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Beneficial effects of an aqueous ginger extract on the immune system cells and antibodies, hematology, and thyroid hormones in male smokers and non-smokers

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HIGHLIGHTS

- Extract had different effects on immune components in smokers and non-smokers.
- Smokers and non-smokers benefited from enhancement of the thyroid gland.
- Enhancement of RBC counts and hemoglobin levels in smokers. Thus, ginger may be beneficial for smokers with anemia.
- Non-smokers had enhanced IgM levels. This may lead to a stronger antibody response against infections.
- Therefore, the extract had benefits for both smokers and non-smokers.

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ABSTRACT

The ginger rhizome is widely used for the treatment of diseases and conditions, such as inflammatory and respiratory ailments, which are prevalent in smokers. This study is the first study of the effects of an aqueous ginger extract on the immune system cells and antibodies, thyroid hormones, and hematology in smokers compared to non-smokers. An aqueous ginger extract was administered to 68 male Saudi healthcare workers (33 smokers and 35 non-smokers) daily for 21 days. Blood samples were collected before and after the experimental period to determine the complete and differential blood counts; and concentrations of C-reactive protein, IgG, IgM, and thyroid hormones. Results showed that before consumption of the extract, smokers had a significantly lower mean neutrophil count and higher mean red blood cell (RBC) count compared to non-smokers. At the end of the experimental period, compared to non-smokers, smokers had a significantly higher mean lymphocyte and RBC counts, and hemoglobin concentration; and a significantly lower mean neutrophil count, and IgM and thyroid stimulating hormone concentrations. In conclusion, the extract had different effects on cells and antibodies of the immune system in smokers and non-smokers, although both benefited from enhancement of the thyroid gland. Smokers experienced increases in mean RBC counts and hemoglobin levels, thus ginger may be beneficial for smokers with anemia. Non-smokers had increased mean IgM levels, which may lead to a stronger antibody response, or humoral immunity, against infections. Therefore, the aqueous ginger extract had benefits for both smokers and non-smokers.

1. Introduction

Tobacco use is estimated to kill more than 7 million active and passive smokers annually, mainly in middle- and low-income countries [1]. Cigarette smoke is known to have thousands of toxic and carcinogenic compounds that affect nearly all systems of the body and lead to increased mortality and risk for heart diseases, stroke, pulmonary diseases, cardiovascular diseases, dyslipidemia, blood vessel diseases, lung cancer and other types of cancers [2]. The immune system is one of the systems affected in smokers as evidenced by the fact that smokers are more prone to infections and tend to have more severe symptoms when sick [2]. Findings of studies [3–5] on the effects of smoking on the immune system are contradictory, with some studies showing inhibition or enhancement of certain functions or components of the immune system, while other studies showing no effects. Additionally, many studies [4,6] have found increased levels of inflammatory cells, such as

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neutrophils, lymphocytes, and others, in smokers compared to non-smokers.

Many studies have been done on the role of natural foods, nutrients, herbs, and vitamins in strengthening the immune response and counteracting the effects of stress and unhealthy lifestyles such as smoking. Many diseases and conditions, such as inflammation, cancer, arthritis, atherosclerosis, and many others, may be modulated or influenced by different foods and nutrients. Therefore, it is worthwhile to find foods that help decrease the damaging effects of smoking on smokers. Ginger is known to contain many very beneficial components with enhancing effects on respiratory ailments, health in general, and the immune system, thereby leading to a stronger resistance to infections and an enhanced response to diseases [7].

The ginger (*Zingiber officinale Roscoe, Zingiberaceae*) rhizome contains many bioactive substances, including minerals, nutrients, vitamins, and antioxidants that are responsible for its many health-related effects. Ginger is very widely consumed worldwide as a food condiment and it has been used for thousands of years in folk, alternative, and ayurvedic medicines. Many studies have shown ginger to be safe to consume in both humans and animals with no harmful side effects and no increased mortality [8], although neither its mode of action nor its safety in the body is fully known [9,10]. Some uses of ginger and its components are in the treatment or inhibition of many ailments and conditions, such as inflammation, platelet aggregation, vomiting, swelling, pain, hypertension, dyslipidemia, cardiovascular diseases, oxidative damage, diabetes, nausea, colds, asthma, allergies, migraines, arthritis, hypertension, and some cancers [11–14]. It has also been reported to help with thyroid function and disease, and to have anti-inflammatory and antioxidant properties, which are linked to many diseases and explain the ability of ginger to treat inflammation and inflammation-related ailments and conditions [13,14].

Saudi Arabia is a major importer of tobacco products and has a high prevalence of tobacco use. Saudi healthcare workers and medical and healthcare students have a surprisingly high prevalence of smoking [15–17]. Although many smokers are aware of the harmful effects of cigarettes, they continue to smoke. Ginger is recommended and is commonly used locally, among other uses, as a natural agent for alleviating the negative effects of smoking on the lungs and the immune system, although this has not been proven scientifically.

Therefore, the aims of this study were to use an aqueous ginger extract as a natural approach to attempt to mitigate the harmful effects of smoking in male hospital healthcare workers and to clarify its effects on the immune system and thyroid hormones in smokers compared to non-smokers. An extensive search in the internet showed no research studies on the effects of aqueous ginger extracts on the immune system and thyroid hormones in smokers compared to non-smokers. Therefore, this study is the first one to study these effects in smokers versus non-smokers. The effects of an aqueous ginger extract on cells of the innate (neutrophils, eosinophils, basophils, and monocytes) and acquired (lymphocytes and antibodies) immunities, thyroid hormones (thyroxine (T4), triiodothyronine (T3), and thyroid-stimulating hormone (TSH)), C-reactive protein (CRP), red blood cells (RBC), hemoglobin, and platelets in the blood of smoker and non-smoker male healthcare workers were determined. This may help in clarifying the effects of ginger on the immune system, inflammatory cells (WBCs and their types), markers of inflammation (CRP and WBCs), thyroid hormones, and general health of male smokers compared to non-smokers.

2. Materials and methods

2.1. Subjects

Subjects recruited for this study were 68 Saudi males working at King Abdullah Medical Complex and living in Jeddah, Saudi Arabia with an age range of 24–38 years. All subjects were healthy and none of them were suffering from any allergies or chronic, hereditary, or immune diseases nor taking any medications on a regular basis. Subjects signed a consent form and they were instructed to fill a daily follow-up schedule to confirm that they took the ginger extract daily for 21 days. Ethical approval for the study was provided by the King Abdullah Medical Complex.

2.2. Preparation and administration of the ginger extract

The aqueous ginger extract was prepared according to the method used locally. Ginger root (4 kg) was peeled, grated, and then boiled in water (15.75 L) for 45 min. Subsequently, the extract was left overnight at room temperature. The extract was then filtered to remove the grated ginger, after which the extract was frozen as cubes of 8.3 g each at −18 °C.

Each participant was instructed to ingest one cube of ginger extract at the same time daily for 3 weeks, by thawing the cube in any warm drink, such as tea, coffee, or warm water.

2.3. Blood sampling and processing

Blood samples were collected from all subjects the day before the beginning of the experiment and the ingestion of the first ginger dose (initial sample), and on the day after the last dose and the end of the experiment (final sample). Blood samples were collected in EDTA vacutainer tubes for the differential CBC analysis, and in plain vacutainer tubes for the determination of thyroid hormones and antibodies concentrations. Blood samples collected in plain tubes were allowed to form a clot after which serum was obtained by centrifugation at 5000 rpm for 10 min. Serum was stored, for a maximum of one week, at −40 °C for use later. Lithium heparin tubes were used for the CRP concentrations, where whole blood was left for some time, after which the tubes were centrifuged at 1500 rpm for 10 min. These samples were stored at −20 °C until the analysis was performed.

2.4. Differential and complete blood count

The differential and complete blood counts (CBC) were done on an ADVIA 2120i Hematology System with Autoslide (Siemens Company, Phnom Penh, Cambodia) at the King Abdullah Medical Complex, Jeddah, Saudi Arabia. The chemicals used were the 1850 CBC/Diff tests (Blue Opportunity Medical Company, Phnom Penh, Cambodia) as specified for the instrument.

2.5. Determination of T3, T4, and TSH concentrations

The concentrations of T3, T4, and TSH were determined on a Cobas e 411 Analyzer (Hitachi High-Technologies Corporation, Tokyo, Japan) at King Fahad Hospital Jeddah, Saudi Arabia. The reagents used were the Roche Diagnostic reagents (Mannheim, Germany) as recommended for the instrument used.

2.6. Determination of IgG, IgM, and CRP concentrations

The serum concentrations of IgG and IgM antibodies, and CRP were determined by using the ARCHITECT c8000 System (Abbott Laboratories Inc., IL, USA) at King Fahad Hospital, Jeddah, Saudi Arabia. The reagents used for the determination of the antibodies concentrations were the Immunoglobulins G and M assays (Abbott, Green Oaks, Illinois, USA) which were used according to the manufacturer's instructions. For the determination of CRP concentrations, the MULTIGENT CRP Vario assay (Randox Company, Milan, Italy), which is a latex immunoassay, was used according to the manufacturer's instructions.

2.7. Statistical analysis

The Megastat statistical program (version 9.4) was used to obtain descriptive and analytical statistics for the data. The minimum and maximum values, mean, standard deviation (± SD), and standard error of the mean (± SE) were determined for all parameters. The P value was calculated to determine the significance of the differences between smokers and non-smokers, using the *t*-test for the normally distributed parameters and the Mann-Whitney *U* test for the none normally distributed parameters. As for the comparison between the initial and final samples for smokers and non-smokers, separately, the paired *t*-test was used for the normally distributed parameters and the Wilcoxon *t*-test was used for the none normally distributed parameters. A significant difference is a P value less than 0.05 and a highly significant difference is a P value less than 0.01.

3. Results

3.1. Subjects of the study

Of the 68 subjects recruited for the study, 33 were smokers and 35 were non-smokers. The median age for smokers was 30 years and for non-smokers 29 years.

3.2. Comparing smokers and non-smokers for the initial and final blood samples

3.2.1. Differential and complete blood counts

For the initial blood samples (Table 1), the mean WBC, lymphocyte, monocyte, eosinophil, basophil, and platelet counts; and the mean hemoglobin concentrations for smokers compared to non-smokers were not significantly different. On the other hand, smokers had a significantly lower mean neutrophil count and a highly significantly higher mean RBC count compared to the respective means in non-smokers.

As for the final blood samples (Table 2), there were no significant differences between smokers and non-smokers for the mean WBC, monocyte, eosinophil, basophil, and platelet counts. On the other hand, smokers had a significantly lower mean neutrophil count, significantly higher mean lymphocyte count, and highly significantly higher mean RBC count and hemoglobin concentration compared to the respective means in non-smokers.

3.2.2. Concentrations of IgG and IgM antibodies, CRP, and thyroid hormones

For the first blood samples (Table 3), there were no significant differences between smokers and non-smokers for the mean IgG, IgM, CRP, TSH, T4, and T3 concentrations. As for the final blood samples (Table 4), there were no significant differences between smokers and non-smokers for the mean IgG, CRP, T4, and T3 concentrations. On the other hand, compared to non-smokers, smokers had a highly significantly lower mean IgM and TSH concentrations.

3.3. Comparing the initial and final blood samples in smokers and non-smokers

3.3.1. Differential and complete blood counts

There were no significant differences between the initial and final blood samples for smokers for the mean hemoglobin concentrations; and the mean counts for the differential and complete WBC, RBC, and platelets (Table 5).

There were no significant differences in non-smokers between the initial and final blood samples for the mean WBC, monocyte, neutrophil, lymphocyte, basophil, RBC, and platelet counts; and the mean hemoglobin concentration. On the other hand, the mean eosinophil count in non-smokers (Table 6) increased highly significantly after consumption of ginger compared to the mean count before extract consumption.

3.4. Concentrations of IgG and IgM antibodies, CRP, and thyroid hormones

The initial and final blood samples for smokers were not significantly different for the mean IgG, IgM, CRP, T4 and T3 concentrations (Table 7). On the other hand, the mean TSH concentration for smokers after extract consumption decreased highly significantly compared to before consumption of the extract.

For non-smokers, the mean IgG, CRP, T4, and T3 concentrations (Table 8) for the initial and final samples were not significantly different. On the other hand, after consumption of the extract, the mean IgM concentration showed a highly significant increase and the mean

Table 1
Descriptive statistics and test of significance for the differences between smokers and non-smokers for the differential complete blood counts for the initial blood samples (before consumption of the extract).

Parameter	Group	n	Min	Max	Mean	± SD	± SE	P value
WBC[b] ($X10^9$/L)	Smokers	33	1.20	12.57	4.77	2.82	0.49	0.074^{NS}
	Non-smokers	35	1.23	30.49	7.10	6.27	1.06	
Neutrophils[a] ($X10^9$/L)	Smokers	33	16.6	90.2	43.4	16.7	2.9	0.045^{S}
	Non-smokers	35	21.9	95.1	53.2	22.1	3.7	
Lymphocytes[a] ($X10^9$/L)	Smokers	33	0.7	63.8	36.4	16.0	2.8	0.232^{NS}
	Non-smokers	35	0.0	53.2	31.5	17.5	3.0	
Monocytes[b] ($X10^9$/L)	Smokers	33	2.7	22.5	8.2	4.7	0.8	0.668^{NS}
	Non-smokers	35	1.6	36.2	8.8	6.2	1.0	
Eosinophils[a] ($X10^9$/L)	Smokers	33	0.0	19.9	8.1	5.1	0.9	0.092^{NS}
	Non-smokers	35	0.0	29.6	5.9	5.8	1.0	
Basophils[a] ($X10^9$/L)	Smokers	33	0.0	9.6	3.5	2.2	0.4	0.051^{NS}
	Non-smokers	35	0.0	9.4	2.4	2.4	0.4	
RBC[a] ($X10^{12}$/L)	Smokers	33	3.94	6.78	5.48	0.73	0.13	0.007^{HS}
	Non-smokers	35	2.98	6.34	4.88	1.00	0.17	
Platelets[a] ($X10^9$/L)	Smokers	33	71	315	198	53	9	0.166^{NS}
	Non-smokers	35	39	692	233	137	23	
Hemoglobin[a] (g/L)	Smokers	33	104	189	153	18	3	0.129^{NS}
	Non-smokers	35	72	186	143	34	6	

NS: Not significant (P ≥ 0.05), S: significant (P < 0.05), HS: Highly significant (P < 0.01).
Max: Maximum, Min: Minimum, n: number of subjects.
[a] T-test was used for the significance test.
[b] Mann-Whitney *U* test was used for the significance test.

Table 2
Descriptive statistics and test of significance for the differences between smokers and non-smokers for the differential complete blood counts for the final blood samples (after consumption of the extract).

Parameter	Group	n	Min	Max	Mean	± SD	± SE	P value
WBC[b] ($X10^9$/L)	Smokers	33	1.53	14.17	4.64	2.52	0.44	0.492[NS]
	Non-smokers	35	1.01	16.65	5.66	3.79	0.64	
Neutrophils[a] ($X10^9$/L)	Smokers	33	20.1	85.7	42.0	15.8	2.8	0.040[S]
	Non-smokers	35	19.4	86.7	51.0	19.2	3.2	
Lymphocytes[a] ($X10^9$/L)	Smokers	33	1.0	64.0	38.1	16.8	2.9	0.017[S]
	Non-smokers	35	0.0	60.7	27.8	17.7	3.0	
Monocytes[b] ($X10^9$/L)	Smokers	33	2.7	41.0	9.3	6.5	1.1	0.329[NS]
	Non-smokers	35	2.6	48.8	10.6	9.9	1.7	
Eosinophils[a] ($X10^9$/L)	Smokers	33	0.4	16.8	7.2	3.8	0.7	0.327[NS]
	Non-smokers	35	0.1	29.6	8.5	6.5	1.1	
Basophils[a] ($X10^9$/L)	Smokers	33	0.2	10.6	3.7	2.1	0.4	0.519[NS]
	Non-smokers	35	0.1	9.4	3.2	3.1	0.5	
RBC[a] ($X10^{12}$/L)	Smokers	33	3.57	7.30	5.58	0.68	0.12	0.000[HS]
	Non-smokers	35	2.66	6.30	4.80	0.97	0.16	
Platelets[a] ($X10^9$/L)	Smokers	33	76	582	199	83	14	0.079[NS]
	Non-smokers	35	90	459	237	96	16	
Hemoglobin[a] (g/L)	Smokers	33	88	183	153	20	4	0.003[HS]
	Non-smokers	35	79	170	134	29	5	

NS: Not significant ($P \geq 0.05$), S: significant ($P < 0.05$), HS: Highly significant ($P < 0.01$).
Max: Maximum, Min: Minimum, n: number of subjects.
[a] T-test was used for the significance test.
[b] Mann-Whitney *U* test was used for the significance test.

Table 3
Descriptive statistics and test of significance for the differences between smokers and non-smokers for the concentrations of antibodies and hormones for the initial blood samples (before consumption of the extract).

Parameter	Group	n	Min	Max	Mean	± SD	± SE	P value
IgG[a] (g/L)	Smokers	17	3.6	27.8	14.0	6.5	1.6	0.099[NS]
	Non-smokers	17	1.5	18.6	10.8	4.5	1.1	
IgM[a] (g/L)	Smokers	17	0.25	3.16	1.17	0.82	0.20	0.464[NS]
	Non-smokers	17	0.35	3.82	1.41	0.99	0.24	
CRP[a] (mg/L)	Smokers	14	1.2	6.9	4.1	2.2	0.6	0.982[NS]
	Non-smokers	14	1.6	8.3	4.1	1.7	0.5	
TSH[b] (Mmol/L)	Smokers	33	0.98	5.47	2.34	1.10	0.19	0.377[NS]
	Non-smokers	35	0.55	6.33	2.18	1.28	0.22	
T4[a] (Mmol/L)	Smokers	33	12.36	33.57	21.44	4.80	0.83	0.719[NS]
	Non-smokers	35	12.81	29.86	21.83	4.02	0.68	
T3[a] (Mmol/L)	Smokers	33	4.40	10.05	6.56	1.14	0.20	0.579[NS]
	Non-smokers	35	4.21	8.81	6.41	1.13	0.19	

NS: Not significant ($P \geq 0.05$).
Max: Maximum, Min: Minimum, n: number of subjects.
[a] T-test was used for the significance test.
[b] Mann-Whitney *U* test was used for the significance test.

Table 4
Descriptive statistics and test of significance for the differences between smokers and non-smokers for the concentrations of immunoglobulins and hormones for the final blood samples (after consumption of the extract).

Parameter	Group	n	Min	Max	Mean	± SD	± SE	P value
IgG[a] (g/L)	Smokers	17	7.0	27.6	13.9	5.9	1.4	0.222[NS]
	Non-smokers	17	2.5	18.3	11.7	4.2	1.0	
IgM[a] (g/L)	Smokers	17	0.25	3.20	1.18	0.83	0.20	0.005[HS]
	Non-smokers	17	0.82	4.56	2.19	1.05	0.25	
CRP[a] (mg/L)	Smokers	14	1.2	6.8	3.8	2.1	0.8	0.906[NS]
	Non-smokers	14	1.3	7.0	3.8	1.6	0.4	
TSH[b] (Mmol/L)	Smokers	33	0.81	4.70	1.64	0.80	0.14	0.000[HS]
	Non-smokers	35	0.54	4.54	1.78	1.05	0.18	
T4[a] (Mmol/L)	Smokers	33	12.11	29.75	21.06	4.27	0.74	0.342[NS]
	Non-smokers	35	12.92	28.65	22.01	3.91	0.66	
T3[a] (Mmol/L)	Smokers	33	4.80	7.92	6.41	0.94	0.16	0.358[NS]
	Non-smokers	35	4.66	9.61	6.64	1.11	0.19	

S: significant ($P < 0.05$), NS: Not significant ($P \geq 0.05$), HS: Highly significant ($P < 0.01$).
Max: Maximum, Min: Minimum, n: number of subjects.
[a] T-test was used for the significance test.
[b] Mann-Whitney *U* test was used for the significance test.

Table 5
Descriptive statistics and test of significance for the differences between the initial and final blood samples for the differential complete WBC counts in smokers.

Parameter	Blood sample	n	Min	Max	Mean	± SD	± SE	P value
WBC[b] ($X10^9$/L)	Initial	33	1.20	12.57	4.77	2.82	0.49	0.796^{NS}
	Final	33	1.53	14.17	4.64	2.52	0.44	
Neutrophils[a] ($X10^9$/L)	Initial	33	16.6	90.2	43.4	16.7	2.9	0.704^{NS}
	Final	33	20.1	85.7	42.0	15.8	2.8	
Lymphocytes[a] ($X10^9$/L)	Initial	33	0.7	63.8	36.4	16.0	2.8	0.683^{NS}
	Final	33	1.0	64.0	38.1	16.8	2.9	
Monocytes[b] ($X10^9$/L)	Initial	33	2.7	22.5	8.2	4.7	0.8	0.249^{NS}
	Final	33	2.7	41.0	9.3	6.5	1.1	
Eosinophils[a] ($X10^9$/L)	Initial	33	0.0	19.9	8.1	5.1	0.9	0.380^{NS}
	Final	33	0.4	16.8	7.2	3.8	0.7	
Basophils[a] ($X10^9$/L)	Initial	33	0.0	9.6	3.5	2.2	0.4	0.755^{NS}
	Final	33	0.2	10.6	3.7	2.1	0.4	
RBC[a] ($X10^{12}$/L)	Initial	33	3.94	6.78	5.48	0.73	0.13	0.276^{NS}
	Final	33	3.57	7.30	5.58	0.68	0.12	
Platelets[a] ($X10^9$/L)	Initial	33	71	315	198	53	9	0.960^{NS}
	Final	33	76	582	199	83	14	
Hemoglobin[a] (g/L)	Initial	33	104	189	153	18	3	0.767^{NS}
	Final	33	88	183	153	20	4	

NS: Not significant (P ≥ 0.05); Max: Maximum, Min: Minimum.
[a] Paired t-test was used for the significance test.
[b] Wilcoxon test was used for the significance test.

Table 6
Descriptive statistics and test of significance for the differences between the initial and final blood samples for the differential complete WBC counts in non-smokers.

Parameter	Blood sample	n	Min	Max	Mean	± SD	± SE	P value
WBC[b] ($X10^9$/L)	Initial	33	1.23	30.49	7.60	6.27	1.10	0.196^{NS}
	Final	33	1.01	16.65	5.66	3.80	0.60	
Neutrophils[a] ($X10^9$/L)	Initial	33	21.9	95.1	53.2	22.1	3.7	0.638^{NS}
	Final	33	19.4	86.7	51.0	19.2	3.2	
Lymphocytes[a] ($X10^9$/L)	Initial	33	0.0	53.2	31.5	17.5	3.0	0.357^{NS}
	Final	33	0.0	60.7	27.8	17.7	3.0	
Monocytes[b] ($X10^9$/L)	Initial	33	1.6	36.2	8.8	6.2	1.0	0.599^{NS}
	Final	33	2.6	48.8	10.6	9.9	1.7	
Eosinophils[b] ($X10^9$/L)	Initial	33	0.2	29.6	5.9	5.8	1.0	0.008^{HS}
	Final	33	0.1	29.6	8.5	6.5	1.1	
Basophils[a] ($X10^9$/L)	Initial	33	0.1	9.4	2.4	2.4	0.4	0.095^{NS}
	Final	33	0.1	9.4	3.2	3.1	0.5	
RBC[a] ($X10^{12}$/L)	Initial	33	2.98	6.34	4.88	1.00	0.17	0.707^{NS}
	Final	33	2.66	6.30	4.80	0.97	0.16	
Platelets[a] ($X10^9$/L)	Initial	33	39	692	233	137	23	0.884^{NS}
	Final	33	90	459	237	96	16	
Hemoglobin[a] (g/L)	Initial	33	72	186	143	34	6	0.112^{NS}
	Final	33	79	170	134	29	5	

NS: Not significant (P ≥0.05), HS: Highly significant (P < 0.01).
Max: Maximum, Min: Minimum.
[a] Paired t-test was used for the significance test.
[b] Wilcoxon test was used for the significance test.

TSH concentration showed a highly significant decrease compared to the respective levels before consumption of the extract.

4. Discussion

Many research studies have shown cigarettes to have stimulatory and/or inhibitory effects on the body. Smoking may lead to cellular damage and effects on most systems and organs of the body, which may lead to many deleterious changes [3–5,18]. These changes may include changes in counts of blood cells and concentrations of secreted hormones. For the past few decades, there has been an extensive interest by the public and many researchers to discover and determine the roles and effects of natural foods in treating, preventing or reducing diseases

Table 7
Descriptive statistics and test of significance for the differences between the initial and final blood samples for the concentrations of antibodies and hormones in smokers.

Parameter	Blood sample	n	Min	Max	Mean	± SD	± SE	P value
IgG[a] (g/L)	Initial	17	3.6	27.8	14.0	6.5	1.6	0.706^{NS}
	Final	17	7.0	27.6	13.9	5.9	1.4	
IgM[a] (g/L)	Initial	17	0.25	3.16	1.10	0.82	0.20	0.601^{NS}
	Final	17	0.25	3.20	1.10	0.82	0.20	
CRP[a] (mg/L)	Initial	14	1.2	6.9	4.1	2.2	0.6	0.097^{NS}
	Final	14	1.2	6.8	3.8	2.1	0.6	
TSH[b] (Mmol/L)	Initial	33	0.98	5.47	2.34	1.10	0.19	0.000^{HS}
	Final	33	0.80	4.70	1.64	0.80	0.14	
T4[a] (Mmol/L)	Initial	33	12.36	33.57	21.44	4.80	0.83	0.634^{NS}
	Final	33	12.11	29.75	21.06	4.27	0.74	
T3[a] (Mmol/L)	Initial	33	4.40	10.05	6.56	1.14	0.20	0.500^{NS}
	Final	33	4.80	7.92	6.41	0.94	0.16	

HS: Highly significant (P < 0.01), NS: Not significant (P ≥ 0.05).
Max: Maximum, Min: Minimum.
[a] Paired t-test was used for the significance test.
[b] Wilcoxon test was used for the significance test.

Table 8
Descriptive statistics and test of significance for the differences between the initial and final blood samples for the concentrations of antibodies and hormones in non-smokers.

Parameter	Blood sample	n	Min	Max	Mean	± SD	± SE	P value
IgG[a] (g/L)	Initial	17	1.5	18.6	10.8	4.5	0.8	0.052^{NS}
	Final	17	2.4	18.3	11.7	4.2	0.7	
IgM[a] (g/L)	Initial	17	0.34	3.82	1.41	0.99	0.17	0.000^{HS}
	Final	17	0.82	4.56	2.19	1.05	0.18	
CRP[a] (mg/L)	Initial	14	1.6	8.3	4.1	1.7	0.3	0.130^{NS}
	Final	14	1.3	7.0	3.8	1.6	0.3	
TSH[b] (Mmol/L)	Initial	33	0.55	6.33	2.18	1.28	0.22	0.003^{HS}
	Final	33	0.54	4.54	1.78	1.05	0.18	
T4[a] (Mmol/L)	Initial	33	12.81	29.86	21.83	4.02	0.68	0.825^{NS}
	Final	33	12.92	28.65	22.01	3.91	0.66	
T3[a] (Mmol/L)	Initial	33	4.21	8.81	6.41	1.13	0.19	0.302^{NS}
	Final	33	4.66	9.61	6.64	1.11	0.19	

NS: Not significant (P≥ 0.05), HS: Highly significant (P < 0.01).
Max: Maximum, Min: Minimum.
[a] Paired t-test was used for the significance test.
[b] Wilcoxon test was used for the significance test.

or their symptoms. Ginger is one of the more popular foods that have been studied and used extensively for its many beneficial effects, although many of these effects have not been proven scientifically. For many natural components, it is essential to consume the natural whole food rather than the active ingredient alone since the active components may need the synergy or influence of other components in the whole food. Thus, in this study, the whole ginger aqueous extract was used rather than using the individual active substances. Another reason for using the whole extract is that it was our goal to assess the effects of ginger as used locally and in other parts of the world to treat different ailments.

The effects of the ginger extract on the immune system and general health of male smokers and non-smokers were determined by measuring the complete and differential blood counts; and levels of thyroid hormones (T3, T4, and TSH), IgG and IgM antibodies, and C-reactive protein. An extensive search of the literature available on the internet showed no other studies on the effects of ginger aqueous extracts on the parameters measured in the current study in smokers and non-smokers. Thus, this is the first study of its kind, which meant that we were not able to compare our results for the blood samples collected at the end of the experiment with other studies.

The aqueous ginger extract was prepared according to the method

used locally, and the subjects were instructed to mix it with a hot liquid, as is advised by folk medicine for best results. None of the subjects reported any adverse symptoms due to the consumption of the extract during the entire experimental period. All the parameters were determined for both the initial (before the consumption of the ginger extract) and final (after the consumption of the extract) blood samples. There was no significant difference between mean ages for smokers and non-smokers as reported previously [19] using the same groups of smokers and non-smokers. In addition, the median ages for smokers and non-smokers (30 and 29 years, respectively) were very close to each other.

The complete and differential blood counts for the initial blood samples showed no significant differences ($P \geq 0.05$) between smokers and non-smokers for the mean WBC, lymphocyte, monocyte, eosinophil, and basophil cell counts. As for the final blood samples, the mean WBC, monocyte, eosinophil, and basophil cell counts for smokers were not significantly different from the respective mean counts for non-smokers. Therefore, the only significant differences between smokers and non-smokers were significantly lower ($P = 0.045$, and $P = 0.040$, respectively) mean neutrophil counts for both the initial and final samples for smokers (Mean ± SD: 43.4 ± 16.7, and 42.0 ± 15.8, respectively) compared to the respective counts in non-smokers (53.2 ± 22.1; and 51.0 ± 19.2, respectively), and a significantly higher ($P = 0.017$) mean lymphocyte count for the final sample for smokers (38.1 ± 16.8) compared to the mean count for non-smokers (27.8 ± 17.7). Comparing the complete and differential blood counts before and after the consumption of the ginger extract in smokers and non-smokers each, neither WBC nor its types showed any significant differences, with the exception of a highly significant increase ($P = 0.008$) in the mean eosinophil count in non-smokers after extract consumption (8.5 ± 6.5) compared to before extract consumption (5.9 ± 5.8).

The findings of the first blood samples do not support previous research studies that demonstrated significantly higher WBC, neutrophil, lymphocyte, monocyte, eosinophil, and basophil counts [20–28] and lower lymphocyte counts [26] in smokers compared to non-smokers. Other studies that agree with the results of the current study showed no significant differences between smokers and non-smokers for lymphocyte, eosinophil, basophil [24], and monocyte counts [24,26] nor for counts of granulocytes in general [28]. As for the results after consumption of ginger, there are no published studies on the effects of ginger on WBC and their types in smokers, as mentioned above, for comparison with the current results. A study done on healthy rats given different doses of ginger extract [29] resulted in significantly lower WBC counts and higher neutrophil counts compared to the control rats that did not consume ginger. These findings contradict our findings of no significant differences for WBC and neutrophil counts between the initial and final blood samples in non-smokers.

Increased counts of white blood cells and their subtypes are indicators of infection, diseases, or an unhealthy lifestyle. Therefore, it is interesting that the ginger extract led to a higher mean lymphocyte count for smokers or, in other words, it led to a lower mean lymphocyte count for non-smokers. On the other hand, neutrophils remained significantly lower for smokers at the end of the experimental period. In addition, WBC and their types did not change significantly for smokers after the consumption of the extract. Lymphocytes are important in both humoral and cellular acquired immunities while neutrophils are important in innate immunity and infections, and both cells are linked to inflammation. Thus, it may be concluded that ginger enhances acquired immunity in smokers compared to not non-smokers, through the increase in the lymphocyte cell count but it does not enhance innate immunity since neutrophils remained low in smokers and the remaining types of WBC did not change.

The mean RBC counts for both the initial and final blood samples were highly significantly higher ($P = 0.007$, and $P = 0.000$, respectively) for smokers (5.48 ± 0.73, and 5.58 ± 0.68, respectively) compared to non-smokers (4.88 ± 1.00, and 4.80 ± 0.97, respectively). The mean platelet count and hemoglobin concentration for the first blood samples did not show significant differences between the two groups ($P > 0.05$). For the final blood samples, the mean platelet counts were not significantly different between smokers and non-smokers, while the mean hemoglobin concentration for the smokers group (15.3 ± 2.0) was highly significantly higher ($P = 0.003$) than for the non-smokers group (13.4 ± 2.9). As for the comparison between the mean RBC and platelet counts and mean hemoglobin concentrations before and after the extract in smokers and non-smokers, there were no significant differences.

The findings for the initial blood samples agree with other studies [22,24,25,29] that found higher RBC counts in smokers compared to non-smokers. On the other hand, these results disagree with studies that found higher hemoglobin levels [22,24,25,28,30–32] in smokers compared to non-smokers. The findings of the present study of no differences in platelet counts between smokers and non-smokers are consistent with the findings of other research studies [22,23,25,33].

The only other study on the effects of ginger extract consumption in health, done on healthy rats, on RBC and platelet counts, and hemoglobin concentrations was the study by Tende et al. [29], mentioned previously. The ginger extract resulted in significantly lower hemoglobin concentration and higher RBC counts. This contradicts the current results of no differences in these parameters between after consumption of the extract and before. In addition, since the mean RBC counts for both the initial and final blood samples were higher for smokers compared to non-smokers, therefore there were no ginger-specific effects on the subjects. As for hemoglobin, ginger led to a significantly higher hemoglobin concentration for smokers compared to non-smokers, or, alternatively, a significantly lower hemoglobin concentration for non-smokers compared to smokers. The lower hemoglobin level in non-smokers agrees with the findings of Tende et al. [29] mentioned above, but the result of a lower RBC count in non-smokers does not.

An explanation [29] for the higher RBC counts in smokers for both blood samples is that the carbon monoxide in cigarette smoke binds to hemoglobin in RBC more successfully than oxygen. This leads to less hemoglobin to carry oxygen and a lower release rate of oxygen carried by hemoglobin. Therefore, to provide the body with the needed amount of oxygen, carried by RBC, the body produces more RBC to compensate. Our findings agree with this explanation since before the consumption of ginger smokers had higher RBC than non-smokers. This held true after consumption of ginger, but now, in addition, smokers had higher hemoglobin concentration compared to non-smokers. Therefore, the ginger extract led to a beneficial effect on smokers where the increased hemoglobin concentration may counteract the reduced amount of hemoglobin available to bind oxygen in smokers.

The results for the mean IgG and IgM concentrations before consumption of the extract did not show any significant differences ($P > 0.05$) between smokers and non-smokers. After consumption of ginger, the mean IgG concentrations for smokers and non-smokers were not significantly different, whereas the mean IgM concentration for smokers (1.18 ± 0.83) was highly significantly lower ($P = 0.005$) than the mean IgM concentration for non-smokers (2.19 ± 1.05). Additionally, the mean IgG and IgM concentrations for smokers before and after extract consumption were not significantly different. As for non-smokers, mean IgG levels were not significantly different before and after extract consumption while the mean IgM level after extract consumption (2.19 ± 1.05) increased highly significantly ($P = 0.000$) compared to before extract consumption (1.41 ± 0.99). These results are in disagreement with the findings of other studies of significantly lower IgG levels [34–37] and increased IgG and IgM levels [38] in cigarette smokers compared to non-smokers. Research work done on healthy fish and sows administered ginger extract showed increased IgM [39], and IgG concentrations [40], which may suggest an enhanced immune system. This agrees with the current result of a significantly

higher IgM level for non-smokers after the consumption of the ginger extract, but disagrees with the results for IgG levels that did not show any significant differences in all comparisons. Thus, it may be that the extract enhances humoral immunity in non-smokers specifically, but not smokers, through higher IgM levels. On the other hand, decreased levels of antibodies lead to a weaker humoral response, which may be partially to blame for the increased susceptibility of smokers to infections and more severe symptoms of infections and diseases.

Mean CRP concentrations did not show any significant differences ($P > 0.05$) between smokers and non-smokers for both the initial and final blood samples, nor before and after ginger extract consumption for smokers and non-smokers. These findings are contradictory to previous studies [20,21,27,38,41] that showed that smokers have a significantly higher CRP level compared to non-smokers. No studies on the effect of ginger or its extract on CRP levels in smokers were found. CRP, important in both the innate and humoral acquired immunities, is used as a marker for inflammation, increasing in inflammatory diseases, such as cardiovascular disease, trauma, infections, and lifestyle choices and conditions that lead to inflammation, such as obesity and smoking. Therefore, it was expected that smokers would have significantly higher CRP levels compared to non-smokers.

The mean thyroid hormones (TSH, T4, and T3) concentrations were not significantly different between smokers and non-smokers ($P > 0.05$) for the initial and final blood samples, with the exception of the mean TSH concentrations after extract consumption which were highly significantly lower ($P = 0.000$) for smokers (1.64 ± 0.80) compared to non-smokers (1.78 ± 1.05). Additionally, the mean T4 and T3 concentrations before and after extract consumption were not significantly different in smokers and non-smokers. On the other hand, the mean TSH concentrations after extract consumption for smokers and non-smokers each (1.64 ± 0.80, and 1.78 ± 1.05, respectively) decreased highly significantly ($P = 0.000$, and $P = 0.003$, respectively) compared to the levels (2.34 ± 1.10, and 2.18 ± 1.28, respectively) before extract consumption by smokers and non-smokers, respectively. Studies conducted by other researchers agree with the current results of no effects of smoking on the serum levels of TSH [42], T3 [42–45], and T4 [43–45]. On the other hand, the findings of the current study do not support other previous research findings that observed that smokers have significantly lower serum TSH levels [46–50] and higher T4 and T3 levels [46,47,49,50] compared to non-smokers. No studies on the effects of ginger or its extracts on thyroid hormones were found.

The thyroid gland, one of the larger glands in the body, regulates growth, energy expenditure, metabolism, and the function of many systems and hormones. The blood concentrations of the major thyroid hormones T3, and T4 are regulated by the blood concentration of TSH, which is produced by the pituitary gland. The TSH stimulates the thyroid to produce more T3 and T4. Therefore, the lower TSH in smokers after consumption of the extract indicates enhanced activity of the thyroid gland and that may result in higher T3 and T4 concentrations if the experimental period were prolonged.

It is noteworthy that the mean TSH levels for smokers and non-smokers were both lower after ingestion of the ginger extract compared to before the beginning of the experiment. Thus, the extract leads to enhancement of thyroid gland function and this would lead to increased T3 and T4 concentrations in both smokers and non-smokers with prolonged consumption of the ginger extract. This effect may be more pronounced in smokers since their mean TSH level was decreased more than for non-smokers.

5. Conclusions and recommendations

In conclusion, before extract consumption, smokers had a significantly lower neutrophil count and higher RBC count compared to non-smokers. After consumption of the ginger extract, these differences remained, but now smokers also had significantly higher lymphocyte count and hemoglobin concentration, and significantly lower IgM and TSH concentrations compared to non-smokers. On the other hand, after consumption of the extract, smokers had significantly decreased TSH levels compared to before consumption of the extract. Non-smokers had significantly increased eosinophil count and IgM concentration, and significantly decreased TSH levels than before consumption of the extract. Therefore, it is clear that the extract leads to enhancement of the thyroid gland function in both smokers and non-smokers since TSH levels were decreased in both smokers and non-smokers. In addition, the extract did not counteract the effects of smoking, since the low neutrophil count and high RBC count in smokers remained unchanged at the end of the experimental period. However, smokers benefited from a higher lymphocyte count and hemoglobin concentration compared to non-smokers, although non-smokers had a higher eosinophil count and IgM concentration. Thus, the extract has different effects on the immune system cells and antibodies in smokers and non-smokers, although both benefited from enhancement of the thyroid gland. Smokers had variable effects on the immune system cells but had enhancement of RBC counts and hemoglobin levels. Non-smokers had enhanced IgM levels, which may lead to a stronger antibody response, or humoral immunity, against infections.

The increased hemoglobin concentration after ginger consumption in smokers may be beneficial for compensating for the reduced hemoglobin molecules available for binding oxygen due to cigarette smoke, as explained above. Therefore, ginger may be beneficial for smokers with anemia. It is recommended that similar studies on smokers be done using more subjects and studying both females and males to determine any gender-specific effects.

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Author contributions

Contribution of author SHM: Was responsible for the conceptualization of the research study, data analysis, funding acquisition, writing of the initial draft, and revising of the initial and subsequent drafts.

Contribution of author OAB: Was responsible for the conceptualization of the research study, data analysis, data collection, sample analysis, data analysis, funding acquisition, writing of the initial draft, and revising of the initial and subsequent drafts.

Compliance with ethical standards

Conflicts of interest

Both authors declare that they have no conflicts of interest.

Human subjects

Ethical approval for the study was provided by the King Abdullah Medical Complex.

"Informed consent was obtained from all individual participants included in the study."

"All procedures performed in the study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards."

Appendix A. Supplementary data

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