*REVIEW*

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# Low-potential homeopathic medicines: historical review and comparative analysis with allopathic and phytotherapeutic approaches

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The relevance of the work is due to the ongoing discussion about the place of homeopathic medicines in the system of evidence-based medicine, as well as the need to distinguish approaches to low and high dilutions.

**The aim.** To systematize information on the use of low homeopathic dilutions; to conduct a comparative group characterization of low-potential homeopathic medicines with allopathic and phytotherapeutic drugs; to identify promising areas for further research.

**Materials and methods.** The data was analyzed, including historical information, theoretical concepts, experimental and clinical studies, as well as regulatory and regulatory documents. The key stages and strategies of using homeopathic remedies in various dilutions are highlighted. The literature was searched in the electronic databases PubMed/MEDLINE, eLibrary for the period from 1990 to 2025. Queries such as "low dilutions homeopathy", "low potency homeopathy", "homotoxicology", "ultra-high dilutions", "homeopathic low potencies", "antihomotoxic therapy" were used. The review included original experimental studies of low-potential homeopathic medicines, clinical studies of complex homeopathic medicines, systematic reviews and meta-analyses, historical and theoretical works on homeopathy, physico-chemical studies of homeopathic dilutions, regulatory documents and economic reviews. The review excluded studies on high and ultra-high dilutions without comparison with low potentials; individual clinical cases; conference abstracts; works in which there was no clear indication of the potency used.

**Results.** According to the main pharmacological criteria, low-potential complex preparations occupy an intermediate position between classical homeopathy on the one hand and allopathic/phytotherapeutic agents on the other. Their effects may have a rational explanation within the framework of hormesis and the direct action of small doses. There are separate RCTs demonstrating the effectiveness of complex drugs, but the overall level of evidence remains lower than for allopathic drugs. In order to formulate definitive conclusions about the place of low-potential homeopathic medicines, large-scale methodologically impeccable clinical studies are needed, as well as continuing the search for confirmation of their mechanisms of action, in particular, in the field of nanopharmacology.

**Conclusion.** The path to the widespread use of low-potential homeopathic remedies in modern medicine lies through the normative separation of low and high homeopathic dilutions, conducting high-quality clinical trials with rigid endpoints.

**Keywords:** homeopathic medicines; phytotherapy; low-potency medicines; allopathy; effectiveness; comparative analysis; evidence-based medicine; regulatory approaches

**Abbreviations:** WHO — World Health Organization; WHA — World Health Assembly World Health Assembly; TKIM — traditional, complementary and integrative medicine: OHLP — general characteristics of the drug; ADV — active ingredient; NMR — nuclear magnetic resonance; RCT — randomized controlled trials; RSCI — Russian Science Citation Index.

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# Низкопотенцированные гомеопатические препараты: исторический обзор и сравнительный анализ с аллопатическим и фитотерапевтическим подходами

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Актуальность работы обусловлена сохраняющейся дискуссией о месте гомеопатических препаратов в системе доказательной медицины, а также необходимостью разграничения подходов к низким и высоким разведениям.

**Цель.** Систематизировать информацию о применении низких гомеопатических разведений; провести сравнительную групповую характеристику низкопотенцированных гомеопатических препаратов с аллопатическими и фитотерапевтическими препаратами; определить перспективные направления для дальнейших исследований.

**Материалы и методы.** Осуществлен анализ данных, включающий исторические сведения, теоретические концепции, экспериментальные и клинические исследования, а также нормативно-правовые и регуляторные документы. Выделены ключевые этапы и стратегии применения гомеопатических средств в различных разведениях. Поиск литературы проводился в электронных базах PubMed/MEDLINE, eLIBRARY за период с 1990 по 2025 гг. Использовались такие запросы, как «low dilutions homeopathy», «low potency homeopathy», «homotoxicology», «ultra-high dilutions», «гомеопатические низкие потенции», «антигомотоксическая терапия». В обзор включались оригинальные экспериментальные исследования низкопотенцированных гомеопатических препаратов, клинические исследования комплексных гомеопатических препаратов, систематические обзоры и метаанализы, исторические и теоретические работы, посвященные гомеопатии, физико-химические исследования гомеопатических разведений, регуляторные документы и экономические обзоры. Из обзора исключались исследования, посвященные высоким и сверхвысоким разведениям без сравнения с низкими потенциями; отдельные клинические случаи; тезисы конференций; работы, в которых отсутствовало четкое указание на использованную потенцию.

**Результаты.** По основным фармакологическим критериям низкопотенцированные комплексные препараты занимают промежуточное положение между классической гомеопатией с одной стороны и аллопатическими/фитотерапевтическими средствами с другой. Их эффекты могут иметь рациональное объяснение в рамках гормезиса и прямого действия малых доз. Существуют отдельные РКИ, демонстрирующие эффективность комплексных препаратов, однако общий уровень доказательств остается ниже, чем для аллопатических препаратов. Для формулировки окончательных выводов о месте низкопотенцированных гомеопатических препаратов необходимы масштабные методологически безупречные клинические исследования, а также продолжение поисков подтверждения их механизмов действия, в частности, в области нанофармакологии.

**Заключение.** Путь к широкому применению низкопотенцированных гомеопатических средств в современной медицине лежит через нормативное разделение низких и высоких гомеопатических разведений, проведение качественных клинических исследований с жесткими конечными точками.

**Ключевые слова:** гомеопатические препараты; фитотерапия; низкопотенцированные препараты; аллопатия; эффективность; сравнительный анализ; доказательная медицина; нормативные подходы

**Список сокращений:** ВОЗ — Всемирная организация здравоохранения; WHA — World Health Assembly Всемирная ассамблея здравоохранения; ТКИМ — традиционная, комплементарная и интегративная медицина; ОХЛП — общая характеристика лекарственного препарата; АДВ —активное действующее вещество; ЯМР — ядерно-магнитный резонанс; РКИ — рандомизированные контролируемые исследования; РИНЦ — Российский индекс научного цитирования.

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## INTRODUCTION

Modern clinical pharmacology and regulatory practice face a complex dilemma related to homeopathic medicines. Currently, the very classification of a drug as homeopathic raises many questions for a significant portion of physicians and hinders the further use of these agents in clinical practice. This position is entirely understandable and justifiable concerning ultra-high dilution (potency) medicines, whose mechanism of action is inexplicable from the standpoint of classical pharmacokinetics and molecular biology, which causes justified scientific skepticism [1, 2]. On the other hand, there is an extensive body of low potency homeopathic remedies (below D8 / C2) containing measurable and often pharmacologically significant amounts of active substances that are used in clinical practice [3, 4]. This fact creates terminological, methodological, and regulatory confusion and complicates the adequate assessment of their efficacy, safety, and potential interactions. A recent systematic review by P.M. Herman et al. (2025) revealed significant shortcomings in the quality of research in the field of homeopathy (42 % of analyzed randomized clinical trials (RCTs) had a high risk of systematic error, and 79 % of studies lacked safety data), indicating the need to improve methodological approaches to conducting research [5]. The presented data suggest a persistent gap between clinical practice and the requirements of evidence-based medicine.

The search for research strategies that reflect the therapeutic principles of homeopathy and meet the standards of modern science [6] is also ongoing.

A systematic review by P. Soni et al. (2025), covering the period from January 2020 to December 2025, highlights contemporary studies confirming the clinical and pharmacological rationale of homeopathic pharmacy [7]. The authors concluded that to expand the role of homeopathy, it is necessary to strengthen analytical standardization and conduct well-designed clinical studies using methods such as chromatography and spectroscopy (including UV spectrophotometry). At the same time, the development of double-blind RCTs for ultra-diluted medicinal products is a methodologically complex task, as is the creation of pharmacokinetic models for substances whose concentration exceeds measurable molecular concentration. Differences in preparation methods and the absence of generally accepted quality control standards further limit reproducibility across different laboratories and institutions. Addressing these issues requires interdisciplinary collaboration between specialists in homeopathy, pharmacologists, chemists, and clinical researchers [7].

The relevance of the aim is due to the need for a clear scientific and legal distinction between two classes of agents—ultra-high dilution medicines and low-potential medicines—as well as the need to develop a differentiated, evidence-based approach to evaluating low-dilution medicines. This work provides a historical analysis of the development of homeopathy using low-potential medicines, systematizes the theoretical foundations and classification of homeopathic dilutions, and performs a comparative analysis of low homeopathic dilutions, allopathy, and phytotherapy based on key pharmacological criteria. The article discusses existing contradictions, limitations of the evidence base for the use of homeopathic remedies, and identifies promising directions for future research in homeopathy.

**THE AIM.** To systematize data on low-potential homeopathic medicines and formulate reasoned conclusions about the place of this group in modern medicine. To conduct a comparative group characterization of low-potential homeopathic medicines with allopathic and phytotherapeutic medicines and to identify promising directions for further research.

## MATERIALS AND METHODS

An analysis of data was carried out, including historical information, theoretical concepts, experimental and clinical studies, as well as regulatory documents, to form a comprehensive understanding of low-potential homeopathic medicines. Key stages and strategies for the use of homeopathic remedies in various dilutions were identified.

A literature search was conducted (first query in October 2025; last query in December 2025) in the databases PubMed / MEDLINE, eLIBRARY (publications in journals and collections included in the RSCI system) for the period from 1990 to 2025. The following search queries and their combinations were used: “low dilutions homeopathy”, “low potency homeopathy”, “homotoxicology”, “ultra-high dilutions”. Additionally, information on the given topic was searched within the reference lists of found publications, and regulatory

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documents were analyzed. The review included original experimental studies of low-potential homeopathic medicines, clinical studies (randomized controlled trials, observational studies, case series) of complex homeopathic medicines, systematic reviews and meta-analyses evaluating the efficacy of homeopathic medicines, historical and theoretical works dedicated to homeopathy and homotoxicology, physicochemical studies of homeopathic dilutions (spectroscopy; electron microscopy; NMR), and regulatory documents. Preference was given to publications in English and Russian. Studies on high and ultra-high dilutions were excluded from the review if they did not include a comparison with low potencies; individual case reports without a control group; publications with limited full-text access; conference abstracts; dissertations, patents, grants, and works where the potency used was not specified.

The search query “low dilutions homeopathy” in PubMed / MEDLINE yielded 80 publications; “low potency homeopathy” yielded 43 publications; “homotoxicology” yielded 13 publications (from 1990 to 2025). Of these, 92 publications were excluded—duplicates and works not relevant to the topic under consideration. The remaining 44 works were included in the review. In eLIBRARY, the query «гомеопатические низкие потенции» yielded 270 publications; «гомотоксикология» yielded 235 publications; after exclusion according to the exclusion criteria, 12 publications were selected for the review.

## RESULTS

### Historical review of homeopathic remedies

Homeopathy was founded by Dr. Samuel Christian Hahnemann in the late 18th century. Over time, it became one of the most frequently used forms of alternative medicine in Europe and the USA. It is based on the principle of “like treats like” or “*similia similibus curentur*,” according to which highly diluted substances that cause symptoms similar to those produced by these substances in healthy individuals are used for therapeutic purposes [8–10]. The method is based on two fundamental principles: the principle of similarity and the principle of dilution [2]. Homeopathy is among the top ten most frequently practiced forms of complementary and alternative medicine worldwide [8, 11]. Its prevalence varies between countries, reaching, according to some data, 24–71.3 % [2].

The widespread use of low homeopathic dilutions in clinical practice became possible due to the formation of the paradigm of “complex” homeopathy, which, unlike classical homeopathy, is based on creating fixed combinations of drugs with clear therapeutic indications aimed at correcting the functions of specific organs and systems. A key role in its development was played by the German company HEEL GmbH, founded in 1936 by physician Hans-Heinrich Reckeweg (1905–1985) [12].

Reckeweg, drawing on Hahnemann’s ideas and mid-20th-century toxicology knowledge, developed the theory of homotoxicology. According to this theory, diseases are considered protective reactions of the body to toxins (homotoxins), and treatment should stimulate the drainage and excretory systems. This theory led to the creation of complex antihomotoxic drugs—fixed combinations of low and medium dilutions of various substances selected to act on specific organs or systems, rather than on the patient’s overall symptom complex [12, 13].

By the mid-20th century, several competing and complementary centers of production and ideology in the field of low dilutions and complex homeopathy had formed. For example, the German school (HEEL, DHU, Schwabe) focused on the theory of homotoxicology, drainage, organotropic effects, and injectable forms; the French school (Boiron, Dolisos) emphasized clinical practice, convenient forms (granules), and widespread distribution through general practitioners; the Soviet / Russian school (Mater Medica, etc.) focused on original scientific research in the field of ultra-low doses, adaptation to the local market, and clinical needs.

This diversity of approaches and commercial strategies has led to the global phenomenon we observe today: low-potency complex homeopathic medicines have become an integral part of the over-the-counter market and the arsenal of many physicians, especially in Europe and Russia [14].

The World Health Organization (WHO) includes homeopathy in its strategy for Traditional, Complementary, and Integrative Medicine [8]. The Global Strategy on Traditional Medicine for 2025–2034, adopted at the 78th World Health Assembly in May 2025 (WHA78(14)), envisages a world where everyone has universal access to people-centered traditional, complementary, and integrative health care (TCIH), contributing to the attainment of the highest possible level of health and well-being [15].

In Russia, the application of homeopathic methods is regulated by Federal Law No. 61-FZ of April 12, 2010 (as amended on July 23, 2025) "On the Circulation of Medicinal Products." According to the instructions for the medical use of homeopathic medicines, there are no restrictions on their prescription by physicians as complex pharmacotherapy for patients with corresponding diseases, which is legally enshrined by the Ministry of Health of the Russian Federation in the current order No. 335 of November 29, 1995 "On the Use of the Homeopathic Method in Practical Healthcare".

Thus, four stages can be identified in the development of low-potency homeopathic medicines:

- Stage 1. Late 18th century–early 20th century: The founding of homeopathy by
- Samuel Hahnemann, who formulated two basic principles: similarity and potentization [8–10]. During this period, individual prescriptions were predominantly used, and dilutions were low to medium.
- Stage 2. Mid-20th century: The formation of the paradigm of complex homeopathy, in which the German company HEEL played a key role in its development, and the development of Reckeweg's theory of homotoxicology.
- Stage 3. Second half of the 20th century: Global spread of complex low-potency medicines and the formation of national schools – German, French, Soviet / Russian.
- Stage 4. Late 20th–early 21st century: Inclusion of homeopathy within regulatory frameworks.

The key result of the historical analysis is the identified evolution from classical individualized homeopathy to standardized organotropic combinations, which has led to a regulatory paradox where drugs with pharmacologically significant doses of active substances are regulated as homeopathic [3, 12, 13].

## Theoretical foundations of homeopathic dilutions

The key process in the creation of a homeopathic medicine is potentization, i.e., dynamization—the sequential dilution of the initial substance (mother tincture) combined with vigorous shaking [9, 10]. It is believed that this releases the "dynamic" therapeutic energy of the substance. The main dilution scales are divided into decimal (D or X) : a 1 : 9 dilution at each step (1D = 1 : 10, 2D = 1 : 100), centesimal (C) : a 1 : 99 dilution at each step (1C = 1 : 100, 2C = 1 : 10,000), introduced by Hahnemann; and the LM (Q) scale : a 1 : 50,000 dilution at each step, developed by Hahnemann in a later period.

Currently, there is no single international or Russian regulatory document that legally enshrines a clear division of homeopathic potencies into low, medium, and high. The boundaries are conventional and vary depending on the source. Some authors indicate that dilutions above D24 and C12 are formally sub-molar, as they lack molecules of the initial substance [16]. Others distinguish low (decimal up to centesimal 12), medium (from centesimal 12 up to centesimal 30 or 50), and high (above centesimal 50) dilutions [17]. According to some authors, homeopathic remedies with high doses of active substances are C2–C3; medium doses are C4, C5 to C12; and high dilution medicine are homeopathic dilutions exceeding Avogadro-Loschmidt's constant [18]. D. Csupor et al. propose dividing all homeopathic medicine into two main classes: potent (with extremely high dilution and low dosage) and weak-acting, or even mother tinctures (dosage close to or equal to allopathic) [3]. The authors of a major systematic review (H.J. Hamre et al., 2023) identified two ranges of homeopathic potencies: low (less than C1 or less than D24) and high (greater than or equal to C12 or greater than or equal to D24) [19]. A summary classification can be presented as follows:

**Classification of potencies**

- Low (mother tinctures, D1-D3 / C1-C2) potencies contain molecules of the initial substance in concentrations accessible for physicochemical analysis. The effects of such drugs may be related to direct pharmacological action [4].
- Medium (D4-D12 / C3-C6) theoretically contain molecules, but in very low concentrations. Their action is determined by the underlying hypothesis of hormesis [10].
- High and ultra-high (above D23 / C12) potencies exceed the Avogadro limit, making the presence of at least one molecule of the initial substance extremely unlikely. Explaining the presumed effects requires alternative (often scientifically questionable) models, the main ones being the hypotheses of "water memory", nanoparticles, and quantum effects [20, 21].

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### Analysis of Low Homeopathic Dilutions, Allopathy, and Phytotherapy

In a systematic review published in 2013, D. Csupor et al. compared an allopathic herbal medicinal product and a homeopathic medicine containing an undiluted mother tincture based on the same plant [3]. Two products (allopathic herbal medicine and homeopathic product) containing *Vitex agnus-castus* extract were analyzed using high-performance liquid chromatography with a diode-array detector for agnuside and casticin content. The agnuside content in the allopathic product was 4 times higher (100.82 vs. 25.19 μg in the homeopathic one), while the amount of casticin showed no statistically significant difference (42.95 μg and 47.03 μg, respectively. The correlation coefficient ($R^2$) was 0.9994). The authors concluded that homeopathic medicines containing active substances in allopathic doses should be treated the same as allopathic drugs in terms of quality assurance and pharmacovigilance. The experiments demonstrated the presence of active ingredients in allopathic dosage in the homeopathic medicine, highlighting the contradiction between the principles of classical and modern homeopathy.

Table 1 illustrates the differences in key pharmacological features of homeopathic dilutions, allopathy, and phytotherapy.

**Table 1 — Pharmacological characteristics of low homeopathic dilutions with allopathy and phytotherapy**

| Criterion | Low-Potency Homeopathy | Classical Allopathy | Phytotherapy (Standardized Extracts) |
|---|---|---|---|
| Mechanism of action | In vitro mechanism of action studies [22–25] are available, as well as transcriptome-level studies [26]. Organotropic, drainage, and regulatory effects are claimed. There are also drugs for which the actual mechanism is often unclear. | Clearly defined: interaction with receptors, enzymes, and ion channels [27]. | Action of a complex of bioactive substances (alkaloids, flavonoids, etc.) on multiple targets [28]. |
| Concentration of Active Pharmaceutical Ingredient (API) | From trace (nanolevel) to pharmacologically significant (mother tinctures) [3]. | High, precisely dosed, sufficient to saturate targets [29]. | High, but variable; depends on the extract. Standardized by marker compounds [30]. |
| Evidence Base | Mixed. Double-blind placebo-controlled RCTs exist for individual complex drugs [31–34], but the overall level of evidence is lower than for allopathy [19]. For some drugs, studies are methodologically weak. | "Gold standard"— randomized double-blind placebo-controlled RCTs with hard endpoints [1]. | The number of RCTs is growing, but soft endpoints are often used. Traditional experience of use plays a significant role [35, 36]. |
| Typical Use | Functional disorders, chronic conditions, pathogenetic, supportive, and drainage therapy, often in complex treatment [4]. | Etiotropic and symptomatic treatment of acute and chronic diseases [37, 38]. | Prevention, treatment of chronic conditions, mild functional correction (e.g., sleep improvement, mild sedative effect) [39, 40]. |

Note: RCT – Randomized Clinical Trial.

## DISCUSSION

### Contradictions, limitations, and prospects

Several main contradictions can be identified in the use of low-dilution homeopathic medicines. Firstly, a regulatory paradox arises: medicines containing pharmacological doses of API (mother tinctures) are regulated as homeopathic, not medicinal products, which weakens the requirements for the evidence base and pharmacovigilance. This raises a number of questions for the scientific community regarding the adequate assessment of their efficacy, safety, potential drug interactions, and legal regulation [3]. Secondly, scientific heterogeneity: studies mix high and low dilutions, individual and complex approaches, making meta-analyses uninformative. The effect of low dilutions can be masked by the placebo effect from high ones.

Limitations of existing studies: most studies on low dilutions are *in vitro* studies, observational studies, or small RCTs with a high risk of systematic error. Overall, there is a lack of large, well-designed pragmatic studies comparing complex low-potency medicines with standard therapy for specific nosologies.

However, there are high-quality placebo-controlled, double-blind RCTs with proven clinical efficacy in certain pathological conditions [31–34],

observational studies in real clinical practice with large patient cohorts [41–45], supported by studies of the mechanism of action at the transcriptome level [26, 46] and mediators [47–51].

An active-controlled RCT compared the efficacy of Traumeel S in a topical dosage form for the treatment of acute ankle ligament sprains [31]. The study showed that in acute ligament sprains (grades 1 and 2), after 7 days of treatment, Traumeel S was not inferior to diclofenac (1% gel) in improving ankle joint function and reducing pain. After 6 weeks, all patients experienced complete pain relief and restoration of joint function.

Studies of some complex low-potency medicines have been included in independent systematic reviews as having a high level of evidence and quality of execution [32, 52]. One systematic review showed that intra-articular administration of complex homeopathic medicines Traumeel®S and Zeel®T in the treatment of osteoarthritis of the knee and hip joints demonstrated therapeutic potential at week 6 compared to placebo (SMD: -0.42, 95 % confidence interval: -0.71 to -0.11, probability of achieving moderate therapeutic efficacy 63.5 % according to one study). However, the authors note that the long-term efficacy of the drugs has not been studied.

The study of the mechanisms of action of homeopathic medicines, along with studies of allopathic drugs, has become possible in modern realities due to the development of technologies and equipment, which is gradually filling the gaps in the evidence base for complex low-dose medicinal products [53, 54].

In an analytical study by S. Duller et al. (2026), a chemical characterization of the low-dose multi-component medicines Neurexan®, containing extracts of *Passiflora incarnata L., Avena sativa L., Coffea arabica L.,* and zinc isovalerate, was performed. Using UPLC-HR-MS and LC-MS / MS methods, flavonoids (vitexin, isovitexin, orientin, apigenin, etc.), alkaloids (caffeine, trigonelline), and caffeic acid were identified in the drug. Quantitative determination showed a vitexin content of 0.95–2.11 ng/tablet and isovitexin content of 3.94–11.5 ng/tablet. The authors conclude that Neurexan® has a complex multi-component composition, including compounds with potential activity against stress and sleep, which requires further research into their functional role [55].

In another analytical study by A. Dunkel et al. (2026), a comprehensive chemical characterization of the low-dose multi-component medicines Vertigoheel®, containing *Anamirta cocculus L., Conium maculatum L.*, Ambra grisea, and *Petroleum rectificatum*, was performed. Using UHPLC-TOF-MS / MS methods, 68,622 molecular features were identified, and t-SNE and ClassyFire classification showed structural diversity of the components. Using targeted UHPLC-MS / MS, 8 marker compounds (two for each ingredient) were quantitatively determined, including picrotoxinin, coniine, ambrinol, and mercaptostearic acid. Their content in drops and tablets varied from 0.0001 to 90.6 µg/L (or µg/g) with low inter-batch variability. The authors conclude that Vertigoheel® retains characteristic compounds from the original ingredients, and the developed protocol is suitable for the quantitative analysis of neuroactive markers and can be used in subsequent studies of mechanisms of action [56].

### Potential fields for study

In 2019, A. Tournier et al. [20] published the results of an analysis of experimental data on the empirical evidence of specific physicochemical properties of homeopathic medicines and the identification of the most promising experimental methods for future research.

The authors identified NMR, optical spectroscopy, and electrical impedance measurement as the most effective methods for confirming the specific physicochemical properties of homeopathic medicines [20].

Currently, research is ongoing to study the mechanism of action of homeopathic medicines. The drop evaporation method [53], ultraviolet and visible spectroscopy (UV-VIS), and transmission electron microscopy are widely used methods for characterizing homeopathic medicines at ultra-low concentrations [20].

P.S. Chikramane et al. (2010) used transmission / scanning electron microscopy to show that the original nanoparticles are preserved in 6 different commercial homeopathic medicines from two different manufacturers at dilutions C6, C30, and C200 [21]. To identify physical differences between potentiated drugs and placebo at the beginning of the 21st century, thanks to nanotechnological developments, numerous experiments have been conducted using a powerful signal amplification method – Raman spectroscopy [54]. Studies have shown differences in the spectra of homeopathic

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medicines at different potencies. For example, significant structural changes were detected in the Raman spectra of homeopathic medicines of Baryta Muriaticum (3X, 6X, and 12X) compared to a control sample of lactose (*saccharum lactis*), confirming the presence of Baryta Muriaticum in the sample. Using a linear regression model to assess the quality of fit, $R_2$ values were obtained (0.6 for 3X, 0.6 for 6X, 0.8 for 12X), indicating the effectiveness of Raman spectroscopy in detecting Raman shift variability ($cm^{-1}$). Raman spectra of the drugs and their medium (90% ethanol) were also obtained in the wavenumber range of 2600–3800 $cm^{-1}$. The ratio of intensities at vibrational frequencies between 3200 and 3420 $cm^{-1}$ (R1) and between 3620 and 3420 $cm^{-1}$ (R2) was calculated for each drug and the control sample.

The study of the effect on the transcriptome reveals the points of action of multi-component medicine, explaining their systemic effect [26, 46].

The study of the action of low-dose multi-component medicinal products at the mediator level demonstrated their effect in the considered links of pathogenesis.

For instance, in one study on adult male mice, the efficacy of Spascuprel® was investigated using an experimental model of electroconvulsive muscle rigidity. The study showed that during myostimulation in mice, the pain threshold decreased by 51.7 % ($p < 0.05$). Administration of Spascuprel® and tizanidine increased the pain threshold by 61.4% ($p < 0.05$) and 55.0% ($p < 0.05$) respectively, compared to the negative control group. Administration of purified water had no significant effect on the change in pain threshold in mice [47].

In an experimental study on a model of LPS-induced inflammation in rats, the mechanisms of action of the multi-component preparation Viburcol® were investigated. The study showed that the use of Viburcol® under conditions of LPS-induced inflammation in animals of both sexes was accompanied by a significant decrease in pro-inflammatory IL-2 (by 19.5–28.6 %, $p < 0.05$) and an increase in anti-inflammatory IL-10 (by 46.9–51.7 %, $p < 0.05$), a decrease in malondialdehyde (by 18.3–37.2%, $p < 0.05$) and medium molecular weight molecules (tendency), indicating a decrease in the intensity of the systemic inflammatory response, oxidative stress, and endogenous intoxication. A significant decrease in prostaglandin E2 (by 23.4–27.4%, $p < 0.05$) and peroxynitrite (by 37.8–43.0 %, $p < 0.05$) in brain tissue pathogenetically justifies the antipyretic effect of the preparation. An increase in endothelial nitric oxide synthase (by 14.3–17.8 %, $p < 0.05$) and cGMP (by 12.7–23.7%, $p < 0.05$) with a decrease in iNOS and peroxynitrite content in smooth muscles explains the antispasmodic effect of Viburcol®. Thus, the multi-component preparation Viburcol® exerts a complex anti-inflammatory, antioxidant, antipyretic, and antispasmodic effect, mediated by the modulation of the nitroergic system and cytokine profile [48].

In another experimental study conducted on a model of pneumococcal respiratory infection in rats, the efficacy of the immunomodulatory preparation Engystol® was investigated. Course administration of the preparation (21 days) reduced neurological deficit by 47.2% ($p < 0.05$) on day 21. Engystol® reduced levels of pro-inflammatory cytokines: IFN-γ—3.5–6.0 times lower than control ($p < 0.05$), IL-6, IL-8—5–7 times lower, while increasing anti-inflammatory IL-10 by 156% ($p < 0.05$). According to flow cytometry data, the preparation reduced T-cell hyperactivity (CD3, CD4, CD25), apoptosis markers (CD95), and vascular wall inflammation (HLA-DR, CD54) to levels comparable to intact animals. The author concludes that Engystol® is effective as an immunomodulatory and detoxifying agent for respiratory pathology, reducing systemic inflammation while maintaining an adequate immune response [49].

Similar studies in the future may shed light on the mechanisms of action of low-dilution homeopathic medicines, improving treatment methods and the integration of multi-component low-dose medicines into mainstream medical practice [38].

## Low-potency complex homeopathic agents using HEEL medicines as an example. Homeopathy or medicinal products?

The paradox of the question's formulation lies in the fact that all HEEL medicines presented on the Russian market are registered by the Ministry of Health of the Russian Federation under the procedure applied to allopathic medicinal products. This fact is explained by the fact that they are positioned with specific therapeutic indications and contain active components in low homeopathic dilutions, at which quantitative determination of trace amounts of initial substances is possible using modern analytical methods [55, 56]. HEEL products undergo full state registration, which allows the company to confirm

the efficacy of its medicines in accordance with the principles of evidence-based medicine and include them in the clinical recommendations of the Ministry of Health of the Russian Federation alongside allopathic drugs[1].

In recent years, particular attention has been paid to elucidating the mechanisms of action of low-dose, multi-component HEEL medicines. Publications demonstrate the influence of these drugs on inflammation resolution, cytokine pathway modulation, and epigenetic markers, as highlighted by recent reviews and experimental studies [47–49].

***Interpretation:***

- In terms of production technology, HEEL products belong to low-potency homeopathy.
- In terms of quantitative substance content and the volume of preclinical / clinical data, the presented drugs meet the requirements for conventional medicinal products.
- The existence of a multi-level experimental base (from molecular to clinical) brings them closer to allopathic pharmacotherapy than to "classical" homeopathy with ultra-high dilutions.

Consequently, HEEL products occupy an intermediate niche: formally – low-potency homeopathic medicines, in practice – medicinal products with confirmed clinical efficacy and multi-level preclinical validation.

Despite skepticism from the perspective of classical pharmacology, homeopathy and homotoxicology continue to be widely used worldwide. According to pharmacological criteria, low-potency complex medicines occupy an intermediate position between classical homeopathy on one hand, and allopathic / phytotherapeutic agents on the other. Modern data, including systematic reviews of clinical studies and fundamental physicochemical research on low-potency homeopathic medicines, indicate their varied efficacy and suggest the presence of certain biological and physicochemical effects that require further study. Criticism of the method in academic literature is less intense than in the public sphere. For definitive conclusions, large-scale, methodologically impeccable clinical studies are necessary, as well as continued research into mechanisms of action, particularly in the field of nanopharmacology. Currently, a number of studies have been published on the mechanism of action of certain medicines, and clinical studies have shown the efficacy of complex medicinal products and helped understand their points of application in various pathological conditions [15–19]. Due to their composition and mechanisms of action, low-potency homeopathic medicines, especially complex ones, deserve independent and unbiased study within the framework of evidence-based medicine. Historically, they have evolved from classical homeopathy to a pragmatic, organotropic model. Theoretically, the effects of low-potency medicines may have a rational explanation within the framework of hormesis or the direct action of small doses, which distinguishes them from ultra-high dilutions. In a comparative aspect, they occupy an intermediate position, but their regulatory status often does not correspond to their actual composition and potential risk.

## CONCLUSION

Thus, the path to integrating rational elements of low-potency homeopathy into modern medicine lies through clear regulatory separation from high dilutions, conducting high-quality clinical studies, and revising regulatory frameworks towards greater transparency and justification.

[1] Respiratory syncytial virus infection in children. Clinical recommendations. Clinical Guidelines Classification; 2025. Available from: https://cr.minzdrav.gov.ru/preview-cr/943_1. Russian

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## CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

## AUTHORS CONTRIBUTION

Sergey K. Zyryanov — conceptualization, formal analysis, writing—original draft, writing—review & editing; Alina B. Strok — conceptualization, formal analysis, writing—original draft. All authors confirm that their authorship meets the international ICMJE criteria (all authors made a significant contribution to the development of the concept, conduct of the study and preparation of the article, read and approved of the final version before the publication).

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