Exploring the Hepatoprotective Mechanisms of *Curcuma longa*: Evidence from Porcine and Human Systems

Nihal Purohit[1], Garima Kalra[1], Sharmin Sultana[1], Varun Asediya[1], Saudeep Karmakar[1], Wojciech Kozera[2], Urszula Czarnik[2], Krzysztof Karpiesiuk[2], Prarthana Sharma[2], Kamila Kibitlewska[2] , Marek Liszowicz[2], Agnieszka Pożarska[2], Malgorzata Ozgo[3], Adam Lepczynski[3], Marta Marynowska[3], Agnieszka Herosimczyk[3], Elżbieta Lichwiarska[3], Brygida Slaska[4], Krzysztof Kowal[4], Angelika Tkaczyk-Wlizło[4], Pawel Grychnik[4], Kaja Ziółkowska[4], Athul P. Kurian[4], Katarzyna Chalaskiwicz[5], Katarzyna kepka-borkowska[5], Ewa Polawska[5], Magdalena Ogluszka[5], Rafal Starzynski[5], Hiroaki Taniguchi[5], Mariusz Pierzchala[5], Avon Augustin Nalpadan[6], Siriluck Wimmers[6], and Klaus Wimmers[6] Chandra Shekhar Pareek[1],

[1]Institute of Veterinary Medicine, Department of Infectious, Invasive Diseases and Veterinary Administration, Faculty of Biological and Veterinary Sciences, Nicolaus Copernicus University, 87-100 Toruń, Poland
[2]Department of Pig Breeding, Faculty of Animal Bio-engineering, University of Warmia and Mazury in Olsztyn, ul. M. Oczapowskiego 5 Str., 10-719 Olsztyn, Poland
[3]Department of Physiology, Cytobiology and Proteomics, West Pomeranian University of Technology, K. Janickiego 32 Str., 71-270 Szczecin, Poland.
[4]Institute of Biological Bases of Animal Production, Faculty of Animal Sciences and Bioeconomy, University of Life Sciences in Lublin, Akademicka 13 Str., 20-950 Lublin, Poland.
[5]Department of Genomics and Biodiversity, Department of Experimental Embryology, Department of Molecular Biology, Institute of Genetics and Animal Biotechnology of the Polish Academy of Sciences, ul. Postepu 36A Str., Jastrzebiec, 05-552 Magdalenka, Poland. [6]Research Institute for Farm Animal Biology (FBN), Wilhelm-Stahl-Allee 2, 18196, Dummerstorf, Germany.

Abstract

Curcuma longa, commonly known as turmeric, is a renowned medicinal herb recognized for its hepatoprotective and gastrointestinal benefits, particularly in counteracting the deleterious effects of poor dietary habits. The principal bioactive compound, curcumin, exhibits significant regulatory potential over gene expression involved in critical biological and metabolic pathways related to detoxification, oxidative stress mitigation, and inflammatory control. Given its multifaceted pharmacological properties, curcumin is increasingly being studied for its molecular mechanisms in the prevention and management of hepatic dysfunction. Transcriptomic analyses are essential to comprehensively understand the hepatoprotective actions of Curcuma longa at the molecular level. Young pigs, due to their highly responsive immune systems and physiological similarities to humans, serve as an ideal model for investigating these effects. In a forthcoming study, immediately following slaughter, a wide array of vital organs and tissue segments were collected from all experimental swine (n = 154), including the liver, kidneys, heart, pancreas, spleen, pituitary gland, stomach (ventriculus), and contents of the gastrointestinal tract (duodenum, jejunum, ileum, cecum, colon), along with blood serum obtained using both heparin and EDTA. Comprehensive haematological and biochemical analyses were performed on blood samples drawn via venipuncture from the external jugular vein (vena jugularis externa) before slaughter and repeated post-mortem. These evaluations encompassed a broad range of parameters, including WBC, RBC, HGB, HCT, MCV, MCH, MCHC, PLT, NEUT, LYM, MONO, EOS, BASO, as well as immunoglobulin classes (IgA, IgE, IgM, IgG), and standard biochemical markers such as TC, HDL, LDL, TG, GLU, ALT, AST, ALP, BIL, and GGTP. Our preliminary findings demonstrated a significant protective effect of CL against AFB1-induced alterations in pigs, specifically reflected in the blood parameters, lymphocyte, and neutrophil counts. Our preliminary results conclude that the genetic and physiological congruence between pigs and humans further underscores the utility of the porcine model in exploring gene expression changes relevant to human health. This enables the identification of therapeutic targets and supports the development of evidence-based interventions for liver diseases. Integrating these findings into modern clinical practice holds promise not only for advancing our understanding of curcumin's protective functions but also for improving outcomes in individuals suffering from chronic hepatic conditions and malignancies that continue to pose significant global health and economic burdens.

Introduction

Curcuma longa, commonly known as turmeric, has long been used in traditional medicine systems such as Ayurveda and Traditional Chinese Medicine for its therapeutic properties, particularly in gastrointestinal and liver-related ailments. The primary active compound of Curcuma longa, curcumin, exhibits pleiotropic biological activity and is known for its ability to modulate various molecular signaling pathways. Key actions include 1) Regulation of Detoxification Enzymes: Curcumin upregulates phase I and phase II detoxifying enzymes, such as cytochrome P450s, glutathione S-transferases (GST), and UDP-glucuronosyltransferases (UGTs), which are vital for the biotransformation and elimination of toxins and xenobiotics, including aflatoxins. 2) Attenuation of Oxidative Stress: It enhances antioxidant defenses by activating the Nrf2–ARE (antioxidant response element) pathway, which upregulates genes encoding antioxidant enzymes like superoxide dismutase (SOD), catalase, and glutathione peroxidase (GPx), thus protecting hepatocytes from reactive oxygen species (ROS)-induced damage. These mechanisms collectively contribute to hepatoprotection, particularly in the context of chemically induced liver injury (e.g., Aflatoxin B1) and diet-related hepatic stress. Given the increasing global burden of chronic liver diseases, there is a growing interest in curcumin as a natural therapeutic agent. However, a comprehensive understanding of its molecular mechanisms, especially through translational animal models such as pigs, is essential for evidence-based application in human health.

Aims and Objectives of Study

- To elucidate the hepatoprotective mechanisms of Curcuma longa at the molecular level
- This study aims to investigate how curcumin, the principal bioactive compound of Curcuma longa, modulates key molecular pathways involved in hepatic protection.
- Specifically, we seek to Identify gene expression changes associated with detoxification, oxidative stress response, and inflammation control.
- Determine curcumin's regulatory impact on hepatic transcriptomic profiles under toxic insult, such as Aflatoxin B1 (AFB1) exposure.Uncover specific biomolecular targets (e.g., transcription factors, enzyme systems) influenced by curcumin that may contribute to hepatic resilience.

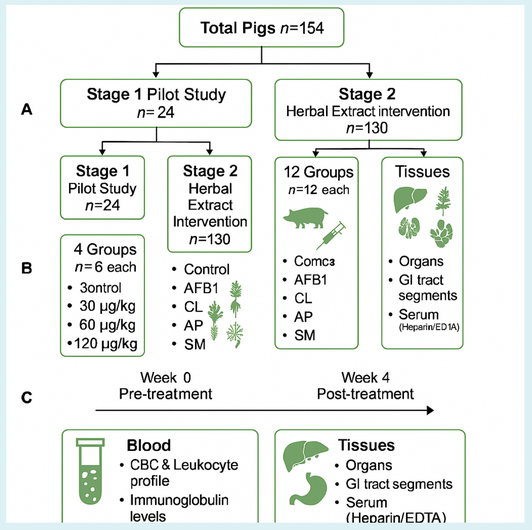
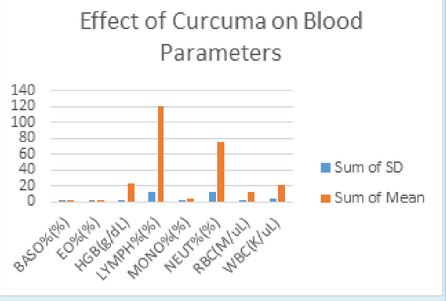


Figure: Schematic overview of the experimental workflow and major findings, highlighting AFB1-induced liver damage, immunological alterations, and the hepatoprotective effects of Curcuma longa *in weaned piglets.*



Sum of Mean	Group	
Parameter	Control	CL
BASO%(%)	0.1	0.09
EO%(%)	0.24	0.49
HGB(g/dL)	2.34	23.08
LYMPH%(%)	13.38	120.37
MONO%(%)	1.23	4.46
NEUT%(%)	13.24	74.59
RBC(M/uL)	1.23	13.43
WBC(K/uL)	3.91	20.93

Table: Hematological comparison showing improved immune and blood parameters in the Curcuma longa *group.*

Results

1. **AFB1-Induced Hepatic Damage**
   - AFB1 exposure caused immune dysregulation: ↓ lymphocytes, ↑ neutrophils.
   - Elevated liver enzymes (ALT, AST, GGTP) indicated hepatocellular injury.
2. **Effects of *Curcuma longa* Supplementation**
   - Restored leukocyte balance (normalized lymphocytes/neutrophils).
   - Reduced liver enzymes (ALT, AST, ALP, GGTP), indicating hepatoprotection.
   - Decreased CRP and improved IgG/IgA profile (if measured).
3. **Transcriptomic Findings**
   - Curcumin upregulated detox genes (Nrf2 pathway: *GSTA1*, *NQO1*, *HO-1*).
   - Downregulated inflammatory markers (NF-κB: *TNF-α*, *IL-6*).
   - Modulated lipid metabolism, suggesting reduced steatosis.

Conclusion

- *Curcuma longa* demonstrates **broad-spectrum hepatoprotective activity** through immunomodulation, antioxidant defense, and detoxification enhancement.
- The use of a well-characterized **porcine model** affirms the relevance and robustness of the experimental outcomes.
- These results underscore the potential of **curcumin as a safe, natural agent** for the **prevention and treatment of liver dysfunction**, warranting further clinical trials and pharmacokinetic evaluations.

ACKNOWLEDGEMENTS:

This research is financed and supported by the scientific project NCN-OPUSLAP (UMO-2021/43/I/NZ9/02612) entitled: Multilevel molecular analysis of the hepatoprotective effect of medicinal herbs extracts in prevention of liver dysfunction caused by aflatoxin B1 in pig as an animal model (in-vivo), and hepatocyte cell culture analysis in human and pig (in-vitro).

NICOLAUS COPERNICUS UNIVERSITY IN TORUŃ
Doctoral Schools

Second Polish RNA Biology Meeting
24-27 June, 2025