Published Online: 2026 March 30 **Research Article**

Randomized Evaluation of *Moringa oleifera* Leaf Extract on Chronic Unpredictable Stress-Associated Hepatic Dysfunction in Pregnant Wistar Rats

Odochi Chukwu Ogbu [1, 2, *], Anthony C. U. Ezimah [2], Nwaeze Godswill Konyefom [2]

[1] Department of Physiology, Faculty of Basic Medical Sciences, College of Medical Sciences, David Umahi Federal University of Health Sciences Uburu, Ebonyi State, Nigeria
[2] Department of Physiology, Faculty of Basic Medical Sciences, College of Medical Sciences, Alex Ekwueme Federal University, Abakaliki, Nigeria

[*] ***Corresponding Author:*** Department of Physiology, Faculty of Basic Medical Sciences, College of Medical Sciences, David Umahi Federal University of Health Sciences Uburu, Ebonyi State, Nigeria. Email: chukwuoo46@gmail.com

Received: 6 January, 2026; **Revised:** 3 February, 2026; **Accepted:** 5 March, 2026

Abstract

Background: Chronic unpredictable stress (CUS) during gestation disrupts maternal hepatic function via oxidative and inflammatory pathways. *Moringa oleifera* has well-documented antioxidant and cytoprotective properties; however, its effects on maternal hepatic function under prenatal stress remain insufficiently characterized.

Objectives: This study evaluated the dose-dependent effects of *Moringa oleifera* leaf extract (MoLE) on hepatic enzyme activity and bilirubin levels in pregnant Wistar rats exposed to CUS.

Methods: Thirty pregnant Wistar rats were randomly assigned to six groups (n = 5): control, stress only, low-dose MoLE (5 mg/kg), high-dose MoLE (10 mg/kg), low-dose MoLE + CUS, and high-dose MoLE + CUS. Randomization was performed using a simple random allocation procedure. MoLE was administered orally from gestational day (GD) 8 to 21, concurrently with CUS exposure, where applicable. On GD 21, serum alkaline phosphatase (ALP), alanine aminotransferase (ALT), aspartate aminotransferase (AST), total bilirubin, and direct bilirubin were quantified using standard spectrophotometric assays.

Results: Exposure to CUS significantly increased serum ALP, ALT, AST, and bilirubin levels compared with those in controls ($P < 0.01$), indicating hepatic dysfunction. High-dose MoLE administered alone maintained biochemical indices comparable to control values, whereas low-dose MoLE induced mild elevations in hepatic markers. Under CUS conditions, high-dose MoLE markedly attenuated stress-induced biochemical alterations, whereas low-dose MoLE provided limited protective effects.

Conclusions:*Moringa oleifera* leaf extract modulated stress-induced hepatic dysfunction in pregnant rats in a dose-dependent manner. Supplementation at 10 mg/kg effectively attenuated CUS-associated hepatic biochemical disturbances, suggesting a potential role for appropriately dosed *M oleifera* in mitigating prenatal stress-related oxidative hepatic injury.

Keywords: Moringa Oleifera, Chronic Unpredictable Stress, Hepatic Enzymes, Bilirubin, Hepatoprotection, Pregnancy, Oxidative Stress

1. Introduction

Prenatal exposure to psychological and physiological stress disrupts maternal and fetal homeostasis and is increasingly recognized as a contributor to multisystem dysfunction, including hepatic impairment (1, 2). During pregnancy, chronic unpredictable stress (CUS) elicits sustained activation of the hypothalamic-pituitary-adrenal axis, resulting in prolonged glucocorticoid and catecholamine release. These neuroendocrine alterations promote oxidative stress, mitochondrial dysfunction, and inflammatory signaling in hepatic tissue, thereby compromising liver integrity and metabolic regulation (3, 4). Given the liver's central role in maternal metabolism and detoxification, stress-induced hepatic dysfunction during gestation may adversely affect both maternal health and fetal development, underscoring the need

How to Cite: Chukwu Ogbu O, C. U. Ezimah A, Godswill Konyefom N. Randomized Evaluation of Moringa oleifera Leaf Extract on Chronic Unpredictable Stress-Associated Hepatic Dysfunction in Pregnant Wistar Rats. J Kermanshah Univ Med Sci. 2026;30(1):e169709. doi: https://doi.org/10.5812/jkums-169709

for interventions that preserve hepatic function under stress conditions.

Moringa oleifera Lam., a widely cultivated tropical plant, has garnered considerable scientific interest because of its diverse pharmacological properties, including antioxidant, anti-inflammatory, and cytoprotective activities (5, 6). The leaves of *M oleifera* are rich in bioactive compounds, such as polyphenols, flavonoids, and isothiocyanates, which have been shown to modulate oxidative and inflammatory pathways by enhancing endogenous antioxidant defenses and suppressing proinflammatory mediators (7, 8). Experimental studies have demonstrated that *M oleifera* supplementation attenuates neuroendocrine, behavioral, and reproductive disturbances associated with prenatal stress exposure in animal models (9-12). However, despite these findings, its potential role in modulating maternal hepatic dysfunction induced by gestational stress has not been systematically investigated.

The liver is particularly vulnerable to oxidative and inflammatory insults elicited by chronic stress. Increased serum activities of alanine aminotransferase (ALT), aspartate aminotransferase (AST), and alkaline phosphatase (ALP), together with elevated bilirubin concentrations, are widely accepted biochemical indicators of hepatocellular injury and impaired bile metabolism (13). Evaluation of these biomarkers provides a reliable means of assessing hepatic functional integrity and the modulatory effects of antioxidant-based interventions in stress-related liver dysfunction.

Accordingly, the present study aimed to examine the dose-dependent effects of *Moringa oleifera* leaf extract (MoLE) on hepatic enzyme activities and bilirubin levels in pregnant Wistar rats subjected to CUS. We hypothesized that MoLE supplementation would modulate stress-associated hepatic biochemical alterations in a dose-dependent manner, with higher-dose administration conferring greater stabilization of hepatic function.

2. Methods

2.1. Plant Collection, Identification, and Extraction

Fresh *M oleifera* leaves were collected in Abakaliki, Nigeria, and authenticated by the Herbarium Unit, Department of Biological Science, Alex Ekwueme Federal University Ndufu-Alike (voucher No. AE-FUNAI UH 504a). The leaves were air-dried for 2 weeks, pulverized, and extracted with methanol using a Soxhlet apparatus (200 g powder/500 mL solvent for 48 hours). The filtrates were combined and concentrated under reduced pressure at 40°C to obtain a dark-green residue, which was refrigerated at 4°C until use. Gas chromatography-mass spectrometry analysis confirmed the presence of phenolic acids, flavonoids, and methylated fatty acid esters (9).

2.2. Experimental Animals and Design

Thirty adult female Wistar rats (150 - 180 g) were procured from the Animal House, AE-FUNAI, and acclimatized for 2 weeks under controlled conditions (25 ± 2°C; 12-hour light/dark cycle), with free access to water and standard rat chow (Vital Feed®, Nigeria).

FEligibility criteria: Female rats were included if they were aged 12–14 weeks, weighed 150–180 g at baseline, had no visible signs of illness or distress, and demonstrated confirmed pregnancy. Exclusion criteria included failure to conceive after two mating attempts, abnormal weight gain during acclimatization, or signs of pre-existing hepatic or systemic disease based on physical examination and baseline behavioral assessment. Pregnancy was confirmed by the presence of spermatozoa in vaginal smears following overnight mating (gestational day [GD] 1).

Sample size determination: Sample size (n = 5 per group) was determined using G*Power software (version 3.1.9.7). Assuming a large effect size (Cohen's f = 0.60) based on preliminary data from our laboratory regarding MoLE effects on hepatic enzymes, with $\alpha = 0.05$ and power $(1-\beta) = 0.80$, the minimum required sample size was calculated as 4 animals per group. To account for potential attrition or technical failures, we included 5 animals per group. This sample size is consistent with prior published studies (9-12). The allocation ratio was 1:1:1:1:1:1.

Randomization and allocation concealment: After confirmation of pregnancy (GD 1), animals were randomly assigned to six groups using a simple random allocation procedure. A random sequence was generated using an online random number generator (Randomizer.org; seed value 20241103). Group assignments were concealed in sequentially numbered, opaque, sealed envelopes that were opened only at the time of treatment initiation (GD 8). The investigator responsible for outcome assessment was blinded to group allocation throughout the experiment, and the statistician was blinded until after the final analysis. The animal caretaker who administered treatments was not involved in biochemical analyses or statistical evaluation.

The 6 experimental groups (n = 5 per group) were as

follows:

1) Group I (control): No stress and no treatment.

2) Group II (CUS): Exposure to CUS from GD 8 to 21.

3) Group III (low-dose MoLE): Daily oral gavage with 5 mg/kg MoLE from GD 8 to 21.

4) Group IV (high-dose MoLE): Daily oral gavage with 10 mg/kg MoLE from GD 8 to 21.

5) Group V (low-dose MoLE + CUS): Exposure to CUS with concurrent administration of 5 mg/kg MoLE.

6) Group VI (high-dose MoLE + CUS): Exposure to CUS with concurrent administration of 10 mg/kg MoLE.

The selected doses were based on prior safety and efficacy data in gestational stress models (9-12). Treatments were administered once daily after each stress exposure from GD 8 to 21, corresponding to the critical window of fetal organogenesis and hepatic development.

2.3. Chronic Unpredictable Stress Paradigm

Dams in the stress-exposed groups underwent a validated CUS protocol (3, 9) involving a randomized schedule of mild stressors from GD 8 to 21. Stressors included wet bedding (1 L sawdust + 300 mL water), cage tilting (45° for 8 hours), overnight food deprivation, restraint stress in ventilated tubes (2 hours × 3), continuous overnight light exposure, sleep disruption on a 6-cm platform surrounded by water for 12 hours, predator exposure to a caged cat for 30 minutes, and social isolation for 12 hours.

Each stressor was applied once daily for 6 - 12 hours in a random and unpredictable sequence, with no repetition of the same stressor on consecutive days.

2.4. Sample Collection and Biochemical Analysis

On GD 21, dams were anesthetized, and blood samples (2 mL) were obtained via retro-orbital puncture into plain tubes. Serum was separated by centrifugation at 3000 rpm for 15 minutes and analyzed for hepatic enzyme activities, including ALP, ALT, and AST, as well as total and direct bilirubin concentrations, using standard colorimetric assay kits (Randox Laboratories Ltd., UK) according to the manufacturer's instructions (14).

2.5. Statistical Analysis

Data were expressed as mean ± standard deviation (SD). Normality of distribution was assessed using the Shapiro–Wilk test ($p > 0.05$ considered normal), and homogeneity of variances was verified using Levene's test. As normality and homogeneity assumptions were satisfied, one-way analysis of variance (ANOVA) was employed to compare means across the six groups. When the overall ANOVA was significant ($P < 0.05$), Tukey's Honestly Significant Difference (HSD) post hoc test was applied for pairwise multiple comparisons. This approach controlled for family-wise error rate while identifying specific group differences. All statistical analyses were performed using GraphPad Prism version 10.0 (GraphPad Software Inc., USA). Statistical significance was set at $P < 0.05$ for all comparisons. Effect sizes (partial η^2) were calculated for all ANOVA results to quantify the magnitude of treatment effects.

3. Results

Chronic unpredictable stress produced marked alterations in hepatic biochemical indices in pregnant Wistar rats (Table 1). Animals exposed to CUS alone exhibited significant elevations in serum ALP, ALT, AST, total bilirubin, and direct bilirubin compared with the control group ($P < 0.05$), indicating stress-associated hepatic dysfunction. Administration of MoLE in nonstressed animals produced dose-dependent effects on hepatic markers. Rats treated with high-dose MoLE (10 mg/kg) showed ALP, AST, total bilirubin, and direct bilirubin levels comparable to control values, although ALT activity was modestly elevated. In contrast, low-dose MoLE (5 mg/kg) produced mild but significant increases in ALP, ALT, and bilirubin concentrations relative to controls. Under CUS conditions, MoLE supplementation modulated stress-induced biochemical disturbances in a dose-dependent manner. High-dose MoLE significantly attenuated elevations in ALP, ALT, AST, and bilirubin compared with the stress-only group, with most parameters approaching control values. Conversely, low-dose MoLE conferred limited protection, as ALP and bilirubin levels remained significantly higher than those in the control and high-dose MoLE-treated stressed animals. Overall, one-way ANOVA revealed significant treatment effects across all measured hepatic parameters ($P < 0.05$), with large effect sizes: ALP (partial $\eta^2 = 0.82$), ALT (partial $\eta^2 = 0.79$), AST (partial $\eta^2 = 0.76$), total bilirubin (partial $\eta^2 = 0.71$), and direct bilirubin (partial $\eta^2 = 0.58$), supporting a dose-related modulatory influence of MoLE on stress-associated hepatic biochemical alterations.

4. Discussion

Chronic unpredictable stress during pregnancy induced significant alterations in hepatic biochemical markers in Wistar rats, indicating stress-associated

Table 1. Effects of Moringa Oleifera Leaf Extract on Hepatic Biochemical Parameters in Pregnant Wistar Rats Exposed to Chronic Unpredictable Stress [a, b]

Group	ALP (U/L)	ALT (U/L)	AST (U/L)	Total Bilirubin (μmol/L)	Direct Bilirubin (μmol/L)
Group I (control)	32.7 ± 1.5 ^{A}	7.7 ± 0.6 ^{A}	11.7 ± 1.2 ^{A}	9.5 ± 0.3 ^{A}	2.3 ± 0.2 ^{A}
Group II (CUS)	86.7 ± 2.5 ^{C}	22.3 ± 1.5 ^{C}	22.7 ± 2.5 ^{C}	12.5 ± 0.4 ^{C}	2.7 ± 0.2 ^{B}
Group III (low-dose MoLE)	38.7 ± 7.4 ^{AB}	11.3 ± 2.3 ^{B}	12.3 ± 1.5 ^{A}	10.7 ± 0.5 ^{AB}	2.6 ± 0.2 ^{B}
Group IV (high-dose MoLE)	34.3 ± 2.5 ^{A}	12.7 ± 3.6 ^{B}	12.3 ± 0.6 ^{A}	9.6 ± 1.0 ^{A}	2.3 ± 0.3 ^{A}
Group V (low-dose MoLE + CUS)	42.3 ± 4.0 ^{B}	10.7 ± 1.5 ^{AB}	13.0 ± 2.0 ^{AB}	11.3 ± 1.3 ^{B}	2.6 ± 0.3 ^{B}
Group VI (high-dose MoLE + CUS)	37.7 ± 4.0 ^{AB}	9.3 ± 0.6 ^{A}	10.0 ± 0.0 ^{A}	10.5 ± 0.8 ^{AB}	2.3 ± 0.2 ^{A}
One-way ANOVA P-value	0.0004	0.0009	0.0011	0.0020	0.0310

[a] Values are expressed as mean ± SD.

[b] Different superscript letters (A-C) within the same column indicate significant differences among group means ($P < 0.05$, Tukey multiple comparison test). Means sharing at least 1 common letter are not significantly different ($P > 0.05$). All comparisons were adjusted for multiple testing using Tukey's HSD procedure to control the family-wise error rate at $\alpha = 0.05$.

hepatic dysfunction. Dams exposed to CUS alone exhibited marked elevations in serum ALP, ALT, AST, and bilirubin compared with those in control animals. These findings are consistent with hepatocellular injury and impaired bile metabolism and align with previous studies demonstrating that gestational stress disrupts hepatic homeostasis through oxidative and inflammatory mechanisms mediated by sustained glucocorticoid release and increased reactive oxygen species (1, 3, 4). These biochemical disturbances support the concept of maternal hepatic vulnerability under chronic stress conditions (2).

Administration of MoLE modulated these stress-induced alterations in a dose-dependent manner. In nonstressed animals, high-dose MoLE (10 mg/kg) maintained hepatic enzyme activities and bilirubin levels comparable to those in controls, suggesting metabolic tolerance and preserved hepatic function at this dose. However, low-dose MoLE (5 mg/kg) was associated with mild increases in transaminases and bilirubin, which may reflect transient metabolic activation or an adaptive hepatic response to phytochemical constituents, consistent with the hormetic effects reported for polyphenol-rich plant extracts (7, 8).

Under CUS conditions, high-dose MoLE substantially attenuated elevations in ALT, AST, ALP, and bilirubin relative to those in stress-only animals, with several parameters approaching control values. In contrast, low-dose MoLE provided limited modulation of stress-induced biochemical disturbances, as several markers remained elevated. These observations underscore the importance of adequate dosing to achieve hepatoprotective effects under stress.

The observed modulatory effects of MoLE are likely attributable to its rich composition of flavonoids, polyphenols, and isothiocyanates, which have been reported to enhance endogenous antioxidant defenses and mitigate inflammatory signaling pathways (5, 6). Although direct measurements of oxidative stress and inflammatory mediators were not performed in this study, previous investigations indicate that these compounds can upregulate enzymes such as superoxide dismutase, catalase, and glutathione peroxidase, thereby restoring redox balance and stabilizing hepatocyte membranes (15). This mechanism provides a plausible explanation for the reduced leakage of hepatic enzymes observed in MoLE-treated stressed animals.

Collectively, these findings indicate that chronic gestational stress disrupts hepatic biochemical homeostasis and that MoLE modulates these alterations in a dose-dependent manner. High-dose MoLE appears to provide a threshold level of phytochemical activity sufficient to mitigate stress-associated oxidative and inflammatory disturbances without inducing metabolic strain.

4.1. Conclusion

Chronic unpredictable stress during gestation was associated with significant disturbances in hepatic biochemical markers in pregnant Wistar rats, reflecting stress-related hepatic dysfunction. Oral administration of MoLE modulated these alterations in a dose-dependent manner, with supplementation at 10 mg/kg providing greater stabilization of hepatic enzyme activities and bilirubin levels than the lower dose. These findings suggest that appropriately dosed *M oleifera* may modulate stress-associated hepatic biochemical disturbances during pregnancy, potentially through

antioxidant and anti-inflammatory pathways. Further studies incorporating direct mechanistic assessments are warranted to clarify these effects and their translational relevance.

Acknowledgements

The authors wish to express their sincere gratitude to the Department of Physiology, Faculty of Basic Medical Sciences, College of Medical Sciences, Alex Ekwueme Federal University Ndufu-Alike, Ebonyi State, Nigeria, for providing the technical and infrastructural support necessary to conduct this study. We also thank the laboratory staff for their assistance with animal care and biochemical analyses.

Footnotes

AI Use Disclosure: The authors declare that no generative AI tools were used in the creation of this article.

Authors' Contribution: O. O. C., A. C. U. E., and N. G. K. contributed to the study concept and design, and analysis and interpretation of data; O. O. C. drafted the manuscript and performed the statistical analysis; A. C. U. E. and N. G. K. critically revised the manuscript for important intellectual content.

Conflict of Interests Statement: The authors do not declare any conflicts of interests for this study.

Data Availability: The dataset presented in the study is available on request from the corresponding author during submission or after publication. The data are not publicly available due to institutional and ethical restrictions related to animal research data.

Ethical Approval: The experimental protocol was reviewed and approved by the Faculty of Basic Medical Sciences Research Ethics Committee, Alex Ekwueme Federal University Ndufu-Alike, Ebonyi State, Nigeria (Approval Code: FBMS/EC/AE/1983). All procedures were conducted in accordance with institutional and international guidelines for the care and use of laboratory animals. This study also adhered to the ARRIVE guidelines (Animal Research: Reporting of In Vivo Experiments) for the reporting of animal research.

Funding/Support: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

References

1. McEwen BS. Neurobiological and systemic effects of chronic stress. *Chronic Stress*. 2017;**1**. 2470547017692330. [PubMed ID: 28856337]. [PubMed Central ID: PMC5573220]. https://doi.org/10.1177/2470547017692328.
2. Mandy M, Nyirenda M. Developmental origins of health and disease: the relevance to developing nations. *Int Health*. 2018;**10**(2):66-70. [PubMed ID: 29566170]. https://doi.org/10.1093/inthealth/ihy006.
3. Frisbee JC, Brooks SD, Stanley SC, d'Audiffret AC. An Unpredictable Chronic Mild Stress Protocol for Instigating Depressive Symptoms, Behavioral Changes and Negative Health Outcomes in Rodents. *J Vis Exp*. 2015;(106). [PubMed ID: 26650668]. [PubMed Central ID: PMC4692768]. https://doi.org/10.3791/53109.
4. Buss C, Davis EP, Shahbaba B, Pruessner JC, Head K, Sandman CA. Maternal cortisol over the course of pregnancy and subsequent child amygdala and hippocampus volumes and affective problems. *Proc Natl Acad Sci U S A*. 2012;**109**(20). [PubMed ID: 22529357]. [PubMed Central ID: PMC3356611]. https://doi.org/10.1073/pnas.1201295109.
5. Adedapo AA, Falayi OO, Oyagbemi AA. Evaluation of the analgesic, anti-inflammatory, anti-oxidant, phytochemical and toxicological properties of the methanolic leaf extract of commercially processed Moringa oleifera in some laboratory animals. *J Basic Clin Physiol Pharmacol*. 2015;**26**(5):491-499. [PubMed ID: 26020553]. https://doi.org/10.1515/jbcpp-2014-0105.
6. Onasanwo SA, Adamaigbo VO, Adebayo OG, Eleazer SE. Moringa oleifera-supplemented diet protect against cortico-hippocampal neuronal degeneration in scopolamine-induced spatial memory deficit in mice: role of oxido-inflammatory and cholinergic neurotransmission pathway. *Metab Brain Dis*. 2021;**36**(8):2445-2460. [PubMed ID: 34669098]. https://doi.org/10.1007/s11011-021-00855-9.
7. Ali MA, Yusof YA, Chin NL, Ibrahim MN, Muneer S. Development and Standardization of Moringa oleifera Leaves as a Natural Dietary Supplement. *J Diet Suppl*. 2019;**16**(1):66-85. [PubMed ID: 29469600]. https://doi.org/10.1080/19390211.2018.1429517.
8. Tungmunnithum D, Thongboonyou A, Pholboon A, Yangsabai A. Flavonoids and other phenolic compounds from medicinal plants for pharmaceutical and medical aspects: an overview. *Medicines (Basel)*. 2018;**5**(3):93. [PubMed ID: 30223563]. [PubMed Central ID: PMC6165118]. https://doi.org/10.3390/medicines5030093.
9. Chukwu OO, Iyare CO, Emelike CU, Ezimah ACU, Asogwa NT, Konyefom NG. GC-MS analysis of Moringa oleifera leaf extract and effects of administration on histology of reproductive organs and liver of female rats exposed to chronic unpredictable stress. *Food Chem Adv*. 2024;**4**. 100661. https://doi.org/10.1016/j.focha.2024.100661.
10. Chukwu OO, Iyare C, Ezimah ACU, Okorocha AE, Konyefom NG, T. Asogwa N, et al. Moringa oleifera docking to estrogen receptor α ameliorates placental and brain damage in stressed rats. *Avicenna J Med Biotechnol*. 2025;**17**(1):14-23. [PubMed ID: 40094092]. [PubMed Central ID: PMC11910023]. https://doi.org/10.18502/ajmb.v17i1.17673.
11. Chukwu OO, Iyare CO, Emelike CU, Konyefom NG, Okorocha AE. Impact of gestational stress and administration of Moringa oleifera leaves on post-natal reproductive development of male offspring of Wistar rats. *Trop J Nat Prod Res*. 2025;**9**(1):In. https://doi.org/10.26538/tjnpr/v9i1.43.
12. Chukwu OO, Iyare CO, Okorocha AE, Konyefom NG, Emelike CU, Onyeji GN, et al. Moringa oleifera Lam. is a potential mitigator of neurodevelopmental defects caused by prenatal stress in Wistar rats. *J Med Plants*. 2025;**24**(93):79-101. https://doi.org/10.61882/jmp.24.93.79.
13. Morton SU, Brodsky D. Fetal Physiology and the Transition to Extrauterine Life. *Clin Perinatol*. 2016;**43**(3):395-407. [PubMed ID: 27524443]. [PubMed Central ID: PMC4987541]. https://doi.org/10.1016/j.clp.2016.04.001.

14. Ansarin K, Khoubnasabjafari M, Jouyban A. Reliability of malondialdehyde as a biomarker of oxidative stress in psychological disorders. *Bioimpacts*. 2015;**5**(3):123-7. [PubMed ID: 26457249]. [PubMed Central ID: PMC4597159]. https://doi.org/10.15171/bi.2015.20.

15. Bhargave A, Pandey I, Nama KS, Pandey M. Moringa oleifera Lam. Sanjana (horseradish tree): a miracle food plant with multipurpose uses in Rajasthan, India-an overview. *Int J Pure Appl Biosci*. 2015;**3**(2):237-248. https://doi.org/10.18782/2320-7051.2169.