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Original Article

Artemisia absinthium L. (Wormwood) Extract Effect on 3,4-Methylenedioxymethamphetamine Withdrawal in Rats: An Animal Study

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Abstract

Background: Methamphetamine is a common addictive industrial substance. Medicinal plants such as *Artemisia absinthium* L. with anti-inflammatory, antioxidant, analgesic, neuroprotective, antidepressant, and antipyretic properties may help patients reduce withdrawal syndrome symptoms.

Methods: Five treatment groups received intraperitoneal (i.p.) injections of 3,4-methylenedioxymethamphetamine (MDMA) and an ethanolic extract of *A. absinthium* diluted in 0.9% normal saline for 7 days. The animals were assigned to five groups: Group I (Control): NaCl 0.9% + Naloxone (SN), administered daily via intraperitoneal (i.p.) injection; Group II: MDMA + NaCl 0.9% + Naloxone (MSN), administered daily via i.p. injection; Groups III, IV, and V: MDMA + NaCl 0.9% + Naloxone + ethanolic Artemisia absinthium extract at concentrations of 5%, 10%, and 25% (MSNA), respectively, administered daily via i.p. injection. To induce withdrawal syndrome, two hours after the last injection of MDMA on the 7th day, naloxone was injected (i.p.) at a dose of 1 mg/kg, and rats were quickly transferred to glass cylinders, and the symptoms of MDMA withdrawal syndrome based on stomach cramp, diarrhea, bruxism, body dragging, and wet dog shakes were recorded within 30 minutes.

Findings: The MSN and MSNA 5% interventions may not be well-tolerated and could require reevaluation to minimize adverse effects; however, MSNA 10% and MSNA 25% showed reduced severity, suggesting potential for better tolerability and effectiveness in managing symptoms like writhing, body dragging, teeth chattering, and diarrhea.

Conclusion: It appears that 10% and 25% ethanolic extracts of *A. absinthium* can lessen certain behavioral signs associated with animal addiction withdrawal. We need more research to optimize dosages for better results.

Keywords: Asteraceae, Complementary therapies, Medicine, Persian, Amphetamine addiction

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Introduction

Addictive drug abuse is a serious problem for physical and mental health,[1] severely reducing a person's social function[2] and potentially leading to death.[1] Amphetamines are addictive,[3] industrial substances and among the most commonly used illegal substances worldwide after hashish.[4] Between 2010 and 2020, the estimated global amphetamine user population varied from 2.9 million in Europe to 13.8 million in Asia, depending on the region. This number was reported at 34.07 million people in 2020 worldwide.[5] Amphetamines stimulate the central nervous system[6] and cause euphoria. Physical and psychological dependence, as well as drug tolerance, develop quickly in users. As the effects diminish, users experience depression,[7] restlessness, and fatigue.[8] To overcome these adverse effects, they become more inclined to consume higher doses and, with continued use, suffer from various physical and mental problems,[9] including weight loss,[10]

chronic skin lesions,[11] ischemic colitis,[12] cerebrovascular disease,[13] myocardial infarction, heart failure,[14] high blood pressure, depression, anxiety, and other mood disorders, confusion, insomnia, and aggressive behavior. In cases of severe abuse, people tend to commit suicide, engage in criminal behavior, and engage in risky sexual behaviors,[15] exposing themselves to sexually transmitted diseases (HIV and hepatitis).[16] Withdrawal symptoms appear after stopping the use of amphetamines[17] or naloxone.[18] Withdrawal syndrome causes cravings, aggression, depression, irritability, lethargy, poor concentration, sleep disturbance, psychosis/hallucinations, loss of pleasure, physical weakness, headache, body aches, tearfulness, runny nose, fatigue, insomnia, diarrhea, and dry mouth, which reach their peak within 24 hours. Therefore, considering the harmful consequences that both abuse and withdrawal of amphetamines impose on the individual and society, measures should be taken to deal with drug addiction and reduce the symptoms and complications caused by withdrawal as much as possible.[17] Using complementary therapies with medicinal plants is one technique to help people experience less pain as they have natural active ingredients and can reduce the cost and side effects of treating various phases of drug addiction and dependency.[19,20] Wormwood, with the scientific name *Artemisia absinthium* L. from the *Asteraceae* family,[21] is a shrub and perennial medicinal plant native to Asia and the Middle East, Europe, and North Africa.[22] In various studies, its antioxidants, its anti-inflammatory, analgesic, and immunomodulatory activity, and its wound healing, neuroprotective, hepatoprotective, antidepressant, and antipyretic effects have been assessed.[21] Benkhaled et al analyzed the essential oil of wormwood and showed its antioxidant properties and its healing effect on wounds of rats.[23] Wubuli et al demonstrated the anti-inflammatory effects of wormwood's phytochemicals using the ultra-performance liquid chromatography (UPLC) method.[24] In an animal study, Bhat et al showed the antipyretic effect of wormwood in rats,[25] and Ivanescu et al demonstrated the analgesic effect of wormwood in mice.[26] Rahimi et al also showed the neuroprotective effect of wormwood in rats.[27] Therefore, *A. absinthium* was chosen for this animal study to take an effective step towards achieving new methods to reduce methamphetamine addiction withdrawal symptoms.

Materials and Methods

Animals and Housing

In this study, young adult male Wistar rats (10 weeks old) weighing 250–280 grams ($n = 40$) were used. The animals were kept in the animal house of the Kerman Neuroscience Research Center, Iran. Every animal was housed in a climate-controlled environment with a relative humidity of 55 ± 15% and a temperature of 25 ± 2 °C, following a 12-hour light/dark cycle. The rats had unlimited access to water and normal pellet food.

Preparation of Drugs

3,4-Methylenedioxymethamphetamine (MDMA) was obtained from Kerman Narcotics Control Headquarters and sent to the Food and Drug Administration Laboratory of Kerman University of Medical Sciences, Iran, for analysis and purity check. The plant extract of *A. absinthium* was procured from the medicinal plant market in Kerman, Iran, and was approved by a botanist. This plant has the herbarium number Kf1414 in Kerman Faculty of Pharmacy, Kerman, Iran. One hundred grams of flower powder from the plant was steeped in 500 milliliters of 80-degree ethanol for 24 hours to prepare the ethanolic extract. The alcoholic extract was then separated using the maceration process. The extract was first concentrated using a rotating apparatus, then strained and dried at 35 °C in an oven.

Experimental Groups

To investigate the protective effects of *A. absinthium* on rats, the rats were ran symptoms of addiction withdrawal in MDMA-exposed domly divided into five treatment groups (eight rats in each). MDMA was dissolved in normal saline (0.9% sodium chloride; 1 mg MDMA per 1 mL normal saline). Stock solutions were prepared and administered via intraperitoneal (i.p.) injection at a daily dose of 5 mg/kg for 7 days. During the 7 days, at the same time as each MDMA injection, a 50 mg/kg *A. absinthium* extract i.p. injection was performed.[28] Naloxone was used to induce withdrawal syndrome syptoms.[29] For this purpose, two hours after the last injection of MDMA on the 7th day, naloxone was injected i.p. at a dose of 1 mg/kg, and rats were quickly transferred to glass cylinders with a diameter of 25 cm and a height of 40 cm, and the symptoms of MDMA withdrawal syndrome were recorded for 30 minutes. The symptoms of MDMA withdrawal, including stomach cramps, diarrhea, bruxism, body dragging, and wet dog shakes, with a rating of zero (absence of symptoms), one (presence of symptoms with low intensity), two (presence of symptoms with moderate intensity), and three (presence of symptoms with high intensity), were recorded.[30] Group I received normal saline (control, NaCl 0.9% + naloxone [SN]), daily, i.p. Group II received MDMA + NaCl 0.9% + naloxone (MSN), daily, i.p. Three groups (III, IV, V) were treated with *A. absinthium* extract, receiving MDMA + NaCl 0.9% + naloxone + ethanolic *A. absinthium* extract 5%, 10%, or 25% (MSNA), daily, i.p. Figure 1 shows the timeline chart of the protocol.

Ethical Issues

To comply with ethical standards, in non-experimental conditions, the rats had free access to water and food. After the experiment, the animals were euthanized using standard and painless methods.

Data Analysis and Statistics

Descriptive statistics, including mean ranks and standard deviation (SD), were calculated for the variables of interest. To assess the differences among intervention groups where the assumptions for parametric tests were not met, a Kruskal-Wallis test was employed. Dunn's multiple comparisons test was conducted to further examine pairwise comparisons between the groups, in case the Kruskal-Wallis test showed a significant difference. Fisher's exact test was conducted to examine the association between groups and the presence of wet dog shakes. A significance level of 0.05 was used throughout the analyses, and statistical significance was interpreted based on this criterion. All analyses were conducted using IBM SPSS version 27, and the graphs were generated using GraphPad Prism version 9.5.1.

Results

Table 1 compares the symptoms of the groups.

The comparison of symptom grades between groups was conducted using the Kruskal-Wallis test. The mean ranks and standard deviations of symptom grades for each group were presented. *P* values were reported based on the results of the Kruskal-Wallis tests for each symptom.

Figure 2 provides a graphical representation of the pairwise comparisons conducted for each symptom, highlighting statistically significant differences between groups.

The figure presents the mean ranks and standard deviations of symptom grades. Dunn's pairwise comparison tests were conducted to investigate differences between groups in symptom grades. Only significant *P* values were displayed in the graphs.

Multiple comparison analyses revealed significant differences in the severity of several behavioral symptoms across the treatment groups. Significant differences were observed in writhing severity between the SN and MSNA 5% groups (*P* value = 0.005), the SN and MSN groups (*P* value = 0.001), and the MSNA 25% and MSN groups (*P* value = 0.003). A significant difference in the intensity of body dragging was found only between the SN and MSNA 5% groups (*P* value = 0.018). Significant differences in teeth chattering intensity were noted in several comparisons: between SN and MSNA 5% (*P* value < 0.001), SN and MSN (*P* value < 0.001), MSNA 25% and MSN (*P* value = 0.001), and MSNA 25% and MSNA 5% (*P* value = 0.004). Significant differences in the severity of diarrhea were found between the SN and MSNA 5% groups (*P* value = 0.010), as well as between the SN and MSN groups (*P* value = 0.001).

The occurrence of wet dog shakes within each group is detailed in Table 2.

The columns display the frequency and relative frequency of the presence and absence of symptoms with low intensity for each group. The *P* value reflects the results obtained from Fisher's exact test.

Table 2 shows that there is a significant difference in the presence of wet dog shakes in different groups (*P* value = 0.005). In the MSN group, this sign was observed in 87.5% of rats.

Discussion

The results of this study demonstrated that the 25% concentration of *A. absinthium* ethanolic extract

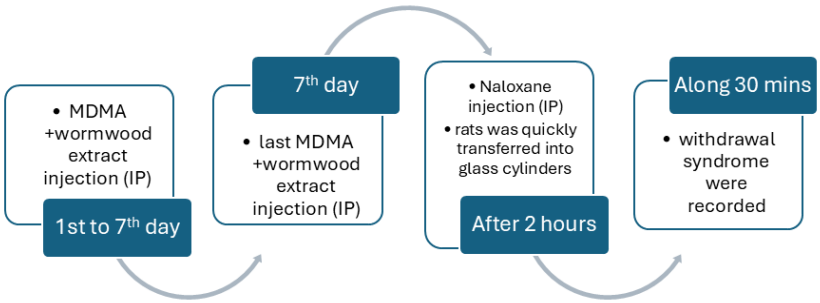

Figure 1. Timeline chart of the protocol

Table 1. Result of the Kruskal-Wallis test for comparison of groups

Group	Writhing	Body dragging	Teeth chattering	Diarrhea
	Mean ranks (SD)			
SN	8.00 (0.00)	11.00 (0.00)	9.00 (0.00)	9.50 (0.00)
MSN	33.63 (6.19)	23.75 (11.04)	33.50 (4.14)	29.88 (9.87)
MSNA 5%	26.88 (5.32)	27.25 (10.85)	31.50 (2.83)	27.13 (8.68)
MSNA 10%	20.00 (7.41)	20.25 (9.89)	16.50 (6.21)	18.00 (9.09)
MSNA 25%	14.00 (8.28)	20.25 (9.89)	12.00 (5.55)	18.00 (9.09)
P value	< 0.001	0.028	< 0.001	0.001

significantly alleviated stomach cramps and bruxism in rats suffering from methamphetamine addiction. Notably, no side effects were observed with this dosage of *A. absinthium* extract. Additionally, a significant improvement in the wet dog shaking behavior was noted across all three administered doses. This research specifically evaluated symptoms associated with withdrawal syndrome, including stomach cramps, bruxism, diarrhea, body dragging, and wet dog shaking, which are commonly reported manifestations of withdrawal from addictive substances.[31] Several neurotransmitters, mainly dopamine, norepinephrine, and serotonin (5-HT), are involved in methamphetamine withdrawal symptoms. Methamphetamine significantly increases dopamine levels in the brain, leading to feelings of euphoria and increased energy during use. However, upon withdrawal, there is a marked depletion of dopamine, which contributes to physical symptoms such as fatigue, lack of motivation, and intense cravings for the drug. The drop in dopamine levels is a major factor in the depressive symptoms experienced during withdrawal, as dopamine is crucial for regulating mood and pleasure. Serotonin is essential for mood stabilization and emotional regulation. Chronic methamphetamine use disrupts serotonin levels, leading to withdrawal symptoms that include anxiety and mood swings. The reduction in serotonin during withdrawal can exacerbate feelings of dysphoria and emotional instability, making the withdrawal experience more challenging. Norepinephrine is involved in the body's stress response and plays a role in arousal and alertness. During withdrawal, the dysregulation of norepinephrine can lead to increased anxiety, agitation, and irritability, which are common physical symptoms associated with methamphetamine withdrawal. The abrupt cessation of methamphetamine use leads to significant changes in these neurotransmitter systems, resulting in a range of withdrawal symptoms that can be both physically and psychologically distressing. Understanding these mechanisms is crucial for developing effective treatment strategies for individuals experiencing methamphetamine withdrawal. Considering the key role of neurotransmitters such as dopamine, serotonin, and norepinephrine in withdrawal symptoms, it can be concluded that the mechanism of action of medicinal plants as complementary treatments for withdrawal syndrome likely works by modulating these very neural pathways.[32] With the same view numerous studies have explored the effects of various medicinal plants on withdrawal symptoms from addictive substances. For instance, in a clinical trial by Hashem-Dabaghian et al, *Sophora alopecuroides var.* seed was shown to safely reduce the symptoms of heroin withdrawal syndrome.[33] The study by Rezaeian et al showed that berberine improved anxiety behaviors and reduced relapses to methamphetamine use in rats by regulating neuroinflammation. Therefore, with further studies, it can be considered as a potential new drug for the treatment of methamphetamine addiction.[34] Another study by Koo et al showed that *Salviae miltiorrhizaen radix* inhibits superoxide generation by rat microglia and mimics the action of amphetamines on rat dopamine release. Therefore, it is a suit option to reduce withdrawal symptoms of amphetamines.[35] In a study by Thangsaard et al the dopaminergic transmission effects of two plants, *Thanbergia laurifolia Linn.* and *Simplocos racemosa Roxb,* were compared to amphetamine. The study showed that the aqueous extract of *Thanbergia laurifolia Linn.*

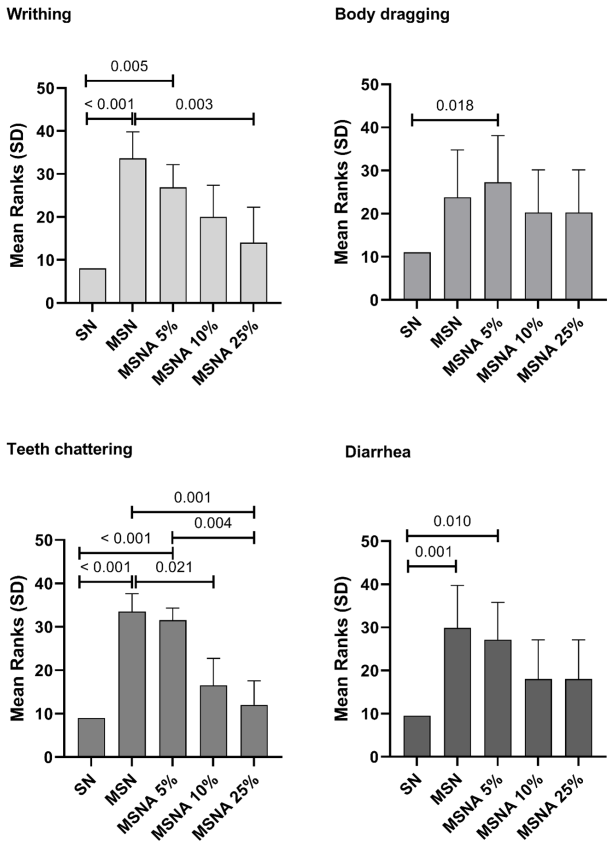

Figure 2. Pairwise comparisons of groups for each symptom

Table 2. The presence of wet dog shakes in different groups

Variables		SN	MSN	MSNA 5%	MSNA 10%	MSNA 25%	*P* value (Fisher's exact test)
		Frequency (relative frequency)					
Wet dog shakes	Absence of symptoms	8 (1.000)	1 (0.125)	4 (0.500)	4 (0.500)	6 (0.750)	0.005
	Presence of symptoms with low intensity	0 (0.000)	7 (0.875)	4 (0.500)	4 (0.500)	2 (0.250)	

significantly increases the stimulation of dopamine release in the brain of rats addicted to amphetamine and can be a good option for reducing the withdrawal symptoms of amphetamine addiction, including methamphetamine, but *Simplocos racemosa Roxb* had no such effect.[36] Also, the therapeutic effects of *A. absinthium* on methamphetamine withdrawal symptoms can be understood through its interaction with the same neurotransmitter systems that are significantly affected during withdrawal.[37] *A. absinthium* has been shown to have several compounds, such as quercetin and rutin, that may positively influence neurotransmitter balance and alleviate withdrawal symptoms.[38] *A. absinthium* may influence dopamine pathways. The plant contains flavonoids and other phytochemicals that may increase serotonin levels. The anxiolytic properties of *A. absinthium* may help stabilize norepinephrine levels.[39] Bora et al found that *A. absinthium* exhibited neuroprotective effects against cerebral damage induced by reperfusion.[40] In a subsequent study, Bora et al highlighted the strong antioxidant properties of *A. absinthium* methanolic extract, suggesting its potential as a preventive measure against diseases related to oxidative stress.[41] The neuroprotective properties of *A. absinthium* may help counteract some of the neurotoxic effects of methamphetamine, supporting brain health during recovery. This could be particularly beneficial in restoring normal neurotransmitter function, thereby aiding in the recovery process. Additionally, *A. absinthium* ethanolic extract has demonstrated cytoprotective and free radical-scavenging properties against oxidative damage in fibroblast-like cells. This plant has been recognized as a significant source of natural antioxidants.[42] Ahmad et al reported that methanolic *A. absinthium* extract demonstrated varying levels of anti-inflammatory activity at doses of 300, 500, and 1000 mg/kg, with a delayed response possibly attributable to the absorption rate of the extracts.[43] Nalbantsoy et al found that *A. absinthium* methanolic extract effectively inhibited carrageenan-induced acute inflammation in rats, reducing inflammation caused by snake venom.[44] Khattak et al reported that aqueous extracts of *A. absinthium* exhibited antipyretic actions compared to aspirin in rabbits, with no adverse effects noted.[45] Zeraati et al found that *A. absinthium* extracts exhibit topical antinociceptive properties in experimental mice.[46] Also, the application of a plant-based ointment can alleviate clinical symptoms in individuals with knee osteoarthritis.[47] Studies found that *A. absinthium* ethanolic extract contains 24-ethyl p-cholesta-7, 22-dien-3, and has antipyretic activity. [21] Therefore, *A. absinthium*, with its analgesic properties, may reduce withdrawal symptoms. The anti-inflammatory properties of *A. absinthium* are likely to be due to its secondary metabolites, particularly flavonoids and sesquiterpene-type compounds.[48] These compounds inhibit inflammatory mediators such as bradykinins, histamine, and prostaglandins. Thus, by potentially enhancing dopaminergic activity, *A. absinthium* may help mitigate the depressive symptoms and cravings associated with decreased dopamine levels during withdrawal. Also, by promoting serotonin synthesis or receptor sensitivity, it can alleviate mood disturbances and anxiety, which are common during methamphetamine withdrawal. As well as its anxiolytic properties, it reduces anxiety and agitation during the withdrawal phase. This stabilization can lead to a more manageable withdrawal experience and decrease the likelihood of relapsing due to heightened stress responses. Also, with its various phytochemicals, it can be effective and useful in reducing withdrawal symptoms of methamphetamine addiction. The study's limitations include a lack of toxicology tests and cellular and molecular investigation of the plant extract's effects on animals, necessitating more detailed research. Without appropriate quality-controlled research, it is difficult to ensure the safety and compatibility of herbal medicines or to make evidence-based recommendations for their use in the treatment of amphetamine withdrawal. More rigorous research is needed to assess the potential benefits and risks of specific herbal medicines before considering policies to integrate them into treatment protocols for amphetamine use disorders. Such studies can facilitate this.

Conclusion

A. absinthium can provide a complementary approach to managing methamphetamine withdrawal symptoms by positively influencing the neurotransmitter systems affected by chronic methamphetamine use. By potentially enhancing dopamine and serotonin levels while stabilizing norepinephrine, this plant could alleviate some of the psychological and physical challenges associated with withdrawal, thereby supporting individuals in their path to recovery. Further research is needed to fully elucidate these mechanisms and establish the efficacy of *A. absinthium* in clinical settings.

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Authors' Contribution

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Project administration: Mohadese Kamali.
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Supervision: Mohadese Kamali.
Validation: Mohadese Kamali.
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Writing–review & editing: Mohadese Kamali.

Competing Interests
The authors have no conflicts of interest to declare.

Ethical Approval
This study was assessed and approved by Kerman University of Medical Sciences, Kerman, Iran (IR.KMU.REC.1397.621).

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References
1. Paknahad S, Akhgari M, Ghadipasha M. An alarming rise in the prevalence of deaths with methamphetamine involved in Tehran, Iran 2011-2018. Forensic Sci Med Pathol. 2021;17(2):208-15. doi: 10.1007/s12024-020-00339-9.
2. Pirnia B, Pirnia K, Aghajanpoor M, Mardan F, Zahiroddin A. Relationship between function of hypothalamic-pituitary-adrenal axis and executive functions in chronic methamphetamine users: a cross-sectional study. Asian J Psychiatr. 2018;35:113-4. doi: 10.1016/j.ajp.2018.05.001.
3. Jones CM, Houry D, Han B, Baldwin G, Vivolo-Kantor A, Compton WM. Methamphetamine use in the United States: epidemiological update and implications for prevention, treatment, and harm reduction. Ann N Y Acad Sci. 2022;1508(1):3-22. doi: 10.1111/nyas.14688.
4. Cumming C, Kinner SA, McKetin R, Young JT, Li I, Preen DB. The predictive validity of the Alcohol, Smoking and Substance Involvement Screening Test (ASSIST) for moderate- to high-risk cannabis, methamphetamine and opioid use after release from prison. Addiction. 2023;118(6):1107-15. doi: 10.1111/add.16138.
5. Citaristi I. United Nations Office on Drugs and Crime—UNODC. In: The Europa Directory of International Organizations 2022. Routledge; 2022. p. 248-52.
6. Čechová B, Šlamberová R. Methamphetamine, neurotransmitters and neurodevelopment. Physiol Res. 2021;70(S3):S301-15. doi: 10.33549/physiolres.934821.
7. Ru Q, Xiong Q, Zhou M, Chen L, Tian X, Xiao H, et al. Withdrawal from chronic treatment with methamphetamine induces anxiety and depression-like behavior in mice. Psychiatry Res. 2019;271:476-83. doi: 10.1016/j.psychres.2018.11.072.
8. Modarresi A, Eslami K, Kouti L, Hassanvand R, Javadi M, Sayyah M. Amantadine reduces persistent fatigue during post-acute withdrawal phase in methamphetamine abstained individuals: a randomized placebo-controlled trial. J Subst Use. 2018;23(6):584-90. doi: 10.1080/14659891.2018.1459904.
9. Guerin AA, Bridson T, Plapp HM, Bedi G. A systematic review and meta-analysis of health, functional, and cognitive outcomes in young people who use methamphetamine. Neurosci Biobehav Rev. 2023;153:105380. doi: 10.1016/j.neubiorev.2023.105380.
10. Duval CJ, Balkchyan AA, Sarkisyan A, Pedersen ER, Nagata JM, Keshishian T, et al. Methamphetamine use and disordered eating: a case study of an understudied phenomenon. Eat Weight Disord. 2022;27(7):2947-51. doi: 10.1007/s40519-022-01380-z.
11. Topcuoğlu M, Erdoğan A, Kulaksızoğlu B. Dermatosis due to methamphetamine use: a case report. Addicta Turk J Addict. 2021;8(2):157-9. doi: 10.5152/addicta.2021.20042.
12. Buddam A, Vellanki M, Chandra S, Rangray R. S1723 Pseudomembranous colitis in ischemic colitis secondary to methamphetamine use: a diagnostic challenge. Am J Gastroenterol. 2020;115:S889. doi: 10.14309/01.ajg.0000708940.76910.f0.
13. Persons JE, Conway KS. Neuropathologic features in chronic methamphetamine use. Am J Forensic Med Pathol. 2023;44(2):77-82. doi: 10.1097/paf.0000000000000817.
14. Manja V, Nrusimha A, Gao Y, Sheikh A, McGovern M, Heidenreich PA, et al. Methamphetamine-associated heart failure: a systematic review of observational studies. Heart. 2023;109(3):168-77. doi: 10.1136/heartjnl-2022-321610.
15. Darke S, Kaye S, McKetin R, Duflou J. Major physical and psychological harms of methamphetamine use. Drug Alcohol Rev. 2008;27(3):253-62. doi: 10.1080/09595230801923702.
16. Feelemyer JP, Richard E, Khan MR, Scheidell JD, Caniglia EC, Manandhar-Sasaki P, et al. Does the association between stimulant use and high-risk sexual behavior vary by injection drug use, sexual minority status, or HIV infection status? A meta-analysis. AIDS Behav. 2023;27(9):2883-90. doi: 10.1007/s10461-023-04012-4.
17. Jan SU, Alam H, Khan A. Effects of methamphetamine withdrawal on the psychological and physiological condition of addicts. J Soc Sci Rev. 2022;2(3):138-44. doi: 10.54183/jssr.v2i3.90.
18. Kaka G, Rahmanzade R, Safee F, Haghparast A. Naloxone induces frequent jumping after chronic morphine and methamphetamine co-administration in rats. Basic Clin Neurosci. 2014;5(1):42-7.
19. Kamali M, Tajadini H, Mehrabani M, Moghadari M. Consequences of opioid abuse and their treatments in Persian medicine: a review study. Addict Health. 2020;12(1):46-57. doi: 10.22122/ahj.v12i1.250.
20. Kamali M, Kamali H, Doustmohammadi M, Sheikhbardsiri H, Moghadari M. Treatment of opium addiction in Persian medicine: a review study. J Educ Health Promot. 2021;10:157. doi: 10.4103/jehp.jehp_5_21.
21. Batiha GE, Olatunde A, El-Mleeh A, Hetta HF, Al-Rejaie S, Alghamdi S, et al. Bioactive compounds, pharmacological actions, and pharmacokinetics of wormwood (*Artemisia absinthium*). Antibiotics (Basel). 2020;9(6):353. doi: 10.3390/antibiotics9060353.
22. Sharopov FS, Sulaimonova VA, Setzer WN. Composition of the essential oil of *Artemisia absinthium* from Tajikistan. Rec Nat Prod. 2012;6(2):127-34.
23. Benkhaled A, Boudjelal A, Napoli E, Baali F, Ruberto G. Phytochemical profile, antioxidant activity and wound healing properties of *Artemisia absinthium* essential oil. Asian Pac J Trop Biomed. 2020;10(11):496-504. doi: 10.4103/2221-1691.294089.
24. Wubuli A, Abdulla R, Zhao J, Wu T, Aisa HA. Exploring anti-inflammatory and antioxidant-related quality markers of *Artemisia absinthium* L. based on spectrum-effect relationship. Phytochem Anal. 2024;35(5):1152-73. doi: 10.1002/pca.3350.
25. Bhat MM, Ansari AP, Ahmad A, Qayoom I, Reshi BM. Antipyretic activity of the hydro-alcoholic extract of *Artemisia absinthium* L. as a standalone and as an adjuvant with barley water against yeast-induced pyrexia in albino Wistar rats. J Complement Integr Med. 2024;21(1):46-52. doi: 10.1515/jcim-2023-0307.
26. Ivanescu B, Corciova A, Vlase L, Gheldiu AM, Miron A, Ababei DC, et al. Analgesic and anti-inflammatory activity of *Artemisia* extracts on animal models of nociception. Balneo

PRM Res J. 2021;12(1):34-9.
27. Rahimi M, Marefati N, Beheshti F, Ahmadabady S, Rakhshandeh H, Hosseini M. The effects of *Artemisia absinthium* L. on scopolamine-induced learning and memory impairment and brain tissue oxidative damage in adult rats. Avicenna J Phytomed. 2023;13(1):70-84. doi: 10.22038/ajp.2022.62851.2991.
28. Saberi A, Sepehri G, Safi Z, Razavi B, Jahandari F, Divsalar K, et al. Effects of methamphetamine on testes histopathology and spermatogenesis indices of adult male rats. Addict Health. 2017;9(4):199-205.
29. Wang ZY, Guo LK, Han X, Song R, Dong GM, Ma CM, et al. Naltrexone attenuates methamphetamine-induced behavioral sensitization and conditioned place preference in mice. Behav Brain Res. 2021;399:112971. doi: 10.1016/j.bbr.2020.112971.
30. Baslam A, Aitbaba A, Lamrani Hanchi A, Tazart Z, Aboufatima R, Soraa N, et al. Modulation of gut microbiome in ecstasy/MDMA-induced behavioral and biochemical impairment in rats and potential of post-treatment with *Anacyclus pyrethrum* L. aqueous extract to mitigate adverse effects. Int J Mol Sci. 2023;24(10):9086. doi: 10.3390/ijms24109086.
31. Brust JC. Abused agents: acute effects, withdrawal, and treatment. Continuum (Minneap Minn). 2004;10(5):14-47. doi: 10.1212/01.CON.0000293607.14958.c3.
32. Taracha E, Czarna M, Turzyńska D, Maciejak P. Amphetamine-induced prolonged disturbances in tissue levels of dopamine and serotonin in the rat brain. Pharmacol Rep. 2023;75(3):596-608. doi: 10.1007/s43440-023-00472-6.
33. Hashem-Dabaghian F, Kianbakht S. A randomized controlled trial on the seeds of *Sophora alopecuroides* var. *alopecuroides* for the treatment of acute heroin withdrawal syndrome. Complement Ther Clin Pract. 2023;51:101740. doi: 10.1016/j.ctcp.2023.101740.
34. Rezaeian L, Kalalian-Moghaddam H, Mohseni F, Khaksari M, Rafaiee R. Effects of berberine hydrochloride on methamphetamine-induced anxiety behaviors and relapse in rats. Iran J Basic Med Sci. 2020;23(11):1480-8. doi: 10.22038/ijbms.2020.47285.10884.
35. Koo BS, Kwon TS, Kim CH. *Salviae miltiorrhizae* Radix inhibits superoxide generation by activated rat microglias and mimics the action of amphetamine on in vitro rat striatal dopamine release. Neurochem Res. 2004;29(10):1837-45. doi: 10.1023/b:nere.0000042210.72927.ec.
36. Thongsaard W, Marsden CA. A herbal medicine used in the treatment of addiction mimics the action of amphetamine on in vitro rat striatal dopamine release. Neurosci Lett. 2002;329(2):129-32. doi: 10.1016/s0304-3940(02)00658-4.
37. Konrath EL, Arbo MD, Arbo BD, Hort MA, Elisabetsky E, Leal MB. Plants with anti-addictive potential. Adv Exp Med Biol. 2021;1308:185-215. doi: 10.1007/978-3-030-64872-5_14.
38. Ali M, Abbasi BH, Ihsan-Ul-Haq M. Production of commercially important secondary metabolites and antioxidant activity in cell suspension cultures of *Artemisia absinthium* L. Ind Crops Prod. 2013;49:400-6. doi: 10.1016/j.indcrop.2013.05.033.
39. Kharoubi O, Slimani M, Aoues A. Neuroprotective effect of wormwood against lead exposure. J Emerg Trauma Shock. 2011;4(1):82-8. doi: 10.4103/0974-2700.76834.
40. Bora KS, Sharma A. Neuroprotective effect of *Artemisia absinthium* L. on focal ischemia and reperfusion-induced cerebral injury. J Ethnopharmacol. 2010;129(3):403-9. doi: 10.1016/j.jep.2010.04.030.
41. Bora KS, Sharma A. Evaluation of antioxidant and free-radical scavenging potential of *Artemisia absinthium*. Pharm Biol. 2011;49(12):1216-23. doi: 10.3109/13880209.2011.578142.
42. Craciunescu O, Constantin D, Gaspar A, Toma L, Utoiu E, Moldovan L. Evaluation of antioxidant and cytoprotective activities of *Arnica montana* L. and *Artemisia absinthium* L. ethanolic extracts. Chem Cent J. 2012;6(1):97. doi: 10.1186/1752-153x-6-97.
43. Ahmad F, Khan RA, Rasheed S. Study of analgesic and anti-inflammatory activity from plant extracts of Lactuca scariola and Artemisia absinthium. J Islam Acad Sci. 1992;5(2):111–4.
44. Nalbantsoy A, Erel SB, Köksal C, Göçmen B, Yıldız MZ, Karabay Yavaşoğlu N. Viper venom induced inflammation with *Montivipera xanthina* (Gray, 1849) and the anti-snake venom activities of *Artemisia absinthium* L. in rat. Toxicon. 2013;65:34-40. doi: 10.1016/j.toxicon.2012.12.017.
45. Khattak SG, Gilani SN, Ikram M. Antipyretic studies on some indigenous Pakistani medicinal plants. J Ethnopharmacol. 1985;14(1):45-51. doi: 10.1016/0378-8741(85)90027-3.
46. Zeraati F, Esna-Ashari F, Araghchian M, Emam AH, Vafaei Rad M, Seif S, et al. Evaluation of topical antinociceptive effect of *Artemisia absinthium* extract in mice and possible mechanisms. Afr J Pharm Pharmacol. 2014;8(19):492-6. doi: 10.5897/ajpp2012.1518.
47. Basiri Z, Zeraati F, Esna-Ashari F, Mohammadi F, Razzaghi K, Araghchian M, et al. Topical effects of *Artemisia absinthium* ointment and liniment in comparison with piroxicam gel in patients with knee joint osteoarthritis: a randomized double-blind controlled trial. Iran J Med Sci. 2017;42(6):524-31.
48. Beigh YA, Ganai AM. Potential of wormwood (*Artemisia absinthium* Linn.) herb for use as additive in livestock feeding: a review. Pharma Innov. 2017;6(8 Pt C):176-87.