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Scope and challenges of network pharmacology in Ayurveda research elucidated towards modelling the efficacy of *Osmium tenuiflorum* (Tulsi) for virus-induced influenza

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Natural products, renowned for their healing properties, are significant in every culture and have been practised for ages. These diverse traditional remedies, spread across various regions, are crucial in advancing humanity. In East Asian societies, conventional healing methods enjoy popularity, contrasting with the deep exploration of traditional Chinese medicine compared to traditional Indian medicine, especially in understanding their mechanisms and effects. These remedies, typically a blend of multiple herbs, target numerous cells, unlike allopathic medicine, which mainly focuses on one or two targets. Tools in network pharmacology offer extensive insights into multi-target interactions, proving invaluable in the study of herbal combinations. This analysis endeavours to uncover the potential within Ayurvedic formulations and present a global outlook on Ayurvedic research. Over time, the world has grappled with viral infections affecting the respiratory system. The study outlines the potential of *Osmium tenuiflorum* (Tulsi) as a remedy for Virus-induced Influenza. Initial virtual screenings suggest that Apigenin exhibits antiviral properties by influencing targets like CFTR and Akt. This review aims to draw the scientific community's attention in that direction by highlighting Ayurvedic formulations.

Keywords: Ayurveda, Network pharmacology, Tulsi, Virus-induced Influenza

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Early human civilization arose around 6000 BCE. The use of animal and plant products in treating aliment was recorded in every civilization; each has adopted its unique style and formulations, often cited with local and region-specific names. The practice of using natural compounds for treating illness has a huge role to play in human colonization. The empirical knowledge preserved in communal experience mainly translates through oral communication across generations or, in other instances, poorly summarized in early scriptures. Gradually enriched across various civilizations and transformed into their dialect and customs. Traditional medicine treating complex diseases is famous in East Asia, Egypt, Greece, and some Islamic cultures (Fig. 1)[1-9].

Ancient medicinal practices: chronological advances and popularization

Due to geographical proximity and cross-culture exchange among habitats, the collections contain duplicated entries. Though repetitive, their posology has attained a distinct shape in every civilization. For example, the therapeutic potential of *Curcuma longa* (turmeric) was recognized in Sushrut Samhita; it recommends its application in treating cough, diabetes, and liver diseases[10]. It might have reached China around 700 BC and be used to treat cardiovascular diseases[11]. Currently, curcumin extracted from turmeric is recognized for some cancers, and the drug is under phase II clinical trials[12]. Century-old references are the seed of recent applications. Although this example delineates the successful utilization of traditional knowledge, such instances are sparse. Region-specific confinement of knowledge, inconsistent practising style, and poor records limit the practice and broader acceptance. It is never recognized by allopathic medicine (AM) practice due to the lack of correlating validation studies and always considered alternative medicines. AM usually acts against symptoms aiming at one or two targets through an effector, omitting the synergistic impact[13]. Contrary to it, traditional medicinal practice effectively utilizes the decoction of multiple compounds that affect different targets. It offers an all-inclusive approach to treatment with minimal side effects.

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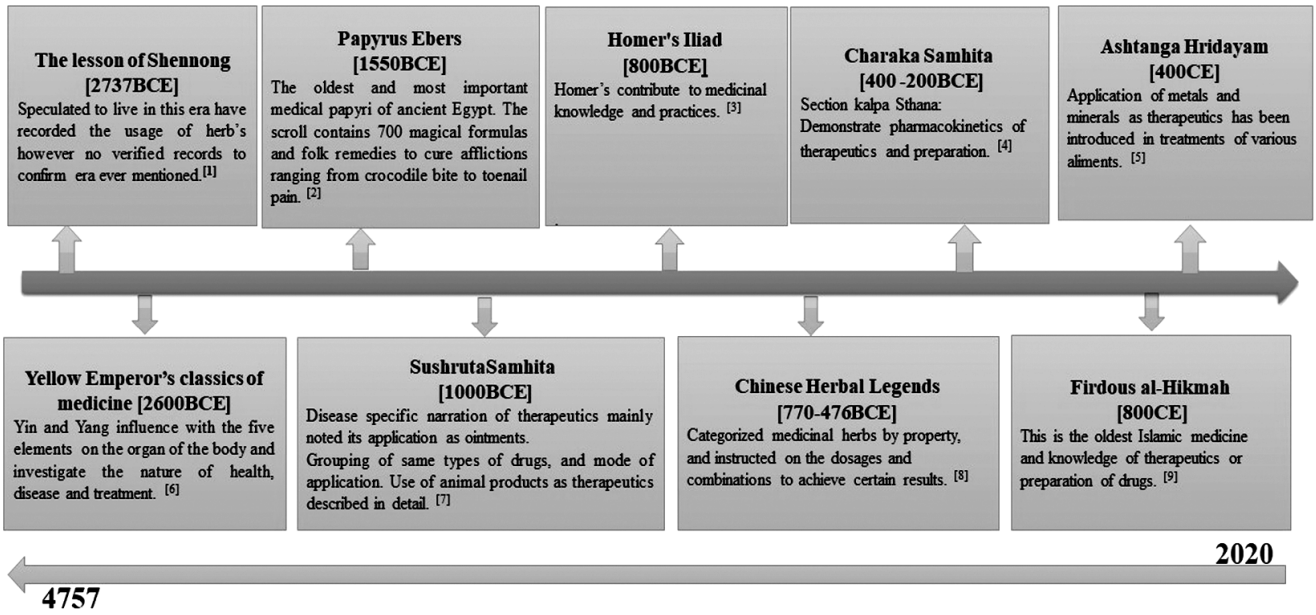

Fig. 1 — Chronicles describing the application of herbs/natural products or animal products for therapeutic applications

The present review mainly focuses on challenges and opportunities for Ayurveda practices. The review further encapsulates the applications of network pharmacology tools in Ayurveda research. First, we summarized the databases with details of monographs of plants and their constituent compounds. Second, the summary of computational tools utilized for impact assessment. Significantly, the evolution of natural compounds from a "potential candidate" to a "marketed drug" is challenging and necessitates highly integrated interdisciplinary approaches. Genomics and proteomics research data flooded the field of Biotechnology, and the bulk amount of data gave rise to the new discipline of bioinformatics[14]. Bio-informatics utilizes various computational and mathematical tools for identifying, screening, predicting, and modelling natural product-based therapeutics. Here, we represent the scope of network pharmacology in modelling and developing the treatment strategies for virus-induced influenza.

Ayurveda and other contemporary medicine practice: A bird's eye view

Each discipline has its code. Traditional Indian medicine (TIM), named Ayurveda, is considered the mother of all healing. Ayurveda has adopted a holistic approach that balances five vital factors that rule our life. The repertoire includes diet, lifestyle, thought modulation, and uses of herbs. The combinatorial practice emphasized the progressive restoration of the body through Panchakarma. The process of Panchkarma follows emesis (vamana), purgation (virechana), evacuative enema (asthapana basti), restorative enema (anuvasana basti), and errhines (shirovirechana) through using various herbal formulations and diet regimens. The practice recommends using a variety of herbs, about 985 formulations, minerals, metal substances, and other animal products for humankind's well-being[15]. It has also illustrated the specific procedure for herb collection, decoction, and applications. For example, in Ayurveda classics, Ashwagandha (*Withania somnifera*) is used for the preparation of Rasayana (therapeutics) prescribed to relieve depression[16]. Ayurveda emphasized the season and time-dependent collection of Ashwagandha roots. Accordingly, it should be collected during the full moon day of the lunar cycle and administered in the morning or evening with a defined amount of milk. The same Rasayana (formulation) can be prescribed to another individual with water for the same ailment, considering the individual's prakruti (physiology). Very few scientific attempts have ever been made to understand the rationale. A handful of scientific reports have noted a rise in total phenolic, flavonoids and carbohydrate concentration in root samples when collected on a full moon day of the lunar cycle. Still, no correlation studies have ever been performed on its physiological impacts on human lives[17]. Considering the integrated nature of the application, preparation

methods, and the multifaceted implications on various targets, the tools available for validating these practices are scarce. Though dissimilar, TIM has a significant challenge in fitting into the existing gold standard for drug discovery. Traditional medicines often fail to mark their impact on one or two key targets nominated by AM.

Since 2010, 1,75,000 articles have been published in the field of drug discovery. Only 729 reports have mentioned Ayurveda or traditional Ayurveda medicines (Fig. 2a & Fig. 2b). Other contemporary disciplines, such as Traditional Chinese Medicines (TCM) and Kampo formulation, are widely recognized in China and Japan. Unlike Ayurveda, TCM has gained appeal in other Western countries. One of the key factors is the early recognition of TCM's potential by Chinese researchers. The research work of Tu *et al.* (2016)[18] on the discovery of the antimalarial drug Artemisinin using TCM has further stirred the practice and motivated researchers towards cataloguing TCM. The intervention of technological developments has led to an organized network of data on traditional Chinese and Kampo formulations. TCMID[19], TCMSP[20], TCM-Mesh[21], KampoDB[22] contain a comprehensive summary of phytochemicals, their protein targets and their similar FDA-approved drugs. Approximately 2069 small molecules with possible therapeutic applications are detailed towards such databases.

Despite immense potential as a therapeutics, the Ayurveda practice is more empirical than experimental and poorly recognized in a region outside the Indian subcontinent. Ayurvedic Pharmacopia by the Ministry of Ayush, Government of India, published in 2016, merely lists 45 monographs, which is insufficient considering the richness of resources. Contrary to its Chinese Pharmacopoeia, it presents 2058 monographs on traditional herbal and animal formulations and single compounds. A few databases are available in the public domain to provide information on Ayurvedic medicines, summarized in (Fig. 3)[23-26]. These catalogues, altogether, merely contain 1700 entries for plants and animal products of therapeutic interest, insufficient to represent the vast body of information.

A bottleneck can be explained towards the following observations:

First, of the four datasets, three lack the minute details of plant varieties, plant parts, collection time, phytochemical names and structures, etc.

According to Ayurvedic practice, phytochemicals should be extracted at a specific time using a defined extraction medium; none of the databases link to Ayurvedic practice and suggest methods for phytochemical extraction.

References related to these compounds' clinical validation and trials are missing or incomplete. Further, no information on posology is summarized in any of the above databases.

Even though these databases provide information on phytochemical constituents for each plant, practically, the quantity of an active molecule is insufficient to cater to the desired effects. Hence, Ayurveda prefers polyherbal formulation, and this herb-herb synergistic interaction can significantly enhance the impact of this chemical compound. Evidence suggests that phytochemicals have not shown any pharmacological activity when used alone, specifying the role of other herbs or active compounds[27]. Henceforth, the assessment should consider the impact of these multiple components on target/targets. Here, the critical need for the network

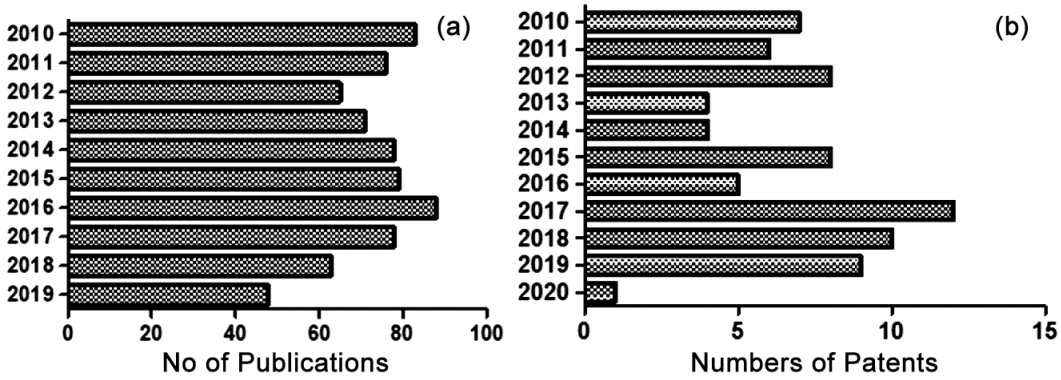

Fig. 2 — (a) Number of publications obtained towards Web of science listed journals through keywords Ayurveda, Ayurveda herbs, traditional Indian medicines; (b) Number of Patents filed at national and International authorities retrieved towards the key words-based search of patentscope (WIPO)

approach is observed, which considers the multiple targets for a single compound of interest.

Network Pharmacology: tools and role in traditional medicine research

Pharmacological research has its own pace and needs detailed background information for candidates. The characterization process is laborious. Early scrutiny of prominent candidates has proven helpful in attaining tangible outcomes in defining the duration. System biology has accelerated research and development in this field by initially screening targets, reducing the cost associated with high-throughput screening assays. Big data accumulation in genomics and proteomics gave a new impetus to the field of drug discovery and drug design. It partially transformed traditional tube reactions into the software's integrated network[28].

Tools designed in the field of network pharmacology can assist in developing an interaction network for compounds of interest. It further integrates the information from system biology and gives a detailed view of associated biological processes and crucial pathways that alter/increase or decrease the compound's efficacy. The druggable properties of compounds can be assessed through pharmacophore mapping and in-silico modelling, as well as by calculating the binding energies. At the same time, the network pharmacology studies provide a cluster for compounds having similar targets. It also illustrates the biological role of this compound. This way, it predicts the interaction of multiple compounds with multiple targets using pre-defined algorithms that operate by calculating the energies for chemical interactions. Seemingly the best methods for Ayurveda and TCM-based poly-pharmacology studies[29]. The standard strategy and tools are presented in (Fig. 4).

The network pharmacology (NP) approach is prevalent in TCM research. A significant boost in reports of virtual screening of compounds of

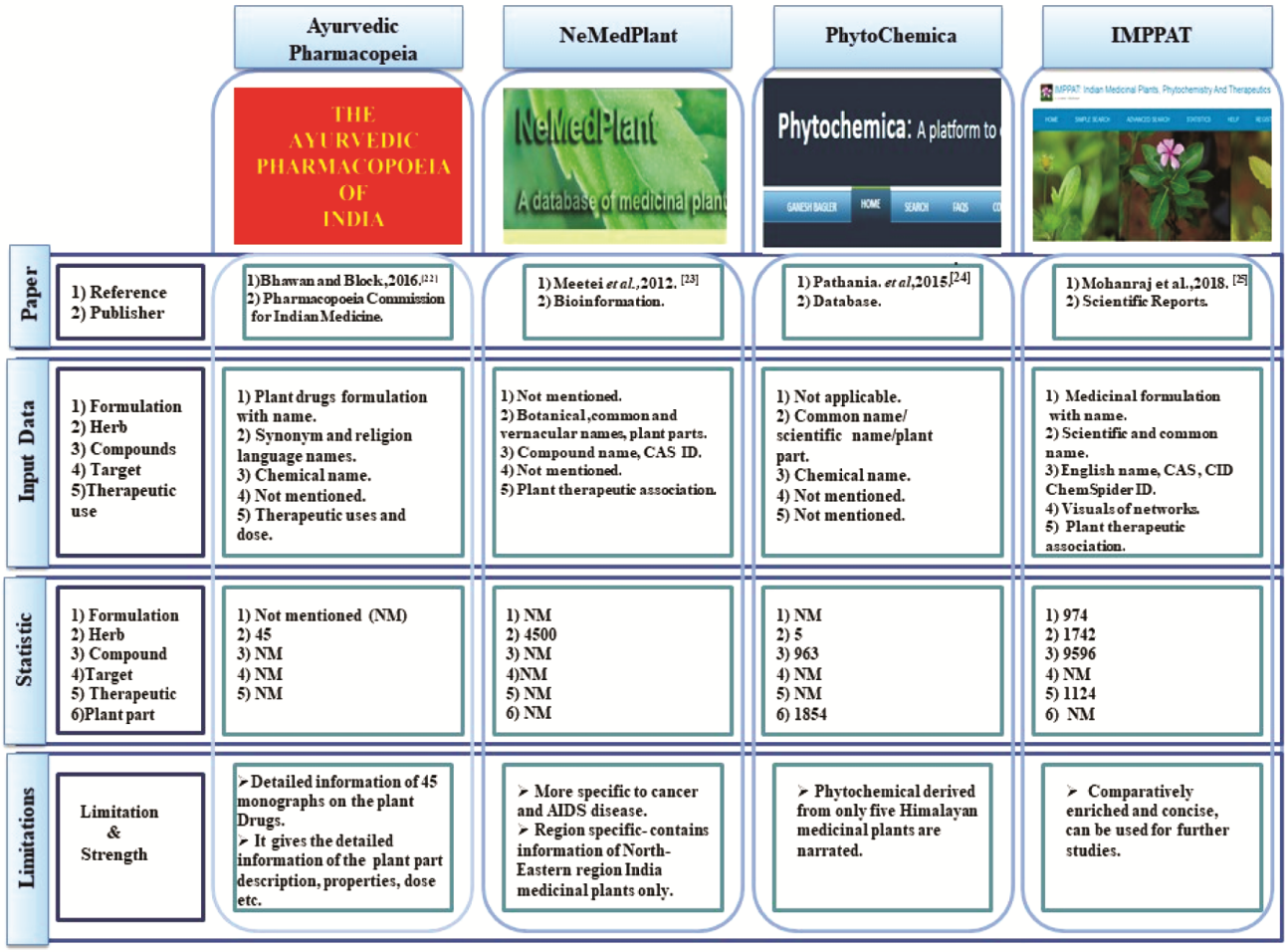

Fig. 3 — Comparative representation of details of traditional Indian medicinal herbs towards various databases available in the public domain

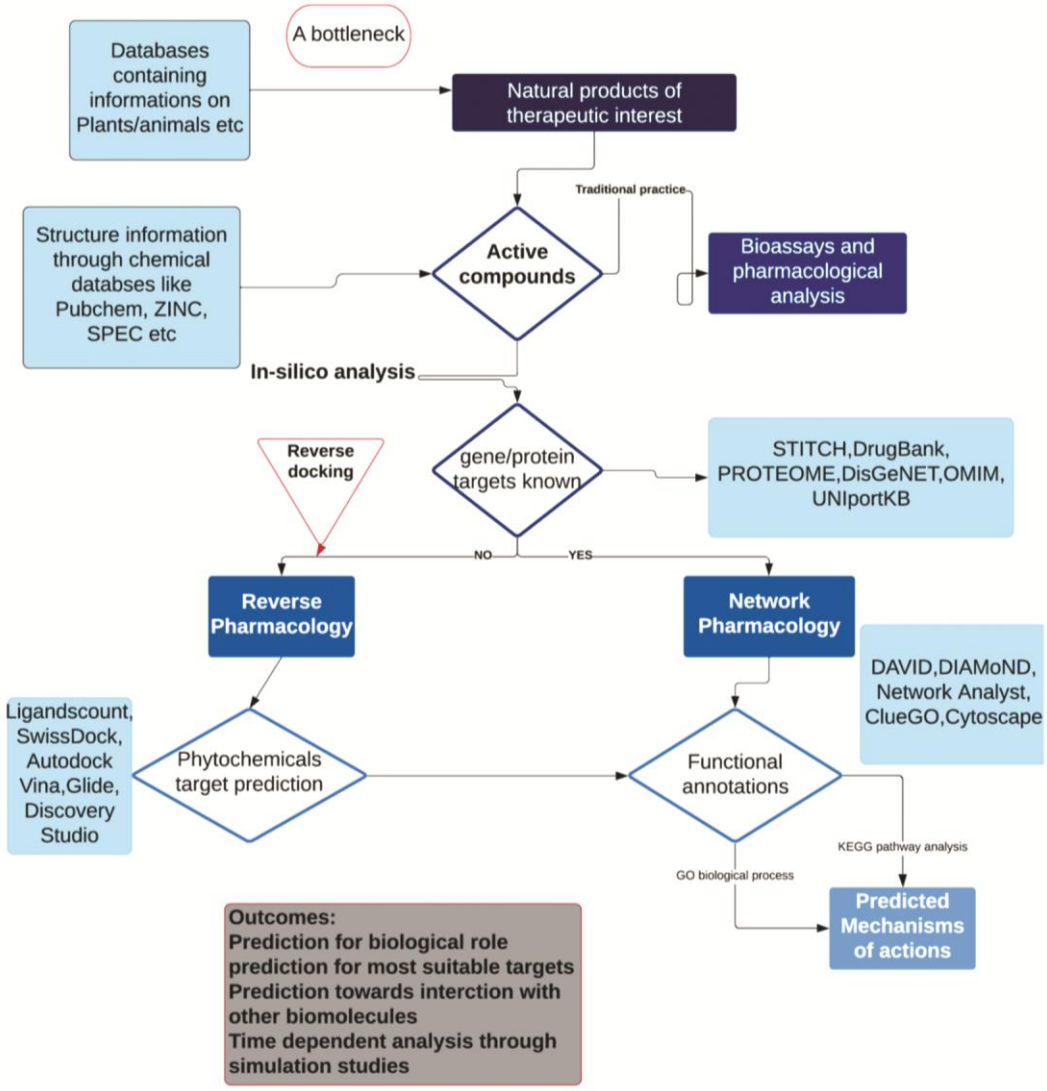

Fig. 4 — Tools of Network pharmacology adopted in traditional medicine research

therapeutic interest was observed in the last decade, leading to the discovery of new active molecules. Hopkins *et al*. (2007)[30] have first published a comprehensive summary of tools of poly-pharmacology. Before that, molecular docking studies were popular among chemists and biologists since the early '90s; within 30 years, these tools were inevitable in TM research. NP is a popular tool among Chinese researchers; almost every compound mentioned in TCM has been surveyed for its benefits. Some are patented for commercial applications.

In contrast, these efforts to compile the information of Ayurveda and Unani formulations are rare. No boost was observed. Out of 45 monographs presented in the Ayush Pharmacopeia (2016), hardly three monographs have been preliminarily assessed towards network pharmacology tools. The comparative analysis of research trends in TCM and Ayurveda research utilizing system biology is represented in (Supplementary Fig. S1).

The review of the last two decades portrays the grim situation for network pharmacology in Ayurveda research. There could be many reasons, but the major is the unfamiliarity of Indian researchers with these open-source tools.

Intuitive networks for target and functional annotation for Ayurveda formulations

Network pharmacology operates by generating available information networks, which helps visualize the most prominent interaction among the candidates under investigation. A disease-specific biomolecule

network usually determines the network's over or under-presents gene/protein targets. Ultimately, it is a related biological process. The recommended targets, usually cellular proteins, are utilized as a prototype for designing therapeutics. The present review elucidates the scope of networks by investigating the therapeutic potential of *Ocimum tenuiflorum* (vernacular name: Tulsi). Leaves and extracts of Tulsi are often used in Ayurveda to treat flu-like symptoms. Briefly, the study was conducted by fetching the names of targets and then investigating their role in influencing cellular processes. A network can be constructed in different ways. The following four types of networks are often used in pharmacological research.

Network for (Tulsi) Compounds of therapeutic interest– associated biomolecular targets: (Compound-target).

Network for Tulsi target – Virus-induced Influenza (Compound target- Disease); fixed to gene targets.

Compound target- Disease; interaction of proteins (PPI).

Compounds- targets (gene+ protein)- Biological pathways.

The networks are presented in (Fig. 5a-d), respectively. (Fig. 5a) elucidates the association of 10 Tulsi components to 100 gene targets. Network (Fig. 5b) represents the network for Tulsi components and host targets involved in virus-induced influenza. A cluster of 6 core genes was obtained. More targets were obtained through the screening of interacting proteins (Fig. 5c). These targets only make sense when they can be correlated with their biological role (Fig. 5d). The functional enrichment analysis for combined targets was carried out to achieve that (Supplementary Table S1). In this supplementary table, a detailed description of (Fig. 5a-d) is provided.

Reports by Maggio *et al.* (2020)[31] have shown that inhibition of TMPRSS2 (Transmembrane Protein Serine 2) through the cancer drug bromhexine can reduce mucus disturbance and secretion in the airway. He has suggested the repurposing of bromhexine for the treatment of COVID-19. Likewise, Apigenin is known to inhibit the Akt phosphorylation, thereby

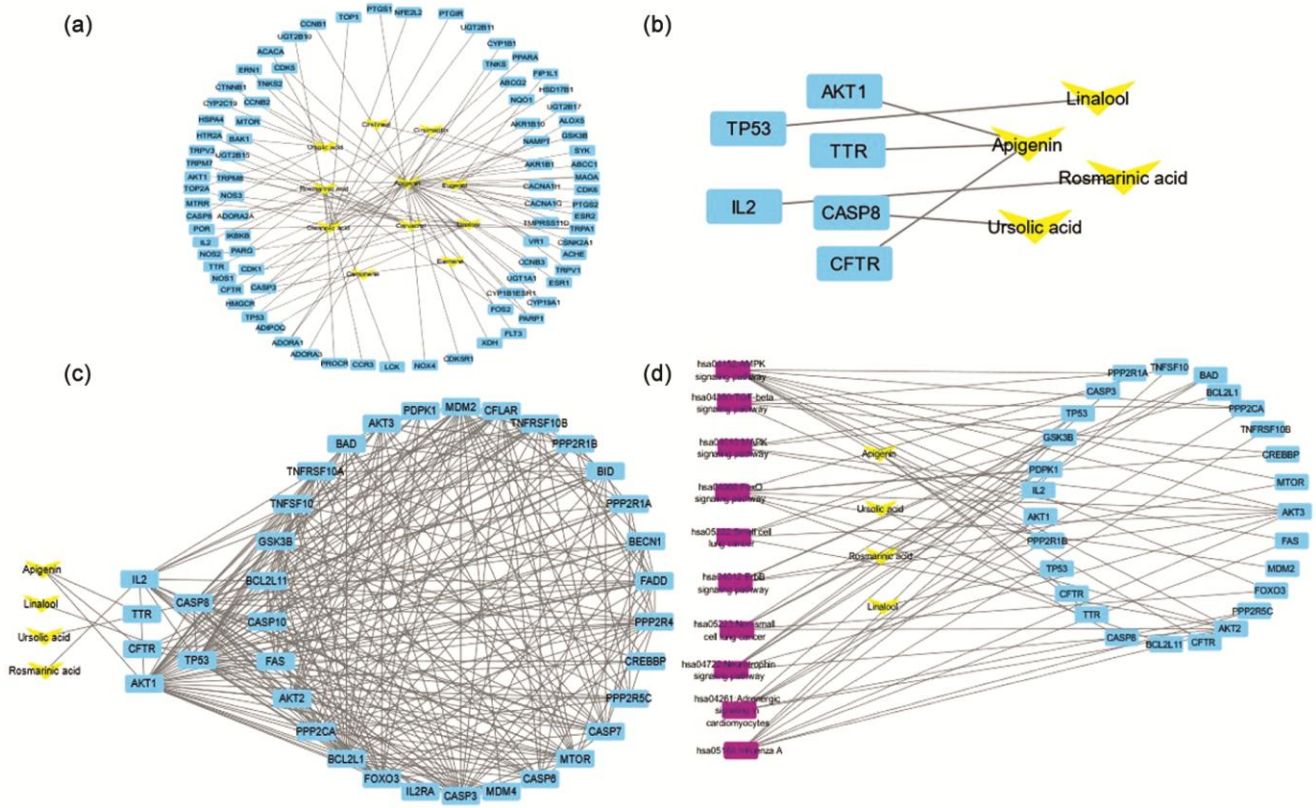

Fig. 5 — Intuitive networks for visualising the ligand-target interactions; (a) Tulsi component and its corresponding disease targets (b) Screened cluster for core gene target (c) Common Disease targets, components and its associated proteins retrieved through protein-protein interactions studies (d) Functional enrichment analysis for targets of network among active common targets, associated proteins and pathways

promoting apoptosis. It promotes apoptosis in tumour cells. The associated edges of the network show that Apigenin can activate the cystic fibrosis transmembrane regulator (CFTR). The earlier laboratory studies unveil the role of CFTR in virus-induced influenza. CFTR is down-regulated and ameliorated to mucous stasis and oedema[32,33]. Repurposing of a therapeutic that affects CFTR dysfunction may be an effective treatment strategy[34]. Here, we introduce Apigenin, a promising candidate that plays a role in CFTR regulation, and it can be further validated in laboratory studies.

Furthermore, the Tulsi component Apigenin interacts with AKT1, AKT2, and AKT3, essential kinases of p53/AKT, and MAPK signalling pathways. The inhibition of this kinase can inhibit the virus's replication in the host cell by provoking the apoptosis of infected cells. This network has provided putative biological insights towards the action of Tulsi. The investigation can be further validated in laboratory studies. Host cellular pathways implicated in influenza infection such as endocytic trafficking, nuclear transport, RNA synthesis, protein translation, and innate immune signaling were systematically categorised. These pathways were mapped to corresponding host-related, viral, and molecular factors influencing influenza susceptibility and disease progression.The interaction between viral proteins and host cellular networks was analysed to understand mechanisms of viral adaptation, replication efficiency, and immune evasion. Identified cellular networks were further correlated with clinical and environmental factors reported to influence influenza severity, thereby integrating molecular mechanisms with epidemiological determinants.

Many investigators have screened host and viral factors that play a role in establishing infection, and our screening amends the details in the current information on annotated factors presented in (Fig. 6)[35-38].

Results and Discussion

Due to Chinese researchers' exhaustive cataloguing and characterization efforts towards TCM, TCM drugs were quickly adopted for treating 2019-nCoV[39,40]. Early clinical trials suggest that gancaoganjiang decoction, qingfei paidu decoction, qingfei touxie fuzheng, and sheganmahuang decoction recipe can be used treatment of 2019-nCoV-induced influenza[41]. Qingfei paidu decoction, which consisted of Ephedrae Herba, Glycyrrhizae Radix et Rhizoma Praeprata cum Melle, effectively treat 2019-nCoV induced pneumonia[42]. Numerous research publications citing TCM applications in 2019-nCoV treatments were published recently[43,44]. Almost all these newly introduced treatment options act through modulating the host cell signalling events. The regulation of host signalling

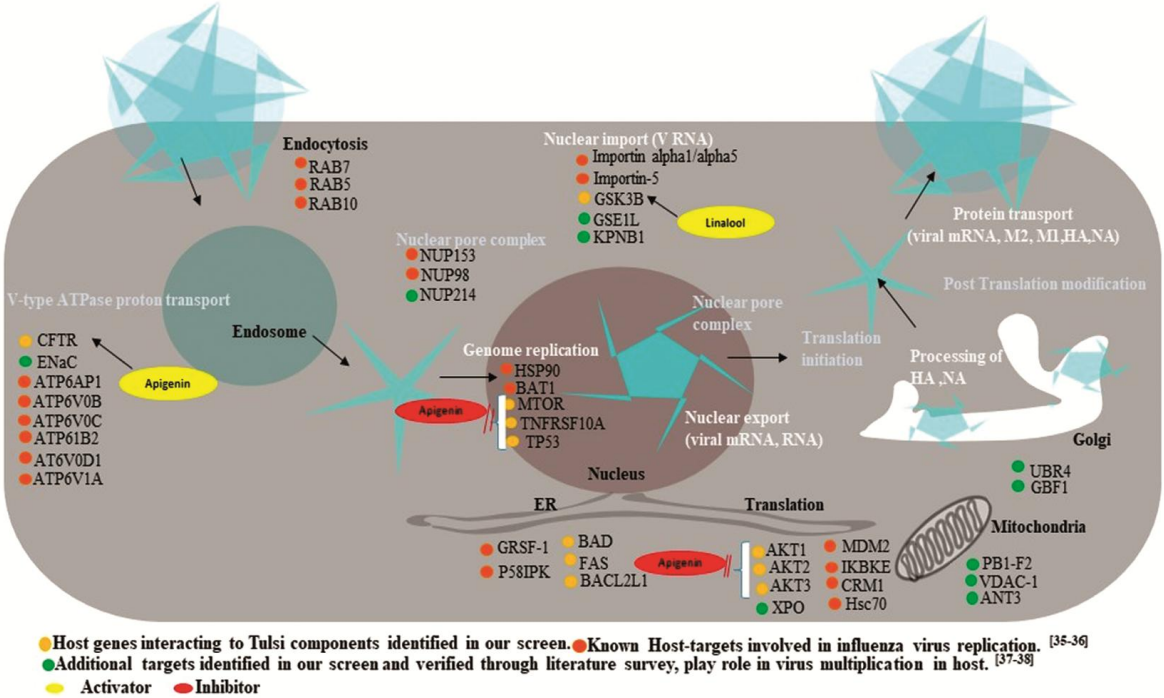

Fig. 6 — Factors associated with Virus-induced influenza

pathways can be an attainable strategy to combat flu viruses. In various studies, the researcher has evaluated the impact of various herbal compounds on modulating host signalling events. Lianhuaqingwen (LH), a TCM formula, exerts broad-spectrum antiviral effects on distinct species of influenza viruses by modulating the functions of host factors NF-α, IL-6, CCL-2/MCP-1, and CXCL-10/IP[45]. Also, a TCM candidate, Liu Shen, inhibits the expression of p-NF-κB p65, p-IκBα, and p-p38 MAPK of the NF-κB/MAPK signalling pathway[46,47]. Recently, one more TCM candidate has been revealed to affect the IFN signalling pathway towards inhibiting the p65 phosphorylation. Henceforth, the nuclear translocation of the virus can be inhibited[48]. Guava flavonoid glycosides regulate the function of host kinases involved in the replication cycle of influenza A viruses (IAV). It further rescues P53 activity. It could represent a new strategy to eradicate IAV[49,50].

Like China, India is also adversely impacted by 2019-nCoV. Locally, Ayurveda physicians prescribed powder/ decoction of *Ocimum tenuiflorum* (Tulsi), *Zingiber officinale* (Ginger), *Cinnamomum cassia* (Cinnamon), *Piper longum* root (Ghanthoda), *Curcuma longa* (Turmeric) as a holistic cure to 2019-nCoV. Though perceived as competent, during this crisis period, very limited systematic reports elaborating on the clinical or in-silico investigation of traditional Indian medicine's efficacy were published. The structural protein NS1 of Influenza viruses interacts with the phosphorylated Akt but not the non-phosphorylated Akt[51] Apigenin is known to inhibit the phosphorylation of Akt and promote apoptosis. It is widely known for promoting apoptosis in cancer cells[52-54]. The Influenza virus replicates in the host by delaying apoptosis. Repurposing Apigenin to treat virus-induced influenza can be a promising alternative. The Scenario is quite horrid; the count of the number of affected individuals is rising worldwide. However, the application of such candidates is not promptly evaluated. None of the above-listed 5 TIM candidates has thoroughly evaluated an established research design as a treatment alternative for virus-induced influenza.

This review attempts to portray a quick way to investigate the speculated efficiency of TIM compounds in treating virus-induced influenza. The study proposes the repurposing of Apigenin to regulate the action of CFTR and threonine-specific protein kinases (Akt) as a treatment alternative for virus-induced influenza. The observations can be further validated towards the research design of biomedical sciences. Furthermore, it elaborates on the scope of Network pharmacology in TIM research.

Conclusion

According to network pharmacology, tulsi has great promise as an antiviral drug against influenza, working via a variety of molecular targets and pathways. Important active substances like apigenin, eugenol, and ursolic acid may reduce inflammatory reactions and viral replication by modulating important signaling pathways like NF-κB, MAPK, and PI3K/Akt. Network pharmacology, combined with databases of Indian medicinal plants, provides a promising foundation for systematically investigating the therapeutic potential of Ayurvedic compositions. This review suggests using apigenin to control the activity of threonine-specific protein kinases (Akt) and CFTR as a substitute therapy for influenza caused by viruses. The observations can be further validated towards the research design of biomedical sciences. It further attempts to draw Indian researchers' attention to the scope of network pharmacology in TIM research.

Supplementary Data

Supplementary data associated with this article is available in the electronic form at https://nopr.niscpr.res.in/jinfo/ijtk/IJTK_25(1)(2026)7-16_SupplData.pdf

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Ethics Statement

This review article did not involve human or animal subjects; therefore, no ethical approval was required.

Conflict of Interest

The authors have no conflict of interest.

Author Contributions

Komal Tilwani wrote the review article; Gayatri Dave contributed to the manuscript's editing and design.

Data Availability

No new data were generated or analyzed for this review. All sources referenced in the manuscript are publicly available.

References

1 Jin R, Zhang B, Xue C-M, Liu S-M, Zhao Q, *et al.*, Classification of 365 Chinese medicines in Shennong's *Materia Medica* Classic based on a semi-supervised incremental clustering method, *Chin J Integr Med*, 9 (6) (2011) 665-674. doi: 10.3736/jcim20110614

2 Barr J, Vascular medicine and surgery in ancient Egypt, *J Vasc Surg*, 60 (1) (2014) 260-263. doi: 10.1016/j.jvs.2014.04.056

3 Hajar R, Learning ancient Greek medicine from Homer, *Heart Views*, 3 (3) (2002) 8.

4 Vinjamury S P, Vinjamury M, Sucharitakul S & Ziegler I, Panchakarma: Ayurvedic detoxification and allied therapies – is there any evidence? In: *Evidence-based Practice in Complementary and Alternative Medicine*, (Springer, Berlin & Heidelberg), (2012) 113-137.

5 Menon I & Spudich A, The Ashtavaidya physicians of Kerala: A tradition in transition, *J Ayurveda Integr Med*, 1 (4) (2010) 245. doi: 10.4103/0975-9476.74424

6 Curran J, The Yellow Emperor's Classic of Internal Medicine, *BMJ*, 336 (7647) (2008) 777. doi: https://doi.org/10.1136/bmj.39527.472303.4E

7 Singh V, Sushruta: The father of surgery, *Natl J Maxillofac Surg*, 8 (1) (2017) 1-3. doi: 10.4103/njms.NJMS_33_17

8 Zhou X, Peng Y & Liu B, Text mining for traditional Chinese medical knowledge discovery: A survey, *J Biomed Inform*, 43 (4) (2010) 650-660. https://doi.org/10.1016/j.jbi.2010.01.002

9 Ali b. Sahl Rabban al-Tabari, *Firdaws al-Hikma* (*Paradise of Wisdom*), Muslim Heritage, Available online: https://muslimheritage.com/al-tabari-paradise-of-wisdom/ (Accessed on 22 May 2022).

10 Li H, Sureda A, Devkota H P, Pittalà V, Barreca D, *et al.*, Curcumin, the golden spice in treating cardiovascular diseases, *Biotechnol Adv*, 38 (2020) 107343. doi: 10.1016/j.biotechadv.2019.01.010.

11 Li H, Sureda A, Devkota H P, Pittalà V, Barreca D, *et al.*, Curcumin, the golden spice in treating cardiovascular diseases, Biotechnology Advances, (38) (2020) 107343. doi:

12 Paliwal R & Paliwal S R, Controlled delivery of chemopreventive agents, In: *Advances in Nanochemoprevention*, (Springer, Singapore), (2020) 29-38. doi:10.1007/978-981-15-9692-6_3

13 Rajkumar R P, Ayurveda and COVID-19: Where psychoneuroimmunology and the meaning response meet, *Brain Behav Immun*, 87 (2020) 8-9. doi: 10.1016/j.bbi.2020.04.056

14 Atanasov A G, Waltenberger B, Pferschy-Wenzig E M, Linder T, Wawrosch C, *et al.*, Discovery and resupply of pharmacologically active plant-derived natural products: A review, *Biotechnol Adv*, 33 (8) (2015) 1582-1614. https://doi.org/10.1016/j.biotechadv.2015.08.001

15 Tilwani K, Patel A, Patel G, Rahevar M & Dave G, AYU search: A repository to facilitate the biochemical understanding of natural products-derived chemical substances, *Curr Sci*, 126 (6) (2024). 706-713. doi:10.18520/cs/v126/i6/706-713.

16 Yadav K D, Reddy K R C & Kumar V, Beneficial effect of Brahmi Ghrita on learning and memory in normal rat, *AYU*, 35 (3) (2014) 325-329. doi:10.4103/0974-8520.153755.

17 Chen S L, Yu H, Luo H M, Wu Q, Li C F, *et al.*, Conservation and sustainable use of medicinal plants: problems, progress, and prospects, *Chin Med*, 11 (1) (2016) 37. doi:10.1186/s13020-016-0108-7.

18 Tu Y, Artemisinin – a gift from traditional Chinese medicine to the world (Nobel lecture), *Angew Chem Int Ed*, 55 (35) (2016) 10210-10226. doi: 10.1002/anie.201601967.

19 Xue R, Fang Z, Zhang M, Yi Z, Wen C, *et al.*, TCMID: Traditional Chinese medicine integrative database for herb molecular mechanism analysis, *Nucleic Acids Res*, 41 (D1) (2012) D1089-D1095. doi: 10.1093/nar/gks1100.

20 Ru J, Li P, Wang J, Zhou W, Li B, *et al.*, TCMSP: A database of systems pharmacology for drug discovery from herbal medicines, *J Cheminform*, 6 (2014) 13. doi: 10.1186/1758-2946-6-13.

21 Zhang R-Z, Yu S-J, Bai H & Ning K, TCM-Mesh: The database and analytical system for network pharmacology analysis for TCM preparations, *Sci Rep*, 7 (2017) 2821. https://doi.org/10.1038/s41598-017-03039-7.

22 Sawada R, Iwata M, Umezaki M, Usui Y, Kobayashi T, *et al.*, KampoDB: Database of predicted targets and annotations of natural medicines, *Sci Rep*, 8 (2018) 11216. https://doi.org/10.1038/s41598-018-29516-1.

23 Ayurvedic Pharmacopoeia of India, (Pharmacopoeia Commission for Indian Medicine & Homoeopathy, Ministry of AYUSH, Government of India), (2016).

24 Meetei P A, Singh P, Nongdam P, Prabhu N P, Rathore R S, *et al.*, Ne Med Plant: Database of medicinal plants from North-East region of India, *Bioinformation*, 8 (4) (2012) 209-211. doi: 10.6026/97320630008209.

25 Pathania S, Ramakrishnan S M & Bagler G, Phytochemica: A platform to explore phytochemicals of medicinal plants, *Database*, 2015 (2015) bav075. doi: 10.1093/database/bav075.

26 Mohanraj K, Karthikeyan B S, Vivek-Ananth R P, Chand R B, Aparna S R, *et al.*, IMPPAT: A curated database of Indian medicinal plants, *Sci Rep*, 8 (2018) 4329. https://doi.org/10.1038/s41598-018-22631-z.

27 Parasuraman S, Thing G S & Dhanaraj S A, Polyherbal formulation: Concept of Ayurveda, *Pharmacogn Rev*, 8 (16) (2014) 73-80. doi: 10.4103/0973-7847.134229.

28 Hussain A & Verma C K, Computational drug repurposing resources and approaches for discovering novel antifungal drugs against Candida albicans N-Myristoyl Transferase, *J Pure Appl Microbiol*, 15 (2) (2021) 556-579. doi:10.22207/JPAM.15.2.49.

29 Cui S, Chen S, Wu Q, Chen T & Li S, A network pharmacology approach to investigate the anti-inflammatory mechanism of effective ingredients of *Salvia miltiorrhiza*, *Int Immunopharmacol*, 81 (2020) 106040. doi: 10.1016/j.intimp.2019.106040.

30 Hopkins A L, Network pharmacology, *Nat Biotechnol*, 25 (2007) 1110-1111. https://doi.org/10.1038/nbt1007-1110.

31 Maggio R & Corsini G U, Repurposing the mucolytic cough suppressant and TMPRSS2 protease inhibitor bromhexine for the prevention and management of SARS-CoV-2 infection, *Pharmacol Res*, 157 (2020) 104837. doi: 10.1016/j.phrs.2020.104837.

32 Londino J D, Lazrak A, Noah J W, Aggarwal S, Bali V, *et al.*, Influenza virus M2 targets CFTR for lysosomal degradation during infection, *FASEB J*, 29 (7) (2015) 2712-2725. doi: 10.1096/fj.14-268755.

33 Brand J D, Lazrak A, Trombley J E, Shei R-J, Adewale A T, *et al.*, Influenza-mediated reduction of lung epithelial ion channel activity leads to dysregulated fluid homeostasis, *JCI Insight*, 3 (20) (2018) e123467. doi: 10.1172/jci.insight.123467.

34 Gaur P, Munjal A & Lal S K, Influenza virus and cell signaling pathways, *Med Sci Monit*, 17 (6) (2011) RA148-RA154. doi: 10.12659/msm.881801.

35 Watanabe T, Watanabe S & Kawaoka Y, Cellular networks involved in the influenza virus life cycle, *Cell Host Microbe*, 7 (6) (2010) 427-439. doi: 10.1016/j.chom.2010.05.008.

36 Saleh M, Rüschenbaum S, Welsch C, Zeuzem S, Moradpour D, *et al.*, Glycogen Synthase Kinase 3β enhances Hepatitis C virus replication by supporting miR-122, *Front Microbiol*, 9 (2018) 2949. doi: 10.3389/fmicb.2018.02949.

37 Miyake Y, Keusch J J, Decamps L, Ho-Xuan H, Iketani S, *et al.*, Influenza virus uses transportin 1 for vRNP debundling during cell entry, *Nat Microbiol*, 4 (4) (2019) 578-586. doi: 10.1038/s41564-018-0332-2.

38 Perwitasari O, Johnson S, Yan X, Howerth E, Shacham S, *et al.*, Verdinexor, a Novel Selective Inhibitor of Nuclear Export, Reduces Influenza A Virus Replication *In vitro* and *In vivo J Virol*, 88 (17) (2014) 10228-10243. doi: 10.1128/JVI.01774-14.

39 Ni L, Chen L, Huang X, Han C, Xu J, *et al.*, Combating COVID-19 with integrated traditional Chinese and Western medicine in China, *Acta Pharm Sin B*, 10 (7) (2020) 1149-1162. doi: 10.1016/j.apsb.2020.06.009.

40 Hu Z, Yang X, Ho P C L, Chan S Y, Heng P W S, *et al.*, Herb-drug interactions: A literature review. *Drugs*, 65 (9) (2005) 1239-1258. doi: 10.2165/00003495-200565090-00005.

41 Mirzaie A, Halaji M, Dehkordi F S, Ranjbar R & Noorbazargan H, A narrative literature review on traditional medicine options for treatment of corona virus disease 2019 (COVID-19), *Complement Ther Clin Pract*, 40 (2020) 101214. doi: 10.1016/j.ctcp.2020.101214.

42 Gao J, Zheng P, Jia Y, Chen H, Mao Y, *et al.*, Mental health problems and social media exposure during COVID-19 outbreak, *PLoS One*, 15 (4) (2020) e0231924. doi: 10.1371/journal.pone.0231924.

43 Caraci F, Iulita M F, Pentz R, Aguilar L F, Orciani C, *et al.*, Searching for new pharmacological targets for Alzheimer's disease in Down syndrome, *Eur J Pharmacol*, 817 (2017) 7-19. doi: 10.1016/j.ejphar.2017.10.004.

44 Chibber P, Haq S A, Ahmed I, Andrabi N I & Singh G, Advances in possible treatment of COVID-19: A review, *Eur J Pharmacol*, 883 (2020) 173372. doi: 10.1016/j.ejphar.2020.173372.

45 Runfeng L, Yunlong H, Jicheng H, Weiqi P, Qinhai M, *et al.*, Lianhuaqingwen exerts antiviral and anti-inflammatory activity against SARS-CoV-2, *Pharmacol Res*, 156 (2020) 104761. doi: 10.1016/j.phrs.2020.104761.

46 Ma Q, Pan W, Li R, Liu B, Li C, *et al.*, Liu Shen capsule shows antiviral and anti-inflammatory activity, *Pharmacol Res*, 158 (2020) 104850. doi: 10.1016/j.phrs.2020.104850.

47 Hou Y, Nie Y, Cheng B, Tao J, Ma X, *et al.*, Qingfei Xiaoyan Wan, a traditional Chinese medicine formula, ameliorates Pseudomonas aeruginosa-induced acute lung inflammation by regulation of PI3K/AKT and Ras/MAPK pathways, *Acta Pharm Sin B*, 6 (3) (2016) 212-221. doi: 10.1016/j.apsb.2016.03.002.

48 Zhou B, Liang X, Feng Q, Li J, Pan X, *et al.*, Ergosterol peroxide suppresses influenza A virus-induced pro-inflammatory response and apoptosis by blocking RIG-I signaling, *Eur J Pharmacol*, 860 (2019) 172543. doi: 10.1016/j.ejphar.2019.172543

49 Zhirnov O P & Klenk H-D, Control of apoptosis in influenza virus-infected cells by up-regulation of Akt and p53 signaling, *Apoptosis*, 12 (8) (2007) 1419-1432. doi: 10.1007/s10495-007-0071-y.

50 Luo L, Jiang J, Wang C, Fitzgerald M, Hu W, *et al.*, Analysis on herbal medicines utilized for treatment of COVID-19, 10 (7) (2020) 1192-1204. doi: 10.1016/j.apsb.2020.05.007.

51 Matsuda M, Suizu F, Hirata N, Miyazaki T, Obuse C, *et al.*, Characterization of the interaction of influenza virus NS1 with Akt, *Biochem Biophys Res Commun*, 395 (3) (2010) 312-317. doi: 10.1016/j.bbrc.2010.03.166.

52 Way T-D, Kao M-C & Lin J-K, Apigenin induces apoptosis through proteasomal degradation of HER2/neu in HER2/neu-overexpressing breast cancer cells via the phosphatidylinositol 3-kinase/Akt-dependent pathway, *J Biol Chem*, 279 (6) (2004) 4479-4489. doi: 10.1074/jbc.M305529200.

53 Shen Z, Lou K & Wang W, New small-molecule drug strategies for resistant influenza A, *Acta Pharm Sin B*, 5 (5) (2015) 419-430. doi: 10.1016/j.apsb.2015.07.006.

54 Yang J, Pi C & Wang G, Inhibition of PI3K/Akt/mTOR pathway by apigenin induces apoptosis and autophagy in hepatocellular carcinoma cells, *Biomed Pharmacother*, 103 (2018) 699-707. doi: 10.1016/j.biopha.2018.04.072.