URGANCH DAVLAT TIBBIYOT INSTITUTI
JANUBIY OROLBO‘YI TIBBIYOT JURNALI
2 - TOM, 3/1 - SON. 2026
14.00.00 - TIBBIYOT FANLARI   ISSN: 3093-8740

UDC: 616.36-002-099:615.322

THERAPEUTIC POTENTIAL OF GINGER EXTRACT IN MITIGATING SECONDARY IMMUNODEFICIENCY AND HEMATOLOGICAL DYSFUNCTIONS IN A MURINE MODEL OF ACUTE TOXIC HEPATITIS

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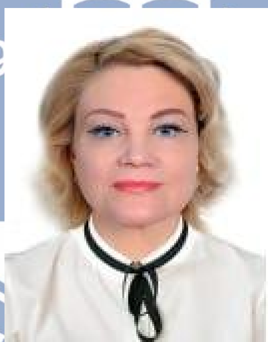

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Abstract

Background: Environmental xenobiotics and various disruptive factors frequently compromise immune system integrity, leading to secondary immunodeficiencies and hematological abnormalities. Plant-based immunomodulators are increasingly recognized for their low toxicity and multifaceted therapeutic potential. This study investigates the immunomodulatory and hematopoietic corrective properties of ginger extract in vivo.

Methods: Acute toxic hepatitis (ATH) was induced in mice via subcutaneous heliotrine administration (3.8 mg/mouse for 3 days). Immunization with sheep red blood cells (SRBCs) was performed on day 4. Ginger extract (0.06 ml/kg and 0.25 ml/kg) or the reference drug Immunomodulin (0.01 ml/kg) was administered intraperitoneally concurrently with SRBCs. Spleen antibody-forming cells (AFCs) and peripheral blood parameters were analyzed.

Results: ATH induced marked immunodeficiency, evidenced by a 4.3-fold reduction in spleen AFCs and a significant drop in peripheral leukocyte counts. Ginger administration (0.25 ml/kg) significantly stimulated immunogenesis, increasing total spleen AFCs by 3.7-fold compared to untreated ATH controls. Furthermore, ginger effectively restored depleted leukocyte populations and stabilized erythrocyte counts, demonstrating efficacy comparable or superior to the reference Immunomodulin.

Conclusion: Ginger acts as a potent natural immunomodulator, effectively mitigating secondary immunodeficiency and correcting peripheral blood dysfunctions associated with acute toxic hepatic injury.

1. Introduction

Recent advancements in clinical disciplines, particularly immunology, indicate that the pathogenesis of numerous contemporary diseases is fundamentally intertwined with systemic immune dysfunction. Emerging research consistently demonstrates that continuous exposure to adverse environmental factors precipitates inevitable disruptions in immune homeostasis, consequently altering the overall immune status of the organism. The immune system is highly susceptible to external damaging agents, serving as a primary target for a vast array of xenobiotics.

Impairments across different immunological cascades contribute to the rising prevalence of autoimmune, allergic, non-infectious, and infectious-inflammatory pathologies. These conditions are typically characterized by rapid progression, a propensity for chronicity, recurrent manifestations, deviations from classical clinical presentations, and frequently, an inadequate response to conventional pharmacotherapy. Consequently, there is an escalating clinical interest in therapeutic agents capable of comprehensively modulating the immune system while addressing the specific magnitude of the underlying immune defect.

Despite significant triumphs in the synthesis of chemical pharmaceuticals, the scientific community maintains a profound interest in phytotherapeutics and their bioactive constituents. Plant-derived agents exhibiting immunotropic activity are particularly valuable for the management of chronic and protracted illnesses. The advent of sophisticated analytical technologies in biology, medicine, and pharmacology has elucidated the unique capacity of phytopreparations to exert comprehensive physiological effects coupled with high efficacy and minimal toxicity. This profile makes them highly suitable not only for therapeutic interventions but also for prophylactic applications. According to the WHO (2019), approximately 130 countries have official programs integrating traditional medicine into their healthcare systems.

Ethnopharmacological studies investigating substances utilized by various cultural groups make substantial contributions to the discovery and refinement of modern therapeutic modalities. Numerous globally utilized herbal medicines are renowned for their anti-infective properties, which operate not solely through direct antimicrobial action, but fundamentally by stimulating the host's innate defense mechanisms. Plant-derived immunomodulators serve as vital alternatives, particularly in cases of compromised immune responses and specific immunosuppression, such as in autoimmune syndromes. In light of recent global health challenges, the application of botanical immunomodulators—including whole plants like betel leaves and turmeric, as well as their biologically active compounds (BACs)—is being rigorously investigated for potential therapeutic roles.

The primary objective of this investigation is to evaluate the dynamics of immunogenesis and hematopoiesis during experimental toxic hepatitis and to determine the potential of the botanical preparation—ginger—in correcting these pathological alterations.

2. Materials and Methods

To construct an in vivo model of acute toxic hepatitis (ATH), experimental mice were subjected to subcutaneous injections of heliotrine for three consecutive days at a dosage of 3.8 mg per animal. Following a four-day interval post-induction, the subjects were immunized via the administration of sheep red blood cells (SRBCs) at a concentration of 2×10^8/ml. Five days subsequent to immunization, the quantitative assessment of antibody-forming cells (AFCs) within the spleen was conducted.

To assess therapeutic efficacy, ginger extract was administered as a single intraperitoneal injection at varying doses concomitantly with the SRBC immunization. To establish a comparative baseline for immunomodulatory effectiveness, an additional cohort of ATH-induced mice received the standard pharmacological agent, Immunomodulin, at a dose of 0.01 ml/kg.

Experimental Group (n=6)	**Drug Dose (ml/kg)**	**Nucleated Spleen Cells (×106/ml)**	**Ratio Index (RI)**	**AFCs per Spleen**	**Ratio Index (RI)**	**AFCs per 106 Splenocytes**	**Ratio Index (RI)**
Intact	-	527.8 ± 14.4	-	7342.0 ± 44.6	-	13.9 ± 0.7	-
Control (ATH)	-	325.7 ± 12.8a	-1.6	1698.0 ± 24.5a	-4.3	5.2 ± 0.3a	-2.7
ATH + Ginger	0.06	432.5 ± 10.3	+1.3	3682.0 ± 16.2a	+2.2	8.5 ± 0.4a	+1.6
ATH + Ginger	0.25	510.2 ± 24.4	+1.6	6335.0	+3.7	12.4 ± 0.5b	+2.4

				± 21.7b			
ATH + Immunomodulin	0.01	492.6 ± 23.3	+1.5	4644.0 ± 26.4b	+2.7	9.4 ± 0.6b	+1.8

3. Results

The experimental data robustly demonstrate that animals afflicted with ATH develop severe secondary immunodeficiency. The quantitative yield of AFCs in the spleens of SRBC-immunized mice subjected to ATH was reduced by a factor of 4.3 compared to the intact cohort.

Table 1: Correction of Immunogenesis by Ginger in Animals with Acute Toxic Hepatitis (ATH) (M±m)

Note: a Statistically significant compared to intact animals; b Statistically significant compared to the ATH control group; (n=6) represents the number of animals per group.

In the cohort receiving a single dose of ginger at 0.06 ml/kg, the humoral immune response to SRBCs amplified 2.2-fold (3682.0 ± 16.2 AFCs) relative to untreated ATH animals. A more profound immunostimulatory effect was achieved with the 0.25 ml/kg dosage, which enhanced splenic antibody genesis 3.7-fold (6335.0 ± 21.7 AFCs). By comparison, the reference pharmaceutical, Immunomodulin, elevated immunogenesis 2.7-fold against the ATH control.

Further analysis of AFC distribution per one million splenocytes revealed that ATH suppressed this metric 2.7-fold (13.9 ± 0.7 in intact vs. 5.2 ± 0.3 in ATH). Ginger administration at 0.06 ml/kg partially recovered this value to 8.5 ± 0.4. Strikingly, the 0.25 ml/kg ginger dosage catalyzed a robust 2.4-fold increase in AFCs per million cells, outperforming Immunomodulin, which yielded a 1.8-fold elevation. Thus, the acquired data indicates that ginger possesses the capacity to correct secondary immunodeficiency in mice with ATH.

Parallel assessments of peripheral blood profiles were conducted for both the ginger and Immunomodulin cohorts.

Table 2: Hematopoiesis Parameters in Animals with Acute Toxic Hepatitis (ATH) (M±m)

Experimental Group (n=6)	**Drug Dose (ml/kg)**	**Erythrocytes (×109/ml)**	**Ratio Index (RI)**	**Leukocytes (×106/ml)**	**Ratio Index (RI)**
Intact	-	7.3 ± 0.04	-	8.4 ± 0.1	-

Experimental Group (n=6)	Drug Dose (ml/kg)	Erythrocytes (×109/ml)	Ratio Index (RI)	Leukocytes (×106/ml)	Ratio Index (RI)
Control (ATH)	-	5.7 ± 0.04a	-1.3	4.1 ± 0.2a	-2.0
ATH + Ginger	0.25	6.9 ± 0.03b	+1.2	8.3 ± 0.2b	+2.0
ATH + Immunomodulin	0.01	7.2 ± 0.02b	+1.3	8.4 ± 0.2b	+2.0

Note: a Statistically significant compared to intact animals; b Statistically significant compared to the ATH control group; (n=6) represents the number of animals per group.

The pathological progression in the liver observably compromised erythropoiesis. However, therapeutic intervention with both ginger and Immunomodulin elicited a modest, yet statistically significant, restoration of circulating erythrocytes.

Leukocytic populations exhibited an even higher vulnerability to the hepatotoxic agent, presenting a twofold depletion in the peripheral blood of ATH mice. A single injection of ginger (0.25 ml/kg) proved highly efficacious, effectively normalizing peripheral white blood cell counts relative to the untreated group. Immunomodulin (0.01 ml/kg) achieved comparable restorative outcomes. Consequently, ginger reliably corrects both secondary immunodeficiency and the formed elements of peripheral blood in ATH models.

4. Conclusions

1. The botanical preparation of ginger possesses substantial corrective properties against secondary immunodeficiency acquired during acute toxic hepatitis in murine models.
2. Therapeutic administration of ginger extract concurrently rehabilitates severe immunodepression and rectifies numerical deficits in peripheral blood formed elements caused by profound hepatotoxic stress.

5. References

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