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A PILOT, PROSPECTIVE, INTERVENTIONAL STUDY ASSESSING SAFETY AND EFFICACY OF HFIM – 01 IN IMPROVING RESPIRATORY IMMUNITY

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ABSTRACT

The coronavirus disease 19 (COVID-19) pandemic is unique and unprecedented in several aspects. It has challenged health care systems globally. The coronavirus pandemic has turned the world's attention to the immune system, the body's defense force against disease-causing bacteria, viruses and other organisms. It is very important to renovate the Ayurveda concept of improving respiratory immunity through a well-developed and standardized product with unique set of ingredients to get incorporated in the lifestyle of an individual. Siddhayu Ayurvedic Research Fdn. Pvt. Ltd. has developed HFIM – 01 decoction. Bitter herbs, such as Woodfordia flower nectar, and Munakka raisins are slowly fermented over 6-weeks to make a therapeutic and subtly sweetened blend formulated which is a potential component of HFIM-01. The aim of present research was to evaluate the safety and efficacy of HFIM – 01 for improving immunity in healthy subjects. The formulation treatment for 30 days to healthy individuals provided improvement in B cell mediated (Humoral immunity) mediated IgG levels and T cell mediated (Acquired immunity) CD4 count. This in turn suggest overall immuno modulation to combat with different stressors, infections of viral and bacterial origin. There is improvement in general health and wellbeing after HFIM-01 treatment indicated by improved GHQ-28 score and reduced fatigue severity score. HFIM-01 can be considered as safe and effective in managing general wellbeing, immunity and gut health.

KEYWORDS: Immunity, Covid 19, Ayurveda.

INTRODUCTION

The coronavirus disease 19 (COVID-19) pandemic is unique and unprecedented in several aspects. It has challenged health care systems globally. The coronavirus pandemic has turned the world's attention to the immune system, the body's defense force against disease-causing bacteria, viruses and other organisms.[1] Alongside the antivirals and vaccines against Covid 19, it will remain fact that we will have to modulate host's fundamental physiological and immunological processes for sailing through Covid 19 as well as other infections.[2]

The COVID-19 has put tremendous psychological distress and significant impact on mental health. Distress with risk of viral respiratory tract infections further potentiate immune dysfunctioning.[3] The clinical manifestation of any infectious disease depend on immune system response against infection. The immune system is the multi-level defense against infections including bacterial, viral and fungal origin. It is well documented research that psychosocial factors play their role in increasing susceptibility to viral respiratory tract infection.[4]

As a result, it is essential to look at respiratory immunity and ways to strengthen the same irrespective of Covid 19. As per classic Ayurveda text Charaka Samhita, immunity is the ability to prevent and arrest the progression of disease for maintaining homeostasis. The Ayurveda accentuates on building strength of mind and body to cope with various stressors, including infection. Ayurveda suggests many herbs and formulations to be used to improve immunity against respiratory illnesses, e.g. immunomodulator (known as Rasayana).[5]

It is very important to renovate the Ayurveda concept of improving respiratory immunity through a well-developed and standardized product with unique set of ingredients to get incorporated in the lifestyle of an individual.

Siddhayu Ayurvedic Research Fdn. Pvt. Ltd. has developed HFIM – 01 decoction. The product HFIM-01 possess specialized ingredients which can modulate the respiratory immunity. Bitter herbs, such as Woodfordia flower nectar, and Munakka raisins are slowly fermented over 6-weeks to make a therapeutic and subtly sweetened

blend formulated which is a potential component of HFIM-01.

The aim of present research was to evaluate the safety and efficacy of HFIM – 01 for improving immunity in healthy subjects.

MATERIALS AND METHODS

Intervention details

The HFIM – 01 is an Ayurvedic formulation with potential ingredients which can modulate the respiratory immunity. Key ingredients of formulation are.

Table 1: Key ingredients of HFIM – 01.

Common name	Botanical name	Common name	Botanical name
Giloy	*Tinospora cordifolia*	Ginger	*Zingiber officinale*
Ashwagandha	*Withania somnifera*	Black pepper	*Piper nigrum*
Vasa/Adulsa	*Adhatoda vasica*	Long pepper	*Piper longum*
Turmeric	*Curcuma longa*	Cinnamon	*Cinnamomum zeylanicum*
Liquorice	*Glycirrhiza glabra*	Cardamom	*Elettaria cardomomum*
Safed musali	*Asperagus racemosus*	Tejpatra	*Cinnamomum tamala*
Vidarikand	*Pueraria tuberosa*	Ativisa	*Aconitum heterophyllum*
Anantmool	*Hemidesmus indicus*	Pittapapada	*Fumaria indica*
Munakka raisin	*Vitis vinifera*	Nagkeshar	*Mesua ferrea*
Dhaiphool	*Woodfordia fruticosa*	Elixir base in Jaggery	

TREATMENT SCHEDULE

All subjects received treatment in the dose of 10 ml of HFIM-01 twice a day daily for 30 days.

METHODOLOGY

The study was sponsored by Siddhayu Ayurvedic Research Fdn. Pvt. Ltd. and the proposal was applied to Institutional ethics committee for review and approval. After approval from institutional EC clinical study was registered on CTRI website and study was conducted at Jyoti Clinic and Research Centre, Pune.

Male and female subjects of age between 18 to 60 years (both inclusive) attending study site(s) were screened for eligibility criteria. On screening visit, a written informed consent was obtained from subjects for their participation in the study. Subject's demographic details were recorded. Subject clinical examination was performed. Subject's medical, surgical and treatment history was recorded. Subject's current medication if any was noted in the case record from (CRF). Subject's vitals were recorded. The subject were considered for further evaluation as per the inclusion and exclusion criteria. Blood samples of all subjects were taken to perform biochemical and hematological tests. The subjective questionnaire score were recorded.

On baseline visit i.e. Day 0, subject fitting in all inclusion criteria and showing absence of all exclusion criteria were randomized. Subjects consumed HFIM-01, 10 ml twice a day for 30 days. The record of concomitant medication was kept in the CRF. All subjects were advised to follow their diet routine as per designed by study center dietician during the entire study period. The presence of any adverse event were strictly monitored and reported. The treatment was followed on subsequent days till day 30. On day 15 the questionnaire, symptom grading and adverse events were checked on telephonic call and day 30 was the physical visit and blood samples were collected for hematological tests and assessment of other scales, scores etc. were performed.

RESULTS AND OBSERVATIONS

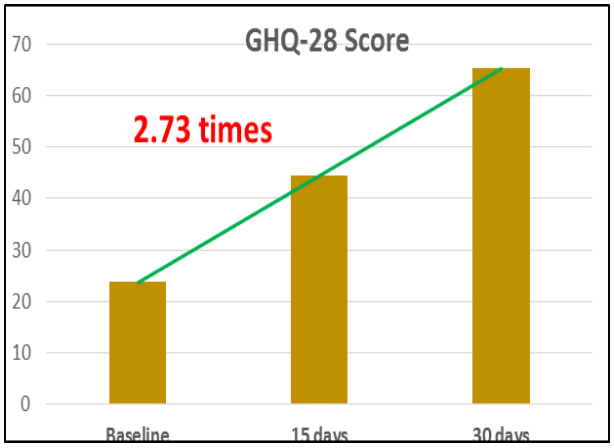
DEMOGRAPHIC DETAILS

In the present study, 33 subjects were screened. Out of 33 subjects, 2 lost to follow up and 1 was screen failure. 30 subjects were considered evaluable cases at the end of the study. The mean age of subjects was 34.8± 5.88 years. There were 15 male and 15 female subjects.

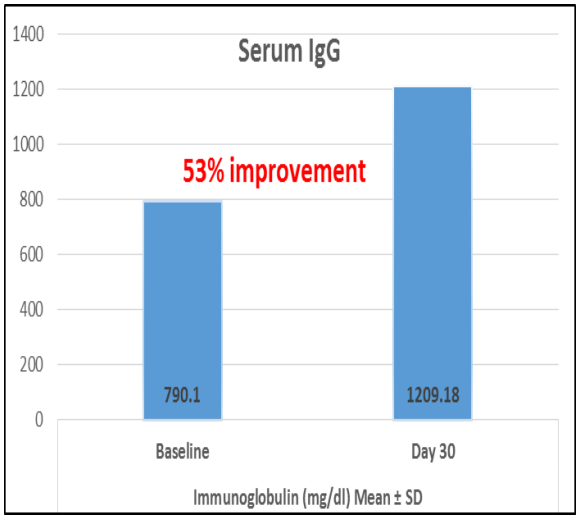
EFFICACY ASSESSMENTS

Assessment of General Heath Questionnaire-28 (GHQ-28) Score

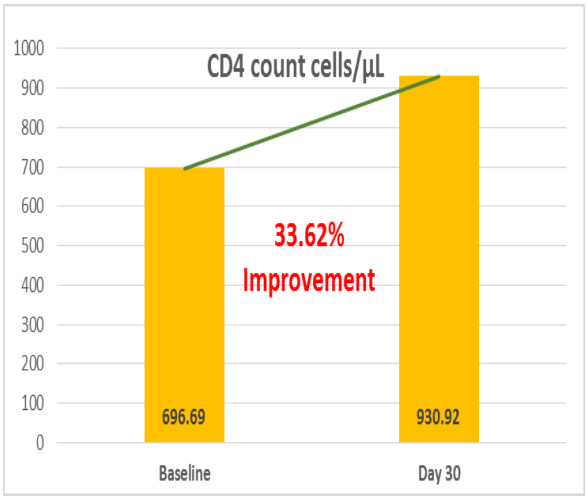
There was significant increase GHQ-28 score in HFIM-01 treated group. After 15 days there was 86.38% and on 30 days around 2.73 times increase in GHQ-28 score in improving Quality of Life.



Graph 1: Assessment of General Heath Questionnaire-28 (GHQ-28) Score between the groups.



Graph 2: Assessment of serum immunoglobulin.



Graph 3: Assessment of CD3, CD4 and CD8 cells.

Assessment of CD3, CD4 and CD8 cells

In the present study, there was significant ($p<0.05$) increase in CD4 counts at day 30. There was increase in CD3 and CD8 counts but was not statistically significant.

Assessment of Digestive Behaviour Score

There was significant reduction in digestive complaints after incorporating HFIM-01 treatment to the subjects. The % reduction is expressed in the table 2.

Table 2: Assessment of Digestive Behaviour Score Mean between the groups.

Parameters	Mean Score ± SD		% reduction
	Baseline	Day 30	
Heartburn	6.10±0.76	3.40±0.29*	44.26
Regurgitation	5.29±0.38	4.26±0.93	19.47
Flatulence	5.11±0.57	2.49±0.20*	51.27
Bloating	8.48±0.98	5.98±0.48*	29.48
Constipation	4.11±0.96	3.53±0.79*	14.11
Loss of Appetite	6.47±0.39	5.29±0.48*	18.24
Post Prandial Fullness	7.88±0.51	6.18±0.74*	21.57

By Student 't' Test, P > 0.05 Not Significant, Significant p< 0.05

Assessment of fatigue by fatigue severity score

There was significant reduction in fatigue severity score after 30 days treatment of HFIM-01.

Table 3: Assessment of fatigue by fatigue severity score.

	Fatigue severity score (Score ± SD)			
	Baseline	Day 30	% decrease	P value
FSS score	48.30 ± 8.34	27.28 ± 9.38	43.51	P<0.05

By Student't' Test, P > 0.05 Not Significant, Significant p< 0.05

Changes in Mean parameters of Complete Hemogram

All the parameters in the complete Hemogram were within normal range. Parameters of complete hemogram were comparable at baseline and at day 30, mean value of parameters of complete hemogram did not show any significant change from baseline and the difference was statistically insignificant.

Table 4: Changes in Mean parameters of Complete Hemogram between the groups.

Parameters	Mean ± SD	
	Baseline	Day 30
Total Leukocyte Count	6273±1980.2	8530.00±2177.34
Neutrophils	66.77 ± 14.16	60.37 ± 9.96
Lymphocytes	24.37 ± 12.19	28.30 ± 8.38
Monocytes	7.40 ± 2.75	8.37 ± 1.99
Eosinophil	1.47 ± 2.27	2.97 ± 2.92
Basophils	0.0 ± 0.0	0.0 ± 0.0
Total RBC Count	4.52 ± 0.51	4.66 ± 0.50
Hemoglobin	12.58 ± 1.72	12.95 ± 1.93
Platelets	279966 ±75360	405500 ±139471

By Student't' Test, P > 0.05 Not Significant

Changes in number of episodes, severity and duration of illness during the study period

There were no subjects reported any episodes of illness, infections etc. in the study population with no events of cough, breathlessness and fever etc.

DISCUSSION

The GHQ-28 requests participants to indicate how their health in general has been over the past few weeks, using behavioral items with a 4-point scale indicating the following frequencies of experience: "not at all", "no more than usual", "rather more than usual" and "much more than usual". The scoring system applied in this study was the same as the original scoring system.[6] In the present study, treatment with HFIM-01 for 30 days led to improvement in general wellbeing index as GHQ-28 score. The general fatigue is one of the important confounder in rating general wellness. In present study, the fatigue severity score is reduced significantly to 43.51% indicating reduced fatigue and improved psycho-physical state.

One of the primary functions of B cells in adaptive immunity is that of effecting a humoral response through the secretion of specific antibodies to combat with infection or foreign antigen. IgG is the most common class of immunoglobulin. It is present in the largest amounts in blood and tissue fluids. IgM is the first class of immunoglobulin made by B cells as they mature, and it is the form most commonly present as the antigen receptor on the B-cell surface.[7] In the present study, HFIM-01 is improving IgG count by 53% and IgM levels by 18%, this can be inferred from the results that HFIM-01 can trigger humoral immune response and help in improving immunoglobulin levels in healthy individuals.

It is now evident that the gut micro biota has a profound effect on the host immune system and that contributes to the response of immune system to infections. The gut micro biota plays an important role in the development of CD4+ T cells, both within and outside the intestine. Intestinal functionality is deeply involved in release of some of the cytokines crucial to modulate the immunity like IL, TNF etc. The gut health needs to be overly emphasized for general wellness and immunity.[8] Probiotics have been shown to promote the production of natural antibodies in the body. They may also boost immune cells like the IgA-producing cells, T lymphocytes and natural killer cells.[9] Functional gastrointestinal disorders, FGIDs, is a collective term for chronic disorders in the gastrointestinal tract, with range of symptoms. It is observed that global prevalence of FGID is 40% ie around 40% population experience one or other kind of GI symptoms.[10] This fact in turn provides us great insight of how GI symptoms can be linked with the compromised immunity and vice versa how improvement in the GI symptoms can improve micro biota which can then regulate immune homeostasis through gut. In the present study we had taken record of GI symptoms of patients on 0-10 VAS. The symptoms included, postprandial fullness, bloating, hyperacidity, flatulence, loss of appetite and constipation. It was observed that in 30 day treatment with HFIM-01, there was much reduction in these symptoms for all subjects. It can be concluded from these results that HFIM_01 through improving gut health can also contribute to immunity modulation.

A T cell is a type of lymphocyte which are one of the important white blood cells of the immune system and play a central role in the adaptive immune response. A different population of T cells, the CD4+ T cells, function as "helper cells" and CD8+ killer T cells, these CD4+ helper T cells function by indirectly killing cells identified as foreign: they determine if and how other parts of the immune system respond to a specific, perceived threat. Helper T cells also use cytokine signaling to influence regulatory B cells directly, and other cell populations indirectly. CD4+ T cells are essential in the formation of protective memory CD8+ T cells following infection or immunization.[11] In the present study, the results show that there is increase in CD3 and CD8 cells post treatment of HFIM-01 for 30 days but in case of CD4 cells there is significant increase from baseline to day 30. This indicated that the CD4/CD8 is improved and which is beneficial to develop the acquired immunity for an individual. Low levels of CD4 and CD8 were also recorded in severe Covid 19 disease[12], it can be linked from this fact that the improvement in CD4 count provides individual's

immunity an edge to combat with the stressors an infections.

No significant post treatment change in any of the hematological investigations was observed in subjects. There were no episodes of illness during the study period to any subjects. There was no abnormality in pulse rate; blood pressure was observed after treatment of HFIM-01. There were no possibly related adverse events due to HFIM-01. The present research confirms safety and efficacy of the treatment of HFIM-01 in improving immunity in healthy adults. However, large scale multi-centric study with larger sample size is warranted.

CONCLUSION

Improving immunity has become basis of health and emphasized more in the era of Covid 19 pandemic. HFIM-01 is carefully formulated Ayurveda preparation which imparts unique concept of bitters fermented to develop a potent sweet component which can potentiate whole formulation. The formulation treatment for 30 days to healthy individuals provided improvement in B cell mediated (Humoral immunity) mediated IgG levels and T cell mediated (Acquired immunity) CD4 count. This in turn suggest overall immuno modulation to combat with different stressors, infections of viral and bacterial origin. As a result of unique manufacturing and selection of ingredients; it is observed that formulation HFIM-01 provides digestive abilities. In the present study all the subjects expressed improvement in gastro intestinal symptoms. The HFIM-01 has beneficial effects in improving gut health which in turn would help develop an immunity homeostasis. There is improvement in general health and wellbeing after HFIM-01 treatment indicated by improved GHQ-28 score and reduced fatigue severity score. HFIM-01 can be considered as safe and effective in managing general wellbeing, immunity and gut health.

REFERENCES

1. Cain, P., 2020. How does your immune system work? World Econ. Forum (accessed on 25th April, 2020). https://www.weforum.org/agenda/2020/04/immune-systemfight-off-disease-coronavirus-covid19-pandemic/.
2. Tay, M.Z., Poh, C.M., Rénia, L., MacAry, P.A., Ng, L.F.P., 2020. The trinity of COVID-19: immunity, inflammation and intervention [published online ahead of print, 2020 Apr 28]. Nat. Rev. Immunol. https://doi.org/10.1038/s41577-020-0311-8.
3. Rajkumar, R.P., 2020a. Ayurveda and COVID-19: Where psychoneuroimmunology and the meaning response meet [published online ahead of print, 2020 Apr 22]. Brain Behav Immun S0889-1591(20)30637-1.
4. Zawada, K., Bratek, A., Krysta, K., 2015. Psychological distress and social factors in patients with asthma and chronic obstructive lung disease. Psychiatr. Danub, 27(Suppl. 1): S462–S464.
5. Acharya, Y. (Ed.), 1992. Charaka Samhita. Chaukhamba Surbharati, Varanasi, India Google Scholar.
6. Goldberg DP, Hillier VF. A scaled version of the general health questionnaire. Psychol Med, 1979; 9(1): 139–145. doi: 10.1017/S0033291700021644.
7. Brian R. Murphy, Chapter 43 - Mucosal Immunity to Viruses, Editor(s): Jiri Mestecky, Michael E. Lamm, Jerry R. McGhee, John Bienenstock, Lloyd Mayer, Warren Strober, Mucosal Immunology (Third Edition), Academic Press, 2005; 799-813.
8. Wu HJ, Wu E. The role of gut microbiota in immune homeostasis and autoimmunity. Gut Microbes, 2012 Jan-Feb; 3(1): 4-14. doi: 10.4161/gmic.19320. Epub 2012 Jan 1. PMID: 22356853; PMCID: PMC3337124.
9. Reid G, Jass J, Sebulsky MT, McCormick JK. Potential uses of probiotics in clinical practice. Clin Microbiol Rev, 2003 Oct; 16(4): 658-72. doi: 10.1128/CMR.16.4.658-672.2003. PMID: 14557292; PMCID: PMC207122.
10. Sperber, A.D., et al. (2020) Worldwide Prevalence and Burden of Functional Gastrointestinal Disorders, Results of Rome Foundation Global Study. Gastroenterology. doi.org/10.1053/j.gastro.2020.04.014.
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