МІНІСТЕРСТВО ОСВІТИ І НАУКИ УКРАЇНИ

УКРАЇНСЬКИЙ ЖУРНАЛ
МЕДИЦИНИ, БІОЛОГІЇ ТА СПОРТУ

Том 9, №4

Заснований у 2016 р.
Видається 4 рази на рік

Миколаїв
2024

УДК 57;60;61;796

ISSN 2415-3060
e-ISSN 2522-4972

Співзасновники:
Чорноморський національний університет ім. Петра Могили
Харківський національний медичний університет
Херсонський державний університет
Національний медичний університет ім. О.О. Богомольця
ТОВ «Наукові журнали»

Видавець: ТОВ «Наукові журнали»

Рекомендовано до друку та поширення
через мережу Інтернет Вченою радою
Чорноморського національного університету ім. Петра Могили
(протокол № 11 від 26 грудня 2024 р.)

Ідентифікатор медіа – R30-02423.
Рішення Національної ради України з питань телебачення і радіомовлення № 249,
протокол № 4 від 01.02.2024 р.

Журнал входить до Переліку наукових фахових видань України
Категорія «Б». Галузі наук: біологічні, медичні, фізичне виховання та спорт.
Спеціальності: 017 – фізична культура і спорт; 091 – Біологія; 221 – Стоматологія; 222 – Медицина,
224 – Технології медичної діагностики та лікування, 226 – Фармація, промислова фармація,
227 – Фізична терапія, ерготерапія, 228 – Педіатрія, 229 – Громадське здоров'я
(Наказ МОН України від 15 жовтня 2019 року № 1301)

Журнал представлено у міжнародних наукометричних базах даних,
репозитаріях та пошукових системах: Crossref, Google Scholar, Polska Bibliografia Naukowa, Національна бібліотека України імені В. І. Вернадського (НБУВ), OUCI, BASE, Ulrichsweb Global Serials Directory, Professional Publications of Ukraine, Elektronische Zeitschriftenbibliothek (EZB), University of Oslo Library, German Union Catalogue of Serials (ZDB), Leipzig University Library

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MINISTRY OF EDUCATION AND SCIENCE OF UKRAINE

UKRAINIAN JOURNAL
OF MEDICINE, BIOLOGY AND SPORTS

Volume 9, No. 4

Established in 2016
Issued 2 times a year

Mykolaiv
2024

UDC 57;60;61;796

ISSN 2415-3060
e-ISSN 2522-4972

Co-founders:
Petro Mohyla Black Sea National University
Kharkiv National Medical University
Kherson State University, Kherson
Bogomolets National Medical University
LLC "Scientific Journals"

Publisher: LLC "Scientific Journals"

Recommended for printing and distribution
via the Internet by the Academic Council
Petro Mohyla Black Sea National University
(Minutes No. 11 of December 26, 2024)

State Registration:
Media identifier R30-02423.
Decision of the National Council of Television and Radio Broadcasting of Ukraine No. 249,
Minutes No. 4, dated 01.02.2024.

The journal is included in the list of Professional Scientific Publications of Ukraine Category "B"
Specialities: 1014 – Sports, 0511 – Biology, 0911 – Dental studies, 0912 – Medicine,
0914 – Medical diagnostic and treatment technology, 0512 – Biochemistry, 0916 – Pharmacy,
0915 – Therapy and rehabilitation, 1021 – Community sanitation
(Order of the Ministry of Education and Science of Ukraine No. 1301, dated 15.10.2019)

The journal is presented international scientometric databases, repositories and scientific systems: Crossref, Google Scholar, Polska Bibliografia Naukowa, National Library of Ukraine after V.I. Vernadskiy (VNLU) OUCI, BASE, Ulrichsweb Global Serials Directory, Professional Publications of Ukraine, Elektronische Zeitschriftenbibliothek (EZB), University of Oslo Library, German Union Catalogue of Serials (ZDB), Leipzig University Library

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UKRAINIAN JOURNAL
OF MEDICINE, BIOLOGY AND SPORTS
Volume 9, No. 4. 2024

Journal homepage: https://uajmbs.com.ua/en
Article's History: Received: 21.08.2024; Revised: 01.11.2024; Accepted: 26.12.2024

UDC 612.172:612.176:612.4:612.826.33:611.73
DOI: 10.63341/ujmbs/4.2024.08

Effect of melatonin on heart rate variability in rats with adrenaline-induced myocardial dystrophy

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Abstract. The pineal hormone melatonin actively regulates the body's adaptive reactions to changes in external environmental conditions and internal homeostasis. Melatonin, as a pharmacological agent with antioxidant properties, is widely used to correct disorders resulting from oxidative stress. The present study aimed to investigate changes in cardiac activity under the influence of this hormone, in particular, the effect of melatonin on heart rate variability in laboratory rats with a model of adrenaline-induced myocardial dystrophy. The degree of regulatory tension and neural control mechanisms and mechanisms of nervous regulation was assessed by mathematical analysis of heart rate variability, which is one of the integrative methods for evaluating the functional activity of the body's regulatory systems. The main results of the study demonstrated that autonomic regulation of the heart showed an increase in the vegetative balance index (VBI), alongside a decrease in heart rate frequency (HRF) and tension index (TI), indicating reduced sympathetic-adrenal stimulation of the heart under conditions of adrenaline-induced myocardial dystrophy. During the 10 day administration of melatonin to rats with adrenaline-induced myocardial dystrophy, an increase in autonomic activity was observed, with an emphasis on heightened parasympathetic nervous system influence on the heart, which contributed to a lower risk of arrhythmias and myocardial infarction. In particular, changes in heart rate were accompanied by HRF fluctuations ranging from 339 to 451 beats/min and an increase in TI from 1,279 to 7,942 units. Twenty-four hours post-adrenaline administration, TI and HRF decreased by 22% and 6.5%, respectively. In rats with pineal hyperfunction, the mean HRF was 414 ± 26 beats/min, TI increased by 27%, and the mean VBI increased by 14%. The observed effects of melatonin indicate that it is a potentially useful tool for preventing adrenaline-induced myocardial damage. The results of the study

Suggest Citation:
Chebotar L, Pshychenko V, Larycheva O, Bila A. Effect of melatonin on heart rate variability in rats with adrenaline-induced myocardial dystrophy. Ukr J Med Biol Sport. 2024;9(4):8–15. DOI: 10.63341/ujmbs/4.2024.08

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offer new possibilities for correcting the functional state of the heart and enhancing understanding of the mechanisms through which different levels of pineal gland activity influence cardiac function

Keywords: melatonin; pineal gland; tension index; heart rate; stress reactions; adrenaline induced myocardial dystrophy

Introduction

The conditions of modern reality in the country are characterised not only by the increasing pace of life but also by military events, uncertainty, social changes, and economic instability. All of these factors, coupled with the sounds of explosions, sirens, a sense of constant danger, and lack of adequate sleep and rest, as well as separation from loved ones, induce constant stress even in healthy people. It is known that stress formation occurs through the activation of the hypothalamicpituitaryadrenal complex. Any stressful event arises due to adrenaline release and is accompanied by the development of oxidative stress, which negatively affects the morphological and functional state of the heart, leading to arrhythmias, heart attacks, coronary syndromes, and hypertensive crises. The negative consequences of oxidative stress, which precede morphofunctional changes, include the intensification of free radical lipid peroxidation and the destabilisation of antioxidant defence. This process is a key factor in the development of cardiac pathologies and is therefore considered a crucial link in the pathogenesis of cardiovascular disease. The chosen research topic is highly relevant, as chronic stress has become an aspect companion of modern life, and cardiovascular disease remains the leading cause of morbidity. At the same time, the effect of melatonin on heart rate variability in rats with adrenaline-induced myocardial dystrophy has been insufficiently studied. This knowledge gap prompted the present study, as these findings may provide new opportunities for correcting the functional state of the heart and enhancing understanding of how varying levels of pineal gland activity affect cardiac function.

The pineal gland is a central endocrine organ actively involved in adaptation processes, homeostasis regulation, and stress response. The pineal hormone melatonin plays a key role in regulating the body's adaptive responses to changes in external environmental conditions and internal homeostasis. Melatonin is known to be an antioxidant with cardioprotective properties. According to V. Pishak *et al.* [1], melatonin plays an important role in blood pressure regulation. Pinealectomy in rats causes hypertension, and melatonin administration reverses this effect. Melatonin has also been found to significantly influence HRF and vascular resistance. In turn, Y-J. Song *et al.* [2] investigated the effect of melatonin supplementation on metabolic status in patients with diabetes and coronary heart disease. Their findings indicated that melatonin supplementation enhanced insulin sensitivity and improved cholesterol levels, as well as significantly reduced certain oxidative biomarkers. These results suggest that melatonin treatment may lower cardiometabolic risk in patients with diabetes and coronary heart disease. According to the research of M. Tobeiha *et al.* [3], melatonin directly interacts with the nervous system and indirectly with blood vessels and the heart. It exerts its direct effects through receptor-dependent signalling pathways, as well as indirect antioxidant actions by scavenging free radicals.

The cardioprotective effects of melatonin are due not only to its antioxidant properties but also to its immunomodulatory, anti-ischaemic and antihypertensive effects. In an experiment conducted by I. Yaremii *et al.* [4], daily administration of melatonin over a two-week period in rats with dexamethasone-induced diabetes led to the normalisation of certain indicators of carbohydrate metabolism in the liver. This confirms the assumption of a possible hypoglycaemic effect of melatonin in diabetes progression. Yu.O. Zolotukhina's research [5] found that patients with coronary heart disease, both those without concomitant conditions and those with diabetes mellitus, exhibit suppressed anticoagulant activity and an increased blood clotting potential, which, in turn, heightens the risk of vascular disease. This was confirmed in the research of A. Stenling [6]. C. MilletBoureima *et al.* [7] demonstrated that melatonin has a beneficial effect on the cardiovascular system (CVS) by regulating heart rate and reducing nighttime blood pressure in patients with hypertension. In addition, it may offer powerful protection for the cardiovascular system and reduce the risk of reperfusion injury following myocardial infarction. Furthermore, according to a study by A. Chrustek & D. Olszewska-Słonina [8], melatonin has a normalising effect on blood pressure, heart rate, and coronary circulation. Y.-J. Song *et al.* [2] found that melatonin can modulate cardiovascular functions such as cardiac output, blood pressure, heart rate, and seasonal rhythms. After pinealectomy, the primary source of melatonin in the bloodstream, blood pressure in rats increased, whereas melatonin administration in hypertensive rats lowered blood pressure, baroreflex response, and heart rate. A study by X. Zhang *et al.* [9] showed a beneficial effect of melatonin on mitochondrial fusion, regulated by the molecule OPA1 (optic atrophy 1), in myocardial infarction and/or reperfusion injury. It has been established that melatonin can preserve myocardial function, reduce infarct size, and prevent cardiac myocyte death in response to reperfusion stress.

Melatonin plays a crucial role in the protective effects of stress adaptation mechanisms. Y.-J. Song *et al.* [2] assessed the effect of melatonin intake on metabolic status in patients with diabetes and coronary heart disease and found that melatonin supplementation enhanced insulin sensitivity and cholesterol levels. A scientific study by A. Chrustek & D. Olszewska-Słonina confirmed that melatonin is a versatile molecule with multiple physiological

functions. It exhibits strong antioxidant properties by activating antioxidant enzymes and safeguards cells from lipid peroxidation. Therefore, melatonin, as a pharmacological agent with antioxidant properties, is widely used to correct disorders resulting from oxidative stress. However, at present, it remains unclear which factor is primary: whether genetically determined disorders of melatonin production, together with other factors, contribute to pathology formation, or whether the increased need for melatonin arises due to the disease itself, as the reserve capacity of the enzymatic (particularly antioxidant) system becomes depleted. Considering the wide range of biological activities of melatonin, including its antioxidant, antistress, and chronobiological effects, this study aimed to investigate the effects of melatonin on heart rate variability in laboratory rats with adrenaline-induced myocardial dystrophy.

Materials and Methods

The experimental component of the study was conducted on adult male Wistar rats, weighing 220-260 g, which were kept under vivarium conditions on a standard diet with exposure to natural light cycles. All stages of the study, including manipulative interventions and euthanasia, were carried out in compliance with the provisions of the "General Ethical Principles for Animal Experiments", adopted by the VII National Congress on Bioethics in 2019 [10], and following the Procedure for Carrying out Experiments and Experiments on Animals by Scientific Institutions (2012) [11], as well as the European Convention for the Protection of Vertebrate Animals Used for Research and Other Scientific Purposes (1986) [12].

Two series of experiments were conducted to study the effects of adrenaline-induced myocardial dystrophy against a background of pituitary hyperfunction, which was complicated by adrenaline-induced cardiac dystrophy. The animals were divided into four groups, with each group consisting of eight animals. Group I (control): rats were maintained under normal vivarium conditions. Group II: rats were exposed to a 10-day period of pituitary hyperfunction. Group III: rats were subjected to 10 days of adrenaline-induced myocardial dystrophy. Group IV: rats developed adrenaline-induced myocardial dystrophy against a background of pituitary hyperfunction.

According to the literature, the maximum single-administered dose of melatonin is 5 mg/kg of body weight; therefore, pituitary hyperfunction was induced by administering melatonin (VitaMelatonin, JSC "Kyiv Vitamin Plant", Ukraine) at a dose of 1 mg/kg of body weight, dissolved in 1.0 ml of solvent, once daily at 19:00 for 10 days [4]. An experimental model of cardiac pathology, specifically adrenaline-induced myocardial dystrophy (AMD), was established by administering adrenaline hydrochloride at a dose of 0.5 mg/kg as a single injection [13, 14]. To record the electrocardiogram (ECG), rats were restrained in the cervical and lumbar regions using a specialised apparatus. The animals' paws were secured with strips of adhesive plaster, and the apparatus containing the restrained animals was placed in a shielded chamber. Alcohol-treated stainless-steel needle electrodes (0.1 mm in diameter) were inserted subcutaneously into the forelimbs of the animals.

ECG recording offers additional possibilities for assessing the mechanisms involved in functional regulation, as well as the adaptive capacity of the body, which reflects the degree of dynamic balance with the environment. In this context, heart rhythm can serve as an indicator of regulatory system function, not only for the heart but also for the body as a whole. Since the cardiovascular system is the first to react to external influences, the body's adaptive response to maintaining balance with the environment manifests through increased tension in regulatory processes [15, 16].

Based on this principle, the degree of regulatory and neural control system tension was assessed through a mathematical analysis of heart rate variability (HRV). According to the literature, HRV is one of the most integrative methods for evaluating the functional activity of the body's regulatory systems, as changes in the key parameters of cardiac variability reflect both cardiac function and the impact of regulatory influences associated with autonomic nervous system activity [17, 18].

During rhythmogram recording, the following indicators were evaluated: Mode (*Mo*) – the duration of the most frequently occurring cardiac interval; Mode amplitude (*AMo*) – the number of cardiac intervals with the value of *Mo*; Variation range of cardiac intervals (ΔX) – the difference between the maximum and minimum values in the sample, and stress index. Mathematical analysis of HRV was conducted based on ECG recordings in the second standard lead at a tape speed of 100 mm/s. For analysis, 100 consecutive R-R intervals were selected. Based on the values of *Mo*, *AMo*, and ΔX, the following indicators were calculated: Regulatory system stress index, using the formula:

$$RSSI = AMo / (2\Delta X \times Mo). \quad (1)$$

Vegetative balance index (VBI) using the formula:

$$VBI = AMo / \Delta X. \quad (2)$$

Statistical analysis of the study results was conducted using the parametric method of variance statistics, specifically the Student's t-test. The arithmetic mean (M), standard deviation ($\bar{o}$), and Student's t-test (t) were determined. A difference between numerical parameters was considered statistically significant if $p < 0.05$. Statistical calculations were performed using a personal computer with the standard STATISTICA 6 software for Windows.

Results and Discussion

According to ECG recordings, the animals in the control group had a regular heart rhythm. Under conditions modelling adrenaline-induced myocardial dystrophy, the HRV parameters changed significantly. Analysis of heart rate frequency (HRF) in rats with adrenaline-induced myocardial dystrophy revealed that the average tension index (TI) ranged from 1,279 to 7,942 units, while HRF ranged from 339 to 451 beats per minute. Thus, adrenaline-induced

myocardial dystrophy had a significant effect on heart rhythm, with animals responding to myocardial dystrophy caused by epinephrine through an increased heart rate. Two hours post-adrenaline administration, the stress index decreased by 2.4%, while the heart rate decreased by 4.8%, reaching 410 ± 13.4 beats per minute. ECG recordings of rats in the experimental group, taken 24 hours post-adrenaline administration, showed a decrease in TI and HRF compared to pre-administration values by 22% and 6.5%, respectively, reaching 403 ± 14.7 beats per minute (Table 1). These changes indicate an increased influence of the sympathetic branch of the autonomic nervous system (ANS) on heart rhythm, which is mediated via the humoral pathway, primarily involving the adrenal glands.

Table 1. Heart rate variability indicators in rats with adrenal-induced myocardial dystrophy

HRV indicators	Before adrenaline administration of	After 2 hours	After 1 day
HRF (beats per minute)	431 ± 14	410 ± 13.4	403 ± 14.7
TI (units)	4,716 ± 467	4,605 ± 381	3,681 ± 460
VBI (units)	1,255 ± 222	1,652 ± 238 $p_1 > 0.05$	1,073 ± 160 $p_2 > 0.05$

Notes: p_1 – comparison with values before adrenaline administration; p_2 – comparison of values observed after 24 hours with those recorded two hours post-adrenaline administration

Source: developed by the authors based on their research

The authors concur with researchers who suggest that phosphoinositide secondary mediators play a role in the formation of limiting systems that mitigate the destructive effects of stress factors, in this case, adrenaline. It is possible that in addition to functional regulation at the systemic level (brain-myocardium), the myocardium itself can counteract negative effects through the selfregulation and oscillatory properties of secondary mediator systems. This process may block adverse effects at the stage of intracellular signalling [19, 20]. The data obtained suggest that epinephrine administration induces changes that result in autonomic regulation disorders. It can be hypothesised that a key trigger in this process is a reduction in melatonin production by the pineal gland.

Testing for adrenaline sensitivity 10 days after administration showed some alterations in HRV parameters; however, these changes were not statistically significant. Two hours post-administration, TI increased by 2%, whereas after 24 hours, it decreased by 30% and 32%, respectively, compared to the baseline level recorded at the two-hour mark. HRF decreased by 10.5% two hours postepinephrine administration. Meanwhile, VBI increased by 27% within two hours but subsequently decreased by 5% over the following 24 hours, relative to pre-administration values. Thus, mathematical analysis of heart rate variability indicated a reduction in TI and HRF, alongside an increase in VBI, two hours post-adrenaline administration. Analysis of heart rate in rats with an experimental model of pituitary hyperfunction revealed an average heart rate of 414 ± 26 beats per minute, with TI increasing by 27% to 5,981 ± 410 units, and VBI rising by 14% to 1,741 ± 197 units (Table 2).

Table 2. Results of mathematical analysis of heart rate in rats under the influence of adrenalineinduced myocardial dystrophy against a background of hypermelatoninaemia

ECG parameters	Before adrenaline administration	After 2 hours	After 1 day
HRF (beats per minute)	414 ± 26	369 ± 18	365 ± 28
TI (units)	5,981 ± 410	2,435 ± 300 $p < 0.01$	3,431 ± 424 $p < 0.001$
VBI (units)	1,741 ± 197	898 ± 77 $p < 0.01$	1,086 ± 100

Notes: p – significant difference between values before adrenaline administration and two hours post-administration within the same group of animals

Source: developed by the authors based on their research

ECG recordings taken two hours post-adrenaline injection in this group of animals revealed a sharp decrease in the stress index and a moderate reduction in heart rate. The average HRF decreased by 10 beats per minute, while the TI value decreased by 47% relative to baseline levels. The TI reduction was statistically significant ($p < 0.001$) compared with both the baseline value and the preadministration TI value recorded in this group ($p < 0.01$). Notably, despite this substantial decline in TI and only a slight reduction in HRF, VBI dropped sharply to 898 ± 77 units. This decrease was significant ($p < 0.01$) compared to control animals. ECG recordings taken 24 hours post-epinephrine administration revealed a further slight reduction in heart rate and an increase in TI and VBI.

It is possible that the administration of epinephrine enhances sympathetic nervous system function, and in the presence of hypermelatoninaemia, parasympathetic nervous system activity is increased, thereby reducing the risk of arrhythmias and myocardial infarction. Melatonin administration may also reduce the intensity of energy metabolism

and, consequently, oxygen consumption. In addition, this effect of melatonin could activate the stress-limiting system in a manner similar to opioid peptides and phosphoinositide systems, ultimately enhancing myocardial resistance to catecholamine-induced stress. With the artificial activation of adrenoceptor structures through adrenaline administration, melatonin may trigger feedback mechanisms that enhance parasympathetic nervous system activity, thereby reducing the risk of arrhythmias, preventing pathological foci, and minimising the likelihood of myocardial infarction.

In contemporary scientific research, the role of the pineal gland has gained increasing significance in understanding the mechanisms of neurohumoral regulation of cardiac function. This growing interest stems from the well-established cardioprotective effects of melatonin. Thus, the results of this study suggest that melatonin administration in the context of AMD exerts an antiischaemic effect, promoting the restoration of cardiac function, enhancing parasympathetic nervous system activity, and mitigating dystrophic manifestations [21, 22].

Mathematical analysis of heart rate under conditions of hypermelatoninaemia in AMD revealed a decrease in HRF and TI in rats two hours after adrenaline administration. However, after 24 hours, the heart rate remained at the two-hour level, while the stress index had increased. This trend did not align with ECG control values following epinephrine administration. Meanwhile, VBI decreased over the 24-hour period. Epinephrine administration may enhance sympathetic nervous system function, while pineal hyperfunction promotes increased parasympathetic nervous system activity, thereby reducing the risk of arrhythmias and myocardial infarction. These data may be attributed to melatonin administration leading to heightened parasympathetic tone, inhibition of free radical reactions, and reduced myocardial electrical instability.

With pineal gland hyperfunction, melatonin production increases, leading to a reduction in sympathetic-adrenal system activity, metabolic rate, and oxygen consumption. Daily fluctuations in autonomic nervous system activity play a crucial role in this process. Thus, the results obtained in this experiment indicate that one of the key advantages of pineal gland hyperfunction, which maximises melatonin's cardioprotective effects, is the predominant role of parasympathetic processes in cardiac adaptation mechanisms under conditions of AMD. The timely and sufficient activation of melatonin enhances the efficiency of compensatory and adaptive responses, thereby increasing myocardial resistance. These findings are consistent with studies conducted by Ukrainian, American, and Chinese researchers. Studies by Y.-J. Song *et al.* [2] have demonstrated that melatonin exerts an antihypertensive effect and alleviates hypertension caused by continuous exposure to light. Similarly, V. Kolesnikova & A. Radchenko [23] found that melatonin affects cardiac function and plays a role in oxidative stress mechanisms. According to V.P. Pishak *et al.* [1], melatonin acts directly on the paraventricular nucleus and the hypothalamic-pituitary-adrenal axis, modulating the baroreflex set point, reducing sympathetic tone, and increasing parasympathetic tone within the medulla oblongata, which regulates heart rate.

The dynamic changes of heart rate variability values in AMD under conditions of pituitary gland hyperfunction exhibited a consistent pattern, characterised by a decrease in heart rate, TI, and VBI (Fig. 1). Comparative analysis of these data and the observed trends suggests that these changes may be attributed to adrenoceptor desensitisation and reduced baroreceptor sensitivity, resulting from structural and metabolic alterations in the myocardium. Such processes may obscure the progressive impairment of neurohumoral regulation. These results also suggest an increase in sympathetic nervous system activity as part of a compensatory response. The decrease in primary HRV parameters highlights the close interrelation between extracardiac heart rate regulation and the functional state of the myocardium during the progression of AMD and the effects of melatonin.

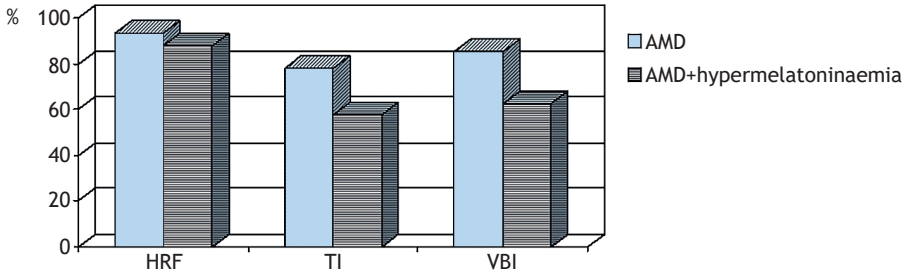

Figure 1. Dynamics of changes in the indicators of mathematical analysis of heart rate under conditions of AMD and AMD + hypermelatoninaemia

Notes: 100% of the values represent indicators in control animals

Source: developed by the authors based on their research

This reduction in heart rate variability suggests a shift in autonomic balance towards increased parasympathetic dominance. Such mechanisms underlying heart rate variability reduction may result from two primary factors: a decrease in the amplitude of autonomic tone oscillations and reduced sinus node sensitivity to autonomic influences.

The results obtained by the present study indicate that melatonin administration under conditions of AMD exerts a general corrective effect by restoring the functional state of the heart. This finding aligns with the studies of M. Tobeiha *et al*. [3], which demonstrated melatonin's role in heart regeneration and its protective effects against cardiac dysfunction. In addition, the absence of significant changes in heart rate, which characterises the central mechanism of heart function, indicates that the observed changes occur at the local level. In other words, these changes take place within the myocardium and are realised at the cellular level rather than within central regulatory circuits.

These results are further supported by the studies of N.O. Bezkorovayna *et al*. [24], found that 10-day exposure to continuous illumination (500 lux) induces a significant increase in parasympathetic influence on heart rate and bradycardia in females, while in males, it leads to an increase in heart rate accompanied by a decrease in parasympathetic influence on the heart. The development of adrenaline-induced myocardial necrosis in females under continuous illumination is associated with cardio-intervalometer dynamics similar to those observed under light-balance conditions, with greater parasympathetic activity within the ANS and a corresponding increase in sympathetic activity. In males, under similar conditions, the ANS response to the development of myocardial necrosis differs from that observed under balanced lighting conditions and demonstrates parasympathetic involvement in heart rhythm regulation while exhibiting sympathetic dominance [24].

The results of the present study indicate that melatonin contributes to reducing oxidative stress under conditions of AMD and normalising the studied parameters. Melatonin demonstrated its antiischaemic effect, significantly improving the functional state of the rat heart in the experiment conducted by T. Senoner & W. Dichtl [25]. For example, studies by F.Gd. Amaral & J. CipollaNeto [26] have shown that the benefits of melatonin's potent protective properties are associated with its ability to lower oxidative stress and reduce the risk of damage following myocardial infarction. Additionally, melatonin functions as a scavenger of reactive oxygen species within mitochondria, thereby providing a beneficial effect in coronary heart disease. According to other studies, notably M. Cherska *et al*. [27], the mechanisms through which melatonin affects vascular tone have been identified, specifically its interaction with its own receptors, its influence on adrenergic pathways of muscle contraction, and its ability to block serotonergic stimulation.

Thus, the findings of this study confirm that melatonin administration under conditions of adrenaline-induced myocardial dystrophy exerts a general corrective effect. It promotes the restoration of the functional state of the heart at the cellular level without significantly affecting central regulatory mechanisms. Melatonin exhibits an anti-ischaemic effect by reducing oxidative stress and improving cardiac function, which corroborates previous studies confirming its role in lowering the risk of damage following myocardial infarction and its involvement in vascular tone regulation.

Conclusions

Based on studies investigating the autonomic regulation of the rat heart under the influence of melatonin in the context of adrenaline-induced myocardial dystrophy, this study has demonstrated the physiological role of melatonin in modulating autonomic status and functional changes in the heart. These effects are attributed to its antioxidant, anti-ischaemic, and stress-protective properties. The dynamics of the studied parameters indicate the adaptive mechanisms of the rat heart, which involve the autonomic nervous system. A comparison with similar parameters in rats with adrenalineinduced myocardial dystrophy led to the following conclusions.

The autonomic regulation of the heart, as assessed by mathematical analysis of heart rate, revealed an increase in VBI values alongside a decrease in HRF and TI values. This pattern indicates a reduction in sympathetic-adrenal stimulation of the heart under conditions of adrenaline-induced myocardial dystrophy. Mathematical analysis of the heart rate in rats with an experimentally induced model of pituitary hyperfunction showed that the average heart rate was 414 ± 26 beats per minute. The average TI increased by 27% to 5,981 ± 410 units, while the average VBI increased by 14% to 1,741 ± 197 units. Given the above findings, these differences may indicate that changes reflecting autonomic balance mechanisms and their influence on adaptive and compensatory responses under adrenaline stress occurred with the vagus nerve playing a dominant role. Experimental data highlight the importance of studying the effects of melatonin in cardiovascular conditions such as myocardial ischaemia, chronic hypoxic heart injury, and atherosclerosis. Therefore, the timely diagnosis of melatonin production disorders, along with its potential therapeutic use in stressful situations, underscores the importance of these measures. In this context, circadian rhythm disturbances – which are crucial for maintaining normal myocardial function – further emphasise the need to investigate melatonin's role in stress and myocardial pathology. The study of heart rate variability is essential for a more precise determination of regulatory mechanisms. This will facilitate the development of effective preventive and therapeutic measures.

The results of this study indicate the need to investigate sex-related differences in heart rate variability. Furthermore, melatonin appears to be a promising agent for the prevention of adrenalineinduced myocardial damage. Future research should focus on examining the effects of melatonin deficiency on heart rate parameters during the development of adrenaline-induced myocardial dystrophy in male and female rats.

Acknowledgements

None.

Conflict of Interest

None.

References

[1] Pishak VP, Kryvchanska MI, Ryznychuk MO, Bulyk OR, Lukan YR. Melatonin: Biological role and optimisation of its use. Buk Med Bull. 2022;2(102):86–90. DOI: 10.24061/2413-0737.28.3.111.2024.1

[2] Song Y-J, Zhong C-B, Wu W. Cardioprotective effects of melatonin: Focusing on its roles against diabetic cardiomyopathy. Biomed Pharmacother. 2020;128:110260. DOI: 10.1016/j.biopha.2020.110260

[3] Tobeiha M, Jafari A, Fadaei S, Mirazimi SM, Dashti F, Amiri A, et al. Evidence for the benefits of melatonin in cardiovascular disease. Front Cardiovasc Med. 2022;9:888319. DOI: 10.3389/fcvm.2022.888319

[4] Yaremii I, Kushnir O, Yaremii K. The effect of melatonin on some indicators of carbohydrate metabolism in the liver of rats with dexamethasone diabetes. Act Probl Modern Med. 2023;23(4):261–5. DOI: 10.31718/2077-1096.23.4.261

[5] Zolotukhina YuO. Peculiarities of changes in anticoagulant and coagulant activity in patients with coronary artery disease combined with type 2 diabetes mellitus. Int J Endocrinol. 2019;15(2):122–7. DOI: 10.22141/2224-0721.15.2.2019.166103

[6] Stenling A, Häggström C, Norberg M, Norström F. Lifetime risk predictions for cardiovascular diseases: Competing risks analyses on a population-based cohort in Sweden. Atheroscler. 2020;312:90–8. DOI: 10.1016/j.atherosclerosis.2020.08.014

[7] Millet-Boureima C, Ennis CC, Jamison J, McSweeney S, Park A, Gamberi C. Empowering melatonin therapeutics with drosophila models. Diseases. 2021;9:67. DOI: 10.3390/diseases9040067

[8] Chrustek A, Olszewska-Słonina D. Melatonin as a powerful antioxidant. Acta Pharm. 2020;71(3):335–54. DOI: 10.2478/acph-2021-0027

[9] Zhang X, Zhu J-X, Ma Z-G, Wu H-M, Xu S-C, Song P, et al. Rosmarinic acid alleviates cardiomyocyte apoptosis via cardiac fibroblast in doxorubicin-induced cardiotoxicity. Int J Biol Sci. 2019;15:556. DOI: 10.7150/ijbs.29907

[10] VII National Congress on Bioethics [Internet]. Kyiv: NASU, NAMSU, MHU; Proceeding; 2019 Sept 30–Oct 2 [cited 2024 Nov 3]. Available from: https://imtuik.org.ua/wp-content/uploads/instytut/nauka/forum/VII_natsionalny_konhres_z_bioetyky.pdf

[11] Procedure for Carrying out Experiments and Experiments on Animals by Scientific Institutions [Internet]. 2012 [cited 2024 November 21]. Available from: https://zakon.rada.gov.ua/laws/show/z0416-12#Text

[12] European Convention for the Protection of Vertebrate Animals Used for Research and Other Scientific Purposes [Internet]. 1986 [cited 2024 November 28]. Available from: https://rm.coe.int/168007a67b

[13] Pshychenko VV, Cherno VS, Davydenko RM, Kucher OO, Gavrilyuk IM. Influence of high adrenalin doses on the morphofunctional status of rats epiphysis under the condition of its hypofunction. World Med Biol. 2020;1(71):211–3. DOI: 0.26724/2079-8334-2020-1-71-211-213

[14] Baliuk OYe, Vazhnichaya EM, Lutsenko RV, Kostenko VO, Akimov OYe. Changes in oxidative stress parameters at local application of minoxidil in rats with chemical depilation. Pharmacol Drug Toxicol. 2023;17(3):189–97. DOI: 10.33250/17.03.189

[15] Brovko MR. Comparison of ECG and echocardiography data in patients with coronary heart disease. In: Achievements of modern medical and pharmaceutical science. Collection of abstracts of the all-Ukrainian scientific and practical conference of students and young scientists. Zaporizhia: Zapozirizhia State Medical University; 2022. P. 8–9.

[16] Liashenko V, Stetsenko S. Peculiarities of heart rate variability against the background of sleep disturbance and stress factors: Theoretical aspect. Sloboda Sci J. 2024;1:43–9. DOI: 10.32782/naturalspu/2024.1.5

[17] Lisun Y, Uglev E. Heart rate variability, use and methods of analysis. Pain Anaesth Int Care. 2020;4(93):83–9. DOI: 10.25284/2519-2078.4(93).2020.220693

[18] Jiryis T, Magal N, Fructher E, Hertz U, Admon R. Resting-state heart rate variability (HRV) mediates the association between perceived chronic stress and ambiguity avoidance. Sci Rep. 2022;12(1):17645. DOI: 10.1038/s41598-022-22584-4

[19] Reva TV, Mandryk OY, Dyriv MO. Influence of chronic stress on the development of cardiovascular diseases under martial law. In: Topical aspects of modern scientific research. Proceedings of the 8th International scientific and practical conference. Tokyo Jap: CPN Publishing Group; 2024 April 18–20. P. 79–83.

[20] Lebedinets NV, Negriy AS. The influence of stress and war on the aging process. In Mechanism of aging in biology. Proceedings of the regional scientific and practical conference. Kyiv: Mykhailo Drahomanov Ukrainian State University; 2024 Mar 27. P. 83–5.

[21] Chu B, Marwaha K, Sanvictores T, Awosika AO, Ayers D. Physiology, stress reaction. StatPearls Publishing; 2024.

[22] Kazakou P, Nicolaides NC, Chrousos GP. Basic concepts and hormonal regulators of the stress system. Horm Res Paediatr. 2022;96(1):8–16. DOI: 10.1159/000523975

[23] Kolesnikova V, Radchenko A. A modern view on the mechanisms of oxidative stress development and its biomarkers in the most common non-communicable diseases. Ukr Therapeutic J. 2020;1:51–61. DOI: 10.30978/UTJ2020-1-51

[24] Bezkorovayna HO, Klishch IM, Khara MR. Heart rate variability in rats of different sexes during the development of adrenaline-induced myocardial necrosis against the background of light desynchronisation. Clin Exp Pathol. 2020;19:1:10–6. DOI: 10.24061/1727-4338.XIX.1.71.2020.2

[25] Senoner T, Dichtl W. Oxidative stress in cardiovascular diseases: Still a therapeutic target? Nutrients. 2019;11(9):20–90. DOI: 10.3390/nu11092090
[26] Amaral FG, Cipolla-Neto J. A brief review about melatonin, a pineal hormone. Arch Endocrinol Metab. 2018;62:472–9. DOI: 10.20945/2359-3997000000066
[27] Cherska M, Kukharchuk K, Haiova O. Oxidative stress in patients with high cardiovascular risk. Endocrinol. 2021;26(3):287–97. DOI: 10.31793/1680-1466.2021.26-3.287

Вплив мелатоніну на варіабельність серцевого ритму у щурів на тлі адреналінової міокардіодистрофії

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Анотація. Активне керування адаптивними реакціями організму на зміни зовнішніх умов середовища і внутрішнього гомеостазу відбувається за участі гормону епіфіза мелатоніну. Мелатонін як фармакологічний препарат із антиоксидантними властивостями широко використовують для корекції розладів, що виникають внаслідок оксидативного стресу. Це дослідження було спрямоване на вивчення змін серцевої активності під впливом даного гормону, зокрема впливу мелатоніну на варіабельність серцевого ритму у лабораторних щурів, які мали модель адреналінової дистрофії міокарда. Ступінь напруги регуляторних механізмів та механізмів нервової регуляції оцінювали за математичним аналізом варіабельності ритму серця, який є одним із інтегративних методів оцінювання функціональної активності регуляторних систем організму. Основні результати дослідження показали, що вегетативна регуляція серця виявила збільшення значення показника вегетативного балансу (ПВБ) при зниженні значень частоти серцевих скорочень (ЧСС) та індексу напруженості (ІН), що свідчить про зниження симпато-адреналової стимуляції серця в умовах адреналінової міокардіодистрофії. Протягом 10-денного введення мелатоніну щурам на тлі розвитку адреналінової міокардіодистрофії спостерігалося підвищення вегетативної активності з акцентом на посилення впливу парасимпатичної нервової системи на серце, що сприяло зниженню ризику аритмій і розвитку інфаркту міокарда. Зокрема, зміни ритму серця супроводжувалися коливаннями ЧСС від 339 до 451 уд./хв. і підвищенням індексу напруженості від 1279 до 7942 од. Через 24 години після введення адреналіну ці показники знижувалися на 6,5 % і 22 %, відповідно. У щурів із гіперфункцією епіфіза середнє значення ЧСС становило 414±26 уд./хв., ІН збільшився на 27 %, а середня величина ПВБ – на 14 %. Виявлені ефекти мелатоніну свідчать, що він є потенційно корисним засобом для запобігання індукованих адреналіном пошкоджень міокарда. Результати дослідження відкривають нові можливості у корекції функціонального стану серця та дозволять розширити рамки розуміння механізмів впливу різної функціональної активності епіфізу на функціональний стан серця

Ключові слова: мелатонін; епіфіз; індекс напруження; серцевий ритм; стресові реакції; адреналінова міокардіодистрофія

UKRAINIAN JOURNAL
OF MEDICINE, BIOLOGY AND SPORTS
Volume 9, No. 4. 2024

Journal homepage: https://uajmbs.com.ua/en
Article's History: Received: 21.08.2024; Revised: 01.11.2024; Accepted: 26.12.2024

UDC 616.53-008.46
DOI: 10.63341/ujmbs/4.2024.016

Evaluating topical treatments for mild to moderate acne: A cross-sectional study

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Abstract. *Acne vulgaris* (AV) is a chronic, inflammatory skin disease affecting 80% of young adults and adolescents, causing lesions, scarring, and pigmentation in the pilosebaceous unit. Managing AV effectively crucial to improving patients' quality of life and preventing long-term dermatological complications. This study aimed to evaluate the efficacy of three widely used topical treatments for AV, which are: benzoyl peroxide, retinoid, and salicylic acid treatments, in managing mild to moderate acne using a cross-sectional observational study design. The study analysed the effectiveness of benzoyl peroxide, retinoid, and salicylic acid treatments for mild to moderate acne over an 8-week period. Participants aged 15 to 50 were randomly assigned to three treatment groups and outcomes were measured through physical exams and questionnaires. The variables assessed included lesion count, acne severity using GAGS scores, scarring, and skin texture and the data was analysed using SPSS, paired T-tests, and ANOVA to identify the most effective treatment. The study found that benzoyl peroxide significantly improved skin texture and eliminated severe inflammatory cases. Retinoids showed the most reduction in non-inflammatory and inflammatory lesions, with 55% of participants showing only mild lesions post-treatment. Retinoids also reduced severe acne scarring and improved skin texture. Salicylic acid produced moderate improvements, reducing non-inflammatory lesions and improving skin texture. Benzoyl peroxide and retinoids significantly improved skin texture, however, benzoyl peroxide showed mixed results in scarring. Paired sample t-tests confirmed significant improvements in skin texture and non-inflammatory lesions for both benzoyl peroxide and retinoid groups. The findings revealed that retinoids are more effective for non-inflammatory acne lesions and benzoyl peroxide for severe inflammatory cases, allowing for personalised treatment plans. This approach offers valuable insights for improving acne management outcomes. The study can help dermatologists in selecting effective treatments for acne based on lesion type and severity

Keywords: Acne Vulgaris; retinoid; benzoyl peroxide; salicylic acid; skin texture

Suggest Citation:
Fahim B, Shaikh MA, Ejaz T, Batool P. Evaluating topical treatments for mild to moderate acne: A cross-sectional study. Ukr J Med Biol Sport. 2024;9(4):16–34. DOI: 10.63341/ujmbs/4.2024.016

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Introduction

Acne vulgaris (AV) is one of the most prevalent dermatological conditions, with a significant impact on the physical and psychological well-being of individuals, particularly young adults and adolescents. AV is a complex condition influenced by hormonal changes, microbial activity and demographic factors. Since acne continues to influence millions of people worldwide, it is essential to comprehend the efficacy and safety of prevalent topical therapies. Despite the availability of a variety of treatment options, the rising incidence of acne and the possibility of treatment resistance, particularly in mild to moderate instances, highlight the need for continuous evaluation of existing treatments. Traditional therapies are limited due to adverse effects and poor patient adherence. The rising prevalence of sensitive skin and antibiotic resistance makes it necessary to provide safer and more effective treatments. Furthermore, with the increased interest in alternative treatments and concerns about the long-term adverse reactions of conventional medicine, it is time to assess the efficacy of established therapies in managing acne symptoms.

In response, recent literature explores advances in acne treatment, therapies and new skin regimens. Hence, researchers are exploring innovative anti-inflammatory and antibacterial agents, such as phytochemicals derived from natural products, as safer and more effective alternatives for combating P. acnes and reducing the impact of acne vulgaris [1, 2]. T. Zhang *et al.* [3] conducted a study comparing 2% supramolecular SSA hydrogel and Davuwen Adapaline gel for treating mild to moderate acne vulgaris. Results showed both treatments were effective, however, SSA showed a lower rate of adverse effects and better outcomes in pore reduction. This suggests SSA as a safer alternative for acne management [4]. For the treatment of mild to moderate AV, A. Gern *et al.* [5] evaluated the safety, effectiveness and tolerability of a unique 3 step skincare routine in comparison to BPO in their randomised, doubl-blinded, clinical research. According to the study, although BPO was quite effective at lowering *P. acnes*, 44% of participants stopped using it within six months due to its adverse effects on sensitive skin.

A study by W. Chen *et al.* [6] found that the prevalence of sensitive skin in the adult population is greater than 71% with women being more likely to report it, suggesting the need for new OTC regimens with comparable efficacy and greater tolerability compared to existing BPO therapies. B.S. Dikicier [7] examined the effectiveness, side effects, and adherence rates of topical acne treatments in 250 patients, primarily female (71.2%). The most prescribed treatments were antibacterial BPO combinations and topical retinoids. Nearly half discontinued therapy due to unresponsiveness and side effects, with severe acne patients more likely to discontinue treatment. Salicylic acid (SA) is a beta-hydroxy acid with keratolytic properties, effective in both comedonal and inflammatory acne. It is used in solutions, creams, and gels with low concentrations depending on the skin [8]. SA acts against both non- inflammatory and inflammatory lesions in active acne vulgaris. Moreover, in a study by R. Sarkar *et al.* [9], SA peels were compared with glycolic acid (GA) peels for treating grade 2 AV. Both peels were found effective in reducing lesions and improving post-acne hyperpigmentation. SA was more effective in addressing comedones, papules, and pustules, however, SA peels have low water solubility.

A systematic review by K. Sattar *et al.* [10] evaluated the efficacy and safety of adapalene and BPO combination therapy for acne vulgaris. The study's results showed that combination of adapalene and BPO is a safe and effective therapeutic option for managing acne and reducing acne lessions. AV has been a common dermatological disease that has important effects on the personal health and well-being of people. Despite the availability of various topical treatments, there is a lack of comprehensive and comparative research analysing their effectiveness. There has been a lack of research focusing on these aspects regarding the efficacy of these treatments, including the possible effects on acne lesion count and skin intensity.

The current literature provides a clear correlation between acne and age as well as gender. Most of the teenagers and young adults are faced with hormonal changes which are essential in growth especially during puberty hence leading to acne [11, 12]. AV is a common skin condition that affects populations worldwide, however, only a few studies have compared its treatment responses between different populations or regions, such as Pakistan. There has been a considerable gap in research regarding the comparative effectiveness of commonly used topical treatments for mild to moderate acne in the Pakistani demographic, considering unique genetic, environmental, and lifestyle factors. This study was designed with the purpose of filling this gap by comparing the effectiveness of Benzoyl peroxide, Retinoid, and salicylic acid in Pakistan.

The aim of this study was to evaluate and determine comparative efficacy of benzoyl peroxide, Retinoid, and SA used topically in patients with mild to moderate acne. This paper represented a corss-sectional observational design that aimed to establish an effective positive therapeutic outcome that might help clinicians to make more informed decisions on acne management practices.

Materials and Methods

Study Design

The study has employed a cross sectional observation design to asses and compare the effectiveness of three treatments: retinoid (tretinoin), benzoyl peroxide and salicylic acid in the patients with mild to moderate acne. The study was conducted on the patients from three dermatological clinics of Pakistan with the span of 8 weeks. Participants were randomly assigned to each treatment group, with all three groups receiving specific assigned treatment method. The effectiveness of each treatment was evaluated at the end of 8-week period, with outcomes assessed based on specific clinical parameters. This design allowed for a comprehensive comparison of the

three treatments within the same timeframe, providing valuable insights into their relative efficacies.

Participants

For the observational study, 60 participants aged 15 to 50 years were selected. Of these, 35% were men (21 participants) and 65% were women (39 participants). The age distribution was as follows: 41.7% were 19 years old and younger, 36.7% were aged 20-29, 16.7% were aged 30-39 and 5.0% were aged 40-50. The majority of participants were under the age of 30, indicating a younger cohort. The gender distribution was skewed towards women, who made up the majority of the sample, as shown in Figure 1.

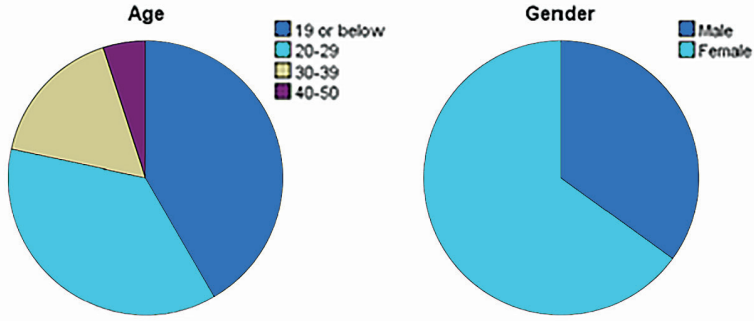

Figure 1. Demographics of the study participants

Source: developed by the authors

Figure 1 demonstrates a disparity in age distribution between males and females, with a greater proportion of females falling within the younger age groups (19 or below and 20-29). This demographic profile provided context for interpreting the treatment outcomes.

The participants were randomly assigned to specific treatment method, dividing 20 participants in each group without any limitation of age or severity of the acne. Consent forms were obtained from each patient and treatments were administered to each patient with the permission of both doctors and patients.

Inclusion and exclusion criteria

The participants were included and excluded by the following criteria.

Inclusion criteria:

- age of participants between 15 and 50;
- patients diagnosed with mild to moderate acne;
- patients that were capable and allowed for the application of treatment method;
- patients that were interested to follow up the treatment method properly and attend follow-up appointments;
- patients with no history of skin allergies or sensitivity to reactions.

Exclusion criteria:

- patients with severe acne or other related medical conditions;
- patients that were allergic to retinoid, salicylic or benzoyl peroxide;
- other medical conditions that might affect their follow-up appointments or treatment method;
- females that were pregnant or on breast feeding period.

Interventions

The study has implemented three distinct interventions for each treatment group. The first group received a 2.5% gel of benzoyl peroxide, which was applied once daily to effected area. The second group was treated with tretinoin lotion, also known as all-trans retinoic acid, which is a topical medication derived from vitamin A with the concentration of 0.05% once daily in the morning. The third group received SA in a 2%gel formulation which was applied twice daily. These interventions were selected to evaluate the effectiveness of mild to moderate acne patients.

Data collection

The data was collected through physical and online questionnaires. Observations were recorded before the treatment and 8 weeks after the treatment. Each participant was assigned to one of three treatment groups. The variables assessed included non-inflammatory lesions (comedones) and inflammatory lesions (papules, pustules, and nodules) [13], the severity of acne using the GAGS (Glycosaminoglycans) score [14], acne scarring [15], and skin texture and appearance [16]. The scales for these observations were clearly defined to ensure consistency and accuracy in the data collection process, providing a comprehensive assessment of the treatment efficacy over the study period. An additional questionnaire of the review process has been undertaken by the patients to analyse the treatment experience of each patient.

Data collection tools and variables

To ensure a comprehensive evaluation of the treatment outcomes, standardised scales and questionnaires were utilised for data collection. These tools assessed various parameters, including non-inflammatory and inflammatory lesions, GAGS scores, acne scarring, skin texture, and treatment satisfaction. The following section details the measurement scales (Table 1) and pre- and post-treatment questionnaires (Table 2 and 3) used to gather participant data systematically.

Table 1. Measurement scales for variables in acne evaluation

Variable	Scale (Range)
Non-inflammatory lesions	1 = 0-20 (mild)
	2 = 21-40 (moderate)
	3 = 41-60 (severe)
	4 = 61 + (extremely severe)
Inflammatory lesions	1 = 0-5 (mild)
	2 = 6 - 20 (moderate)
	3 = 21 - 50 (severe)
	4 > 50 (very severe)
GAGS (glycosaminoglycans) score	1 = 0 - 18 (mild)
	2 = 18 - 30 (moderate)
	3 = 31 - 38 (severe)
	4 > 38 (very severe)
Acne scarring	1 = Macular
	2 = Mild
	3 = Moderate
	4 = Severe
Skin texture	0 = None
	1 = Minimal
	2 = Moderate
	3 = Severe
	4 = Extreme

Source: developed by the authors

Table 2. Pre-treatment questionnaire

Question	Response options
1. Age	19-25 26-35 36-45 46-50
2. Gender	Male Female
3. Do you use sunscreen regularly?	Yes No
4. If yes, what is the SPF of the sunscreen you use?	SPF 15 or lower SPF 16-30 SPF 31-50 SPF 51 or higher
5. Do you use any additional skin care products (e.g., moisturizer, exfoliator)?	Yes (please specify): No
6. How often do you apply these additional skin care products?	Daily Weekly Monthly Rarely
7. Do you have any known hormonal issues (e.g., polycystic ovary syndrome, thyroid issues)?	Yes (please specify): No
8. Are you currently taking any medications other than for acne?	Yes (please specify): No
9. Are you currently on any hormonal treatments or birth control?	Yes (please specify): No
10. Do you experience significant stress or lifestyle changes regularly?	Yes No
11. Do you have a history of any skin conditions (e.g., eczema, psoriasis)?	Yes (please specify): No
12. Have you had any recent changes in your skin condition?	Yes (please specify): No
13. Do you have any known allergies?	Yes (please specify): No
14. Are you currently pregnant or breastfeeding?	Yes No

Continued Table 2

Question	Response options
15. How often do you experience acne flare-ups?	Daily Weekly Monthly Rarely
16. On average, how many hours per day do you spend outdoors?	Less than 1 hour 1-2 hours 2-4 hours More than 4 hours
17. Do you use any specific acne or skin treatments, such as over-the-counter medications or home remedies?	Yes (please specify): No
18. On a scale of 1 to 10, how would you rate the overall condition of your skin prior to starting treatment?	1 (Very poor) to 10 (Excellent)

Source: developed by the authors

Table 3. Post-treatment questionnaire

Question number	Question	Options/scale
Participant information		
1	Participant ID	
2	Age	
3	Gender	Male, female, other
Baseline assessment		
4	Non-inflammatory lesions (comedones) count	0-20 (mild), 21-40 (moderate), 41-60 (severe), 61+ (extremely severe)
5	Inflammatory lesions (papules, pustules, nodules) count	0-5 (mild), 6-20 (moderate), 21-50 (severe), >50 (very severe)
6	GAGS (glycosaminoglycans) score	0-18 (mild), 18-30 (moderate), 31-38 (severe), >38 (very severe)
7	Acne scarring	Macular, mild, moderate, severe
8	Skin texture and appearance	0 (none), 1 (minimal), 2 (moderate), 3 (severe), 4 (extreme)
8-week follow-up assessment		
9	Non-inflammatory lesions (comedones) count	0-20 (mild), 21-40 (moderate), 41-60 (severe), 61+ (extremely severe)
10	Inflammatory lesions (papules, pustules, nodules) count	0-5 (mild), 6-20 (moderate), 21-50 (severe), >50 (very severe)
11	GAGS (glycosaminoglycans) score:	0-18 (mild), 18-30 (moderate), 31-38 (severe), >38 (very severe)
12	Acne scarring:	Macular, mild, moderate, severe
13	Skin texture and appearance:	0 (none), 1 (minimal), 2 (moderate), 3 (severe), 4 (extreme)
Treatment experience and satisfaction		
14	How satisfied are you with the treatment overall?	1 (very dissatisfied) — 5 (very satisfied)
15	Did you experience any side effects during the treatment?	Yes, no
16	If yes, please describe the side effects experienced:	
17	How would you rate the ease of use of the treatment?	1 (very difficult) — 5 (very easy)
18	Would you recommend this treatment to others?	Yes, no
19	How has the treatment impacted your confidence and social interactions?	1 (no impact) — 5 (significant impact)
20	Any additional comments or feedback on the treatment:	

Source: developed by the authors

Ethical considerations

Consent forms were obtained from each patient and treatments were administered to each patient with the permission of both doctors and patients. Additionally, approval for the study was granted by the three dermatology clinics in Pakistan involved in the research. However, per their request, the names of these clinics have been kept confidential to respect their privacy policies. All procedures adhered to ethical guidelines to protect the participants' rights, safety, and well-being throughout the study in accordance with the rules of the Declaration of Helsinki [17].

Reliability of the study

The reliability of the study was assessed by determining the internal consistency of the questionnaire by using Cronbach's Alpha. It was found that for a 10-item scale, the Cronbach's Alpha was 0.409. This suggested a fair degree of internal consistency though implying that some modification might be made to improve reliability with respect to this scale. However, rigorous methodology was observed throughout the investigation of questionnaire and treatments validation by dermatological experts and consideration of ethical issues thereby enhancing dependability and trustworthiness of results.

Outcome Measures

The outcomes of each treatment group were measured as primary and secondary outcomes. The primate outcomes included the changes in the inflammatory and non-inflammatory lesions count and the improvements in the GAGS score. Secondary outcomes of the treatment groups included the improvement in skin smoothness and reduction in the acne scarring. These outcomes were measured to determine the comparative analysis of each treatment and the determination of an effective treatment for the patients with mild to moderate acne.

Statistical Analysis

The study used SPSS for data analysis, utilising descriptive statistics to summarise baseline demographics and study endpoints. The Paired T-test was used to compare pre- and post-treatment outcomes within each treatment group, assessing the effectiveness of each treatment method in reducing acne severity over an 8-week period. ANOVA was used to compare mean outcome measures across the three treatment groups, identifying the most effective treatment method (Benzoyl Peroxide, Tretinoin, or Salicylic Acid) in improving acne outcomes. This statistical test provided a comprehensive understanding of the relative efficacy of each treatment, ensuring observed differences were not due to chance.

Results and Discussion

Acne Vulgaris: Pathophysiology, treatment challenges, and hormonal influences

Acne vulgaris (AV) is a chronic inflammatory skin disease affecting around 80% of young adults and adolescents [1, 7]. AV affects the pilosebaceous unit and is characterised by both inflammatory and non-inflammatory lesions, scarring, and pigmentation that persist throughout life [18]. It has been characterised by open and closed comedones, lesions with inflammatory nodules, pustules, and papules, typically affecting the face, chest, and back [5].

Another human commensal bacterium that inhabits the skin's pilosebaceous ducts is *Propionibacterium acnes*, or *P. acnes*. The pathophysiology of acne vulgaris is significantly influenced by *P. acnes,* a bacterium that colonises the sebaceous glands and hair follicles. Its proliferation triggers inflammation, leading to the development of acne lesions and contributing to both physical discomfort and emotional distress [19]. Notably, the rise in *P. acnes*-related infections, such as shoulder infections after surgery, underscores the growing challenge of managing this bacterium. Compounding the issue is the increasing incidence of antibiotic resistance, which limits the effectiveness of traditional treatments [20].

Treatment adherence is a significant issue, especially for topical treatments, as it can lead to side effects and prolonged treatment time, resulting in acne recurrence, patient dissatisfaction, and increased medical costs [7]. International treatment guidelines recommend a topical retinoid plus antimicrobial as the first-line therapy for most acne patients. Topical Retinoid, such as tretinoin and adapalene, were essential for acne management, but they are often primarily effective in comedonal acne and associated with significant cutaneous irritation [21]. Benzoyl peroxide (BPO) is a widely used topical therapy for acne vulgaris, with its bactericidal effect on *P. acnes* being well documented.

Androgens are hormones that are present in both male and female, play a pivotal role in the development of acne, particularly during puberty when their levels rise rignificantly. This hormonal surge stimulates an increase in sebum production, contributing to pore formation and the subsequent onset of acne [22]. The condition of acne, is caused by increased androgen production by the gonads and adrenal glands and increased sensitivity to androgen receptors. This leads to blockage of the pilosebaceous canal, follicular hyperkeratinisation, sebaceous gland enlargement, and keratinocyte shedding, resulting in a follicular plug all influenced by androgens. This blockage creates a microcomedo, which progresses into a visible comedo as sebum flow is obstructed [23]. Although acne is commonly associated with adolescence, it may be severe in adulthood, especially among women because of hormonal fluctuations caused by the menstrual cycle, pregnancy, or Polycystic Ovary Syndrome (PCOS) [24]. Understanding these demographic characteristics is crucial in delivering suitable acne therapies and setting the appropriate anticipations for each group of patients.

Results of acne treatment according to the severity of the disease

The acne grading system is an essential part of dermatological practice aimed at classifying acne according to its severity, offering therapy options, and providing prognostic estimations. It consists of several measurements: the non-inflammatory lesions scale, the inflammatory lesions scale, the GAGS (glycosaminoglycans) score, the acne scarring scale, and the skin texture scale. One scale measures various aspects of acne and ranges from mild to extremely severe ensuring that every aspect is considered.

Non-inflammatory acne lesions include comedones, which are divided into open (blackheads) and closed (whiteheads). They occur due to the blockage of hair follicles by sebum, dead epidermal cells, and microorganisms, with no signs of inflammation such as redness or pain. The main causes are hyperkeratinisation and increased sebum production, which create a favourable environment for the growth of *P. acnes*. These lesions typically do not cause

discomfort but may progress to an inflammatory stage without proper care. Figure 2 shows the distribution of non-inflammatory lesions in three groups before therapy. Most patients in all groups had moderate to severe non-inflammatory lesions, with moderate category being the most prevalent. Figure 3 shows the post treatment results of all groups for non-inflammatory lesions. This highlights a common issue that treatment aims to address.

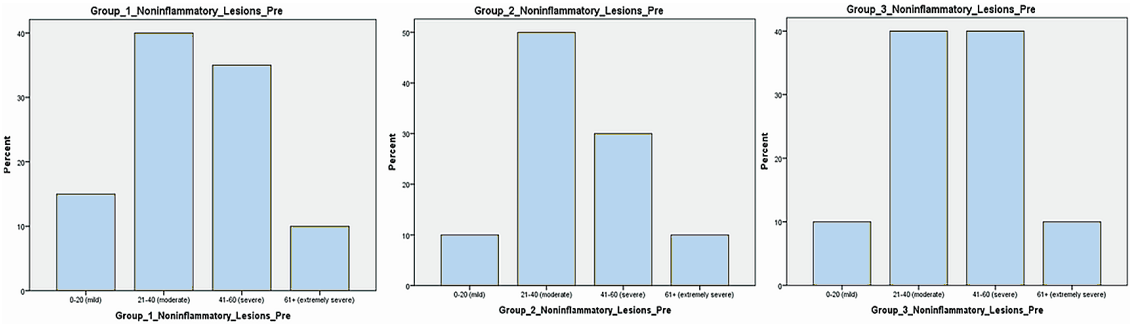

Figure 2. Non-inflammatory lesions – all 3 groups (pre-treatment)

Source: developed by the authors

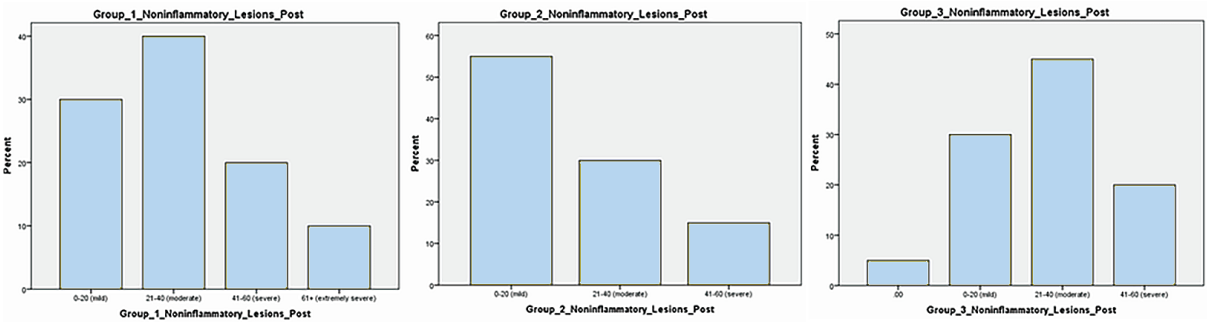

Figure 3. Non-inflammatory lesions – all 3 groups (post-treatment)

Source: developed by the authors

The analysis found that in all three groups, after treatment, there was a tendency to reduce the percentage of patients with severe and extremely severe lesions. This indicates the overall effectiveness of the treatment. In parallel with the decrease in the number of severe cases, the number of patients with mild or moderate lesions increased. Despite the overall trend towards improvement, there are certain differences in the dynamics of changes between the groups. In particular, Group 3, which used salicylic acid, showed the greatest treatment effectiveness. In particular, after treatment, no extremely severe cases were detected at all, and the number of severe cases was halved. Inflammatory lesions are skin conditions causing redness, swelling, and pain due to the body's immune response to perceived threats. Examples include acne, eczema, psoriasis, and dermatitis, with severity ranging from mild to severe. Figure 4 shows the results of the distribution of inflammatory skin lesions before treatment in the three experimental groups. In particular, in all groups, the majority of participants had moderate to severe inflammatory lesions. Figure 5 shows the results of treatment of inflammatory lesions.

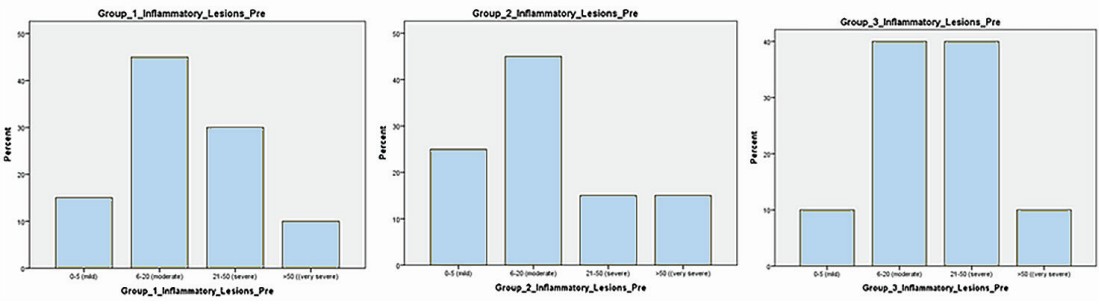

Figure 4. Inflammatory lesions – all 3 groups (pre-treatment)

Source: developed by the authors

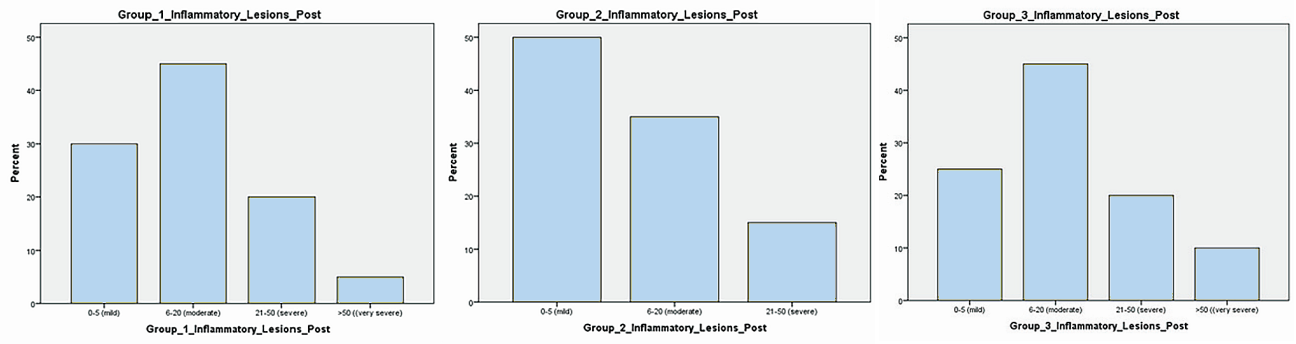

Figure 5. Inflammatory lesions – all 3 groups (post treatment)

Source: developed by the authors

The results showed improvement in all groups. In particular, the number of patients with mild lesions increased and the number of severe and very severe lesions significantly decreased. In Group 1 (benzoyl peroxide), the number of patients with mild lesions doubled to 30%, and the number of patients with very severe lesions decreased by half. Group 2 (retinoids) showed the most significant improvement: 50% of participants had mild cases (which is 2 times more than before treatment), and no very severe cases were recorded. Group 3 (salicylic acid) showed a significant increase in mild cases and a halving of severe cases (from 40 to 20%). however, the number of very severe lesions remained the same. Thus, while all groups showed a reduction in disease severity, treatment with retinoids (group 2) produced the most significant reduction in inflammation.

GAGS Score. To evaluate the effectiveness of the drugs, it is important to analyse the distribution of disease severity in patients in all three groups. For this purpose, we used the Global Acne Grading System (GAGS), a quantitative scoring system used to assess the severity of acne vulgaris. It measures the severity of acne in six areas of the face, chest and back, ranging from 0 to 4. The total score of all six areas determines the severity of acne. The total score is then used to classify acne as mild, moderate, severe or very severe. The GAGS can be used for clinical monitoring, epidemiological studies and clinical trials. Figure 6 shows the overall results of the GAGS score before treatment.

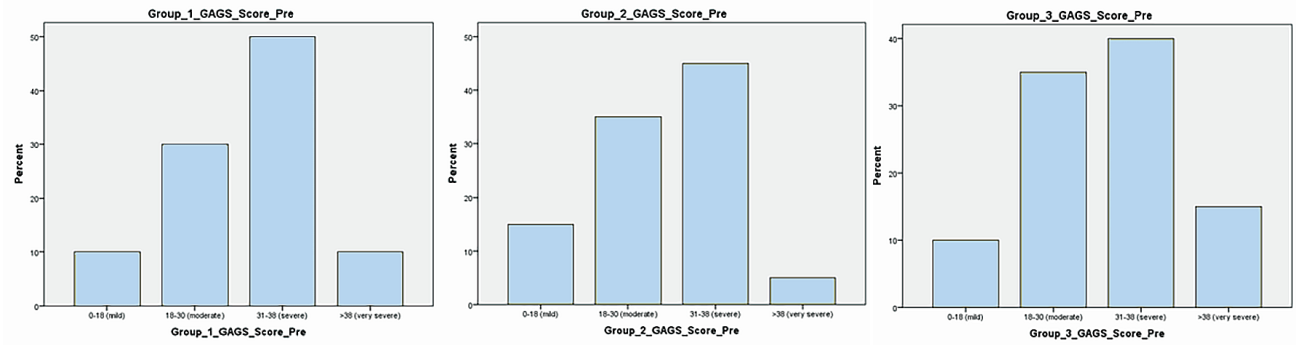

Figure 6. GAGS score – all 3 groups (pre-treatment)

Source: developed by the authors

Figure 6 shows the GAGS score distribution for three groups before treatment. Most participants had moderate or severe acne, with fewer cases of mild or very severe acne. In Group 1, about 50% had severe acne, 30% moderate, 10% very severe, and 10% mild. Group 2 had around 45% with severe acne, 35% moderate, 15% mild, and a small percentage very severe. Group 3 had 40% severe, 35% moderate, 10% mild, and 15% very severe cases. This suggests that moderate to severe acne was the most common. These results indicated a predominance of moderate to severe GAGS scores in all groups prior to treatment. Post-treatment data should reveal changes in these categories to assess the effectiveness of each treatment in reducing GAGS severity (Fig. 7).

In Figure 7, the GAGS score post-treatment showed that group 1 (BPO) had a higher number of severe cases compared to pre-treatment, suggesting it may not have been as effective in reducing GAGS severity. group 2 (Retinoid) showed modest improvement, while group 3 (SA) showed a slight reduction in very severe cases but overall stability. Thus, the most significant improvement was shown by group 2, which was treated with tretinoin lotion.

Acne scarring is a condition where the skin's healing process is disrupted, leading to excessive or insufficient

collagen production. This can be caused by factors like acne severity, picking, delayed treatment, hormonal changes, and men developing more severe acne. It's crucial to address acne promptly to prevent scarring. Causes include cysts or nodules burst, and picking or squeezing acne can also contribute to scarring [25].

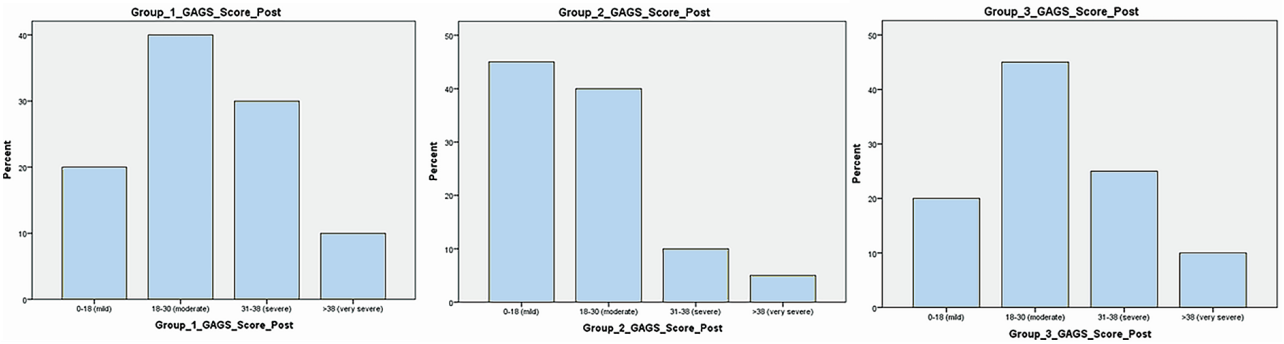

Figure 7. GAGS score – all 3 groups (post treatment)

Source: developed by the authors

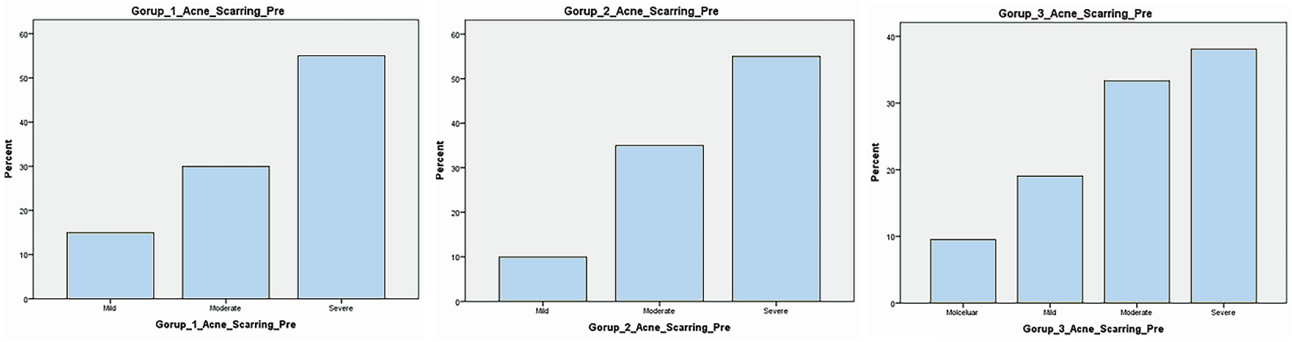

Figure 8. Acne scarring – all 3 groups (pre-treatment)

Source: developed by the authors

Figure 8 shows the distribution of acne scarring severity across three treatment groups before treatment. The data suggests that moderate and severe scarring were the most common types among participants, with fewer cases of mild or molecular scarring. All three groups show a similar pattern, where the proportion of severe scarring is notably higher than the mild category. This indicates that most participants had significant acne-related scarring prior to treatment. The differences in scarring severity across groups provide a baseline for assessing how well each treatment reduces acne scars in the post-treatment phase (Fig. 9).

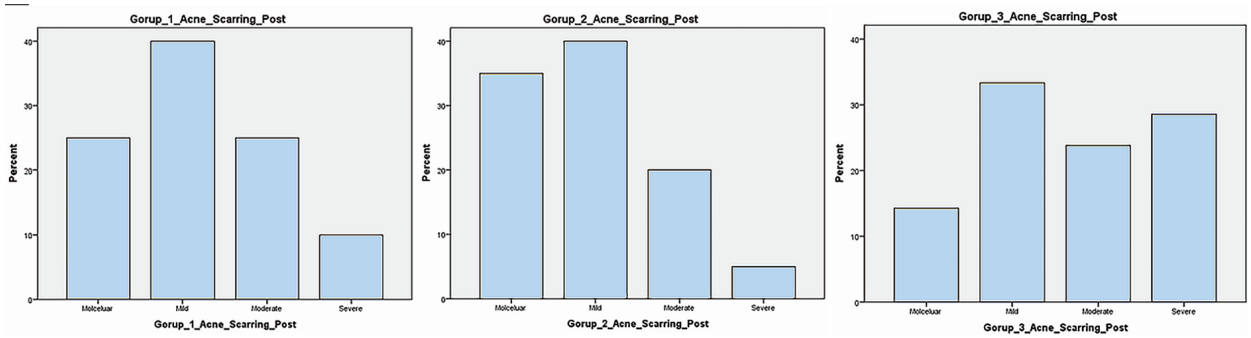

Figure 9. Acne scarring – all 3 groups (post treatment)

Source: developed by the authors

Figure 9 shows the post treatment results for acne scarring which demonstrates that Group 1 (Benzoyl Peroxide) showed most significant shift, with a notable rise in mild scarring and a reduction in severe cases. Group 2 (Retinoid) showed the best improvement, showing the highest proportion of molecular and mild scarring, indicating

effective scar healing. Group 3 (Salicylic Acid) showed some improvement but retained a higher percentage of severe scarring. Overall, Retinoids were the most effective in reducing acne scars, followed by Benzoyl Peroxide, while Salicylic Aci showed limited impact.

Skin Texture. Skin texture issues result from inflammation, scarring, and irregular healing processes. Common complications include rough patches, enlarged pores, and raised scars. Factors such as hormonal imbalances, and environmental pollutants contribute to the deterioration [26]. The analysis of the skin texture of the participants by group showed the following results (Fig. 10). In all groups, a large number of severe and very severe skin texture problems were recorded. However, in the first group, the number of moderate, severe and very severe cases was almost the same (30, 30 and 35%, respectively). In the second and third groups, severe cases significantly prevailed. However, Group 3 had the highest proportion of severe skin texture problems before treatment.

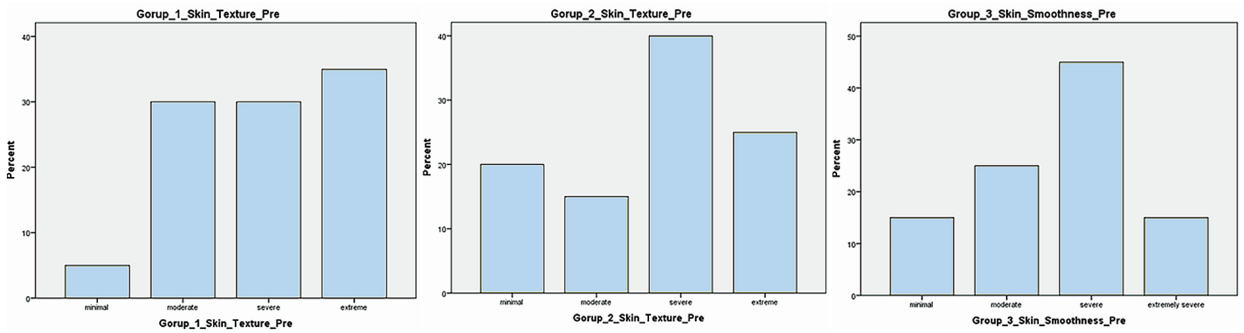

Figure 10. Skin texture – 3 groups (pre-treatment)

Source: developed by the authors

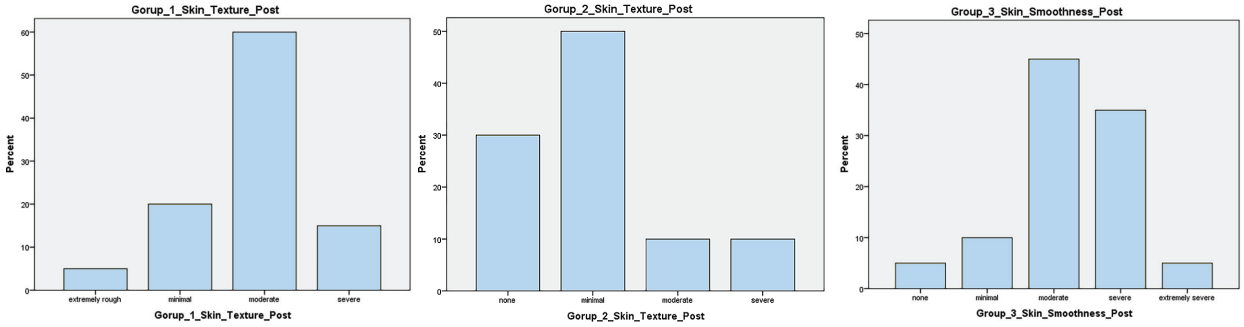

Figure 11. Skin texture – all 3 groups (post treatment)

Source: developed by the authors

Figure 11 shows the results of the skin treatment for all groups. The analysis showed that all groups achieved an improvement in the patients' skin texture. At the same time, after treatment, at least 5% of patients in each group were found to be completely free of problems. There were two times fewer severe cases and no extremely severe cases in groups 1 and 2. Group 3 showed improvement in skin texture, however, retained severe textures than Groups 1 and 2. BPO and Retinoid treatments showed better outcomes, with many achieving moderate or minimal improvements, suggesting they may be more effective than SA.

Assessing the safety and effectiveness of topical acne treatments

Paired Sample T-test

The paired T-test is a statistical method used to compare the mean values of two related samples, particularly before and after a given intervention. In this study, paired sample t-test was conducted to evaluate the safety and efficacy of topical the treatment for mild to moderate acne. The analysis compared pre-treatment and post-treatment outcomes to assess significant differences in spasticity reduction and functional improvement. This approach allows for an objective evaluation of each treatment's effectiveness and enables conclusions to be drawn about their impact.

Benzoyl Peroxide Group

Table 4 shows the paired sample t-test statistics for Group 1 (Benzoyl Peroxide) which showed that skin texture improved significantly, with a mean score reduction from 2.95 (pre-treatment) to 1.85 (post-treatment), a mean difference of 1.100. Other parameters did not exhibit significant changes: non-inflammatory lesions (mean difference = 0.300), inflammatory lesions (mean difference = 0.350), and acne scarring (mean difference = 0.100). GAGS scores even increased by 0.250, which may indicate a deterioration in the overall condition of the skin.

Table 4. Benzoyl Peroxide group-paired samples statistics

Paired samples statistics					
		Mean	N	Std. deviation	Std. error mean
Pair 1	Non_Inflammatory_Lesions_Pre	2.40	20	.883	.197
	Non_Inflammatory_Lesions_Post	2.10	20	.968	.216
Pair 2	Inflammatory_Lesions_Pre	2.35	20	.875	.196
	Inflammatory_Lesions_Post	2.00	20	.858	.192
Pair 3	GAGS_Score_Pre	2.35	20	.933	.209
	GAGS_Score_Post	2.60	20	.821	.184
Pair 4	Acne_Scarring_Pre	2.30	20	.923	.206
	Acne_Scarring_Post	2.20	20	.951	.213
Pair 5	Skin_Texture_Pre	2.95	20	.945	.211
	Skin_Texture_Post	1.85	20	.745	.167

Source: developed by the authors

Table 5 shows the paired sample t-test statistics for Group 1 (BPO) which indicated the following outcomes: ehe skin texture showed a statistically significant value of p = 0.000, reflecting a significant improvement after treatment. However, non-inflammatory lesions showed p = 0.083, and inflammatory lesions p = 0.149, neither of which reached statistical significance. That is, the treatment did not have a confirmed effect. GAGS scores (p = 0.309) and acne scarring (p = 0.725) showed no statistically significant changes. The most notable improvement was in skin texture, highlighting its effectiveness in this area.

Table 5. Benzoyl Peroxide group-paired sample test

Paired samples test									
		Paired differences					t	df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. erro r mea n	95% Confidence interval of the difference				
					Lower	Upper			
Pair 1	Non_Inflammatory_Lesions_Pre - Non_ Inflammatory_Lesions_Post	.300	.733	.164	-.043	.643	1.831	19	.083
Pair 2	Inflammatory_Lesions_Pre - Inflammatory_Lesions_Post	.350	1.040	.233	-.137	.837	1.505	19	.149
Pair 3	GAGS_Score_Pre - GAGS_Score_Post	-.250	1.070	.239	-.751	.251	- 1.04	19	.309
Pair 4	Acne_Scarring_Pre - Acne_Scarring_Post	.100	1.252	.280	-.486	.686	.357	19	.725
Pair 5	Skin_Texture_Pre - Skin_Texture_Post	1.100	.912	.204	.673	1.527	5.395	19	.000

Source: developed by the authors

The analysis reveals that BPO significantly improves skin texture post-treatment, with a mean difference of 1.100. However, changes in non-inflammatory and inflammatory lesions did not reach statistical significance. Reductions in GAGS scores and acne scarring showed no significant impact. These findings highlight the targeted effectiveness of BPO in improving skin texture, while other acne-related measures showed limited or nonsignificant changes.

Retinoid Group

Table 6 shows the paired sample t-test statistics for Group 2 (Retinoid) which showed the following outcomes: Non-inflammatory lesions improved significantly, with a mean reduction of 0.80 (p = 0.000), indicating substantial effectiveness in reducing these lesions. Inflammatory lesions also decreased by 0.55 (p = 0.002), demonstrating a significant improvement. GAGS scores increased by 0.15 (p = 0.375), reflecting no significant change. Acne scarring worsened slightly by 0.35 (p = 0.168), and skin texture showed a significant improvement with a mean reduction of 1.70 (p = 0.000). The most notable improvements were observed in non- inflammatory lesions and skin texture, suggesting the effectiveness of Retinoid in these areas.

Table 6. Retinoid group-paired samples statistics

Paired samples statistics					
		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	Non_Inflammatory_Lesions_Pre	2.40	20	.821	.184
	Non_Inflammatory_Lesions_Post	1.60	20	.754	.169
Pair 2	Inflammatory_Lesions_Pre	2.20	20	1.005	.225
	Inflammatory_Lesions_Post	1.65	20	.745	.167
Pair 3	GAGS_Score_Pre	2.25	20	.851	.190
	GAGS_Score_Post	2.40	20	.821	.184
Pair 4	Acne_Scarring_Pre	1.75	20	.851	.190
	Acne_Scarring_Post	2.10	20	.968	.216
Pair 5	Skin_Texture_Pre	2.70	20	1.081	.242
	Skin_Texture_Post	1.00	20	.918	.205

Source: developed by the authors

Table 7 shows the paired sample t-test results for Group 2 (Retinoid) which demonstrates significant improvements in several areas. Non-inflammatory lesions were significantly reduced, demonstrating a statistically significant difference of $p = 0.001$. Inflammatory lesions also improved, showing a significant reduction $p = 0.037$. GAGS scores showed a minor decrease ($p = 0.614$), which was not significant. That is, the treatment did not have a significant effect on the overall acne severity scale. Acne scarring slightly worsened ($p = 0.309$), but the change was not statistically significant, that is, the acne scars have not changed significantly Skin texture changes showed a statistically significant difference $p = 0.000$, indicating significant improvement after treatment. The most pronounced improvements were in non-inflammatory lesions and skin texture.

Table 7. Retinoid group-paired sample test

Paired samples test									
		Paired differences					t	df	Sig. (2-tailed (p)
		Mean	Std. deviation	Std. error mean	95% confidence interval of the difference				
					Lower	Upper			
Pair 1	Non_Inflammatory_Lesions_Pr e - Non_ Inflammatory_Lesions_P ost	.800	.951	.213	.355	1.245	3.760	19	.001
Pair 2	Inflammatory_Lesions_Pre - Inflammatory_Lesions_Post	.550	1.099	.246	.036	1.064	2.238	19	.037
Pair 3	GAGS_Score_Pre - GAGS_Score_Post	-.150	1.309	.293	-.763	.463	-.513	19	.614
Pair 4	Acne_Scarring_Pre - Acne_Scarring_Post	-.350	1.496	.335	- 1.050	.350	- 1.046	19	.309
Pair 5	Skin_Texture_Pre - Skin_Texture_Post	1.700	1.031	.231	1.217	2.183	7.373	19	.000

Source: developed by the authors

The test showed that Retinoids effectively reduce both non-inflammatory and inflammatory rashes ($p < 0.05$). At the same time, the overall acne severity score (GAGS Score) and the condition of the scars did not change significantly after treatment ($p > 0.05$). The most pronounced improvements were observed in skin texture ($p < 0.001$), which may be an important cosmetic effect. In general, retinoids show significant efficacy in the treatment of acne, especially in reducing rashes and improving skin texture, but do not significantly affect existing scars.

Salicylic Acid Group

Table 8 shows the paired sample t-test statistics results in the SA group which indicated the following outcomes: Non-inflammatory lesions decreased significantly by 0.70, reflecting improvement. Inflammatory lesions also showed a reduction of 0.35. GAGS scores increased slightly by 0.25 ($p = 0.299$), indicating a minimal change or slight deterioration in the condition. Acne scarring worsened by 0.35, but this change was not significant. Skin texture improved by 0.35 ($p = 0.125$), showing a modest enhancement. The most significant improvements were observed in non-inflammatory lesions, while other measures showed minimal or no significant change. Table 9 shows the paired sample t-test results for the SA group which revealed the following outcomes: Salicylic acid statistically significantly reduced the number of non-inflammatory rashes ($p = 0.000$), indicating a notable improvement. The inflammatory lesions showed a result of $p = 0.110$, i.e. this change was not statistically significant. GAGS scores increased slightly ($p = 0.367$), showing minimal change. Acne scarring worsened ($p = 0.286$), which was not significant. The skin texture improved significantly, as evidenced by the p value of 0.005. The most notable results were the significant reduction in non-inflammatory lesions and improvement in skin texture.

Table 8. Salicylic acid-paired samples statistics

Paired samples statistics					
		Mean	N	Std. deviation	Std. error mean
Pair 1	Non_Inflammatory_Lesions_Pre	2.50	20	.827	.185
	Non_Inflammatory_Lesions_Post	1.80	20	.834	.186
Pair 2	Inflammatory_Lesions_Pre	2.50	20	.827	.185
	Inflammatory_Lesions_Post	2.15	20	.933	.209
Pair 3	GAGS_Score_Pre	2.35	20	.875	.196
	GAGS_Score_Post	2.60	20	.883	.197
Pair 4	Acne_Scarring_Pre	2.25	20	.910	.204
	Acne_Scarring_Post	2.60	20	1.046	.234
Pair 5	Skin_Texture_Pre	2.60	20	.940	.210
	Skin_Texture_Post	2.25	20	.910	.204

Source: developed by the authors

Table 9. Salicylic Acid group-paired sample test

Paired Samples Test									
		Paired Differences					t	df	Sig. (2-tailed)
		Mean	Std. deviation	Std. error mean	95% confidence interval of the difference				
					Lower	Upper			
Pair 1	Non_Inflammatory_Lesions_Pre- Non_ Inflammatory_Lesions_Post	.700	.657	.147	.393	1.007	4.765	19	.00
Pair 2	Inflammatory_Lesions_Pre- Inflammatory_Lesions_Post	.350	.933	.209	-.087	.787	1.677	19	.110
Pair 3	GAGS_Score_Pre-GAGS_Score_Post	-.250	1.209	.270	-.816	.316	-.925	19	.367
Pair 4	Acne_Scarring_Pre- Acne_Scarring_Post	-.350	1.424	.319	- 1.017	.317	- 1.099	19	.286
Pair 5	Skin_Texture_Pre - Skin_Texture_Post	.350	.489	.109	.121	.579	3.199	19	.005

Source: developed by the authors

Salicylic acid is effective in reducing the number of non-inflammatory breakouts and improving skin texture, which is confirmed by statistically significant results ($p < 0.01$). At the same time, its effect on inflammatory rashes, general acne condition (GAGS Score) and acne scars is not statistically significant, and in some cases, there is even a tendency to worsen. Thus, salicylic acid can be an effective treatment for patients with comedonal acne, but its use in the treatment of inflammatory acne and post-acne scars requires additional research or a combined approach with other therapeutic methods.

One-way ANOVA for comparing gender and treatment measures

A one-way ANOVA analysis was conducted to evaluate the impact of gender on various acne treatment outcomes, including non-inflammatory lesions, inflammatory lesions, GAGS score, acne scarring, and skin texture. Table 10 shows the results of the ANOVA analysis, which shows whether there is a statistically significant difference between the groups (men and women) for each acne treatment indicator. A p-value of < 0.05 is statistically significant and indicates that gender has an effect on this indicator. A P-value ≥ 0.05 means that there is no such effect.

Table 10. Results of one-way ANOVA analysis

		Sum of Squares	df	Mean Square	F	Sig.
Non_Inflammatory_Lesions_Pre	Between Groups	.059	1	.059	.085	.772
	Within Groups	40.674	58	.701		
	Total	40.733	59			
Non_Inflammatory_Lesions_Post	Between Groups	.165	1	.165	.216	.643
	Within Groups	44.168	58	.762		
	Total	44.333	59			
Inflammatory_Lesions_Pre	Between Groups	.514	1	.514	.633	.429
	Within Groups	47.136	58	.813		
	Total	47.650	59			

Continued Table 10

		Sum of Squares	df	Mean Square	F	Sig.
Inflammatory_Lesions_Post	Between Groups	.847	1	.847	1.145	.289
	Within Groups	42.886	58	.739		
	Total	43.733	59			
GAGS_Score_Pre	Between Groups	.405	1	.405	.526	.471
	Within Groups	44.579	58	.769		
	Total	44.983	59			
GAGS_Score_Post	Between Groups	.003	1	.003	.004	.949
	Within Groups	40.930	58	.706		
	Total	40.933	59			
Acne_Scarring_Pre	Between Groups	.264	1	.264	.312	.578
	Within Groups	49.136	58	.847		
	Total	49.400	59			
Acne_Scarring_Post	Between Groups	4.344	1	4.344	4.643	.035
	Within Groups	54.256	58	.935		
	Total	58.600	59			
Skin_Texture_Pre	Between Groups	1.653	1	1.653	1.724	.194
	Within Groups	55.597	58	.959		
	Total	57.250	59			
Skin_Texture_Post	Between Groups	6.336	1	6.336	7.032	.010
	Within Groups	52.264	58	.901		
	Total	58.600	59			

Source: developed by the authors

The results of ANOVA analysis showed no significant gender-related differences in the severity of non-inflammatory lesions pre- or post-treatment, suggesting minimal variability between genders. Inflammatory lesions showed no significant gender-related differences pre- or post-treatment, suggesting no statistically meaningful differences between genders. The GAGS scores also showed no significant gender differences pre- or post-treatment, indicating no significant variability between genders. However, a notable gender-related difference was observed in post-treatment acne scarring, indicating that gender significantly affects the outcomes for acne scarring. Gender differences were also significant for skin texture post-treatment, suggesting that gender significantly influences the improvement of skin texture after treatment. These findings highlight the importance of considering gender-specific factors when assessing treatment efficacy for acne scarring. Table 11 displays the reliability test findings for the study's items. The Case Processing Summary shows that all 60 cases (100%) were legitimate, with no exclusions, resulting in a complete dataset for study. In Reliability Statistics, the Cronbach's Alpha score for 10 items is 0.709, suggesting satisfactory internal consistency. A Cronbach's Alpha greater than 0.7 indicates good reliability, implying that the questions included in the questionnaire are relatively consistent, however minor changes might potentially increase reliability even further.

Table 11. Reliability test

Case Processing Summary			
		N	%
Cases	Valid	60	100.0
	Excluded[a]	0	.0
	Total	60	100.0
a. Listwise deletion based on all variables in the procedure.			

Reliability Statistics	
Cronbach's Alpha	N of Items
.709	10

Source: developed by the authors

The study evaluated the efficacy of three topical treatments for acne by Benzoyl Peroxide, Retinoid, and SA in five parameters including non-inflammatory and inflammatory lesions, GAGS scores, acne scarring, and skin texture. BPO showed significant improvement only in skin texture, with a mean reduction of 1.10 ($p = 0.000$), while other parameters, including non-inflammatory and inflammatory lesions, GAGS scores, and acne scarring, did not show statistically significant changes.

The paired sample t-test analysis revealed that all three treatment groups demonstrated significant improvements in certain areas. For the BPO group, significant

enhancement was observed in skin texture (p = 0.000), but no significant changes were found in non-inflammatory lesions, inflammatory lesions, GAGS scores, or acne scarring. The Retinoid group showed significant reductions in non-inflammatory lesions (p = 0.001) and inflammatory lesions (p = 0.037), along with improved skin texture (p = 0.000). The SA group exhibited significant reductions in non-inflammatory lesions (p = 0.000) and improvements in skin texture (p = 0.005). These findings highlight the efficacy of each treatment in improving specific acne-related parameters. In general, the results show that the choice of drug depends on the type of acne, and each drug has its own advantages for specific patient groups.

Discussion

This study highlights the comparative efficacy of three commonly used topical treatments for mild-to-moderate acne, namely benzoyl peroxide, retinoids, and salicylic acid. The findings not only emphasise the strengths of each treatment but also underscore the need for personalised approaches to acne management, particularly considering the unique profiles and responses of the study participants. Studies conducted by H. Baldwin *et al.* [27], P. Szczuraszek *et al.* [28] have shown that Retinoid derived from vitamin A works by unclogging pores, reducing inflammation and preventing the formation of new acne lesions in the treatment of AV and psoriasis by altering cellular protein that affects multiple pathways involved in the pathogenesis of acne. This is confirmed by the results of the current study. The results of this study aligned with J.C. Harper *et al.* [29] and D. Pariser & E. Guenin [30] demonstrating that Tretinoin 0.05% lotion was significantly more effective than vehicle in achieving treatment success and reducing inflammatory and non-inflammatory lesions.

According to S.K. Tyring *et al.* [31], lotion comprising 0.05% Tretinoin improved quality of life for patients with moderate-to-severe acne after 12 weeks of treatment, with clinical improvements in acne symptoms specifically in female with moderate or severe acne if used once in daily routines. Moreover, G. Han *et al.* [32] showed that this lotion effectively reduced non-inflammatory acne lesions in an Asian population, improving quality of life without any adverse events or concerns about skin dryness, irritation, or hyperpigmentation.

The American Academy of Dermatology (AAD) recommends using topical benzoyl peroxide and retinoid as the first treatment for mild acne, followed by oral antibiotics for moderate- grade disease [2]. T. Matin & M.B. Goodman [33] noted Benzoyl peroxide is an effective topical treatment for AV due to its antibacterial, irritant, and anti-inflammatory properties. The results of the current study also coincide with the findings of the following authors. According to B. Dréno *et al.*, [34] topical benzoyl peroxide 2.5% gel effectively reduces atrophic acne scars and acne lesions in moderate to severe acne patients, with up to 48 weeks of treatment being safe and well- tolerated. The 2.5% gel formulation of benzoyl peroxide was found to be more effective by H. Tanizaki *et al.* [35] in preventing the worsening of scars in Japanese patients with AV.

Benzoyl peroxide, being a popular acne treatment can cause skin irritation, bleaching effects, allergic reactions, antibiotic resistance, and increased sun sensitivity [36]. Due to these complications, several studies has demonstrated the combination of other agents with benzoyl peroxide to improve the effeteness of the treatment method for acne patients. M.P. Amrutha *et al.* [37] suggested that the combination gel of 0.1% adapalene and 2.5% benzoyl peroxide is more effective for treating mild-to-moderate acne vulgaris, with comparable tolerability. However, G. Kosmoski *et al.* [38] suggested that a daily regimen of benzoyl peroxide (2.5%) in the morning and retinol (0.1%) in the evening effectively reduces acne count, severity, and lesions, while improving skin complexion and quality of life without causing facial irritation. Although the current study did not investigate combination treatments for acne, the authors agree that combining different drugs that demonstrate specific positive effects on different problems can be effective.

SA effectively treats AV by suppressing the AMPK/SREBP1 pathway and NFB pathway in human sebocytes. This is confirmed by the study by J. Lu *et al.* [39]. According to S.E. Dal Belo *et al.* [40], DC-Eff, a multi-targeted salicylic acid-based dermocosmetic cream, is as effective as benzoyl peroxide 5% in improving mild-to-moderate acne, with better tolerance and high appreciation. Due to several limitations of using SA along such as skin irritation, dryness, peeling, and increased sun sensitivity, especially during initial treatment has suggested the combination of SA with other agents for effective outcomes. For instance, T. Zhang *et al.* [3] suggested that Poly (ionic liquid)-based microneedles containing SA showed potential in improving acne treatment by effectively delivering therapeutics through the skin barrier. Moreover, D. Ye *et al.* [41] revealed that the low-dose oral isotretinoin combined with 30% SA chemical peeling effectively and safely treats AV in Asian patients.

The ANOVA analysis conducted in the current study showed that gender did not significantly affect the overall severity of non-inflammatory and inflammatory lesions. However, significant gender differences were found in the treatment of scars and skin texture, which is supported by numerous studies. Gender differences in acne treatment outcomes can be influenced by hormonal fluctuations, treatment response, and side effects. Women experience more hormonal fluctuations due to menstrual cycles, pregnancy, and menopause, which can affect acne [24]. Research of K.D. Gardner [42] suggested that women may respond differently to acne treatments, benefiting from hormonal therapies like oral contraceptives. Women may also experience different side effects from topical treatments, such as irritation and dryness, which can influence adherence to treatment regimens and potentially affect overall outcomes [43]. Overall, these researches highlighted the need for tailored treatment plans that consider individual patient characteristics, including skin type, acne severity, and potential side effects, to achieve optimal outcomes in acne management.

Conclusions

The study successfully achieved its goal of evaluating the comparative efficacy of benzoyl peroxide, retinoids, and salicylic acid in managing mild-to-moderate acne. Using a robust cross-sectional design, the research analysed outcomes across parameters such as non-inflammatory and inflammatory lesions, skin texture, and acne scarring. Each treatment demonstrated unique strengths. Retinoids showed superior efficacy in improving non-inflammatory and inflammatory lesions and enhancing skin texture. Benzoyl peroxide significantly improved skin texture, but its effect on inflammatory and non-inflammatory rashes was less pronounced, and no statistically significant changes were observed. Salicylic acid demonstrated a positive effect on non-inflammatory rashes and skin texture, but its effect on inflammatory lesions and acne scars was less pronounced and not statistically significant. This indicates the need for a combined approach in the treatment of complex forms of acne.

The study results also demonstrated that the effectiveness of treating inflammatory and non-inflammatory acne lesions does not depend on gender. At the same time, it was emphasised that gender is important in terms of the impact of acne treatment on scarring and skin texture, highlighting the role of hormonal influences on the course of treatment. Women showed more pronounced improvements in skin texture, while men showed less of an effect on scarring, indicating the need for individualised treatment approaches depending on gender. While gender-related differences were observed, age-related variations and hormonal fluctuations were not extensively explored. Thus, for optimal treatment of acne and its consequences, it is necessary to take into account the type of drug, gender differences and the specificity of skin lesions.

The study's short follow-up period may limit long-term outcomes assessment and treatment durability. Further research is needed to explore the long-term effectiveness and safety of these treatments, considering larger, more diverse populations and extended follow-up periods. Factors like age, hormonal changes, and individual factors could provide more comprehensive insights for treatment tailoring.

Acknowledgements

The authors acknowledge and express their gratitude to all participants, dermatology clinics, and research teams who contributed to this study. Their support and collaboration were invaluable in completing this research.

Conflict of Interest

None.

References

[1] Lueangarun S, Sriviriyakul K, Tempark T, Managit C, Sithisarn P. Clinical efficacy of 0.5% topical mangosteen extract in nanoparticle-loaded gel in treatment of mild-to-moderate acne vulgaris: A 12-week, split-face, double-blinded, randomized, controlled trial. J Cosmet Dermatol. 2019;18(5):1395–1403. DOI: 10.1111/jocd.12856

[2] Bhatt S, Kothari R, Tripathy DM, Sandhu S, Babaei M, Goldust M. Emerging drugs for the treatment of acne: A review of phase 2 & 3 trials. Expert Opin Emerg Drugs. 2022;27(3):241–51. DOI: 10.1080/14728214.2022.2110239

[3] Zhang T, Sun B, Guo J, Wang M, Cui H, Mao H, et al. Active pharmaceutical ingredient poly(ionic liquid)-based microneedles for the treatment of skin acne infection. Acta Biomater. 2020;115:136–47. DOI: 0.1016/j.actbio.2020.08.023

[4] Ye CX, Yi J, Su Z, Gao X, Jiang X, Yu N, et al. 2% supramolecular salicylic acid hydrogel vs. adapalene gel in mild to moderate acne vulgaris treatment: A multicenter, randomized, evaluator-blind, parallel-controlled trial. J Cosmet Dermatol. 2024;23(6):2125–34. DOI: 10.1111/jocd.16238

[5] Gern A, Xu S, Walter J, Vakharia P. A randomized controlled double-blinded split-face prospective clinical study to assess the efficacy, safety, and tolerability of a novel 3-step routine compared to benzyl peroxide for the treatment of mild to moderate acne vulgaris. Arch Dermatol Res. 2024;316:230. DOI: 10.1007/s00403-024-02874-9

[6] Chen W, Dai R, Li L. The prevalence of self-declared sensitive skin: A systematic review and meta-analysis. J Eur Acad Dermatol Venereol. 2020;34(8):1779–88. DOI: 10.1111/jdv.16166

[7] Dikicier BS. Topical treatment of acne vulgaris: Efficiency, side effects, and adherence rate. J Int Med Res. 2019;47(7):2987–92. DOI: 10.1177/0300060519847367

[8] Jorgaqi E, Savo I, Koraqi A, Doci X, Cela R, Vasili E, et al. Efficacy of acne vulgaris treatment protocols according to its clinical forms. Dermatol Ther. 2020;33(4):e1361. DOI: 10.1111/dth.13611

[9] Sarkar R, Ghunawat S, Garg VK. Comparative study of 35% Glycolic acid, 20% Salicylic-10% Mandelic acid, and Phytic acid combination peels in the treatment of active Acne and postacne pigmentation. J Cutan Aesthet Surg. 2019;12(3):158–63. DOI: 10.4103/JCAS.JCAS_135_18

[10] Sattar K, Sakina S, Mumtaz S, Behram F, Akbar A, Jadoon SK, et al. Safety and efficacy of fixed-dose combination of adapalene and benzoyl peroxide in acne vulgaris treatment: A systematic review of clinical trials. Cureus. 2024;16(9):e69341. DOI: 10.7759/cureus.69341

[11] Bhadra P. A literature review on acne due to hormonal changes and lifestyle. Indian J Nat Sci. 2020;10(59):18507–21.

[12] Kostecka M, Kostecka J, Szwed-Gułaga O, Jackowska I, Kostecka-Jarecka J. The impact of common acne on the well-being of young people aged 15-35 years and the influence of nutrition knowledge and diet on acne development. Nutrients. 2022;14(24):5293. DOI: 10.3390/nu14245293

[13] Bae IH, Kwak JH, Na CH, Kim MS, Shin BS, Choi H. A comprehensive review of the acne grading scale in 2023. Ann Dermatol. 2024;36(2):65–73. DOI: 10.5021/ad.23.094
[14] Alsulaimani H, Kokandi A, Khawandanh S, Hamad R. Severity of acne vulgaris: Comparison of two assessment methods. Clin Cosmet Investig Dermatol. 2020;13:711–6. DOI: 10.2147/ccid.s266320
[15] Kravvas G, Al-Niaimi F. A systematic review of treatments for acne scarring. Part 1: Non-energy-based techniques. Scars Burns Healing. 2017;3:2059513117695312. DOI: 10.1177/2059513117695312
[16] Donofrio L, Carruthers A, Hardas B, Murphy DK, Carruthers J, Jones D, et al. Development and validation of a photonumeric scale for evaluation of facial skin texture. Dermatol Surg. 2016;42:S219–S226. DOI: 10.1097/dss.0000000000000852
[17] WMA Declaration of Helsinki – Ethical Principles for Medical Research Involving Human Participants (2013). [cited 2024 November 22]. Available from: https://www.wma.net/policies-post/wma-declaration-of-helsinki
[18] Ghosh A, Das K. Efficacy and safety of nadifloxacin and benzoyl peroxide versus adapalene and benzoyl peroxide in acne vulgaris: A randomized open-label phase IV clinical trial. J Pharmacol Pharmacother. 2018;9(1):27–31. DOI: 10.4103/jpp.JPP_20_18
[19] Tuchayi SM, Makrantonaki E, Ganceviciene R, Dessinioti C, Feldman SR, Zouboulis CC. Acne vulgaris. Nat Rev Dis Primers. 2015;1(1):15029. DOI: 10.1038/nrdp.2015.29
[20] Scheer VM, Jungeström MB, Lerm M, Serrander L, Kalén A. Topical benzoyl peroxide application on the shoulder reduces Propionibacterium acnes: A randomized study. J Shoulder Elbow Surg. 2018;27(6):957–61. DOI: 10.1016/j.jse.2018.02.038
[21] See JA, Goh CL, Hayashi N, Suh DH, Casintahan FA. Optimizing the use of topical retinoids in Asian acne patients. J Dermatol. 2018;45(5):522–28. DOI: 10.1111/1346-8138.14314
[22] Bharti S, Vadlamudi HC. A strategic review on the involvement of receptors, transcription factors and hormones in acne pathogenesis. J Recept Signal Transduct Res. 2021;41(2):105–16. DOI: 10.1080/10799893.2020.1805626
[23] Leung AK, Barankin B, Lam JM, Leong KF, Hon KL. Dermatology: How to manage acne vulgaris. Drugs Context. 2021;10:1–18. DOI: 10.7573/dic.2021-8-6
[24] Branisteanu DE, Toader MP, Porumb EA, Serban IL, Pinzariu AC, Branisteanu CI, et al. Adult female acne: Clinical and therapeutic particularities. Exp Ther Med. 2022;23(2):151. DOI: 10.3892/etm.2021.11074
[25] Jennings T, Duffy R, McLarney M, Renzi M, Heymann WR, Decker A, et al. Acne scarring – pathophysiology, diagnosis, prevention and education: Part I. J Am Acad Dermatol. 2024;90(6):1123–34. DOI: 10.1016/j.jaad.2022.04.021
[26] Sullivan JV, Myers S. Skin structure and function, wound healing and scarring. In: Rostam DF, Neil WB, Babak JM, Cugno S, editors. Plastic Surgery – Principles and Practice [Internet]. Amsterdam: Elsevier; 2022:1–14. [cited 2024 December 12]. DOI: 10.1016/B978-0-323-65381-7.00001-0
[27] Baldwin H, Webster G, Stein Gold L, Callender V, Cook-Bolden FE, Guenin E. 50 years of topical retinoids for acne: Evolution of treatment. Am J Clin Dermatol. 2021;22:315–27. DOI: 10.1007/s40257-021-00594-8
[28] Szczuraszek P, Szczuraszek H, Sałata P, Paluch M, Tomkiewicz M, Tomkiewicz J, et al. The role of the retinoids in topical treatment of skin diseases-the review of the literature. J Educ Health Sport. 2023;13(3):309–19. DOI: 10.12775/JEHS.2023.13.03.040
[29] Harper JC, Baldwin H, Stein Gold L, Guenin E. Efficacy and tolerability of a novel Tretinoin 0.05% lotion for the once-daily treatment of moderate or severe Acne vulgaris in adult females. J Drugs Dermatol. 2019;18(11):1147–54.
[30] Pariser D, Guenin E. Tretinoin 0.05% lotion for the once-daily treatment of moderate and severe acne vulgaris in females: Effect of age on efficacy and tolerability. J Drugs Dermatol. 2019;18(12):1218–25.
[31] Tyring SK, Kircik L, Pariser DM, Woolery-Lloyd HC, Harper JC, Bhatt V, et al. The effects of once-daily tretinoin 0.05% lotion on quality of life in patients with moderate-to-severe acne vulgaris. Am J Clin Dermatol. 2020;21:891–9. DOI: 10.1007/s40257-020-00559-3
[32] Han G, Armstrong AW, Desai SR, Guenin E. Novel tretinoin 0.05% lotion for the once-daily treatment of moderate-to-severe acne vulgaris in an Asian population. J Drugs Dermatol. 2019;18(9):910-916.
[33] Matin T, Patel P, Goodman MB. Benzoyl Peroxide. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 [cited 2024 November 25]. Available from: https://pubmed.ncbi.nlm.nih.gov/30725905/
[34] Dréno B, Bissonnette R, Gagné-Henley A, Barankin B, Lynde C, Chavda R, et al. Long-term effectiveness and safety of up to 48 weeks' treatment with topical adapalene 0.3%/benzoyl peroxide 2.5% gel in the prevention and reduction of atrophic acne scars in moderate and severe facial acne. Am J Clin Dermatol. 2019;20:725–32. DOI: 10.1007/s40257-019-00454-6
[35] Tanizaki H, Hayashi N, Abe M. Evaluation of the efficacy of maintenance therapy for acne vulgaris using adapalene 0.1%/benzoyl peroxide 2.5% gel and benzoyl peroxide 2.5% gel for 24 weeks and assessment of atrophic acne scars using three-dimensional image analysis. J Dermatol. 2023;50(12):1513–22. DOI: 10.1111/1346-8138.16942
[36] Dubey A, Amane H. Comparative clinical study of efficacy and safety of adapalene 0.1% gel versus benzoyl peroxide 2.5% gel for the treatment of acne vulgaris. Int J Basic Clin Pharmacol. 2019;8:2317–21. DOI: 10.18203/2319-2003.ijbcp20194279

[37] Amrutha MP, Bifi J, Anoop T, Ajayakumar S, Radhakrishnan K, Rajiv S. Topical 0.1% adapalene gel versus 0.1% adapalene and 2.5% benzoyl peroxide combination gel in the treatment of mild-to-moderate acne vulgaris: An open-label randomized controlled pilot study. Indian J Drugs Dermatol. 2021;7(1):20–3. DOI: 10.4103/ijdd.ijdd_29_20
[38] Kosmoski G, Miller D, Coret C, Atillasoy E. A topical combination regimen of benzoyl peroxide and retinol moisturizer for mild to moderate acne. J Drugs Dermatol. 2022;21(12):1340–6. DOI: 10.36849/jdd.6845
[39] Lu J, Cong T, Wen X, Li X, Du D, He G, et al. Salicylic acid treats acne vulgaris by suppressing AMPK/SREBP 1 pathway in sebocytes. Exp Dermatol. 2019;28(7):786–94. DOI: 10.1111/exd.13934
[40] Dal Belo SE, Kanoun-Copy L, Lambert C, Cornillon C, Muller B, Jouni H, et al. Efficacy of a multitargeted, salicylic acid-based dermocosmetic cream compared to benzoyl peroxide 5% in acne vulgaris: Results from a randomized study. J Cosmet Dermatol. 2024;23(3):891–7. DOI: 10.1111/jocd.16052
[41] Ye D, Xue H, Huang S, He S, Li Y, Liu J, Wang Z, Zeng W. (2022). A prospective, randomized, split-face study of concomitant administration of low-dose oral isotretinoin with 30% salicylic acid chemical peeling for the treatment of acne vulgaris in Asian population. Int J Dermatol. 2022;61(6):698–706. DOI: 10.1111/ijd.16127
[42] Gardner KD. Cis-men's perspectives on male birth control [dissertation on the internet]. Arizona, USA: Arizona State University; 2022. [cited 2024 December 25]. Available from: https://keep.lib.asu.edu/items/171559
[43] Otlewska A, Baran W, Batycka-Baran A. Adverse events related to topical drug treatments for acne vulgaris. Expert Opin Drug Saf. 2020;19(4):513–21. DOI: 10.1080/14740338.2020.1757646

Оцінка засобів місцевого лікування вугрів легкого та помірного ступеня: перехресне дослідження

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Анотація. *Acne vulgaris* (AV) – це хронічне запальне захворювання шкіри, яке вражає 80 % молодих людей і підлітків, спричиняючи ураження, рубці та пігментацію волосисто-сальних відділів. Ефективне лікування AV має вирішальне значення для покращення якості життя пацієнтів і запобігання довгостроковим дерматологічним ускладненням. Це дослідження було спрямоване на оцінку ефективності трьох широко використовуваних місцевих методів лікування AV: лікування пероксидом бензоїлу, ретиноїдом і саліциловою кислотою в лікуванні вугрів легкого та середнього ступеня тяжкості за допомогою плану перехресного обсерваційного дослідження. Проаналізовано ефективність бензоїлпероксиду, ретиноїду та саліцилової кислоти для лікування акне легкого та середнього ступеня тяжкості протягом 8-тижневого періоду. Учасників віком від 15 до 50 років випадковим чином розподілили на три групи лікування, а результати оцінювали за допомогою фізичних обстежень і опитувальників. Змінні, які оцінювали, включали кількість уражень, тяжкість акне за допомогою балів GAGS, рубці та текстуру шкіри, а дані аналізували за допомогою SPSS, парних Т-тестів та дисперсійного аналізу для визначення найбільш ефективного лікування. Дослідження показало, що пероксид бензоїлу значно покращив текстуру шкіри та усунув важкі запальні процеси. Ретиноїди продемонстрували найбільше зменшення незапальних і запальних уражень, причому у 55 % учасників після лікування спостерігалися лише легкі ураження. Ретиноїди також зменшили серйозні рубці від прищів і покращили текстуру шкіри. Саліцилова кислота викликала помірне поліпшення, зменшуючи незапальні ураження та покращуючи структуру шкіри. Перекис бензоїлу та ретиноїди значно покращили структуру шкіри, однак пероксид бензоїлу продемонстрував неоднозначні результати щодо утворення рубців. Т-тести парних зразків підтвердили значні покращення текстури шкіри та незапальних уражень як для груп пероксиду бензоїлу, так і для ретиноїдів. Отримані дані показали, що ретиноїди є більш ефективними для незапальних уражень від вугрів, а пероксид бензоїлу – для важких запальних випадків, що дозволяє складати індивідуальні плани лікування. Цей підхід пропонує цінну інформацію для покращення результатів лікування акне. Дослідження може допомогти дерматологам у виборі ефективних методів лікування акне на основі типу та тяжкості ураження

Ключові слова: *Acne Vulgaris*; ретиноїд; бензоїл пероксид; саліцилова кислота; текстура шкіри

UKRAINIAN JOURNAL
OF MEDICINE, BIOLOGY AND SPORTS
Volume 9, No. 4. 2024

Journal homepage: https://uajmbs.com.ua/en
Article's History: Received: 03.09.2024; Revised: 12.11.2024; Accepted: 26.12.2024

UDC 615.322:634.67:612.063 **DOI:** 10.63341/ujmbs/4.2024.035

Experimental evidence on the therapeutic effects of ashwagandha on the human body: A literature review

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Abstract. Ashwagandha-based preparations are gaining increasing global popularity as effective natural therapeutic agents. However, the lack of consensus regarding the scientific validity of this plant's effects and the absence of comprehensive biochemical studies highlight the need for a systematic analysis of its efficacy, particularly within the framework of evidence-based medicine. The purpose of this study was to assess the effectiveness of ashwagandha-based preparations through the analysis of experimental research. To achieve this, a systematic review and analysis of literature sources from scientific databases were conducted using an analytical approach. A range of experimental studies demonstrate that the application of the leaves and roots of two ashwagandha species, *Withania somnifera* and *Withania coagulans*, is the most effective. Both aqueous extracts and alcohol-based extracts exhibit comparable therapeutic value. The most commonly available formulations are in capsule or tablet form. Notably, a positive impact and improvements in cognitive functions, psychological well-being, and physical performance have been observed among volunteers participating in experiments. Improvements have also been reported in conditions such as depression, anxiety, hormonal imbalances, muscle weakness, and sexual dysfunction. The antioxidant and anti-inflammatory properties of *Withania somnifera* contribute to slowing down ageing processes, inhibiting tumour development, and supporting the proper functioning of the cardiovascular, nervous, and muscular systems. Combined preparations containing ashwagandha demonstrate particularly high efficacy, enhancing the studied health parameters. Furthermore, incorporating this herbal extract into primary medical treatments has been shown to accelerate patient recovery. Importantly, ashwagandha is not contraindicated for older adults; on the contrary, experimental evidence suggests that its consumption reduces muscle atrophy, improves overall well-being, and regulates hormonal balance in elderly men. According to experimental findings, ashwagandha possesses a range of therapeutic properties that can substantially improve human health indicators, particularly in men. Therefore, the integration of this medicinal plant into contemporary medical practice may yield highly beneficial results

Keywords: protective properties; anti-inflammatory and anti-tumour effects; antioxidant activity; hormonal regulation; antidepressant effects

Suggest Citation:
Mandziuk M, Pylypenko O, Goldenko D. Experimental evidence on the therapeutic effects of ashwagandha on the human body: A literature review. Ukr J Med Biol Sport. 2024;9(4):35–43. DOI: 10.63341/ujmbs/4.2024.35

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Introduction

The rising prevalence of chronic diseases, heightened levels of anxiety and stress, frequent depressive states, weakened immunity, and muscle atrophy due to physical inactivity are direct consequences of global and social factors. These include climate change, the modern pace of life, and environmental issues, which have become particularly pronounced in the 21st century. Consequently, researchers face the challenge of identifying new, commercially viable, natural therapeutic agents with broad-spectrum effects that enhance physical and mental well-being. Ashwagandha has been attracting increasing attention from physicians and scientists due to its adaptogenic properties and its alignment with contemporary healthcare demands. Experimental studies confirm the high biological activity of this medicinal plant, demonstrating its positive effects on psycho-emotional well-being, the nervous system, and physical endurance. Its antioxidant properties contribute to cellular protection, thereby reducing the risk of chronic diseases.

Ashwagandha, also known as Indian ginseng, has been used in Indian medicine since ancient times as a sedative, diuretic, immunostimulant, anti-stress agent, anthelmintic, and treatment for constipation, haemorrhoids, and other ailments [1–3]. In recent years, an increasing number of scientists have provided evidence supporting the therapeutic potential of this plant in modern medicine. Two species of ashwagandha are most commonly used for medicinal purposes: *Withania somnifera* and *Withania coagulans*. The immunomodulatory effects of leaf and root extracts from these species were experimentally analysed by A. Tharakan [4] in healthy adult volunteers. Their findings indicate that the positive immunomodulatory effects extend not only to adaptive immunity but also to innate immunity. As a result, the researchers recommend this plant as a dietary supplement.

The efficacy of *Withania somnifera* in promoting mental health was examined by W. Sobota *et al.* [5], who discovered that this medicinal plant can reduce glucocorticoid levels, particularly cortisol. Participants demonstrated improved results in stress, anxiety, and depression assessments. According to the authors, ashwagandha is a safe and efficacious means of stress management when prescribed by a physician. Furthermore, numerous researchers highlighted the beneficial effects of ashwagandha on sleep regulation. Specifically, A. Deshpande *et al.* [6] conducted a clinical evaluation of the impact of *Withania somnifera* root extract on sleep in individuals suffering from insomnia and healthy volunteers. Their findings indicated that the root extract not only enhances sleep quality but also effectively mitigates insomnia. Moreover, this medicinal preparation was well tolerated by all participants.

Overall, ashwagandha has demonstrated a positive impact on cognitive functions. American researchers M. Leonard *et al.* [7] conducted clinical trials confirming improvements in short-term memory, reduced reaction times, and enhanced attention and alertness in men and women. According to their findings, the potential applications of this medicinal plant are evident, necessitating further research into its nootropic effects.

In establishing the efficacy of a medicinal product, researchers conduct experiments involving laboratory animals. For instance, a study by Z.F. Khattak *et al.* [8] tested a crude methanolic extract of *Withania coagulans* fruit on mice to demonstrate the anticonvulsant effects of ashwagandha. Their findings indicated a positive trend and a reduction in seizure manifestations, supporting further research into the development of a safe anticonvulsant treatment for humans. This approach allowed for a comprehensive evaluation of the plant's effectiveness, minimisation of adverse effects, and determination of the minimum therapeutic doses.

To assess the efficacy and safety of ashwagandha for human consumption, clinical trials were conducted to evaluate the tolerability of certain ashwagandha-containing formulations. V.G. Vaidya *et al.* [9] conducted a four-week study involving 500 volunteers who received 500 mg capsules of *Withania somnifera* root extract twice daily. According to the researchers, no adverse effects were identified, which represents the plant's suitability for therapeutic use.

Given the growing body of research on ashwagandha, there arises a need for the systematic organisation of experimental data to provide a clearer perspective on the plant's medicinal potential. A key aspect that has received limited attention is the identification of the most relevant experimental studies related to contemporary human diseases and dysfunctions. A rigorous analysis of well-selected studies enables a deeper understanding of the prospects and benefits associated with the use of this medicinal plant.

The purpose of this study was to determine the efficacy of ashwagandha-based medicinal products through an analysis of experimental research, with a particular focus on current health conditions. To achieve this, a systematic review was conducted, employing a comprehensive and transparent approach to the search, selection, evaluation, and synthesis of scientific literature on the subject. The inclusion criteria for analysis encompassed experimental studies on the effects of ashwagandha-based preparations on the human body, published in peer-reviewed scientific papers within the last ten years, and available in English or Ukrainian. Exclusion criteria included studies lacking methodological transparency and those that did not align with the research subject. The primary sources of information were scientific databases such as PubMed, Scopus, Google Scholar, and Web of Science. A total of 41 papers were selected, of which 32 were experimental studies, while the remainder were review publications. Each study underwent a critical quality assessment using appropriate evaluation methodologies.

The impact of ashwagandha on stress levels and depressive states

A thorough review and analysis of the experimental evidence regarding ashwagandha's effects on the human body demonstrated that the majority of studies focused on its beneficial impact on physiological states and

bodily systems. However, there was a notable scarcity of information concerning potential side effects or negative influences, and therefore, these aspects were not discussed in detail in this review. The most relevant studies, along with their findings, are elaborated on further.

In the contemporary world, stress levels and the prevalence of depressive conditions have increased. Consequently, researchers are actively developing and investigating a range of ashwagandha-based formulations to address these dysfunctions. For instance, to establish the efficacy and safety of a novel standardised root extract of *Withania somnifera*, known as Witholytin, in adults experiencing high levels of stress and fatigue, S.J. Smith *et al.* [10] conducted a study involving 120 adult participants with these symptoms. The participants were randomly assigned to either an experimental group, which received Witholytin at a daily dose of 600 mg, or a placebo group. The study lasted for 12 weeks, and the efficacy of the intervention was assessed using various psychometric scales. The results demonstrated statistically significant improvements in all evaluated parameters among those taking Witholytin compared to the placebo group. Specifically, stress levels decreased by 34.2% in the experimental group, compared to 12.1% in the placebo group; fatigue levels declined by 29.5% versus 8.7% in the placebo group; and overall quality of life improved. Witholytin was well tolerated, with minimal reported side effects. These findings indicate that this novel standardised ashwagandha root extract is an effective and safe means of reducing stress and fatigue in adults.

A similar study examining ashwagandha in the form of the Shoden supplement was conducted by D.N. Mishra & M. Kumar [11] to evaluate its effects on stress and anxiety levels in healthy adults experiencing frequent stress. The experiment involved 100 healthy adults with high stress levels, who were divided into an experimental group receiving Shoden and a placebo group. The study lasted for eight weeks, with efficacy assessed using standardised questionnaires measuring stress and anxiety levels, as well as physiological indicators such as blood pressure and heart rate. The intake of Shoden over eight weeks resulted in a statistically significant reduction in stress and anxiety levels, and an improvement in physiological parameters compared to the placebo group. Specifically, anxiety levels decreased by 59% in the experimental group, while morning serum cortisol levels were reduced by 66%, compared to only a 2.22% reduction in the placebo group.

Further evidence supporting the positive effects of *Withania somnifera* on individuals experiencing chronic stress was provided by S. Pandit *et al.* [12]. This study investigated the impact of an aqueous extract of ashwagandha root and leaves on adult participants reporting persistent stress. A total of 131 adults were enrolled in the study and were administered Sensoril, an aqueous extract of ashwagandha root and leaves, in doses of 125 mg, 250 mg, or 500 mg. The study lasted for eight weeks and demonstrated that even the lowest administered dose exerted beneficial effects. According to the researchers, participants experienced a reduction in stress symptoms, improved sleep parameters, and enhanced overall well-being. The supplement was well tolerated, with no reported adverse effects. The researchers thus recommend Sensoril as a safe and effective intervention for alleviating mild to moderate stress and improving general well-being.

A similar perspective is shared by S.M. Ross [13], who argues that the broad spectrum of ashwagandha's effects has a positive impact on patients' psychological well-being. A.B. Speers *et al.* [14] also investigated the neuropsychiatric effects of *Withania somnifera*, specifically examining its influence on disorders such as stress, depression, anxiety, and insomnia. The findings indicated that ashwagandha root extract exhibited both anti-stress and anxiolytic properties. The researchers suggest that these effects occur through the modulation of the hypothalamic-pituitary system and GABAergic pathways.

Depression and anxiety can cause chronic stress, which can trigger certain inflammatory processes in the body. To address such symptoms, A.V. Krishna Raju *et al.* [15] employed a slow release ashwagandha extract (AshwaSR) and conducted both *in vivo* and *in vitro* experiments. The antidepressant and anxiolytic effects of AshwaSR were assessed *in vivo*, where test animals subjected to chronic stress for 28 days were subsequently administered the extract. The efficacy of the treatment was evaluated through behavioural tests, including the open field test, elevated plus maze, forced swimming test, and Morris water maze test. This formulation improved behavioural outcomes in rats, manifesting as a reduction in symptoms of depression and anxiety. In the *in vitro* phase, the anti-inflammatory activity of ashwagandha extract was examined by assessing its inhibitory effects on cytokine production in macrophage cell lines. The results demonstrated that the extract exerted an inhibitory effect on interleukin-6 (IL-6) and tumour necrosis factor-alpha (TNF-α). These findings support the potential application of ashwagandha as a natural remedy for maintaining mental health and mitigating inflammation, which may be associated with the development of depression and anxiety.

The ability of ashwagandha to reduce stress levels was also highlighted in a pharmacological review by A.S. Chopra [16]. The author provides a detailed account of ashwagandha's pharmacological properties, including its capacity to lower stress and anxiety levels, improve sleep quality, support the immune system, and exhibit antioxidant and anti-inflammatory effects. Similarly, systematic reviews conducted by C. Akhgarjand *et al.* [17], P. Mikulska *et al.* [18] and V. Arumugam *et al.* [19] confirmed the efficacy of ashwagandha as a systemic treatment for stress and anxiety. Consequently, the use of this medicinal plant appears highly appropriate for managing stress-related conditions and depressive disorders.

Experimental studies on antioxidant and anti-inflammatory properties

Numerous studies on the therapeutic potential of ashwagandha focused on its antioxidant and anti-inflammatory

properties. A research team led by I.M. Khalil [20] demonstrated the protective effects of *Withania somnifera* leaf extract against oxidative stress and myocardial damage in rats induced by isoproterenol. The extract was administered to the rats for 28 days prior to isoproterenol induction. The effects of the extract were assessed through the analysis of biochemical markers of oxidative stress and myocardial damage in blood serum and myocardial tissue and through histopathological examination of cardiac tissue. These results support the potential of *Withania somnifera* as a natural antioxidant and a therapeutic agent for cardiovascular diseases associated with oxidative stress. The authors also emphasised the need for further research to investigate the molecular mechanisms of action of this extract and assess its efficacy and safety in clinical settings.

The antioxidant and neuroprotective properties of ashwagandha were also identified by J.N. Saykally *et al.* [21], who conducted an experiment simulating traumatic brain injury in mouse embryos. Following the injury, neurons were treated with varying concentrations of ashwagandha extract. The effects of the extract were evaluated through analyses of neuronal survival, morphological changes, and levels of inflammatory and oxidative stress markers. Based on the collected data, the authors concluded that *Withania somnifera* extract exhibits protective effects on neurons subjected to traumatic injury *in vitro*. These findings may have important implications for the development of novel therapeutic strategies for brain injuries and other neurodegenerative disorders.

In the study by P. Kumar *et al.* [22], evidence was provided that ashwagandha leaf extract exerts a glioprotective effect against lead-induced toxicity in rats. This protective action is attributed to the plant's antioxidant and anti-inflammatory properties, which help mitigate oxidative stress and neuroinflammation while safeguarding glial cells. These findings suggest that ashwagandha may serve as a potential therapeutic agent for alleviating the neurotoxic effects of lead exposure and related neurological disorders.

To further investigate the anti-tumour and anti-inflammatory properties of ashwagandha, a team of Chinese researchers led by S. Lee [23] conducted an experiment on human skin fibroblast cell cultures. The cells were exposed to TNF-α to induce an inflammatory response and cellular damage, followed by treatment with varying concentrations of the plant extract. The study demonstrated a reduction in oxidative stress and inflammatory cytokines, such as interleukin-6 (IL-6) and interleukin-8 (IL-8), in damaged skin fibroblasts. Furthermore, the extract enhanced the activity of antioxidant enzymes, including superoxide dismutase and catalase, and inhibited the activation of detrimental signalling pathways associated with inflammation and oxidative stress.

S. Wankhede *et al.* [24] linked their successful trials to the antioxidant, anti-inflammatory, and anabolic properties of *Withania somnifera* extract, investigating its effects on muscle strength and post-exercise recovery in healthy men. The study included 60 healthy male participants aged between 18 and 50, who were randomly assigned to two groups: an experimental group (n = 30), which received ashwagandha extract at a dose of 500 mg twice daily for eight weeks, and a placebo group (n = 30), which received a placebo under the same regimen. All participants simultaneously followed a standardised strength training programme three times per week throughout the study period. Muscle strength and recovery were assessed at baseline and after four and eight weeks of training, using various tests, including maximal weightlifting for squats and bench press and measurements of creatine kinase levels as a marker of muscle damage. The findings confirm that incorporating *Withania somnifera* extract into a strength training regimen may enhance muscle strength and accelerate muscle recovery in healthy men. These effects could be beneficial for athletes, fitness enthusiasts, and individuals engaged in intensive physical activity.

Further experimental research led by M. Sarbishegi [25] demonstrated that *Withania coagulans* root extract reduced prostate gland size in rats with benign prostatic hyperplasia compared to the control group. In addition, the extract was found to induce apoptosis in prostate cells and inhibit the expression of cyclooxygenase-2, a key enzyme involved in inflammatory processes. Similar studies by these researchers were described in another publication, where the efficacy of biologically active compounds in *Withania coagulans* extract was demonstrated. These compounds, including flavonoids, steroids, and alkaloids, were shown to possess anti-cancer and antioxidant properties [26].

An experimental study conducted by A.A. Alghamdi *et al.* [27] focused on the anti-inflammatory and anti-angiogenic effects of *Withania somnifera* extract in mitigating liver toxicity induced by silver nanoparticles (AgNPs). The study was performed on male albino rats, which were divided into four groups: a control group, a group receiving injections of AgNPs, a group receiving oral administration of *Withania somnifera* (WS), and a group receiving both AgNPs and WS. The experiment lasted for 28 days. Following the completion of the study, biochemical blood analyses, histopathological examination of the liver, and measurements of inflammatory cytokine levels and angiogenesis markers were conducted. Exposure to silver nanoparticles resulted in an increase in biochemical markers of liver dysfunction, such as aspartate aminotransferase (AST), alanine aminotransferase (ALT), and lactate dehydrogenase (LDH), as well as histopathological alterations in the liver, including oedema, fatty degeneration, and inflammation. Concurrent administration of ashwagandha extract markedly reduced these indicators, restoring normal liver structure and function. Furthermore, WS lowered levels of pro-inflammatory cytokines, including interleukin-6 (IL-6) and tumour necrosis factor-alpha (TNF-α), as well as angiogenesis markers such as vascular endothelial growth factor (VEGF). The researchers concluded that *Withania somnifera* extract exhibits anti-inflammatory and anti-angiogenic properties, enabling it to mitigate AgNP-induced

liver toxicity in rats. Thus, a substantial body of research demonstrated the beneficial effects of ashwagandha as an antioxidant and anti-inflammatory agent.

Evidence of improved physiological parameters and overall well-being with ashwagandha supplementation

A series of experimental studies investigated the effects of ashwagandha on physiological parameters in elderly individuals. Notably, A.L. Lopresti *et al.* [28] examined the impact of *Withania somnifera* on hormonal status and vitality in older men exhibiting signs of obesity. The study assessed hormone levels (testosterone, cortisol), physical endurance, and participants' overall well-being. Ashwagandha supplementation resulted in a statistically significant 17% increase in free testosterone levels and a 28% reduction in cortisol levels compared to the placebo group. Furthermore, improvements were observed in physical endurance and overall well-being among those receiving ashwagandha. Adverse effects were minimal and comparable to those in the placebo group. The study provides evidence supporting the potential benefits of *Withania somnifera* in managing age-related hormonal changes and enhancing quality of life.

Another research team from Korea, led by J.-S. Ko [29], investigated the effects of an ethanolic extract of ashwagandha on age-related muscle atrophy (sarcopenia). The study aimed to evaluate the anti-inflammatory and anti-atrophic effects of *Withania somnifera* extract on muscle tissue. Over a 12-week period, 20-month-old mice were administered ashwagandha extract at a dosage of 200 mg/kg body weight per day. The results demonstrated an increase in muscle mass and improved muscle fibre morphology compared to the control group. Furthermore, the extract reduced levels of pro-inflammatory cytokines such as interleukin-6 (IL-6) and tumour necrosis factor-alpha (TNF-α) and inhibited the expression of muscle atrophy biomarkers. The authors suggest that these effects may be linked to the activation of signalling pathways that support muscle maintenance and function, as well as the reduction of chronic inflammation commonly associated with ageing. The findings highlight the potential of *Withania somnifera* extract as a natural intervention for the prevention and treatment of sarcopenia in elderly individuals.

The beneficial effects of combining multiple medicinal plants with ashwagandha were observed by Z.A. Rizvi *et al.* [30], who examined the synergistic effects of *Withania somnifera* and Tinospora cordifolia (Guduchi). The study demonstrated antiviral activity against SARS-CoV-2 in vitro and revealed an immunomodulatory effect, stimulating the differentiation of T-helper 1 (Th1) and T-regulatory (Treg) cells, both crucial for immune system balance. Moreover, the extracts enhanced neutrophil function, increasing their phagocytic and chemotactic capabilities. These findings suggest that these plant extracts may contribute to the development of novel therapeutic strategies aimed at enhancing immune responses and antiviral defence mechanisms.

A. Saiyed *et al.* [31] investigated the combined effects of ashwagandha (*Withania somnifera*) and tribulus *(Tribulus terrestris)* extracts on letrozole-induced polycystic ovary syndrome (PCOS) in rats. The study demonstrated a statistically significant improvement in ovarian structure, a reduction in androgen levels, and enhanced fertility outcomes compared to the group receiving letrozole alone. While both ashwagandha and tribulus individually exhibited beneficial effects, their combination proved to be more effective.

A research team led by S. Chauhan [32] identified that the root of ashwagandha exhibits potency-enhancing properties comparable to those of Chinese ginseng. A standardised extract of ashwagandha root was shown to have a positive impact on sexual function, overall well-being, and stress levels in adult men. These findings support the standard use of ashwagandha and open new avenues for its application in modern medicine for the treatment of sexual dysfunctions and the enhancement of male quality of life. Furthermore, participants who consumed ashwagandha demonstrated improvements in overall well-being and reductions in stress levels. Similar experimental results were obtained by K. Sahin *et al.* [33], who conducted trials using a polyherbal formulation containing ashwagandha root.

An intriguing study was conducted by D. Xing *et al.* [34], which aimed to assess the effects of a single dose of *Withania somnifera* extract on cognitive function in healthy individuals. Thirty participants aged 18-35 were randomly assigned to either an experimental group (receiving 300 mg of standardised ashwagandha extract) or a control group (receiving a placebo). Before supplementation and 60 minutes after administration, participants completed a series of cognitive tests assessing various aspects of cognitive function, including attention, memory, information processing speed, and executive function. The results demonstrated that participants in the experimental group exhibited statistically significant improvements in most cognitive tests compared to the placebo group. Specifically, enhancements were observed in attention, short-term memory, information processing speed, and executive functions. No serious adverse effects were reported following the intake of the extract. These findings suggest that even a single dose of ashwagandha extract may have a beneficial impact on cognitive function in adults.

K.G. Choudhary *et al.* [35] conducted a detailed analysis of ashwagandha's ability to stimulate appetite, improve digestion, supply essential vitamins, and promote overall recovery in children. Based on their analysis, the authors concluded that due to its adaptogenic and nutritional properties, ashwagandha represents an effective and safe intervention for children with poor dietary intake.

Several other experimental studies demonstrated ashwagandha's positive influence on human hormonal balance, regulating the function of the thyroid, pancreas, adrenal glands, and reproductive system [36–38]. This wide-ranging physiological activity can be attributed to the abundance of biologically active compounds present in different parts of the plant.

Researchers increasingly recognise the potent therapeutic properties of ashwagandha, highlighting its potential for medical applications. Experimental studies provide valuable insights into the efficacy of this plant, underscoring its relevance in modern medicine. The broad spectrum of therapeutic effects associated with Ashwagandha positively influences multiple physiological systems and organs. Notably, its role in regulating hormonal activity is particularly sought after in medical applications, a perspective also supported by M. Wiciński *et al.* [39]. As numerous studies demonstrated, Ashwagandha-based formulations are widely used in the treatment of psychosomatic and psychiatric disorders. When combined with other medicinal plants or pharmaceutical agents, its effects appear to be further enhanced. A key advantage of Ashwagandha is its minimal incidence of side effects, low toxicity, and overall safety, even for paediatric use. This is supported by several of the reviewed studies and the pharmacological assessment conducted by D.S. Mandlik *et al.* [40]. Furthermore, elderly individuals report improvements in general well-being and muscle strength with regular intake of Ashwagandha-based supplements, findings that align with the study by S.B. Kelgane *et al.* [41]. However, some experimental studies were conducted on animal models, necessitating further evidence to confirm their efficacy in human subjects. It is also noteworthy that much of the literature supporting the long-standing and effective use of *Withania somnifera* and *Withania coagulans* was produced by researchers from China and India. However, a review of recent publications indicates a growing interest in Ashwagandha among scientists in Europe, Australia, and the United States. This suggests that ongoing experimental research holds considerable promise for the development of effective medicinal products derived from ashwagandha.

The potential applications of ashwagandha extend beyond general well-being to the treatment of various serious health conditions. Consequently, researchers from multiple countries are actively engaged in experimental studies investigating different formulations of this plant. The majority of studies report promising results in the treatment of multiple concurrent diseases or disorders. Through the integration of experimental research, scientific theories, and systematic analysis, it is possible to develop highly effective therapeutic formulations based on ashwagandha.

Conclusions

The analysis of experimental studies investigating the therapeutic properties of ashwagandha species *Withania somnifera* and *Withania coagulans* provides compelling evidence supporting the efficacy of plant-based formulations in addressing contemporary health concerns. A systematic review of the literature demonstrated that ashwagandha possesses a broad range of therapeutic properties, including anti-stress, antioxidant, anti-inflammatory, immunomodulatory, and adaptogenic effects. These properties contribute to the overall improvement of numerous physiological parameters in younger individuals and the elderly. This study synthesised data on the effects of ashwagandha on various aspects of health, including physical endurance, recovery following exercise, and hormonal regulation, particularly its role in increasing testosterone levels and supporting reproductive health. Furthermore, findings indicate its efficacy in reducing stress, anxiety, and depressive symptoms while improving sleep quality and general well-being, making it especially relevant in modern clinical and preventative medicine. The antioxidant properties of ashwagandha contribute to reducing oxidative stress, thereby potentially preventing the development of cardiovascular diseases, oncological conditions, and neurodegenerative disorders. In addition, ashwagandha-based formulations demonstrated anti-inflammatory effects, which may be beneficial in the treatment of chronic inflammatory diseases.

The results obtained confirm the substantial therapeutic potential of ashwagandha in contemporary medicine. Its multifunctionality and safety profile suggest that this plant represents a promising candidate for integration into preventative and clinical practices. However, existing studies present certain limitations, including an insufficient number of clinical trials involving human participants, small sample sizes, and a lack of long-term assessments of efficacy and safety.

Thus, ashwagandha emerges as a multifunctional therapeutic agent with the potential for medical application. Future research should focus on expanding the scope of its therapeutic indications, investigating its combined use with other pharmaceutical agents, and optimising dosage regimens to maximise efficacy. Particular attention should be given to evaluating the long-term effects of ashwagandha consumption and its impact on specific patient populations, including the elderly and individuals with chronic health conditions.

Acknowledgements

None.

Conflict of Interest

None.

References

[1] Behl T, Sharma A, Sharma L, Sehgal A, Zengin G, Brata R, et al. Exploring the multifaceted therapeutic potential of Withaferin A and its derivatives. Biomedicines. 2020;8(12):571. DOI: 10.3390/biomedicines8120571

[2] Wiciński M, Fajkiel-Madajczyk A, Kurant Z, Liss S, Szyperski P, Szambelan M, et al. Ashwagandha's multifaceted effects on human health: Impact on vascular endothelium, inflammation, lipid metabolism, and cardiovascular outcomes – a review. Nutrients. 2024;16(15):2481. DOI: 10.3390/nu16152481

[3] Paul S, Chakraborty S, Anand U, Dey S, Nandy S, Ghorai M, et al. *Withania somnifera* (L.) Dunal (Ashwagandha): A comprehensive review on ethnopharmacology, pharmacotherapeutics, biomedicinal and toxicological aspects. Biomed Pharmacother. 2021;143:112175. DOI: 10.1016/j.biopha.2021.112175
[4] Tharakan A, Shukla H, Benny IR, Tharakan M, George L, Koshy S. Immunomodulatory effect of *Withania somnifera* (Ashwagandha) extract – a randomized, double-blind, placebo controlled trial with an open label extension on healthy participants. J Clin Med. 2021;10(16):3644. DOI: 10.3390/jcm10163644
[5] Sobota W, Piskorz P, Zemsta K, Zwoliński M, Tyniec M, Morshed K. Ashwagandha and stress. J Educ Health Sport. 2024;70:55514. DOI: 10.12775/JEHS.2024.70.55514
[6] Deshpande A, Irani N, Balkrishnan R, Rosanna Benny I. A randomized, double blind, placebo controlled study to evaluate the effects of ashwagandha (*Withania somnifera*) extract on sleep quality in healthy adults. Sleep Medicine. 2020;72:28–36. DOI: 10.1016/j.sleep.2020.03.012
[7] Leonard M, Dickerson B, Estes L, Gonzalez DE, Jenkins V, Johnson S, et al. Acute and repeated ashwagandha supplementation improves markers of cognitive function and mood. Nutrients. 2024;16(12):1813. DOI: 10.3390/nu16121813
[8] Khattak ZF, Ansari B, Jamal M, Awan AA, Sherkheli MA, ul Haq R. Anticonvulsant activity of methanolic extract of *Withania cogulans* in mice. Metab Brain Dis. 2021;36(8):2437–43. DOI: 10.1007/s11011-021-00850-0
[9] Vaidya VG, Gothwad A, Ganu G, Girme A, Modi SJ, Hingorani L. Clinical safety and tolerability evaluation of *Withania somnifera (L.) Dunal* (Ashwagandha) root extract in healthy human volunteers. J Ayurveda Integr Med. 2024;15(1):100859. DOI: 10.1016/j.jaim.2023.100859
[10] Smith SJ, Lopresti AL, Fairchild TJ. Exploring the efficacy and safety of a novel standardized ashwagandha (Withania somnifera) root extract (Witholytin®) in adults experiencing high stress and fatigue in a randomized, double-blind, placebo-controlled trial. J Psychopharmacol. 2023;37(11):1091–104. DOI:10.1177/02698811231200023
[11] Mishra DN, Kumar M. Shoden promotes Relief from stress and anxiety: A randomized, double-blind, placebo-controlled study on healthy subjects with high stress levels. Heliyon. 2024;10(17):e36885. DOI: 10.1016/j.heliyon.2024.e36885
[12] Pandit S, Srivastav AK, Sur TK, Chaudhuri S, Wang Y, Biswas TK. Effects of *Withania somnifera* extract in chronically stressed adults: A randomized controlled trial. Nutrients. 2024;16(9):1293. DOI:10.3390/nu16091293
[13] Ross SM. Ashwagandha. Holist Nurs Pract. 2023;37(5):298–300. DOI: 10.1097/hnp.0000000000000607
[14] Speers AB, Cabey KA, Soumyanath A, Wright KM. Effects of *Withania somnifera* (ashwagandha) on stress and the stress-related neuropsychiatric disorders anxiety, depression, and insomnia. Current neuropharmacology. 2021;19(9):1468. DOI: 10.2174/1570159X19666210712151556
[15] Krishna Raju AV, Somepalli V, Thanawala S, Shah R. Efficacy and Anti-Inflammatory Activity of Ashwagandha Sustained-Release Formulation on Depression and Anxiety Induced by Chronic Unpredictable Stress: in vivo and in vitro Studies. J Exp Pharmacol. 2023;15:291–305. DOI: 10.2147/jep.s407906
[16] Chopra AS. Ashwagandha. Zeitschrift für Komplementärmedizin. 2023;15(04):28–30. DOI: 10.1055/a-2117-5841
[17] Akhgarjand C, Asoudeh F, Bagheri A, Kalantar Z, Vahabi Z, Shab-bidar S, et al. Does Ashwagandha supplementation have a beneficial effect on the management of anxiety and stress? A systematic review and meta-analysis of randomized controlled trials. Phytother Res. 2022;36(11),4115–24. DOI: 10.1002/ptr.7598
[18] Mikulska P, Malinowska M, Ignacyk M, Szustowski P, Nowak J, Pesta K, et al. Ashwagandha (*Withania somnifera*) – current research on the health-promoting activities: A narrative review. Pharmaceutics. 2023;15(4):1057. DOI: 10.3390/pharmaceutics15041057
[19] Arumugam V, Vijayakumar V, Balakrishnan A, Bhandari RB, Boopalan D, Ponnurangam R, et al. Effects of ashwagandha (*Withania Somnifera*) on stress and anxiety: A systematic review and meta-analysis. Explorer. 2024;20(6):103062. DOI: 10.1016/j.explore.2024.103062
[20] Khalil MI, Ahmmed I, Ahmed R, Tanvir EM, Afroz R, Paul S, et al. Amelioration of isoproterenol-induced oxidative damage in rat myocardium by *Withania somnifera* leaf extract. BioMed Res Int. 2015;2015(1):624159. DOI: 10.1155/2015/624159
[21] Saykally JN, Hatic H, Keeley KL, Jain SC, Ravindranath V, Citron BA. *Withania somnifera* extract protects model neurons from in vitro traumatic injury. Cell Transplant. 2017;26(7):1193–1201. DOI: 10.1177/0963689717714320
[22] Kumar P, Singh R, Nazmi A, Lakhanpal D, Kataria H, Kaur G. Glioprotective effects of ashwagandha leaf extract against lead induced toxicity. BioMed Res Int. 2014:2014(1):182029. DOI: 10.1155/2014/182029
[23] Lee S, Choi YJ, Lee S, Kang KS, Jang TS, Kim KH. Protective effects of Withagenin A Diglucoside from Indian ginseng (*Withania somnifera*) against human dermal fibroblast damaged by TNF-α stimulation. Antioxidants. 2022;11(11):2248. DOI: 10.3390/antiox11112248
[24] Wankhede S, Langade D, Joshi K, Sinha SR, Bhattacharyya S. Examining the effect of *Withania somnifera* supplementation on muscle strength and recovery: A randomized controlled trial. J Int Soc Sports Nutr. 2015;12(1). DOI: 10.1186/s12970-015-0104-9

[25] Sarbishegi M, Khajavi O, Arab MR. *Withania coagulans* extract induces cell apoptosis and inhibits COX-2 expression in a rat model of benign prostatic hyperplasia. Nephro-Urol Mon. 2016;8(5):e39284. DOI: 10.5812/numonthly.39284
[26] Sarbishegi M, Khani M, Salimi S, Valizadeh M, Sargolzaei Aval F. Antiproliferative and antioxidant effects of *Withania coagulans* extract on benign prostatic hyperplasia in rats. Nephro-Urol Mon. 2016;8(1):e33180. DOI: 10.5812/numonthly.33180
[27] Alghamdi AA, Abdallah EA, El-Refaei MF. Anti-inflammatory and anti-angiogenic effects of *Withania somnifera* extract on liver toxicity induced by silver nanoparticles in vivo. J Med Life. 2024;17(7):728–38. DOI: 10.25122/jml-2024-0050
[28] Lopresti AL, Drummond PD, Smith SJ. A randomized, double-blind, placebo-controlled, crossover study examining the hormonal and vitality effects of Ashwagandha (*Withania somnifera*) in aging, overweight males. Am J Mens Health. 2019;13(2). DOI: 10.1177/1557988319835985
[29] Ko J-S, Chang B-Y, Choi Y-J, Choi J-S, Kwon H-Y, Lee J-Y, et al. Ashwagandha ethanol extract attenuates sarcopenia-related muscle atrophy in aged mice. Nutrients. 2024;16(1):157. DOI: 10.3390/nu16010157
[30] Rizvi ZA, Babele P, Madan U, Sadhu S, Tripathy MR, Goswami S, et al. Pharmacological potential of *Withania somnifera* (L.) Dunal and *Tinospora cordifolia* (Willd.) Miers on the experimental models of COVID-19, T cell differentiation, and neutrophil functions. Front Immunol. 2023;14. DOI: 10.3389/fimmu.2023.1138215
[31] Saiyed A, Jahan N, Makbul SA, Ansari M, Bano H, Habib SH. Effect of combination of *Withania somnifera* Dunal and *Tribulus terrestris* Linn on letrozole induced polycystic ovarian syndrome in rats. Integr Med Res. 2016;5(4):293–300. DOI: 10.1016/j.imr.2016.10.002
[32] Chauhan S, Srivastava MK, Pathak AK. Effect of standardized root extract of ashwagandha (*Withania somnifera*) on well-being and sexual performance in adult males: A randomized controlled trial. Health Sci Rep. 2022;5(4):e741. DOI: 10.1002/hsr2.741
[33] Sahin K, Tuzcu M, Orhan C, Gencoglu H, Sahin N, Akdemir F, Turk G, Yilmaz I, Juturu V. MAT, a novel polyherbal aphrodisiac formulation, enhances sexual function and Nrf2/HO-1 pathway while reducing oxidative damage in male rats. Evid Based Complement Altern Med. 2018;2018:8521782. DOI: 10.1155/2018/8521782
[34] Xing D, Yoo C, Gonzalez D, Jenkins V, Nottingham K, Dickerson B, et al. Effects of acute ashwagandha ingestion on cognitive function. Int J Environ Res Public Health. 2022;19(19):11852. DOI: 10.3390/ijerph191911852
[35] Choudhary KG, Sinha N, Ojha NK. A Critical review of ashwagandhadi leha on malnutrition in children. Int J Res Ayurveda Pharm. 2023;14(2):118–22. DOI: 10.7897/2277-4343.140253
[36] Abdel-Wahhab KG, Mourad HH, Mannaa FA, Morsy FA, Hassan LK, Taher RF. Role of ashwagandha methanolic extract in the regulation of thyroid profile in hypothyroidism modeled rats. Mol Biol Rep. 2019;46(4):3637–49. DOI: 10.1007/s11033-019-04721-x
[37] Gopal S, Ajgaonkar A, Kanchi P, Kaundinya A, Thakare V, Chauhan S, et al. Effect of an ashwagandha (*Withania somnifera*) root extract on climacteric symptoms in women during perimenopause: A randomized, double-blind, placebo-controlled study. J Obstet Gynaecol Res. 2021;47(12), 4414–25. DOI: 10.1111/jog.15030
[38] Gómez Afonso A, Fernandez-Lazaro D, Adams DP, Monserdà-Vilaró A, Fernandez-Lazaro CI. Effects of *Withania somnifera* (Ashwagandha) on hematological and biochemical markers, hormonal behavior, and oxidant response in healthy adults: A systematic review. Curr Nutr Rep. 2023;12:465–77. DOI: 10.1007/s13668-023-00481-0
[39] Wiciński M, Fajkiel-Madajczyk A, Kurant Z, Kurant D, Gryczka K, Falkowski M, et al. Can ashwagandha benefit the endocrine system?–A review. Int J Mol Sci. 2023;24(22):16513. DOI: 10.3390/ijms242216513
[40] Mandlik (Ingawale) DS, Namdeo AG. Pharmacological evaluation of Ashwagandha highlighting its healthcare claims, safety, and toxicity aspects. J Diet Suppl. 2021;18(2):183–226. DOI: 10.1080/19390211.2020.1741484
[41] Kelgane SB, Salve J, Sampara P, Debnath K. Efficacy and tolerability of ashwagandha root extract in the elderly for improvement of general well-being and sleep: A prospective, randomized, double-blind, placebo-controlled study. Cureus. 2020;12(2):e7083. DOI: 10.7759/cureus.7083

Дослідження експериментальних доказів позитивного впливу ашваганди на організм: огляд літератури

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Анотація. Препарати на основі ашваганди набирають дедалі більшої популярності у світі як ефективні засоби природної терапії. Однак відсутність єдиної позиції щодо наукової обґрунтованості дії цієї рослини та ґрунтовних біохімічних досліджень створює запит на систематичний аналіз ефективності використання ашваганди, особливо в контексті доказової медицини. Метою роботи було встановити ефективність використання препаратів на основі лікарської рослини ашваганди, шляхом аналізу експериментальних досліджень науковців. Для цього було здійснено систематичний огляд та аналіз літературних джерел з наукових баз з використанням аналітичного методу. Ряд експериментальних досліджень доводять, що застосування листя та коренів двох видів ашвагади *Withania somnifera* та *Withania coagulans* є найбільш дієвими. Водні витяжки та спиртові екстракти мають однакову терапевтичну цінність. Найбільш поширеними є капсульні або таблетовані форми препаратів. Відзначається позитивний ефект та динаміка покращення когнітивних функцій, психологічних та фізичних якостей у добровольців, які брали участь в експериментах. Також спостерігається покращення таких станів як депресія, тривожність, гормональний дисбаланс, м'язова слабкість, сексуальна дисфункція. Антиоксидантні та протизапальні властивості *Withania somnifera* забезпечують зниження процесів старіння, розвитку пухлин та нормальній роботі серцево-судинної та нервової системи та м'язів. Високі показники ефективності мають комбіновані препарати, які в своєму складі містять ашваганду, що помітно покращує досліджувані показники. Також додавання даного рослинного екстракту до медичних препаратів основної дії, сприяє швидшому одужанню пацієнтів. Важливо, що людям похилого віку не протипоказано приймання даної лікарської рослини, навпаки, експериментально доведено, що вживання ашваганди знижує м'язову атрофію, покращує загальне самопочуття, регулюючи гормональний баланс у чоловіків пенсійного віку. Згідно з результатами експериментів, ашваганда є рослиною, що має ряд терапевтичних властивостей, здатних суттєво покращити життєві показники людини, особливо чоловіків, тому застосування цієї лікарської рослини в сучасній медичній практиці може мати досить дієві результати

Ключові слова: захисні властивості; протизапальна та протипухлинна дія; антиоксидантна активність; гормональна регуляція; антидепресивна дія

УКРАЇНСЬКИЙ ЖУРНАЛ
МЕДИЦИНИ, БІОЛОГІЇ ТА СПОРТУ

Том 9, № 4
2024

(Англійською мовою)

Відповідальний редактор:
В. Пшиченко

Редагування бібліографічних списків:
І. Вишневська

Редагування англомовних текстів:
С. Воровський, К. Касьянов

Комп'ютерна верстка:
О. Глінченко

Підписано до друку 26.12.2024
Формат 60*84/8
Ум. друк. арк. 5,3
Наклад 50 прим.

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UKRAINIAN JOURNAL
OF MEDICINE, BIOLOGY AND SPORTS

Volume 9, No. 4
2024

Managing Editor:
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Editing bibliographic lists:
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Editing English-Language Texts:
S. Vorovsky, K. Kasianov

Desktop publishing:
O. Glinchenko

Signed to the print 26.12.2024
Format 60*84/8
Conventional Printed Sheet 5.3
Circulation 50 copies

Address for contacts:
54003, 10 68 Desantnykiv Str., Mykolaiv, Ukraine
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https://ijmr.com.ua/