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Fabrication of functional dairy drink using grapefruit peel extract and studying its health effects

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ABSTRACT

Background: With increasing consumer demand for functional foods, this study developed and assessed a functional dairy drink fortified with grapefruit peel extract. The use of grapefruit peels will reduce pollution and promote the sustainable disposal of orange peels.

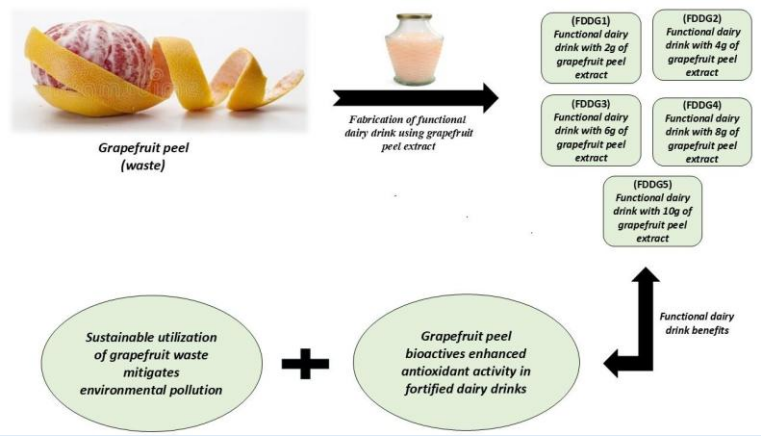
Objective: This study aimed to determine the importance of functional dairy drinks with grapefruit peel extract in people's diets, as they contain important compounds that help reduce harmful reactive free radicals, which can lower the risk of oxidative stress. Reusing grapefruit peels will facilitate their sustainable disposal and mitigate pollution.

Materials and methods: The experimental formulations incorporated grapefruit peel extract at five concentrations (2, 4, 6, 8, and 10 grams) into dairy drinks.

Results: Sensory evaluation revealed superior acceptability for formulations containing 2, 4, 6, and 8 grams of extract, demonstrating successful integration of this bioactive ingredient without compromising consumer appeal. The functional significance of these fortified dairy drinks stems from the rich bioactive compound profile of grapefruit peels, which exhibit substantial antioxidant capacity. These compounds effectively reduce reactive oxygen species. In addition to their health benefits, this approach offers an environmentally sustainable solution for grapefruit processing waste, reducing the pollution associated with conventional disposal methods.

Conclusion: This research establishes a viable pathway for developing commercially acceptable functional dairy products with enhanced health-promoting properties while simultaneously addressing food industry waste management challenges.

Keywords: antioxidant capacity, anthocyanins, beta-pinene, dairy drink, free radicals, grapefruit peel, linoleic acid, mitigate pollution



Graphical abstract: Fabrication of functional dairy drink using grapefruit peel extract and studying its health effects.

INTRODUCTION

Functional foods confer health advantages beyond those of food supplements and nutraceuticals [1]. The primary impetus for individuals to seek more affordable and effective methods of safeguarding their health is the high cost of medical care [2]. Products manufactured from grapefruit peel waste play a significant role in the functional food market and dairy-based functional beverages [3]. Grapefruit (Citrus paradisi) is mostly farmed for its juice [4]. People have regarded grapefruit peels as trash [5]. Recent research, however, has revealed a wealth of bioactive components in these peels, such as limonene, oleic acid, linoleic acid, butyric acid, catechins, and other active compounds [6-7]. The comprehensive and accurate investigation of the chemical and bioactive components of grapefruit peels has produced remarkable discoveries with considerable significance for several sectors, including the food industry and pharmaceuticals [5]. Furthermore, it contains polyphenols and essential oils, both of which protect against free radicals [8]. Grapefruit peel contains compounds capable of treating cancer [9]. Additionally, grapefruit peel compounds are recognized for their antibacterial and antioxidant properties [10]. Functional dairy drinks can play a significant role in the human diet, as they may contain essential bioactive compounds that aid in treating and preventing chronic diseases [11]. Nonetheless, the taste and flavor quality of these drinks are paramount to their popularity [12]. To achieve the recommended consumption levels for disease prevention, health promotion, and chronic illness treatment, high-quality drinks with optimal flavor and aroma are necessary [13]. Although many studies have examined phytochemical components, there is a need to explore how a healthy dairy drink made from grapefruit peel extract can benefit health, to address a gap in

literature. This study aimed to determine the potential importance of functional dairy drinks containing grapefruit peel extract in people's diets, as they contain compounds that help reduce harmful reactive free radicals, which may lower the risk of oxidative stress. Reusing grapefruit peels will facilitate their sustainable disposal and mitigate pollution.

METHODOLOGY

Chemicals and reagents: Scharlab S.L. (Spain) provided analytical-grade solvents, whereas Elabscience (USA) supplied sandwich ELISA kits.

Grapefruit peel extract preparation and GC–MS compositional analysis: Grapefruit peel extraction was conducted via cold maceration. To summarize, 30 g of powdered peel was combined with 270 mL of distilled water and 80% ethanol in conical flasks. The sealed flasks were agitated at 200 rpm for 24 hours at 25°C in a shaking incubator (Heidolph Inkubator 1000 with Unimax 1010, Germany). The resulting mixtures were vacuum-filtered through Whatman No. 1 filter paper before being concentrated at 40°C using a rotary evaporator system (IKA RV8) that included a water bath (IKA HB10) and a vacuum pump (IKA MVP10, IKA Werke, Staufen, Germany). To minimize loss, the extracts were collected in small amounts, placed in preweighed Petri dishes, and dried at 40°C until fully evaporated [14]. The compositional analysis of the grapefruit peel extract was performed using a modified method based on Chao Han et al. [15].

Fabrication of functional dairy drinks using grapefruit peel extract: Figure 1 illustrates the entire experimental scheme. A functional dairy drink was made by combining 8 grams of sucrose and 500 ml of milk, with a constant amount of 0.75 grams of gum Arabic; the mixture was shaken at medium speed in a domestic shaker. The prepared drinks were heated to 85°C for 15 minutes, cooled, and then supplemented with grapefruit peel extract (2, 4, 6, 8, and 10 g/500 ml milk) and refrigerated at 8–10°C. The functional dairy drink is made in five concentrations: FDDG1: functional dairy drink with 2 g of grapefruit peel extract; FDDG2: functional dairy drink with 4 g of grapefruit peel extract; FDDG3: functional dairy drink with 6 g of grapefruit peel extract; FDDG4: functional dairy drink with 8 g of grapefruit peel extract; and FDDG5: functional dairy drink with 10 g of grapefruit peel extract. The prepared beverage was packed into presterilized glass bottles and sealed with crown caps.

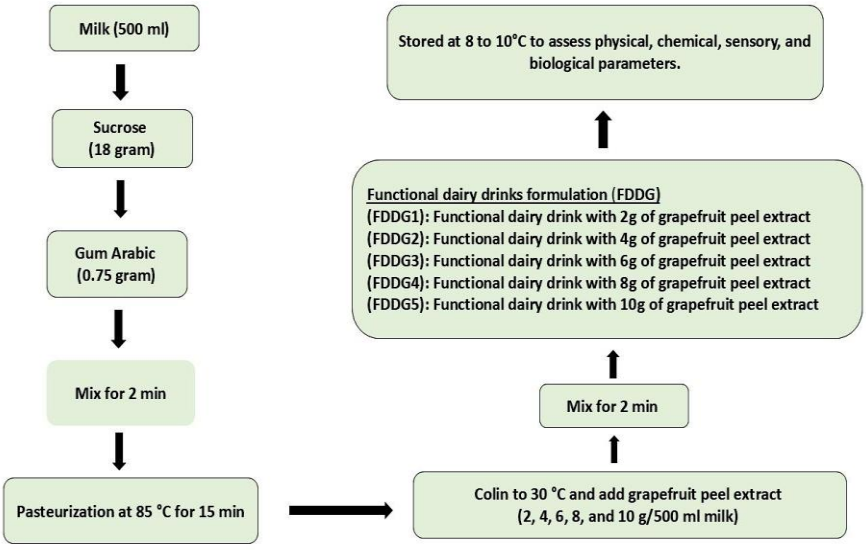


Figure 1. Workflow diagram illustrating the manufacturing of functional dairy drinks enriched with grapefruit peel extract.

Chemical and physical composition of functional dairy drinks. Density and Viscosity: The density and viscosity were assessed via the modified method of [16].

Titratable acidity and pH: Titratable acidity and pH were determined using the methods of [17].

Fat content: Fat content was measured following the method described by [18].

Protein Content: The modified technique of [19] was used to assess the protein content.

Total solid content and Moisture: The percentage of moisture and total solid content was estimated according to the methods of [20].

Aash: The percentage of ash content was estimated according to previous methods [21].

Total carbohydrates: The concentrations of total carbohydrates in functional dairy drinks were calculated via the following equations:

$$Totalcarbohydrates = 100 - (moisture\% + Fat\% + Protein\% + Ash\%)$$ [22].

Calories: The caloric content of functional dairy drinks was calculated via the following equation:

$$Calories = (proteins \times 4) + (Carbohydrates \times 4) + (Fats \times 9)$$[23].

Sensory evaluation: The sensory evaluation was conducted via the approach described by [24]. Five sensory variables were used to evaluate five functional dairy drink samples: FDDG1, FDDG2, FDDG3, FDDG4, and FDDG5. A panel of 30 trained assessors rated the samples on a 10-point scale, with 1 representing minimal preference and 10 denoting maximum preference.

Animals and experimental design: Male albino rats, aged 11-14 weeks and weighing between 170 and 230 grams, were obtained from the principal animal facility at Mosul University, Mosul, Iraq. The rats were maintained in a filtered, climate-controlled environment with a 12-hour light period, a constant temperature of 21–25°C, and 50–60% humidity. Each cage contained three rats that had unrestricted access to regular food. Every effort was made to minimize the number of animals used in the experiment and to prevent any unintentional stress or discomfort. Twenty-one rats were assigned at random to one of seven groups. A small amount of carbon tetrachloride (CCl_4) was injected subcutaneously to induce oxidative stress and evaluate the impact of functional dairy beverages on metabolic markers. We divided the animals into the following groups: Group 1 (positive control) rats served as controls; Group 2 (negative control) rats were injected with 1 ml of CCl_4/kg under the skin for the entire study period of 60 days; Group 3 (FDDG1+ CCl_4) animals received 8 ml of functional dairy drink with 2 g of grapefruit peel extract/ kg bw/day for 8 weeks with 1 ml of CCl_4/kg under the skin for the entire study period; Group 5 (FDDG3+ CCl_4) animals received only once for the entire study period; Group 4 (FDDG2+ CCl_4) animals received 8 ml of functional dairy drink with 4 g of grapefruit peel extract/ kg bw/kg for 8 weeks, with 1 ml of CCl_4/kg under the skin, for the entire study period; Group 6 (FDDG4+ CCl_4) animals received 8 ml of functional dairy drink with 6 g of grapefruit peel extract/kg bw/day for 8 weeks, with 1 ml of CCl_4/kg under the skin, for the entire following the final treatment on day 61, all the rats were fasted for 24 hours while having unrestricted access to water. After the animals were sedated with chloroform, a blood sample was obtained intracardially and centrifuged at 4000 rpm for 15 minutes to isolate the serum. The serum was then stored at −80°C before its biochemical properties were analyzed.

Parameters:

Parameter measurement: The biochemical parameters were determined using a Roche/Hitachi cobas system (model C-501/502). Also, the total antioxidant capacity was analyzed by sandwich ELISA kits according to the manufacturer's instructions (Elabscience, USA).

Calculation of study parameters: The following equations were used to determine the concentrations of globulin, VLDL-C, LDL-C, and phospholipids:

$Globulin(g/dl) = TotalProteinconcentration - Albuminconcentration$[25,26]

$VLDL - C(mg/100ml) = \frac{Triglycerideconcentration}{5}$ [27].

$LDL - C(mg/100ml) = Totalcholesterol - HDL + 0.20(TG)$ [27-28].

$Phospholipids(mg/100ml) = (Totalcholesterolconcentration \times 0.89) + 68$ [29].

Statistical analysis: All analyses were performed in triplicate, and the findings are presented as the means ± standard deviations (SDS). To determine significant differences between treatments, one-way ANOVA was used, followed by Duncan's multiple range test.

RESULTS AND DISCUSSION

Grapefruit peel extract composition: The GC–MS analysis of active compounds in grapefruit peel extract is presented in Figures 2 and 3 and Table 1. The results of the GC/MS analysis revealed that the grapefruit peel extract contains components derived from natural medicinal materials and those that can be developed into value-added materials. 14 compounds were identified. The major compounds were D-limonene (0.94%), nootkatone (1.04%), alpha-pinene (0.89%), beta-pinene (0.31%), gamma-terpinene (1.70%), butyric acid (0.39%), catechins (8.94%), hesperidin (4.08%), oleic acid (4.81%), rutin (55.20%), linoleic acid (86.05%), anthocyanins (0.83%), quercetin (0.66%), and kaempferol (0.21%). Compounds such as D-limonene, nootkatone, alpha-pinene, beta-pinene, gamma-terpinene, butyric acid, catechins, hesperidin, oleic acid, rutin, linoleic acid, anthocyanins, quercetin, and kaempferol are recognized for their involvement in redox activity, significantly influencing the efficacy of medicinal plants, fruits, and vegetables [30]. Owing to their redox activity, natural medicinal chemicals in grapefruit peel extract function as hydrogen donors, reducers, oxygen radical scavengers, and metal-chelating agents [31].

Table 1. GC–MS compositional analysis of grapefruit peel extract

Peak No:	RT (min)	Name of the compound	MF and CAS	MW (g/mol)	Area %	Probability %
1	5.01	Limonene	$C_{10}H_{16}$ CAS: 138-86-3	136.24	0.94	85
2	8.03	Nootkatone	$C_{15}H_{22}O$ CAS: 4674-50-4	218.33	1.04	98
3	10.51	Alpha-Pinene	$C_{10}H_{16}$ CAS:80-56-8	136.23	0.89	92
4	11.09	Beta-Pinene	$C_{10}H_{16}$ CAS: 127-91-3	136.24	0.31	95
5	16.38	Gamma-Terpinene	$C_{10}H_{16}$ CAS: 99-85-4	136.23	1.70	95
6	18.05	Butyric acid	$C_4H_8O_2$ CAS:623-42-7	89.10	0.39	92
7	22.01	Catechins	$C_{15}H_{14}O_6$	290.27	8.94	73

Peak No:	RT (min)	Name of the compound	MF and CAS	MW (g/mol)	Area %	Probability %
			CAS: 18829-70-4			
8	24.52	Hesperidin	$C_{28}H_{34}O_{15}$ CAS: 520-26-3	610.60	4.08	73
9	27.61	Oleic acid	$C_{19}H_{36}O_2$ CAS:56554-45-1	296.00	4.81	72
10	30.99	Rutin	$C_{27}H_{30}O_{16}$ CAS: 153-18-4	610.5	55.20	74
11	34.69	Linoleic acid	$C_{18}H_{32}O_2$ CAS:60-33-3	280.00	86.05	75
12	39.81	Anthocyanins	$C_{52}H_{54}O_{26}$ CAS: 528-58-5	1095.0	0.83	83
13	42.59	Quercetin	$C_{15}H_{10}O_7$ CAS: 117-39-5	302.23	0.66	100
14	47.46	Kaempferol	$C_{15}H_{10}O_6$ CAS: 520-18-3	286.24	0.21	96

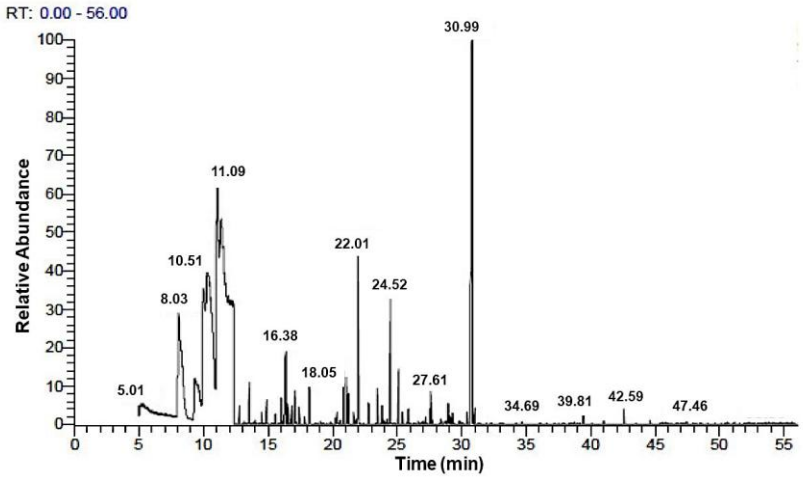


Figure 2: GC–MS analysis of grapefruit peel extract.

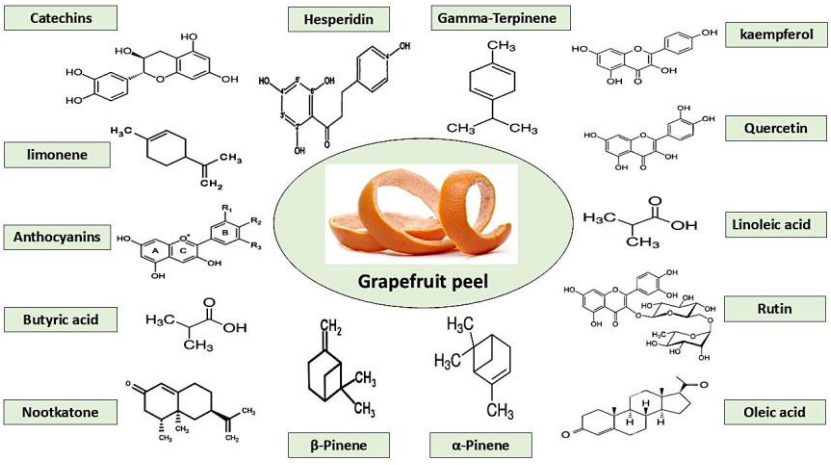


Figure 3. Structures of the active compounds in the grapefruit peel extract.

Chemical and physical composition of functional dairy drinks: Table 2 presents the chemical and physical compositions of the functional dairy drink formulations (FDDG1, FDDG2, FDDG3, FDDG4, and FDDG5) used in the study. The density percentages in the formulations were 1.19, 1.18, 1.17, 1.19, and 1.20, respectively. The maximum density was observed in sample FDDG5, which contained the highest concentration of grapefruit peel extract (10 g). Viscosity has a significant effect on both the stability and efficiency of drug release. The viscosities of all the samples—FDDG1, FDDG2, FDDG3, FDDG4, and FDDG5—prepared with varying concentrations of grapefruit peel extract were 47.08, 47.09, 47.11, 47.12, and 47.13, respectively (Table 2). Sample FDDG1 had the lowest viscosity (47.08) because of its relatively low concentration of grapefruit peel extract. The low viscosity may be a consequence of the high water content and the low concentration of grapefruit peel extract [32]. The total solid contents from the functional dairy drinks FDDG1, FDDG2, FDDG3, FDDG4, and FDDG5 were 35.45, 35.44, 35.44, 35.46, and 35.46, respectively (Table 2). Compared with the other samples, the functional dairy drink samples FDDG4 and FDDG5 presented greater total solid contents. The moisture contents of the functional dairy drink samples, FDDG1, FDDG2, FDDG3, FDDG4, and FDDG5, were 64.55, 64.56, 64.56, 64.54, and 64.54, respectively. The functional dairy drink samples FDDG2 and FDDG3 had higher moisture content than the other samples. The percentages of total acidity were 0.16, 0.17, 0.18, 0.19, and 0.20 for all formulations. With the addition of grapefruit peel extract, the pH of the samples changed. The highest pH value observed was 6.69 for the FDDG1 sample, with the addition of 2 g of grapefruit peel extract. When 4 g was added to FDDG2, the pH decreased to 6.68; when 6 g was added to FDDG3, the pH decreased to 6.67; when 8 g was added to FDDG4, the pH decreased to 6.66; and when 10 g was added to FDDG5, the pH decreased to 6.65. The lowest pH was observed in sample FDDG5, which had the highest percentage of grapefruit peel extract, suggesting greater acidity. In general, the addition of grapefruit peel extract resulted in a substantial decrease in pH because of the high content of active compounds and phenolic compounds in the grapefruit peel extract. The ash contents of the functional dairy drink samples FDDG1, FDDG2, FDDG3, FDDG4, and FDDG5 were 0.92, 0.93, 0.93, 0.94, and 0.95, respectively. The functional dairy drink sample FDDG5 presented a greater ash content than the other samples. The protein contents of the functional dairy drink samples FDDG1, FDDG2, FDDG3, FDDG4, and FDDG5 were 3.71, 3.72, 3.72, 3.73, and 3.73, respectively. Compared with the other samples, samples FDDG4 and FDDG5 presented higher protein contents. The fat contents of the functional dairy drink samples FDDG1, FDDG2, FDDG3, FDDG4, and FDDG5 were 3.31, 3.32, 3.32, 3.32, and 3.33, respectively. There was a similarity in fat content among all formulations, with no significant differences between them. The total carbohydrate contents of all the samples, including FDDG1, FDDG2, FDDG3, FDDG4, and FDDG5, which were prepared with different grapefruit peel extract concentrations, were different: 27.51, 27.48, 27.46, 27.47, and 27.47, respectively. Sample FDDG1 had a high level of carbohydrates (27.51) because of its relatively low concentration of grapefruit peel extract. The low carbohydrate content may be a consequence of the low concentration of grapefruit peel extract. The highest caloric content observed was 154.75 for the FDDG5 sample, with the addition of 10 g of grapefruit peel extract. The addition of 2 g of grapefruit peel extract (FDDG1) changed the caloric content to 154.67, the formulation of FDDG2 with 4 g of grapefruit peel extract changed the caloric content to 154.64, the formulation of

FDDG3 with 6 g of grapefruit peel extract changed the caloric content to 145.63, and the formulation of FDDG4 with 8 g of grapefruit peel extract changed the caloric content to 154.75. Sample FDDG3 had the lowest caloric content. The chemical composition of functional dairy drinks reveals that they contain all the essential nutrients required by a living organism. These nutrients, in addition to a variety of active compounds derived from grapefruit peel extract, include d-limonene, nootkatone, alpha-pinene, beta-pinene, gamma-terpinene, butyric acid, catechins, hesperidin, oleic acid, rutin, linoleic acid, anthocyanins, quercetin, and kaempferol.

Table 2. Chemical and physical composition of the functional dairy drinks.

Chemical and Physical Composition	Functional dairy drinks formulation (FDDG)				
	FDDG1	FDDG2	FDDG3	FDDG4	FDDG5
Density(g/cm3)	1.19±0.010 ^{ab}	1.18±0.010 ^{ab}	1.17±0.010 ^{b}	1.19±0.010 ^{ab}	1.20±0.021^{a}
Viscosity	47.08±0.010^{ab}	47.09±0.006 ^{ab}	47.11±0.015^{b}	47.12±0.021^{b}	47.13±0.015^{a}
Total acidity	0.16±0.010^{a}	0.17±0.020 ^{a}	0.18±0.021^{a}	0.19±0.021^{a}	0.20±0.032^{a}
pH	6.69±0.010^{b}	6.68±0.021^{a}	6.67±0.015 ^{ab}	6.66±0.010 ^{ab}	6.65±0.010 ^{ab}
Moisture %	64.55±0.010^{ab}	64.56±0.010^{ab}	64.56±0.015^{a}	64.54±0.010^{b}	64.54±0.010^{b}
Total solid	0.586^{a}±35.45	35.44±0.010^{a}	35.44±0.015^{a}	35.46±0.010^{a}	35.46±0.010^{a}
Ash%	0.92±0.010^{a}	0.93±0.015^{a}	0.93±0.021^{a}	0.94±0.026^{a}	0.95±0.032^{a}
Protein%	3.71±0.010^{a}	3.72±0.015^{a}	3.72±0.021^{a}	3.73±0.026^{a}	3.73±0.026 ^{a}
Fat%	3.31±0.010^{a}	3.32±0.015^{a}	3.32±0.015^{a}	3.32±0.021^{a}	3.33±0.025 ^{a}
Carbohydrates%	27.51±0.026^{a}	27.48±0.053^{a}	27.46±0.067^{a}	27.47±0.059^{a}	27.47± 0.061^{a}
Calories	154.67±0.046^{a}	154.64±0.032^{a}	154.63±0.049^{a}	154.66±0.075^{a}	154.75±0.206^{a}

Different letters within each row indicate significant differences ($p \leq 0.05$). The following formula was used: FDDG1, functional dairy drink with 2 g of grapefruit peel extract; FDDG2, functional dairy drink with 4 g of grapefruit peel extract; FDDG3, functional dairy drink with 6 g of grapefruit peel extract; FDDG4, functional dairy drink with 8 g of grapefruit peel extract; and FDDG5, functional dairy drink with 10 g of grapefruit peel extract.

Sensory evaluation of functional dairy drinks: Based on the panelists' views, a nine-point hedonic scale—from strongly hate (1) to extremely like (10)—was used for the sensory evaluation (Table 3 and Figure 4). The functional dairy drinks FDDG1, prepared with 2 g of grapefruit peel extract, FDDG2 with 4 g, FDDG3 with 6 g, and FDDG4 with 8 g, were judged to have an acceptable flavor, indicating that the taste ratings were unaffected. Nevertheless, worse taste ratings were obtained when the content of grapefruit peel extract was increased to 10 g (FDDG5). A harsh flavor is imparted by high amounts of grapefruit peel extract, which probably influences customer impressions. On the other hand, no discernible variations in scent, hue, or appearance were found among all the formulations (FDDG1, FDDG2, FDDG3, FDDG4, and FDDG5). Sensory analysis revealed that all formulations had high overall acceptance (average score of 8.00-9.00), average color (average score of 7.00-9.00), average odor (average score of 7.67-9.00), and average appearance (average score of 8.67-9.00) values. However, testers' perceptions were impacted when the concentration of grapefruit peel extract was increased to 10 g/500 ml (FDDG5), as they noticed a harsh flavor in their mouth. Therefore, based on overall acceptability and taste evaluations, the best formulas were FDDG1, FDDG2, FDDG3, and FDDG4.

Table 3. Sensory evaluation of functional dairy drinks.

Sensory evaluation	Functional dairy drinks formulation (FDDG)				
	FDDG1	FDDG2	FDDG3	FDDG4	FDDG5
Taste (1-10)	9.00±1.000 [a]	8.33±1.528 [a]	8.33±1.528 [a]	8.33±1.528[a]	8.31±1.528[a]
Odor (1-10)	9.00±1.000 [a]	9.00±1.000 [a]	9.00±1.000 [a]	8.00±1.000[a]	7.67±1.528[a]
Color (1-10)	9.00±1.000 [a]	8.00±1.000[a]	8.00±1.000 [a]	7.67±1.528 [a]	7.00±1.000[a]
Appearance (1-10)	9.00±1.000[a]	9.00±1.000 [a]	9.00±1.000 [a]	9.00±1.000[a]	8.67±1.528 [a]
Overall acceptability (1-10)	9.00±1.000 [a]	8.38±1.528 [a]	8.37±2.000 [a]	8.33±1.528[a]	8.00±2.000[a]

Different letters within each row indicate significant differences ($p \leq 0.05$). The following formula was used: FDDG1, functional dairy drink with 2 g of grapefruit peel extract; FDDG2, functional dairy drink with 4 g of grapefruit peel extract; FDDG3, functional dairy drink with 6 g of grapefruit peel extract; FDDG4, functional dairy drink with 8 g of grapefruit peel extract; and FDDG5, functional dairy drink with 10 g of grapefruit peel extract.

Figure 4. Functional dairy drink with grapefruit peel extract, (FDDG1): functional dairy drink with 2 g of grapefruit peel extract; (FDDG2): functional dairy drink with 4 g of grapefruit peel extract; (FDDG3): functional dairy drink with 6 g of grapefruit peel extract; (FDDG4): functional dairy drink with 8 g of grapefruit peel extract; and (FDDG5): functional dairy drink with 10 g of grapefruit peel extract.

Effects of functional dairy drinks on metabolic markers: When the rats received 1 mL of CCl_4/kg subcutaneously, their blood serum total antioxidant capacity significantly decreased (Table 4). Numerous mechanisms are responsible for this decrease, most notably increased intake of superoxide dismutase, catalase, and glutathione, which are essential endogenous antioxidants that reduce free radicals caused by oxidative stress and protect cell membranes from oxidative damage [33-34]. The total antioxidant capacity was measured at 0.66 mol/ml in the group of mice exposed to oxidative stress by CCl_4 (G2). In G3, G4, G5, G6, and G7, the total antioxidant capacity of the animals was 1.47, 1.49, 1.50, 1.51, and 1.55 mol/ml, respectively, after being given the functional dairy drink produced from grapefruit peel extract. In contrast, in G2, the total antioxidant capacity was only 1 ml of CCl_4/kg under the skin. The functional dairy drink made from grapefruit peel extract effectively increased the total antioxidant capacity because of the presence of compounds such as limonene, nootkatone, alpha-pinene, beta-pinene, gamma-terpinene, butyric acid, catechins, hesperidin, oleic acid, rutin, linoleic acid, anthocyanins, quercetin, and kaempferol. As a first line of defense against the

dangers presented by free radicals during oxidative stress, these exogenous dietary antioxidants, which are included in grapefruit peel extract, function to eradicate the free radicals that are continuously generated [35–40]. The glucose levels of the mice in group G2, which were exposed to CCl_4-induced oxidative stress, significantly increased (170.56 mg/dl). After CCl_4 oxidative stress, the animals given functional dairy drinks had glucose levels of 81.41, 79.37, 78.44, 77.52, and 76.56 mg/dl in groups G3, G4, G5, G6, and G7, respectively. The formation of H_2O_2 due to oxidative stress led to increased free radical production, which damaged pancreatic beta cells. Consequently, insulin inhibition causes an increase in blood glucose levels, which impedes glucose metabolism and promotes gluconeogenesis and glycogenolysis [33-53]. A reduction in blood serum glucose content was observed in rats fed functional dairy drinks. This could be because these substances can reduce glucose synthesis in cells [41-54] or because they may, directly or indirectly, increase peripheral glucose use from muscle and adipose tissues by increasing insulin sensitivity and simultaneously decreasing glucose synthesis [8].

Table 4 presents the total protein, albumin, and globulin levels in animals administered functional dairy drinks derived from grapefruit peel extract. CCL4-induced oxidative stress in G2 rats resulted in total protein, globulin, and albumin levels of 3.46, 1.77, and 1.69 g/dL, respectively. In contrast, the corresponding values for groups G3–G7 were as follows: 5.64, 3.41, and 2.23 mg/dL (G3); 5.64, 3.56, and 2.23 mg/dL (G4); 5.68, 3.67, and 2.01 mg/dL (G5); 5.76, 3.70, and 2.06 mg/dL (G6); and 5.86, 3.73, and 2.19 mg/dL (G7). These differences can be attributed to the metabolic shifts observed in animals under oxidative stress, in which they rely on alternative energy sources such as fat and protein breakdown, including amino acid catabolism and gluconeogenesis from noncarbohydrate precursors [41]. Conversely, protein levels may decrease due to kidney dysfunction caused by diabetes, which can lead to diabetic nephropathy, a condition characterized by proteinuria (excess protein in the urine) [42-55]. Notably, the rats given functional dairy drinks had a significantly greater total protein content than did those not given the drink (G2). This improvement could be attributed to several factors, including the antioxidant activity of grapefruit peel extracts. Antioxidants neutralize free radicals and prevent protein oxidation [43].

The results revealed that the rats given 1 ml of CCl_4/kg subcutaneously presented increased levels of ALT and AST enzymes (Table 4). Pathogenic infection of hepatocytes causes the release of these enzymes into the bloodstream, resulting in elevated concentrations compared with normal levels in standard groups. The oral administration of functional dairy drinks resulted in ALT and AST levels approaching normal levels, which was attributed to the active components in the grapefruit peel extract that reduce oxidative stress by inhibiting free radicals [44-56].

Creatinine levels were reduced in the animal groups that received functional dairy beverages. This change is attributed to the action of active molecules that prevent oxidative damage to the glomeruli and renal cells. These molecules are derived from the active ingredients in grapefruit peel extract, which inhibit free radicals from causing oxidative stress. These antioxidants prevent renal hypertrophy by keeping the glomerular filtration rate within normal limits [45-57]. When animals lose a direct energy source due to oxidative stress, they turn to proteins as alternative energy sources, resulting in significant urea production [46]. This is the cause of the high urea levels observed under these conditions. The

urea concentration of the animals given functional dairy beverages was significantly lower than that of the animals not given the beverage (G2). The antioxidants eliminate free radicals and prevent the oxidation of proteins and amino acids, reducing the body's urea production [47]. Another possible explanation is that active ingredients protect the liver from oxidative damage to renal cells and glomeruli, reducing protein disruption and degradation and lowering blood urea levels, Uric acid levels are reduced due to its antioxidant function, which can impede lipid peroxidation and prevent LDL-C oxidation by binding with ferrous ions (Fe2+) or Cu2+, interrupting the Fenton reaction and thus inhibiting free radical generation [47].

The blood serum of the experimental group (G2) included considerably more phospholipids (PLs), LDL-C, VLDL-C, triglycerides, and cholesterol than did that of the control group (G1). This could be linked to improved intestinal cholesterol absorption caused by increased cholesterol acyltransferase activity. This enzyme aids in cholesterol absorption and is activated by insulin deficiency, which results from oxidative stress on pancreatic beta cells caused by reactive oxygen species; CCl4 increases ROS formation [48]

An increase in malondialdehyde levels, caused by oxidative stress [49] or oxidative stress by reactive oxygen species (ROS), triggers the release of the hormones norepinephrine and adrenaline, resulting in an increase in LDL-C levels in blood serum. LDL-C levels are increased because of the activation of two hormones by the hormone-sensitive enzyme lipase in adipocytes, which triggers rapid triglyceride breakdown and fatty acid release [50]. The increased concentration of free radicals in the body due to oxidative stress, which damages adipose tissue and beta cells in the pancreas, may be the reason for elevated VLDL-C levels. This increases the release of free fatty acids, which the liver heavily employs to produce VLDL-C [51]. An imbalance in lipid concentrations and increased triglyceride levels in the serum may also occur from increased oxidative stress caused by elevated free radical levels, which in turn reduces the activity of the enzyme lipoprotein lipase in body tissues. The concentration of VLDL-C in blood serum increases due to its production [52].

Increased phospholipid concentrations may be due to increased phospholipid peroxidation, particularly inside cell membranes, which facilitates phospholipid transport into the bloodstream. This transfer occurs in response to oxidative stress caused by free radical production and elevated malondialdehyde levels [48].

Oral administration of the functional dairy drink derived from grapefruit peel extract to CCl4-induced oxidatively stressed animals resulted in significantly elevated HDL-C levels compared with those in the untreated control group (G2). This is due to the active ingredients in beverages, which increase HDL-C levels to near-normal ratios. The elevated levels of HDL-C can be ascribed to both increased activity of certain liver enzyme antioxidants and active molecules that, via their antioxidant properties, particularly reactive oxygen species [50]. In contrast to those in the G2 group, the animals that received the functional dairy drink orally presented a reduction in phospholipids, VLDL-C, triglycerides, and cholesterol. This is due to active compounds such as limonene, nootkatone, alpha-pinene, beta-pinene, gamma-terpinene, butyric acid, catechins, hesperidin, oleic acid, rutin, linoleic acid, anthocyanins, quercetin, and kaempferol, which reduce damage to reactive oxygen species and increase the activity of enzymatic antioxidants such as glutathione-S-transferase, which play crucial roles in neutralizing free radicals within the body [38].

Table 4. Effects of functional dairy drinks on metabolic markers

Metabolic Markers	G 1	G 2	G 3	G 4	G 5	G6	G 7
Total antioxidant capacity (µmol/ml)	1.56±0.021 ^{a}	0.66±0.010 ^{d}	1.47±0.015 ^{c}	1.49±0.025 ^{bc}	1.50±0.021 ^{b}	1.51±0.020 ^{b}	1.55±0.010 ^{a}
Glucose *(mg/dl)*	77.81±0.577 ^{d}	170.56±1.010^{a}	81.41±1.010^{b}	79.37±0.015 ^{c}	78.44±0.049 ^{cd}	77.52±0.010 ^{de}	76.56±0.010 ^{e}
Total Protein *(g/dl)*	6.91±0.072^{a}	3.46±0.025 ^{e}	5.64±0.047 ^{d}	5.64±0.040 ^{d}	5.68±0.010 ^{cd}	5.76±0.010 ^{bc}	5.86±0.119 ^{b}
Albumin *(g/dl)*	3.77±0.015 ^{a}	1.77±0.015 ^{g}	3.41±0.010^{f}	3.56±0.010 ^{e}	3.67±0.010 ^{d}	3.70±0.015 ^{c}	3.73±0.010 ^{b}
Globulin*(g/dl)*	3.14±0.061 ^{a}	1.69±0.026 ^{d}	2.23±0.050 ^{b}	2.23±0.235 ^{b}	2.01±0.020 ^{c}	2.06±0.015 ^{bc}	2.19±0.025 ^{b}
Cholestrol *(mg/dl)*	77.66±0.084 ^{b}	352.42±2.661 ^{a}	76.96±0.044 ^{b}	77.35±0.050 ^{b}	77.42±0.015 ^{b}	77.59±0.010 ^{b}	77.61±0.010 ^{b}
Triglycerides *(mg/dl)*	69.36±0.608 cd	231.28±1.010 ^{a}	71.30±0.050 ^{b}	70.52±0.059 ^{b}	70.50±0.081 ^{b}	69.59± 0.095^{c}	68.62±0.038 ^{d}
Phospholipids *(mg/100 ml)*	137.12±0.072 ^{b}	381.65±2.370 ^{a}	136.49±0.044 ^{b}	136.8±0.045 ^{b}	136.90±0.015 ^{b}	147.05±17.321 ^{b}	137.0±0.010 ^{b}
ALT *(U/L)*	28.82±1.042 ^{c}	49.03±1.015 ^{a}	30.23±0.010 ^{b}	30.08±0.010 ^{b}	30.08±0.010 ^{b}	29.45±0.035 ^{bc}	28.66±0.554 ^{c}
AST *(U/L)*	17.14±0.586 ^{e}	78.02±1.010 ^{a}	25.63±0.575 ^{b}	21.53±1.752 ^{c}	19.39±0.423 ^{d}	18.74±0.061 ^{d}	18.86±0.044 ^{d}
Creatinine (mg/dl)	0.46±0.015 ^{g}	1.77±0.026 ^{a}	1.56±0.015 ^{b}	1.46±0.010 ^{c}	0.83±0.031 ^{d}	0.66±0.010 ^{e}	0.54±0.010 ^{f}
Uric Acid *(mg/dl)*	2.44±0.015 ^{e}	6.95±0.015 ^{a}	3.57±0.021 ^{b}	3.50±0.021 ^{c}	2.57±0.021 ^{d}	2.41±0.036 ^{ef}	2.38±0.010 ^{f}
Blood Urea *(mg/dl)*	30.17±0.025 ^{e}	61.21±0.592 ^{a}	50.27±0.015 ^{b}	49.63± 0.020^{c}	30.87± 0.015^{d}	30.57±0.021 ^{de}	30.46±0.010 ^{de}
Bloodurea nitrogen *(mg/dl)*	16.15± 1.020^{f}	29.72±0.702 ^{a}	20.82±0.015 ^{b}	19.77±0.017 ^{c}	18.66± 0.015^{d}	18.53±0.021 ^{d}	17.26±0.010 ^{e}
HDL *(mg/dl)*	73.48±10.978 ^{a}	17.35±1.163 ^{e}	49.18±0.552 ^{d}	52.59±0.569 ^{d}	54.97±4.070 ^{cd}	62.83±0.990 ^{bc}	64.56±0.990 ^{b}
VLDL-C *(mg/100 ml)*	13.87±0.122 ^{de}	46.25±0.200 ^{a}	14.26±0.010 ^{b}	14.10± 0.010^{c}	14.09±0.015 ^{c}	13.91± 0.020^{d}	13.72± 0.010^{e}
LDL-C *(mg/100 ml)*	18.05±10.826 ^{d}	381.33± 1.730^{a}	42.70±1.469 ^{b}	38.86± 0.613^{b}	36.55±4.048 ^{b}	28.67±1.005 ^{c}	26.77±1.010 ^{c}

Different letters (a, b, c) within each row indicate significant differences ($p \leq 0.05$), and the data are presented as the means ± standard deviations. (G1) Positive control and (G2) (negative control) rats were injected with 1 ml of CCl_4/kg under the skin, (G3) FDDG1+ CCl_4, (G4) FDDG2+ CCl_4, (G5) FDDG3 + CCl_4, (G6) FDDG4+ CCl_4, or (G7) FDDG5+ CCl_4, and there were 3 rats in each experimental group.

CONCLUSION

The use of grapefruit peels will reduce pollution and promote sustainable disposal of grapefruit peels. The antioxidant system was significantly enhanced, and oxidative stress was effectively reduced by the administration of a functional dairy beverage made from grapefruit peel extract. While much of what we know about the health benefits of different functional dairy beverages comes from personal stories, we still need research on how these drinks are processed in the body, their active ingredients, and evidence of their effectiveness, consistency, safety, and stability. Such investigations may begin with in vitro and animal studies, but definitive evidence may require clinical trials. Functional dairy beverages can benefit most individuals, but depending on their lifestyle and genetic makeup, some may need to weigh the risks and rewards.

Abbreviations: GC–MS: Gas Chromatography-Mass Spectrometry; ROS: Reactive Oxygen Species; RT: Retention Time; MF: Molecular formula; CAS: Chemical Abstracts Service; MW: Molecular Weight; AST: Aspartate aminotransferase; FDDG: Functional dairy drinks formulation; G1,2,3,4,5,6,7: Group 1,2,3,4,5,6,7; CCl4: Carbon tetrachloride; ALT: Alanine aminotransferase; PL: Phospholipids.

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