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Assessment of the Impact of Consuming Enriched Flours with Anti-Inflammatory and Antioxidant Properties among People with Sickle Cell Anemia in Togo

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Abstract

Background: Sickle cell disease remains a hereditary condition for which there is no widely accessible curative treatment in sub-Saharan Africa. Growing interest in nutrition as a means of reducing morbidity has led to the development of adapted local nutritional alternatives. **The Objective** of this study was to evaluate the impact of consuming an enriched flour with anti-inflammatory and antioxidant properties among undernourished patients with sickle cell disease. **Methods:** This was a prospective interventional study conducted from July 1, 2024, to July 31, 2025, at the National Center for Sickle Cell Disease Reference and Follow-up in Togo. Of the 233 patients recruited, 154 were identified as undernourished; 75 of them were enrolled in the intervention phase, and 57 completed the 6-month follow-up period while consuming the enriched flour porridge. **Results:** The prevalence of malnutrition was 66.1%. After 6 months of intervention, vaso-occlusive crises decreased by 86% (from 1.46 to 0.20 episodes/month, $p < 0.001$), and quantitative CRP levels decreased by 64%. Paired analysis (McNemar's test) showed a significant improvement in CRP levels (OR = 7.33; 95% CI 2.20 - 24.50; $p < 0.001$) and albumin levels (OR = 7.00; 95% CI 1.59 - 30.80; $p = 0.004$), with no significant paired change for alpha-1-glycoprotein (OR = 1.08; 95% CI 0.51 - 2.29; $p = 1.000$), alpha-2-glycoprotein (OR = 0.22; 95% CI 0.05 - 1.03; $p = 0.065$), or beta-2-glycoprotein

(OR = 2.40; 95% CI 0.85 - 6.81; p = 0.143). The proportion of patients with normal muscle mass increased by 21%. **Conclusion:** Enriched flour made from local products showed a positive and clinically significant impact on nutritional status, inflammatory status, the incidence of vaso-occlusive crises, and quality of life in undernourished patients with sickle cell disease, although this effect was not consistent across the inflammatory markers studied. Systematic integration of nutritional management into the overall care of sickle cell patients is recommended.

Keywords

Sickle Cell Disease, Undernutrition, Enriched Flour, Anti-Inflammatory, Antioxidant, Vaso-Occlusive Crisis, Togo

1. Introduction

Sickle cell disease is an autosomal recessive hereditary hemoglobinopathy resulting from a point mutation in the beta-globin gene (chromosome 11), leading to the substitution of glutamic acid with valine at position 6 of the beta chain. This abnormality leads to the synthesis of a mutant hemoglobin (HbS) that polymerizes under hypoxic conditions, causing erythrocytes to become sickle-shaped [1] [2]. It is the most common monogenic genetic disorder worldwide, with a pooled prevalence of 1.43% (95% CI: 1.08% - 1.88%) in Africa, where approximately 80% of global cases are reported [3]. In sub-Saharan Africa, it constitutes a major public health problem, exacerbated by insufficient diagnostic, therapeutic, and preventive resources [4].

From a pathophysiological perspective, sickle cell disease is characterized by four interconnected processes: HbS polymerization, blood rheology disorders and vascular occlusion, intravascular hemolysis, and the activation of chronic sterile inflammation [5]. This inflammation, mediated by the TLR-4 and inflammasome pathways, perpetuates a vicious cycle of ischemia-reperfusion and endothelial damage, which explains the frequency and severity of vaso-occlusive crises (VOCs) [5] [6]. CRP, alpha-globulins, and gamma-globulins are markers of acute and chronic inflammation that are commonly elevated in these patients [7].

Patients with sickle cell disease have increased nutritional needs due to chronic hypermetabolism (persistent hemolytic anemia), recurrent infections, and inflammation. These factors contribute to widespread undernutrition, the consequences of which include worsening anemia, increased susceptibility to infection, and a higher frequency of complications [8]. Recent systematic reviews have highlighted a high prevalence of stunted growth and malnutrition among African patients with sickle cell disease, while emphasizing the glaring lack of interventional studies in this area [9] [10].

Given this situation, the development of functional foods based on local resources is of major interest in terms of accessibility and cultural adaptation. Tur-

meric (*Curcuma longa*), moringa (*Moringa oleifera*), baobab (*Adansonia digitata*), soy (*Glycin max*), and sesame (*Sesamun indicum*) are recognized for their well-documented anti-inflammatory and antioxidant properties [11]-[14]. A composite flour formulation combining these ingredients was developed with funding from FAO-Togo. Its design and production were made possible through a tripartite collaboration between the Laboratory of Biomedical, Agri-Food, and Environmental Health Sciences (LaSBASE), the Togolese Institute for Agronomic Research (ITRA), and the National Reference and Monitoring Center for Sickle Cell Disease (CNRSD) [15]. This flour could offer a multimodal nutritional approach capable of modulating the oxidative stress and chronic inflammation that characterize sickle cell disease.

The objective of this study is to prospectively evaluate the impact of an enriched flour with anti-inflammatory and antioxidant effects, administered as porridge to malnourished patients with sickle cell disease being treated at the CNRSD in Togo.

2. Material and Methods

2.1. Study Type, Setting, and Duration

This was a single-arm, prospective, interventional study conducted from July 1, 2024, to July 31, 2025 (13 months) at the CNRSD in Togo, located in Lomé. This facility served as the site for recruitment, anthropometric measurements, bioimpedance analysis, and follow-up of malnourished patients with sickle cell disease who came to pick up their flour kits. The Togolese Institute of Agricultural Research (ITRA) produced the batches of flour needed for ongoing distribution. The National Institute of Hygiene and Public Health (INH) served as the site for conducting biochemical tests.

2.2. Data Collection Equipment

The weight of children and adults with sickle cell disease was measured using an M321600 electronic scale (ADE Germany, China) with a digital display capable of weighing up to 250 kg in 0.1-kg increments. Height was measured using a Shorr height rod with 0.1-cm increments. Arm circumference was measured using a Shakir tape-. Harpenden calipers were used for triceps skinfold thickness, and the Z-Metrix (Bioparhom, France) was used for body composition analysis. The Cobas c311 and e411 biochemical and immunochemical analyzers (Roche Diagnostics, Switzerland) were used for the various biochemical assays. The Minicap Flex Piercing (SEBIA, France) was used to perform protein electrophoresis. Data were collected during face-to-face interviews using a pre-established questionnaire. The questionnaire was pre-tested, including reproducibility exercises for the use of the Harpenden caliper. At the end of each day, the completed forms were reviewed and corrected as necessary to ensure the completeness and accuracy of the data.

2.3. Selection and Inclusion of Volunteers

2.3.1. Study Population

Based on the 10% attendance rate of individuals with sickle cell disease seen at the CNRSD representing 343 subjects expected for the assessment of protein-energy nutritional status a study population size consistent with the prevalence of sickle cell disease was determined. Taking into account the estimated prevalence of major sickle cell disease of between 3% and 5% [16] and using Cochran's formula, a sample size of 73 patients was determined.

2.3.2. Inclusion Criteria

The study population consisted of HbSS and HbSC sickle cell patients. The inclusion criteria were: a confirmed diagnosis of sickle cell disease by hemoglobin electrophoresis; the presence of malnutrition diagnosed according to at least one validated WHO criterion, primarily through anthropometric measurements (weight, height, BMI, upper arm circumference, and triceps skinfold thickness) and secondarily through body composition assessment and measurement of certain biochemical parameters. Age over 5 years, and informed consent from the patient or their legal guardian.

2.3.3. Exclusion Criteria

Patients with severe uncontrolled comorbidities, those on immunosuppressive therapy, or those who had received a transfusion within the 3 months prior to enrollment were excluded.

2.3.4. Follow-Up Method

Selected patients with sickle cell disease underwent assessment of sociodemographic information, dietary habits, and anthropometric measurements (weight, height, BMI, upper arm circumference, and triceps skinfold thickness) to diagnose malnutrition. Once consent was obtained for a 6-month follow-up, a blood sample was collected and body composition was measured using bioelectrical impedance analysis for each subject at the beginning and end of the 6-month follow-up period. Kits containing 100 g of enriched flour with anti-inflammatory and antioxidant properties, produced by [15], were provided at a rate of 2 kits per day for adolescents and children under 18 years of age and 3 kits per day for adults over 19 years of age during the 6-month follow-up period. Biochemical testing methods were used to assess malnutrition and inflammatory processes.

2.3.5. Vaso-Occlusive Crises (VOCs)

Vaso-occlusive crises (VOC) were defined as any painful episode of sufficient intensity to require analgesic treatment and/or a medical consultation or hospitalization, lasting at least two hours, with no other identifiable cause [17]. The baseline VOC rate (prior to intervention) was determined through review of the medical records of participants followed at the CNRSD, as well as through structured interviews conducted at enrollment, during which patients reported the number of VOC episodes occurring in the six months preceding their inclusion. Following

enrollment, participants were monitored over a six-month follow-up period through scheduled visits (T1 to T5) for flour stock renewal and verification of any use of transfusion or hydroxyurea, supplemented by regular telephone contacts between visits and a follow-up booklet provided to each patient. Any VOC episode occurring during the follow-up period, including those managed outside the study center, was systematically recorded through these various means.

2.4. Assessment of Nutritional Status

2.4.1. Anthropometric Measurements

Measurements were performed according to WHO procedures [18]. Malnutrition was assessed using a three-tier classification (severe, moderate, normal) based on five indicators: weight-for-length z-score (12 - 59 months), height-for-age z-score (5 - 18 years), body mass index (BMI) (≥ 19 years), upper arm circumference (UAC), and triceps skinfold thickness (TSFT). The TSC thresholds were based on WHO growth charts for children under 5 years of age, the tables by Soylu *et al.* (2021) for 6 - 18-year-olds [19], and the reference values from Hasselmann & Alix (2003) for adults aged 19 and older, defining depletion of fat reserves as a value below 50% of the mean reference value for the respective sex (*i.e.*, <6 mm in men and <11.5 mm in women) [20] [21]. A patient was classified as malnourished if they exhibited severe or moderate malnutrition on at least one indicator.

2.4.2. Body Composition Measurements: Bioimpedance Analysis

Impedance measurement is a method of measuring resistance to the flow of an electric current. This test relies on the electrical properties of biological tissue and involves passing a harmless, low-intensity electric current (approximately 70 mA) through the body via electrodes in contact with the skin, and measuring its conduction within the body. The impedance measurement was performed using electrodes placed precisely on the limbs, with the subject standing with legs slightly apart. Electrode placement: four electrodes labeled 1, 2, 5, and 6 are placed on the skin. Electrodes 1 and 2 (higher up) are placed on the hand, and electrodes 5 and 6 (lower down) are placed on the ankle. Formulas are then used to convert the impedance, which measures body water into an estimate of the fat mass. The Metabolic Activity Index (MAI) indicates healthy ion channels, the ability to restore osmotic pressure, and proper transfer of ions and proteins. MAI < 4.63 (abnormal metabolic activity) MAI 4.63 - 7.63 (reference range).

Muscle Mass (MM) or Muscle Mass Index (MMI) measures the total weight of the cells that make up the muscles and is a good indicator of lean body mass. Muscle Mass Index (MMI):

M < 7.0 and F < 5.7

Non-fat mass represents lean body mass (LBM), which accounts for visceral protein mass, intracellular and extracellular water, and bone mass. It includes muscles, bones, organs, water, and blood, and is used to assess malnutrition in obese individuals. Non-fat mass index: M < 17, F < 15 kg/m^2.

Fat Mass (FM) or Fat Mass Index (FMI) is the amount of fat in the body; it

is a better indicator of body composition than BMI, since BMI does not distinguish between muscle mass and fat mass. A decrease in FM is the best indicator of weight loss.

2.4.3. Evaluation Using Biochemical Measures

The following tests were performed on the blood samples collected, taking into account the standard reference values [22] [23].

- Spectrophotometry: albumin, calcium, magnesium, phosphorus,
- Particle-based immuno-turbidimetry: CRP and ferritin;
- Indirect potentiometric ISE: sodium, potassium, and chloride;
- Capillary technique using Minicap Flex Piercing: protein electrophoresis. The relevant fractions analyzed were Alpha 1 and Alpha 2 for monitoring the inflammatory status.

1) Albumin

Principle: At a pH of 4.1, albumin is sufficiently cationic to combine with bromocresol green (BCG) in the form of an anion to form a blue-green complex [24]. The intensity of the blue-green color developed is directly proportional to the albumin concentration and is measured by photometry. Wavelengths (sec/primary) 505/570 nm.

Reference range: Adults 35 - 52 g/L (532 - 790 µmol/L).

Interpretation: Moderate malnutrition 30 - 35 g/L, Severe malnutrition 25 - 30 g/L.

2) Calcium

Principle: Calcium ions react with 5-nitro-5'-methyl-BAPTA (NMBAPTA) in an alkaline medium to form a complex. Subsequently, this complex reacts in the presence of EDTA. The intensity of the color developed by the complex is directly proportional to the calcium concentration and is measured by photometry. Wavelengths (absorbance/reference) 376/340 nm.

Reference range depend on age.

0 - 10 days 76 - 104 mg/L

10 days - 2 years 90 - 110 mg/L

2 - 12 years 88 - 108 mg/L

12 - 18 years 84 - 102 mg/L

18 - 60 years 86 - 100 mg/L

60 - 90 years 88 - 102 mg/L

>90 years 82 - 96 mg/L

Interpretation: Hypocalcemia below reference values

Hypercalcemia above reference values

3) Magnesium

Principle: Magnesium ions form a purple complex in an alkaline medium with xylidyl blue (diazonium salt). Magnesium concentration is measured photometrically by the decrease in the absorbance of xylidyl blue [25]. Wavelength (sec/princ) 505/600 nm.

Reference range depend on age.

5 months - 6 years 15 - 22 mg/L

6 - 12 years 17 - 23 mg/L

12 - 20 years 17 - 21 mg/L

20 - 60 years 17 - 22 mg/L

60 - 90 years 1 - 24 mg/L

>90 years 17 - 23 mg/L

Interpretation: Hypomagnesemia below reference values

Hypermagnesemia above reference values

4) Phosphorus

Principle: In the presence of sulfuric acid, inorganic phosphate reacts with ammonium molybdate to form an ammonium phosphomolybdate complex with the formula $(NH_4)_3[PO_4(MoO_3)_{12}]$. The concentration of phosphomolybdate formed is directly proportional to the concentration of inorganic phosphate and is measured by UV photometry [26]. Wavelength (sec/princ) 700/340 nm.

Reference range depend on age.

Infants: 50 - 70 mg/L

Children: 32 - 57 mg/L

Adults: 25 - 45 mg/L

Interpretation: Hypophosphatemia below reference values

Hyperphosphatemia above reference values

5) C-Reactive Protein (CRP)

Principle: Immunoturbidimetric assay using on latex particles. Human CRP binds on latex particles coated with anti-CRP monoclonal antibodies. The agglomerates of particle are measured by turbidimetry [27] [28]. Wavelength (sec/princ): 800/570 nm.

Reference range for adults: <6 mg/L (<57.12 nmol/L)

Interpretation: Acute inflammation, CRP > 6 mg/L

6) Ferritin

Principle: Immunoturbidimetric assay using latex particles. Human ferritin binds to latex particles coated with anti-ferritin antibodies. The precipitate is measured by turbidimetry at 570/800 nm [29].

Reference rang

Men (20 to 60 years): 30 - 400 µg/L (67 - 899 pmol/L, 30 - 400 ng/mL)

Women (17 to 60 years): 15 - 150 µg/L (34 - 337 pmol/L, 15 - 150 ng/mL)

Interpretation: Hypoferritinemia below reference values

Hyperferritinemia above reference values

7) Sodium Na^+, Potassium K^+, Chloride Cl^-

Principle: Ion-selective electrode, using automatically diluted serum/plasma or urine samples. The sodium, potassium, and chloride electrodes are based on ion-exchange systems [30]-[33].

Calculation: The equation below is used for calculating sample and/or quality control (QC) results:

$$Cs = C_{IS} \times \log\left(\frac{\mathrm{ES} - \mathrm{EIS}}{\pm \mathrm{S}}\right)$$

where:

CS: Concentration of the ion in the sample

CIS: Concentration of the ion in the ISE (Internal Standard Electrode) solution

ES: Electromotive Force (EMF) of the sample

EIS: EMF of the Internal Standard Electrode (ISE) solution

S: Slope of electrode

Log: decimal logarithm

The complete measurement system for a specific ion consists of the ISE, a reference electrode, and electronic circuits that measure and process the EMF to determine the concentration of the measured ion (K^+, Cl^-, Na^+).

Reference rang

- Sodium

Normal 136 - 145 mmol/L

Interpretation: Hyponatremia below reference values

Hypernatremia above reference values

- Potassium

Normal 136 - 145 mmol/L

Interpretation: Hypokalemia below reference values

Hyperkalemia above reference values

- Chloride

Adult 98 - 107 mmol/L

>90 years 98 - 111 mmol/L

Interpretation: Hypochloremia below reference values

Hyperchloremia above reference values

2.4.4. Protein Electrophoresis

The basic principles of separation were:

- Electric field: Proteins migrate through a capillary filled with electrolyte under the influence of a high voltage.
- Electrophoretic mobility: The migration rate depends on the charge and size of each protein.
- Electroosmotic Flow (EOF): EOF, a fluid flow caused by charges on the capillary wall, accelerates or decelerates the molecules, enabling the detection of all fractions.
- Detection: A UV detector at the capillary outlet measures the absorbance of the separated proteins, generating an electropherogram.

The presence of an inflammatory state by protein electrophoresis was assessed as follows:

- Moderate inflammatory syndrome: alpha-1 > 4 g/L and < 6 g/L and/or alpha-2 > 9 g/L and < 12 g/L
- Severe inflammatory syndrome: alpha-1 > 6 g/L and/or alpha-2 > 12 g/L
- Inflammatory state due to C3 hypercomplementemia: 5 g/L < Beta2 < 8 g/L
- Prevalence of hypoalbuminemia: Moderate (albumin < 35 g/L and >30 g/L), Severe (albumin < 30 g/L),

- hypergammaglobulinemia: moderate (gamma > 15 g/L < 20 g/L), severe (>20 g/L).

2.5. Fortified Flour (Composition and Administration)

The enriched flour was formulated using six local ingredients, selected for their complementary nutritional, anti-inflammatory, and antioxidant properties, which have been documented in the scientific literature. The detailed composition is presented in Table 1.

Table 1. Composition of 100 g of enriched flour and profile of active compounds [15].

Ingredients	Active Compounds and Nutritional Objectives
Yellow corn (*Zea mays*) 48.8 g	Complex carbohydrates, phenolic compounds, carotenoids, minerals [34] [35].
Soybean (*Glycine max*) 19.5 g	Complete proteins, phytoestrogens (genistein, daidzein, glycitein), minerals [36] [37].
Baobab (*Adansonia digitata*) 22.2 g	Vitamin C (200 - 500 mg/100g), flavonoids, proanthocyanidins, beta-carotene, minerals [38] [39].
Moringa (*Moringa oleifera)* 7 g	Vitamins A and E, carotenoids, flavonoids, glucosinolates, isothiocyanates, minerals [40] [41].
Turmeric (*Curcuma longa*) 1.02 g	Curcumin (anti-inflammatory via NF-κB), curcuminoids, minerals [42] [43].
Sesame (*Sesamum indicum*) 1.48 g	Unsaturated fats, sesamine, sesamolin, antioxidant lignans, minerals [44] [45].

2.6. Statistical Analyses

The data were entered and analyzed using appropriate statistical software. Quantitative variables are expressed as mean ± standard deviation ($\bar{x} \pm$ SD). Before-and-after comparisons were performed using the Wilcoxon test for quantitative variables and the McNemar test for paired categorical variables. Mated odds ratios (OR) were calculated as the ratio of discordant pairs (b/c), with 95% confidence intervals (95% CI) obtained using the Wald method on a logarithmic scale. The rate of change (RC) was defined as $(\bar{y} - \bar{x})/\bar{x}$. The threshold for statistical significance was set at $p < 0.05$.

3. Results

3.1. Characteristics of the Study Population

A total of 233 patients with sickle cell disease participated in the study, including 119 (51.07%) males and 114 (48.93%) females, for a sex ratio of 1.04 males to 1 female.

Among the 233 participants, the prevalence of malnutrition based on at least one diagnostic criterion was 66.09% (n = 154). Of the 154 malnourished patients, 75 (48.7%) agreed to undergo laboratory testing and body composition analysis using bioimpedance analysis. Of these, 57 (76%) attended the 6-month follow-up appointment, while 18 participants were lost to follow-up. Figure 1 shows the flowchart of participants.

The distribution of the 57 and 75 patients by age group and genotype is presented in Table 2.

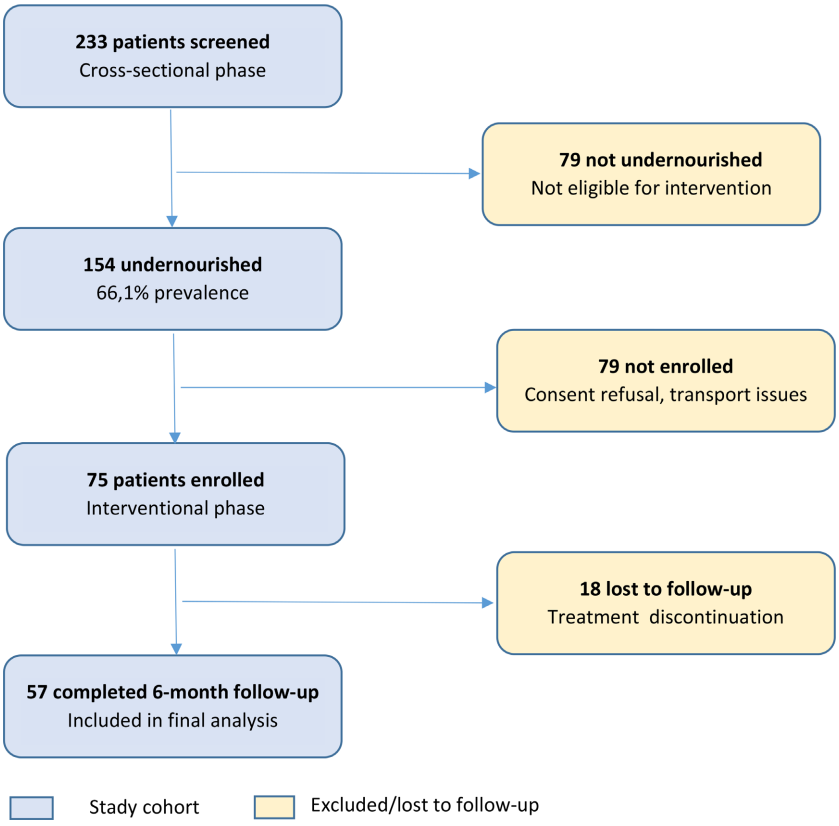

Figure 1. Participant flowchart.

Table 2. Distribution of patients by age group, genotype, and sex (75 = enrollment; 57 = 6-month follow-up).

Age Groups	Group of 75				Group of 57			
	Male		Female		Men		Female	
	SS n (%)	SC n (%)	SS n (%)	SC n (%)	SS n (%)	SC n (%)	SS n (%)	SC n (%)
6 to 9 years	2 (2.7)	0 (0.0)	3 (4.0)	0 (0.0)	2 (3.5)	0 (0.0)	2 (3.5)	0 (0.0)
Ages 10 - 14	10 (13.3)	3 (4.0)	9 (12.0)	1 (1.3)	7 (12.3)	5 (8.8)	8 (14.0)	0 (0.0)
Ages 15 - 18	4 (5.3)	1 (1.3)	4 (5.3)	1 (1.3)	4 (7.0)	1 (1.8)	1 (1.8)	1 (1.8)
19 and over	19 (25.3)	6 (8.0)	10 (13.3)	2 (2.7)	12 (21.1)	6 (10.5)	7 (12.3)	1 (1.8)
Total	**35 (46.7)**	**10 (13.3)**	**26 (34.6)**	**4 (5.3)**	**25 (43.9)**	**12 (21.1)**	**18 (31.6)**	**2 (3.5)**

3.2. Biochemical and Inflammatory Parameters at Enrollment

Initial biochemical evaluation of the 75 undernourished patients revealed significant abnormalities:

- Electrolyte imbalances: hyperkalemia in 28%, hyponatremia in 32%, hypochloremia in 29%, hypocalcemia in 9.33%, and hypercalcemia in 8%.
- Acute inflammatory syndrome: 46.67% of patients had a CRP > 6 mg/L, 42.66% had elevated alpha-1 and/or alpha-2 glycoproteins, and 68% had hypercomplementemia.
- Chronic inflammatory syndrome: 72% had hypergammaglobulinemia.

- Bioelectrical impedance analysis: At least one tissue, fluid, or metabolic index was abnormal in 96% of undernourished patients.

3.3. Impact on the Inflammatory State

After 6 months of consuming the enriched flour, a significant improvement was observed in all inflammatory markers among the 57 subjects who returned for the final follow-up. Table 3 presents the results, showing the decrease in the proportion of subjects exhibiting an inflammatory (PEI) state after consuming the flour.

3.4. Impact on Biochemical and Anthropometric Parameters

A total of 13,180 kits were used out of the 25,200 planned for the initial cohort of 75 patients over a 6-month period, representing an overall utilization rate of 52.30%. Table 4 presents the comparative results before and after the intervention

Table 3. Impact of consuming enriched flour on inflammatory markers.

Parameter	Before n (%)	After n (%)	a	b	c	d	McNemar's p-value	Paired OR (95% CI)
CRP (>6 mg/L)	28 (49.12%)	9 (15.79%)	6	22	3	26	0.00016* (0.00032†)	7.33 (2.20 - 24.50)
Alpha-1 glycoprotein (>4 g/L)	25 (43.86%)	24 (42.11%)	11	14	13	19	1.000* (1.000†)	1.08 (0.51 - 2.29)
Alpha-2 glycoprotein (>9 g/L)	4 (7.02%)	11 (19.31%)	2	2	9	44	0.065* (0.070†)	0.22 (0.05 - 1.03)
Albumin (<35 g/L)	14 (24.56%)	2 (3.51%)	0	14	2	41	0.00418* (0.006†)	7.00 (1.59 - 30.80)
Beta-2 glycoprotein (5 - 8 g/L)	39 (68.42%)	32 (56.14%)	27	12	5	13	0.143* (0.146†)	2.40 (0.85 - 6.81)

PEI: pathological inflammatory element. a, b, c, d: cells in the 2 × 2 paired contingency table (before × after). The paired OR is calculated as b/c (discordant pairs), with a 95% CI obtained using the Wald method on a logarithmic scale. *Exact McNemar's test. †McNemar's χ^2 test with continuity correction. a: PEI → PEI, b: PEI → Normal, c: Normal → PEI, d: Normal → Normal

Table 4. Impact of enriched flour on biochemical and anthropometric parameters.

Parameters	Before ($\bar{X}$ ± ET)	After ($\bar{Y}$ ± SE)	Difference ($\bar{Y}$ − $\bar{X}$)	Rate of change
Weight (kg)	39.73 (±1.84)	40.84 (±1.75)	+1.11	+3%
Upper arm circumference (mm)	197.05 (±7.68)	205.48 (±6.12)	+8.43	+4%
MPCT (mm)	6.63 (±0.26)	7.40 (±0.28)	+0.77	+12%
Vaso-occlusive crises/month	1.46 (±0.07)	0.20 (±0.05)	−1.26	−86%
Serum calcium (mg/L)	96.73 (±4.81)	90.08 (±0.89)	−6.65	−7%
Magnesium level (mg/L)	21.66 (±0.36)	21.25 (±0.28)	−0.41	−2%
Serum phosphorus (mg/L)	46.04 (±1.30)	51.21 (±2.33)	+5.17	+11%
Serum potassium (mmol/L)	4.91 (±0.11)	4.88 (±0.17)	−0.03	−1%
Serum sodium (mmol/L)	135.86 (±0.52)	134.39 (±1.15)	−1.47	−1%
Chloride (mmol/L)	98.38 (±0.58)	98.17 (±0.98)	−0.21	0%
Quantitative CRP (mg/L)	12.77 (±2.35)	4.56 (±1.64)	−8.21	**−64%**
Albumin (g/L)	42.64 (±0.46)	43.66 (±0.48)	+1.02	+2%

$\bar{X}$: average of the values before adding the flour; $\bar{Y}$: mean of values after consuming the flour.

for the main biochemical and anthropometric parameters, as well as the frequency of vaso-occlusive crises (n = 57).

3.5. Impact on Body Composition

The bioelectrical impedance analysis at 6 months revealed significant improvements in body composition (Table 5).

Table 5. Impact of enriched flour on body composition parameters (N = 57).

Parameters Assessed	Before x (%) N = 57	After y (%) N = 57	Difference (y-x)	Progression
Good cellular vitality (IAM)	26 (45.61)	31 (54.38)	+5	+16%
Very healthy lifestyle (MCA)	22 (38.60)	27 (47.37)	+5	+19%
Normal body fat (BF)	31 (54.39)	37 (64.91)	+6	+14%
Normal muscle mass (IMM)	26 (45.61)	33 (57.89)	+7	**+21%**
Normal bone quality (CMO)	53 (92.98)	57 (100.0)	+4	+7%
Normal tissue hydration (HMNG)	33 (57.89)	33 (57.89)	0	0%
Normal extracellular volume (Ve)	26 (45.61)	25 (43.86)	−1	−4%

x: number of patients in a normal state before consuming the flour kits. y: number of patients in normal condition after taking the flour kits.

4. Discussion

The objective of this study was to prospectively evaluate the impact of an enriched flour with anti-inflammatory and antioxidant effects, administered as porridge, on the nutritional status of malnourished patients with sickle cell disease being treated at the CNRSD in Lomé, Togo. This objective builds on the previously conducted cross-sectional phase, which had revealed an overall prevalence of malnutrition of 66.1% in this population, thereby justifying the need for a targeted nutritional intervention. The assessment of the nutritional impact of this intervention was based on a multidimensional anthropometric approach combining five complementary indicators: the weight-for-height z-score (W/H), the BMI-for-age z-score (BMI/A), body mass index (BMI), upper arm circumference (UAC), and triceps skinfold thickness (TSFT). This methodological choice is based on the principle that no single indicator can account for all dimensions of nutritional status. In fact, overall body composition indices such as the W/H z-score and BMI tend to underestimate undernutrition in a hypermetabolic population such as that of patients with sickle cell disease, whereas body composition measures, particularly the TSC, allow for earlier detection of depletion of fat reserves [46] [47]. Defining overall undernutrition as the presence of at least one positive criterion among the five selected indicators was intended to maximize detection sensitivity, at the cost of a possible overestimation of prevalence, which must be interpreted with caution [48]. Furthermore, the prospective longitudinal follow-up used in

this study, unlike a cross-sectional approach, made it possible to establish a temporal relationship between the consumption of enriched flour and changes in nutritional status, thereby strengthening the inferential value of the results obtained. It is within this methodological framework that the results presented here concerning the impact of enriched flour on nutritional status and the occurrence of vaso-occlusive crises in malnourished patients with sickle cell disease followed at the CNRSD are situated.

4.1. Prevalence of Malnutrition: An Alarming Reality in Sub-Saharan Africa

The prevalence of malnutrition observed in our cohort (66.09%) is consistent with data from the African literature. A systematic review conducted according to PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) criteria, covering the period 1995-2020, reported that African studies consistently described malnutrition and stunted growth among pediatric and adolescent patients with sickle cell disease, though no robust interventional studies were identified [9]. In Nigeria, an analysis of data from the Demographic and Health Survey which included neonatal screening for sickle cell disease for the first time showed that the prevalence of stunting and underweight was 55.4% and 38.9%, respectively, among children with sickle cell disease, with a 2.39-fold higher risk of stunting (adjusted OR: 2.39; 95% CI: 1.26 - 4.54) than among children without sickle cell disease [10]. The prevalence found in the present study exceeds these figures, which can be explained by the inclusion of adults in the cohort and the use of sensitive diagnostic criteria (TSFT, PB, BMI-for-age, weight-for-height z-score) in accordance with WHO recommendations [9].

The predominance of TSFT as the most sensitive criterion (58.80%) was notable. This result suggests that malnutrition in our population is primarily of the marastic type, characterized by loss of subcutaneous adipose tissue, which can be explained by chronic hypermetabolism associated with hemolysis and repeated episodes of infection. The imbalance between nutritional intake and requirements in sickle cell disease is well documented, resulting from a combination of increased energy expenditure (hemolysis: 20% - 40% of basal metabolism), reduced food intake during crises, and malabsorption associated with episodes of intestinal ischemia [8] [11].

4.2. Inflammatory Syndrome: Pathophysiological Mechanisms and Markers Used

The initial inflammatory profile of our patients (CRP > 6 mg/L: 46.67% of subjects; elevated alpha-glycoproteins: 42.66%; hypercomplementemia: 68%) is characteristic of the acute multifactorial inflammation associated with sickle cell disease. The pathophysiology of this inflammation is based on a vicious cycle involving: the polymerization of HbS leading to erythrocyte sickling, the adhesion of sickled erythrocytes to the vascular endothelium mediated by P-selectin, VCAM-1 (Vascular Cell Adhesion Molecule-1), and integrins, the activation of neutro-

phils and platelets, followed by the release of pro-inflammatory mediators and free radicals [5] [6].

The hypercomplementemia observed in 68% of patients is explained by the fact that free hemin released during hemolysis interacts with complement molecules (C1q, CRP, immunoglobulins), notably activating the classical pathway and leading to increased cleavage of C4 and C3 [7]. This complement activation sustains endothelial inflammation and contributes to recurrent vascular occlusion.

CRP, synthesized by the liver under the influence of interleukin-6 (IL-6) and interleukin-1β (IL-1β), is a sensitive marker of systemic inflammation. In this study, 49.12% of malnourished patients had pathologically elevated CRP at enrollment, with a mean quantitative value of 12.77 (±2.35) mg/L. This level is consistent with a moderate chronic inflammatory state, which is consistent with the presence of recurrent vaso-occlusive episodes and frequent subclinical infections in this population [5] [7]. Immune responses to these infections lead to hypergammaglobulinemia. Hypergammaglobulinemia (72%) reflects chronic stimulation of the adaptive immune system, secondary to repeated infections and autoimmunization linked to the release of erythrocyte antigens during chronic hemolysis [7].

4.3. Effects of Enriched Flour on Inflammation: Molecular Mechanisms

Paired analysis using the McNemar test confirmed a significant improvement in CRP levels, with 22 patients moving from pathological to normal levels compared to only 3 in the opposite direction ($p = 0.00016$; paired OR = 7.33, 95% CI: 2.20 - 24.50), which is consistent with the expected anti-inflammatory effect of the intervention. In contrast, no significant change was observed for alpha-1-glycoprotein ($p = 1.000$; matched OR = 1.08, 95% CI: 0.51 - 2.29), with an almost equal number of patients showing improvement (n = 14) and worsening (n = 13).

Serum albumin showed the most marked improvement among all the protein parameters studied: 14 patients who were hypoalbuminemic at enrollment returned to normal levels at 6 months, compared with only 2 who showed the opposite trend ($p = 0.00418$; matched OR = 7.00, 95% CI: 1.59 - 30.80), reflecting a significant restoration of visceral protein status. It should be noted that albumin is not solely a nutritional marker: it is also a negative acute-phase protein, whose hepatic synthesis decreases under the influence of IL-6 in favor of positive acute-phase proteins such as CRP, and whose level can also be lowered by increased vascular permeability in an inflammatory context [49]. In sickle cell disease, where chronic undernutrition and systemic inflammation coexist and are mutually reinforcing, the concurrent improvement in CRP and albumin strengthens the biological coherence of the enriched flour's combined anti-inflammatory and nutritional effect. Beta-2-glycoprotein showed a comparable favorable trend (27 patients normalized versus 5 who worsened), though it did not reach the threshold for statistical significance ($p = 0.143$; matched OR = 2.40, 95% CI: 0.85 - 6.81),

which may reflect a lack of statistical power rather than an actual absence of effect.

This discrepancy among markers suggests that acute-phase proteins and visceral proteins do not respond uniformly or synchronously to the nutritional intervention, with CRP and albumin appearing to be more sensitive indicators of short-term changes in this population than alpha-1- and beta-2-glycoprotein. The significant reduction in inflammatory marker s after 6 months of intervention can be explained by the combined and synergistic effects of the bioactive compounds in the flour on the molecular pathways of inflammation.

Curcumin from *Curcuma longa* is the most well-documented anti-inflammatory compound in the formulation. It exerts its effects by inhibiting the degradation of cytoplasmic Inhibitor of Nuclear Factor kappa-B alpha (IκBα) and by reducing the phosphorylation of the transcription factor nuclear factor kappa-B (p65/NF-κB), thereby blocking the transcription of numerous pro-inflammatory cytokines (TNF-α, IL-1β, IL-6, IL-8) [50]. At the same time, curcumin inhibits the Mitogen-Activated Protein Kinase (MAPK) pathways Extracellular Signal-Regulated Kinase 1 and 2 (ERK1/2), c-Jun N-terminal Kinase (JNK), and 38 kDa protein (p38), which are involved in the propagation of the inflammatory signal, and activates the Keap1-Nrf2/ARE pathway (Kelch-like ECH-Associated Protein 1/Nuclear factor Erythroid 2-related factor 2/Antioxidant Response Element), which strengthens endogenous antioxidant defenses (superoxide dismutase (SOD), catalase, glutathione) [50] [51]. In mouse models of sickle cell disease, curcumin has been shown to significantly reduce hyperalgesia, hemolysis, oxidative stress, and inflammation (decreased levels of IL-2, IL-4, IL-6, and monocyte chemoattractant protein-1 (MCP-1)), as well as an improvement in hematological parameters, suggesting a disease-modifying effect [51].

Moringa oleifera also contributes to reducing inflammation by inhibiting the nuclear translocation of NF-κB and upregulating Nrf2, leading to a reduction in the expression of pro-inflammatory genes and an increase in the production of anti-inflammatory cytokines [52]. An umbrella review of 26 meta-analyses confirmed these effects, attributing moringa's anti-inflammatory and antioxidant activity to its glucosinolates, flavonoids, and phenolic acids [53]. In in vitro models, *Moringa oleifera* extracts at 4 mg/mL inhibited HbS sickling by 95.6% (±2.47%), with iron-chelating activity capable of reducing erythrocyte oxidative stress [54]. Moringa's high content of antisickling amino acids (phenylalanine, lysine, arginine, histidine, and tryptophan) provides a complementary mechanism of action against HbS polymerization [54].

The baobab (*Adansonia digitata*) is an exceptional source of vitamin C (200 - 500 mg/100g, or 7 to 10 times the content of oranges), polyphenols (proanthocyanidins, flavonoids, catechins, tannins), and minerals (calcium, potassium, iron, magnesium, phosphorus, sodium, zinc, and manganese). Among these minerals, zinc is particularly relevant in sickle cell disease due to its documented antisickling activity and its role as a cofactor for superoxide dismutase (SOD), while iron helps correct the iron-deficiency anemia frequently associated with this condition [55]

[56]. These compounds exhibit antioxidant properties (neutralization of reactive oxygen species or free radicals, ROS), anti-inflammatory properties (inhibition of the lipoxygenase and xanthine oxidase pathways), antibacterial properties (bactericidal or bacteriostatic), and analgesic properties (pain-relieving) [55]. The high vitamin C content of baobab is particularly relevant in sickle cell disease, where erythrocyte oxidative stress is intense and reserves of water-soluble antioxidants are frequently insufficient [8].

The soy isoflavones (genistein, daidzein, glycitein) present in the soy component of the formulation are phytoestrogens with well-documented anti-inflammatory and antioxidant properties. They inhibit LPS-induced nitric oxide production (by inhibiting inducible nitric oxide synthase, or iNOS) and reduce pro-inflammatory cytokines (IL-6, IL-8, TNF-α, IL-12) in various types of immune cells [57] [58]. Genistein, which has the highest antioxidant activity among isoflavones, outperforms ascorbate and alpha-tocopherol in protecting cells against oxidative stress. It also inhibits the MAPK/NF-κB pathways and activates the NRF2/HO-1 pathway [59].

Sesame contributes through its lignans (sesamin, sesamolin), which exert antioxidant effects by inhibiting lipid peroxidation and modulating antioxidant enzymes.

This synergistic combination of antioxidant and anti-inflammatory effects among the compounds in the enriched flour explains the extent of the reduction in inflammatory metabolites: pathological quantitative CRP levels decreased from 49.12% to 15.79% of patients ($p = 0.0001$), quantitative CRP levels decreased from 12.77 to 4.56 mg/L (64%).

4.4. Reduction in Vaso-Occlusive Crises: A Clinically Significant Association

The 86% reduction in VOCs is the most clinically significant result of this study. This association between improved inflammatory status and reduced VOCs is mechanistically consistent.

By reducing systemic inflammation (CRP, complement), the enriched flour attenuates endothelial activation and the overexpression of adhesion molecules. Furthermore, the reduction in erythrocyte oxidative stress (vitamins C and E from baobab and moringa, polyphenols, curcumin) improves erythrocyte deformability and reduces their propensity for sickling. This dual anti-inflammatory and antioxidant action is the most likely mechanism to explain the observed reduction in CVOs [5] [60]. A study conducted in the Democratic Republic of the Congo involving 838 patients documented the relationship between inflammatory status and the frequency of CVOs in an African context, highlighting the importance of integrated care [11].

4.5. Impact on Body Composition and Biochemical Parameters

The improvement in normal muscle mass (+21%, from 45.61% to 57.89% of pa-

tients) and normal fat mass (+14%) reflects the anabolic effect of soy protein intake on muscle synthesis, combined with the energy provided by corn and the reduction in inflammatory hypercatabolism. These results are particularly significant in sickle cell disease, where muscle wasting is common and contributes to chronic fatigue and low exercise tolerance [8].

The normalization of bone quality (BMD) in 100% of patients at 6 months is a remarkable result, likely explained by the combined intake of calcium (baobab: 250 - 655 mg/100g), vitamin D, and protein (soy), as well as by the reduction of chronic inflammation, which promotes osteolysis via osteoclast activation mediated by the Receptor Activator of Nuclear Factor Kappa-B Ligand (RANKL) [8]. Soy isoflavones (genistein, daidzein), due to their estrogenic activity, may also contribute to the inhibition of bone resorption, as demonstrated in other contexts [59].

The increase in serum phosphorus levels (+11%) is consistent with improved intestinal absorption linked to overall nutritional status and a reduction in ischemic episodes in the intestine that contribute to malabsorption. Electrolyte levels (sodium, potassium, chloride) remained relatively stable, suggesting that the enriched flour did not disrupt the patients' fluid and electrolyte balance.

4.6. Strengths, Limitations, and Future Directions

The strengths of this study include: its prospective design with pre- and post-intervention assessments, the multimodal nature of the diagnostic tools used (anthropometry, laboratory tests, bioimpedance analysis), the use of a reproducible and accessible locally developed formulation, and the reasonable sample size for an African population with sickle cell disease.

The main limitations are the absence of a randomized control group (which does not allow for the formal exclusion of a seasonal effect or the impact of standard care on certain parameters). The interpretation of TSFT must be qualified due to the documented fat redistribution in patients with sickle cell disease [61] [62] and the limitations of predictive equations when applied to general populations [63]. Furthermore, the lack of specific pro-inflammatory cytokine assays (TNF-α, IL-6, IL-1β) prevents a precise characterization of the predominant molecular mechanism of action of the flour. The kit utilization rate 43.43% for the initial cohort (n = 75) and 52.30% for the 57 patients who completed follow-up reflects moderate adherence, and the gap between the two groups suggests a selection bias favoring more adherent patients. This adherence level is likely explained by logistical constraints (distance to the center, patient availability), the daily burden of twice- or thrice-daily intake over six months, and progressive sensory fatigue: the initial hedonic evaluation had already shown only a moderate score (6.22 ± 1.55) [15]; and patients reported a decline in taste, smell, and color appreciation of the porridge by the end of follow-up. This low adherence represents a major limitation, likely to attenuate the true magnitude of the intervention's effects, and calls for improvement strategies (closer support, organoleptic reformulation) in future similar interventions.

5. Conclusion

This prospective study demonstrates that a flour fortified with locally sourced ingredients (yellow corn, soybeans, baobab, moringa, turmeric, and sesame), administered as porridge for 6 months to malnourished patients with sickle cell disease in Togo, has a positive and clinically significant impact on nutritional status, the frequency of vaso-occlusive crises, and certain key inflammatory markers, notably CRP and albumin, although this effect was not consistent across all inflammatory parameters studied. These results underscore the critical importance of systematically integrating nutritional management into the overall follow-up protocol for patients with sickle cell disease. The development of fortified flours made from local produce represents an accessible, culturally appropriate, inexpensive, and effective nutritional alternative for improving the quality of life and reducing morbidity in these patients.

Declarations

All procedures complied with ethical standards and were approved by the Bioethics Committee for Health Research (CBRS) pursuant to Opinion No. 013/2022/CBRS dated May 24, 2022. This research was conducted in accordance with the Declaration of Helsinki.

Informed consent was obtained from each study participant. The anonymity of the subjects included in this study was preserved. The results obtained in this study were used exclusively for scientific purposes.

Availability of Data and Materials

All data obtained are presented in the form of tables and figures: counts, medians, standard deviations, and percentages, as well as statistical relationships. Raw data are available from the research organization LASBASE.

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Authors' Contributions

Kouassi Kafui Codjo: Report writing, Study design, review, and validation.

Ouro-bere Tchagbélé: Field survey, report drafting, Corresponding author, review.

Hezouwe Magnang: Patient recruitment design.

Bouka Ekpetsi Chantal: Design and sharing of experiences regarding sickle cell disease.

Paka Essodolom: Review for proofreading.

Madjalani Hèzouwè: Manuscript revision.

Tchacondo Tchadjobo: Critical intellectual contribution.

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Pauling, L., Itano, H.A., Singer, S.J. and Wells, I.C. (1949) Sickle Cell Anemia, a Molecular Disease. *Science*, **110**, 543-548. https://doi.org/10.1126/science.110.2865.543

[2] Ware, R.E., de Montalembert, M., Tshilolo, L. and Abboud, M.R. (2017) Sickle Cell Disease. *The Lancet*, **390**, 311-323. https://doi.org/10.1016/s0140-6736(17)30193-9

[3] Jonani, B., Kasule, E.C., Herman, B.R., Arturo, J.F., Mugambwa, M.C., Stephen, S., *et al.* (2025) Burden of Sickle Cell Anemia in Africa: A Systematic Review and Meta-Analysis. *PLOS ONE*, **20**, e0337090. https://doi.org/10.1371/journal.pone.0337090

[4] Esoh, K., Wonkam-Tingang, E. and Wonkam, A. (2021) Sickle Cell Disease in Sub-Saharan Africa: Transferable Strategies for Prevention and Care. *The Lancet Haematology*, **8**, e744-e755. https://doi.org/10.1016/s2352-3026(21)00191-5

[5] Sundd, P., Gladwin, M.T. and Novelli, E.M. (2019) Pathophysiology of Sickle Cell Disease. *Annual Review of Pathology*: *Mechanisms of Disease*, **14**, 263-292. https://doi.org/10.1146/annurev-pathmechdis-012418-012838

[6] Manwani, D. and Frenette, P.S. (2013) Vaso-Occlusion in Sickle Cell Disease: Pathophysiology and Novel Targeted Therapies. *Blood*, **122**, 3892-3898. https://doi.org/10.1182/blood-2013-05-498311

[7] Silva-Junior, A.L., Garcia, N.P., Cardoso, E.C., Dias, S., Tarragô, A.M., Fraiji, N.A., *et al.* (2021) Immunological Hallmarks of Inflammatory Status in Vaso-Occlusive Crisis of Sickle Cell Anemia Patients. *Frontiers in Immunology*, **12**, Article ID: 559925. https://doi.org/10.3389/fimmu.2021.559925

[8] Obeagu, E.I. and Obeagu, G.U. (2024) Malnutrition in Sickle Cell Anemia: Prevalence, Impact, and Interventions: A Review. *Medicine*, **103**, e38164. https://doi.org/10.1097/md.0000000000038164

[9] Nartey, E.B., Spector, J., Adu-Afarwuah, S., Jones, C.L., Jackson, A., Ohemeng, A., *et al.* (2021) Nutritional Perspectives on Sickle Cell Disease in Africa: A Systematic Review. *BMC Nutrition*, **7**, Article No. 9. https://doi.org/10.1186/s40795-021-00410-w

[10] Williams, T.N. (2021) Undernutrition: A Major but Potentially Preventable Cause of Poor Outcomes in Children Living with Sickle Cell Disease in Africa. *BMC Medicine*, **19**, Article No. 17. https://doi.org/10.1186/s12916-020-01892-4

[11] Kaponda, A., Muya, K., Panda, J., Koto, K.K. and Bonnechère, B. (2024) Unraveling the Complexity of Vaso-Occlusive Crises in Sickle Cell Disease: Insights from a Re-

source-Limited Setting. *Journal of Clinical Medicine*, **13**, Article 2528. https://doi.org/10.3390/jcm13092528

[12] Kim, I.S. (2021) Current Perspectives on the Beneficial Effects of Soybean Isoflavones and Their Metabolites for Humans. *Antioxidants*, **10**, Article 1064. https://doi.org/10.3390/antiox10071064

[13] Pareek, A., Pant, M., Gupta, M.M., Kashania, P., Ratan, Y., Jain, V., *et al.* (2023) Moringa Oleifera: An Updated Comprehensive Review of Its Pharmacological Activities, Ethnomedicinal, Phytopharmaceutical Formulation, Clinical, Phytochemical, and Toxicological Aspects. *International Journal of Molecular Sciences*, **24**, Article 2098. https://doi.org/10.3390/ijms24032098

[14] Silva, M.L., Rita, K., Bernardo, M.A., Mesquita, M.F.d., Pintão, A.M. and Moncada, M. (2023) Adansonia Digitata L. (Baobab) Bioactive Compounds, Biological Activities, and the Potential Effect on Glycemia: A Narrative Review. *Nutrients*, **15**, Article 2170. https://doi.org/10.3390/nu15092170

[15] Tchagbele, O., Codjo, K., Chantal, B., Essodolom, P., Mouawiyatou, B. and Moudassirou, B. (2025) Physical, Chemical, and Microbiological Characterization of a Flour with Antioxidant and Anti-Inflammatory Properties for Patients with Sickle Cell Anemia in Togo. *International Journal of Nutrition and Food Sciences*, **14**, 383-394. https://doi.org/10.11648/j.ijnfs.20251406.13

[16] Layibo, Y., Kuéviakoé, I.M., Padaro, E., Magnang, H., Vovor, A. and Agbonon, A. (2019) Prévalence de l'albuminurie chez les drépanocytaires au centre hospitalier universitaire campus de lomé au togo. *Annales de Biologie Clinique*, **77**, 79-86. https://doi.org/10.1684/abc.2018.1404

[17] Farrell, A.T., Panepinto, J., Carroll, C.P., Darbari, D.S., Desai, A.A., King, A.A., *et al.* (2019) End Points for Sickle Cell Disease Clinical Trials: Patient-Reported Outcomes, Pain, and the Brain. *Blood Advances*, **3**, 3982-4001. https://doi.org/10.1182/bloodadvances.2019000882

[18] Cashin, K. and Oot, L. (2018) Guide to Anthropometry: A Practical Tool for Program Planners, Managers, and Implementers. Food and Nutrition Technical Assistance III Project (FANTA)/FHI 360. https://www.fantaproject.org/tools/anthropometry-guide

[19] Soylu, M., Şensoy, N., Doğan, İ., Doğan, N., Mazıcıoğlu, M.M. and Öztürk, A. (2021) Four-Site Skinfolds Thickness Percentiles of Schoolchildren and Adolescents in Turkey. *Public Health Nutrition*, **24**, 5414-5425. https://doi.org/10.1017/s1368980021003323

[20] Hasselmann, M. and Alix, E. (2003) Outils et procédures de dépistage de la dénutrition et de son risque en milieu hospitalier. *Nutrition Clinique et Métabolisme*, **17**, 218-226. https://doi.org/10.1016/j.nupar.2003.09.004

[21] Kouassi, K., Bagny, A., Kaaga, L., Bouglouga, O., Lawson Anani-Soh, L., Lamboni, C., and Redah, D. (2014). Prevalence of Protein-Energy Undernutrition Evaluated by the Measurement of Triceps Skinfold Thickness and Mid-Arm Muscle Circumference of 103 Adults with Cirrhosis of the Liver Hospitalized in the Department of Hepatology and Gastroenterology of the Lomé Campus University Hospital (Togo). *Médecine et Santé Tropicales*, **24**, 208-213. https://doi.org/10.1684/mst.2014.0334

[22] Caquet, R. (2015) 250 Examens de laboratoire. 12th Edition, Elsevier-Masson.

[23] Durand, G. and Beaudeux, J.L. (2011) Biochimie Médicale. 2nd Edition, Lavoisier.

[24] Doumas, B.T., Ard Watson, W. and Biggs, H.G. (1971) Albumin Standards and the Measurement of Serum Albumin with Bromcresol Green. *Clinica Chimica Acta*, **31**, 87-96. https://doi.org/10.1016/0009-8981(71)90365-2

[25] Mann, C.K. and Yoe, J.H. (1956) Spectrophotometric Determination of Magnesium with Sodium 1-Azo-2-Hydroxy-3-(2,4-Dimethylcarboxanilido)-Naphthalene-1'-(2-Hydroxybenzene-5-Sulfonate). *Analytical Chemistry*, **28**, 202-205. https://doi.org/10.1021/ac60110a016

[26] Henry, R. (1974) Clinical Chemistry. 2nd Edition, Harper & Row, 723 p.

[27] Eda, S., Kaufmann, J., Roos, W. and Pohl, S. (1998) Development of a New Microparticle-Enhanced Turbidimetric Assay for C-Reactive Protein with Superior Features in Analytical Sensitivity and Dynamic Range. *Journal of Clinical Laboratory Analysis*, **12**, 137-144. https://doi.org/10.1002/(sici)1098-2825(1998)12:3<137::aid-jcla2>3.0.co;2-6

[28] Price, C.P., Trull, A.K., Berry, D. and Gorman, E.G. (1987) Development and Validation of a Particle-Enhanced Turbidimetric Immunoassay for C-Reactive Protein. *Journal of Immunological Methods*, **99**, 205-211. https://doi.org/10.1016/0022-1759(87)90129-3

[29] Dubois, S., McGovern, M. and Ehrhardt, V. (1988) Eisenstoffwechsel-Diagnostik mit Boehringer Mannheim/Hitachi-Analysensystemen: Ferritin, Transferrin und Eisen. *GIT Labor-Medizin*, **9**, 468-471.

[30] Hartman, K., Luterotti, S., Osswald, H.F., Oehme, M., Meier, P.C., Ammann, D., *et al.* (1978) Chloride-Selective Liquid-Membrane Electrodes Based on Lipophilic Methyl-Tri-N-Alkyl-Ammonium Compounds and Their Applicability to Blood Serum Measurements. *Mikrochimica Acta*, **70**, 235-246. https://doi.org/10.1007/bf01201614

[31] Shibata, Y., Maruizumi, T., & Miyagi, H. (1992) Characteristics of Sodium Ion-Selective Electrodes Based on Neutral Carriers and Their Application to Analysis of Physiological Fluids. *NIPPON KAGAKU KAISHI*, 961-967. https://doi.org/10.1246/nikkashi.1992.961

[32] Shono, T., Okahara, M., Ikeda, I., Kimura, K. and Tamura, H. (1982) Sodium-Selective PVC Membrane Electrodes Based on Bis(12-Crowns-4)S. *Journal of Electroanalytical Chemistry and Interfacial Electrochemistry*, **132**, 99-105. https://doi.org/10.1016/0022-0728(82)85009-2

[33] Pioda, L.A.R., Stankova, V. and Simon, W. (1969) Highly Selective Potassium Ion Responsive Liquid-Membrane Electrode. *Analytical Letters*, **2**, 665-674. https://doi.org/10.1080/00032716908051343

[34] Adom, K.K. and Liu, R.H. (2002) Antioxidant Activity of Grains. *Journal of Agricultural and Food Chemistry*, **50**, 6182-6187. https://doi.org/10.1021/jf0205099

[35] Lim, T.K. (2012) Edible Medicinal and Non-Medicinal Plants: Volume 4, Fruits. Springer.

[36] Messina, M. (2010) Insights Gained from 20 Years of Soy Research. *The Journal of Nutrition*, **140**, 2289S-2295S. https://doi.org/10.3945/jn.110.124107

[37] Bhagwat, S., Haytowitz, D. and Holden, J. (2008) USDA Database for the Isoflavone Content of Selected Foods, Release 2.0. U.S. Department of Agriculture, Agricultural Research Service, Nutrient Data Laboratory.

[38] Chadare, F.J., Linnemann, A.R., Hounhouigan, J.D., Nout, M.J.R. and Van Boekel, M.A.J.S. (2008) Baobab Food Products: A Review on Their Composition and Nutritional Value. *Critical Reviews in Food Science and Nutrition*, **49**, 254-274. https://doi.org/10.1080/10408390701856330

[39] Cisse, M., Sakho, M., Dornier, M., Diop, C.M., Reynes, M. and Sock, O. (2009) Caractérisation du fruit du baobab et étude de sa transformation en nectar. *Fruits*, **64**,

19-34. https://doi.org/10.1051/fruits/2008052

[40] Fahey, J.W. (2005) Moringa Oleifera: A Review of the Medical Evidence for Its Nutritional, Therapeutic, and Prophylactic Properties. Part 1. *Trees for Life Journal*, **1**, 1-15.

[41] Nouman, W., Basra, S.M.A., Siddiqui, M.T., Yasmeen, A., Gull, T. and Alcayde, M.A.C. (2014) Potential of *Moringa oleifera* L. as Livestock Fodder Crop: A Review. *Turkish Journal of Agriculture and Forestry*, **38**, 1-14. https://doi.org/10.3906/tar-1211-66

[42] Aggarwal, B.B. and Harikumar, K.B. (2009) Potential Therapeutic Effects of Curcumin, the Anti-Inflammatory Agent, against Neurodegenerative, Cardiovascular, Pulmonary, Metabolic, Autoimmune and Neoplastic Diseases. *The International Journal of Biochemistry & Cell Biology*, **41**, 40-59. https://doi.org/10.1016/j.biocel.2008.06.010

[43] Gupta, S.C., Sung, B., Kim, J.H., Prasad, S., Li, S. and Aggarwal, B.B. (2012) Multitargeting by Turmeric, the Golden Spice: From Kitchen to Clinic. *Molecular Nutrition & Food Research*, **57**, 1510-1528. https://doi.org/10.1002/mnfr.201100741

[44] Bhat, K.V., Kumari, R., Pathak, N. and Rai, A.K. (2014) Value Addition in Sesame: A Perspective on Bioactive Components for Enhancing Utility and Profitability. *Pharmacognosy Reviews*, **8**, 147-155. https://doi.org/10.4103/0973-7847.134249

[45] Suja, K.P., Jayalekshmy, A. and Arumughan, C. (2005) Antioxidant Activity of Sesame Cake Extract. *Food Chemistry*, **91**, 213-219. https://doi.org/10.1016/j.foodchem.2003.09.001

[46] Barden, E.M., Kawchak, D.A., Ohene-Frempong, K., Stallings, V.A. and Zemel, B.S. (2002) Body Composition in Children with Sickle Cell Disease. *The American Journal of Clinical Nutrition*, **76**, 218-225. https://doi.org/10.1093/ajcn/76.1.218

[47] Salman, E.K., Haymond, M.W., Bayne, E., Sager, B.K., Wiisanen, A., Pitel, P., *et al.* (1996) Protein and Energy Metabolism in Prepubertal Children with Sickle Cell Anemia. *Pediatric Research*, **40**, 34-40. https://doi.org/10.1203/00006450-199607000-00007

[48] Chawla, A., Sprinz, P.G., Welch, J., Heeney, M., Usmani, N., Pashankar, F., *et al.* (2013) Weight Status of Children with Sickle Cell Disease. *Pediatrics*, **131**, e1168-e1173. https://doi.org/10.1542/peds.2012-2225

[49] Gabay, C. and Kushner, I. (1999) Acute-Phase Proteins and Other Systemic Responses to Inflammation. *New England Journal of Medicine*, **340**, 448-454. https://doi.org/10.1056/nejm199902113400607

[50] Cui, J., Li, H., Zhang, T., Lin, F., Chen, M., Zhang, G., *et al.* (2025) Research Progress on the Mechanism of Curcumin Anti-Oxidative Stress Based on Signaling Pathway. *Frontiers in Pharmacology*, **16**, Article ID: 1548073. https://doi.org/10.3389/fphar.2025.1548073

[51] Liu, M., Wang, J., Song, Z. and Pei, Y. (2025) Regulation Mechanism of Curcumin Mediated Inflammatory Pathway and Its Clinical Application: A Review. *Frontiers in Pharmacology*, **16**, Article ID: 1642248. https://doi.org/10.3389/fphar.2025.1642248

[52] Villegas-Vazquez, E.Y., Gómez-Cansino, R., Marcelino-Pérez, G., Jiménez-López, D. and Quintas-Granados, L.I. (2025) Unveiling the Miracle Tree: Therapeutic Potential of Moringa Oleifera in Chronic Disease Management and Beyond. *Biomedicines*, **13**, Article 634. https://doi.org/10.3390/biomedicines13030634

[53] da Silva Parente, T.S.J., Sarandy, M.M., de Araújo, E.R.D., Gonçalves, R.V. and Zucolotto, S.M. (2025) Effect of Moringa Oleifera on Inflammatory Diseases: An Umbrella

Review of 26 Systematic Reviews. *Frontiers in Pharmacology*, **16**, Article ID: 1572337. https://doi.org/10.3389/fphar.2025.1572337

[54] Obiekwe, C.L., Ibegbulem, C.O., Ujowundu, C.O., Igwe, C.U. and Nwaoguikpe, R. (2025) Proximate Analysis, Phytochemical Content and the Antioxidant Effect of Moringa Oleifera Leaf Methanol Extract in Sickle Cell Disease Management. *International Journal of Science and Research Archive*, **16**, 334-348. https://doi.org/10.30574/ijsra.2025.16.1.1963

[55] Abdulwaliyu, I., Arekemase, S.O., Batari, M.L., Oshodin, J.O., Mustapha, R.A., Ibrahim, D., *et al.* (2024) Nutritional and Pharmacological Attributes of Baobab Fruit Pulp. *Food Production, Processing and Nutrition*, **6**, Article 98. https://doi.org/10.1186/s43014-024-00283-z

[56] Monteiro, S., Reboredo, F.H., Lageiro, M.M., Lourenço, V.M., Dias, J., Lidon, F., *et al.* (2022) Nutritional Properties of Baobab Pulp from Different Angolan Origins. *Plants*, **11**, Article 2272. https://doi.org/10.3390/plants11172272

[57] Goh, Y.X., Jalil, J., Lam, K.W., Husain, K. and Premakumar, C.M. (2022) Genistein: A Review on Its Anti-Inflammatory Properties. *Frontiers in Pharmacology*, **13**, Article ID: 820969. https://doi.org/10.3389/fphar.2022.820969

[58] Omoni, A.O. and Aluko, R.E. (2005) Soybean Foods and Their Benefits: Potential Mechanisms of Action. *Nutrition Reviews*, **63**, 272-283. https://doi.org/10.1111/j.1753-4887.2005.tb00141.x

[59] Wu, Z. and Liu, L. (2022) The Protective Activity of Genistein against Bone and Cartilage Diseases. *Frontiers in Pharmacology*, **13**, Article ID: 1016981. https://doi.org/10.3389/fphar.2022.1016981

[60] Goel, Y., Arellano, M.A., Fouda, R.T., Kerr, D., Jana, S., Lomeli, R.A., *et al.* (2023) Mechanism-Based Targeting of Sickle Cell Pathobiology and Pain with Novel Transdermal Curcumin. *Blood*, **142**, 2490-2490. https://doi.org/10.1182/blood-2023-182512

[61] Wood, K.C., Hsu, L.L. and Gladwin, M.T. (2008) Sickle Cell Disease Vasculopathy: A State of Nitric Oxide Resistance. *Free Radical Biology and Medicine*, **44**, 1506-1528. https://doi.org/10.1016/j.freeradbiomed.2008.01.008

[62] Stevens, M.C.G., Hayes, R.J. and Serjeant, G.R. (1983) Body Shape in Young Children with Homozygous Sickle Cell Disease. *Pediatrics*, **71**, 610-614. https://doi.org/10.1542/peds.71.4.610

[63] Orsi, B.C., Gorski, D., Krul, N.E., Wiens, A., Brito, M., Tonin, F.S., *et al.* (2025) The Effects of Nutritional Supplementation for Children and Adolescents with Sickle Cell Disease: A Systematic Review and Meta-Analyses. *Clinical Nutrition*, **47**, 157-168. https://doi.org/10.1016/j.clnu.2025.02.016

Abbreviations

BMD	Bone Mineral Density
CNRSD	National Center for Sickle Cell Disease Reference and Monitoring.
CRP	C-Reactive Protein
VOC	Vaso-occlusive crises
IAM	Muscle Adiposity Index **or** Mass Adiposity Index
BMI	Body Mass Index,
MMM	Muscle Mass Index
iNOS	Inducible Nitric Oxide Synthase
ITRA	Togolese Institute of Agricultural Research
HbSS	Homozygous sickle cell anemia
HbSC	Compound heterozygous sickle cell disease
HMNG	Hydration of Lean Body Mass
LPS	Lipopolysaccharide
MCA	Active Cell Mass
WHO	World Health Organization
BP	Upper arm circumference
TSFT	Triceps Skinfold
TLR-4	Toll-like receptor 4
PRISMA	Preferred reporting items for systematic reviews and meta-analyses.
Keap1-Nrf2/ARE	Kelch-like ECH-associated protein 1/Erythropoietic nuclear factor 2-related factor 2/Antioxidant response element
IκBα	Nuclear factor kappa B alpha inhibitor
MAPK	Mitogen-activated protein kinase
ERK1/2	Extracellular signal-regulated kinase 1 and 2
JNK	c-Jun N-terminal kinase
p38	38 kDa protein