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REVIEW ARTICLE

Herbal Research: Gaps Affecting the Quality and Validity of Research Findings

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KEYWORDS

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ABSTRACT: Traditional and herbal medicines are rich and promising sources for drug development. The number of articles published on traditional medicines and their applications is rapidly increasing. However, despite the extensive ongoing research on herbal medicines, the results of such research are not remarkable. Against this background, this study aims to highlight some existing research gaps, the bridging of which will increase the quality and validity of the results of herbal research. To this end, Iranian and non-Iranian articles on *Allium sativum* L. were reviewed for compliance with standards and requirements for herbal research. Botanical nomenclature, processing and extraction procedures, and history of traditional medicine were identified as the main gaps in the reviewed herbal research. Researchers and authors should keep in mind that familiarity with the history, characteristics, and potential of traditional medicine systems is a key factor accelerating the process of developing nature-based medicines. Essential standards that have a great impact on the validity and reliability of the results of herbal research should not be ignored, either. In addition, there are still numerous areas that need to be considered by scientists and researchers, including the status of medicinal herbs, toxicological assessments, biological and pharmacological mechanisms of diseases, and research issues.

INTRODUCTION

Traditional medical knowledge, including the use of herbal medicines and broader medical practices, is part of local folklore in many cultures worldwide. The importance of medicinal herbs and their use as a distinctive approach of traditional medicine in human civilization is widely recognized [1].

Thousands of articles on ethnopharmacological topics are now published annually. However, despite the extensive and intensive herbal research, the time and budget spent on this research, and the review and publication of its findings, the successes in treating diseases using traditional medicine or the discovery of new nature-based medicines are not outstanding. A review of the titles of the articles published in this field shows that a significant concern of research articles is to demonstrate the practical and impressive potentials and superiority of a certain type of traditional medicine. In almost all original articles, the efficacy of herbal medicines and their preparations (HMP) is investigated in an *in vitro* or *in vivo* manner, and their promising potentials are discussed. Apart from the problems associated with this approach to scientific results, [2,3], some serious concerns about herbal medicines and HMP, such as the effects of cultivation conditions on plant constituents, contaminants of HMP, side effects, and herb-

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drug interactions [4-6], do not seem to be the primary concern of the researchers and scientists in the field of traditional medicine.

Previous studies have noted the strengths and weaknesses of research on herbal management of diabetes mellitus, as a model [7], the need for an encyclopedia of herbs-diseases [8], and the impact of journals' policies on the quality and validity of publications on traditional medicine [9]. Against this background, this article aims to highlight existing research gaps that adversely affect the quality and validity of the findings, accuracy and misunderstanding, and the time and cost of herbal research. To this end, *Allium sativum* L. was selected as a typical herb to investigate the research gaps in articles published by Iranian and non-Iranian researchers and scientists alike. Based on our previous studies, [7, 8], a wide range of pharmacological effects have been attributed to this herb, including hypoglycemic, hypolipidemic, anticoagulant, antihypertensive, antihepatotoxic, anticancer, immunomodulatory and antioxidant properties, as well as antibiotic and antifungal activities. *A. sativum*, called sir in Persian, has nutritional values and numerous applications in medicine and is highly valued by herbal researchers.

Major gaps in herbal research

The increasing number of publications on traditional medicine shows how much time and money is devoted to this subject. In our opinion, it seems that researchers' tendency to see promising results in their research efforts [10], the pressure to present something novel [11] and the looming specter of the "publish-or-perish" culture [10], have taken the focus off the inaccuracy of the general belief in the innocuousness of medicinal herbs thanks to their nature-based origin [4-6,12]. In addition, there are a number of significant concerns regarding the manufacture, processing, and delivery of herbal products [13, 14]. The impact of botanical nomenclature, identification of plants and plant parts used, processing, and extraction procedures on the validity and reproducibility of publications on herbal medicines has been emphasized previously [15, 16]. Over and above all, there are still numerous areas that need to be considered by researchers, including the history of traditional medicine, the status of medicinal herbs, toxicological assessments, biological and pharmacological mechanisms of disease, and research questions.

Botanical nomenclature

The importance of standard terminology to describe herbal medicines and their products has already been highlighted [17]. Despite the great importance of plant identification and botanical nomenclature and given the fact that some toxicities are a direct result of herb misidentification [4,6], botanical nomenclature is still being ignored in various publications. For example, in a study, none of the reviewed articles on herbal treatment of diabetes reached the maximum score of Chan's scoring system [15] because they did not cite botanical nomenclature and did not include information on processing and extraction methods [7]. Rivera et al. showed that the Latin scientific names of plants were used incorrectly or even erroneously in many articles [16]. Or, the species of the studied herbs were not indicated in the titles and abstracts of the articles in the Iranian articles studied [7, 8].

Ethnopharmacology is a rapidly developing and interdisciplinary field of research. Researchers from diverse backgrounds, including pharmacists, pharmacologists, anthropologists, biologists, botanists, toxicologists, and practitioners/researchers of various medical traditions, are all involved in this research1. We assume that botanical nomenclature is a common gap in herbal research because researchers and scientists are unfamiliar with this botanical concept. Accordingly, we devote a portion of this article to introducing the system of botanical nomenclature to many herbal researchers, who may not be familiar with the scientific nomenclature. However, in a remarkable article [16], Rivera et al. have already described the method of giving the exact scientific names of plants.

The International Code of Nomenclature for algae, fungi, and plants is a 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 molds, and photosynthetic protists with their taxonomically related non-photosynthetic groups (but excluding Microsporidia). Prior to 2011, it was called the *International Code of Botanical Nomenclature* (ICBN) [18].

The plant's scientific name consists of three parts: 1- the genus name or generic name, 2- the specific epithet or species epithet, and 3- the author's name. In the genus name, the first letter is always capitalized, and the remaining letters are lowercase. The name is always in Latin and in the singular. It could be named after a famous person (e.g., *Avicennia* in honor of Abu Ali Sinai-Avicenna), the Latin name of a plant (e.g., *Viola* of Viola) could be chosen for its name, or the appearance of the plant (e.g., *Pinus* for its needle-like leaves) could contribute to its naming. All letters of the species epithet are lowercase and could be based on the name of a person, a place, or the characteristics of a plant. The genus name and species epithet should be underlined or italicized. The author's name is the name of the person(s) who first identified or validly introduced a plant. The author's name is usually abbreviated (e.g., L. is the abbreviation of the Swedish botanist Carl Linnaeus) and comes after the genus name and species epithet [19].

In previous works [7, 8], the omission of the author's name was widespread. For example, garlic (Sir in Persian) was introduced as *Allium sativum* instead of *Allium sativum* L.

However, it is worth noting that constant changes in the new classification principles are due to the continuous progress of science. Accordingly, the scientific name of plants may appear to be incorrect when writing these articles based on newly adopted criteria. In addition, the identification of plant specimens obtained from grocery stores is impossible because the samples are usually prepared from various plant parts such as flowers, branches, leaves, roots, etc. in dried and powdered form. However, it must be mentioned that the recognized names must replace synonymous names.

Researchers and students can introduce plants with great confidence by referring to the International Plant Name Index (IPNI, 2012) [20]. In the Authors option on the left side of IPNI, you can get the abbreviation of the author by entering the full name. However, IPNI, as the most complete reference for published plant names, does not provide information on accepted names and synonyms. The Plant List (http://www.theplantlist.org/) is a good choice in this regard because it contains the accepted Latin names, the unresolved names, or the synonyms of all known plant species, but not the vernacular or common plant names. In addition, The Plant List does not include algae or fungi. Therefore, an international consensus is needed to establish an online database that contains all the necessary information and rules for the scientific nomenclature of algae, fungi and plants.

History of traditional medicine

The knowledge of traditional medicine that has been passed down to us from previous generations is closely related to the people's cultures. Each nation has its own traditional medicine systems. The "holistic" approach that integrates medical and psychological therapies is the foundation of traditional medicine systems [1]. The reverse pharmacology strategy is a guide to research the traditional use of phytopharmaceuticals in a specific population for screening natural products. This approach saves time and costs in drug development [reviewed in 21]. Traditional use could have the same value as a case series or a poor-quality cohort and case-control study [21]. Modern ethnopharmacological research involves the study of written historical sources for knowledge about the use of plants in different cultures around the world. The growing evidence of the rational basis and pharmacological relevance of many of the remedies described in these sources demonstrate the value of using historical texts as a starting point for searching for new medicines. Despite some potential pitfalls associated with the study of historical texts, many researchers believe that comparative analysis of these texts helps provide new insights into the use of plants and the development of relevant medical systems. It bears noting that identifying a plant or herbal substance and interpreting symptoms or diseases are also the most important steps in the ethnopharmacological analysis of historical texts [1].

The historical approach to traditional medicine and ethnopharmacology helps preserve the local or indigenous knowledge of each culture, protect the rights of the holders of traditional knowledge, and provide important clues to the safety of herbal medicines. Essential requirements for most studies are 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 requirements for most studies [1].

Status of medicinal herbs

Traditional medicine is linked to biodiversity, as local and indigenous peoples and/or healers usually use biological resources for their medicinal uses [1, 22 and 23]. Plants, animals, and microorganisms constitute the raw material of ethnopharmacology. So far, plants have been the main source of active ingredients used in medicines compared to animals. However, the potential biological activity of less than 10% of the world's biodiversity has been evaluated. For example, only about 4-5% of the world's 350,000-400,000 plant species have been studied ethnomedically. Moreover, the geographic distribution of medicinal herbs and the number of commercially used plants vary across continents. Access to the large number of useful natural lead compounds awaiting discovery will present many technical, scientific, social, and legal challenges1.

The destructive impact of ecosystem collapse on human civilization is believed to be no less than that of nuclear war or global warming [3]. Several multifaceted problems and issues have arisen in the context of biodiversity conservation and indigenous peoples' rights to their knowledge and resources [22-24]. The practice of traditional medicine is not immune to the current environmental problems facing the planet, such as the overexploitation of numerous species around the globe. But traditional medicine itself is also known to be implicated in this problem. For example, wild harvesting and over-collecting of plants are of concern in the context of biodiversity conservation. Accordingly, researchers should address the cultural and ecological aspects of the traditional use of plants and animals in traditional medicine [reviewed in 1, 23, and 25]. Because of the importance of medicinal herbs to the environment, we introduce the status of herbs, e.g., whether they are endemic or endangered, as an important factor to be considered in publications on herbal medicines.

Approaches and methods

Iranian and non-Iranian articles published on *A. sativum* were reviewed to investigate the existing gaps in herbal research.

Data source and selection of studies

First, a search limited to Iran was conducted using *Allium sativum* or *Allium sativum* L. in the data source PubMed in a 12-year period ending in 2012. Second, a search not limited to Iran was repeated with the keywords in the previous year (2020/08/21) to compare the status of research gaps in the articles based on searching keywords in two searches.

Included criteria and data extraction

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

Excluded criteria

The reviewed articles or those that did not study the medicinal use of *A. sativum* and letters to the editor were excluded. Two reviewers independently checked the title and abstract of each article to avoid duplication. In the case of duplicate publications, we attempted to extract all available data and relate them to the baseline study.

Evaluation of the reviewed articles

The reviewed articles were evaluated using a three-score system developed by Chan K et al. [15] to assess the

following aspects of the herbs or plant materials: (i) identity of the plants and plant parts used; (ii) processing procedure; and (iii) extraction process. In addition to Chan's scoring system, the status of botanical nomenclature and the history of traditional medicine were also examined in the selected articles.

RESULTS

Searches for the keywords *Allium sativum* + Iran and *Allium sativum* L. + Iran yielded a total of 228 and 47 articles, respectively. After excluding the reviewed articles or articles unrelated to medical use, a total of 144 articles were evaluated [26-169]. In the second search, which was limited to the previous year but not Iran, 447 queries with *Allium sativum* were found. However, when *Allium sativum* L. was used as a keyword, only 94 articles were found. In this case, we decided to evaluate the articles found with *Allium sativum* L. Of these, 32 articles were reviewed using the inclusion and exclusion criteria [170-201]. The information from the reviewed Iranian articles and the articles found by the second search are summarized in Tables 1 and 2, respectively.

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

Botanical nomenclature used in the title/abstract	*Allium sativum* L. was used through the main text	Referring to Persian medicine or the traditional usage	Score (max = 25)	Reference
Garlic	Yes	No	5	25
Garlic	Yes	No	15	26
***Allium sativum*, Garlic**	Yes	No	14	27
***Allium sativum*, Garlic**	Yes	No	12	28
***Allium sativum* 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
***Allium sativum*, Garlic**	Yes	No	14	34
***Allium sativum*, Garlic**	Yes	No	10	35
Garlic	No	No	0	36
***Allium sativum*, Garlic**	No	No	0	37
***Allium sativum*, Garlic**	No	No	11	38
***Allium sativum*, Garlic**	No	No	9	39
Garlic	Yes	No	4	40
***Allium sativum*, 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
***Allium sativum*, Garlic**	No	No	8	46
Garlic	No	No	7	47
***Allium sativum*, Garlic**	No	No	5	48
Garlic	No	No	3	49
***Allium sativum*, Garlic**	Yes	No	0	50
***Allium sativum*, Garlic**	No	No	0	51
Garlic	No	No	0	52
Garlic	No	No	6	53
Garlic	No	No	9	54
***Allium sativum*, Garlic**	Yes	No	9	55
Garlic	Yes	Yes	7	56
***Allium sativum*, Garlic**	No	No	7	57
Garlic	No	No	0	58
Garlic	No	No	11	59
***Allium sativum*, Garlic**	No	No	11	60

Garlic	No	No	11	61
***Allium sativum*, Garlic**	Yes	No	8	62
Garlic	No	No	8	63
Garlic	Yes	No	7	64
***Allium sativum*, Garlic**	No	No	5	65
Garlic	No	No	3	66
Garlic	No	No	3	67
***Allium sativum*, Garlic**	Yes	No	3	68
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
***Allium sativum*, Garlic**	Yes	No	14	75
***Allium sativum*, Garlic**	No	No	10	76
Garlic	No	No	6	77
Allium sativum	No	No	6	78
Garlic	No	No	3	79
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
***Allium sativum*, Garlic**	No	No	0	85
Garlic	No	No	0	86
Garlic	No	No	0	87
***Allium sativum*, Garlic**	Yes	No	17	88
Garlic	No	No	13	89
Garlic	Yes	No	11	90
***Allium sativum*, Garlic**	Yes	No	10	91
Garlic	No	No	9	92
***Allium sativum*, Garlic**	Yes	No	9	93
***Allium sativum*, Garlic**	No	No	8	94
Garlic	No	No	8	95
***Allium sativum*, 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
***Allium sativum*, Garlic**	No	No	3	101
Garlic	No	No	3	102
Garlic	No	No	2	103
Garlic	No	No	0	104
Allium sativum	No	No	0	105
***Allium sativum*, Garlic**	No	No	0	106
Garlic	No	No	0	107
Garlic	No	No	0	108
Garlic	No	No	8	109
Allium sativum	No	Yes	5	110
Garlic	No	No	5	111
***Allium sativum*, 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
***Allium sativum*, Garlic**	No	No	0	118
Garlic	No	No	0	119
***Allium sativum* L., Garlic**	Yes	No	14	120
***Allium sativum*, Garlic**	Yes	No	10	121
***Allium sativum*, Garlic**	No	No	10	122
Allium sativum	Yes	No	7	123
***Allium sativum*, Garlic**	Yes	No	6	124
***Allium sativum*, 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
Garlic	Yes	No	0	131
***Allium sativum*, Garlic**	No	No	17	132
***Allium sativum*, Garlic**	Yes	No	14	133
***Allium sativum*, Garlic**	No	No	11	134
***Allium sativum* L., Garlic**	Yes	No	9	135
***Allium sativum*, 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
***Allium sativum*, Garlic**	Yes	No	12	143
***Allium sativum*, Garlic**	No	No	11	144
Garlic	No	No	10	145
Garlic	Yes	No	10	146
Allium sativum	Yes	No	8	147
***Allium sativum*, 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
Allium sativum	No	No	16	155
***Allium sativum*, Garlic**	No	No	15	156
Allium sativum	No	No	11	157
Allium sativum	No	No	8	158
***Allium sativum*, Garlic**	No	No	7	159
Garlic	No	No	4	160
Garlic	No	No	3	161
***Allium sativum*, Garlic**	No	No	2	162
Garlic	No	No	0	163
Garlic	No	No	0	164
Garlic	No	No	0	165
***Allium sativum*, Garlic**	No	No	0	166
Garlic	Yes	No	11	167
Garlic	Yes	No	8	168

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

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

Botanical Nomenclature used in the title/abstract	*Allium sativum* L. was used through the main text	Referring to the traditional medicine or the traditional usage	Country	Score (max = 25)	Reference
Allium sativum	Yes	Yes	Sri Lanka	19	169
***Allium sativum*, Garlic**	Yes	No	Brazil	18	170
***Allium sativum*, Garlic**	Yes	No	India	14	171
Garlic	Yes	No	Italy	14	172
***Allium sativum*, Garlic**	Yes	No	Japan	13	173
Allium, Garlic	No	No	Mexico	13	174
Garlic	Yes	No	Japan	13	175
***Allium sativum*, Garlic**	Yes	No	Japan	11	176
***Allium sativum*, Garlic**	Yes	No	Japan	11	177
***Allium sativum*, Garlic**	Yes	No	China	11	178
***Allium sativum*, Garlic**	Yes	No	Japan	8	179
Garlic	No	No	China	8	180
***Allium sativum*, Garlic**	Yes	No	Iran	8	181
***Allium sativum*, Garlic**	Yes	No	China	7	182
Garlic	No	No	China	7	183
***Allium sativum*, Garlic**	Yes	Yes	Indonesia	7	184
Garlic	No	No	Canada	6	185
Garlic	No	No	China	6	186
Garlic	No	No	Korea	5	187
***Allium sativum*, Garlic**	No	No	Saudi Arabia	4	188
Garlic	No	No	Poland	3	189
Garlic	No	No	Tunisia	0	190
***Allium sativum*, Garlic**	Yes	Yes	Australia and China	18	191
***Allium sativum*, Black garlic**	No	No	China	16	192
***Allium sativum*, Garlic**	Yes	Yes	Taiwan	15	193
Garlic	No	No	China	10	194
***Allium sativum*, Garlic**	Yes	No	Korea	10	195
***Allium sativum*, Garlic**	No	No	Iran	9	196
Garlic	No	No	Japan	8	197
Allium sativum	No	No	Indonesia	7	198
***Allium sativum*, Garlic**	Yes	No	Algeria	6	199
***Allium sativum*, Garlic**	Yes	No	United Arab Emirates	4	200

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

Botanical nomenclature

Of the total 144 Iranian publications reviewed, the scientific name of *Allium sativum* L. had been mentioned in the main text of 37 articles (25.7%). In other words, the scientific nomenclature had not been mentioned in the main text in 74.3% of the articles. It is noteworthy that the non-use of scientific nomenclature was also observed in journals with an impact factor of about five. In a review of the botanical nomenclature used in the titles/abstracts of these reviewed articles, *Allium sativum* L. had been mentioned along with garlic in only three articles. In eight reviewed articles, *Allium sativum* had been mentioned alone, and in 45 articles, the name *A. sativum* had been mentioned together with garlic. In comparison, 87 articles had mentioned garlic alone. One article had also mentioned both *Allium* and garlic (Table 1). In addition, Iranian authors had rarely mentioned the Persian generic name of *A. sativum* (Sir) in their publications.

In the 36 articles found by the second search using the keyword *Allium sativum* L. and limited to the previous year but not Iran, *Allium sativum* L. had been mentioned in the

main text of 18 articles reviewed (56.3%). In contrast, in the overview of article titles/abstracts, *Allium sativum* L. had not been mentioned in the titles/abstracts of any of the reviewed articles. In 17 articles, *Allium sativum* had been used together with garlic, and in one article, it had been used together with black garlic. In 11 articles, only garlic had been mentioned. In one of the reviewed articles, *Allium sativum* had been used alone, and in one article, *Allium* had been mentioned together with garlic (Table 2). In some cases, the first letter of the genus *sativum* was written with a capital letter as *Sativum*.

History of traditional medicine

Of the reviewed Iranian articles, only two articles (1.4%) had mentioned the traditional use of *A. sativum* (Table 1) without citing the known historically valid literature76, 139. Similarly, only four of the 32 reviewed articles (12.5%) found in the second search had referred to *A. sativum* as a traditional folk medicine used in Sri Lanka [170], Indonesia [185], Australia and China [192], and Taiwan [195] (Table 2). The history of Iranian traditional medicine or other traditional medicine systems related to historical literature had not been addressed in any of the articles reviewed.

Status of the medicinal herb

A. sativum (Plantae > Asparagales > Amaryllidaceae > Allium) is believed to have originated in Central Asia (Kazakhstan, Uzbekistan, and western China). This was confirmed by phylogenetic analysis based on molecular and biochemical markers, indicating a secondary center of diversity in the Caucasus. Currently, garlic is cultivated worldwide from the equator to latitudes of 50° in both hemispheres [202]. In other words, garlic is not an endangered herb. Therefore, it was not assessed from this perspective in the articles reviewed.

Chan's scoring system

All the reviewed articles were evaluated using Chan's scoring system [15]. The total scores of 144 Iranian articles and the articles published in the previous year are shown in Tables 1 and 2. Of the total 144 Iranian articles reviewed, 44 cases (30.6%) scored zero, 27 articles (18.75%) scored 1-4, 42 articles (29.2%) scored 5-9, 26 articles (18.1%) scored 10-14, and the remaining 5 articles (3.5%) scored 15-17 points (Table 1). In other words, about 97% of the articles scored < 15 points, and about 80% of the articles scored < 10 points.

Of the total 32 articles published in the previous year, one article (3.1%) scored zero, three articles (9.4%) scored 1-4, 13 articles (40.6%) scored 5-9, 10 articles scored 10-14 (31.3%), and five articles (15.6%) scored 15-19 points (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 found in two searches reached the total score of 25.

DISCUSSION

There are various types of traditional and alternative medicine and traditional health practices [1, 22, and 203]. According to reports from the World Health Organization (WHO), about 88% of its member countries have recognized the use of traditional and complementary medicine, and many of them have a national research institute and a national policy on traditional medicine and regulation of herbal medicines. This article highlights some existing gaps in research on herbal medicines, such as the history of traditional medicine and botanical nomenclature, which have a great impact on the validity of results and the speed of drug development.

Based on the current data, previously published research results, and unpublished data, most Iranian researchers do not address the history and traditional uses of the studied herbal medicines in their articles. In fact, with a few exceptions, the history of Iranian traditional medicine, the scholars of Persian medicine, and the plants endemic to Iran have not received adequate attention from researchers, especially Iranian researchers [7,204]. Non-Iranian researchers have only mentioned that *A. sativum* has been used traditionally and have also not cited the historical sources and the related literature. In some cases, Iranian researchers mention the use of the studied herbs in

traditional medicines other than Iranian traditional medicine. Several possible reasons for this need further investigation. For example, Scholars interested in herbal research might not be familiar with the traditional history of a remedy and its historical sources. Furthermore, the journals' guidelines that publish in these areas do not set much store by the historical aspects of the research. The guidelines of the journals have a great influence on the quality and validity of the publications [9].

Traditional and complementary medicine is a recognized healthcare system around the world. Many traditional medicine systems are commonly categorized as Ayurveda, Kampo, traditional Chinese medicine, traditional Korean medicine, and Unani [205]. However, Iranian traditional medicine does not seem to be as well known and carry the cachet of the above. There is also no reference to Persian medicine or its historical influence on traditional medicine in the world in the WHO Traditional Medicine Strategy 2014-2023 [206]. This is while the history of Persian medicine dates back to thousands of years before Christ [reviewed in 207-211]. According to Cyril Elgood, the English medical historian, Greeks adopted the elements of the medical system from Persians that have come to be known as Greek medicine [212]. Hippocrates, the father of medicine, was not uninfluenced by the medical teachings of ancient Iran [213,214]. Simorgh, the legendary bird of Iran, which has occupied a special place in the ancient culture and literature of Iran for more than 2500 years, is also older than some medical symbols of the world and Greece [215,216]. In ancient and traditional Iranian medicine, medicinal herbs and healing methods are prescribed according to each person's characteristics, called temperament and humors of a person [210, 212, 213, 217 and 218]. In other words, traditional Iranian healers believe in personalized medicine in the prevention, diagnosis, and treatment of diseases. In personalized medicine, efforts are made to identify specific biomarkers to determine the best drug and treatment method for each patient [219-221].

The history of Iranian traditional medicine and its scholars are not as well known as that of traditional Chinese medicine and, to some extent, Ayurveda. Ignorance of the Pahlavi language or other ancient Iranian languages has been cited as a reason for neglecting pre-Islamic medicine [212]. John Bernal also states that the contribution of Iranians to science has been underestimated because the books of ancient Iran have been destroyed, and there is no access to sufficient evidence [214]. Considering the importance of a historical view of traditional health care [1, 22, and 23], knowing the historical and cultural background of all types of traditional medicine systems and conducting ethnobotanical and ethnomedical research should be the primary concern of herbalists and traditional medicine activists.

In Iranian folklore, garlic is consumed raw or cooked. Its base oil is also used as a spice in the food industry. Garlic is traditionally used to lower hypertension and hyperglycemia, stimulate appetite, and prevent cholera and typhoid infections. However, the main disadvantage of garlic is its repulsive odor [222].

According to Chan's scoring system, the evaluation of the reviewed articles confirmed the results of previous studies [7, 15] and showed that issues such as plant identification, processing, and extraction methods have not yet attracted attention. None of the reviewed articles, Iranian or non-Iranian, scored the maximum 25 points. In comparison, more than half of the reviewed articles scored < 10, one of the non-Iranian (5%) and 44 of the Iranian (30.6%) reviewed articles scored zero points.

A look at the impact factor of the journals in which the reviewed articles had been published (the mean of the impact factor of the reviewed articles = 1.89, maximum and minimum = 5.80 and 0.349, respectively; the impact factor of 71 journals was zero; data not shown). The peer Chan's evaluation score for each reviewed article also showed that even in high-impact journals, there is no guarantee that important aspects, such as documentation of herbal quality, are adequately addressed, as previously emphasized [7,15]. It is noteworthy that impact factor is already accepted as a benchmark between researchers and scholars despite considerable criticism of it being used as a touchstone against which the quality of journals, the quality of individual manuscripts, and scholars' merits are measured [223-226].

Suggestions for further evaluations and studies

Such time-consuming studies require a thorough review of hundreds of publications. Therefore, to limit the number of articles selected, two time periods with an interval were chosen to select publications on a well-known herb, here *A. sativum*, to show that the majority of herbal publications suffer from some common research gaps, regardless of the time, journals, or research team. Furthermore, we emphasize that in addition to the gaps mentioned above, other issues need to be considered in ethnopharmacological research, including research questions, toxicological assessments, and biological and pharmacological disease mechanisms. These issues were not explored because they are beyond the scope of this paper. However, because they significantly impact the quality and scope of research on traditional and herbal medicines, they are briefly presented below.

Research questions

The starting point of any research project is a research question. Research questions can be categorized as descriptive, predictive, or causal [227]. Although the question guides the study design and influences reporting [228], the question type and the study design are two completely different issues. The results of a study are interpreted provided that a well-defined question is matched with the correct study design and reported correctly [227]. Ethnopharmacological projects may be either applied research or basic research, or a combination of both1. The impact of the nature of the questions and study design on the results of published and ongoing herbal research must be studied by experts.

Toxicological assessments

Medicinal plants and their products must be safe for patients and consumers. Contaminants of herbs and HMP are classified into biological (microorganisms) and chemical (e.g., mycotoxins, heavy metals, and pesticides) contaminants [5], correctly identified medicinal plants with unknown toxicity, misidentified medicinal plants with toxic activity, and unprofessional processing that differs from safe traditional preparation [reviewed in 6]. The last three items again demonstrate the importance of botanical nomenclature and the history of traditional knowledge of herbal medicines, as emphasized in the current study. In addition, the interactions of medicinal herbs with conventional drugs represent another source of herbal toxicity [reviewed in 6]. The quality and safety of the herbs studied and the phytochemical and toxicological evaluations have a significant impact on the quality of the final herbal publications [14]. Quality standards for herbal medicines and HMP have evolved considerably in recent decades [229]. However, some toxicological studies are not feasible for all research teams due to high costs and technical instrumentation.

Biological and pharmacological mechanisms of disease

In a previous study, it was shown that most studies investigated the effects of the studied herbs on some known signs of diabetes, but the biological mechanism of diabetes and diabetes-related complications were not studied in depth [7]. In a proposed encyclopedia of herb-disease, the topics and diseases studied in herbal research were classified into 18 groups [8]. We suggest that specialized and continuous collaboration between physicians, pharmacists, and herbal medicine researchers focusing on the biological and pharmacological mechanisms of diseases will accelerate discoveries and improve the final results of herbal research.

CONCLUSIONS

In order to obtain valid and fruitful results, the essential standards required for the validity and reliability of herbal research should be observed. In the current study, more than 170 articles on *A. sativum* were evaluated, underscoring some existing gaps and topics that are usually not adequately addressed in publications on herbal research and traditional medicine despite their great importance, such as botanical nomenclature, history of traditional medicine, research issues, and biological and

pharmacological disease mechanisms. In addition, the existing valid reference databases for plants, such as IPNI or The Plant List, do not provide all the necessary information for all members of the plant kingdom in one place. The proposed solution was to establish an online database containing all the necessary information and rules.

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Conflicts of interest

The authors declare that they have no conflicts of interest.

Abbreviations

HMP, Herbal Medicines and their Preparation

ICBN, International Code of Botanical Nomenclature

IPNI, International Plant Name Index

WHO, World Health Organization

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Availability of data and materials

All data generated or analyzed as part of this study are included in this article.

Competing Interests

The authors declare that they have no competing interests.

Authors' Contribution

AR participated in the conception and design of the study and contributed to the analysis and interpretation of the data. She wrote the article in collaboration with AA on botanical issues. AA and VP contributed to the data collection from the reviewed articles. All the authors contributed to the critical revision of the manuscript and approved the final manuscript.

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