1	The Effectiveness of Garlic (Allium sativum) Consumption on		
2	Improving Anosmia and Dysgeusia in Patients with COVID-19		
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Abstract

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Background: Coronavirus disease has been declared a pandemic worldwide. Anosmia and dysgeusia are symptoms associated with coronavirus infection. Moreover, there is no effective treatment for coronavirus. Garlic is a well-known herb that has antimicrobial and antiviral properties. This study evaluated the potential therapeutic effect of garlic consumption on reducing the recovery time from anosmia and dysgeusia symptoms among participants with coronavirus-19 infection. **Methods**: A sample of 388 Jordanian participants with coronavirus-19 infection was enrolled in an online computer-assisted web survey during the period from 20th September 2021 to 20th January 2022. The survey consisted of three constructs; sociodemographic profile, symptoms associated with COVID-19, and frequency of garlic and onion consumption used during coronavirus infection. Results: The results of this study showed that almost half of the participants were between 20-40 years (193, 49.7%); most of them significantly complaining of fever, fatigue, anosmia, and dysgeusia. Also, most of them used onion (20, 93%) and garlic (29, 23%) to alleviate symptoms of the disease. In total, 40.7% of the participants who used garlic recovered from anosmia within the first 11-15 days followed by 35.3% of participants who recovered within 6-10 days. The results, also revealed that there is no correlation between garlic consumption and recovery from dysgeusia. Hence, there is a weak inverse association between garlic consumption and recovery time from anosmia. Conclusion: We suggest that consumption of garlic will enhance the immune system during the fight against COVID-19. There is need for further study to identify the proper amount of garlic consumption to relieve from anosmia during COVID-19.

Key word: Garlic intake, anosmia, dysgeusia, COVID-19

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Introduction

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Coronavirus disease (COVID-19) is a disease caused by a new mutation of coronavirus (Wu and McGoogan 2020). Thus, COVID-19 was declared a global pandemic in 2020 (Alam et al. 2021). An interaction between virus COVID-19 and the immune system results in a clinical manifestation (Li et al. 2020; Paces et al. 2020) which range from mild influenza symptoms, fever, headache, dry cough, myalgia, fatigue, loss of appetite, Anosmia (loss of smell), and dysgeusia (loss of taste) to severe acute respiratory tract infection (Calder 2020; Li et al. 2020; Moscatelli et al. 2020). Unfortunately, till now there is no treatment to cure COVID-19. As a result, many strategies were adopted to limit the spread of COVID-19 such as: vaccination; social distance; proper nutrition (Murthy, Gomersall, and Fowler 2020; Hiedra et al. 2020). Proper nutrition intervention should be at the forefront of the strategies to control spreading of COVID-19 (Alam et al. 2021) due to the cost-effectiveness, safety, and efficiency to enhance the body's immune system (Alam et al. 2021; Hiedra et al. 2020; Murthy, Gomersall, and Fowler 2020). Several recent studies have reported the positive influence of nutritional status and food intake in COVID-19 patients (Moscatelli et al. 2020). In this regard, garlic (Allium sativum) has been used for therapeutic purposes in many countries (Bayan, Koulivand, and Gorji 2014); also, garlic has anti-viral properties that can be added to the COVID-19 prevention and treatment strategies programs (de Wit and Cook 2014). Garlic contains a variety of minerals such as Ca, Fe, K, Cu, and Mg as well as different vitamins. Moreover, garlic is full of water-soluble organosulfur compounds (Suleria et al. 2015), and rich in various phytochemicals, especially allicin. Allicin has anti-microbial; anti-viral; anti-fungal potential which interacts with the viral phospholipids and amino acids involved in infection that also prevents them from attachment to the host cell by

denaturing these viruses (Razavi, Azizolahi, and Rahimi 2006). Even though, many studies have suggested that garlic use could be beneficial in helping the immune system cope better with the viral infection by enhancing the response to viruses, balancing the inflammatory response and it can help prevent immune overreaction to viral infection (Cunningham-Rundles, McNeeley, and Moon 2005). Therefore, to the best of our knowledge, no previous study has been conducted yet to evaluate the effectiveness of garlic consumption on COVID-19 symptoms. This study evaluated the potential therapeutic effect of garlic consumption on reducing the recovery time from anosmia and dysgeusia symptoms among participants with coronavirus-19 infection.

Materials and Methods

Study design and participants: A sample of 388 Jordanian participants with laboratory confirmed COVID -19 infection were enrolled in this online computer-assisted web survey study during the period from 20th September 2021 to 20th January 2022. The sample size was determined using Mendenhall's (1983) equation (Larson 1982). The online self-administered structured questionnaire was constructed in Arabic language using google forms. The link of the questionnaire was distributed using different social media platforms. The inclusion criteria were the following: participants were ≥ 18 years old, laboratory-confirmed COVID-19, clinically be able to fulfill the questionnaire, and without medical history of any respiratory disease. The exclusion criteria were the history of anosmia and dysgeusia before the epidemic as well as the participants who were in the intensive-care unit at the time of the study. Development of the Questionnaire: The online questionnaire items were collected from previous research articles about strengthening immune defenses

against COVID-19 through nutrition. The questionnaire was divided into four parts: the first part of google questionnaire asked participants to provide written informed consent prior the administration of the questionnaire. The second part includes the demographic profile which consist of multiple-choice questions related to age, sex, and educational level. Whereas self-reported weight and height are provided by openended questions. Moreover, in the third part the participants were asked to choose from a list of the symptoms that they had suffered from during their COVID-19 infection (dyspnea, fever, headache, fatigue, anosmia, and dysgeusia). Finally, the fourth part the participants were asked to choose from a list of the types of herbs or plants they had used to relieve anosmia and dysgeusia symptoms which include: garlic, onion, lemon, black pepper, Curcuma, ginger, and nutritional supplementation. The questionnaire is expected to take 5 - 10 minutes to fill. The online survey was performed according to the ethical principles of the World Medical Association Declaration of Helsinki. Data analysis: Data were extracted as a Microsoft excel spreadsheet then coded and prepared for analysis. Statistical analysis was performed using Statistical Package for the Social Sciences for Windows (SPSS version 22,0; IBM Corp, Armonk, NY, USA). The descriptive analysis is expressed as frequencies, percentages, and numbers. The potential associations between binary or categorical variables have been assessed through cross-tab generation and the Chi-square test. Linear regression analyses were conducted to investigate the association between variables, garlic intake as a dependent variable and anosmia, and dysgeusia as independent variables. On the other hand, certain demographic variables, nutritional supplementation, plants, and herbs were used as adjusting variables. A P value of <0.05 will be considered to be statistically significant in all analyses.

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Results:

The sociodemographic characteristics of the study participants in **Table 1** shows that the participants were nearly distributed equally among females (51.5%) and males (48.5%). Almost half of the participants (49.7%) were between the ages of 20 and 40 years, and nearly more than half of them (52%.6%) was within an educational level of bachelor's degree.

Figure 1 shows the participants consumption of some common herbs and plants. The results showed that nearly (75%) of the participants used garlic (29.23%), black pepper (24.43%), and onion (20.93%). Furthermore, **Figure 2** shows the distribution of participants according to the common symptoms of COVID-19. Results show that fatigue, fever, anosmia, and dysgeusia were the most common symptoms among the participants (21.3%, 19.3%, 19.9%, and 15.5%, respectively).

Table 2 shows the association between garlic intake, anosmia, and dysgeusia. The results show a significant but negative and weak correlation between garlic consumption and anosmia (-0.313 ± 0.069 , p <0.05) as well as a significant and very weak correlation between garlic consumption and dysgeusia. Thus, **Figure 3** shows the different recovery times from the anosmia among participants who reported using garlic during COVID-19. 40.7% of the participants recovered from anosmia within the first 11-15 days followed by 35.3% of participants who recovered within 6-10 days.

Discussion:

The results of this study indicated that the prevalence of confirmed COVID-19 infection among 388 participants in this study was substantially higher among younger participants. Also, there is a significantly higher prevalence of anosmia and dysgeusia symptoms among participants, more than half of them used garlic during the COVID-19 infection. Interestingly, the study showed that the recovery time from anosmia symptoms was also significantly reduced among garlic consumers during COVID-19 infection. Moreover, after adjusting of confounding variables, it was found that the association between garlic consumption and recovery time from anosmia among participants were inversely related. Furthermore, the pathological mechanisms leading to anosmia during COVID-19 infection are still unknown. The results of available clinical evaluations indicated that anosmia was the main form of neurological injury in patients with COVID-19 (La Rosa et al. 2020). DNA and RNA of COVID-19 viruses could be directly or indirectly responsible for mild to severe infection of mucosal epithelium in the oral cavity which may lead to ulceration or lesions of the oral tissue (La Rosa et al. 2020). Similarly, only one study worldwide reported hyposmia as a symptom of COVID-19 infection (Mao, Zhang, and Huang 2014). The pathological mechanism which supported that some patients had hyposmia during COVID-19 infection suggested that COVID-19 virus may invade CNS through a retrograde neuronal route (Lechien et al. 2020). Garlic (Allium sativum L) is a functional food containing a bioactive compound that may be able to pre-exposure and post-exposure prophylaxis which exhibits a role in antimicrobial, antiviral, immunomodulator and antioxidant activities (Sivaram et al. 2004; Aly, Atti, and Mohamed 2008). Previous research suggested that the beneficial health properties of garlic are mainly attributed to the bioactive compounds, including Sulphur containing compounds, particularly thiosulfinates, such as: allicin, allin, and

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196 diallyl sulfides (Amagase and Milner 1993; Block 1992). Hence, garlic compound may be able to enhance the activity of cytokine suppressors, promotion of lymphocyte 197 synthesis, natural killer cells, and macrophages; also, garlic improves outcomes of 198 COVID -19 by decreasing the inflammation and respiratory symptoms (Mohajer 199 Shojai et al. 2016; Kyo et al. 1998). 200 In a randomized clinical study, garlic extracts have been evaluated for their inhibitory 201 202 effect on infectious bronchitis virus during replication. Participants were randomly 203 allocated either garlic or placebo during viral infectious bronchitis. It was shown that virus titters in the treatment groups were significantly decreased as compared to the 204 205 control group (Chen et al. 2014). A similar finding was observed on the inhibitory 206 effect of garlic against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) multiplication that suggested a beneficial preventive measure before being infected 207 208 with the SARS-CoV-2 virus. Garlic decreases the expression of proinflammatory cytokines and reverse the immunological abnormalities to more acceptable levels 209 210 probably due to the formation blocking of structural proteins and genetic materials (Chen et al. 2006). Several randomized double-blind trials were conducted to assess 211 212 the effect of garlic supplementation on common cold infections. A randomized 213 control trial was conducted on 146 participants who were allocated to either garlic (180 mg allicin) powder once per day or a placebo group. Self-reported common cold 214 infection was significantly less common in the garlic group as compared to the 215 216 placebo group. As a result, the severity and duration of common cold symptoms were significantly reduced in the garlic group compared to the placebo (Josling 2001; 217 Lissiman, Bhasale, and Cohen 2012). 218 On the other hand, vaccines are expensive and may not be available against the 219 220 diseases. Therefore, there is a need for alternative nutritional intervention as one of the efficient strategies to fight against COVID-19. On the whole, the findings of this study indicated that the prevalence of nutritional supplementation intake was significantly higher among participants with COVID-19 infection. Several researchers are focusing on nutrition to control COVID-19 worldwide for its role in the development and maintain the immune system thus alter the susceptibility to infection (Alam et al. 2021; Sasi et al. 2021).

This study has several limitations. First, only 388 patients were studied which could cause biases in clinical observation. Therefore, it would be better to include more participants in the study. Second, all data was extracted from the electronic web survey based on the participants self-reported data of COVID— 19 symptoms and intake of supplementation and herbs during the disease.

Conclusion

The results indicating that because of the emergency state, there are numerous effective, safe treatments and preventive measures against COVID-19. Within the scope of preventive measures, garlic may be an acceptable therapeutic measure against COVID-19 infection and seems to counteract the symptoms caused by COVID-19 infection. We suggest that the administration of this functional food will enhance the immune system during the fight against COVID-19.

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Conflict of interest

The authors declare that there are no conflicts of interest.

Authors' contribution

Baha'a Abu Salma: wrote the paper, conduct research, analyze the data and draft the paper; Hanen Tarawneh and Nizar Al-Rabadi conduct and design the research idea, revision the final content of the paper; Mohammed Omar Ibrahim had primary responsibility to revise the final content of the paper; Ali Ibrahim Elmoumani conducted the research and wrote the paper. All authors read and approved the final version of the paper.

References:

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- Alam, S., F. R. Bhuiyan, T. H. Emon, and M. Hasan. 2021. 'Prospects of nutritional interventions in the care of COVID-19 patients', *Heliyon*, 7: e06285.
- Aly, SM, NM Abdel Atti, and Mohamed Fathi Mohamed. 2008. "Effect of garlic on the survival, growth, resistance and quality of Oreochromis niloticus." In From the pharaohs to the future. Eighth International Symposium on Tilapia in Aquaculture. Proceedings. Cairo, Egypt, 12-14 October, 2008, 277-96. AQUAFISH Collaborative Research Support Program.
- Amagase, H., and J. A. Milner. 1993. 'Impact of various sources of garlic and their constituents on 7,12-dimethylbenz[a]anthracene binding to mammary cell DNA', *Carcinogenesis*, 14: 1627-31.
- Bayan, L., P. H. Koulivand, and A. Gorji. 2014. 'Garlic: a review of potential therapeutic effects', *Avicenna J Phytomed*, 4: 1-14.
- Block, Eric. 1992. 'The organosulfur chemistry of the genus Allium–implications for the organic chemistry of sulfur', *Angewandte Chemie International Edition in English*, 31: 1135-78.
- Calder, P. C. 2020. 'Nutrition, immunity and COVID-19', *BMJ Nutr Prev Health*, 3: 74-92.

- Chen, C., D. M. Zuckerman, S. Brantley, M. Sharpe, K. Childress, E. Hoiczyk, and A.R. Pendleton. 2014. 'Sambucus nigra extracts inhibit infectious bronchitis virus at an early point during replication', *BMC Vet Res*, 10: 24.
- Chen, L., J. Li, C. Luo, H. Liu, W. Xu, G. Chen, O. W. Liew, W. Zhu, C. M. Puah, X. Shen, and H. Jiang. 2006. 'Binding interaction of quercetin-3-beta-galactoside and its synthetic derivatives with SARS-CoV 3CL(pro): structure-activity relationship studies reveal salient pharmacophore features', *Bioorg Med Chem*, 14: 8295-306.
- Cunningham-Rundles, S., D. F. McNeeley, and A. Moon. 2005. 'Mechanisms of nutrient modulation of the immune response', *J Allergy Clin Immunol*, 115: 1119-28; quiz 29.
- de Wit, J. J., and J. K. Cook. 2014. 'Factors influencing the outcome of infectious bronchitis vaccination and challenge experiments', *Avian Pathol*, 43: 485-97.
- Hiedra, R., K. B. Lo, M. Elbashabsheh, F. Gul, R. M. Wright, J. Albano, Z.
 Azmaiparashvili, and G. Patarroyo Aponte. 2020. 'The use of IV vitamin C for patients with COVID-19: a case series', *Expert Rev Anti Infect Ther*, 18: 1259-61.
- Josling, P. 2001. 'Preventing the common cold with a garlic supplement: a double-blind, placebo-controlled survey', *Adv Ther*, 18: 189-93.
- Kyo, E., N. Uda, A. Suzuki, M. Kakimoto, M. Ushijima, S. Kasuga, and Y. Itakura. 1998. 'Immunomodulation and antitumor activities of Aged Garlic Extract', *Phytomedicine*, 5: 259-67.
- La Rosa, G. R. M., M. Libra, R. De Pasquale, S. Ferlito, and E. Pedulla. 2020.

 'Association of Viral Infections With Oral Cavity Lesions: Role of SARS-CoV-2 Infection', *Front Med (Lausanne)*, 7: 571214.

- Larson, Harold J. 1982. 'Introduction to probability and statistical inference', *JOHN WILEY & SONS, INC., 605 THIRD AVE., NEW YORK, NY 10158, 1982, 480.*
- Lechien, J. R., C. M. Chiesa-Estomba, D. R. De Siati, M. Horoi, S. D. Le Bon, A. Rodriguez, D. Dequanter, S. Blecic, F. El Afia, L. Distinguin, Y. Chekkoury-Idrissi, S. Hans, I. L. Delgado, C. Calvo-Henriquez, P. Lavigne, C. Falanga, M. R. Barillari, G. Cammaroto, M. Khalife, P. Leich, C. Souchay, C. Rossi, F. Journe, J. Hsieh, M. Edjlali, R. Carlier, L. Ris, A. Lovato, C. De Filippis, F. Coppee, N. Fakhry, T. Ayad, and S. Saussez. 2020. 'Olfactory and gustatory dysfunctions as a clinical presentation of mild-to-moderate forms of the coronavirus disease (COVID-19): a multicenter European study', *Eur Arch Otorhinolaryngol*, 277: 2251-61.
- Li, G., Y. Fan, Y. Lai, T. Han, Z. Li, P. Zhou, P. Pan, W. Wang, D. Hu, X. Liu, Q. Zhang, and J. Wu. 2020. 'Coronavirus infections and immune responses', J Med Virol, 92: 424-32.
- Lissiman, E., A. L. Bhasale, and M. Cohen. 2012. 'Garlic for the common cold', *Cochrane Database Syst Rev*: CD006206.
- Mao, S., A. Zhang, and S. Huang. 2014. 'Meta-analysis of Zn, Cu and Fe in the hair of Chinese children with recurrent respiratory tract infection', *Scand J Clin Lab Invest*, 74: 561-7.
- Mohajer Shojai, T., A. Ghalyanchi Langeroudi, V. Karimi, A. Barin, and N. Sadri. 2016. 'The effect of Allium sativum (Garlic) extract on infectious bronchitis virus in specific pathogen free embryonic egg', *Avicenna J Phytomed*, 6: 458-267.
- Moscatelli, Fiorenzo, Anna Valenzano, Rita Polito, Sessa Francesco, Angelo Montana, Monica Salerno, Antonietta Messina, Marcellino Monda, Giuseppe Cibelli, and Vincenzo Monda. 2020. 'Ketogenic diet and sport performance', *Sport Mont*, 18: 91-94.

- Murthy, S., C. D. Gomersall, and R. A. Fowler. 2020. 'Care for Critically Ill Patients With COVID-19', *JAMA*, 323: 1499-500.
- Paces, J., Z. Strizova, D. Smrz, and J. Cerny. 2020. 'COVID-19 and the immune system', *Physiol Res*, 69: 379-88.
- Razavi, SM, B Azizolahi, and H Rahimi. 2006. 'An investigation on antiviral effect of garlic extract on herpes simplex virus via cell culture'.
- Sasi, M., S. Kumar, M. Kumar, S. Thapa, U. Prajapati, Y. Tak, S. Changan, V.
 Saurabh, S. Kumari, A. Kumar, M. Hasan, D. Chandran, Radha, S. P. Bangar,
 S. Dhumal, M. Senapathy, A. Thiyagarajan, A. Alhariri, A. Dey, S. Singh, S.
 Prakash, R. Pandiselvam, and M. Mekhemar. 2021. 'Garlic (Allium sativum
 L.) Bioactives and Its Role in Alleviating Oral Pathologies', *Antioxidants* (*Basel*), 10.
- Sivaram, V, MM Babu, G Immanuel, S Murugadass, T Citarasu, and M Pt Marian. 2004. 'Growth and immune response of juvenile greasy groupers (Epinephelus tauvina) fed with herbal antibacterial active principle supplemented diets against Vibrio harveyi infections', *Aquaculture*, 237: 9-20.
- Suleria, Hafiz Ansar Rasul, Masood Sadiq Butt, Nauman Khalid, Saira Sultan, Ali Raza, Muhammad Aleem, and Munawar Abbas. 2015. 'Garlic (Allium sativum): diet based therapy of 21st century—a review', *Asian Pacific journal of tropical disease*, 5: 271-78.
- Wu, Z., and J. M. McGoogan. 2020. 'Characteristics of and Important Lessons From the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72314 Cases From the Chinese Center for Disease Control and Prevention', *JAMA*, 323: 1239-42.

Table 1: Socio-demographics of the Participants

Items	N (%)
Participants	N = 388
Age	
18 - 20 years	36 (9.3%)
20 - < 40 years	193 (49.7%)
40 - < 60 years	140 (36.1%)
> 60 years	19 (4.9%)
Gender	
Male	188 (48.5%)
Female	200 (51.5%)
Educational level	
≤ Secondary degree	62 (61%)
Diploma degree	35 (9%)
Bachelor degree	204 (52.6%)
Higher education degree	87 (22.4%)
Body mass index (kg/m ²)	
≤ 18.5	29 (7.5%)
18.5- 24.9	146 (37.9%)
25 – 29.9	144 (37.4%)
30 – 34.9	53 (13.8%)
35 - 39.9	8 (2.1%)
≥ 40	5 (1.3%)

Data are expressed as number of replicates (N), and percentage (%).

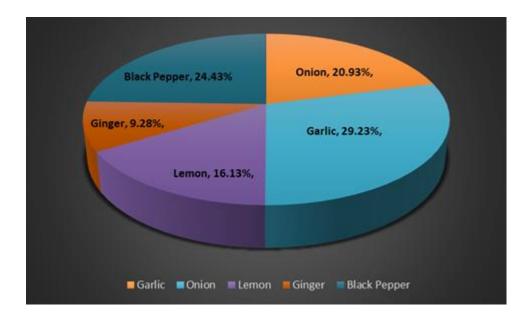


Figure 1: Participants distribution according to the common herbs and plants consumption.

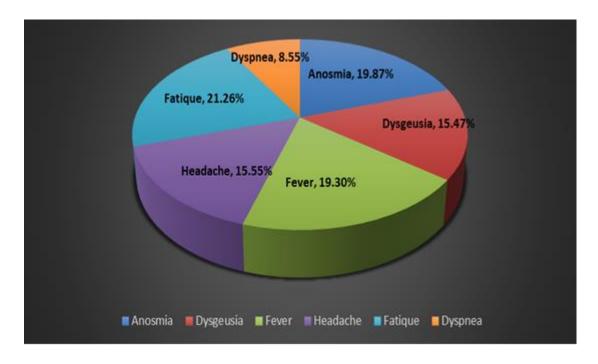


Figure 2: Distribution of participants according to common symptoms of COVID-19.

Table 2: Association between garlic consumption and recovery from anosmia and dysgeusia:

Symptoms	Garlic intake	P- value
	$\mathbf{B} \pm \mathbf{SEM}$	
Anosmia	- 0.313 ± 0.069	0.001
Dysgeusia	-0.022 ± 0.006	0.01

Model adjusted for age, sex, vitamin D, vitamin C, lemon, ginger, curcuma, and onion intake.

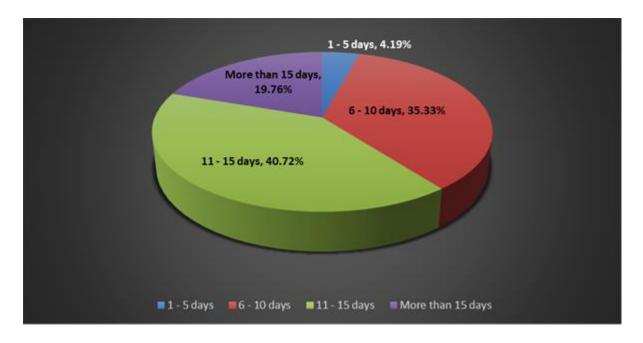


Figure 3: Distribution of participants with Anosmia according to garlic consumption and recovery time