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NMPB Medicinal Plants for COVID-19 Care

India is an emporium of medicinal plants. Indian systems of medicine as well as folkloric systems are utilizing medicinal plant wealth from very ancient times for combating a wide array of human ailments. There exists a history of facing several pandemics including Small pox, Tuberculosis, Spanish Flu, Malaria etc. using traditional herbal medicines. National Medicinal Plant Board had suggested selected twenty medicinal plants including Amla, Aswagandha, Basil, Giloe, Cinnamon, Clove etc. as a prophylaxis or support therapy for curing COVID-19 related ailments. In addition, *in silo*, *in vitro* and pre-clinical evidences exhibiting the anti-COVID-19 activity of these medicinal plants revealed the scope for development of plant derived anti-COVID drugs.

INTRODUCTION

COVID-19 (Corona virus disease-2019) or SARS-CoV-2 (Severe Acute Respiratory Syndrome Corona Virus -2) pandemic teaches people to think for health than wealth. The best way to improve our immune system is the use of medicinal plants based natural remedies. Recently, on the International Biodiversity Day, NMPB (National Medicinal Plant Board), Ministry of AYUSH has published 20 different medicinal plants conventionally using as antipyretic and immune boosters for health care during the COVID -19 scenarios.

MEDICINAL PLANTS

The 20 medicinal plants are, Amla (*Phyllanthus emblica* L.), Ashwagandha (*Withania somnifera* L.), Basil (*Ocimum basilicum* L.), Blue flowered glory tree (*Clerodendrum serratum* L.), Chiretta (*Swertia chirata* Buch.-Ham. Ex Wall.), Cinnamon (*Cinnamomum verum* Bercht. & Presl.), Clove (*Syzygium aromaticum* (L.) Merr. & L. M.

Perry), Elicampane (*Inula racemosa* Hook.f.), Giloe (*Tinospora cordifolia* (Willd.) Miers Hook F. & Thomas), Ginger (*Zingiber officinale* Roscoe), Kalmegh (*Andrographis paniculata* (Burm. f.) Wall. Ex Nees), Kutki (*Picrorhiza kurroa* Royle ex Benth.), Oil grass (*Cympopogon jwarancusa* (Jones) Schult.), Liquorice (*Glycyrrhiza glabra* L.), Malabar nut (*Adhatoda vasica* Nees.), Neem (*Azadirachta indica* A. Juss), Sacred basil (*Ocimum tenuiflorum* L.), Star anise (*Illicium verum* Hook.f.), Spiked ginger lily (*Hedychium spicatum* (Buch-Ham) and Turmeric (*Curcuma longa* L.). Scientific evidences showing anti-COVID-19 activity (most of them being *in silico* studies) of these plants are discussed here with.

COVID-19 OR SARS-COV-2

COVID-19 or SARS-CoV-2 (Severe Acute Respiratory Syndrome Corona Virus -2) has a protein coat containing the targets – spike (S) protein and E or N protein. The enveloped S protein could bind the functional receptor ACE2 (Angiotensin Converting Enzyme 2) in the host's lung alveolar cell and helps in membrane fusion and thus facilitating virus entry into the cells. SARS-CoV-2 also contains a protease enzyme, MPrO [3-chymotrypsin – like protease (3CLPro)] which stimulates the maturation process of the virus by the production of different proteins *viz.*, exoribonuclease, endoribonuclease and RNA polymerase. Once COVID -19 infects the body, it may create a cytokine storm/ blast, a life-threatening immune reaction. The RNA synthesis and replication can be prevented by targeting 3C-like main protease (3CLpro), Papin-like protease (PLpro), RNA-dependent RNA polymerase (RdRp) and helicase. In addition, SARS-CoV-2 can be inhibited by targeting its virulence factors – Nsp1, Nsp3c and ORF7.

ANTI-COVID-19 ACTIVITY

Kalmegh is a potential medicinal plant showing 3CLpro inhibitory activity due to the presence of andrographolide (Enmozhi *et al.*, 2020). Methyl eugenol, oleanolic acid and ursolic acid in Basil (Kumar, 2020) and taraxerol present in *C. serratum* (Kar *et al.*, 2020) showed binding efficiency against surface spike protein, RNA polymerase and Mpro of SARS-CoV-2. Glycyrrhizic acid, liquiritigenin and Glabridin present in Liquorice (Srivastava *et al.*, 2020) as well as of epoxyazadiradione and Gedunin present in Neem (Kumar, 2020) could bound with the Mpro of SARS-CoV-2 which could help to prevent virus multiplication.

Curcumin and cyclocurmin in turmeric could inhibit SARS-CoV-2 main protease enzyme (Rajagopal *et al.*, 2020). Pandey *et al.* (2020) proclaimed that Gingerone A had maximum inhibitory potential and found effectively bound 7JTL target of SARS-CoV-2. Besides, Obeta (2020) observed that consumption of Ginger along with vitamin C rich garlic, giloe, turmeric and lime could effectively manage COVID-19 infection in Enugu-Nigeria.

Sagar and Kumar (2020) found out that Berberine, isocolumbin, magnoflorine and tinocordiside in Giloe showed highest binding efficiency with surface glycoprotein (6VSB; receptor binding domain- 6MOJ), RNA dependent RNA polymerase (6MJ1) and main protease (6Y84). In Amla, an *in silico* analysis done using the phytoconstituents *viz.*, phyllaemblicin- B, phyllaemblicin-G7 and phyllaemblinol revealed that phyllaemblicin-G7 had high binding affinity to spike protein as like Withaferin A present in Ashwagandha (Balkrishna *et al.*, 2020a) whereas phyllaemblicin- B and phyllaemblinol could bind helicase protein of SARS-CoV-2. (Wu *et al.*, 2020). Compounds in Ashwagandha *viz.*, Withanone and Withanoside V could inhibit the activity of SARS-CoV-2 main protease (MPrO) as well (Tripathi *et al.*, 2020). Besides, Coronil is a tri-herbal medicine containing *W. somnifera* (L.) Dunal, *T. cordifolia* (Willd.) Miers Hook F. & Thomas and *O. tenuiflorum* L. developed in India found efficient to regulate cytokine secretion and thus claimed to control cytokine blast during SARS-CoV-2 infection under *in vitro* conditions (Balkrishna *et al.*, 2020b).

Flavonoid derivatives present in Malabar nut showed its potentiality to inhibit/ bind with 3CLpro, PLpro, RdRp, ACE2, NSP14 and NSP16 (Gheware *et al.*, 2021). In Kalmegh, not only andrographolide its analogues were proved for its binding efficiency against key targets like spike protein, ACE2, RdRp, 3CLpro, PLpro etc. of SARS-CoV-2 through several *in silico* studies (Xin *et al.*, 2021). Quercetin present in Cinnamon could block ADP ribose phosphate protein (a unit of NSP3) and NSP3 enzyme SARS-CoV-2 through molecular docking studies done by Sahu *et al.* (2021) which evinced the blockage of host-immune response. Eugenol, eugenol acetate, eugenol benzoate, methyl eugenol, triterpenoids, eugenin, eugenitin and campesterol in Clove could bind with 6LU7 and 7JTL, two crucial protein targets of SARS-CoV-2 (Pandey *et al.*, 2020). Nevadensin in Basil showed high binding affinity against RdRp of SARS-CoV-2 (Shafiq *et al.*, 2021). Swetiapuniside present in

S. chirata could inhibit RdRp which helps to prevent the cytokine storm and proved *in silico* the efficiency for using in COVID-19 management (Koulgi *et al.*, 2021).

These evidences indicate the capacity of medicinal plants to restrict the entry of virus into the host and its multiplication within. This could highlight the scope for using the proven medicinal plants for prophylactic therapy of COVID-19 since, it could attenuate lung injury, thrombosis, fibrosis and related responses due to COVID-19 infection.

AYUSH in collaboration with CSIR had done several clinical trials by administering AYUSH-64 a formulation containing Kutki to COVID-19 patients and reported an improved general wellness and reduced anxiety, stress, sleeplessness etc. Thus, it is recommended for asymptomatic and mild to moderate COVID-19 infections since it could prevent worsening of the disease. The possibility of using Elicampane for using as an immune booster for fighting against COVID-19 infection was also suggested. Oil grass could function against skin diseases, rheumatism, gout, arthritis. Spiked ginger could relieve breathing difficulty (NMPB 2021). NMPB (2021) recommends the consumption of star anise fruit powder for alleviating abdominal pain, cough, digestive disorders etc. On the whole its broad therapeutic and immunomodulatory properties might put forth NMPB (2021) to repurpose star anise for COVID-19 mitigation and management.

CONCLUSION

NMPB recommended medicinal plants are potential for fighting against COVID-19. Several *in silico* studies done with phytochemicals has proven that, these medicinal plant-based products work in improving immune system and thus, helps in prevention and management of COVID-19 along with other standard drugs. Nevertheless, *in vitro*, *in vivo* as well as clinical studies are required for its authentication. Although these plant-based products are safe there exist a few limitations for some individuals hence, required consultation with a medicinal practitioner before its administration.

REFERENCE

Balkrishna, A., Pokhrel, S., Singh, J., & Varshney, A. (2020). Withanone from *Withania somnifera* may inhibit novel coronavirus (COVID-19) entry by disrupting interactions between viral S-protein

receptor binding domain and host ACE2 receptor. *Research Square*.

Balkrishna, A., Solleti, S. K., Verma, S., & Varshney, A. 2020. Application of humanized zebrafish model in the suppression of SARS-CoV-2 spike protein induced pathology by tri-herbal medicine coronil via cytokine modulation. *Molecules*, 25(21), 1-25.

Enmozhi, S. K., Raja, K., Sebastine, I., & Joseph, J. 2020. Andrographolide as a potential inhibitor of SARS-CoV-2 main protease: an *in silico* approach. *Journal of Biomolecular Structure and Dynamics*, 39(9), 3092-3098.

Gheware, A., Dholakia, D., Kannan, A., Panda, L., Rani, R., Pattnaik, B. R., Jain, V., Parekh, Y., Enayathullah, M. G., Bokara, K. K., Subramanian, V., Mukarji, M., Agrawal, A., & Prasher, B. (2021). *Adhatoda vasica* attenuates inflammatory and hypoxic responses in preclinical mouse models: potential for repurposing in COVID-19-like conditions. *Respiratory Research*, 22 (1), 1-15.

Kar, P., Sharma, N. R., Singh, B., Sen, A., & Roy, A. (2020). Natural compounds from *Clerodendrum* spp. as possible therapeutic candidates against SARS-CoV-2: An *in silico* investigation. *Journal of Biomolecular Structure and Dynamics*.

Koulgi, S., Jani, V., Uppuladinne, V. N. M., Sonavane, U., & Joshi, R. (2021). Natural plant products as potential inhibitors of RNA dependent RNA polymerase of Severe Acute Respiratory Syndrome Coronavirus-2. *Plos One*, 16 (5).

Kumar, A. (2020). Molecular docking of natural compounds from tulsi (*Ocimum sanctum*) and neem (*Azadirachta indica*) against SARS-CoV-2 protein targets. *Research Square*.

NMPB (National Medicinal Plant Board). 2021. 20 Medicinal Plants of '21 for COVID-19 care. Ministry of Ayush, Government of India, 49p.

Obeta, M. U. (2020). Anti-COVID-19 Properties of ginger (*Zingiber officinale*) assisted Enugu - Nigerian people during the pandemic. *Journal of Bacteriology and Infectious Diseases*, 4(3), 1-5.

- Pandey, P., Singhal, D., Khan, F., & Arif, M. (2020). An *In Silico* screening on *Piper nigrum*, *Syzygium aromaticum* and *Zingiber officinale roscoe* derived compounds against SARS-CoV-2: A drug repurposing approach. *Biointerface Research in Applied Chemistry*, 11 (4), 11122 – 11134.
- Rajagopal, K., Varakumar, P., Baliwada, A., & Byran, G. (2020). Activity of phytochemical constituents of *Curcuma longa* (turmeric) and *Andrographis paniculata* against coronavirus (COVID-19): an *in silico* approach. *Future Journal of Pharmaceutical Sciences*, 6, 1-12.
- Sagar, V. & Kumar, A. H. S. (2020). Efficacy of natural compounds from *Tinospora cordifolia* against SARS-CoV-2 protease, surface glycoprotein and RNA polymerase. *Journal of Virology*, 1-10.
- Sahu, P. K., Sarangi, S., Bhoi, B., & Gadtya, A. S. (2020). *In Silico* analysis of COVID-19 prevention using *Cinnamomum verum* extract by blocking ADP ribose phosphates protein of NSP3 enzyme. *Indian Journal of Natural Sciences*, 10 (60), 21483-21485.
- Shafiq, M., Saif, R., Ali, L., Ahmad, T., & Sohail, A. (2021). Computer-aided drug designing of *Ocimum basilicum* compounds as therapeutic agents against RdRp of SARS-CoV2.
- Srivastava, V., Yadav, A., & Sarkar, P. (2020). Molecular docking and ADMET study of bioactive compounds of *Glycyrrhiza glabra* against main protease of SARS-CoV2. *Materials Today: Proceedings*. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7556787/>
- Tripathi, M. K., Singh, P., Sharma, S., Singh, T. P., Ethayathulla, A. S., & Kaur, P. (2020). Identification of bioactive molecule from *Withania somnifera* (Ashwagandha) as SARS-CoV-2 main protease inhibitor. *Journal of Biomolecular Structure and Dynamics*, 1–14.
- Wu, C., Liu, Y., Yang, Y., Zhang, P., Zhong, W., & Wang, Y. (2020). Analysis of therapeutic targets of SARS-CoV-2 and discovery of potential drugs by computational methods. *Acta Pharmaceutica Sinica B-Journal*, 10 (5), 766-788.
- Xin, Y. L., Janice, S. W. C., Terence, Y. C. T., Bee, P. T., Razak, M. R. M. A., Mohamad, S., & Mohamed, A. F. (2021). *Andrographis paniculata* (Burm. F.) Wall. Ex Nees, andrographolide, and andrographolide analogues as SARS-CoV-2 antivirals. A rapid review. *Natural Product Communications*, 16 (5), 1-15.