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The immune-boosting activity of mulmina® mango and mulmina® amla orange health drinks in Covid-19 patients: Findings from a prospective, open label, three arms, single center, controlled study

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ABSTRACT

Objective: The present study was aimed to evaluate safety and efficacy of two poly herbal formulations Mulmina®Mango and Mulmina® Amla Orange, as supplements in COVID-19 patients when compared to control group that received standard treatment alone. Methodology: Total 120 subjects were divided into 3 arms, each arm of 40 subjects received orally either Mulmina® Mango or Mulmina®Amla Orange along with standard treatment or standard treatment alone, for a period of 28 days. After obtaining the ethics committee approval subjects were screened and only eligible volunteers were enrolled into the study. The subjects were classified as asymptomatic, mildly symptomatic COVID-19 patients and also health care workers who were willing to use the products. In addition to clinical, haematology & serum chemistry parameters, various immune markers like cytokines (serum amyloid A, IL-4, IL-6, IFN-γ, and IgA) and anti-oxidant parameters (SOD, MDA, CAT, GSH) were assessed. Results: There were no drop-outs in this study, the efficacy assessments both from immune and antioxidant parameters prove that the 2 products under investigations, Mulmina® Mango and Mulmina®Amla Orange, have potential and statistically significant ($p<0.05$) immune boosting (IL-6 &IFN-γ) and anti-oxidant activities (SOD& CAT) in healthcare workers and mild asymptomatic subjects by Day 28. Physician's assessment and patient feedback also reiterates the same results. Conclusion: From the study results it can be safely concluded that the products Mulmina® Mango and Mulmina® Amla Orange are completely safe for oral administration with good tolerability and also excellent immune boosting & anti-oxidant activities.

Keywords: Mulmina, COVID-19, immunity, RT-PCR, biomarkers, cytokines, anti-oxidant

ABBREVIATIONS

ARDS – Acute Respiratory Distress Syndrome, COVID-19: Corona Virus – 2019, CFR – Code of Federal Regulations, CRP – C Reactive Protein, CAT- Catalase, COX-2 – Cyclic-Oxygenase, CRF – Case Record Form, EC – Ethics Committee, ELISA – Enzyme Linked Immunosorbent Assay, IL-Interleukin, IFN-Interferon, SOD – Superoxide dismutase, GSH – Reduced Glutathione, ICH – International Conference on Harmonization, Ig – Immunoglobin, iNOS –inducible Nitric Oxide Synthase, LFT – Liver Function Test, NF-κB– Nuclear Factor-kappa B, MAPK- Mitogen-Activated Protein Kinase, MDA – Malon-dialdehyde, ORAC - Oxygen Radical Absorbance Capacity, RFT – Renal Function Test, RT-PCR – Reverse transcription polymerase chain reaction, SAA - Serum amyloid A, SARS-CoV-2 - Severe Acute Respiratory Syndrome Corona virus 2, TE - trolox equivalent, WHO – World Health Organization.

INTRODUCTION

The pandemic caused by the Severe Acute Respiratory Syndrome Corona virus 2 (SARS-CoV-2) was first identified on December 29, 2019, whereas identified in India in March 2020. Initially it was under the impression of a "pneumonia of unknown etiology" similar to that of the 2003 severe acute respiratory syndrome (SARS)outbreak[1]However, WHO made it to public about this pandemic outbreak, with common symptoms being fever, cough, myalgia, and fatigue. In severe cases, the disease can progress to organ disorders including acute respiratory distress syndrome (ARDS), acute cardiac injury, liver injury, kidney injury, and even death[1]. Corona virus has certainly put the world in an extremely panic situation. Whilst the whole world is struggling to fight against Corona virus, the WHO (World Health Organization) recommends people to have an excellent immunity to fight the pandemic.

Indian Ayurvedic system has rich source of herbal medicines used for multiple therapeutic benefits, and various combinations are viable for formulations that can boost human's immune system. Indian or Asian ethnics have natural immunity acquired due to their regular use of herbs in their daily food recipe. However, due to various factors not all individuals shall have high immunity against infections, specifically if the source of infection is from viral origin. Jagdale Pharma has multiple health care products with key ingredients from natural sources. Few such formulations are very active in fighting against infections and increase one's immunity. The immunity booster and anti-oxidant product Mulmina® Mango, under study here is a very tasty drink that contains several ingredients that would achieve the goal of wellness and compliance. The specific and special herbs used work synergistically to provide a very high ORAC value that is expected to promote good health. Accordingly, the invention provides for a wholly natural formulation that contains a wellness product wherein the herbs, fruit extract and essential agents act synergistically to provide a high ORAC value of 5668 µmol TE/200 ml. The said product is carefully formulated with a meticulously chosen set of herbs - *Curcuma longa* and *Centella asiatica* that is meant to act as anti-inflammatory, immune-boosting and free-radical scavenging agents. These herbs so formulated are combined with the healthy vitamin rich, anti-oxidant mango extract with the necessary vitamins and minerals to result in a very tasty product for good health. The taste factor makes the herbal concoction palatable and hence ensures compliance.

Mulmina®Amla Orange, with its ORAC value is 5400 µmol TE/200 ml and the synergism of the formulation is accentuated since there are essential vitamins and minerals to the orange fruit juice with Amla (Emblica officinalis) which has also got multi-vitamins &minerals, polyphenols and tannins, which increases compatibility between all. The rich ORAC score of Orange-1819 µmol TE/100g and as per USDA, Amla (Emblica officinalis) - 2,61,500 µmol TE/100g makes the formulation still more comprehensive and all together synergistically provide immune boosting activity and rich antioxidant. The aim of the present study was to evaluate safety and efficacy of two poly herbal formulation Mulmina® Mango and Mulmina®Amla Orange, as supplements in COVID-19 patients when compared to control group that received standard treatment alone.

METHODS

The clinical trial protocol and other study related documents were reviewed by the institutional ethics committee of Bangalore medical hospital and research institute (BMCRI), Bangalore, India, prior to study initiation. The trial received a favorable opinion on 16 MAY 2020 and the study was conducted in compliance with Part 56 of Title 21 of the Code of Federal Regulations (CFR) and International Conference on Harmonization (ICH) guidelines. With Dr.Jayanthi C R., as Principal Investigator, and the trial was prospectively registered in the Indian Clinical Trial Registry, CTRI/2020/06/025702.Written and oral information about the study in a language understandable by the subject was provided to all subjects. Each subject was informed by the investigator, prior to the screening evaluation, of the purpose of this clinical trial, including possible risks and benefits and documented the informed consent process in the subject's source notes. Assessment of complete recovery from COVID infection as assessed by the treating physician and improvement in biomarkers that enhance immune-boosting activity are the anticipated outcomes of this trial.

The study was initiated on 17June 2020 and first subject was enrolled on 18June 2020. The last subject's last visit completed on 07 August 2020. Volunteers who otherwise had no abnormal medical history were screened. A detailed physical examination at screening visit was done to understand whether the subjects are healthy volunteers with no medical condition, except they are asymptomatic, mild symptomatic and also health care workers who were in primary contact with COVID-19 patients. Subjects were enrolled after evaluating their eligibility criteria (Table 1); informed consent from individual subjects was obtained in writing. Enrolled subjects were assessed for various study assessments, inclusive of clinical and biomarker parameters (Table 2). Around 120 subjects were distributed equally between the three groups of 40 each between A & B products and C group did not receive any treatment serving as control arm. Each of 3 groups comprised of asymptomatic, mild symptomatic COVID -19 patients, and health care workers posted to COVID wards (Fig. 1). Subjects were instructed to administer either Investigational Product A (Mulmina® Mango) or Product B (Mulmina®Amla Orange) for a period of 4 consecutive weeks (28 days) from the baseline visit. On the baseline day0 of the study, basic hematology and biochemistry tests were done prior to dosing. Post dosing, blood samples were collected for the measurements of biomarkers. In this study, total 2 (1x5 ml each) blood samples were collected from each subject in pre-chilled and labeled EDTA plastic tubes and stored in an ultra-freezer at a temperature -80^{0}C. The plasma samples were analyzed using ELISA kits for serum immune biomarkers and serum anti-oxidant markers estimation as per the procedures mentioned in the leaflets in respective ELISA kits. The expected outcome measures were a) assessment of complete recovery from COVID infection as assessed by the treating physician and b) assess improvement in biomarkers that enhance immune-boosting activity.

Table 1.Inclusion and exclusion criteria

Eligibility Criteria	
Inclusion	i. Volunteer aged between 18-60 years (both inclusive) ii. Asymptomatic, Mildly Symptomatic COVID -19 Patients and Health Care Workers posted to COVID wards.
Exclusion	i. Pregnancy or breast feeding. ii. Patients with pre-existing severe systemic disease necessitating long-term medication. iii. Evidence of significant uncontrolled co-morbid disease, like diabetes (Type I or II), which in the investigator's opinion would jeopardize patient participation. iv. History of cancer, including solid tumors, hematologic malignancies and carcinoma in situ. v. Any neurological (congenital or acquired), vascular or systemic disorder which could affect any of the efficacy assessments. vi. Participation in the current or previous treatment with any approved or investigational health supplement(s) during the past 1 month.

Table 2. Schedule of Assessments

Activity	Screening (-7 day)	Day 0	Day 14 (Week 2)	Day 28 (Week 4)
Informed consent	X	-	-	-
Demographics	X	-	X	-
Physical examination	X	X	X	X
Medical and medication history	X	-	-	-
Vitals	-	X	X	-
Blood tests (Basic Hematology & Biochemistry)	X			X
Urine pregnancy test	X	-	-	-
Inclusion & Exclusion criteria	-	X	-	-
Randomization	-	X	-	-
IP dispensing	-	X	X	-
Collection of unused IPs	-	-	X	X
Diet chart	-	X	X	X
Serum Immuno biomarkers: • Serum amyloid A - SAA, • IL-4, IL-6, IFN-gamma • CRP • Lymphocyte Count-L & • Mitochondrial gene Nsp-4 • IgA	-	X	X	X
Serum Antioxidant Markers: • Superoxide dismutase (SOD) • Catalase (CAT) • Malondialdehyde (MDA) • Glutathione (GSH)				
Physician's assessment of disease progression	X	-	X	X
Feedback questionnaire on health product	-	-	X	X
Adverse events	-	X	X	X
Concomitant medications.	-	X	X	X

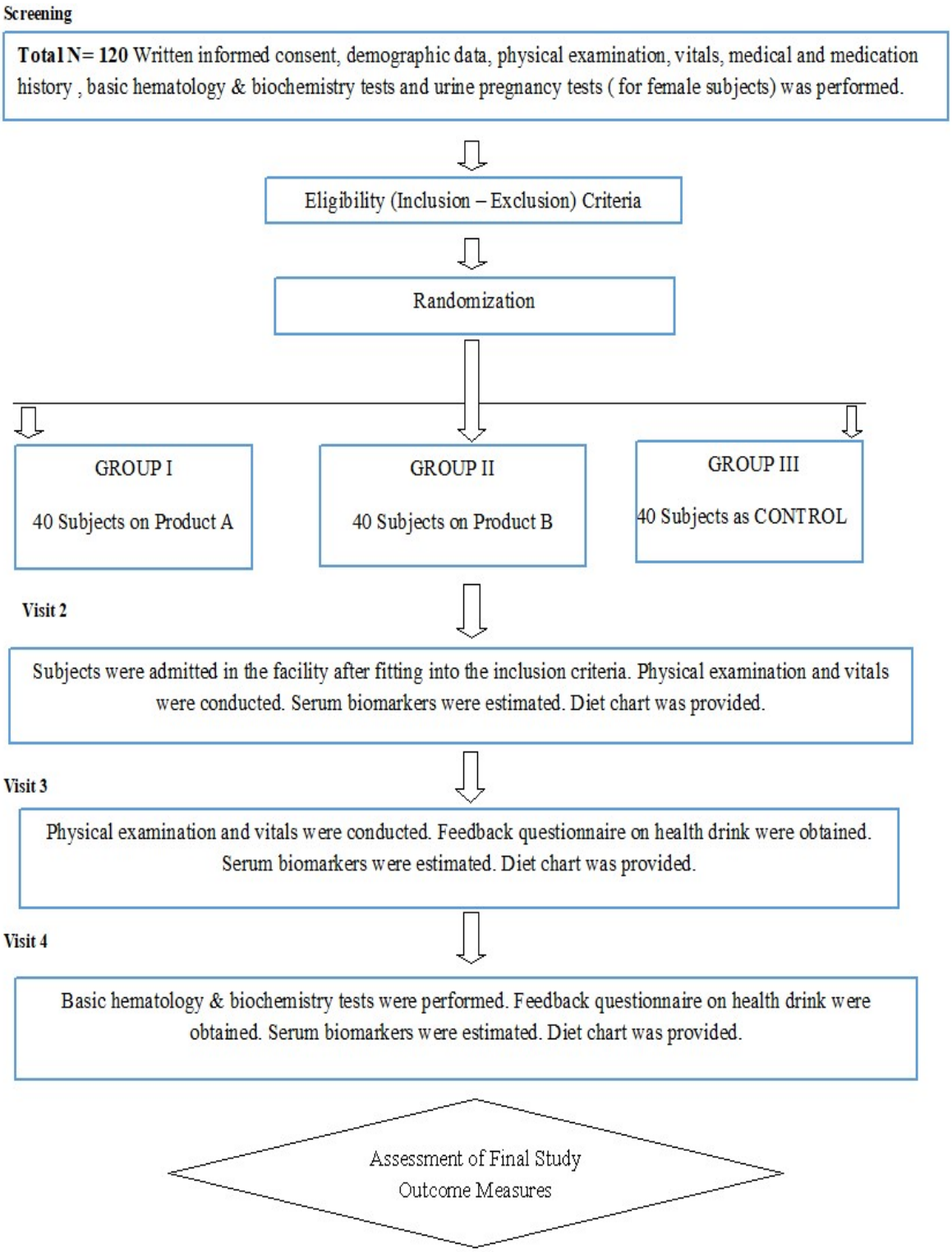

Fig 1. Flow chart of patients screened, enrolled and completed the study

RESULTS

Randomization to achieve equal number of subjects in all the arms was done by appropriate statistical software (SAS® Version 9.1.3 or higher).In the present study 29 patients (72 %) cleared the virus and became negative for RT PCR test within 10- 14 days. Vitals like temperature, systolic and diastolic blood pressure, pulse rate, heart rate and respiratory rate measured and recorded at all the visits. None of the patients progressed to severe COVID 19 and none of the patients succumbed to the disease. There was no clinically significant abnormality observed both the groups inferring the active product is safe for administration. However, there were 4 adverse events (2 nausea, 1 head ache, 1 stomach

upset) observed for 4 different subjects which were categorized as mild to moderate in severity with none of the events were judged to be related to study product in the Investigator's opinion. Subjects were followed up telephonically on respective day 30, for evaluating their overall well-being and safety/adverse events (if any). None of the enrolled subjects had serious adverse events requiring prolonged hospitalization or death. The safety laboratory parameters CBC, RFT and LFT were within normal limits at screening and on day 14. There was one protocol deviation, i.e. Mitochondrial NSP-4 which is one of the parameters to be assessed as per the ethics committee (EC) approved protocol, was not analyzed, due to logistical reasons. The deviation has been notified to the EC and there was no impact on this study and the outcomes due to this protocol deviation. There were no adverse or serious adverse events reported in this study. As there were no abnormal vital signs (temperature, blood pressure, heart rate, pulse rate) and no AEs/SAEs, the products under study are completely safe for oral consumption. 'Student t' test was employed for analyzing all the biomarker values with baseline data as co-variate, while 'p' value <0.05 was considered as statistical significance for the study.

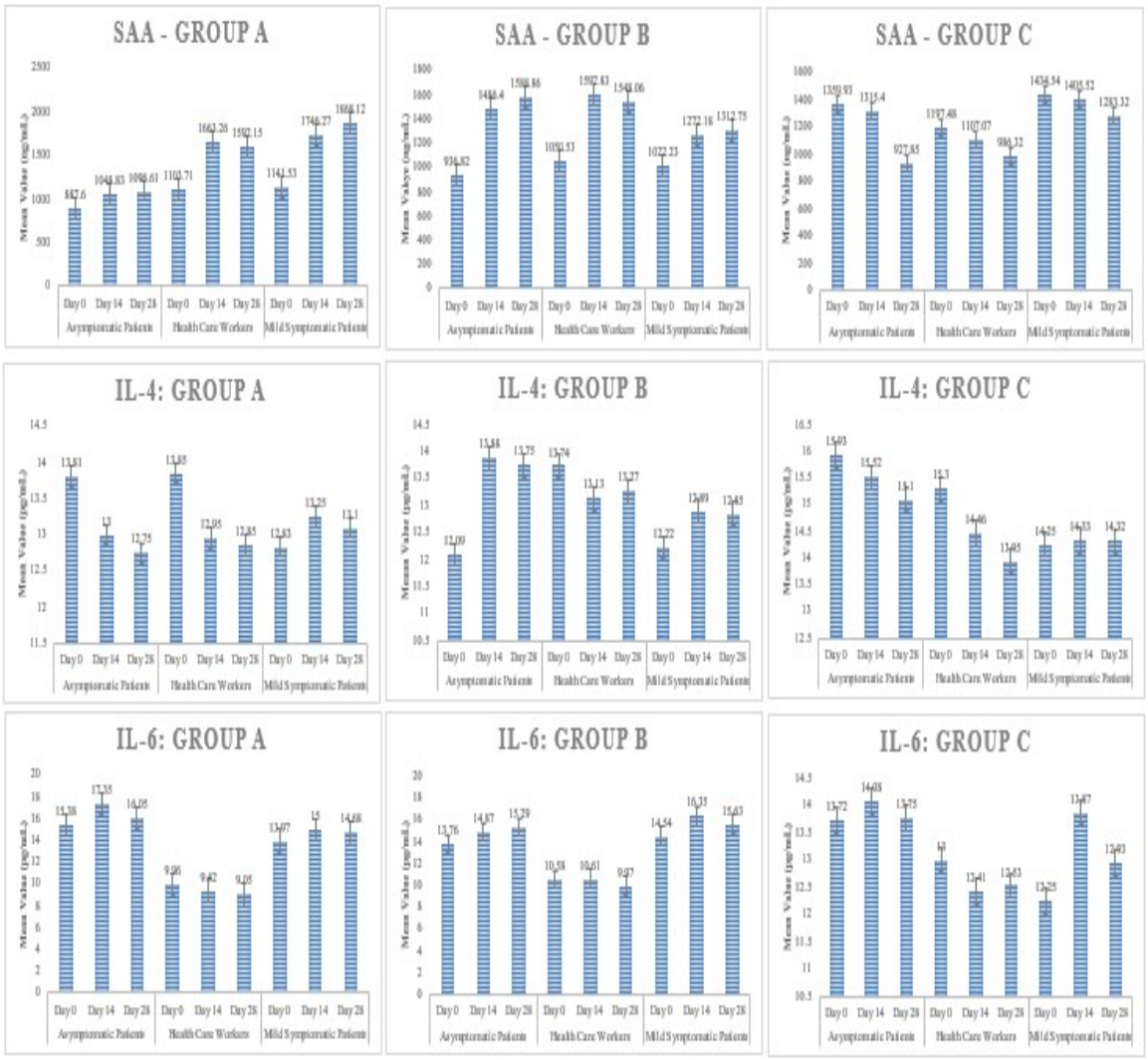

Fig 2. SAA, IL-4 & IL-6 were compared across all the 3 groups having asymptomatic, healthcare workers and mild symptomatic patients on Day 0, 14 & 28. Serum Amyloid A (SAA) values increased in all the sub-groups of asymptomatic, healthcare workers and mild symptomatic subjects. However, the increase is statistically significant ($p<0.05$) between treatment group A Vs C (Control Group) and also between Group B Vs Group C. However, the difference did not reach statistical significance when compared between Group A Vs Group B. Interleukin 4 (IL-4) values between the Treatment Groups suggest that the cytokine values had not changed much from Day 0 through Day 28. While the other cytokine Interleukin 6 (IL-6) values were kept intact across all the treatment sub-groups in all the arms, indicating that though the harmful cytokines increased by Day 14, they were brought back to control by Day 28 with the study products($p<0.05$).

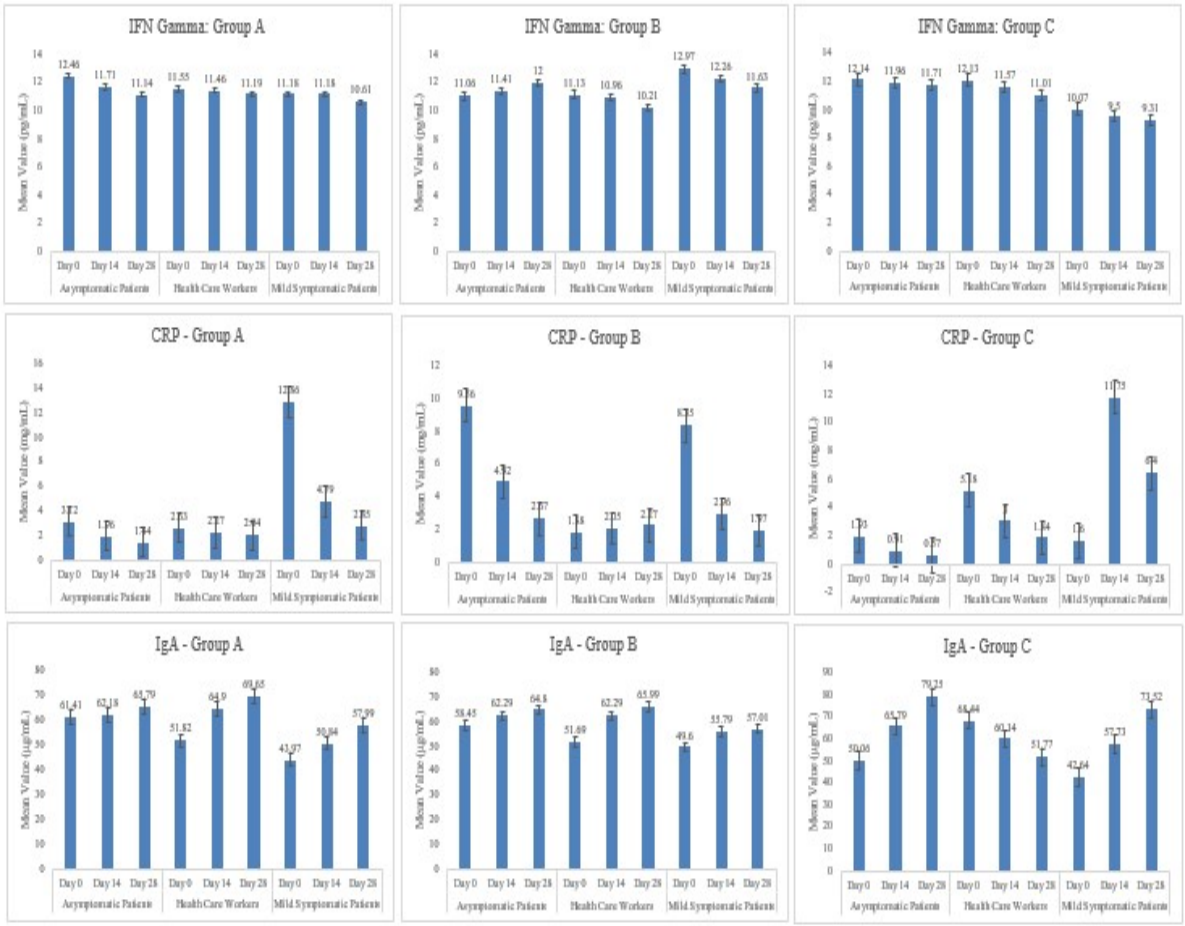

Fig 3.Average Interferon gamma (IFN-γ) values, a pathological immune marker, were drastically reduced in treatment group A amongst all the three sub-groups, whereas in the treatment group B the values decreased significantly ($p<0.05$) in the healthcare workers and mild asymptomatic subjects by Day 28 which implies that the product has a potential role in controlling the dysregulated or imbalanced immune system. Another important inflammatory marker C - reactive protein (CRP) values results comprehend the same results. CRP values are elevated in inflammatory conditions and both the study products were able to curtail the elevated CRP values on Day 0 by end of the study (Day 28) in all the 3 sub-group population which indicates that the product has an excellent anti-inflammatory activity starting Day 14 itself and continued to show its good effects even at Day 28, with an exception of asymptomatic and healthcare workers in both the active treatment groups when compared to the control group C. Lymphocyte Count also shows a similar trend.. The antibodies, Immunoglobulin A (IgA) values, are the key players in COVID-19 and primary contacts, and in this study the results are clear that the antibodies have been increased in all the 3 sub-groups both the treatment groups (A & B) by Day 28 when compared to that of control group C.

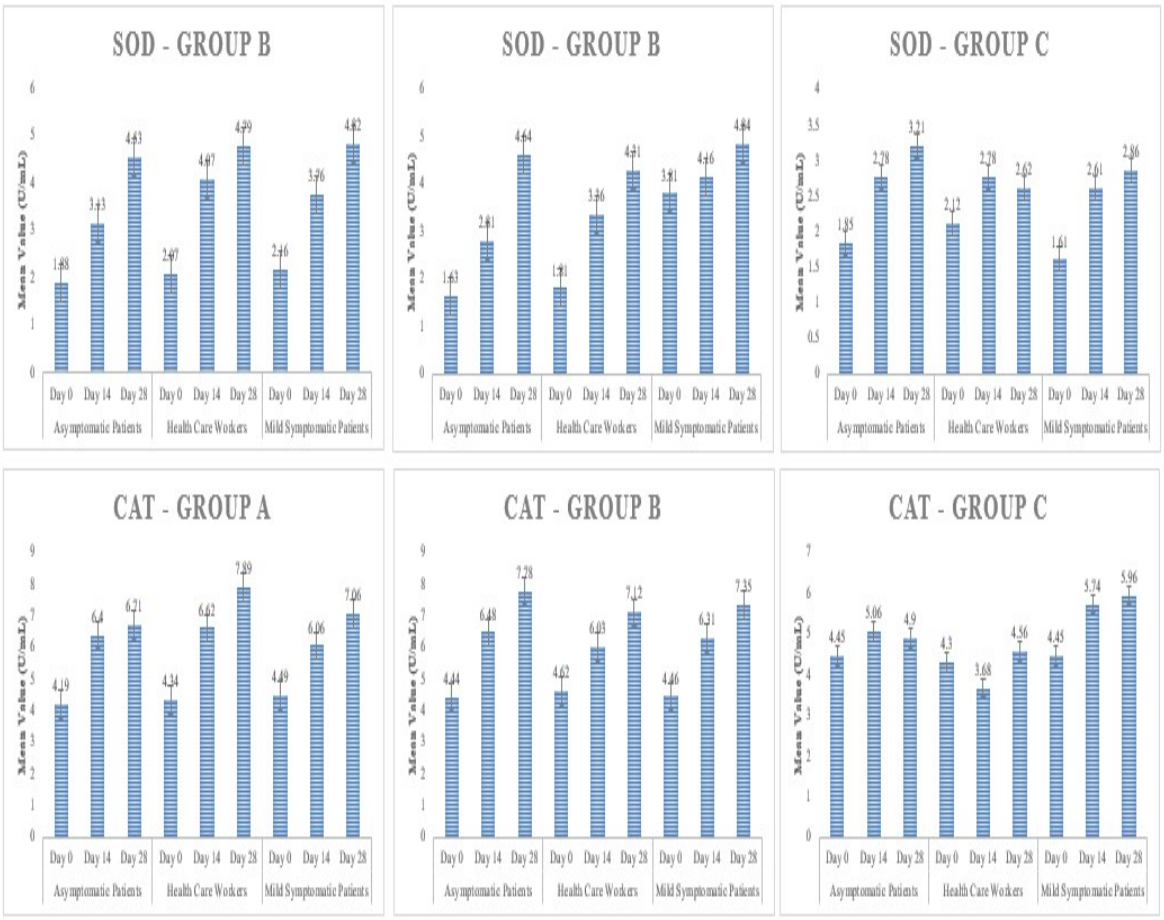

Fig 4.Superoxide Dismutase, Catalase were compared across all the 3 Groups having asymptomatic, healthcare workers and mild symptomatic patients on Day 0, 14 & 28. Superoxide dismutase average values comparison on Day 0, Day 14 & Day 28 for both the treatment groups/arms receiving the 2 study products against the Control Group C. It showed in the 3 sub-groups SOD values increased by Day 14 and continued to increase and reached statistically significant ($p<0.05$) in the Treatment A and B groups Vs Group C, whereas there is no difference in performance between the two Treatment Groups A Vs B even by Day 28 of the study period. Other important antioxidant is Catalase and its average values in the 3 sub-groups across various study visits also exhibits similar positive results with $p<0.05$.

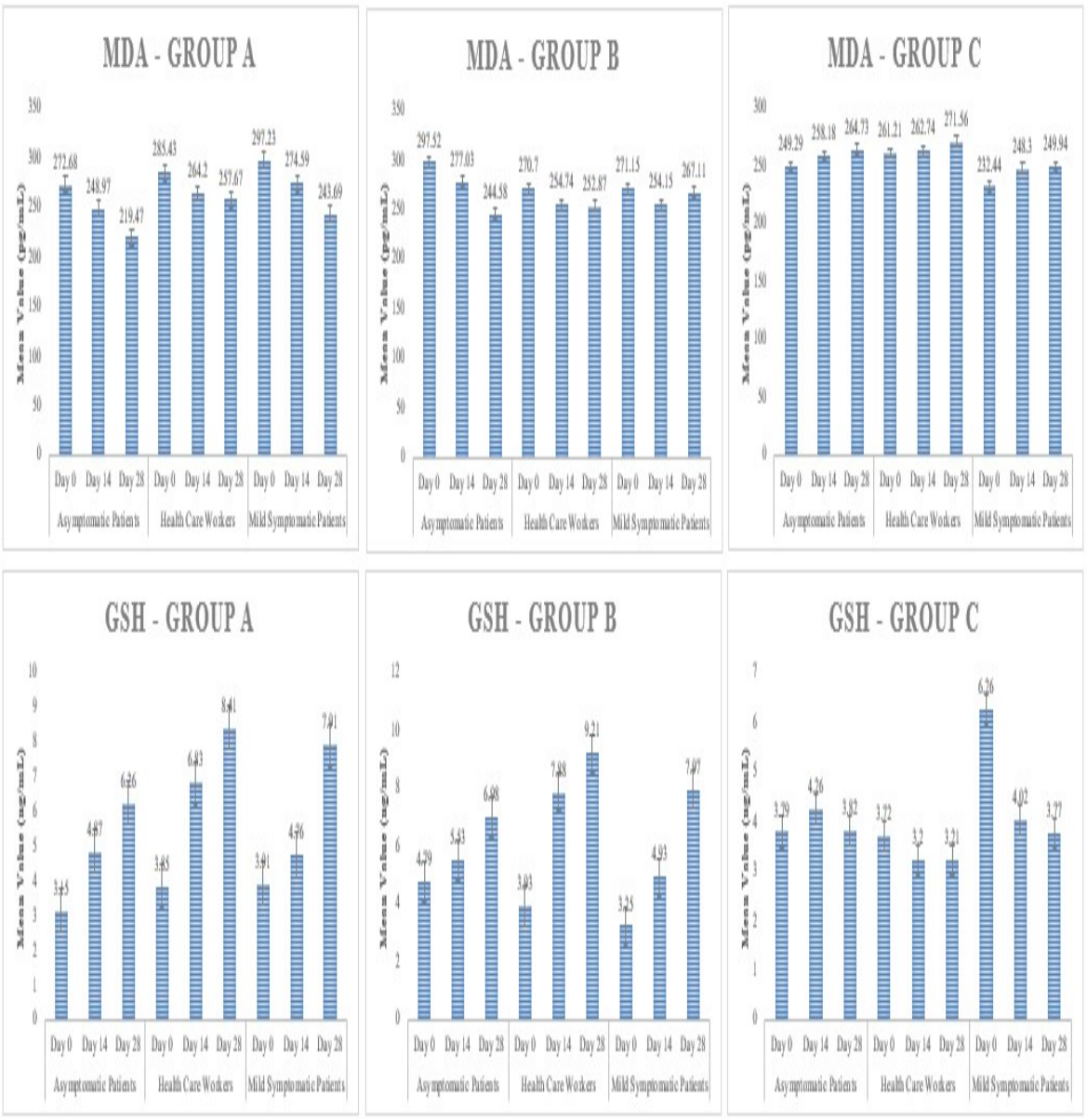

Fig 5.Malondialdehyde, Glutathione was compared across all the 3 Groups having asymptomatic, healthcare workers and mild symptomatic patients on Day 0, 14 & 28. Malondialdehyde (MDA) and its mean values across the study groups indicates that this oxidant marker reduced by Day 14 and further declined by Day 28 between all the 3 sub-groups in both the treatment arms (A & B) when compared with control group C respectively, which is a positive sign from the study product's perspective. One more antioxidant analyzed in this study was Glutathione (GSH) and this marker increased by Day 28 amongst all the groups.

DISCUSSION

In the treatment group A, 8 subjects asymptomatic, 20 were healthcare workers and 12 subjects were mild symptomatic patients. While in the treatment group B, same categories were 8, 23 and 9 in respective sub-groups (Table 2). Sex, age, height, weight, BMI and other demographics were recorded during the screening visit.

The vital signs like heart rate, pulse, respiratory rate, temperature, systolic and diastolic blood pressure were reflected for all the 3 sub-group category of subjects in both the treatment arms (A and B) and found to be normal as throughout the study duration recorded on Day 0 & Day 28.

There were no abnormal values (clinically non-significant) noted in any of the hematology and serum biochemistry parameters and it can be interpreted that the two products (A & B) tested had demonstrated absolute safety in all the three subject sub-groups when tested on Day 0 and Day 28.

Health drinks (Mulmina® Mango and Mulmina®Amla Orange) wherein the herbs, fruit extract and essential agents act synergistically to provide a rich Meso-nutrients contributing Antioxidant and Immune Boosting Property through their high ORAC values. The said health drinks are formulated with a carefully chosen herbs–that are meant to act as anti-inflammatory, immune-boosting and free-radical scavenging agents, the herbs so formulated are combined with a healthy vitamin and mineral rich, anti-oxidant fruit

juices and is fortified with the necessary vitamins and minerals to result in a very tasty drink for good health. The taste factor makes the herbal concoction palatable and hence ensures compliance. Hence these preparations has all the three categories of nutrients namely Macro-nutrients (Carbohydrates, Protein, Dietary Fibres etc.), Micro Nutrients (Vitamins and Minerals), Meso-nutrients (Curcumin, Mangiferin, Asiatic acid, Gallic acid, Naringenin, Hesperidin, Meso/α-β-crypto zeaxanthin, Carotenoids etc.), which are required for the body to perform wellness.

Oxidative stress is encountered by cells after bacterial infection and in a state of inflammation and is in fact part of the primary innate immune defense of the body, including also the well-known oxidative burst of macrophages and monocytes[3]. Also oxidative stress determines structure modifications and function modulation in nucleic acids, lipids and proteins. The imbalance between the oxidant species and the antioxidant defense system may trigger specific factors responsible for oxidative damage in the cell: over-expression of oncogene genes, generation of mutagen compounds, and promotion of atherogenic activity, senile plaque occurrence or inflammation. This leads to cancer, immune disorders, neuro degeneration, cardiovascular, diabetes, and kidney diseases. Hence the formulation is designed to cope up this oxidative stress and to boost immunity.

Immune boosting and anti-oxidant drinks for wellness with particular emphasis as a health promoter. The formulation is meant for general health and well-being with the herbs concerned acting synergistically to provide immune boosting properties and high anti-oxidant benefit without any attenuating side-effects. Cardinal to the invention is the synergistic play between the natural ingredients and meso-nutrients which provide an Immune Boosting Activity and rich Anti-oxidant through its higher ORAC values[5].

Yip et al[6] suggested that Serum Amyloid A (SAA) could monitor the extent of pneumonia in severe acute respiratory syndrome (SARS) and currently, there are few recent reports about the relationship between SAA and COVID-19. One more study[7] confirmed that SAA was more efficient in predicting severity of COVID-19 and SAA serves an important role in inflammation and relates to the severity of inflammation. Cytokines, specifically Interleukins (IL-4, IL-6, and IFN-γ) are found to be elevated in COVID-19 patients and is a good immune marker in predicting the disease progression[8]. Interleukin 4 (IL-4) values between the Treatment Groups suggest that the cytokine values had not changed much from Day 0 through Day 28 (no statistical difference). Interleukin 6 (IL-6) values were kept intact across all the treatment sub-groups in all the arms, indicating that though the harmful cytokines increased by Day 14, they were brought back to control by Day 28 with the study products (to a mild extent) as seen in Fig 2. Average Interferon gamma (IFN-γ) values were mildly reduced in treatment group A amongst all the three sub-groups, whereas in the treatment group B the values decreased drastically in the healthcare workers and mild asymptomatic subjects by Day 28 which implies that the product has a potential role in controlling the dysregulated or imbalanced immune system. Other inflammatory or immune marker that plays a critical role in severe inflammation or infections is C - reactive protein (CRP). Both the study products were able to curtail the elevated CRP values from Day 0 by end of the study (Day 28) in all the 3 sub-group population which indicates that the product has an excellent anti-inflammatory activity starting Day 14 itself and continued to show its good effects even at Day 28, with an exception of asymptomatic and healthcare workers in both the active treatment groups when compared to the control group C. The antibodies, Immunoglobulin A (IgA) values, are the key players in COVID-19 and primary contacts, and in this study the results are clear that the antibodies have been increased in all the 3 sub-groups both the treatment groups (A & B) by Day 28 when compared to that of control group C (Fig 3).

A recent article[9] confirms that the herbal alternative to vaccination, being sources of antioxidant is noteworthy, especially as there has yet to be any approved vaccine (or recently approved) for the corona viruses that caused pandemic since over 10years. The article emphasizes that the immune-compromised status contraindicates about 25% of COVID-19 vaccines being researched. Low immunity could be improved by antioxidants, but contrariwise worsened by side-effects of anti-inflammatories that constitute 52% of drugs currently being developed. In the current study, the 3 sub-groups SOD and CAT values increased by Day 14 and continued to increase and reached statistically significant ($p<0.05$) in the Treatment A and B groups Vs group C, whereas there is no difference in performance between the two Treatment Groups A Vs B even by Day 28 of the study period (Fig 4). MDA and its mean values across the study groups indicates that this oxidant marker reduced by Day 14 and further declined by Day 28 between all the 3 sub-groups in both the treatment arms (A & B) when compared with control group C respectively, which is a positive sign from the study product's perspective. Glutathione (GSH) increased by Day 28 amongst all the groups which indicates strong antioxidant potential of the tested products (Fig 5).

The two products tested (Mulmina® Mango and Mulmina®Amla Orange) have excellent herbal medicinal ingredients like *Curcuma longa, Centella asiatiaca, Emblica officinalis,* Mangiferin, Naringenin, Hesperidin and other essential vitamins & minerals which were proved time and again for their potent antioxidant and immune-boosting activities. Curcumin, one of the most studied is the anti-inflammatory natural component that may be useful in both acute and chronic inflammation[10]. The immunomodulatory abilities of curcumin arise from its interaction with various immunomodulators, including not only cellular components, such as dendritic cells, macrophages, and both B and T lymphocytes, but also molecular components involved in the inflammatory processes, such as cytokines and various transcription factors with their downstream signalling pathways. The modulation of cytokine levels by curcumin has been related to the inhibition of NF-κB signalling pathway[11]. Preclinical studies proved that, Curcumin significantly attenuates endotoxin induced release of NO and pro-inflammatory cytokines, as well as iNOS expression and NF-κBactivation[12]. These anti-inflammatory effects have been demonstrated to be mediated by iNOS, COX-2, HO-1, MAPK and NF-κB, thus suggesting that curcumin plays an important role in the attenuation of inflammatory responses[13]. Curcumin is an extremely potent lipid soluble antioxidant and has been suggested to act through its pro-oxidant/antioxidant effects, because, formation of ROS by curcumin and curcuminoids correlates with their apoptotic activity on tumour cells. The free radical scavenging activity of curcumin can arise either from the phenolic OH group or from the CH2 group of the β-diketonemoiety[14].

Mangiferin is a naturally occurring xanthone glucoside and it is found widely distributed in plants and preclinical studies proved its antioxidant and immune boosting activities[15]. Mangiferin found to play immunoprotective role mediated through the inhibition of reactive intermediate-induced oxidative stress in lymphocytes, neutrophils and macrophages[16].Centella asiatica L. is important herbal medicinal plant used for various applications and used in Indian ayurvedic medicine as a nerve tonic[17]. Utilization of Centella asiatica have been known for many years in treating all kind of diseases such as gastrointestinal disease, gastric ulcer, asthma, wound healing and eczema[18]. The use of Centella in food and beverages has increased over the years basically due to its health benefits such as antioxidant, as anti-inflammatory, wound healing, memory enhancing property and many others. The potential of Centella as an alternative natural antioxidant especially of plant origin and its protection against age-related changes in brain antioxidant defense system, have notably increased in recent years[19]. Mulmina® Mango composed of *Curcuma longa* and *Centella asiatica* has exhibited antioxidant and immune boosting properties in the present trial on COVID-19 confirming the benefits of these ingredients.

Mulmina®Amla Orange health drink is composed of Orange and Amla extracts. Amla is a powerful super fruit loaded with vitamin C, vitamin B complex and many essential minerals known as excellent antioxidant and immunity booster. It has been reported that amla protects against the harmful action of free radicals and exhibit its ameliorating effects in biological system[20, 21]. It is also reported that the antioxidant potential of amla may be due to the presence of many phyto-constituents, which provide maximum conjugation with free radical species, thus reducing the number of free radicals available and the extent of cellular damage[22]. It is also reported that immunosuppressive effects on lymphocyte proliferation has been ameliorated following treatment with amla and it also restored the altered levels IL-2 and IFN-γ proving its immune modulatory potential[23]. Orange contains a high amount of antioxidant compounds, such as polyphenols and vitamins. Orange majorly comprises of vitamin C, which is known for its antioxidant activity and also to boost immunity. In the present trial, treatment with Mulmina®Amla Orange health drink has elevated the antioxidant levels in COVID-19 patients and also helping them in the maintenance of health immune health. Present study results established these traditional ingredients once again for their excellent antioxidant properties and therefore mild immune-potentiating effects that played vital role in COVID-19 patients by boosting their immunity.

The feedback questionnaires from the study subjects' gave a very positive note on the product smell and taste and therefore the compliance to its usage during the study period was 100%. None of the subjects had missed the product during the course of the study duration implying that the product is liked by all the study participants.The protocol was amended once during the course of trial execution, as per which 40 additional subjects, receiving standard treatment of care for COVID-19, was included and served as a control group. The IEC has been duly notified with this protocol amendment. We find that lack of control arm receiving SoC treatment alone is the limitations for this study. A randomized, double blind, placebo controlled with SoC treatment arm would have given more insights about the trial.

CONCLUSION

The efficacy assessments both from immune and antioxidant parameters prove that the 2 products under investigations, Mulmina® Mango and Mulmina®Amla Orange, have potential immune boosting and anti-oxidant activities. Physician's assessment also reiterates the same results. From the study results it can be concluded that the products Mulmina® Mango and Mulmina®Amla Orange are completely safe for oral administration with good tolerability and also excellent immune boosting & anti-oxidant activities.

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DECLARATION

We wish to confirm that there are no known conflicts of interest associated with this publication and there has been no significant financial support for this work that could have influenced its outcome. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

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