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An Encyclopedia of Herb-Disease, a Quick Shortcut for Herbal Research: A Comprehension Based on Iranian Herbal Studies

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Abstract

The use of herbal medicine has been faced with a huge welcome by patients and scientists, as well as drug industries. It seems that reducing the time of research, economizing investments with better safety, and conducting high-quality botanical research are essential and indispensable. This study aimed to introduce the first reciprocal herb-disease encyclopedia and to recount some of the salient points of herbal research based on Iranian studies. A search limited to Iran was conducted using 36 search terms in the data banks Pubmed, Scopus, ScienceDirect, Wiley, and SpringerLink up to the end of 2012. Data including the investigated disease(s) and common and scientific names of the investigated herbs were extracted from the titles and abstracts of 1310 articles. Investigated subjects and diseases have been categorized in 18 groups: cancer, cardiovascular, cellular-molecular, embryology, endocrinology, genito-urology, gastrointestinal, gynecology, immunology, infectious, metabolism, mucocutaneous, musculoskeletal, neuroscience, ophthalmology, renal, reproductive, and respiratory topics. Herbs including *Crocus sativus L.*, *Allium sativum L.*, and *Zataria multiflora* Boiss from totally 560 studied herbs were the most studied ones. Only 69 of 560 studied (12.5%) herbs were endemic to Iran. Due to the vast majority of information available for herbs and diseases, an herb-disease encyclopedia comes to the help of herbal researchers and enthusiasts to find that which herb is useful or recommended for which kind(s) of health problems, and/or for the management, pretreatment or treatment of a specific disease or disorders.

Keywords: Encyclopedia; Herbal medicine; Traditional medicine; Research; Iran

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Introduction

The use of medicinal plants in therapy has been known for centuries in every culture and civilization [1,2]. Traditional medicine is an important part of human health care and there is an increasing worldwide demand for botanicals in all countries [1,3]. In other words, patients desire to benefit from the use of complementary and alternative medicine (CAM) such as herbal medicine. However, sometimes they are not informed that herbal therapy, especially over a proven conventional therapy, may be toxic and dangerous [4]. In order to decrease this kind of risks, clinicians and pharmacists need to be informed about herbs and other CAM practices [5,6], especially with their own country endemic, traditional herbs [7].

On the other hand, the drug discovery process is becoming extremely expensive for the pharmaceutical industry. Natural drug discovery based on ethnopharmacology and traditional medicines is becoming an attractive area [8]. Medicinal herbs and related herbal products are important targets of patent claims since they have become of great interest to the international drug and cosmetic industry [1]. However, there are many problems associated with botanicals research, for instance limited data exist on the safety and efficacy of botanical products [7,9]. Therefore, reducing the time of research, economizing investments with better safety and conducting high-quality botanicals research are essential and indispensable. To do this, a quick access to valid information is requisite.

The aim of this article is to introduce a framework for a compendious and reciprocal encyclopedia of herb-disease based on Iranian herbal studies. Such an encyclopedia helps researchers and enthusiasts on herbal medicine to find out that the effects of an herb have been investigated on the treatment of which kind of disease or the management of a particular disease has been examined using which herbs, in a shortest possible time.

Materials and Methods

This review is based on Winslow et al. [4] and WHO [10] definition of herb. A search limited to Iran was conducted using 36 search terms listed in **Table 1** in the data sources PubMed, Scopus, ScienceDirect, Wiley, and SpringerLink up to the end of 2012.

Inclusion and exclusion criteria

All human, animal and *in vitro* studies were included. Review articles, letters to editor, unpublished data such as thesis and published studies from countries other than Iran were omitted. Two reviewers independently examined the title and abstract of each article to avoid duplications.

Data extraction and classification

Data including investigated disease(s), common and scientific names of investigated herbs were extracted from the titles and abstracts of articles. Investigated subjects and diseases have been categorized in 18 groups, including cancer, cardiovascular, cellular and molecular (Cell. Mol.) studies, embryology, endocrinology, genitourology, gastrointestinal (GI), gynecology, immunology, infectious, metabolism, mucocutaneous, musculoskeletal, neuroscience, ophthalmology, renal, reproductive, and respiratory systems **(Table 2)**.

Botanical scientific nomenclature

The appropriate scientific name and endemicity of all herbs introduced in the reviewed articles were validated taxonomically according to Ghahreman and Attar [11], Mozaffarian [12] and www.theplantlist.org [13]. Botanical scientific nomenclatures applied in the reviewed articles were evaluated according to Rivera et al. [14].

Findings

Studied herbs and the aims of the treatments were extracted from the titles and abstracts of 1319 articles written by Iranian scientists and researchers from 1969 up to the end of 2012. Information on the studied herbs including their division, family, scientific names and names used in the reviewed articles, Persian names, and the aims of the studies are shown in **appendix 1**. Totally, the efficacy of 560 herbs belonging to 100 families was studied. Of them, 511 herbs belonging to 77 families were *Angiosperm-dicotyledon* and 49 herbs belonged to *Angiosperm- monocotyledon, Gymnosperm, rhodophyta* (red algae), *phaeophyta* (brown algae), *basidiomycota* (fungi), *and chlorophyta* (green algae) in a descending order **(Table 3)**. *Lamiaceae (Labiatae), Apiaceae (Umbelliferae), Asteraceae (Compositae)* and *Fabaceae (Leguminosae)* were the most studied families with 412, 211, 179 and 75 studies in each, respectively. Most of the studied herbs belonged to *Lamiaceae (Labiatae), Asteraceae (Compositae), Apiaceae (Umbelliferae), Fabaceae (Leguminosae)* with 118, 72, 60 and 38 studied herbs in each, respectively. Among 100 studied herbal families, only one species was studied in 45 families, of them 41 were studied less than 10 times. The herbs including *Crocus sativus L. (Iridaceae), Camellia sinensis (L.) Kuntze (Theaceae), Urtica dioica L. (Urticaceae)* and *Peganum harmala L. (Nitrariaceae)* were the most frequently studied species within 66, 16, 13 and 11studies, respectively. Of 560 studied herbs, the species of 31 studied herbs (5.5%) were not specified in the titles and abstracts of 55 articles. Only 69 of 560 studied herbs (12.3%) were endemic **(Table 4)** and the remained 491 studied herbs (87.6%) were not endemic to Iran. Five herbs (0.9%) including *C. sativus, Allium sativum L. (Amaryllidaceae), Zataria multiflora Boiss. (Lamiaceae) and Nigella sativa L. (Ranunculaceae)* and *Teucrium polium L. (Lamiaceae)* were the most studied herbs with 66, 51, 41, 35 and 27 studies, respectively. The efficacy of *C. sativus* and *A. sativum* was studied on cardiovascular, Cell. Mol., immune, infectious, metabolism, mucocutaneous, neuroscience and renal systems. *C. sativus* was also examined in embryology, genitourinary, gynecology, musculoskeletal and respiratory systems. Cancer, GI and ocular system were additional aims for research on *A. sativum*. The effects of *Z. multiflora, N. sativa* and *T. polium* were also studied on the same items. The herbs were studied one time in 295 (52.7%) herbs, 2 to 9 times in 236 (42.1%) herbs and 10 to 21 times in 24 (4.3%) **(Appendix 1)**.

Appendix 2 shows the herbs studied for the management of the investigated subjects and diseases in each category. The efficacy of most herbs was investigated in infectious system, metabolism, neuroscience, Cell. Mol. and immunology with 289, 218, 122, 115 and 92 studied herbs in each, respectively **(Table 2)**.

Features and Limitations of our Study

Our study is focused on Iranian research on herbal medicine up to the end of 2012. Data were extracted from titles and abstracts without any evaluation according to available scoring systems [15] and were not checked with the information in the full text of

Table 1 Search terms used in combination with Iran to find Iranian studies investigating herbal medicines in the management of different aspects of health and disease.

Botanical, medicine	Herb, pharmaceutical	Herbalism	Plant, pharmaceutical
Botany, medicinal herb	Herb, pharmacodynamic	Herbalism, medical	Plant, pharmacodynamic
Botany, medicinal plants	Herb, pharmacokinetic	Herbology	Plant, pharmacokinetic
Flora, medicinal	Herb, pharmacology	Medicinal, vegetation	Plant, pharmacotherapy
Folk, medicine	Herb, pharmacotherapy	Phytomedicine	Plant, pharmacy
Galenical	Herb, pharmacy	Phytopharmacy	Plant, remedy
Herb, drug	Herb, remedy	Phytotrapy	Plant, medicinal
Herb, medicinal	Herbage, medicinal	Plant, drug	Plant, pharmacology
Herb, narcotic	Herbal, medicine	Plant, narcotic	Traditional medicine

Table 2 A categorization of issues investigated in 18 subjects and diseases studied by Iranian herbal researchers.

Category	Number of herbs (studies)	Subject
Cancer	46 (35)	adhesive property; anticancer, antitumor and antiproliferative effects; cancerogenesis; cell adhesion; chemopreventive effects, tumor growth
Cardiovascular system	49 (69)	angiogenesis; antiangiogenic, antihemolytic, antihypertensive and antihypoxic effects; cardiac cell injury; cardiotoxicity; cardioprotective; cardiovascular; fibrinolytic, hypotensive and vasodilator effects; arterial blood and oxygen pressure; atherosclerosis; biochemical blood parameters; blood platelet adhesion, aggregation and secretion; heart failure; coronary vasodilatation; fatty streaks; hematological and hemolytic indices; ischaemic arrhythmias; isolated heart activity; myocardial ischemia-reperfusion; myocardial oxidative damage; normotensive and hypertensive; reactivity of isolated aorta
Cell Mol study	115 (141)	allelopatic and cytotoxic effects; antigenotoxic effects; apoptosis; cell cycle arrest; cell cycle analysis; cell viability ; cell death; differentiation; DNA damage; enzyme activity/ inhibition; fibrillation of apo-alpha-lactalbumin; gene expression and regulation; lead toxicity; karyorrhexis; microtubule assembly; mutagenicity; necrosis; nucleic acid synthesis; piknosis; radioprotective effects; teratogenicity
Embryology	4 (4)	embryotoxicity; fetal development; microstructure of placenta
Endocrine system	6 (7)	antiandrogenic and antihirsutism effects; endocrinotoxicity; levels of hormones
Genitourinary system	11 (17)	erectile dysfunction; gonadal and sex hormone levels; impotence; semen quality; sexual behaviors; sexual impairment; spermatogenesis; sperm quality; sperm parameters
GI	58 (69)	antispasmodic and anti-diarrhoeal effects; aphthous stomatitis; aphthous ulcers; coeliac disease; colitis; delayed gastric emptying; gastric acid and pepsin secretions; gastric irritation; gastric ulcer; gastroprotective effects; heaptotoxic and hepatoprotective effects; ileum antispasdomic effects; ileum contractions; Ileal relaxation; iron absorption; liver cirrhosis; liver injury; nausea and vomiting in pregnancy; oral toxicity; pancreatitis; pediatric functional constipation; peptic ulcer; salivation; sclerosing cholangitis; small intestinal damage; spasmogenic activity in small intestine; steatohepatitis; stoma care; stomach and intestinal disorders; stomatitis
Gynecology	21 (34)	abortifacient effects; amenorrhea; dysmenorrhea; estrus Cycle; menstrual bleeding; milk Production; ovarian cysts; pregnancy; nausea and vomiting in pregnancy; premenopausal, perimenopausal, menopausal and postmenopausal symptoms; premenstrual syndrome; striae gravidarum in pregnancy; uterine bleeding; uterus contraction
Immunology	92 (116)	acquired immune deficiency syndrome; allergic inflammation; allergic Rhinitis; anti-Behçet armamentarium; antihistaminic effects; anti-inflammatory and anti-pyreticeffects; autoimmune encephalomyelitis; bowel inflammation; inflammatory bowel diseases; irritable bowel syndrome; chronic rhinosinositis; colitis; immunologic colitis; complement activity; cytokine release and pattern; denture stomatitis; dermatitis; diaper dermatitis; immune responses; humoral immunity; antibody production; immunoinhibitory, immunomodulatory and effects; immunotherapy; inflammation; inflammatory biomarkers; inflammatory diseases; innate immunity; lung inflammation; allergic airway inflammation; lupus nephritis; mucositis; multiple sclerosis; oral allergy syndrome; osteoarthritis; pancreatitis; peritoneal macrophages activity; rhinosinusitis; steatohepatitis
Infectious system	289 (308)	anthelmintic effects; antibacterial, antifungal, antimicrobial, antiprotozoal and antiviral effects; anti-Leishmanial effects; leishmaniasis; anti-malarial and antiplasmodial effects, malaria; bioactivity; biological activity; biofilm formation; fermentation parameters; hydatid cyst; hydatid cyst protoscolices; larvicidal activity; microbial mortadella sausage; multidrug-resistancy; necrotic dermatitis; preventing sepsis
Metabolism	218 (295)	antiglycating effects; antioxidative effects; free-radical-scavenging properties; bioenergetic status independently of age; biological properties; bone mineralisation; bone strength; bone turnover indicators; cartilage thickness; diabetes and related complications; blood glucose; insulin release; insulin resistance; nasal absorption of insulin; dyslipidemia, hypercholesterolemia, hyperglycemia, hyperlipidemia; histological changes of pancreatic beta-cells; hypoglycemic effect; hypouricemic effects; LDL oxidation; metabolic syndrome; obesity; oxidant-related diseases; removal of cadmium ions; resting energy expenditure; safety evaluation; serum levels of bilirubin, cholesterol, creatinine, glucose, iron, lipids, lipoproteins, nitrogen and urea
Mucocotaneous system	34 (47)	acne vulgaris; alopecia areata; anti-keloid armamentarium; antiplaque effects, dental biofilm; dental caries, dental plaque, gingivitis, gingival disease, periodontal diseases; antisolar and moisturizing activities; burn wounds;Skin lesions ; wound healing effects; dermal toxicity; dermatology; dermatophytosis; eczema; mouthwashes; nipple crack, nipple sore; non-healed ulcers; oral aphthous lesions; oral lichen planus; periodontal disease; peristomal skin lesions; pityriasis versicolor; psoriasis vulgaris

Musculoskeletal system	7 (7)	chondrogenesis and osteogenesis; chondroprotective effects; ischemia-reperfusion in skeletal muscle; knee joint; muscle relaxant effects
Neuroscience	122 (217)	acute stress; Alzheimer's disease; amnesia; analgesic, anesthetizing, anticonvulsant and antinociceptive effects; anorexia; anti-cholinergic and anticholinesterase effects; anticholinergic effects; antidepressant effects; depression; attention-deficit/ hyperactivity disorders; autistic disorders; brain injury; spinal cord injury; cerebral ischemia-reperfusion injury; carpal tunnel syndrome; epilepcy, epileptic seizures, seizures; hippocampal neurites; hyperalgesia and motor nerve conduction velocity; learning and memory, recognition; migraine headache; morphine analgesic tolerance, morphine antinociceptive tolerance, morphine dependence, morphine withdrawal syndrome, opiates withdrawal; motor coordination; neurodegenerative disorders; neuronal hyperexcitability; neuroprotective effects; neurotoxicity; obsessive-compulsive disorder; pain; pentobarbital hypnosis; sedative, hypnotic and anxiolytic effects; antianxiety effects; anxiety; preoperative anxiety; hypnotic effect; sleep-prolonging effect
Ophthalmology	4 (4)	cataract; cataractogenesis; corneal neovascularization; ocular abnormalities; ocular toxicity; uveitis;
Renal system	28 (34)	diabetic nephropathy; diuretic effect; hemodialysis patients; kidney calculi; kidney disease; morphometric indices of kidney; nephroprotective effects; nephrotoxicity; nephrolithiasic; peritoneal dialysis patients; renal ischemia; renal reperfusion injury; renal transplant recipients; renal-transplanted patients; urinary clearance of nicotine; urolithiasis ; antiurolithic (antiurolithiatic) effects
reproductive system	12 (15)	antifertility effects; fertility; maturation of oocytes; offspring sex ratio; reproduction stimulatory properties; reproductive and neurobehavioral end points; reproductive indices; reproductive system; reproductive tract histology; testicular damages
Respiratory system	16 (32)	antitussive effect; asthma; antiasthmatic effect; bronchodilatory effect; cough associated with ACE inhibitors; histamine (H(1)) receptors of tracheal chains; hypoxia; lung injury; lung lavage; lung pathology and lung inflammation; pulmonary fibrosis; respiratory symptoms and pulmonary function tests; tracheal chains; tracheal muscle responsiveness

Table 3 Division, number of families, total studies, number of studied herbs, number of endemic and unknown species per division of studied herbs in Iranian herbal research.

Division	Number of families	Total studies/ division	Number of studied herbs/ division	Number of endemic	Unknown species
Angiosperm- Dicotyledon	77	1469	511	66	28
Angiosperm- Monocotyledon	10	194	25	3	1
Gymnosperm	5	30	13	-	1
Monilophytes	3	5	4	-	-
Thallophyta	5	7	7	-	-
Total	**100**	**1705**	**560**	**69**	**30**

the reviewed articles. Accordingly, the beneficial or side effects of the studied herbs were not reviewed. However, we think our categorization gives a good point of view to researchers and scientists to have a concurrent glance to diseases and recommended herbs for them in traditional medicines. Thus, the benefits and importance of a reciprocal encyclopedia of herb-diseases can be seen.

From an Herb-disease Encyclopedia to an Herb-disease Database

An herb- disease encyclopedia comes to the help of herbal researchers and enthusiasts to find that a desired herb is useful or recommended for which kind(s) of health problems, and/or the management, pretreatment or treatment of a specific disease or disorders has been examine using which herb(s) or herbal product(s). Information on the history of traditional uses of herbs or traditional management of known health problems can be included as well. As mentioned earlier, due to the vast amount of information available for herbs and diseases, it is worth to emphasize that a comprehensive database in which the valid and assessed results of herbal research on various aspects of diseases are updated in detail is an ideal tool to increase the efficiency of research and to shorten the way of the herbal management and control of diseases [7]. The authors are currently working on the schema of an ideal herbal database, which will be published in future.

Recounting Some of the Salient Points of Herbal Research

Knowing the gaps in studies and research, including research on medicinal herbs is of value to find out suitable guideline and policy for defining an efficient research. In our pervious review, the efficacy of medicinal herbs on the management of different aspects of diabetes mellitus (DM), including parameters in DM, pharmacological mechanisms, and the effects on the functions of organs were collected and compared **(Table 4)** [7] here, we showed that some important aspects of DM other than the blood glucose and HbA1C levels were not considered in both Iranian and non-Iranian herbal research. We think that providing and improving such a standard framework for diseases and health problems help herbal researchers to design their studies according to unexamined items which are also appropriate to

Table 4 Division, family, scientific name and Persian name of studied herbs endemic to Iran extracted from Iranian herbal research.

Division	Family	Scientific name	Persian name
Angiosperm-Dicotyledon	Apiaceae (Umbelliferae)	Dicyclophora persica Boiss.	Chatr gorzi
		Diplotaenia damavandica Mozaff., Hedge & Lamond	Kozal
		Echinophora cinerea (Boiss.) Hedge & Lamond	Khosharizeh kuhestani
		Echinophora platyloba DC.	Khosharizeh
		Ferula persica Willd	Koma, Barijeh, Anghouzeh
		Haussknechtia elymaitica Boiss.	Johour
		Heracleum rechingeri Manden.	Golpar
		Kelussia odoratissima Mozaff.	Karafs e bakhtiari
		Narthex asafoetida Falc. ex Lindl. (syn: Ferula asafoetida H.Karst.)	Koma, Barijeh, Anghouzeh
		Semenovia tragioides (Boiss.) Pimenov & V.N. Tikhom.	-
	Asteraceae (Compositae)	Achillea kellalensis Boiss. & Hausskn.	Boumadaran
		Achillea talagonica Boiss.	Boumadaran
		Cirsium bracteosum DC.	Kangar bargedar
		Tanacetum budjnurdense (Rech. f.) Tzvelev	Mina-e bojnurdi
		Tanacetum sonbolii Mozaff.	Mina
	Boraginaceae	Alkanna frigida Boiss.	Shangar
		Onosma bulbotrichum DC.	Zangulei
	Buxaceae	Buxus sempervirens subsp. hyrcana (Pojark.) Takht. (syn: Buxus hyrcana Pojark.)	Shemshad
	Euphorbiaceae	Euphorbia hebecarpa Boiss.	Farfioun
		Euphorbia kopetdaghi (Prokh.) Prokh. (syn: Euphorbia aellenii Rech.f.)	Farfioun
	Fabaceae (Leguminosae)	Astragalus gypsocola Maassoumi & Podlech	Gavan
		Astragalus stepporum Podlech	Gavan
		Oreophysa microphylla (Jaub. & Spach) Browicz	Niam hobabi
		Parkinsonia aculeata L.	Darman aghrab
	Grossulariaceae	Ribes khorasanicum Saghafi & Assadi	Angur farangi
	Lamiaceae (Labiatae)	Ajuga chamaecistus subsp. tomentella (Boiss.) Rech.f.	Lobdisi
		Dracocephalum kotschyi Boiss.	Badranjbuyeh
		Dracocephalum polychaetum Bornm.	Badranjbuyeh
		Dracocephalum surmandinum Rech.f.	Badranjbuyeh
		Hymenocrater yazdianus Rech.f.	Gol-e ervaneh
		Lagochilus hispidus (Bél.) Fisch. & C.A.Mey. (syn:Lagochilus kotschyanus Boiss.)	Lob khargushi
		Nepeta crispa Willd. (syn:Nepeta asterotricha Rech.f.)	Pune sa
		Nepeta menthoides Boiss. & Buhse	Puneh sa
		Phlomis anisodonta Boiss.	Goush barreh
		Phlomis olivieri Benth.	Goush barreh
		Phlomis persica Boiss.	Goush barreh
		Rydingia persica (Burm.f.) Scheen & V.A.Albert (syn: Otostegia persica (Burm.f.) Boiss.)	Golder
		Salvia eremophila Boiss.	Maryam goli
		Salvia hypoleuca Benth.	Maryam goli
		Salvia lachnocalyx Hedge	Maryam goli
		Salvia mirzayanii Rech.f. & Esfand.	Maryam goli

Angiosperm-Dicotyledon	Lamiaceae (Labiatae)	Salvia reuteriana Boiss.	Maryam goli
		Salvia sahendica Boiss. & Buhse	Maryam goli
		Satureja bachtiarica Bunge	Marzeh bakhtiari
		Satureja intermedia C.A. Mey.	Marzeh taleshi
		Satureja khuzistanica Jamzad	Marzeh khuzestani
		Satureja sahendica Bornm.	Marzeh sahandi
		Stachys acerosa Boiss.	Sonbolei
		Stachys laxa Boiss. & Buhse	Sonbolei
		Stachys obtusicrena Boiss.	Sonbolei
		Stachys subaphylla Rech.f.	Sonbolei
		Teucrium persicum Boiss.	Maryam nokhodi shirazi
		Thymus carmanicus Jalas	Avishan kermani
		Thymus daenensis Celak.	Avishan denaei
		Thymus migricus Klokov & Des. Shost.	Avishan azarbaijani
		Thymus persicus (Ronniger ex Rech.f.) Jalas	Avishan irani
		Thymus trautvetteri Klokov & Des.-Shost.	Avishan taleshi
		Zhumeria majdae Rech.f. & Wendelbo	Mohr-e khosh
	Linaceae	Linum persicum Boiss.	Katan
	Malvaceae	Alcea hyrcana Grossh.	Khatmi
	Moringaceae	Moringa peregrina (Forssk.) Fiori	Gaz roghani
	Polygonaceae	Polygonum hyrcanicum Rech.f.	Alafee haftband
	Primulaceae	Dionysia termeana Wendelbo	Aroos-e sang
		Primula heterochroma Stapf	Pamchal
	Rosaceae	Geum iranicum Khat.	Alaf-e mobarak
	Rutaceae	Haplophyllum canaliculatum Boiss.	Sodaby
Angiosperm-Monocotyledon	Amaryllidaceae	Allium elburzense Wendelbo	Piaz alborzi
		Allium jesdianum Boiss. & Buhse	Piaz Yazdi
		Allium stipitatum Regel (syn: Allium hirtifolium Boiss.)	Mousir

their fund. It is clear that being familiar with the traditional uses of medicinal herbs is a prerequisite for experimental designing. Furthermore, as others and we have raised [7] journals need to define unanimous guidelines with emphasis on criteria such as botanical scientific nomenclature, the quality and safety of herbs, phytochemical, pharmacological and toxicological information to improve the validity and quality of the final publications.

Discussion and Conclusion

The most obvious finding is the little attention to endemic herbs to Iran in Iranian research, whereas Iran is a country with a known ancient history in traditional medicine, as well as diverse and rich vegetation. Endemic plants are unique genetic resources which worth further investigation. As we found, most herbs (52.7%) were studied once and the research on them was discontinued. Infectious system was the most investigated area (23.3% of reviewed studies) of Iranian herbal research. Despite the worldwide importance of infectious diseases, we believe that most common health problem of a society should be a priority. As well as, due to the widespread and popular use of herbal medicines, medical staffs should be familiar with traditionally used herbs, including endemic ones. Accordingly, it is expected that herbal researchers prioritize ethnopharmacological research on medicinal herbs, especially endemic ones which are traditionally used in their own country [7]. However, considering the time and expenditure that are spent to such studies, it is crucial to find reasons and motivations of designing such herbal research.

The finding 560 herbs were studied and that most of them possibly have beneficial effects is very promising. None of the five most studied herbs, including *C. sativus, A. sativum, Z. multiflora, N. sativa* and *T. polium* were endemic to Iran. *C. sativus* and *A. sativum* are among most known medicinal herbs with available phytochemical information [7]. Information collected in **Appendix 1** makes it easy to define a research study; however, it is recommended that general considerations for herbal research, as well as specific issues for studies on a specific disease [7] in addition to the history of traditional usages of desired herb(s) are carefully examined from the beginning of an experiment to the end. Botanical scientific nomenclature is another critical case that should never be overlooked [14].

It was interesting for us that most reviewed herbs (95.7%) belonged to angiosperms, possibly due to their vast diversity and geographical distribution. Biogeographers and evolutionary biologists are also surprised with the dramatic rise in the abundance of angiosperms around the world. Various parameters have been hypothesized that play important roles during the early and later stages of angiosperm expansion, as well as the slowdown in the diversification of gymnosperms [16-19]. Perhaps, phytochemical and metabolome comparison between herbs from different plant kingdoms provides more evolutionary clues other than geographical distribution and diversification for more medicinal utilization of angiosperms. It has been reported that chemometric analyses such as reversed-phase high-performance liquid chromatography and biochemical markers can be used for

analyzing and classifying intra-specific genetic relationship of plant populations [20,21]. Nowadays, scientists are encouraged to bioinformatics technics and the omics-based approaches in traditional medicine and ethnomedicine studies [22-25] which can be of help to manage the herbal research as large-scale data-rich studies.

Clearly, there is still much to be done to discover the appropriate herbal medicine for the treatment and management of diseases due to the exhausting labor of the investigation on items such as the quality, safety, side effects, toxicity, and pharmacological mechanism for each herb. However, appropriate mechanisms, including standard frameworks for different aspects of diseases and pharmacological mechanisms of medicinal herbs, as well as a specialized database for herbal medicine can be defined to make easier overcoming such obstacles.

Finally, to compensate some features such as industrialization that seems unlikely to be omitted from new human modern life, the human kind restored to use traditional medicine for maintaining his/her health. However, every day more than over, it is needed to admit seriously that the lifestyle is the most effective and appropriate way for maintaining health by the prevention and management of diseases. According to an Iranian proverb, prevention is better than treatment.

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