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EFFECT OF SUPPLEMENTAL ANTIOXIDANT-BASED THERAPY ON THE OXIDATIVE STRESS LEVEL IN COVID-19 PATIENTS

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ABSTRACT

Background: COVID-19 is a disease in several stages starting with virus replication to dysregulation in immune system response, organ failure and recovery/death. Our aim was to determine the effect of Ganoderma lucidum, lycopene, sulforaphane, royal jelly and resveratrol extract on markers of oxidative stress, inflammation, routine laboratory analyses and duration of symptoms in COVID-19 patients.

Methods: The oxidative stress parameters and interleukines 6 and 8 (IL-6, IL-8), tumor necrosis factor alpha (TNF-α) were determined in order to estimate the antioxidant and the anti-inflammatory effect of the product using a spectrophotometric and a magnetic bead-based multiplex assay in serum of 30 patients with mild form of COVID-19.

Results: Statistically significant differences were obtained for all investigated parameters between the treated patients and the control group. Moreover, significant differences were observed for leukocytes, neutrophil to leukocyte ratio and iron. The average duration of the symptoms was 9.4±0.487 days versus 13.1±0.483 days in the treatment and the control group, respectively (p=0.0003).

Conclusion: Our results demonstrated the promising effect of Ge132+Natural™ on reducing the oxidative stress and the IL-6, IL-8 and TNF-α levels, and symptoms duration in COVID-19 patients. The evidence presented herein suggest that the combination of Ganoderma lucidum extract, lycopene, sulforaphane, royal jelly and resveratrol could be used as a potent an adjuvant therapy in diseases accompanied by increased oxidative stress and inflammation.

Keywords: oxidative stress, anti-inflammatory, Ge132+ Natural™, Ganoderma lucidum, lycopene, sulforaphane, royal jelly, resveratrol, COVID-19

INTRODUCTION

The SARS-CoV-2 virus is responsible for the development of COVID-19, an infectious-inflammatory disease that has so far affected over 400 million people globally, with over 5 million deaths. The largest number of deaths, approximately 73%, is among those over 65 years of age [1].

Laboratory tests in COVID-19 patients showed abnormalities associated with the so-called cytokine storm presented elevated values of systemic inflammatory parameters such as: C-reactive protein (CRP), ferritin, bradykinin, interferon gamma, tumor-necrotizing factor alpha, interleukins as well as high neutrophil-lymphocyte ratio (NLR). The cytokine storm occurs as a result of activation of the inflammatory signal cascade which results in hypercoagulation in the small blood vessels, leading to tissue damage as well as systemic failure of vital organs. Elevated D-dimer values, a prognostic marker for disseminated intravascular coagulation, and elevated interleukin-6 (IL-6) values are associated with an increased risk of fatal outcome. This condition is accompanied by an increased level of systemic oxidative stress. In patients with a severe clinical picture, the high value of NLR is associated with extremely high levels of reactive oxygen radicals. Angiotensin converting enzyme-2 (ACE-2) dysfunction (reduced levels due to SARS-CoV-2 infection) also contributes to the formation of reactive oxygen radicals [2-8].

In addition to the above, the data from our previous research indicate that vitamin D deficiency was observed in patients with COVID-19, accompanied by increased oxidative stress index in the severe group of patients. Oxidative stress index also showed a good correlation with the cytokine profile (IL-2, IL-4, IL-6, IL-8, IL-10, vascular endothelial growth factor (VEGF), interferon gamma (IFN-γ), tumor necrosis factor alpha (TNF-α), IL-1α, monocyte chemoattractant protein 1 (MCP-1) and endothelial growth factor (EGF)) in COVID-19 patients with the severe form of the disease [9-11]. The application of natural components, vitamins and minerals, as a promising supportive therapy, for the reduction of the existing inflammation and oxidative stress in COVID-19, is of great global interest.

With a proper literature survey, copious data from studies conducted in order to investigate the efficacy of sulforaphane, medicinal mushrooms, melatonin, vitamin D, zinc, vitamin C, acetylcysteine, resveratrol, propolis, elderberry, barberry, etc., on viral infections including COVID-19 disease can be found [12–34].

Cuadrado et al., suggest that the antioxidant and cytoprotective effects of nuclear factor erythroid 2 related factor 2 (Nrf-2) activators such as sulforaphane are long-lasting and persist for several days after its elimination, providing robust cytoprotection by restoring redox and protein homeostasis, promoting resolution of inflammation and rapid healing in COVID-19 patients due to its cytoprotective and anti-inflammatory effects [15].

Different research groups provide in vitro evidence that resveratrol shows potent antiviral properties suggesting its efficacy in reducing inflammatory cytokine levels, oxidative stress, regulating ACE-2 receptors and improving the immune response [20-25].

The reishi mushroom has a proven antiviral effect against some RNA and DNA viruses through the protective action of cells by increasing CD4+ T lymphocytes subsets [26]. Its use in COVID-19 patients is discussed by some authors as a natural strategy for reducing duration and severity of respiratory tract infections [27-30].

Habashi et al., prove a vital interaction between royal jelly proteins, i.e., its X1 isoform with the vital SARS-CoV-2 protein. These proteins are thought to be effective in preventing SARS-CoV-2 cell binding to ACE-2 receptors through their sialidase activity and can prevent viral complications in the lungs (hypoxia) [31].

Based on the available scientific research that confirms the immunomodulatory and antiviral properties of several natural substances, given their long history of use, we believe that the use of similar components can provide benefits to COVID-19 patients in terms of reducing oxidative stress, and thus the inflammatory response as part of the pathogenesis of this disease, which would reduce tissue damage and reduce the possibility of disease progression to severe form or death. Until now, the available data dealing on this topic generally came from review articles or several in vitro studies, and only a limited number of in vivo studies.

Hence, in order to prove the concept in vivo, we have chosen a product that is a combination of reishi mushroom extract (Ganoderma lucidum), royal jelly, sulforaphane, resveratrol and lycopene

with previously in vitro proven antioxidant and immunomodulatory effect. We have conducted an observational study with a goal to determine the effect of the product (combination of Ganoderma lucidum extract, lycopene, sulforaphane, royal jelly and resveratrol) on oxidative stress markers, inflammatory cytokines (IL-6, IL-8 and TNF-α), routine laboratory parameters and duration of symptoms in patients with mild form of SARS-CoV-2 infection.

MATERIAL AND METHODS

2.1. Study design and patients

This was an open-label study carried out from November 2021 to January 2022 with ambulatory male and female patients diagnosed with COVID-19 at the University Clinic for Infectious Diseases and Febrile Conditions, Skopje, Republic of North Macedonia. The flow chart of the study is shown in Figure 1. The inclusion criteria were: infection with SARS-CoV-2 confirmed by real-time reverse transcriptase-polymerase chain reaction assay (RT-PCR) from nasal and pharyngeal swab specimen or with rapid antigen test, older than 18 years with presence of COVID-19 symptoms. The exclusion criteria included COVID-19 vaccination, positive history of allergic reaction to pollen and/or to any of the components in the dietary supplement, use of Ganoderma lucidum extract, royal jelly, sulforaphane, resveratrol and/or lycopene in the past three months, patients with clinically significant immunodeficiency conditions (organ transplantation, use of immunosuppressive drugs, etc.), patients with clinically significant liver or kidney disease, with active malignant disease, for female patients - pregnancy or lactation, patients receiving anticoagulants (e.g., warfarin, acenocoumarol), patients with a history of drug and/or alcohol abuse in the past 12 months or participation in other clinical studies in the past two months. All patients were symptomatic, but without evidence of viral pneumonia or hypoxia, thus classified as mild according to the guideline of World Health Organisation for clinical management of COVID-19.

In this study, 30 patients (15 males and 15 females) were enrolled in the treatment group and the control group was consisted of 15 ambulatory COVID-19 patients (8 males and 7 females) who were not treated with the product.

After signing the informed consent form, anthropometric data (weight, height) and medical history (previous illness, medications, concomitant therapy) was obtained from each patient. Additionally, the patients used a diary during the treatment in order to obtain data about their nutritional intake. Medical doctors contacted the patients by telephone to check on any health changes between the hospital visits and to confirm the regular intake of the product. Duration of symptoms of patients who received the product (Ge132+ Natural™) was compared with the patients who were not treated (control group). Blood samples were taken for routine laboratory analysis (differential blood count, ferritin, cholesterol, triglycerides, bilirubin, urea, creatinine, glucose, ALT, AST, LDH, CK, iron, CRP, D-dimer), as well as for measurement of oxidative stress parameters and inflammation markers on admission and after 15 days of treatment.

2.2. Treatment and study product

All patients (30) in the treatment group received two capsules per day of Ge132+ Natural™, formula for adults which contains the extract of

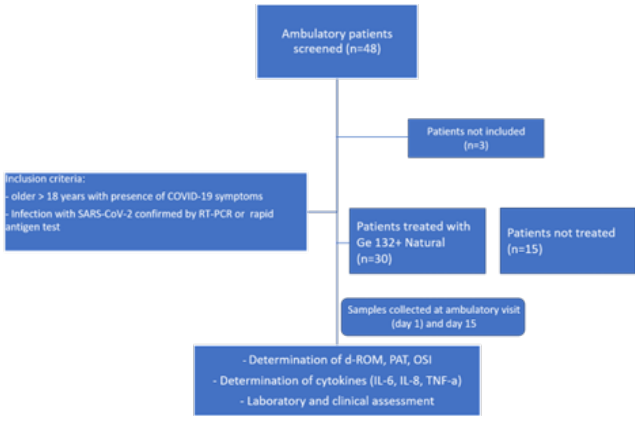


Figure 1. *Flow-chart of the study*

Ganoderma lucidum (180 mg), royal jelly (160 mg), resveratrol (100 mg), tomato extract (lycopene, 35 mg) and sulforaphane (25 mg) per capsule, for a period of 15 days. According to the manufacturer (Alphacaps GmbH, Germany), this product was formulated in Japan and is completely natural, free of preservatives, medicines and heavy metals. The analysis of the results was done independently by researchers outside of the investigators team.

2.3. Methods for determination of oxidative stress parameters and cytokines

Total antioxidant power, iron reducing (PAT) and plasma peroxides (d-ROMs) were measured using FRAS5 analytical photometric system and are reported in equivalents of ascorbic acid and H_2O_2, respectively. The oxidative stress index (OSI) was automatically calculated by the software (OB manager, FRAS5, H&D, Parma, Italy) with the normal reference range up to 40 given by the manufacturer.

Quantitative detection of IL6, IL8 and TNF-α in the patients' serum samples was performed using magnetic bead-based multiplex assay (R&D Systems, Minneapolis, MN USA) and the fluorescence was read using Luminex 200™ analyzer.

2.3. Statistical analyses

Data were presented as a number or mean with standard errors of mean (SEM). In order to investigate the differences between groups t-test was used. P-values less than 0.05 were considered as statistically significant. Analyses were performed using statistical program GraphPad Prism 9 (USA).

RESULTS

3.1. Patient characteristics and laboratory findings

All included patients in the study had a mild form of COVID-19. The mean age in the treatment group was 40.13±2.83 years and the mean age for the control group was 42.6±3.81 years ($p>0.05$). The most prominent and disturbing symptoms reported by the patients on admission were increased body temperature (62.2%), malaise (57.1%), nasal congestion (42.8%), headache (28.6%) and cough (54.76%). Abnormal values were observed for CRP and glucose, 16.97±4.884 mg/L and 6.057±0.1509 mmol/L, respectively. The other clinical parameters used for classification of COVID-19 patients were in the range of the normal values but either on lower or higher side of the range which is expected since these patients had mild form of the disease and their follow-up was in the outpatient facility. Namely, WBC were 5.817 x 103±0.28 mL, iron 9.363±0.9426 mmol/L, D-dimers 433.4±60.14 ng/mL, LDH 204.3±10.31 U/L and NLR 2.619±0.2919. The laboratory values of the control group at their initial visit were comparable to the treatment group. Namely, the mean values of all clinical laboratory parameters are presented in Table 1a and Table 1b. None of the patients had disease deterioration and none of them were hospitalized. Additionally, no adverse

Table 1a. *Hematological laboratory parameters of ambulatory COVID-19 patients treated with Ge132+ Natural™ (n=30) and control group (n=15) (Mean ± SEM).*

Parameter	Pre-treatment	Post-treatment, (15 days)	Control	Control (15 days)	Reference values
Hemoglobin	145.5±2.61	143.4±2.563	140.6±5.593	138.56±6.689	115-180 g/L
RBC	4996±83.58	4946±95.33	5226±173.4	5208±219.2	4000-5500 x10^3 µL
WBC	**5.817±0.28**	**7.66±0.4336**	6.011±0.6029	**9.925±1.285**	4.0-11.0 x10^3 µL
PLT	228.7±10.15	328.5±18.59	217.6±27.42	272.8±20.14	150-400 x10^3 µL
HCT	0.4627±0.006	0.4203±0.006	0.4244±0.014	0.415±0.0162	0.35-0.50
Neutrophil	0.559±0.021	0.5762±0.02	0.5822±0.451	0.6175±0.034	0.40-0.70
Lymphocyte	0.295±0.017	0.3145±0.0164	0.2956±0.0425	0.2725±0.327	0.21-0.25
Monocyte	0.1337±0.008	0.0927±0.0046	0.1056±0.0123	0.0875±0.006	0.02-0.10
Eosinophils	0.012±0.002	0.0165±0.002	0.0166±0.0071	0.0215±0.003	0.01-0.06
NLR	**2.619±0.2919**	**1.904±0.1375**	2.663±0.6768	**2.725±0.1716**	< 3.0

***Bold**, $p<0.05$ between pretreatment and post treatment; **bold and underlined**, $p<0.05$ between post treatment and control after 15 days

Table 1b. *Clinical biochemistry parameters of ambulatory COVID-19 patients treated with Ge132+ Natural™ (n=30) and control group (n=15) (Mean ± SEM).*

Parameter	Pre-treatment	Post-treatment, (15 days)	Control	Control (15 days)	Reference values
Triglycerides	1.198±0.1495	1.552±0.1158	1.515±0.1406	1.47±0.302	0.2-2 mmol/L
Cholesterol	4.31±0.1337	4.98±0.21	4.311±0.2997	5.089±0.228	3.1-5.2 mmol/L
Ferritin	146.6±20.47	112.3±16.79	103.1±21.35	78.77±21	males:20-274 ng/ml females:10-204 ng/ml
Bilirubin	6.962±0.9837	8.786±0.773	7.25±2.33	6.5±1.746	0-20 □mol/L
Direct bilirubin	1.769±0.2735	2.321±0.2245	2±0.866	1.667±0.494	0-5 □mol/L
Indirect bilirubin	5.2969±0.1737	6.429±0.5621	5.25±1.719	4.833±1.276	0-15 □mol/L
Urea	3.473±0.1718	4.007±0.2489	3.133±0.3223	4.138±0.4238	1.7-8.3 mmol/L
Creatinine	61.54±3.224	63.72±2.753	61.44±4.35	65.71±5.384	62-133 µmol/L
Glucose	**6.057±0.1509**	**5.5±0.1158**	5.833±0.1247	5.4±0.1138	3.9-5.6 mmol/L
ALT	25.93±4.686	20.17±1.794	20.89±4.489	23.75±3.255	10-52 U/L
AST	23.03±2.667	18.41±0.866	20.89±2.557	18.5±1.427	10-47 U/L
LDH	**204.3±10.31**	**175.6±8.252**	208.7±20.08	172.3±9.017	120-246 IU/mL
CK	68.63±5.264	65.28±7.826	62.56±10.88	65.88±13.74	30-170 U/L
Iron	**9.363±0.9426**	**20.69±1.384**	11.22±2.328	**13.59±2.598**	6.6-32.4 mmol/L
CRP	**16.97±4.884**	**2.55±0584**	23.33±11.1	4±1.118	0-10 mg/L
D-dimer	433.4±60.14	367.8±39.87	370.3±42.8	324.8±74.36	0-500 ng/mL

***Bold**, p<0.05 between pretreatment and post treatment; **bold and underlined**, p<0.05 between post treatment and control after 15 days

Table 2. *Mean values of oxidative stress markers and serum cytokines in ambulatory COVID-19 patients treated with Ge132+ Natural™ for 15 days.*

Parameter	Pre-treatment (n=30)	Post treatment (n=30)	p –value (t-test)
d-ROM (U.Carr)	416±14.67	315.5±10.98	0.0001
PAT (U.Carr)	2933±90.41	2827±81.23	0.3860
OSI	87.40±6.619	37.70±4.452	0.0001
IL-6 (pg/mL)	2.767±1.118	0.4527±0.0	0.00291
IL-8 (pg/mL)	10.87±0.768	2.809±0.353	0.0001
TNF-α (pg/mL)	4.354±0.417	1.027±0.071	0.0001

events were reported by the patients during the treatment with the product.

3.2. Effect of Ge132+ Natural™ treatment on oxidative stress markers and serum cytokines

The results of this observational study suggest that adjuvant treatment with Ge132+ Natural™ could lead to attenuation of oxidative stress and inflammation. The results presented in Table 2 show that the parameters of the oxidative stress d-ROM (416±14.67 U.Carr) and OS index (87.40±6.619) were significantly higher (p<0.05, t-test) before treatment when compared to the post treatment values. Moreover, the investigated cytokines were significantly lower after an intervention of 15 days (p<0.05, t-test). Statistically significant differences were obtained for all investigated parameters presented in Figure 2.

3.3. Effect of Ge132+ Natural™ treatment on laboratory parameters and duration of symptoms

After the treatment period of 15 days, significant differences between the levels of the markers used to follow up the disease were observed, such as, LDH (p=0.0351), NLR (p=0.0369), leukocytes (p=0.007), iron (p<0.0001), CRP (p=0.0056) and glucose (p=0.0051). The control group demonstrated no significant differences in the clinical parameters, except for leukocytes which increased after 15 days (6.01±0.6029 versus 9.925±1.285, p=0.0120). By comparison between the treatment and the control group,

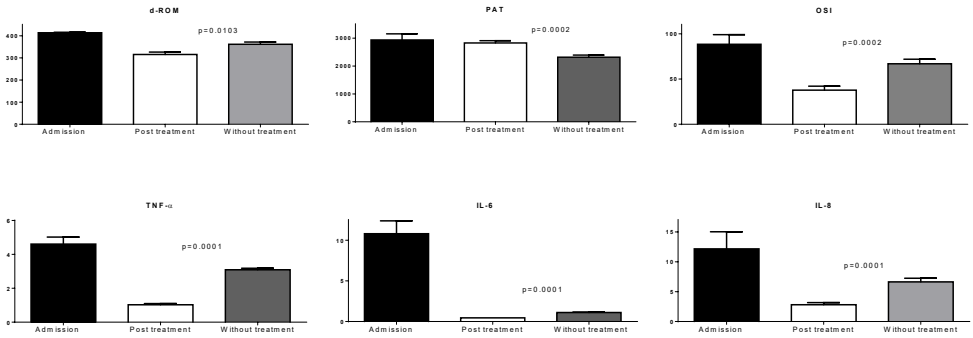


Figure 2. *Effect on Ge132+ Natural™ on the investigated parameters in ambulatory COVID-19 patients (at admission, n=45). Comparison between treated patients (n=30) and patients without treatment (n=15).*

significantly differences were observed for leukocytes (p=0.0392), NLR (p=0.0047) and iron (p=0.0266). The average duration of the symptoms was 9.4±0.487 days versus 13.1±0.483 days in the treatment and the control group, respectively (p=0.0003).

DISCUSSION

In general, the present study shows that daily consumption of Ge132+Natural™, a mixture of five natural components (*Ganoderma lucidum* extract, lycopene, sulforaphane, royal jelly and resveratrol) during infection with SARS-CoV-2 is effective in reducing the oxidative stress and inflammation. The mild form of COVID-19 was chosen because it can be considered a model of acute inflammatory disease where the potential effects of the investigated product can be evaluated without significant interference of other concomitant therapies which are administered more frequently with the severe form of the disease.

This is in line with one previously published paper for in vitro analyses of the antioxidant activity of Ge132+ Natural™, where authors suggested that this formula may contribute to the maintenance of the physiological levels of free radicals and redox balance in the body [34]. On the other hand, the in vitro effect of Ge132+ Natural™ on IL-6, IL-8 and TNF-α cytokine release in lipopolysaccharides treated primary human monocytes shows that this formula has a strong anti-inflammatory potential and thus can be useful in the treatment of diseases with an inflammatory background (unpublished results from Viva-Cell biotechnology GmbH) [35]. The generation of oxidative stress and inflammation after infection with SARS-CoV-2 was the subject of investigation in our previously published papers, and almost the same results were obtained here, compared to healthy non-infected individuals where the normal ranges were: d-ROM (266±12.3), PAT (2554±76.74), OSI (36±4.1) IL-6 (1.25±0.213 pg/mL), IL-8 (6.954±1.201 pg/mL) and TNF-α (1.956±0.353 pg/mL) [9-11]. In this study, the anti-inflammatory effect of the combined product is evidenced by the normalization of IL-6, IL-8 and TNF-α values after the treatment, which is not the case in the control group where more time was needed for normalization of the cytokine levels. Namely, in the control group, IL-6 and IL-8 were normalized on the upper level of the normal values, but more than two-fold in comparison to the patients that used Ge-132+ Natural™. TNF-α was still increased after 15 days in the patients that did not use the product as adjuvant therapy. Our results are in agreement with some recently presented evidence, showing that sulforaphane inhibits the expression of IL-6 and IL-8 in bronchial epithelial IB3-1 cells when exposed to SARS-Cov-2 spike protein[16], and it improves the immune system response [17-19]. In terms of some of the components present in the product, Ho *et al*. [36] have discussed Ganoderma lucidum elicited antiviral activities against SARS-CoV-2 by interfering virus binding to host cells and spike mediated cell fusion and this has been approved by the Food and Drug Administration (FDA) as dietary substances.

Published reviews discuss that these components have both antioxidant and anti-inflammatory effects. Among them, Andric *et al*. [37]

have summarized that the antiviral, antioxidant, antibacterial, anti-tumor, antifungal, anti-inflammatory and neuroprotective activity of *Ganoderma lucidum* can be attributed mainly due to the high content of polysaccharides and can be used as a potential treatment in COVID-19. Ordonez *et al*. [38], have used experimental model of K18-hACE2 mice treated with sulforaphane, prior SARS-CoV-2 infection, as prophylactic agent, where reduced pulmonary and lung changes were observed. In order to reduce the clinical effects of COVID-19, McCreary *et al*. [39], performed a randomized double-blind placebo-controlled trial with resveratrol in patients with a mild form of the disease. In this study, better response in the clinical endpoints were observed when resveratrol was included in the treatment as soon as possible after viral infection. In this line, Brummelen et al. [40], comment on the well-known antioxidant capacity of resveratrol and its part in immune stimulation, down regulation of pro-inflammatory cytokines expression and its role in decreasing the oxidative stress that further results in reduced lung injury. Lycopene as part of the studied substances in the product of interest, also has anti-inflammatory and antioxidant effects. Khongthaw *et al*. [41] presented that lycopene reduced intestinal damage and immunoglobulin A depletion, as well inhibition of pro-inflammatory cytokine and chemokine production in severe COVID-19 patients leading to reduced inflammation. Considering the scientific data regarding the above-mentioned components and their long history of use as functional foods, sharing similar mechanisms for exerting their antioxidant and anti-inflammatory activity, we believe that a potential synergism exists between the components of the product in this study. Herein, we have shown in vivo evidence for the first time that this mixed combination as a single product has beneficial effect in ambulatory patients with COVID-19. Namely, the oxidative stress index and the d-ROMs as oxidative stress markers were significantly increased at the beginning of the disease in the treated and the control group. However, the patients who were treated with Ge132+ Natural™ have demonstrated faster reduction of the free radicals concentration and hence the oxidative stress index when compared to the patients who did not use Ge132+ Natural™ as adjuvant therapy. Moreover, the level of the total antioxidant capacity (PAT) in the control group was significantly decreased compared to the treated group. We can most likely attribute this to the decreased antioxidant reserve and the need to take an additional pool of specific antioxidants (physiological modulators). Royal jelly, together with other bee products, can respond effectively against SARS-CoV-2 because of its antiviral, anti-inflammatory properties and its effect on the stimulation of the innate and adaptive immune responses [32,33]. Our results support these findings as our control group has elevated leukocytes (close to the upper reference limit), slightly increased neutrophils and decreased lymphocytes, hence increased NLR, as one of the most important markers of disease progression. This could reflect the possible antiviral and antimicrobial activity of Ge132+ Natural™. Moreover, iron levels are reduced during viral infections, and after the treatment period they were restored faster in the treated group as compared to the control group.

This study has some limitations such as the small sample size and the possibility to investigate the product in patients with mild form of COVID-19, only. However, the power of prediction has shown promising results for future confirmation in larger population. Also, it would be of great interest to evaluate if a longer duration of treatment could have additional benefits in the treatment of this disease.

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Institutional Review Board Statement: The study was conducted in accordance with the Declaration of Helsinki and The Ethical Committee of the Medical faculty, Skopje, Republic of North Macedonia approved this study (No 03-4731/6).

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: Not applicable.

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Conflicts of Interest: Part of this work has been presented as a poster at the Redox Biology Congress, Ghent, Belgium held in August 2022.

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Резиме

ЕФЕКТИ НА ДОПОЛНИТЕЛНА АНТИОКСИДАТИВНА ТЕРАПИЈА ВРЗ НИВОТО НА ОКСИДАТИВЕН СТРЕС КАЈ ПАЦИЕНТИ СО КОВИД-19

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Цели: КОВИД-19 е болест што може да поминува низ неколку стадиуми, започнувајќи со вирусна репликација, па сè до дисрегулација на системскиот имунолошки одговор, органска слабост и заздравување/смрт. Целта на оваа студија беше да се утврди ефектот на екстракт од Ganoderma lucidum, ликопен, сулфорафан, матичен млеч и ресвератрол врз параметрите на оксидативниот стрес, инфламаторните маркери, рутинските лабораториски анализи и времетраењето на симптомите кај пациенти со КОВИД-19.

Методи: Параметрите на оксидативниот стрес (d-ROM, PAT, OS индекс) и IL-6, IL-8, TNF-α беа определени со цел да се евалуира антиоксидативниот и антиинфламаторниот ефект на препаратот со употреба на спектрофотометриски и мултиплексен метод базиран на магнетни гранули во серум од 30 пациенти со лесна форма на КОВИД-19.

Резултати: Статистички сигнификантна разлика беше добиена за сите истражувани параметри меѓу третираната и контролната група. Дополнително, значајна разлика беше утврдена за бројот на леукоцити, односот неутрофили/леукоцити и серумското железо. Просечното времетраење на симптомите беше 9,4 ± 0,487 дена во третираната група наспроти 13,1 ± 0,483 дена во контролната група ($p = 0,0003$).

Заклучок: Нашите резултати покажаа поволен ефект на препаратот Ge132+ Natural™ во намалување на оксидативниот стрес и вредностите на IL-6, IL-8 и TNF-α, како и на времетраењето на симптомите кај пациентите со КОВИД-19. Презентираните резултати сугерираат дека комбинацијата од екстракт на Ganoderma lucidum, ликопен, сулфорафан, матичен млеч и ресвератрол би можела да се користи како адјувантна терапија кај болестите придружени со зголемен оксидативен стрес и инфламација.

Клучни зборови: оксидативен стрес, Ge132+ Natural™, Ganoderma lucidum, ликопен, сулфорафан, матичен млеч, ресвератрол, КОВИД-19