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Research article

Use of vitamin/zinc supplements, medicinal plants, and immune boosting drinks during COVID-19 pandemic: A pilot study from Benha city, Egypt

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ABSTRACT

Background: The COVID-19 infection is characterized by a wide spectrum of severity that ranges from mild to severe lethal symptoms. The optimal status of vitamins and minerals in the body is important to maintain proper immune response to overcome infections including COVID-19. Certain foods and medicinal plants have been shown to boost the immune system.

Objectives: In the current study, the use of vitamin and zinc supplements, medicinal plants, honey, garlic, and immune-boosting drinks among Egyptian living in Benha city were investigated during the corona pandemic.

Methods: An online questionnaire was distributed through Google forms. A total of 301 adult participants (age range: 18–82) from Benha city, Egypt were included in the study. The Chi2 goodness of fit test was used to determine the differences in the distribution of the participant responses.

Results: The use of vitamin C and D were reported by 27% and 17.7% of participants. About one-third of participants reported the use of immune-boosting drinks, honey, and garlic during the pandemic to strengthen the body immunity. The use of *Zingiber officinale* and *Curcuma longa* was reported by 47.2% and 31.6% respectively. Concerning zinc supplements, only 5.6% of the sample reported using it during the pandemic. The use of examined nutrients was found to be associated with age ($P < 0.05$) and the fear score from the virus ($P < 0.05$), but not with other factors such as sex, income, and educational level.

Conclusion: The uses of supplements, medicinal plants, and immune-boosting drinks to strengthen the immune system during the pandemic were common among the participants. The present findings may help comprehend some health practices related to the COVID-19 pandemic that might be considered by health policymakers.

1. Introduction

COVID-19 belongs to the corona group of enveloped viruses with a single-stranded RNA genome (Esakandari et al., 2020). Coronaviruses can infect mammals from bats to humans and usually cause respiratory illnesses (Muniyappa and Gubbi, 2020). While some coronaviruses have caused devastating epidemics such as SARS-1 COV and MERS-COV, the majority infect the upper respiratory tract and leads to light to moderate symptoms similar to the common cold (García, 2020).

The immune system is the major protective system of the body, which is responsible for response against foreign bodies such as viruses. There are two types of immune responses, the innate immune response, which includes a group of cells protecting the body against any foreign invading material engulfing and releasing chemicals that ultimately kills the foreign agent (Thaiss et al., 2016). The acquired immunity is the other type of immune response. It is mostly concerned with detailed and more specific action against invading microbes (Lovely and Sen, 2016).

Malnutrition is the most common cause of immunodeficiency by interfering with cell-mediated immune responses, functions of phagocytes, cytokine synthesis, and immunoglobulin A secretion (Galmés and Serra, 2020; Iddir et al., 2020). Deficiency of a single nutrient such as zinc, selenium, manganese, vitamins, and folic acid could significantly alter the immune response to infections (Ali, 2020; Galmés and Serra, 2020; Zemb et al., 2020). Thus, nutritional status, as a modifiable factor, plays a key role in the functioning and maintaining of the immune system integrity.

Current literature identified risk factors that contribute to the development of the severe form of COVID-19 infection. These factors include malnutrition such as vitamin deficiency, and having chronic conditions such as diabetes mellitus, pulmonary dysfunction, heart

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diseases, and immune system disorders (Esakandari et al., 2020; García, 2020; Muniyappa and Gubbi, 2020; Weir et al., 2020).

Recent studies showed that vitamin D supplementation could reduce COVID-19 infection and death (Ali, 2020; Rhodes et al., 2020; Weir et al., 2020). Besides, zinc status has been shown to modulate responses to COVID-19 medications (Jothimani et al., 2020; Prasad, 2008). High doses of vitamin C were shown to be associated with better treatment outcomes, including a significant reduction in the course of the infection and less time in the intensive care unit (Waqas Khan et al., 2020). Therefore, nutritional support is highlighted as an essential part of the management of COVID-19 infection. On the other hand, maintaining good nutritional status is suggested as a useful strategy to prevent/avoid complications of the infection (Iddir et al., 2020).

In a USA study, a slight increase in the use of supplements including zinc and vitamin C was reported among older adults (Brown et al., 2020). In Italy, the majority of study participants believed that strengthening immune defenses through nutrition elements that enhance the function of the immune system is important to reduce the risk of COVID-19 infection (Savarese et al., 2020). In a survey study that includes several countries, increased consumption of ginger, garlic, onion, turmeric, and lemon during the pandemic was reported (Pieroni et al., 2020). However, the use of supplements and foods that boost the immune system was not yet investigated in Egypt. Therefore, in this study, the use of supplements and foods that boost the immune response among Egyptians was examined by taking Benha city as an example. The study highlights the importance of using available nutrients to maintain the integrity of the immune system and avoid complications of COVID-19 infection.

2. Method

2.1. Subjects

In the current study, Egyptian adults (age: 18+) from both sexes and living in Benha city, were invited to participate. The population of Benha was 166,000 in 2012. The study is a cross-sectional survey conducted during the period from April to June of 2020. The study was approved by the Ethical Committee of Scientific Research at Ein Shams University. Consent of the participants was taken electronically before the participants started filling the questionnaire. The study objectives, procedures, and voluntary participation were described in the cover webpage of the questionnaire. The questionnaire was anonymous and thus the privacy of the participants was maintained.

2.2. Questionnaire

An electronic survey form was developed by the researchers to cover the aims of the study. The survey consisted of four domains. The first domain covered demographics such as age, sex, education, income, and health status. The second domain asked questions about the use of the supplement (vitamins, minerals, and immune-boosting) during the COVID-19 pandemic. The selection of such supplements was based on previous studies that showed their beneficial effects in the management/prevention of COVID-19 infection complications (Ali, 2020; Rhodes et al., 2020; Weir et al., 2020). The third domain asked questions about the consumption of drinks and foods known to enhance the functions of the immune system and are available and affordable by the studied population. Immune boosting drinks include the use of any of the following drinks during the pandemic to enhance immunity: green tea, star anise, mint, marjoram, hibiscus, orange juice, and lemon juice. Foods include garlic and honey (Pieroni et al., 2020). The last domain used a validated fear scale (Ahorsu et al., 2020) to measure the fear of the participants of COVID-19 infection. The first draft of the questionnaire was content, and face validated by three expert colleagues in the fields of public health, nutrition, and pharmacology/medicinal plants. Then, the revised draft of the questionnaire was pilot tested online with 15 subjects from both sexes to provide their advice regarding the clarity and comprehensibility of the different items. Feedback obtained from the pilot testing was incorporated in the final form of the questionnaire. The questionnaire was distributed anonymously and electronically via social media groups such as Facebook and Whatsapp. The anonymity was insured by avoiding sharing the link with particular individuals. The questionnaire did not ask questions that might identify the participants. All questions were optional and participants had the choice to skip any question they don't like to answer. The English translation of the questionnaire is provided as supplementary material, whereas the Arabic version is available upon request.

2.3. Fear scale

A fear of COVID-19 scale was used in the study as described previously (Ahorsu et al., 2020). The scale is a valid instrument that assesses fear of COVID-19 among the general populations. It is based on a five-item Likert type scale. The answers included “strongly disagree,” “disagree,” “neither agree nor disagree,” agree”, and “strongly agree”. The scores range from 1 for “strongly disagree,” to 5 for “strongly agree”. The fear score is calculated by totaling the scores of the seven items (ranging from 7 to 35). Fear of COVID-19 is proportionate with the total score.

2.4. Statistics

Data were obtained from Google forms as an EXCEL spreadsheet. Data were then exported into the SPSS statistical program (version 21). The Chi^2 goodness of fit test was used to determine the differences in the distribution of the participant responses. The G*Power program (version 3.1.92) was used to compute the sample size. A significance level of 0.05, a power of 0.80, with an effect size of 0.15 resulting in a minimum number of subjects being 270. Cross-tabulation was used to link the participant responses to demographics (age, sex, income, and education). For statistical significance, α was set apriori at 0.05.

3. Results

A total of 301 participants completed the questionnaire. The mean age of participants was 36.8 ± 14.4 years. About 20% of the sample were 50 or more years old (Table 1). Females represent 64.5% and the majority (59.8%) had a bachelor's degree (Table 1). About one third had chronic diseases such as diabetes and cardiovascular diseases. The majority (61.8%) were of low income (<10,000 Egyptian pounds, Table 1). The mean fear scale from COVID-19 was 23.66 ± 5.32 out of 35.

Table 2 showed vitamin use among the participants. The percentages of users were 27%, 17.7%, 13%, and 13% for vitamins C, D, A, and B respectively. Vitamin use was strongly associated with age ($P < 0.05$, Table 2). For example, vitamin C use was higher among ≥50 years old participants (45.8%) compared to younger ones (19.7–25.0%, $P < 0.001$). Similarly, vitamin use was strongly associated with fear scores as the percentage of users increased with an increase in the fear score ($P < 0.05$, Table 2). Concerning other factors such as sex, education, income, and the presence of chronic diseases, no or weak associations were observed (Table 2).

Table 3 showed the use of immune-boosting nutrients to strengthen the immune system. About 39.3%, 32.2%, and 37.2% reported the use of immune-boosting drinks, honey, and garlic respectively. With respect to zinc supplements, only 5.6% of the sample reported using it during the COVID-19 pandemic. The use of immune-boosting drinks was found to be associated with age, income, presence of chronic diseases, and fear score ($P < 0.05$). The use of honey was found to be associated with age and fear score ($P < 0.05$). The use of garlic was found to be associated with age only ($P < 0.05$). None of the examined parameters were found to be associated with zinc use ($P > 0.05$, Table 3).

Concerning medicinal plants (Table 4), high use of *Zingiber officinale* (47.2%) and *Curcuma longa* (31.6%) was reported. On the other hand,

Table 1. Demographics of participants.

Parameter	Sub-group	N (%)*
Mean age (years ±SD$)	36.8 ± 14.4	-
Age groups	18–29	124 (41.2)
	30–49	117 (38.9)
	≥50	60 (19.9)
Sex	Male	104 (34.6)
	Female	194 (64.5)
Education	=<High school	64 (21.3)
	Bachelor	180 (59.8)
	Master/PhD	55 (18.3)
Income (Egyptian pound)	<10000	187 (61.8)
	10,000–49,000	89 (29.6)
	>50,000	19 (6.3)
Chronic diseases	Yes	88 (29.6)
	No	212 (70.4)
Fear from COVID-19	Mean ± SD	23.66 ± 5.32
Mean age	Mean ± SD	36.86 ± 14.4

* N(%): Number (percentage).
$ SD: Standard deviation.

low use of most examined medicinal plants was reported and they include *Origanum majorana* (7.7%), *Carum carvi* (8.6%), *Trigonella foenum-graecum* (13.0%), *Salvia rosmarinus* (13.6%), and *Ocimum basilicum* (10.0%). Use of *Zingiber officinale* and *Curcuma longa* during COVID-19 was found to be associated with age and fear score. The rest of investigated medicinal plants were not associated with any of studies variables.

4. Discussion

In the current study, the use of vitamin supplements, immune-boosting foods, and medicinal plants during the COVID-19 pandemic was investigated. Relatively, higher use of vitamin C and D, and the immune system boosting drinks, honey, and garlic were reported. In addition, in about one-third of participants, the use of *Zingiber officinale* and *Curcuma longa* was also reported.

One of the characteristics of the COVID-19 infection is the wide spectrum of severity that ranges from no (asymptomatic carriers) into severe lethal symptoms (Esakandari et al., 2020; Harapan et al., 2020). Different factors have been shown to contribute to such a wide range and include age, health status, and immune response (García, 2020; Paces et al., 2020). The severity of the infection is higher in the elderly compared to young and children (Ludvigsson, 2020; Nikolich-Zugich et al., 2020; She and Liu, 2020). The presence of chronic conditions significantly increases the risk of developing severe forms of the infection (Huang et al., 2020; Muniyappa and Gubbi, 2020). Moreover, deficiency in some nutrients such as vitamins and minerals can modulate response to the virus infection (Carr, 2020; Weir et al., 2020).

In the current study, the use of vitamin C and D were reported by 27% and 17.7% of participants during the pandemic, whereas less increase in the use of other vitamins was indicated. Using Google Trends, the interest in immune-boosting agents, vitamin and mineral supplements, and some foods (such as garlic and ginger) was increased during the COVID-19 pandemic (Hamulka et al., 2020). In a European study, the belief in the importance of dietary supplements in overcoming infections became significantly more pronounced during the pandemic (Karbownik et al., 2020). In a USA study, a slight increase in the use of supplements including zinc and vitamin C was reported in a study that was conducted among older adults (Brown et al., 2020). An association between vitamin D blood level and immune response and the subsequent enhanced risk of

Table 2. Vitamin use during COVID-19 pandemic.

Parameter	Vitamin A			Vitamin B complex			Vitamin C			Vitamin D		
	Yes: N(%)	No: N(%)	#*P* value	Yes: N(%)	No: N(%)	#*P* value	Yes: N(%)	No: N(%)	#*P* value	Yes: N(%)	No: N(%)	#*P* value
Total	39 (13)	261(87)		39(13)	261(87)		81(27.0)	219(73.0)		53(17.7)	247(82.3)	
Age groups												
18–29	13(10.5)	111(89.5)	0.024	10(8.1)	114(91.9)	0.000	31(25.0)	93(75.0)	0.001	18(14.5)	106(85.5)	0.016
30–49	12(10.3)	105(89.7)		11(9.4)	106(90.6)		23(19.7)	94(80.3)		17(14.5)	100(85.5)	
≥50	14(23.7)	45(76.3)		18(30.5)	41(69.5)		27(45.8)	32(54.2)		18(30.5)	41(69.5)	
Sex												
Male	13(12.6)	90(87.4)	0.948	13(12.6)	90(87.4)	0.948	23(22.3)	80(77.7)	0.192	17(16.5)	86(83.5)	0.740
Female	25(12.9)	169(87.1)		25(12.9)	169(87.1)		57(29.4)	137(70.6)		35(18.0)	159(82.0)	
Education												
=<High school	12(19.0)	51(81.0)	0.164	14(22.2)	49(77.8)	0.053	22(34.9)	41(65.1)	0.039	12(19.0)	51(81.0)	0.930
Bachelor	23(12.8)	157(87.2)		19(10.6)	161(89.4)		51(28.3)	129(71.7)		32(17.8)	148(82.2)	
Master/PhD	4(7.3)	51(92.7)		6(10.9)	49(89.1)		8(14.5)	47(85.5)		9(16.4)	46(83.6)	
In come												
<5000	28(15.1)	157(84.9)	0.228	27(14.6)	158(85.4)	0.434	59(31.9)	126(68.1)	0.03	36(19.5)	149(80.5)	0.444
5000–10000	7(7.9)	82(92.1)		10(11.2)	79(88.8)		15(16.9)	74(83.1)		12(13.5)	77(86.5)	
>10000	3(15.8)	16(84.2)		1(5.3)	18(94.7)		6(31.6)	13(68.4)		4(21.1)	15(78.9)	
Chronic diseases												
Yes	14(15.9)	74(84.1)	0.334	24(11.3)	188(88.7)	0.179	52(24.5)	160(75.5)	0.134	38(17.9)	174(82.1)	0.856
No	25(11.8)	187(88.2)		15(17.0)	73(83.0)		29(33.0)	59(67.0)		15(17.0)	73(83.0)	
Fear Score												
<3.0	5(6.3)	74(93.7)	0.012	4(5.1)	75(94.9)	0.023	14(17.7)	65(82.3)	0.026	10(12.7)	69(87.3)	0.397
3.0–3.99	19(13.7)	120(86.3)		19(13.7)	120(86.3)		37(26.6)	102(73.4)		27(19.4)	112(80.6)	
>4.0	15(18.3)	67(81.7)		16(19.5)	66(80.5)		52(63.4)	52(63.4)		16(19.5)	66(80.5)	

*N(%): Number(percentage).
# indicates Chi-square P value.

Table 3. Use of Immune boosters during COVID-19 pandemic.

Parameter	Immune system boosting drinks			Immune system boosting: honey			Immune system boosting: Garlic			Zinc supplements		
	Yes: N(%)	No: N(%)	#P value	Yes: N(%)	No: N(%)	#P value	Yes: N(%)	No: N(%)	#P value	Yes: N(%)	No N (%)	#P value
Total	118(39.3)	182(60.7)		97(32.2)	204(67.8)		112(37.2)	189(62.8)		17(5.6)	283(94.4)	
Age groups												
18–29	57(46.0)	67(54.0)	0.011	32(25.8)	92(74.2)	0.000	40(32.3)	84(67.7)	0.018	7(5.6)	117(94.4)	0.343
30–49	48(41.0)	69(59.0)		26(22.2)	91(77.8)		42(35.9)	75(64.1)		5(4.3)	112(95.7)	
≥50	14(23.3)	46(76.7)		39(65.0)	21(35.0)		30(50.0)	30(50.0)		5(8.5)	54(91.5)	
Sex												
Male	41(39.4)	63(60.6)	0.967	40(38.5)	64(61.5)	0.060	38(36.5)	66(63.5)	0.477	6(5.8)	97(94.2)	0.573
Female	76(39.2)	118(60.8)		56(28.9)	138(71.1)		73(37.5)	79(62.4)		11(5.7)	183(94.3)	
Education												
=<High school	21(32.8)	43(67.2)	0.268	24(37.5)	40(62.5)	0.198	25(39.1)	39(60.9)	0.220	3(4.8)	60(95.2)	0.348
Bachelor	72(40.0)	108(60.0)		56(31.1)	124(68.9)		70(38.9)	110(61.1)		14(7.8)	166(92.2)	
Master/PhD	26(47.3)	29(52.7)		17(30.9)	38(69.1)		16(29.1)	39(70.9)		0(0.0)	55(100.0)	
In come												
<5000	63(33.9)	123(66.1)	0.023	68(36.6)	118(63.4)	0.051	76(40.9)	110(59.1)	0.102	13(7.0)	172(93.0)	0.376
5000–10000	42(47.2)	47(52.8)		23(25.8)	66(74.2)		29(32.6)	60(67.4)		2(2.2)	87(97.8)	
>10000	9(47.4)	10(52.6)		5(26.3)	14(73.7)		6(31.6)	13(68.4)		2(10.5)	17(89.5)	
Chronic diseases												
Yes	91(42.9)	121(57.1)	0.041	67(31.6)	145(68.4)	0.410	78(36.8)	134(63.2)	0.458	12(5.7)	200(94.3)	1.000
No	28(31.5)	61(68.5)		30(33.7)	59(66.3)		34(38.2)	55(61.8)		5(5.7)	83(94.3)	
Fear Score												
<3.0	36(45.6)	43(54.4)	0.025	13(16.5)	66(83.5)	0.000	25(31.6)	54(68.4)	0.063	2(2.5)	77(97.5)	0.144
3.0–3.99	60(43.2)	79(56.8)		50(36.0)	89(64.0)		50(36.0)	89(64.0)		10(7.2)	129(92.8)	
>4.0	23(27.7)	60(72.3)		34(41.0)	49(59.0)		37(44.6)	46(55.4)		5(6.1)	77(93.9)	

*N(%): Number(percentage).
# indicates Chi-square P value.

pneumonia and coronavirus upper respiratory tract infection is well documented (Ali, 2020; Weir et al., 2020). Besides, vitamin D supplements decrease acute respiratory infections as indicated by randomized controlled trial studies (Zemb et al., 2020). Vitamin D might modulate the inflammatory response and viral infection through increasing angiotensin II hydrolysis via shifting the ratio of angiotensin-converting enzyme 2 (ACE2) to ACE (Rhodes et al., 2020). Vitamin C has strong antioxidant, anti-inflammatory, and antiviral properties (Boretti and Banik, 2020; Feyaerts and Luyten, 2020). Studies have suggested the usefulness of vitamin C in reducing the length of mechanical ventilation and ICU stay and the duration of the infection in COVID-19 patients with severe symptoms (Iddir et al., 2020; Waqas Khan et al., 2020). Vitamin A and B could also be useful in the management of COVID-19 infection (Li et al., 2020; Takhar, 2020). The present study showed also increases in the use of zinc supplements. Zinc plays an important role in the development of immune cells such as neutrophils, natural killer cells, and macrophages (Prasad, 2008). Zinc deficiency in COVID-19 patients may be associated with poor outcomes (Galmés and Serra, 2020; Jothimani et al., 2020). Thus, the observed use of vitamin and zinc supplements during the COVID-19 pandemic is justified by the available literature.

Table 4. Use of Medicinal plants during COVID-19.

Medicinal Plant	Common name	Use during pandemic
Pimpinella anisum	Aniseed	71(23.6)
Origanum majorana	Sweet marjoram	23(7.7)
Carum carvi	caraway	26(8.6)
Trigonella foenum-graecum	Fenugreek	39(13.0)
Curcuma longa	Turmeric	91 (31.6)
Glycyrrhiza glabra	Licorice	48(15.9)
Salvia rosmarinus	Rosemary	41(13.6)
Zingiber officinale	Ginger	142(47.2)
Ocimum basilicum	Basil	30(10.0)

The present findings showed increases in the use of immune-boosting drinks, honey, and garlic. The drinks include lemon juice, orange juice, green tea, star anise, mint, marjoram, and hibiscus. These drinks are rich in minerals and vitamins that boost the immune system (Alkhatib, 2020). In a study that conducted in Italy, about 60.9% of respondent believed that strengthening immune defenses through nutrition (includes supplements and immune-boosting foods) is important to lower COVID-19 infection (Savarese et al., 2020). In a survey study that includes five metropolises and twelve countries, the use of ginger, onion, and lemon to fight COVID-19 was reported(Pieroni et al., 2020). Honey and bee products enhance the function of the immune system via enhancing immunoglobulin production, maturation of immune cells, and triggering of the different immune responses (Lima and Brito, 2020). Honey has been shown to boost the immune system in HIV carriers by improving CD4 counts and reducing viral load (Wan Yusuf et al., 2019). Garlic, on the other hand, is a potent stimulant of the immune system (Ried, 2016). Garlic has also strong antiviral activity and is suggested to be useful in the prevention and management of COVID-19 infection (Rizzo et al., 2020; Rouf et al., 2020).

The results showed that the use of some medicinal plants during the COVID-19 pandemic among Egyptians. The examined plants are traditionally used as medications in Egypt. The most common method of use is soaking the plant parts in hot water for some time and then drinking the liquid. The plant part can also be used as food additives. A notable use of *Zingiber officinale* (47.2%) and *Curcuma longa* (31.6%) was observed. *Zingiber officinale* is very rich in gingerols, shogaols, paradols, and volatile compounds (Dall'Acqua et al., 2019; Sultan et al., 2014), whereas *Curcuma longa* is very rich in curcumin. These compounds are effective mediators of the immune system (Catanzaro and Corsini, 2018; Pereira et al., 2011; Sultan et al., 2014) and thus can modulate COVID-19

infection (Gupta et al., 2020; Thota and Balan, 2020). *Pimpinella anisum* was reported to be used by about one-fourth of participants. It contains lignin-carbohydrate-protein complexes that possess antiviral and immune-stimulating effects (Lee et al., 2011). The other examined medicinal plants (*Origanum majorana*, *Carum carvi*, *Glycyrrhiza glabra*, *Ocimum basilicum*) were used but less frequently. Such plants have also been shown to possess immune enhancement effects (Garg et al., 2020; Mardani et al., 2016; Sun et al., 2019; Yousefi et al., 2021). Thus, the use of available and natural boosters of the immune system that help in the management of COVID19 should be encouraged. Enhancing the public knowledge and awareness regarding the benefits of such natural nutrients is an urgent demand.

The increase in the use of vitamin and zinc supplements, honey, garlic, and medicinal plants among Egyptians is associated with age and fear from COVID-19. As mentioned above, complications of COVID-19 infection are associated with age. Thus, the observed associations between age/fear and the use of agents that modulate COVID-19 symptoms and infection are expected and logical. However, level of education and income seem to play a minor role in modulating such use. More studies are required to confirm these findings.

Among the limitations of the current study is the relatively small sample size. In addition, an online sampling approach was utilized and this might prevent the participation of individuals with no/limited internet services. Thus, a larger study that covers major areas in Egypt is strongly recommended.

5. Conclusion

The study examined the use of supplements, medicinal plants, and immune-boosting drinks among the Egyptian population during the COVID-19 pandemic. The use of such nutrition was reported by approximately one-third of the study participants and was found to be associated with age and fear of the virus. The present findings may help understand certain health practices related to the COVID-19 pandemic that might be considered by health policymakers. Understanding factors associated with supplements/immune booster foods use may assist to design interventions that aim to disseminate accurate information and to motivate individuals towards healthy use of supplements, immune boosters, and medicinal plants for the sake of COVID-19 prevention during the pandemic.

Declarations

Author contribution statement

Omar F. Khabour, Salwa F. M. Hassanein: Conceived and designed the experiments; Performed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

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Data availability statement

Data will be made available on request.

Declaration of interests statement

The authors declare no conflict of interest.

Additional information

No additional information is available for this paper.

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