The Eurasia Proceedings of Science, Technology, Engineering & Mathematics (EPSTEM)
ISSN: 2602-3199

The Eurasia Proceedings of Science, Technology, Engineering & Mathematics (EPSTEM), 2024

Volume 28, Pages 81-89

ICBASET 2024: International Conference on Basic Sciences, Engineering and Technology

Investigation of Oxidative Stress Parameters and Pro-Inflammatory Cytokines in a Neuropathy Model Created with Taraxacum Officinale L. Leaf Extract and Cisplatin

Mehmet Erdem
Gaziantep University

Mehmet Ozaslan
Gaziantep University

Abstract: The aim of this study was to investigate the effect of *Taraxacum officinale* leaf extract, a plant known for its potent antioxidant and anti-inflammatory properties, on cisplatin-induced neurotoxicity. Cancer treatment has demonstrated platinum drugs, particularly cisplatin, as among the most effective treatments. However, the drug comes with serious side effects. The use of cisplatin is limited due to its cytotoxic effects, potentially preventing patients from benefiting optimally from anticancer agents. *Taraxacum officinale* has been used for various diseases for years, observed clinically in conditions such as dyspepsia, liver, gallbladder, and urinary disorders. Nowadays, *Taraxacum officinale* has entered our lives in various forms as a dietary supplement. However, this plant possesses many bioactivities, particularly potent anti-inflammatory, antioxidant, and hepatoprotective properties.In this study, chronic cisplatin administration was used to induce a peripheral neuropathy model, administered intraperitoneally (i.p) once a week for 5 weeks at a dose of 3 mg/kg. *Taraxacum officinale* leaf extract was administered intragastrically once daily at a dose of 500mg/kg for the same duration to determine its potential effects on cisplatin neuropathy. After drug administration, motor performance was evaluated using the rotarod test, while sensory transmission status was assessed using tail withdrawal and hot/cold plate tests. Oxidative stress parameters and proinflammatory cytokine markers were analyzed biochemically. In animals exposed to cisplatin, thermal hypoalgesia and cold hypoalgesia were observed ($p<0.001$), motor coordination balance was prolonged with the rotarod test ($p<0.001$), and tail withdrawal time was extended ($p<0.001$). Biochemically, oxidative stress parameters TOS ($p<0.05$), OSI ($p<0.05$), and MDA ($p<0.05$) levels significantly increased compared to the cisplatin control group. TAS levels provided a statistically significant increase compared to the cisplatin-administered group ($p<0.05$). Proinflammatory cytokine markers TNF-α ($p<0.05$), IL-6 ($p<0.001$), and NFKB ($p<0.05$) levels were found to be higher compared to the cisplatin control group. It was determined that *Taraxacum officinale* improved these side effects induced by cisplatin both behaviorally and biochemically. In conclusion, *Taraxacum officinale* leaf extract is a plant with potent antioxidant and anti-inflammatory activity.

Keywords: Cisplatin neurotoxicity, Taraxacum officinale, Oxidative stress, Proinflammatory

Introductıon

Cancer ranks second among the leading causes of death worldwide, following cardiovascular diseases. Despite the development of new chemotherapy treatment strategies, the disease continues to maintain its significance (Bray et al., 2018). While aggressive treatments have led to increased cancer survival rates, new anticancer drugs often come with serious side effects that may persist for years. Peripheral neuropathy associated with chemotherapy is the most dose-limiting side effect of anticancer agents commonly used in the treatment of

various tumors such as paclitaxel, vincristine, and platinum. Most of these drugs affect the nervous system, with neurotoxicity being one of the most significant side effects (Brown et al., 2019). Cisplatin exhibits neurotoxic effects through various mechanisms, with oxidative stress being one of the most important. Peripheral neuropathy typically manifests as neuropathic pain syndrome characterized by painful symptoms. However, in many severe cases, it can progress to sensory loss. Additionally, motor and/or autonomic peripheral neuropathies can also occur (Brown et al., 2019). Chemotherapy-induced peripheral neuropathy adversely affects the quality of life of patients and may result in dose limitations or even discontinuation of treatment (Miltenburg & Boogerd, 2014). Therefore, patients may not be able to benefit optimally from the effects of anticancer agents. Neurotoxicity is one of the most serious problems associated with cisplatin chemotherapy (McWhinney et al., 2009). Among these, oxidative stress is the most important (Hashem et al., 2015). Additionally, DNA-mediated apoptotic pathways, mitochondrial damage, activation of proinflammatory cytokines, disturbances in ion channels, and glial activation are mechanisms responsible for cisplatin neurotoxicity. Studies have shown that cisplatin administration increases free radical formation and consequently enhances oxidative damage (Areti et al., 2014; Rehman et al., 2019). These findings indicate that oxidative stress plays a significant role in cisplatin toxicity. Consequently, oxidative products such as malondialdehyde and protein carbonyls increase. However, since chronic complications seen in cancers cannot be completely prevented with existing drugs, and there are toxic side effects of existing pharmaceutical treatments and sometimes long-term use leads to the development of tolerance, the importance of herbal medicines as supportive agents has emerged. Many studies have shown that phenolic compounds in plant essential oils exhibit antioxidant activity as a result of their free radical scavenging capacities. Natural antioxidants are thought to be beneficial agents in preventing diseases. Antioxidant substances have strong scavenging activities and the ability to upregulate cellular antioxidant systems. *Taraxacum officinale* is one of the plants with phenolic content that has been used as a herbal medicine for years. When the relationship between chemical content and bioactivity studies is examined, it is determined that phenolic compounds such as luteolin, chicoric acid, and taraxasterol in the composition of T. officinale significantly contribute to anti-inflammatory activity (Park et al., 2011; Piao et al., 2015). It has been observed to have strong antioxidant activity by reducing lipid peroxidation and scavenging free radicals with its rich flavonoid structure (Schütz et al., 2006). It has been recorded to significantly reduce liver toxicity due to its sesquiterpene and various polysaccharides (Mahesh et al., 2010; Park et al., 2010). The antioxidant activity of T. officinale is attributed to phenolic hydroxyl groups and activation of endogenous antioxidant enzymes (Park et al., 2014). Applying *Taraxacum officinale* roots and leaves to rats, in particular, leads to the development of an endogenous antioxidant profile (Kuntz & Kuntz, 2008; Harvey & Ferrier, 2017). Represented by 51 species, the Taraxacum genus of the Asteraceae family includes 16 endemic species in Turkey. The use of the *Taraxacum officinale* L. genus found in the natural flora of our country as a herbal drug from past to present, its herbal properties, and its possibilities of being cultured are important. (Özenirler, 2018). The aim of this study is to investigate the effect of *Taraxacum officinale* leaf extract, a plant known for its potent antioxidant and anti-inflammatory properties, on cisplatin-induced peripheral neuropathy.

Materials and Methods

Plant Collection

Plant Material: The aerial parts of Taraxacum officinale in leafy period were collected from the Gaziantep Region and washed before being dried in the shade.

Extraction Procedure

In the laboratory, the dried plant samples were ground using a laboratory grinder. The powdered sample weighing 50 g of *Taraxacum officinale* leaves was extracted in 1L of ethanol (96%) at room temperature for two weeks. The mixture was occasionally shaken during the waiting period. Afterward, it was filtered (Whatman No. 4 filter). Following the removal of the solvent using a rotary evaporator, the extracts were stored at +4°C in a refrigerator (Colle et al., 2012).

Experimental Animals and Housing Conditions

In this study, 28 male Wistar Albino rats aged 8-10 weeks were used. The experimental animals were obtained from the Gaziantep University Animal Research Center (GAÜNDAM). Male Wistar Albino rats (250-300±5 g) were acclimatized to the environment for 10 days under a 12-hour light/12-hour dark cycle, at a room

temperature of 21±2°C, with 50-60% relative humidity and a ventilation system. Throughout the research period, the animals were fed standard pellet feed and given ad-libitum access to drinking water to control their nutrition. The cages were cleaned daily, and the animals received regular care.

Experimental Model

The neuropathic pain model induced by cisplatin, as described by Han et al. (2014), was used. In the first group (n=7), an equivalent amount of saline solution was injected as the Control group. In the second group, rats were injected with cisplatin at a dose of 3 mg/kg intraperitoneally once a week for 5 weeks. To prevent the development of cisplatin-associated nephrotoxicity, 1 ml of saline solution was simultaneously injected intraperitoneally with cisplatin. In the third group, referred to as the treatment group, *Taraxacum officinale* L. leaf extracts (500mg/kg) were administered intragastrically daily for 5 weeks, along with a single dose of cisplatin (3mg/kg) intraperitoneally once a week for 5 weeks. The fourth group, the positive control, received *Taraxacum officinale* L. leaf extract (500mg/kg) intragastrically daily for 5 weeks. Injections were administered at the same time every week (between 12:00 - 13:00) throughout the 35-day experiment.

In Vivo Experiments

Motor Performance and Coordination Assessment

Rotarod

The Rotarod test is commonly used to measure motor performance and coordination (Ugo Basile, Comerio, Italy). In our experimental protocol, animals were acclimatized to the apparatus and environment before being subjected to the test. The Rotarod test involved gradually increasing the speed from 5 (rpm) to 40 (rpm) over 300 seconds (ramp protocol) (Griffiths et al., 2018). Animals were run on the Rotarod apparatus three times with a 5-minute rest period between each run. The duration each animal remained on the rod was recorded, and the arithmetic mean of three measurements was calculated for each group. The presence of differences between groups was determined, and any significant variations were assessed.

Sensory Evaluation

Hot Plate

In this test, thermal hyperalgesia was evaluated. A floor enclosed with glass or plexiglass cylinders was heated to 55°C as descrided (model 35100, Ugo Basile, Comerio, Italy). The animal was placed on the heated floor, and the time until the animal withdrew its paw was recorded (Animals exhibit stereotypical movements such as paw licking, jumping, paw withdrawal, etc., when experiencing pain). The normal reaction time typically ranges from 5 to 20 seconds, but rats were not allowed to remain on the heated surface for more than 30 seconds to prevent tissue damage (cut-off) (Yamamoto et al., 2002).

Cold Plate

In this test, cold hyperalgesia conditions among groups were evaluated according to (model 35100, Ugo Basile, Comerio, Italy). Its effect was examined at 5°C. The working principle of the cold plate test is similar to the hot plate test. Rats were not allowed to remain on the plate for more than 50 seconds to prevent tissue damage (cut-off) (Sakurai et al., 2009).

Pain Evaluation

Tail Flick

The tail flick test is used to evaluate the central effects of pain threshold (model 37360, Ugo Basile, Comerio, Italy). A photosensor is located beneath the area where the tail is placed. When heat is applied to the tail, the animal withdraws its tail when it feels pain, and this movement is detected by the photosensor. The time from the

onset of heat application to tail withdrawal was recorded. This time was kept less than 10 seconds to prevent the animal from experiencing excessive pain (Singh et al., 2018). The spinal reflex, evaluated as tail withdrawal latency, determines the animal's pain threshold.

Biochemical Analyses

Sampling and Preparation of Samples

After completion of behavioral experiments, blood samples and sciatic nerve samples were taken from each rat for biochemical analyses. Two blood samples were taken from each rat, one in normal biochemical tubes and the other in biochemical tubes containing EDTA. Similarly, two sciatic nerve samples were taken from each rat. These samples would be used in biochemical analyses.

The collected blood samples were centrifuged at 4000 (rpm) for 10 minutes at +4°C to separate serum/plasma. Depending on the parameters to be analyzed, serum/plasma samples were divided into Eppendorf tubes and stored at -80°C until analysis. It was estimated that approximately 5 ml of blood sample would be sufficient for biochemical analyses.

Statistical Analysis of Data

The Shapiro-Wilk normality test was conducted to compare differences between groups and observations concerning the measured data. One-way analysis of variance (ANOVA) was used for normally distributed data, while the Kruskal-Wallis H test was applied for non-normally distributed data. For pairwise comparisons between groups, the Post Hoc Tukey test was used if the data were homogeneously distributed; otherwise, the Games-Howell test was applied for ANOVA. For Kruskal-Wallis, Dunnett (as a Post Hoc test), Tukey, or Duncan tests were used. The results were expressed as mean ± standard deviation. A significance level of $p < 0.05$ was considered in the study.

Results

Evaluation of Motor Coordination and Balance

Rota Rod Results

In the results, the sisplatin group significantly shortened the time spent on the rod compared to the control group ($p < 0.01$). The treatment group significantly extended the shortened time on the rod compared to the sisplatin group ($p < 0.05$).

Sensory Experiments Findings

Hot Plate

According to the hot plate results, the sisplatin group significantly prolonged the time spent on the hot plate compared to the control group ($p < 0.001$). The treatment group significantly reduced the prolonged time in the sisplatin group ($p < 0.001$).

Cold Plate

According to the results on the Cold Plate at 5°C, the sisplatin group significantly prolonged the time spent on the cold plate compared to the control group ($p < 0.001$). The treatment group significantly reduced the prolonged time observed in the sisplatin group ($p < 0.001$).

Pain Experiment Findings

Tail Flick Results

According to the tail flick results, the sisplatin group significantly increased the tail flick latency compared to the control group ($p < 0.001$). The treatment group significantly decreased the prolonged tail flick latency observed in the sisplatin group ($p < 0.001$).

Biochemical Analyses

One-way ANOVA and Tukey's post-hoc test were used for evaluating biochemical analyses. Oxidative stress parameters such as TOS, TAS, OSI, MDA, and proinflammatory markers including NFkB, TNF-α, IL-6 were assessed in the sciatic nerve tissue samples from control, sisplatin, treatment, and positive groups.

According to our results, there was a statistically significant increase in NFkB levels in the sisplatin group compared to the control group ($p < 0.001$), while the treatment group showed a significant decrease compared to the sisplatin-administered groups ($p < 0.05$).

For TNF-α levels, there was a statistically significant increase in the sisplatin group compared to the control group ($p < 0.05$), but the treatment group did not show a significant decrease compared to the sisplatin-administered groups ($p > 0.05$).

IL-6 levels showed a statistically significant increase in the sisplatin group compared to the control group ($p < 0.001$), whereas the treatment group exhibited a significant decrease compared to the sisplatin-administered groups ($p < 0.05$).

MDA levels showed a statistically significant increase in the sisplatin group compared to the control group ($p < 0.001$), while the treatment group showed a significant decrease compared to the sisplatin-administered groups ($p < 0.05$).

TOS and OSI levels showed a statistically significant increase in the sisplatin group compared to the control group ($p < 0.05$). TAS levels showed a statistically significant increase in the treatment group compared to the sisplatin-administered group ($p < 0.05$).

Discussion

Cisplatin is a chemotherapeutic agent used in the treatment of many solid tumors, including colorectal cancer, ovarian cancer, testicular cancer, bladder cancer, esophageal cancer, stomach cancer, and lung cancer. Due to the neurotoxicity caused by cisplatin treatment, effective combat against tumors cannot be achieved if treatment is discontinued or dose-reduced. In this study, we demonstrated that Taraxacum officinale leaf extract reduces the side effects of cisplatin, both behaviorally and biochemically, likely by reducing oxidative stress in the sciatic nerve tissue.

In this study, the motor activity and balance skills of the cisplatin group were significantly impaired by cisplatin. This finding is consistent with previous research findings. Over the course of five weeks, Taraxacum officinale leaf extract (500 mg/kg, i.g) significantly reduced the effects of cisplatin and extended the time spent on the rotarod. Platinum compounds like cisplatin are widely known to cause significant sensory neuropathies, but previous research has also shown a serious impact on the motor system, disrupting motor coordination. The role of Taraxacum officinale leaf extract in correcting motor performance impaired by cisplatin may be associated with its neuroprotective effects. Consequently, Taraxacum officinale leaf extract significantly improved the impaired motor function in this study.

Thermal hyperalgesia was observed in the hot plate tests. The perception of the thermal stimulus on the hot plate decreased after intraperitoneal administration of cisplatin. Thermal hyperalgesia was observed in the cold plate tests. The perception of the thermal stimulus on the cold plate decreased after intraperitoneal administration of cisplatin. Previous studies have reported that cisplatin induces thermal hyperalgesia and cold allodynia in rats. However, there are also studies showing that cisplatin induces thermal hypoalgesia. Taraxacum officinale leaf extract reduced the prolonged paw withdrawal latency in the hot/cold plate test induced by cisplatin and approached the control group averages. According to the tail flick results, the cisplatin group significantly

prolonged the tail withdrawal latency compared to the control group. However, the treatment group significantly reduced the prolonged tail withdrawal latency of the cisplatin group.

Conclusion

The aim of this study was to minimize the neurotoxic effects of cisplatin, an effective chemotherapeutic agent, and to eliminate or reduce the side effects that limit the use of this drug. Traditionally, Taraxacum officinale has been used in the treatment of various diseases and its use has been observed clinically in conditions such as dyspepsia, liver, gallbladder, and urinary disorders. Today, *Taraxacum officinale* has become part of our lives as a food supplement in various forms. However, this plant has many bioactivities, especially strong anti-inflammatory, antioxidant, anticancer, and hepatoprotective properties. Considering its side effects and toxicity, it is seen to not have serious side effects or toxicity. Although it is not naturally found in our country, it is a plant suitable for its culture. In light of this information, it is evaluated that it may be effective in the treatment of common diseases such as cancer, liver, and gallbladder, due to its strong antioxidant, hepatoprotective, and anti-inflammatory effects, if it is converted into herbal medicine form.

Due to the neurotoxicity caused by chemotherapy, effective combat against tumors cannot be achieved when treatment is discontinued or doses are reduced. As a result of this study, the side effects of cisplatin have been partially reduced with the application of Taraxacum officinale leaf extract. Consistent with the literature, Taraxacum officinale leaf extract reduced oxidative stress, decreased the destructive effect of cisplatin, and this effect was confirmed behaviorally and biochemically. Among the significant limitations of this study are the lack of histopathological examination of the sciatic nerve tissue and the lack of mRNA expression of antioxidant enzymes.

Traditionally, oxidative stress has been defined as an imbalance between prooxidants and antioxidants in biological systems. Increased oxidative stress is defined as an imbalance between cellular defense mechanisms and cellular free radical formation, and MDA is considered one of the most important oxidative stress markers (Ince et al., 2010). In this study, we observed that Taraxacum officinale leaf extract significantly reduced the elevated MDA levels in serum and nerve tissue induced by cisplatin.

Taraxacum officinale flowers, leaves, stems, and roots extracts have been evaluated for their antioxidant effects by measuring lipozomal lipid peroxidation induced by Fe+2 and ascorbic acid, either alone or in combination with toxic agents such as CCl4. It has been reported that *Taraxacum officinale* extract exhibited antioxidant effects by reducing lipid peroxidation (Yan et al., 2009).

In another study, it was reported that a mixture of *Taraxacum officinale* and various green leafy vegetables applied to mice exhibited protective effects on hepatocytes in liver tissue by reducing lipid peroxidation (Kim et al., 2009). According to the study by Sumanth and Rana, an extract made from *Taraxacum officinale* roots was administered orally at two different doses, namely 50 and 100 mg/kg. At the dose of 100 mg/kg, a significant decrease in MDA levels compared to the toxicity group was observed ($p<0.01$). Additionally, there was a significant increase in MDA levels when compared to the toxicity group with the control group ($p<0.001$) (Sumanth and Rana, 2006).

You et al. reported that liver damage induced by alcohol toxicity was significantly associated with increased ROS production and lipid peroxidation ($p<0.05$) (You et al.,2010). Furthermore, it was found that the increase in MDA levels in the liver induced by toxicity decreased with the administration of lutein, luteolin-7-O-glucoside, and polyphenols contained in *Taraxacum officinale* (Hagymasi et al., 2000; Popovic et al., 2001).

Park et al. stated that there was a significant increase in MDA levels in the toxicity-induced group compared to the control group ($p<0.05$). Additionally, they observed that the water extract of *Taraxacum officinale* leaves showed a decrease in MDA levels for the dose of 0.5 g/kg compared to the toxicity-induced group, but the dose of 2 g/kg showed a greater decrease ($p<0.05$) (Park et al., 2010).

In our study, we observed a significant increase in MDA levels in both serum ($p<0.05$) and sciatic nerve tissue ($p<0.001$) in the cisplatin-induced neurotoxicity group treated with *Taraxacum officinale* leaf ethanol extract. The treatment group showed a statistically significant decrease in both serum and sciatic nerve tissue compared to groups treated with cisplatin alone ($p<0.05$). These findings are consistent with previous studies. We believe that *Taraxacum officinale* achieves this effect by reducing oxidative stress. Cisplatin-induced neuropathy has been associated with oxidative damage, inflammation, mitochondrial dysfunction, DNA damage, and apoptosis

in nerve system cells. DNA damage caused by cisplatin leads to abnormal protein synthesis and reduces the activity of antioxidant enzymes such as catalase, glutathione peroxidase, and superoxide dismutase. Mitochondrial physiological dysfunction reduces cellular metabolism, increases the production of reactive oxygen species (ROS), and enhances oxidative stress. Increased intracellular ROS production triggers inadequate antioxidant defense, leading to demyelination of peripheral nerve cytoskeleton and sensitization of signal transmission processes. As a result, cisplatin induces structural changes in peripheral nerves by disrupting enzymes, proteins, and lipids, leading to peripheral neuropathy.

In a study involving humans, a combination of seven plants including T. officinale was found to significantly reduce anal bleeding and decrease disease activity in patients with inflammatory bowel disease. Although the etiology of this disease remains unclear, the current treatment is generally aimed at systemic immunosuppression due to the significant feature of damage to the gastrointestinal mucosal layer. It should be noted that a combination of various plant compounds may lead to reduced leukocyte infiltration and mucosal ulceration, which could improve acute colonic inflammation. A herbal medicine with synergistic mechanisms of action inhibited the pro-inflammatory transcription factor NF-kB activity, reduced the expression of COX-2, TNF-a, IL-1, IL-6, and iNOS, and decreased the production of nitric oxide, reactive oxygen species, leukotrienes, and prostaglandins, indicating its potential use as an adjunctive therapy for inflammatory bowel disease (Jackson et al., 2008).

Koh et al. investigated the anti-inflammatory effects of *Taraxacum officinale* methanolic leaf extract and fractions on lipopolysaccharide-stimulated mouse macrophage RAW 264.7 cell line. They found that the extract dose-dependently inhibited LPS-induced production of NO, pro-inflammatory cytokines, and PGE(2). The analysis included the activation of iNOS, COX-2, and mitogen-activated protein kinases, as well as the levels of pro-inflammatory cytokines such as TNF-α, IL-1β, and IL-6. It was found that Taraxacum officinale methanolic leaf extract dose-dependently inhibited NO production, PGE, and pro-inflammatory cytokines such as TNF-α and IL-1β (Koh et al., 2010).

A study investigating the hepatoprotective effects of polysaccharides isolated from *Taraxacum officinale* showed that this plant has hepatoprotective effects through alleviating oxidative damage and triggering anti-inflammatory response. In toxicity-induced studies, polysaccharides found in *Taraxacum officinale* were found to reduce liver damage by regulating iNOS, COX-2, TNF-α, and IL-1 levels (Park et al., 2010).

Another study demonstrated that combined treatment with luteolin and chicoric acid derived from *Taraxacum officinale* reduced cellular nitric oxide (NO) and prostaglandin E2 (PGE2) concentrations synergistically in lipopolysaccharide (LPS)-stimulated RAW 264.7 cells. Additionally, the combined treatment inhibited inducible nitric oxide synthase (iNOS) and cyclooxygenase-2 (COX-2) expression. Furthermore, the combined treatment decreased the levels of pro-inflammatory cytokines such as tumor necrosis factor (TNF)-α and interleukin (IL)-1β. Both luteolin and chicoric acid individually suppressed oxidative stress but did not exhibit any synergistic activity. When applied together, luteolin and chicoric acid inhibited the phosphorylation of NF-κB and Akt, but had no effect on extracellular signal-regulated kinase (ERK), c-Jun NH2-terminal kinase (JNK), and p38. This anti-inflammatory signaling cascade overlapped only with luteolin treatment. The results suggest that luteolin plays a central role in improving LPS-induced inflammatory cascades through inactivation of NF-κB and Akt pathways, and chicoric acid enhances luteolin's anti-inflammatory activity by reducing NF-κB activation (Park et al., 2011a).

In another study, it was found that taraxasterol isolated from T. officinale dose-dependently inhibited nitric oxide (NO), prostaglandin E(2) (PGE(2)), tumor necrosis factor-α, interleukin IL-1β, and IL-6 production in LPS-stimulated RAW 264.7 macrophages. Taraxasterol was shown to prevent the translocation of NF-κB from the cytoplasm to the nucleus induced by LPS. The evaluation showed that taraxasterol inhibited NO, PGE(2), TNF-α, IL-1β, and IL-6 production in a dose-dependent manner, and further studies demonstrated that taraxasterol prevented NF-κB translocation induced by LPS. The results suggest that taraxasterol has an anti-inflammatory effect by inhibiting the NF-κB pathway (Zhang et al., 2012).

According to our findings, *Taraxacum officinale* demonstrated antioxidant activity by reducing levels of pro-inflammatory markers such as NF-κB, TNF-α, and IL-6 in both nerve tissue and serum. These findings are consistent with previous studies. The antioxidant activity of Taraxacum officinale has been demonstrated in previous research as well. Given its potential as a treatment approach in the pathophysiology of oxidative stress in various diseases, Taraxacum officinale is suggested to be utilized to mitigate the adverse effects of chemotherapeutics. It should be noted that in the positive control group, *Taraxacum officinale* did not exhibit any adverse effects in behavioral and biochemical tests.

Scientific Ethics Declaration

The authors declare that the scientific ethical and legal responsibility of this article published in EPSTEM journal belongs to the authors.

Acknowledgements or Notes

* This article was presented as an oral presentation at the International Conference on Basic Sciences, Engineering and Technology (www.icbaset.net) held in Alanya/Turkey on May 02-05, 2024.

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Author Information

Mehmet Erdem
Department of Health Services Vocational School, Gaziantep University, 27310, Gaziantep-Türkiye

Mehmet Özaslan
Department of Biology, Gaziantep University, 27310, Gaziantep-Türkiye
Contact e-mail: *ozaslanmd@gantep.edu.tr*

To cite this article:

Erdem, M. & Ozaslan, M. (2024). Investigation of oxidative stress parameters and pro-inflammatory cytokines in a neuropathy model created with taraxacum officinale L. leaf extract and cisplatin. *The Eurasia Proceedings of Science, Technology, Engineering & Mathematics (EPSTEM), 28,* 81-89.