GEORGIAN MEDICAL NEWS

ISSN 1512-0112

NO 9 (366) Сентябрь 2025

ТБИЛИСИ - NEW YORK

ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии

საქართველოს სამედიცინო სიახლენი

GEORGIAN MEDICAL NEWS

Monthly Georgia-US joint scientific journal published both in electronic and paper formats of the Agency of Medical Information of the Georgian Association of Business Press. Published since 1994. Distributed in NIS, EU and USA.

GMN: Georgian Medical News is peer-reviewed, published monthly journal committed to promoting the science and art of medicine and the betterment of public health, published by the GMN Editorial Board since 1994. GMN carries original scientific articles on medicine, biology and pharmacy, which are of experimental, theoretical and practical character; publishes original research, reviews, commentaries, editorials, essays, medical news, and correspondence in English and Russian.

GMN is indexed in MEDLINE, SCOPUS, PubMed and VINITI Russian Academy of Sciences. The full text content is available through EBSCO databases.

GMN: Медицинские новости Грузии - ежемесячный рецензируемый научный журнал, издаётся Редакционной коллегией с 1994 года на русском и английском языках в целях поддержки медицинской науки и улучшения здравоохранения. В журнале публикуются оригинальные научные статьи в области медицины, биологии и фармации, статьи обзорного характера, научные сообщения, новости медицины и здравоохранения. Журнал индексируется в MEDLINE, отражён в базе данных SCOPUS, PubMed и ВИНИТИ РАН. Полнотекстовые статьи журнала доступны через БД EBSCO.

GMN: Georgian Medical News – საქართველოს სამედიცინო სიახლენი – არის ყოველთვიური სამეცნიერო სამედიცინო რეცენზირებადი ჟურნალი, გამოიცემა 1994 წლიდან, წარმოადგენს სარედაქციო კოლეგიისა და აშშ-ის მეცნიერების, განათლების, ინდუსტრიის, ხელოვნებისა და ბუნებისმეტყველების საერთაშორისო აკადემიის ერთობლივ გამოცემას. GMN-ში რუსულ და ინგლისურ ენებზე ქვეყნდება ექსპერიმენტული, თეორიული და პრაქტიკული ხასიათის ორიგინალური სამეცნიერო სტატიები მედიცინის, ბიოლოგიისა და ფარმაციის სფეროში, მიმოხილვითი ხასიათის სტატიები.

ჟურნალი ინდექსირებულია MEDLINE-ის საერთაშორისო სისტემაში, ასახულია SCOPUS-ის, PubMed-ის და ВИНИТИ РАН-ის მონაცემთა ბაზებში. სტატიების სრული ტექსტი ხელმისაწვდომია EBSCO-ს მონაცემთა ბაზებიდან.

WEBSITE

www.geomednews.com

К СВЕДЕНИЮ АВТОРОВ!

При направлении статьи в редакцию необходимо соблюдать следующие правила:

1. Статья должна быть представлена в двух экземплярах, на русском или английском языках, напечатанная через **полтора интервала на одной стороне стандартного листа с шириной левого поля в три сантиметра**. Используемый компьютерный шрифт для текста на русском и английском языках - **Times New Roman** (**Кириллица**), для текста на грузинском языке следует использовать **AcadNusx.** Размер шрифта - **12**. К рукописи, напечатанной на компьютере, должен быть приложен CD со статьей.

2. Размер статьи должен быть не менее десяти и не более двадцати страниц машинописи, включая указатель литературы и резюме на английском, русском и грузинском языках.

3. В статье должны быть освещены актуальность данного материала, методы и результаты исследования и их обсуждение.

При представлении в печать научных экспериментальных работ авторы должны указывать вид и количество экспериментальных животных, применявшиеся методы обезболивания и усыпления (в ходе острых опытов).

4. К статье должны быть приложены краткое (на полстраницы) резюме на английском, русском и грузинском языках (включающее следующие разделы: цель исследования, материал и методы, результаты и заключение) и список ключевых слов (key words).

5. Таблицы необходимо представлять в печатной форме. Фотокопии не принимаются. **Все цифровые, итоговые и процентные данные в таблицах должны соответствовать таковым в тексте статьи**. Таблицы и графики должны быть озаглавлены.

6. Фотографии должны быть контрастными, фотокопии с рентгенограмм - в позитивном изображении. Рисунки, чертежи и диаграммы следует озаглавить, пронумеровать и вставить в соответствующее место текста **в tiff формате**.

В подписях к микрофотографиям следует указывать степень увеличения через окуляр или объектив и метод окраски или импрегнации срезов.

7. Фамилии отечественных авторов приводятся в оригинальной транскрипции.

8. При оформлении и направлении статей в журнал МНГ просим авторов соблюдать правила, изложенные в «Единых требованиях к рукописям, представляемым в биомедицинские журналы», принятых Международным комитетом редакторов медицинских журналов - http://www.spinesurgery.ru/files/publish.pdf и http://www.nlm.nih.gov/bsd/uniform_requirements.html
В конце каждой оригинальной статьи приводится библиографический список. В список литературы включаются все материалы, на которые имеются ссылки в тексте. Список составляется в алфавитном порядке и нумеруется. Литературный источник приводится на языке оригинала. В списке литературы сначала приводятся работы, написанные знаками грузинского алфавита, затем кириллицей и латиницей. Ссылки на цитируемые работы в тексте статьи даются в квадратных скобках в виде номера, соответствующего номеру данной работы в списке литературы. Большинство цитированных источников должны быть за последние 5-7 лет.

9. Для получения права на публикацию статья должна иметь от руководителя работы или учреждения визу и сопроводительное отношение, написанные или напечатанные на бланке и заверенные подписью и печатью.

10. В конце статьи должны быть подписи всех авторов, полностью приведены их фамилии, имена и отчества, указаны служебный и домашний номера телефонов и адреса или иные координаты. Количество авторов (соавторов) не должно превышать пяти человек.

11. Редакция оставляет за собой право сокращать и исправлять статьи. Корректура авторам не высылается, вся работа и сверка проводится по авторскому оригиналу.

12. Недопустимо направление в редакцию работ, представленных к печати в иных издательствах или опубликованных в других изданиях.

При нарушении указанных правил статьи не рассматриваются.

REQUIREMENTS

Please note, materials submitted to the Editorial Office Staff are supposed to meet the following requirements:

1. Articles must be provided with a double copy, in English or Russian languages and typed or compu-ter-printed on a single side of standard typing paper, with the left margin of **3** centimeters width, and **1.5** spacing between the lines, typeface - **Times New Roman** (**Cyrillic**), print size - **12** (referring to Georgian and Russian materials). With computer-printed texts please enclose a CD carrying the same file titled with Latin symbols.

2. Size of the article, including index and resume in English, Russian and Georgian languages must be at least 10 pages and not exceed the limit of 20 pages of typed or computer-printed text.

3. Submitted material must include a coverage of a topical subject, research methods, results, and review.

Authors of the scientific-research works must indicate the number of experimental biological species drawn in, list the employed methods of anesthetization and soporific means used during acute tests.

4. Articles must have a short (half page) abstract in English, Russian and Georgian (including the following sections: aim of study, material and methods, results and conclusions) and a list of key words.

5. Tables must be presented in an original typed or computer-printed form, instead of a photocopied version. **Numbers, totals, percentile data on the tables must coincide with those in the texts of the articles.** Tables and graphs must be headed.

6. Photographs are required to be contrasted and must be submitted with doubles. Please number each photograph with a pencil on its back, indicate author's name, title of the article (short version), and mark out its top and bottom parts. Drawings must be accurate, drafts and diagrams drawn in Indian ink (or black ink). Photocopies of the X-ray photographs must be presented in a positive image in **tiff format**.

Accurately numbered subtitles for each illustration must be listed on a separate sheet of paper. In the subtitles for the microphotographs please indicate the ocular and objective lens magnification power, method of coloring or impregnation of the microscopic sections (preparations).

7. Please indicate last names, first and middle initials of the native authors, present names and initials of the foreign authors in the transcription of the original language, enclose in parenthesis corresponding number under which the author is listed in the reference materials.

8. Please follow guidance offered to authors by The International Committee of Medical Journal Editors guidance in its Uniform Requirements for Manuscripts Submitted to Biomedical Journals publication available online at: http://www.nlm.nih.gov/bsd/uniform_requirements.html
http://www.icmje.org/urm_full.pdf
In GMN style for each work cited in the text, a bibliographic reference is given, and this is located at the end of the article under the title "References". All references cited in the text must be listed. The list of references should be arranged alphabetically and then numbered. References are numbered in the text [numbers in square brackets] and in the reference list and numbers are repeated throughout the text as needed. The bibliographic description is given in the language of publication (citations in Georgian script are followed by Cyrillic and Latin).

9. To obtain the rights of publication articles must be accompanied by a visa from the project instructor or the establishment, where the work has been performed, and a reference letter, both written or typed on a special signed form, certified by a stamp or a seal.

10. Articles must be signed by all of the authors at the end, and they must be provided with a list of full names, office and home phone numbers and addresses or other non-office locations where the authors could be reached. The number of the authors (co-authors) must not exceed the limit of 5 people.

11. Editorial Staff reserves the rights to cut down in size and correct the articles. Proof-sheets are not sent out to the authors. The entire editorial and collation work is performed according to the author's original text.

12. Sending in the works that have already been assigned to the press by other Editorial Staffs or have been printed by other publishers is not permissible.

Articles that Fail to Meet the Aforementioned Requirements are not Assigned to be Reviewed.

ავტორთა საყურადღებოდ!

რედაქციაში სტატიის წარმოდგენისას საჭიროა დავიცვათ შემდეგი წესები:

1. სტატია უნდა წარმოადგინოთ 2 ცალად, რუსულ ან ინგლისურ ენებზე,დაბეჭდილი სტანდარტული ფურცლის 1 გვერდზე, 3 სმ სიგანის მარცხენა ველისა და სტრიქონებს შორის 1,5 ინტერვალის დაცვით. გამოყენებული კომპიუტერული შრიფტი რუსულ და ინგლისურენოვან ტექსტებში - **Times New Roman (Кириллица)**, ხოლო ქართულენოვან ტექსტში საჭიროა გამოვიყენოთ **AcadNusx.** შრიფტის ზომა – 12. სტატიას თან უნდა ახლდეს CD სტატიით.

2. სტატიის მოცულობა არ უნდა შეადგენდეს 10 გვერდზე ნაკლებს და 20 გვერდზე მეტს ლიტერატურის სიის და რეზიუმეების (ინგლისურ, რუსულ და ქართულ ენებზე) ჩათვლით.

3. სტატიაში საჭიროა გაშუქდეს: საკითხის აქტუალობა; კვლევის მიზანი; საკვლევი მასალა და გამოყენებული მეთოდები; მიღებული შედეგები და მათი განსჯა. ექსპერიმენტული ხასიათის სტატიების წარმოდგენისას ავტორებმა უნდა მიუთითონ საექსპერიმენტო ცხოველების სახეობა და რაოდენობა; გაუტკივარებისა და დაძინების მეთოდები (მწვავე ცდების პირობებში).

4. სტატიას თან უნდა ახლდეს რეზიუმე ინგლისურ, რუსულ და ქართულ ენებზე არანაკლებ ნახევარი გვერდის მოცულობისა (სათაურის, ავტორების, დაწესებულების მითითებით და უნდა შეიცავდეს შემდეგ განყოფილებებს: მიზანი, მასალა და მეთოდები, შედეგები და დასკვნები; ტექსტუალური ნაწილი არ უნდა იყოს 15 სტრიქონზე ნაკლები) და საკვანძო სიტყვების ჩამონათვალი (key words).

5. ცხრილები საჭიროა წარმოადგინოთ ნაბეჭდი სახით. ყველა ციფრული, შემაჯამებელი და პროცენტული მონაცემები უნდა შეესაბამებოდეს ტექსტში მოყვანილს.

6. ფოტოსურათები უნდა იყოს კონტრასტული; სურათები, ნახაზები, დიაგრამები - დასათაურებული, დანომრილი და სათანადო ადგილას ჩასმული. რენტგენოგრამების ფოტოასლები წარმოადგინეთ პოზიტიური გამოსახულებით **tiff** ფორმატში. მიკროფოტოსურათების წარწერებში საჭიროა მიუთითოთ ოკულარის ან ობიექტივის საშუალებით გადიდების ხარისხი, ანათალების შეღებვის ან იმპრეგნაციის მეთოდი და აღნიშნოთ სურათის ზედა და ქვედა ნაწილები.

7. სამამულო ავტორების გვარები სტატიაში აღინიშნება ინიციალების თანდართვით, უცხოურისა – უცხოური ტრანსკრიპციით.

8. სტატიას თან უნდა ახლდეს ავტორის მიერ გამოყენებული სამამულო და უცხოური შრომების ბიბლიოგრაფიული სია (ბოლო 5-8 წლის სიღრმით). ანბანური წყობით წარმოდგენილ ბიბლიოგრაფიულ სიაში მიუთითეთ ჯერ სამამულო, შემდეგ უცხოელი ავტორები (გვარი, ინიციალები, სტატიის სათაური, ჟურნალის დასახელება, გამოცემის ადგილი, წელი, ჟურნალის №, პირველი და ბოლო გვერდები). მონოგრაფიის შემთხვევაში მიუთითეთ გამოცემის წელი, ადგილი და გვერდების საერთო რაოდენობა. ტექსტში კვადრატულ ფჩხილებში უნდა მიუთითოთ ავტორის შესაბამისი N ლიტერატურის სიის მიხედვით. მიზანშეწონილია, რომ ციტირებული წყაროების უმეტესი ნაწილი იყოს 5-6 წლის სიღრმის.

9. სტატიას თან უნდა ახლდეს: ა) დაწესებულების ან სამეცნიერო ხელმძღვანელის წარდგინება, დამოწმებული ხელმოწერითა და ბეჭდით; ბ) დარგის სპეციალისტის დამოწმებული რეცენზია, რომელშიც მითითებული იქნება საკითხის აქტუალობა, მასალის საკმაობა, მეთოდის სანდოობა, შედეგების სამეცნიერო-პრაქტიკული მნიშვნელობა.

10. სტატიის ბოლოს საჭიროა ყველა ავტორის ხელმოწერა, რომელთა რაოდენობა არ უნდა აღემატებოდეს 5-ს.

11. რედაქცია იტოვებს უფლებას შეასწოროს სტატია. ტექსტზე მუშაობა და შეჯერება ხდება საავტორო ორიგინალის მიხედვით.

12. დაუშვებელია რედაქციაში ისეთი სტატიის წარდგენა, რომელიც დასაბეჭდად წარდგენილი იყო სხვა რედაქციაში ან გამოქვეყნებული იყო სხვა გამოცემებში.

აღნიშნული წესების დარღვევის შემთხვევაში სტატიები არ განიხილება.

GEORGIAN MEDICAL NEWS
NO 9 (366) 2025

Содержание:

GEORGIAN MEDICAL NEWS
No 9 (366) 2025

THE USE OF HERBAL MEDICINES IN PREVENTING CANCER MUTATIONS IN ANIMAL MODELS EXPOSED TO TOXICANTS: A SYSTEMATIC REVIEW

Yerbolat Iztleuov[1]*, Marat Iztleuov[2], Anar Tulyayeva[3], Gulmira Iztleuova[4], Elyanora Kydyrbayeva[5].

[1]Department of Radiology, Department of Radiology, NJSC "Marat Ospanov West Kazakhstan Medical University", Aktobe, Kazakhstan.

[2]Department of Natural Sciences, NJSC "Marat Ospanov West Kazakhstan Medical University", Aktobe, Kazakhstan.

[3]Department of Oncology, NJSC «Marat Ospanov West Kazakhstan Medical University», Aktobe, Kazakhstan.

[4]Department of Phthisiology and Dermatovenereology, NJSC «Marat Ospanov West Kazakhstan Medical University», Aktobe, Kazakhstan.

[5]Department of Obstetrics and Gynecology, NJSC «Marat Ospanov West Kazakhstan Medical University», Aktobe, Kazakhstan.

Abstract.

Aim of the Study: To systematically evaluate preclinical evidence on the protective effects of herbal interventions against toxicant-induced genetic and epigenetic alterations in animal models.

Materials and Methods: A systematic review (2015-2025) across PubMed, Scopus, Web of Science, Cochrane, and Google Scholar identified six animal studies on herbal protection against toxicant-induced mutations. SYRCLE's tool showed generally robust designs.

Results and Discussion: Six rodent studies investigated exposures such as BPA, busulfan, testosterone propionate, OVA, and prenatal stress. Herbal treatments (carob, ginger, ASHMI, BSTJF, Cuscuta flavonoids) were administered via diverse routes and durations. All studies reported significant improvements ($P < 0.05$ to $P < 0.001$) in genetic and epigenetic outcomes, including enhanced sperm DNA integrity, reduced inflammation, improved neurobehavior, hormonal regulation, and restored DNA methylation patterns. Transgenerational assessments consistently supported the potential of herbal therapies to mitigate inheritable mutation risks. Herbal medicines show protective effects against toxicant-induced genetic and epigenetic changes in animal models, suggesting potential preventive strategies, while long-term and mechanistic studies are needed to confirm human applicability.

Key words. Herbal medicine, environmental toxicants, genetic mutations, epigenetics, cancer prevention, rodent models.

Introduction.

Cancer remains a leading cause of morbidity and mortality worldwide, with genetic mutations playing a central role in its development [1,2]. Environmental toxicants such as heavy metals, pesticides, and industrial chemicals can induce genetic alterations not only in directly exposed individuals but also in their offspring, raising concerns about transgenerational health risks [3]. Herbal medicines, known for antioxidant and anti-mutagenic activities, have been investigated for their potential to reduce radiation- or toxicant-induced genomic damage. Constituents of turmeric, green tea, and garlic have demonstrated the ability to preserve DNA integrity across multiple experimental models [4-7].

Despite encouraging findings, the literature reveals inconsistencies. While some studies report strong protective effects of specific herbal extracts, others show minimal benefits. Variations in toxicant type, herbal preparation, study design, and outcome measures contribute to these discrepancies [8]. Toxicant exposure during gestation and early postnatal life is of particular concern, as it can compromise genomic integrity, promote oxidative stress, and induce epigenetic reprogramming, thereby increasing cancer susceptibility in progeny [9-11]. Protecting early developmental stages is therefore a priority in environmental health.

Herbal medicines, long valued in traditional practice, have gained attention for mitigating genotoxic and carcinogenic effects of xenobiotics [12]. Evidence indicates that phytochemicals such as flavonoids, polyphenols, and alkaloids exhibit antioxidant, anti-inflammatory, and DNA repair-enhancing properties, intervening in key steps of carcinogenesis [13-16]. In vivo and in vitro studies show that herbal preparations can prevent DNA lesions, chromosomal aberrations, and epigenetic changes such as DNA methylation and histone modification, events particularly harmful during embryonic development [17-19].

Epigenetic inheritance further complicates mutagenic risks. Prenatal toxin exposure can imprint signatures that affect gene expression across generations [20-23]. Herbal compounds that can reverse or stabilize these epigenetic alterations present a unique and timely opportunity for cancer prevention at the germline level [24-26]. Herbs like Cuscuta chinensis, ginger, Ganoderma lucidum, and Valeriana Fauriei showed protective, restorative effects in animal models [27-30]. However, mechanistic insights remain fragmented, with only limited exploration of ROS regulation, DNA repair, or modulation of oncogenes and tumor suppressors [31-34].

Challenges also include variability in herbal formulation quality, concentrations of active compounds, and safety profiles, complicating reproducibility and translation to humans [35,36]. Another challenge is the absence of long-term follow-up in most studies, which mainly assess short-term outcomes after prenatal toxicant exposure and herbal treatment [37,38]. Longitudinal research is needed to confirm whether benefits such as improved neurodevelopment, hormonal balance, or immune function translate into reduced heritable cancer mutations, requiring molecular validation like mutation burden reduction or restored epigenetic marks [39-41].

A systematic evaluation of the evidence is therefore warranted. The objectives of this review are to assess the protective effects of herbal medicines against toxicant-induced genetic and epigenetic alterations in animal models, focusing on DNA integrity, gene expression, hormonal regulation, and prevention of transgenerational inheritance. The review also examines dosage, timing, administration, and existing research gaps to guide future investigations.

Research Question.

This review examines herbal medicines' role in preventing toxicant-induced mutagenesis in animal models, focusing on DNA integrity, gene expression, hormonal regulation, dosage, timing, administration, transgenerational effects, and evidence gaps.

Materials and Methods.

Study design: A systematic review from 1 January 2015 - 20 July 2025.

PICO Criteria.

Population: animal models (including progeny or transgenerational effects) exposed to environmental toxicants.

Intervention: Herbal medicines (e.g., Carob, Ginger, ASHMI, Cuscuta flavonoids, Valeriana fauriei, Bu-Shen-Tian-Jing formula) administered during or post-toxicant exposure to prevent genetic mutations or epigenetic modifications.

Comparison: No herbal intervention or placebo treatment.

Outcome: Reduction in cancer-related genetic mutations in animal models, improved DNA integrity, epigenetic modifications (e.g., DNA methylation), and overall health outcomes related to mutagenesis.

Inclusion Criteria:

Experimental rodent studies (mice or rats) published in English between 2015 and 2025 assessing herbal medicines against toxicant-induced genetic mutations, DNA damage, or epigenetic alterations were included. Outcomes considered were genetic integrity, epigenetic changes, transgenerational effects, and related endpoints (e.g., sperm DNA integrity, neurodevelopment, immunity, behavior).

Exclusion Criteria:

Review articles, editorials, conceptual papers, non-experimental studies, non-rodent or human research, non-herbal interventions, irrelevant outcomes, studies without direct mutation or epigenetic data, or articles not peer-reviewed or without full-text access were excluded.

Comprehensive Search Strategy:

A comprehensive search was conducted across PubMed, Scopus, Web of Science, Cochrane Library, and Google Scholar for studies (1 July 2015 to 31 July 2025) on herbal medicines preventing toxicant-induced cancer mutations in animal models. Both MeSH and free-text terms were used, applying Boolean operators (AND, OR). The primary search string was: "herbal medicine" AND ("offspring" OR "progeny" OR "transgenerational") AND "cancer", ensuring broad coverage of herbal interventions, toxicant exposures, mutagenic outcomes, and transgenerational effects.

Study Selection Process:

The study selection process, outlined in Figure 1 (PRISMA), followed predefined inclusion criteria to identify evidence on herbal medicines mitigating toxicant-induced cancer-related mutations. Titles and abstracts were screened by two independent reviewers, followed by full-text eligibility

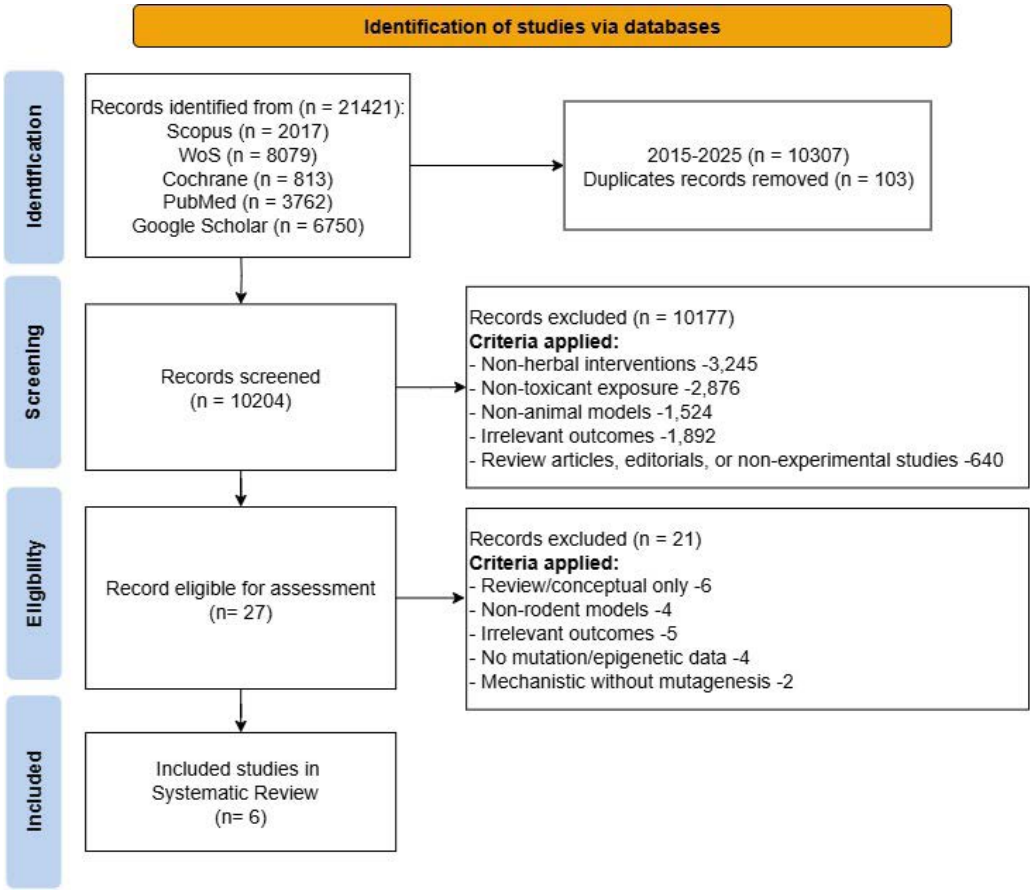

Figure 1. *Study Selection Process.*

assessment. Interventions were tabulated by type, dosage, route, timing, and matched against synthesis groups. Filters included publication period (2015-2025), peer-reviewed English articles, and open-access availability. From 21,421 records across Scopus (2,017), Web of Science (8,079), Cochrane Library (813), PubMed (3,762), and Google Scholar (6,750), the number was reduced to 10,307 after applying the publication period filter, with 103 duplicates subsequently removed. After screening 10,204 records, 10,177 were excluded (non-herbal interventions = 3,245; non-toxicant exposure = 2,876; non-animal models = 1,524; irrelevant outcomes = 1,892; reviews/editorials/non-experimental studies = 640). A total of 27 full-text articles were assessed, of which 21 were excluded (review/conceptual only = 6; non-rodent models = 4; irrelevant outcomes = 5; no mutation/epigenetic data = 4; mechanistic without mutagenesis = 2). Ultimately, 6 studies were included, addressing genetic, epigenetic, and transgenerational outcomes.

Data Extraction:

Data extraction was performed independently by two reviewers, with disagreements resolved by consensus or third reviewer (Cohen's kappa = 0.87). Extracted variables included study design, animal model, sample size, toxicant type, herbal intervention (type, dosage, route, duration, timing), and outcomes. Outcomes encompassed mutation type (genetic/epigenetic), DNA integrity, epigenetic changes, transgenerational effects, methods (e.g., comet assay, PCR, methylation assays), statistical significance, effect size, findings, limitations, and cancer-prevention implications. For multiple measures, preference was given to primary endpoints, longest follow-up, and complete statistical reporting.

Risk of Bias Assessment:

Risk of bias (Figure 2) showed low risk in randomization, baseline balance, allocation concealment, random housing, and completeness of outcome data. However, unclear risk remained for blinding and selective reporting. Using GRADE, most outcomes were rated moderate confidence, constrained by small sample sizes and some methodological limitations, though consistency across studies strengthened reliability of findings.

Figure 3 outlines bias risk in six studies most domains were low risk, but blinding and selective reporting remained unclear. Together with GRADE, this provides integrated quality appraisal for interpreting findings. Risk of bias was systematically assessed using SYRCLE's Risk of Bias tool [42] ensuring a comprehensive evaluation of methodological rigor across included studies.

Results.

Table 1 summarizes six experimental rodent studies (sample sizes 4–100) on herbal medicines against toxicant-induced effects. Exposures included busulfan, BPA, testosterone propionate, OVA, ginger extract, and prenatal stress, providing foundational evidence for herbal interventions reducing mutation risk and improving outcomes.

Table 2 outlines herbal interventions across studies, detailing dosage (20–600 mg/kg), route (mostly oral gavage, one intraperitoneal), and duration (2.5–8 weeks). Administration timing varied (prenatal, post-exposure, or continuous), reflecting diverse strategies yet consistently supporting protective herbal effects.

Table 3 summarizes mutation-related outcomes and methods. Most studies assessed transgenerational effects via neurobehavior, DNA methylation, hormones, and immunity, using ELISA, RT-qPCR, histology, SDFA, and behavioral tests. Findings highlight diverse evaluations of herbal interventions against toxicant-induced genetic and functional disruptions.

Table 4 presents effect sizes, significance, and epigenetic impacts. All studies showed improvements ($P < 0.05–0.001$) in sperm DNA integrity, neurodevelopment, immunity, and hormones, with epigenetic changes (e.g., ERα, H19/Igf2). Transgenerational analyses confirmed herbal interventions influence health and gene regulation post-toxicant exposure.

Table 5 summarizes findings from six studies, all showing protective herbal effects against toxicant-induced mutagenesis, improving sperm recovery, neurodevelopment, immunity, hormones, DNA methylation, and behavior. Herbs like Carob, Ginger, ASHMI, and Cuscuta showed promise, though

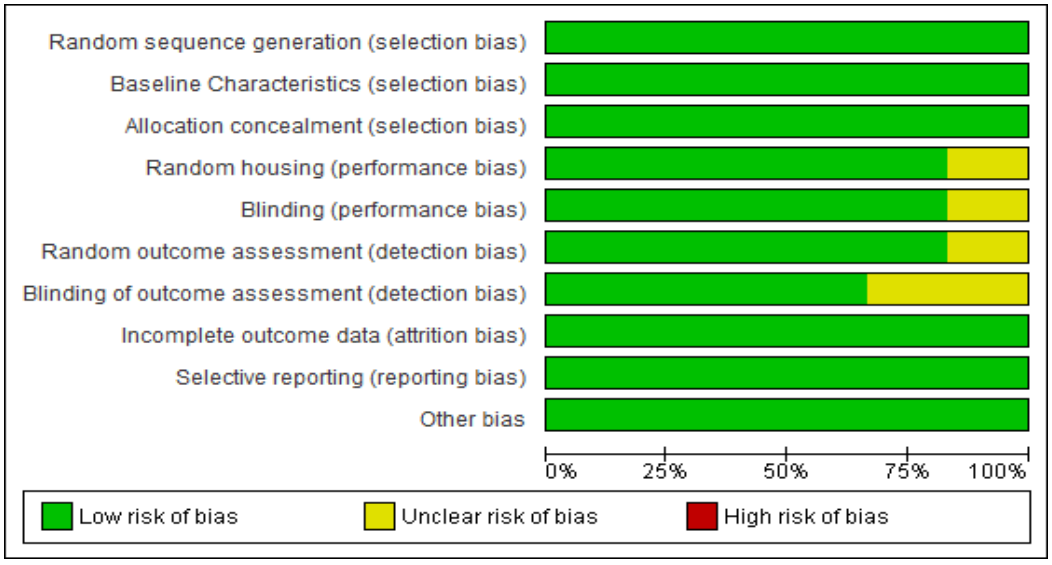

Figure 2. *SYRCLE's Risk of bias graph.*

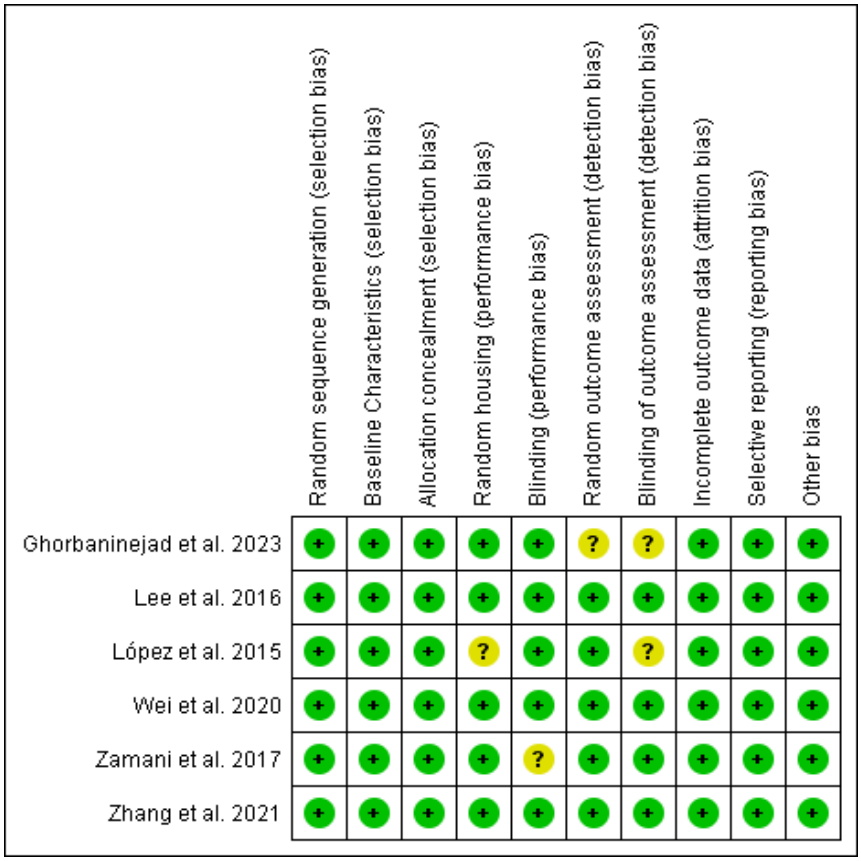

Figure 3. *SYRCLE's Risk of bias summary.*

Table 1. *Included Studies Overview.*

Study	Study Design	Species/ Population	Sample Size	Type of Exposure
Ghorbaninejad et al. 2023 [43]	Experimental animal	NMRI mice, 8-10 weeks old	4 mice	Busulfan (45 mg/kg intraperitoneally to induce azoospermia)
Zhang et al. 2021 [44]	Experimental animal	Sprague-Dawley rats (neonatal, adult rats)	45 rats	Testosterone propionate (PCOS)
López et al. 2015 [45]	Experimental animal	BALB/c mice (6-week-old)	9 mice	OVA sensitization (asthma model)
Zamani et al. 2017 [46]	Experimental animal	Wistar rats (pregnant females)	40 rats	Hydro-alcoholic ginger extract
Wei et al. 2020 [47]	Experimental animal	Kunming mice (9-week-old)	100 mice	Bisphenol A (BPA)
Lee et al. 2016 [48]	Experimental animal	Sprague-Dawley rats (pregnant)	16 rats	Prenatal stress (PNS)

Table 2. *Dosage, administration, and timing on included studies.*

Study	Herb/ Intervention	Dosage	Route of Administration	Duration of Treatment	Timing Relative to Exposure
Ghorbaninejad et al. 2023 [43]	Carob extract (Ceratonia siliqua)	75–600 mg/kg	Oral gavage	5 weeks	After azoospermia induction
Zhang et al. 2021 [44]	Bu-Shen-Tian-Jing formula (BSTJF)	333 mg/200 g	Oral gavage	4 weeks	After PCOS induction
López et al. 2015 [45]	ASHMI (Ganoderma, Sophora, Glycyrrhiza)	4.5 mg	Oral gavage	6 weeks	Post-OVA challenge
Zamani et al. 2017 [46]	Ginger (Zingiber officinale)	50–100 mg/kg	Intraperitoneal injection	8 weeks	Daily during pregnancy
Wei et al. 2020 [47]	Cuscuta chinensis flavonoids (CCFs)	20–40 mg/kg	Oral gavage	2.5 weeks	Prenatal exposure
Lee et al. 2016 [48]	Valeriana fauriei extract (VF)	100 mg/kg	Oral administration	3 weeks	Postnatal stress exposure

Table 3. *Mutation Outcome and Measurement Method.*

Study	Mutation Outcome Measured	Measurement Method	Mutagenesis Type
Ghorbaninejad et al. 2023 [43]	Spermatogenesis recovery, sperm count, motility, DNA integrity	CASA, SDFA, histology, ROS	Spontaneous mutagenesis
Zhang et al. 2021 [44]	Neurobehavioral changes, dendritic spine density	Morris Water Maze, Nissl Staining	Transgenerational mutagenesis
López et al. 2015 [45]	Airway inflammation, immune response	BALF, serum assays, histology	Transgenerational mutagenesis
Zamani et al. 2017 [46]	Testosterone, LH, FSH in serum, sperm lineage cells	ELISA, cell counts, histology	Transgenerational mutagenesis
Wei et al. 2020 [47]	DNA methylation of ERα and H19/Igf2	BSP, RT-qPCR, hormone assays	Transgenerational mutagenesis
Lee et al. 2016 [48]	Behavioral patterns, protein expression	Behavioral tests, Western blot	Epigenetic programming

Table 4. *Effect Size, Statistical Significance, and Epigenetic Changes.*

Study	Effect Size	Statistical Significance	DNA/Genetic Integrity	Epigenetic Changes	Transgenerational Analysis
Ghorbaninejad et al. 2023 [43]	Significant dose-dependent improvement in sperm count and DNA integrity ($P < 0.05$, $P < 0.001$)	$P < 0.05$	Improved sperm DNA integrity with reduced fragmentation	Changes in spermatogenesis-related genes	Yes, male sperm production after busulfan-induced infertility
Zhang et al. 2021 [44]	Improved neurobehavioral performance and dendritic spine density ($P < 0.05$)	$P < 0.05$	Improved neurodevelopment	Changes in neuronal protein expression	Yes, offspring behavior and protein expression in hippocampus
López et al. 2015 [45]	Reduced inflammation and mucus hyperproduction in offspring ($P < 0.05$)	$P < 0.05$	No DNA damage observed	Changes in cytokine production	Yes, immune response in offspring from treated mothers
Zamani et al. 2017 [46]	Increased hormone levels and spermatogenesis in offspring ($P \leq 0.01$)	$P \leq 0.01$	Improved sperm cell lineage	Epigenetic regulation of spermatogenesis	Yes, maternal effects on offspring spermatogenesis
Wei et al. 2020 [47]	Decreased DNA methylation at ERα and H19/Igf2 loci ($P < 0.01$)	$P < 0.01$	Down-regulated DNA methylation at promoter regions	Epigenetic changes at ERα and H19/Igf2 loci	Yes, BPA-induced DNA methylation in offspring
Lee et al. 2016 [48]	Improved behavioral responses ($P < 0.05$)	$P < 0.05$	No significant DNA damage	Epigenetic regulation of neurodevelopmental genes	Yes, maternal prenatal stress effects on offspring

Table 5. *Summary of Results and Implications.*

Study	Effect on Mutagenesis	Cancer Prevention Implications	Key Findings	Limitations
Ghorbaninejad et al. 2023 [43]	Significant improvement in spermatogenesis recovery	Supports Carob extract in sperm recovery from toxic exposure	Improved sperm count, motility, morphology, and DNA integrity	Small sample size, no long-term follow-up
Zhang et al. 2021 [44]	Improved neurodevelopment in offspring	BSTJF could help reverse epigenetic damage from PCOS exposure	Improved neurobehavioral performance and dendritic spine density	Limited focus on neurodevelopment; no epigenetic markers assessed
López et al. 2015 [45]	Reduced inflammation in offspring	ASHMI could reduce inflammation and prevent immune-related mutations	Reduced inflammation and immune response in offspring	Limited to immune responses; no broader epigenetic analysis
Zamani et al. 2017 [46]	Improved hormone levels and spermatogenesis	Ginger extract (HEG) may prevent transgenerational mutagenesis in male offspring	Increased testosterone, LH, FSH, and spermatogenesis in offspring	Focus on hormonal levels, no epigenetic data
Wei et al. 2020 [47]	Significant decrease in DNA methylation	Cuscuta chinensis flavonoids can reverse BPA-induced mutations	Restored DNA methylation at ERα and H19/Igf2 loci	Short follow-up; lacks behavioral analysis in offspring
Lee et al. 2016 [48]	Improved behavior and protein expression	Valeriana fauriei (VF) may reverse prenatal stress-induced mutagenesis	Improved behavioral responses and protein expression in offspring	Focus on protein expression; no direct mutagenesis assessment

limitations included small samples, short follow-ups, and narrow outcome focus.

Discussion.

This SLR of six rodent studies shows herbal medicines (Ceratonia siliqua, ASHMI, Zingiber officinale, Cuscuta chinensis) protected against toxicant-induced mutagenesis, enhancing DNA integrity, spermatogenesis, neurobehavior, airway inflammation, hormone balance, immunity, and epigenetics. Broader evidence links phytochemicals like curcumin, resveratrol, ginsenosides, and berberine to anticancer effects [49,50]. Similarly, animal and in vitro studies confirm herbal bioactive reduce DNA mutations [51,52], while multi-component formulations from traditional medicine mitigate chemotherapy-induced toxicity [53,54].

To further support the review examined dosage, timing, and administration of herbal interventions. Most were delivered orally at 20-600 mg/kg for 2.5-8 weeks, used either preventively or therapeutically. Early or continuous supplementation during critical windows appeared most effective. Similar to preclinical studies on curcumin, resveratrol, and green tea polyphenols, oral routes ensured clinical relevance and safety [55]. The dose range aligns with prior reports (e.g., curcumin 50–500 mg/kg) [56] Preventive use likely modulates early mutagenic events or strengthens antioxidant defenses [57]. Yet, lack of extract standardization raises reproducibility concerns, while metabolomics offers mechanistic insights complementing efficacy assessments [58,59].

Expanding to Outcomes included ELISA, RT-qPCR, comet assays, and behavior tests. Studies assessed transgenerational mutagenesis, DNA damage, and epigenetic programming. Herbs like luteolin and triptolide modulate DNMTs/HDACs, suppress oncogenes, and enhance genomic stability [60]. Epigenetic modifications from phytochemicals may be heritable [61], with paternal exposures also affecting germline mutations [62]. Yet effects are context-dependent; some extracts show mutagenicity or genotoxicity under certain conditions, such as the Ames test [63-67]. Spermatogenesis outcomes highlight germline protection against heritable mutations linked to cancer. Neurobehavioral improvements indicate reduced neurotoxicity and oxidative stress, integral to systemic cancer pathways. Herbal modulation of airway inflammation mitigates tumor-promoting chronic inflammation, while hormone normalization prevents endocrine disruption, reducing risks of breast, ovarian, and prostate cancers. Together, these outcomes demonstrate preventive mechanisms.

Overall, findings suggest herbal medicines act as promising chemopreventive agents with multi-targeted effects. However, the six included studies displayed considerable variability in target species, toxicant exposures (e.g., BPA, busulfan, stress), herbal remedies (e.g., carob, ginger, ASHMI), dosages, and treatment durations. This heterogeneity complicates direct comparison and limits generalizability, making it inappropriate to conclude that herbal medicines are broadly effective against all mutagenic exposures. Instead, efficacy has been demonstrated only for specific herb–toxicant combinations under defined conditions. Small sample sizes, inconsistent extract standardization, and limited clinical validation further restrict reliability, emphasizing the necessity for deeper mechanistic exploration and rigorous human trials [68-70]. Many acts via epigenetic pathways in parallel with regulation of reproductive, neurological, inflammatory, and endocrine functions, thereby supporting the potential to reverse inherited genomic risks and lower systemic cancer susceptibility [71]. However, evidence remains incomplete; most studies address anticancer effects in cell lines or adult models, not transgenerational impacts [72,73]. Standardization issues, compound complexity, and toxicity risks also limit translation, and safety in preventing inherited mutations requires further validation [74,75].

Current SLR demonstrates that herbal medicines mitigate toxicant-induced mutagenesis via genetic and epigenetic pathways, supporting cancer prevention, DNA repair, and immune regulation. Despite promising effects, limited mechanistic depth and small samples warrant standardized formulations, metabolomic profiling, and human trials [76]. A meta-analysis reported that traditional herbal medicines alleviate chemotherapy-induced side effects while enhancing efficacy, though it stressed the need for RCTs and safety data [77]. Similarly, trigonelline inhibits tumor growth and chemotherapy toxicity but requires further mechanistic insight [78,79]. Biological mechanisms include antioxidant defense, DNA repair modulation, apoptosis regulation, immune enhancement, and epigenetic remodelling (e.g., Cuscuta chinensis). These reduce heritable mutations and cancer risk. Strengths were controlled toxicant exposures and validated assays, though limitations sample size, blinding, and heterogeneity restrict generalizability.

Conclusion.

Herbal medicines demonstrate potential in mitigating toxicant-induced mutagenesis through multiple pathways, including antioxidant defense, epigenetic remodelling, and immune modulation. By influencing DNMTs, HDACs, and oncogene expression, compounds like luteolin, triptolide, and curcumin can restore genomic stability. Transgenerational studies further highlight their ability to reduce inherited DNA damage and normalize gene regulation, offering a unique avenue for cancer prevention. Nonetheless, considerable variation in toxicants, herbal formulations, and experimental designs across studies constrains external validity. Efficacy should therefore be interpreted as context-specific, rather than universally applicable across all herbal medicines and exposures. Integrating standardized experimental designs, advanced omics-based profiling, and human studies will be essential to confirm reproducibility, optimize therapeutic formulations, and strengthen translational evidence for clinical applications.

Implications for Clinical Practice and Public Health.

Herbal formulations like Carob, Ginger, and ASHMI may aid reproductive and neurodevelopmental health in toxicant-exposed groups. Yet, clinical translation must proceed cautiously, given that current evidence supports only certain herb exposure pairings. Clinical trials remain essential, but public health messaging could emphasize safe prenatal use and epigenetic protection.

Recommendations for Future Research.

Future studies should use larger, blinded, randomized designs, assess multigenerational effects, and standardize dosages. Integrating omics-based biomarkers and conducting human cohorts or phase I trials are urgently needed to translate promising animal evidence into preventive strategies.

This study was funded by the Science Committee, Ministry of Science and Higher Education of Kazakhstan (Grant AR19678225; reg. no. 0123RK00613), focused on oncogenesis prevention in irradiated rat offspring.

REFERENCES

1. Mattiuzzi C, Lippi G. Current cancer epidemiology. J Epidemiol Glob Health. 2019;9:217-22.
2. Asiri A, Ali A Al, Abu-Alghayth MH. Understanding the Role of Genetics in Tumour and Cancer Biology. Adv Life Sci. 2025;12:35-48.
3. Imran M, Zia R, Arshad M, et al. Exploration of the genetic and environmental determinants of male infertility: a comprehensive review. Egyptian Journal of Medical Human Genetics. 2025;26:1-17.
4. Tan L, Cao Z, Chen H, et al. Curcumin reduces apoptosis and promotes osteogenesis of human periodontal ligament stem cells under oxidative stress in vitro and in vivo. Life Sci. 2021;270:119125.
5. El-Saadony MT, Yang T, Korma SA, et al. Impacts of turmeric and its principal bioactive curcumin on human health: Pharmaceutical, medicinal, and food applications: A comprehensive review. Front Nutr. 2023;9:1040259.
6. Makhuvele R, Naidu K, Gbashi S, et al. The use of plant extracts and their phytochemicals for control of toxigenic fungi and mycotoxins. Heliyon. 2020;6:e05291.
7. Kusnir P, Baig S. The Neuropathy as an Adverse Effect of Chemotherapy Diminished After Administration of Dietary Supplement with Iron Citrate – Case Study. Futur Med. 2024;3:60-67.
8. Wang H, Chen Y, Wang L, et al. Advancing herbal medicine: enhancing product quality and safety through robust quality control practices. Front Pharmacol. 2023;14:1265178.
9. Ogunjobi TT, Gbayisomore TJ, Nneji PO, et al. Environmental Epigenetics and Its Impacts on Disease Susceptibility: A Comprehensive Review. Medinformatics. 2024.
10. Bala S, Garg D, Thirumalesh BV, et al. Recent Strategies for Bioremediation of Emerging Pollutants: A Review for a Green and Sustainable Environment. Toxics. 2022;10.
11. Briffa J, Sinagra E, Blundell R. Heavy metal pollution in the environment and their toxicological effects on humans. Heliyon. 2020;6:e04691.
12. Malik S, Kaur K, Prasad S, et al. A perspective review on medicinal plant resources for their antimutagenic potentials. Environmental Science and Pollution Research. 2021;29:62014-29.
13. Jităreanu A, Trifan A, Vieriu M, et al. Current Trends in Toxicity Assessment of Herbal Medicines: A Narrative Review. Processes. 2023;11.
14. Pop S, Enciu AM, Tarcomnicu I, et al. Phytochemicals in cancer prevention: modulating epigenetic alterations of DNA methylation. Phytochemistry Reviews. 2019;18:1005-24.
15. Pandit K, Garg C, Bhat AH, et al. Harnessing Dietary Phytochemicals to Modulate Signaling Pathways in Cancer Chemoprevention—A Review. Phytotherapy Research. 2025;39:3271-99.
16. Fakhri KU, Sharma D, Fatma H, et al. The Dual Role of Dietary Phytochemicals in Oxidative Stress: Implications for Oncogenesis, Cancer Chemoprevention, and ncRNA Regulation. Antioxidants. 2025;14:620.
17. Mbemi A, Khanna S, Njiki S, et al. Impact of Gene–Environment Interactions on Cancer Development. International Journal of Environmental Research and Public Health. 2020;17:8089.
18. Sciarra T, Ciccotti M, Aiello P, et al. Polypharmacy and nutraceuticals in veterans: pros and cons. Frontiers in Pharmacology. 2019;10.
19. Ming T, Tao Q, Tang S, et al. Curcumin: An epigenetic regulator and its application in cancer. Biomedicine & Pharmacotherapy. 2022;156:113956.
20. Tando Y, Matsui Y. Inheritance of environment-induced phenotypic changes through epigenetic mechanisms. Environ Epigenet. 2023;9.
21. Breton CV, Landon R, Kahn LG, et al. Exploring the evidence for epigenetic regulation of environmental influences on child health across generations. Communications Biology. 2021;4:1-15.
22. Sobral AF, Cunha A, Costa I, et al. Environmental Xenobiotics and Epigenetic Modifications: Implications for Human Health and Disease. Journal of Xenobiotics. 2025;15:118.
23. Legoff L, D'Cruz SC, Tevosian S, et al. Transgenerational Inheritance of Environmentally Induced Epigenetic Alterations during Mammalian Development. Cells. 2019;8:1559.
24. Carlos-Reyes Á, López-González JS, Meneses-Flores M, et al. Dietary compounds as epigenetic modulating agents in cancer. Front Genet. 2019;10.
25. Jasek K, Kubatka P, Samec M, et al. DNA Methylation Status in Cancer Disease: Modulations by Plant-Derived Natural Compounds and Dietary Interventions. Biomolecules. 2019;9:289.
26. El Omari N, Bakrim S, Bakha M, et al. Natural Bioactive Compounds Targeting Epigenetic Pathways in Cancer: A Review on Alkaloids, Terpenoids, Quinones, and Isothiocyanates. Nutrients. 2021;13:3714.
27. Hamamouch N. Use of Ethnomedicinal Plants by the People Living in the Middle Atlas Mountains in Morocco. Med Aromat Plants (Los Angel). 2020;9.
28. Kamel N, El Boullani R, Cherrah Y. Use of Medicinal Plants during Pregnancy, Childbirth and Postpartum in Southern Morocco. Healthcare. 2022;10:2327.
29. Zhao Q, Liu Y, Wang X, et al. Cuscuta chinensis flavonoids reducing oxidative stress of the improve sperm damage in bisphenol A exposed mice offspring. Ecotoxicol Environ Saf. 2023;255:114831.
30. Zhao Q, Liu Y, Chuo Y, et al. Cuscuta chinensis flavonoids alleviate ovarian damage in offspring female mice induced by BPA exposure during pregnancy by regulating the central carbon metabolism pathway. Ecotoxicol Environ Saf. 2024;275:116253.

31. Zandi P, Schnug E. Reactive Oxygen Species, Antioxidant Responses and Implications from a Microbial Modulation Perspective. Biology. 2022;11:155.
32. Farooqi AA, Rakhmetova V, Kapanova G, et al. Suppressive effects of bioactive herbal polysaccharides against different cancers: From mechanisms to translational advancements. Phytomedicine. 2023;110:154624.
33. Mohanta B, Sen DJ, Mahanti B, et al. Extraction, characterization, haematocompatibility and antioxidant activity of linseed polysaccharide. Carbohydrate Polymer Technologies and Applications. 2023;5.
34. Khrustalev D, Yedrissov A, Vetrova A, et al. Synthesis of 2,7-dibromo-9H-carbazole and its N-alkylation under microwave activation conditions in a flow-type microwave reactor. Mater Today Proc. 2022;49:2449-54.
35. Wu P, Zhang C, Yin Y, et al. Bioactivities and industrial standardization status of Ganoderma lucidum: A comprehensive review. Heliyon. 2024;10.
36. Ren S, Liu H, Sang Q, et al. A Review of Bioactive Components and Pharmacological Effects of Ganoderma lucidum. Food Sci Nutr. 2025;13:e70623.
37. Salm S, Rutz J, van den Akker M, et al. Current state of research on the clinical benefits of herbal medicines for non-life-threatening ailments. Front Pharmacol. 2023;14:1234701.
38. Belayneh YM, Yoseph T, Ahmed S. A cross-sectional study of herbal medicine use and contributing factors among pregnant women on antenatal care follow-up at Dessie Referral Hospital, Northeast Ethiopia. BMC Complement Med Ther. 2022;22:146.
39. Aiello P, Sharghi M, Mansourkhani SM, et al. Medicinal Plants in the Prevention and Treatment of Colon Cancer. Oxid Med Cell Longev. 2019;2019:2075614.
40. Virolainen SJ, VonHandorf A, Viel KCMF, et al. Gene–environment interactions and their impact on human health. Genes Immun. 2022;24:1.
41. Donayeva A, Kulzhanova D, Amanzholkyzy A, et al. Relationship between vitamin D and adolescents' hypothyroidism – a cross-sectional study. Menopause Review/ Przegląd Menopauzalny. 2023;22:186-190.
42. Hooijmans CR, Rovers MM, De Vries RBM, et al. SYRCLE's risk of bias tool for animal studies. BMC Med Res Methodol. 2014;14.
43. Ghorbaninejad Z, Eghbali A, Ghorbaninejad M, et al. Carob extract induces spermatogenesis in an infertile mouse model via upregulation of Prm1, Plzf, Bcl-6b, Dazl, Ngn3, Stra8, and Smc1b. J Ethnopharmacol. 2023;301:115760.
44. Zhang X, You L, Zhang X, et al. Neurobehavioral alternations of the female offspring born to polycystic ovary syndrome model rats administered by Chinese herbal medicine. Chinese Medicine (United Kingdom). 2021;16:1-19.
45. López-Expósito I, Srivastava KD, Birmingham N, et al. Maternal antiasthma simplified herbal medicine intervention therapy prevents airway inflammation and modulates pulmonary innate immune responses in young offspring mice. Annals of Allergy, Asthma and Immunology. 2015;114:43-51.e1.
46. Zamani N, Hosseini E, Modaresi M, et al. Investigating the prenatal exposure of hydro-alcoholic extract of ginger on the function of Pituitary – Gonad axis in male mature offspring rats. World Family Medicine Journal/Middle East Journal of Family Medicine. 2017;6:141-148.
47. Wei Y, Han C, Li S, et al. Cuscuta chinensis flavonoids down-regulate the DNA methylation of the H19 / Igf2 imprinted control region and estrogen receptor alpha promoter of the testis in bisphenol A exposed mouse offspring. Food Funct. 2020;11:787-798.
48. Lee H, Won H, Im J, et al. Effect of Valeriana fauriei extract on the offspring of adult rats exposed to prenatal stress. Int J Mol Med. 2016;38:251-8.
49. Jenča A, Mills DK, Ghasemi H, et al. Herbal Therapies for Cancer Treatment: A Review of Phytotherapeutic Efficacy. Biologics. 2024;18:229.
50. Cui D, Zhang C, Zhang L, et al. Natural anti-cancer products: insights from herbal medicine. Chin Med. 2025;20:82.
51. Simón L, Mariotti-Celis MS. Bioactive compounds as potential alternative treatments to prevent cancer therapy-induced male infertility. Front Endocrinol (Lausanne). 2023;14:1293780.
52. Sharma A, Sharma L, Nandy SK, et al. Molecular Aspects and Therapeutic Implications of Herbal Compounds Targeting Different Types of Cancer. Molecules. 2023;28:750.
53. Fu B, Wang N, Tan HY, et al. Multi-Component Herbal Products in the Prevention and Treatment of Chemotherapy-Associated Toxicity and Side Effects: A Review on Experimental and Clinical Evidences. Front Pharmacol. 2018;9:1394.
54. Carvajal-Otaño NM, Ruiz Reyes D, Águila Carbelo M, et al. Pediatric oncology: past, present, and future. South Health Policy. 2025;4:233.
55. Qiang Y, Li Q, Xin Y, et al. Intake of Dietary One-Carbon Metabolism-Related B Vitamins and the Risk of Esophageal Cancer: A Dose-Response Meta-Analysis. Nutrients. 2018;10:835.
56. Bhatt HD, McClain SA, Lee HM, et al. The Maximum-Tolerated Dose and Pharmacokinetics of a Novel Chemically Modified Curcumin in Rats. J Exp Pharmacol. 2022;14:73.
57. Intharuksa A, Arunotayanun W, Takuathung MN, et al. Therapeutic Potential of Herbal Medicines in Combating Particulate Matter (PM)-Induced Health Effects: Insights from Recent Studies. Antioxidants. 2024;14:23.
58. Polgar O, Patel S, Walsh JA, et al. Minimal clinically important difference for daily pedometer step count in copd. ERJ Open Res. 2021;7.
59. Oyenihi OR, Oyenihi AB, Erhabor JO, et al. Unravelling the Anticancer Mechanisms of Traditional Herbal Medicines with Metabolomics. Molecules. 2021;26:6541.
60. Wu YY, Xu YM, Lau ATY. Epigenetic effects of herbal medicine. Clin Epigenetics. 2023;15:85.
61. Vatov E, Gechev T. Recent evidence for transgenerational adaptation resulting from stress induced changes in the cytosine methylation landscape of plants. Plant Stress. 2025;16:100812.
62. Dehghanbanadaki H, Jimbo M, Fendereski K, et al. Transgenerational effects of paternal exposures: the role of germline de novo mutations. Andrology. 2025;13:101-118.
63. Fasiku V, Kyagaba D, Hlalele A, et al. A perspective review on factors that influence mutagenicity in medicinal plants and their health implications. Toxicological Sciences. 2025;204:121.

64. Dantas FG da S, Castilho PF de, Almeida-Apolonio AA de, et al. Mutagenic potential of medicinal plants evaluated by the Ames Salmonella/microsome assay: A systematic review. Mutat Res Rev Mutat Res. 2020;786:108338.
65. Qari SH, Alrefaei AF, Ashoor AB, et al. Genotoxicity and Carcinogenicity of Medicinal Herbs and Their Nanoparticles. Nutraceuticals. 2021;1:31-41.
66. Drobchak M, Kitsera N, Osadchuk Z, et al. Neurodevelopmental manifestations and birth defects in Prader-Willi syndrome: findings from a study in Western Ukraine. Biomed Pharmacol J. 2023;16:233-240.
67. Govbakh IO, Zavodovskiy DO, Bulgakova NV, et al. Nerve conduction and neuromuscular transmission in C57Bl/6 mice with genetically determined peripheral neuropathy. Neurophysiology. 2019;51:248-252.
68. Wu HC, Tsai CC, Hsu PC, et al. Herbal Medicine in Breast Cancer Therapy: Mechanisms, Evidence, and Future Perspectives. Current Issues in Molecular Biology. 2025;47:362.
69. Tayeb BA, Kusuma IY, Osman AAM, et al. Herbal compounds as promising therapeutic agents in precision medicine strategies for cancer: A systematic review. J Integr Med. 2024;22:137-162.
70. Kooti W, Servatyari K, Behzadifar M, et al. Effective Medicinal Plant in Cancer Treatment, Part 2: Review Study. J Evid Based Complementary Altern Med. 2017;22:982.
71. Sulaiman C, George BP, Balachandran I, et al. Cancer and Traditional Medicine: An Integrative Approach. Pharmaceuticals. 2025;18:644.
72. Adico MDW, Bayala B, Bunay J, et al. Contribution of Sub-Saharan African medicinal plants to cancer research: Scientific basis 2013–2023. Pharmacol Res. 2024;202:107138.
73. Youn BY, Kim JH, Jo YK, et al. Current Characteristics of Herbal Medicine Interventions for Cancer on Clinical Databases: A Cross-Sectional Study. Integr Cancer Ther. 2023;22.
74. Bayatmanesh H, Javadi N, Nejhad TSN, et al. The role of herbal medicine in the side effects of chemotherapy. Revista Latinoamericana de Hipertensión 2020;15:64-70.
75. Shapoval LM, Dmytrenko OV, Sagach VF, et al. Systemic administrations of water-dispersible single-walled carbon nanotubes: activation of NOS in spontaneously hypertensive rats. Neurophysiology. 2020;52:101-109.
76. Figini M, De Francesco V, Finato N, et al. Dermoscopy in adult colloid milium. Journal of Dermatology. 2020;47:e127-128.
77. Kim EH, Jin H, Lee SH, et al. Traditional herbal medicine for the prevention of chemotherapy-induced peripheral neuropathy: a systematic review and meta-analysis with association rule analysis. Front Pharmacol. 2025;16:1607181.
78. Zhu Y, Ding D, Shen F, et al. Unveiling the Therapeutic Potential of Trigonelline: A Promising Approach in Cancer Prevention and Treatment. Anticancer Agents Med Chem. 2025;25:1175-87.
79. Trikur I, Batori-Tartsi Z, Sichka M, et al. Design of chemically modified bacteriorhodopsin films for information protection systems. East Eur J Enterp Technol. 2022;5:6-14.