Original article

Antioxidants, Antidiabetic and antihyperlipidemic effects of the spice ginger rhizome (*Zingiber officinale*) and cinnamon (*Cinnamomum zeylanicumon*) in diabetic rats

Abstract

This study aimed to evaluate the effects of two medicinal plants, ginger rhizome (*Zingiber officinale*) and cinnamon bark (*Cinnamomum zeylanicum*), on reducing blood sugar, triglycerides, cholesterol, and LDL-cholesterol levels. The analysis of the phenolic compounds in these plants revealed that both ginger rhizome and cinnamon bark are rich in antioxidants, containing high levels of hypoglycemic and hypocholesterolemic phenolic acids, such as cinnamic acids. The study found that ginger rhizome and cinnamon bark could be added at concentrations of 1% and 2%, respectively, to a basal diet. Diabetic rats were fed a diabetic diet for 5 weeks, with the normal control (G1) receiving the basal diet. The results showed that the addition of ginger rhizome and cinnamon bark to the diabetic diet significantly reduced serum glucose and improved the lipid profile (cholesterol, triglycerides, LDL, and VLDL cholesterol). Furthermore, HDL cholesterol levels increased in all treatment groups, while LDL- cholesterol levels significantly decreased compared to the positive control.

Key words: Ginger, cinnamon, rats, diabetic

Introduction

Diabetes mellitus (DM), commonly referred to as diabetes, is a chronic metabolic disorder characterized by prolonged elevated blood sugar levels and insulin resistance, often linked to oxidative stress. If untreated, it can lead to a wide range of complications and irreversible damage. **[1]** A study conducted on 180,000 insured dogs aged 5 to 12 years in the United States revealed that Australian Terriers, Samoyeds, Swedish Elkhounds, and Swedish Lapphunds exhibited the highest rates of diabetes mellitus. Genetic differences among animals may predispose certain breeds to specific forms of diabetes. Furthermore, factors such as breed, a history of hyperadrenocorticism, and female gender were identified as risk factors for developing the condition. Diabetes mellitus (DM) is categorized into three types. Type 1 DM, also known as "insulin-dependent diabetes mellitus" (IDDM) or "juvenile diabetes," has an unknown cause. Type 2 DM, the most common form, referred to as "non-insulin-dependent diabetes mellitus" (NIDDM) or "adult-onset diabetes," is primarily associated with insulin resistance due to excess body weight and lack of physical activity. Type 3 DM, or "gestational diabetes," arises during pregnancy and is characterized by elevated blood sugar levels without a prior history of diabetes. Among animals, Types 1 and 2 are the most commonly observed forms **[2].** The management of diabetes mellitus (DM) generally requires a combination of medications, dietary adjustments, and regular physical activity. Hypoglycemic drugs, including insulin, biguanides, sulfonylureas, and alpha-glucosidase inhibitors, may cause various adverse effects, such as severe hypoglycemia, abdominal pain, lactic acidosis, and other complications **[3]**. Herbal remedies present an alternative approach to treatment, offering a rich source of bioactive compounds with antidiabetic effects. They are associated with fewer side effects, lower costs, and improved accessibility, especially in rural regions. Natural resources are regarded as a safe and affordable source of these beneficial compounds **[4-5].** The genus *Cinnamomum*, belonging to the Lauraceae family, was first identified in 1760 and includes around 250 species distributed across tropical and subtropical regions, mainly in Asia, as well as in South and Central America and Australia **[6].** Worldwide, cinnamon is known for its culinary and therapeutic uses. **[7]** Cinnamon has been recognized as one of the most potent plants with antidiabetic properties. In the Philippines, 25 species of *Cinnamomum* are found, 18 of which are endemic. Among these, three economically significant species—*Cinnamomum cebuense*, *C. mercado*, and *C. burmannii* (also known as *C. mindanaense Elmer*)—are primarily found in the Visayas and Mindanao regions. Despite their potential, these species are underutilized and sparsely distributed in the country. Philippine cinnamon holds promise as a sustainable forest-based livelihood through the utilization of its bark, leaves, and fruits in various products **[8].**

Ginger (*Zingiber officinale*), a non-toxic spice **[9]**, is frequently utilized in herbal therapy to treat a range of chronic illnesses **[10–12]**. Extensive research has examined the anti-inflammatory properties of ginger, which is regarded as a safe and effective complementary therapy for reducing inflammation. This is especially beneficial, as inflammation is a major risk factor in various diseases, including those affecting healthy individuals and those with chronic illnesses or gastrointestinal disorders **[13–15].** According to certain research, ginger lowers low-density lipoprotein (LDL), systolic blood pressure (SBP), diastolic blood pressure (DBP), total cholesterol (TC), triglycerides (TG), and fasting blood sugar (FBS) in people with type 2 diabetes **[16, 17]**. The aim of this manuscript is to study the effect of antioxidants present in cinnamon and ginger and their lowering effect on serum glucose, blood lipids and cholesterol.

MATERIAL AND METHODES

Materials.

Ginger rhizome (*Zingiber officinale*):

The item was purchased from a marketplace in Kafrelsheikh, Egypt.

Cinnamon barks *(Cinnamon zeylanicum)*:

The item was purchased from a marketplace in Kafrelsheikh, Egypt.

Animals.

The study utilized 30 mature male albino rats acquired from the experimental animal facility at the Food Technology Research Institute, Agricultural Research Center in Giza, Egypt. The rats selected for the experiment had body weights ranging from 68 to 78 grams.

Phenolic and flavonoid compounds

The scientists employed high-performance liquid chromatography to identify and measure phenolic and flavonoid compounds in the samples, utilizing a technique described in **[18-19].**

Animal feeding:

In the current study, a total of thirty (30) adult male albino rats, weighing between 67 and 79 grams, were utilized. The experiment took place at the animal facility of the Food Technology Research Institute, Agricultural Research Center, located in Giza, Egypt. The rats were maintained under standard healthy conditions for a period of ten days. During this time, they were provided with a standard diet (basal diet) as outlined in List 1, which included 4% salt mixture and 1% vitamin mixture. The animals had unrestricted access to tap water and were fed a uniform basic diet in accordance with **[20].**

List 1: The consistent of the basal diet.

Ingredient	g/100g diet	Ingredient	g/100g diet
Casein	20	Vitamin mixture	1
Corn oil	10	Cellulose	5
Salt mixture	4	Corn starch	60

Design of experiment:

Following a ten-day adaptation period on a basal diet, five rats were designated as the control group (G1, normal control) and continued to receive the basal diet throughout the experiment. The remaining 25 rats were subjected to a 24-hour fast before receiving an alloxan solution injection (120mg/kg body weight) to induce hyperglycemia **[21].** Blood glucose levels were measured four days post-injection. Diabetes was confirmed according to the criteria reported by **[22].**

Subsequently, the 25 diabetic rats were divided into five subgroups, each containing five animals.

Hyperglycemia experiment of spices:

G1: Received the standard diet (negative control).

G2: Received the standard diet (Positive diabetic control).

G3: Received the standard diet enhanced with powdered ginger at a 1% concentration.

G4: Received the standard diet enhanced with powdered ginger at a 2% concentration.

G5: Received the standard diet enhanced with powdered cinnamon at a 1% concentration.

G6: Received the standard diet enhanced with powdered cinnamon at a 2% concentration.

Blood analysis

To assess the separated serum, various tests were conducted. For biochemical analyses, blood samples were centrifuged at 3000 rpm for 5 minutes to obtain serum, which was then utilized for specific tests (Glucose, total cholesterol TC, HDL-C, triglyceride TG,LDL-C).

a. Serum glucose determination followed the method outlined in [23].

Glucose concentration was calculated using equation 1:

Glucose (mg/dl) = (A sample)/ (A standard) x 100 (1)

b. Blood triglyceride [TG] levels were measured.

Serum triglyceride concentration was estimated using the approach described in equation 2 [24]:

Triglycerides (mg/dL) = (A sample)/ (A standard) x 200 (2)

c. Cholesterol profile analysis included assessment of total cholesterol levels (TC).

The enzymatic method for colorimetric cholesterol measurement, as described by [25], was employed. Cholesterol concentration was determined using equation 3:

Total cholesterol = (A sample)/ (A standard) x 200 (3)

High-density lipoprotein cholesterol (HDL-cholesterol) was evaluated using the method detailed in [26]. Very-low-density lipoprotein cholesterol (VLDL-C) was calculated using equation 4:

VLDL-C (mg/dL) = Triglycerides/5 (4)

Low-density lipoprotein cholesterol [LDL-C] levels were determined using equation 5:

LDL-C [mg/dL] = TC – [VLDL + HDL] (5)

Statistical analysis:-

Data were subjected to the proper statiscal analysis according to the method prescribed by **[27].** Means were verified according to the **[28].**

Results and Discussion

Isolation and identification of phenolic compounds of ginger rhizomes and cinnamon bark (powder).

The phenolic compounds in ginger and cinnamon powder were separated and identified using high-performance liquid chromatography (HPLC), as presented in Table 1. The analysis detected eleven phenolic compounds in total.

In ginger powder, coumarin was the most abundant phenolic compound, present at 858 mg/100g. Chlorogenic acid followed at 2.1 mg/100g, with vanillic acid at 1.3 mg/100g. Other compounds were found in smaller amounts: caffeine (0.59 mg/100g), gallic acid (0.55 mg/100g), caffeic acid (0.4 mg/100g), cinnamic acid (0.23 mg/100g), catechin (0.22 mg/100g), ferulic acid (0.05 mg/100g), catechol (0.08 mg/100g), and syringic acid (0.0733 mg/100g).

Cinnamon powder contained higher levels of certain phenolic compounds compared to ginger, with coumarin being the most prevalent at 526.9 mg/100g, followed by chlorogenic acid at 19 mg/100g. Vanillic acid was found at 4.4 mg/100g, and gallic acid at 4.8 mg/100g. Other compounds were present in lower concentrations: ferulic acid (1.7 mg/100g), cinnamic acid (1.02 mg/100g), caffeine (0.9 mg/100g), caffeic acid (0.6 mg/100g), syringic acid (0.4 mg/100g), catechin (0.8 mg/100g), and catechol (0.5 mg/100g).

Research by [29] investigated the antidiabetic effects of cinnamon polyphenols (CPS), finding that both dimethyldiguanide and CPS significantly reduced blood glucose levels in diabetic mice. [30] explained how polyphenols enhance glucose uptake by increasing the activity of glucose transporter 4 (GLUT 4), which is responsible for absorbing glucose from the bloodstream and operates under insulin regulation. Diabetes mellitus, however, leads to insufficient insulin sensitivity or absence, disrupting GLUT 4 function and causing hyperglycemia. [31] proposed that these polyphenols could become a valuable asset in the anti-diabetic pharmaceutical market. Additionally, studies and clinical trials have shown that phenolic phytochemicals can help alleviate diabetes symptoms and potentially prevent long-term diabetic complications.

Table (1): Phenolic compound from ginger rhizome and cinnamon bark using (HPLC).

Identification phenolic compounds	Relation time (min.)	Ginger rhizome (mg/100g)	Cinnamon bark (mg/100g)
Cinnamic acid	11.643	0.23	1.02
Chlorogenic acid	6.882	2.1	19
Vanlic acid	7.537	1.3	4.4
Syringic acid	7.704	0.0733	0.4
Caffeic acid	7.511	0.4	0.6
Ferrulic acid	9.050	0.05	1.7
Catechol	6.503	0.08	0.5
Caffeine	7.543	0.59	0.9
Gallic acid	4.316	0.55	4.8
Coumarin	10.986	858	526.9
Catechin	6.703	0.22	0.8

Effect of ginger rhizomes and cinnamon bark powder on blood glucose level of diabetic rats.

Table 2 presented the average blood glucose levels of the control and diabetic groups throughout the study. Blood glucose levels in the diabetic groups (72 hours after alloxan-induced diabetes) were significantly higher than those in the normal control group (G1). The data indicated no significant differences between diets containing 1% and 2% ginger rhizome powder. However, cinnamon bark powder at both 1% and 2% concentrations significantly reduced blood glucose levels in the diabetic groups (G3, G4, G5, and G6) compared to the diabetic group on the control diet (G2). This reduction was observed from the first week of feeding and continued to intensify over the course of the study. Additionally, the results showed that 2% cinnamon bark powder had a more substantial effect on lowering blood glucose levels than 2% ginger rhizome powder. Furthermore, the higher 2% concentration of both ginger and cinnamon powders produced a greater reduction in blood glucose levels than the 1% concentration.

Table 2 results showed that diabetic rats consuming a basal diet with 1% ginger rhizome addition maintained blood glucose levels above 248.4 mg/dl, staying within the diabetic range.

Studies have shown that cinnamon extract can substantially reduce blood glucose levels in vivo in models of alloxan-induced experimental diabetes as described by [32-33], Alloxan, a urea derivative, selectively targets and destroys pancreatic islet β-cells, leading to experimental diabetes. It is commonly used alongside streptozotocin to induce diabetes in various animals, including rats, rabbits, mice, and dogs, with dosages tailored to achieve different levels of severity. This chemical method of induction is regarded as the most effective, reliable, and practical approach for inducing diabetes in rodents [34]. Research conducted by [35] demonstrated that administering cinnamon extract orally significantly lowered blood glucose levels. These results are consistent with the findings of a study by [36], The study examined the impact of cinnamon (C. zeylanicum) powder supplementation on glucose levels in alloxan-induced diabetic Wistar rats. The findings revealed that cinnamon effectively inhibited the rise in blood glucose levels. Diabetes was induced in the rats with a single subcutaneous injection of alloxan at a dose of 15 mg/kg. [37] examined the effects of increasing doses of C. verum aqueous extract on fasting plasma glucose levels in alloxan-induced diabetic male rats. The results indicated that the lowest dose of cinnamon extract (200 mg/kg) was the most effective in significantly ($P < 0.05$) reducing fasting blood glucose levels. Furthermore, the study reported notable improvements in the extract's hypoglycemic effects, which were associated with increased body weight gain, food intake, and food efficiency ratio. These findings suggest that cinnamon extract can help regulate glycemic profiles in alloxan-diabetic rats and shows considerable potential as a complementary treatment for diabetes. However, further research is needed to fully understand its biological activity.

Type 2 diabetes mellitus is characterized by elevated blood sugar levels caused by malfunctioning insulin receptors. This high glucose concentration damages cells directly and triggers lipid peroxidation [38]. Researchers have investigated the potential blood sugar-lowering effects of cinnamon in diabetic animal models through in vivo studies. Proposed mechanisms for cinnamon's hypoglycemic action include the inhibition of glycogen synthase kinase 3 (GSK-3), which enhances glucose uptake or reduces blood sugar levels. Mammals express two widely distributed homologs of GSK-3: GSK-3α and GSK-3β. As noted in [39], GSK-3 has emerged as a target for diabetes treatment due to its functional partitioning, tissue selectivity, and acute dosage-dependent inhibition effects. GSK-3, a serine protein kinase, plays a critical role in regulating various cellular processes, such as glycogen metabolism and gene transcription. The inability of insulin to suppress GSK-3, which is typically active in a cell's basal state, may contribute to the development of type 2 diabetes mellitus.

Cinnamic acid (3-phenyl-2-propenoic acid), a key component of C. cassia, is present in many fruits, vegetables, and beverages [40]. This antioxidant phytochemical is known for mitigating diabetic complications and reducing hyperglycemia [41]. High levels of cinnamic acid in cinnamon supplements have been shown to improve diabetic control in experimental rat models, as evidenced by reduced blood glucose levels, better glucose tolerance, and increased insulin secretion in a time- and dose-dependent manner [42].

The therapeutic effects of ginger in addressing diabetic complications are believed to stem from its ability to reduce oxidative stress and inflammation, partly through the inhibition of the NF-κB signaling pathway [43]. Research suggests that ginger, which contains compounds like Zerumbone, can help reduce kidney damage in diabetic rats. Thanks to its anti-inflammatory properties, ginger may also be effective in managing conditions such as gout, osteoarthritis, and rheumatoid arthritis. Its benefits include regulating blood sugar levels, relieving pain, enhancing heart function, and offering antiemetic, antimicrobial, and antifungal effects [44]. Ginger has shown protective effects against diabetic complications in the liver, kidneys, eyes, and nervous system. Multiple studies have demonstrated that ginger extract can lower blood glucose levels in both types of diabetes, with its effectiveness increasing in a dose-dependent manner [45].

Table 2. Effect of ginger rhizome and cinnamon bark powder on blood glucose level of normal and diabetic rats.

Group	Diets	After 72 hr mg/dl	After 1 week mg/dl	After 2 week mg/dl	After 3 week mg/dl	After 4 week mg/dl	After 5 week mg/dl
G1	**Normal control**	97.87 b ±1.85	99.40 d ±1.10	104.33 d ±9.25	102.01 d ±7.56	103.52 e ±3.09	91.84 f ±4.10
G2	**Diabetic control**	300.33 a ±12.15	303.33 a ±12.62	308.92 a ±8.90	313.25 a ±13.57	311.89 a ±7.73	311.38 a ±4.74
G3	**Ginger rhizome 1%**	302.00 a ±1.61	290.30 b ±4.95	281.30 b ±9.66	269.06 b ±7.74	265.70 b ±4.90	260.23 b ±4.95
G4	**Ginger rhizome 2%**	304.33 a ±6.66	275.40 c 4.80	257.27 c ±5.86	240.50 c ±10.10	238.33 c ±2.78	227.03 d ±5.92
G5	**Cinnamon bark 1%**	304.63 a ±7.15	287.97 b ±2.62	266.13 bc ±5.19	258.63 b ±2.89	245.67 c ±5.13	238.40 c ±2.46
G6	**Cinnamon bark 2%**	305.50 a ±6.49	282.07 bc ±7.28	272.17 bc ±12.41	240.37 c ±10.15	208.66 d ±2.98	191.63 e ±3.20
LSD at p ≤ 0.05		**12.39**	**11.89**	**15.80**	**16.47**	**8.480**	**7.790**

Effect of ginger rhizomes and cinnamon bark powder on some serum lipid parameters of diabetic rats.

After five weeks of dietary intervention, blood samples were collected from rats to assess the serum concentrations of various lipid markers, including total cholesterol, low-density lipoprotein cholesterol (LDL-C), very low-density lipoprotein cholesterol (VLDL-C), high-density lipoprotein cholesterol (HDL-C), triglycerides, and total lipids. The results, shown in Table 3, revealed notable findings.

At the end of the experiment, the normal control group had a total cholesterol level of 116.80 mg/dl. In comparison, the diabetic control group had a higher total cholesterol concentration of 194.03 mg/dl. Diabetic rats given 1% and 2% ginger rhizome powder showed total cholesterol levels of 181.08 and 165.35 mg/dl, respectively. Diabetic rats treated with 1% and 2% cinnamon bark powder (G5 and G6) had total cholesterol levels of 165.51 and 130.58 mg/dl, respectively. These findings indicated that rats fed ginger and cinnamon powder had significantly lower cholesterol levels compared to the diabetic control group ($P \leq 0.05$).

In terms of triglycerides, the normal control group had a plasma level of 112.73 mg/dl, while the diabetic control group had a triglyceride concentration of 188.11 mg/dl. Diabetic rats treated with 1% and 2% ginger rhizomes (G3 and G4) showed triglyceride levels of 170.48 and 160.51 mg/dl, respectively. Rats fed with 1% and 2% cinnamon bark powder (G5 and G6) displayed triglyceride values of 140.57 and 120.65 mg/dl, respectively. Notably, the decrease in triglycerides was more pronounced in the 2% cinnamon bark group (G6) than in the 2% ginger rhizome group (G4).

Regarding HDL cholesterol, the normal control group had a level of 72.67 mg/dl, while the diabetic control group showed a lower level of 40.30 mg/dl. Diabetic rats fed 1% and 2% ginger rhizomes (G3 and G4) had HDL cholesterol values of 45.92 and 49.55 mg/dl, respectively. The HDL levels in G5 and G6 groups, which were fed cinnamon bark powder at 1% and 2%, were 55.25 and 59.94 mg/dl, respectively.

The LDL cholesterol levels for the normal control diet were 21.59 mg/dl, while the diabetic control group had an average of 116.11 mg/dl. Rats fed ginger rhizomes and cinnamon bark powder had LDL cholesterol values of 101.06, 83.70, 82.70, and 46.94 mg/dl, respectively.

For VLDL cholesterol, the normal control diet resulted in a value of 22.55 mg/dl, whereas the diabetic control group had an average of 37.62 mg/dl. Rats fed ginger rhizomes and cinnamon (1% and 2%) exhibited VLDL cholesterol levels of 34.09, 32.10, 28.11, and 24.13 mg/dl, respectively.

At the experiment's conclusion, the normal control group's plasma total lipid content was 1.35 mg/dl, while the diabetic control had a value of 3.35 mg/dl. The G3 and G4 groups, treated with 1% and 2% ginger rhizome powder, showed total lipid values of 3.06 and 2.84 mg/dl, respectively, while the G5 and G6 groups, fed 1% and 2% cinnamon bark powder, had total lipid values of 2.88 and 1.89 mg/dl, respectively.

Overall, the data in Table 3 revealed that diabetic rats treated with ginger rhizomes and cinnamon bark powder at 1% and 2% had significantly lower serum levels of total cholesterol, triglycerides, LDL cholesterol, VLDL cholesterol, and total lipids compared to the diabetic control group ($P \leq 0.05$). Additionally, these groups exhibited significantly higher HDL cholesterol levels. The normal control group or basal diet-fed rats had significantly lower values for total cholesterol (TC), triglycerides (TG), and LDL-C.

Metabolic syndrome, a complex condition associated with poor dietary choices and lack of physical activity【46], poses a significant global public health risk and is a major contributor to cardiovascular disease [47]. Commonly recognized factors contributing to metabolic syndrome include obesity [48], dyslipidemia [49], hyperglycemia [50], hypertension [51], and insulin resistance [52]. According to the National Cholesterol Education Program (NCEP) criteria, metabolic syndrome is diagnosed when at least three of the following factors are present: central obesity (waist circumference > 102 cm for males and > 89 cm for females, or BMI > 30 kg/m2), elevated triglycerides (TG ≥ 150 mg/dL), low HDL cholesterol (HDL < 40 mg/dL for males or < 50 mg/dL for females), high blood pressure (≥130/85 mmHg), and fasting blood sugar (FBS between 110-125 mg/dl)[53]. Cardiovascular disease (CVD), which is the leading cause of morbidity and mortality worldwide, is closely linked to metabolic risk factors such as diabetes, high LDL-cholesterol, hypertension, and obesity. As a result, considerable efforts are being made to address and manage metabolic syndrome to prevent CVD. This work confirms the great importance of applied science in bakery products for diabetes people [54-77]

Table 3. Effect of ginger rhizome and cinnamon bark powder on some lipid profile of normal and diabetic rats.

Group	Diets	T. cholesterol mg/dl	Triglyceride mg/dl	HDL mg/dl	LDL mg/dl	VLDL mg/dl	T. lipids mg/dl
G1	**Normal control**	116.80 e ±3.18	112.73 e ±4.36	72.67 a ±1.80	21.59 e ±1.56	22.55 e ±0.87	1.350 e ±0.11
G2	**Diabetic control**	194.03 a ±1.66	188.12 a ±2.11	40.30 f ±2.09	116.11 a ±3.43	37.62 a ±0.43	3.35 a ±0.09
G3	**Ginger rhizome 1%**	181.08 b ±6.08	170.48 b ±4.83	45.92 e ±2.05	101.06 b ±5.66	34.09 b ±0.97	3.06 b ±0.04
G4	**Ginger rhizome 2%**	165.35 c ±4.93	160.51 c ±4.94	49.55 d ±2.15	83.70 c ±6.62	32.10 c ±0.99	2.48 c ±0.14
G5	**Cinnamon bark 1%**	165.5 1 c ±5.20	140.57 d ±4.84	55.25 c ±0.85	82.15 c ±4.91	28.11 d ±0.97	2.88 c ±0.12
G6	**Cinnamon bark 2%**	130.58 d ±5.06	120.65 e ±5.21	59.51 b ±1.31	46.99 d ±4.38	24.13 e ±1.04	1.89 d ±0.06
LSD at $p \leq 0.05$		**8.175**	**8.009**	**3.140**	**8.387**	**1.604**	**0.1688**

* Each value was an average of three determination ± standard deviation

* Values followed by the same letter in columns are not significantly different at LSD at $p \leq 0.05$

Conclusion

The findings in this paper suggest that ginger, and cinnamon powder possess significant potential as food or feed ingredients. Their high levels of phenols, flavonoids, antioxidants, and fiber contribute to reducing blood glucose levels in diabetic rats, making them beneficial for human nutrition.

Ethical Approval

Animal Ethic committee approval has been collected and preserved by the author(s)

Disclaimer (Artificial intelligence)

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1.

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