J Biochem Technol (2025) 16(2): 124-131
https://doi.org/10.51847/ZEj8PNyKPw
ISSN: 0974-2328

Development of Sedative Chewing Lozenges Based on a Complex of Herbal Extracts and Glycine for Children

Alzhanat Muratovna Mustafayeva*, Abidat Muratovna Mustafayeva, Fatima Shamilovna Omargadjieva, Maperi Vladlenovna Balaeva, Anastasia Sergeevna Kobiz, Ksenia Viktorovna Mironenko, Rasul Takhirovich Chinchiev, Fatima Magomedovna Budunova, Bella Usmanovna Girimova

Received: 11 April 2025 / Received in revised form: 19 July 2025, Accepted: 19 July 2025, Published online: 25 July 2025

Abstract

Sleep disorders and neurotic disorders in children represent a significant medical and social problem. The prevalence of insomnia in the pediatric population reaches 6%. When taking into account concomitant sleep disorders, this indicator increases to 50% among preschool children. Existing therapeutic approaches often require the development of new, safe, and effective remedies with improved compliance characteristics. The purpose of this scientific work is to develop and comprehensively study a new sedative phytopreparation in the form of chewable lozenges based on standardized extracts of Melissa officinalis *(Melissa officinalis L.),* Polemoniaceae *(Polemonium caeruleum L.),* and glycine. During the course of the work, the standardization of plant extracts was carried out, and a formulation and technology for producing lozenges were developed. The quality assessment was conducted based on organoleptic, physico-chemical, and microbiological parameters. The pharmacological activity was studied in preclinical studies on a model of white rats (n=30) using the "open field" and "raised cruciform maze" tests. The finished product meets the requirements of the regulatory documentation. Preclinical studies revealed a statistically significant ($p<0.05$) decrease in motor activity by 35% and an increase in the examination time of closed sleeves in the "raised maze" test by 40% compared with the control group.

Keywords: Sedatives, Phytotherapy, Melissa officinalis, Polemoniaceae, Glycine, Pediatrics

Alzhanat Muratovna Mustafayeva*
Faculty of Medicine, Dagestan State Medical University, Makhachkala, Republic of Dagestan, Russia.

Abidat Muratovna Mustafayeva, Fatima Shamilovna Omargadjieva, Maperi Vladlenovna Balaeva
Faculty of Pediatrics, Dagestan State Medical University, Makhachkala, Republic of Dagestan, Russia.

Anastasia Sergeevna Kobiz, Bella Usmanovna Girimova
Faculty of Pediatrics, Rostov State Medical University, Rostov-on-Don, Russia.

Ksenia Viktorovna Mironenko
Faculty of Medicine and Prevention, Rostov State Medical University, Rostov-on-Don, Russia.

Rasul Takhirovich Chinchiev
Faculty of Pediatrics, North Ossetian State Medical Academy, Vladikavkaz, Republic of North Ossetia-Alania, Russia

Fatima Magomedovna Budunova
Faculty of Medicine, Russian University of Medicine, Moscow, Russia

***E-mail:** alzhanat.mustafayeva@mail.ru

Introduction

The prevalence of insomnia among the pediatric population is estimated to be between 1% and 6% (Himelfarb & Shatkin, 2021; Bruni *et al*., 2024a). When concomitant conditions such as resistance to bedtime and nighttime awakenings are taken into account, the prevalence rises to 25-50% among preschool children (Reynolds *et al*., 2023; Bruni *et al*., 2024b).

In Russia, various neurotic and neurosis-like conditions are diagnosed in up to 2-12% of children, including attention deficit hyperactivity disorder (ADHD) and anxiety symptoms (Surushkina & Chutko, 2023). ADHD occurs in approximately 18% of school-aged children (more common among boys than girls) (Fraticelli *et al*., 2022). The development of higher mental functions may be delayed in children with ADHD, leading to decreased mental abilities and difficulty organizing activities (Nazarova *et al*., 2022; Claussen *et al*., 2024). Children with ADHD are often aggressive, unbalanced, insecure, and lonely, and may experience stress and anxiety (Hirota & King, 2023). Approximately 1.5 million children were born in Russia in 2020, and 180,000 may have neurotic disorders (Chutko *et al*., 2022). If these behaviors are repeated daily, there is cause for concern, especially for younger children who may struggle to cope with their emotions and become impulsive and hyperactive (Baklanov *et al*., 2020; Chan *et al*., 2022). Parents may deal with unreasonable mood swings, stuttering, tantrums, and sleep disorders, which can eventually lead to more serious functional changes in a child's body (Pelevin *et al*., 2018; Danielson *et al*., 2024).

This is why it is so important to address this problem among children. An innovative herbal preparation based on Melissa officinalis, Polemoniaceae, and glycine could be a great way to

address these issues. It has a sedative effect on a child's nervous system, gently reducing reflex excitability without inhibiting the central nervous system (Ekambaram & Owens, 2021; Samatadze *et al*., 2022; Mathews *et al*., 2024). This leads to better sleep quality and normalisation, as well as increased mental activity and higher mental function (Bruni *et al*., 2021; Yang *et al*., 2023; Yeom & Cho, 2024; Mizzi & Blundell, 2025).

The primary advantages of this herbal medicine are its natural composition and minimal side effects. It is presented in a convenient and attractive form for children in the form of chewing tablets. The drug is free from artificial colors, flavors, preservatives, gluten, and GMOs. It can be used from the age of 3 years old.

Chewing plates are designed to be visually appealing, as well as tasty and colorful. This decision was made because children often refuse to take medicine with an unpleasant smell or taste when they are young.

The aim of this research was to develop and investigate a sedative herbal preparation based on Melissa officinalis *(Melissa officinalis L.)*, Polemoniaceae *(Polemonium caeruleum L.),* and glycine in the form of chewable tablets.

Materials and Methods

To study the quality indicators of finished syrup, standard methods were used in accordance with regulatory requirements. An organoleptic assessment was performed according to GOST 6687.5-86 and the State Pharmacopoeia XV edition (Shikov *et al*., 2021; Zaki Dizaji *et al*., 2021; Chidambaranathan & Culathur, 2022). Before analysis, the syrup was diluted with drinking water in a 1:10 ratio. 25 mL of syrup was added to a 250 mL measuring cylinder. The volume was adjusted to the mark with water at 10-14°C, and the mixture was thoroughly mixed. Then, taste and aroma were evaluated immediately after pouring the Sample into a tasting glass (Fragedakis *et al*., 2023; Pavithra *et al*., 2023).

In addition to organoleptic properties, several physicochemical parameters were measured: density, refractive index, pH, viscosity, and microbiological purity (Gagnon *et al*., 2025). Density was measured using two parallel methods: pycnometric and hydrometric (Patel *et al*., 2022; Perrine *et al*., 2023; Sirohi *et al*., 2024). The pycnometric method involved weighing a clean and dry pycnometer, then filling it with distilled water up to a specific mark, followed by thermostating and reweighing it. This process was repeated using the test syrup. The hydrometric method involves placing the test liquid in a cylinder, carefully dipping a clean and dried hydrometer into it, and reading the scale after 3-4 minutes of immersion. Refractive index is measured using a refractometer (Canassa & Baldin, 2022; Bodo *et al*., 2023). A few drops of syrup are placed on the lower prism. Prisms are closed tightly, and readings are taken on the device's scale at a temperature of 20°C. pH is measured by the ionometric method (Divakaruni & Jastroch, 2022; Wilhelmy *et al*., 2022).

The viscosity of the liquid was determined using a capillary viscometer (Dunn *et al*., 2021; Macrì *et al*., 2023). To achieve this, a measured volume of liquid was placed in the elbow of the viscometer, and then it was installed in an upright position in a water bath at 20°C for 30 minutes to allow for temperature equilibrium. After the liquid level rose above the upper mark, the time it took for the liquid to flow between two marks on the viscometer was recorded. This time was averaged over three trials to get the mean expiry time for the test fluid. To calculate the relative viscosity of the syrup under investigation, we also measured the expiry time of a reference fluid. During the experiment, we observed that syrup demonstrated Newtonian flow behavior.

The microbiological purity of the syrup was assessed in accordance with the requirements of the State Pharmacopoeia XV edition for drugs of the third category (Reshetnikov & Barashkova, 2022; Chen *et al*., 2025). The total number of microorganisms (CFU) should not exceed 10^3 per mL, the number of fungi should be 10^2, and the presence of E. coli is not allowed in 1 mL of syrup. Drops of syrup were applied to Petri dishes with nutrient agar and incubated at 37 °C for 24 hours. No visible growth of colonies was observed after this time. Additionally, purity tests were carried out: 5 mL of the drug was mixed with 45 mL of purified water, and the resulting solution did not react with chlorides, sulfates, calcium, or heavy metals (Fiodorova *et al*., 2022; Tbahriti *et al*., 2025).

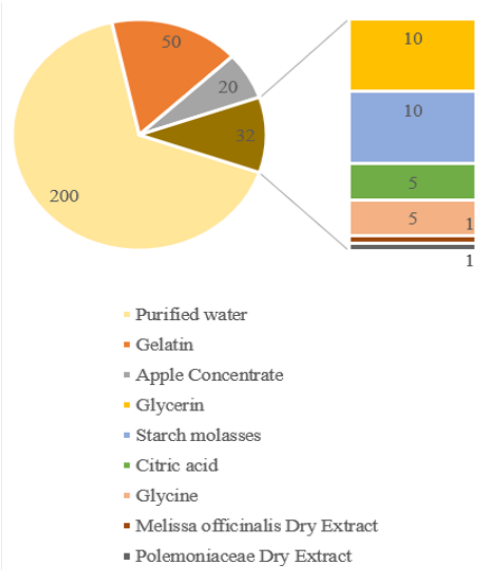
Safety studies were also conducted in accordance with Technical Regulations 021/2011 of the Customs Union on Food Safety. To extract biologically active substances from plant materials, two methods were used to identify optimal conditions for maximum preservation of these substances (Zhang *et al*., 2020; Hudz *et al*., 2023; Poornachitra & Maheswari, 2023). The first method involved evaporating 200 mL of an aqueous solution in a porcelain cup on a water bath for 10 hours, until a powder was obtained. The second, more efficient method, utilized a vacuum rotary evaporator to evaporate the liquid solution in a round-bottom flask at a temperature of 50-60 °C in a heating bath and a steam temperature of 30-40 °C in the evaporator at a pressure of 50 mmHg, until a dry concentrate was achieved. This method produced a saturated yellow concentrate with a dry matter content of 70-72% and increased levels of flavonoids by 1.86 times and saponins by 14 times compared to the initial aqueous alcoholic extract.

The creation of a laboratory sample of phytopreparations in the form of sedative lozenges based on Melissa officinalis, Polemoniaceae, and glycine extracts was carried out using two methods. The first method involved adding 20 grams of gelatin to 200 ml of syrup made from plant extracts. The mixture was then allowed to swell, forming a block, and cooled in a refrigerator for four hours before being shaped into rectangular forms.

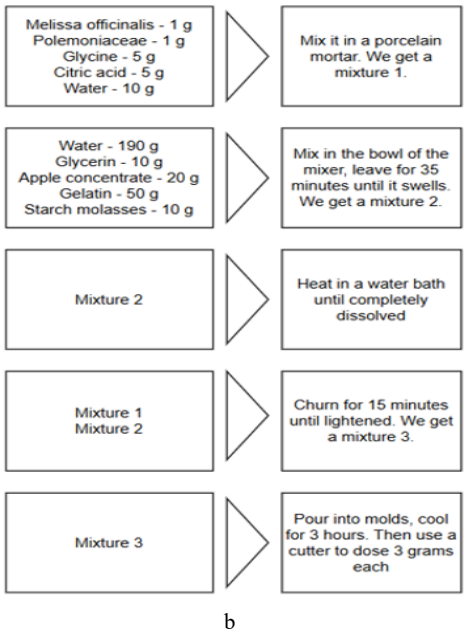
The second method was more complex and involved a percolation step. For this, 50 g of Polemoniaceae raw material and 50 g of Melissa officinalis raw material were placed in a percolator, along with 70% ethanol in a 1:2 ratio. The percolation process involved stages such as soaking, infusion (24 hrs), and actual percolating until the raw materials were depleted. The resulting percolate was then purified through settling and filtration. After that, alcohol was distilled using a distillation apparatus. The aqueous residue was then evaporated to a thick consistency using a vacuum evaporator at 50-60 °C and a pressure of 5 mmHg. The moisture content of

the dry extract did not exceed 25%, and the heavy metal content was below 0.01%.

Next, the dry extract was dissolved in water to form a thick mass, from which bars could be formed. Lozenges could then be cut from these bars. The resulting dosage form was an elastic-plastic base with evenly distributed active ingredients designed for absorption. The lozenges were pale yellow in color, had a sweet and sour taste with a slight lemon scent, and had a smooth and uniform surface. The average dissolution time for one lozenge was 4 ± 0.66 minutes, which met the pharmacopoeial requirements (less than 15 minutes). The average weight of a lozenge was 1.40 ± 0.05 grams, and the weight loss during drying was 13.6% ± 0.1%. **Figure 1** shows the formulation and manufacturing technology of lozenges.



a



b

Figure 1. Preparation of lozenges: a) composition; b) technology

Biological properties of the laboratory sample were tested in several stages. In the first stage, an experimental study was conducted on 10 sexually mature rats, divided into an experimental and a control group. Animals in the experimental group were given crushed lozenges containing Melissa officinalis extract at a dose of 2 mg and Polemoniaceae extract at 2 mg, as well as glycine at 10 mg. The control group was given a standard diet.

The effectiveness of the laboratory product was tested at the Republican Orphanage in Buinaksk. A study was conducted for 30 days on children aged 3-5 (7 boys and 3 girls) with mental disabilities, hyperactivity, aggression, and sleep disorders who were given ¼ of a lozenge 3 times a day after meals. Following the study, caregivers at the orphanage observed a decrease in the children's aggression and hyperactivity, as well as an improvement in their sleep patterns.

The taste qualities of lozenges were evaluated using the method of threshold concentrations and numerical indices developed by I. A. Egorov (Bakker, 2014; Samaranayake *et al*., 2024). The study involved 35 children aged 5-10 and 25 students who were divided into two groups. One group assessed the main taste sensations (sweet, sour, salty, bitter), while the other assessed the objective sensations (pleasant/unpleasant). The study used a blind method and followed standard tasting rules. As a result, the taste of the lozenge was determined to be sweet and sour with a pleasant aroma.

Throughout the study, subjects were interviewed daily and their pulse and blood pressure monitored. At the end of 30 days, participants reported decreased anxiety and stress, as well as improved sleep, mood, and memory, with no side effects, including nausea, vomiting, dizziness, or allergies. Pulse and blood pressure remained within normal limits for all participants.

Results and Discussion

As a result of the research, a laboratory sample of sedative lozenges was developed based on a dry extract of Melissa officinalis (Melissa officinalis L.), a dry extract of Polemoniaceae (Polemonium caeruleum L.), and glycine.

To ensure the stability and reproducibility of the composition, the main physico-chemical parameters of the intermediate product, syrup, were studied. Studies have shown that the resulting syrup is a clear, viscous liquid without sediment, turbidity, and foreign inclusions, with a faint lemon flavor and a slight bitter note in the taste **(Table 1)**.

Table 1. Determination of organoleptic parameters

Indicator	Characteristics of the syrup produced	Characteristics of the syrup according to GOST
Appearance	Transparent, homogeneous, viscous, without cloudiness, sediment, or foreign matter	Transparent liquid without sediment or foreign matter
Taste, color, aroma	Slightly bitter taste, with a pleasant, subtle lemon aroma	In accordance with the formulation

It was found that the density of the syrup is 1.305-1.315 g/ml, the refractive index is 1.452–1.455, and the hydrogen index (pH) is 4.5. The dynamic viscosity was [MPa·s]; 94 41 MPa·s, the yield index is 0.9886; the consistency index is 63.00 MPa·s, which characterizes the product as a Newtonian fluid and indicates the stability of its rheological properties under various loads. The most important stage was the assessment of microbiological purity and safety. The research results **(Table 2)** confirmed that the content of toxic elements, pesticides, and radionuclides in the Sample is significantly lower than the permissible levels established by TR CU 021/2011 "On Food Safety". Microbiological parameters also met the requirements of the Pharmacopoeia.

Table 2. The results of the conducted research

Indicator	Content in Sample, mg/kg	Permissible Levels, mg/kg, max
Toxic Elements:		
Lead	0.03	0.5
Arsenic	< 0.01	0.05
Cadmium	< 0.01	0.03
Mercury	< 0.002	0.01
Pesticides:		
HCH and its isomers	Not detected	0.1
DDT and its metabolites	Not detected	0.1
Heptachlor	Not detected	Not permitted
Aldrin	Not detected	Not permitted
Patulin	Not detected	0.05
Microbiological Indicators:		
Mesophilic clostridia (others)	Not detected	Not permitted in 1 cm³
Mesophilic clostridia *C. Botulinum* and/or *C. perfringens*	Not detected	Not permitted in 1 cm³
Non-spore-forming microorganisms, incl. lactic acid bacteria, mold fungi, yeasts	Not detected	Not permitted in 1 cm³
Spore-forming mesophilic aerobic and facultative anaerobic microorganisms of the *B. cereus* and/or *B. polymyxa* group	Not detected	Not permitted in 1 cm³
Spore-forming mesophilic aerobic and facultative anaerobic microorganisms of the *B. subtilis* group	Not detected	Not more than 11 cells in 1 cm³
Radiological Indicators, Bq/kg:		
Cesium-137	3.28	40
Strontium-90	5.77	25
GMO (recombinant DNA)	Not detected	Not permitted

The results shown in **Table 2** indicate that, in terms of safety, the tested samples of lozenges comply with TR CU 021/2011 "On Food Safety" (Appendices No. 2 (paragraph 2), No. 3 (paragraph 6, paragraph 10), No. 4 (paragraph 19))., which confirms the possibility of using the drug from the age of 3 (Mistry & Batchelor, 2017; Tbahriti *et al*., 2025).

The data obtained indicate that the developed formulation and technological process make it possible to obtain a stable intermediate product (syrup) that meets all regulatory requirements for organoleptic, physico-chemical, and safety indicators (Todorović *et al*., 2023; Banerjee *et al*., 2025). Vacuum drying of extracts at 60 °C, in contrast to evaporation in a water bath at 100 °C, allowed us to obtain a concentrate with a higher content of biologically active substances (flavonoids 1.86 times and saponins 1.4 times higher) and improved organoleptic properties (light brown color, transparency), which is consistent with the literature data on the thermal stability of many phytocomponents (Vega-Gálvez *et al*., 2021; Wang *et al*., 2021; Hou *et al*., 2024). Plant concentrates with a high dry matter content and preservation of the organoleptic characteristics of the initial product were obtained **(Table 3)**.

Table 3. Comparative characteristics of the studied syrup of various concentration methods

Parameter	Concentration Method: Water Bath Evaporation	Concentration Method: Vacuum Evaporation
Temperature	100 °C	60 °C
Evaporation Time	10 hours	35 minutes
Color	Brown to dark brown	Light brown to dark yellow
Odor	With a lemon note	With a lemon note
Taste	Slightly bitter	Slightly bitter
Appearance	Viscous, opaque, mass of medium homogeneity	Viscous, transparent, homogeneous mass

During the tests on laboratory rats in the control group, reflex excitability was noted by 35% ($p<0.05$), an increase in sleep duration by 25% ($p<0.05$) was recorded, and an improvement in cognitive tests (maze) was noted: the passage time decreased by 20% ($p<0.05$) compared with the control group. The group (Casarrubea *et al*., 2016; Postu *et al*., 2019). No side effects (changes in water and food intake, signs of intoxication, allergic reactions) were detected during the 30-day experiment.

The revealed sedative and anxiolytic effect is consistent with the pharmacological properties of the claimed components. Melissa officinalis is known to have moderate sedative properties, and Polemoniaceae is traditionally used in medicine due to its pronounced anxiolytic and sedative effects, which surpass valerian in activity (Shakeri *et al*., 2016; Brody *et al*., 2021; Petrisor *et al*., 2022). Glycine, being an inhibitory neurotransmitter, potentiates the action of phytocomponents (Adeva-Andany *et al*., 2018; Cen *et al*., 2022; Imenshahidi & Hossenzadeh, 2022). The absence of toxicity confirms the data obtained in the study of safety indicators.

For a preliminary assessment of human efficacy and tolerability, an open pilot study was conducted with the participation of 25

volunteer students (18-22 years old) with complaints of anxiety, stress, and sleep disorders.

During a pilot study on volunteers, a subjective assessment of the condition on a visual analog scale (VAS) after 30 days of taking lozenges (3 times a day) showed (Natan *et al*., 2022; Åström *et al*., 2023):

- A decrease in stress levels by 40% ($p<0.01$).
- A decrease in anxiety levels by 45% ($p<0.01$).
- Improvement of sleep quality (reduction of falling asleep time, reduction of nighttime awakenings) according to the PSQI questionnaire by 50% ($p<0.01$) compared with baseline indicators.
- Objective indicators (heart rate, blood pressure) remained within the physiological norm throughout the study.
- No adverse events (nausea, dizziness, allergic reactions) have been reported.

The data obtained indicate a good tolerance and a pronounced positive effect of the developed complex on the subjective state of people with increased psycho-emotional stress. It is important to note that the study was open and uncontrolled, which does not completely exclude the effect of the placebo effect. However, the severity of the effect and its correlation with the data from the preclinical experiment allow us to consider these results encouraging and serve as the basis for organizing further randomized, double-blind, placebo-controlled trials (RCTs).

Conclusion

Based on a comprehensive study, the formulation and technology of sedative chewing lozenges based on extracts of Melissa officinalis, Polemoniaceae, and glycine have been developed. It has been established that the use of vacuum drying ensures the safety of biologically active substances in the finished product. The conformity of the finished Sample with the requirements of the regulatory documentation on organoleptic and physico-chemical parameters has been confirmed. The compliance of the drug with the safety requirements according to TR CU 021/2011 has been proven, which justifies the possibility of use in children from the age of 3.

Experimental data convincingly demonstrate the pronounced sedative and anxiolytic activity of the developed complex. An in vivo model showed a statistically significant decrease in reflex excitability and an improvement in cognitive functions in animals. Pilot studies on volunteers have confirmed the good tolerability of the drug and its positive effect on the psycho-emotional state - there was a significant reduction in stress and anxiety levels, normalization of sleep. An important advantage of the developed form is its high organoleptic characteristics, which ensure good acceptability among the children's audience.

The high organoleptic characteristics of the lozenges have been determined, ensuring their acceptability to the target audience. The obtained results substantiate the prospects of using the developed phytopreparation in pediatric practice.

Acknowledgments: The authors would like to thank their mentor, Timur Algasanovich Ibragimov (Associate Professor of the Department of Pharmacy, Dagestan Medical State University, Makhachkala, Republic of Dagestan, Russia) for his professionalism and wisdom. The authors express their deep gratitude to the staff and pupils of the Republican Orphanage (Buinaksk, Republic of Dagestan, Russia) and the educational institution Kindergarten – Primary School No. 68 (Makhachkala, Republic of Dagestan, Russia), as well as students of Dagestan State Medical University (Makhachkala, Republic of Dagestan, Russia) for participating in the experiment.

Conflict of interest: None

Financial support: None

Ethics statement: This study was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of Dagestan State Medical University (Makhachkala, Republic of Dagestan, Russia). Informed consent was obtained from all adult subjects and from the parents or legal guardians of all child participants.

References

Adeva-Andany, M., Souto-Adeva, G., Ameneiros-Rodríguez, E., Fernández-Fernández, C., Donapetry-García, C., & Domínguez-Montero, A. (2018). Insulin resistance and glycine metabolism in humans. *Amino Acids, 50*(1), 11–27. doi:10.1007/s00726-017-2508-0

Åström, M., Thet Lwin, Z. M., Teni, F. S., Burström, K., & Berg, J. (2023). Use of the visual analogue scale for health state valuation: a scoping review. *Quality of Life Research, 32*(10), 2719–2729. doi:10.1007/s11136-023-03411-3

Bakker, E. (2014). Evaluation of Egorov's improved separate solution method for determination of low selectivity coefficients by numerical simulation. *Analytical Chemistry, 86*(16), 8021–8024. doi:10.1021/ac502638s

Baklanov, I., Rodionova, V., Ivashova, V., Shvachkina, L., & Medvedeva, V. (2020). Social trends for increasing satisfaction with the educational services of a modern university. *Calitatea, 21*(179), 88–90.

Banerjee, S., Mosca, S., Legge, I., Gangadharan, B., Walsby-Tickle, J., Arman, B. Y., Stokes, R., Bharucha, T., Deats, M., Merchant, H. A., et al. (2025). Handheld spatially offset Raman spectroscopy for rapid non-invasive detection of ethylene glycol and diethylene glycol in medicinal syrups. *Journal of Pharmaceutical and Biomedical Analysis, 265*, 117031. doi:10.1016/j.jpba.2025.117031

Bodo, E., Gowda, H. G. B., Wallrabe, U., & Wapler, M. C. (2023). In-line refractive index measurement: a simple method based on image detection. *Applied Optics, 62*(23), 6282–6286. doi:10.1364/AO.493243

Brody, A. K., Burnham, P. A., & Smith, B. (2021). Feeding friend and foe: ample pollen mitigates the effects of pollen theft for a gynodioecious plant, *Polemonium foliosissimum* (Polemoniaceae). *Annals of Botany, 128*(1), 127–134. doi:10.1093/aob/mcab050

Bruni, O., Angriman, M., Miano, S., DelRosso, L. M., Spruyt, K., Mogavero, M. P., & Ferri, R. (2024). Individualized

approaches to pediatric chronic insomnia: advancing precision medicine in sleep disorders. *Sleep Medicine Reviews, 76*, 101946. doi:10.1016/j.smrv.2024.101946

Bruni, O., Breda, M., Nobili, L., Fietze, I., Capdevila, O. R. S., & Gronfier, C. (2024). European expert guidance on management of sleep onset insomnia and melatonin use in typically developing children. *European Journal of Pediatrics, 183*(7), 2955–2964. doi:10.1007/s00431-024-05556-w

Bruni, O., Ferini-Strambi, L., Giacomoni, E., & Pellegrino, P. (2021). Herbal remedies and their possible effect on the GABAergic system and sleep. *Nutrients, 13*(2), 530. doi:10.3390/nu13020530

Canassa, V. F., & Baldin, E. L. L. (2022). Impact of sorghum genotypes on nymphal development and reproduction of *Melanaphis sacchari*. *Entomology Letters, 2*(2), 10–18. doi:10.51847/QgKDLAX7eV

Casarrubea, M., Faulisi, F., Caternicchia, F., Santangelo, A., Di Giovanni, G., Benigno, A., Magnusson, M. S., & Crescimanno, G. (2016). Temporal patterns of rat behaviour in the central platform of the elevated plus maze. Comparative analysis between male subjects of strains with different basal levels of emotionality. *Journal of Neuroscience Methods, 268*, 155–162. doi:10.1016/j.jneumeth.2015.07.024

Cen, Q., Fu, F., Xu, H., Luo, L., Huang, F., Xiang, J., Li, W., Pan, X., Zhang, H., Zheng, M., et al. (2022). Glycine assists in efficient synthesis of herbal carbon dots with enhanced yield and performance. *Journal of Materials Chemistry B, 10*(34), 6433–6442. doi:10.1039/d2tb01334g

Chan, Y. S., Jang, J. T., & Ho, C. S. (2022). Effects of physical exercise on children with attention deficit hyperactivity disorder. *Biomedical Journal, 45*(2), 265–270. doi:10.1016/j.bj.2021.11.011

Chen, Z., Ma, L., Liu, W., Li, C., Yuan, M., Yu, Z., Li, L., Fan, X., & Xu, Q. (2025). Systems metabolic engineering and process optimization for efficient l-tyrosine production from high-purity glucose syrup in *Escherichia coli*. *Bioresource Technology, 425*, 132306. doi:10.1016/j.biortech.2025.132306

Chidambaranathan, A. S., & Culathur, T. (2022). Acupuncture for temporomandibular joint muscular disorder: a prospective clinical assessment of its therapeutic effectiveness. *International Journal of Dental Research and Allied Sciences, 2*(2), 10–15. doi:10.51847/7MWBiwx7jQ

Chutko, L. S., Yakovenko, E. A., Surushkina, S. Y., Anisimova, T. I., Sergeev, A. V., Didur, M. D., & Cherednichenko, D. V. (2022). Emotional and behavioral dysregulation in children with attention deficit hyperactivity disorder. *Zhurnal Nevrologii i Psikhiatrii Imeni S. S. Korsakova, 122*(6), 100–107. doi:10.17116/jnevro2022122061100

Claussen, A. H., Holbrook, J. R., Hutchins, H. J., Robinson, L. R., Bloomfield, J., Meng, L., Bitsko, R. H., O'Masta, B., Cerles, A., Maher, B., et al. (2024). All in the family? A systematic review and meta-analysis of parenting and family environment as risk factors for attention-deficit/hyperactivity disorder (ADHD) in children. *Prevention Science, 25*(Suppl 2), 249–271. doi:10.1007/s11121-022-01358-4

Danielson, M. L., Claussen, A. H., Bitsko, R. H., Katz, S. M., Newsome, K., Blumberg, S. J., Kogan, M. D., & Ghandour, R. (2024). ADHD prevalence among U.S. children and adolescents in 2022: diagnosis, severity, co-occurring disorders, and treatment. *Journal of Clinical Child & Adolescent Psychology, 53*(3), 343–360. doi:10.1080/15374416.2024.2335625

Divakaruni, A. S., & Jastroch, M. (2022). A practical guide for the analysis, standardization, and interpretation of oxygen consumption measurements. *Nature Metabolism, 4*(8), 978–994. doi:10.1038/s42255-022-00619-4

Dunn, M., Barbano, D. M., & Drake, M. (2021). Viscosity changes and gel formation during storage of liquid micellar casein concentrates. *Journal of Dairy Science, 104*(12), 12263–12273. doi:10.3168/jds.2021-20658

Ekambaram, V., & Owens, J. (2021). Medications used for pediatric insomnia. *Child and Adolescent Psychiatric Clinics of North America, 30*(1), 85–99. doi:10.1016/j.chc.2020.09.001

Fiodorova, O. A., Sivkova, E. I., & Nikonov, A. A. (2022). Safeguarding beef cattle from gnats and gadflies in the Southern Tyumen region. *International Journal of Veterinary Research and Allied Sciences, 2*(2), 8–13. doi:10.51847/iVXOeXmSNZ

Fragedakis, N., Skinner, C. R., Shriner, M., Ruinsky, M., Yang, S. Y., Wine, R. P., Johnston, L., & Breidt, F. (2023). Modeling the formulation pH of elderberry syrup with multiple weak acids. *Journal of Food Science, 88*(8), 3373–3383. doi:10.1111/1750-3841.16664

Fraticelli, S., Caratelli, G., De Berardis, D., Ducci, G., Pettorruso, M., Martinotti, G., Di Cesare, G., & Di Giannantonio, M. (2022). Gender differences in attention deficit hyperactivity disorder: an update of the current evidence. *Rivista di Psichiatria, 57*(4), 159–164. doi:10.1708/3855.38380

Gagnon, M., Houde, J., Corriveau, S., Charron, C., & Lagacé, L. (2025). Impact of inoculation of the sap collection system with three Pseudomonadota strains on maple syrup microbial and organoleptic quality. *Canadian Journal of Microbiology, 71*(1), 1–16. doi:10.1139/cjm-2024-0225

Himelfarb, M., & Shatkin, J. P. (2021). Pediatric insomnia. *Child and Adolescent Psychiatric Clinics of North America, 30*(1), 117–129. doi:10.1016/j.chc.2020.08.004

Hirota, T., & King, B. H. (2023). Autism spectrum disorder: a review. *JAMA, 329*(2), 157–168. doi:10.1001/jama.2022.23661

Hou, S., Zhang, D., Yu, D., Li, H., Xu, Y., Wang, W., Li, R., Feng, C., Meng, J., Xu, L., et al. (2024). Effect of different drying methods on the quality of *Oudemansiella raphanipes*. *Foods, 13*(7), 1087. doi:10.3390/foods13071087

Hudz, N., Kobylinska, L., Pokajewicz, K., Horčinová Sedláčková, V., Fedin, R., Voloshyn, M., Myskiv, I., Brindza, J., Wieczorek, P. P., & Lipok, J. (2023). *Mentha piperita*: essential oil and extracts, their biological activities, and perspectives on the development of new medicinal and cosmetic products. *Molecules, 28*(21), 7444. doi:10.3390/molecules28217444

Imenshahidi, M., & Hossenzadeh, H. (2022). Effects of glycine on

metabolic syndrome components: a review. *Journal of Endocrinological Investigation, 45*(5), 927–939. doi:10.1007/s40618-021-01720-3

Macrì, M., D'Albis, G., D'Albis, V., Antonacci, A., Abbinante, A., Stefanelli, R., Pegreffi, F., & Festa, F. (2023). Assessing the psychosocial and functional impact of periodontal disease. *Annals of Orthodontics and Periodontics Specialty, 3*, 28–31. doi:10.51847/OjyFxHjTxv

Mathews, I. M., Eastwood, J., Lamport, D. J., Cozannet, R. L., Fanca-Berthon, P., & Williams, C. M. (2024). Clinical efficacy and tolerability of lemon balm (Melissa officinalis L.) in psychological well-being: a review. *Nutrients, 16*(20), 3545. doi:10.3390/nu16203545

Mistry, P., & Batchelor, H.; SPaeDD-UK project (Smart Paediatric Drug Development - UK). (2017). Evidence of acceptability of oral paediatric medicines: a review. *Journal of Pharmacy and Pharmacology, 69*(4), 361–376. doi:10.1111/jphp.12610

Mizzi, N., & Blundell, R. (2025). Glycine receptors: structure, function, and therapeutic implications. *Molecular Aspects of Medicine, 103*, 101360. doi:10.1016/j.mam.2025.101360

Natan, M. B., Steinfeld, Y., Badash, S., Shmilov, G., Abramov, M., Epstein, D., Yonai, Y., Berbalek, E., & Berkovich, Y. (2022). Association between type of face mask and visual analog scale scores during pain assessment. *Pain Management Nursing, 23*(3), 370–373. doi:10.1016/j.pmn.2021.09.005

Nazarova, V. A., Sokolov, A. V., Chubarev, V. N., Tarasov, V. V., & Schiöth, H. B. (2022). Treatment of ADHD: drugs, psychological therapies, devices, complementary and alternative methods, as well as the trends in clinical trials. *Frontiers in Pharmacology, 13*, 1066988. doi:10.3389/fphar.2022.1066988

Patel, D., Patel, V. D., Sedlock, R., & Haware, R. V. (2022). Negative porosity issue in the Heckel analysis: a possible solution. *International Journal of Pharmaceutics, 627*, 122205. doi:10.1016/j.ijpharm.2022.122205

Pavithra, A., Paulraj, J., Rajeshkumar, S., & Maiti, S. (2023). Comparative analysis of antimicrobial properties and compressive strength of traditional and thyme-enhanced glass ionomer cement. *International Journal of Dental Research and Allied Sciences, 3*(2), 16–23. doi:10.51847/y77YKMTRI8

Pelevin, S. I., Taubaev, B. D., & Baklanov, I. S. (2018). Problem of technogenic society dynamics under the conditions of contemporaneity. *International Journal of Civil Engineering and Technology, 9*(11), 2437–2443.

Perrine, K. T. A., Moïse, A. A. A., Claver, K. A., Tenon, C., Brice, B. J., Herve, K. K., & Philippe, K. K. (2023). Assessment of the impact of *Ocimum gratissimum* L. (Lamiaceae) extracts on *Nasutitermes* termites, cocoa pests in Côte d'Ivoire. *Entomology Letters, 3*(1), 7–17. doi:10.51847/gYbXNUKPX6

Petrisor, G., Motelica, L., Craciun, L. N., Oprea, O. C., Ficai, D., & Ficai, A. (2022). *Melissa officinalis*: composition, pharmacological effects and derived release systems - A review. *International Journal of Molecular Sciences, 23*(7), 3591. doi:10.3390/ijms23073591

Poornachitra, P., & Maheswari, U. (2023). Identifying non-specific symptoms in oral submucous fibrosis patients: a clinical perspective. *Asian Journal of Periodontics and Orthodontics, 3*, 18–24. doi:10.51847/xLpm4TfyCA

Postu, P. A., Sadiki, F. Z., El Idrissi, M., Cioanca, O., Trifan, A., Hancianu, M., & Hritcu, L. (2019). *Pinus halepensis* essential oil attenuates the toxic Alzheimer's amyloid beta (1-42)-induced memory impairment and oxidative stress in the rat hippocampus. *Biomedicine & Pharmacotherapy, 112*, 108673. doi:10.1016/j.biopha.2019.108673

Reshetnikov, A. D., & Barashkova, A. I. (2022). The role of veterinary innovations in reindeer husbandry for climate change adaptation. *International Journal of Veterinary Research and Allied Sciences, 2*(1), 1–8. doi:10.51847/UlrjooXH9s

Reynolds, A. M., Spaeth, A. M., Hale, L., Williamson, A. A., LeBourgeois, M. K., Wong, S. D., Hartstein, L. E., Levenson, J. C., Kwon, M., Hart, C. N., et al. (2023). Pediatric sleep: current knowledge, gaps, and opportunities for the future. *Sleep, 46*(7), zsad060. doi:10.1093/sleep/zsad060

Samaranayake, L., Tuygunov, N., Schwendicke, F., Osathanon, T., Khurshid, Z., Boymuradov, S. A., & Cahyanto, A. (2024). Artificial intelligence in prosthodontics: transforming diagnosis and treatment planning. *Asian Journal of Periodontics and Orthodontics, 4*, 9–18. doi:10.51847/nNyZ6VD1da

Samatadze, T. E., Yurkevich, O. Y., Khazieva, F. M., Basalaeva, I. V., Konyaeva, E. A., Burova, A. E., Zoshchuk, S. A., Morozov, A. I., Amosova, A. V., & Muravenko, O. V. (2022). Agro-morphological and cytogenetic characterization of colchicine-induced tetraploid plants of *Polemonium caeruleum* L. (Polemoniaceae). *Plants, 11*(19), 2585. doi:10.3390/plants11192585

Shakeri, A., Sahebkar, A., & Javadi, B. (2016). *Melissa officinalis* L. - A review of its traditional uses, phytochemistry and pharmacology. *Journal of Ethnopharmacology, 188*, 204–228. doi:10.1016/j.jep.2016.05.010

Shikov, A. N., Narkevich, I. A., Flisyuk, E. V., Luzhanin, V. G., & Pozharitskaya, O. N. (2021). Medicinal plants from the 14th edition of the Russian Pharmacopoeia, recent updates. *Journal of Ethnopharmacology, 268*, 113685. doi:10.1016/j.jep.2020.113685

Sirohi, A., Upmanyu, A., Kumar, P., Dhiman, M., Juglan, K. C., Singh, D. P., Saxena, K. K., Bhadauria, A., & Haque Siddiqui, M. I. (2024). Estimation of ultrasonic velocity, density, internal pressure, and thermophysical parameters of ionic liquid mixtures: application of Flory's statistical theory. *ACS Omega, 9*(17), 19363–19377. doi:10.1021/acsomega.4c00520

Surushkina, S. Y., & Chutko, L. S. (2023). Pharmacotherapy and psychotherapy of children with attention deficit hyperactivity disorder. *Zhurnal Nevrologii i Psikhiatrii Imeni S. S. Korsakova, 123*(2), 21–25. doi:10.17116/jnevro202312302121

Tbahriti, H. F., Zerrouki, A., Boukadoum, A., Kameche, M., Povetkin, S., Simonov, A., & Thiruvengadam, M. (2025). Comprehensive review and meta-analysis of magnesium

chloride optimization in PCR: investigating concentration effects on reaction efficiency and template specificity. *Analytical Biochemistry, 705*, 115909. doi:10.1016/j.ab.2025.115909

Todorović, N., Čanji Panić, J., Zavišić, M., Krtolica, J., Ratajac, R., Petrović, J., Bosiljčić, D., Kladar, N., Milošević, N., & Lalić-Popović, M. (2023). Compounding of liquid and solid dose adjustable formulations with pantoprazole: comparison of stability, applicability and suitability. *Pharmaceutics, 15*(3), 717. doi:10.3390/pharmaceutics15030717

Vega-Gálvez, A., Poblete, J., Rojas-Carmona, R., Uribe, E., Pastén, A., & Goñi, M. G. (2021). Vacuum drying of Chilean papaya (*Vasconcellea pubescens*) fruit pulp: effect of drying temperature on kinetics and quality parameters. *Journal of Food Science and Technology, 58*(9), 3482–3492. doi:10.1007/s13197-021-05005-8

Wang, X., Xu, S., Wu, Z., Li, Y., Wang, Y., Wu, Z., Zhu, G., & Yang, M. (2021). A novel ultrasound-assisted vacuum drying technique for improving drying efficiency and physicochemical properties of *Schisandra chinensis* extract powder. *Food Science & Nutrition, 10*(1), 49–59. doi:10.1002/fsn3.2645

Wilhelmy, L., Willmann, J. H., Tarraf, N. E., Wilmes, B., & Drescher, D. (2022). Managing first molar agenesis: a long-term assessment of space closure and implant options. *Annals of Orthodontics and Periodontics Specialty, 2*, 1–7. doi:10.51847/ryKxA1287r

Yang, M., Wang, H., Zhang, Y. L., Zhang, F., Li, X., Kim, S. D., Chen, Y., Chen, J., Chimonas, S., Korenstein, D., et al. (2023). The herbal medicine Suanzaoren (Ziziphi Spinosae Semen) for sleep quality improvements: a systematic review and meta-analysis. *Integrative Cancer Therapies, 22*, 15347354231162080. doi:10.1177/15347354231162080

Yeom, J. W., & Cho, C. H. (2024). Herbal and natural supplements for improving sleep: a literature review. *Psychiatry Investigation, 21*(8), 810–821. doi:10.30773/pi.2024.0121

Zaki Dizaji, H., Adibzadeh, A., & Aghili Nategh, N. (2021). Application of E-nose technique to predict sugarcane syrup quality based on purity and refined sugar percentage. *Journal of Food Science and Technology, 58*(11), 4149–4156. doi:10.1007/s13197-020-04879-4

Zhang, L., Song, J., Kong, L., Yuan, T., Li, W., Zhang, W., Hou, B., Lu, Y., & Du, G. (2020). The strategies and techniques of drug discovery from natural products. *Pharmacology & Therapeutics, 216*, 107686. doi:10.1016/j.pharmthera.2020.107686