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REVIEW ARTICLE

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Anti-hypertensive plants of rural Pakistan: Current use and future potential

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ABSTRACT

Aim/Background: Hypertension is surging around the world and negatively affecting lives and livelihoods along its way. This plight is felt especially hard by the world's rural population in developing nations, where many barriers to medical care exist. These barriers can exhibit themselves as monetary or distance barriers. In Pakistan, where barriers to medical care caused by the remoteness and financial hardship are strong, people have drawn on traditional medicinal plants to treat this plight of hypertension.

Materials and Methods: In this review, we assess the interface between hypertension and plant-based medicine among a population with limited health care access. We queried the scientific databases of Google Scholar, PubMed, Scopus, and Web of Science for the search terms: "medicinal plants of Pakistan, ethnobotany of Pakistan, and anti-hypertension plants of Pakistan".

Results: This search revealed about 114 species that are used to combat hypertension in Pakistan. It also showed how the majority of species are harvested from sustainable aerial plant parts or leaves.

Conclusion: The promotion of cultivation and validation studies may prove promising for these remedies that people in need of health care turn to.

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Hypertension; medicinal plants; anti-hypertensive activity; traditional uses; Pakistan

Introduction

Hypertension deteriorates patient health, and it is a dangerous risk factor for death [1–3]. Currently, hypertension affects over a quarter (26.4%) of the global adult population, and it is projected to increase [4,5]. This prevailing risk factor of hypertension led to 12.8% of deaths worldwide in 2004, and a daunting 92 million disability-adjusted life years and 7.6 million premature deaths in 2001 [6,7]. A major cause of uncontrolled hypertension is poor patient compliance. The World Health Organization (WHO) estimates that 50–70% of the hypertensive patient population does not take their anti-hypertensive medication as prescribed [8]. Hypertension, especially uncontrolled hypertension, severely elevates the risk of cardiovascular disease, ischemic heart disease, stroke, and kidney failure [9–12]. The decline in health and longevity, the potential of medical emergencies, and the projected increase in hypertension show the burden of hypertension in the world.

In Pakistan, hypertension is a significant health problem that has taken root. Over 28% (male 28.8% and female 28.0%) of adults over the age of 25 have hypertension [13]. This has increased since the early 1990s, when the percentage of hypertension in rural areas was 16.2% and that in urban areas was 21.6% [14]. Overall, Pakistan is an unfortunate world leader in the number of people who have hypertension. Interestingly, it is also a country where there is a strong presence and use of ethnobotany—especially regarding medicinal plants

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[15]. In all, Pakistan serves as an excellent region of the world, to study the interface of hypertension and plant-based remedies.

Medicinal plants as part of traditional remedies play an intricate part of human health care. Molecular evidence shows that even Neanderthals made use of medicinal plants [16–18]. Modern humans also have treated, and continue to treat, diseases with medicinal plants in the form of traditional medicine. Although percentages of traditional medicine use around the globe are difficult to pinpoint, estimates show that the majority of the population in developing nations consistently rely on traditional medicine and a large percentage, just under 50%, of the population in many developed nations, have incorporated traditional medicine into their personal health care [7,19,20].

The development of many synthetic drugs has been originated from plant compounds. Seventy-five percent of the drugs have been approved for infectious diseases between 1981 and 2002 that are originated from natural sources [21]. Additionally, some estimates show that about 25% of modern medicines has originated from tropical forest plants, and out of these, 74% were derived from plants with traditional herbal medicine use [22]. It is worth noting that out of the estimated 3,50,000 plant species on earth [23,24], about 50,000 species are used for medicinal purposes [25]. Thus, searching for new, active compounds in plants can be seen as a productive strategy for drug development [26]. Interestingly, herbal remedies are often believed to be safer than synthetic drugs [27,28]. Further, price often hinders the availability of synthetic drugs [29]. Thus, patients, including many low-income patients, may seek out and use local and traditional treatments.

In Pakistan, a large majority of the population seeks and relies on traditional medicine such as herbal medicine [30]. Significantly, out of the 6,000 flowering plants in the country, 400–600 plants are considered medicinally important [31]. Of these, many are traded both locally and on national and international markets [32].

A number of studies on medicinal plants used in the management of hypertension in different parts of the world exist [1,12,33–43], as well as in Pakistan [44–52]. In this review, we aim to analyze, identify, and describe the species and plant parts harvested for the treatment of hypertension throughout Pakistan. We do this to reveal the interplay between populations with hypertension, who, at the same time, experience monetary barriers to medical treatment.

Material and Methods

We conducted a systematic search of the literature regarding anti-hypertensive medicinal plant species in Pakistan. For this, we queried the scientific databases of Google Scholar, PubMed, Scopus, and Web of Science for the search terms: medicinal plants of Pakistan, ethnobotany of Pakistan, and "anti-hypertensive plants of Pakistan". For extra rigor, we also queried these same terms in a general search engine, Google. All pertinent articles up to December 2017 were reviewed.

In this review, we follow current taxonomy and naming of species as found in the International Plant Names Index (www.ipni.org) and The Plant List (www.theplantlist.org). We arranged and categorized species by botanical family, growth form, status, and locality.

Result

Quantitative review of ethnomedicinal plants used for hypertension

Our review is based on the publications found on Web of Science, Google Scholar, Scopus, and PubMed up to 2017 with the term "medicinal plants of Pakistan, "ethnobotany of Pakistan" or "anti-hypertensive plant of Pakistan" in the title", which resulted in 902 studies in the past 27 years (**Table 1**).

Table 1. Database with accompanying range of years and search terms.

Database	Search term	Range of year	Total articles	Selected articles
Web of Science	"Anti-hypertensive plants in Pakistan"	1990–2018	221	12
	"Ethnobotany of Pakistan"	2000–2018		25
Google Scholar	"Anti-hypertensive plants of Pakistan"	1990–2017	415	30
Scopus	"Anti-hypertensive plants of Pakistan"	1990–2018	156	8
	"Ethnobotany of Pakistan"	2000–2018		25
PubMed	"Anti-hypertensive plants of Pakistan"	2016–2017	110	7
	"Ethnobotany of Pakistan"			17
Google		1990–2016		16

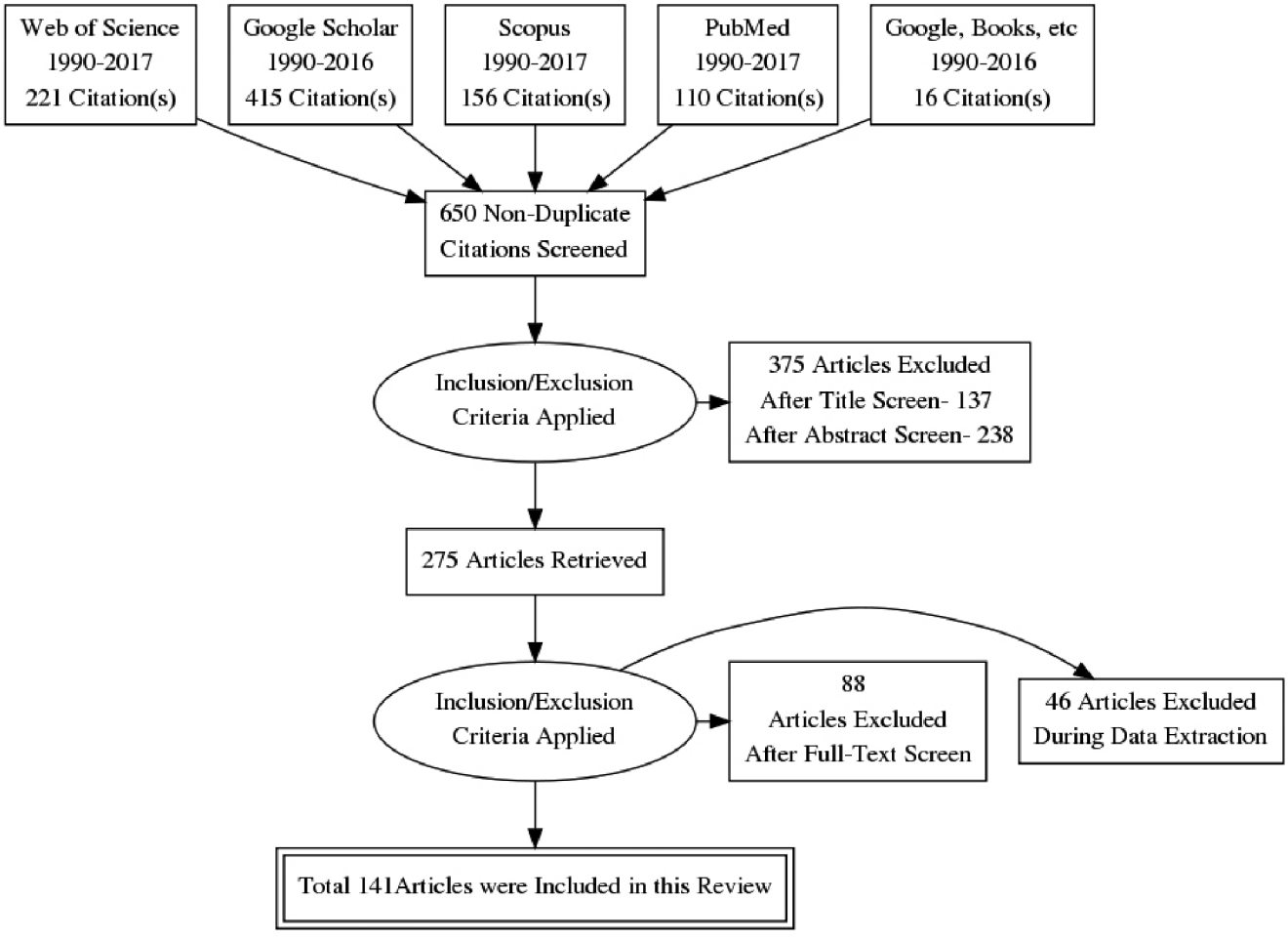

Figure 1. A flow of information through the different phases of a systematic review.

We omitted published studies outside the focus of our aim. After reading the abstracts and keywords of published articles; by focusing only on articles pertaining to hypertensive activities, medicinal plants used to treat hypertension, or ethno-botanical studies which show the species was against hypertension. This reduced the sample articles to 141 publications. Most articles were selected from Scopus; followed by Google Scholar, and Web of Science. Figure 1 represents the different phases of our methodology for our review article.

The spatial distribution of medicinal plants use for hypertension in Pakistani regions shows that the northern regions of Pakistan like Malakand Division (Dir, Swat, Chitral, Kohistan, and Buner), Hazra Division (Abbatabad, Mansehra, and Battagram), Azad Kashmir, and Gilgit-Baltistan have the most studies (Fig. 2). We suspect that this is due to the rich floristic diversity in the northern regions of the country.

Taxonomic diversity of medicinal plant

In this review, we identified 114 medicinal plant species belonging to 97 genera, and 55 botanical families that are used to treat hypertension in Pakistan (Table 2). Additionally, the frequency of citation, growth form, status, part used, and location are given (Table 2). The most dominant botanical families with more cited species included Lamiaceae (14 species), followed by Asteraceae (7 species), Apiaceae (6 species), Fabaceae (5 species), Amaryllidaceae (4 species), Myrtaceae and Brassicaceae (4 species), Poaceae (3), Solanaceae (3 species), Linaceae, Amaranthaceae, Rosaceae, Papaveraceae, Ranunculaceae, Asclepiadaceae, Chenopodiaceae, Oleaceae, Verbenaceae, Zingiberaceae, Zygophyllaceae, Scrophulariaceae, and Euphorbiaceae (2 species), while the rest of the families have one cited species each (Fig. 3).

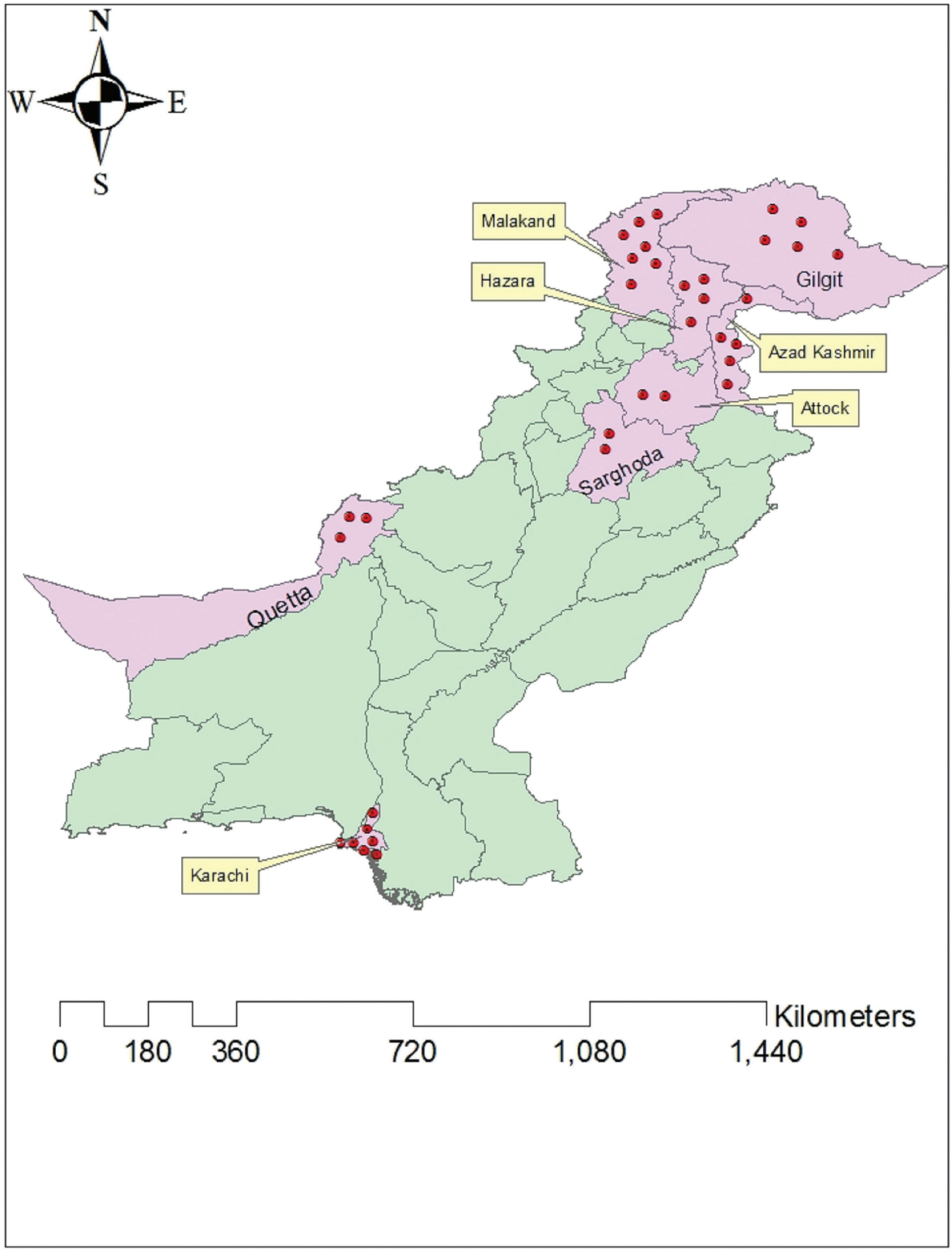

Figure 2. Geographical distribution of case studies of Pakistan in the review, red dots shows the number of anti-hypertensive case studies per division.

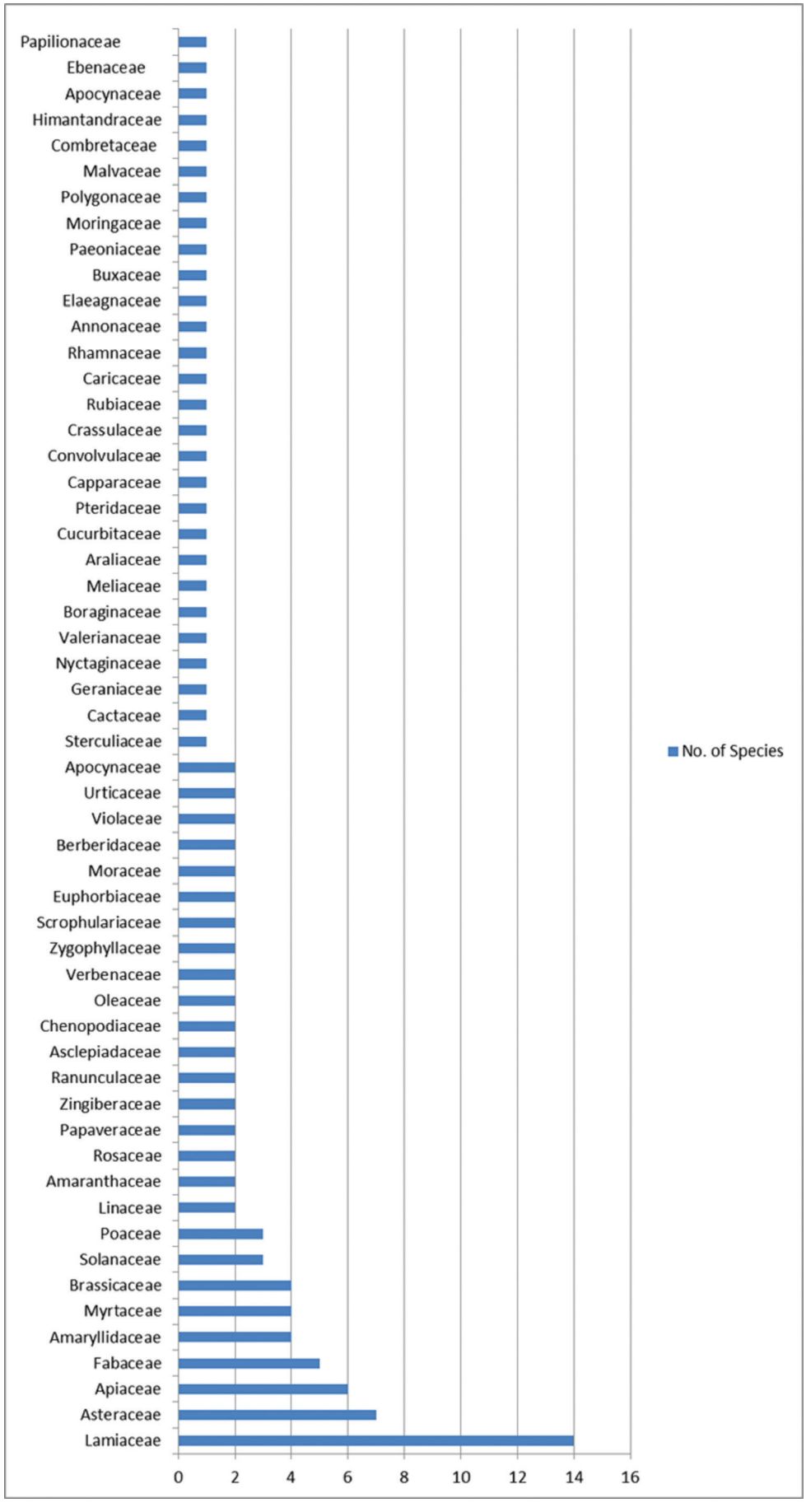

Figure 3. Number of plant species in across families.

Table 2. Ethnomedicinal plants used to relieve hypertension in Pakistan.

Family	Plant name	Growth form	Status	Part used[a]	Study area[b]	References
Lamiaceae	*Salvia bucharica* Popov	Herb		Lv, Fl	Kalat and Khuzdar, Baluchistan	[53]
	Otostegia limbata Benth. ex Hook.f.	Shrub	Wild	R, Lv	Dir, KPK	[52]
					Allai Valley	[54]
	Origanum vulgare L.	Herb	Wild	AP	Dir, KPK	[52]
	Ocimum basilicum L.	Herb	Cultivated	Lv	Dir, KPK	[52]
					Swat, KPK	[55]
	Lavandula stoechas L.	Herb	Wild	AP	Karachi, Pakistan	[56]
	Mentha viridis (L.) L.	Herb	Wild Cultivated	AP	Dir, KPK	[52]
	Mentha longifolia (L.) L.	Herb	Wild	AP		[109]
	Isodon rugosus (Wall. ex Benth.) Codd	Shrub	Wild	Lv	Bugrote valleys, Gilgit	[57]
				Lv	Toli Peer, Azad Kashmir	[114]
	Teucrium stocksianum Boiss.	Herb	Wild	WP	Dir, KPK	[52]
	Lamium album L.	Herb	Wild	YS, Lv	Swat, KPK	[58]
	Ajuga bracteosa Wall. ex Benth.	Herb	Wild	WP	Dir, KPK,	[52]
					Swat, KPK	[59]
					Leepa Valley, Azad Kashmir	[60]
				Lv	Kotli, Azad Kashmir	[115]
					Swat, KPK	[55]
					Swat, KPK	[61]
	Ajuga parviflora Benth.	Herb	Wild	Lv	Swat, KPK	[55]
	Mentha longifolia (L.) L.	Herb	Wild	WP	Dir, KPK	[52]
					Mastung, Baluchistan	[62]
	Nepeta erecta (Royle ex Benth.) Benth.	Herb	Wild	Fl	Toli Peer, Azad Kashmir	[114]
Asteraceae	*Inula royleana* DC.	Herb	Wild	R	Batagram, KPK	[63]
	Artemisia annua L.	Shrub	Wild	Lv	Dir, KPK	[52]
	Achillea millefolium L.	Herb	Wild	AP	Karachi, Sindh	[64]
	Cichorium intybus L.	Herb	Wild	Se, AP	Dir, KPK	[52]
	Artemisia vulgaris L.	Shrub	Wild	AP	Dir, KPK	[52]
				Lv	Dir, KPK	[135]
	Artemisia parviflora Roxb. ex D.Don	Shrub	Wild	Se, Lv	Chitral, KPK	[65]
	Sonchus asper (L.) Hill	Herb	Wild	AP	Sargodha, Punjab	[111]
Apiaceae	*Daucus carota* L.	Herb	Cultivated	AP	Karachi, Sindh	[66]
	Carum copticum (L.) Benth. & Hook.f. ex C.B.Clarke	Herb	Wild	PE	Karachi, Sindh	[45]
	Ammi visnaga (L.) Lam.	Herb	Wild	WP	Various study sites from	[67]
	Apium graveolens L.	Herb	Cultivated Wild	Se	Pakistan	[67]
	Coriandrum sativum L.	Herb	Cultivated	Fr	Dir, KPK	[52]
					Swat, KPK	[55]
					Karachi, Sindh	[50]
	Foeniculum vulgare Mill.	Herb	Cultivated Wild	Fr	Dir, KPK	[52]
Fabaceae	*Cassia absus* Sesse & Moc.	Shrub	Wild	Se, Lv	Gujrat, Punjab	[68]
	Medicago polymorpha L.	Herb	Wild	AP	District Tank, KPK	[69]
	Medicago sativa L.	Herb	Wild	Lv	Ghizer district, Gilgit-Baltistan	[70]
	Castanospermum australe A.Cunn. & C.Fraser	Tree	Cultivated	PE	Karachi, Sindh	[71]
	Melilotus officinalis (L.) Pall.	Herb	Wild	Fl, Lv	Ghizer district, Gilgit-Baltistan	[72]
Amaryllidaceae	*Allium jacquemontii* Kunth	Herb	Wild	Bu	Dir, KPK	[52]
	Allium sativum L.	Herb	Cultivated	Bu	Narowal, Punjab	[73]
					District Tank, KPK	[69]
					Chitral, KPK	[74]
					Swat, KPK	[56]
					Dir, KPK	[75]
				Bu	Talagang, Punjab	[136]

(Continued)

Table 2. Ethnomedicinal plants used to relieve hypertension in Pakistan. (Continued)

Family	Plant name	Growth form	Status	Part used[a]	Study area[b]	References
	Allium cepa L.	Herb	Cultivated	Bu	Attock, Punjab	[76]
	Narcissus tazetta L.	Herb	Wild	Bu	Dir, KPK	[52]
Myrtaceae	*Myrtus communis* L.	Shrub	Wild	Lv	Dir, KPK	[52]
	Psidium guajava L.	Shrub	Cultivated	Lv	Narowal,Punjab	[73]
	Eucalyptus camaldulensis Dehnh.	Tree	Cultivated	Lv	Dir, KPK	[52]
	Eucalyptus globulus Labill.	Tree	Cultivated	Lv	Dir, KPK	[52]
Brassicaceae	*Sisymbrium brassiciforme* C.A. Mey.	Herb	Wild	Se	Dir, KPK	[52]
	Raphanus sativus L.	Herb	Cultivated	Se	Karachi, Sindh	[44]
	Eruca sativa Mill.	Herb	Cultivated	WP	Abbottabad, KPK	[77]
	Nasturtium officinale R. Br.	Herb	Wild	WP	Chitral, KPK	[116]
Solanaceae	*Solanum nigrum* L.	Herb	Wild	Lv	Dir, KPK	[52]
				Lv	Dir, KPK	[135]
	Withania somnifera (L.) Dunal	Herb	Wild	R, Lv	Dir, KPK	[52]
	Capsicum annuum L.	Herb	Cultivated	Fr	Swat, KPK	[56]
Poaceae	*Arundo donax* L.	Herb	Wild	R	Bahawalnagar, Punjab	[102]
	Andropogon muricatus Retz.	Herb	Wild	Ap	Karachi, Sindh	[105]
	Desmostachya bipinnata (L.) Stapf	Herb	Wild	RT	Toli Peer, Azad Kashmir	[114]
Linaceae	*Linum usitatissimum* L.	Herb	Cultivated	Se	Chitral, KPK	[65]
	Linum perenne L.	Herb	Wild	Se	Chitral, KPK	[78]
Amaranthaceae	*Achyranthes bidentata* Blume	Herb	Wild	AP	Islamabad, Pakistan.	[79]
	Achyranthes aspera L.	Herb	Wild	Lv, Sm	D. G. Khan, Punjab	[80]
Rosaceae	*Rosa brunonii* Lindl.	Shrub	Wild	Fr	Dir, KPK	[52]
	Rosa indica L.	Shrub	Cultivated	Fl	Mastung, Baluchistan	[63]
Papaveraceae	*Papaver somniferum* L.	Herb	Wild Cultivated	Fruit	Mastung, Baluchistan	[63]
	Fumaria indica (Hausskn.) Pugsley	Herb	Wild	AP	Dir, KPK	[52]
					Swat, KPK	[55]
				AP	Dir, KPK	[135]
Zingiberaceae	*Zingiber officinale* Roscoe	Herb	Cultivated	Rz	Karachi, Sindh	[81]
	Elettsaria cardamomum (L.) Maton.	Herb	Cultivated	Fr	Karachi, Sindh	[49]
Violaceae	*Viola canescens* Wall.	Herb	Wild	AP	Dir, KPK	[52]
	V. odorata L.	Herb	Wild	AP	Karachi, Sindh	[103]
Berberidaceae	*Berberis lycium* Royle	Shrub	Wild	Rz	Dir, KPK	[52]
				Rz	Kotli, Azad Kashmir	[115]
	Berberis vulgaris Royle	Shrub	Wild	Rz	Chitral, KPK	[116]
Moraceae	*Morus nigra* L.	Tree	Wild	Fr	Abbottabad, KPK	[77]
	Ficus carica L.	Shrub	Wild	Fr	Sargodha, Punjab	[117]
Ranunculaceae	*Nigella sativa* L.	Herb	Wild Cultivated	Se	Karachi, Sindh	[82]
	Clematis orientalis L.	Shrub	Wild	R	Azad Kashmir, Pakistan	[83]
Asclepiadaceae	*Caralluma tuberculata* N.E.Br.	Herb	Wild	AP	Dir, KPK	[52]
					Waziristan agency, Pakistan	[84]
					Mastung, Baluchistan	[62]
					Kalat and Khuzdar, Baluchistan	[53]
	Calotropis procera (Aiton) Dryand.	Shrub	Wild	WP	Islamabad, Pakistan.	[85]
Chenopodiaceae	*Chenopodium botrys* L.	Herb	Wild	AP	Dir, KPK	[52]
	Chenopodium ambrosiodes L.	Herb	Wild	Lv	Dir, KPK	[52]
Oleaceae	*Olea europaea* L.	Tree	Cultivated	FR	Karachi, Sindh	[46]
	Olea ferruginea Royle	Tree	Wild	Lv	Dir, KPK	[52]
Verbenaceae	*Phyla nodiflora* (L.) Greene	Herb	Wild	Lv	Jhelum, Punjab	[86]
	Verbena officinalis L.	Herb	Wild	Lv	Dir, KPK	[52]
Zygophyllaceae	*Peganum harmala* L.	Herb	Wild	PE	Karachi, Sindh	[87]
	Tribulus terrestris L.	Herb	Wild	Lv	Dir, KPK	[52]
Scrophulariaceae	*Scrophularia deserti* Delile	Herb	Wild	R	Mansehra, KPK	[88]
	Pedicularis punctata Decne.	Herb	Wild	Fl	Deosai, Gilgit-Baltistan	[89]

(Continued)

Table 2. Ethnomedicinal plants used to relieve hypertension in Pakistan. (Continued)

Family	Plant name	Growth form	Status	Part used[a]	Study area[b]	References
Euphorbiaceae	*Euphorbia thymifolia* L.	Herb	Wild	WP	Thar Desert, Sindh	[90]
	Euphorbia hirta L.	Herb	Wild	WP	Dir, KPK	[52]
Sterculiaceae	*Firmiana simplex* (L.) W.Wight	Tree	Wild	Gum, Se	Thar Desert, Sindh	[90]
Cactaceae	*Opuntia dillenii* (Ker Gawl.) Haw.	Herb	Wild	Sm	Dir, KPK	[52]
Geraniaceae	*Geranium wallichianum* D.Don ex Sweet	Shrub	Wild	Rz	Waziristan agency, Pakistan	[84]
					Chitral, KPK	[78]
					Mohmand Agency, Pakistan	[141]
Nyctaginaceae	*Boerhavia diffusa* L.	Herb	Wild	AP	Azad Kashmir, Pakistan	[91]
Valerianaceae	*Valeriana wallichii* DC.	Herb	Wild	Rz	Karachi, Sindh	[47]
Boraginaceae	*Onosma hispida* Wall. ex G. Don	Herb	Wild	AP	Dir, KPK	[52]
Meliaceae	*Melia azedarach* L.	Tree	Cultivated Wild	Fr	Batagram, KPK	[53]
Araliaceae	*Hedera nepalensis* K.Koch	Shrub	Wild	Lv	Dir, KPK	[52]
					Malakand, KPK	[92]
					Swat, KPK	[93]
Cucurbitaceae	*Memordica charantia* L.	Herb	Cultivated	Fr	Malakand, KPK	[92]
Pteridaceae	*Adiantum capillus-veneris* L.	Herb	Wild	WP	Allai Valley	[55]
Convolvulaceae	*Cuscuta reflexa* Roxb.	Herb	Wild	WP	Dir, KPK	[52]
					Karachi, Sindh	[94]
Capparaceae	*Capparis cartilaginea* Decne.	Shrub	Wild	PE	Karachi, Sindh	[95]
Crassulaceae	*Bryophyllum pinnatum* (Lam.) Oken	Herb	Wild	Le	Azad Kashmir, Pakistan	[96]
Rubiaceae	*Morinda citrifolia* L.	Tree	Cultivated	R	Karachi, Sindh	[51]
Caricaceae	*Carica papaya* L.	Tree	Cultivated	Se, Fr		[97]
Rhamnaceae	*Ziziphus oxyphylla* Edgew.	Shrub	Wild	R	Dir, KPK	[52]
					Swat, KPK	[61]
					Poonch Valley, Azad Kashmir	[98]
Annonaceae	*Polyalthia longifolia* (Sonn.) Thwaites	Tree	Cultivated	Sm, R	Lodhran,Gujrat, Punjab	[99] [100,108]
Elaeagnaceae	*Hippophae tibetana* Schltdl.	Shrub	Wild	Lv, Fr	Gilgit-Baltistan	[71]
Buxaceae	*Sarcococca saligna* Müll.Arg.	Shrub	Wild	Lv, R	Dir, KPK	[52]
				Lv	Chiral, KPK	[116]
Paeoniaceae	*Paeonia emodi* Royle	Herb	Wild	Rz	Dir, KPK	[52]
Moringaceae	*Moringa oleifera* Lam.	Tree	Cultivated	Gum	Thar Desert, Sindh	[90,104]
Polygonaceae	*Polygonum hydropiper* L.	Herb	Wild	Lv	Gilgit, Gilgit-Baltistan	[101]
Malvaceae	*Malva neglecta* Wallr.	Herb	Wild	WP	Mastung, Balochistan	[63]
Urticaceae	*Forrskalea tenacissima* L.	Herb	Wild	WP	Dir, KPK	[106]
Apocynaceae	Ervatamia coronaria (Jacq.) Stapf	Herb	Wild	LV	Karachi, Sindh	[112]
	Gymnema sylvestre (Retz.) R.Br. ex Sm.	Shrub	Wild	LV	Sarghoda, Punjab	[118]
Combretaceae	Terminalia actinophylla Mart.	Tree	Wild	Fr	Karachi, Sindh	[107]
Orchidaceae	Orchis mascula (L.) L.	Herb	Wild	Plant extract	Karachi, Sindh	[113]
Ebenaceae	Diospyros kaki L.f.	Tree	Wild	LV	R Sawabi, KPK	[119]
Leguminosae	Trigonella foenum-graecum L.	Herb	Wild	Plant extract	Karachi, Sindh	[120]

Parts used[a]: Leaves = Lv, Seed = Se, Fruit = Fr, Stem = Sm, Aerial part = AP, Whole plant = WP, Bulb = Bu, Flower = Fl, Rhizome = Rz, Root = R, Plant extract = PE, Study area[b]**:** KPK = Khyber Pakhtunkhwa.

Life form and status of medicinal plants treating hypertension

In this review, we categorized medicinal species as herb, shrub, or tree life forms (Fig. 4). Herbaceous plants dominated the life form of medicinal species used in remedies. The predominant use of herbaceous plants by local patients may be due to their availability and ease of collection [121].

This review identified 71% wild and 29% cultivated medicinal species**.** Almost all tree plants used to treat hypertension were cultivated, except *Olea ferruginea* Royle and *Firmiana simplex* (L.) W.Wight.

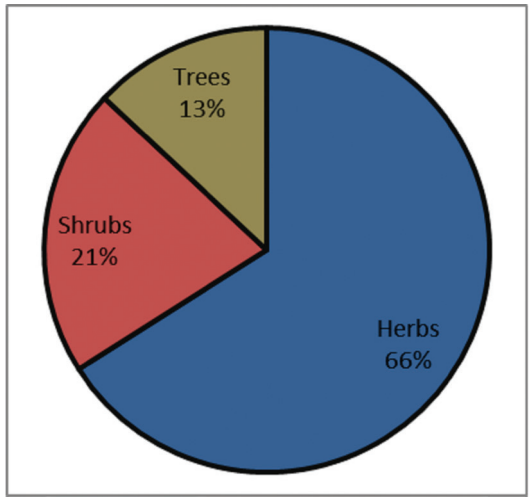

Figure 4. Life form of medicinal plants for the treatment of hypertension.

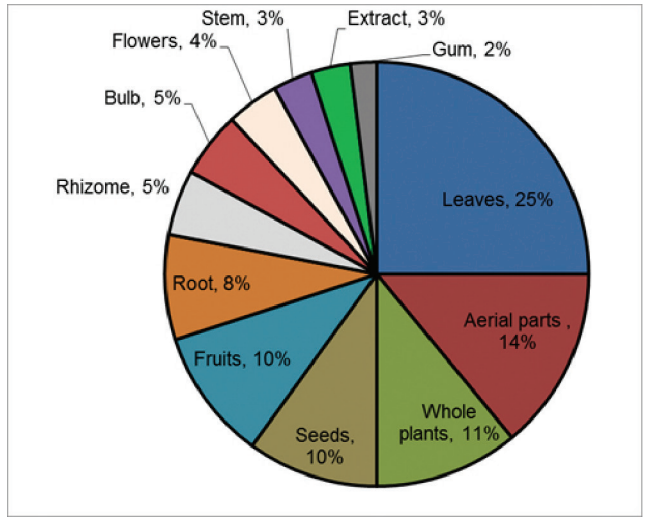

Figure 5. Percentage of plant parts used for herbal preparations to treat hypertension in Pakistan.

Some herbs present in the wild habitat can be cultivated, such as *Mentha viridis* (L.) L., *Papaver somniferum* L., *Nigella sativa* L., *Foeniculum vulgare* Mill., and *Apium graveolens* L.

Medicinal plant parts

Leaves along with aerial plant parts constituted the majority of usage specified. The whole plant, seeds, fruits, roots, and bulbs trailed with lesser use frequency (Fig. 5). This is promising since some research suggests that the use of aerial plant parts and leaves is sustainable with a minimal environmental impact and harm to plant populations [122].

Discussion

Hypertension is a significant public health problem, with a global prevalence of 40.8% and a control rate of 32.3%. Moreover, it is an increasingly common public health problem in low-income developing countries [123]. In the case of Pakistan, the prevalence of hypertension was found to be 19.1% [124].

Most of the local rural inhabitants in Pakistan use medicinal plants for curing hypertension, due to easy availability in these areas, while in addition the allopathic drug shops are scarce, and out of reach for the rural poor. In Pakistan, there are almost 50,000 herbalists scattered in the whole country. They are running their clinics both in rural and urban areas by using medicinal plants with minimal processing form [125].

The review reports the highest number of anti-hypertensive plants (63%) from Northern Pakistan—the Pan-Himalaya region (Figure 2). The majority of studies were reported from Northern Pakistan because of the many traditional practices and rich floral diversity. Understanding and applying the indigenous knowledge of mountain communities for biodiversity resource management is one of the key elements for achieving sustainable development [126]. The local people of Pakistan use at least 114 medicinal plants for the management of hypertension. The majority of the Pakistani population lives in rural villages [127]. Also, approximately 75% of that population relies on traditional medicines to treat ailments [128]. Much of the population lives at a great distance from medical facilities and often cannot afford the high price of health care [129,130]. Correspondingly, many of these people turn to herbal remedies for their health care needs.

In this review, we focused on ethnobotanical and ethnopharmacological uses of medicinal plants for hypertension treatment. Some of these plants have active ingredients and documented pharmacological anti-hypertensive effects and mechanism. These plants are: *Lavandula stoechas, Daucus carota, Carum copticum, Coriandrum sativum, Castanospermum australe, Allium sativum, Raphanus sativus, Eruca sativa, Zingiber officinale, Elettsaria cardamomum, Nigella sativa, Olea europaea, Peganum harmala, Valeriana wallichii, Cuscuta reflexa, Capparis cartilaginea, Carica papaya, Mentha longifolia, Sonchus asper, Moringa oleifera, Andropogon muricatus, Viola odorata, Forrskalea tenacissima, Terminalia bellerica, Polyalthia longifolia var. pendula, Galbulimima baccata,* and *Orchis mascula* represented in Table 2.

Medicinal herbs play a very important role in the development and discovery of drugs. They are a

leading basis for the development of pharmaceuticals [131]. Often, synthetic drugs are very expensive and a large population cannot pay for these medicines.

According to a report in 2011, in the United States, the total costs associated with hypertension were $46 billion in health care services, missed days of work, and medications [132]. In Cameroon, it was reported by Nole et al. [133] that in cases of non-complicated arterial hypertension the diabetic patients', with arterial hypertension, monthly cost of treatment was 60,500 Central African CFA franc Fcfa (1 US $ = 528 Fcfa), and certain pharmaceutical products and their cost like Actrapid HM (14,510 Fcfa), Lodoz (10,415 Fcfa) Insulatard HM (14,525 Fcfa), and Hexen 50 (13,860 Fcfa), etc., are rare in rural zones or expensive for patients. At the same time, using these anti-hypertensive drugs can cause numerous adverse effects and reactions, including orthostatic hypotension, dizziness, headache, and also decreased sexual function [134].

In China, the study of Chinese herbal formulas, for the management of hypertension, is an important area of research within integrative medicine and Traditional Chinese Medicine [134]. It was reported that approximately 80% population of Morocco and 21% population of Nigeria use alternative and complementary medicine in the management and treatment of hypertension [37,137]. In 2003, it was reported that about 63.9% of hypertensive patients use traditional herbal medicine in India [138]. Attempts by the low-income groups in rural areas of developing countries to control hypertension and its complications, when faced with scarce economic resources, often include adopting herbal remedies [139]. In many parts of the world, people use ethnomedicinal plants for the treatment of high blood pressure, because of its easy availability, less expensive, and also, due to lack of other health facilities. Such plants like Catharanthus roseus, Allium cepa, Momordica charantia, Azadirachta indica, Ocimum spp., Zanthoxylum spp. [133], Scutellaria spp., Achyranthis spp., Eucommia spp., Scrophularia spp., Epimedium spp., Cassia spp., Allium sativum, [134], and Mentha spp., Artemisia spp., Ajuga bracteosa, Ocimum basilicum, Foeniculum vulgare, Berberis lycium [52] are easily available in the wild as well as in cultivated habitats and make an attractive choice for the treatment of hypertension.

Hypertension affects both developed and underdeveloped countries. Barriers to health care combined with a strong tradition of medicinal plant use make Pakistan an excellent model for research on ethnomedicine. According to the National Health Survey of Pakistan, nearly 18% of all adults and 33% of all adults above 45 years old in Pakistan suffer from hypertension. In another study, it was reported that 18% of people in Pakistan were affected from hypertension with every third person over the age of 40 becoming susceptible to an extensive range of diseases [130–140].

Limitations, Conclusion, and Future Perspective

In this review, we reviewed ethno-botanical reports of species used for hypertension in Pakistan. These types of data are obtained from the authors conducting studies in the field, while interviewing community members such as elders of indigenous communities. These reports provide the parts of the plants used, mode of preparation of herbal medicines, and other traditional practices. In most cases, there are no experimental comparisons reported on these plants. So, potential future experiments or clinical studies are inferred from examining traditional collective knowledge of plant use. Having said that, this review brings to light the 30 (26% of resulting species) species which have been tested in animal models. While these articles delve into the mode and sometimes for the mechanism of action of these species, the phytochemistry is very limited. It is yet to be seen that what active compounds are present in these species that provide the rationale for age-old ancestral use for controlling hypertension.

The inexpensive nature of herbal medicine allows the low-income households access to health care. This is reflected in studies that show that a higher percentage of people in developing countries compared to developed countries rely on traditional medicine [19]. This is especially true in Pakistan, where a high percentage of the population lives in remote rural settings and access to health care is often cost prohibitive [126,129,130]. Given the alarming nature of hypertension trends around the globe, especially in developing nations, Pakistan served as an excellent model to investigate the interface between anti-hypertensive medicinal plants and the humans who depend on them. In this review, we identified 114 medicinal plant species that were used by people across Pakistan for the management of hypertension. The promotion and planting of these commonly accepted species may provide a benefit to people who cannot afford and/or may not be compliant with synthetic medications. Ethno-botanical studies of medicinal plant species used to treat hypertension in various regions of Pakistan suggest that people actively seek alternative treatments for

hypertension. Therefore, well-planned mechanistic studies on these species should be carried out in future work, along with studies on safety and toxicity.

Conflict of interest

The authors declare that there are no conflicts of interest.

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