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Efficacy and Tolerance of Thymus Vulgaris Extract in Patients with Covid-19

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ABSTRACT

The coronavirus disease 19 (COVID-19) has been a pandemic since February 2020. So far, no effective treatment has been found. WHO has recommended research on medicinal plants as an alternative treatment course. Several studies conducted on *Thymus vulgaris* have established its antioxidant, antiviral and immunomodulatory properties that induce the elimination of viruses such as Herpes simplex Virus 1 and 2. Following this, we initiated a study entitled Efficacy and tolerance of *Thymus vulgaris* extract in patients with coronavirus 2019.

Material and method: *Thymus vulgaris* powder was used in this study. A consent letter and a questionnaire about the patients' symptoms were prepared to be used by a research investigator. According to the statistical calculations of this cohort study, 161 patients testing positive for COVID-19 PCR were consecutively recruited, of which 75 patients were not exposed to *Thymus vulgaris* and 86 patients were exposed. Information from the questionnaire was gathered from the patients before the initiation of conventional treatment (vitamin C 1000 1 tablet/day, Zinc 20 mg 1tablet/day, Azithromycin 500 1cp day and amoxicillin/clavulamic acid 1g/125 1 tablet per 12 hours for six days in both cohorts) and by combining *Thymus vulgaris* (1 teaspoon, i.e. 5g, in 100 ml of hot water to be taken every 8 hours) by the patients in the exposed cohort. After three days of this treatment, the evaluative part of the questionnaire was completed to assess the impact of taking or not taking *Thymus vulgaris* on early symptoms and tolerance; on the 10th day after the start of treatment, the PCR control test was carried out. Thereafter, the various statistical analyses were performed.

Results: Statistical evaluation after three days of treatment shows that taking *Thymus vulgaris* has a statistically significant positive effect on cough ($p < 0.01$), dyspnoea ($p < 0.001$), dizziness ($p < 0.029$), fatigue ($p < 0.001$), anorexia ($p < 0.001$), chest pain ($p < 0.001$), fever ($p < 0.024$), agueusia ($p < 0.029$) and anosmia ($p < 0.001$). There was a significant decrease in neutrophils ($p < 0.01$); in addition, the lymphocyte count increased significantly ($p < 0.001$) as did the serum calcium level ($p < 0.03$). Blood urea level decreased significantly ($p < 0.01$). Significant negative results of the COVID-19 PCR were obtained at Day 10 in the exposed group ($p < 0.001$). In addition, there was no significant change in other biological parameters such as creatinine, blood glucose, aspartate amino transferase.

Conclusion: Results of this study show that the use of the powder of *Thymus vulgaris*, a medicinal plant, with antioxidant, immunomodulatory and antiviral properties, was very effective on coronavirus-induced symptoms and virus elimination. Moreover, there was good tolerance after taking *Thymus vulgaris*.

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Introduction

Coronavirus was first identified in 1960 [1]. Between 2002 and 2003, more than 8,000 people were infected and 774 deaths were recorded as a result of Severe Acute Respiratory Syndrome (SARS) [2]. In 2019, the new generation of Coronavirus Disease 19 (COVID-19) induced Severe Acute Respiratory Syndrome (SARS Cov -2) [3]. In 2020, there was a resurgence of the virus affecting millions of people worldwide. The virus brings about flu-like symptoms with the potential to induce similar severe acute respiratory syndrome and other symptoms such as agueusia, anosmia, fatigue, dyspnoea, cough etc [4]. Africa is also contaminated, with many different types among its regions In the absence of a universal treatment protocol, general measures and methods are used to treat the symptoms and try to eliminate the virus according to the recommendations of WHO, which has focussed on training in clinical management [5]. In addition, WHO recommends and encourages scientific research into therapeutic avenues that can contribute to better managing this pandemic. One of the research avenues is pharmacopoeia. Plants are rich in chemical components that can reduce the pathogenicity of the virus by neutralising it through contact or by inhibiting intracellular replication [6,7]. One of the plants that should be investigated for its efficacy in preventing and treating the novel corona virus is *Thymus vulgaris*. This edible plant contains components such as polyphenols, tannins, terpenic derivatives; and these substances, in the form of essential oils, have antiviral, immunomodulatory, antioxidant, anti-cough effects (anti-spasmodic effect on the respiratory tract and reduction of interleukin -1 β production) Considering these respiratory and antiviral effects, we proposed to conduct a study to assess its efficacy and tolerance on COVID-19 patients [8-10].

Material and Method

We used the prepared concentrated dry powder of *Thymus vulgaris* (after harvesting the leaves of *Thymus vulgaris* in the wild, they were soaked in food grade vinegar, and then sun dried and kept in a room containing the desiccator. They were ground in a mill and the powder was sieved and bottled by a technician under aseptic conditions).

A consent form and questionnaire were prepared.
The inclusion criteria for this cohort study were any COVID-19 PCR positive, mild to moderate symptomatic patients admitted to the Promoteurs de la Bonne Santé clinic who have taken *Thymus vulgaris or not*. Exclusion criteria: pregnant women, patients who refused to participate, patients in intensive care, patients with heart, liver and kidney failure.

The successively recruited patients were divided into two groups or cohorts:
Thymus vulgaris exposed group (EG): Oral administration of 5 grams (one teaspoon) *Thymus vulgaris* extract powder in 100 ml of warm water to be taken every 8 hours for 5 days combined with conventional treatment of acute pneumonitis (azithromycin 500 mg 1tab/day and amoxicillin + clavulanic acid 1g/125 1tab per 12 hours for 6 days)

***Thymus vulgaris* unexposed group (UEG):** administration of conventional treatment (Azithromycin 500 mg 1 tablet/day and amoxicillin + clavulanic acid 1g/125 1 tablet every 12 hours for 6 days). The sample size was 161 COVID-19 PCR-positive patients, i.e. 75 patients in the unexposed group and 86 in the exposed group. This statistically significant sample size was calculated using the Kelsey and Schlesselman formula.)

Sample size justification: (According to Kelsey and Schlesselman)
The incidence of this disease is presently $2.4x10^{-3}$.
We assumed that due to psychosis and fear of death, 90% of the patients would accept to take the plant extract and only 10% would refuse for various reasons.
Unexposed (UE)/Exposed (E) ratio: Ɣ (gamma): 1-0.1/0.9:0.88
Estimated annual incidence:
Patient not exposed to *Thymus vulgaris extract*: Π UE: $2.4*10^{-3}$
Patient Exposed to *Thymus vulgaris extract*: Π E: 9*Π U: 0.0216
Difference: 8: Π E–Π UE: 0.0192
Average: Π: Π E + Y Π UE/1+Ɣ: 0.115
ß: 0.2 ά: 0.05 Z1: 1.935
The number of patients to be exposed in our study is calculated using the formula:

$$\frac{z1 - \frac{\alpha}{2} * \sqrt{(1+\gamma)*\Pi*(1-\Pi)} + z1-\beta * \sqrt{\gamma.\Pi E(1-\Pi E)+\Pi UE.(1-\Pi UE)2.}}{\gamma * 8^2}$$

Equals: 86.03 patients
Number of patients not to be exposed: **patients to be exposed * gamma:** 75 patients.
Our sample size is: 86 + 75: 161 patients.

An investigator filled in the questionnaire by questioning the patients. Thereafter, consenting patients were given *Thymus vulgaris*. After 72 hours of treatment, the questionnaire was filled in to assess the effect of *Thymus vulgaris* on early symptoms and tolerance. The control PCR test was performed at Day 10 after initiation of treatment.

To assess the efficacy of *Thymus vulgaris* on each of the early symptoms, we used the SPSS 22 software (SPSS Inc. Chicago,III. USA). Descriptive results are presented in tabular form, as number, percentage, median and interquartile range (IQR), Odds Ratio (OR). Chi-square, Mann-Whitney, logistic regression tests were used to compare the results between the two groups.

Differences were considered statistically significant for p values <0.05. Static adjustment of the P-value was performed to reduce error in multiple comparisons.

This study was validated by the Cameroon Scientific **Ethics Committee with the granting of Ethics Clearance No. 2020/07/1278/CE/CNERSH/SP**.

Results

In this cohort study, the sample size was 161 patients divided into two groups: the unexposed group (UEG) consisting of 48 women (64%) and 27 men (36%) with a mean age of 48.7 years; and the exposed group (EG) consisting of 51 women (59.3%) and 35 men (40.7%) with a mean age of 47.6 years.

Table 1: Distribution of the frequency of symptoms before treatment in the two groups

	Variable	UEG N (%)	Group to be exposed N (%)	P-value
sex	Female Male	48 (64%) 27 (36%)	51 (59.3%) 35 (40.7%)	0.061
cough	Present Absent	72 (96%) 04 (4%)	80 (93%) 6 (7%)	0.939
dyspnoea	Present Absent	54 (74.6%) 21 (25.4%)	76 (88.4%) 10 (11.6%)	0.083
Headache	Present Absent	48 (64%) 27 (36%)	68 (79%) 18 (21%)	0.438
Anosmia	Present Absent	48 (64%) 27 (36%)	56 (65.1%) 41 (34.9%)	0.831
dizziness	Present Absent	37 (48.6) 38 (41.4)	35 (40.7%) 51 (59.3%)	0.692
Muscle ache	Present Absent	48 (64%) 27 (36%)	68 (79%) 18 (21%)	0.222
Cold	Present Absent	12 (16%) 63 (84%)	10 (11.6%) 76 (88.4%)	0.834

Fever	Present Absent	48 (64 %) 27 (36 %)	40 (46.6 %) 46 (53.4 %)	0.064
Diarrhoea	Present Absent	10 (13.3) 65 (86.6%)	12 (13.9%) 74 (86.1)	0.352
Fatigue	Present Absent	54 (74.6%) 21 (25.4%)	76 (88.4%) 10 (11.6%)	0.083
Sputum	Present Absent	27 (36%) 48 (64%)	41 (47.6%) 45 (52.4%)	0.351
Anorexia	Present Absent	48 (64%) 27 (36%)	56 (65.1%) 31 (34.9%)	0.831
Chest pain	Present Absent	48 (64%) 27 (36%)	56 (65.1%) 30 (34.9%)	0.651
Sore throat	Present Absent	48 (64%) 27 (36%)	56 (65.1%) 41 (34.9%)	0.831
Agueusia	Present Absent	37 (48.6) 38 (41.4)	35 (40.7%) 51 (59.3%)	0.692

There was no significant difference in symptomatic expression of COVID-19 between the two groups before initiation of treatment.

Table 2: Distribution of the frequency of different symptoms on day 4 after initiation of treatment in both groups

	Variable	UEG N (%)	EG N (%)	P-value	OR (95%)	P-value adjusted
cough	Present Absent	52 (69.3%) 23 (30.7%)	5 (5.8%) 81 (94.2%)	0.941	0.02 (0.004 -0.14)	<0.001
dyspnoea	Present Absent	51 (68%) 24 (32%)	5 (5.8%) 81 (94.2%)	0.083	0.03 (0.005 -0.1)	<0.001
Anosmia	Present Absent	35 (46.6%) 40 (53.4%)	2 (2.3%) 84 (97.7%)	0.651	0.03 (0.003 -0.23	<0.001
Headache	Present Absent	35 (46.6%) 40 (53.4%)	12 (13.9%) 74 (86.1%)	0.438	0.14 (0.05 -0.5)	<0.001
dizziness	Present Absent	30 (40%) 45 (60%)	10 (11.6%) 76 (88.4%)	0.692	0.13 (0.04 -0.4)	<0.029
Muscle ache	Present Absent	60 (78.9%) 15 (21.1%)	6 (6.9%) 79 (93.1%)	0.222	0.02 (0.005 -0.16)	<0.001
Cold	Present Absent	11 (14.6%) 64 (85.4%)	6 (6.9%) 79 (93.1%)	0.834	0.56 (0.13 -2.4)	0.388
Fever	Present Absent	15 (20 %) 60 (80 %)	3 (3.4 %) 83 (96.6 %)	0.062	0.07 (0.01 -0.8)	<0.024
Diarrhoea	Present Absent	2 (2.6%) 73 (96.4%)	2 (2.3%) (97.7%)	0.352	1.09 (0.18 -8.8)	0.894
Fatigue	Present Absent	51 (68%) 24 (32%)	5 (5.8%) 81 (94.2%)	0.083	0.03 (0.005 -0.1)	<0.001
Sputum	Present Absent	16 (21.3%) \59 (78.7%)	23 (26.7%) 53 (73.3%)	0.351	1.78 (0.58 -5.1)	0.298
Anorexia	Present Absent	55 (73.3%) 2 (26.7%)	28 (32.5%) 58 (67.5%)	0.831	0.16 (0.05-0.4)	<0.001
Chest pain	Present Absent	35 (46.6%) 40 (53.4%)	2 (2.3%) 84 (97.7%)	0.651	0.03 (0.003 -0.23	<0.001
Agueusia	Present Absent	30 (40%) 45 (60%)	10 (11.6%) 76 (88.4%)	0.692	0.13 (0.04 -0.4)	<0.029

According to the results, a very significant improvement of symptoms was achieved in patients exposed to *Thymus vulgaris*.

Table 3: Age and blood test results of both groups before treatment.

Variable	UEG	EG	P-value
	Median (IQR)	Median (IQR)	
Age	55.4 (37)	56.5 (34)	0.677
Urea	0.36 (0.19)	0.33 (0.09)	0.186
Creatine	8 (3)	9 (2.5)	0.679
Serum calcium level	88.7 (8.5)	89 (13.3)	0.333
Aspartate aminotransferase	38 (7)	39 (6)	0.462
Leucocytes	5.4 (3.2)	5.5 (3.5)	0.672
Red blood cells	4.43 (1.32)	4.69 (1.22)	0.821
Platelets	184 (73)	178 (83)	0.682
Lymphocyte %	24.3 (18.9)	24.6 (12.8)	0.368
Neutrophil %	62.6 (28.2)	68 (19)	0.074
Na +	138.2 (8)	138.3 (7)	0.463
K +	4 (0.7)	4.2 (0.65)	0.614
CRP	77.65 (27.6)	81.2 (18.9)	0.621
Blood sugar	0.8 (0.3)	0.9 (0.25)	0.677

Before exposure to *Thymus vulgaris*, there was no significant difference in biological and age parameters between the two groups

Table 4: Blood test results of both groups after treatment

Variable	UEG	EG	P-value
	Median (IQR)	Median (IQR)	
Urea	0.33 (0.16)	0.23 (0.08)	<0.003
Creatine	9 (3)	9 (3)	0.48
Serum calcium level	80 (8.5)	89 (13.3)	0.034
Aspartate aminotransferase	40 (7)	40.2 (7)	0.482
Leucocytes	6.23 (2.28)	5.69 (3.45)	0.376
Red blood cells	4.53 (1.32)	4.59 (1.22)	0.501
Lymphocyte %	20.3 (20.60)	38 (12.8)	<0.001
Neutrophil %	63.6 (29.2)	52.3 (21)	<0.001
Platelets	205 (146.8)	192 (133)	0.582
Na	138.1 (6)	138.2 (7)	0.563
K	4 (0.63)	4.1 (0.8)	0.564
CRP	51.65 (21.6)	20.2 (12.9)	<0.001
Blood sugar	0.82 (0.29)	0.92 (0.26)	0.578

The results in Table 4 show that patients who received *Thymus vulgaris* had a significant decrease in blood urea and CRP; and a significant increase in calcium. Furthermore, in the same group of exposed patients, there was a significant increase in lymphocytes and a significant decrease in neutrophils.

Table 5: Assessment of PCR negative result at Day 10 after treatment initiation

	NEGATIVE on Day 10 Unexposed group Number (%)	NEGATIVE on Day 10 Exposed group Number %)	P-value
PCR	37 (49.3)	84 (97.6 %)	<0.001

The difference in obtention of PCR negative results is highly significant in favour of the effects of *Thymus vulgaris* on COVID-19.

Discussion

This study was conducted on COVID-19 patients to investigate the therapeutic effect of Thymus vulgaris on the symptoms presented by these patients. Results show that *Thymus vulgaris* has a positive effect on symptoms such as fever, cough, dyspnoea, fatigue and chest pain. Another study analysed the analgesic effect of Thymus resulting from the anti-inflammatory action brought about by decreasing interleukin 1 beta and IL-8 and intracellular calcium [8]. These results corroborate those of SardariS et al [11]. It was also noted that *Thymus vulgaris* induces an increase in lymphocytes which provide a better defence against the coronavirus (Schonknecht

Karina et al and SardariS et al) [11, 12]. However, in our subjects, the clinical improvement occured earlier as the evaluation was done at Day 4 against Day 5 on average, post-initiation of the treatment (Schonknecht Karina et al and SardariS et al.) [11,12]. This would be justified by the use by our patients of concentrated dry powder extract containing several active components which supposedly acted better than the isolated essential oil extract of *Thymus vulgaris*. There was no significant variation in renal, hepatic and pancreatic function in patients who took *Thymus vulgaris*. This finding leads us to evoke good therapeutic tolerance; this same observation has been made by other authors [13,14].

In our study, *Thymus vulgaris* demonstrated a 97.6% PCR negative result obtention rate in COVID positive patients. Lenz E et al. obtained a positive result of the action of essential oil of Thymus on viral infections of the respiratory area [10]; according to Akbar S et al (2020), the strong antiviral activity of the aqueous extract of *Thymus vulgaris* was demonstrated against Herpes simplex virus-1 (HSV-1) and Herpes simplex virus-2 (HSV-2) and the acyclovir-resistant strain HSV1 [15]. Furthermore, it has been shown that thyme extract reduces the production and expression of inflammatory mediators, tumour necrosis factor alpha, IL-1 B, IL - 6, and carvacrol revealing their ability to activate the expression of Peroxisome Proliferator-activated Receptor-alpha (PPARalpha) and Peroxisome Proliferator-activated Cyclooxygenase -2 (COX-2) and inhibition of acetylcholinesterase (ACh E) [15].

Limitations of the study

Although the active ingredients of *Thymus vulgaris* were identified, selective extraction, measurement of bioavailability and half-life could not be carried out due to very limited financial resources.

Conclusion

Results of this study show that the use of *Thymus vulgaris*, a medicinal plant with antioxidant, immunomodulatory and antiviral properties, proved very effective on coronavirus-induced symptoms and virus elimination. The absence of significant variation in biological parameters allows us to conclude that there was good tolerance following the intake of *Thymus vulgaris* [16,17].

Ethical considerations

Ethical factors (plagiarism, informed consent, redundancy, falsification, etc.) have been respected by the authors.

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Conflict of interest

The authors declare no conflict of interest.

References

1. Lau SK, Lee P, Tsang AK, Cyril C Y Yip, Herman Tse, et al. (2011) Molecular epidemiology of human coronavirus 0C43 reveals evolution of different genotypes over time and recent emergence of a novel genotype due to natural combination. virol. 85: 11325-11337.
2. Organization WHO (2019) Middle East respiratory syndrome coronavirus (MERS-CoV).
3. Le Chang Y, Lunan Wang (2020) Coronavirus disease 2019: Coronaviruses and blood safety. Trans Med Rev. 34: 75-80.
4. Balboni A, Battilani M, Prosperi, JM QJoMS (2012) The SAAR-Like coronaviruses: the role of bats and evolutionary relationships with SARS coronavirus New. Microbiol. 35: 1-16.
5. OMS (2020) Riposte à la COVID-19 dans la Région africaine de l'OMS. OMS 36 p février-juillet.
6. Peiris J, Lai S, Poon L, Y Guan, L Y C Yam, et al. (2003) Coronavirus as possible cause of severe acute respiratory syndrome. Lancet. 3. 361: 1319-1325.
7. Gonzalez-Molina E, Moreno DA, Garcia-Viguera CJSh (2009) Comparison of Verna lemon juice quality for new ingredients and food products. Scientiahorticulturae. 12: 353-359
8. Moubarack LO, Amaye SY, Sambane Yade (2020) La covid-19 en Afrique : bilan d'étape et perspectives. Policy Center for the South. 1-35.
9. Tang LI, Ling AP, KohRY, Chye SM, Voom KGJBC (2012) Screening of anti-dengue activity in methanolic extracts of medicinal plants. BMC complement Altern Med. 12: 3.
10. Nabissi M (2018) Antiviral effect assay of Thymus extract increases mucocilliary-beating frequency in primary cells lines from chronic obstructive pulmonary disease patients. Biomed Pharcother.
11. Santoyo S, Jaime L, Garcia-Risco M, Lopez-Hazas M, Reglero GJIC, et al. (2014) Products. Supercritical fluid extraction as an alternative process to obtain antiviral from thyme species. Indust crops Products. 52: 475-480.
12. Lenz, E., Müller, C., Mostafa, A., et al. Authorized medicinal product Aspect on Oral Drops containing thyme extract KMT v 24497 shows antiviral against viruses which cause respiratory infections. J Herbal Med. 2018.
13. Sardari S, Mobaien A, Ghassenmifard L, Kamali K, Khavasi N et al. (2021) Therapeutic Effect of Thyme (Thymus Vulgaris) Essential oiil on patients with COVID19: A Randomized TrialAdv. med. Biomed Res. 29: 83-11.
14. Schonknechtk, Krauss H, Jambor J, Fal A, MJWI (2016) Treatment of cough in respiratory tract infection. The effect of combining the natural active compounds with thymol. Wiadomoscilekarskie. 69: 791-798.
15. Abd El Kader M A, Mohamed N Z (2012) Evaluation of Protective and Antioxidant Activity of Thyme (Thymus Vulgaris) Extract on Paracetamol-Induced Toxicity in Rats. Australian Journal of Basic and Applied Sciences. 6: 467-474.
16. Fachini-Queiroz F C, Kummer R, Estev˜ao-Silva C F, De Barros Carvalho M D, Cunha JM, et al. (2012) Effects of Thymol and Carvacrol, Constituents of Thymus vulgaris L. Essential Oil, on the Inflammatory Response. Hindawi Publishing Corporation. ID 657026-10.
17. Akbar S (2020) Thymus vulgaris. (Lamiaceae). Handbook of 200 Medicinal Plants:Springer 1795-I810.