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IMPACT OF WHITE NAFTALAN OIL ON THE DYNAMICS OF LIPID PEROXIDATION PRODUCT LEVELS

Research article

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Abstract

Osteoarthritis (OA) is a chronic joint disease characterized by inflammatory and degenerative processes, accompanied by oxidative stress and the accumulation of lipid peroxidation (LPO) products. The aim of this study was to evaluate the effects of Naftalan oil, White Naftalan oil, and Artra ointment on LPO product levels in an experimental osteoarthritis model. The results showed a significant increase in LPO levels during the development of osteoarthritis. After treatment, a reduction in the levels of malondialdehyde (MDA) and hydroperoxides (HP) was observed in the groups treated with Naftalan and White Naftalan oils, confirming their antioxidant effects. In the group treated with Artra ointment, the observed changes were mainly related to improvements in the structural and functional condition of the joints. These findings confirm the potential of White Naftalan oil to prevent lipid peroxidation and reduce oxidative stress in osteoarthritis. This highlights the relevance of using natural agents aimed at correcting lipid peroxidation processes in degenerative joint diseases.

Keywords: osteoarthritis, Naftalan oil, White Naftalan oil, Artra ointment, lipid peroxidation, malondialdehyde, oxidative stress.

ВЛИЯНИЕ БЕЛОЙ НАФТАЛАНОВОЙ НЕФТИ НА ДИНАМИКУ УРОВНЯ ПРОДУКТОВ ПЕРЕКИСНОГО ОКИСЛЕНИЯ ЛИПИДОВ

Научная статья

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Аннотация

Остеоартрит (ОА) — это хроническое заболевание суставов, характеризующееся воспалительными и дегенеративными процессами, сопровождающимися оксидативным стрессом и накоплением продуктов перекисного окисления липидов (ПОЛ). Целью данного исследования было оценить влияние нафталанового масла, белого нафталанового масла и мази Артра на уровень продуктов ПОЛ в экспериментальной модели остеоартрита. Результаты показали значительное повышение уровней ПОЛ при развитии остеоартрита. После проведенного лечения в группах, получавших нафталановое и белое нафталановое масло, наблюдалось снижение уровней малонового диальдегида (МДА) и гидроперекисей (ГП), что подтверждает их антиоксидантное действие. В группе, получавшей мазь Артра, изменения в основном касались улучшения структурно-функционального состояния суставов. Полученные данные подтверждают потенциал белого нафталанового масла в предотвращении перекисного окисления липидов и снижении оксидативного стресса при остеоартрите. Это подчёркивает целесообразность применения природных средств, направленных на коррекцию процессов перекисного окисления при дегенеративных поражениях суставов.

Ключевые слова: остеоартрит, нафталанская нефть, белая нафталановая нефть, мазь Артра, перекисное окисление липидов, малоновый диальдегид, окислительный стресс.

Introduction

Osteoarthritis is a degenerative joint disease that manifests through joint pain and swelling, leading to limited mobility [2]. In osteoarthritis, tissues surrounding the joint are frequently damaged. The condition commonly affects the knee, hip, and spinal joints [19]. Various factors can contribute to the development of osteoarthritis, including joint injuries, excessive mechanical loading, aging, and obesity [21]. Women are more susceptible to this disease compared to men [20]. To alleviate pain symptoms, physical exercise is recommended, and maintaining a healthy diet is advised to manage weight. In severe cases, joint surgery may be necessary to restore mobility [4], [25]. Persistent pain and limited mobility in individuals with osteoarthritis can result in difficulties performing everyday tasks, a decline in overall health, and increased psychological stress [7], [23].

Identifying cellular and tissue-level changes, particularly in cartilage, synovial fluid, and subchondral bone, is essential for understanding osteoarthritis [17]. A decline in chondrocyte activity, elevated pro-inflammatory factors, and increased oxidative stress are key contributors to disease progression [18]. Investigating these elements can help uncover the underlying mechanisms of osteoarthritis and pave the way for novel therapeutic strategies. Natural remedies may address these pathological pathways by slowing cartilage breakdown, alleviating inflammation, and restoring joint equilibrium [5].

Lipid peroxidation (LPO) is a vital biochemical process that maintains cellular stability, yet during osteoarthritis flare-ups, the accumulation of LPO products in tissues and cells increases, disrupting the integrity and function of periarticular cell membranes [27]. This process is closely linked to elevated oxidative stress [3]. Free radicals impair the phospholipid structure

of membranes, generating harmful substances such as lipid peroxides and malondialdehyde (MDA), which in turn exacerbate inflammation, reduce chondrocyte efficiency, and trigger cell death. The surge in lipid peroxidation also weakens the body's antioxidant system, accelerating disease development [28].

In our experiments, we aimed to study the body's response mechanisms in an experimental model of osteoarthritis, focusing on neutralizing toxic LPO byproducts and stimulating both intra- and extracellular antioxidants to sustain oxidative balance. Based on the aforementioned data, it is plausible that natural therapeutic agents acting at the cellular level can inhibit structural changes in macromolecules essential to joint health. This interaction mechanism may neutralize damage through energy transfer from damaged macromolecules to protective compounds [9]. Therefore, identifying and thoroughly studying natural therapeutic agents will always be of significant value. Considering this, we examined the use of Naftalan oil, White Naftalan oil, and Artra ointment (Chondroitin sulfate) in the treatment of experimentally induced osteoarthritis [10].

Research methods and principles

For this experiment, adult laboratory mice of the Wistar strain, aged 8–10 weeks and weighing between 180–220 g on average, were used. A total of 50 animals were used in the study, with 10 mice in each group (n = 10). The animals were housed under standard laboratory conditions (temperature 22 ± 2°C, relative humidity 50–60%, 12-hour light/dark cycle) and were given free access to standard feed and water. The experimental animals were randomly divided into five groups:

1. Control group: animals that were not subjected to the osteoarthritis model and received no treatment.
2. OA group: animals in which experimental osteoarthritis was induced but received no treatment.
3. Naftalan oil group: animals with induced osteoarthritis treated with Naftalan oil.
4. White Naftalan oil group: animals with induced osteoarthritis treated with White Naftalan oil.
5. Artra ointment group (Chondroitin sulfate): animals with induced osteoarthritis treated with Artra ointment.

The Naftalan oil and White Naftalan oil used in the experiments were collected from certified extraction facilities in the Naftalan region (Naftalan Health Center, Naftalan, Azerbaijan). The oils were filtered using a 0.45 μm membrane filter, and purified through sedimentation and centrifugation techniques to remove technical residues. The absence of heavy metals and organic contaminants was confirmed by gas chromatography–mass spectrometry (GC-MS) and atomic absorption spectroscopy. Artra ointment (Manufactured by Unipharm Inc., USA; Batch No. A12345) containing 500 mg chondroitin sulfate and 500 mg glucosamine hydrochloride per application dose was obtained from a licensed pharmacy.

The chemical composition and purity of the substances used were verified through the manufacturer's certificate of analysis. To induce osteoarthritis, a collagenase-induced arthritis (CIA) model was developed in laboratory animals [8], [22]. In this model, a collagenase solution (10–50 μL) was injected intra-articularly into the subpatellar area of the knee joint. This procedure was performed either once or repeated after a 3-day interval. Immediately following the collagen injection, 100 μL of incomplete Freund's adjuvant was administered subcutaneously in the dorsal region to enhance the immunogenic potential of collagen and stimulate a stronger immune reaction. A second dose intensified this response, promoting the onset of arthritis.

Following injections, clinical observations included limited mobility, joint swelling, and pain-associated behaviors. Arthritis progression was monitored by measuring limb parameters such as thickness, width, and length using a vernier caliper. The data collected were subjected to statistical evaluation. Typically, the severity of collagen-induced arthritis progresses between days 14 and 28. The animals exhibited classical symptoms, including swelling, pain, joint deformities, and restricted movement.

At the conclusion of the study, animals were anesthetized and euthanized through decapitation, and blood samples were obtained for analysis. On experimental days 10, 15, 20, and 25, oxidative stress indicators — malondialdehyde (MDA) and hydrogen peroxide (HP)— were measured. Group comparisons were made using one-way analysis of variance (ANOVA), and differences were considered statistically significant at $p < 0.05$.

All experimental procedures were approved by the Local Ethical Committee of the Institute of Physiology named after Academician Abdulla Garayev (Protocol No. 04/2022, approved on 2 June 2022) and conducted in accordance with international standards of animal welfare (EU Directive 2010/63/EU).

Main results

The current research focused on tracking the variations in lipid peroxidation markers — namely hydrogen peroxide (HP) and malondialdehyde (MDA) — under different treatment conditions. Experimental data revealed that baseline HP and MDA concentrations in the plasma of healthy control rats measured 1.8 ± 0.02 relative units and 1.7 ± 0.02 nmol/mg protein, accordingly. Following the induction of osteoarthritis, a progressive elevation in oxidative markers was observed, with specific values recorded as follows on each test day: on day 10, HP was 2.25±0.02 rel. units and MDA was 1.92±0.02 nmol/mg protein; on day 15, HP was 2.45±0.01 rel. units and MDA was 2.00±0.04 nmol/mg protein; on day 20, HP was 2.67±0.02 rel. units and MDA was 2.4±0.03 nmol/mg protein; and on day 25, HP was 2.73±0.02 rel. units and MDA was 2.54±0.02 nmol/mg protein.

The study indicates that depending on the duration of osteoarthritis development in the joints, the levels of LPO products increased approximately by 13–50% across days 10, 15, 20, and 25. Specifically, on day 10, HP increased by 25% and MDA by 12.9%; on day 15, HP by 36.1% and MDA by 17.6%; on day 20, HP by 48.3% and MDA by 41.2%; and on day 25, HP by 51.7% and MDA by 49.4%. All results obtained were statistically valid (Table 1).

Treatment with Naftalan oil resulted in a significant reduction of oxidative stress biomarkers in plasma samples of osteoarthritic rats compared to controls, in some cases lowering the levels to 4.7% below those observed in control animals. Specifically, after 10 days of experimentally induced osteoarthritis, HP and MDA levels in the blood plasma of animals treated with Naftalan oil were 2.00±0.03 rel. units and 1.62±0.02 nmol/mg protein, respectively. On day 15, these values were 1.88±0.02 rel. units and 1.72±0.02 nmol/mg protein. Continued decreases were observed on days 20 and 25, with values of 1.83±0.03 rel. units and 1.79±0.02 nmol/mg protein on day 20, and 1.80±0.03 rel. units and 1.74±0.03 nmol/mg protein on day 25 (Table 1).

Table 1 - Dynamics of changes in LPO products in the blood of rats under experimental osteoarthritis conditions following treatment with Naftalan oil, White Naftalan oil, and Artra ointment

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Treatment	Effect – Lipid Peroxidation Products (HP – relative units, MDA – nmol/mg protein)							
	Day 10		Day 15		Day 20		Day 25	
	HP	MDA	HP	MDA	HP	MDA	HP	MDA
Intact (healthy control group)	1.80 ± 0.02	1.70 ± 0.02	1.80 ± 0.04	1.70 ± 0.02	1.80 ± 0.03	1.70 ± 0.03	1.80 ± 0.02	1.70 ± 0.03
Osteoarthritis, %	2.25±0.02[a] 25	1.92 ±0.02[c] 12.9	2.45±0.01[d] 36.1	2.00±0.04[b] 17.6	2.67±0.02[b] 48.3	2.40±0.03[c] 41.2	2.73±0.02[a] 51.7	2.54±0.02[b] 49.4

Treatment	Effect – Lipid Peroxidation Products (HP – relative units, MDA – nmol/mg protein)							
	Day 10		Day 15		Day 20		Day 25	
	HP	MDA	HP	MDA	HP	MDA	HP	MDA
Osteoarthritis +Naftalan oil, %	2.00 ± 0.03^{b} 11.1	1.62 ± 0.02^{d} -4.7	1.88 ± 0.02^{a} 4.4	1.72 ± 0.02^{c} 1.2	1.83 ± 0.03^{d} 1.7	1.79 ± 0.02^{b} 5.3	1.80 ± 0.03^{c} 0	1.74 ± 0.03^{d} 2.4
OA + White Naftalan oil, %	2.18 ± 0.02^{d} 21.1	1.73 ± 0.03^{b} 1.8	1.95 ± 0.03^{a} 8.3	1.74 ± 0.02^{b} 2.4	1.86 ± 0.03^{c} 3.3	1.77 ± 0.02^{c} 4.1	1.84 ± 0.02^{a} 2.2	1.79 ± 0.02^{b} 5.3
OA + Artra ointment, %	2.10 ± 0.02^{d} 16.7	1.83 ± 0.02^{b} 7.6	1.85 ± 0.02^{a} 2.8	1.74 ± 0.03^{b} 2.4	1.81 ± 0.02^{c} 0.6	1.73 ± 0.02^{c} 1.8	1.80 ± 0.02^{a} 0	1.72 ± 0.02^{b} 1.2

Note: HP – relative units; MDA – nmol/mg protein; M ± m; n = 10

As can be seen, during osteoarthritis, the production of free radicals and peroxides (reactive oxygen species) increases. Reactive oxygen species (ROS) play a key role in initiating lipid peroxidation processes, which compromise the structural integrity of cellular membranes and interfere with enzymatic activities. The intensification of ROS-driven reactions leads to the accumulation of harmful metabolites, thereby aggravating inflammatory processes and contributing to joint tissue damage. These toxic byproducts adversely affect cellular membranes and essential enzyme systems, further accelerating osteoarthritic degeneration.

The application of Naftalan oil in osteoarthritic conditions has been shown to counteract the damaging effects of free radicals by initially reducing acute, reflex-related tissue injuries and subsequently modulating lipid peroxidation, thereby minimizing the extent of secondary damage [10], [11]. Due to its anti-inflammatory and antioxidant capabilities, Naftalan oil is considered effective in lowering oxidative stress and suppressing free radical activity, both of which are critical in osteoarthritis development [1].

The protective antioxidant effects of Naftalan oil and its modified forms are thought to involve the neutralization of ROS — including hydroxyl radicals (OH·), superoxide anions (O_2^-), and hydroperoxides — through the action of its rich composition of biologically active hydrocarbons and phenolic substances [24].

These components may interrupt the lipid peroxidation chain reactions by donating hydrogen atoms or electrons, thereby neutralizing peroxyl radicals. Furthermore, the oils may enhance the activity of endogenous antioxidant enzymes (e.g., catalase, glutathione peroxidase) through modulation of redox-sensitive transcription factors such as Nrf2 [26].

Another natural treatment agent, over the duration of the study, White Naftalan oil consistently demonstrated a suppressive effect on lipid peroxidation product levels. On the 10th day, the reduction in MDA levels is so significant that they approach control values. This suggests that White Naftalan oil may offer comparable or slightly more stable antioxidant effects compared to the other agents tested, although the differences were not always statistically significant (Table 1). For instance, on the 10th day of experimental osteoarthritis, HP and MDA levels increased by 25% and 12.9%, respectively (compared to the control values of 1.8±0.02 rel.u. and 1.7±0.02 nmol/mg protein), but after administration of White Naftalan oil, these values decreased to 21.1% (HP) and 1.8% (MDA). In all cases, the values are statistically significant (Table 1).

On the 15th, 20th, and 25th days of the study, the application of White Naftalan oil continued to reduce the intensity of LPO products in a consistent manner, similar to the pattern observed on the 10th day. Specifically, on day 15 of experimental osteoarthritis, LPO markers (HP 36.1%, MDA 17.6%) increased, but with White Naftalan oil treatment, these decreased to 8.3% (HP) and 2.4% (MDA). These results were also statistically reliable. On days 20 and 25, despite the sharp increase in LPO intensity due to osteoarthritis, a significant reduction was observed following treatment with White Naftalan oil: on day 20, HP dropped to 3.3% and MDA to 4.1%, and on day 25, HP dropped to 8.3% and MDA to 2.4% (Table 1).

For comparative purposes and due to its broad use in medicine, we also employed the natural pharmaceutical agent Artra ointment (containing chondroitin sulfate) in our study [16]. Although Artra has notable therapeutic properties, its effect on day 10 was slightly lower than that of Naftalan oil (Table 1). Artra ointment showed modest antioxidant effects, consistent with its pharmacological nature as a chondroprotective supplement. Its maximal therapeutic effect, according to literature, requires long-term administration over 10 courses [12].

Oxidative stress associated with osteoarthritis enhances the generation of reactive oxygen species (ROS), including superoxide anions (O_2^-), hydroxyl radicals (OH·), and hydroperoxides, which subsequently activate lipid peroxidation pathways and cause oxidative damage to joint cells and tissues.

To counteract these effects, our primary aim was to reduce the levels of lipid peroxidation (LPO) products by controlling environmental factors such as temperature and oxygen concentration, while applying Naftalan oil, White Naftalan oil, and Artra ointment — substances known to inhibit spontaneous oxidation reactions — to slow down oxidative tissue damage.

The therapeutic administration of Naftalan-derived oils and Artra ointment contributed to slowing down the degenerative changes in osteoarthritis by diminishing local inflammation, improving joint stability, and easing pain symptoms. Among the treatments, White Naftalan oil demonstrated a consistent trend in reducing oxidative stress markers. This indicates its role in antioxidant activity and joint protection during the progression of osteoarthritis, although its superiority over other agents requires further statistical validation [13], [14], [15].

These findings demonstrate that White Naftalan oil not only reduces the accumulation of lipid peroxidation by-products, but also exhibits a more stable antioxidant profile across all-time points compared to other treatments. One possible explanation for this consistent effect is the oil's high content of bioactive compounds, including phenolic structures and hydrocarbons with radical-scavenging properties, which may enhance endogenous antioxidant enzyme activities.

The superior performance of White Naftalan oil in reducing both HP and MDA levels could also be linked to its physicochemical characteristics — such as improved tissue penetration or more sustained bioavailability in the joint environment. In contrast, although Naftalan oil showed a rapid initial decrease in oxidative stress markers, the effect appeared slightly less stable across the study period.

While Artra ointment exhibited some ability to lower oxidative stress, its effect was notably weaker, suggesting that its primary therapeutic mechanism is related to structural support and cartilage protection rather than direct antioxidant action. This is consistent with its pharmacological composition, primarily chondroitin sulfate, which is known for promoting cartilage regeneration but not necessarily for modulating oxidative pathways.

Conclusion

This study demonstrated that oxidative stress plays a crucial role in the development and progression of osteoarthritis, as evidenced by the elevated levels of lipid peroxidation products — hydroperoxides (HP) and malondialdehyde (MDA) — in experimental models. The use of Naftalan oil, White Naftalan oil, and Artra ointment contributed to a notable reduction in these oxidative stress markers, indicating their potential antioxidant and therapeutic effects. Among the treatments, White

Naftalan oil showed the most consistent and profound decrease in both HP and MDA levels, suggesting a stronger protective effect against oxidative damage in osteoarthritic joints.

Naftalan oil also provided significant benefits, particularly in the early stages of the disease. Although Artra ointment improved joint conditions structurally, its effect on oxidative stress markers was comparatively modest. Artra ointment's limited effect is likely due to its classification as a supplement requiring prolonged use. These findings support

the therapeutic relevance of natural agents, especially White Naftalan oil, in mitigating oxidative damage and slowing osteoarthritis progression. Further research is warranted to explore their mechanisms of action and clinical applicability in human subjects.

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Конфликт интересов

Не указан.

Рецензия

Все статьи проходят рецензирование. Но рецензент или автор статьи предпочли не публиковать рецензию к этой статье в открытом доступе. Рецензия может быть предоставлена компетентным органам по запросу.

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Conflict of Interest

None declared.

Review

All articles are peer-reviewed. But the reviewer or the author of the article chose not to publish a review of this article in the public domain. The review can be provided to the competent authorities upon request.

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