

**EVALUATION OF EFFECTS OF SWAMALA (FORTIFIED *CHYAWANPRASH*) ON IMMUNITY AND QUALITY OF LIFE IN HEALTHY HUMAN VOLUNTEERS: AN OPEN LABELLED, RANDOMIZED, CONTROLLED EXPLORATORY STUDY.**

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**Abstract**

**Background:** The immune system defends against invading pathogenic microorganisms and cancer. Ayurved interventions can restore immune functions. Swamala is an ayurvedic formulation containing *Chyawanprash* fortified with processed gold, silver, mica, coral, iron, etc. The study was planned to assess the effect of Swamala on immune functions and Quality of Life in healthy volunteers.

**Methods:** A prospective, randomized, open-label, parallel arm, single-centre exploratory clinical study was conducted involving thirty-two healthy volunteers. They were randomly assigned to the Swamala Group (n=21) or Control Group (n=11) after conducting haematological, biochemical, X-ray, ECG, urine routine & immunological (IgG, TNF- $\alpha$ , CD4 cell count, anti-COVID antibody) investigations along with Quality of Life (QoL) assessment. Participants in the Swamala group were instructed to consume two teaspoonfuls (10 grams) of Swamala twice daily for 90 days. Control group participants did not receive any treatment. Weekly follow-up was done by means of telephonic interviews, and blood investigations were repeated after 45 & 90 days.

**Results:** Swamala group showed significant improvement in CD4 cell count, neutrophils, platelets & quality of life scores, and significant reduction in TNF- $\alpha$  levels & eosinophil counts during the subsequent follow-up visits (p<0.05). Incidence of general illness (80% vs. 35%),

and absenteeism (30 % vs. 0) were higher in the control group during the treatment period. The control group showed significant decrease in IgG levels and an increase in CRP levels during follow-up ( $p < 0.05$ ); no such variations were observed in the Swamala group. However, all the changes observed were within the physiological range. Swamala was found to be well-tolerated and safe.

**Conclusion:** The current exploratory pilot study findings suggest that Swamala possesses potential immunostimulant and anti-inflammatory properties.

**Keywords:** *Chyawanprash*, *Suvarna bhasma*, COVID-19, Immunostimulant, Anti-inflammatory agent

## Introduction

A well-functioning immune system is essential for protection from a variety of infections. Studies have revealed that immune cells decline steadily as age advances. Age-related changes influence the host immune response as people get older, which weakens the ability to fight infections and mount efficient immunological responses to vaccinations.<sup>1,2</sup> Declining immunity is associated with several diseases, including HIV, Tuberculosis, respiratory tract infections, cancer, etc. The COVID-19 pandemic has revealed a striking demographic bias in the number of cases and deaths, with the elderly population being the most severely affected. Besides genetics and underlying comorbidities, aging causes numerous physiologic changes within the immune system broadly categorized into Immunosenescence and inflamm-aging. They cause a progressive decline in the ability to fight latent and novel infections like COVID-19 and determine the disease course and clinical outcomes.<sup>3</sup> Interventions that can combat immunosenescence by restoring cellular immune function are highly desired. Previous research has shown that dietary supplementation with micronutrients enhanced some aspects of cellular immunity.<sup>2</sup>

*Chyawanprash*, referred to as a Rasayana (rejuvenating tonic), is a classical product containing time-tested ayurvedic ingredients. It is effective as an immunity booster and vitalizer, which also helps to prevent common infections and allergies such as common cold, cough, etc.<sup>4</sup> Authoritative texts recognized by the Drugs and Cosmetics Act of India, describe *Chyawanprash* as an immunity enhancer, and tonic meant for improving lung functions in diseases with compromised immunity.<sup>5</sup> Swamala is a *Chyawanprash* fortified with other ingredients like processed gold, silver, mica, coral, iron, etc. Swamala has been widely used by Ayurved practitioners across India for many decades to support health and immunity, especially in the geriatric population. *Suvarna Bhasma* (Processed Gold) possesses anti-stress/anxiolytic effect and has proven safety.<sup>6</sup> Other ingredients like *Rajata Bhasma* (Processed Silver), *Abhraka Bhasma* (Processed Mica), *Pravala Pishti* (Processed Coral), *Kantalooha Bhasma* (Processed Iron) and *Poornachandrodaya Makardhwaja* possess rejuvenating effects.

The documented clinical studies from electronic databases and Ayurved scriptures reported that individuals consuming *Chyawanprash* regularly showed improvement in immunity and overall health.<sup>5</sup> *Chyawanprash* has been reported to enhance immune function and significantly decrease the number of episodes of general illness and allergic illnesses in children.<sup>7</sup> However, it was found that no such study has been conducted in healthy adults to prove its effect on immunogenicity using immune markers and Quality of Life (QoL) so far. Hence, this pilot

study was planned to assess the effect of Swamala consumption on immune functions and QoL in healthy human volunteers.

#### METHODS:

The study was a prospective, randomized, controlled, open-label, parallel arm, single-center exploratory clinical study. It was carried out at the special OPD for Clinical Trials, D.Y. Patil Deemed to be University, School of Ayurveda, Nerul after Institutional Ethics Committee (IEC) approval & CTRI registration (CTRI/2021/05/033767). The total duration of the study was 14 months (August 2021- November 2022).

The participants were screened in accordance with the inclusion and exclusion criteria. Those who voluntarily agreed to participate and give written informed consent were included in the study. A detailed medical history, drug use (including nutritional supplements, ayurvedic/ herbal remedies, Immunoglobulin) or blood product/s infusion, alcohol/ substance use, occupation & pregnancy (in females) was obtained. Physical examination (temperature, pulse, respiratory rate, BP & SpO<sub>2</sub>), & systemic examination were done. Enquiry about COVID-19 symptoms/testing positive was done by the investigator. All participants had received two doses of vaccine for COVID-19.

Baseline investigations like CBC, Hb, ESR, LFT (Aspartate Transaminase and Alanine Transaminase), RFT (Blood Urea Nitrogen and Creatinine), C-reactive protein & urine routine were done along with X-ray & ECG. Participants with abnormal findings were excluded from the trial. Additional assessments of immunological markers (IgG, TNF-  $\alpha$ , CD4 cell count & COVID-19 antibody) and Quality of Life (QoL) were done for the enrolled participants.

The study medication, Swamala, was provided by Shree Dhootapapeshwar Limited, it was manufactured according to GMP standards. The composition of Swamala (Quantity/10 g) is as follows: *Chyawanprash (Ashtavarga)* 9.959 g, *Suvarna Bhasma* (Processed Gold) 1 mg, *Rajata Bhasma* (Processed Silver) 1 mg, *Abhraka Bhasma* (Processed Mica) 5 mg, *Pravala Pishti* (Processed Coral) 10 mg, *Kantaloha Bhasma* (Processed Iron) 10 mg, *Poornachandrodaya Makardhwaja* 14 mg. The certificate of analysis for the batch used in the study was obtained.

It was an exploratory study, so no formal sample size calculation was done. The participants were randomly allocated into Swamala or control groups in a 2:1 ratio using a computer-generated random code system. All information recorded by the investigator was entered in the case record form (CRF).

Swamala Group participants (n=21) were advised to consume Swamala in a dose of 10 g (2 teaspoons) twice a day (before breakfast and before dinner) with sufficient water for 90 days. Control Group (n=11) participants did not receive any medication.

The follow ups were taken on 45<sup>th</sup> day & 90<sup>th</sup> day, during which immunological parameters and QoL were assessed. All baseline investigations were repeated on the last day. Furthermore, telephonic follow-ups were done weekly, and compliance & inter-current illnesses were noted. **Figure 1** depicts details of participant recruitment, visits & investigations in the form of flowchart.

Graph Pad (Version 3.06) was used to analyse the data and it was presented as percentages and Mean  $\pm$  SD. An unpaired t-test & Mann Whitney test were used to compare the data between the two groups. The paired t-test and repeated measures ANOVA were used to compare data within the groups. The significance threshold was set at 0.05. To avoid bias, the data analyst was kept blinded to treatment allocations.

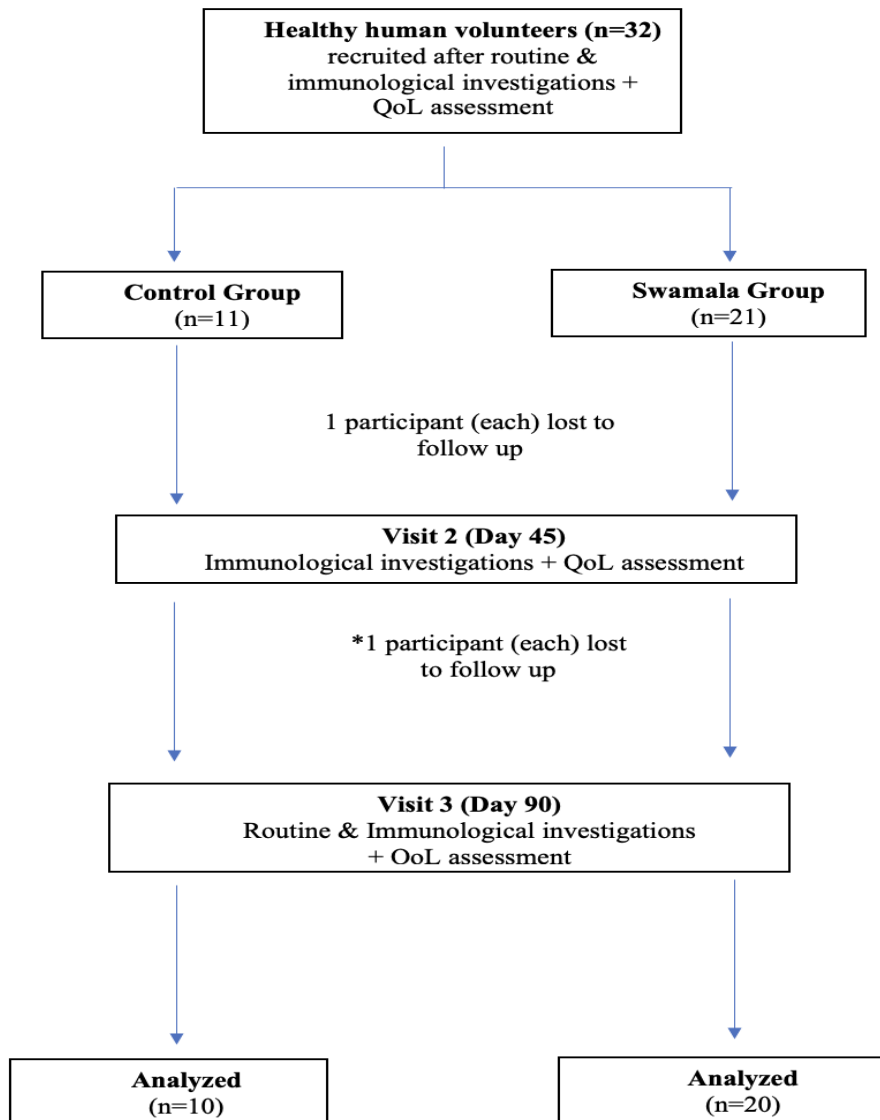


Figure 1: CONSORT Flow Chart

\* Last observations of 2 participants who lost to follow-up after completing the second visit were carried forward. Hence, the final analysis was done for 10 & 20 participants for the control & Swamala group, respectively

**RESULTS:**

Thirty-two healthy participants were recruited in this study. Of these, 21 participants were randomly assigned to the Swamala Group and 11 to the Control Group. Four participants (2 in each group) lost to follow-up. However, one participant in each group completed their second visit on Day 45, and their last observed data were carried forward and imputed for Day 90.<sup>8,9</sup> Hence, for the final analysis, 20 & 10 participants were considered for the Swamala and Control group, respectively.

The mean age of participants in the Swamala and Control Group was  $36.95 \pm 10.51$  and  $35 \pm 10.07$  years, respectively. There were more males (11 out of 20) in the Swamala group & more females (7 out of 10) in the control group. All routine investigations were comparable at baseline. [Table 1] All the volunteers had more than 80% compliance with the study

medication, as reported by them during the OPD and telephonic follow-ups.

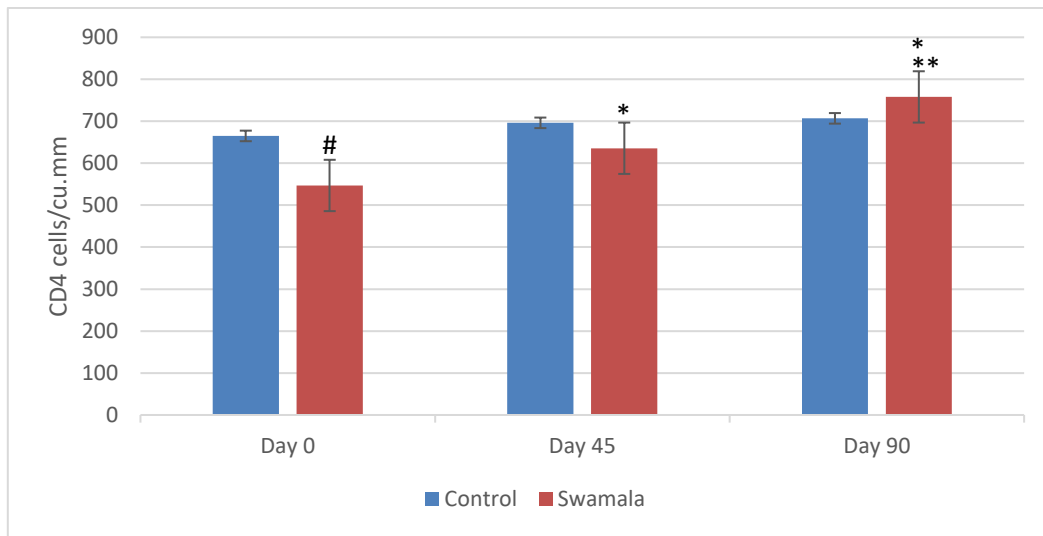
**Table 1: Routine Investigations at Baseline and Day 90**

	Baseline		Day 90	
	Control Group (n =10)	Swamala Group (n=20)	Control Group (n =10)	Swamala Group (n=20)
<b>Hemoglobin [g/dl]</b>	12.83 ± 1.46	13.67 ± 1.90	12.50 ± 1.34	13.65 ± 1.64
<b>Red Blood Cell count</b>	4.66 ± 0.43	4.76 ± 0.41	4.55 ± 0.40	4.75 ± 0.37
<b>Total Leukocyte Count</b>	7630 ± 2211	6645 ± 1126	7933 ± 2421	6805 ± 823
<b>Platelet count (lakhs)</b>	2.68 ± 0.51	2.72 ± 0.71	2.83±0.36	2.83 ± 0.58*
<b>Neutrophils (%)</b>	59.10 ± 4.09	61.30 ± 4.84	62.11 ± 7.74	63.26 ± 3.97*
<b>Lymphocyte (%)</b>	37.10 ± 4.12	35.00 ± 4.70	35.11 ± 8.02	33.89 ± 3.89
<b>Basophil (%)</b>	0	0	0	0
<b>Eosinophil (%)</b>	2.80 ± 1.23	2.65 ± 0.99	1.89 ± 0.78	1.89 ± 0.32**
<b>Monocyte (%)</b>	1.00 ± 0.94	1.05 ± 0.51	1.11 ± 0.33	0.95 ± 0.23
<b>Aspartate aminotransferase</b>	20.40 ± 5.49	20.90 ± 5.32	18.78 ± 5.20	20.32 ± 5.24
<b>Alanine aminotransferase</b>	21.72 ± 7.20	22.80 ± 4.83	21.03 ± 5.69	22.98 ± 5.78
<b>Blood Urea Nitrogen</b>	9.45 ± 2.73	9.60 ± 2.02	8.43 ± 2.61	10.00 ± 1.91
<b>Serum Creatinine</b>	0.98 ± 0.13	1.00 ± 0.14	1.02 ± 0.13	1.00 ± 0.15

Mean ± SD. \*p<0.05 & \*\*p<0.001 vs Swamala baseline (Mann Whitney U Test, paired & unpaired t-test)

We observed variations in the routine & immunological parameters in both groups throughout the study, and only a few were statistically significant; however, all the variations were within the normal physiological limits. Routine investigations repeated on Day 90 revealed no significant changes in the control group. Swamala group participants showed no significant difference as compared to the control, but there was significant increase in neutrophils & platelets and a decrease in eosinophils compared to its baseline. [Table 1]

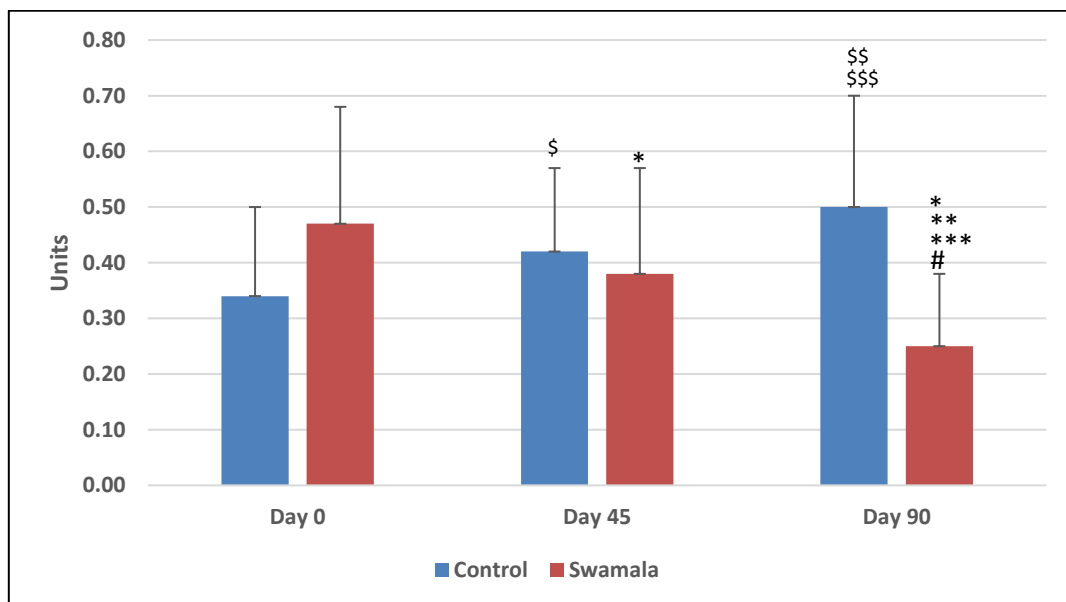
The Baseline CD4 cell count in the Swamala Group participants was significantly lower compared to the Control Group; it increased significantly on the subsequent visits. No significant change was observed in the control group [Figure 2]



**Figure 2: Effect on CD4 Cell Count**

Mean± SD; (Control group n=10 & Swamala group n=20), <sup>#</sup> p < 0.001 vs. Control Group (unpaired t-test), \*p < 0.001 vs baseline & \*\*p<0.001 vs Day 45 of Swamala group (Repeated measure ANOVA)

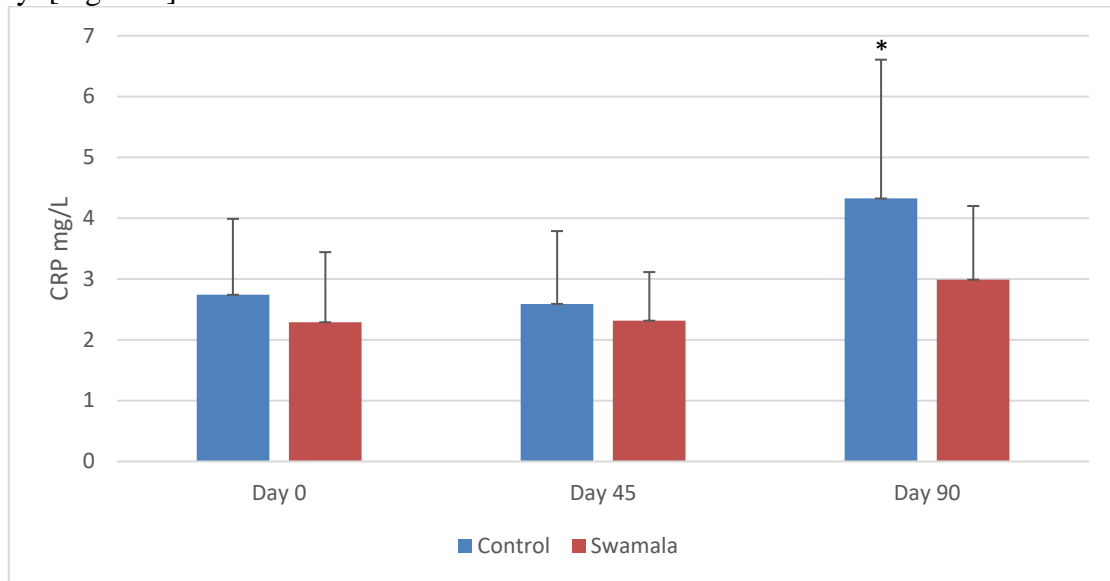
TNF-α levels showed a statistically significant increase in the control group on day 45 and day 90 as compared to the baseline levels, and a significant increase in the TNF-α levels was reported on Day 90 as compared to Day 45 in the control group participants. Swamala Group exhibited a significant reduction in TNF-α levels on Day 45 and Day 90 compared to the baseline levels. Reduction at Day 90 in the Swamala group was significant compared to its Day 45 value and with the corresponding control group.



**Figure 3: Effect on TNF alpha levels**

Mean± SD; (Control group n=10 & Swamala group n=20), \*p<0.05 & \*\*p<0.001 vs Swamala group baseline and \*\*\*p<0.01 vs Swamala group on Day 45 (Repeated measure ANOVA), <sup>#</sup>p<0.001 vs Control Group (Unpaired t-test), <sup>\$</sup>p< 0.05 & <sup>\$\$</sup>p<0.001 vs Control group baseline and <sup>\$\$\$</sup>p<0.01 vs Control group on Day 45 (Repeated measure ANOVA)

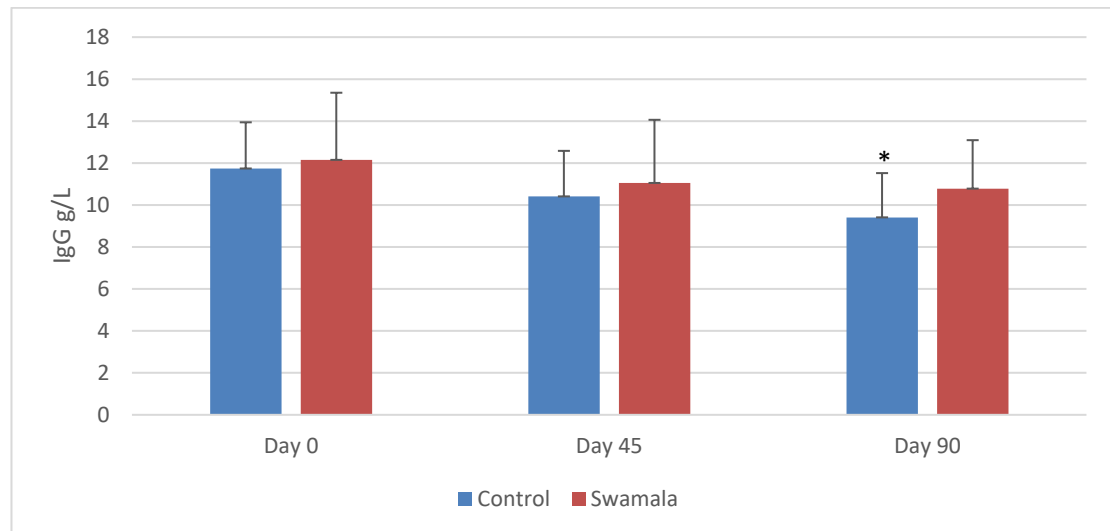
CRP levels in the Control Group significantly increased on Day 90 compared to Day 45. The Swamala Group participants did not exhibit significant change in CRP levels throughout the study. [Figure 3]



**Figure 4: Effect on C-Reactive Protein**

Mean± SD; (Control group n=10 & Swamala group n=20), \*p<0.05 as compared to Day 45 (Repeated measure ANOVA, Unpaired t-test)

Serum IgG levels did not change significantly in the control group during the second visit but reduced significantly on Day 90. Swamala Group participants showed no significant changes. [Figure 4]

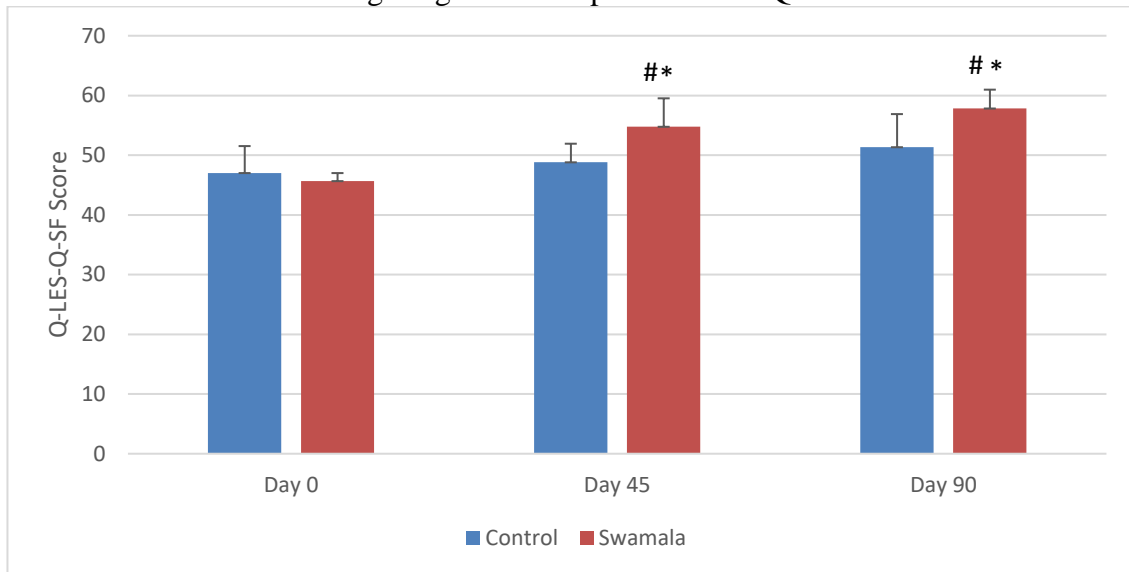


**Figure 5: Effect on Serum IgG levels**

Mean± SD; (Control group n=10 & Swamala group n=20), \*p<0.05 as compared to Baseline (Repeated measure ANOVA, Unpaired t-test)

Quality of life (QoL) was measured using Q-LES-Q-SF scores. It did not vary significantly in the control group. It improved significantly in a graded fashion on Day 45 & Day 90 in the Swamala group compared to its baseline and corresponding control group scores. [Figure 6]

Among the sixteen variables assessed, six (Physical health; Work; Household activities; Mood; Overall life satisfaction and contentment during the past week; Overall sense of well-being) contributed the most in showing a significant improvement in QoL.



**Figure 6: Effect on Quality of Life (Q-LES-Q-SF Score)**

Mean± SD; (Control group n=10 & Swamala group n=20), # p<0.01 vs Control Group (Unpaired t-test), \*p<0.001 vs Swamala group baseline (Repeated measure ANOVA)

All of the participants received COVID vaccination. The vaccine-induced antibody was present among all participants. The antibody titre did not change significantly in both groups [Table 2]. None of the participants developed COVID-19 infection or COVID-19-related symptoms during the study duration.

**Table 2: Effect on COVID-19 Antibodies**

	Control Group (n=10)	Swamala Group (n=20)
<b>Baseline</b>	1.77 ± 1.33	1.19 ± 0.95
<b>Day 45</b>	1.60 ± 0.95	1.69 ± 1.78
<b>Day 90</b>	1.58 ± 0.91	1.09 ± 0.78

(Reference range: Negative < 0.80, Equivocal: 0.80-1.00, Positive: > 1)

Mean ± SD; (Control group n=10 & Swamala group n=20) (Repeated measure ANOVA; Unpaired t-test)

It was observed that 8/10 (80%) participants in the Control Group suffered from general illnesses during the study duration of 90 days; in comparison, only 7/20 participants (35%) in the Swamala group reported them. [Table 3] The Majority had cough and cold that lasted one to two days. 3 (30 %) participants in the Control Group reported absenteeism, but it no absenteeism was reported in the Swamala group.



**Table 3: Episodes of General Illness Among Study Participants**

Description	Control group (%) (n=10)	Swamala group (%) (n=20)
No. of participants having cold and cough	7 (70)	6 (30)
No. of participants having fever	1 (10)	0
No. of participants having diarrhoea	0	1 (5)*
Number of participants reporting absenteeism from work	3 (30)	0

\* The participant also reported a headache

### Discussion:

Swamala is a multi-ingredient ayurvedic formulation containing *Chyawanprash* as a principal constituent. The effects of Swamala on immunological markers like IgG, TNF, CD4 count, and CRP levels, as well as changes in Quality of Life (QoL) & routine blood investigations, were evaluated over three months. Swamala was found to improve CD4, neutrophil, and platelet counts, as well as QoL significantly. It also lowered the eosinophil counts and CRP levels along with the incidence of general illnesses. It was found to be well tolerated & safe as it did not alter other variables, including the liver & renal functions.

Several pre-clinical and clinical studies have been conducted to evaluate the safety and efficacy of *Chyawanprash*. It provides various health benefits like protection and improvement in digestive, metabolic, respiratory, and endocrinal functions. It possesses antioxidant, nootropic, cardiogenic, immunogenic, aphrodisiac, radioprotective, cytoprotective, genoprotective, antimutagenic, and anticarcinogenic effects along with favourable effects on lipid profile and glycaemic levels.<sup>4,5,7</sup>

Swamala Group exhibited anti-inflammatory activity by lowering TNF- $\alpha$  levels significantly. Similar findings were seen in a previous study.<sup>7</sup> TNF- $\alpha$  is an inflammatory mediator that plays an essential role in the development of cancer and bone resorption. Moreover, TNF- $\alpha$  has a role in the emergence of insulin resistance, endothelial dysfunction, and dyslipidemia. Low-grade systemic elevations in TNF- $\alpha$  have been associated with cardiovascular diseases, and elevated TNF- levels have been reported to be connected to Alzheimer's disease.<sup>10,11</sup> As a result, Swamala may have a potential role in the treatment of the illnesses indicated above.

A significant rise in the CD4 cell count was observed in the Swamala Group over the treatment period of 3 months. Human helper T cells express the CD4 immunoglobulin family molecule, primarily mediating adhesion to major histocompatibility complex components, leading to an enhanced immune response. Li et al. found that a considerable reduction in CD4 T cells increases the likelihood of opportunistic infections in humans.<sup>12</sup> HIV, infections, autoimmune diseases, immunosuppressive drugs, cancer, and idiopathic CD4 lymphocytopenia are some of the known causes of CD4 lymphocytopenia in humans.<sup>13</sup> No prior studies have investigated how *Chyawanprash* affects CD4 count. The effects of Swamala (which contains *Chyawanprash* as one of its ingredients) on CD4 in healthy individuals were investigated for the first time in this study. In our study, CD4 cell counts in the Swamala group increased steadily over three months. So it can be assumed that Swamala may be useful in treating lymphocytopenia and impaired immunity. Testing its potential impact on diseases, including HIV, autoimmune disorders, and other immunodeficiency syndromes, may be worthwhile.

CRP is an acute-phase reactant protein primarily activated during the acute phase of an inflammatory or viral event by the action of IL-6 on the gene in control of CRP transcription. Increased C-reactive protein levels can be caused by viral or non-infectious diseases, and they can occur in both acute and chronic disorders. Nonetheless, markedly elevated CRP values are

often attributable to an infectious cause.<sup>14</sup> Although both groups experienced an increase in CRP levels, the increase in the Swamala group at day 90 was less than that seen in the Control Group. However, a decline in CRP levels in the Zebrafish model due to *Chyawanprash* was demonstrated by Balkrishna *et. al.*<sup>15</sup> *Chyawanprash*'s anti-inflammatory properties may have contributed to the decrease in CRP levels seen in that study.<sup>15</sup> Further studies may be needed to confirm the role of Swamala on CRP levels.

No significant changes were found when the IgG levels were compared within Swamala and Control Groups in our study. Participants in the Swamala Group maintained their IgG levels throughout the trial; however, those in the Control Group showed a declining trend, but they were within normal limits. Serum IgG is a marker of the humoral immune response indicating the body's natural defenses against pathogens. Testing for IgG antibodies can be used to diagnose persistent (latent or chronic) infections as well as to determine immunological status, such as a marker of immunity following a wild viral infection or active immunization.<sup>16</sup> Participants in the Swamala Group exhibited a significant improvement in QoL score than those in the Control Group. Among the sixteen variables assessed, six (physical health, work, household activities, mood, overall life satisfaction & contentment and sense of well-being) contributed the most to a significant change in QoL. These findings are in accordance with a study done on the use of *Chyawanprash* in 313 healthy children, which showed improvement in QoL, energy levels, physical fitness levels, strength & stamina, and protection from illnesses.<sup>7</sup>

None of the participants developed COVID-19 infection, and their COVID-19 antibody titers remained within a range. Previous studies utilizing *Chyawanprash* on healthcare professionals at high risk of contracting COVID-19 revealed a statistically significant elevation in blood IgG levels, but they were within their normal range.<sup>17</sup> During the study period, the physical examinations for both groups revealed no abnormal findings. In the Swamala Group, the levels of platelets and neutrophils showed a significant increase, and the eosinophil count showed a significant decrease. Eosinophils have a significant role in the pathophysiology of allergic reactions and asthma and are linked to the severity of the condition. They cause tissue damage and inflammation in numerous disorders, including asthma.<sup>18</sup> Validating the anti-allergic and immunogenicity potential indicated by Swamala in the present study will require additional research with a bigger sample size.

The number of participants developing episodes of general illnesses during the course of the study was lower in the Swamala Group as compared to the Control Group. Cough & cold were the most common, followed by fever and diarrhoea. Participants in the Swamala group reported episodes of cough, cold, and diarrhoea but no fever. These illnesses were mild to moderate in severity and lasted an average of two days. The increase in the number of individuals with cough and cold seen in the control group may be attributed to the rise in the TNF- $\alpha$  levels. On the other hand, Swamala Group showed a significant decrease in the TNF- $\alpha$  levels and eosinophil count, indicating its anti-allergic properties. Similar-findings were seen in earlier studies on *Chyawanprash*.<sup>17</sup> During the trial, participants in both groups were asked about absenteeism due to general illness. It was found that no participants taking Swamala were absent from work due to illness, whereas three participants in the Control Group were absent for one day each due to cough and cold. Even though a smaller number of Swamala Group participants became sick, they were still able to go to work, suggesting that those illnesses were of mild severity due to the protective effects of Swamala.

Various studies have highlighted the complex interactions that underlie the relationships among stress, immunity, and health outcomes. Chronic stress affects a variety of clinically meaningful immune parameters, including susceptibility to infectious illnesses, the ability of the immune system to suppress latent viruses, and various inflammatory processes.<sup>19</sup>

*Suvarna Bhasma* (Processed Gold), another ingredient in Swamala, has demonstrated anti-stress and anxiolytic effects and safety.<sup>6</sup> Gold has also been shown to have anti-inflammatory action by suppressing NF-kappa B binding activity as well as the activation of the I-kappa B-kinase.<sup>20</sup> This results in reduced production of pro-inflammatory cytokines, most notably TNF- $\alpha$ , interleukin-1, and interleukin-6.<sup>20</sup> In addition to *Chyawanprash*, these properties of gold might have also contributed to the immunostimulant effects of Swamala.

Based on the above findings, it may be worthwhile to test the potential beneficial effects of Swamala in conditions such as Tuberculosis, upper respiratory tract infections, lower respiratory tract infections, HIV, autoimmune diseases, and other immunodeficiency syndromes. Swamala appeared to be well tolerated by healthy volunteers in our study, but clinical trials with a larger sample size are needed to further assess its safety and efficacy.

### Conclusion:

The present study found that Swamala has potential immunostimulant effects, as shown by the increase in CD4 & neutrophil counts along with improvement in the quality of life. It has also demonstrated anti-inflammatory properties by decreasing TNF- $\alpha$  levels and eosinophil counts. Hence, Swamala might have a role in treating conditions associated with immunodeficiency and allergy which should be explored in future studies.

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