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Commentary

Comments on "*Hypericum perforatum* Alleviates Ovalbumin-Induced Asthma through Downregulating TH2 and Upregulating TH1 Related Parameters in BALB/C Mice"

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In the publication by Rostamabadi *et al.*[1] the efficacy of *Hypericum perforatum* (HP) extract in an animal model of allergic asthma has been investigated. The study involved sensitizing BALB/c mice with ovalbumin to induce asthma, followed by treatment with the HP extract (50, 150, and 300 mg/kg) via intraperitoneal injection. To evaluate the HP efficacy, both histological analyses and cytokine measurements were conducted. The findings indicated that HP significantly alleviated the severity of asthma and reduced inflammatory cell infiltration in the lungs of affected mice. Additionally, HP treatment was associated with increased levels of TH1-associated cytokines (IFN-γ and IL-10) and decreased levels of TH2-associated cytokines (IL-4 and GATA3). They reported that the histological examinations confirmed a reduction in inflammation and an improvement in airway morphology among the treated mice. Overall, the article presents evidence for the use of HP in managing allergic asthma, emphasizing its role in immune modulation.

However, upon critical review of the article, I contend that the study's results are fundamentally flawed. Serious weaknesses affect the interpretation of the findings, particularly regarding the histological reports. The most significant issue is the misidentification of lung tissue. Specifically, figures 2 A-E in the Rostamabadi *et al.*[1] study are purported to depict lung tissue micrographs; however, they actually represented adipose tissue. To clarify this matter, I have included accurately labeled micrographs of lung tissue (Figure 1) which is previously published in the Pharmaceutical Sciences.[2] Additionally, I provide micrographs of adipose tissue (Figure 2) obtained from a mouse sample studied in my lab.

Fat tissue and lung tissue differ significantly in structure and function. Adipose tissue is a specialized form of connective tissue that plays a crucial role in energy homeostasis. In contrast, lung tissue is part of the respiratory system and varies from adipose tissue in terms of structure, cellular composition, and function.[3,4]

Adipose tissue is situated in proximity to various organs and tissues, including muscles, glands, and kidneys; however, it does not exert a direct influence on their physiological functions. Anatomically, the lungs are located within the chest cavity, surrounded by a connective tissue membrane referred to as the pleura. The space between the two lungs, encompassing the mediastinum where the heart and blood vessels are found, contains small amounts of connective and adipose tissue, all of which are separated from the lungs by the pleura.[5] While some adipose tissue near the hilum of the lungs—where the main vessels and bronchi enter and exit—may be in closer proximity to lung tissue, the pleura effectively prevents direct contact between the two. In the study by Rostamabadi *et al.*[1], it appears that during animal sampling, the mediastinal fat was not adequately separated from the lungs and was processed alongside lung tissue. Since histological slides were not examined by a pathologist or histologist, this oversight has led to inaccurate reports regarding lung tissue.

Connective tissue septa and blood vessels are typically present in adipose tissue. As illustrated in Figure 2, the nuclei of adipocytes are displaced by the fat droplets stored within them, positioning them adjacent to the cell membrane. While lung tissue may appear somewhat similar to fat tissue (just looking at the slide with the naked eye), a closer examination at 100x and 400x magnification reveals significant complexities in lung tissue compared to adipose tissue. The walls of the alveoli are rich in blood vessels (Figure 1), and the primary cells constituting the alveolar walls are known as pneumocytes, which exist in two types: type 1 and type 2. Additionally, macrophages are naturally present in lung tissue. In asthma conditions induced by stimulating mouse lungs with agents such as ovalbumin or lipopolysaccharide (LPS), several changes can be observed, including thickening of the alveolar walls, edema, capillary bleeding, and infiltration of lymphocytes into the interstitial tissue and alveoli.[6,7] Notably, none of these pathological changes were reported in the study by Rostamabadi *et al.*[1]

Despite notable progress in the field of molecular biology

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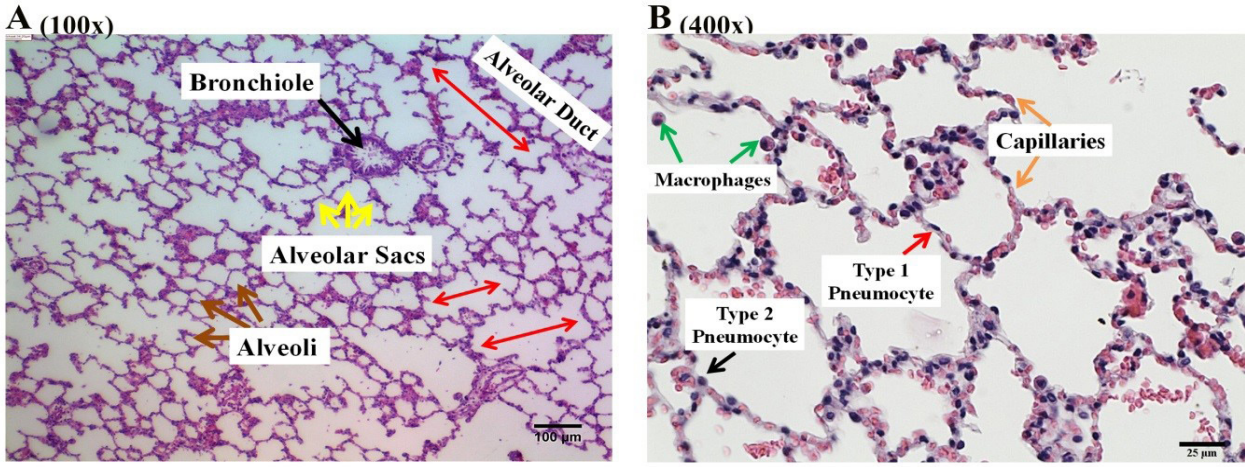

Figure 1. Histological architecture of the lung in BALB/c mice. Micrographs depict the normal histological features of respiratory bronchioles, alveolar ducts, and alveoli at 100X (A) and 400X (B) magnifications. The slide was stained with hematoxylin and eosin. In panel A, the micrograph labels various lung structures, including a bronchiole (black arrow), alveolar ducts (red double-headed arrows), alveolar sacs (yellow arrows), and alveoli (brown arrows). In panel B, microcapillaries within the walls of the alveoli (light brown), macrophages (green arrows), pneumocyte type 1 (red arrow), and pneumocyte type 2 (black arrow) are labeled.[2]

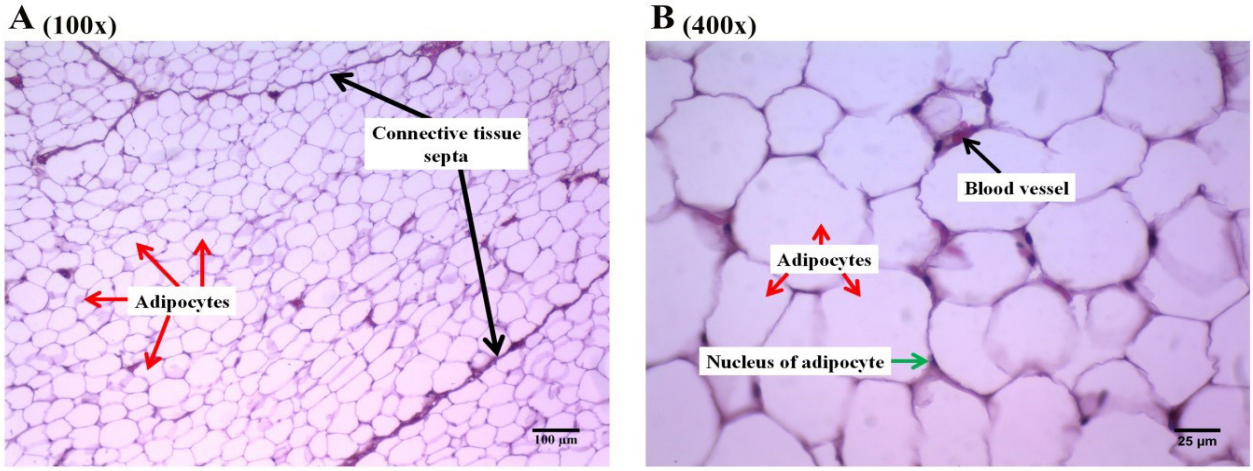

Figure 2. Histological architecture of the white adipose tissue in BALB/c mice. The micrographs exhibit the normal histological features of the white adipose tissue at 100X (A) and 400X (B) magnifications. The slide was stained with hematoxylin and eosin. In panel A, adipocytes (red arrows) and the septa of connective tissue (black arrows) are labeled. In panel B, adipocytes (red arrows), the nucleus of an adipocyte (green arrow), and a blood vessel (black arrow) located between adipocytes are identified.

and the emergence of advanced techniques, histological evaluations continue to serve as a fundamental and conclusive diagnostic approach. Nonetheless, the accuracy of these evaluations may be compromised if they are not performed by qualified professionals, potentially leading to significant diagnostic inaccuracies. This commentary emphasizes the necessity of engaging a pathologist or histologist in studies that incorporate histological assessments.

Author Contributions

Mehran Hosseini: Writing - Original Draft.

Conflict of Interest

There are neither ethical nor financial conflicts of interest involved in the manuscript.

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