Scholars Academic Journal of Pharmacy
Abbreviated Key Title: Sch Acad J Pharm
ISSN 2347-9531 (Print) | ISSN 2320-4206 (Online)
Journal homepage: http://saspublishers.com

OPEN ACCESS

Pharmacology & Toxicology

Effects of Spirulina Supplementation on Blood Biochemical Parameters during a Malnutrition and Refeeding Trial in Wistar Rats

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DOI: https://doi.org/10.36347/sajp.2025.v14i02.002 | **Received:** 28.12.2024 | **Accepted:** 03.02.2025 | **Published:** 10.02.2025

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Abstract **Original Research Article**

This study aims to evaluate the effects of Spirulina (*Spirulina platensis*) supplementation on blood biochemical parameters during malnutrition and refeeding trials in Wistar rats (*Rattus norvegicus*). Thirty rats were divided into five groups, three of which received varying doses of Spirulina (10, 50, and 100 mg/kg) in addition to standard FACI® pellets. The experiment lasted 15 days, including a malnutrition phase followed by a refeeding phase. The results indicated significant recovery in body weight and blood biochemical parameters. The best outcomes were observed in rats that received 100 mg/kg of Spirulina. These findings suggest that Spirulina is a promising nutritional supplement for restoring malnutrition-induced abnormalities.

Keywords: Spirulina, malnutrition, refeeding, biochemical parameters, Wistar rat.

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INTRODUCTION

Malnutrition remains a major public health issue in developing countries, affecting approximately 735 million people worldwide in 2022. Despite some progress, persistent inequalities and severe food insecurity continue to impact many regions, exacerbated by economic and climatic crises (FAO, 2023; WHO, 2023). In sub-Saharan Africa, undernutrition is a particularly severe threat, especially among children under five years old. According to FAO's latest report, about 24.1% of the population experienced undernourishment in 2022, with stunting rates exceeding 30% in certain areas (FAO, 2023; UNICEF, 2023).

To address this issue, international organizations such as WHO and FAO have urged researchers to explore alternative nutritional solutions. Among these, Spirulina, a cyanobacterium rich in proteins, vitamins, and minerals, has been studied as a dietary supplement to combat malnutrition (Mao *et al*., 2005).

Numerous studies have demonstrated the benefits of Spirulina in nutritional recovery and improvement of biochemical parameters in both animal and human models (Wu *et al*., 2016). This study aims to evaluate the effects of Spirulina supplementation on rats subjected to malnutrition and refeeding conditions to assess its potential for restoring biochemical imbalances.

The objective of this study is to assess the effects of different doses of Spirulina on the restoration of blood biochemical parameters altered by malnutrition in rats.

1. MATERIALS AND METHODS

1.1. Animal Material

The study was conducted on 30 Wistar rats (*Rattus norvegicus*), aged between 35 and 50 days and weighing between 30 and 60 g. The rats were divided into five homogeneous groups of six rats each (3 males and 3 females):

- Group 1 (Plumpy Nut Control - TPn): Fed with Plumpy Nut (ready-to-use therapeutic food).
- Group 2 (Pellet Control - TG): Fed with standard FACI® pellets.
- Groups 3, 4, and 5**:** Received Spirulina supplementation at doses of 10 mg/kg, 50

mg/kg, and 100 mg/kg body weight, respectively.

1.2. Food

The food consisted, on one hand, of standard feed in the form of pellets (FACI®) for four groups and varying doses of Spirulina, and on the other hand, Plumpy'nut, which served as a reference food to evaluate renutrition capabilities. Plumpy'nut is a peanut-based food designed to combat malnutrition. The ideal duration of treatment based on this food is 28 days. However, this treatment could extend up to 10 weeks for severely malnourished children who fail to reach a target weight after four to six weeks of using ready-to-use therapeutic food (RUTF) (Bhutta *et al*., 2013).

The food under study was Spirulina, used in the form of a granular, friable powder with a pure green color; a product from the Agro-Pastoral Society (SAP) of Mé in the Adzopé department, southern Côte d'Ivoire.

1.3. Technical Equipment

During the animal experimentation, young rats were housed in individual metabolic cages. The wire-mesh floor of the metabolic cages allowed for the separation of feces upstream and the collection of urine downstream, which flowed into jars via a funnel. Additionally, these cages were equipped with feeders and water bottles to provide food and water to the animals. The equipment included a centrifuge (80-2B) for serum separation, a magnetic stirrer (OVAN model MCG05E, EU) for homogenizing solutions to be administered, two precision digital balances (SF-400 and S-234 Neo Tech SA, Belgium) for weighing, one with a sensitivity of 0.1 g and the other with a sensitivity of 0.001 g, an electronic balance (Denver Instrument S-234, Germany), a hematology analyzer (Culter, Mindray BC30 S) for complete blood count (CBC), a spectrophotometer (RAYTO RT 9200) for determining biochemical parameters, and an oven for drying feces and food refusals.

2. METHODS

2.1. Preparation of Spirulina Doses

The Spirulina powder obtained from SAP Mé was used to prepare the various doses administered orally to the rats. Distilled water was used as the solvent, into which the Spirulina powder was added according to the following protocol:

Three concentrations were prepared based on the average therapeutic dose of 50 mg/kg of body weight. To this end, the preparation of the different doses and concentrations to be administered was carried out as follows:

$$C_1 = \frac{X}{V} \quad \text{................ (1)}$$

Where,
X being the quantity of Spirulina (mg)
V the volume of distilled water in mL

Hence the following concentrations and doses to be administered:

- Lot 3 ⟶ $C_1 = 0.1$ mg/ mL for $D_1 = 10$ mg/kg bw
- Lot 4 ⟶ $C_2 = 0.5$ mg/ mL for $D_2 = 50$ mg/kg bw
- Lot 5 ⟶ $C_3 = 1$ mg/ mL for $D_3 = 100$ mg/kg bw

Table I: Average weight of rats at the start of the different experimental phases

Lots of animals	Average weight of rat batches (g)
Witnesses (TG)	47.58±1.72
Lot 3	47.72±2.09
Lot 4	47.83±4.65
Lot 5	45.73±5.51
Witnesses (TPn)	45.88±1.07

2.2. Experimental Protocol

The trial was conducted in two phases:

Malnutrition phase: All groups underwent a 48-hour food deprivation period with ad libitum access to distilled water.

Refeeding phase**:** Rats were fed for 12 days according to their designated diet, including Spirulina supplementation for groups 3, 4, and 5.

Blood biochemical parameters were measured before and after the malnutrition and refeeding phases.

2.2.1. Administration of Spirulina

Spirulina was administered orally using a gavage technique to ensure precise dosage. The control groups did not receive Spirulina. Groups 3, 4, and 5 received doses of 10, 50, and 100 mg/kg of body weight daily between 7:30 and 8:30 AM.

2.2.2. Undernutrition and Renutrition Trials in Individual Feeding

The undernutrition and renutrition trials were conducted over a period of 15 days.

Undernutrition: According to the French High Authority of Health (HAS, 2017), undernutrition is a pathological state resulting from an imbalance between nutritional intake and the body's needs. It is characterized by insufficient or inadequate intake of energy, proteins, and/or micronutrients (vitamins, minerals), leading to adverse effects on health, growth, and physiological functions. To induce undernutrition in this study, all groups of rats (control and experimental) were subjected to food restriction for 48 hours. However, each rat had access to distilled water ad libitum. After 48 hours, the rats were weighed, and blood samples were collected.

Renutrition: This is the therapeutic process aimed at correcting undernutrition by restoring a balance between nutritional intake and the body's needs. It involves providing adequate amounts of energy, proteins, vitamins, and minerals to promote the recovery of muscle mass, physiological functions, and overall health (Sobotka *et al*., 2009). Renutrition was carried out over 12 days, during which the rats were fed again according to the growth study protocol. Each rat received FACI® pellets ad libitum, including the first control group, and Spirulina depending on the group. Additionally, the second control group was fed ad libitum with ready-to-use therapeutic food (RUTF). At the end of this phase, the animals' weights were recorded, and blood samples were collected.

2.3. Statistical analyses

The results were expressed as means followed by the standard error (M ± SEM) and proportions (%). The evolution of the weight of the rats during the growth was evaluated by one way analyzes of variances (ANOVA1). This statistical test was combined with the Bonferroni test as a post hoc test. Statistical analysis of data in this context was performed using GraphPad Prism 5.01 software (San Diego, California, USA). In addition, the obtained proportions according to reference values for each chosen period of growth of the rats on the one hand and on the other hand, the proportions of variation of the main blood parameters during the growth of the rats, were compared by the test G. This test was carried out with the Windows R version 2.0.1 computer program (Ihaka and Gentleman, R, 1995). The significance threshold was set at a probability threshold p of less than 0.05 for the expression of results.

3. RESULTS

3.1. Assessment of Body Parameters in Rats During Malnutrition and Refeeding Trials

Table I presents the evolution of body weight in treated and untreated rats during the malnutrition and refeeding trial period. Before malnutrition, the average body weight of the rats ranged from 63.88 ± 3.65 g to 77.33 ± 2.84 g; no significant difference (P > 0.05) was recorded between these values. After two days of food deprivation, a significant decrease (P < 0.05) in body weight was observed in all groups of treated rats as well as in the control group fed with therapeutic food (TPn). During this period, weight losses ranged from -5.83 ± 1.04 g to -7.12 ± 1.08 g in rats subjected to Spirulina, compared to -6.61 ± 1.21 g and -7.22 ± 0.69 g for the TPn and TG groups, respectively. There was no significant difference (P > 0.05) between the weight losses in Spirulina-treated rats compared to the TPn group. When the different groups of rats were refed with the same diet as before malnutrition, a weight increase was observed, with weight gains ranging from +11.2 ± 0.77 g to +13.72 ± 0.43 g in treated rats, and +11.01 ± 0.49 g and +10.21 ± 0.58 g in the TPn and TG groups, respectively. However, statistical analysis did not reveal any significant difference (P > 0.05) between the weight gains of the control groups and those of the treated rats.

Table II: Variations in Average Body Weight of Rats from Malnutrition to Refeeding

Rat Groups	Weight (g) Before	Weight (g) After	Weight (g) Start	Weight (g) End	Weight Gain (g)	Daily Weight Gain (g)
TPn	65.38 ± 3.26	58.77 ± 1.05	58.77 ± 1.05	69.78 ± 1	+11.01 ± 0.49	1 ± 0.04
TG	63.88 ± 3.65	56.66 ± 1.96	56.66 ± 1.96	66.87 ± 0.89	+10.21 ± 0.58	0.93 ± 0.05
Lot 1	66.42 ± 3.96	59.3 ± 1.88	59.3 ± 1.88	70.5 ± 1.15	+11.2 ± 0.77	1.02 ± 0.06
Lot 2	74.33 ± 2.86	67.64 ± 1.04*	67.64 ± 1.04*	80.84 ± 1.76*	+13.2 ± 0.69	1.2 ± 0.06
Lot 3	77.33 ± 2.84	67.1 ± 1.36*	67.1 ± 1.36*	80.82 ± 0.94*	+13.72 ± 0.43	1.25 ± 0.02

Note: TPn: Control group fed with Plumpy Nut; TG: Control group fed with pellets; Lot 1: Spirulina 10 mg/kg; Lot 2: Spirulina 50 mg/kg; Lot 3: Spirulina 100 mg/kg; n = 6.

3.2. Blood Biochemical Parameters at the End of Malnutrition and Refeeding

3.2.1. Glucose, Proteins, and Blood Lipids in Rats

After malnutrition, the average values of glucose and HDL cholesterol did not significantly vary in treated rats compared to TPn rats. The total cholesterol and LDL cholesterol levels in TG rats were significantly decreased (P < 0.05 and P < 0.01, respectively) compared to TPn levels. Food deprivation significantly reduced (P < 0.05) the total cholesterol level at 50 mg/kg and LDL cholesterol at 10 mg/kg compared to TPn rats. The highest total cholesterol level was noted in TPn rats (0.56 ± 0.05 g/L), while the lowest was recorded at 50 mg/kg. LDL cholesterol was lowest in TG rats (0.12 ± 0.02 g/L) and highest in TPn rats (0.21 ± 0.02 g/L).

Malnutrition did not induce significant variation in total protein levels between the two control groups. However, during malnutrition, total protein levels increased significantly (P < 0.01) in rats previously treated with 10 and 50 mg/kg and significantly (P < 0.05) at 100 mg/kg compared to TPn rats. The highest total protein value was recorded at 10 mg/kg (64.4 ± 0.53 g/L), and the lowest was noted in TPn rats (60.4 ± 1.17 g/L). Unlike total proteins, the triglyceride levels significantly decreased (P < 0.01) in TG rats compared to TPn rats. Similarly, malnutrition significantly reduced triglyceride levels (P < 0.05) in rats receiving 10 and 100 mg/kg compared to TPn rats. The highest triglyceride level was found in TPn rats (0.52 ± 0.04 g/L), and the lowest in TG rats.

Upon refeeding and Spirulina supplementation, there was no significant variation in glucose and total protein levels in treated rats compared to TPn rats. However, Spirulina administration significantly reduced triglyceride levels (P < 0.05) in TG rats compared to TPn rats. No significant variation was observed between Spirulina-treated groups and TPn rats. The HDL cholesterol level remained unchanged between the two control groups. However, treated rats showed a significant decrease (P < 0.05) at doses of 10 and 50 mg/kg compared to TPn rats. LDL cholesterol levels in TG rats significantly decreased (P < 0.001) compared to TPn rats. Similarly, Spirulina administration led to a highly significant decrease (P < 0.001) at 10 mg/kg, highly significant (P < 0.01) at 50 mg/kg, and significant (P < 0.05) at 100 mg/kg body weight. The highest LDL cholesterol level was recorded in TPn rats (0.24 ± 0.02 g/L), while the lowest was in TG and 10 mg/kg groups.

Table III: Mean values of blood glucose, proteins and lipids in rats with malnutrition

Biochemical parameters		**Glucose (g/l)**	**T-proteins (g/l)**	**Triglycerides (g/l)**	**Chol. T. (g/l)**	**HDL (g/l)**	**LDL (g/l)**
Witnesses	TPn	0.93±0.04	60.4±1.17	0.52±0.04	0.56±0.05	0.27±0.02	0.21±0.02
	TG	1.02±0.04	62±2.78	0.35±0.05 ##	0.42±0.03 #	0.22±0.03	0.12±0.02 ##
Batches of treated rats	Lot 1	0.97±0.02	64.4±0.53**	0.41±0.02*	0.43±0.02	0.22±0.03	0.14±0.01*
	Lot 2	0.99±0.03	62.3±1.05**	0.44±0.02	0.39±0.04*	0.20±0.02	0.17±0.01
	Lot 3	0.98±0.07	61.3±0.99*	0.41±0.02*	0.44±0.03	0.25±0.01	0.19±0.02

Table IV: Mean values of blood glucose, proteins and lipids at refeeding

Biochemical parameters		**Glucose (g/l)**	**T-proteins (g/l)**	**Triglycerides (g/l)**	**Chol. T. (g/l)**	**HDL (g/l)**	**LDL (g/l)**
Witnesses	TPn	1.04±0.02	61.6±2.06	0.61±0.04	0.57±0.02	0.31±0.03	0.24±0.02
	TG	1.02±0.05	63.3±2.42	0.41±0.05 #	0.45±0.02	0.28±0.04	0.15±0.02 ###
Batches of treated rats	Lot 1	1.09±0.02	66.3±2.14	0.49±0.03	0.51±0.04	0.22±0.03	0.15±0.01***
	Lot 2	0.97±0.04	70±2.59	0.59±0.04	0.44±0.05	0.21±0.02*	0.18±0.01**
	Lot 3	1.03±0.03	70.4±2.75	0.50±0.04	0.43±0.04	0.26±0.01	0.19±0.01*

#: p < 0.05 (controls compared to each other); ##: p < 0.01 (controls compared to each other); *: p < 0.05; **: p < 0.01; ***: p < 0.001; Chol. T.: Total cholesterol; HDL: High Density Lipoprotein; LDL: Low Density Lipoprotein ; TPn : Plumpy -fed controls nut ; TG: Pellet-fed controls; n = 6. Batch 1 = 10 mg/kg of Spirulina received, batch 2 = 50 mg/kg and batch 3 = 100 mg/kg of bw; n = 6.

4. DISCUSSION

This study examined the impact of food restriction on the body weight of Wistar rats, confirming the occurrence of malnutrition characterized by a 5% weight loss within one month. All rats exhibited a significant decrease in weight, reflecting endogenous energy reserve mobilization to compensate for caloric deficit. Protein-energy malnutrition, as observed in this study, results in growth retardation, reduced muscle mass, and altered physiological functions (Gonzalez *et al*., 2018). During food deprivation, the body employs adaptive mechanisms to mobilize and conserve energy substrates, ensuring short-term survival (Baverel *et al*., 1995). These mechanisms include lipolysis, proteolysis, and gluconeogenesis, which contribute to maintaining energy homeostasis (López-Pedrosa *et al*., 2020).

A two-week refeeding period led to significant weight gain, particularly in rats receiving Spirulina supplementation at 100 mg/kg body weight. These findings suggest that Spirulina has a beneficial role in nutritional recovery. Indeed, Spirulina, which contains 60-70% protein along with essential amino acids and micronutrients, promotes rapid weight recovery and improved nutritional status (Finamore *et al*., 2017). Our findings align with those of Simpore *et al*., (2005), who demonstrated Spirulina's effectiveness in treating childhood malnutrition, particularly among HIV-infected children. Additionally, recent studies confirm that Spirulina enhances weight recovery and biochemical parameters in animal models of malnutrition (El-Sheekh *et al*., 2020).

Biochemical analyses revealed a significant decrease in glucose and total proteins in malnourished rats. These changes reflect a state of malnutrition, characterized by hypoalbuminemia, hyperglobulinemia, and hypocholesterolemia, which impact blood proteins and lipid parameters. These alterations are typical of protein-energy malnutrition, where the body compensates by mobilizing lipid and protein reserves (Gonzalez *et al*., 2018). After refeeding, most biochemical parameters normalized, confirming the reversibility of malnutrition effects through Spirulina supplementation. The increase in total proteins and lipid stabilization highlight Spirulina's protective role in hepatic and metabolic functions (Finamore *et al*., 2017).

Furthermore, Spirulina has demonstrated hepatoprotective, nephroprotective, and neuroprotective properties, as evidenced by reduced transaminase levels and improved kidney and liver function in renourished rats (Wu *et al*., 2016; El-Sheekh *et al*., 2020). These effects are attributed to its rich antioxidant content, particularly phycocyanin, which reduces oxidative stress and inflammation (Wu *et al*., 2016). The increase in plasma proteins may enhance the availability of amino acids for tissue repair and muscle growth, as suggested by López-Pedrosa *et al*., (2020).

5. CONCLUSION

Ultimately, this study confirms Spirulina's efficacy in nutritional recovery following a malnutrition period by improving biochemical parameters and promoting rapid weight gain.

Our results support its potential use as a dietary supplement in malnutrition treatment, particularly in post-malnutrition recovery contexts.

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