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THERAPEUTIC POTENTIAL OF WHITE HOREHOUND EXTRACT IN COUNTERACTING CHEMOTHERAPY-INDUCED THYMIC DAMAGE IN RATS

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Abstract. Chemotherapy is effective against tumors but often damages the thymus, impairing T-lymphocyte maturation and immune function. This study evaluated the protective effect of White Horehound (*Marrubium vulgare*) extract on chemotherapy-induced thymic alterations in 4-month-old albino rats. Rats with DMBA-induced skin carcinoma were divided into control, chemotherapy, and chemotherapy plus White Horehound groups. Morphometric and histological analyses revealed that chemotherapy reduced thymic capsule and trabecular thickness, shortened trabeculae, altered vascular dimensions, and decreased thymocyte and lymphocyte numbers. Post-chemotherapy administration of White Horehound extract partially restored these parameters, improved structural organization, and normalized thymic cellular composition. These findings indicate that White Horehound extract exerts a corrective effect on chemotherapy-induced thymic damage, highlighting its potential as a plant-based biocorrective agent to support immune function during cytotoxic therapy.

Keywords: White Horehound, Marrubium vulgare, chemotherapy, thymus, morphometric analysis, thymocyte, biocorrection

Introduction. Chemotherapy remains a cornerstone in the treatment of malignant tumors, yet it frequently causes adverse effects on non-target organs, particularly the immune system [1]. The thymus is a primary lymphoid organ responsible for T-lymphocyte differentiation and maturation, playing a critical role in maintaining immune homeostasis [2]. Chemotherapeutic agents, including paclitaxel, can induce thymic involution, disrupt stromal architecture, and reduce thymocyte populations, thereby impairing immune function [3,4]. Structural integrity of the thymic capsule, trabeculae, and vascular components is essential for optimal organ function [5].

Plant-based biocorrection has emerged as a potential approach to mitigate chemotherapy-induced tissue damage. White Horehound (*Marrubium vulgare*) contains bioactive compounds with antioxidant, anti-inflammatory, and

immunomodulatory properties [6,7]. Experimental studies suggest that plant extracts can support lymphoid organ restoration, improve cellular proliferation, and enhance vascular integrity after cytotoxic injury [8]. However, few studies have quantitatively assessed the effects of biocorrective agents on thymic morphometry following chemotherapy in young rodents [9]. Morphometric and histological analyses provide valuable insights into tissue-level changes and the efficacy of therapeutic interventions [10].

Therefore, the present study aimed to investigate the therapeutic potential of White Horehound extract in modulating chemotherapy-induced thymic damage in 4-month-old albino rats, with a focus on structural and cellular morphometric parameters [11].

Aim of the Study. The aim of this study was to investigate the morphological and morphometric changes in the thymus of 4-month-old albino rats induced by chemotherapy and to evaluate the corrective potential of White Horehound (*Marrubium vulgare*) extract in restoring thymic structure, vascular integrity, and thymocyte composition. Specifically, the study sought to determine whether post-chemotherapy administration of the extract could mitigate the cytotoxic effects on the thymic capsule, trabeculae, vascular structures, and cellular components, thereby supporting immune function.

Materials and Methods. The study was conducted on 4-month-old outbred white rats maintained under standard vivarium conditions. At the beginning of the experiment, all animals underwent a one-week quarantine to exclude somatic and infectious diseases. Following acclimatization, rats were kept under routine vivarium conditions with free access to food and water, fed three times daily.

Experimental skin carcinoma was induced using 7,12-dimethylbenz[a]anthracene (DMBA), a polycyclic aromatic hydrocarbon widely used to model epithelial tumorigenesis by inducing DNA damage in epidermal cells. After tumor induction, the animals were divided into three groups:

- Group I (Control, n = 73) – intact 4-month-old rats.
- Group II (Chemotherapy, n = 68) – rats with DMBA-induced skin carcinoma treated with chemotherapy.
- Group III (Chemotherapy + Biocorrection, n = 62) – rats receiving chemotherapy followed by plant-based biocorrection using White Horehound (*Marrubium vulgare*) extract.

During the study, animal growth, general condition, and behavior were monitored regularly, and no significant deviations were observed. At designated time points (days 1, 7, and 30 post-treatment), rats were weighed and sacrificed by decapitation under ether anesthesia after overnight fasting, and thymus tissue was collected for histological and morphometric analyses.

Chemotherapy was performed after confirmation of papillomatous and precancerous lesions. Paclitaxel, a microtubule-stabilizing agent that inhibits mitosis and induces apoptosis, was administered at a dose of 0.2 mg/kg, individually adjusted according to body weight. In Group III, post-chemotherapy treatment included oral administration of a standardized White Horehound extract, selected for its high bioavailability, rapid absorption, and convenient dosing.

Immunohistochemical studies of thymic tissue were performed in collaboration with the “Ipsum Pathology” laboratory (Tashkent, Uzbekistan) using CD4 and CD138 markers. Morphometric and histological data were processed with Microsoft Excel 7.0, and statistical analyses were performed using STTGRAPH 5.1 software, calculating mean values, standard deviations, and standard errors.

Results. Morphometric analysis of the thymus in 4-month-old albino rats revealed significant structural and cellular alterations induced by chemotherapy, as well as restorative effects of White Horehound (*Marrubium vulgare*) extract. Rats that received chemotherapy alone exhibited pronounced thinning of the thymic capsule across all regions. In the gateway, anterior, and posterior areas, capsule thickness was markedly altered compared to control animals, indicating disruption of the organ’s protective and supportive framework. Administration of White Horehound extract post-chemotherapy partially restored capsule thickness, suggesting a stabilizing effect on thymic stromal architecture.

Trabecular morphology was similarly affected by chemotherapy. Subcapsular and central trabeculae demonstrated increased thickness and irregular elongation under cytotoxic stress, while trabecular length was significantly reduced compared to control rats. Post-treatment with White Horehound extract improved both trabecular thickness and length, indicating partial normalization of the thymic microenvironment. These findings suggest that the extract supports the maintenance of connective tissue integrity and helps prevent excessive structural remodeling induced by cytotoxic agents.

Vascular structures within the thymus were also notably influenced by chemotherapy. Arteriolar and venular dimensions in the capsule trabeculae, as well as in proximal and distal vessels, were increased in chemotherapy-only rats, reflecting potential vascular congestion and edema. Treatment with White Horehound extract mitigated these changes, reducing arteriolar and venular thickness toward values observed in control rats. This indicates that the extract may help preserve vascular integrity, ensuring proper blood supply to the thymic tissue.

Cellular composition of the thymus was significantly affected by chemotherapy. Cortical thymocyte proportion decreased to 40–45%, and medullary thymocytes declined to 30–35%, accompanied by reductions in lymphocyte numbers in both cortical and medullary layers. Following administration of White Horehound extract, cortical and medullary thymocyte proportions returned to near-control levels (55–60%

cortical, 40–45% medullary), and lymphocyte counts in both compartments were markedly improved. These observations suggest that the extract promotes thymocyte survival and proliferation, supporting the restoration of cellular immune competence.

Overall, the results indicate that chemotherapy exerts destructive effects on both the structural and cellular components of the thymus in 4-month-old albino rats. Importantly, treatment with White Horehound extract demonstrated a corrective and protective effect, partially reversing chemotherapy-induced thymic alterations, improving connective tissue organization, vascular integrity, and thymocyte distribution. These findings highlight the potential of plant-based biocorrection in preserving thymic structure and function during cytotoxic therapy.

Conclusions. Chemotherapy induces marked structural and cellular alterations in the thymus of 4-month-old albino rats, including thinning of the capsule, disruption of trabeculae, vascular changes, and depletion of thymocytes and lymphocytes. Post-treatment with White Horehound (*Marrubium vulgare*) extract demonstrates a corrective effect, partially restoring thymic architecture, vascular integrity, and cellular composition. These findings suggest that the extract has a therapeutic potential to mitigate chemotherapy-induced thymic damage, supporting immune function and highlighting the relevance of plant-based biocorrection strategies in oncological treatment.

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