Original Article

Safety and efficacy of COROPROTECT kit as an add-on therapy in the management of mild-to-moderate COVID-19: A randomized, placebo-controlled trial

Chetan Savaliya[1], Shridhar Pandya[1], Kamalesh Thumar[1], Dheeraj Nagore[2]

[1]Research and Development Department, Gplife Healthcare Pvt., Ltd., Surat, Gujarat, [2]Director, Mprex Healthcare Pvt., Ltd., Pune, Maharashtra, India

Abstract

Background: The constructive role of Ayurveda in managing COVID 19 has been widely discussed, with identified herbs showing immunomodulatory and antiviral potential. However, clinical trials examining their safety and efficacy are limited. **Aim:** The aim of this study is to determine the efficacy of COROPROTECT kit, a proprietary Ayurvedic formulation, in COVID 19. **Materials and method:** Randomized, placebo controlled trial with 312 mild to moderate hospitalized COVID 19 patients. Groups received COROPROTECT or placebo for 10 days alongside standard care. **Results:** The outcome measures included the number of days taken to reverse the reverse transcriptase polymerase chain reaction (RT PCR) status, reduction in symptoms and inflammatory markers. Fisher exact test was used to analyze the changes between categorical variables, whereas the comparative effect of therapy in both groups on inflammatory markers and safety biochemical parameters was analyzed using Student's *t* test. A total of 300 patients completed the study without any adverse events. The COROPROTECT kit group exhibited a statistically significant higher percentage of patients testing negative on days 4, 7, and 10 compared to the placebo group. A within group analysis showed that trial group to significantly reduced the levels of C reactive protein ($P = 0.03$), lactate dehydrogenase ($P < 0.001$), and interleukin 6 ($P = 0.01$). Subjects of the trial group experienced complete relief from cough (69.33%), breathlessness (65.33%), and fatigue (62.67%) within 4 days. In contrast, the placebo group had 20%–40% of participants with mild symptoms persisting until day 10. **Conclusion:** This study suggests potential future implications, indicating a faster RT PCR negativity, reduced COVID 19 severity, and inflammatory markers, along with early symptomatic recovery. The COROPROTECT kit proved safe, facilitating an accelerated clinical recovery compared to conventional care.

Keywords: Anti viral, *Ashwagandha*, Ayurveda, COVID 19, immunomodulation

Introduction

COVID 19, an acute respiratory disease, caused due to the coronavirus has so far affected more than 315 million people worldwide.[1] This has posed lot of challenges to the health care systems and general public, where majority of confirmed cases were asymptomatic, mild or moderate. Vaccines are considered as the primary mode of prevention, but still there are many cases getting reported with evidence of the breakthrough infections. Considerable attention is paid on development of prophylactic and therapeutic drugs against COVID 19 in past 2 years.[2] The constructive role of Ayurveda in the management of COVID 19 has been widely discussed in medical literature since emergence of COVID 19. Studies demonstrating effectiveness of Ayurvedic medicines and principles in the management of COVID 19 envisage the use of *Ahara* (nutritional principles) and *Aushadha* (medication) in combination to alleviate various ramifications of COVID 19.[3] Ayurveda philosophies advocate the use doctrines of *Doshahara* (modulation of host characteristics) and *Prativisha* (anti viral)[3] and *Rasayana* botanicals (modulating immunity and boosting the immune system) in the prophylaxis as well as the management of

Access this article online

Quick Response Code:

Website: www.ayujournal.org

DOI: 10.4103/ayu.ayu_92_22

Address for correspondence: Dr. Dheeraj Nagore, Mprex Healthcare Pvt., Ltd., 501-514, Crossroad, Wakad, Pune - 411 057, Maharashtra, India.
E-mail: dheeraj@mprex.in

How to cite this article: Savaliya C, Pandya S, Thumar K, Nagore D. Safety and efficacy of COROPROTECT kit as an add on therapy in the management of mild to moderate COVID 19: A randomized, placebo controlled trial. AYU 2023;44:9 16.

Submitted: 19 Apr 2022 **Revised:** 14 Dec 2023
Accepted: 26 Dec 2023 **Published:** 21 Feb 2024

diseases, which can be applied for COVID 19 management as well.[4]

Numerous herbs such as *Asparagus racemosus* Willd. whole plant extract, *Tinospora cordifolia* (Thunb.) Miers stem extract, and *Withania somnifera* (L.) Dunal root extract were identified as potential botanicals with immunomodulatory and immune boosting capacity specific to SARS CoV 2.[5,6] Successful utilization of many Ayurvedic formulations and regimens in the prevention and management of COVID 19 has been witnessed since its emergence[2,7,8] Numerous Ayurveda medicines such as AYUSH 64, *Indukantham Kwatham*, *Vilvadi Gulika,* and *Mukkamukkatuvadi Gulika* have been studied to be beneficial in COVID 19 due to its anti viral and immunomodulatory effects.[9,10]

Considering the nature of the virus, clinical scenario and the mutations and waves of the infections coming in, holistic management of COVID 19 should be contemplated, integrating Ayurvedic medication into the standard supportive care protocol, with an integration of Ayurvedic medication in the standard supportive care protocol. The integration can improve clinical outcomes and can help in managing any long term complications as well as by fundamentally supporting host immunity.

There is a need of rigorous experimental studies to strengthen the clinical practice of Ayurveda especially in COVID 19,[11] keeping clinical recovery, symptom regression, and safety of the intervention as the primary goals.[12]

The objective of the present study is to explore the efficacy of COROPROTECT kit, a poly herbal Ayurvedic formulation in preventing the progression of disease, reducing symptoms and bringing faster clinical recovery in mild to moderate COVID 19 as an adjuvant to the standard care and secondary outcome is to document its safety.

Materials and methods

Study design and settings

This was a prospective, randomized, double blind, parallel group, placebo controlled trial conducted during March–October 2021 at Lokmanya Medical Research Center, Lokmanya Hospital Pune, Maharashtra and Health Nexus Research Centre, Pune, Maharashtra.

The treatment duration was of 10 days. Medication was started on day 1. Three days window before baseline was kept to receive reverse transcriptase polymerase chain reaction (RT PCR) reports of patients. Patients eligible for the study were those diagnosed with mild to moderate COVID 19, determined by a positive RT PCR report and a clinical assessment using the national early warning score (NEWS) with a score of ≤8.[13]

The day on which the patient was identified with symptoms to the receipt of the RT PCR positive report as well as to the receipt of other biochemical parameter report (liver function test [LFT], renal function test [RFT] etc.,) was considered as the screening period.

Randomization and blinding

The eligible patients at each site underwent randomization using SPSS version 10.0 software (SPSS 10.0 for Windows Student Version, IBM, Chicago) and were allocated by a ratio of 1:1 to either in to the COROPROTECT kit (intervention) arm or placebo arm. A certified statistician developed a randomization scheme, and the investigator subsequently assigned individuals to their respective study groups.

This study was registered as a trial on Clinical Trials Registry of India (CTRI), CTRI/2021/08/036010. Further the study protocol and study report also complied with the CONSORT guidelines. The overall scheme of study is depicted in Figure 1. All the investigators followed ICH Good Clinical Practice (GCP) to monitor and record the adverse events of the study.[13,14] The study participants were covered by appropriate insurance, facilitated by the study team.

Ethical considerations

The study was carried out in accordance with the Declaration of Helsinki (Ethical Principles for Medical Research Involving Human Subjects, 64th World Medical Association General Assembly, Fortaleza, Brazil, October 2013), GCP (International Council for Harmonization E6 (R2) Guidelines. The study was approved by the Institutional ethics committee of Lokmanya Medical Research Centre and Royal Independent ethics committee Pune, India.

Study participants

Patients diagnosed with mild and moderate COVID 19 were screened for eligibility to participate in this study after obtaining a signed informed consent. All the patients were provided with study information, in their vernacular/understandable language about the purpose and nature of the study and its procedures as well as potential risks and benefits associated with study drugs as per the patient information sheet, prior to participation in the study.

Inclusion criteria

Male and females aged between 18 and 65 years (both inclusive), who tested positive for COVID 19 through RT PCR on a nasal and/or throat swab, exhibited a mild to moderate clinical status with a NEWS score[7] <8, were included in the study.

Exclusion criteria

The study excluded special populations, such as pregnant or lactating women. In addition, patients requiring intensive care admission at screening, with a past history of myocardial infarction, epileptic episodes, or any other co morbidity (such as uncontrolled diabetes or severe hypertension, defined as blood pressure exceeding 180/110 mmHg from the subject's history or clinical examination at screening), were also excluded. Any participant from the investigator perspective

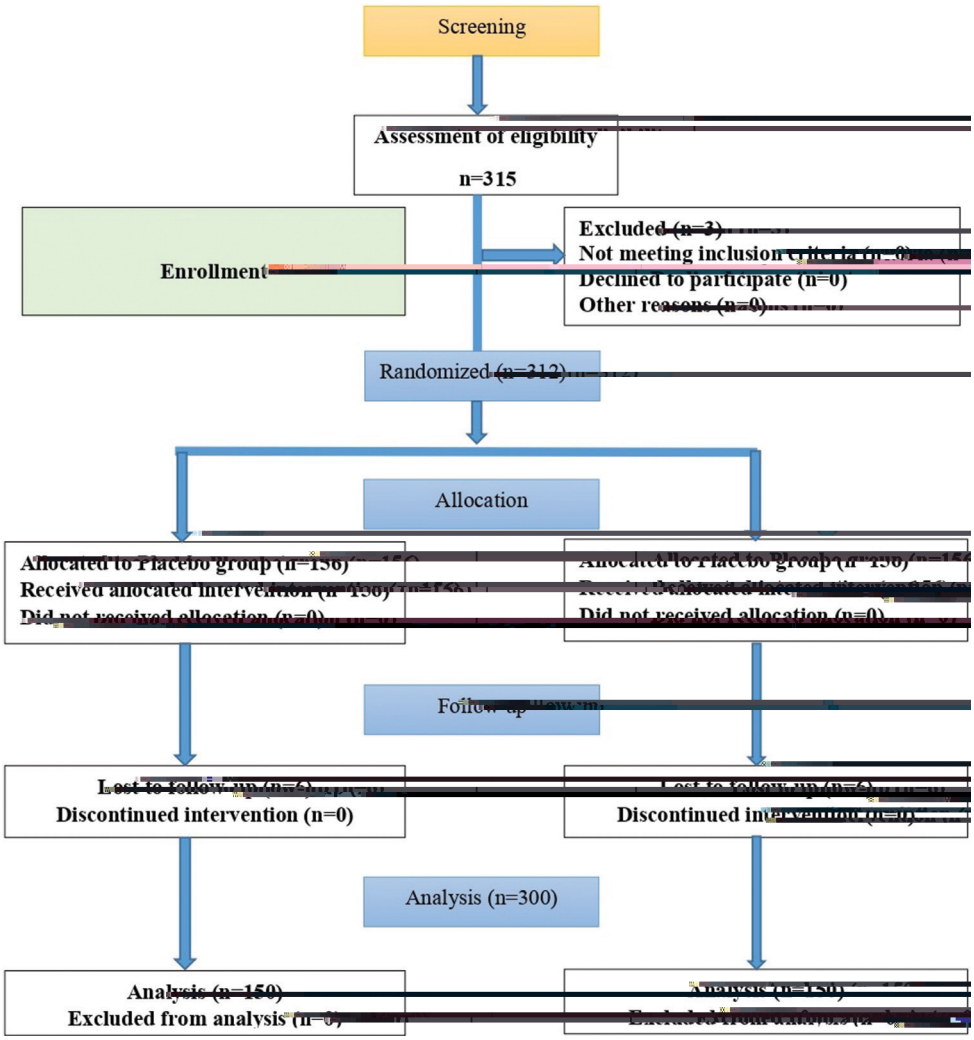

Figure 1: Consort flow chart

presenting critical comorbidity at screening was not included in the study.

Sample size calculation

Hypothesizing that the percentage of the population with a negative RT PCR result on day 3 would be 71.1% in the COROPROTECT group and 50% in the placebo group,[15] the sample size was calculated by a qualified statistician as 298 (149 in each group) to assess the study objective at 80% power and a 5% level of significance. Considering dropouts, the final targeted sample size was 315 patients.

Interventions

Both the groups received the standard of care as per the Indian Council of Medical Research guidelines.[16] All the patients were monitored throughout the study period by a team of physicians which consisted of modern medical and Ayurvedic physicians.

Investigational drug

The investigational medicinal product (IMP) is an Ayurvedic kit containing COROPROTECT Tablet 1000 mg and COROPROTECT dry syrup 25 g. The IMP was developed by Gplife Healthcare Pvt., Ltd. The manufacturing facility followed the guidelines of good manufacturing practice Ayurvedic Pharmacopoeia of India. The study products (COROPROTECT kit and placebo) were packaged and labeled based on the randomization schedule generated prior to the start of the study. The investigator ensured that study medication was stored in a safe, limited access location, as per the condition noted in the label.

Each COROPROTECT tablet contained key extracts of *Withania somnifera* (L.) Dunal root, *Tinospora cordifolia* (Thunb.) Miers stem, *Punica granatum* L. fruit, *Curcuma longa* L. rhizomes, *Moringa oleifera* Lam. whole plant, *Bacopa monnieri* (L.) Pennell whole plant, *Carica papaya* L. leaves, *Trigonella foenum-graecum* L. seeds, *Boerhaavia diffusa* L. nom. cons bark, *Andrographis paniculata* (Burm.f.) Nees roots used. Similarly, COROPROTECT dry syrup contained the key extracts of *Glycyrrhiza glabra* L. stems, *Trachyspermum ammi* (L.) Sprague ex Turrill whole plant, *Ocimum sanctum* L. leaves, *Piper longum* L. fruits, *Zingiber officinale* Roscoe

rhizomes, *Piper nigrum* L. fruit, *Adhatoda vasica* Nees leaves, *Cinnamomum zeylanicum* Blume bark, *Syzygium aromaticum* (L.) Merr. and L. M. Perry seeds, *Piper betle* L. leaves, *Curcuma longa* L. rhizome, *Solanum nigrum* L. fruit, *Inula racemose* Hook.f. whole plant, *Mentha spicata* L. leaves. [Supplementary File]

The COROPROTECT kit group was provided with 2 COROPROTECT tablets twice a day and 10 mL COROPROTECT syrup thrice a day (25 g of COROPROTECT dry syrup was reconstituted to 100 mL by patients and considered for further dosing) with warm water. The placebo group received placebo tablets and dry syrup (formulated out of the inert additives to mimic similar organoleptic characters) in similar doses. Additionally, standard of care such as antipyretic, antiviral, antihistaminic, anti inflammatory, and antibiotics were used as per the discretion of the investigator in both the groups.

Outcome measures

The primary efficacy measures were (i) number of days taken for negative RT PCR test for SARS CoV 2, performed using a nasopharyngeal swab on days 4, 7, and 10; (ii) Change in clinical symptom presentation from baseline to day 4, 7, and 10 in cough, breathlessness, fatigue, chest congestion on a 5 point ordinal scale (none [1], mild [2], moderate [3], severe [4], extremely severe [5]); (iii) change in serum C reactive protein (CRP), lactate dehydrogenase (LDH), ferritin, interleukin 6 (IL 6); (iv) immunity panel levels (CD3, CD4, CD8) from baseline to end of the study.

In addition, the trial had following secondary efficacy measures pertaining to, (i) change in plasma levels of COVID specific immunoglobulin G (IgG) antibodies; (ii) change in clinical status expressed in percentage of subjects reporting each severity rating on a 6 point ordinal scale; (iii) change in NEWS; (iv) assessment of changes in complete blood count, liver and RFTs; (v) need for admission to the intensive care unit (ICU); and (vi) duration of hospitalization.

If the RT PCR report was found negative on day 4 or 7, the subsequent swabs were not repeated. The need of admission to ICU, supplemental oxygen was assessed. The number of days of hospitalization was recorded for each patient. There was a telephonic follow up for symptom assessment if the patient is discharged from hospitals or home isolated.

Statistical analysis

All the data were analyzed using the Statistical Package for the Social Sciences (SPSS) version 10.0 software. Demographic details were expressed as mean, percentage, and frequencies. Efficacy metrics, including the percentage of patients exhibiting a negative RT PCR and experiencing symptom relief, was assessed using the Fisher exact test. Other data, such as inflammatory markers and safety hematological and biochemical measures, underwent analysis utilizing the Student's *t* test.

Results

Out of 315 screened, 312 patients were enrolled in to the study, of which 300 participants completed the study (150 subjects in each group). The COROPROTECT kit group had 62% males and 38% females with a mean age of 35.8 ± 11.3 years, whereas the placebo group consisted of 57% males and 43% females with a mean age of 35.35 ± 10.20 years. A Chi square test revealed that gender and age distribution was comparable between groups ($P > 0.05$). [Table 1]

Changes in percent population with negative reverse transcriptase-polymerase chain reaction test between groups

In COROPROTECT kit group, 70.67% of patients turned RT PCR negative on day 4, 99.33% of subjects turned RT PCR negative on day 7, and 100% of subjects turned RT PCR negative on day 10. The percentage of patients who turned negative on days 4, 7, and 10 was significantly higher in the COROPROTECT kit group than in the placebo group. The results are depicted in Table 2 and Figure 2.

Table 1: Demographic details

Parameter	COROPROTECT kit	Placebo	P
Number of subjects	150	150	>0.05
Male	93	86	
Female	57	64	
Mean age (years)	35.8±11.3	35.35±10.20	

Data was analyzed by Chi square test. Not significant as $P>0.05$

Table 2: Summary of changes in the number of subjects getting negative reverse transcription-polymerase chain reaction between groups

Duration	Group	Number of subjects (%)
Day 4	COROPROTECT kit	106 (70.67)*,#
	Placebo	56 (37.30)*
Day 7	COROPROTECT kit	149 (99.33)*,#
	Placebo	130 (86.67)*
Day 10	COROPROTECT kit	150 (100)*,#
	Placebo	140 (93.30)*

*Significant at $P<0.05$ for within group analysis, #Significant at $P<0.05$ for between group analysis. Data analyzed by Fisher's exact tests

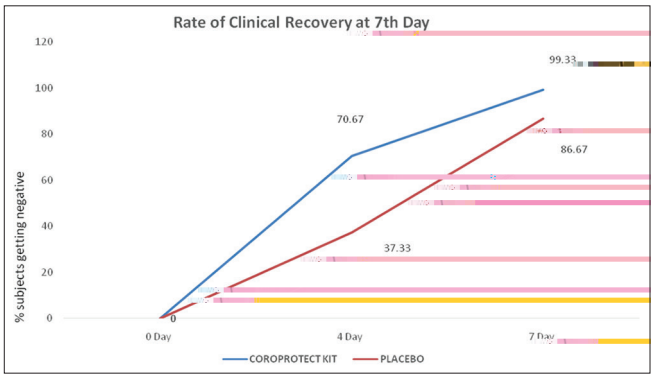

Figure 2: Rate of clinical recovery with negative RT-PCR between groups

C-reactive protein

The COROPROTECT kit group demonstrated a statistically significant decrease in CRP levels on day 10 when compared to the baseline ($P = 0.03$), whereas the changes in the placebo group were not significant. There was a 40% reduction in elevated CRP levels in the COROPROTECT kit group compared to 3.01% in the placebo group. [Figure 3]

Ferritin

In placebo group, the serum ferritin levels were increased from baseline to day 10. In the COROPROTECT kit group, there was no significant rise in the serum ferritin levels.

Serum lactate dehydrogenase

There was a significant reduction in the LDH levels in both COROPROTECT kit group and the placebo group ($P < 0.001$). However, magnitude wise COROPROTECT kit group showed greater reduction (16.71%) compared to the placebo group (10.28%).

Interleukin-6

Significant reduction in IL 6 levels were observed in both the groups ($P = 0.01$) compared to the baseline. There was a 53.53% reduction in IL6 levels in the COROPROTECT kit groups compared to 39.45% in placebo group were noted.

There were no significant differences between the groups in the other parameters such as D Dimer, IgG levels, CD3, CD4, and CD8 absolute cells. The detailed results are tabulated in Table 3 and Figure 4.

Changes in symptoms

In the present study, symptoms such as cough, breathlessness, fatigue, and persistent pain in the chest were assessed from baseline to day 10. At the baseline, all subjects were experiencing mild to moderate symptoms, indicating a consistent symptom profile across the groups. In 4 days, 69.33% of subjects were completely relieved of cough in COROPROTECT kit groups compared to 38% from placebo. At day 4, around 65.33% of subjects were relieved of breathlessness in COROPROTECT kit groups compared to 18% population in placebo group, similarly in 4 days, around 62.67% of subjects were relieved of fatigue in COROPROTECT kit groups compared to 27.33% in placebo group. The detailed results are tabulated in Table 4.

Safety parameters

No adverse events or serious adverse events were reported in both the groups. No participants in the COROPROTECT

Table 3: Summary of changes in the blood parameters between groups

Parameter tested	COROPROTECT group		P value within group	Control group		P value within group	P value in-between groups
	Pre (mean±SD)	Post (mean±SD)		Pre (mean±SD)	Post (mean±SD)		
CRP (mg/dL)	5.75±13.55	3.45±3.35	0.03	5.30±15.98	5.14±10.73	0.91	0.79
Ferritin (ng/mL)	105.98±178.8	121.93±101.26	0.33	82.10±50.81	113.68±86.12	<0.001	0.11
LDH (U/L)	259.76±148.77	216.33±74.96	<0.001	265.30±156.73	265.30±156.73	0.0011	0.75
D dimer (µg/mL)	213.97±199.32	239.18±133	0.17	221.54±340.55	237.21±128.06	0.59	0.81
IL6 (pg/mL)	10.18±25.89	4.73±3.13	0.01	10.62±26.61	6.43±9.25	0.01	0.88
IgG (S/C)	7.17±16.18	6.25±14.77	0.28	5.60±13.79	5.45±9.02	0.89	0.42
CD 3 absolute cells/µL	1129.68±488.94	1116.13±438.51	0.65	1175.52±500.18			

Table 4: Changes in percent population with improving symptom scores between groups

Symptom score	Day 0		Day 4		Day 7		Day 10	
	Test	Placebo	Test	Placebo	Test	Placebo	Test	Placebo
Cough								
1 (none)	0	0	104*,# (69.33)	57* (38.00)	130*,# (86.67)	74* (49.33)	149*,# (99.33)	93* (62.00)
2 (mild)	82 (54.67)	79 (52.67)	42 (28.00)	74 (49.33)	40 (26.67)	68 (45.33)	1 (0.67)	57 (38.00)
3 (moderate)	68 (45.33)	71 (47.33)	4 (2.67)	19 (12.67)	0	8 (5.33)	0	0
Breathlessness								
1 (none)	0	0	98*,# (65.33)	27* (18.00)	130*,# (86.67)	85* (56.67)	150*,# (100.00)	113* (75.33)
2 (mild)	82 (54.67)	79 (52.67)	48 (32.00)	81 (54.00)	20 (13.33)	62 (41.33)	0	37 (24.67)
3 (moderate)	68 (45.33)	71 (47.33)	4 (2.67)	42 (28.00)	0	3 (2.00)	0	0
Fatigue								
1 (none)	0	0	94*,# (62.67)	41* (27.330)	121*,# (80.67)	90* (60.00)	143*,# (95.33)	101* (67.33)
2 (mild)	69 (46.00)	62 (41.33)	53 (35.33)	87 (58.000)	29 (19.33)	56 (37.33)	7 (4.67)	48 (32.00)
3 (moderate)	81 (54.00)	88 (58.67)	3 (2.00)	22 (14.67)	0	4 (2.67)	0	1 (0.67)
Persistent pain in chest								
1 (none)	79 (52.67)	71 (47.33)	144* (96.00)	132* (88.00)	150* (100)	150* (100)	150* (100)	150* (100)
2 (mild)	58 (38.67)	69 (46.00)	6 (4.00)	18 (12.00)	0	0	0	0
3 (moderate)	13 (8.67)	10 (6.67)	0	0	0	0	0	0

*Within group signi f cance at $P<0.05$, #Between group signi f cance at $P<0.05$. Data analyzed by Fisher's exact test

kit group required oxygen supplementation or intensive care support during the study period.

Both group participants did not experienced any COVID 19 related complications, including pneumonia, acute respiratory distress syndrome, sepsis, and arrhythmia throughout the 10 day study period. Further, no clinically signi f cant changes (i.e., beyond normal limits) were observed in the laboratory parameters such as LFTs, RFTs, lipid pro f le, and complete blood count in both groups. [Table 5]

Discussion

This placebo controlled randomized trial assessed e f ectiveness of an Ayurvedic formulation, COROPROTECT kit treatment, in a COVID 19 population along with its safety. The study took a comprehensive approach, considering multiple aspects/factors such as viral load clearance, improved symptoms and quality of life, reduction in elevated pro in f ammatory marker status, and immunity ultimately contributing to clinical recovery. This trial was conducted on mild to moderate patients who were positive for SARS CoV 2 on RT PCR. The primary outcomes indicated a reduction in the time to recovery in response to the treatment. Although the patients were recovering in the placebo group, their speed of recovery was comparatively slow than those in the treatment group. Converging RT PCR negativity data with clinical symptom alleviation, it was observed that there was a much faster signi f cant reduction in cough, breathlessness, and fatigue due to COROPROTECT kit than placebo. There was substantially more reduction in in f ammatory mediators like CRP and IL 6 observed in COROPROTECT kit treated group than placebo, suggesting that the treatment might have curbed these pro in f ammatory markers. T cell subsets (CD3, 4, 8, and 45) which have a role in immunomodulation in COVID 19 were recovered better in COROPROTECT kit treated group. This suggests that the immunomodulatory capabilities of the COROPROTECT kit could be responsible for the accelerated clinical recovery observed in COVID 19 patients. The consistent baseline characteristics of patients in both groups enhanced the reliability of the data and the robustness of the outcomes.

In the present study, COROPROTECT kit, i.e., COROPROTECT tablet and COROPROTECT dry syrup were compared with placebo for its safety and clinical e f cacy along with standard care treatment in COVID 19 patients. The results are promising as it has shown improvement in multiple variables tested compared to the placebo group. Integrating COROPROTECT kit in COVID 19 care will be very strategic to accelerate recovery of COVID 19 patients reducing chances of mild to moderate severity to getting into the advanced COVID 19 disease stages.

The COROPROTECT kit has shown to signi f cantly curb the disease progression and reverse in the RT PCR status to negative for the majority of the participants in 4 days compared to the control group. This suggests a positive role of COROPROTECT kit in inducing immunomodulation and facilitating faster clinical recovery. A previous pilot study also reported Ayurvedic formulations to curtail the hospital stay and recovery period when administered as an add on treatment for COVID 19 patients.[17] Early recovery may have considerable amount of impact on improving mental health status and reducing the health care burden such as need for advanced care. The e f cacy of COROPROTECT kit may be attributed to its ingredients like *W. somnifera* root extract, *G. glabra* stem extract, *T. cordifolia* stem extract, etc., which has multifaceted clinical properties speci f c to COVID 19 such as anti in f ammation, anti oxidant, organ protection, and induce homoeostasis.[18 20]

Table 5: Changes in hematological and biochemical parameters between the groups

Parameters	Baseline		Day 10	
	Test	Placebo	Test	Placebo
Complete blood count				
Hemoglobin (g/dL)	13.30±2.41	13.39±2.02	13.29±1.83	13.16±2.04
Total leucocytes (10^3/μL)	7267.55±2442.92	7966.69±2735.96	7540.49±2570.52	7696.31±2653.76
Platelet count (10^3/μL)	122.87±137.75	119.50±137.49	121.96±142.85	128.63±150.00
RBC count (×10^6/μL)	4.57±0.70	4.59±0.62	4.49±0.63	4.52±0.62
PCV (%)	41.42±6.22	41.96±5.86	42.22±5.71	41.56±5.72
Neutrophils (%)	67.24±10.32	67.95±10.75	66.01±10.41	65.97±10.24
Eosinophils (%)	4.29±3.96	4.18±3.44	5.19±6.46	4.68±4.52
Basophils (%)	0.43±0.41	0.44±0.39	0.43±0.33	0.44±0.39
Lymphocytes (%)	21.36±9.95	20.29±9.53	21.11±9.07	21.55±9.53
Monocytes (%)	6.72±3.05	6.89±3.16	7.05±3.47	7.29±3.88
Lipid profile (mg/dL)				
Total cholesterol	163.54±29.96			

COROPROTECT Kit group reported to have 40%, 53.53%, and 17% reduction in elevated CRP, IL 6, and LDH levels, respectively, which was certainly better than the placebo group. The anti inflammatory effect stimulated by the COROPROTECT kit is worth considering, as down regulation of inflammation is considered as one of the important strategy in the management of COVID 19.[21]

Studies suggest the elevated levels of LDH to heighten the severity of COVID 19.[22 24] In the present study, COROPROTECT kit group has lowered the LDH levels by 17%, this may be viewed as the better prognosticating effect of COROPROTECT kit group in COVID 19.

Elevated ferritin levels are postulated to increase the severity of complication among COVID 19 patients.[25] Significant increase in the ferritin levels among the placebo group, whereas very minimal rise among COROPROTECT kit group was observed. This may be viewed as a protective effect of COROPROTECT kit in alleviating the severity of COVID 19. No marked changes were observed in other inflammatory markers such as D Dimer, IgG levels, CD3, CD4, and CD8 absolute cells in 10 days of duration.

Earlier studies also reported that symptom alleviation is positively correlated to the clinical recovery and improved quality of life in COVID 19 through Ayurveda intervention.[17,24] As discussed earlier the clinical recovery rate in COROPROTECT kit group by the end of day 4 was around 60%–70% compared to 20%–30% in placebo group. By the end of 10 days, none of the patients from COROPROTECT group had any symptoms, whereas 40% participants from placebo group remained with mild symptoms. This reinstates the usefulness of COROPROTECT kit an adjunct with standard of care over using the standard of care alone. It was observed that the participants from COROPROTECT kit group returned to their normal daily activities with 5–7 days on the contrary subjects from the placebo group required more than 10 days' time to return to their normal daily activity level.

No adverse events were reported throughout the entire study, and there were no significant alterations in the complete blood count, lipid profile, and liver profile. This suggests the safety of the COROPROTECT kit in COVID 19 patients. The strength of the study lies in its comprehensive assessment of various aspects of clinical recovery within a single trial. However,

the potential positive effects of the COROPROTECT Kit in moderate to severely comorbid COVID 19 patients can be explored in the future research. The findings of this study may carry socioeconomic implications, particularly in developing countries such as India, where a reduction in the severity of COVID 19, early clinical recovery, and shorter hospital stays can be considered valuable clinical outcomes. The results of this study can be only generalized among the mild to moderate COVID 19 patients, as severe COVID 19 patients were not included in this study which could be viewed as the limitation of the study.

Conclusion

COROPROTECT kit as an adjuvant to conventional care is safe and offers faster clinical recovery, viral clearance, and symptom relief along with reduction in inflammatory markers and restoration in the immune cell levels in patients with mild to moderate COVID 19. Therefore, it can be considered as a safe and effective add on regimen in the management of mild to moderate COVID 19.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. World Health Organization. WHO Coronavirus (COVID 19) Dashboard | WHO Coronavirus (COVID 19) Dashboard with Vaccination Data. Available from: https://covid19.who.int/. [Last accessed on 2022 Apr 07].
2. Reddy RG, Gosavi RV, Yadav B, Rai AK, Holay MP, Talekar M, *et al*. AYUSH 64 as an add on to standard care in asymptomatic and mild cases of COVID 19: A randomized controlled trial. Ayu 2020;41:107 16.
3. Adluri US, Tripathi AC. Understanding COVID 19 pandemic – A comprehensive Ayurvedic perspective. J Ayurveda Integr Med 2022;13:100348.
4. Borse S, Joshi M, Saggam A, Bhat V, Walia S, Marathe A, *et al*. Ayurveda botanicals in COVID 19 management: An *in silico* multi target approach. PLoS One 2021;16:e0248479.
5. Patwardhan B, Chavan Gautam P, Gautam M, Sci GT, Ayurveda Rasayana in Prophylaxis of COVID 19; 2020. Available from: https://media.curofy.com/pdfuploaduser/o95An6taiU7JfppQsFmB2k.pdf [Last accessed on 2022 Mar 28].
6. Singh R, Goel S, Bourgeade P, Aleya L, Tewari D. Ayurveda Rasayana as antivirals and immunomodulators: Potential applications in COVID 19. Environ Sci Pollut Res Int 2021;28:55925 51.
7. Devpura G, Tomar BS, Nathiya D, Sharma A, Bhandari D, Haldar S, *et al*. Randomized placebo controlled pilot clinical trial on the efficacy of Ayurvedic treatment regime on COVID 19 positive patients. Phytomedicine 2021;84:153494.
8. Thakar A, Panara K, Patel F, Bhagiya S, Goyal M, Bhinde S, *et al*. Add on Ayurveda treatment for early stage COVID 19: A single center retrospective cohort study from Gujarat, India. J Evid Based Integr Med. 2021;26. doi: 10.1177/2515690X211020685.
9. Sulaiman CT, Deepak M, Ramesh PR, Mahesh K, Anandan EM, Balachandran I. Chemical profiling of selected Ayurveda formulations recommended for COVID 19. Beni Suef Univ J Basic Appl Sci 2021;10:2.
10. Ali H. "Ayush 64" – A new anti malarial herbal compound. Indian J Pathol Microbiol 1996;39:499 500.
11. Payyappallimana U, Patwardhan K, Mangalath P, Kessler CS, Jayasundar R, Kizhakkeveettil A, *et al*. The COVID 19 pandemic and the relevance of Ayurveda's whole systems approach to health and disease management. J Altern Complement Med 2020;26:1089 92.
12. Siddiqi HK, Mehra MR. COVID 19 illness in native and immunosuppressed states: A clinical therapeutic staging proposal. J Heart Lung Transplant 2020;39:405 7.
13. Central Council for Research in Ayurvedic Sciences. General Guidelines for Clinical Evaluation of Ayurvedic Interventions. Available from: https://www.ayush.gov.in/docs/clinical_evaluation.pdf. [Last accessed on 2022 Mar 22].
14. Indian Council of Medical Research. National Guidelines of Ethics Committees Reviewing Biomedical and Health Research during COVID 19 Pandemic. Available from: https://main.icmr.nic.in/sites/default/files/guidelines/EC_Guidance_COVID19_06_05_2020.pdf. [Last accessed on 2022 Mar 22].
15. Baker KF, Hanrath AT, Schim van der Loef I, Kay LJ, Back J, Duncan CJ. National early warning score 2 (NEWS2) to identify inpatient COVID 19 deterioration: A retrospective analysis. Clin Med (Lond) 2021;21:84 9.
16. AIIMS/ICMR COVID 19 National Task Force MG. Clinical Guidance for Management of Adult COVID 19 Patients; 2021. Available from: https://www.icmr.gov.in/pdf/covid/techdoc/COVID19_Management_Algorithm_22042021_v1.pdf. [Last accessed on 2021 May 20].
17. Kataria S, Sharma P, Ram JP, Deswal V, Singh M, Rana R, *et al.* A pilot clinical study of an add on Ayurvedic formulation containing *Tinospora cordifolia* and *Piper longum* in mild to moderate COVID 19. J Ayurveda Integr Med 2022;13:100454.
18. Saggam A, Limgaokar K, Borse S, Chavan Gautam P, Dixit S, Tillu G, *et al. Withania somnifera* (L.) Dunal: Opportunity for clinical repurposing in COVID 19 management. Front Pharmacol 2021;12:623795.
19. Diomede L, Beeg M, Gamba A, Fumagalli O, Gobbi M, Salmona M. Can antiviral activity of licorice help fght COVID 19 infection? Biomolecules 2021;11:855.
20. Balkrishna A, Khandrika L, Varshney A. Giloy Ghanvati (*Tinospora cordifolia* (Willd.) Hook. F. and Thomson) reversed SARS CoV 2 viral spike protein induced disease phenotype in the xenotransplant model of humanized zebrafsh. Front Pharmacol 2021;12:635510.
21. Garcia LF. Immune response, inflammation, and the clinical spectrum of COVID 19. Front Immunol 2020;11:1441.
22. Liu Y, Yang Y, Zhang C, Huang F, Wang F, Yuan J, *et al.* Clinical and biochemical indexes from 2019 nCoV infected patients linked to viral loads and lung injury. Sci China Life Sci 2020;63:364 74.
23. Henry BM, Aggarwal G, Wong J, Benoit S, Vikse J, Plebani M, *et al*. Lactate dehydrogenase levels predict coronavirus disease 2019 (COVID 19) severity and mortality: A pooled analysis. Am J Emerg Med 2020;38:1722 6.
24. Singh H, Srivastava S, Yadav B, Rai AK, Jameela S, Muralidharan S, *et al.* AYUSH 64 as an adjunct to standard care in mild to moderate COVID 19: An open label randomized controlled trial in Chandigarh, India. Complement Ther Med 2022;66:102814.
25. Vargas Vargas M, Cortés Rojo C. Ferritin levels and COVID 19. Rev Panam Salud Publica 2020;44:e72.

Supplementary File

About the trial drug

Gplife “COROPROTECT tablet and COROPROTECT dry syrup” are successfully tested and demonstrated good e f cacy in

हिन्दी सारांश

हल्के से मध्यम कोविड-19 के प्रबंधन में ऐड-ऑन थेरेपी के रूप में कोरोप्रोटेक्ट किट की अहानिकारकता और प्रभावकारिता: एक यादृच्छिक प्लेसबो नियंत्रण परीक्षण

श्रीधर पंड्या, चेतन सावलिया, कमलेश ठुमर, धीरज नागोरे

पृष्ठभूमि: कोविड-19 के उद्भव के बाद से चिकित्सा क्षेत्र में कोविड-19 के प्रबंधन में आयुर्वेद की रचनात्मक भूमिका पर व्यापक रूप से चर्चा की गई है। कई आयुर्वेदिक औषधियों में कोविड-19 के प्रति इम्यूनोमॉड्यूलेटरी और एंटी-वायरल क्षमता होने की पहचान की गई है। इन औषधियों की अहानिकारकता और प्रभावकारिता की जांच करने वाले नैदानिक परीक्षण सीमित हैं। **उद्देश्य:** इस अध्ययन का उद्देश्य कोविड-19 में आयुर्वेद उत्पाद कोरोप्रोटेक्ट-किट की अहानिकारकता और प्रभावकारिता निर्धारित करना। **सामाग्री एवं विधि:** यह एक यादृच्छिक, प्लेसबो नियंत्रित परीक्षण था जिसमें अस्पताल में भर्ती हल्के से मध्यम स्तर के 312 कोविड-19 रोगी शामिल थे जिन्हें एड-ऑन के रूप में 10 दिनों के लिए कोरोप्रोटेक्ट समूह (सीपी) या प्लेसबो समूह (पीबी) में यादृच्छिक समूहों में बांटा गया। आरटी-पीसीआर परीक्षण के नकारात्मक होने में लगने वाले दिनों की संख्या, लक्षणों और सूजन के मार्करों में कमी को अवलोकन में शामिल किया गया। फिशर सटीक परीक्षण का उपयोग श्रेणीबद्ध अस्थिरता के बीच परिवर्तनों का विश्लेषण करने के लिए किया गया था, जबकि इन्फ़्लेमेटरी मार्करों और जैव रासायनिक मापदंडों पर दोनों समूहों के परिणाम के तुलनात्मक प्रभाव का विश्लेषण 'छात्र-टी परीक्षण' का उपयोग करके किया गया था। **परिणाम:** 300 रोगियों ने बिना किसी प्रतिकूल प्रभाव के अध्ययन पूरा किया। 4, 7, और 10वें दिन निगेटिव होने वाले रोगियों का प्रतिशत प्लेसीबो समूह की तुलना में कोरोप्रोटेक्ट किट समूह में अधिक था, जो सांख्यिकीय रूप से सार्थक था। समूहों के परिणाम विश्लेषण से पता चला कि कोरोप्रोटेक्ट समूह (सीपी) ने सीआरपी (पी=0.03), एलडीएच (पी<0.001), इंटरल्यूकिन-6(पी=0.01) के स्तर को काफी कम कर दिया था। कोरोप्रोटेक्ट समूह (सीपी) के लगभग 60-70% रोगियों को 4 दिनों में खांसी, सांस फूलना और थकान से पूरी तरह से राहत मिल गई, जबकि प्लेसीबो समूह में 10 दिन तक हल्के लक्षणों वाले 20-40% रोगियों में थे। **निष्कर्ष:** इस अध्ययन के संभावित परिणाम हो सकते हैं आरटी-पीसीआर निगेटिव होने की तेज दर, कोविड-19 की गंभीरता, इन्फ़्लेमेशन के निशान में कमी, शीघ्र रोगसूचक पुनर्प्राप्ति जैसे भविष्य के प्रभावों को मूल्यवान नैदानिक परिणामों के रूप में देखा जा सकता है। कोरोप्रोटेक्ट किट को सुरक्षित पाया गया और पारंपरिक देखभाल की तुलना में इससे तेजी से क्लिनिकल रिकवरी प्राप्त हुई।

मुख्य शब्द: अश्वगंधा, आयुर्वेद, इम्यूनोमॉड्यूलेशन, एंटी-वायरल, कोविड-19