Scientific rationale of Indian AYUSH Ministry advisory for COVID-19 prevention, prophylaxis, and immunomodulation

Prashant Kumar Gupta1 · Kishor Sonewane1 · Mariappan Rajan2 · Nitin J. Patil3 · Trapti Agrawal4 · Ena Ray Banerjee5 · Nagendra Singh Chauhan6 · Awanish Kumar7

Abstract
The current outbreak of COVID-19 is caused by the SARS-CoV-2 virus that has affected > 210 countries. Various steps are taken by different countries to tackle the current war-like health situation. In India, the Ministry of AYUSH released a self-care advisory for immunomodulation measures during the COVID-19 and this review article discusses the detailed scientific rationale associated with this advisory. Authors have spotted and presented in-depth insight of advisory in terms of immunomodulatory, antiviral, antibacterial, co-morbidity associated actions, and their probable mechanism of action. Immunomodulatory actions of advised herbs with no significant adverse drug reaction/toxicity strongly support the extension of advisory for COVID-19 prevention, prophylaxis, mitigations, and rehabilitation capacities. This advisory also emphasized Dhyana (meditation) and Yogasanas as a holistic approach in enhancing immunity, mental health, and quality of life. The present review may open-up new meadows for research and can provide better conceptual leads for future researches in immunomodulation, antiviral-development, psychoneuroimmunology, especially for COVID-19.

Keywords COVID-19 · Indian AYUSH advisory · Ayurveda · Immunomodulation · Therapy

Introduction
Today whole world is battling with the current pandemic of COVID-19 (Corona Virus Disease-2019). Increasing patient trend, high extend of spread, the unpredictability of manifestation of the clinical disease spectrum, and the uncertainty of cure are some worrisome concerns behind such social and mental stress in COVID-19. Information on COVID-19 is evolving very fast and it unlikely to have any definite treatment in near future. Drug discovery is a costly and large gestational affair while repurposing can cut short both cost/gestational time and bypass the pre-clinical and safety studies hence a push for Hydroxychloroquine repurposing is emphasized and exhibiting with a mixed response from scientists and clinicians (Rodrigo et al. 2020). Amid such situations, where modern medical science and traditional medicine are standing on the same platform, we must explore all possibilities to prevent, mitigate, and control this pandemic. It is the right time to integrate critical care and complication management skills of allopathy and preventive, immunomodulatory, and mental health management through traditional medicine. The development of traditional medicine with the perspectives...
of safety, efficacy, and quality would help not only to preserve the traditional heritage but also to rationalize the use of herbal medicine in human healthcare (Mukharjee et al. 2017). Integration of traditional Chinese medicine and modern medicine had formed the dominant treatment strategy in all COVID-19 affected areas across China (Jia and Yunfei 2020). Following a rich heritage of traditional medicine, the Indian AYUSH (Ayurveda, Yoga, Unani, Siddha, and Homeopathy) ministry has released an advisory for preventive health and immunity-boosting measures for self-care during the COVID-19 crisis (https://ayush.gov.in). It underscores the concept of “Prevention is better than cure”.

The author has screened the capacity of AYUSH-advisory in the prevention, prophylaxis, mitigations, and rehabilitation of COVID-19 cases. Advisory broadly divided into 3 categories i.e. general measures, immunity promoting measures, and the Ayurveda procedures to follow. General measures of advisory advocate drinking warm water throughout the day in COVID-19 outbreak and practice of Yogasana, Pranayama, and Dhayana (meditation) for 30 min daily (https://ayush.gov.in). According to Ayurveda, drinking hot water helps in digesting Aama (a pro-inflammatory marker of impaired metabolism) followed by Samprapti Vighatan (break of disease cascade). It is advocated in Naveen Jwara (fever) (Vaidya and Trikamji 2004). It is a good natural remedy to treat nasal congestion. A clinical study done in 15 healthy subjects, the nasal mucus velocity was measured before and at 5 and 30 min after drinking hot water increased from 6.2 to 8.4 mm/min five minutes after administration in patients drinking hot water by sip, again value returned to their baseline at 30 min. The above study concludes increased nasal mucus velocity might be helpful in the management of upper respiratory tract infections (Saketkhoo et al. 1978).

On the line of advisory, the author emphasized how Yoga, Dhyana, and Pranayama practices can be helpful in fighting psychoneuroimmuno perturbation during COVID-19. Among general measures, Yoga therapy is a form of mind–body medicine that integrates an individual’s physical, psychological, social, and spiritual components to enhance health, with a primary focus on stress and related illnesses (Atkinson and Permuth-Levine 2009). Yoga therapy comprises yogic physical postures (Asanas), Yogic breathing techniques (Pranayama), meditation (Dhyana)/Mindfulness, Yogic cleansing techniques (Kriya), Yogic gestures (Mudras), and locks (Bandhas) (Sengupta 2012). Evidence suggests Yoga as a therapeutic tool in alleviating fear, depression, anxiety, negative thinking, and enhance the quality of sleep (Cabral et al. 2011). With mounting scientific literature/research in the field of Yoga, it is regarded as a form of Complementary and Alternative Medicine (CAM) by National Centre for Complementary and Integrative Health (NCCIH), USA.

Spices like Curcumin longa Linn. (Haldi), Cuminum cyminum Linn. (Jeera), Coriandrum sativum Linn. (Dhaanvakya), and Allium sativum Linn. (Lahsun) are recommended for cooking. Herbal medicines like Ocimum sanctum Linn. (Tulsi), Piper nigrum Linn. (Maricha), Dry Zingiber officinale Roscoe (Shunthi), Cinnamomum species (Tvaka), Dry Vitis vinifera Linn. (Munnaka), Raisin, dried grapes are recommended to make herbal tea/decoction and consume twice daily. Chyawanprasha (Herbo-mineral ayurvedic preparation) 10 g daily in the morning is also advised (https://ayush.gov.in). Herbal drug screening revealed the presence of phytoconstituents such as polyphenol, terpenoid, flavonoid, curcumin, anthocyanin, proteins like lectins or agglutinins, piperine, vitamin C, gingerols, anethraquinone, and so on. These phytochemicals showed wide pharmacological actions but here we are documenting immunomodulatory, antiviral, and antibacterial actions, co-morbidity preventive action, and their probable mechanism of action.

The third section i.e. Ayurvedic procedures advocates oil pulling therapy (Kawala) by sesame or coconut oil for 2–3 min followed by the warm water rinse, nasal application (Pratimash Nasya) of sesame oil or coconut oil or ghee in morning and evening. Daily steam inhalation with Mentha arvensis Linn. (Pudina) or Trachyspermum ammi Linn. (Ajwain), and Syzygium aromaticum Linn. (lavang) powder with honey orally is advised for ailment like sore throat or cough (ayush.gov.in). Recently, Indian states like Kerala, Delhi, Gujarat, Goa, and so on, allowed to treat COVID-19 confirm cases through dedicated Ayurveda/integrative approach using Ayurveda and modern medicine through projects like ‘Sukhayusham’, ‘Swasthyam’, and ‘AyurRaksha’ clinics. The herbal medicines and Ayurveda procedures mentioned in the advisory are being used for the purpose of immunomodulation, antiviral, and stress management in various traditional medicine the system of the world since ancient period (Table 1). In the next section, AYUSH recommended herbs, their present antimicrobial, immunomodulatory, and antiviral actions are discussed in detail and how these medicines and procedures are vindicated in retaliation of COVID-19.

### Immunomodulatory and antimicrobial actions of herbs advised by Indian Ayush Ministry

The current advisory supports the scientific background of Ayurvedic plants and their phytochemicals support the immune system and have antimicrobial action (Fig. 1a,b). Apart from that, we have also discussed the detailed role of advised herbs because each phytochemical influences...
| Herb name | Traditional uses | Study/study model | Preparation (dose) | Results | References |
|-----------|-----------------|-------------------|-------------------|---------|------------|
| **Rasona (Allium sativum)** | Athletes for increasing stamina during the earliest Olympics in Greece. (2) Oil as an antimicrobial in Ayurveda. (3) In Turkish traditional medicine cloves and bulb of garlic as an immuno-tonic, anthelmintic, ringworm management, cardio-protective and rheumatism | In vivo study, BALB/c mice | Aged garlic extract (AGE) (10 µl/kg/day/I.p. route) | Protective Altering of cytokine production through raised levels of IFN-γ and IL-4. Reduced lymphocytes in the spleen | Larypoor et al. (2013) |
|         |                 | In vitro study, tumor cells, S180 sarcoma cell line | Dially ltrisulfide (DATS) higher concentration dose (50 µg/ml) | T cell proliferation inhibition | Feng et al. (1994) |
|         |                 | In vivo study, Broiler chicks | Garlic or ginger dietary supplementation (garlic extract at concentrations of 10–15% and ginger extract at a concentration of 15 g/kg diet) | Augmented the proliferation of T cells to Con A | Elmowalid et al. (2019) |
| **Jiraka (Cuminum cyminum/Nigella sativa)** | Hoarseness, jaundice, leprosy, chronic diarrhoea, bronchopulmonary disorders, and as a cough remedy. (2) Bloody diarrhea, inflamed eczema, and headache in Indonesia. (3) In Unani system of medicine, used for the treatment of ulcers, boils, stye, and cough. (4) Used to treat pneumonia in Russia. (5) Gastrointestinal, gynecological, and respiratory disorders in Iranian traditional medicine | Cyclosporine-A immune-suppressed Swiss albino mice | Cuminum cyminum seed powder (25, 50, 100 and 200 mg/kg) | A dose-dependent increase in CD4 and CD8, and Th1 predominant immune response | Chauhan et al. (2010) |
|         |                 | Ovalbumin-induced allergic diarrhea in BALB/c mice | Nigella sativa seed hexanic extract and thymoquinone (intragastric gavage once a day for 4 days) | Improved symptoms and immune parameters | Duncker et al. (2012) |
|         |                 | BALB/c mice | Methanolic extract of N. sativa (sublethal dose-20 mg/dose/animal/I.p.) | Protective increase in total WBC count, increased spleen weight, and enhanced splenocyte proliferation | Ghonime et al. (2011) |
|         |                 | Typhoid vaccination challenged long Evan rat model | N. sativa seed oil | Decreased antibody production with decreased splenocytes and neutrophil counts | Ahmad et al. (2013) |
|         |                 | Pigeons (Columbalivia) | Co-administration of N. sativa (2.5%) with oxytetracycline (OXT) (0.05 g/kg of feed) | Blocks the inhibitory effects on TLC and lymphocyte counts | Al-Ankari (2005) |
| **Dhaanyaka (Coriandrum sativum)** | (1) Juice of fresh leaves used as a gargle in sore throat and stomatitis. (2) Seeds are used for the treatment of fever and diarrhea. (3) A decoction of leaves used in conjunctivitis | Broiler chicks (Ross 308) | Seed extract (750, 1000 ppm) in drinking water+control diet without coriander | IgG antibody against sheep red blood cells improved, IgM was higher in fed animals | Hesam et al. (2014) |
| Herb name | Traditional uses                                                                 | Study/study model                                                                 | Preparation (dose)                                                                 | Results                                                                                       | References                             |
|-----------|----------------------------------------------------------------------------------|------------------------------------------------------------------------------------|------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------|----------------------------------------|
| **Tulsi** (Ocimum sanctum, Ocimum basilicum, Ocimum americanum) | (1) A decoction of leaves is a remedy for cold. (2) As prophylaxis against malaria, fresh Tulsi leaves with black pepper in the morning | Male Wistar rats, male Swiss albino mice, and guinea pigs                           | Ocimums sanctum seed oil (3 ml/kg/l.p.)                                                   | Modulates GABAergic humoral and cell-mediated immune response                               | Mediratta et al. (2002)                |
|           |                                                                                  | Wistar albino rats infected with LD50 dose of S. typhimurium infection             | Aqueous extract of O. sanctum leaves (250 mg/kg)                                   | Increased number of S. typhimurium engulfed peritoneal macrophages An elevated level of TNF-α, IFN-γ, and IL-2 cytokines in serum |                                                       |
|           |                                                                                  | 60 crossbred lactating cow sub-clinical mastitis (SCM)                             | Aqueous extract of O. sanctum leaf (100 mg/teat/ intramammary route/OD for 7 days) | Inhibited bacterial growth by increased phagocytic activity and phagocytic index. Enhanced lysosomal enzyme contents of the milk polymorphonuclear cells | Mukharjee et al. (2005)                |
|           |                                                                                  | Wistar albino rats                                                                | Aqueous extract of O. sanctum leaf (100, 200 mg/kg/day/P.o. for 45 days)             | Increased level of total protein, stimulated antibody production, enhanced production of WBC, RBC, and Hb Decreased SGPT | Jebe et al. (2011)                     |
|           |                                                                                  | Swiss albino mice                                                                 | Ethanal and aqueous extracts of O. basilicum leaves (400 mg/kg/day/P.o.)            | Increase in circulating antibody titer production, percentage neutrophil adhesion (p < 0.01) to nylon fibers, phagocytic activity, and primary and secondary hemagglutination antibody titer (p <0.01) Potentiate delayed-type hypersensitivity reaction | Neelam and Nilofer (2010)              |
|           |                                                                                  | In vitro study, Cell preparation from Sprague–Dawley male rat and suspended in RPMI 1640 medium | Methanolic extract of O.basilicum (250 µg/ml)                                       | Lymphoproliferation up to 80%                                                            | Flores et al. (2008)                   |
|           |                                                                                  |                                                                                    | Aqueous extract of O.basilicum (250 µg/ml)                                          | lymphoproliferation up to 83%                                                            |                                                       |
|           |                                                                                  | Stress-induced anxiety and depression model of male albino rats                    | Aqueous extract of Ocimum sanctum (100 mg/kg)                                      | Anxiolytic and antidepressant-like effect mediated through central monoaminergic neurotransmitter system | Tabassum et al. (2010)                 |
| Herb name       | Traditional uses                                                                 | Study/study model                                      | Preparation (dose)                                                                 | Results                                                                                                                                                                                                 | References         |
|-----------------|----------------------------------------------------------------------------------|-------------------------------------------------------|----------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------|
| Haridra (Curcuma longa) | (1) Used with cow’s urine in eosinophilia. (2) with curry leaves in asthma. (3) Turmeric powder, honey, and bitter gourd leaves extract used for measles. (4) Turmeric powder, powdered black pepper with milk used for Malaria. (6) Honey and turmeric powder mixed with the juice of Indian gooseberry treats urine discharges | NP-OVA immunized C57BL female mice                      | Curcumin, extracted from *Curcuma longa* (200 µg/day/l.p.) | Increases humoral immunity by antibody production mediated by increased TFH cells in the draining lymph nodes. Production of high-affinity antibodies of the IgG1 and IgG2b isotypes | Kim et al. (2019)  |
|                 |                                                                                  | In vitro, RAW 264.7 cells derived from murine macrophages and clone-9 rat hepatocytes | Concentrations of 20% turmeric polysaccharides ukonan A, B, C, and D extracted with water (TurP) | Promotes cellular immune responses, and tissue repair (improves telomer function)                                                                                                                        | Pan et al. (2017) |
|                 |                                                                                  | C57BL/6 mice infected with LP-BM5 murine leukemia virus (MuLV) | A mixture of *Curcuma longa* and sweet purple potato (CPM) (CPM low—2 g/kg Bw/P.o.) (CPM high—5 g/kg Bw/P.o.) | Increased expression of MHC class I and CD8(+) T helper cells, T cell proliferation, phagocytic activity and improved the imbalance of Th1/Th2 type cytokines | Park et al. (2018) |
|                 |                                                                                  | Swiss albino male mice                               | Nanoparticulate curcumin (doses of 5 mg/kg/day, 10 mg/kg/day/P.o.) | Stimulated primary humoral immunity with 9.00 ± 1.00 antibody titer (p < 0.05) white blood cells increased and the weight of the lymphoid organs was also increased | Afolayan et al. (2018) |
|                 |                                                                                  | Pacific white shrimp (Lito penaeus vannamei Boone) against *V. harveyi* | *Curcuma longa* Linn. extract containing 25.726% (w/w) curcuminoids (0, 12.5, 25.0 and 50.0 mg/kg feed) | Better resistance against *V. harveyi* in shrimps. Enhanced phenoloxidase activity and phagocytic activity                                                                                       | Kittima et al. (2010) |
|                 |                                                                                  | Splenocyte culture made from swiss albino male mice | NR-INF-02 (an aqueous-based extract of *C. longa*) ((0.8–500 µg/mL) | Immunostimulatory activity by macrophage activation, splenocytes proliferation, and cytokine release down-regulating PGE2 and IL-12 secretion                                                                 | Chandrasekaran et al. (2013) |
|                 |                                                                                  | C57BL/6−Min/+(Min+/+) mice                           | A diet containing 0.1% curcumin                                                  | Increased mucosal CD4(+) T cells and B cells                                                                                                                                                    |                    |
| Herb name | Traditional uses                                                                 | Study/study model                                                                 | Preparation (dose)                                                                 | Results                                                                                                                                                                                                 | References                  |
|----------|----------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------|
| Tvaka (genus Cinnamomum) | (1) In Ayurveda, used for the common cold, cough, fever, sore throat, sinusitis, and herbal toothpaste to reduce dental caries. (2) In traditional Chinese medicine (TCM), used for cold, diarrhea, asthma and as an appetiser. (3) In Europe, used for ailments associated with cold. (6) In western herbal medicine, used in toothpaste because of its antimicrobial property | In vivo study, Nile tilapia, *Oreochromis niloticus* (L.). Fish challenged against hypoxia stress or pathogenic bacteria | 0.0, 0.25, 0.5, 1.0, 3.0, 5.0, and 10.0 g cinnamon nanoparticles (CNP)/kg/P.o | Raised Innate immunity variables (nitrous oxide, nitro blue tetrazolium) and lysozyme activity were higher. No mortality in fish fed 3.0–10.0 g CNP/kg diet | Abdel-Tawwab et al. (2018) |
|          |                                                                                  | In vitro, Peripheral blood lymphocyte (PBL) culture                                  | 0.01% extract of Chinese medicinal herbs (CMH) containing Cinnamomum cassia (at the dilution of 40°) | Stimulated human lymphocytes to proliferate                                                                                                   | Shan et al. (1999)          |
Table 1 (continued)

| Herb name       | Traditional uses                                                                 | Study/study model                  | Preparation (dose)                                                                 | Results                                                                                                                                                                                                 | References |
|-----------------|----------------------------------------------------------------------------------|------------------------------------|----------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------|
| *Maricha (Piper nigrum)* | (1) In Ayurveda, used to treat respiratory congestion. (2) Used in cold and flu prevention in western herbalism. (3) Used in ear–nose–throat-related problems, including a cough, sinusitis, throat pain, throat infection, and earache. (4) Used against skin diseases, fever, and jaundice | *L. donovani* infected BALB/c mice | *Piper nigrum* hexane (PNH) (100 mg/kg, 200 mg/kg/I.P. and *P. nigrum* ethanolic (PNE) (100 mg/kg, 200 mg/kg/I.p.) | Increased secretion of Th1 (INF-γ, TNFα, and IL-2) cytokines and Decreased IL-4 and IL-10, Increased production of IgG2a, Upregulated expression of co-stimulatory molecules CD80 and CD86, Augmented splenic CD4 + and CD8 + T cell population, Induced strong lymphoproliferative and DTH responses and partially stimulated NO production | Chouhan et al. (2015) |
|                 |                                                                                 | In vitro, murine cultured splenocytes | Aqueous extracts of black pepper or cardamom four doses (1, 10, 50, and 100 µg/mL) | All doses (except 1 µg/mL) enhanced splenocyte proliferation A dose-dependent increase in IFN-γ release, IL-6 and TNFα release by macrophages | Maurya et al. (2020) |
|                 |                                                                                 | BALB/c mice                         | AC II, a registered Ayurvedic preparation (1 g/kg BW/P.o.)                        | The enhanced mitogen-induced proliferation of spleen cell lymphocytes Enhanced NK cell activity in normal and tumor-bearing animals, Elevated levels of IL-2, TNF-α, and IFN-γ in normal mice, Antibody-dependent cellular cytotoxicity was raised | Kesavan et al. (1998) |
| Herb name                          | Traditional uses                                                                                                                                                                                                 | Study/study model           | Preparation (dose)                                                                 | Results                                                                 | References                  |
|-----------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------|----------------------------------------------------------------------------------|------------------------------------------------------------------------|-----------------------------|
| **Shunthi (Dry Zingiber officinale)** | (1) Ginger given orally for the common cold in India. (2) Ginger and palm tree juice (htan-nyat) are boiled and given orally to prevent the flu in Burma. (3) In China, sliced cooked ginger with brown sugar is used in the common cold. Dried ginger candies are used for coughing | Rainbow trout fish (*Oncorhynchus mykiss*) | Diet (1% of a dried aqueous ginger extract) used at a rate of 2% of body wt. for 3 weeks | Increased Non-specific immunity | Dugenci et al. (2003)       |
|                                  |                                                                                                                                       | BALB/c mice                 | 50% ethanolic ginger extract (25 mg/kg/P.o.)                                      | Improved humoral immunity (higher antibodies and plaque-forming cells) | Puri et al. (2000)          |
|                                  |                                                                                                                                       | Cyclophosphamide immunosuppressed male swiss mice | Essential oil from *Zingiber officinale* (100, 200 and 400 mg/kg/OD/P.o. for 7 days) | Recovered humoral immune response in immunosuppressed mice              | Carrasco et al. (2009)       |
| **Chyawanprash**                  | (1) In Ayurveda, It is Rasayana (rejuvenating tonic) that helps in attaining longevity, memory, intellect, freedom from disease, youthfulness, luster, complexion, voice, and optimum strength of physique and sense organs | In vitro study done in dendritic cell (DC) and NK cell cultures from murine bone marrow | D-CHY (Dabar-Chyawanprash) (20–500 µg/ml for 24 h)                             | Discussed in manuscript                                                | Madaan et al. (2015)        |
|                                  |                                                                                                                                       | Ovalbumin induced allergy in mice | D-CHY (1 g/kg/P.o.)                                                                 | Antiallergic activity by reducing plasma histamine levels and serum immunoglobulin E (IgE) release | Sastry et al. (2014)         |
| Herb name          | Traditional uses                                                                                                                                     | Study/study model         | Preparation (dose)                                                                                           | Results                                                                                                                                                                                                                     | References                               |
|--------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------|----------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------|
| *Lavang* *(Syzygium aromaticum)* | (1) In tropical Asia, cloves are used to treat scabies, cholera, malaria, tuberculosis, diarrhea, and asthma. (3) It has been traditionally used in inhibiting food-borne pathogens in America | Albino Wistar rats       | Flower bud oil of *Syzygium aromaticum* (200, 400, 800 mg/kg p.o.)                                           | Exhibited increase in haemagglutinating antibody titer and delayed-type hypersensitivity response in dose-dependent manner                                                                                      | Umanskark and Nambikkainj (2018)        |
|                    |                                                                                                                                                      | Male Swiss mice           | Clove essential oil (CEO) (100, 200 and 400 mg/kg p.o.) 400 mg/kg p.o.                                         | Increase in total WBC count and stimulating cell-mediated immunity in a dose-dependent manner                                                                                                                       | Carrasco et al. (2009)                  |
|                    |                                                                                                                                                      | In vitro, macrophage cells isolated from BALB/c mice               | Clove ethanolic extracted essential oil (containing eugenol) or aqueous extract (ranging from 0.001 to 1000 µg/ml) | Both extracts enhance NO release by non-LPS (unstimulated) treated macrophages at a concentration of (0.001–1 µg/ml) Ethanol sample extract and aqueous extract (doses up to 1 µg/ml) showed suppression of TNF-α release while aqueous extract (doses > 1 µg/ml) showed stimulation of TNF-α release |                                                                                                              |
| *Pudina* *(Mentha arvensis)* | (1) Used to treat cold, cough, fever, headache, and asthma. (2) Leaves have anti-inflammatory action. (3) A decoction is used to treat diarrhea and influenza | Sprague-Dawley rats       | *Mentha arvensis* (MA) extract (100 mg/kg P.o.) and fermented *Mentha arvensis* (FMA) (100 mg/kg P.o.)       | Pretreatment reduced the serum and hippocampus level of malondialdehyde (MDA) Ameliorated the serum and hippocampus nitric oxide (NO) levels in immobilized rats                                              | Weishun et al. (2018)                   |
| *Ajwain* *(Trachyspermum ammi)* | (1) Ajwain seeds, clove, and common salt are used as lozenges for pharyngitis, sore throat, and hoarseness of voice. (2) Steam inhalation with Ajwain seed in common cold | Wistar rats               | Crude methanolic extract of *T. ammi* (500 mg/kg P.o.)                                                     | Effective immunomodulation on skin thickness (DTH reaction) The induced proliferation of murine splenocytes activates peritoneal exudate cells for the synthesis of NO (nitric oxide) and phagocytosis | Siddiqui et al. (2019)                   |
|                    |                                                                                                                                                      | In vitro, murine splenocyte cells                                 | Ajowan immunomodulatory component (ImC) (1 µg/ml)                                                         |                                                                                                              | Shruthi et al. (2017)                   |
(a) **Haridra** (Curcuma longa)

- Curcumin, Anthocyanin, Poly saccharides
- Mannaka (Raisin)
  - Oleanolic acid, Oleanolic aldehyde, Lindoric acid, Flavonol glycosides
- Rasna (Allium sativum)
  - Lectins, Agglutinins, Allicin, SAC
- Maricha (Piper nigrum)
  - Piperine
- Shunthi (Zingiber officinale)
  - Gingerol, Shogaols, Zingerone, Gingerdiones

| Immuno modulation & Anti microbial Action |
|------------------------------------------|
| **Jiraka** (Cuminum cyminum)              |
| - Coumarine, Thymoquinone, Anthraquinone |
| - Total WBCs count, splenocyte proliferation and impairing bacterial cell membrane |
| - T cells (CD4 and CD8) count and Th1 predominant immune response |
| **Tulsi** (Ocimum sanctum)                |
| - Terpenoid, Polyphenol                   |
| - Elevated level of TNF-α, IFN-γ and IL-2 cytokines, GABAergic pathway, Lymphoproliferation |
| - Inhibited virus replication, Anxiolytic antidepressant effect |
| **Twak** (Cinnamomum)                    |
| - Cinnamaldehyde derivatives BCA & HCA    |
| - Stimulated lymphoproliferation, induced T cell differentiation, Inhibition of virus-induced cytopathogenicity |
| **Lavang** (Syzgium aromaticum)           |
| - Eugenin, Eugenol, Flavonoids            |
| - Inhibiting viral DNA polymerase, showed virucidal activity, Inhibited release of cytokines (IL-1, TNF-α, IL-6 and IL-8) |
| - Haemagglutinating antibody titre, WBCs count and DTH response |
| **Chywanprash**                           |
| - Vitamin C, Polyphenolic, Flavonoids      |
| - Inhibitions of TNF-α, MIP-1α, IL-1β and NK cell activity and phagocytic activity |
| - Modulated IgE and immunity markers C3 and C4 levels |

(b) Innate and Adoptive arm, Optimum sequestration of transcriptional factors STAT3, 6, & NF-kB, Recognize and prevents viral entry, replication, and translation
the immune cells as well as microbes that could also provide useful insights to the development of potentially useful new pharmacological agents (Fig. 2). Rasona is an Ayurvedic Sanskrit name for Garlic (Allium sativum L.; Family: Amaryllidaceae) that enhances the functioning of the immune system by stimulating macrophages, lymphocytes, natural killer (NK) cells, dendritic cells, and eosinophils, through mechanisms like modulation of cytokine secretion, immunoglobulin production, phagocytosis, and macrophage activation (Arreola et al. 2015). Garlic compounds, like sulfur-containing components, showed a modulatory effect on T cell proliferation. Cuminum cyminum (Jiraka) possesses immune stimulatory property possibly through thymoquinone (TQ). The black cumin seeds are proved effective for the treatment of diseases such as asthma, bronchitis, rheumatism, and other inflammatory diseases (Srinivasan 2018). Cuminum cyminum stimulated the T cells (CD4 and CD8) and Th1 cytokines expression in normal and immune-suppressed swiss albino mice (Chauhan et al. 2010). Antibacterial activities of cumin, cardamom, and dill weed essential oils were evaluated against Campylobacter jejuni and Campylobacter coli showed inhibition of Campylobacter species by impairing the bacterial cell membrane (Ingok and Guler 2017). Coriandrum sativum (Dhaanyaka) leaves contain vitamins, minerals (phosphorous, calcium and iron) and it is a major source of lipids, petroselinic acid, and monounsaturated fatty acid (Mandal and Mandal 2015). Plantaricin C. sativum, an antimicrobial peptide isolated from coriander leaf extract and coriander essential oil exhibited antimicrobial activities against different strains of bacteria’s in two different studies (Masoud et al. 2014). Immunomodulatory and antimicrobial in vivo/in vitro and clinical studies of all recommended spices/herbs are summarised in Table 1.

An open level, comparative clinical study administering add-on Ayurvedic treatment with Standard of Care (SoC) in COVID-19 positive cases expressed fast recovery and early discharge in patients received Dasamooladuthrayam Kashaya and Guduchi Kwatham with SoC than SOC alone (Khedkar et al. 2020). Results of undergoing Ayurvedic herbs trials on recovery rate, virus loads, and immunological markers of COVID-19 are awaited (Rangnekar et al. 2020).

### Ayurvedic procedures

Ayurveda advocates Nasya (instillation of medicine through nostrils) for the prevention and mitigation of diseases. Absorption of drugs from the nasal cavity occurs through two routes i.e. paracellular (slow, passive, and aqueous route of transport) and transcellular (rate dependent, active and lipophilic route of transport) (Bale et al. 2015). Advisory recommended applying sesame oil/ coconut oil or ghee in both the nostrils twice daily (morning and evening) called Praimarsha nasya. This therapy cleanses, purifies, and strengthens the nasal passages, likely to act as a “physiological mask” and may prevent virus fatty acid layer adherence to moist mucosa of the nasal or oral cavity (Tillu et al. 2020).

The sesame seed oil contains important active compounds such as major lignans, phytosterols, and vitamin E especially γ-tocopherol which has immunomodulatory and antimicrobial activity (Nonaka et al. 1997). Advisory also recommended oil pulling therapy (Kavala or Gandusha: a traditional procedure in which the practitioner rinses or swishes oil in his mouth). It is supposed to cure oral and systemic diseases. It is a powerful detoxifying ayurvedic technique that is preventive as well as curative (Hooda et al. 2017). Cosco nucifera Linn. (Coconut) oil is an easily available edible oil that contains predominantly medium-chain fatty acids (lauric acid) that have proven anti-inflammatory and antimicrobial effects (Peedikayil et al. 2015). In an observer-masked, randomized, volunteer-based cross-over clinical trial, coconut oil pulling seems to have similar plaque inhibition activity as 2% chlorhexidine gluconate (CHX) with less tooth staining than CHX (Sezgin et al. 2019).

Non-pharmacological procedures like Yogasan, Pranayama, and Dhyaan (meditation) have been advised routinely at least 30 min/day in AYUSH guidelines to reduce stress, anxiety, enhance immunity, etc. Every day, an instructor displays the Asanas technique on the website of the AYUSH ministry in the form of a video for the people to follow. Pranayama (breath regulation) an essential component of Yoga, positively influences the physiology of the human body. Stress hurts the immune system and prolonged exposure is linked to physical and mental health problems (Segerstrom and Miller 2004). Yoga modulates levels of immunoglobulins and viral recognition cells (NK cells) and moderates C-reactive protein and other inflammatory cytokines in the blood (Shete et al. 2017). Yoga practice optimizes sympathetic responses of the body to stressful stimuli and restores autonomic regulatory reflex mechanisms by inhibition of the posterior or sympathetic area of the hypothalamus. It inhibits median forebrain centers and other areas liable for...
fear, aggressiveness, and rage, coupled with stimulation of the rewarding pleasure centers resulting in a state of bliss and pleasure (Woodyard 2011) and increase multiple anti-depressant neurotransmitters and hormones such as GABA, serotonin, dopamine (Stephens 2017) and decrease the levels of monoamine oxidase that breaks down neurotransmitters and cortisol (Kamble 2019). Yoga practices may inhibit the activity of the paraventricular nuclei of the hypothalamus, resulting in reduced ACTH production and decreased synthesis of cortisol, and aldosterone lead to down-regulate stress responses (Arora and Bhattacharjee 2008). The process and interrelation between stress, immunity, morbidity susceptibility, co-morbidities, and Yogic practices are summarised in Fig. 3.

**Dhyaan** (meditation) increases the expression of brain-derived neurotrophic factor (BDNF) and the thickness of the left hippocampus that essentially plays a role in the resiliency to chronic stress and depressive states (Taliaz et al. 2011). Chronic stress flare-up the aging process in association with decreased telomerase activity and telomere shortening. A big positive association between comprehensive lifestyle changes (including Yoga, meditation, breathing, healthy whole-food, and plant-based diet), and increased telomerase activity in human peripheral blood mononuclear cells was found (Ornish et al. 2008). An open-label cohort study performed on 54 depression patients (high serum cortisol level), subjects in the Yoga groups (Yoga alone and Yoga with drug therapy) had significant drops in their cortisol levels in comparison to the drug-only group ($p < 0.008$). In Yoga only group, there was a high correlation between decreased cortisol levels and lower scores on the HDRS (Hamilton Depression Rating Scale) indicating a positive antidepressant effect as well ($p < 0.001$) (Thirthalli et al. 2013). A randomized controlled clinical test performed among high stressed college students assessed the consequences of sun salutations or *Suryanamaskar* (a series of 12 physical postures in conjunction with breathing). After 14 days of practice, the experimental group scored higher on mental calmness, joy, strength, physical relaxation and feeling at ease, and scored lower on physical fatigue, somatic stress, and negative emotional feelings in comparison with the control group (Godse et al. 2015).

**Pranayama** or breath regulation includes modulation of the pace of breathing, viz. slowing down or pacing the breath, manipulation of nostrils, chanting of humming sounds, retention of breath, etc. Pranayama techniques are also beneficial for treating a range of stress-related disorders. *Anuloma-Viloma-Pranayama* (AVP), i.e., alternate nasal breathing exercise creates negative pressure within the cavity hence improves oxygenation (better surface
availability) and ventilation of the paranasal sinuses and nasal respiratory epithelium (Bhardwaj et al. 2013). A set of 3 Pranayama breathing exercises was found to increase lung functions (PEF and FEV1) after only 6 weeks of three 10-min each practice sessions per week in healthy volunteers (Kupershmidt and Barnable 2019). The Intervention arm, COPD assessment test scores after 3 months of Pranayama practice, showed improvement in the subjective experience of health, disease severity, and functional status for COPD patients, with airflow limitation not fully reversible but usually progressive (Gupta et al. 2014). In an observational, prospective, quasi-experimental study done on elderly COVID-19 patients (65 yrs or above) recruited from Hainan General Hospital and Huanggang central hospital, six-week respiratory rehabilitation improved respiratory function (FEV1, FVC, FEV1/FVC%, and DLCO%), Quality of life, anxiety and depression scores (Liu et al. 2020).

Yoga is effective in improving dyspnea, inflammatory markers, respiratory functions (Tidal volume, vital capacity, minute ventilation, respiratory rate, forced expiratory volume (FEV1) and forced vital capacity (FVC)), cardiac functions (blood pressure, heart rate, pulse duration, upstroke time, ejection duration index, diastolic time) and Quality of life as a standard cardiopulmonary rehabilitation.
immunity (Masram et al. 2014). The immunity used in modern medicine (Masram et al. 2014).

The word “Kshamatwa” has many broad implications than the term “Immunity” used in modern medicine (Masram et al. 2014). Immunity, immunomodulation, and SARS-CoV-2

The immune components have continuing inside-out and outside-in communication at molecular, cellular, historical, and systems levels to maintain the body homeostasis. This routine house-keeping vs. concerted strategized response to an incumbent situation (altered normal) dialogue is what keeps a human body healthy and able to overcome challenging situations. Host immunity against viral is largely innate (first and second lines of defense) and also auto-regulated. Acquired or memory-directed immunity usually does not need to kick in during a virus lytic cycle. When a virus changes from lytic to lysogenic cycle (i.e. assumes a more long-term association with the body), it leads to a powerful and unregulated innate immune response leading to devastating results.

For SARS-CoV-2, an unregulated cytokine storm seems to be an important watershed reaction leading to mortality. Just like in allergic response, some persons may and some may not respond to an allergen in the environment because of ‘primed’ dendritic and other antigen presentation cells that process and activate the allergenic circuit. Similarly, 80% of individual do not show symptoms of SARS-CoV-2 although they harbour the virus in their body and may act as carriers, while others (15%) show moderate symptoms, and only 5% show the severe form of disease requiring ventilation and...
these individuals (with or without co-morbidity) tend to succumb to the COVID-19. SARS-COV-2 manifestation is akin to other influenza viruses such as HKU-1, NL6, and OC43 which cause mild forms of pneumonia. SARS-COV-2 on the other hand is unusual in the sense, it quickly unlocks its replicon and usurps the host’s transcriptome using its enzymes 3CLpro, RDRP, and other NSPs. ACE-2 is expressed on all blood vessel cells, monocytes, dendritic cells, and macrophages in tissue spaces that interact with spike protein of virus for internalization inside the host cell. It resulted in inflammation (innate immune response), release low levels of IFN-γ, and then the mononuclear macrophages start secreting high levels of IL-6, TNF-α, IL-1b, etc. Soon potent inflammation-inducing cytokines secreted in large quantity relentlessly and lost regulatory mechanism to stop it. A positive feedback loop seems to be the hyper-response to the viral proteins that cannot be controlled. Under these circumstances, an efficient immune system needs to have the right proportion of all cells. The signal reception nodes of all the immune circuits must be in good functioning so that once they can respond, certain stimuli be interrupted, and once mounted it must not go on for a very long-time unabated unchecked. The other important thing is the rejuvenation (regeneration, replacement, and repair) of damaged and used-up components of the immune system. The preventive, mitigation, and rehabilitation role of immunity to viral threat is shown in Fig. 1b. AYUSH advisory’s phytochemicals and Yoga may induce the Th1/Th17 response for macrophage activation and elimination of SARS-COV-2 pathogens. They could support regenerating the required repertoire for the development of certain cell types to be efficiently and correctly occurring during infection (Rastogi et al. 2020; Kar et al. 2015; Das et al. 2016).

From data generated by scientific experiments, curcumin, piperine and various phenolic compounds (Paul et al. 2018; Das et al. 2015) have already shown immunoboosting not in the sense of activation but rather to maintain, regenerate, and ensure the efficiency of key immune components and their connecting circuitry in the rest of the systems (none of them exist in isolation). Nutritional ligands of PPAR-y like Curcuma Longa and others are under scrutiny as a potential candidate for cytokine storm modulation in COVID-19 (Ciavarella et al. 2020). Pro-inflammatory innate responses are not misfired and in case there is an over-stimulation, they act as inflammation regulatory elements to bring responses not misfired and in case there is an over-stimulation, they act as inflammation regulatory elements to bring

hence Chyawanprash could also be extended to COVID-19 care if trials post positive results.

Suffice it to say, the functional food, prophylactic-therapeutic phytochemicals, Ayurvedic procedures, frequency and synchronicity of important diurnal events for maximum efficacy by the chrono-biological system of the body’s cells and their bioavailability to affected tissue, may ensure transcriptomic and/or metabolomic sequestration of the required components (cellular and non-cellular) and their proper communication in the body with time to ensure optimum balance to keep the immunity (Vyadhukshamata), samprapti-vigathan (break of disease cascade), etc. in synchrony. Self-care advisory can streamline and maintain immunological, social, diurnal, and mental balance. Ayurveda fortified by Yoga, Dhyana, and Pranayaam ensure perfect rhythm and well-stocked repertoire of an already efficient and well-endowed immune system to combat the current pandemic situation.

**Apprehensions about AYUSH advisory**

**Evidence, drug interaction, efficacy, and safety**

An international advisory released by WHO, welcoming innovation like drug repurposing and traditional medicine in search of a potential treatment for COVID-19. This advisory also expressed concern for safety, efficacy and adverse side effects of certain remedies like Artemisia annua Linn. (family—Asteraceae) (Sweet wormwood, Chinese name-qinghao and famous as COVID-ORGANICS) touted as possible treatment backed by several African nations. “Natural and safe” a perception linked with herbal products is not always true. Many herbs have reported toxicity and adverse drug reactions. Clinical, in vivo and in vitro safety and toxicity profile studies for advised drugs are searched, analyzed, and discussed in Table 2. Although most of these herbs are food or dietary supplements so pharmacological vigilance is not compulsory. Sufficient works had been carried out on Chyawanprash, no evident information on toxicity has been available to date. It is considered safe in prescribed dosage (10 g/P.o. in the morning as recommended by AYUSH advisory). Agbaje et al. (2009), concluded that indiscriminate and long-term use of Syzgium aromaticum could be hazardous to body health so must be ingested with caution. (already in below table). No study has shown any significant toxicity except few in doses much higher than therapeutic limits. We searched Uppsala Monitoring Centre (UMC) (www.vigiaccess.org) and Ayushsuraksha (AYUSH pharmacovigilance reporting site) (www.ayushsuraksha.com) for adverse drug reactions (ADRs) associated with these herbs. UMC on date 23rd May 2020, ADRs reported for P. nigrum, O. sanctum, C. cyminum, Cinnamomum, and M. arvensis are 2, 1, 6, 68, and 26 respectively. ADRs for A. sativum, Z. officinalis and
| Herb name       | Study                        | Preparation            | Study model                      | Dose/route                        | Results                                                                                                                                                                                                 | References                        |
|-----------------|------------------------------|------------------------|----------------------------------|-----------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------|
| *Allium sativum*| Sub-chronic toxicity study   | Methyl propyl trisulfide| Sprague–Dawley rats              | 0, 0.5, 2, and 6 mg/kg/day/P.o    | No adverse effects in clinical observations, hematological findings, clinical bio-chemistry parameters, and histopathological examinations                                                              | Bastaki et al. (2018)             |
|                 | (90 days)                    |                        |                                  |                                   |                                                                                                                                                                                                       |                                   |
| *Cuminum cyminum*| Sub-chronic toxicity study  | Essential oil          | Healthy female wistar rats       | 0, 250, 500, and 1000 mg/kg/day/P.o| No adverse effects on clinical signs, body weight, hematological, biochemical parameters, and organ histology. No mortality                                                                                      | Taghizadeh et al. (2017)          |
|                 | (45 days)                    |                        |                                  |                                   | Increased serum alanine transaminase (ALT) level                                                                                                                                                      |                                   |
| *Coriandrum sativum*| Acute toxicity study      | Seeds extract          | Female swiss albino mice         | 1000, 3000 and 5000 mg/kg/OD/P.o | No behavioral changes and no mortality                                                                                                                                                                  | Patel et al. (2012)               |
|                 | Sub-chronic toxicity study  | Seeds extract          | Female swiss albino mice         | 1000 mg/kg/P.o                    | No alterations in hematological profile, histology, relative organ weights, and plasma markers of vital organs tissue damage                                                                             |                                   |
|                 |                              |                        |                                  | 2000 and 3000 mg/kg/P.o          | Significant reduction in food intake, body weight, and plasma lipid profiles                                                                                                                                              |                                   |
| Herb name                  | Study                           | Preparation                                      | Study model          | Dose/route | Results                                                                 | References                        |
|---------------------------|---------------------------------|--------------------------------------------------|----------------------|------------|-------------------------------------------------------------------------|-----------------------------------|
| *Ocimum basilicum*        | Acute toxicity test             | 50% ethanolic leaf extract of *O. Sanctum*       | Swiss albino mice    | 200, 600, & 2000 mg/kg/P.o | No hazardous symptoms like Central nervous system and Autonomic nervous system toxicities or death | Gautam and Goel (2014)            |
|                           |                                 |                                                  |                      |            |                                                                         |                                   |
|                           | Sub-chronic toxicity study      | Hydroalcoholic leaves extract of *O. basilicum*  | Wistar rats          | 500 mg/kg/day/P.o | Reduced hematocrit, platelets, and RBC count                            |                                   |
|                           | (45 days)                       |                                                  |                      | 50, 500, 1000 & 2000 mg/kg/day/P.o | Neither deaths nor adverse effects were seen on serum parameters (glucose, creatinine, albumin, cholesterol, LDL, HDL, VLDL, SGPT, SGOT) |                                   |
|                           | Acute toxicity study            | The essential oil of *O. basilicum*              | Wistar albino rats   | 5–1000 mg/kg/P.o gavage | No abnormalities on day 1                                               |                                   |
|                           |                                 |                                                  |                      | 1500 mg/kg/P.o gavage | Brief torpor just after gavages disappeared after few minutes          |                                   |
|                           |                                 |                                                  |                      | 2000 and 3000 mg/kg/P.o gavage | Stayed torpid throughout the day with no mortality                    |                                   |
|                           |                                 |                                                  |                      | 3500 mg/kg/P.o. gavage | Mortality 100%                                                          |                                   |
|                           | *Curcuma longa*                 | Sub-chronic toxicity study                       | Demethylatedcurcuminoids | Sprague–Dawley rats | No mortality and no signs of toxicity during the observation (14 days) and thereafter | Krishnaraju et al. (2009)         |
|                           |                                 |                                                  |                      | 5000 mg/kg/P.o |                                                                      |                                   |
|                           |                                 |                                                  |                      |                  |                                                                         |                                   |
|                           | *Cinnamon species*              | Sub-acute toxicity study                        | Aqueous extract      | 0.1 g/kg/P.o | No adverse effects on behavior, water intake, food consumption, hematological parameters, and mortality | Ahmad et al. (2015)               |
|                           |                                 |                                                  | Female Sprague–Dawley rats | 0.5 and 2 g/kg/P.o | A slight decrease in weight of kidney and liver                         |                                   |
| Herb name       | Study                                   | Preparation                        | Study model                  | Dose/route | Results                                                                                           | References |
|-----------------|-----------------------------------------|------------------------------------|------------------------------|------------|---------------------------------------------------------------------------------------------------|------------|
| Piper nigrum    | Acute toxicity study                    | Aqueous extract                    | Sprague–Dawley rats of either sex | 5000 mg/kg/P.o./OD | No signs of toxicity, No behavioral changes, No mortality, No histopathological changes in selected internal organs | Siharat et al. (2007) |
|                 | Sub-chronic toxicity study (90 days)    | Aqueous extract                    | Sprague–Dawley rats          | 300, 600 and 1200 mg/kg/P.o | No abnormalities in body weight, hematological parameters, biochemical parameters, and histopathology |           |
| Zingiber officinale | Sub-chronic toxicity study (45 days)   | Ginger powder                      | Sprague–Dawley rats          | 500 mg/kg/P.o | No abnormalities in general conditions, behavior, growth, food and water consumption and hematological parameters, No mortality | Rong et al. (2009) |
|                 |                                        |                                    |                              | 1000 and 2000 mg/kg/P.o | No changes in biochemical parameters except a dose-dependent decrease in serum lactate dehydrogenase |           |
|                 | Sub-chronic toxicity study (13 weeks)  | Ginger oil                         | Wistar rats                  | 2000 mg/kg/P.o | Reduced weight of testes                                                                         |           |
|                 |                                        |                                    |                              | 100, 250, and 500 mg/kg/day/P.o | No mortality                                                                                     |           |
|                 |                                        |                                    |                              |                                  | No adverse effects on body weight, organ weights, food consumption, hematological parameters, biochemical parameters, and histopathology of selected organs |           |
| Raisin (dried grapes) | Sub-chronic toxicity study (90 days) | Grape seed extract with less than 5% catechin monomers | Sprague–Dawley rats | 0, 0.5, 1.0, or 2.0% of diet | No toxicologically significant changes in clinical signs, hematological parameters, ophthalmology evaluations, and histopathological findings | Wren et al. (2002) |
| Acute toxicity study | Proanthocyanidin-rich extract from grape seeds | Fischer 344 rats                  |                              | 2 and 4 g/kg/P.o | No evidence of acute oral toxicity                                                               |           |
| Herb name               | Study                          | Preparation                  | Study model                                      | Dose/route         | Results                                                                                                                                                                                                 | References         |
|------------------------|--------------------------------|-----------------------------|-------------------------------------------------|--------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------|
| *Syzigium aromaticum*  | Acute toxicity study          | Aqueous extract             | Healthy Swiss albino mice and Wistar rats of both sexes | 500–5000 mg/kg/P.o | No physical changes in the skin, fur, eyes, respiratory system. No change in behavioral pattern. Abdominal writhing was found, few animals died before the end of the study. LD50 was 2500 mg/kg/P.o               | Agbaje et al. (2009) |
|                        | Sub-chronic toxicity study (90 days) | Aqueous extract            | Swiss albino mice and wistar rats               | 300 and 700 mg/kg/P.o | Showed effects on hematological parameters. Altered (decreased) serum electrolytes and increased serum urea. Severe and irreversible histological changes in brain, kidney, liver, stomach               |                     |
| *Mentha arvensis*      | Subchronic toxicity study (for 20, 40, and 60 days) | Petroleum ether extract of the leaves | Male albino mice                                | 10 and 20 mg/mouse/day/P.o | Dose and duration-dependent reduction in the number of offspring of treated male mice mated with normal females. Reversible fall in weight of testis, epididymis, and sperm count. No alterations of serum protein, bilirubin, SGOT, SGPT, acid phosphatase, blood urea, and hematological indices | Sharma and Jacob (2001) |
| *Trachyspermum ammi*   | Acute toxicity study          | Methanolic seed extract     | Wistar rats                                      | 400, 800, 1600, and 3200 mg/kg/P.o | Two deaths occurred after 24 h in rats administering crude extract up to 3200 mg/kg/P.o                                                                                                               | Siddiqui et al. (2019) |
C. longa are 216, 399, and 226 respectively while Chyawanprash, S. aromaticum, and T. ammi has no reported ADR to date. These numbers are negligible in comparison to ADRs reported of another prophylactic drug like hydroxychloroquine (23,994) and paracetamol (149,820). The above data support the safety of advisory for longer human uses. Although limited access and information are available may be due to under-reporting or less known reporting procedure. Ayursuraksha, an Indian ASU pharmacovigilance reporting site, has no available data for public access to get an idea of ADRs reported to date for a particular herb, active ingredient, and their combination.

Guidelines issued are self-care, so no unsubstantial claims and no Ayurveda professional practice is promoted. Ministry of AYUSH issued a notification prohibiting themongering of unsubstantiated and unauthenticated claims of curing COVID-19 through AYUSH medicines. It stated that all Indian states and Union Territories are directed to stop or prevent publicity and advertisement of AYUSH related claims for COVID-19 treatment in television, print media, and electronic media. This step has fairly regulated the claims made through e-platforms and print media (Anonymous 2020).

International relevance

More than 30 traditional medicine guidelines (for treatment alone 26 from china, 2 from South Korea) for prevention, prophylaxis, and treatment of COVID-19 have been issued till 12 May 2020. Many nations have adopted the translated version like Japan has adopted the translated version of Traditional Chinese Medicine (Lin et al. 2020). Indian AYUSH self-care guideline is translated in 5 united nation (UN) languages and 3 other international languages; hence it was eminent to see such advisory in light of current science and public health prospect.

Stress, anxiety, depression, fear, psychosis, psychoneuroimmunological correlations, and Yoga

The concept of the psychosomatic phenomenon has its roots in one of the traditional/classical Yoga texts (The Yoga Vashista, codified nearly 5000 years ago) termed as Adhija-Vyadhi. Uncontrolled, long-standing stress at Manomaya Kosha (Mental body) may lead to disturbances in the Prana (vital energy—similar to Qi), and manifest the disturbances in the Annamaya Kosa (Physical body) may result in several psychosomatic diseases. Stress, anxiety, depression, fear psychosis, sleep disturbances, loneliness (lockdown effect) are associated with the ongoing COVID-19 pandemic. Psychoneuroimmunology (PNI) studies showed correlation between the state of mind and the state of physical health (Singh et al. 2015). Eustress helps to cope with the demanding situation at the physical, mental or emotional level, but uncontrolled long-standing stress/chronic stress can have an immunosuppressive effect, a risk factor for COVID-19. Stress may dysregulate different immune parameters (e.g. inflammatory pathways) and lead to disease. Elevated pro-inflammatory cytokine production may generate sustained upper respiratory infection symptoms. Limited studies are carried out to evaluate the effect of Yoga on the immune system and it may decrease IL-1β, IL-6, and TNF-α in inflammatory stages and reflects immunomodulation (Falkenberg et al. 2018). Increasing psychological resources (mindfulness, body consciousness, self-transcendence, spiritual peace, and social connectedness) may bring about salutary effects on emotional wellbeing. PNI correlation and protective effect of Yoga in modulation of acute stress, chronic stress, comorbidity, and immune system are explained in Fig. 3.

Endocrine, nervous and immune systems are interconnected, so disruption in one creates an impact on the other. Yoga activates neurohormonal mechanisms by inhibiting the posterior or sympathetic area of the hypothalamus, optimizes sympathetic responses to stressful stimuli, restores autonomic reflexes associated with stress, increases the parasympathetic activity thus reduces stress, anxiety, balances autonomic functions and hormonal secretions (Balasubramaniam et al. 2013). Yoga therapy was also found beneficial in enhancing immunity, sleep, cardio-pulmonary fitness, and telomere length in regular practitioners (Ornish et al. 2008; McCall et al. 2013). The above discussion supports that Yoga, Pranayama, and Dhyana can be a better way of managing stress in the current pandemic situation.

Co-morbidities management through drugs and non-pharmacological procedures

Emerging data suggest an increased association and a heightened mortality in patients of COVID-19 with co-morbidities (Singh et al. 2020). Co-morbidities predispose the patients to multi-organ failure during an infection. According to a recently published study on laboratory-confirmed cases of COVID-19, patients with any comorbidity yielded poorer clinical outcomes than those without. A systematic review and meta-analysis on the prevalence of co-morbidities and their effects in COVID-19 patients revealed that underlying disease, including hypertension, respiratory system disease, and cardiovascular disease, may be risk factors for severe patients compared with non-severe patients (Yang and Zhou 2020). Hence advised drugs were screened for various morbidities associated with COVID-19. It was observed that all herbs protect from single or multiple co-morbidities collectively or individually. The role of advised herbs and their mechanism of action against co-morbidities associated with COVID-19 is explained in
Scientific rationale of Indian AYUSH Ministry advisory for COVID-19 prevention, prophylaxis,…

Fig. 2 and Table 3. Yoga has also gained popularity as an adjunct therapeutic tool in the management of diabetes, hypertension, obesity, respiratory disorders, autoimmune disorders and other psychosomatic illnesses (Ornish et al. 2008; McCall et al. 2013) hence may equally contribute to co-morbidities management.

Post-COVID-19 rehabilitations

Evidence from China has shown that recovery will be longer and more complex in COVID-19 patients due to neurological, cardiovascular, and respiratory after effects. The symptoms of COVID-19 disease can range from very mild to severe. Community-acquired pneumonia, ARDS, acute cardiac injury, stress, depression, and acute kidney injury in COVID-19 patients results in decreased activities of daily living and quality of life accompanied by decreased physical and mental function. Many research studies support that Yoga therapy is reported to relieve post-traumatic stress disorder symptoms in war veterans, tsunami survivors, hurricane refugees, and flood survivors (Tyagi 2013). Based on the above discussion, Yoga therapy may prove a beneficial rehabilitative strategy in patients having a history of severe symptoms of COVID-19 in improving dyspnea, inflammatory markers, respiratory functions, cardiac functions, quality of life, and post-traumatic stress disorder as shown in Fig. 4. AYUSH guidelines can help to get back, improve the functioning system of the body as standard rehabilitation therapy (Fig. 5).

There is a need to document the feedbacks of self-care advisory and in this regard, the Indian AYUSH ministry’s attempt of “Ayush Sanjeevani” mobile application (covered > 100 thousand downloads and > 1 million cumulative feedbacks as of 19 June 2020) and Arogyaduta are appreciable. Advisory has streamlined the AYUSH human resources (> 7 lakh AYUSH practitioners) and associated infrastructure (near 25,000 health facilities) in India.

Conclusion

From time to time, scientific advisory released by the national government of a country has great significance and is considered as an important medical guideline but

| Activity | Herb               | Mechanistic property                                                                 |
|----------|--------------------|--------------------------------------------------------------------------------------|
| Anti-obesity | *Allium sativum*     | Decreased fat accumulation in 3T3-L1 adipocytes and stimulates apoptosis              |
|          | *Zingiber officinalis* | Decreases the level of fatty acid synthase                                           |
|          | *Piper nigrum*       | Reduces LDL, VLDL, HMGCoA reductase                                                  |
|          | *Cinnamomum*         | Reduces Serum cholesterol                                                              |
|          | *Cuminum cyminum*    | Reduces Serum cholesterol, LDL, and triglycerides                                     |
| Anti-diabetic | *Ocimum sanctum*     | Enhances Insulin secretions                                                           |
|          | *Curcuma longa*      | Act through PPAR-activation                                                            |
|          | *Zingiber officinalis* | Increases cell-mediated glucose uptake                                               |
|          | *Cinnamomum*         | Enhances Insulin secretions and their action                                          |
| Antihypertensive | *Allium sativum*     | Reduces induction of NHE and activation of Na pump activity                          |
|          | *Cinnamomum*         | Increases level of ANF                                                                 |
|          | *Cuminum cyminum*    | Reduces Sr. Cholesterol, LDL, triglycerides, act as a diuretic                       |
| Cardioprotective | *Allium sativum*     | Free radical scavenger, Controls cardiac Na/K ATPase activity                        |
|          | *Piper nigrum*       | Reduces LDL, VLDL, HMGCoA reductase                                                  |
|          | *Chywanprash*        | Free radical scavenging                                                               |
|          | *Cinnamomum*         | Reduces Serum cholesterol, and total lipid level                                      |
| Nephroprotective | *Ocimum sanctum*     | Anti oxidative and free radical scavenging                                           |
|          | *Curcuma longa*      | Reduces oxidative stress and increases kidney glutathione content                     |
|          | *Cuminum cyminum*    | Diuretic action                                                                      |
|          | *Chywanprash*        | Free radical scavenging                                                               |
| Hepato-protective | *Ocimum sanctum*     | Increase bile synthesis, reduces liver lipid synthesis                               |
|          | *Zingiber officinalis* | Anti-oxidant action                                                                 |
|          | *Piper nigrum*       | Reduces superoxide dismutase, catalase, glutathione reductase                        |
| Pulmo-protective | *Curcuma longa*      | Anti-inflammatory activity                                                            |
|          | *Cuminum cyminum*    | Manages inflammatory pulmonary response, increase activity of surfactant protein D    |
|          | *Chywanprash*        | Settle pulmonary ailments, immunomodulatory                                           |

Table 3 The activity and mechanistic properties of the herbs advised by Indian AYUSH for COVID-19
the modern medical fraternities have some apprehension for the unconventional method like AYUSH. The information discussed in this article is the rationale behind advisory and will gradually increase the wisdom to provide an alternative to a large Indian community. The detailed immunological and other scenarios of herbal medicine are portrayed in Fig. 1a in terms of B-cell/T-cell response, cytokines release, and antimicrobial activity. It can be concluded that AYUSH-advised herbs and Yoga promote the state of immunity preparedness to threat, and equipoise the immunity in COVID-19, COVID-19 related co-morbidities (Fig. 2) and stress management. It may be a simple, safe, cost-effective, accessible, acceptable, infrastructure compatible, pragmatic for a longer duration, and sustainable preventive and prophylaxis approach for COVID-19. AYUSH ministry advisory not only supports the health of COVID-19 people but also creating a mental state that one can remain safe following home remedies (Rajkumar 2020). It is adoptive in nature and in the long run, it will change an individual’s habits that may reduce the burden of overall health care. It was an advisory release for pan India which may have a pan globe following. We have thoroughly searched the scientific domain for each component of advisory for its pharmacological relevance. We conclude
that this advisory comes up with a strong scientific rationale and further indicated more precise research in clinical/observational trials concerning COVID-19 and prevention of other infections. This advisory can pave the way to overcome this pandemic and may open a new window for the effective use of traditional medicines throughout the world. Considering the properties of flora, Yoga, and procedures, this advisory encouraging us to get closer to the natural way of healing.

Acknowledgements Authors are thankful to their parent institutions for the support and assistance during the work and scientific writing. We acknowledge Dr. Kathrina Petterson Sjorup, World Health Organisation, Uppsala Monitoring System, Sweden for giving guidance of public access website www.vigiaccess.org, We thank Prof. Brij Mohan Singh & Prof. Kishor Patwardhan, Banaras Hindu University, Varanasi, India for guiding and conceptual structuring. We thank Dr. Neelam Singh, Research Officer, CCRAS, Gwalior, India for information about Ayush Sanjivani mobile application. Authors are thankful to their parent institutions for providing all kind of support. The authors have no financing to disclose.

Declarations

Ethical Statement This article does not contain any studies involving animals performed by any of the authors. This article does not contain any studies involving human participants performed by any of the authors.

Conflict of interest Prashant Kumar Gupta, Kishor Sonewane, Mariappan Rajan, Nitin J Patil, Trapti Agrawal, Ena Ray Banerjee, Nagendra Singh Chauhan, Awanish Kumar declare that they have no conflict of interest.

References

Abdel-Tawwab M, Samir F, Abd El-Naby AS, Monier MN (2018) Antioxidative and immunostimulatory activity of dietary cinnamon nanoparticles on the performance of Nile tilapia, Oreochromis niloticus (L.) and its susceptibility to hypoxia stress and Aeromonas hydrophila infection. Fish Shellfish Immunol 74:19–25

Afelayan FID, Eriniwusi B, Oyeyemi OT (2018) Immunomodulatory activity of curcumin-entrapped poly D, L-lactic-co-glycolic acid nanoparticles in mice. Integ Med Res 7:68–175

Agbaje EO, Adeneye AA, Daramola AO (2009) Biochemical and immunological studies of aqueous extract of Syzygium aromaticum (L.) Merr. & Perry(Myrtaceae) in rodents. Afr J Tradit Complement Altern Med 6(3):241–254

Ahmad A, Husain A, Mujeeb M (2013) A review on therapeutic potential of Nigella sativa: a miracle herb. Asian Pac J Trop Biomed 3(5):337–352

Ahmad RA, Nouri HS, Majid FAA et al (2015) Assessment of potential toxicological effects of Cinnamon bark aqueous extract in rats. Int J Biosci Biochem Bioinformatic 5(1):36–44

Al-Ankari AS (2005) Immunomodulating effects of black seed and oxytetracycline in pigeons. Immunopharmacol Immunotoxicol 27:515–520

Anonymous (2020) Order no. F.no. Z 25023/09/2018-2020-DCC (AYUSH), Government of India, Ministry of AYUSH

Arora S, Bhattacharjee J (2008) Modulation of immune responses in stress by Yoga. Int J Yoga 1(2):45–55

Arreola R, Quintero-Fabian S, Lopez-Roa RI et al (2015) Immunomodulation and anti-inflammatory effects of garlic compounds. J Immunol Res 2015:401630

Atkinson NL, Permut-Levine R (2009) Benefits, barriers, and cues to action of yoga practice: a focus group approach. Am J Health Behav 33(1):3–14

Balasubramaniam M, Telles S, Doraishwamy PM (2013) Yoga on our minds: a systematic review of yoga for neuropsychiatric disorders. Front Psychiatry 3:117

Bale AP, Manerikar V, Tengse VG (2015) Review on pharmacodynamics of nasya. Int Ayu Med J 3(6):1780–1784

Bastaki M, Anbanel M, Cachet T (2018) Absence of adverse effects following the gavage administration of methyl propyl trisulfide to Sprague–Dawley rats for 90 days. Food Chem Toxicol 120:544–551

Bezerra LA, De Melo HF, Garay AP et al (2014) Do 12-week yoga program influence respiratory function of elderly women? J Hum Kinet 43:177–184

Bhardwaj A, Sharma MK, Gupta M (2013) Endoscopic evaluation of therapeutic effects of “Anuloma-Viloma Pranayama” in Pratyushayaw.s.r. to mucociliary clearance mechanism and Benoulli’s principle. Ayu 34(4):361–367

Byagdi PS (2011) Concept of immunity in Ayurveda. J Appl Pharm Sci 1(5):21–24

Cabral P, Meyer HB, Ames D (2011) Effectiveness of yoga therapy as a complementary treatment for major psychiatric disorders: a meta-analysis. Prim Care Companion CNS Disord 13(4):PCC.10r1068

Carrasco FR, Schmidt G, Romero AL et al (2009) Immunomodulatory activity of Zingiber officinale Roscoe, Salvia officinalis L. and Syzygium aromaromaticum L. essential oils: evidence for humor- and cell-mediated responses. J Pharm Pharmacol 61(7):961–967

Chandrasekarann CV, Sundarajan K, Guduraj GM, Mundkinajeddu D, Agarwal A (2013) Immune-stimulatory and anti-inflammatory activities of Curcuma longa extract and its polysaccharide fraction. Phcog Res 5:71–79

Chauhan PS, Satti NK, Suri KA, Amina M, Bani S (2010) Stimulatory effects of Cuminum cyminum and flavonoid glycoside on cyclosporine-A and restraint stress induced immune-suppression in Swiss albino mice. Chem Biol Interact 185(1):66–72

Chauragan G, Islanuddin M, Muzamil YW (2015) Leishmanicidal activity of Piper nigrum bioactive fractions is interceded via apoptosis in vitro and substantiated by Th1 immunostimulatory potential in vivo. Front Microbiol 6:1368

Ciavarella C, Motta I, Valente S, Pasquinelli G (2020) Pharmacological (or synthetic) and nutritional agonists of PPAR-γ as candidates for cytokine storm modulation in COVID-19 disease. Molecules 25(9):2076

Das R, Mitra S, Mukherjee K, Paul P, Singh UP, Banerjee E (2015) Anti-oxidant and anti-inflammatory activities of different varieties of piper leaf extracts (Piper betle L.). OMICS Nutr Food Sci 5:5

Das R, Biswas S, Banerjee E (2016) Nutraceutical—prophylactic and therapeutic role of functional food in health and disease. J Nutr Food Sci 6:4

Devpura G, Tomar BS, Nathiya D et al (2021) Randomised placebo-controlled pilot clinical trials on the efficacy of Ayurvedic treatment regime on COVID-19 positive patients. Phytomedicine 53:110356

Duncker SC, Philippe D, Martin-Paschoud C et al (2012) Nigella sativa (black cumin) seed extract alleviates symptoms of allergic diarrhea in mice, involving opioid receptors. PLoS ONE 7:e359841

Dugenci SK, Arda N, Candan A (2003) Some medicinal plants as immunostimulant for fish. J Ethnopharmacol 88(1):99–106
Elmowalid GA, AbdEl-Hamid MI, AbdEl-Wahab AM et al (2019) Garlic and ginger extracts modulated broiler chicks innate immune responses and enhanced multidrug resistant Escherichia coli O78 clearance. Comp Immun Microbiol Infect Dis 66:101334

 Falkenberg RI, Eising C, Peters ML (2018) Yoga and immune system functioning: a systematic review of randomized controlled trials. J Behav Med 41(4):467–482

 Feng ZH, Zhang GM, Hao TL et al (1994) Effect of diallyl trisulfide on the activation of T cell and macrophage-mediated cytotoxicity. J Tongji Med Univ 14:142–147

 Flores GA, Rodriguez VL, Licea QR, Guerra RC (2008) In vitro lymphocyte proliferation induced by Ocimumbasilicum, Perseaamericana, Plantago virginica and Rosa spp. extracts. J Med Plants Res 2(1):5–10

 Gautam MK, Goel RK (2014) Toxicological study of Ocimum sanctum Linn leaves: hematological, biochemical, and histopathological studies. J Toxicol 2014:135654

 Ghonime M, Eldomany R, Abdelaziz A, Soliman H (2011) Evaluation of immunomodulatory effect of three herbal plants growing in Egypt. Immunopharmacol Immunotoxicol 33:141–145

 Godse AS, Shejwal BR, Godse AA (2015) Effects of suryanamaskar on relaxation among college students with high stress in Pune, India. Int J Yoga 8(1):15–21

 Guleria R, Arora S, Mohan A et al (2015) Yoga as is effective as standard pulmonary rehabilitation in improving dyspnea, inflammatory markers, and quality of life in patients with COPD. Chest J 148(4):907A. https://doi.org/10.1378/chest.2266469

 Gupta A, Gupta R, Sood S et al (2014) Pranayam for treatment of chronic obstructive pulmonary disease: results from a randomized controlled trial. Integr Med (Encinitas) 13(1):26–31

 Hesam H, Qobi AAA, Seidavi A, Norris D (2014) Effects of different levels of coriander (Coriandrum sativum) seed powder and extract on serum biochemical parameters, microbiota, and immunity in broiler chick. Sci World J 2014:628979

 Hooda R, Hooda S, Sharma R (2017) Oil pulling: a wonderful ayurvedic Therapy. Int J Pharmacogn Chin Med 1(2):000112 https://ayush.gov.in

 Ingok AM, Guler FK (2017) Cardamom, cumin, and Dill weed essential oils: chemical compositions, antimicrobial activities, and mechanisms of action against Campylobacter spp. Molecules 22(7):1191

 Jeba RC, Vaidyanathan R, Rameshkumar G (2011) Immunomodulatory activity of aqueous and ethanolic leaves extracts of Ocimum sanctum in rat. Int J Pharm Biochem Res (IJPBR) 2(1):33–38

 Jia Xu, Yunfei Z (2020) Traditional Chinese Medicine treatment of COVID-19. Complement Ther Clin Pract 39:101165

 Jbabdi SH (2013) Definition of a Yoga breathing (Pranayama) protocol that improves lung function. Holist Nurs Pract 33(4):197–203

 Jarypoor M, Bayat M, Zuhair MH et al (2013) Evaluation of the number of CD4(+) CD25(+)/FoxP3(+) treg cells in normal mice exposed to AFB1 and treated with aged garlic extract. Cell J 15:37–44

 Lin A, Hye WL et al (2020) Herbal medicine and pattern identification for treating COVID-19: a rapid review of guidelines. Integr Med Res 9(2):100407. https://doi.org/10.1016/j.imr.2020.100407

 Liu K, Zhang W, Yang Y et al (2020) Respiratory rehabilitation in elderly patients with COVID-19: a randomized controlled study. Complement Ther Clin Pract 39:101166

 Madaan A, Satayajyoti Kanjilal AG et al (2015) Evaluation of immunomodulatory activity of Chyanwanshurax using in vitro assays. Indian J Exp Biol 53:158–163

 Mandal S, Mandal M (2015) Coriander (Coriandrum sativum L.) essential oil: chemistry and biological activity. Asian Pac J Trop Biomed 5(6):421–428

 Masoud ZS, Mohammad A, Leila E (2014) Biological activities of a new antimicrobial peptide from Coriandrum sativum. Int J Biosci 4(6):89–99

 Masram P, Chaudhary S, Patel KS (2014) A brief review on ayurvedic concept of immunity and immunization. Ayurpharm Int J Ayur Alli Sci 3:230–240

 Maurya VK, Kumar S, Prasad AK et al (2020) Structure-based drug design for potential antiviral activity of selected natural products from Ayurveda against SARS-CoV-2 spike glycoprotein and its cellular receptor. Virus Dis. https://doi.org/10.1007/s13337-020-00598-8

 McCall MC, Ward A, Roberts NW, Heneghan C (2013) Overview of systematic reviews: yoga as a therapeutic intervention for adults with acute and chronic health conditions. Evid Based Complement Altern Med 2013:945895. https://doi.org/10.1155/2013/945895

 Mediratta PK, Sharma KK, Singh S (2002) Evaluation of immunomodulatory potential of Ocimum sanctum seed oil and its possible mechanism of action. J Ethnopharmacol 80:15–20

 Mukherjee NJ, Dash PK, Ram GC (2005) Immunotherapeutic potential of ocimum sanctum (L.) in bovine subclinical mastitis. Res Vet Sci 79:37–43

 Mukherjee PK, Bahadur S, Harwansh RK et al (2017) Paradigm shift in natural product research: traditional medicine inspired approaches. Phytochem Rev 16:803–826

 Neelam LD, Nilofer SN (2010) Preliminary immunomodulatory activity of aqueous and ethanolic leaves extracts of Ocimum basilicum Linn in mice. Int J PharmTech Res 2(2):1342–1349

 Nonaka M, Yamashita K, Lizuka Y et al (1997) Effects of dietary sesaminol and sesamin on eicosanoid production and immunological function of mice. Jpn J Pharmacol 61:836–839

 Ornish D, Lin J, Daubennier J et al (2008) Increased telomerase activity and comprehensive lifestyle changes: a pilot study. Lancet Oncol 9(11):1048–1057

 Pandkar DP, Sachdeva V (2020) Pathophysiology of COVID-19 and host centric approach of Ayurveda. J Ayurveda Integr Med. https://doi.org/10.1016/j.jaim.2020.11.010

 Pan MH, Wu JH, Ho CT (2017) Effects of water extract of curcuma longa (L.) roots on immunity and telomerase function. J Compl Integr Med 2017:20150107
