

POST PANDEMIC ERA: THE RELEVANCE OF INDIAN TRADITIONAL SYSTEM OF MEDICINE AS A PROSPECTIVE ALTERNATIVE IN BUILDING THE IMMUNE SYSTEM

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Healing from infectious diseases requires strong immunity. So, an immunocompromised host is unable to respond to the infection. The World Health Organization recognizes the traditional and alternative medicine of proven quality and safety, for health care. The Indian Traditional Medicine System is a pathfinder for several natural sources, which protects us from illnesses and strengthens our immunity. Among several medicinal plants, we have discussed here the relevancy of Amlaki, Ashwagandha, Guduci, Haldi and Neem as immune boosting agent for post-COVID complications.

The recent pandemic Covid-19 has resulted in a deep crisis and challenge. The researchers and scientists around the globe are putting a tireless effort to defeat this biological menace. From microbiologists to chemists everyone is in search for a molecule which can destroy this virus invaded in human body. Across the world the efforts are going on to find or to synthesize a novel molecule which can arrest the propagation of this virus in our body.

Vaccination is the most practiced method of treatment of viral infections. Vaccination is a way of triggering the immune system which may be called as immunization. Therefore, direct triggering of the immune system is the main motto of vaccination. Hence, vaccination may be called as adaptive immunity towards a particular infection or infectious disease. In most viral infections, the immune

system has the opportunity of attacking viral particles in some stages of the infection. Immunity that is developed against virus infections is known as viral immunity. An immune response against virus appears first during the primary infection. In nutshell it could be stated that Cytotoxic T lymphocytes, natural killer (NK) cells and antiviral macrophages can recognize and kill virus-infected cells. Helper T cells can recognize virus-infected cells and produce a number of important cytokines. Therefore, immunity is the key factor to combat against viral invasion¹.

It is the antibody, an immunoglobulin protein generated by the immune system, arrests the replication or multiplication of virus nucleotide. It has been estimated that humans generate about 10 billion different antibodies, each capable of binding a distinct epitope of an antigen i.e. each antibody is unique in attaching a specific pathogen. Therefore, 10 billions of antibodies are capable of destroying innumerable different pathogens. A good immune system can produce a good numbers of several antibodies and *vice versa*. It means a strong immune system which is potent enough with large reservoir of antibodies is capable to combat several pathogens².

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The Indian Traditional System of Medicine (ITSM) has clearly shown the way for attainment of a strong immune system. Ayurveda has vividly mentioned the guidelines for acquiring a powerful immune system through food, medicines and life styles. Good food, potent medicines (here it is attributed to medicinal plants) and curbed life style are the ingredients of good health. Generation of antibodies is directed by the metabolic system, which in turn depends upon the food and nutrition, medicines and life style. Hence, the viral causes may be turned down by enhancing the potential of the immune system aided by the use of medicinal plants described in ITSM. These natural sources may boost up the immune system which definitely gives a good fight against this virus. The present review is aimed at discussing the relevancy of ITSM to minimize the infection due to SARS virus and to restrict the subsequent socio economic fall off.

Outbreak of Coronaviruses:

Let us have a brief glance on coronaviruses before discussing the main issue. Three new corona viruses which have emerged since the turn of the century have caused respiratory disease outbreaks (SARS-CoV-1 in 2003, MERS-CoV in 2012 and SARS-CoV-2 in 2019) belong to the RNA enveloped coronaviridae family. All these have a common mode of transmission through droplets produced by coughing, sneezing, talking and breathing. In humans they can cause mild infections in the upper respiratory tracts, like common cold but also more serious lower respiratory tract infection. These infections can be manifested as bronchitis, pneumonia or a severe respiratory illness, such as SARS, MERS or Covid-19 due to SARS-CoV, MERS-CoV or SARS-CoV-2 respectively³.

There are many similarities between severe acute respiratory syndrome (SARS) and coronavirus disease 2019 (COVID-19) from the virus homology to the origin and transmission routes. The progression for patients with severe disease follows a similar pattern in both viruses, with progression to acute respiratory distress syndrome approximately 8–20 days after onset of first symptoms, whereby the lung abnormalities on chest CT show greatest severity approximately 10 days after initial onset of symptom⁴⁻⁷. The similarities between SARS-CoV and SARS-CoV-2 are striking, not only in name. The whole genome of SARS-CoV-2 has a 86% similarity with SARS-CoV⁸. Both viruses share high degrees of homology to SARS-like coronaviruses isolated in bats, suggesting that bats are the probable origin of both SARS-CoV and SARS-CoV-2.

Few studies claim that after entering through mouth or nose, this virus resides at upper respiratory tract for 4–5 days, causing a superficial primary infection manifested by mild fever and cough. Real danger occurs when the virus rolls down to lower respiratory tract and reaches lungs. The angiotensin-converting enzyme 2 (ACE2), found in the lower respiratory tract of humans, has been identified as the receptor used for cell entry for both SARS-CoV and SARS-CoV-2^{9,10}.

Immunocompromising Situations:

Immunocompromised is a situation where a person is having an impaired immune system. Such situation may arise in a person mainly due to three reasons. Natural immune deficiency, acquired immune deficiency and person undergoing medications with immunosuppressive drugs. In the last case immunity is lowered deliberately for the sake of treatment of some particular diseases. Withdrawn of such medication brings back the body to its natural immunity profile. It means restoration is possible at any point of time. But in first two cases immunity strength is impaired or lost. Natural immune deficiency may be observed in persons of any age. People roughly above age 60 are expected to be immune deficient due to the natural degeneration. On the other hand children below 15 years are also immuno susceptible as their immune system is under development. Persons dwelling between these age groups are found to be normal, but may also be immune deficient due to their lifestyle, food habit and medications. Therefore, persons of any age may be the host of viral infections, considering aged persons and children as a soft target. Therefore, a mass population is under the surveillance of immunity issue to provide proper immunity. Hence, there is a huge scope to strengthen the immunity in those persons.

Indian Traditional System of Medicine and Immunity:

The Indian Traditional System of Medicines (ITSM) has several components and contributors, like, Ayurveda, Siddha, Unani and Folklore healer. Each of these avenues has inputs in healing, protecting and boosting of human health. Among all these Ayurveda is being considered as a frontline healing system. It is the indigenous system which contributes to the nation about 80%, which is far higher than the all other indigenous systems put together. This is because the abundance of Ayurvedic medicinal plants and knowledgeable Ayurvedic Physician across the country. By considering these aspects, we streamline our discussion in the realm of Ayurveda.

Vyadhikshamatva or immunity in Ayurveda is defined by different Ayurvedic scholars from different perspectives. It has been described in *Caraka Samhita* that certain factors are enhancing it which are *Janma-desh-characteristic* of the persons native land, *Suhkashcha kalayoga* or favourable climate, *Veeja Kshetra guna sampata* or inherent qualities, *Aahara samapata*, *Sharer sampata*, *Satmya sampata* or absence of hypersensitivity, *Satva sampata* or absence of mental stress, *Swabhava samsiddhi* or favourable disposition of the race and species, *Yauvanam* or youthfulness, *Karma* or proper exercise and *Saharsha* or cheerful disposition etc¹¹. In a nutshell, this is the capacity of the body to resist the disease. *Swabhava*, *Bala*, *Prakriti* are the terminologies homologous to *Vyadhikshamatva*, especially of *Sahaja* or innate variety¹². The other variety, *Yuktikrita Vyadhikshamatva* is the type which is to be acquired. Several factors like diet, climate, inherent qualities, are reported in Ayurveda, which are responsible to maintain *Vyadhikshamatva*. Time or season is also another important factor to control *Vyadhikshamatva*. Several drugs from plant origin, metal and mineral origin are described in Ayurveda which are *Rasayana* in nature and control *Vyadhikshamatva*. The pharmacological approach of *Rasayana* drugs broadly divided into two groups, viz., *Kama Rasayana* for improving health, vigour and vitality of healthy person and *Naimittika Rasayana* is specially indicated for patients suffering from particular disease to enhance their immunity¹³. According to Ayurveda, *Rasayanas* are powerful Ayurvedic herbs for immunity building, which strengthen, nourish and repair all the *Dhatus* of the body – the fundamental constituents involved in the healthy functioning and upkeep of the body. These *Rasayanas* can be applied to skin,

Table 1. Major Class of Phytocompounds in amlaki.

Class of Compounds	Major Compounds
Alkaloids	Phyllantine, Phyllembain, Phyllantidine
Polyphenol	Gallic acid, Chlorogenic acid, Ellagic acid, Chebulinic acid, Chebulagic acid, Corilagin
Flavonoids	Kaempferol-3-O- α -L-(600-methyl)-rhamnopyranoside, Kaempferol-3-O- α -L-(600-ethyl)-rhamnopyranoside, Myricetin, Quercetin
Tannins	Emblicanin-A, Emblicanin-B, Punigluconin, Pedunculagin
Amino acids	Glutamic acid, Proline, Aspartic acid, Alanine, and Lysine
Vitamins	Vitamin C as Ascorbagin

and taken through the diet, to improve immunity. Ayurveda suggests that strong immunity is the outcome of healthy digestion or a strong *Agni* (*Agni* or Fire is one of the five elements namely, Ether, Air, Fire, Water, and Earth) the digestive or metabolic fire. A good metabolism is the reservoirs of antibodies, the soldiers of body's defence system. Intake of immunity enhancing herbs is an important way to enhance the *Agni*¹⁴.

Ayurveda advocates the names of several plants as

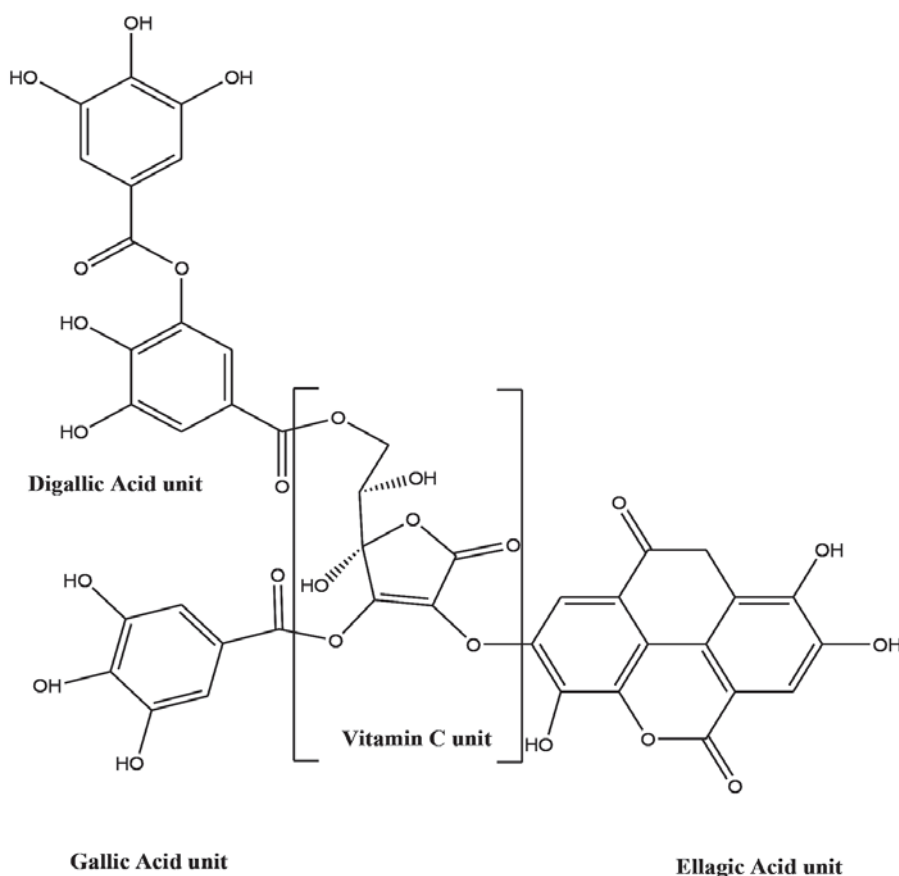


Fig. 1. Vitamin C in amlaki enveloped by different polyphenols

immune boosting herbs. The plants which are abundant across the subcontinent and one can avail these with no difficulties, are selected here for discussion. From a plethora of medicinal plant database of Ayurveda, only five plants have been chosen.

Amlaki: Amlaki or *Phyllanthus emblica* Gaertn. is also known as Indian gooseberry. The fruits find use in several Ayurvedic compound formulations and also used as a single plant drug. Several classes of compounds mentioned in Table 1 present in amlaki make it a highly potential. Being rich in polyphenols¹⁵, it is one of the best natural antioxidant which protect cells and cell components from undesired destruction. Most importantly, this fruit is a reservoir of vitamin C, which plays a paramount role in building a strong immune system and resists declination of immunity. It also contributes to immune defense by supporting various cellular functions of both the innate and adaptive immune system. Vitamin C supports epithelial barrier function against pathogens and promotes the oxidant scavenging activity of the skin, thereby potentially

protecting against environmental oxidative stress. The compound accumulates in phagocytic cells, such as neutrophils, and can enhance chemotaxis, phagocytosis, generation of reactive oxygen species, and ultimately microbial killing¹⁶. It is also needed for apoptosis and clearance of the spent neutrophils from sites of infection by macrophages, thereby decreasing necrosis/NETosis and potential tissue damage. The role of vitamin C in lymphocytes is less clear, but it has been shown to enhance differentiation and proliferation of B- and T-cells, likely due to its gene regulating effects¹⁷. The advantage of using this natural source of vitamin C over synthetic vitamin C tablet is its bioavailability. The Vitamin C molecule in amlaki fruit is enveloped with several polyphenols (Fig. 1) like ellagic acid, gallic acid, catechuic acid and therefore makes it highly bioavailable¹⁸. The matured fruits can be used like other fruits.

Ashwagandha: *Withania somnifera* (L.) Dunal is also known as Indian Ginseng. Plant roots are rich source¹⁹⁻²¹ of phytosterols, steroidal saponins, steroidal lactones like

withanolides, withaferin etc are summarized in Table 2. Alteration of T-cell functions and corresponding cytokines pattern by withanolides A is reported²² as an immunomodulatory model. A group of researchers²³ claimed that Ashwagandha administered with milk has an impact on cell activation of lymphocytes' components (Natural Killer cells, which are a major component of the immune system and best known for their ability to respond to virally-infected cells and tumors; B-cells, which make antibodies that bind to a virus or microorganism and then destroy it; CD4+ T cells (also known as helper cells), which coordinate the immune system's response; and CD8+ T cells, which kill cells that become infected). They found a statistical significance of overall increase in the level of white blood cell activation. Cell activation was most pronounced in the CD56+ Natural Killer cells. This is important, since these cells play a critical role in the body's response to flu, mumps, or tumors. Study²⁴ reports that water soluble

Table 2. Major Class of Phytochemicals in Ashwagandha

Class of Compounds	Major Compounds
Alkaloids	Ashwagandhine, Cuscohygrine, Anahygrine, Tropine, Anaferine (bis (2-piperidylmethyl) ketone) , Isopelletierine, Pseudotropine, 3 α -tigloyloxypine, 3- tropylogloate, dl-Isopelletierine, Hygrine, Mesoaniferine, Choline, Somniferine, Withanine, Withanamine; Hentriacontane, Visamine, Withasomnine, Pseudowithanine.
Glycosides	Withanoglycosides as Withanosides (I-VII),
Steroids	Withaferin A-J, Withanolides A-Y, Withasomniferin-A, Withasommidienone, Withasomniferols A-C, Withanone, Withanol, Withanolal, Sitoindosides (I-X),

Table 3. Major Class of Phytochemicals in Guduchi

Class of Compounds	Major Compounds
Alkaloids	Berberine, Palmatine, Tembetarine, Magnoflorine , Choline, Tinosporin, Isocolumbin, Palmatine, Tetrahydropalmatine.
Glycosides	Norclerodane glucoside, Tinocordiside, Tinocordifolioside, Cordioside, Cordifolioside, Cordifolioside, Syringin, Syringin-apiosylglycoside, Palmatosides, Palmatosides F , Cordifolioside A, Cordifolioside B, Cordifolioside C, Cordifolioside D, Cordifolioside E,
Terpenoids	Furanoid diterpene glucoside, Tinosporon, Tinosporides, Jateorine, Columbin, Tinocordifolin.
Steroids	β -sitosterol, δ -sitosterol, 20 β -hydroxy ecdysone, Ecdysterone, Makisterone A, Giloinsterol.
Others minor class	Octacosanol, Heptacosanol, Nonacosan-15-one, 3, (α ,4-di hydroxy-3-methoxy-benzyl)-4-(4-hydroxy-3-methoxy-benzyl)-tetrahydrofuran, Jatrorrhizine, Tinosporidine, Cordifol, Cordifellone, N-trans-feruloyl tyramine acetate, Giloin, Giloinin, Tinosporic acid.

extract of ashwagandha significantly increases the number of CD4+ T helper cells while both CD8+ T helper cells and B cells are also increased. Immunomodulatory evidences are reported in animal studies¹⁹.

Guduchi: *Tinospora cordifolia* (Willd.) Miers ex Hook. F & Thoms. is mentioned in Ayurveda as *Amrita* due to its several health benefit. An wide range of phytoconstituents, summarized in Table 3 are present^{25,26} in the stem. The water and ethanol extract of stem containing arabinosides inhibit immunosuppression produced by cyclophosphamide²⁷. Glycosides from stem show polyclonal mitogenic activity against B-cell²⁸. Fresh extract improves the phagocytic function without effecting the humoral or cell mediated immune system²⁹. Syringin and Cardinol two active principles possess anticcomplimentary and immunomodulatory activities. These compounds also give rise to significant increases in IgG antibodies in serum³⁰. In immunomodulation studies humoral immunity was enhanced as evidenced by haemagglutination titre³¹. Several studies claim that the water extract and or guduchi sarasa is found to be more potent than other extract.

Haldi: *Cucuma longa* (L.) plays an augustus role in building body's defense system through one of its active compounds³² curcumin. Major classes of compounds are listed in Table 4. Curcumin is a potent immunomodulatory agent that can modulate the activation of T cells, B cells, macrophages, neutrophils, natural killer cells, and dendritic cells. Curcumin can also downregulate the expression of various proinflammatory cytokines including TNF, IL-1, IL-2, IL-6, IL-8, IL-12, and chemokines, most likely through inactivation of the transcription factor NF-kappaB. Interestingly, however, curcumin at low doses can also enhance antibody responses³³. Immunomodulatory effects of curcumin on various facets of the immune response, including its effect on lymphoid cell

populations, antigen presentation, humoral and cell-mediated immunity, and cytokine production is reported by researchers³⁴. Effect of curcumin has been reported on mitogen/antigen induced proliferation of splenic lymphocytes, induction of cytotoxic T lymphocytes (CTLs), lymphokine activated killer (LAK) cells, and the production of cytokines by T lymphocytes and macrophages. Mitogen, interleukin-2 (IL-2) or alloantigen induced proliferation of splenic lymphocytes, and development of cytotoxic T lymphocytes is significantly suppressed by certain concentration of curcumin³⁵. Curcumin most likely inhibits cell proliferation, cell-mediated cytotoxicity (CMC), and cytokine production by inhibiting NF-kappaB target genes involved in induction of these immune responses³⁶. While talking about curcumin and SARS, the efficacy of curcumin to inhibit the influenza causing virus is a proven fact³⁷.

Table 4. Major Class of Phytocompounds in Haldi

Class of Compounds	Major Compounds
Cucuminoids (diphenyl heptanoids)	Curcumin, Demethoxycurcumin, Bisdemethoxycurcumin, Dihydrocurcumin, Diferuloylmethane, Feruloyl-p-coumaroylmethane, Di-p-coumaroylmethane, Dehydrocuridone, Germacrone, Cyclocurcumene.
Terpenoids	Alpha-phellandrene, 1,8-Cineole, Alpha-Terepnine, Alpha-Turmerone, Beta-Turmerone,, Alpha-Pinene, Gamma-Terpinene, Para-Cymene, Alpha-Terpenolene,
Steroids	Bisbolene, Bisacumul, , Curcumene, Curnole
Alkaloids	Guaiacol, Zingerone, Styrenes, methyl-3-methoxy-4-hydroxystyryl ketone, Bisacurone A, Bisacurone B, Bisacurone C, Turmeronol.
Others minor class	Turmerin, Cucumenone, Curcumenol, Isoprocucumenol, Procucumenol, Epiprocucumenol, Zedoaronediol,

Table 5. Major Class of Phytocompounds in Neem

Class of Compounds	Major Compounds
Terpenoids	Azadirachtolide, Azadirachtanin, Nimbocinone, Meliantriol, Nimocinolide, Isonimocinolide, Isonimbocinolide, Nimbin, Nimbinene, Nimbolide, Nimbandiol, Nimbocinolide, Nimocinol, Isomeldenin, Gedunin, Vilasinin, Morgosone, Morgosolone, Morgolone, Morgolonone
Flavonoids	Quercetin, Isorhamnetin, Nimbaflavone, Rutin
Flavonoglycosides	Myrcetin-3'-larabinoside
Tannins	Gallic acid, (+)-Gallocatechin, (-)-Epicatechin, (+)-Catechin, Epigallocatechin
Coumarins	Scopoletin
Hydrocarbons	Octadecane, Nonadecane, Hexacosane, Nonacosane, Tetratriacontane, n-Hexacosanol, β -Carotene, Xanthophyll.
Sulfur compound	Cyclic trisulfide, Cyclic tetrasulfide
Carbohydrates	Polysachcharides GIa, GIb, Polysaccharides GIIa, GIIIA

Neem: Binomially this plant is known as *Azadirachta indica* (L.). Every part of this plant is found to be a potential immunoboster and immunomodulator. Bark and leaves of this plant are found to possess immense medicinal and therapeutic values attributed by phytochemicals³⁸ present in it. A brief list of classes of phytoconstituents is represented in Table 5. Flow cytometric analysis study^{39,40} of lymphocyte subpopulations documented increased counts of CD-4 and CD-8 cells and an increased activation marker expression on lymphocytes (CD-25) and monocytes (MAC-3) in neem-treated mice compared to the control animals. Application of neem leaf extract and determination of peripheral blood cells revealed significant up-regulations of leukocyte subsets, the lymphocytes and monocytes. Supplementation of neem leaf diet significantly increased phagocytic activity, superoxide anion production, serum lysozyme, serum bactericidal activity, serum anti-protease activity⁴¹. Biomedical research⁴² has revealed that neem is antagonistic to human immune deficiency disease through phagocytic activity and antigen presenting limit with macrophages. It vivifies IL-I, TNF- α , IFN- γ reflecting start of Th1 sort of response. Very recent experiment⁴³ revealed that the methanol extract of Neem Bark divulged potent anti-viral activity against Mouse hepatitis virus (MHV) by retarding cell-to-cell fusion, viral spread, viral replication by targeting direct binding to Spike protein. Thus it has been suggested that the Neem bark extract might be effective against the Spike expressing human coronaviruses like SARS, SARS-CoV-2, OC43.

Community Immunity and its Significance

It is well known to us that the pandemic due to Covid-19 was fought by lockdown or social distancing. It was the most observed way of prevention of spreading of corona virus. State declared lockdown and that was to be obeyed by all classes of people to avoid public aggregation. There was no doubt that this strategy was efficient for a densely populated country like India. Countries which followed this protocol had lower infection rate and mortality.

Now the most important question rises as to whether it is possible for any country to continue lockdown for a prolonged period? The answer is in the negative for a country like India where most of the earners are engaged in unorganised sector and depend upon daily wages. A prolonged lockdown will definitely pull down the financial situation of the poorer sector which contributes 55-60% of the Indian population. Elongation of lockdown period invites a big fall in nation's economy and a huge drop in

socioeconomic index. The worst scenario would be jeopardised law & order and rise in crime.

An alternative solution can be adopted in the country for combating the pandemic. The idea of community immunity is an important solution where country needs to cater immunisation programs aggressively among the community simultaneously with running the lockdown. For corona virus till date there is no proven vaccine for immunisation. Hence, the only solution is community immunisation through the use of indigenous medicinal plants. Exploitation of these indigenous immune boosting sources may develop herd immunity. When sufficient portion of community get immunised, the pathogens would hardly find a weak or new host and thereby stops spreading. Lockdown and community immunisation would be able to arrest the spreads and shorten the period of lockdown. With this expectation herd immunity may be the prime target at this point.

The herd immunity strategy, which would allow a majority of the population to gain resistance to the virus by becoming infected and then recovering, could result in less economic devastation and human suffering than restrictive lockdowns designed to stop the spread of the virus. Nation may be able to reach a point of herd immunity without infection. When herd immunity reaches a sufficient number the outbreak will stop, and the elderly are also safe. Cultivating herd immunity may be the best of various options.

Policy of Rationing Immunisation through Indigenous System and Resources

The rationing system is a process in which the government through the public distribution system (PDS) distributes various resources like food and medicines. Health care rationing may be adopted in this situation where government will distribute immune boosting items to achieve herd immunity. A policy may be framed and adopted in this regard. This mass rationing system not only creates awareness and belief on indigenous therapy but also make a nation stronger and healthier.

Conclusion

Prevention is better than cure, this words again becomes relevant in this context. We must boost up the defense system of our body through our food and medications. A strong immune system can give a better fight against pathogens. When community gains power to fight the pandemic, it can stop this to be a pandemic. Adaptation of new policies may make a Nation strong,

proud and developed. Lastly, it may be concluded this discussion is that, boosting immunity through indigenous system is a way out to give a better fight against any viral outbreak. This scenario gave us a retrospective look to the potency of Indian traditional system of medicines. □

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