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Molecular Docking and Network Pharmacology Based Approach To Explore Potential Targets for Influnza Virus

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I. INTRODUCTION

Influenza, usually known as the flu, is a tremendously contagious respiration contamination due to influenza viruses. These viruses belong to the Orthomyxoviridae family and are known for their capacity to motive seasonal epidemics and coffee pandemics. Influenza viruses often infect the top and decrease respiratory tract, leading to symptoms together with fever, cough, sore throat, muscle aches, fatigue, and, in severe instances, pneumonia or dying. The virus is a widespread public health challenge due to its excessive mutation price, zoonotic ability, and capability to steer clear of immune responses.

Influenza viruses are enveloped, single-stranded, bad-sense RNA viruses with a segmented genome (eight segments for Influenza A and B, 7 for Influenza C and D). Key structural additives consist of:

Hemagglutinin (HA): A floor glycoprotein that binds to sialic acid receptors on host cells, facilitating viral access.

Neuraminidase (NA): An enzyme that cleaves sialic acid, allowing viral launch from infected cells.

Matrix Protein (M1): Provides structural stability.

Ion Channel Protein (M2): Facilitates viral uncoating.

Nucleoprotein (NP): Encapsulates viral RNA.

RNA-dependent RNA Polymerase (PB1, PB2, PA): Essential for viral replication.

The segmented nature of the genome allows for genetic reassortment, a key mechanism at the back of the emergence of pandemic strains.

II. MATERIALS AND METHOD

1. Data Collection: By the beneath steps:

Screening of Active Antiviral Phyto-parts, Pharmacokinetic ADME Prediction, Potential Target Screening for Anti-Viral Phyto-constituents and Influnza, binding DB database, KEGG Mapper database, DisGeNet Database, intersection of phytoconstituent and disease goal, String database, Metascape database.

2. Data Preparation: by way of underneath steps:

Molecular docking, the preparation of small molecule ligand documents, education of macromolecular receptor documents, the development of matting pockets, docking and visualization, community production, intersection of phytoconstituent and sickness goal, Protein protein interplay.

BIOINFORMATICAL ANALYSIS:

Molecular Docking

Molecular docking analyzed interactions among phytoconstituents (ligands) and target proteins, revealing binding modes (e.G., hydrogen bonds, π-alkyl interactions). Isochlorogenic Acid A confirmed hydrogen bonds (green), π-cation (orange), and π-alkyl (red) interactions.

ADME Prediction (SwissADME)

- Physicochemical Properties: Evaluated molecular weight, H-bond donors/acceptors, rotatable bonds, and many others.
- Lipophilicity: Predicted through models (XLOGP3, WLOGP, and many others.); higher log P = more lipophilicity.
- Solubility: Classified the use of ESOL and SILICOS-IT models (log S scale: insoluble → particularly soluble).
- Pharmacokinetics:
  - BOILED-Egg Model: Predicts GI absorption (white) and brain permeability (yellow).
  - SVM Algorithm: Assesses substrate/inhibitor capacity.

- Lipinski's Rule of Five (Ro5): Orally active pills commonly have:
  - Molecular weight <500
  - H-bond donors <five
  - H-bond acceptors <10
  - Log P ≤five

III. RESULT

1. Molecular docking: Molecular docking studies have been carried out to investigate the binding interactions between decided on phytoconstituents and target proteins, providing insights into their ability mechanisms of motion. The docking simulations were accomplished the usage of AutoDockVina, with results visualized thru Chimera software program. Binding affinity, measured in kcal/mol devices, served as the important thing metric for comparing interaction energy, wherein lower values indicate stronger binding. For the 3TRK protein, amentoflavone verified the best binding affinity (-nine.Eight kcal/mol), observed carefully by using fisetin (-9.7 kcal/mol) and isochlorogenic acid A (-nine.6 kcal/mol). In the case of the 3GPO protein, punicalagin showed the most powerful binding (-10.1 kcal/mol), with geranin (-nine.8 kcal/mol) and isochlorogenic acid A (-nine.5 kcal/mol) additionally exhibiting considerable interactions. Notably, even as punicalagin and chebulagic acid displayed the most powerful binding affinities for each proteins, they were excluded from further analysis. This choice become based totally on their lack of goal additives relevant to viral contamination pathways, making other phytoconstituents with slightly decrease but still sturdy binding affinities more appropriate for next investigations. These findings provide treasured preliminary records for expertise the molecular interactions of bioactive plant compounds with healing goals.

2. For pharmacokinetic houses: Pharmaco-kinetic observe (absorption, distribution, metabolism, excretion, and toxicity) of the phytoconstituents was studied through using the ADME calculator and AdmetSAR databases Their effects have been received for simplest the ones Phyto-components that display the highest binding affinity from molecular docking results.According to the Lipinski Rule of Five, baicalein, fisetin, and luteolin follow the guideline, while Isochlorogenic Acid A, and Proanthocyanidin B2 violate 3 parameters: molecular weight, H-bond acceptors, and H-bond donors.

3. Result for community Pharmacology: Network evaluation gives insights into drug-ailment associations and molecular pathways. Using Cytoscape, key community metrics had been calculated: average shortest route duration (data performance), betweenness centrality (bridge feature), closeness centrality (average node distance), and connectivity (neighbor be counted).
Four awesome networks were analyzed:
Network 1: 488 nodes, 901 edges (density: 0.008, centralization: 0.178). Top objectives: PTGS2 (diploma=11), ABCB1 (eight), MMP9 (eight).
Network 2: 476 nodes, 932 edges (density: 0.008, centralization: zero.203). Top targets: PSMA4 (eleven), PSMA3 (11), ALOX12 (6).
Network 3: 358 nodes, 759 edges (density: 0.012, centralization: 0.213). Top goals: PTGS2 (6), CYP1A1 (6), VEGFA (4).
Network 4: 171 nodes, 301 edges (density: 0.021, centralization: 0.431). Top targets: PRKCH (three), PRKCA (3), AKR1B1 (2).
Phytoconstituent stages numerous (forty nine–a hundred), reflecting their connectivity. These metrics highlight crucial nodes and community robustness, helping drug discovery.

4. Result for intersection of phytoconstituents and influenza targets: The intersection of expected targets from phyto-parts and influenza disease found out eleven mutual targets, suggesting ability for drug repurposing. These goals had been analyzed using the GeneCards "Analyze" tool, which diagnosed their associations with various diseases across species. This method highlights promising applicants for further investigation in influenza treatment.

5. Result for protein protein interplay network of targets: To discover phytoconstituents' mechanisms towards influenza, a PPI community changed into built the use of STRING v11.Zero (Homo sapiens, high-self assurance interactions). Key findings:
Isochlorogenic Acid A:
Nodes: 90 Edges: 465 diploma: 10.3 0 Edges: 566 diploma: eleven.1 zero.587
Proanthocyanidin B2:
Nodes: 48 degree: 9.25 zero.704
Conclusion: Luteolin, Baicalein, and Proanthocyanidin B2 showed the very best connectivity, suggesting their potential as key modulators in influenza remedy.

6. Result for PPI network Analysis and hub gene verification: The CytoHubba plugin in Cytoscape identified the pinnacle 10 hub genes crucial for community connectivity. These key genes and their primary functions are:
-ESR1 - Estrogen receptor regulating hormonal responses
-VEGFA - Promotes angiogenesis and blood vessel formation
-EGFR - Regulates cell boom and differentiation
-PTGS2 (COX-2) - Mediates inflammation through prostaglandin synthesis
-SNCA - Involved in synaptic feature and neurotransmitter release
-CYP3A4 - Key drug metabolism enzyme
-CFTR - Regulates chloride ion shipping
-AR - Mediates androgen hormone outcomes

-MMP9 - Important for tissue remodeling
-PPARG - Regulates fats mobile differentiation and metabolism
Additional large genes covered:
- PRKCA/PRKCB - Protein kinases in cell signaling
- AKR1B1- Glucose metabolism enzyme
- TRPC1/TRPC4 - Ion channel regulators
- HSP90AB1 - Molecular chaperone
- APP - Neuronal improvement
- PTPN1 - Tyrosine phosphatase signaling
- PSMA3/PSMB10 - Proteasome additives for protein degradation
These hub genes constitute critical molecular targets with diverse features in cell procedures, metabolic regulation, and signaling pathways, making them ability applicants for therapeutic intervention.

7. Result for module evaluation of protein protein interplay network: We diagnosed key protein interaction modules for three phytocompounds the usage of MCODE:
Isochlorogenic Acid A:
Module 1 (Score=15.6): 16 nodes/117 edges (PSMB6, SNCA, PSMA1)
Module 2 (Score=eight.Zero): 8 nodes/28 edges (KIT, ESR1, TERT)
Module three (Score=5.0): five nodes/10 edges (PLA2G10, ALOX12)
Luteolin:
Module 1 (Score=16.Five): 17 nodes/132 edges (PSMB8, SNCA, PSMA5)
Module 2 (Score=6.4): 15 nodes/45 edges (APP, PTPN1, KDR)
Module three (Score=4.5): 12 nodes/25 edges (ABCB1, AKR1C3)
Proanthocyanidin B2:
Module 1 (Score=4.0): four nodes/6 edges (PRKCH, PRKCB)
Module 2 (Score=15.6): sixteen nodes/117 edges (PSMB6, SNCA)
Module 3 (Score=8.Zero): eight nodes/28 edges (KIT, ESR1)
Key objectives like SNCA, ESR1, and PSMA proteins seemed throughout multiple compounds, suggesting shared mechanisms. Higher-scoring modules suggest extra densely linked useful clusters. Eight.Result for gene ontology functional enrichment analysis: Through the functional enrichment evaluation of GO, the primary capabilities of the targets are enriched to Proteasome middle complex, Proteasomal ubiquitin-impartial protein catabolic process, Carbonate dehydratase hobby, Cyclooxygenase pathway and so on. Among them, the 2 capabilities fProteasomal ubiquitin-unbiased protein catabolic method, Cyclooxygenase pathway hobby are enriched to the maximum genes with high importance, so they'll imply that they're the principle features of the target.

IV. CONCLUSION

In this study, the molecular mechanism of Phytoconstituents inside the remedy of influenza virus was explored by means of network pharmacology and molecular docking. It turned into found that the potentially important Phytoconstituents within the treatment of influenza virus have been Isochlorgenic Acid A, Luteolin, and pronthtocynadin B2 Through the PPI network analysis, it is found that the ability Phytoconstituents in the treatment of influenza virus are Luteolin, Isochlorgenic Acid A and Proanthocyanidin B2 and the network may be divided into 3 modules. GO practical enrichment evaluation showed that the target specifically achieved Proteasomal ubiquitin-independent protein catabolic system and other capabilities. Finally, it's miles of first rate importance to check and discover the binding among the lively components and the goal via molecular docking. Further take a look at on the antiviral activity of phytoconstituents and the underlying mechanism are nonetheless urgently to be investigated in different techniques along with in vitro, in vivo, and clinical take a look at assessment to verify this in silico look at.

V. REFERENCES

1). Oliveira Silva Martins D, de A ndrade Santos 1, Moraes de Oliveira D, RiquenaGrosche V. Carolina Gomes Jardim 7 Antivirals against influenza virus: is the answer in nature?. Viruses. 2020 Feb 29;12(three):272
2). Battisti V, Urban E, Langer T. Antivirals towards the influenza virus Viruses 2021 2. Jul five:thirteen(7):1307
3). Raghavendhar S Tripati PK. Ray P, Patel AK Evaluation of medicinal herbs for a.Anti- Influnz interest Virology 2019 Jul 1:533:forty five-9 Roongaraya P. Boonyasuppayakorn S. Influenza vaccines: An update in 2023. Asian four. Pacific Journal of Allergy and Immunology 2023 Mar 1;41():1-1, five. Hakim MS, Aman AT Understanding the Biology and Immune Pathogenesis of influenza Virus Infection for Diagnostic and Vaccine Development. Viruses. 2022 Dec 23;15(1):forty eight
4). Vora J, Patel S, Sinha S, Sharma S, Srivastava A, Chhabria M, Shrivastava N. Structure o. Based digital screening, 3-D-QSAR, molecular dynamics and ADMET studies for choice of herbal inhibitors in opposition to structural and non-structural objectives of influenza. Journal of Biomolecular Structure and Dynamics. 2019 Aug thirteen:37(12):3150-sixty one.
Five) de Lima Cavalcanti TY, Pereira MR, de Paula SO, Franca RF. A evaluate on influenza virus epidemiology, pathogenesis and modern-day vaccine development.A. Viruses. 2022 May five;14(5):969.

6). Rausalu, K.; Utt, A.; Quirin, T.; Varghese, F.S.; Zusinaite, E.; Das, P.K.; Ahola, T:; Merits, A. Influenza virus infectivity, RNA replication and non-structural polyprotein processing rely upon the nsP2 protease's lively web site cysteine residue. Sci. Rep. 2016, 6,37124

7). Freire, M.; Basso, L.G.M.; Mendes, L.F.S.; Mesquita, N.; Mottin, M.; Fernandes, R.S.; Policastro, L.R.; Godoy. A.S.; Santos, LA.: Ruiz, U.E.A.; et al. Characterization of the RNA-structured RNA polymerase from influenza virus and discovery of a unique ligand as a capacity drug candidate. Sci. Rep. 2022, 12, 10601.

Eight) Silva, LA; Dermody, T.S. Influenza virus: Epidemiology, replication, ailment mechanisms, and prospective intervention techniques. J. Clin. Investig. 2017, 127, 737-

nine) Translational Research Consortia (TRC) for influenza Virus in India. Current reputation 749. Of influenza in India. Frontiers in Microbiology. 2021 Jun 24:12:695173.

10). Kapoor R, Sharma B, Kanwar SS. Antiviral phytochemicals: an outline. BiochemPhysiol Open Access. Gabrani R. Phytochemicals.