

Herbal Research: Gaps With the High Impact on the Quality and Validity of Outcomes

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Abstract

Purpose Traditional medicine and herbal therapy, as a health-care approach of traditional medicine, are receiving increased attention from both the public and scientific society. The number of articles presented on traditional medicine and its applications is increasing rapidly. However, compared with extensive ongoing herbal research, achievements are not remarkable. The objective of the present article is to highlight some existing research gaps, which bridging the gaps will increase the quality and validity of the results of herbal research. Methods Iranian and non-Iranian articles on *Allium sativum* L. were reviewed for compliance with standards and requirements for herbal research. Results Botanical nomenclature, the processing and the extraction procedures, and the history of traditional medicine were the most important gaps in the herbal research. Conclusions Traditional and herbal medicines are rich and promising sources for drug development. Researchers and authors should consider that the familiarity with the history, characteristics, and potentials of traditional medicine systems is an important factor, accelerating the process of natural-based drug development. Moreover, essential standards with a high impact on the validity and reliability of the results of herbal research must not be ignored. Also, numerous fields remain to be considered by scientists and researchers, including the status of medicinal herbs, toxicological assessments, biological and pharmacological mechanisms of disease, and research questions.

Herbal Research: Gaps With the High Impact on the Quality and Validity of Outcomes

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Abstract

Purpose

Traditional medicine and herbal therapy, as a health-care approach of traditional medicine, are receiving increased attention from both the public and scientific society. The number of articles presented on traditional medicine and its applications is increasing rapidly. However, compared with extensive ongoing herbal research, achievements are not remarkable. The objective of the present article is to highlight some existing research gaps, which bridging the gaps will increase the quality and validity of the results of herbal research.

Methods

Iranian and non-Iranian articles on *Allium sativum* L. were reviewed for compliance with standards and requirements for herbal research.

Results

Botanical nomenclature, the processing and the extraction procedures, and the history of traditional medicine were the most important gaps in the herbal research.

Conclusions

Traditional and herbal medicines are rich and promising sources for drug development. Researchers and authors should consider that the familiarity with the history, characteristics, and potentials of traditional medicine systems is an important factor, accelerating the process of natural-based drug development. Moreover, essential standards with a high impact on the validity and reliability of the results of herbal research must not be ignored. Also, numerous fields remain to be considered by scientists and researchers, including the status of medicinal herbs, toxicological assessments, biological and pharmacological mechanisms of disease, and research questions.

Keywords: Herbal medicine, research gaps, botanical nomenclature, standards of herbal research, validity, Iranian traditional medicine

1- Introduction

The traditional medical knowledge, including the use of herbal medicines and the broader medical practices, is available from many cultures with a different local language all around the world. The importance of medicinal herbs and their application, as a characteristic health-care approach of traditional medicine in human civilization, is well recognized¹.

Annually thousands of papers on ethnopharmacological topics are now published. However, despite the extensive and intensive herbal research, the time and budget spent on this research, as well as reviewing and publication of their findings, the achievements for the treatment of diseases, using traditional medicine or the discovery of new natural-based drugs, are not salient. An overview of the titles of the articles published in this field indicates that a major concern in research articles is to demonstrate the effective and impressive potentials and the superiority of a specific type of traditional medicine. Almost, in all original articles, the efficacy of herbal medicines and their preparation (HMP) in an *in vitro* or *in vivo* model is studied and their promising potentials are discussed. Apart from the problems associated with this approach to scientific outcomes^{2,3}, some serious concerns about herbal medicines and HMP, such as the effects of cultivation conditions on plant compounds, contaminants of HMP, side effects, and herb-drug interactions⁴⁻⁶, seem not to be the major problem of the researchers and scientists in the field of traditional medicine.

In the previous works, the strengths and weaknesses of research on herbal management of diabetes mellitus, as a model⁷, and the necessity of an encyclopedia of herbs-diseases⁸, have been noticed. In the present article, Iranian and non-Iranian research on *Allium sativum* L. were chosen as models to highlight some

existing research gaps, which bridging the gaps will increase the quality and validity of the results, decrease the inaccuracy and misunderstanding, and also save the time and expenditure required for herbal research.

2- Important gaps of herbal research

The increasing number of publications and literature on traditional medicine presents the significant budget and time, which are spent on this topic. In our opinion, it seems that the tendency of researchers and scientists to see promising findings in their research efforts⁹, as well as the pressures such as to be novel and first¹⁰, and the desperation to publish or perish⁹ have taken the inaccuracy of the general belief in the safety of medicinal herbs due to their natural origin^{4-6,11} out of the scientists' spotlight. Moreover, there are a number of substantial concerns about the production, processing, and supply of herbal products^{12,13}. The importance of botanical nomenclature, identification of plants and plant parts used, the processing, and the extraction procedures on the validity and reproducibility of publications on herbal medicine has been previously emphasized^{14,15}. In addition to the above mentioned items, numerous fields remain to be considered by scientists and researchers, including the history of traditional medicine, the status of medicinal herbs, toxicological assessments, biological and pharmacological mechanisms of disease, and research questions.

2-1- Botanical nomenclature

The importance of a standard terminology to describe herbal medicine and their products has been highlighted¹⁶. Despite the significant importance of plant identification and botanical nomenclature, as some toxicity happens due to the incorrect identification of herbs^{4,6}, botanical nomenclature is already often ignored in herbal publications. For instance, in the previous study, none of the reviewed articles about the herbal management of diabetes scored the maximum of Chan's scoring system¹⁴, as they failed to cite botanical nomenclature and include information on the processing procedure and extraction processes⁷. Rivera et al. showed that the Latin scientific name of plants have been used improperly or even by mistake in many articles¹⁵. As an extra example, the species of studied herbs in the reviewed Iranian articles were not specified in the titles and abstracts of articles^{7,8}.

Ethnopharmacology is a fast-developing and interdisciplinary area of research. Researchers with diverse backgrounds, including pharmaceutical scientists, pharmacologists, anthropologists, biologists, botanists, toxicologists and practitioners/researchers of the diverse medical traditions are all involved in such research¹. We guess that a reason for botanical nomenclature to be a common gap in the herbal research is unfamiliarity of the researchers and scientists with this botanical concept. Accordingly, we have dedicated a part of the present article to introduce botanical nomenclature system to many herbal researchers, who may not be familiar with the scientific nomenclature. Although, Rivera et al. described the method of presenting the exact scientific name of plants in their noteworthy paper¹⁵.

The "International Code of Nomenclature for algae, fungi, and plants" is the set of rules and recommendations that govern the scientific naming of all organisms traditionally treated as algae, fungi, or plants, whether fossil or non-fossil, including blue-green algae (*Cyanobacteria*), chytrids, oomycetes, slime moulds, and photosynthetic protists with their taxonomically related non-photosynthetic groups (but excluding *Micropodidia*). Before 2011, it was called the *International Code of Botanical Nomenclature* (ICBN)¹⁷.

The scientific name of a plant consists of three parts, including: 1- the name of genus or the generic name, 2- specific epithet or species epithet, and 3- the author's name. For the name of genus, the first letter is always written with a capital letter, and the rest of its letters is written small. The name is always in Latin and singular, and may be taken from the name of a famous person (for instance, *Avicennia* in honor of Abu Ali Sinai- Avicenna), the Latin name of a plant (like the *Viola* from viola) or the appearance of the plant (for example, *Pinus* for its needles leaves). All letters of species epithet are written small and may be taken from the name of a person, location or characteristics of a plant. The genus name and species epithet should be written as underlined or italicized. The author's name is the name of a person or persons who first identified or validly introduced a plant. The author's name is usually given in brief (for example, L. is the abbreviation of Swedish botanist Carl Linnaeus) and comes after the name of the genus and species epithet¹⁸.

In the previous works^{7,8}, not mentioning the author's name was seen in abundance. For instance, garlic (Sir in Persian) was introduced *Allium sativum* instead of *Allium sativum* L. However, it is noteworthy to mention that the constant changes in the new classification principles are due to the continuous progression of science. Accordingly, it is possible that the scientific name of the plants, at the time of writing those articles, seems to be incorrect based on the new criteria. Furthermore, the identification of plant specimens, obtained from grocery stores, is impossible; as samples are usually prepared from different parts of plants, such as flowers, branches, leaves, roots, etc., in dried and powdered forms. However, it is necessary to mention that the synonym names must be replaced by the accepted names.

Researchers and students could introduce plants with great confidence by referring to the International Plant Name Index (IPNI, 2012)¹⁹. In the Authors option on the left side of IPNI, the abbreviation for the author can be obtained by entering the full name. However, IPNI as the most complete reference for published names of herbs does not provide any information on the accepted names and synonyms. The Plant List (<http://www.theplantlist.org/>) is a proper choice in this regard that provides the accepted Latin names, unresolved names, or synonyms of all known plant species, but not vernacular or common plant names. As well, The Plant List does not include algae or fungi. Accordingly, it needs an international consensus to establish an online database, which covers all necessary information and rules on scientific nomenclature of algae, fungi, and plants. In Figures 1 and 2, the steps to find the accepted name for *Allium sativum* in IPNI and The Plant List are presented, respectively.

Figure 1- (a). Steps 1 to 3 to find the accepted name for *Alliumsativum* are presented by arrows and numbers in "IPNI". (b). Steps to achieve abbreviation for the author by entering the full name in IPNI are shown by arrows and numbers.

Figure 2. Steps 1 to 3 to find the accepted name for *Alliumsativum* are presented by arrows and numbers in "the plant list".

2-2- The history of traditional medicine

The knowledge of traditional medicine, which has been transferred from the previous generations to us, is closely linked to the people cultures. Every nation has its traditional medicine systems. The 'holistic' approach integrating medicinal and psychological therapies forms the basis of traditional medicine systems¹. Reverse pharmacology strategy is a guide to explore the traditional use of phytopharmaceuticals in a certain population for the screening of natural products. This approach will save time and expenses in drug development^{reviewed in 20}. The traditional use might have the same value as the case-series or a poor quality cohort and case-control study²⁰. Modern ethnopharmacological research involves the study of historical written sources for the knowledge about the use of plants available in the various cultures all around the world. The increasing evidence for the rational basis and pharmacological relevance of many remedies, described in these sources, demonstrates the validity of using historical texts as a starting point in the search for new medicines. Despite some potential pitfalls linked with the investigation of historical texts, many researchers subscribe to the view that a comparative analysis of these texts helps to provide new insights into the plant usage and also the development of the related medicinal systems. It is noteworthy that the identification of the plant or plant substances and the interpretation of the symptoms or diseases are also the most crucial steps in the ethnopharmacological analysis of historical texts¹.

The historical approach to traditional medicine and ethnopharmacology helps to the preservation of local or indigenous knowledge of the respective culture, protection of the rights of holders of traditional knowledge, and also providing important clues about the safety of herbal medicines. An adequate understanding of the ethnopharmacognostic background of the herbal medicines, the medical concepts and beliefs of the respective culture, a relevant research question, and time are essential prerequisites in most studies¹.

2-3- The status of medicinal herbs

Traditional medicine is interlinked with biodiversity, as local and indigenous peoples and/or healers usually use biological resources regarding their medicinal use^{1,21,22}. Plants, animals and microorganisms make up

the raw material of ethnopharmacology. So far, plants have been the main source for the active compounds used in medicines compared to animals. However, the potential biological activity of less than 10% of the world's biodiversity has been evaluated. For instance, only about 4–5% of the world's 350,000–400,000 plant species have been reported on ethnomedically. In addition, the geographical distribution of medicinal herbs and the number of those that have been developed commercially from the different continents vary. Accessing the large number of useful natural lead compounds awaiting discovery will pose many technical scientific, social and legal challenges¹.

It has been assumed that the destructive effects of ecosystem collapse on human civilization are no less than those of nuclear war or global warming³. Several multi-layered issues and questions have arisen regarding biodiversity conservation and the rights of indigenous peoples to their knowledge and resources^{21–23}. The practice of TM is not immune to the current environmental issues facing Earth, such as the overexploitation of numerous species around the globe. Although, the traditional medicine itself is known to be involved in this issue. For instance, wild harvesting and over-collection are causes of concern in the context of biodiversity conservation. Accordingly, researchers should concern about both the cultural and ecological aspects associated with the traditional uses of plants and animal in TM^{reviewed in 1,22, and 24}. In this regard, due to the importance of medicinal herbs in terms of environmental issues, we introduce the status of herbs, e.g. being endemic or endangered, as an important factor needed to be addressed in publications on herbal medicines.

3- Approaches and methods

3-1- Selection of the herb

Based on the results of previous studies^{7,8}, we selected *Allium sativum* L. as a typical plant to investigate the research gaps in articles published by Iranian and non- Iranian researchers and scientists. *A. sativum* has both nutritional values and numerous applications in medicine. Thanks to various biologically active substances, a wide range of pharmacological effects has been attributed to this herb, including hypoglycemic, hypolipidemic, anticoagulant, antihypertensive, antihepatotoxic, anticancer, immunomodulatory, antioxidant properties, as well as antibiotic and antifungal activities. These properties result from the combined curative effect of^{reviewed in 7}.

3-2- Data source and study selections

Firstly, a search limited to Iran was conducted with *Allium sativum* or *Allium sativum* L. in the data source PubMed up to the end of 2012. Secondly, a search, which was not limited to Iran, was repeated using the keywords in the past year (2020/08/21) to compare the statuses of research gaps in the articles, obtained by searching keywords in two searches.

3-2-1- Included criteria and data extraction

All human, animal and in vitro studies on *A. sativum* were included. Two reviewers independently extracted the data, including common and scientific names of herbs, study design, experimental groups, dose, duration, processing and extraction procedure of herbs and HPM, and sample size from the articles.

3-2-2- Excluded criteria

The reviewed articles or those in which the medicinal application of *A. sativum* were not investigated, and letters to the editor were excluded. Two reviewers independently examined the title and abstract of each article to avoid duplications. In case of duplicated publications, we tried to extract all available data and refer them to the base study.

3-4- Evaluation of the reviewed articles

The reviewed articles were evaluated by a three-score system developed by Chan K et al.¹⁴ for assessing the following aspects of the herbs or herbal materials: (i) identity of plants and plant parts used; (ii) processing

procedure; (iii) extraction process. Besides the Chan's scoring system, the status of botanical nomenclature and the history of traditional medicine were examined in the selected articles.

4- Results

In the search using the keywords *Allium sativum* + Iran and *Allium sativum* L. + Iran, totally 228 and 47 articles were found, respectively. After excluding the reviewed articles or those unrelated to medicinal application, totally 144 articles were evaluated²⁵⁻¹⁶⁸. In the second search, which was limited to the past year but not Iran, about 447 queries were found using *Allium sativum*. However, using *Allium sativum* L. as the keyword, 94 articles were found. In this case, we chose to evaluate the articles found using *Allium sativum* L. from which 32 articles were reviewed based on the included and excluded criteria¹⁶⁹⁻²⁰⁰. Information extracted from the Iranian reviewed articles and the articles found through the second search are summarized in Tables 1 and 2, respectively. (Please Find Attached Tables 1 and 2 at the end of the manuscript).

Table 1- Botanical nomenclature and referring to Persian medicine or the traditional usage in Iranian reviewed articles with the total score based on the Chan's scoring system.

Table 2- Botanical nomenclature, referring to the traditional medicine or the traditional usage in reviewed articles published in the last year with the total score based on the Chan's scoring system and the country mentioned in the affiliation.

4-1- Botanical nomenclature

From the total of 144 reviewed Iranian publications, the scientific name of *Allium sativum* L. was mentioned through the main text of 37 articles (25.7 %). In other words, the scientific nomenclature was not mentioned in 74.3 % of the articles' main text. It is noteworthy that not using the scientific nomenclature was also seen in journals with the impact factor as high as about five. In a review of botanical nomenclature used in the title/abstract of these reviewed articles, *Allium sativum* L. was mentioned in only three articles along with garlic. In eight reviewed articles, *Allium sativum* alone and in 45 articles the name *A. sativum* along with garlic was mentioned. In comparison, in 87 articles, only garlic was mentioned. Furthermore, one article cited only *Allium* and garlic (Table 1). In addition, Iranian authors rarely mentioned the Persian generic name of *A. sativum* (Sir) in their publications.

Considering 36 articles, which are obtained through the second search, using *Allium sativum* L. as the keyword that are limited to the past year but not Iran, *Allium sativum* L. was mentioned in the main text of 18 reviewed articles (56.3 %). Whereas, in the overview of the articles' title/abstract, *Allium sativum* L. was not mentioned in the title/abstract of any of the reviewed articles. In 17 articles, *Allium sativum* was used along with garlic, and in one article it was used along with black garlic. In 11 articles, only garlic was mentioned. *Allium sativum* alone was used in one of the reviewed article, and one article mentioned *Allium* along with garlic (Table 2). In some cases, the first letter of genus sativum was written with a capital letter as Sativum.

4-2- The history of traditional medicine

Among the Iranian reviewed articles, only two articles (1.4%) mentioned the traditional application of *A. sativum* (Table 1) without any citation to the known historical valid literature^{75,138}. In the same way, only four of the 32 reviewed articles (12.5%), obtained in the second search, referred to *A. sativum* as a traditional folk medicine that have been adopted in Sri Lanka¹⁶⁹, Indonesia¹⁸⁴, Australia and China¹⁹¹, and Taiwan¹⁹³ (Table 2). The history of Iranian traditional medicine (ITM) or other traditional medicine systems, referring to historical literature, was not addressed in none of the reviewed articles.

4-3- The status of medicinal herb

A. sativum (Plantae>Asparagales>Amaryllidaceae>Allium) is believed to have been originated from Central Asia (Kazakhstan, Uzbekistan and western China). This was confirmed by phylogenetic analysis based on

molecular and biochemical markers, also indicating a secondary diversity center in the Caucasus. At present, garlic is grown all over the world from the equator to latitudes of 50° in both hemispheres²⁰¹. In other words, garlic is not an endangered herb. Therefore, it was not assessed from this point of view in the reviewed articles.

4-4- Chan's scoring system

All the reviewed articles were evaluated based on Chan's scoring system¹⁴. The total score of 144 Iranian reviewed articles and the articles published in the past year is shown in Tables 1 and 2, respectively. From the total of 144 reviewed Iranian articles, 44 cases (30.6%) scored zero, 27 articles (18.75%) scored from 1-4, 42 articles (29.2%) ranged from 5-9, 26 articles (18.1%) scored 10-14, and the remaining 5 ones (3.5%) scored from 15- 17 points (Table 1). In other words, about 97% of them scored < 15 and about 80% of the articles scored < 10 points.

In comparison, from the totally 32 articles published in the past year, one article (3.1%) scored zero, three articles (9.4%) scored 1-4, and 13 articles (40.6%) scored 5-9, 10 articles scored (31.3%) and five articles (15.6%) scored 10-14 and 15-19 points, respectively (Table 2). In other words, about 84% of the reviewed articles scored < 15 points and about 53% of the articles scored < 10 points. Obviously, none of the reviewed articles, obtained in two searches, received the total score of 25.

5- Discussion

There are various kinds of traditional and alternative medicines and traditional health care practices^{1,21, 202}. According to the World Health Organization (WHO) reports, about 88% of its member states have acknowledged the use of traditional and complementary medicine, and many of them have a national research institute, as well as national policy on traditional medicine and regulation of herbal medicines. It is noteworthy that these percentages are increasing²⁰². In the present article, some existing gaps in the herbal research such as the history of traditional medicines and botanical nomenclature have been highlighted, which have high impact on the validity of outcomes and the rate of drug development.

Based on the current data and the previously published research, as well as our unpublished data, the majority of Iranian researchers do not address the history and traditional applications of the studied herbal medicines in their articles. In fact, except in limited cases, the history of ITM, scholars of Persian medicine and plants endemic to Iran have not got appropriate attention from researchers, especially Iranian ones^{7,203}. As seen in the present article, non-Iranian researchers just mentioned that *A. sativum* was traditionally used and did not cite the historical sources and literatures, either.

Traditional and complementary medicine is a well-known health care system in all of the developed, developing and undeveloped countries. WHO covers regional offices, including African, the Americas, Eastern Mediterranean, European, South-East Asia, and Western Pacific regions²⁰². Many traditional medicine systems used around the world are usually categorized as Ayurveda, Kampo, traditional Chinese medicine (TCM), traditional Korean medicine, and Unani²⁰⁴. However, ITM seems to be not so well known. As seen, ITM is not known as an independent traditional medicine system. As well as, in the WHO *Traditional Medicine Strategy 2014–2023*²⁰⁵, there is no reference to Persian medicine or its historical impact on traditional medicines of world. Whereas, the history of Persian medicine roots backs to thousand years before Christ^{reviewed in 206-210}. According to Cyril Elgood, the English medical historian, Persian thoughts the Greeks the elements of the medical system, which has been known as Greek medicine²¹¹. Hippocrates, the father of medicine, was not unaffected by the medical teachings of ancient Iran^{212,213}. Also, Simorgh, the legendary bird of Iran for more than 2500 years, with a special place in the ancient culture and literature of Iran is older than some medical symbols in the world and Greece^{214,215}. In the ancient and traditional Iranian medicine, medicinal herbs and cure approaches are prescribed according to the personal characteristics of each person, which is called the temperament and humors of a person^{209,211,212,216,217}. In other words, Iranian traditional healers believe in personal medicine in the prevention, diagnosis and treatment of disorders. In personal medicine, an attempt is made to identify specific biomarkers to determine the best drug and treatment method for each patient²¹⁸⁻²²⁰.

The history of ITM and its scholars are not known the same as TCM and to some extent Ayurveda, which are exceptions in this regard. The unfamiliarity with the Pahlavi language or other ancient Iranian languages has been introduced as a reason for neglecting pre-Islamic medicine²¹¹. John Bernal also states that the contribution of Iranians in science has been underestimated because of the destruction of the books of ancient Iran and the lack of access to sufficient evidence²¹³. Considering the importance of having a historical view on traditional health care approach^{1,21,22}, acquaintance with the historical and cultural background of all kinds of traditional medicine systems and conducting the ethnobotanical and ethnomedical research should be the innermost concern of herbal researchers and traditional medicine activists.

In Iranian folklore, garlic is consumed raw or cooked. Its base oil is also used as spice in the food industry. Garlic has been traditionally used for reducing hypertension and hyperglycemia, stimulating the appetite, and preventing the contamination of places for cholera, typhoid and typhoid. However, the largest disadvantage of garlic is its repugnant smell²²¹.

Evaluation of the reviewed articles by Chan's scoring system, in confirmation of the past research^{7,14}, also showed that the appropriate references to issues such as the identification of plants, the processing, and the extraction procedures are still forgotten. None of the reviewed articles, either Iranian or non-Iranian, scored the maximum point of 25. In comparison, more than half of the total reviewed articles scored < 10, one of the non-Iranian (5%) and 44 of the Iranian (30.6%) reviewed articles scored zero.

Looking at the impact factor (IF) of journals in which the current reviewed articles were published (the mean of IF (144 + 32) of the reviewed articles = 1.89, maximum and minimum of IF = 5.80 and 0.349, respectively; The IF of 71 journals was zero; data not shown) and peer Chan's evaluation score for each reviewed article demonstrated that even in high impact journals, there is no guarantee that the important aspects, such as herbal quality documentation, were not overlooked, as was highlighted previously^{7,14}. It is noteworthy that despite significant criticism of IF as a valid measure of journal quality, the quality of individual manuscripts and the merits of scientists²²²⁻²²⁵, and the proposed alternatives²²⁵, it is already accepted as a measure between researchers and scientists.

5-1- Suggestions for further evaluation and study

We have found that there are other extra issues except the historical approach, the status of herbs, botanical nomenclature, and the items highlighted in Chan's scoring system that need further considerations in ethnopharmacological research, including research questions, toxicological assessments, and biological and pharmacological mechanisms of disease. These items have not been examined as they are beyond the scope of the present paper. However, due to their significant impact on the quality and the rate of research on traditional and herbal medicines, a brief introduction of them is provided in the following.

5-1-1 Research questions

The starting point of every research project is a research question. Research questions can be categorized into descriptive, predictive, or causal²²⁶. Although the question directs study design and influence on reporting²²⁷, the question type and study design are two thoroughly distinct issues. The study findings will be interpreted, provided that a well-defined question is matched to the right study design, and reported correctly²²⁶. Ethnopharmacological projects may be intended for either applied, or a basic research or a combination of both aspects¹. We are of the opinion that the impact of the type of questions and study design on the outcomes of the published and ongoing herbal research must be examined by experts.

5-1-2- Toxicological assessments

Medicinal plants and their products must be safe for the patients and consumers. Contaminants of herbs and HMP have been categorized into biological contaminants (microorganisms), chemical contaminants (e.g. mycotoxins, heavy metals, and pesticide)⁵, correctly identified medicinal plants with unknown toxicity, incorrectly identified medicinal plants with toxic activity, and unprofessional processing, which differs from safe traditional preparation^{reviewed in 6}. The last three items again show the critical importance of botanical nomenclature and the history of traditional knowledge on herbal medicines, as was emphasized in the current

study. Furthermore, the interactions of medicinal herbs with conventional drugs represent other sources for herbal toxicity^{reviewed in 6}. The quality and safety of the studied herbs, phytochemical and toxicological assessments significantly impact on the quality of final herbal publications¹³. Quality standards for herbal drugs and herbal medicinal products have been developed over recent decades significantly²²⁸. However, some toxicological investigations are not feasible for all research teams due to the high cost and technical instruments. In our opinion, toxicological assessments must be considered as a main part of the study by researchers, who have adequate financial resources to conduct this kind of research.

5-1-3- Biological and pharmacological mechanisms of disease

In the previous study on the herbal management of diabetes, it has been shown that the majority of studies investigated the effects of the studied herbs on some well-known signs of diabetes, but the biological mechanism of diabetes and diabetes-related complications were not investigated in depths⁷. In a proposed encyclopedia of herb-disease, the investigated subjects and diseases of herbal research have been categorized into 18 groups⁸. We suggest that a specialized and continuous collaboration between physicians, pharmacist, and researchers of herbal medicine with a focus on the biological and pharmacological mechanisms of disease will accelerate new discoveries and improve the final outcomes of the herbal research.

6- Conclusion

Exploration of traditional knowledge has gained increasing interest in rational drug design and development^{20,24}. To achieve valid and fruitful outcomes, the essential standards necessary for the validity and reliability of herbal research should be concerned but not forgotten. In the current study, we aimed to draw attention to existing gaps and some issues that are not usually addressed properly in the publications on herbal research and traditional medicine in spite of their importance, such as botanical nomenclature, the processing, and the extraction procedures. Moreover, the impact of the traditional medicine history on the protection of the rights of traditional knowledge holders, the safety of herbal medicines, the quality and reliability of outcomes and finally shortening and speeding up drug development was the focus of our attention. Research questions and also biological and pharmacological mechanisms of disease are another important issues that should be considered, when evaluating publications on herbal and traditional medicine. Furthermore, available valid reference databases for plants, such as IPNI or The Plant List, do not provide all necessary information for all members of the plant kingdom in one place. The proposed solution was to establish an online database, which covers all necessary information and rules.

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Abbreviations

HMP, Herbal Medicines and their Preparation

ICBN, *International Code of Botanical Nomenclature*

IF, Impact Factor

IPNI, International Plant Name Index

ITM, Iranian traditional medicine

TCM, Traditional Chinese medicine

WHO, the World Health Organization

Availability of data and materials

All data generated or analyzed during this study are included in the present article.

Ethics approval and consent to participate

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Consent for publication

Not applicable.

Disclosures

The authors declare no conflicts of interest.

Author contribution

AR involved in the conception and design of the study and also contributed to analysis and interpretation of data. She wrote the article with the collaboration of AA in botanical issues. AA and VP have made contributions to data collection from the reviewed articles. AA has also prepared the provided figures. All authors involved in critical revision of the manuscript and approved the final manuscript.

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Table 1- Botanical nomenclature and reference to Persian medicine or the traditional usage of *Allium sativum* L. in Iranian reviewed articles with the total score based on the Chan's scoring system.

Botanical nomenclature used in the title/abstract	<i>Allium sativum</i> L. was used through the main text	Referring to the Persian medicine or the traditional usage	Score (max = 25)	Reference
Garlic	Yes	No	5	25
Garlic	Yes	No	15	26
<i>Allium sativum</i> , Garlic	Yes	No	14	27
<i>Allium sativum</i> , Garlic	Yes	No	12	28

Botanical nomenclature used in the title/abstract	<i>Allium sativum</i> L. was used through the main text	Referring to the Persian medicine or the traditional usage	Score (max = 25)	Reference
<i>Allium sativum</i> L., Garlic	Yes	No	10	29
Garlic	No	No	5	30
Garlic	Yes	No	4	31
Garlic	No	No	0	32
Garlic	No	No	0	33
<i>Allium sativum</i> , Garlic	Yes	No	14	34
<i>Allium sativum</i> , Garlic	Yes	No	10	35
Garlic	No	No	0	36
<i>Allium sativum</i> , Garlic	No	No	0	37
<i>Allium sativum</i> , Garlic	No	No	11	38
<i>Allium sativum</i> , Garlic	No	No	9	39
Garlic	Yes	No	4	40
<i>Allium sativum</i> , Garlic	No	No	3	41
Garlic	No	No	0	42
Garlic	No	No	0	43
Garlic	No	No	0	44
Garlic	No	No	11	45
<i>Allium sativum</i> , Garlic	No	No	8	46
Garlic	No	No	7	47
<i>Allium sativum</i> , Garlic	No	No	5	48
Garlic	No	No	3	49
<i>Allium sativum</i> , Garlic	Yes	No	0	50
<i>Allium sativum</i> , Garlic	No	No	0	51

References were arranged by year of publication from 2000 to 2020. For each year, the reviewed articles were ranked based on the score from the highest to the lowest.

Table 1- Botanical nomenclature and referring to Persian medicine or the traditional usage of *Allium sativum* L. in Iranian reviewed articles with the total score based on the Chan's scoring system (continued).

Botanical nomenclature used in the title/abstract	<i>Allium sativum</i> L. was used through the main text	Referring to the Persian medicine or the traditional usage	Score (max = 25)	Reference
Garlic	No	No	0	52

Botanical nomenclature used in the title/abstract	<i>Allium sativum</i> L. was used through the main text	Referring to the Persian medicine or the traditional usage	Score (max = 25)	Reference
Garlic	No	No	6	53
Garlic	No	No	9	54
<i>Allium sativum</i> ,	Yes	No	9	55
Garlic				
Garlic	Yes	Yes	7	56
<i>Allium sativum</i> ,	No	No	7	57
Garlic				
Garlic	No	No	0	58
Garlic	No	No	11	59
<i>Allium sativum</i> ,	No	No	11	60
Garlic				
Garlic	No	No	11	61
<i>Allium sativum</i> ,	Yes	No	8	62
Garlic				
Garlic	No	No	8	63
Garlic	Yes	No	7	64
<i>Allium sativum</i> ,	No	No	5	65
Garlic				
Garlic	No	No	3	66
Garlic	No	No	3	67
<i>Allium sativum</i> ,	Yes	No	3	68
Garlic				
Garlic	No	No	0	69
Garlic	No	No	0	70
Garlic	No	No	0	71
Garlic	No	No	0	72
Garlic	No	No	0	73
Garlic	No	No	0	74
<i>Allium sativum</i> ,	Yes	No	14	75
Garlic				
<i>Allium sativum</i> ,	No	No	10	76
Garlic				
Garlic	No	No	6	77
<i>Allium sativum</i>	No	No	6	78
Garlic	No	No	3	79

References were arranged by year of publication from 2000 to 2020. For each year, the reviewed articles were ranked based on the score from the highest to the lowest.

Table 1- Botanical nomenclature and referring to Persian medicine or the traditional usage of *Allium sativum* L. in Iranian reviewed articles with the total score based on the Chan's scoring system (continued).

Botanical nomenclature used in the title/abstract	<i>Allium sativum</i> L. was used through the main text	Referring to the Persian medicine or the traditional usage	Score (max = 25)	Reference
Garlic	No	No	0	80
Garlic	No	No	0	81
Garlic	No	No	0	82
Garlic	No	No	0	83
Garlic	Yes	No	0	84
<i>Allium sativum</i> , Garlic	No	No	0	85
Garlic	No	No	0	86
Garlic	No	No	0	87
<i>Allium sativum</i> , Garlic	Yes	No	17	88
Garlic	No	No	13	89
Garlic	Yes	No	11	90
<i>Allium sativum</i> , Garlic	Yes	No	10	91
Garlic	No	No	9	92
<i>Allium sativum</i> , Garlic	Yes	No	9	93
<i>Allium sativum</i> , Garlic	No	No	8	94
Garlic	No	No	8	95
<i>Allium sativum</i> , Garlic	No	No	7	96
Garlic	No	No	6	97
Garlic	No	No	6	98
Garlic	No	No	5	99
Garlic	No	No	5	100
<i>Allium sativum</i> , Garlic	No	No	3	101
Garlic	No	No	3	102
Garlic	No	No	2	103
Garlic	No	No	0	104

References were arranged by year of publication from 2000 to 2020. For each year, the reviewed articles were ranked based on the score from the highest to the lowest.

Table 1- Botanical nomenclature and referring to Persian medicine or the traditional usage of *Allium sativum* L. in Iranian reviewed articles with the total score based on the Chan's scoring system (continued).

Botanical nomenclature used in the title/abstract	<i>Allium sativum</i> L. was used through the main text	Referring to the Persian medicine or the traditional usage	Score (max = 25)	Reference
<i>Allium sativum</i>	No	No	0	105
<i>Allium sativum</i> , Garlic	No	No	0	106
Garlic	No	No	0	107
Garlic	No	No	0	108
Garlic	No	No	8	109
<i>Allium sativum</i>	No	Yes	5	110
Garlic	No	No	5	111
<i>Allium sativum</i> , Garlic	No	No	3	112
Garlic	No	No	3	113
Garlic	No	No	3	114
Garlic	No	No	1	115
Garlic	Yes	No	1	116
Garlic	No	No	1	117
<i>Allium sativum</i> , Garlic	No	No	0	118
Garlic	No	No	0	119
<i>Allium sativum</i> L., Garlic	Yes	No	14	120
<i>Allium sativum</i> , Garlic	Yes	No	10	121
<i>Allium sativum</i> , Garlic	No	No	10	122
<i>Allium sativum</i>	Yes	No	7	123
<i>Allium sativum</i> , Garlic	Yes	No	6	124
<i>Allium sativum</i> , Garlic	Yes	No	5	125
Garlic	No	No	2	126
Garlic	Yes	No	2	127
Garlic	No	No	1	128
Garlic	No	No	0	129
Garlic	No	No	0	130

References were arranged by year of publication from 2000 to 2020. For each year, the reviewed articles were ranked based on the score from the highest to the lowest.

Table 1- Botanical nomenclature and referring to Persian medicine or the traditional usage of *Allium sativum* L. in Iranian reviewed articles with the total score based on the Chan's scoring system (continued).

Botanical nomenclature used in the title/abstract	<i>Allium sativum</i> L. was used through the main text	Referring to the Persian medicine or the traditional usage	Score (max = 25)	Reference
Garlic	Yes	No	0	131

Botanical nomenclature used in the title/abstract	<i>Allium sativum</i> L. was used through the main text	Referring to the Persian medicine or the traditional usage	Score (max = 25)	Reference
<i>Allium sativum</i> , Garlic	No	No	17	132
<i>Allium sativum</i> , Garlic	Yes	No	14	133
<i>Allium sativum</i> , Garlic	No	No	11	134
<i>Allium sativum</i> L., Garlic	Yes	No	9	135
<i>Allium sativum</i> , Garlic	No	No	7	136
Garlic	No	No	6	137
Garlic	No	No	3	138
Garlic	No	No	1	139
Garlic	No	No	0	140
Garlic	No	No	0	141
Garlic	No	No	0	142
<i>Allium sativum</i> , Garlic	Yes	No	12	143
<i>Allium sativum</i> , Garlic	No	No	11	144
Garlic	No	No	10	145
Garlic	Yes	No	10	146
<i>Allium sativum</i>	Yes	No	8	147
<i>Allium sativum</i> , Garlic	No	No	8	148
Garlic	No	No	7	149
Garlic	No	No	6	150
Garlic	Yes	No	4	151
Garlic	No	No	4	152
Allium, Garlic	No	No	0	153
Garlic	No	No	0	154
<i>Allium sativum</i>	No	No	16	155
<i>Allium sativum</i> , Garlic	No	No	15	156

References were arranged by year of publication from 2000 to 2020. For each year, the reviewed articles were ranked based on the score from the highest to the lowest.

Table 1- Botanical nomenclature and referring to Persian medicine or the traditional usage of *Allium sativum* L. in Iranian reviewed articles with the total score based on the Chan's scoring system (continued).

Botanical nomenclature used in the title/abstract	<i>Allium sativum</i> L. was used through the main text	Referring to the Persian medicine or the traditional usage	Score (max = 25)	Reference
<i>Allium sativum</i>	No	No	11	157

Botanical nomenclature used in the title/abstract	<i>Allium sativum</i> L. was used through the main text	Referring to the Persian medicine or the traditional usage	Score (max = 25)	Reference
<i>Allium sativum</i>	No	No	8	158
<i>Allium sativum</i> , Garlic	No	No	7	159
Garlic	No	No	4	160
Garlic	No	No	3	161
<i>Allium sativum</i> , Garlic	No	No	2	162
Garlic	No	No	0	163
Garlic	No	No	0	164
Garlic	No	No	0	165
<i>Allium sativum</i> , Garlic	No	No	0	166
Garlic	Yes	No	11	167
Garlic	Yes	No	8	168

References were arranged by year of publication from 2000 to 2020. For each year, the reviewed articles were ranked based on the score from the highest to the lowest.

Table 2- Botanical nomenclature, referring to the traditional medicine or the traditional usage of *Allium sativum* L. in the reviewed articles published in the last year with the total score based on the Chan's scoring system and the country mentioned in the affiliation.

Botanical Nomenclature used in the title/abstract	<i>Allium sativum</i> L. was used through the main text	Referring to the traditional medicine or the traditional usage	Country	Score (max = 25)	Reference
<i>Allium sativum</i>	Yes	Yes	Sri Lanka	19	169
<i>Allium sativum</i> , Garlic	Yes	No	Brazil	18	170
<i>Allium sativum</i> , Garlic	Yes	No	India	14	171
Garlic	Yes	No	Italy	14	172
<i>Allium sativum</i> , Garlic	Yes	No	Japan	13	173
Allium, Garlic	No	No	Mexico	13	174
Garlic	Yes	No	Japan	13	175
<i>Allium sativum</i> , Garlic	Yes	No	Japan	11	176

Botanical Nomenclature used in the title/abstract	<i>Allium sativum</i> L. was used through the main text	Referring to the traditional medicine or the traditional usage	Country	Score (max = 25)	Reference
<i>Allium sativum</i> , Garlic	Yes	No	Japan	11	177
<i>Allium sativum</i> , Garlic	Yes	No	China	11	178
<i>Allium sativum</i> , Garlic	Yes	No	Japan	8	179
Garlic	No	No	China	8	180
<i>Allium sativum</i> , Garlic	Yes	No	Iran	8	181
<i>Allium sativum</i> , Garlic	Yes	No	China	7	182
Garlic	No	No	China	7	183
<i>Allium sativum</i> , Garlic	Yes	Yes	Indonesia	7	184
Garlic	No	No	Canada	6	185
Garlic	No	No	China	6	186
Garlic	No	No	Korea	5	187
<i>Allium sativum</i> , Garlic	No	No	Saudi Arabia	4	188
Garlic	No	No	Poland	3	189
Garlic	No	No	Tunisia	0	190
<i>Allium sativum</i> , Garlic	Yes	Yes	Australia and China	18	191
<i>Allium sativum</i> , Black garlic	No	No	China	16	192
<i>Allium sativum</i> , Garlic	Yes	Yes	Taiwan	15	193
Garlic	No	No	China	10	194
<i>Allium sativum</i> , Garlic	Yes	No	Korea	10	195
<i>Allium sativum</i> , Garlic	No	No	Iran	9	196
Garlic	No	No	Japan	8	197

Botanical Nomenclature used in the title/abstract	<i>Allium sativum</i> L. was used through the main text	Referring to the traditional medicine or the traditional usage	Country	Score (max = 25)	Reference
<i>Allium sativum</i>	No	No	Indonesia	7	198
<i>Allium sativum</i> , Garlic	Yes	No	Algeria	6	199
<i>Allium sativum</i> , Garlic	Yes	No	United Arab Emirates	4	200

References were arranged by the year of publication from 2019 to 2020. For each year, the reviewed articles were ranked based on the score from the highest to the lowest.

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