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Data Availability Statement

The data supporting the findings of this study are publicly available and are included within this published article.

AI Usage Declaration

AI was not used during the writing of this article.

ORIGINAL ARTICLE

Preliminary Assessment of Hematopoietic Cell Kinase Gene Expression in Wistar Rats Fed SAMPEA-11 and SAMPEA 20T Diets

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Abstract

Dietary factors play a crucial role in modulating immune responses and inflammatory processes. This study investigates the expression of the hematopoietic cell kinase (HCK) gene in Wistar rats fed exclusively with two novel cowpea cultivars, SAMPEA-11 and SAMPEA 20T, to evaluate their potential immunomodulatory effects. The experiment employed a randomized controlled design with six Wistar rats divided into three groups: SAMPEA-11, SAMPEA 20T, and a control group fed a standard diet. Gene expression analysis was performed using real-time quantitative PCR (qPCR), with GAPDH serving as the reference gene for normalization. The results demonstrated significant upregulation of HCK gene expression in rats fed with SAMPEA-11 and SAMPEA 20T compared to the control group. SAMPEA-11 exhibited the highest expression fold change (38.6394), followed by SAMPEA 20T (3.7542), indicating a strong activation of HCK expression. The $\Delta\Delta Ct$ values further confirmed this trend, showing the greatest upregulation in SAMPEA-11 (−5.272) and a moderate increase in SAMPEA 20T (−1.9085). Statistical analysis revealed a strong inverse correlation between $\Delta\Delta Ct$ and expression fold change ($r = -0.955$, $p = 0.191$), aligning with expected qPCR trends. Also, regression analysis indicated that $\Delta\Delta Ct$ was a strong predictor of expression levels ($R^2 = 0.913$). These findings suggest that the consumption of SAMPEA-11 and SAMPEA 20T influences immune-related gene expression, potentially impacting immune cell signaling and inflammatory responses. The observed variations between the two cowpea cultivars highlight the need for further investigation into their bioactive components and mechanistic pathways underlying HCK gene regulation. This study contributes to the growing body of knowledge on the dietary modulation of immune function and underscores the potential health benefits of SAMPEA-11 and SAMPEA 20T in immune regulation.

Keywords: HCK gene, SAMPEA-11, SAMPEA 20T, Gene expression, Immune response

1. Introduction

Dietary factors have increasingly been recognized as pivotal environmental modifiers of immune cell signaling pathways and inflammatory responses. Recent studies underscore the influence of specific diets on immune modulation and inflammation [1–5].

SAMPEA-11 and SAMPEA 20T are two recently introduced cowpea cultivars in Nigeria [6–11] that have garnered significant attention due to their promising agronomic traits and potential to contribute positively to nutritional health and food security; SAMPEA-11 is known for its resistance to nematodes and aphids, good seed quality, field tolerance to major insect pests, and an average yield of 2.0 tons per hectare, while SAMPEA 20T exhibits resistance to the legume pod borer, early maturity, and a higher yield potential of 2.9 tons per hectare, with both varieties being well-suited for cultivation

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in the Guinea and Sudan Savanna agroecological zones [12].

Inflammation is a crucial biological response that can lead to various pathological conditions when dysregulated [13–15]. Understanding how dietary components like SAMPEA-11 and SAMPEA 20T influence inflammatory markers in animal models can provide valuable insights into their immune modulatory properties and potential health implications.

The HCK gene encodes the hematopoietic cell kinase (HCK), a member of the Src family of non-receptor tyrosine kinases [16–18]. HCK is predominantly expressed in myeloid lineage cells such as monocytes, macrophages, granulocytes, and certain dendritic cell populations [19]. It plays a vital role in intracellular signal transduction pathways that regulate immune cell functions, including allergic reactions, phagocytosis, respiratory burst activity, adhesion, migration, and cytokine production [20–22]. Dysregulated HCK expression can significantly impact inflammatory responses, with its overexpression linked to hyper-reactive immune cells and excessive inflammation [23].

This study examines the effects of exclusive diets of SAMPEA-11 and SAMPEA 20T on HCK gene expression in Wistar (*Rattus norvegicus*) rats, providing insight into their immunomodulatory potential and laying the groundwork for future research on their bioactive components.

2. Methodology

2.1. Experimental design

A randomized controlled design was implemented using six healthy Wistar rats (both sexes), of average weight of 150 g. Health assessments were conducted to exclude rats with pre-existing health conditions. The animals were divided into two treatment groups (SAMPEA-11 and SAMPEA 20T treated groups) and a control group, with two rats in each.

2.2. Ethical considerations

This research adheres to the ARRIVE 2.0 and Helsinki guidelines. And the animals were treated in accordances with the guideline of National Research Council's Guide for the Care and Use of Laboratory Animals. The welfare and humane treatment of the Wistar rats were prioritized, with all procedures conducted in accordance with institutional and regulatory ethical standards and the National Research Council's Guide for the Care and Use of Laboratory Animals guidelines.

2.3. Administration of SAMPEA-11 and SAMPEA 20T diet

The experimental group were administered a strict diet of SAMPEA-11 and SAMPEA 20T *ad libitum* for 6 days, while the control group was maintained on a standard grower mash diet (Vital feeds, Nigeria). The administration of the diet was closely monitored, and the nutritional composition was precisely controlled.

2.4. Samples collection

The Wistar rats were anesthetics humanely using isoflurane and blood samples were collected by jugular puncture on the 6th day in EDTA blood RNA tube and preserved at −20 °C to maintain the integrity of the genetic material as previously described by Hussein et al. [24].

2.5. RNA extraction

RNA was extracted using AccuPrep® Universal RNA Extraction kit (K-3140, K-3141) according to the supplier's instructions. 1 ml of blood were homogenized in a new 1.5 ml tube, and 500 μl of RB buffer was added. The content was centrifuged for 3 min at full speed, and the supernatant was transferred to a new 1.5 ml tube. Subsequently, 200 μl of absolute ethanol was added and mixed using a pipette. The misture was transferred to a binding column in a 2 ml collection tube, closed, and centrifuged at 14,000 rpm for 20 s. The flow-through was discarded, and 700 μl of RWA1 buffer was added, followed by centrifugation at 14,000 rpm for 20 s. This step was repeated with 500 μl of RWA2 buffer, and the sample was centrifuged for 1 min to remove ethanol.

2.6. cDNA synthesis

The extracted RNA was mixed with primers in a sterile tube, incubated at 70 °C for 5 min, and then placed on ice. The incubated mixture was transferred into an AccuPower® RT premix tube and filled with deionized, distilled water treated with diethyl pyrocarbonate (DEPC). The vacuum-dried blue pellets were dissolved by vortexing and brief spins. cDNA synthesis was performed at 42 °C for 60 min, and the RTase was inactivated at 94 °C for 5 min. From the cDNA synthesis tubes, 5 μl were pipetted to perform PCR.

2.7. Primers

Wistar rat's HCK was targeted in this study which was compared with glyceraldehyde-3-phosphate dehydrogenase as reference.

HCK gene:

Forward: 5'-CACTAGAGCATGGGTACC-3'.

Reverse: 5'-CAGCTATAGATTGAATTC-3'.

Glyceraldehyde-3-phosphate dehydrogenase (GAPDH) gene:

Forward: 5′-ATGGTGAAGGTCGGAGTC-3'.

Reverse: 5′-CATGGACTGTGGTGGTCATGAG-3'.

These were primer extensively used for the investigations of HCK and GAPDH genes [25–28].

2.8. Real-time PCR conditions

Real-time PCR was performed using AccuPower® 2X GreenStar™ qPCR MasterMix and an CFX96 Real-Time PCR Detection System (Bio-Rad). Fluorescence produced during each cycle was measured to quantify the target DNA. TaqMan primers were used for the PCR, as described by Yang et al. [29] with GAPDH serving as the reference gene due to its consistent expression levels across most cells and tissues.

The reagents were thawed before use. AccuPower® 2X GreenStar™ qPCR MasterMix, template DNA, and primers were added to the real-time PCR tubes as per the manufacturer's instructions. The tubes were sealed with optical adhesive film or optically clear cap strips, thoroughly mixed by pipetting up and down several times, and then centrifuged at 3000 rpm for 2 min. The tubes were loaded onto the real-time PCR instrument, and the reaction was performed under the following conditions:

Pre-denaturation: 95 °C for ~15 min in the first cycle.

Denaturation: 95 °C for 15 s for 45 cycles.

Annealing/extension: 60 °C for 30 s.

2.9. Statistical analysis

Gene expression was quantified using the $2^{-\Delta\Delta Ct}$ method. Pearson correlations and regression analyses were conducted with SPSS v27. A p-value <0.05 was considered statistically significant.

3. Results and discussion

3.1. Expression levels of HCK gene

3.2. Expression levels and fold changes

Table 1 and Fig. 1 presents the expression levels of the HCK gene in Wistar rats fed with SAMPEA-11 and SAMPEA 20T diets compared to a control group, using GAPDH as a reference gene for normalization. Gene expression was quantified using cycle threshold (Ct) values, with differences analyzed through ΔCt, ΔΔCt, and expression fold changes.

The results show significant differences in HCK gene expression across the groups (Table 1). The ΔCt values, which represent the difference between the Ct values of HCK and GAPDH, reveal that SAMPEA-11 has the lowest ΔCt (−3.795), followed by SAMPEA 20T (−0.4315), while the control has the highest value (1.477). This suggests that the target

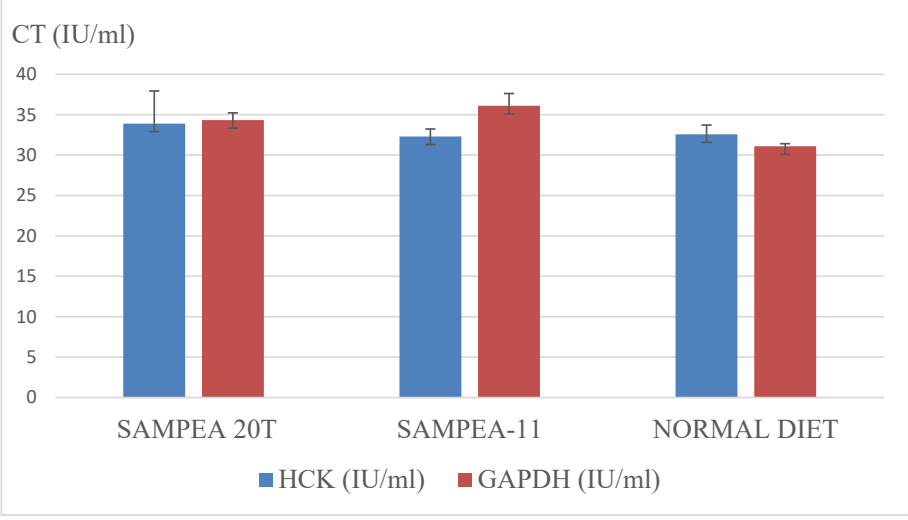

Fig. 1. Cycle threshold of HCK and GAPDH expressed in Abino rats treated with SAMPEA-11 and SAMPEA 20T.

Table 1. Gene expression of target HCK and GAPDH reference genes in Wistar rats treated with SAMPEA 20T and SAMPEA-11.

	HCK (IU/ml)	GAPDH (IU/ml)	ΔCT	ΔΔCT	Expression Fold
SAMPEA 20T	33.8965 ± 4.0329	34.3280 ± 0.8952	−0.4315	−1.9085	3.7542
SAMPEA-11	32.2988 ± 0.9275	36.0938 ± 1.519	−3.795	−5.272	38.6394
CONTROL	32.5705 ± 1.1434	31.0935 ± 0.3146	1.477	0	1

$p < 0.05$, $\chi^2 = 0.000$ (Kappa measure of agreement).

Table 2. Correlations.

		HCK	GAPDH	ΔCT	ΔΔCT	Fold
HCK	Pearson correlation	1				
	Sig. (2-tailed)					
GAPDH	Pearson correlation	0.008	1			
	Sig. (2-tailed)	0.995				
ΔCT	Pearson correlation	0.312	−0.947	1		
	Sig. (2-tailed)	0.798	0.208			
ΔΔCT	Pearson correlation	0.312	−0.947	1.000[a]	1	
	Sig. (2-tailed)	0.798	0.208	0.000		
Fold	Pearson correlation	−0.579	0.81	−0.955	−0.955	1
	Sig. (2-tailed)	0.607	0.398	0.191	0.191	
	N	3	3	3	3	3

[a] Correlation is significant at the 0.01 level (2-tailed).

Table 3. Model analysis.

	ANOVA	Regression
R		0.955
R square		0.913
Adjusted R square		0.825
F	10.458	
Sig.	0.191[a]	

[a] Regression model is not statistically significant.

gene is more actively expressed in SAMPEA-11 compared to both SAMPEA 20T and the control. The ΔΔCt values confirm this trend, with SAMPEA-11 showing the greatest upregulation (−5.272), while SAMPEA 20T also exhibits upregulation (−1.9085), though to a lesser extent. Consequently, the expression fold change is highest in SAMPEA-11 (38.6394), followed by SAMPEA 20T (3.7542), with the control set as the baseline (1.00).

The expression fold change results (Table 1) indicate that HCK gene expression is upregulated nearly 3.8-fold in the SAMPEA 20T-treated rats compared to the control. In contrast, SAMPEA-11 shows a dramatic 39.19-fold increase, implying a much stronger activation of the gene. The relatively high standard deviation in HCK values for SAMPEA 20T (±4.0329) suggests variability in expression levels within this group, while the smaller standard deviation in SAMPEA-11 (±0.9275) implies more consistent expression levels. The control group provides the baseline for comparison, with a stable GAPDH expression (±0.3146), confirming its reliability as a reference gene.

3.3. Statistical analysis and correlation

A strong inverse relationship between ΔΔCt and expression fold change was observed ($r = -0.955$, $p = 0.191$) (Tables 2 and 3), aligning with expected qPCR trends where lower ΔΔCt values correspond to higher gene expression. GAPDH showed a significant negative correlation with ΔCt ($r = -0.947$), supporting its stability as a reference gene. Regression analysis suggests that ΔΔCt is a strong predictor of expression levels ($R^2 = 0.913$), although the significance value ($p = 0.191$) suggests a need for further validation with larger sample sizes.

Descriptive statistics indicate that HCK levels vary minimally across groups (mean = 32.92, SD = 0.85), while GAPDH exhibits higher variation (mean = 33.83, SD = 2.54). The mean ΔCt (−0.9165) and ΔΔCt (−2.3935) values reflect the overall trend of HCK upregulation in both SAMPEA varieties compared to the control. The chi-square test ($\chi 2 = 0.157$) confirms that observed expression values do not significantly deviate from expected values, supporting the reliability of the data.

3.4. Biological implications

The upregulation of HCK in both SAMPEA 20T and SAMPEA-11 treated rats suggests enhanced immune activation. The significant increase in HCK expression, particularly in the SAMPEA-11 group, suggest activation of immune cells, potentially enhancing pathogen defense. However, the dramatic

upregulation in SAMPEA-11 raises concerns about possible immune system overactivation, which could lead to excessive inflammation or autoimmune reactions. Conversely, the more moderate upregulation in SAMPEA 20T suggests a balanced enhancement of immune function, which might be beneficial without significantly disrupting immune homeostasis.

Research on other cowpea varieties, reported significant impacts on immune pathways by primary component of their diets. Ojwang et al. [30] demonstrated that cowpea polyphenolic extracts possess anti-inflammatory properties, down-regulating proinflammatory cytokines (IL-8, TNF-α, VCAM-1) and modulating microRNA-126 in LPS-stimulated cells. This aligns with the concept that moderate immune activation, as seen with SAMPEA 20T, could be beneficial by enhancing pathogen defense while mitigating excessive inflammation. Furthermore, Adjei-Fremah et al. [31] highlighted the influence of cowpea phenolic extract (CPE) on the *Wnt* signaling pathway, which is critical in inflammation and immunity. Their findings showed that CPE modulated *Wnt* signaling genes and impacted mononuclear cell populations, suggesting a direct effect on immune homeostasis. This explains the observed immune activation in our study, as the *Wnt* pathway is known to interact with HCK signaling [32]. In another study, Adjei-Fremah et al. [33] investigated the effects of CPE on galectin gene expression, their result revealing that CPE decreased pro-inflammatory gene expression (TNFA and COX2) and increased anti-inflammatory gene expression (IL10 and IL4), further supporting the immunomodulatory role of cowpea. These findings suggest that cowpea components may fine-tune immune responses, potentially explaining the differential HCK upregulation observed between SAMPEA 20T and SAMPEA-11.

Furthermore, Gomes et al. [34] demonstrated that cowpea extracts influence gut microbiota and intestinal morphology, which are critical for immune function. A healthy gut microbiome is essential for maintaining immune homeostasis, and alterations can significantly impact systemic immune responses [35]. They observed reduction in *Clostridium* and *E. coli* abundance, along with improved intestinal morphology, suggests that cowpea components in Cowpea diets can contribute to immune modulation by influencing gut health.

Adjei-Fremah et al. [36] further corroborated these findings by showing that CPE impacts global gene expression in bovine blood, affecting Toll-like receptor and inflammation response pathways. This suggests that cowpea components can induce a wide range of immunomodulatory effects, potentially explaining the complex HCK expression patterns observed in our study.

The observed HCK upregulation may reflect a complex interplay of immunomodulatory effects mediated by SAMPEA-11 and SAMPEA 20T. Future studies should focus on understanding the specific mechanisms through which cowpea components influence HCK expression and immune responses, and also evaluate the long-term effects of these diets on immune health.

4. Conclusions

This study demonstrates that diets of SAMPEA-11 and SAMPEA 20T modulate HCK gene expression in Wistar rats, with SAMPEA-11 exerting a more pronounced effect. The gene expression analysis reveals significant upregulation of the HCK gene in Wistar rats treated with SAMPEA-11 and SAMPEA 20T, with SAMPEA-11 showing a more substantial effect. These findings suggest that the genetically modified cowpea cultivars can markedly influence immune responses. While this may enhance immune response capabilities, the potential for adverse effects due to overactivation of immune pathways warrants further study. Understanding these effects is crucial for evaluating the safety and efficacy of genetically modified crops in promoting health and combating diseases.

Author's contribution statement

Conceptualization, Stephen Dio Titus, Salisu Muhammed, Priscila Benjamin; methodology, Stephen Dio Titus, Salisu Muhammed, Priscila Benjamin; validation, Stephen Dio Titus Salisu Muhammed, Priscila Benjamin; formal analysis, Stephen Dio Titus; investigation, Stephen Dio Titus, Salisu Muhammed, Priscila Benjamin; resources, All authors; data curation, Stephen Dio Titus, Achilus Francis, Christian Nelson; writing—original draft preparation, Stephen Dio Titus, Kennedy Banja Samuel, Salisu Muhammed, Priscila Benjamin; writing— review and editing, Stephen Dio Titus, Samuel Gadzama Ishaya; visualization, Stephen Dio Titus, Achilus Francis; supervision, Bala M. Shuaibu.

Ethical statement

This research adheres to the ARRIVE 2.0 and Helsinki guidelines. And the animals were treated in accordances with the guideline of National Research Council's Guide for the Care and Use of Laboratory Animals.

Use of AI

AI was not used during the writing of this article.

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Conflict of interest

The authors declare that there is no conflict of interest.

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