

- The Model was created using priority hub gene TP53 stringdb sequence and was save in PDB format further used as Receptor for molecular modelling.
- The template 8f2h.1.A cellular tumor antigen p53 has 100% similarity with the sequence and was used as Receptor Obtained from TP53 Sequence Modelling.

3.2.5 LIBRARY PREPARATION :

With the assistance of literature study, a distinct list of phytocompounds that have the potential to have a therapeutic impact against silicosis was compiled. There were a total of twenty-five phytochemical compounds that were acquired, and the list was compiled using the canonical smile structure of those phytocompounds that were retrieved from Pubchem [51]. Following the screening process, these phytochemicals will be used as ligands for the purpose of docking. Shown in Table 1

PHYTOCHEMICAL	PLANT SOURCE	CANONICAL SMILES
Sodium tanshinone IIA sulfonate	Salvia miltiorrhiza (Red Sage)	CC1=C(OC2=C1C(=O)C(=O)C3=C2C=CC4=C3CCCC4C)C)S(=O)(=O)[O-].[Na+]
Kaempferol	Kale, beans, tea	C1=CC(=CC=C1C2=C(C(=O)C3=C(C=C(C=C3O2)O)O)O)O
Astragaloside IV	Astragalus membranaceus	CC1(C(CCC23C1C(CC4C2(C3)CCC5(C4(CC(C5C6(CCC(O6)C(C)(C)O) C)O)C)C)OC7CC(C(C(O7)CO)O)O)O)OC8C(C(C(CO8)O)O)O)C
Dioscin	Dioscoreaceae, Lili acae and Solanacae	CC1CCC2(C(C3C(O2)CC4C3(CCC5C4CC=C6C5(CCC(C6)OC7C(C(C(C(O7)CO)OC8C(C(C(C(O8)C)O)O)O)O)OC9C(C(C(C(O9)C)O)O)O)C)C)C)OC1
Oleanolic acid	Olea europaea	CC1(CCC2(CCC3(C(=CCC4C3(CCC5C4(CCC(C5(C)C)O)C)C)C2C1)C)C(=O)O)C
Hesperetin	Citrus fruits	COC1=C(C=C(C=C1)C2CC(=O)C3=C(C=C(C=C3O2)O)O)O
Emodin	Reynoutria japonica Houtt, and Rheum	CC1=CC2=C(C(=C1)O)C(=O)C3=C(C2=O)C=C(C=C3O)O

	officinale Baill.	
Curcumin	Curcuma longa	COC1=C(C=CC(=C1)C=CC(=O)CC(=O)C=CC2=CC(=C(C=C2)O)OC)O
Resveratrol	Grapes , Berries, Peanuts	C1=CC(=CC=C1C=CC2=CC(=CC(=C2)O)O)O
Quercetin	Apples, Onions, Berries	C1=CC(=C(C=C1C2=C(C(=O)C3=C(C=C(C=C3O2)O)O)O)O)O
Genistein	Soybeans	C1=CC(=CC=C1C2=COC3=CC(=CC(=C3C2=O)O)O)O
Epigallocatechin gallate (EGCG)	Green tea	C1C(C(OC2=CC(=CC(=C21)O)O)C3=CC(=C(C(=C3)O)O)O)OC(=O)C4=CC(=CC(=C4)O)O)O
Naringenin	Citrus fruits	C1C(OC2=CC(=CC(=C2C1=O)O)O)C3=CC=C(C=C3)O
Silibinin	Silybum marianum (Milk thistle)	COC1=C(C=CC(=C1)C2C(OC3=C(O2)C=C(C=C3)C4C(C(=O)C5=C(C=C(C=C5O4)O)O)O)CO)O
Apigenin	Parsley, Celery, Chamomile	C1=CC(=CC=C1C2=CC(=O)C3=C(C=C(C=C3O2)O)O)O
Luteolin	Green peppers, celery, chammomile tea	C1=CC(=C(C=C1C2=CC(=O)C3=C(C=C(C=C3O2)O)O)O)O
Baicalin	Scutellaria baicalensis	C1=CC=C(C=C1)C2=CC(=O)C3=C(C(=C(C=C3O2)OC4C(C(C(C(O4)C(=O)O)O)O)O)O)O
Ellagic Acid	Berries, nuts	C1=C2C3=C(C(=C1O)O)OC(=O)C4=CC(=C(C(=C43)OC2=O)O)O
Apocynin	Picrorhiza kurroa	CC(=O)C1=CC(=C(C=C1)O)OC
Sulforaphane	Broccoli, Brussels sprouts	CS(=O)CCCCN=C=S
Thymoquinone	Nigella sativa (black cumin)	CC1=CC(=O)C(=CC1=O)C(C)C
Berberine	Berberis species (eg Barberry)	COC1=C(C2=C[N+]3=C(C=C2C=C1)C4=CC5=C(C=C4CC3)OCO5)OC
Glycyrrhizin	Licorice root (Glycyrrhiza glabra)	CC1(C2CCC3(C(C2(CCC1OC4C(C(C(C(O4)C(=O)O)O)O)OC5C(C(C(C (O5)C(=O)O)O)O)O)C)C(=O)C=C6C3(CCC7(C6CC(CC7)(C)C(=O)O)C) C)C)C
Allicin	Allium sativum	C=CCSS(=O)CC=C
Aloin	Alovera	C1=CC2=C(C(=C1)O)C(=O)C3=C(C2C4C(C(C(C(O4)CO)O)O)O)C=C(C=C3O)CO

3.2.6 MOLECULAR DOCKING:

Molecular docking was performed using Seam Dock and Swiss Dock to identify potential drug candidates. Ligands were selected from phytocompounds following Lipinski's Rule of Five, while the receptor was a modeled structure of a hub gene using Swiss Model. The receptor structure, saved as a PDB file, was used in docking to determine the optimal binding orientation and stability between the ligand and protein target.

3.2.7 Rejected Phytochemicals That DO Not Follow the Lipinski's Rule:

When the screening was performed on these phytocompounds, they were found to be unsuccessful in the process. Furthermore, they did not adhere to Lipinski's Rule of five, which resulted in their subsequent rejection during the selection of the ligand. TABLE-2 is given for rejected compounds.

PHYTOC HEMICA L	PLANT SOURCE	CANONICAL SMILES	LIPINSKI 'S RULE
ASTRAGAL OSIDE IV	Astragalus membranaceu s	CC1(C(CCC23C1C(CC4C2(C3)CCC5(C4(CC(C5C6CCC(O6)C(C)(C)O)C)O)C)C)OC7C(C(C(C(O7)CO)O)O)OC8C(C(C(CO8)O)O)O)C	REJECTED
DIOSCIN	Dioscoreaceae , Liliacae and Solanacae	CC1CCC2(C(C3C(O2)CC4C3(CCC5C4CC=C6C5(CCC(C6)OC7C(C(C(C(O7)CO)OC8C(C(C(C(O8)C)O)O)O)O)OC9C(C(C(C(O9)C)O)O)O)C)C)C)OC1	REJECTED
EPIGALLO CATECHIN GALLATE (EGCG)	Green tea	C1C(C(OC2=CC(=CC(=C21)O)O)C3=CC(=C(C(=C3)O)O)O)OC(=O)C4=CC(=C(C(=C4)O)O)O	REJECTED
BAICALIN	Scutellaria baicalensis	C1=CC=C(C=C1)C2=CC(=O)C3=C(C(=C(C=C3O2)OC4C(C(C(C(O4)C(=O)O)O)O)O)O)O	REJECTED
GLYCYRRH IZIN	Licorice root (Glycyrrhiza glabra)	CC1(C2CCC3(C(C2(CCC1OC4C(C(C(C(O4)C(=O)O)O)O)OC5C(C(C(C(O5)C(=O)O)O)O)O)C)C(=O)C=C6C3(CCC7(C6CC(CC7)(C)C(=O)O)C)C)C)C	REJECTED

3.2.8 VIRTUAL SCREENING:

The phytocompounds were eliminated via the usage of ADMET Lab in accordance with Lipinski's rule of five. Those phytocompounds that adhered to the specifications of Lipinski's rule were taken into consideration and used for the docking stage. This allowed for the construction of a hypothetical library of compounds that were used in further research[50].The phytocompounds that adhered to the rule were utilized as ligands. Shown in Table 2

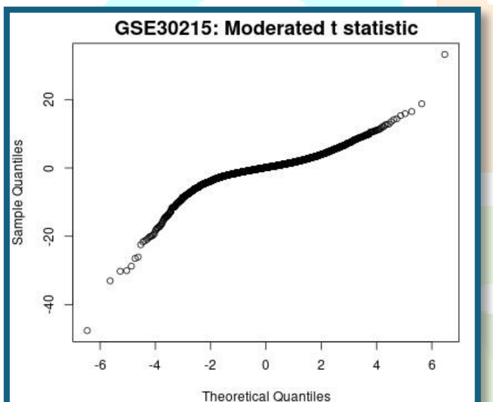
Table-3:

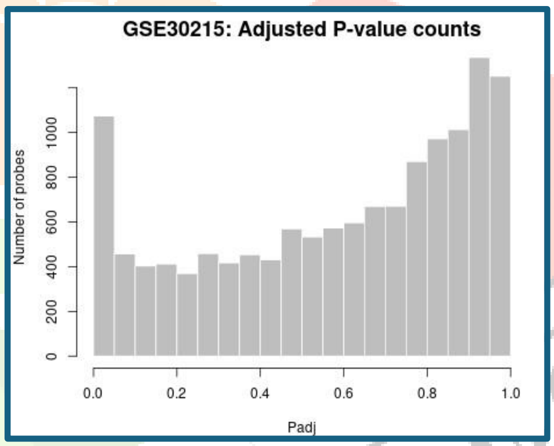
PHYTOCHEMICAL	LIPINSKI'S RULE
SODIUMTANSHINONE IIA SULFONATE	ACCEPTED
KAEMPFEROL	ACCEPTED
OLEANOLIC ACID	ACCEPTED
HESPERETIN	ACCEPTED
EMODIN	ACCEPTED
CURCUMIN	ACCEPTED
RESVERATROL	ACCEPTED
QUERCETIN	ACCEPTED
GENISTEIN	ACCEPTED

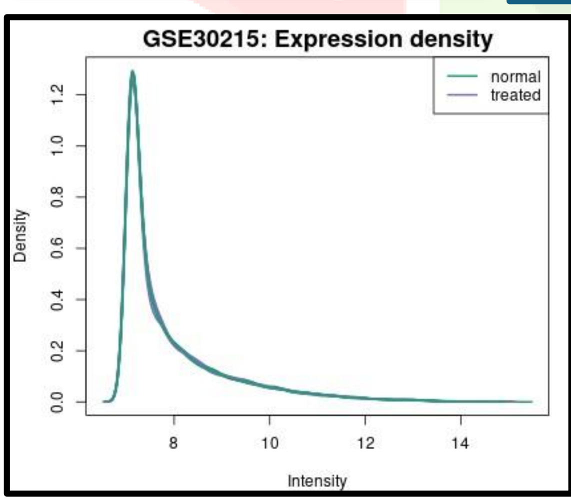
NARINGENIN	ACCEPTED
SILIBININ	ACCEPTED
APIGENIN	ACCEPTED
LUTEOLIN	ACCEPTED
ELLAGIC ACID	ACCEPTED
APOCYNIN	ACCEPTED
SULFORAPHANE	ACCEPTED
THYMOQUINONE	ACCEPTED
BERBERINE	ACCEPTED
ALLICIN	ACCEPTED
ALOIN	ACCEPTED

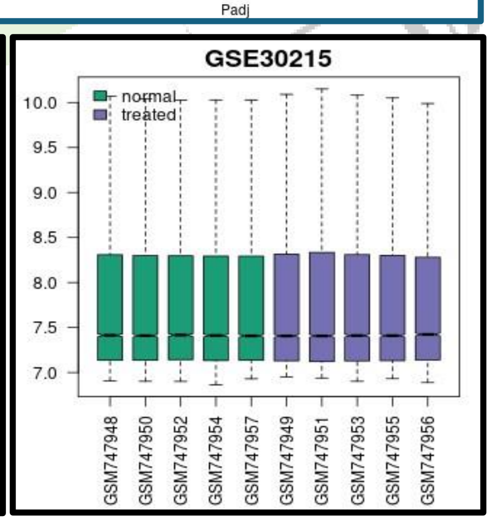
4. RESULTS :

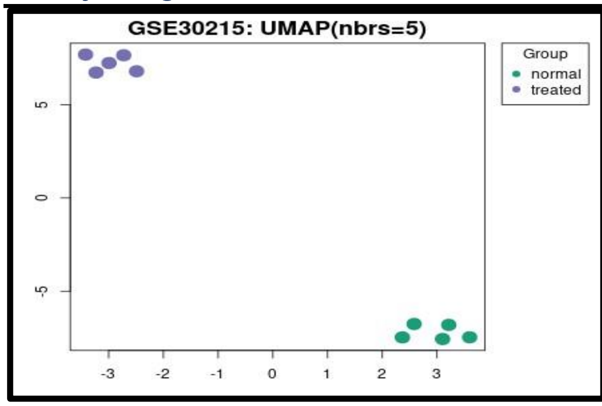
The process of assessing the results from 13528 genes led to the identification of a total of 1075 genes that were expressed differently. Among those genes, every single one of them was significant, with a padj value that was lower than 0.05. There were a total of 559 genes that were upregulated, meaning they had a higher expression, and there were 517 genes that were downregulated, meaning they had a lower expression.The following eight plots were obtained: a box plot, an MA plot, a histogram, a principal component analysis plot, a volcano plot, a BCV plot, and a Venn diagram.

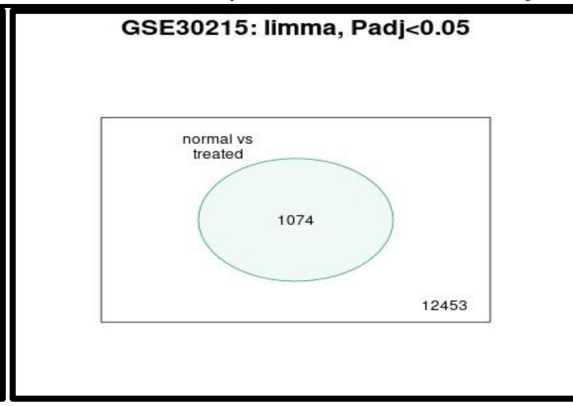


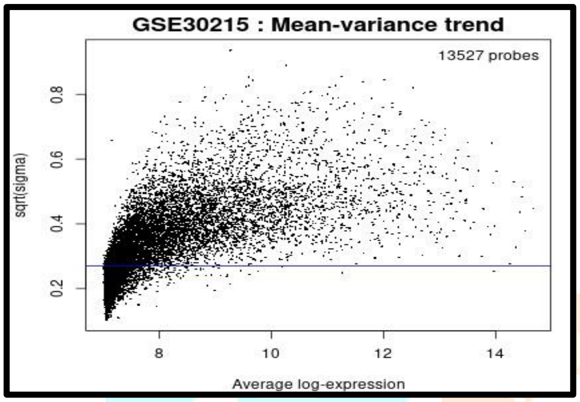


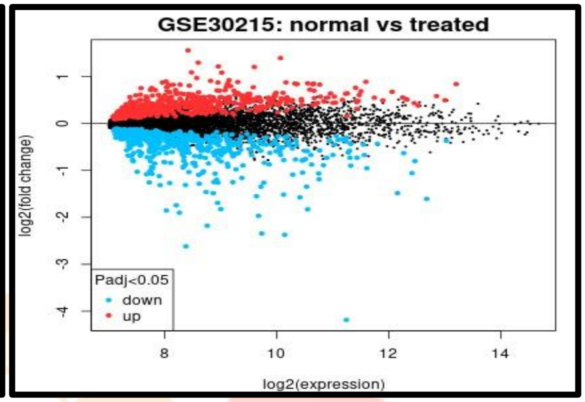


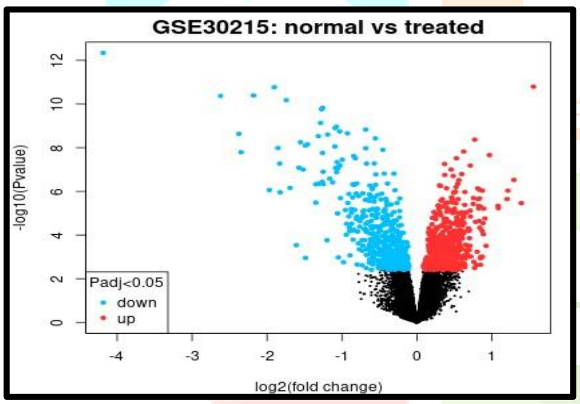












To determine the target gene, a string network was constructed in Cytoscape by using 343 genes. This was done following the elimination of duplicate genes and the conclusion of the functional enrichment analysis. A protein-protein interaction network work with 250 nodes and 526 edges was constructed in relation to Silicosis. The TP53 gene was taken as the priority hub gene because, in the end, three genes were identified that showed the presence of the same gene in all and every one of the 12 parameters. These genes were TP53, JUN, and IL6. Out of these three genes, TP53 was chosen as the hub gene because it showed a hundred percent similarity with template while the model was being constructed.

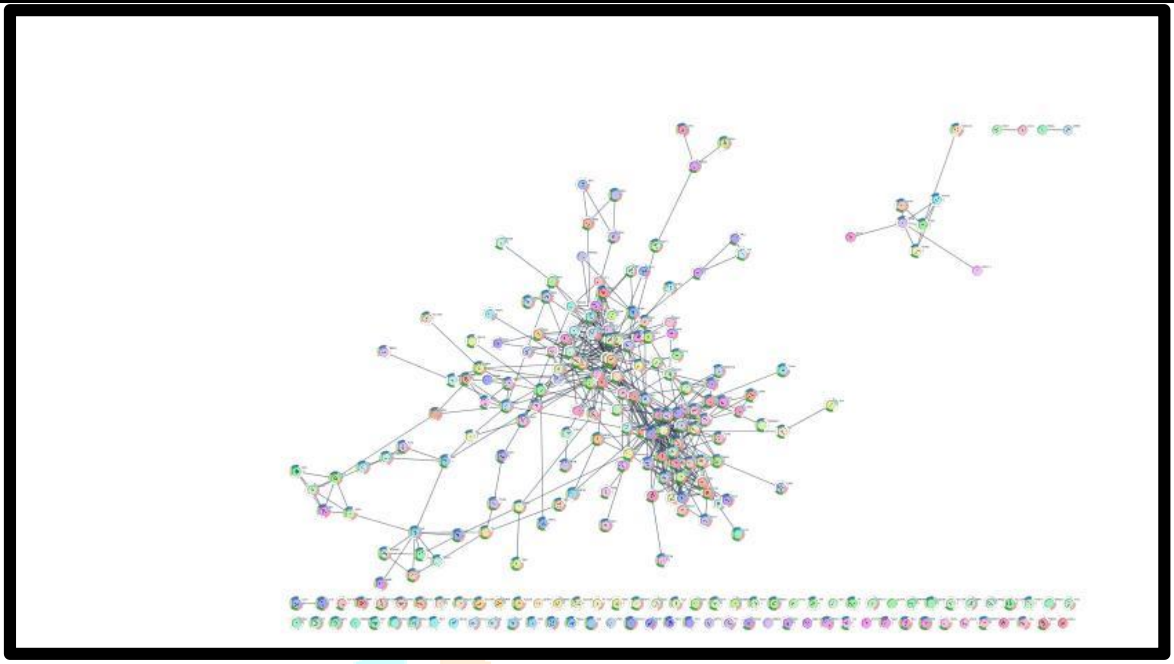


Figure1: string network construction

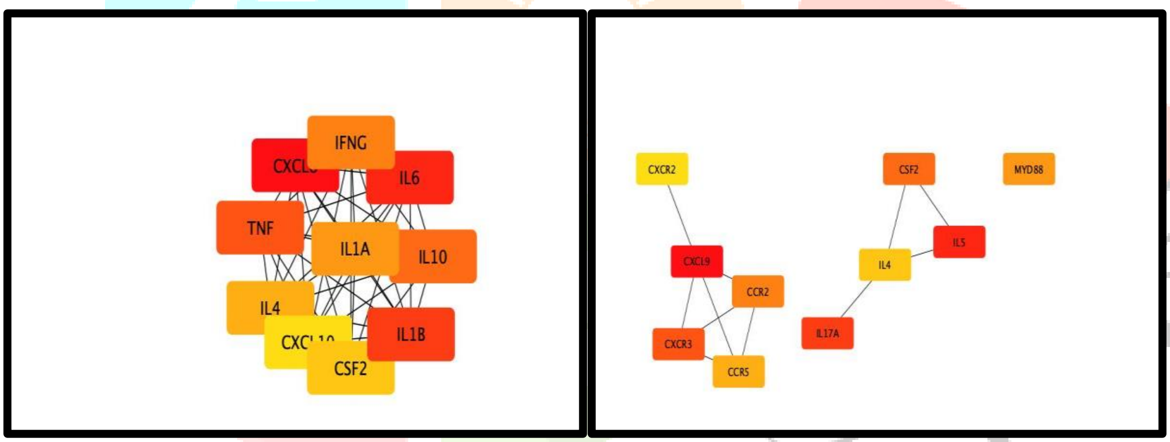


Figure2: MCC And DMNC GENE NETWORK VISUALIZATION BASED PARAMETERS RESULTING IN THE IDENTIFICATION OF KEY TARGET GENE.

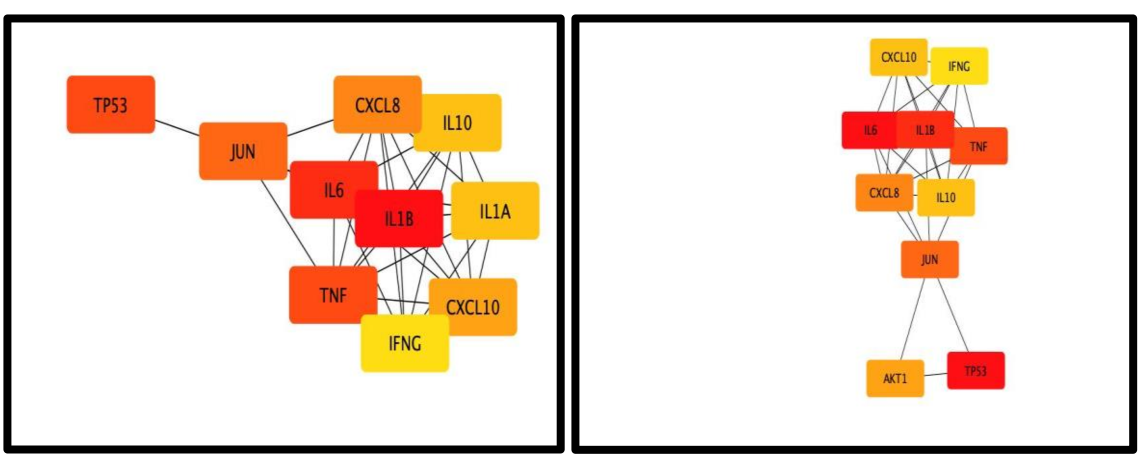


Figure3: MNC And DEGREE GENE NETWORK VISUALIZATION BASED PARAMETERS RESULTING IN THE IDENTIFICATION OF KEY TARGET GENE

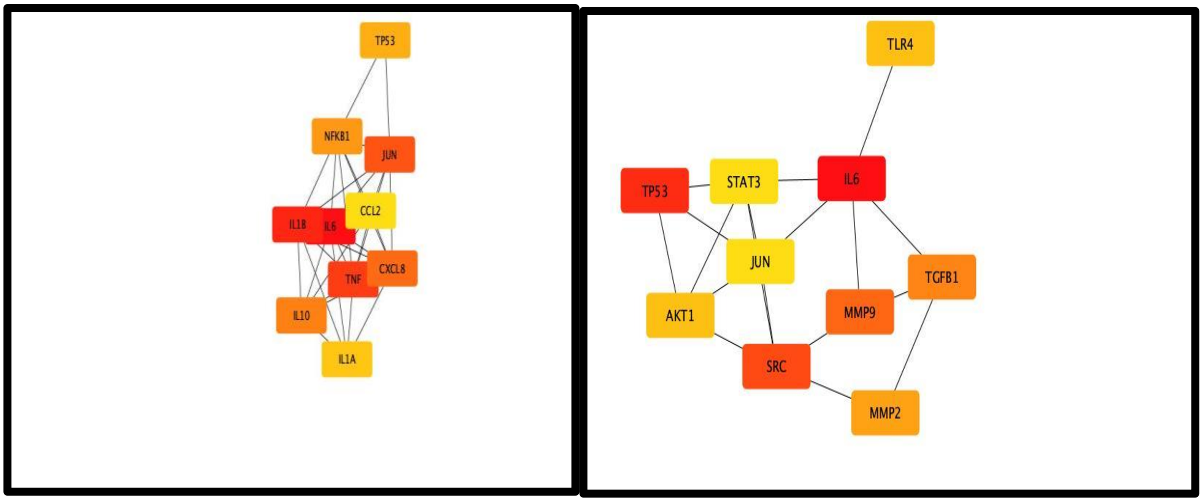


Figure4: EPC And BOTTLENECK GENE NETWORK VISUALIZATION BASED PARAMETERS RESULTING IN THE IDENTIFICATION OF KEY TARGET GENE

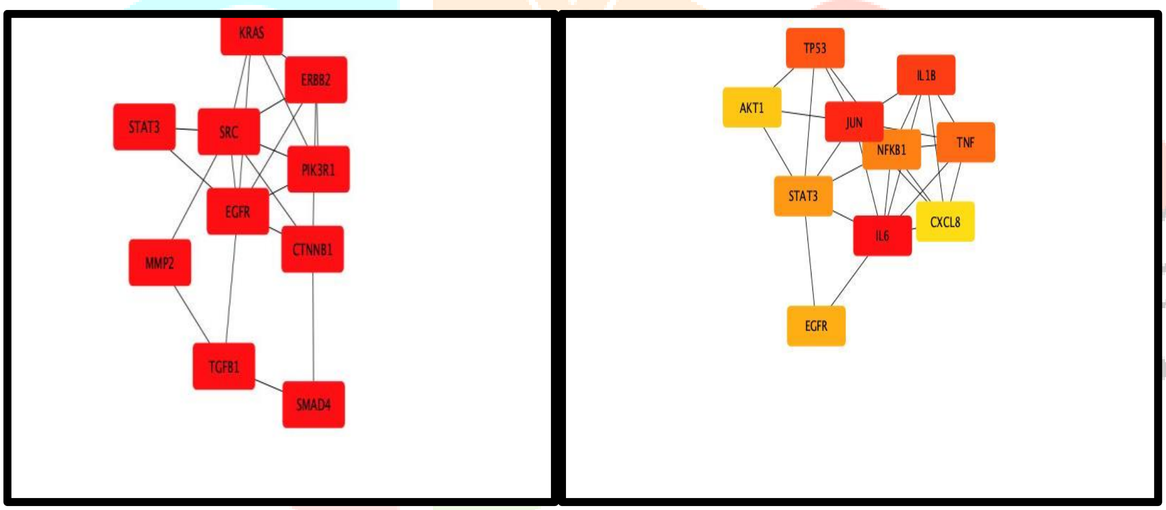


Figure5: ECCENTRICITY And CLOSENESS GENE NETWORK VISUALIZATION BASED PARAMETERS RESULTING IN THE IDENTIFICATION OF KEY TARGET GENE

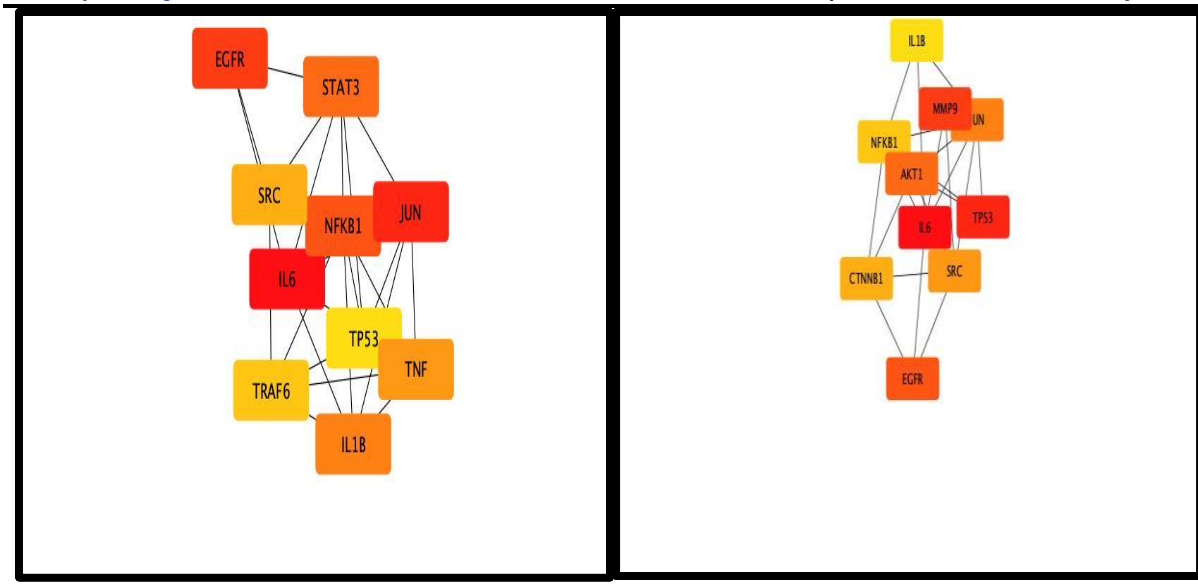


Figure6: RADIALITY And BETWEENNESS GENE NETWORK VISUALIZATION BASED PARAMETERS RESULTING IN THE IDENTIFICATION OF KEY TARGET GENE

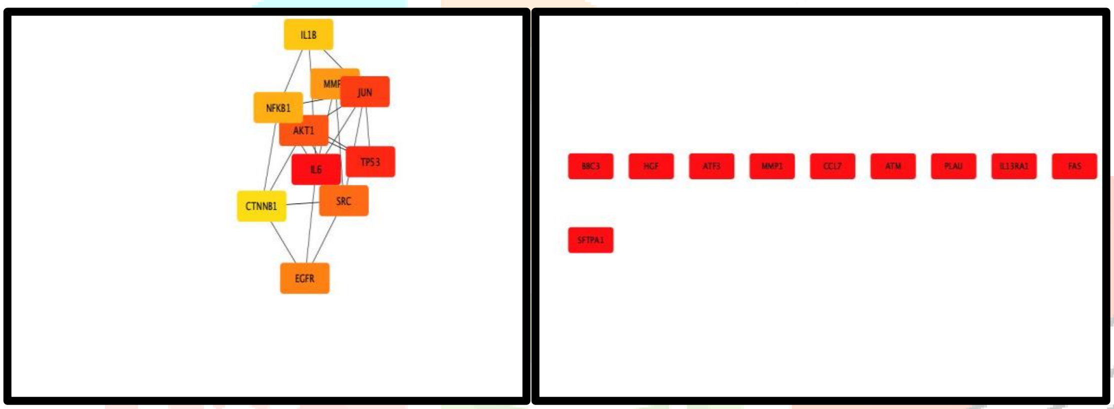
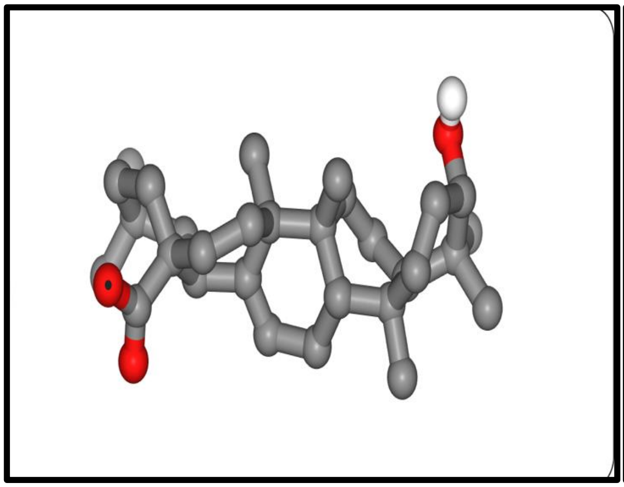
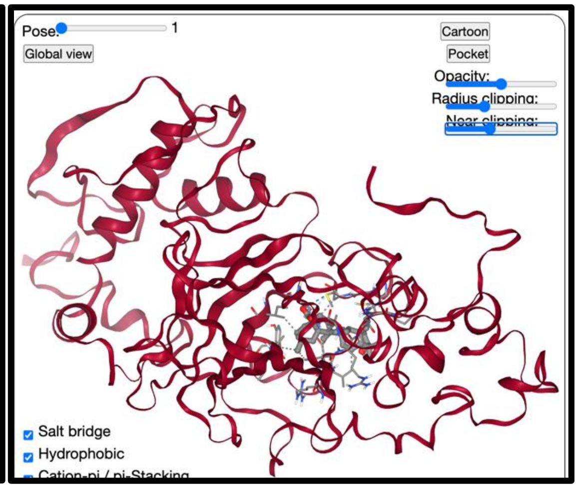


Figure7: STRESS And CLUSTERING COFFICIENT GENE NETWORK VISUALIZATION BASED PARAMETERS RESULTING IN THE IDENTIFICATION OF KEY TARGET GENE

Using TP53 modelled structure, Molecular Docking was performed for 20 phytocompounds that accepted the Lipinski's. Rule, other five were rejected. The best binding score that was obtained was from the phytocompound **Oleanolic Acid** obtained from *Olea europae*. with binding energy of **(-9.24kcal)** with the receptor **TP53** obtained in PDB format. All the other **24 phytochemicals** were also assessed with molecular docking.

Oleanolic Acid As Ligand and Docking was performed and had highest binding affinity of -9.24kcal and amino acid residues M 246, Y163,E171,V172,V173,R249,I251

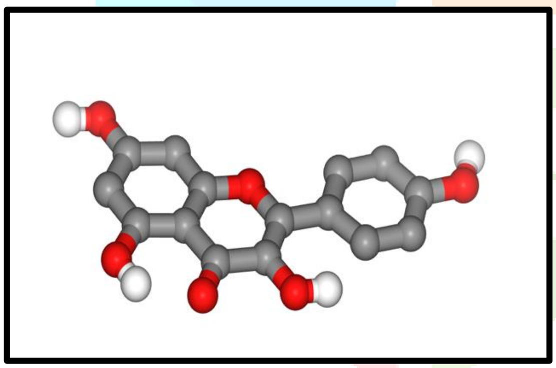


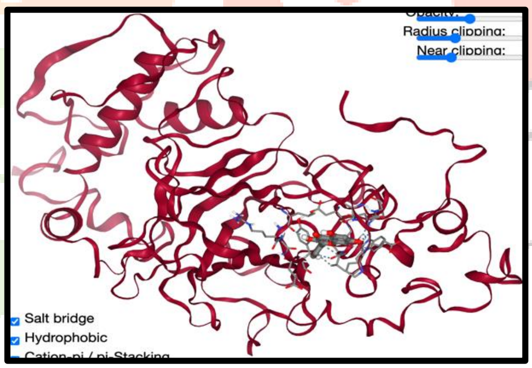


OTHER 19 PHYTOCOMPOUNDS WITH THEIR BINDING ENERGIES AND AMINO ACID RESIDUES Results Given Below

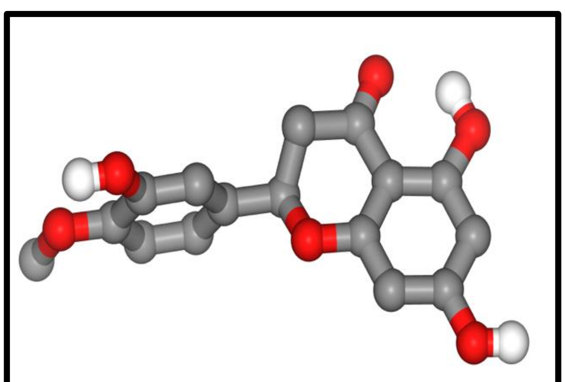
TABLE-4

Kaempferol

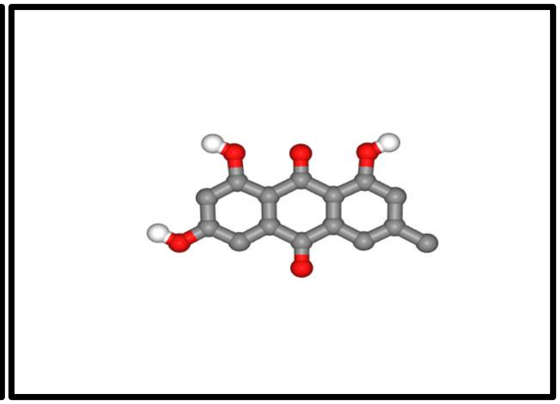




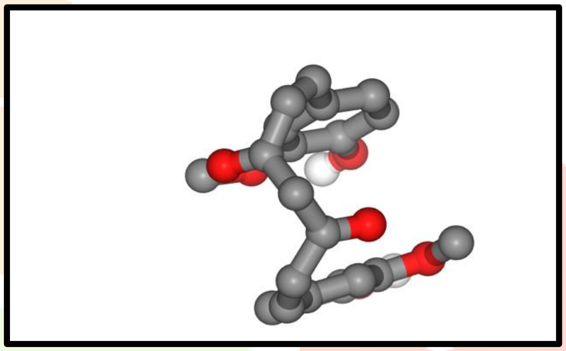
Hesperetin



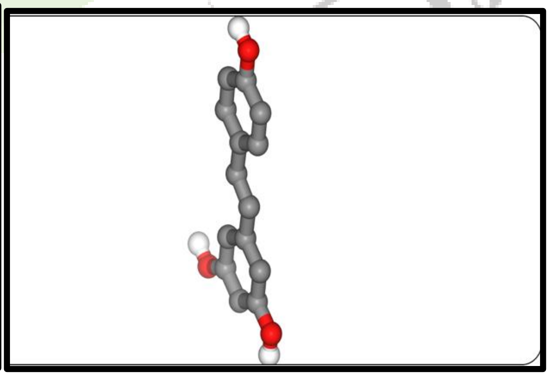
Emodin



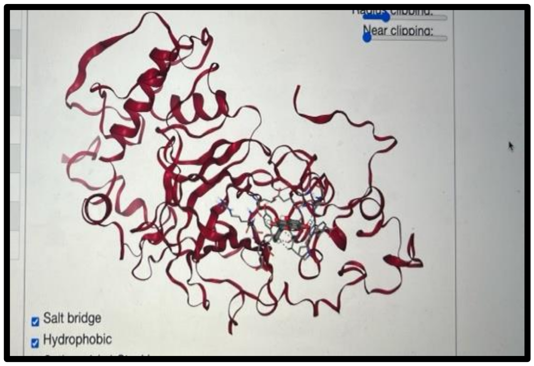
Curcumin

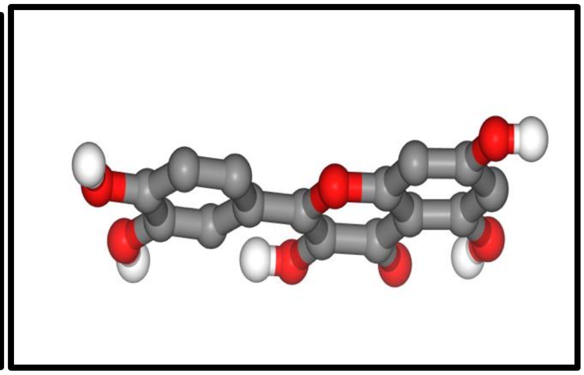


Resveratrol

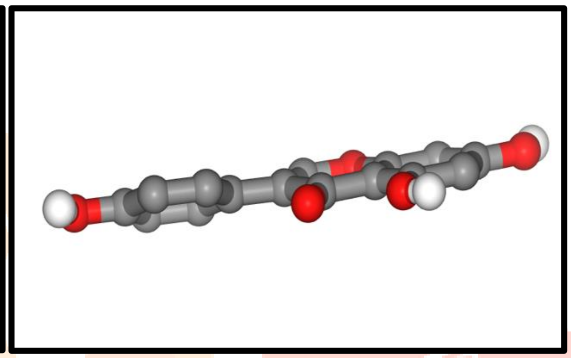


Quercetin

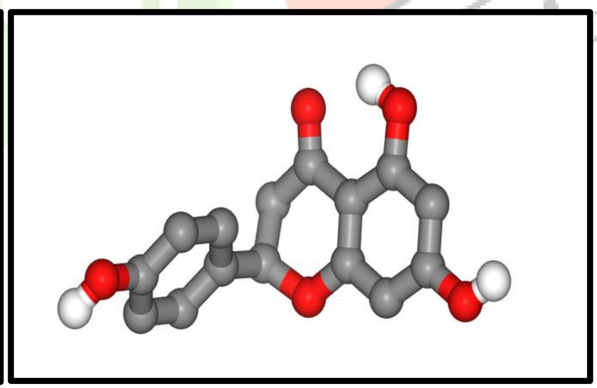




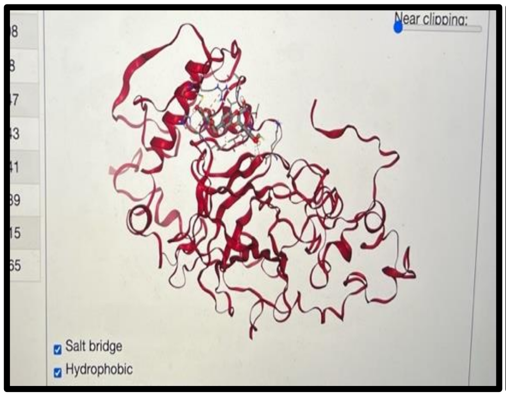
Genistein

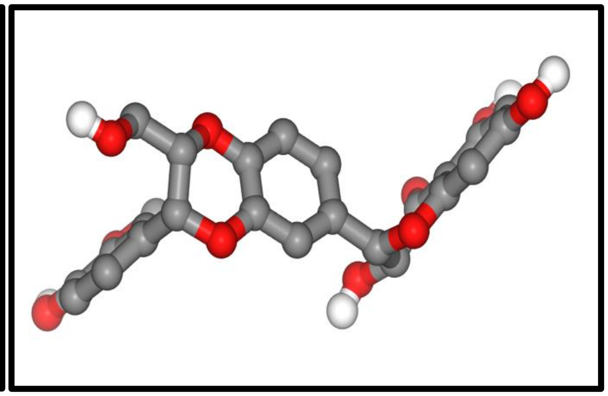


Naringenin

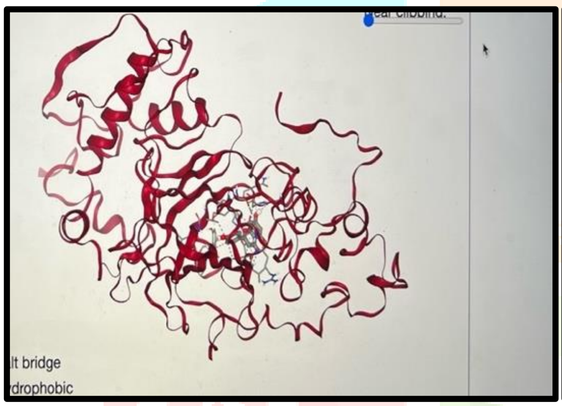


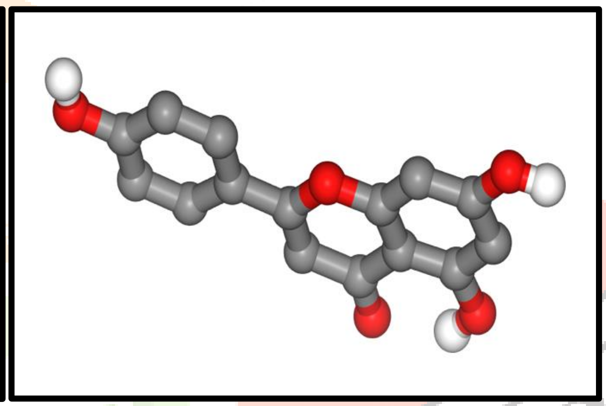
Silibinin



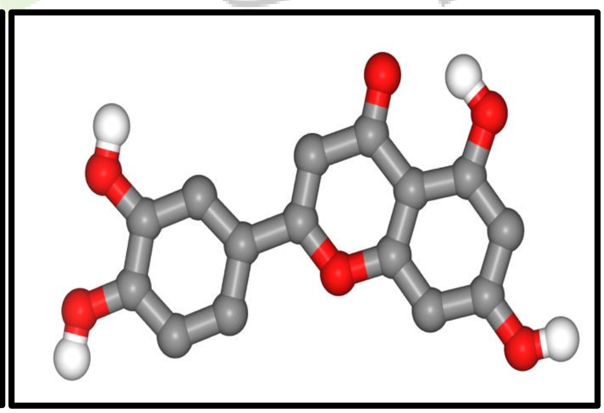


Apigenin

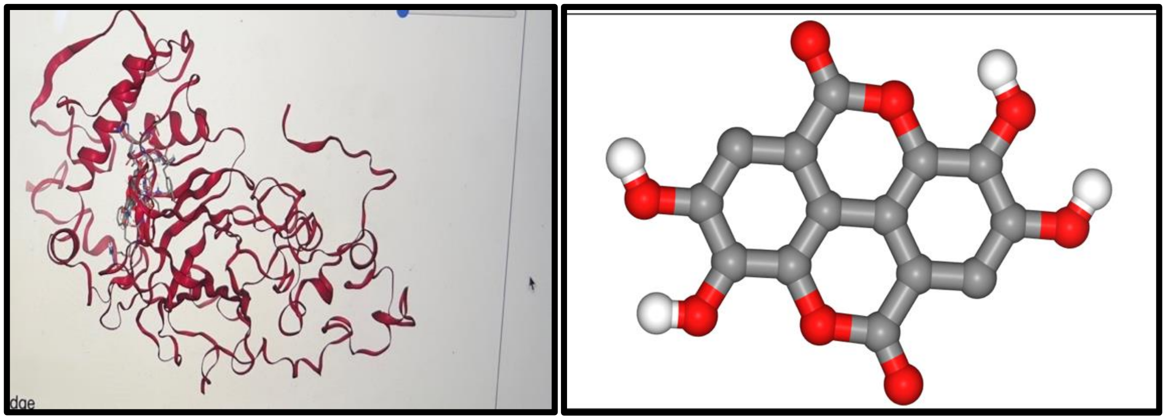




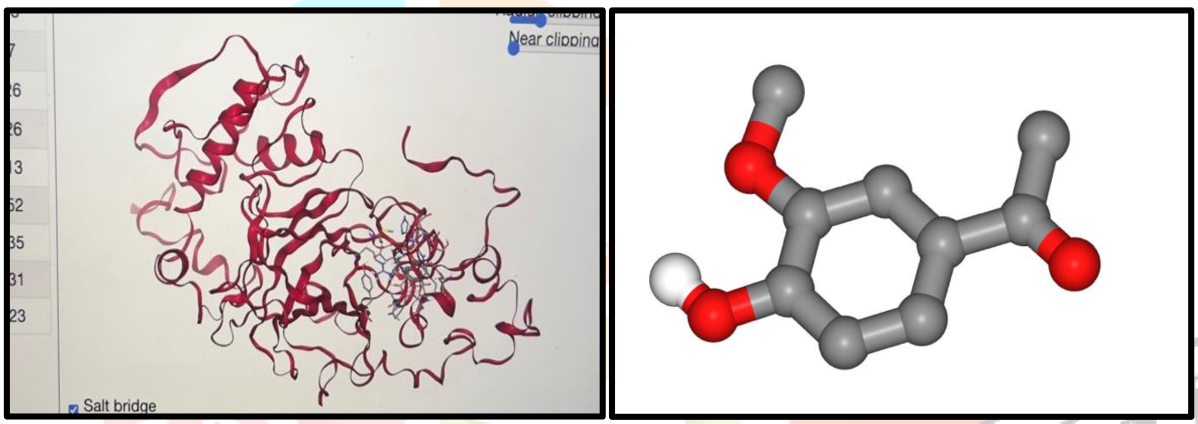
Luteolin



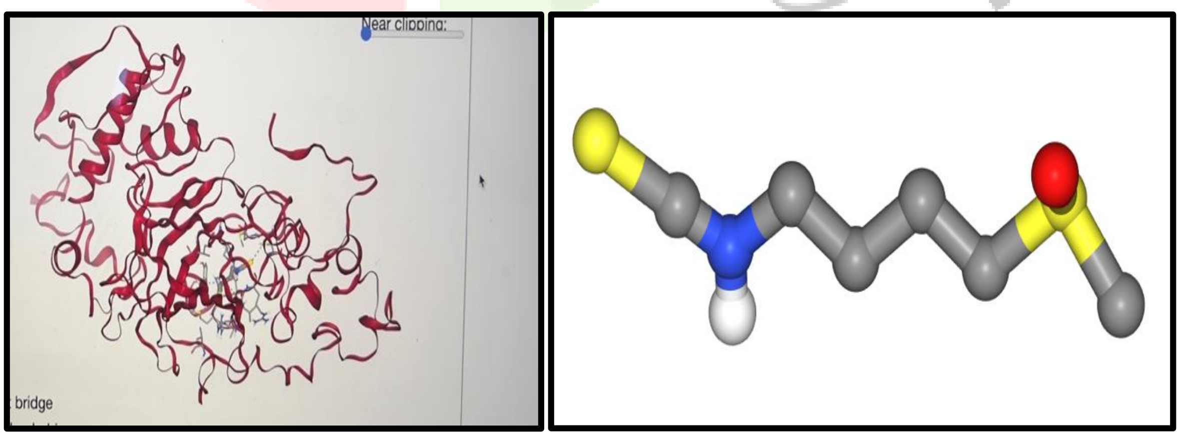
Ellagic Acid



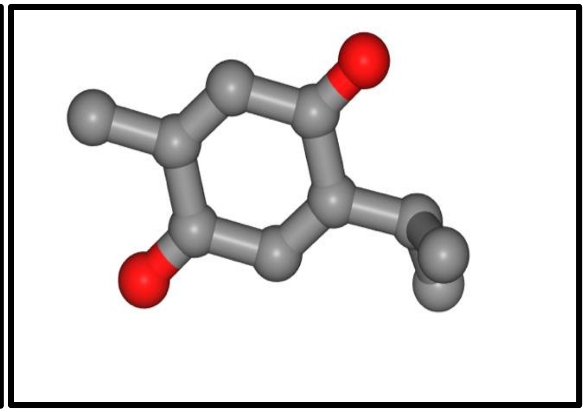
Apocynin



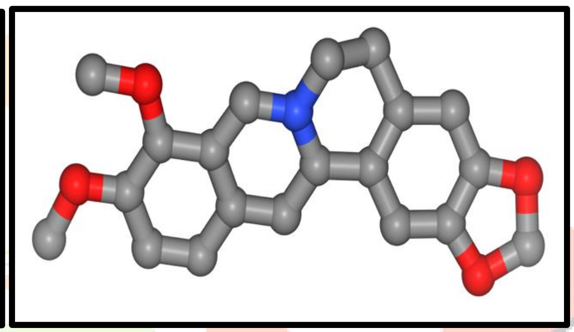
Sulforaphane



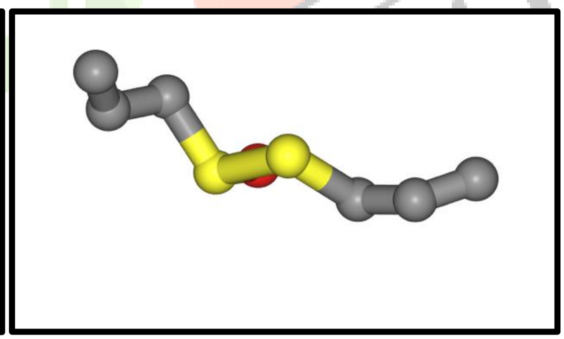
Thymoquinone



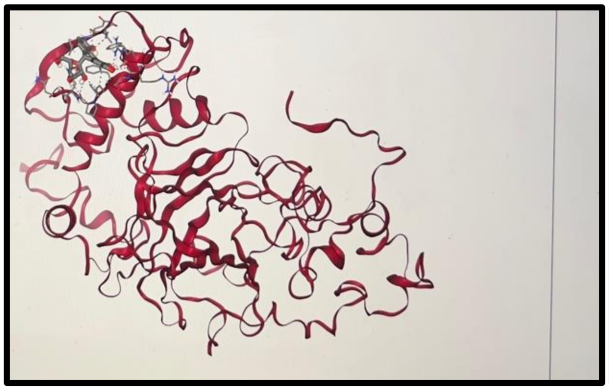
Berberine

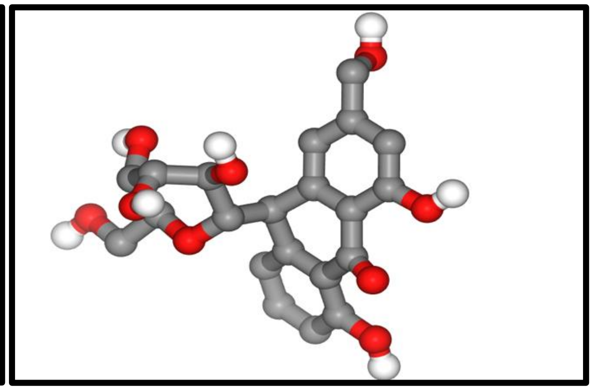


Allicin



Aloin





PHYTOCOMPOUNDS	BINDING ENERGY	AMINOACID RESIDUE
SODIUM TANSHINONE IIA SULFONATE	-6.601	-
KAEMPFEROL	-6.17	W23,L188,Y205,E28,L201,N30,E204
Hesperetin	-6.74	W23,P34,D186,L201,V203,S33,N29,E28
EMODIN	-6.65	Y163,M246,R249,I251,E171,V172,R174,R175,G244,V173,C176
CURCUMIN	-6.73	W23,P27,P34,L188,L201,V203,N29,S33,G187
RESVERATROL	-6.05	Y236,Y163,I251,E171,V173,L194,M169,M246,H168,R249
QUERCETIN	-5.73	E171,V173,V172,R174,C176,G244,G245
GENISTEIN	-6.62	I251,M246,V173,Y163,E171,G244,V172,R174,C176
NARINGENIN	-7.59	Y163,E171,V173,M246,R249,M169,C176,H168,R213,R174,G245,V172
SILIBININ	-6.53	L114,H115,R306,V122,T140,T125,C124,T123,S116
APIGENIN	-6.04	Y163,I251,E171,V173,R249,M246,V172,G245

LUTEOLIN	-6.28	F113,Y126,N131,L111,H115,S116,L114,G112,P128
ELLAGIC ACID	-6.83	L111,F113,L114,N131,P128,G112
APOCYNIN	-5.86	Q16,P191,F19,A189,R175,G187,S20,S185
SULFORAPHANE	-4.53	Y163,E171,M169,C176
THYMOQUINONE	-5.96	Q16,F19,P190,R196,P191
BERBERINE	-7.04	L114,F113,L111,N131,W146
ALLICIN	-4.68	Q16,F19,D184,R196,S185
ALOIN	-5.69	L308,L330,I332,R306,P309,Q331,N310,R337

5. CONCLUSION:

For the purpose of analyzing the impacts of silica on illnesses that affect Homo sapiens, transcriptome sequencing was used, and the GEO Accession Id GSE30215 was employed for the investigation. During the course of the research, 13528 genes were examined, and 1075 genes were found to have unique expression patterns. By using network biology techniques, the top 10 genes were discovered, and the sequence of the target gene as well as the protein sequence was determined. Through the utilization of the Swiss Model tool, the priority hub gene that is accountable for the therapy of silicosis was discovered. A list of phytocompounds that have the potential to have therapeutic effects on silicosis was compiled via the process of conducting a literature review. There were twenty-five phytochemical compounds that were acquired as ligands for docking, and a hypothetical library of chemicals was developed. Molecular docking was performed with the use of tools such as Swiss dock and Seam dock in order to determine which target chemical would be the most appropriate for the creation of a drug. Because it is identical to the template in every way, the TP53 gene was chosen to be the priority hub gene among the candidates. The phytocompound Oleanolic Acid, which is produced from Olea europae, was shown to have the highest binding score. The research emphasizes the significance of gaining a knowledge of the function that phytocompounds play in the treatment of silicosis as well as the prospective therapeutic advantages that these compounds may provide.

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