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Article

Effect of Silymarin on the Levels of Thyroid Hormones in Rats Induced Hypothyroidism by Propylthiouracil (PTU)

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Abstract: The purpose of this research was to identify any potential protective benefits of silymarin against the thyroid-damaging effects of PTU in male rats, with a focus on antioxidants and thyroid hormones. The following is the breakdown of the six groups comprised of four male rats with an average weight of 190 ± 10 grammes and an age of 90 days: C: For 30 days, 10 male rats in the control group were given distilled water orally. Phase 1: Ten male rats were given PTU (10 mg/kg b.w.) for 30 days. Subject 2: Ten male rats were given silymarin orally at a dosage of 200 mg/kg body weight for a duration of 30 days. T3: 10 male rats were given PTU (10 mg/kg b.w.) and Silymarin (200 mg/kg b.w.) for 30 days. Rats given PTU or silymarin had significantly different thyroid hormone levels, according to the present study. These results show that silymarin may have the ability to regulate thyroid hormone levels in hypothyroidism caused by PTU and imply that there is a complicated interaction between the three factors. To further understand how silymarin works and how long it takes to see results in treating thyroid diseases, more studies are required. Research also shows that silymarin may help with PTU-induced hypothyroidism by increasing GSH levels, decreasing lipid peroxidation, and improving antioxidant enzyme activity. One possible way to combat the oxidative stress that hypothyroidism causes is to take silymarin supplements. To further understand how silymarin works and how long it takes to see results in treating thyroid diseases, more studies are required.

Keywords: PTU, Silymarin, T3, T4, TSH, SOD, GSH

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1. Introduction

Hormones produced by the thyroid gland are essential for maintaining homeostasis, growth, development, and metabolism, among other bodily functions. Significant health consequences, such hypothyroidism or hyperthyroidism, can result from disturbances in thyroid hormone levels [1]. An inhibitor of thyroid hormone production, propylthiouracil (PTU) is frequently used in animal models to intentionally induce hypothyroidism, which is characterised by low thyroid hormone levels [2]. The natural chemical silymarin, found in milk thistle (Silybum marianum), is being studied for its possible medicinal uses. It has properties that protect the liver, reduce inflammation, and act as an antioxidant.

Silimarin may have regulatory effects on thyroid function, according to recent investigations [3]. It has not been thoroughly investigated, however, how silymarin affects thyroid hormone levels in PTU-induced hypothyroidism. It is critically important to understand how silymarin affects hypothyroidism thyroid hormone levels. The possible utility of silymarin as an auxiliary treatment for hypothyroidism can be better understood with a better understanding of these consequences. Furthermore, future research and treatment interventions can be informed by studying the effects of silymarin on thyroid hormone

levels, since this can shed light on the molecular processes that regulate thyroid hormone [4]. So, we're doing this study to find out how silymarin affects thyroid hormone levels in rats that have hypothyroidism caused by PTU. The effects of silymarin on hypothyroidism thyroid function can be better understood by analysing the changes in thyroid hormone levels, which this study will do. Thyroid shape and function in iodine-deficient rats after silymarin administration. The study's authors discovered that taking silymarin supplements raised thyroid hormone levels and strengthened the gland's cellular matrix. According to [5], silymarin may have a protective impact on thyroid function, which might make it a useful treatment for thyroid problems.

The role of silymarin as a protective factor against rat thyroid damage in an experimental setting. Taking silymarins helped the thyroid gland hormone levels and oxidative stress indicators go down, according to the data. Based on these results, silymarin may be useful as a treatment for thyroid problems as it can reduce damage to the thyroid and bring hormone levels back into balance [6]. These new findings provide credence to the idea that silymarin could improve hormone levels and thyroid function. In order to find out how much silymarin to take and for how long for PTU-induced hypothyroidism, more studies are needed to understand the exact processes at work.

2. Materials and Methods

2.1. Study design

The following is the breakdown of the four groups comprised of forty male rats with an average weight of 190 ± 10 grammes and an age of 90 days: C: For 30 days, 10 male rats in the control group were given distilled water orally. Time 1: Ten male rats were given PTU (10 mg/kg b.w.) for 30 days. Group 2: 10 male rats were given silymarin orally at a dosage of 200 mg/kg body weight for a duration of 30 days. T3: 10 male rats were given PTU (10 mg/kg b.w.) and Silymarin (200 mg/kg b.w.) for 30 days. The experimental periods have been accompanied by continuous monitoring of male rats. Male rats were put to sleep with an intraperitoneal injection of 0.3 ml ketamine and 0.1 ml xylazine per kilogram of body weight. After each treatment and control subgroup period, the rats were dissected and blood samples were taken from their abdominal veins using non-heparinized tubes. Prior to analysing the amounts of T3, T4, TSH, MDA, SOD, CAT, and GSH, blood serum samples were isolated by centrifugation at 3000 rpm for 5 minutes and stored at -20 °C.

2.2. Measure of triiodothyronine (T3), tetraiodothyronine (T4) and thyroidstimulating hormone (TSH) and Antioxidants (SOD, GSH, CAT and MDA)

The Hormones T3, T4, and TSH levels using ELISA kits (BioSolar, Beijing, China) in accordance with the manufacturer instructions. The Antioxidants (SOD, GSH, CAT and MDA) levels using Spectrophotometer kits (BioSolar, Beijing, China) in accordance with the manufacturer instructions.

2.3. Statistical analysis

We used SPSS16.0 (SPSS, Inc., Chicago, IL, USA) to analyse all the data. The average ± standard error of at least three separate experiments was used to represent the data from the experiments. To compare the two groups' continuous variables before and after the intervention, we utilised a paired t-test, and to compare the two groups' continuous variables after the intervention, we employed analysis of variance with repeated measures. The connection was examined using the Spearman method. Statistical significance was determined when $P \leq 0.05$.

3. Results

3.1. Hormones profile

The present study's findings indicate a statistically significant decline at (P≤0.05). Regarding the PTU group as comparison to the control group. In contrast to the T1 treated with PTU, the T2 treated with silymarin exhibited a statistically significant rise in T3 and T4 (P≤0.05) in the study. Researchers found that when T3 was treated with a combination of PTU and silymarin, the levels of T3 and T4 hormones were significantly higher compared to T1, and lower compared to T2 and the control group. This difference was statistically significant (P≤0.05). The present study's findings indicate a statistically significant improvement at (P≤0.05). Regarding the PTU group as comparison to the control group. The study found that TSH levels in the T2 group treated with silymarin decreased significantly (P≤0.05) as compared to T1 group treated with PTU. According to the study's findings, the TSH hormone level decreased significantly (P≤0.05) in the T3 group treated with a combination of PTU and silymarin compared to the T1 group, whereas it increased in the T2 and control group.

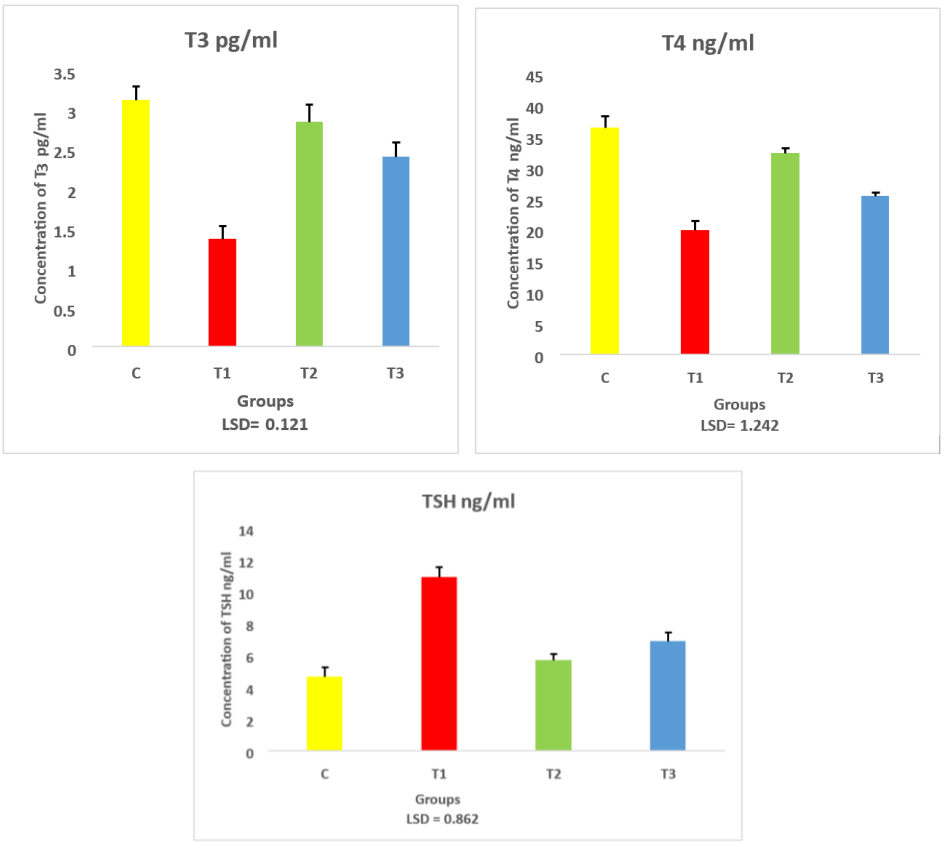

Figure 1. Effect of Silymarin on thyroid hormones in rat induced hypothyroidism by PTU

3.2. Antioxidants status

The present study's findings indicate a statistically significant decline at (P≤0.05). Compared to the control group, the PTU-treated group had higher levels of SOD, GSH, and CAT. The study found that when T2 was treated with silymarin, compared to T1 treated with PTU, there was a substantial increase in SOD, GSH, and CAT (P≤0.05). In contrast to the T1 group, the T3 group treated with a combination of PTU and silymarin had a significantly higher level of the T3 and T4 hormones compared to the control group, and the SOD, GSH, and CAT hormone levels were lower in the T3 group treated with PTU and silymarin compared to the T2 group and the control group, according to the study's results. The present study's findings indicate a statistically significant improvement at (P≤0.05). In the MDA group that received PTU treatment, as opposed to the control group.

The study found that the MDA in the T2 group treated with silymarin decreased significantly (P≤0.05) compared to the T1 group treated with PTU. Researchers found that when T3 was treated with a combination of PTU and silymarin, the MDA hormone level decreased significantly (P≤0.05) compared to T1, and it increased when compared to T2 and the control group.

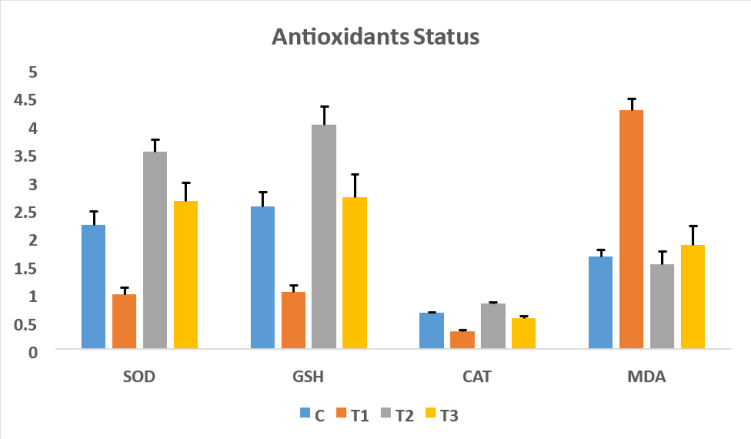

Figure 2. Effect of Silymarin on antioxidants status in rat induced hypothyroidism by PTU

4. Discussion

One famous anti-thyroid medication, PTU, blocks the enzymes thyroid peroxidase and peripheral deiodinase, therefore preventing the body from making thyroid hormones. Similar to what was previously described by [7], we also found that after PTU treatment, serum T3 and T4 levels decreased significantly, TSH levels increased, and body weight decreased, confirming the onset of hypothyroidism. Negative alterations in the histo-architecture of the thyroid gland provided more evidence of hypothyroidism. In order to keep one's weight in check, thyroid hormones are crucial. As a result, the fact that animals lose weight after receiving PTU therapy implies that the procedure interferes with their normally functioning thyroid glands. This confirms what had been seen in rats before [8]. When looking for thyroid problems, serum T3, T4, and TSH levels are the ones to use. There are positive and negative control components that can influence the hypothalamic-pituitary-testis axis.

Norepinephrine, according to studies [9], [10], affects the axis. Scientific studies on white mice have demonstrated that silymarin increases concentrations of norepinephrine, serotonin, and dopamine in their brains [11]. The current study found that an increase in gonadotropin hormone synthesis by the pituitary gland was correlated with an increase in norepinephrine release. This study's higher testosterone heights may be explained by silymarin's central effects on the hypothalamus-pituitary-testis axis, which regulates the production and metabolism of this hormone. Among the most powerful aromatase inhibitors is silymarin [12]. The enzyme aromatase is responsible for converting testosterone into oestrogen. Unintentionally, blocking this enzyme raises testosterone heights [12]. Antioxidant therapy has demonstrated promising outcomes in the treatment of diabetes. Unfortunately, it seems that traditional antioxidants, such as vitamins E and C, are ineffective [13].

Our results show that heights of antioxidant molecules such as catalase and superoxide dismutase were much higher than normal; as a result, we may look into using silymarin to block the mechanisms that cause oxidative stress to develop in diabetes. This provides more evidence that silymarin has the potential to block the process that leads to diabetic problems. As part of this inquiry into the antioxidant defence system, catalase, glutathione, and superoxide dismutase (SOD) were explored. Possible mechanism by which silymarin decreases lipid peroxidation includes elevating blood glutathione heights in the livers of rats that have been administered the compound. An integral part of the

antioxidant defence mechanism in cells, glutathione protects biomolecules from oxidation, detoxifies lipid peroxides and hydrogen peroxide, and neutralises reactive oxygen species [14]. An increase in serum MDA heights was linked to hyperlipidemia, a condition that promotes lipid peroxidation, while a reduction in MDA heights was linked to hypolipidemia, a condition that inhibits lipid peroxidation. So, comparing serum MDA heights in the treatment and control groups is a good way to evaluate silymarin's effectiveness [15]. Because of its effects on free radical load, glutathione (GSH) heights, and superoxide dismutase (SOD) activity, silymarin may be able to keep these two important detoxification pathways from being exhausted. All of the cell's components, including DNA and RNA, are negatively impacted [16].

5. Conclusion

Based on its ability to suppress lipid peroxidation, boost antioxidant levels, and decrease inflammatory and hepatic marker levels, Silymarin is hepato-protective and helpful in hypothyroidism regulation, according to the current data. It is now abundantly obvious from these results that the TSHR receptor may be a therapeutic target for hypothyroidism caused by PTU, and that silymarin may provide an alternate natural agonist for this condition. Based on these new results, we expect that Silymarin may be refined into a powerful medicine to treat hypothyroidism. More research on this topic, particularly on how to standardise dosages, would be beneficial.

REFERENCES

[1] L. F. L. Rizzo, D. L. Mana, and H. A. Serra, "Drug-induced hypothyroidism," *Medicina (Buenos Aires)*, 2017, [Online]. Available: http://www.scielo.org.ar/scielo.php?pid=S0025-76802017000500008&script=sci_arttext

[2] P. N. Taylor, D. Albrecht, A. Scholz, and ..., "Global epidemiology of hyperthyroidism and hypothyroidism," *Nature Reviews …*, 2018, [Online]. Available: https://www.nature.com/articles/nrendo.2018.18

[3] V. Křen and D. Walterová, "Silybin and silymarin-new effects and applications," *Biomed papers*, 2005, [Online]. Available: https://biomed.papers.upol.cz/pdfs/bio/2005/01/02.pdf

[4] C. A. Burgess, *Silybum marianum (milk thistle)*. sid.ir, 2003. [Online]. Available: https://www.sid.ir/paper/532916/en

[5] W. Borymska, M. Zych, S. Dudek, and I. Kaczmarczyk-Sedlak, "Silymarin from milk thistle fruits counteracts selected pathological changes in the lenses of type 1 diabetic rats," *Nutrients*, 2022, [Online]. Available: https://www.mdpi.com/2072-6643/14/7/1450

[6] S. Meng, "Silymarin ameliorates diabetic cardiomyopathy via inhibiting TGF-β1/Smad signaling," *Cell Biol Int*, vol. 43, no. 1, pp. 65–72, 2019, doi: 10.1002/cbin.11079.

[7] M. López-Torres, M. Romero, and G. Barja, "Effect of thyroid hormones on mitochondrial oxygen free radical production and DNA oxidative damage in the rat heart," *Mol Cell Endocrinol*, 2000, [Online]. Available: https://www.sciencedirect.com/science/article/pii/S0303720700003026

[8] E. Pucci, L. Chiovato, and A. Pinchera, "Thyroid and lipid metabolism," *Int J Obes*, 2000, [Online]. Available: https://www.nature.com/articles/0801292

[9] D. J. Selvage and C. A. Johnston, "Interaction between norepinephrine, oxytocin, and nitric oxide in the stimulation of gonadotropin-releasing hormone release from proestrous rat basal hypothalamus …," *J Neuroendocrinol*, 2004, doi: 10.1111/j.1365-2826.2004.01235.x.

[10] J. Całka, "The role of nitric oxide in the hypothalamic control of LHRH and oxytocin release, sexual behavior and aging of the LHRH and oxytocin neurons.," *Folia Histochem Cytobiol*, 2006, [Online]. Available: https://journals.viamedica.pl/folia_histochemica_cytobiologica/article/view/4581

[11] M. Osuchowski, V. Johnson, Q. He, and ..., "Alterations in regional brain neurotransmitters by silymarin, a natural antioxidant flavonoid mixture, in BALB/c mice," *Pharmaceutical …*, 2004, doi: 10.1080/13880200490519712.

[12] H. G. Oufi, N. N. Al-Shawi, and S. A. R. Hussain, "What are the effects of silibinin on testicular tissue of mice?," *Journal of Applied …*, 2012, [Online]. Available: http://japsonline.com/abstract.php?article_id=688

[13] A. Ceriello and R. Testa, "Antioxidant anti-inflammatory treatment in type 2 diabetes," *Diabetes Care*, 2009, [Online]. Available: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2811469/

[14] X. Wu, G. R. Beecher, J. M. Holden, D. B. Haytowitz, and ..., "Hydrophilic Antioxidant Capacities of Common Foods in the United States., 2004, 52," *DOI: https://doi. org/10.1021 …*.

[15] R. Shukla, S. Gupta, J. K. Gambhir, K. M. Prabhu, and ..., "Antioxidant effect of aqueous extract of the bark of Ficus bengalensis in hypercholesterolaemic rabbits," *Journal of …*, 2004, [Online]. Available: https://www.sciencedirect.com/science/article/pii/S0378874104000613

[16] H. Wiseman, "Dietary influences on membrane function: importance in protection against oxidative damage and disease," *J Nutr Biochem*, 1996, [Online]. Available: https://www.sciencedirect.com/science/article/pii/0955286395001522

[17] A. Schuh, "Presentation of Graves' orbitopathy within European Group On Graves' Orbitopathy (EUGOGO) centres from 2012 to 2019 (PREGO III)," *British Journal of Ophthalmology*, vol. 108, no. 2, pp. 294–300, 2023, doi: 10.1136/bjo-2022-322442.

[18] Y. Horie, "Adverse effects of thyroid-hormone-disrupting chemicals 6-propyl-2-thiouracil and tetrabromobisphenol A on Japanese medaka (Oryzias latipes)," *Comparative Biochemistry and Physiology Part - C: Toxicology and Pharmacology*, vol. 263, 2023, doi: 10.1016/j.cbpc.2022.109502.

[19] I. Rani, "An Appraisal on Synthetic and Medicinal Aspects of Fused Pyrimidines as Anti Neoplastic Agents," *Anticancer Agents Med Chem*, vol. 23, no. 5, pp. 525–561, 2023, doi: 10.2174/1871520622666220701113204.

[20] P. Pannetier, "Reversibility of Thyroid Hormone System–Disrupting Effects on Eye and Thyroid Follicle Development in Zebrafish (Danio rerio) Embryos," *Environ Toxicol Chem*, vol. 42, no. 6, pp. 1276–1292, 2023, doi: 10.1002/etc.5608.

[21] S. Alam, "Antidiabetic Phytochemicals From Medicinal Plants: Prospective Candidates for New Drug Discovery and Development," *Front Endocrinol (Lausanne)*, vol. 13, 2022, doi: 10.3389/fendo.2022.800714.

[22] B. Akbari, "The role of plant-derived natural antioxidants in reduction of oxidative stress," *BioFactors*, vol. 48, no. 3, pp. 611–633, 2022, doi: 10.1002/biof.1831.

[23] C. H. Wong, "Effect of Inactivated and mRNA COVID-19 Vaccination on Thyroid Function among Patients Treated for Hyperthyroidism," *Journal of Clinical Endocrinology and Metabolism*, vol. 108, no. 5, 2023, doi: 10.1210/clinem/dgac684.

[24] S. Y. Lee, "Comparison of Propylthiouracil vs Methimazole for Thyroid Storm in Critically Ill Patients," *JAMA Netw Open*, vol. 6, no. 4, 2023, doi: 10.1001/jamanetworkopen.2023.8655.

[25] B. M. Sahoo, "Microwave Induced Green Synthesis: Sustainable Technology for Efficient Development of Bioactive Pyrimidine Scaffolds," *Curr Med Chem*, vol. 30, no. 9, pp. 1029–1059, 2023, doi: 10.2174/0929867329666220622150013.

[26] N. A. N. Hanafy, "Silymarin/curcumin loaded albumin nanoparticles coated by chitosan as muco-inhalable delivery system observing anti-inflammatory and anti COVID-19 characterizations in oleic acid triggered lung injury and in vitro COVID-19 experiment," *Int J Biol Macromol*, vol. 198, pp. 101–110, 2022, doi: 10.1016/j.ijbiomac.2021.12.073.

[27] K. U. Khan, "Overview of nanoparticulate strategies for solubility enhancement of poorly soluble drugs," *Life Sci*, vol. 291, 2022, doi: 10.1016/j.lfs.2022.120301.

[28] A. Chauhan, "Phytochemicals targeting NF-κB signaling: Potential anti-cancer interventions," *J Pharm Anal*, vol. 12, no. 3, pp. 394–405, 2022, doi: 10.1016/j.jpha.2021.07.002.

[29] S. Fakhri, "Modulation of dysregulated cancer metabolism by plant secondary metabolites: A mechanistic review," *Semin Cancer Biol*, vol. 80, pp. 276–305, 2022, doi: 10.1016/j.semcancer.2020.02.007.

[30] J. W. Jang, "KASL clinical practice guidelines for management of chronic hepatitis B," *Clin Mol Hepatol*, vol. 28, no. 2, pp. 276–331, 2022, doi: 10.3350/cmh.2022.0084.