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RESEARCH PAPER

Genetic polymorphisms influence runners' responses to the dietary ingestion of antioxidant supplementation based on pequi oil (*Caryocar brasiliense* Camb.): a before-after study

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ABSTRACT Genes have been implicated in the levels of oxidative stress, lipids, CVD risk, immune reactivity, and performance. Pequi oil (*Caryocar brasiliense*) has shown anti-inflammatory and hypotensive effects, besides reducing exercise-induced DNA, tissue damages, and anisocytosis. Given that diet can interact with the human genome to influence health and disease, and because genetic variability can influence response to diet, we aim to investigate the influence of 12 gene polymorphisms on inflammatory markers, postprandial lipids, arterial pressure, and plasma lipid peroxidation of runners ($N = 125$), before and after 14 days of 400 mg pequi-oil supplementation, after races under closely comparable conditions. Arterial pressure was checked before races; blood samples were taken immediately after racing to perform leukogram and plateletgram, Tbars assay, lipid, and CRP dosages and genotyping. CAT, GST-M1/T1, CRP-G1059C, and MTHFR-C677T polymorphisms influenced post-pequi-oil responses in leukogram; Hp and MTHFR-C677T, in plateletgram; Hp, ACE, GSTT1, and MTHFR-A1298C, in lipid profile; MTHFR-A1298C, in C-reactive protein (CRP) levels; and Hp and MnSOD, in Tbars assay. Differences between ACE genotypes in leukogram and total cholesterol disappeared after pequi, and the same occurred for Hp and MnSOD in Tbars assay and for MTHFR-A1298C with CRP levels. Because genetic inheritance is one of the factors that drive atherosclerosis-related lipid abnormalities, results can contribute to a greater understanding of the influence of genetic polymorphisms in situations that push up free radicals. Knowledge is also expanded on how antioxidant supplementation affects an individual's genes and how athletic genetic makeup can affect the way a person responds to antioxidant supplements.

Keywords *Caryocar brasiliense* Camb. · Genetic polymorphisms · Postprandial serum lipids · Inflammatory markers · TBARS assay

Abbreviations

ROS	Reactive oxygen species
LDL	Low-density lipoproteins
HDL	High-density lipoproteins
VLDL	Very low-density lipoproteins
TG	Triglycerides
Hp	Haptoglobin
MnSOD	Manganese superoxide dismutase
CAT	Catalase
GPX	Glutathione peroxidase
CRP	C-reactive protein
hs-CRP	High-sensitivity C-reactive protein
MTHFR	Methylenetetrahydrofolate reductase
MPV	Mean platelet volume
PDW	Platelet distribution width
CVD	Cardiovascular disease
CAD	Coronary artery disease
CHD	Coronary heart disease

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Introduction

Many athletes and individuals participating in regular exercise programs consume antioxidant supplements to avoid enhanced production of reactive oxygen and nitrogen species (RONS) in response to exercise, which may lead to modifications in lipids, proteins, nucleic acid, and other cellular compounds due to oxidative stress [37, 44, 109, 128, 144]. Some production of RONS is necessary for normal contractile activity of skeletal muscles [72, 144], and physical training is a known to induce antioxidant enzymes [44, 61]. However, strenuous exercise, mainly if above habitual intensity of effort, or training with very elevated frequency, generally overloads the endogenous antioxidant system's capacity, leading to an increase in plasma lipid peroxidation [44] plus oxidative damage to muscles and other tissues [44, 61, 128, 132]. These damaging effects, with their consequent inflammatory processes, can jeopardize performance and may lead to overtraining syndrome, besides potentially contributing to an increased future risk of cardiovascular disease (CVD) [37, 44, 109, 131, 136]. These observations have led to research into whether antioxidant supplementation could prevent the damaging effects of RONS and thereby enhance performance [144]. It should be taken into account that: (1) the human physical performance phenomenon has always been of interest to specialists in sports medicine and exercise physiologists [42]; (2) certain characteristics related to performance are to some extent genetically determined [13, 19, 42, 76, 124]; and (3) exhausting exercise can also contribute to an increased future risk of CVD in athletes [118, 131]. Given this, knowledge on how individual genetic differences can affect response to antioxidant supplementation and how diet interacts with the human genome to influence performance, health, and disease is of unquestionable importance to the athlete's performance and health.

Many potentially significant genetic variants related to oxidative stress have already been identified [45, 55]. These include single-nucleotide polymorphisms (SNPs): Val9Ala in the mitochondrial targeting sequence of the manganese (MnSOD) gene (NCBI, refSNP ID: rs1799725), −21A/T in the promoter region of the catalase (CAT) gene (NCBI, refSNP ID: rs7943316), and Pro198Leu of the glutathione peroxidase 1 (GPx-1) gene (NCBI, refSNP ID: rs1050450) [45]. The effect of these variations has not yet been clarified; however, most of the polymorphisms result in changes in the levels or the activities of these enzymes, which can lead to a reduction in protection against oxidative stress [12]. Genes have also been implicated in changed lipid levels [18, 22], increased CVD risk [15, 23, 34, 62, 85, 95], immune reactivity [69], biotransformation of many substances, including products of oxidative stress [36, 68, 147], and athletic performance [20, 42, 78].

In previous studies by our group, we demonstrated that the carotenoid-rich oil extracted from pequi pulp (*Caryocar brasiliense* Camb.), a typical fruit found in the Brazilian Cerrado, had anti-inflammatory properties, besides reducing arterial pressure, exercise-induced DNA, tissue damages, and anisocytosis [88, 89, 92]. Although the protective effects of pequi oil are unquestionable, some of these responses were influenced by genetic polymorphisms related to oxidative stress.

Diet can interact with the human genome to influence health and disease, and genetic variability can also influence the response to diet [63, 126]. We therefore aim in the present study to investigate the influence of genetic polymorphisms of haptoglobin (Hp), MnSOD (Val9Ala), CAT (−21A/T), GPx-1 (Pro198Leu), angiotensin I-converting enzyme (ACE), glutathione S-transferases M1 (GSTM1) and T1 (GSTT1), creatine kinase muscle type (CK-MM *Taq*I and *Nco*I), C-reactive protein (CRP G1059C), and methylenetetrahydrofolate reductase (MTHFR C677T and A1298C) on the runners' responses to the dietary ingestion of antioxidant supplementation based on pequi oil (*Caryocar brasiliense* Camb.). Their effects were evaluated after races in the same environment and under the same type, intensity and length of weekly training conditions.

Materials and methods

Study design and participants

The trial was conducted after preclinical and toxicological tests in mice [87]. Volunteers of both genders (76 men and 49 women) and different age groups (15–67) were recruited in high schools, colleges, universities, clubs, and companies in Brasília (Federal District/Brazil). The selection criterion (inclusion/exclusion criteria) used for the runners was that they had at least a 4,000-m run performance, keeping the race of the same type, intensity and length of weekly training, to guarantee no additional physical stress beyond what they are accustomed to, in order to avoid differences in training amount or intensity and consequent increased oxidative stress. They should participate in two races of the same route and time, before (control group) and after (treatment group) ingestion of 400 mg of pequi oil in capsules supplied daily for 14 consecutive days. The choice of this daily ingestion took into account the data from pequi literature and the maximum daily dose of provitamin A carotenoids (25 mg) recommended by the National Agency for Sanitary Surveillance (ANVISA). To avoid plasma volume changes as function of individual variability, each athlete participated as control group and treatment group, being compared in the statistical tests with him(her)self. There was no significant change in the daily

Table 1 Relative composition of pequi (*Caryocar brasiliense* Camb.) pulp-oil capsules

Saturated	Fatty acids[a]			Carotenoids[b]			Quantity (mg/100 g)
	Carbon number	Quantity (%)	*Mono-unsaturated*	Carbon number	Quantity (%)	Types	
Palmitic	C16:0	41.78	Oleic	C18:1 (ω9)	54.28	Provitamin A	6.26–11.5
Stearic	C18:0	1.28	Palmitoleic	C16:1 (ω7)	0.67	Lycopene	1.12–2.08
Araquidic	C20:0	0.12	*Bi-unsaturated*				
			Linoleic	C18:2 (ω6)	1.36		
			Tri-unsaturated				
			Linolenic	C18:3 (ω3)	0.51		
	Total	43.18		Total	56.82	Total	6.75–28.66

The Omega nomenclature, which is defined according to carbon numeration associated with the first double bonds (3rd, 6th, 7th, or 9th) from the methyl group, is correlated to unsaturated fatty acids

[a] Present study and Miranda-Vilela et al. [90]

[b] Ramos et al. [110], Azevedo-Meleiro and Rodriguez-Amaya [9], Oliveira et al. [101] and Lima et al. [75]

routine, training, or lifestyle of all runners between the first race and the second race, except for ingestion of pequi-oil capsules.

The races before and after ingestion of pequi oil were run outdoors on flat tracks, under the same environmental conditions, and the athletes could choose the distance that they would cover (4–21 km), according to their type, intensity and length of weekly training; both races for each athlete were the same distance. The time needed by each athlete to finish the races was similar in the two races, guaranteeing the same intensity (time needed to finish the race) of races before and after pequi-oil supplementation. The volunteers were informed about the purpose of the study; all of them received a random number generated by computer and were free to withdraw at any time during the study. After the first race, they received the capsules and were instructed to take them for 14 days during or immediately after lunch until the second race.

This study was conducted according to the guidelines laid down in the Declaration of Helsinki, and all procedures involving human subjects were approved by the Ethics Committee for Health Sciences Faculty Research of the University of Brasília and by the National Commission for Ethics in Research (CONEP), number 0.001668/2005–2018. Written informed consent was obtained from all subjects.

Preparation of capsules

Pequi fruit was obtained *in natura* from the local markets of Brasília/DF (Brazil) and surrounding areas. The internal mesocarp was peeled to obtain the pulp, which was packed in a covered pot and frozen at −86°C until the moment of its use. Pequi oil was extracted by cold maceration using chloroform as a solvent. The extract was submitted to evaporation under reduced pressure for solvent removal and dried at high vacuum. Pequi oil, whose relative composition is shown in Table 1, was then incorporated in Aerosil (colloidal silicon dioxide) q.s.p., so that the users ingested a daily dose of 400 mg of pequi oil. The capsule production was patented as number PI0601631-6 (National Institute of Industrial Property—INPI).

Procedures and measurements

Waist circumference (WC), hip circumference, waist-hip ratio, and body mass index (BMI) were checked before the first race as previously described [88]. All volunteers had their arterial pressure checked before each race. Blood samples were drawn with EDTA immediately after races in two rounds: (1) race without pequi-oil supplementation and (2) race after ingestion of 400 mg of pequi oil in capsules supplied daily for 14 consecutive days. Blood samples were used to count white blood cells and platelets, and for genotyping of the polymorphisms, while serum samples were submitted to TBARS assay and dosages of postprandial lipid profile and C-reactive protein (CRP and high-sensitivity CRP—hs-CRP).

Biochemical analyses and cell counts

Serum postprandial lipid profile and CRP analyses were run on the automated chemistry analyzer ADVIA 1650 (Bayer Diagnostics), using the appropriate Advia chemistry reagents. Leukocyte and platelet counts were carried out in the automated analyzer Cell-Dyn 3700 (Abbott Diagnostics), and hs-CRP was measured by an immunometric assay (Immulite 2000, DPC, Medlab). The TBARS assay was carried out according to Wasowicz et al. [141].

Genotyping of the polymorphisms

Peripheral blood samples were collected in Vacutainer tubes containing EDTA, and genomic DNA was isolated from the buffy-coat layer using the GFX purification kit (GE Healthcare, Buckinghamshire, England). DNA samples were stored at −20°C until analysis.

Hp genotypes were determined by allele-specific PCR (Polymerase Chain Reaction) as described by Yano et al. [143]. Identification of alleles Hp^{*1F}, Hp^{*1S}, and Hp^{*2} was based on product analysis of three independent PCR. MnSOD, CAT, GPx-1, CK-MM, CRP, and MTHFR genotypes were determined by polymerase chain reaction (PCR)-based restriction fragment length polymorphism (RFLP) assays performed as described by Mitrunen et al. [94] (MnSOD), Ukkola et al. [134] (CAT), Zhao et al. [147] (GPx-1), Rivera et al. [113], Zhou et al. [148, 149] (CK), Suk et al. [127] (CRP), and Yi et al. [145] (MTHFR). DNA fragments containing I/D polymorphism in intron 16 of the ACE gene were amplified by PCR as previously described by Rigat et al. [112], using DMSO (dimethyl sulfoxide) as recommended by Odawara et al. [100], to avoid mistyping of the DD genotype. The glutathione S-transferase (GST) GSTM1 and GSTT1 fragments were amplified simultaneously as proposed by Chen et al. [29], using β-globin as positive control. The absence of an amplification product combined with the presence of a positive control band (268-bp DNA fragment of β-globin) indicated the null (variant) type for both polymorphisms (Table 2). PCR and PCR-based RFLP products were separated by electrophoresis in 10 (GPX1) and 6% (other polymorphisms) non-denaturing polyacrylamide gels and visualized by staining with silver nitrate.

Statistical analyses

Allelic and genotypic frequencies were estimated by gene counting, and the goodness of fit of the genotype distribution to Hardy–Weinberg equilibrium (HWE) was assessed by the chi-square (χ^2) test. Values of $P > 0.05$ indicated HWE. Data for genetic diversity were assessed by comparing the observed and expected heterozygosities; F_{IS} (inbreeding coefficient), probability (P) values, and linkage disequilibrium test for the two polymorphisms of CK and MTHFR were generated using Genepopweb Statistical Program version 4.0 (http://genepop.curtin.edu.au). Although for the used biochemical markers and cell counts there are no differences between sexes for clinical purposes, the distribution frequencies of the genotypes of each polymorphism between sexes were also tested through the Mann–Whitney U test.

Statistical analysis was carried out using SPSS (Statistical Package for the Social Sciences) version 15.0. Data were expressed as mean ± SEM (standard error of mean) and values of $P < 0.05$ were considered statistically significant. Because the possible correlations between sex/age groups, sex/distance covered, and age groups/distance covered have been previously reported [88], the correlations analyzed here through chi-square correlation test were limited to the following parameters: genetic markers/sex, genetic markers/age groups, and genetic markers/distance covered. The continuous variables were tested for normal distribution with Shapiro–Wilk. For the analyzed parameters, statistical analyses on the influences of pequi-oil intake on the total and sex groups, as well as on the age groups and distance covered, have also been previously described [88]. Therefore, this study evaluated only the influences of the genetic polymorphisms on plasma lipid peroxidation, postprandial serum lipids, inflammatory response, and arterial pressure of runners before and after pequi-oil supplementation. For GSTM1, GSTT1, and CRP G1059C, the influence of the polymorphisms was investigated through the independent samples t-test or the Mann–Whitney U test (when the data were not normally distributed); for the other genetic markers, these influences were verified by ANOVA or by the Kruskall–Wallis test (when the data were not normally distributed). For significant ANOVA results, Bonferroni's post hoc test was chosen to carry out 2-to-2 comparisons; for significant Kruskal–Wallis results, Mann–Whitney U test was performed. To verify differences in the comparison of before-after pequi-oil supplementation, the statistical significance was assessed by the paired-samples t-test or the Wilcoxon matched pairs test (when the data were not normally distributed).

Results

Allele and genotype frequencies and Hardy–Weinberg equilibrium

There were significant deviations from Hardy–Weinberg equilibrium (HWE) for the Hp, MnSOD, GSTM1, and GSTT1 loci. For the Hp locus, it was appropriate to a heterozygote deficit ($P = 0.0012$), while for the MnSOD locus, to a heterozygote excess ($P = 0.0000$). For GSTM1 and GSTT1, results were compatible with heterozygote deficit, due to homozygous (+/+, wild type) and heterozygous (±) being considered together within non-null genotypes, given that the PCR method is not suitable for distinguishing these genotypes. According to data of heterozygosity-observed (H_o) and heterozygosity-expected (H_e) of the Hp locus, the main factors that contributed to deviation from HWE were the higher frequencies of Hp1F-1F and Hp1S-1S with regard to the expected as well as the lower observed frequency of Hp1F-1S. When the Hp^{*1}

Table 2 Chromosome location, primer sequences, and restriction enzymes used in the genotyping of Haptoglobin (Hp), MnSOD, CAT, GPx-1, ACE, GSTM1, GSTT1, CK-MM, CRP, and MTHFR genes' polymorphisms

Genetic Markers	Chromosome location	Primer sequences	Restriction enzymes	References
Hp*1F	16q22.1		–	[143]
F3		5′ CAGGAGTATACACCTTAAATG 3′		
C72		5′ AATTTAAAATTGGCATTTCGCC 3′		
Hp*1S				
C51		5′ GCAATGATGTCACGGATATC 3′		
S2		5′ TTATCCACTGCTTCTCATTG 3′		
Hp*2				
F3		5′ CAGGAGTATACACCTTAAATG 3′		
C42		5′ TTACACTGGTAGCGAACCGA 3′		
MnSOD	6q25.3		*Ngo* MIV	[94]
Sense		5′ ACCAGCAGGCAGCTGGCGCCGG 3′		
Antisense		5′ GCGTTGATGTGAGGTTCCAG 3′		
CAT	11p13		*Hinf* I	[134]
Sense		5′ AATCAGAAGGCAGTCCTCCC 3′		
Antisense		5′ TCGGGGAGCACAGAGTGTAC 3′		
GPx-1	3p21.3		*Apa* I	[147]
Sense		5′AGCCCAACTTCATGCTCTTC 3′		
Antisense		5′CAGGTGTTCCTCCCTCGTAG 3′		
ACE	17q23		–	[100, 112]
Sense		5′ CTGCAGACCACTCCCATCCTTTCT 3′		
Antisense		5′ GATGTGGCCATCACATTCGTCAGAT 3′		
GSTM1	1p13.3		–	[29]
GSTM1/6		5′ GCTTACCGTGTTATGGAGGTTC 3′		
GSTM1E7A		5′ TTGGGAAGGCGTCCAAGCGC3′		
GSTM1E7		5′ TTGGGAAGGCTGCCAAGCAG 3′		
GSTT1	22q11.2		–	
Sense		5′ TTGGGAAGGCGTCCAAGCGC3′		
Antisense		5′ TTGGGAAGGCGTCCAAGCGC3′		
β-globin	11p15.5	Positive control	–	
Beta 1		5′ CAACTTCATCCACGTTCACC3′		
Beta 2		5′ GAAGAGCCAAGGACAGTTAC3′		
CK-MM	19q13.2–q13.3		*Nco*I e *Taq*I	[113, 148, 149]
Sense		5′ GTGCGGTGGACACAGCTGCCG 3′		
Antisense		5′ CAGCTTGGTCAAAGACATTGAGG 3′		
CRP G1059C	1q21–q23		*Mae*III	[127]
Sense		5′GCCCAGGGTGAGGAAGAGTCT 3′		
Antisense		5′ CCCGCCAGTTCAGGACATTAG 3′		
MTHFR C677T	1p36.3			[145]
Sense		5′ TGAAGGAGAAGGTGTCTGCGGGA 3′	*Hinf*I	
Antisense		5′ AGGACGGTGCGGTGAGAGTG 3′		
MTHFR A1298C				
Sense		5′ CAAGGAGGAGCTGCTGAAGA 3′	*Mbo*II	
Antisense		5′ CCACTCCAGCATCACTCACT 3′		

alleles were treated as a single block, the genotypic distributions were in accordance with the EHW ($P = 0.2133$). The MnSOD locus presented a heterozygosity-observed (H_o) value higher than the heterozygosity-expected (H_e) value, and an F_{IS} (inbreeding coefficient) value compatible with selection in favor of heterozygotes. The genotypic distributions of CAT, GPx-1, ACE, CK *Nco*I, CK *Taq*I, CRP G1059C, MTHFR C677T, and MTHFR A1298C loci were in accordance with HWE (Table 3). A strong linkage disequilibrium was detected only between the CK *Nco*I

Table 3 Distribution of Haptoglobin (Hp), MnSOD, CAT, GPx-1, ACE, GSTM1, GSTT1, CK *Nco*I, CK *Taq*I, CRP G1059C, MTHFR C677T and MTHFR A1298C allele frequencies, genetic diversity parameters, genotype frequencies, and Hardy–Weinberg equilibrium data for chi-square (χ^2) test

Genetic Markers	Allele frequencies		Heterozygosity-observed (H_o)	Heterozygosity-expected (H_e)	F_{IS} (Inbreeding coefficient)	Genotypes	Genotype frequencies	Number of observed individuals	Number of expected individuals	HWE test (P values)
Hp*	Hp^{*1F}	0.176	0.504	0.617	+0.1831	1F-1F	0.064	8	3.87	0.0117
						1F-1S	0.064	8	14.61	
	Hp^{*1S}	0.332				1S-1S	0.160	20	13.78	
						1F-2	0.160	20	21.65	
	Hp^{*2}	0.492				1S-2	0.280	35	40.84	
						2-2	0.272	34	30.25	
MnSOD*	Val	0.568	0.800	0.491	−0.6293	Val/Val	0.168	21	40.33	0.0000
	Ala	0.432				Val/Ala	0.800	100	61.34	
						Ala/Ala	0.032	4	23.33	
CAT	A	0.396	0.424	0.478	+0.1130	AA	0.184	23	19.60	0.3173
	T	0.604				AT	0.424	53	59.80	
						TT	0.392	49	45.60	
GPx-1	Pro	0.688	0.400	0.429	+0.0676	Pro/Pro	0.488	61	59.17	0.4458
	Leu	0.312				Pro/Leu	0.400	50	53.66	
						Leu/Leu	0.112	14	12.17	
ACE	D	0.604	0.488	0.478	−0.0209	DD	0.360	45	45.60	0.8225
	I	0.396				ID	0.488	61	59.80	
						II	0.152	19	19.60	
GSTM1*	Null	0.648	–	–	–	Null	0.648	81	52.49	0.0000
	Present	0.352				Non-null	0.352	44	72.51	
GSTT1*	Null	0.136	–	–	–	Null	0.136	17	2.31	0.0000
	Present	0.864				Non-null	0.864	108	122.69	
CK *Nco*I	A	0.720	0.448	0.403	−0.1117	AA	0.496	62	64.80	0.2141
	G	0.280				AG	0.448	56	50.40	
						GG	0.056	7	9.80	
CK *Taq*I	1	0.336	0.480	0.446	−0.0762	1-1	0.096	12	14.11	0.5479
	2	0.664				1-2	0.480	60	55.78	
						2-2	0.424	53	55.11	
CRP G1059C	G	0.948	0.104	0.099	−0.0508	GG	0.896	112	112.34	0.5394
	C	0.052				GC	0.104	13	12.32	
MTHFR C677T	C	0.672	0.400	0.441	+0.0930	CC	0.472	59	56.45	0.3008
	T	0.328				CT	0.400	50	55.10	
						TT	0.128	16	13.45	
MTHFR A1298C	A	0.796	0.376	0.325	−0.1569	AA	0.608	76	79.20	0.0779
	C	0.204				AC	0.376	47	40.60	
						CC	0.016	2	5.20	

* $P < 0.05$ indicates deviation from Hardy–Weinberg equilibrium, appropriate to a heterozygote deficit for Hp locus ($p = 0.0012$) and a heterozygote excess for MnSOD locus ($P = 0.0000$). P values were generated using statistical program Genepopweb version 4.0 (http://genepop.curtin.edu.au). For GSTM1 and GSTT1, genotypes were considerate as follows: Null = −/−; Non-null = +/+ and ±

and the *Taq*I RFLPs ($P = 0.00047$), with 11 individuals carrying AA/1-1 haplotype, 32 carrying AA/1-2 haplotype, 19 carrying AA/2-2 haplotype, 1 carrying AG/1-1 haplotype, 28 carrying AG/1-2 haplotype, 27 carrying AG/2-2 haplotype, and 7 carrying GG/2-2 haplotype; nobody presented GG/1-1 or GG/1-2 haplotypes (data not provided in Tables). Between the sexes, there was a significant difference in the distribution frequencies of the genotypes only for the CAT polymorphism ($P = 0.030$; Fig. 1).

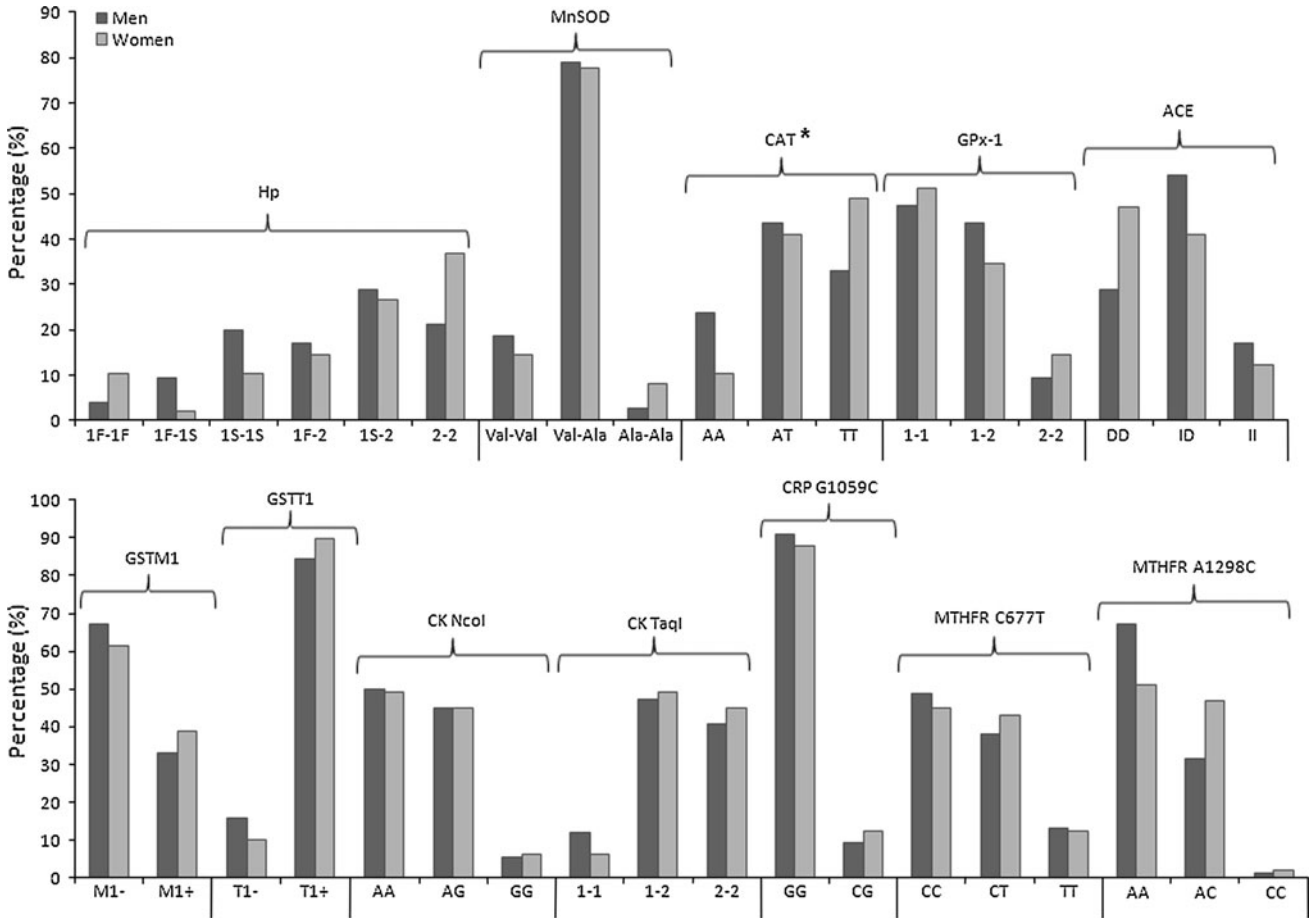

Fig. 1 Distribution frequencies of the genotypes of Haptoglobin (Hp), MnSOD, CAT, GPx-1, ACE, GSTM1, GSTT1, CK NcoI, CK TaqI, CRP G1059C, MTHFR C677T, and MTHFR A1298C polymorphisms between sexes. *P* values were generated by the Mann–Whitney *U* test. Asterisks indicate significant differences between the distribution frequencies of the genotypes between sexes ($P = 0.030$)

Correlation test

There was a significant correlation between sex and CAT ($P = 0.027$), and distance covered and CK*Taq*I ($P = 0.035$; Fig. 2).

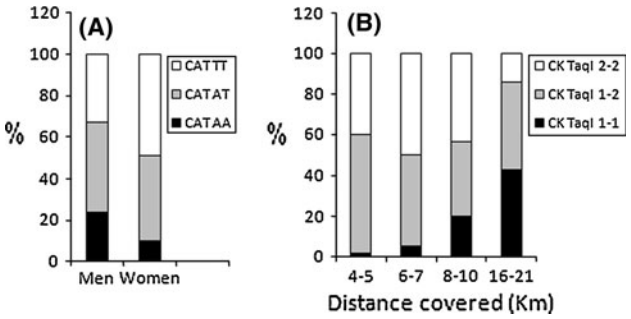

Fig. 2 Significant correlations between **a** sex and CAT-21A/T genotypes; **b** distance covered and CK-MM *Taq*I genotypes. *P* values were generated by the chi-square correlation test: **a** $P = 0.027$; **b** $P = 0.035$

Leukogram

For total leukocytes, significant differences in the comparison of before-after pequi-oil supplementation were showed for CRP CG ($P = 0.043$) genotype, whose values increased after pequi. For lymphocytes, GPx-1 Pro/Pro ($P = 0.033$) and CK *Nco*I AA ($P = 0.035$) genotypes presented decreased values after supplementation, while the number of segmented increased for CRP GC ($P = 0.011$) genotype. CAT AT ($P = 0.008$), GPx-1 Pro-Leu ($P = 0.036$), CK *Nco*I AG (0.010), MTHFR677 CC (0.018), and MTHFR1298 AA ($P = 0.013$) genotypes showed significant increase in the values of basophils after pequi-oil treatment, while eosinophils were enhanced for Hp 1S-2 ($P = 0.024$), CAT AA ($P = 0.017$), GPx-1 Leu/Leu ($P = 0.046$), GSTM1 null ($P = 0.027$), and MTHFR677 TT ($P = 0.036$) genotypes, but all of them were inside the reference values. Pequi oil also resulted in increased monocytes for MnSOD Val/Ala ($P = 0.027$),

CAT AT ($P = 0.033$), GPx-1 Pro/Leu ($P = 0.001$), GSTM1 null ($P = 0.006$), GSTT1 non-null ($P = 0.002$), CK *Nco*I AG ($P = 0.017$), CK *Taq*I 2-2 ($P = 0.006$), CRP CG ($P = 0.028$), and MTHFR677 CC ($P = 0.040$) genotypes; for GSTT1 null ($P = 0.023$), values dropped after supplementation (Table 4).

Concerning the influences of the genetic polymorphisms, significant differences before pequi-oil supplementation were presented for ACE, in the values of total leukocytes ($P = 0.009$) and segmented (0.028); for GSTT1 ($P = 0.014$) and MTHFR C677T ($P = 0.038$), in the values of eosinophils; and for GSTT1 ($P = 0.001$) and MTHFR C677T ($P = 0.018$), in the values of monocytes. For ACE, significant differences in the number of total leukocytes appeared between ID and DD ($P = 0.013$) and between ID and II (0.013) genotypes, where ID genotype presented increased values; a similar increase in eosinophils was showed for ID genotype with respect to DD genotype ($P = 0.017$). For GSTT1, the null genotype presented significantly higher eosinophils ($P = 0.014$) and monocytes ($P = 0.001$) compared with non-null genotypes, with the same result occurring with MTHFR677 CT with respect to CC genotype ($P = 0.014$ for eosinophils; $P = 0.007$ for monocytes). Although Kruskall–Wallis test detected significant differences between MTHFR1298 genotypes ($P = 0.038$) in the values of basophils "before", these were not related to two specific genotypes. After pequi-oil supplementation, no significant differences were observed for ACE polymorphism in the values of total leukocytes or segmented, nor for GSTT1 and MTHFR C677T polymorphisms in the values of monocytes, with only those related to eosinophils remaining ($P = 0.047$ for GSTT1; $P = 0.029$ for MTHFR C677T). Nevertheless, for the MTHFR C677T polymorphism, individuals carrying T allele presented increased eosinophils compared with the C homozygous ($P = 0.020$ between CC and CT; $P = 0.049$ between CC and TT). Besides these results, other significant differences appeared for CAT, in the values of basophils ($P = 0.004$); for GSTM1, in the values of rods ($P = 0.003$); for GSTT1 ($P = 0.038$) and MTHFR A1298C ($P = 0.024$), in the values of lymphocytes; and for CRP G1059C, in the values of total leukocytes ($P = 0.003$), segmented ($P = 0.020$), and monocytes ($P = 0.004$). For CAT, basophils showed a significant increase for AT genotype compared with AA (0.001) or TT ($P = 0.039$) genotypes. Similarly, significant increases in the values of rods were observed for GSTM1 non-null genotypes, while GSTT1 null genotype presented increased lymphocytes. Individuals carrying MTHFR1298 AA ($P = 0.043$) or CC ($P = 0.045$) genotypes showed a fall in the number of lymphocytes compared with heterozygous, while the carriers of CRP1059 variant allele presented a significant increase in total leukocytes, segmented, and monocytes (Table 4).

Plateletgram

In the comparison between before and after pequi-oil supplementation, significant differences appeared for Hp 1F-1F ($P = 0.036$), 1F-1S ($P = 0.018$), 1F-2 ($P = 0.012$), and 1S-2 ($P = 0.012$), MnSOD Val/Val ($P = 0.010$) and Val/Ala ($P = 0.000$), CAT TT ($P = 0.000$), GPx-1 Pro/Pro ($P = 0.002$) and Pro/Leu ($P = 0.001$), ACE ID ($P = 0.000$), GSTM1 null (0.000), GSTT1 null ($P = 0.003$) and non-null ($P = 0.000$), CK *Nco*I AA ($P = 0.003$) and AG ($P = 0.000$), CK *Taq*I 1-2 ($P = 0.002$) and 2-2 ($P = 0.001$), CRP GG ($P = 0.000$), MTHFR677 CC ($P = 0.000$) and TT ($P = 0.001$), and MTHFR1298 AA ($P = 0.003$) and AC ($P = 0.000$) genotypes in the values of platelets, which fell after pequi-oil treatment. For plateletocrit, the same downward trend occurred after pequi, with significantly decreased values for Hp 1F-1F ($P = 0.046$), 1F-1S ($P = 0.018$), 1S-1S ($P = 0.022$), and 1S-2 ($P = 0.022$), MnSOD Val/Ala ($P = 0.004$), CAT TT ($P = 0.000$), GPx-1 Pro/Pro ($P = 0.001$) and Pro/Leu ($P = 0.035$), ACE ID ($P = 0.011$, GSTM1 null ($P = 0.002$) and non-null ($P = 0.035$), GSTT1 null ($P = 0.021$) and non-null ($P = 0.002$), CK *Nco*I AA ($P = 0.020$) and AG ($P = 0.001$), CK *Taq*I 1-2 ($P = 0.039$) and 2-2 ($P = 0.003$), CRP GG ($P = 0.000$), MTHFR677 CC ($P = 0.000$), and MTHFR1298 AA ($P = 0.029$) and AC ($P = 0.000$) genotypes. Significant reductions in mean platelet volume (MPV) values were seen only for Hp 1S-1S ($P = 0.018$) and ACE ID ($P = 0.011$) genotypes after pequi treatment, while for platelet distribution width (PDW), a significant increase in the values was observed for Hp 2-2 genotype ($P = 0.012$; Table 5).

As regards the influence of genetic polymorphisms before pequi-oil supplementation, significant differences appeared only for MTHFR C677T polymorphism in the values of platelets ($P = 0.016$) and for CK *Nco*I polymorphism in the values of PDW ($P = 0.045$). For MTHFR677, significant differences were showed between CC and TT ($P = 0.008$), with increased platelet values for TT genotypes. For CK *Nco*I, AG genotype presented higher PDW values compared with AA genotype. Although the Kruskall–Wallis test showed a P value of 0.056 for Hp in the values of MPV "before", the Mann–Whitney U test detected significant differences between Hp 1S-1S and Hp 1F-2 ($P = 0.017$), between 1S-1S and 1S-2 ($P = 0.012$), and between Hp 1S-2 and 2-2 ($P = 0.044$) in the 2-to-2 comparisons. Similarly, the Mann–Whitney U test also detected a significant difference between Hp 1F-1S and 1F-2 ($P = 0.015$) in the values of PDW "before". After pequi-oil supplementation, significant

Table 4 Influences of Haptoglobin (Hp), MnSOD, CAT, GPx-1, ACE, GSTM1, GSTT1, CK *Nco*I, CK *Taq*I, CRP G1059C, MTHFR C677T and MTHFR A1298C genes' polymorphisms on the leukogram before and after pequi-oil supplementation

Genetic Markers	Total leukocytes (/mm^3)		Lymphocytes (/mm^3)		Segmented (/mm^3)		Rods (/mm^3)		Basophils (/mm^3)		Eosinophils (/mm^3)		Monocytes (/mm^3)	
	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After
Hp														
1F-1F	6,425.00 ± 290.78	6,850.00 ± 548.05	2,313.75 ± 197.11	2,359.00 ± 299.70	3,435.25 ± 268.34	3,704.00 ± 488.19	13.25 ± 13.25	11.38 ± 11.38	79.13 ± 16.48	91.88 ± 11.19	149.00 ± 22.29	112.13 ± 19.04	434.63 ± 68.44	571.63 ± 66.68
1F-1S	7,487.50 ± 1,291.93	7,000.00 ± 853.77	1,923.75 ± 193.56	2,297.63 ± 276.28	4,740.13 ± 1,176.15	3,909.50 ± 607.49	101.00 ± 64.76	26.50 ± 26.50	83.00 ± 14.49	79.50 ± 13.40	101.25 ± 23.42	134.38 ± 47.93	539.50 ± 93.29	549.88 ± 94.59
1S-1S	7,994.12 ± 715.15	7,764.71 ± 605.61	2,719.56 ± 209.79	2,586.89 ± 184.12	4,470.89 ± 596.70	4,343.22 ± 465.01	28.22 ± 19.38	26.35 ± 16.53	74.17 ± 12.39	89.22 ± 12.95	175.56 ± 32.29	173.44 ± 36.23	524.50 ± 52.14	556.72 ± 49.65
1F-2	7,515.00 ± 414.49	7,690.00 ± 329.03	2,840.05 ± 199.83	2,651.90 ± 169.33	3,914.45 ± 265.02	4,024.95 ± 301.57	3.32 ± 3.32	5.11 ± 5.11	88.45 ± 12.73	105.30 ± 10.36	158.55 ± 31.11	152.05 ± 29.82	491.60 ± 40.33	586.10 ± 47.22
1S-2	7,103.12 ± 419.06	7,090.63 ± 356.60	2,599.75 ± 206.66	2,656.38 ± 237.66	3,788.91 ± 267.41	3,644.50 ± 218.58	37.81 ± 18.06	43.25 ± 20.76	77.03 ± 8.51	93.22 ± 7.83	129.69 ± 18.90	155.41 ± 15.49*	462.44 ± 36.09	495.66 ± 31.21
2-2	7,696.87 ± 311.91	7,771.88 ± 316.01	2,885.69 ± 164.48	2,743.87 ± 169.69	4,021.81 ± 229.42	4,156.53 ± 234.81	11.72 ± 6.90	26.28 ± 15.44	100.56 ± 9.21	111.13 ± 8.73	149.75 ± 20.97	165.34 ± 26.74	524.69 ± 46.44	569.59 ± 39.20
P values	0.433	0.437	0.070	0.810	0.728	0.517	0.314	0.857	0.373	0.276	0.625	0.684	0.816	0.607
MnSOD														
Val/Val	7,305.26 ± 508.09	7,136.84 ± 423.87	2,871.68 ± 304.69	2,597.79 ± 210.58	3,711.79 ± 270.98	3,670.47 ± 326.61	8.72 ± 6.03	15.78 ± 15.78	75.16 ± 9.94	87.16 ± 8.91	176.84 ± 33.90	183.74 ± 25.56	457.11 ± 50.54	500.42 ± 49.65
Val/Ala	7,484.95 ± 237.47	7,523.66 ± 206.72	2,644.79 ± 93.08	2,628.18 ± 107.11	4,076.53 ± 188.75	4,042.41 ± 151.86	30.39 ± 9.44	29.99 ± 9.24	87.04 ± 5.51	101.46 ± 5.06	141.76 ± 11.36	149.90 ± 13.50	503.16 ± 23.01	557.33 ± 21.27*
Ala/Ala	7,240.00 ± 1,027.91	7,380.00 ± 673.35	2,403.00 ± 242.8	2,651.20 ± 286.97	4,078.60 ± 839.11	3,898.40 ± 458.03	11.20 ± 11.20	0.00 ± 0.00	94.80 ± 10.50	85.80 ± 10.32	118.00 ± 42.3	163.40 ± 37.81	534.40 ± 102.24	581.20 ± 79.12
P values	0.908	0.823	0.793	0.924	0.865	0.675	0.803	0.442	0.298	0.346	0.764	0.178	0.567	0.413
CAT														
AA	7,280.00 ± 558.83	6,920.00 ± 425.85	2,739.43 ± 230.87	2,728.10 ± 209.69	3,856.81 ± 472.24	3,473.38 ± 261.02	13.43 ± 13.43	24.81 ± 20.49	77.90 ± 11.97	75.19 ± 7.82	139.24 ± 18.77	180.71 ± 29.16**, $^{\neq}$	482.86 ± 45.05	551.43 ± 44.30
AT	7,540.00 ± 309.01	7,728.00 ± 283.23	2,799.60 ± 141.04	2,746.08 ± 157.72	3,975.84 ± 224.25	4,037.00 ± 220.21	26.34 ± 11.78	27.62 ± 12.62	84.94 ± 7.33	113.96 ± 6.87**, $^{a,\neq}$, *, ^{c}	151.48 ± 18.82	145.54 ± 18.38	490.68 ± 28.67	563.22 ± 27.78*, $^{\neq}$
TT	7,414.89 ± 332.48	7,391.49 ± 274.95	2,503.81 ± 129.93	2,448.28 ± 127.73	4,134.60 ± 249.53	4,136.74 ± 204.45	31.98 ± 13.55	26.02 ± 11.17	89.38 ± 7.14	92.45 ± 6.49	144.19 ± 16.11	155.89 ± 17.48	510.21 ± 36.45	533.23 ± 32.21
P values	0.757	0.412	0.407	0.525	0.393	0.151	0.311	0.917	0.758	0.004	0.954	0.556	0.942	0.805
GPx-1														
Pro/Pro	7,787.93 ± 324.14	7,484.48 ± 272.35	2,689.93 ± 131.51	2,516.60 ± 128.63*, $^{\neq}$	4,312.79 ± 266.69	4,168.45 ± 196.70	39.59 ± 13.99	32.38 ± 11.54	90.53 ± 6.19	102.28 ± 7.12	138.02 ± 15.27	129.81 ± 13.62	512.07 ± 31.61	529.48 ± 24.85
Pro/Leu	7,030.43 ± 286.62	7,373.91 ± 263.72	2,619.77 ± 143.84	2,692.94 ± 143.41	3,706.91 ± 188.07	3,806.43 ± 195.90	7.09 ± 3.17	25.98 ± 13.24	77.57 ± 7.95	94.28 ± 5.89*	160.64 ± 18.16	184.49 ± 22.07	480.04 ± 29.17	582.83 ± 32.73*, $^{\neq}$
Leu/Leu	7,384.62 ± 622.63	7,607.69 ± 558.67	2,772.46 ± 221.73	2,856.31 ± 323.78	3,826.46 ± 446.38	3,734.31 ± 433.76	36.75 ± 28.07	0.00 ± 0.00	91.31 ± 15.08	96.85 ± 9.09	132.31 ± 22.70	169.15 ± 27.42	491.69 ± 61.19*, $^{\neq}$	515.38 ± 58.35
P values	0.427	0.981	0.678	0.454	0.588	0.712	0.307	0.196	0.294	0.918	0.639	0.109	0.791	0.355

Table 4 continued

Genetic Markers	Total leukocytes (/mm^3)		Lymphocytes (/mm^3)		Segmented (/mm^3)		Rods (/mm^3)		Basophils (/mm^3)		Eosinophils (/mm^3)		Monocytes (/mm^3)	
	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After
ACE														
DD	7,036.59 ± 356.98	7,319.51 ± 328.45	2,686.63 ± 157.06	2,667.78 ± 170.95	3,607.46 ± 240.84	3,794.80 ± 228.24	29.61 ± 13.42	35.52 ± 15.41	77.85 ± 7.34	92.05 ± 8.44	131.80 ± 14.50	131.90 ± 11.56	503.29 ± 36.44	562.56 ± 33.02
ID	8,013.79 ± 301.45*,[a,c]	7,632.76 ± 266.94	2,761.20 ± 120.09	2,657.81 ± 123.92	4,461.86 ± 253.69*,[a]	4,136.25 ± 186.21	28.93 ± 12.17	19.05 ± 10.08	91.68 ± 6.93	103.07 ± 5.48	157.92 ± 17.25	179.22 ± 20.77	505.51 ± 29.13	560.44 ± 28.43
II	6,544.44 ± 374.97	7,188.89 ± 269.21	2,340.22 ± 239.79	2,415.17 ± 226.57	3,497.50 ± 213.75	3,866.22 ± 349.23	9.89 ± 5.74	30.39 ± 18.08	82.39 ± 12.27	98.17 ± 10.63	141.89 ± 25.58	134.28 ± 18.46	455.22 ± 45.57	481.78 ± 32.80
P values	0.009	0.482	0.188	0.625	0.028	0.360	0.774	0.512	0.287	0.352	0.891	0.576	0.577	0.345
GSTM1														
Null	7,306.49 ± 235.12	7,254.55 ± 208.22	2,735.84 ± 107.97	2,661.48 ± 115.81	3,853.82 ± 180.95	3,758.60 ± 142.72	18.24 ± 8.04	14.75 ± 8.35	82.04 ± 5.54	93.56 ± 5.00	135.21 ± 12.70	153.01 ± 13.27*,[≠]	481.71 ± 24.97	553.49 ± 24.08**,[≠]
Non-null	7,712.50 ± 412.00	7,840.00 ± 335.69	2,549.44 ± 157.54	2,554.37 ± 152.86	4,326.02 ± 307.62	4,385.51 ± 264.55	41.07 ± 15.98	48.80 ± 15.72**,[a]	91.88 ± 8.62	107.76 ± 8.03	167.41 ± 19.26	161.39 ± 22.51	525.90 ± 35.38	541.07 ± 31.07
P values	0.627	0.276	0.268	0.543	0.232	0.092	0.077	0.003	0.367	0.153	0.102	0.966	0.247	0.828
GSTT1														
Null	8,482.35 ± 680.41	8,176.47 ± 552.77	2,970.29 ± 236.03	2,957.88 ± 195.32	4,511.65 ± 601.57	4,132.41 ± 460.59	6.24 ± 6.24	27.59 ± 21.49	100.12 ± 12.43	97.65 ± 7.70	218.76 ± 37.75	201.12 ± 33.01	651.76 ± 44.99	577.47 ± 48.18*,[≠]
Non-null	7,269.00 ± 212.09	7,332.00 ± 186.69	2,620.71 ± 95.92	2,568.11 ± 101.73*,[a]	3,934.78 ± 157.17	3,950.17 ± 135.82	29.64 ± 8.89	26.30 ± 8.42	82.99 ± 5.05	98.63 ± 4.89	134.22 ± 10.38*,[a]	148.32 ± 12.29*,[a]	471.03 ± 21.63**,[a]	544.42 ± 20.71**,[≠]
P Values	0.068	0.106	0.141	0.038	0.280	0.696	0.224	0.989	0.138	0.646	0.014	0.047	0.001	0.476
CK *Nco*I														
AA	7,337.29 ± 256.20	7,222.03 ± 233.48	2,663.32 ± 118.60	2,493.18 ± 115.56*,[≠]	3,904.80 ± 178.46	3,926.12 ± 189.84	32.19 ± 11.64	36.68 ± 13.30	89.42 ± 6.84	94.27 ± 6.13	151.63 ± 13.04	155.70 ± 14.87	504.23 ± 30.06	527.20 ± 25.19
AG	7,634.62 ± 363.81	7,671.15 ± 293.73	2,727.71 ± 146.35	2,773.42 ± 154.12	4,164.98 ± 295.52	3,996.40 ± 202.09	20.25 ± 11.12	17.82 ± 8.71	80.98 ± 6.63	104.15 ± 6.57*	146.19 ± 18.94	161.17 ± 19.94	484.15 ± 28.76	554.10 ± 29.57*,[≠]
GG	6,866.67 ± 644.29	7,866.67 ± 742.37	2,257.83 ± 262.59	2,642.33 ± 393.94	3,874.00 ± 462.32	4,306.33 ± 509.29	19.67 ± 12.70	0.00 ± 0.00	84.67 ± 25.48	91.67 ± 14.85	95.83 ± 17.64	112.67 ± 20.94	537.33 ± 106.28	726.33 ± 80.91
P values	0.777	0.490	0.570	0.581	0.994	0.761	0.198	0.437	0.688	0.748	0.299	0.826	0.922	0.094
CK *Taq*I														
1-1	7,272.73 ± 564.74	7,081.82 ± 602.69	2,666.27 ± 256.58	2,288.09 ± 229.55	4,021.91 ± 525.48	4,095.00 ± 592.83	7.91 ± 7.91	17.09 ± 11.47	66.45 ± 16.36	97.36 ± 13.93	94.45 ± 18.88	92.09 ± 15.60	406.18 ± 60.78	492.18 ± 51.26
1-2	7,284.21 ± 279.22	7,335.09 ± 223.92	2,658.65 ± 124.93	2,600.11 ± 120.46	3,849.95 ± 216.42	3,873.40 ± 178.49	23.18 ± 11.43	23.21 ± 11.14	87.58 ± 6.17	95.77 ± 5.66	140.67 ± 14.55	150.67 ± 15.99	513.60 ± 23.92	536.18 ± 25.51
2-2	7,671.43 ± 359.75	7,677.55 ± 315.25	2,686.30 ± 146.77	2,725.76 ± 160.63	4,208.46 ± 262.99	4,067.78 ± 205.00	33.92 ± 12.55	32.35 ± 13.25	87.22 ± 7.79	101.84 ± 7.36	164.36 ± 18.26	175.96 ± 19.74	498.22 ± 37.33	576.54 ± 32.13**,[≠]
P values	0.809	0.822	0.983	0.534	0.538	0.676	0.284	0.64	0.508	0.919	0.244	0.138	0.308	0.402

Table 4 continued

Genetic Markers	Total leukocytes (/mm^3)		Lymphocytes (/mm^3)		Segmented (/mm^3)		Rods (/mm^3)		Basophils (/mm^3)		Eosinophils (/mm^3)		Monocytes (/mm^3)	
	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After
CRP G1059C														
GG	7,349.04 ± 225.92	7,257.69 ± 183.85	2,626.70 ± 95.98	2,556.44 ± 92.16	3,976.72 ± 174.77	3,874.71 ± 139.61	28.91 ± 8.59	27.36 ± 8.63	86.35 ± 5.00	97.85 ± 4.68	142.18 ± 10.72	151.23 ± 11.39	488.79 ± 21.44	526.35 ± 18.48
GC	8,215.38 ± 488.70	9,030.77 ± 507.30**,$^{a,*,\neq}$	3,029.46 ± 217.56	3,172.08 ± 357.89	4,350.38 ± 335.73	4,797.92 ± 373.79*,$^{a,\neq}$	4.85 ± 4.85	19.62 ± 13.72	78.23 ± 13.83	103.69 ± 10.63	180.46 ± 44.49	193.85 ± 52.30	563.92 ± 65.40	733.54 ± 69.46**,$^{a,*,\neq}$
P values	0.092	0.003	0.079	0.096	0.173	0.020	0.351	0.757	0.692	0.484	0.594	0.674	0.173	0.004
MTHFR C677T														
CC	7,201.79 ± 352.16	7,155.36 ± 249.82	2,592.72 ± 127.15	2,580.26 ± 130.98	3,941.67 ± 281.28	3,796.54 ± 183.41	27.58 ± 9.12	19.51 ± 8.28	78.79 ± 6.69	95.70 ± 5.67*,$^{\neq}$	120.11 ± 13.46	137.16 ± 17.79	445.26 ± 32.54	512.04 ± 26.05
CT	7,597.83 ± 276.69	7,784.78 ± 303.59	2,645.91 ± 144.50	2,636.72 ± 148.85	4,101.87 ± 199.01	4,245.48 ± 227.81	31.52 ± 15.92	40.07 ± 16.77	92.13 ± 7.65	98.91 ± 7.96	176.26 ± 18.90*,^{a}	171.61 ± 16.08*,^{a}	545.30 ± 26.25	585.04 ± 31.33
TT	7,886.67 ± 462.38	7,560.00 ± 464.64	3,046.00 ± 244.37	2,753.27 ± 277.07	4,050.00 ± 289.17	3,834.87 ± 339.58	3.43 ± 3.43	11.29 ± 11.29	90.33 ± 12.86	107.80 ± 10.17	154.73 ± 29.35	179.13 ± 36.43*,$^{a,\neq}$	546.00 ± 55.65	580.33 ± 54.72
P values	0.129	0.347	0.235	0.932	0.172	0.386	0.339	0.791	0.401	0.481	0.038	0.029	0.018	0.394
MTHFR A1298C														
AA	7,512.86 ± 278.82	7,625.71 ± 241.07	2,713.39 ± 109.73	2,746.48 ± 118.22	4,039.68 ± 230.33	4,030.17 ± 180.08	29.75 ± 10.28	20.54 ± 8.21	76.96 ± 5.87	99.90 ± 6.08*	145.48 ± 13.49	164.86 ± 16.04	512.66 ± 28.33	566.37 ± 25.67
AC	7,175.56 ± 263.14	7,093.33 ± 252.39	2,520.11 ± 134.50	2,348.73 ± 130.06*,^{a,c}	3,919.56 ± 184.62	3,883.69 ± 200.39	18.11 ± 11.56	34.36 ± 15.80	96.33 ± 7.62	94.84 ± 5.97	148.02 ± 18.46	144.49 ± 16.90	460.69 ± 27.20	516.60 ± 27.83
CC	11,150.00 ± 4,950.00	9,600.00 ± 2,700.00	4,565.50 ± 1,713.50	4,485.00 ± 1,173.00	5,457.00 ± 2,915.00	4,155.00 ± 1,257.00	80.50 ± 80.50	61.50 ± 61.50	142.50 ± 18.50	130.50 ± 7.50	142.50 ± 18.50	96.00 ± 27.00	762.00 ± 204.00	672.00 ± 189.00
P values	0.715	0.255	0.167	0.024	0.944	0.880	0.241	0.279	0.038	0.363	0.898	0.542	0.149	0.456

Data are expressed as mean ± SEM (standard error of mean). For GSTM1, GSTT1, and CRP G1059C, *P* values were generated by the Mann–Whitney *U* test; for the other genetic markers, *P* values were generated by the Kruskall–Wallis test. The lower case letters indicate differences between two specific genotypes detected by the Mann–Whitney *U* test. Asterisks indicate significant (* $P < 0.05$) and highly significant (** $P < 0.01$) differences. The lower case letters indicate a significant differences between two specific genotypes, with a = significant compared with the first genotype of each genetic marker; b = significant compared with the second genotype of each genetic marker; c = significant compared with the third genotype of each genetic marker. The symbol ≠ indicates significant differences in the comparison of before–after pequi-oil supplementation detected by the Wilcoxon matched pairs test

Table 5 Influences of Haptoglobin (Hp), MnSOD, CAT, GPx-1, ACE, GSTM1, GSTT1, CK *Nco*I, CK *Taq*I, CRP G1059C, MTHFR C677T and MTHFR A1298C genes' polymorphisms on the plateletgram before and after pequi-oil supplementation

Genetic markers	Platelet (thousand/mm^3)		Plateletocrit (%)		MPV (fl)		PDW (%)	
	Before	After	Before	After	Before	After	Before	After
Hp								
1F-1F	313.75 ± 13.54	277.38 ± 12.83*,≠	0.31 ± 0.02	0.25 ± 0.01*,≠	10.27 ± 0.60	9.18 ± 0.60	18.18 ± 0.49	17.63 ± 0.37
1F-1S	324.87 ± 25.18	280.88 ± 22.57*,≠	0.34 ± 0.03	0.27 ± 0.03*,≠	10.59 ± 0.40	9.67 ± 0.35	18.70 ± 0.38	17.6 ± 0.07
1S-1S	328.42 ± 20.64	306.05 ± 18.46	0.37 ± 0.03	0.32 ± 0.02*,a,≠	11.52 ± 0.50	10.58 ± 0.33*,≠	18.39 ± 0.31	18.19 ± 0.18
1F-2	369.35 ± 17.74	339.90 ± 13.66*,≠	0.37 ± 0.02	0.34 ± 0.02*,a	10.06 ± 0.28*,b,c	9.92 ± 0.32	17.55 ± 0.15	17.71 ± 0.22
1S-2	332.31 ± 10.98	306.75 ± 11.57*,≠	0.34 ± 0.01	0.31 ± 0.01*,a,≠	10.10 ± 0.28*,c	10.13 ± 0.29	17.83 ± 0.21	18.03 ± 0.20
2-2	328.97 ± 10.19	320.37 ± 9.86	0.37 ± 0.02	0.36 ± 0.01*,a,b,e	10.76 ± 0.27*,e	11.18 ± 0.33**,a,*,b,d,e	18.07 ± 0.23	18.58 ± 0.20**,b,d,*e,≠
P values	0.451	0.099	0.566	0.002	0.056	0.023	0.140	0.027
MnSOD								
Val/Val	352.26 ± 16.72	317.58 ± 14.90*,≠	0.37 ± 0.02	0.32 ± 0.02	10.11 ± 0.35	9.94 ± 0.37	17.77 ± 0.24	17.92 ± 0.29
Val/Ala	332.88 ± 7.08	312.28 ± 6.66**,≠	0.35 ± 0.01	0.33 ± 0.01**,≠	10.60 ± 0.18	10.47 ± 0.18	18.03 ± 0.12	18.15 ± 0.11
Ala/Ala	316.00 ± 25.3	289.20 ± 27.99	0.41 ± 0.08	0.31 ± 0.03	10.95 ± 0.27	10.13 ± 0.54	18.48 ± 0.68	17.96 ± 0.22
P values	0.306	0.563	0.456	0.786	0.261	0.351	0.683	0.618
CAT								
AA	347.59 ± 14.97	326.50 ± 15.01	0.35 ± 0.02	0.32 ± 0.02	10.03 ± 0.31	9.76 ± 0.28	17.78 ± 0.25	18.04 ± 0.22
AT	337.66 ± 9.52	318.64 ± 8.87	0.36 ± 0.01	0.34 ± 0.01	10.62 ± 0.23	10.67 ± 0.25	17.96 ± 0.15	18.19 ± 0.15
TT	326.96 ± 10.35	298.55 ± 9.11**,≠	0.36 ± 0.02	0.31 ± 0.01**,≠	10.68 ± 0.26	10.34 ± 0.26	18.17 ± 0.20	18.04 ± 0.16
P values	0.434	0.120	0.901	0.235	0.268	0.099	0.380	0.782
GPx-1								
Pro/Pro	348.84 ± 9.96	323.69 ± 9.34**,≠	0.37 ± 0.01	0.33 ± 0.01**,≠	10.51 ± 0.23	10.16 ± 0.19	17.99 ± 0.15	18.00 ± 0.12
Pro/Leu	321.1 ± 8.77	298.88 ± 8.23**,≠	0.34 ± 0.01	0.32 ± 0.01*,≠	10.62 ± 0.25	10.59 ± 0.28	18.11 ± 0.19	18.27 ± 0.17
Leu/Leu	327 ± 16.24	309.77 ± 14.69	0.34 ± 0.02	0.33 ± 0.02	10.31 ± 0.30	10.49 ± 0.48	17.68 ± 0.16	17.94 ± 0.35
P values	0.346	0.122	0.390	0.535	0.877	0.697	0.640	0.457
ACE								
DD	320.05 ± 10.88	311.21 ± 11.45	0.34 ± 0.01	0.34 ± 0.02	10.80 ± 0.27	10.94 ± 0.31	18.04 ± 0.20	18.31 ± 0.18
ID	348.32 ± 9.08	313.42 ± 7.98**,≠	0.37 ± 0.01	0.32 ± 0.01**,≠	10.53 ± 0.21	10.04 ± 0.19*	18.11 ± 0.15	18.00 ± 0.13
II	328.00 ± 13.67	310.22 ± 12.47	0.32 ± 0.02	0.32 ± 0.01	9.97 ± 0.38	10.22 ± 0.34	17.59 ± 0.24	18.02 ± 0.24
P values	0.189	0.948	0.081	0.525	0.132	0.082	0.237	0.621
GSTM1								
Null	335.19 ± 6.78	307.97 ± 6.60**,≠	0.35 ± 0.01	0.32 ± 0.01**,≠	10.31 ± 0.16	10.25 ± 0.19	17.94 ± 0.12	18.13 ± 0.12
Non-null	335.40 ± 13.09	319.83 ± 11.63	0.37 ± 0.02	0.34 ± 0.01*,≠	10.97 ± 0.32	10.61 ± 0.27	18.14 ± 0.22	18.06 ± 0.18
P values	0.621	0.443	0.749	0.135	0.120	0.153	0.519	0.519

Table 5 continued

Genetic markers	Platelet (thousand/mm^3)		Plateletocrit (%)		MPV (fl)		PDW (%)	
	Before	After	Before	After	Before	After	Before	After
GSTT1								
Null	365.53 ± 16.58	329.41 ± 15.32**,≠	0.40 ± 0.03	0.33 ± 0.02*,≠	10.23 ± 0.43	9.86 ± 0.36	18.28 ± 0.37	17.79 ± 0.25
Non-null	330.23 ± 6.76	309.28 ± 6.40**,≠	0.35 ± 0.01	0.32 ± 0.01**,≠	10.59 ± 0.16	10.46 ± 0.17	17.96 ± 0.11	18.16 ± 0.11
P values	0.053	0.302	0.263	0.720	0.262	0.207	0.569	0.197
CK *Nco*I								
AA	336.88 ± 9.25	315.88 ± 7.29**,≠	0.35 ± 0.01	0.33 ± 0.01*,≠	10.51 ± 0.22	10.29 ± 0.20	17.79 ± 0.16	18.02 ± 0.13
AG	332.96 ± 9.52	305.47 ± 9.91**,≠	0.36 ± 0.01	0.32 ± 0.01**,≠	10.55 ± 0.23	10.41 ± 0.26	18.23 ± 0.15*,a	18.09 ± 0.15
GG	339.50 ± 19.06	334.00 ± 29.86	0.37 ± 0.03	0.37 ± 0.05	10.67 ± 0.49	10.92 ± 0.68	18.08 ± 0.50	18.98 ± 0.40
P values	0.932	0.728	0.822	0.321	0.888	0.668	0.045	0.103
CK *Taq*I								
1-1	370.91 ± 36.07	331.36 ± 24.45	0.40 ± 0.04	0.35 ± 0.03	10.29 ± 0.41	10.06 ± 0.30	17.72 ± 0.30	18.20 ± 0.18
1-2	325.21 ± 7.91	304.90 ± 8.52**,≠	0.34 ± 0.01	0.32 ± 0.01*,≠	10.53 ± 0.23	10.44 ± 0.24	17.96 ± 0.16	18.03 ± 0.15
2-2	339.10 ± 8.89	316.36 ± 8.51**,≠	0.37 ± 0.01	0.33 ± 0.01**,≠	10.59 ± 0.23	10.36 ± 0.24	18.12 ± 0.17	18.17 ± 0.15
P values	0.379	0.310	0.069	0.572	0.894	0.941	0.580	0.493
CRP G1059C								
GG	332.34 ± 6.43	309.26 ± 6.31**,≠	0.35 ± 0.01	0.32 ± 0.01**,≠	10.54 ± 0.16	10.30 ± 0.15	18.03 ± 0.12	18.05 ± 0.10
GC	359.15 ± 24.70	335.77 ± 16.05	0.40 ± 0.04	0.37 ± 0.03	10.51 ± 0.39	10.98 ± 0.69	17.83 ± 0.31	18.50 ± 0.34
P values	0.380	0.180	0.211	0.056	0.819	0.431	0.601	0.151
MTHFR C677T								
CC	324.63 ± 9.52	299.47 ± 8.47**,≠	0.35 ± 0.01	0.31 ± 0.01**,≠	10.73 ± 0.25	10.26 ± 0.23	18.18 ± 0.18	18.06 ± 0.14
CT	336.83 ± 9.21	323.74 ± 9.26**,a	0.34 ± 0.01	0.33 ± 0.01	10.32 ± 0.21	10.30 ± 0.20	17.76 ± 0.13	18.01 ± 0.14
TT	370.80 ± 17.73**,a	324.07 ± 16.81**,≠	0.41 ± 0.03*,a	0.36 ± 0.03*,a	10.49 ± 0.39	11.12 ± 0.64	18.16 ± 0.34	18.59 ± 0.36
P values	0.016	0.015	0.066	0.047	0.627	0.435	0.312	0.359
MTHFR A1298C								
AA	331.28 ± 8.32	312.60 ± 8.15**,≠	0.35 ± 0.01	0.33 ± 0.01*,≠	10.54 ± 0.20	10.52 ± 0.21	18.00 ± 0.14	18.15 ± 0.13
AC	343.09 ± 10.15	311.44 ± 8.73**,≠	0.36 ± 0.01	0.32 ± 0.01**,≠	10.58 ± 0.24	10.21 ± 0.23	18.04 ± 0.18	18.06 ± 0.14
CC	303.00 ± 6.00	312.50 ± 16.50	0.29 ± 0.04	0.30 ± 0.09	9.50 ± 1.20	9.30 ± 2.10	17.35 ± 0.45	17.60 ± 1.60
P values	0.539	0.980	0.227	0.748	0.643	0.525	0.686	0.808

Data are expressed as mean ± SEM (standard error of mean) *MPV* mean platelet volume, *PDW* platelet deviation weight, *fl* femtoliters. For GSTM1, GSTT1, and CRP G1059C, *P* values were generated by the Mann–Whitney *U* test; for the other genetic markers, *P* values were generated by the Kruskall–Wallis test. The lower case letters indicate differences between two specific genotypes detected by the Mann–Whitney *U* test. Asterisks indicate significant (* $P < 0.05$) and highly significant (** $P < 0.01$) differences. The lower case letters indicate significant differences between two specific genotypes, with a = significant compared with the first genotype of each genetic marker; b = significant compared with the second genotype of each genetic marker; c = significant compared with the third genotype of each genetic marker. For Hp polymorphism, the lower case letters d, e, and f were also added, with d = significant compared with 1F-2; e = significant compared with 1S-2; and f = significant compared to 2-2 genotypes. The symbol ≠ indicates significant differences in the comparison of before-after pequi-oil supplementation detected by the Wilcoxon matched pairs test

differences were presented for MTHFR C677T ($P = 0.015$) polymorphism in the values of platelets; for Hp ($P = 0.002$) and MTHFR C677T ($P = 0.047$) polymorphisms, in the values of plateletocrit; for Hp ($P = 0.023$), in the values of MPV; and for Hp ($P = 0.027$), in PDW values. For MTHFR C677T polymorphism, the number of platelets presented a significant increase in CT genotype compared with CC genotype ($P = 0.007$), while the plateletocrit values were higher for T homozygous compared with C homozygous ($P = 0.032$). For Hp polymorphism, significant differences in the plateletocrit values appeared between 1F-1F and 1S-1S (0.025), 1F-1F and 1F-2 ($P = 0.005$), 1F-1F and 1S-2 ($P = 0.025$), 1F-1F and 2-2 ($P = 0.001$), with lower values for 1F-1F; and between 1F-1S and 2-2 ($P = 0.017$), and 1S-1S and 2-2 ($P = 0.008$), where 2-2 genotype presented higher values. Significant differences were also seen for MPV values in the comparisons between 1F-1F and 2-2 ($P = 0.001$), 1F-1S and 2-2 ($P = 0.012$), 1F-2 and 2-2 ($P = 0.038$), 1S-2 and 2-2, with higher values for individuals carrying 2-2 genotype. PDW values also presented significant differences between 1F-1S and 2-2 ($P = 0.004$), 1F-2 and 2-2 ($P = 0.006$), 1S-2 and 2-2 ($P = 0.048$) genotypes, with 2-2 genotype maintaining higher values (Table 5).

Postprandial lipid profile

For total cholesterol, significant differences in the comparison of before-after pequi-oil supplementation were showed for MnSOD Ala/Ala ($P = 0.016$) and GPx-1 Pro/Leu ($P = 0.048$) genotypes, whose values decreased after pequi-oil supplementation. For triglycerides (TG), differences were detected for Hp 1F-2 ($P = 0.044$), MnSOD Val/Ala (0.016), CAT AA (0.023), and CK *Nco*I GG (0.046) genotypes, whose values increased after pequi. Individuals carrying Hp 1F-1F (0.048) genotype presented a significant increase in high-density lipoprotein (HDL) values after supplementation, as did subjects carrying GPx-1 Pro/Pro (0.034) genotype. After pequi treatment, a significant reduction in low-density lipoproteins (LDL) values was showed for GPx-1 Pro/Leu ($P = 0.025$) genotype, while a significant increase in the very low-density lipoproteins (VLDL) values was observed for Hp 1F-2 (0.044), CAT AA (0.023), and CK *Nco*I GG ($P = 0.046$) genotypes (Table 6).

Regarding genetic markers, significant differences between the genotypes before pequi-oil supplementation were showed for ACE (0.029), in the values of total cholesterol; for GSTT1, in the values of TG and VLDL (0.017 for both); and for ACE ($P = 0.024$), in the values of LDL. ACE ID genotype presented higher total cholesterol ($P = 0.047$) and LDL (0.022) values than DD genotype and similar results of increased TG were observed for GSTT1 null genotype. After pequi-oil treatment, no significant difference in the values of total cholesterol was observed between ACE genotypes, but ID genotype kept significantly higher values of LDL than did DD genotype ($P = 0.007$). GSTT1 null genotype also kept higher values of TG ($P = 0.031$) and VLDL ($P = 0.031$) than non-null genotype. Similar increased TG were observed for MTHFR1298 AA ($P = 0.019$) and CC ($P = 0.022$) compared with AC genotype, and the same occurred with VLDL ($P = 0.019$ for AA; $P = 0.022$ for CC). For HDL, values were higher for Hp 2-2, compared with Hp 1S-1S ($P = 0.003$) and 1S-2 (0.033; Table 6).

CRP and hs-CRP

CRP values increased significantly after pequi-oil supplementation for individuals carrying MTHFR1298 AC genotype (0.024). However, before pequi treatment, MTHFR1298 AA genotype presented higher CRP values than AC genotype ($P = 0.002$). For MTHFR677, although the Kruskall–Wallis test did not show significant differences between MTHRF677 genotypes before pequi-oil supplementation, the Mann–Whitney *U* test indicated differences between CC and TT genotypes in CRP values ($P = 0.026$), which were significantly higher for TT genotype. After pequi, no significant differences were observed between these genotypes (Table 7).

Arterial pressure

There are downward trends to reduced systolic and diastolic pressures after pequi-oil supplementation. Significant decreases in systolic pressure were observed for Hp 1F-1S ($P = 0.046$), 1S-1S ($P = 0.047$), and 1S-2 ($P = 0.016$); for MnSOD Val/Val (0.018) and Val/Ala ($P = 0.021$); for CAT AA ($P = 0.032$) and AT ($P = 0.026$); for GPx-1 Pro/Pro ($P = 0.026$) and Pro/Leu ($P = 0.002$); for ACE ID ($P = 0.035$) and II ($P = 0.012$); for GSTM1 null ($P = 0.021$) and non-null (0.011); for GSTT1 non-null ($P = 0.002$); for CK *Nco*I AA ($P = 0.011$) and AG ($P = 0.010$); for CK *Taq*I 1-1 ($P = 0.035$) and 1-2 ($P = 0.011$); for CRP GG ($P = 0.002$); for MTHFR677 CC ($P = 0.006$); and for MTHFR1298 AA ($P = 0.013$) and AC ($P = 0.042$) genotypes. For diastolic pressure, significant reduction after pequi was observed for MnSOD Val/Ala ($P = 0.003$); for CAT AT ($P = 0.033$) and TT ($P = 0.011$); for GPx-1 Pro/Pro ($P = 0.003$); for GSTM1 null ($P = 0.026$) and non-null ($P = 0.017$); for GSTT1 non-null ($P = 0.001$); for CK *Nco*I AA ($P = 0.007$); for CK *Taq*I 1-2 ($P = 0.023$); for CRP GG ($P = 0.007$); for MTHFR677 CC ($P = 0.013$) and CT ($P = 0.025$); and

Table 6 Influences of Haptoglobin (Hp), MnSOD, CAT, GPx-1, ACE, GSTM1, GSTT1, CK *Nco*I, CK *Taq*I, CRP G1059C, MTHFR C677T, and MTHFR A1298C genes' polymorphisms on the postprandial lipid profile before and after pequi-oil supplementation

Genetic markers	Total cholesterol (mg/dL)		Triglycerides (mg/dL)		HDL (mg/dL)		LDL (mg/dL)		VLDL (mg/dL)	
	Before	After	Before	After	Before	After	Before	After	Before	After
Hp										
1F-1F	192.37 ± 13.88	186.88 ± 8.54	165.38 ± 36.12	137.50 ± 20.71	55.50 ± 4.14	59.38 ± 4.42*,≠	103.80 ± 12.99	100.00 ± 7.12	33.08 ± 7.22	27.50 ± 4.14
1F-1S	184.88 ± 9.42	187.75 ± 9.92	106.88 ± 21.20	111.50 ± 18.72	54.00 ± 3.89	55.13 ± 3.73	109.50 ± 7.75	110.33 ± 8.29	21.38 ± 4.24	22.30 ± 3.74
1S-1S	178.50 ± 11.91	176.06 ± 10.57	116.33 ± 11.69	128.50 ± 16.56	45.94 ± 3.63	46.61 ± 3.84	109.29 ± 11.21	103.74 ± 9.08	23.27 ± 2.34	25.70 ± 3.31
1F-2	190.3 ± 8.71	190.45 ± 7.70	98.26 ± 9.77	117.32 ± 12.37*,≠	52.85 ± 2.81	51.50 ± 2.82	115.93 ± 6.44	113.64 ± 6.42	19.65 ± 1.95	23.46 ± 2.47*,≠
1S-2	186.28 ± 6.60	182.87 ± 6.07	104.44 ± 7,62	115.63 ± 8.17	54.61 ± 1.57	53.21 ± 1.81	111.24 ± 5.69	106.53 ± 5.44	20.89 ± 1.52	23.13 ± 1.63
2-2	192.36 ± 6.27	195.76 ± 5.91	117.09 ± 12.67	112.76 ± 8.08	59.03 ± 2.67*,c	60.48 ± 2.61**,c,*e	110.33 ± 4.34	112.49 ± 4.16	23.42 ± 2.53	22.55 ± 1.62
P values	0.881	0.495	0.562	0.889	0.166	0.011	0.882	0.511	0.562	0.889
MnSOD										
Val/Val	196.05 ± 7.93	193.00 ± 7.95	115.32 ± 14.99	100.53 ± 8.22	57.05 ± 3.96	56.11 ± 3.74	115.94 ± 6.49	116.79 ± 6.53	23.06 ± 3.00	20.11 ± 1.64
Val/Ala	185.41 ± 4.08	186.27 ± 3.69	111.29 ± 5.75	122.62 ± 5.55*,≠	53.31 ± 1.30	53.92 ± 1.41	109.72 ± 3.48	107.23 ± 3.05	22.26 ± 1.15	24.53 ± 1.11
Ala/Ala	198.67 ± 13.73	185.17 ± 10.96*,≠	134.00 ± 47.03	106.83 ± 29.81	60.33 ± 2.54	58.17 ± 1.70	111.53 ± 5.36	105.63 ± 4.98	26.80 ± 9.41	21.37 ± 5.96
P values	0.429	0.742	1.000	0.130	0.130	0.390	0.560	0.330	1.000	0.130
CAT										
AA	184.41 ± 7.79	187.82 ± 6.81	98.68 ± 11.13	128.27 ± 14.16*,≠	49.27 ± 2.67	48.41 ± 2.35	116.30 ± 7.64	113.45 ± 7.18	19.74 ± 2.23	25.66 ± 2.83*,≠
AT	189.86 ± 5.95	188.61 ± 4.85	120.74 ± 10.21	117.44 ± 7.26	55.53 ± 1.80	56.45 ± 2.03	109.41 ± 4.69	107.83 ± 3.72	24.15 ± 2.04	23.49 ± 1.45
TT	187.09 ± 5.23	185.57 ± 5.54	111.67 ± 7.26	114.37 ± 6.84	55.19 ± 2.02	55.17 ± 2.01	109.86 ± 4.28	107.47 ± 4.32	22.34 ± 1.45	22.87 ± 1.37
P values	0.849	0.912	0.383	0.956	0.274	0.117	0.886	0.868	0.383	0.956
GPx-1										
Pro/Pro	187.14 ± 5.09	190.45 ± 4.66	117.12 ± 8.60	119.63 ± 6.71	54.76 ± 1.93	56.49 ± 1.91*,≠	108.70 ± 4.10	109.07 ± 3.65	23.43 ± 1.72	23.93 ± 1.34
Pro/Leu	189.09 ± 5.55	183.55 ± 5.22	106.34 ± 6.61	117.81 ± 8.29	53.28 ± 1.85	51.68 ± 1.99	114.54 ± 5.07	108.31 ± 4.60*,≠	21.27 ± 1.32	23.56 ± 1.66
Leu/Leu	186.07 ± 11.21	186.71 ± 8.59	119.36 ± 22.86	114.21 ± 12.62	55.36 ± 2.07	55.36 ± 2.54	106.84 ± 6.90	108.51 ± 6.55	23.87 ± 4.57	22.84 ± 2.52
P values	0.953	0.608	0.948	0.790	0.828	0.363	0.810	0.787	0.948	0.790
ACE										
DD	178.44 ± 5.97	178.41 ± 5.01	107.71 ± 10.01	116.83 ± 8.20	54.43 ± 2.20	55.21 ± 2.21	102.98 ± 3.95	99.27 ± 3.65	21.54 ± 2.00	23.37 ± 1.64
ID	197.22 ± 5.01*,a	194.86 ± 4.78	116.26 ± 8.11	119.90 ± 7.29	54.64 ± 1.75	54.81 ± 1.90	118.80 ± 4.65*,a	115.49 ± 4.12**,a	23.25 ± 1.62	23.98 ± 1.46
II	178.63 ± 7.80	182.89 ± 7.46	115.05 ± 11.59	116.37 ± 10.19	52.63 ± 2.49	51.79 ± 2.35	102.99 ± 6.39	107.83 ± 5.80	23.01 ± 2.32	23.27 ± 2.04
P values	0.029	0.057	0.461	0.911	0.880	0.779	0.047	0.024	0.461	0.911
GSTM1										
Null	192.33 ± 4.50	190.22 ± 4.00	110.27 ± 7.04	114.19 ± 5.77	55.14 ± 1.60	55.37 ± 1.61	114.67 ± 3.78	111.50 ± 3.31	22.06 ± 1.41	22.84 ± 1.15
Non-null	179.12 ± 5.47	181.71 ± 5.37	118.39 ± 9.15	125.90 ± 8.66	52.60 ± 1.78	52.81 ± 2.01	103.42 ± 4.39	103.31 ± 4.30	23.68 ± 1.83	25.18 ± 1.73
P values	0.076	0.210	0.291	0.224	0.194	0.239	0.065	0.205	0.291	0.224

Table 6 continued

Genetic markers	Total cholesterol (mg/dL)		Triglycerides (mg/dL)		HDL (mg/dL)		LDL (mg/dL)		VLDL (mg/dL)	
	Before	After	Before	After	Before	After	Before	After	Before	After
GSTT1										
Null	193.25 ± 6.89	189.44 ± 6.83	145.12 ± 16.9	143.81 ± 14.92	52.88 ± 3.20	53.63 ± 4.09	111.35 ± 6.65	107.05 ± 5.22	29.03 ± 3.38	28.76 ± 2.98
Non-null	186.93 ± 3.94	186.95 ± 3.57	108.07 ± 5.76*,[a]	114.25 ± 4.99* ,[a]	54.46 ± 1.32	54.61 ± 1.32	110.74 ± 3.25	108.96 ± 2.95	21.61 ± 1.15* ,[a]	22.85 ± 1.00* ,[a]
P values	0.544	0.793	0.017	0.031	0.988	0.616	0.824	0.956	0.017	0.031
CK *Nco*I										
AA	189.62 ± 4.32	184.72 ± 4.19	118.90 ± 8.20	113.75 ± 6.33	52.49 ± 1.45	51.52 ± 1.52	113.62 ± 4.05	110.47 ± 3.88	23.78 ± 1.64	22.75 ± 1.27
AG	186.58 ± 6.11	189.60 ± 5.32	107.69 ± 7.99	121.71 ± 7.59	56.28 ± 2.07	57.72 ± 2.13	108.17 ± 4.66	106.47 ± 3.86	21.54 ± 1.60	24.34 ± 1.52
GG	180.00 ± 14.11	192.50 ± 12.08	101.83 ± 24.04	133.50 ± 28.11* ,≠	54.17 ± 6.06	55.83 ± 5.26	105.47 ± 9.75	109.97 ± 9.97	20.37 ± 4.81	26.70 ± 5.62* ,≠
P values	0.809	0.713	0.543	0.618	0.406	0.067	0.624	0.979	0.543	0.618
CK *Taq*I										
1-1	198.00 ± 7.70	191.17 ± 9.04	129.50 ± 21.22	123.50 ± 12.82	55.58 ± 4.47	53.42 ± 4.48	116.52 ± 8.09	113.05 ± 8.07	25.90 ± 4.24	24.70 ± 2.56
1-2	185.04 ± 5.46	184.30 ± 4.64	106.27 ± 7.46	115.00 ± 6.61	54.00 ± 1.94	53.98 ± 1.99	110.30 ± 4.66	107.07 ± 3.67	21.25 ± 1.49	23.00 ± 1.32
2-2	188.39 ± 5.39	189.65 ± 5.13	116.80 ± 8.84	120.66 ± 8.19	54.22 ± 1.58	55.27 ± 1.71	110.04 ± 4.22	109.45 ± 4.32	23.36 ± 1.77	24.13 ± 1.64
P values	0.570	0.680	0.327	0.701	0.942	0.857	0.680	0.732	0.327	0.701
CRP G1059C										
GG	186.33 ± 3.72	185.17 ± 3.40	113.89 ± 6.04	117.83 ± 5.00	54.02 ± 1.29	54.00 ± 1.35	109.41 ± 3.11	107.06 ± 2.79	22.78 ± 1.21	23.57 ± 1.00
GC	199.62 ± 11.08	204.54 ± 8.89	106.69 ± 14.05	121.77 ± 17.61	56.15 ± 3.73	58.38 ± 3.64	122.12 ± 8.59	121.80 ± 7.61	21.34 ± 2.81	24.35 ± 3.52
P values	0.243	0.060	0.973	0.867	0.518	0.145	0.146	0.055	0.973	0.867
MTHFR C677T										
CC	187.31 ± 5.20	185.64 ± 4.71	110.75 ± 8.18	116.51 ± 7.38	52.89 ± 1.60	53.11 ± 1.72	112.86 ± 4.80	109.02 ± 4.02	22.15 ± 1.64	23.30 ± 1.48
CT	187.98 ± 5.79	190.12 ± 5.10	115.00 ± 8.77	121.15 ± 7.56	56.08 ± 2.09	56.19 ± 2.24	108.02 ± 4.28	108.86 ± 4.15	23.00 ± 1.75	24.23 ± 1.51
TT	188.81 ± 9.02	184.44 ± 9.16	115.56 ± 16.26	115.81 ± 12.19	53.50 ± 3.56	54.13 ± 2.98	112.20 ± 6.79	107.15 ± 6.83	23.11 ± 3.25	23.16 ± 2.44
P values	0.990	0.766	0.858	0.773	0.653	0.767	0.735	0.980	0.858	0.773
MTHFR A1298C										
AA	189.15 ± 4.69	187.17 ± 4.14	119.32 ± 7.84	125.41 ± 6.55	55.85 ± 1.54	55.51 ± 1.56	109.07 ± 3.62	105.95 ± 3.28	23.87 ± 1.57	25.08 ± 1.31
AC	185.27 ± 5.60	187.00 ± 5.38	102.51 ± 7.63	103.42 ± 6.36* ,[a,c]	52.07 ± 2.01	53.20 ± 2.22	113.06 ± 5.19	112.96 ± 4.58	20.50 ± 1.53	20.68 ± 1.27* ,[a,c]
CC	195.00 ± 16.00	198.00 ± 9.00	130.00 ± 2.00	198.50 ± 30.50	45.00 ± 3.00	45.50 ± 2.50	124.00 ± 12.60	112.80 ± 12.60	26.00 ± 0.40	39.70 ± 6.10
P values	0.841	0.911	0.212	0.010	0.181	0.265	0.641	0.659	0.212	0.010

Data are expressed as mean ± SEM (standard error of mean). For GSTM1, GSTT1 and CRP G1059C, *P* values were generated by the independent samples *t*-Test (total cholesterol) or Mann–Whitney *U* test (other variables); for the other genetic markers, *P* values were generated by ANOVA (total cholesterol) or by the Kruskall–Wallis test (other variables). Asterisks indicate significant (* $P < 0.05$) and highly significant (** $P < 0.01$) differences. The lower case letters indicate significant differences between two specific genotypes, with a = significant compared with the first genotype of each genetic marker; b = significant compared with the second genotype of each genetic marker; c = significant compared with the third genotype of each genetic marker. For Hp polymorphism, the lower case letters d, e, and f were also added, with d = significant compared with 1F-2; e = significant compared with 1S-2; and f = significant compared with 2-2 genotypes. The symbol ≠ indicates significant differences in the comparison of before-after pequi-oil supplementation detected by the Wilcoxon matched pairs test

Table 7 Influences of Haptoglobin (Hp), MnSOD, CAT, GPx-1, ACE, GSTM1, GSTT1, CK *Nco*I, CK *Taq*I, CRP G1059C, MTHFR C677T, and MTHFR A1298C genes' polymorphisms on the CRP, hs-CRP, arterial pressure and TBARS assay before and after pequi-oil supplementation

Genetic Markers	CRP (mg/dL)		hs-CRP (mg/dL)		Systolic pressure (mmHg)		Diastolic pressure (mmHg)		TBARS (nmol/mL of MDA)	
	Before	After	Before	After	Before	After	Before	After	Before	After
Hp										
1F-1F	0.24 ± 0.07	0.31 ± 0.11	1.02 ± 0.27	1.41 ± 0.53	111.43 ± 4.59	112.86 ± 2.86	68.57 ± 4.04	65.71 ± 2.97	0.029 ± 0.003	0.030 ± 0.002
1F-1S	0.28 ± 0.12	0.35 ± 0.09	1.97 ± 0.80	1.39 ± 0.39	120.00 ± 1.89	115.00 ± 1.89*,≠	77.50 ± 3.13	72.50 ± 2.50	0.032 ± 0.002	0.030 ± 0.003
1S-1S	0.30 ± 0.05	0.37 ± 0.07	1.49 ± 0.51	1.95 ± 0.43	116.00 ± 1.97	111.00 ± 1.76*,≠	73.50 ± 1.67	69.00 ± 1.76	0.023 ± 0.001*,[b]	0.025 ± 0.001
1F-2	0.32 ± 0.08	0.38 ± 0.07	1.70 ± 0.50	2.00 ± 0.65	115.26 ± 1.77	113.16 ± 2.17	71.05 ± 2.28	70.00 ± 1.87	0.028 ± 0.002	0.026 ± 0.002
1S-2	0.36 ± 0.06	0.36 ± 0.05	1.37 ± 0.38	1.34 ± 0.33	116.88 ± 1.23	111.87 ± 1.76*,≠	72.19 ± 1.54	68.12 ± 1.45	0.029 ± 0.001	0.026 ± 0.001
2-2	0.36 ± 0.07	0.38 ± 0.06	1.82 ± 0.46	1.36 ± 0.24	112.50 ± 1.00	111.87 ± 1.14	73.13 ± 1.52	69.69 ± 1.52	0.024 ± 0.001	0.025 ± 0.001
P values	0.827	0.969	0.912	0.604	0.060	0.680	0.358	0.599	0.005	0.249
MnSOD										
Val/Val	0.34 ± 0.06	0.33 ± 0.04	1.38 ± 0.37	1.62 ± 0.31	116.50 ± 1.67	110.50 ± 1.85*,≠	71.00 ± 2.16	68.50 ± 1.82	0.031 ± 0.002	0.028 ± 0.002
Val/Ala	0.33 ± 0.04	0.37 ± 0.03	1.59 ± 0.24	1.54 ± 0.20	114.95 ± 0.79	112.69 ± 0.85*,≠	73.01 ± 0.89	69.35 ± 0.84*,≠	0.026 ± 0.001*,[a]	0.026 ± 0.001
Ala/Ala	0.30 ± 0.11	0.60 ± 0.31	2.58 ± 0.99	1.51 ± 0.52	114.00 ± 4.00	110.00 ± 3.16	72.00 ± 4.90	68.00 ± 4.90	0.026 ± 0.003	0.026 ± 0.003
P values	0.885	0.872	0.398	0.478	0.786	0.501	0.575	0.853	0.024	0.493
CAT										
AA	0.33 ± 0.05	0.42 ± 0.08	1.97 ± 0.54	2.10 ± 0.60	115.22 ± 1.65	110.87 ± 1.39*,≠	70.87 ± 1.65	69.13 ± 1.65	0.027 ± 0.001	0.027 ± 0.001
AT	0.35 ± 0.05	0.39 ± 0.05	1.39 ± 0.30	1.31 ± 0.21	114.58 ± 1.07	111.46 ± 1.33*,≠	73.75 ± 1.32	69.79 ± 1.21*,≠	0.026 ± 0.001	0.025 ± 0.001
TT	0.31 ± 0.05	0.33 ± 0.03	1.61 ± 0.33	1.56 ± 0.23	115.74 ± 1.13	113.62 ± 1.11	72.34 ± 1.30	68.51 ± 1.18*,≠	0.027 ± 0.001	0.028 ± 0.001
P values	0.877	0.735	0.344	0.262	0.628	0.212	0.332	0.740	0.837	0.133
GPx-1										
Pro/Pro	0.36 ± 0.05	0.34 ± 0.04	2.12 ± 0.38	1.57 ± 0.23	115.69 ± 0.99	112.76 ± 1.15*,≠	73.97 ± 1.04	68.97 ± 1.03*,≠	0.027 ± 0.001	0.026 ± 0.001
Pro/Leu	0.29 ± 0.03	0.38 ± 0.04	1.08 ± 0.17	1.69 ± 0.31	115.53 ± 1.13	111.06 ± 1.02**,≠	71.28 ± 1.35	68.94 ± 1.23*,≠	0.027 ± 0.001	0.026 ± 0.001
Leu/Leu	0.32 ± 0.06	0.45 ± 0.12	1.04 ± 0.22	0.97 ± 0.22	111.54 ± 1.91	113.85 ± 2.67	71.54 ± 2.96	70.77 ± 2.39	0.027 ± 0.002	0.026 ± 0.002
P values	0.851	0.542	0.118	0.507	0.227	0.377	0.204	0.726	0.998	0.912
ACE										
DD	0.33 ± 0.06	0.39 ± 0.05	1.72 ± 0.42	1.57 ± 0.28	113.33 ± 1.06	111.54 ± 1.01	71.03 ± 1.41	68.46 ± 1.25	0.027 ± 0.001	0.026 ± 0.001
ID	0.33 ± 0.04	0.34 ± 0.03	1.55 ± 0.27	1.55 ± 0.25	115.67 ± 1.02	112.83 ± 1.01*,≠	72.67 ± 1.11	70.00 ± 1.01	0.027 ± 0.001	0.027 ± 0.001
II	0.34 ± 0.05	0.43 ± 0.08	1.41 ± 0.33	1.49 ± 0.41	117.37 ± 1.85	111.58 ± 2.79*,≠	75.79 ± 2.07	67.89 ± 2.24**,≠	0.026 ± 0.002	0.026 ± 0.001
P values	0.590	0.653	0.993	0.922	0.141	0.448	0.206	0.407	0.840	0.639
GSTM1										
Null	0.36 ± 0.04	0.36 ± 0.03	1.83 ± 0.30	1.54 ± 0.19	115.26 ± 0.93	112.50 ± 0.90*,≠	72.63 ± 1.05	69.61 ± 0.98*,≠	0.027 ± 0.001	0.027 ± 0.001
Non-null	0.27 ± 0.03	0.38 ± 0.05	1.12 ± 0.18	1.57 ± 0.33	115.00 ± 1.04	111.67 ± 1.36*,≠	72.62 ± 1.28	68.33 ± 1.13*,≠	0.025 ± 0.001	0.026 ± 0.001
P values	0.443	0.902	0.513	0.652	0.978	0.674	0.915	0.503	0.183	0.436

Table 7 continued

Genetic Markers	CRP (mg/dL)		hs-CRP (mg/dL)		Systolic pressure (mmHg)		Diastolic pressure (mmHg)		TBARS (nmol/mL of MDA)	
	Before	After	Before	After	Before	After	Before	After	Before	After
GSTT1										
Null	0.33 ± 0.06	0.27 ± 0.06	1.68 ± 0.47	1.30 ± 0.44	114.71 ± 2.12	111.76 ± 2.14	70.00 ± 2.10	68.82 ± 2.08	0.029 ± 0.001	0.027 ± 0.002
Non-null	0.33 ± 0.03	0.38 ± 0.03	1.57 ± 0.23	1.59 ± 0.18	115.25 ± 0.74	112.28 ± 0.81**,≠	73.07 ± 0.88	69.21 ± 0.80**,≠	0.026 ± 0.001	0.026 ± 0.001
P values	0.665	0.083	0.409	0.492	0.825	0.851	0.216	0.864	0.152	0.791
CK *Nco*I										
AA	0.35 ± 0.05	0.38 ± 0.04	1.63 ± 0.33	1.74 ± 0.27	115.25 ± 0.92	111.97 ± 0.87*,≠	73.11 ± 1.11	69.02 ± 1.01**,≠	0.026 ± 0.001	0.027 ± 0.001
AG	0.32 ± 0.04	0.36 ± 0.04	1.63 ± 0.29	1.47 ± 0.23	115.10 ± 1.10	111.76 ± 1.33*,≠	71.76 ± 1.24	69.02 ± 1.20	0.028 ± 0.001	0.026 ± 0.001
GG	0.25 ± 0.09	0.33 ± 0.05	0.85 ± 0.30	0.59 ± 0.12	115.00 ± 4.28	118.33 ± 3.07	75.00 ± 4.28	71.67 ± 3.07	0.026 ± 0.003	0.026 ± 0.002
P values	0.836	0.939	0.737	0.287	0.976	0.157	0.635	0.682	0.276	0.780
CK *Taq*I										
1-1	0.37 ± 0.08	0.43 ± 0.08	1.60 ± 0.49	2.11 ± 0.50	117.27 ± 2.37	110.91 ± 2.11*,≠	77.27 ± 2.73	72.73 ± 2.37	0.026 ± 0.002	0.028 ± 0.002
1-2	0.30 ± 0.04	0.40 ± 0.05	1.29 ± 0.24	1.71 ± 0.30	115.00 ± 0.93	111.90 ± 1.06*,≠	71.55 ± 1.04	67.93 ± 1.07*,≠	0.026 ± 0.001	0.026 ± 0.001
2-2	0.35 ± 0.06	0.32 ± 0.02	1.91 ± 0.39	1.26 ± 0.16	114.90 ± 1.17	112.86 ± 1.24	72.86 ± 1.37	69.80 ± 1.15	0.028 ± 0.001	0.027 ± 0.001
P values	0.828	0.625	0.362	0.157	0.701	0.617	0.161	0.128	0.341	0.638
CRP G1059C										
GG	0.34 ± 0.03	0.37 ± 0.03	1.67 ± 0.23	1.60 ± 0.18	115.14 ± 0.73	112.19 ± 0.83**,≠	72.48 ± 0.85	69.43 ± 0.78**,≠	0.027 ± 0.001	0.026 ± 0.001
GC	0.27 ± 0.06	0.35 ± 0.08	0.86 ± 0.25	1.14 ± 0.45	115.38 ± 2.43	112.31 ± 1.22	73.85 ± 2.67	66.92 ± 2.63	0.025 ± 0.002	0.026 ± 0.002
P values	0.645	0.785	0.144	0.103	0.974	0.996	0.568	0.197	0.349	0.666
MTHFR C677T										
CC	0.28 ± 0.05	0.36 ± 0.04	1.30 ± 0.29	1.49 ± 0.24	115.18 ± 1.05	111.43 ± 1.12**,≠	72.50 ± 1.20	68.93 ± 0.94*,≠	0.028 ± 0.001	0.027 ± 0.001
CT	0.36 ± 0.05	0.39 ± 0.05	1.76 ± 0.33	1.74 ± 0.31	115.00 ± 1.02	112.61 ± 1.22	72.39 ± 1.21	68.48 ± 1.20*,≠	0.025 ± 0.001	0.026 ± 0.001
TT	0.39 ± 0.05*,[a]	0.33 ± 0.04	1.99 ± 0.61	1.19 ± 0.24	115.63 ± 2.23	113.75 ± 1.80	73.75 ± 2.56	71.88 ± 2.77	0.026 ± 0.002	0.023 ± 0.002
P values	0.063	0.992	0.648	0.944	0.899	0.670	0.879	0.557	0.133	0.079
MTHFR A1298C										
AA	0.38 ± 0.04	0.38 ± 0.04	1.65 ± 0.26	1.49 ± 0.22	115.35 ± 0.82	112.68 ± 0.98*,≠	72.82 ± 1.05	68.73 ± 0.96**,≠	0.027 ± 0.001	0.026 ± 0.001
AC	0.25 ± 0.04**,[a]	0.35 ± 0.04*	1.51 ± 0.36	1.71 ± 0.28	114.67 ± 1.30	111.33 ± 1.21*,≠	72.22 ± 1.34	69.56 ± 1.23	0.026 ± 0.001	0.027 ± 0.001
CC	0.34 ± 0.16	0.33 ± 0.18	0.67 ± 0.07	0.56 ± 0.06	120.00 ± 0.00	115.00 ± 5.00	75.00 ± 5.00	75.00 ± 5.00	0.036 ± 0.001	0.034 ± 0.004
P values	0.006	0.760	0.397	0.727	0.511	0.692	0.894	0.459	0.123	0.208

Data are expressed as mean ± SEM (standard error of mean). MDA = malondialdehyde. For GSTM1, GSTT1 and CRP G1059C, *P* values were generated by the independent samples *t*-Test (Tbars assay) or Mann–Whitney *U* test (other variables); for the other genetic markers, *P* values were generated by ANOVA (Tbars assay) or by the Kruskall–Wallis test (other variables). Asterisks indicate significant (* $P < 0.05$) and highly significant (** $P < 0.01$) differences. The lower case letters indicate significant differences between two specific genotypes, with a = significant compared with the first genotype of each genetic marker; b = significant compared with the second genotype of each genetic marker; c = significant compared with the third genotype of each genetic marker. For Hp polymorphism, the lower case letters d, e, and f were also added, with d = significant compared with 1F-2; e = significant compared with 1S-2; and f = significant compared with 2-2 genotypes. The symbol ≠ indicates significant differences in the comparison of before-after pequi-oil supplementation detected by the Wilcoxon matched pairs test

for MTHFR1298 AA ($P = 0.002$) genotypes. However, no significant differences were observed between genotypes before or after pequi-oil supplementation (Table 7).

TBARS assay

No significant differences were observed in MDA values in the comparison of before-after pequi-oil treatment. However, Hp (0.005) and MnSOD ($P = 0.024$) polymorphisms presented significant differences between genotypes before supplementation. Hp 1F-1S showed higher MDA values than 1S-1S ($P = 0.019$), and the same occurred with MnSOD Val/Val compared with Val/Ala ($P = 0.019$). After pequi, no significant differences between genotypes were observed (Table 7).

Discussion

The integration of genomics into nutritional sciences has illuminated the complexity of genome responses to nutritional exposures, offering opportunities to increase the effectiveness of nutritional interventions [126]. Dietary chemicals can affect gene expression directly or indirectly to act as ligands for transcription factor receptors, to be metabolized by primary or secondary metabolic pathways, altering concentrations of substrates or intermediates, or to affect signal pathways positively or negatively [63]. Thus, nutrients elicit multiple physiological responses that affect genome stability, imprinting, expression, and viability [126]. These effects confer both health benefits and risks, some of which may not become apparent until later in life [63, 126], besides potentially being able to affect athletic performance [49]. Other reports with lower or equal intervention times have also shown physiological effects, with significant changes in the used markers [16, 48, 66, 77, 104]. Pequi oil is composed mostly of oleic acid and palmitic acid, which are involved in modulating the ratio of triacylglycerol to cholesterol in postprandial lipemia, as well as cell viability and cycling in human monocytes [77]. It also contains several carotenoids, recognized as an effective antioxidant under low PO_2 conditions [17, 43] such those undergone by various tissues and organs during races. In addition, it has been reported that a postprandial monounsaturated fattyacid–rich meal (such as those provided by the Mediterranean diet and by pequi-oil supplementation) increases both plasma carotenoids and human serum paraoxoanase activity (PON1) with a decrease in CRP levels [16]. It has also been suggested that an increased intake of monounsaturated fatty acids is inversely related to blood pressure [125], and our previous report corroborates all these reports and suggestions [88]. Hence, the present study can help broaden knowledge of how antioxidant supplementation affects a person's genes and how individual athletic genetic makeup can affect the way athletes respond to antioxidant supplementation.

As previously mentioned, genes have been implicated in the levels of oxidative stress, lipids, CVD risk, immune reactivity, and performance [12, 15, 18, 20, 22, 23, 34, 36, 42, 45, 55, 62, 68, 69, 78, 85, 95, 147]. Although it is difficult for any study to control all the involved variables, the following were controlled in this study: (1) only trained sportsmen were included; (2) the athletes could choose the distance that they would cover, according to the type, intensity and length of weekly training, guaranteeing no additional physical stress beyond what they are accustomed to; (3) the volunteers were grouped for distance chosen, so that the same route was covered in both races inside the same time for each group of athletes, guaranteeing also the same intensity (time needed to finish the races); (4) although the athletes had a variable degree of training intensity, the amount of training per week was similar (in number of days and hours of training); (5) the volunteers ran the same distance in both races in the same sample time interval and under the same environmental conditions; consequently, the same plasma expansion would be expected in both races; (6) the only change in the athletes' routine between the two races was the supplementation with pequi oil; (7) for the analyzed parameters, differences between sexes are not considered for clinical purposes [46, 67, 137]; (8) for the lipid profile, differences between age groups (up to and from 19 years old) are only clinically considered in fasting [46]; we, however, worked with postprandial lipid profile, and the sample size of this age group was only 20 individuals, which we consider too small to influence the overall result, mainly because there was no correlation between age groups and the analyzed genetic markers. Thus, the significant differences presented in this study are more likely to be related to the pequi-oil supplementation affecting genes/alleles and the genetic factors affecting responses to this supplementation than to the differences between sexes, age, training amount, or intensity.

It is a well-known fact that blood parameters vary in accordance with the stress, duration, and type of exercise. There can be changes in blood values during and after intensive exercise caused by differences such as the state of individual training, environmental factors, and nutrition [14, 35, 41, 71, 135, 139], and the only change in the athletes' routine between the two races was the supplementation with pequi oil. Moreover, previous results of our group which investigated the antioxidant effects of pequi oil on the same runners through measurements of creatine kinase (CK), aspartate aminotransferase (AST), and alanine aminotransferase (ALT) [89] corroborate the suggestion

above, since they did not exceed the reference values proposed for clinical purposes [46, 67, 120] and much less for athletes [96] in both before and after pequi-oil supplementation, besides reducing DNA damage after pequi. Additionally, in the immediate post-exercise period an increment of 50–100% of total leukocytes occurs, mainly due to neutrophilia and lymphopenia, as well as monocytosis, which also occurs at a lower rate [35], and results of leukogram and plateletgram were inside the reference values [67, 137] after both races, independently of sex, age group, or distance covered. As the effects of pequi oil on leukogram, plateletgram, posprandial lipid profile, CRP, and arterial pressure have been previously reported and discussed [88], including correlations between sex/age group, sex/distance covered, and age group/distance covered, we will not discuss them here.

Hp polymorphism has been suggested as a candidate genetic marker in essential hypertension [39] and showed playing a role in predicting an individual's total serum cholesterol [22] and HDL levels [18]. Hp^{*1} allele frequency (when it is treated as a single block, without differentiating Hp 1F or 1S) is high among patients with essential hypertension [40, 92]. Our study was carried out with athletes. However, the different responses obtained for Hp 1F and 1S alleles, even before pequi-oil supplementation, as well as the significant deviation from HWE (which disappeared when these alleles are considered as a single block), indicates that there are differences in biological responses among the Hp^{*1} alleles and that they cannot be treated as a single block in the association studies.

Our study also indicates that before pequi-oil supplementation, lipid peroxidation (evaluated by the Tbars assay) can perhaps be the main predisposition factor for essential hypertension associated with Hp^{*1} allele. It also suggests that Hp 1F-1S genotype may contribute to spurious associations with Hp^{*1} allele. Nevertheless, after pequi-oil supplementation, the responses became more homogeneous and no more significant differences were observed among Hp genotypes, demonstrating that the supplement's protective antioxidant effects affected differential responses to the exercise-induced lipid peroxidation. On the other hand, the Hp 2-2 genotype has been associated with increased risk for essential hypertension [107] and with accumulation of atherosclerotic lesions in essential hypertension, besides showing higher therapeutic needs and more refractory hypertension [40]. Hp 2-2 has been also associated with increased CVD risk, mainly in patients with diabetes [69, 73, 114]. Because atherosclerosis is an inflammatory disease, strenuous exercise can exacerbate this condition and favor atherosclerosis and cardiovascular risk, increasing oxidative stress in the vascular endothelium, blood viscosity, and leukocytosis [70, 118, 119]. In addition, evidence has emerged indicating interactions between neutrophils and platelets and suggesting an ability of platelets to enhance neutrophil-induced endothelial dysfunction [60]. It is noteworthy that (1) HDL has direct anti-atherothrombotic properties that result from inhibition of platelet aggregation, reduced blood viscosity, and suppression of platelet activation factors [83, 86, 115] and (2) in our study, no significant differences in the analyzed biochemical profiles or arterial pressure were found before pequi-oil treatment, but after pequi the Hp 2-2 was differentiated from other Hp genotypes, particularly in the plateletgram, despite having higher HDL values ("good cholesterol"). These results suggested that such associations may be related to increased platelet activation for this genotype in response to the lipid diet rather than to the lipid profile alone. In this context, increased dietary ingestion of lipids for individuals carrying Hp 2-2 genotype could increase thrombolytic effects, contributing to CVD events. Evidence to support this includes the fact that MPV is an indicator of platelet activation [117], and Hp 2-2 presented higher plateletocrit, MPV, and PDW values than any of the other Hp genotypes after pequi-oil supplementation.

Because reactive oxygen species (ROS) play a pivotal role in the pathogenesis of endothelial dysfunction [26], which may involve the development of hypertension and coronary artery disease [74], polymorphisms in the antioxidant enzymes' genes and glutathione S-transferases (GSTs) should also be better analyzed in this context. Whereas antioxidant enzymes act by directly neutralizing ROS [43, 57], most GST substrates are xenobiotics or products of oxidative stress [36].

At the cellular and molecular levels, the endothelium is a likely central focus for the effects of hypertension and the pathogenesis of atherosclerosis [4]. It has even been suggested that superoxide anions might trigger the development of hypertension in some models, presumably by inactivating endothelium-derived nitric oxide and thus mitigating this important vasodilator mechanism [4, 98]. Thus, the polymorphisms in the MnSOD gene can affect superoxide dismutase enzyme efficiency against oxidative stress due to superoxide production in the vascular endothelium, in turn favoring hypertension. Similarly to the Hp polymorphism, before pequi the Val/Val genotype presented higher MDA values than did Val/Ala genotypes, a fact that may contribute to the significant deviation from HWE in favor of heterozygous. Deviations from HWE might be explained by natural selection or recent ethnic admixture [121], but the latter is not the case of our population, although miscegenation continues to occur. Because natural selection can act at the level of genes, if particular genotypes allow for increased fitness in specific environments [11], results suggest a possible adaptive advantage for MnSOD heterozygosis for our population.

Further, they are in accordance with results obtained by our research group with other population groups from Brasília [58, 92]. Although the variant −9Ala allele has been associated with diseases related to oxidative stress and abnormal free radical defense mechanisms [2, 31, 94, 102], our results are not contrary to these findings: the small sample size and also the large standard deviation of the Ala/Ala genotype were already expected, because we worked with athletes. So these aspects made any significant difference in the used markers impossible when it was compared with other genotypes. Moreover, while another area of the MnSOD gene or another unknown gene located in its close vicinity of the MnSOD gene should also be taken into account, heterozygote gives a selective advantage in the global aspect of diseases. However, after pequi-oil supplementation, no further significant differences were observed among MnSOD genotypes, demonstrating once again that its protective antioxidant effects affected the differential responses to the exercise-induced lipid peroxidation.

The CAT-21A/T polymorphism has not been associated with any alteration in catalase activity [51, 79], but individuals carrying the variant T allele presented non-significant higher HDL and lower LDL levels, both before and after pequi-oil supplementation, indicating that this variant allele could be more protective. Although there were differences in the genotype frequencies between the sexes, for clinical purposes, the reference values of lipid profile are equal for men and women [46, 67, 137], not affecting the results. However, the significant and greater increase in number of basophils after pequi-oil supplementation, which differentiated AT genotype from the other CAT genotypes, could indicate a certain predisposition of this genotype to allergic reactions related to the diet. However, this is a question that needs more investigation, mainly in view of the fact that the basophil number was still inside the reference values and all adverse effects disappeared after 3-4 days of pequi-oil treatment [88].

Glutathione S-transferases (GST) are phase II biotransformation enzymes that play an important role in the organism's antioxidant capability, by catalyzing the conjugation of reduced GSH to a variety of endogenous and exogenous substrates [30, 36, 52]. Because GST M1 and T1 null genotypes result in a complete absence of activity in their respective enzymes [52, 68], these common deletion polymorphisms have been widely investigated for their effect on the risk of myocardial infarction [142], hypertension [80, 103], and smoking-related and non-related coronary artery disease (CAD); [1, 50, 54, 84, 130, 140]. However, these studies have yielded contradictory results, with some studies showing a significant association, and others showing no such association [140]. Nevertheless, at least in part, such contradictory results can be explained by the inter-ethnic and intra-ethnic differences known to exist in the allele frequencies of GST null genotypes [30, 36, 68]. Thus, studies mapping the distribution of these alleles' frequency in several ethnicities can be important to gain a better understanding of their biological significance.

The GSTM1 null genotype has been associated both with a risk factor for CAD [1, 140] and with decreased risk of myocardial infarction, although the mechanisms underlying this association are still unexplained [142]. Our study corroborates the latter report and perhaps offers some explanation, given that the GSTM1 null genotype presented a downward trend in leukocyte and platelet numbers compared with the GSTM1 non-null genotypes, both before and after pequi-oil supplementation. It also presented non-significant lower TG and VLDL values, besides higher HDL and LDL values. An association between leukocytosis and increased morbidity and mortality from ischemic vascular disease has been observed for more than half a century. Leukocytosis is simply a marker of inflammation which can directly enhance acute thrombosis and chronic atherosclerosis [33]. Moreover, evidence is increasing that raised serum triglyceride levels are associated with an increased risk of atherosclerotic events [82], and VLDL is the main carrier of triglycerides in plasma [116]. In this context, results suggest that pequi oil had a beneficial effect for the GSTM1 null genotype, at least with regard to leukocytes. For the GSTT1 polymorphism, a meta-analysis of 19 studies including 8,020 cases and 11,501 controls [140] has indicated no correlation between GSTT1 null genotype and CAD risk [140]. GSTT1 null genotype has been also reported as a protective factor against CAD [50] and hypertension [80], as well as a risk factor for CAD independent of genotype-smoking interaction [1]. Our study corroborates the last of these results, given that this genotype presented a greater number of leukocytes and platelets as well as higher and significant values of TG and VLDL, mainly before pequi-oil supplementation. Because after pequi oil such differences decreased or disappeared, results suggest that pequi oil showed protective cardiovascular effects for individuals carrying GSTT1 null genotype.

The renin-angiotensin system (RAS) plays an important role in the regulation of blood pressure (BP), fluid and electrolyte homeostasis, and cardiovascular and renal pathophysiologic processes [24, 106]. For these reasons, genes coding for components of this system are attractive candidates for the investigation of the genetic basis of essential hypertension [106] and for the elucidation of the pathogenesis of CVD [25]. ACE is an important enzyme of the RAS that converts angiotensin I to angiotensin II, a potent vasoconstrictor [24, 123, 138]; since the beginning of the 1990s an association between the insertion/deletion

(I/D) polymorphism of ACE gene and phenotypic expression of CVD has been reported [27]. This polymorphism has also been reported as the main determinant of plasma and tissue ACE levels [111, 138], which are highest in individuals carrying the DD genotype, lowest in those carrying II genotype, and intermediate for heterozygotes [111, 138]. The ACE D allele has been also associated with increased ACE activity [3, 133], and an increase in plasma ACE activity may increase blood pressure through increased production of angiotensin II [123]; as a result, the ACE I/D polymorphism has been associated with hypertension [10, 81, 99, 123]. However, this association is controversial and no correlation has been found in other studies [5, 32, 91, 93, 146]. In contrast, other studies suggest that ethnicity affects both ACE I/D allele frequency and the relationship between ACE I/D genotype and serum ACE concentration [47]. This suggestion reinforces the need for studies mapping the distribution of the alleles' frequency in a number of ethnicities to gain a better understanding of their biological significance and to avoid inconsistent genotype–phenotype associations in pharmacogenetic studies. This is because the considerable range of variation in human populations may reflect, in part, distinctive processes of natural selection and adaptation to variable environmental conditions [11]. Hence, common genetic causes of hypertension for particular populations are more likely to be demonstrated than those for the general population. Although our study does not evaluate serum ACE concentration or activity, ACE I/D polymorphism significantly influenced the results of total leukocytes, segmented, total cholesterol, and LDL levels, with higher values for ID genotype. Pequi oil significantly reduced systolic pressure in athletes carrying this genotype, besides apparently canceling the pre-pequi differences between genotypes seen in the values of total leukocytes, segmented, and total cholesterol. Furthermore, the pequi supplement reduced LDL values for ID genotype, although non-significantly. These results suggest that pequi oil can potentially influence CAD and hypertension risk related to this polymorphism. In view of the fact that these are important factors which can jointly contribute to CAD risk and hypertension, our study also indicates that there are more physiologic factors related to ACE I/D polymorphism than remain to be investigated in associative studies with these diseases.

It has been reported that CK-MM polymorphism influence physiological responses to exercise [42, 56]. Although our results did not demonstrate this association with the analyzed parameters, at least for the CK-MM *Taq*I polymorphism, the correlation found between this polymorphism and distance covered could compromise any possible association.

CRP is an inflammatory marker that contributes to the prediction of CVD and has been associated with atherosclerosis-related phenotypes, such as measures of obesity, insulin resistance, and subclinical atherosclerosis [53, 122]. Because common genetic variants within the CRP gene have been reported to affect baseline CRP levels [8, 122], the CRP gene is an important candidate gene for atherosclerosis and some of its related phenotypes [28]. In our study, CRP and hs-CRP levels were higher for the GG genotype. However, this genotype also presented lower numbers of leukocytes, platelets, lower levels of total cholesterol, TG, and LDL, besides presenting arterial pressure below that of the GC genotype before pequi-oil supplementation. Although these differences were not significant, they were probably due to the small sample size of GC genotype. Moreover, pequi oil mainly favored the GG genotype in significantly reducing leukocytes, platelets, and systolic and diastolic pressures. In this context, our results suggest that the variant C allele could contribute to the prediction of CVD, perhaps being an independent risk factor, but this possible effect needs to be more deeply investigated. Moreover, the frequency of the C allele varies among regions [28] and possibly among ethnicities, and these are important aspects to investigate, in order to avoid spurious associations.

Increased plasma homocysteine (Hcy) is considered a risk factor for CAD [7, 15] and genetic alterations of the MTHFR enzyme could reduce its thermolability and alter the Hcy metabolism, contributing to the development of atherosclerotic lesions [15]. With this in mind, some studies have correlated the C677T and A1298C polymorphisms within MTHFR gene with elevated levels of plasma homocysteine and/or with an increased risk of CVD [21, 38, 95, 105, 129], while other studies have not found such associations [15, 59, 65, 97]. Besides other risk factors involved, ethnic and geographic variations in the allele frequencies of these polymorphisms could perhaps explain these controversial results. Before pequi-oil supplementation, our results showed significant differences in the leukogram, plateletgram, and CRP levels for the MTHFR C677T polymorphism, with increased values for T variant, corroborating results of association between this allele and CAD risk. Because after pequi there is a significant fall in the platelet number, this may indicate some protection. Results also showed significant differences for MTHFR A1298C polymorphism in the TG, VLDL, and CRP levels. However, for this polymorphism, both homozygous presented higher values than heterozygous, indicating that heterozygosis could protect against CAD, but this suggestion needs to be further investigated. After pequi-oil supplementation, there was a significant increase in CRP levels for MTHFR1298 AC genotype, but these levels remained inside the normal range, and results of leukogram, plateletgram, and lipid profile indicated protective effects of pequi.

In Brazil, there are few studies that describe these studied polymorphisms. The Brazilian population as a whole is very mixed and heterogeneous, primarily as a result of five centuries of interethnic crosses among Europeans, Africans, and Amerindians [6], and this miscegenation can influence the distribution of certain polymorphisms. The Federal District was formed in the late 1950s by a wide-ranging mixture of migrants from all regions of Brazil [108], so its population tends to reflect the constitution of the Brazilian population better than populations of other Brazilian regions.

To conclude, CAT, GST-M1/T1, CRP-G1059C, and MTHFR-C677T polymorphisms influenced pequi-oil's responses in leukogram; Hp and MTHFR-C677T, in plateletgram; Hp, ACE, GSTT1, and MTHFR-A1298C, in lipid profile; MTHFR-A1298C, in C-reactive protein (CRP) levels; and Hp and MnSOD, in Tbars assay. Differences between ACE genotypes in the leukogram and total cholesterol disappeared after pequi, and the same occurred for Hp and MnSOD in Tbars assay and for MTHFR-A1298C with CRP levels. Genetic inheritance is one of the factors that drive the lipid abnormalities involved with the progression of atherosclerosis [64]. Consequently, our results can contribute to a greater understanding of the influence of genetic polymorphisms in situations that promote increased ROS. They may also add substantially to the knowledge of how antioxidant supplementation affects a person's genes and how individual athletic genetic makeup can affect the way the athlete responds to antioxidant supplements.

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Conflicts of interest Nothing to declare.

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