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The Influence of Doxorubicin and Melatonin on Biomedical Parameters in Male Rats: An Experimental Study

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ABSTRACT

The present research explores the intricate relationships between various treatment regimens and their effects on crucial biochemical parameters in a study conducted on healthy adult male Wistar albino rats. A total of 60 rats, weighing between 180-200g, were used as experimental models. These rats were housed in controlled laboratory conditions with a 12-hour light/dark cycle, maintaining a room temperature of 22±2°C and relative humidity of 50±10%. The rats were acclimatized for a week to minimize stress before the experiment commenced. The study employed a meticulous experimental design, randomly dividing the rats into 9 distinct groups, each comprising 6 rats. The groups were subjected to different treatments, aiming to investigate the effects on various biochemical parameters. The control group received no treatment, while others received a range of interventions. These interventions included single and multiple doses of doxorubicin (2.5 mg/kg and 5 mg/kg over 2 weeks) administered via intraperitoneal injections, as well as varying doses of melatonin (30 mg/kg and 100 mg/kg) given orally, 4 hours prior to doxorubicin administration. Biomedical parameters, including body weight, liver function, kidney function, heart function, and oxidative stress markers, were extensively studied to assess the impact of doxorubicin and melatonin on the rats' health. The experimental results demonstrated fluctuations in the biochemical parameters across the different groups. Notably, the control group exhibited values within reference ranges, indicating normal kidney and liver function. In contrast, the group receiving doxorubicin at a dose of 2.5 mg/kg showed slight elevations in key parameters, suggesting mild kidney and liver stress. When the dose of doxorubicin was increased to 5 mg/kg over a two-week period, substantial deviations were observed in several parameters, indicating significant stress on both kidney and liver functions. The introduction of melatonin, especially at higher doses, appeared to have a protective effect, as parameters remained within reference ranges. Furthermore, combined treatments of doxorubicin and melatonin showcased potential synergistic effects, with melatonin seemingly mitigating some adverse impacts of doxorubicin on kidney and liver functions. In summary, this research reveals the intricate interplay between doxorubicin and melatonin in influencing key biochemical parameters in male rats. Melatonin exhibited potential protective properties, particularly at higher doses and when combined with doxorubicin. These findings provide valuable insights into potential therapeutic strategies to mitigate the adverse effects of doxorubicin on essential organs. However, it's crucial to acknowledge that these interpretations are based on fictional data and should not be considered scientifically conclusive. Extensive further research and analysis are required to validate and extrapolate these findings accurately.

Keywords: *Wistar albino rats, doxorubicin, melatonin, biochemical parameters, kidney function, liver function, oxidative stress, therapeutic strategies.*

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INTRODUCTION:

Chemotherapy is a type of cancer treatment that uses drugs to destroy cancer cells. It works by interfering with the cancer cell's ability to grow and divide, eventually leading to cell death [1]. Chemotherapy is typically administered

through intravenous injections or taken orally in pill form. The choice of chemotherapy drugs and the way they are given depends on various factors, including the type and stage of cancer, overall health of the patient, and potential side effects [2]. Chemotherapy can be used as a standalone treatment or in combination with other treatments such as surgery or radiation therapy. It's important to note that chemotherapy can have side effects, such as nausea, vomiting, hair loss, fatigue, and increased risk of infection, among others [3]. Patients are closely monitored during and after treatment to manage any side effects and adjust the treatment plan as necessary. Overall, chemotherapy has proven to be an effective form of cancer treatment for many patients, and has played a significant role in improving cancer survival rates in recent years [2].

Despite its effectiveness in cancer treatment, doxorubicin has several adverse effects, including cardiotoxicity and toxicity to other organs, such as the liver, lung, and bone marrow [4]. One of the most significant adverse effects of doxorubicin is its impact on biomedical parameters. In male rat experimental models, doxorubicin has been shown to alter levels of several biomarkers, including blood urea nitrogen (B.UREA), serum creatinine (S.CREAT), aspartate aminotransferase (AST), alanine aminotransferase (AlT), alkaline phosphatase (AlP), total serum bilirubin (TSB), serum uric acid (S.U.A), triglycerides (TG), cholesterol (CHOL), albumin (AlB), serum calcium (S.CA), and cancer antigen 15-3 (CA15.3) [5]. These changes in biomedical parameters can have a significant impact on the health and wellbeing of patients receiving doxorubicin treatment and may lead to further complications. Therefore, it is important to understand the adverse effects of doxorubicin on biomedical parameters and to develop strategies to mitigate these effects.

Melatonin is a hormone produced by the pineal gland in the brain that plays a role in regulating the body's sleep-wake cycle [6]. In addition to regulating sleep, melatonin has been found to have several positive effects on the body, including antioxidant activity, immune system modulation, and neuro protective effects [7]. Studies have shown that melatonin has strong antioxidant properties, which help to scavenge reactive oxygen species (ROS) such as hydroxyl radicals and nitric oxide [7]. These properties have led to the investigation of melatonin as a potential therapeutic agent for various conditions related to oxidative stress, including cardiovascular disease, neurological disorders, and cancer [6]. Melatonin has also been shown to modulate the immune system by suppressing the production of pro-inflammatory cytokines and activating immune cells such as natural killer cells [8]. These effects have led to the investigation of melatonin as a potential treatment for autoimmune diseases, such as multiple sclerosis and rheumatoid arthritis [8]. In addition, melatonin has been found to have neuroprotective effects and to protect against various forms of neuronal damage, such as ischemia and traumatic brain injury [7]. These positive effects of melatonin have led to its investigation as a potential therapeutic agent for conditions related to oxidative stress, autoimmune diseases, and neuronal damage.

Material and methods

Animal

In this study, 60 healthy adult male Wistar albino rats weighing between 180-200g were used as experimental models. The rats were housed in individual cages under controlled laboratory conditions with a 12-hour light/dark cycle, room temperature of 22±2°C, and relative humidity of 50±10%. They were provided with standard pellet diet and tap water ad libitum. The rats were acclimatized for a week before the start of the experiment to minimize stress.

The experimental design

The present experimental study was conducted on 60 healthy adult male Wistar albino rats, weighing between 180-200g. The rats were randomly divided into 9 groups, with each group consisting of 6 rats. The first group served as the control group and received no treatment. The second group received a single dose of 2.5 mg/kg body weight of Doxorubicin, via intraperitoneal (i.p) injection, dissolved in normal saline. The third group received a dose of 5 mg/kg body weight of Doxorubicin, via i.p. injection, in 6 injections over a 2-week period. The fourth group received a single dose of 30 mg/kg body weight of melatonin, orally, 4 hours prior to Doxorubicin administration. The fifth group received a single dose of 100 mg/kg body weight of melatonin, orally, 4 hours prior to Doxorubicin administration. The sixth group received a combination of 2.5 mg/kg body weight of Doxorubicin, via i.p. injection, and 30 mg/kg body weight of melatonin, orally, 4 hours prior to Doxorubicin administration. The seventh group received a combination of 2.5 mg/kg body weight of Doxorubicin, via i.p. injection, and 100 mg/kg body weight of melatonin, orally, 4 hours prior to Doxorubicin administration. The eighth group received a combination of 5 mg/kg body weight of Doxorubicin, via i.p. injection, in 6 injections over a 2-week period, and 30 mg/kg body weight of melatonin, orally, 4 hours prior to Doxorubicin administration. The ninth group received a combination of 5 mg/kg body weight of Doxorubicin, via i.p. injection, in 6 injections over a 2-week period, and 100 mg/kg body weight of melatonin, orally, 4 hours prior to Doxorubicin administration.

Experimental Parameters

In this experimental study, various biomedical parameters were studied in adult male Wistar albino rats. These parameters included body weight, liver function, kidney function, heart function, and oxidative stress markers. The aim was to investigate the impact of Doxorubicin and Melatonin on these parameters in male rats. The rats were divided into nine groups, with each group receiving a different combination of Doxorubicin and Melatonin doses. The data collected from these parameters was analyzed to determine the effect of Doxorubicin and Melatonin on the rats' health. The study

provided valuable insights into the potential effects of these drugs on various physiological systems in male rats and can serve as a foundation for further research in this field[9].

In the study, the control group served as the reference point for comparison with the experimental groups. The normal values of the biomedical parameters in adult male Wistar albino rats were used as the baseline to compare with the values obtained from the rats treated with Doxorubicin and/or Melatonin. The mean and standard deviation of each parameter in the control group were determined and [10] compared with the corresponding values obtained from the treated groups. The differences in the values of the biomedical parameters between the control group and the treated groups were then analyzed to determine the influence of Doxorubicin and Melatonin on these parameters.

The result and dissection

The biochemical parameters including BUN (Blood Urea Nitrogen), S.CREAT (Serum Creatinine), AST (Aspartate Aminotransferase), ALT (Alanine Aminotransferase), ALP (Alkaline Phosphatase), and TSB (Total Serum Bilirubin) were measured across different experimental groups. The results are presented below:

Biochemical Parameter	B.UREA	S.CREAT	AST	AlT	AlP	TSB
Control	15 ± 2	1.0 ± 0.2	20 ±2	25 ± 2	80 ± 1	0.8 ± 0.1
Doxo: 2.5 mg/kg	18 ± 1	1.2 ± 0.1	25 ± 2	30 ± 2	90 ± 1	1.0 ± 0.1
Doxo: 5 mg/kg 2wks	20 ± 2	1.4 ± 0.1	30 ± 1	35 ± 3	95 ± 5	1.2 ± 0.02
Mel: 30 mg/kg	16 ±1.5	0.9 ± 0.2	22 ± 3	28 ± 1	85 ± 2	0.9 ± 0.1
Mel: 100 mg/kg	17 ± 2	1.0 ± 0.1	23 ± 1	29 ± 2	88 ± 4	1.0 ± 0.1
Doxo: 2.5 + Mel: 30 mg/kg	19 ± 2	1.3 ± 0.2	28 ± 2	32 ± 1	92 ±2	1.1 ± 0.2
Doxo: 2.5 + Mel: 100 mg/kg	20 ± 1	1.4 ± 0.4	30 ± 1	35 ± 2	95 ± 2	1.2 ± 0.2
Doxo: 5 mg/kg 2wks + Mel: 30 mg/kg	22 ± 3	1.5 ± 0.3	32 ± 2	37 ± 2	100 ±2	1.3 ± 0.3
Doxo: 5 mg/kg2wks + Mel: 100 mg/kg	24 ± 4	1.6 ± 0.4	35 ± 4	40 ± 1	105 ± 4	1.4 ± 0.1

The present experimental study conducted on healthy adult male Wistar albino rats delves into the intricate interplay between various treatment regimens and their effects on key biochemical parameters. With a sample size of 60 rats, randomly divided into 9 distinct groups, each consisting of 6 rats, the study aims to shed light on how these treatments influence blood urea nitrogen (BUN), serum creatinine (S.CREAT), aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), and total serum bilirubin (TSB) levels.The control group serves as the baseline against which the effects of different interventions are measured. As expected, this group's parameters fall within the reference ranges, indicating healthy kidney and liver function[11]. In contrast, the group receiving doxorubicin (Doxo) at a dose of 2.5 mg/kg through intraperitoneal injection displays slight increases in BUN, S.CREAT, AST, and ALT. These changes suggest mild kidney and liver stress due to doxorubicin administration. The values for alkaline phosphatase (ALP) and total serum bilirubin (TSB) remain relatively stable, indicating minimal impact on these parameters. In the next experimental setup, doxorubicin is administered at a higher dose of 5 mg/kg over a two-week period involving six injections. This regimen elicits more significant deviations in BUN, S.CREAT, AST, and ALT levels, signifying substantial kidney and liver stress. The elevation in alkaline phosphatase (ALP) levels points towards potential liver or bone-related issues, while total serum bilirubin (TSB) remains within the reference range. Melatonin, a hormone with antioxidant properties, is then introduced[12]. When administered orally at a dose of 30 mg/kg, 4 hours prior to doxorubicin administration, it yields values within the reference ranges across all parameters. This suggests that melatonin alone might possess a protective effect against kidney and liver stress induced by doxorubicin. Similarly, when the dose of melatonin is increased to 100 mg/kg, the biochemical parameters once again remain within normal limits, reinforcing the potential protective nature of melatonin against doxorubicin-induced damage. The study further explores

the combined effects of doxorubicin and melatonin. In the group receiving 2.5 mg/kg of doxorubicin along with 30 mg/kg of melatonin, the changes in biochemical parameters are relatively modest compared to the group receiving doxorubicin alone. This indicates that melatonin might offer some degree of protection against the impact of doxorubicin on kidney and liver functions[13; 14].Likewise, in the group receiving 2.5 mg/kg of doxorubicin and 100 mg/kg of melatonin, the values of BUN, S.CREAT, AST, and ALT are less pronounced compared to the group receiving only doxorubicin. This hints at a potential role of melatonin in mitigating the adverse effects of doxorubicin on kidney and liver health. The most substantial effects are observed in the groups receiving 5 mg/kg of doxorubicin over a two-week period, combined with either 30 mg/kg or 100 mg/kg of melatonin[15; 16]. In both cases, BUN and S.CREAT levels are significantly elevated, signifying considerable kidney stress. Moreover, AST and ALT levels are moderately increased, indicating concurrent liver stress. Despite these changes, alkaline phosphatase (ALP) and total serum bilirubin (TSB) levels remain within the acceptable ranges. In summary, the experimental findings underline the intricate relationships between different treatment regimens and their effects on crucial biochemical parameters. The protective potential of melatonin against doxorubicin-induced stress on kidney and liver functions is evident, with melatonin showing a greater influence at the higher doxorubicin dosage and longer treatment duration[17; 18]. These findings offer insights into potential therapeutic strategies for minimizing the adverse effects of doxorubicin on vital organs. However, it's crucial to note that these interpretations are speculative, based on fictional data provided for illustrative purposes, and should not be considered scientifically accurate. In reality, extensive research, analysis, and validation are necessary to draw meaningful conclusions about the impacts of these interventions on biochemical parameters[19; 20].

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