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Review

Ethnopharmacology and toxicology of Pakistani medicinal plants used to treat gynecological complaints and sexually transmitted infections

A. Tariq [a,b,*], M. Adnan [c], A. Iqbal [c], S. Sadia [d,**], Y. Fan [e,**], A. Nazar [c], S. Mussarat [c], M. Ahmad [f,g], O.A. Olatunji [a,b,h], S. Begum [i], P. Mazari [d], B. Ambreen [j], S.N. Khan [k], R. Ullah [l], A.L. Khan [m]

[a] Key Laboratory of Mountain Ecological Restoration and Bioresource Utilization & Ecological Restoration Biodiversity Conservation Key Laboratory of Sichuan Province, Chengdu Institute of Biology, Chinese Academy of Sciences, Chengdu 610041, Sichuan, China
[b] University of Chinese Academy of Sciences, Beijing, China
[c] Department of Botany, Kohat University of Science and Technology, Kohat 26000, Pakistan
[d] College of Life Sciences, Beijing Normal University, Haidian District, Beijing 100875, China
[e] The Medical Center of General Practice, Sichuan Academy of Medical Science and Sichuan Provincial People's Hospital, Chengdu 610041, Sichuan, China
[f] Center for Natural Products Lab, Chengdu Institute of Biology, Chengdu -610041, Sichuan, China
[g] Department of Plant Sciences, Quaid-i-Azam University, Islamabad 45320, Pakistan
[h] Department of Biological Sciences, Faculty of Basic and Applied Sciences, Osun State University, Osogbo, Osun State, Nigeria
[i] Department of Environmental Sciences, Fatima Jinnah Women University, 46000 The Mall, Rawalpindi, Punjab, Pakistan
[j] Department of Chemistry, Kohat University of Science and Technology, Kohat 26000, Pakistan
[k] Department of Zoology, Kohat University of Science and Technology, Kohat 26000, Pakistan
[l] Department of Pharmacognosy and Medicinal, Aromatic & Poisonous Plants Research Center (MAPPRC), College of Pharmacy, King Saud University, P.O. Box 2457, Riyadh 11451, Saudi Arabia
[m] Chair of Oman's Medicinal Plants & Marine Natural Products, University of Nizwa, Nizwa 616, Oman

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ABSTRACT

Gynecological problems and sexually transmitted infections (STIs) are greatly affecting women health especially in developing countries due to lack of modern reproductive health facilities, poverty and different cultural norms. Consequently, a large population of Pakistan turns toward ethno-medicinal healthcare systems due to accessibility, affordability, availability and an inherent trust in this method. The present review was framed by searching different search engines for the collection of fragmented literature on indigenous knowledge of medicinal plants used by Pakistani women to treat gynecological complaints and STIs. In total, 116 plant species used in Pakistan to treat a variety of gynecological complaints and STIs. The dominant plant families used for the preparation of herbal remedies are Asteraceae and Amaranthaceae. Majority of the plants were reportedly found to be used against menses (46 plant species) followed by gonorrhea (30 plant species). The frequency of citation was also found higher for these two complications, which might be due to the higher prevalence of these problems in Pakistan. The highest number of plant species (59) was reported from Khyber Pakhtunkhwa (KPK) province of Pakistan due to more cultural resistance as compared to other provinces. Sørensen similarity index showed the highest consensus between Pashtun and Punjabi cultures of Pakistan in terms of plants and parts usage for species *Convolvulus arvensis, Justicia adhatoda, Achyranthes aspera, Berberis lycium, Punica granatum* and *Withania somnifera*. Interestingly, these plants were also reported to treat multiple reproductive problems indicating their high bioactivity. Thirteen plants including *A. aspera* and *P. granatum* have also been reportedly evaluated pharmacologically and found active confirming the efficacy of traditional medicines. Few plants (17% of total) were reportedly evaluated for toxicity, among which *Nerium oleander, Euphorbia hirta* and *Acacia nilotica* showed toxic effects on living systems. The present findings stress the need for further in-depth studies on the phytochemical, pharmacological and toxicological aspects of commonly important medicinal plants used for multiple gynecological complaints and STIs in different cultures in order to provide reliable information to the primary users and development of novel drugs.

* Correspondence to: A. Tariq, Key Laboratory of Mountain Ecological Restoration and Bioresource Utilization & Ecological Restoration Biodiversity Conservation Key Laboratory of Sichuan Province, Chengdu Institute of Biology, Chinese Academy of Sciences, Chengdu 610041, Sichuan, China.
** Corresponding authors.
E-mail addresses: akash.malik786@mails.ucas.ac.cn (A. Tariq), sehrish@mail.bnu.edu.cn (S. Sadia), yangfan_peg@sina.com (Y. Fan).

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Contents

1. Introduction

Plant-based medicines are widely used across the world today. According to a report, over three-fourths of the world population cannot afford allopathic medicines and have to rely on traditional medicines of plant origin (WHO, 2001a). In the context of the present day scenario, it is very important to find alternate medicines for the treatment of certain diseases, which do not need prolonged treatment and may be cured by the use of herbal products.

Pakistan has about 6000 species of flowering plants, of which 600 are reported to be medicinal plants (Nasir and Ali, 1991). More than 50% of all modern drugs have natural origin; therefore, these products have a significant role in the pharmaceutical sciences for drug development (Deka et al., 2011). Poor reproductive health accounts for up to 18% of the global burden of diseases and 32% of the total burden of diseases for women at reproductive age (Singh et al., 2010). Over 50,000 flowering plants are being used for medicinal purposes across the world (Schippmann et al., 2002); however, ethno-gynecological literature is scarce (Sahu, 2011).

Pakistan has diverse cultures, ethnicities and languages; however, Punjabi, Pashtun, Sindhi and Balochi are the major ethnic groups (Fig. 1). Punjabi culture is a mixture of different ethnic communities due to historical invasions by Afghan and Turks (Chopra, 1977), and also share border with Indian Punjab. It consists of different tribes including Gujars, Juts, Awan, and Arain. Pashtun culture is the most dominant culture in Khyber Pakhtunkhwa province reflecting the ethnic tribal society and the second largest ethnic group in the country. Sindhi culture constitutes multi-clan group of people who are highly influenced by Sufism (a way of life). At the time of the Indo-Pak partition in 1947, refugees influenced the socio-ethnic factor of Sindhi society. Baloch society is located at tribal areas of Western Pakistan and has a rich treasure of cultural heritage (Shehzad, 2011) and a treasure of natural resources. Parts of Balochistan region are extremely cold in winter, from where many people migrate to Punjab and Sindh, thus also being influenced by other cultures. Rural women of these ethnic groups are heavily dependent on forest resources to sustain livelihood including the collection of medicinal plants for the treatment of different kind of gynecological complaints and STIs.

Documentation of ethno-gynecological knowledge by ethnic minorities is not only important to understand and analyze these practices but also to conserve it from being lost. Pakistani women in rural areas commonly face gynecological problems because of malnutrition, unhygienic living conditions, and extensive physical activities (Bhat et al., 2013). Some rural women are specialized to treat diseases by using locally available plants. However, the number of traditional healers is decreasing due to modernization and lack of interest by the younger generation in ethnomedicines. Herbal drugs have fewer side effects on the living system compared to allopathic medicines. It is therefore, important to systematically analyze the values of plants systematically for the chemical agents involved in medicinal activities. Pharmacological studies revealed that activity of plant extracts on uterine-ovarian axis may produce variation in the pattern of the reproductive cycle (Shukla et al., 1988). Pharmacological studies have immense importance to show the exact mechanism of action in a particular agent used to cure an ailment. As an example, the estrogenic activity of plants acts on the pituitary action of Luteinizing and Follicle Stimulating Hormones to reduce their secretion and block ovulation (Shibeshi et al., 2006). However, safety assessment of pharmacological agents may be carried out through toxicological assays (Ernst, 2005). Toxicological studies play a significant role in understanding the harmful actions of active agents or the phytochemicals on tissues. It gives an insight of the chemical actions, reactions, interactions, consequential changes of structure in biological tissues and a range of concentration for the safely use of plants to cure a particular disease (Olejniczak et al., 2001). For example, Chowdhury et al. (2004) evaluated the toxicity of *Nerium oleander*, a folk medicine being used in gynecological complaints. They found the lowest dose (300 mg/kg) was non-toxic, while high doses were lethal.

Two of the most important health indicators of a country are life expectancy and maternal mortality rates (Nepal Census Report, 2001; WHO, 2001b). A worldwide leading cause of morbidity and mortality in pregnant women is related to reproductive health complications (Cohen, 2009). Periodic blood discharge from the uterus every month at a regular interval in the whole active reproductive life of women is known as menstruation (Critchley, 1986), and abnormalities related to it may lead to serious disorders. Leucorrhea and dysfunctional uterine bleeding are very common and create distress in females (Tewiri et al., 2001). In developing countries, due to a high population rate and absence of family planning practices, many pregnancies are leading to unsafe abortions and eventually mortality and morbidity. According to a survey, approximately 180 women die every day due to unsafe

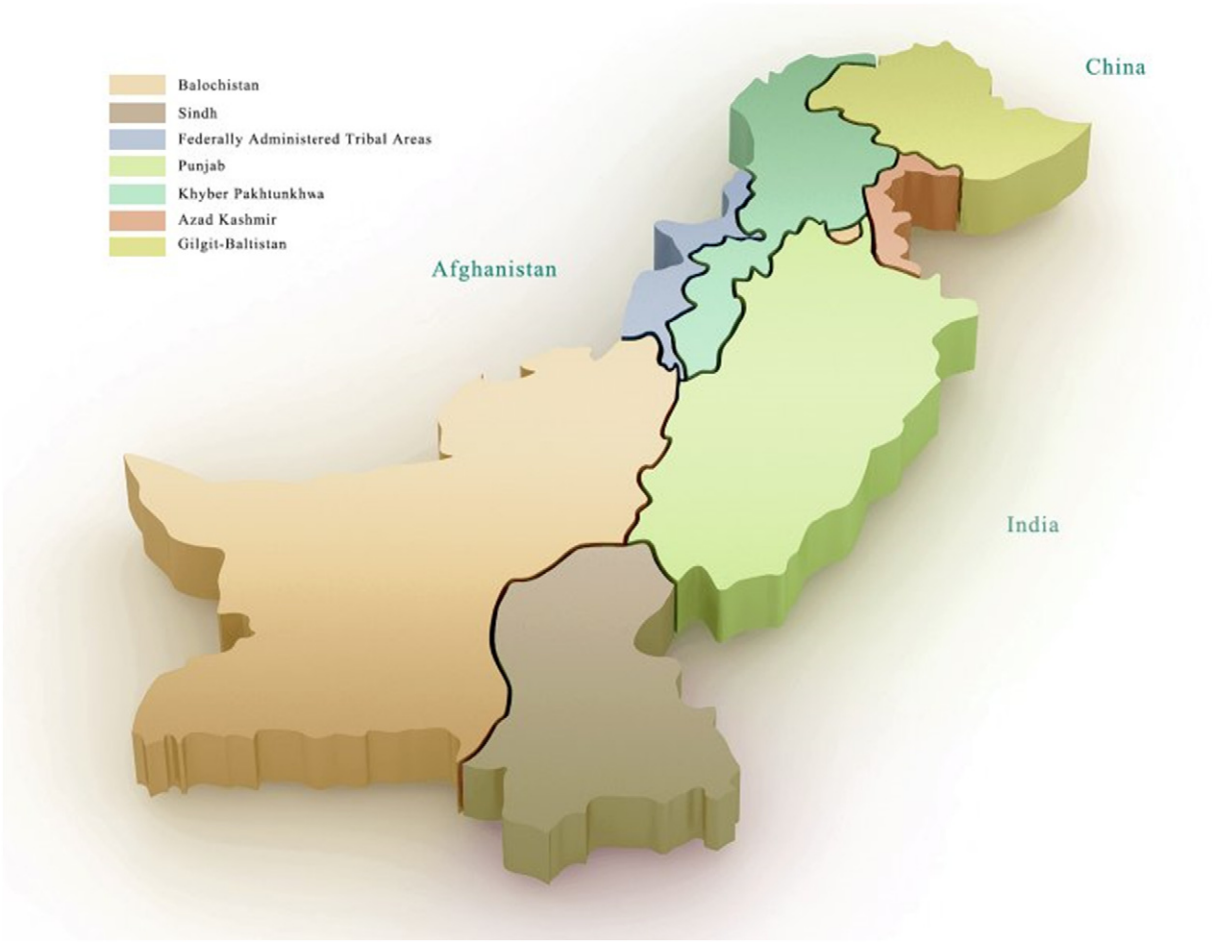

Fig. 1. Map of Pakistan indicating four provinces (Punjab, Khyber Pakhtunkhwa, Sindh and Balochistan), and three independent divisions (Federally administered areas, Azad Kashmir and Gilgit-Baltistan) under the federal control. The provinces are dominated by Punjabi, Pashtun, Sindhi and Balochi cultures respectively.

abortions (Biswas et al., 2012). Moreover, vomiting, anemia, nausea, backache, and headache are pregnancy related complications in women. Eighty-five percent of women are affected by nausea during early stages of pregnancy and almost half of those include vomiting (Gadsby et al., 1992). Additionally, sexually transmitted diseases including gonorrhea, syphilis, AIDS are also affecting the life expectancy and mortality rate of women in many countries.

To the best of our knowledge, this is the first attempt to compile published information on Pakistani medicinal plants used for gynecological complications and STIs. The present review will explore the efficacy of medicinal plants by combining the phytochemical, pharmacological, and toxicological aspects. This will help in identifying potential candidate medicinal plant species for further *in-vitro*, *in-vivo* and phytochemical investigation.

2. Methodology

This review paper was designed by consulting and compiling a large number of mostly peer-reviewed scientific articles on the traditional uses of plants in different provinces of Pakistan (Fig. 1) related to gynecological complaints and STIs. In Pakistan there are four provinces (Punjab, Khyber Pakhtunkhwa, Sindh and Balochistan) and three independent divisions (Federally administered areas, Azad Kashmir and Gilgit-Baltistan) under the federal control. The main focus of this review was on the major ethnic groups belonging to the four provinces of the country, because majority of the literature related with ethno-gynecological plants was available from these regions. PubMed, Scopus, Google Scholar, Medline, Web of Science, and Flora of Pakistan were searched as the source of literature. Indicators like Pakistani flora used for gynecological problems, ethnomedicinal uses of plants, medicinal uses of plants against gonorrhea, abortion, and leucorrhea *etc.* were applied for searching the literature. To limit the data to accessible digitized literature, we focused mostly on English literature containing maximum relevant information. The authors did not find the relevant useful literature in their local languages. A total of 220 articles were accessed, of which only 163 scientific articles fulfilled the inclusion criteria. Fifty seven articles were excluded based on different criteria (Fig. 2) such as, biased information, ambiguous knowledge, least information, duplicate references, lack of information regarding focused ethnic groups and absence of voucher/herbarium specimens (Fig. 2).

Relevant plants from the selected papers were all entered in separate excel files. A detailed ethno-medicinal table was formulated for all the plants used for gynecological complications and STIs in a systematic manner. In the ethno-medicinal table, we included the plants scientific names, local names, habit, distribution, part used, and types of problems. Two more tables regarding pharmacological evidence and safety profiles were also developed. Further taxonomic corrections in the publication author of plants and family names were rectified according to the plant list (www.plantlist.com) and Tropicos (www.tropicos.org). Pakistani culture was divided into four main types *i.e.* Punjabi, Pashtun, Balochi and Sindhi culture. Cultural similarity for the use of plants and plant parts was calculated by using Sørensen similarity index (SS), and the correlation between the use of plants and plant parts were found out by using linear regression function of MS Excel 2016. Results of Sørensen index were summarized in the form of a table and a figure.

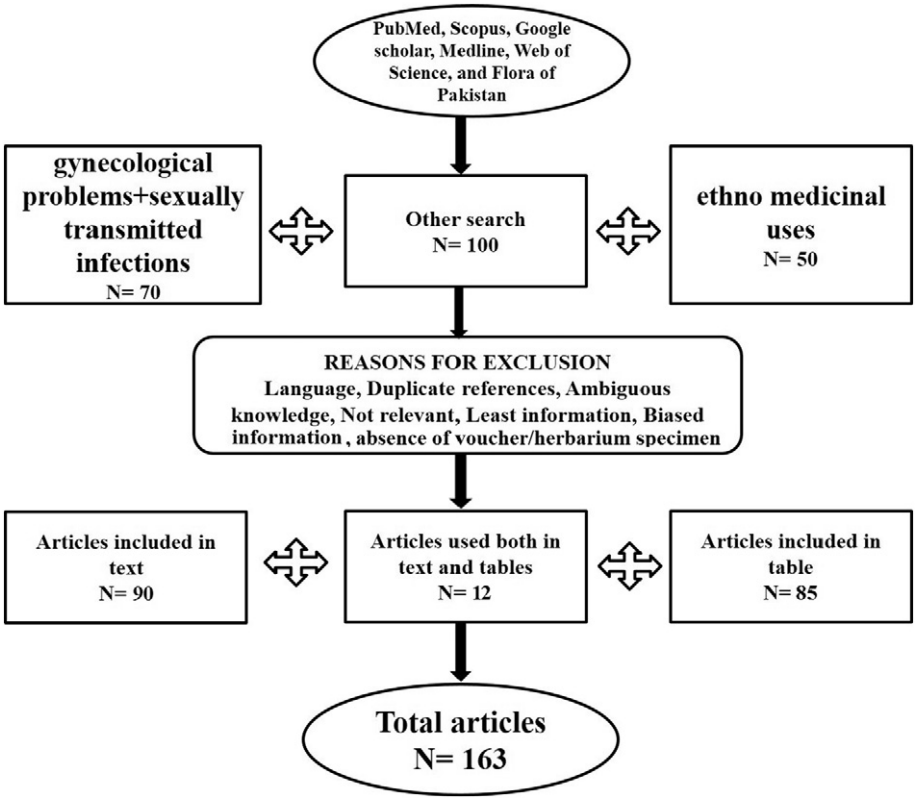

Fig. 2. Flow diagram of literature search and screening process.

3. Results and discussion

Majority of studies were reported from the Western Himalayan regions located in the Eastern and North-Western parts of the Pakistan. Hence, most of the included literature belongs to the Indo-Malayan eco-zone of Pakistan as compared to Palearctic eco-zone. In most of the reported studies, the majority of informants were women (midwives, traditional healers, health workers and experienced elder women) at the ages between 40 and 80 years. In almost all studies, number of informants or interviewees was above 60. Mostly, field surveys were reportedly conducted, in which group discussions, semi-structured questionnaires and interviews were carried out from local inhabitants to collect the data. However, in some of the studies, direct interviews were also observed. A brief overview of the results is presented in the following sections.

3.1. Medicinal plants used against gynecological complaints in Pakistan

Pakistani women are using majority of plants against gonorrhea and menstrual complications. In Pakistan, a total of 116 medicinal plants are being used against different gynecological complications (Table 1). The most commonly used and reported medicinal plants against reproductive problems include *Justicia adhatoda*, *Achyranthes aspera*, *Nerium oleander*, *Berberis lycium*, *Cannabis sativa*, *Citrullus colocynthis*, *Cyperus rotundus*, *Rhynchosia minima*, *Thymus serpyllum*, *Abutilon indicum, Acacia nilotica*, *Prosopis cineraria*, *Ficus benghalensis*, *Punica granatum*, *Withania somnifera*, *Peganum harmala*, and *Tribulus terrestris* (Table 1). However, five of them including *Achyranthes aspera*, *Cannabis sativa*, *Citrullus colocynthis*, *Punica granatum* and *Abutilon indicum* have been validated pharmacologically so far and have reportedly shown good biological activities. The highest number of plant species (59) was reported from Khyber Pakhtunkhwa (KPK) province of Pakistan due to more cultural resistance as compared to other provinces (Fig. 3). Majority of the reported plants belongs to the family Asteraceae (10), Amaranthaceae (7), Solanaceae (6), and Mimocaceae (5). Asteraceae has also been reported as a dominant plant family in ethno-gynecological studies conducted in other countries (Steenkamp, 2003; Yadav et al., 2006). Species dominance of these families might be due to their extensive distribution, herbaceous locality, and affluence in the study area. Additionally, the large exploitation of plant species from these families may be associated with the incidence of useful, proactive ingredients against disease (Gazzaneo and Albuquerque, 2005). Conversely, Borokini et al. (2013) reported Poaceae and Caesalpiniaceae are dominant families against gynecological problems, which might be due to the difference in culture and traditional beliefs. According to the present review, herbs (63%) were the dominant life form (Fig. 4) used in herbal formulations for the treatment of gynecological problems followed by trees (20%) and shrubs (16%). In most rural areas, medicinal herbs are the chief constituents of local plants and are generally considered the first choice (Shinwari, 2010). The utmost uses of medicinal herbs gives a sign of existence in large quantities in the studied regions and can be grown in various places like farmland, home ground, road sides and wild areas. Pakistani women mostly use the whole plant (45 plant species) followed by leaves (39 plant species) for making different kind of recipes (Fig. 5). Most recipes include more than one part of a specific plant, for instance bark, root, and fruit of *Schinus molle* are used for a particular gynecological complaint.

The present review reveals that Pakistani women are having adequate traditional knowledge about the utilization of herbal medicines for their reproductive healthcare. Pakistani women use medicinal plants for the treatment of sixteen different kind of gynecological complaints such as abortion, gonorrhea, leucorrhea, removal of the dead fetus, menstrual complications, *etc.* Plants are also used to cure prevalent sexual diseases such as gonorrhea, syphilis, vulvovaginal yeast infections caused by *Candida albicans*, dysmenorrhea (painful menstruation), menorrhagia (abnormally heavy and prolonged periods), amenorrhea (absence of monthly periods), leucorrhea (vaginal discharge), premature menopause, and sexual dysfunction in many other countries. Moreover, traditional and herbal medicines also supply health care during

Table 1
Ethno-medicinal uses of plants in gynecological problems.

Families	Plant species	Local name	Habit	Part used	Locality	Medicinal use	Reference
Acanthaceae	*Justicia adhatoda* L. (=*Adhatoda zelyanica.* Medic., *Adhatoda vasica.* Nees)	Baikar, Barg-e-baansa, Arrusa	S	Leaves, whole plant	Malakand, Bannu, Islamabad, Dir, Azad Kashmir, Punjab	Decoction of leaves is used as abortifacient. It is also used to treat gonorrhea.	Alamgeer et al. (2013), Khan et al. (2015), Rauf et al. (2012)
Amaranthaceae	*Achyranthes aspera* L.	Phut kanda	H	Whole plant; roots, leaves, stem	Dera Ghazi Khan, Bannu, Abbottabad	It is used to treat gonorrhea, menstrual, and post-partum pain. One cup of decoction of whole plant is given in case of painful delivery on daily basis.	Khan et al. (2015), Iqbal et al. (2011), Gulshan et al. (2012), Shah et al. (2013)
	Amaranthus angustifolius var. silvester Thell. (=*Amaranthus Sylvestris* Desf.)	Phulari	H	Leaves	Sialkot, Gujrat	It is used to treat gonorrhea.	Arshad et al. (2011), Hussain et al. (2010)
	Amaranthus spinosus. L	Ganair	H	Leaves	Abbottabad	Fresh leaves are cooked and eaten to cure leucorrhea.	Shah et al. (2013)
	Amaranthus viridis L.	Phut booti, Ganar	H	Whole plant, Root	Dera Ghazi Khan, AJK	Internally used for excessive menstruation and externally used for vaginal discharge.	Gulshan et al. (2012), Ajaib et al. (2014)
	*Achyranthus bidentate*Blume	Chaff flower	H	Roots	Bannu	Roots are used for placenta retention.	Khan et al. (2015)
	Alternanthera pungens Kunth	Keshtto lata	H	Whole plant.	Makerwal & Gulla Khel, Bannu	It is used to treat gonorrhea.	Khan et al. (2015)
	Haloxylon salicornicum	Lana	S	NA	Bahawalpur	It is used in abortion, excessive bleeding and leucorrhea.	Wariss et al. (2012)
Anacardiaceae	*Schinus molle* L.	Toor maruch	T	Bark, leaves, fruits	Bannu, KPK	It is used to treat menstrual disorder.	Khan et al. (2015), Rehman et al. (2013)
Apiaceae	*Foeniculum vulgare* Mill.	Saunf	H	Seeds, fruits	Rural urban areas of Sindh, Bannu	Decoction and powder form is preferred in most of disease treatments such as for leucorrhea, menses, abortion, infertility, and other reproductive diseases.	Khan et al. (2015)
	Cuminum cyminum	Zira, Zankai	H	Fruit	KPK	It is orally given to pregnant women to cure their stomach problem due to stress or light work schedule.	Jan et al. (2008)
	Ferula narthex	Sup, Hing	H	Root, Stem, Resin	Gilgit, Astore	Gum resin is used to treat habitual abortion.	Khan and Khatoon (2009)
	Anethum graveolens	Soey	H	Fruit	Bahawalpur	It is given to lactating mothers to increase milk flow.	Wariss et al. (2012)
	Centella asiatica(Linn.)	NA	H	Whole plant	Rawalpindi	Hepatitis, syphilis, and leucorrhea	Zahra et al. (2014)
Apocynaceae	*Nerium oleander* L. (=*Nerium indicum.* Mill.)	Kaner, Kanhera	S	Root, Flowers	Bannu, Gujrat	Root powder is used as abortifacient.	Khan et al. (2015), Hussain et al. (2010), Parvaiz (2014)
Asclepiadaceae	*Oxystelma esculentum* (L.f) Sm.	Dudhi, Dudhani	H	Fruit, Whole plant	Kohistan khirthar national park, Cholistan	Fruit juice is used to treat Gonorrhea and leukoderma.	Panhwar and Abro (2007), Ahmad et al. (2012)
	Leptadenia pyrotechnica	Khip	S	Leaves, Shoot	Cholistan	Decoction and powder form is used to treat dysmenorrhea.	Ahmad et al. (2012)
	Calotropis procera	Ak	S	Latex, leaves, flower buds	Cholistan	Sexually transmitted diseases	Malik et al. (2015)
Asteraceae	*Artemisia absinthium* L.	Dhada Tarkha/Vilayathi afsanthin	H	Whole plant, shoots	Bannu	It is used to conceive pregnancy.	Ahmad et al. (2011), Khan et al. (2015)
	Carthamus oxycantha M. Bieb.	Kandiyari; Azghibotay	H	Flower, seeds	Dera Ghazi Khan	It is used to stimulate menstrual flow.	Gulshan et al. (2012), Ahmad et al. (2011)
	Erigeron bonariensis L. (=*Conyza bonariensis* L.	Chabal grass, Shpelaye	H	Whole plants, oil, Shoot, Leaves	Dera Ghazi Khan, KPK	This tonic herb is internally used to treat hemorrhage. Infusion is taken in painful menstruation.	Gulshan et al. (2012), Khan et al. (2013)
	Cichorium intybus L.	Bhangara	H	Leaves, root	Tehsil Birmal, S.W Agency,	Decoction is used to stimulate menstruation	Farooq et al. (2012)
	Launea procumbens Roxb.	Kandiyari/Bhatter	H	Whole plant	Mianwali	Used to treat painful urination in gonorrhea and also in pregnancy.	Ghani et al. (2012)
	Achillea millefolium L.	Kungi	H	Whole plant	Bannu, KPK, Poonch Valley Azad Kashmir,	Decoction (20 ml for 3 days) is used to treat menstrual disorder. It also acts as febrifuge.	Khan et al. (2015), Khan et al. (2012)
	Aster molliusculus C.B. Clarke	Aster	H	Flower	Bannu	Used to treat amenorrhea.	Khan et al. (2015)
	Eclipta prostrata (L.) L.	Pattrati	H	Whole plant	Dera Ghazi Khan	It is used to treat post-partum or abnormal uterine bleeding.	Gulshan et al., 2012
	Anaphalis nepalensis	Chikee, Chora	H	Flowers	Astore, Chaprote, Gilgit	It is used for gynecological infections.	Khan et al. (2015)
	Conyza Canadensis	NA	H	Whole plant	Gilgit	Uterine hemorrhage	Akhter et al. (2016)
Brassicaceae	*Brassica campestris*	Sharsham saag	H		Mardan, KPK	It is used in dysmenorrhea	Bahadur et al. (2013)

Table 1 (*continued*)

Families	Plant species	Local name	Habit	Part used	Locality	Medicinal use	Reference
Berbaridaceae	*Berberis lycium* Royle.	Kali sumbali/Kashmal, Kwarary	S	Roots, Bark of root, Fruit	Bannu, Poonch Valley Azad Kashmir, KPK, Shangla	The bark is given as a tonic in pregnancy. Gonorrhea, leucorrhea, and menses are also treated by this.	Khan et al. (2015), Khan et al. (2012), Ibrar et al. (2007)
	Berberis aristata	Churku, Sumlo, Ishkeen, Sumbal	S	Root, Stem	Balochistan, Dir, Hazara, Murree, AJK, Sindh	It is used to treat gonorrhea.	Khan et al. (2015)
Bignoniaceae	*Tecomella undulata* Seem.	palwana/Rohira, Lohiro, Lahora	T	Leaf	Khirthar, AJK, Bahawalpur	It is used as abortifacient and to treat leucorrhea and menstrual pain.	Panhwar and Abro (2007)
Burseraceae	*Commiphora wightii* (Arnot) Bhaudari	Gugur	T	Gum	Kirther National park, Sindh	Gum is used for syphilis and menses problems	Mehmood et al. (2012)
Boraginaceae	*Arnebia hispidissima*	Sorkhi butti	H	Whole plant	Cholistan	Diffusion and decoction is used to treat dysmenorrhea.	Ahmad et al. (2012)
Caricaceeae	*Carica papaya*	Papeeta	T	Fruit	Gujrat	It is used for abortion.	Parvaiz (2014)
Caesalpiniaceae	*Cassia fistula* L.	Amaltas, Kinjol	T	Legume	Barroha, Bhara Kahu and Maanga in Islamabad	Decoction of legume is given to the women after expelling the birth material and to control obesity.	Rauf et al. (2012)
Cannabaceae	*Cannabis sativa*	Banga, Bang, Thoonchi	H	Leaves and bark, root, flowering tops, resin, seed	KPK, Gilgit, Astore, Diamer, Baltistan	It is used in abortion, gonorrhea and post-partum hemorrhage. Leaves are used as antimenorrhea. Leaves are also used for tetanus. Infusion of seeds is useful for gonorrhea.	Rehman et al. (2013), Ajaib et al. (2014), Khan and Khatoon (2009)
Chenopodiaceae	*Chenopodium murale* L.		H	Whole plant	Bannu	Used to treat abnormal menstrual flow.	Khan et al. (2015)
Convolvulaceae	*Convolvulus arvensis* L.	Pryvatay, Wanvary	H	Whole plant	Takht-e-Nasrati, Karak, Bannu, Bahawalpur	It is used in excessive menstrual bleeding and leucorrhea.	Khan et al. (2015), Wariss et al. (2012)
	Ipomoea eriocarpa	Lagaco cozinho	S	Leaves, Roots	District Sialkot, Punjab	It is used to relief menstrual pain.	Arshad et al. (2011)
Cucurbitaceae	*Citrullus colocynthis* L.	Maraginye/Truh, Tumma	H	Roots and fruits	Kpk, Cholistan, Bahawalpur	Used as abortifacient and in menses.	Rehman et al. (2013), Ahmad et al. (2012), Wariss et al. (2012)
Cuscutaceae	*Cuscuta reflexa* Roxb.	Amarbail, akashbail, dodder	H	Whole plant.	Jhelum, Bannu	It is used as antifertility agent	Khan et al. (2015)
Cupressaceae	*Juniperus excelsa*	Pencil cedar	T	Berries	Ziarat, Dir, Chitral, Swat, Gilgit	They are used to treat leucorrhea and gonorrhea.	Khan and Khatoon (2009)
Cyperaceae	*Cyperus rotundus* L.	Delloca	H	Whole plant, Rhizome	Bannu, KPK	Dysmenorrhea is treated by this plant.	Khan et al. (2015), Panhwar and Abro (2007), Khan et al. (2013)
Equisetaceae	*Equisetum ramosissimum* Desf.	Jorter, Horse tail	H	Whole plant	Kaghan Valley, Mansehra, Bannu	It is used to treat gonorrhea.	Khan et al. (2015)
Euphorbiaceae	*Riccinus communis* L.	Harnoli	S	Whole plant, seed, leaves	Mianwali, Bannu	It is used to start labor pain at the time of delivery. Also used to treat gonorrhea, and leucorrhea.	Ghani et al. (2012), Khan et al. (2015)
	Euphorbia hirta	Chaghji boti	H	Latex	Shangla	It is used to treat gonorrhea.	Ibrar et al. (2007)
Fabaceae	*Rhynchosia minima*	Jungli moath	C	Whole plant	Sialkot, Mianwali	It is used to take bath after child birth for body care.	Arshad et al. (2011), Ghani et al. (2012), Hussain et al. (2010)
	Quercus floribanda Lindle	Hawthorn	T	Fruit	Bannu	It is used to treat gonorrhea.	Khan et al. (2015)
	Medicago sativa L.	Alfalfa	H	Leaves	Bannu	Menstrual problems	Khan et al. (2015)
	Tephrosiauniflora Pers.	Siringh	H	Leaves	Nara Desert	Boiled leaves are used for syphilis	Qureshi et al. (2010)
	Butea monosperma (Lam.) Taub.	Chichra	H	Gum	Islamabad	Gum is useful for syphilis	Ahmad et al. (2009)
	Cassia fistula L.	Amaltas	T	Root	Islamabad	Powdered seeds used for syphilis	Ahmad et al. (2009)
Gentianaceae	*Geranium wallichianum* D. Don	NA	H	Roots	Bannu	It is used to treat leucorrhea.	Khan et al. (2015)
	Swertia petiolata	Chirayetta	H	NA	Bagh	It is used to treat leucorrhea and vomiting in pregnancy.	Qureshi et al. (2007)
Lamiaceae	*Ajuga bracteosa*	NA	H	Whole plant	Gilgit	Whole plant is used for amenorrhea	Akhter et al. (2016)
	Mentha piperita L.	NA	H	Leaves	Bannu	It is used to induce labor pain at the time of child birth.	Khan et al. (2015)
	Thymus serpyllum L.	Mervezei	H	Whole plant	Tehsil Birmal, S.W Agency, Bagh	It is used for suppression of menstruation.	Farooq et al. (2012), Khan et al. (2015), Qureshi et al. (2007)
Liliaceae	*Aloe vera*	Quargandal	S	Juicy extract	Fiasalabad	Genital herpes	Qadir (2009)
				Acemannan	Fiasalabad	HIV AIDS	Qadir (2009)

(*continued on next page*)

Table 1 (*continued*)

Families	Plant species	Local name	Habit	Part used	Locality	Medicinal use	Reference
Lythraceae	*Woodfordia fruiticosa* Kurz.	Dhaawi, Taavi	S	Flowers, Fruits	Bannu, New Murree	It is used to treat leucorrhea. Powder of dried flowers is taken by females for abortion. Lesser quantity is also used to ease menstruation.	Khan et al. (2015), Ahmed et al. (2013)
Malvaceae	*Abutilon indicum* L.	Koso beta, Kangi	S	Whole plant, leaves, flower	Bannu, Siran Valley, Mansehra	It is used to treat gonorrhea, leucorrhea, and Abortion. Root extract is mixed with egg albumin used for syphilis	Shah et al. (2006), Ishtiaq et al. (2012)
	Malva parviflora L.	Tikalai, Khubazi	H	Leaves	Tehsil Birmal, S.W Agency, Jhehlam	Used in menses.	Khan et al. (2013), Iqbal et al. (2011)
	Abelmoschus esculentus (L.) Moench	Bhindi, Okra	H	Seeds	AJK	Seeds are used to treat gonorrhea.	Ajaib et al. (2014)
Meliaceae	*Melia azedarach* L.	Bakana	T	Bark, fruits and gum	Humzoni, KPK, Bannu	It is used to treat gonorrhea.	Khan et al. (2015), Rehman et al. (2013)
Mimosaceae	*Acacia farnesiana*	Vilayate kikar	T	Gum	Bannu	It is used to treat leucorrhea.	Khan et al. (2015)
	Acacia jacquemontii	Banwali	T	Gum	Bahawalpur	Gum is used to treat gonorrhea.	Wariss et al. (2012)
	Acacia nilotica L.	Kikar, Babool, Babul	T	Leaves, Bark, Pod, fruit, flower, gum	Sialkot, Islamabad, Gujrat Cholistan	Mixture of green lomentum, sugar candy and cardamoms is used orally to cure leucorrhea. Warmed gum is also used for leucorrhea. Leaves, fruits, flowers and gum mixed with sugar, powdered and used thrice a day to treat leucorrhea.	Arshad et al. (2011), Hussain et al. (2010), Rauf et al. (2012), Ahmad et al. (2012)
	Albizia lebbek L.		T	Bark, Seeds	Bannu	It is used to treat gonorrhea.	Khan et al. (2015)
	Prosopis cineraria	Jandi, Kanda, Kandee, jhand	T	Leaves, Bark, Flowers, pods and wood	Cholistan, Bahawalpur, Khirthar National Park, Jhehlum	Decoction is used to treat menstrual disorders. It is also used as contraceptive. Flowers are pounded and mixed with sugar and taken to prevent abortion.	Ahmad et al. (2012), Wariss et al. (2012), Panhwar and Abro (2007), Ghani et al. (2012), Iqbal et al. (2011)
Menispermaceae	*Tinosporea cordifolia* (Willd.) Miers.	NA	H	Leaves, Gum	Bannu	Used as sexual tonic and to cure weakness after delivery.	Khan et al. (2015)
Moraceae	*Ficus benghalensis* L.	Boher, Banyan	T	Latex, Bark, Fruit	Sialkot, Gujrat	It is used to treat gonorrhea and menstrual pain.	Arshad et al. (2011), Hussain et al. (2010), Parvaiz (2014)
Molluginaceae	*Mollugo cerviana*	Padi or Sarr	H	Whole plant	Cholistan	Decoction is used to treat gonorrhea other sexually transmitted diseases.	Ahmad et al. (2012), Malik et al. (2015)
Myrtaceae	*Psidium guajava*	Amrood	T	Leaves, fruit and juice	KPK	It is used to treat menstrual problems.	Rehman et al. (2013)
Nyctaginaceae	*Boerhaavia procumbens*	Padrawash	H	Whole plant	KPK, Cholistan	Juice (50 ml thrice a day) is orally taken in menstrual pain and sexually transmitted diseases.	Khan et al. (2013), Malik et al. (2015)
Papaveraceae	*Papaver somnineferum* L.	Khash khash	H	Seeds	Muzaffar Abad	Seeds crushed with almonds and milk, are given to pregnant women for health and development of fetus. Abortificient, Pregnancy	Ishtiaq et al. (2012)
Papilionaceae	*Butea monosperma* Lam.	Chichra	T	Leaves, whole plant, flowers	Mirpur, AJK, Bannu	It is used to treat gonorrhea. Also used in pregnancy.	Khan et al. (2015)
	Dalbergia sisso Roxb.	Talhi, Shisham, Shawa	T	Whole plant, Roots, Leaves, Bark	Lahore-Islamabad motorway; Bahawalpur	Used as abortificient and to treat gonorrhea. Bark and leaves are used to treat menstrual bleeding.	Shah et al. (2006), Rehman et al. (2013), Wariss et al. (2012)
	Medicago sativa	Malkindye	H	Leaves, Stem	KPK	It is used to treat menstrual disorders.	Khan et al. (2013)
Pinaceae	*Pinus wallichiana* A. B. Jacks.	Biar	T	Leaf, resin	Leepa Valley, Muzaffarabad (AJK)	It is used to treat gonorrhea.	Khan et al. (2013)
Plantiginaceae	*Veronica agrestis*	Khoso beta	H	Whole plant	KPK	Decoction is used to treat menstrual pain.	Khan et al. (2013)
Poaceae	*Arundo donax* L.	NA	H	Stem, leaves and fruits	Bannu,	Used in menstrual pain.	Khan et al. (2015), Khan et al. (2013)
	Cynodon dactylon (L.) Pers	NA	H	Whole plant	Gilgit	Whole plant is crushed, mixed with rice soup for amenorrhea	Akhter et al. (2016)
Pinaceae	*Pinus wallichiana* A. B. Jacks.	Biar	T	Leaf, resin	Leepa Valley, Muzaffarabad (AJK)	It is used to treat gonorrhea.	Khan et al. (2015)
Plantiginaceae	*Veronica agrestis*	Khoso beta		Whole plant	KPK	Decoction is used to treat menstrual pain.	Khan et al. (2013)
Poaceae	*Arundo donax* L.	NA	H	Stem, leaves and fruits	Bannu,	Used in menstrual pain.	Khan et al. (2015), Khan et al. (2013)
	Desmostachya bipinnata Stapf.	Ghar Chichona	H	Leaves	Gujrat	Used to treat menorrhagia.	Hussain et al. (2010)
	Cynodon dactylon L.	Chhabbar.	H	roots	Kohistan khirthar	Decoction of roots is used to	Panhwar and Abro

Table 1 (*continued*)

Families	Plant species	Local name	Habit	Part used	Locality	Medicinal use	Reference
Poaceae					national park	treat gonorrhea and other urinogenital diseases.	(2007)
Polygonaceae	*Polygonum amplexicaule* D.Don	Mosloom	H	Flowers, leaves, Whole plant	Galliyat, Bannu	It is used to treat leucorrhea and menstrual pain.	Khan et al. (2015)
	Rumex dentatus L.	NA	H	Leaves	Bannu	Used in abortion.	Khan et al. (2015)
	Polygonum dichotomum Blume.	NA	H	Whole plat	Bannu	It is used to treat gonorrhea.	Khan et al. (2015)
	Polygonum biaristatum	Howar	H	Whole plant	KPK	Mostly used to treat gonorrhea.	Khan et al. (2013)
Punicaceae	*Punica granatum* L.	Anar, Daruna, Daruni	S	Exocarp of fruit, stem bark, flowers	KPK, Mandi Bahaudin, Gujrat, Poonch Valley Azad Kashmir	It is used to treat leucorrhea and hemorrhage. Flower powder (20 g thrice a day) with water is given to treat the leucorrhea and vomiting during pregnancy. It is also used to treat menstrual irregulation.	Jan et al. (2008), Khan et al. (2012), Hussain et al. (2010)
Rananculaceae	*Ranunculus scleratus* L.	Gul-e-ashrafi	H	Whole plant	Dera Ghazi Khan	It is used externally to treat hemorrhoids and perineal damage after child birth.	Gulshan et al. (2012)
Rhamnaceae	*Zizyphus spina-christi*	Beri	T	Fruit, Bark, Leaves, Seeds	Cholistan	Powder and decoction form is used to treat hemorrhage and leucorrhea.	Ahmad et al. (2012)
Rosaceae	*Crataegus songarica* K. Koch.	Ghonii	T	Leaves, stem, bark	Chitral	Bark is boiled to make extract. One glass of this extract is given to women at the time of delivery to reduce labor pain.	Hussain et al. (2007)
Rubiaceae	*Randia tetrasperma* Roxb.	Mainphal, Gangeri, Kikra, Kukal, Khukhuri, Mindla	S	Fruit	Kaghan valley, KPK	Fruit pulp is used as abortifacient.	Jan et al. (2008)
Salicaceae	*Salix acmophylla* Boiss.	Chekar	H	Leaves	Chitral	Fresh leaves extract is used orally to regulate menses.	Hussain et al. (2007)
Salvadoraceae	*Salvadora oleiodes* Decne.	Pilu	S	Whole plant	Mianwali, Bannu	It is used to regulate menstruation period. It reduces labor pain.	Ghani et al. (2012), Khan et al. (2015)
Saxifragaceae	*Bergenia stracheyi*	Korat, Zakhm-i-Hayat	H	Leaves, Flower	Babosar, Naltar, Astore, Juglot, Nagar	It is used for post-partum recovery.	Khan and Khatoon (2009)
Solanacae	*Solanum surattense* Burm. f.	Azghai/Kandiyari/-Candairi/-Manraghonay/-Mahokri, Mohkri	H	Whole plant	Bannu, AJK	The roots are used to increase fertility in women. Also used to treat gonorrhea and menstrual complications.	Khan et al. (2015), Ajaib et al. (2014)
	Withania somnifera L.	Kotilal, asgand, Jangli paneer, Shapyange	S	Seeds, leaves, roots	Dera Ghazi Khan, Bannu, Khan, Valley Alladand Dehri Malakand, Jhehlam, Mardan, KPK	Seeds are used in pregnancy to control body temperature. Leaves poultice locally applied to keep the breast shape. Root powder is taken with milk or butter to treat leucorrhea and for pregnancy. Its seeds are also used to regulate the menstrual cycle.	Khan et al. (2015), Alamgeer et al. (2013), Iqbal et al. (2011), Bahadur et al. (2013), Khan et al. (2013)
	Datura metel L.	Barbaka	S	Whole plant	Lakki Marwat	It is used to treat gonorrhea.	Khan et al. (2013)
	Datura alba	Burbaka	H	Seeds, fruit, leaves, bark	KPK	It is used to treat hemorrhoids.	Rehman et al. (2013)
	Physalis angulata	Hotelie	H	Leaves	KPK	Leaves are used to facilitate childbirth. Also used to treat infertility in women.	Khan et al. (2013)
Tamaracaceae	*Tamarix aphylla*	Ukhan, Frash	T	Leaves, Bark	Cholistan	Decoction is used to treat leucorrhea and menstrual disorders.	Ahmad et al. (2012)
			T	Bark	Kohat	Bark is used for syphilis	Iqbal et al. (2012)
Tiliaceae	*Corchorus depressus* L.	Bundairy/Mundairy	H	Whole plant	Kalat and Khuzdar regions of Balochistan	It is used to treat gonorrhea.	Khan et al. (2013)
	Grewia villosa Willd.	Jalidar	S	Whole plant	Cholistan	Urinary tract infections, and sexually transmitted diseases.	Malik et al. (2015)
Typhaceae	*Typha latifolia* L.	Typha	H	Leaves and Pollens	Gujrat, Lodheran, Punjab	It is used to treat painful menstruation, hemorrhage, post-partum pains and uterine bleeding. Not given to pregnant women. Menses	Gulshan et al. (2012), Hussain et al. (2010)
	Typha domingensis Pers.	Barya	H	Rhizome	AJK	It is used to treat amenorrhea.	Ajaib et al. (2014)
Urticaceae	*Urtica dioica* L.	NA	H	Leaves	Bannu	Used to treat menstrual complications.	Khan et al. (2015)
Verbenaceae	*Verbena officinalis* L.	Chandni	H	Whole plant	Dera Ghazi Khan	It is used to increase lactation.	Gulshan et al. (2012)
	Phyla nodiflora	Bhukan boti	H	Whole plant	Bahawalpur	Decoction of whole plant is used to ease the delivery and to treat post-partum discharge	Wariss et al. (2012)

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Table 1 (*continued*)

Families	Plant species	Local name	Habit	Part used	Locality	Medicinal use	Reference
Zygophyllaceae	*Fagonia indica* Burm.f.	Dhamasa, Damaho	S	Whole plant	Jhehlam, Sothern Punjab	Dried plant in powder form is used for gynae problems. Menses	Iqbal et al. (2011)
	Peganum harmala L.	Harmal, Hurmal, Sponda/Spellanii	H	Whole plant, Seeds	Dera Ghazi Khan, Khirthar, KPK	It is used to treat painful Menstruation. Seeds are used as abortifacient and in retention of urine.	Gulshan et al. (2012), Panhwar and Abro (2007), Rehman et al. (2013)
	Tribulus terrestris L.	Puncture Vine, Bhakra	H	Seeds, leaves, whole plant	Sialkot, Gujrat, New Murree, Dera Ghazi Khan	It is used to treat gonorrhea, menstrual complications and urinogenital diseases. Dried powdered whole plant is used to ease the menstrual flow and its high dose is also used in abortion.	Arshad et al. (2011), Hussain et al. (2010), Ahmed et al. (2013)
Zingeberaceae	*Elettaria cardamomum* (L.) Maton	Chotti illaichi	S	Seeds	Rural urban areas of Sindh	It is used to treat leucorrhea and female impotency.	Arshad et al. (2011)

the whole birthing process, from pregnancy through conception to postpartum (Shah et al., 2013). Usually, the rural women prefer medicinal plants on allopathic drugs for their personal illness due to deficiency of modern amenities in remote areas (Adnan et al., 2015).

3.2. Cultural similarities in use of plants and their parts

Punjabi, Pashtun, Sindhi, and Balochi are the four major groups of diverse culture of Pakistan (Chandio, 2012; Siddiqi, 2012), which are based on the ethnicity of four provinces including Punjab, Khyber Pakhtunkhwa, Sindh, and Baluchistan, respectively. Pashtun women are using the highest number (65%) of plants against gynecological complaints and STIs followed by Punjabis (53%). There might be several reasons behind this finding. Pashtun culture is the leading culture in ethno-gynecological uses of plants in Pakistan. Such as, the Pashtun women in Pakistan are facing cultural resistances, lack of modern reproductive health facilities, dry mountainous ecosystem, and susceptibility to different kinds of infections (Abbas et al., 2016). Moreover, another reason could be the occurrence of Pashtun culture in a large geographic area between Pakistan and Afghanistan called Pashtun tribal belt which is also one of the largest ethno-linguistic tribal groups around the globe (Nawaz, 2009; Munoz, 2010). Punjabi culture is the largest ethnic group of Pakistan because (Veach and Williamson, 2010) most of Punjabis are the inhabitants of Indus valley civilization and Punjab is rich in plant species of economic importance due to a vast irrigation system, moist monsoon climate and fertile land (Zereen et al., 2013). In addition, there is also an effect of the traditional medicinal system on the use of plant species in different regions of Punjabi culture *i.e.* Ayurvedic, Tibetan and Unani system of medicine (Gairolaa et al., 2014). Indus civilization is among the earliest urban cultures, hence, possessing a treasure of historical ethnobotanical knowledge. Outer influences made this culture very different from the rest of Pakistani cultures (Allana, 2010). Tribal communities mostly live in association with nature and play crucial roles in the development of native knowledge in order to conserve and protect biodiversity, ethno-medicine, and the environment (Jaiswal, 2010). These communities also cause the inter-cultural transfer of ethno-botanical knowledge when they travel among different provinces. Sørensen similarity index indicated that highest consensus was found between Punjabi and Balochi culture (PJB*BC) followed by Punjabi and Pashtun culture (PJB*PC) in terms of the use of plants (Table 2). In terms of plant parts use, highest similarity was found between Punjabi and Sindhi culture (PJB*SC) followed by Punjabi and Pashtun culture (PJB*PC). These findings are interesting because Punjabi and Pashtun cultures showed higher similarity for plant usage and their parts in using ethno-medicines, which might be due to similarities in phytodiversity, geographical conditions, and ethno-medicinal knowledge of local healers in these regions. *Cuscuta reflexa, Citrullus colocynthis, Convolvulus arvensis, Justicia adhatoda, Achyranthes aspera, Nerium oleander, Erigeron bonariensis, Achillea millefolium, Berberis lycium, Ricinus communis, Woodfordia fruticosa, Malva parviflora, Butea monosperma, Punica granatum*, and *Withania somnifera* were found to be commonly used by Punjabi and Pashtun cultures. *Juniperus excels* was commonly used between Balochi and Pashtun culture. *Foeniculum vulgare* was commonly used between Sindhi and Pashtun culture. *Tecomella undulata, Prosopis cineraria*, and *Oxystelma esculentum* were found to be commonly used between Sindhi and Punjabi culture. *Berberis lycium* and *Peganum harmala* were commonly used in more than two cultures. Therefore, all the above mentioned plant species must be subjected to further pharmacological screening for the development of safe drugs and to facilitate women in improving their reproductive health. Consensus between Sindhi and Balochi cultures was almost negligible, which might be due to the significant distinction between the two cultures or lack of documentation of traditional ethno-gynecological knowledge. Linear regression showed positive and direct correlation between similarities

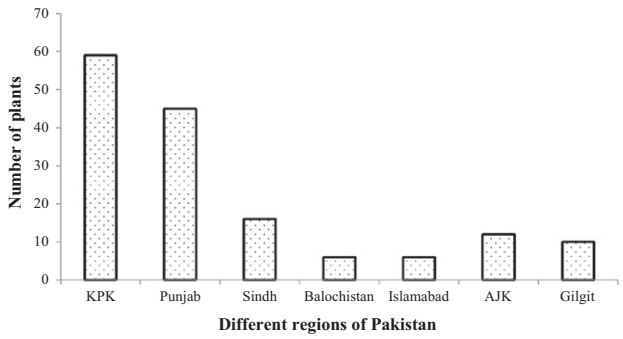

Fig. 3. Utilization of plants to treat gynecological and sexually transmitted problems in different regions of Pakistan.

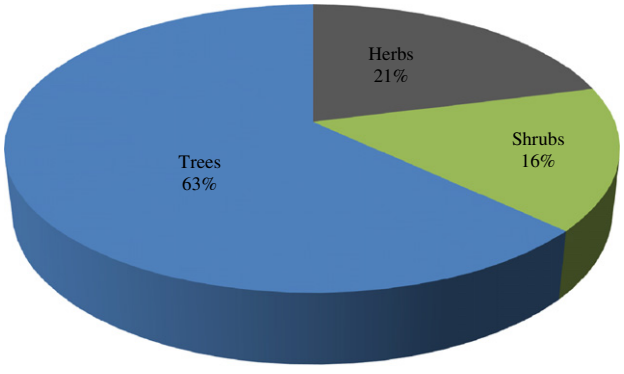

Fig. 4. Habits of plants used for various gynecological and sexually transmitted diseases.

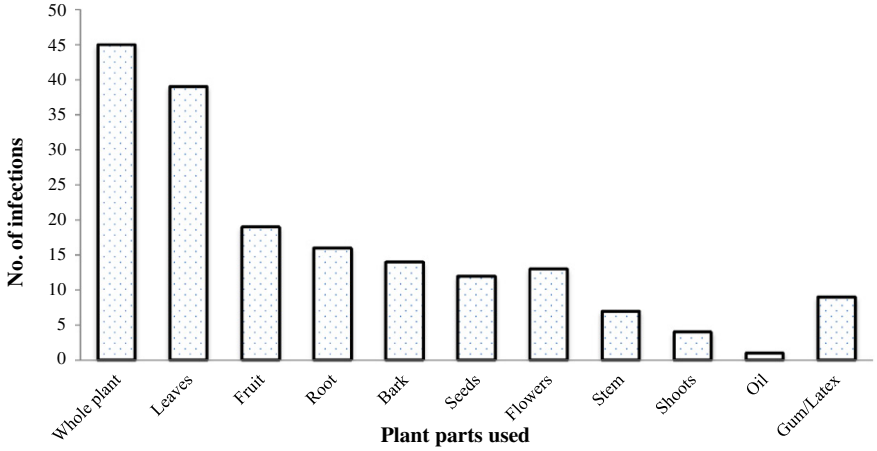

Fig. 5. Parts used for treatment of gynecological and sexually transmitted diseases in Pakistan.

regarding plant and their parts uses among four cultures (Fig. 6). The highest percentage of reports was found in Punjabi culture (46%) followed by Pashtun (33%), Sindhi (10%) and Balochi (10%) cultures. Least documentation is the major reason behind the differences in the extent of medicinal plant uses or knowledge between different cultures. The documentation of ethno-gynecological knowledge about plants in Punjab is found to be well conducted as compared to other provinces of Pakistan. Hence, it is the need of time to pay more attention in this regard to conserve this precious treasure of folk knowledge in less focused areas. Present finding also indicates a reasonable similarity in ethno-medicinal knowledge of plants to treat gynecological complaints in different cultures, which could provide useful information to the researchers for selecting potential medicinal plants for future pharmacological studies.

3.3. Pharmacological profile of reported plants

Literature review revealed that among 116 reported medicinal plants, very few (13 plant species) were found to be pharmacologically evaluated (Table 3). In these reported studies, different activities were checked such as antifertility, abortifacient, antiovulatory, anti-implantation, regulation of estrous cycle and pregnancy inhibition. Female rats and Guinea pigs were mostly used as model organisms to evaluate plant extract activities through oral administration. Majority of the reported studies were carried out in India, whereas, none of the studies found in Pakistan which clearly indicates the lack of *in-vitro* and *in-vivo,* studies in the country, and might be attributed to the dearth of modern well-equipped laboratories. A previous study proved that the crude aqueous extract of *Mangifera indica* and *Centella asiatica* carries antiherpes simplex virus activities (Yoosook et al., 2000). More attention should be given to the ethno-medicinally used plants against gynecological diseases in order to validate the pharmacological efficacy and reliability of herbal medicines against the reproductive problems.

Table 2
Sørensen similarity index (SS). PJC, PC, SC and BC represents Punjabi culture, Pashtun culture, Sindhi culture and Balochi culture, respectively.

Cultures	SS of plant species	SS of plant parts
Punjabi*Pashtun	0.311	0.514
Punjabi*Sindhi	0.131	0.593
Punjabi*Balochi	0.351	0.182
Pashtun*Sindhi	0.053	0.154
Pashtun*Balochi	0.056	0.286
Sindhi*Balochi	0	0

3.4. Toxic potential of plants used to treat gynecological complaints

This literature review reported toxicity tests for 22 medicinal plants (Table 4). Most of these plants were found safe against different model organisms. Aqueous extract of *Anethum graveolens* was proved to be more toxic than alcoholic extract (Hosseinzadeh et al., 2002). High dose of aqueous extract of *Nerium oleander* leaves also showed toxicity (Chowdhury et al., 2004). Aqueous extract of *Carica papaya* showed a little dehydration in blood investigation but no lethality was observed (Halim et al., 2011). Alcoholic extract of *Citrullus colocynthis* (Dehghani and Panjehshahin, 2006) and aqueous extract of *Psidium guajava* (Attawsih et al., 1995) showed the signs of hepatotoxicity. Methanolic extract of leaves, stems, flowers and roots of *Euphorbia hirta* showed mild toxicity (Rajeh et al., 2012). A single dose was found to be safe, but hepatotoxicity was found in repeated doses of aqueous extracts of *Acacia nilotica* roots (Alli et al., 2015). There are no toxic effects of *Centella asiatica* but at high doses it causes burning sensations, skin allergy, nausea, headache, dizziness, upset stomach, and extreme drowsiness (Zahra et al., 2014).

Herbal drugs are widely used across the world because of their natural origin. However, it does not assure their safety, as chemical compounds present in plants may exhibit toxic effects, because every chemical is safe up to a specific level of dosage (Sharwan et al., 2015). Lack of sufficient knowledge about the safety profile of herbal medicines could be dangerous if taken in very high doses or taken repeatedly over a period of time (Rodriguez-Fragoso et al., 2008; Alli et al., 2015). In toxicology, observational data is gathered and used to predict the results of exposure to animals as well as humans (Sharwan et al., 2015). Toxicology is helpful to determine the range of doses, responsible for producing the maximum effect (Reddy and Kamble, 2014). Most common toxic

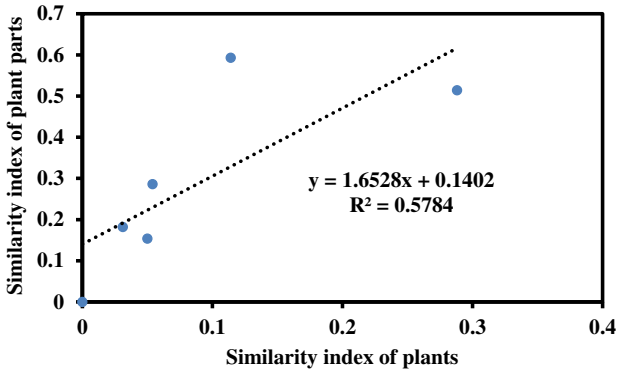

Fig. 6. Sorensen index correlation between plants and parts usage.

Table 3
Pharmacological activities of medicinal plants against gynecological problems.

Family	Plant name	Part used	Extract	Model Animal	Dose (mg/kg/day)	Mode of administration	Duration (days)	Effect (%age)	Country	Activity	Reference(s)
Amaranthaceae	*Achyranthes aspera* L.	Leaves	Methanolic	Female rats	1 g/kg	Gavage	21	>90	Ethiopia	Antifertility	Shibeshi et al. (2006)
Apiaceae	*Cuminum cyminum*	Seeds	Aqueous and alcoholic	Female rats	150 mg/kg 200	P.O.	7	100 80	India	Anti-infertility	Dhaliwal et al. (2016)
	Anithum graveolense	Whole plant	Aqueous Alcoholic	Female rats	0.04 g/kg 0.45 0.5 5	Oral	10	NA	Iran	Regulation of estrous cycle	Monsefi et al. (2006)
Asteraceae	*Cichorium intybus*	Seeds	Ethanolic	Female rats	NA	Oral	NA	NA	NA	Contraceptive	Keshri et al. (1998)
Cannabaceae	*Cannabis sativa*	Leaves	Alcoholic	Female rats	100 200 400	Oral	5	9.09 20 42	India	Abortifacient	Zade et al. (2013)
			Chloroform		100 200 400	Oral	5	10.90 20 42			
Caricaceeae	*Carica papaya*	Roots	Composite ethanolic	Female rats	1000	Oral	12	NA	India	Menstrual regulation	Sarma and Mahanta (2000)
		Seeds	Aqueous	Female rats	100 800	Oral	10	NA	Nigeria	Abortifacient	Oderinde et al. (2002)
		Whole plant	Alcoholic	Rabbits	NA	NA	NA	40	India	Antiovulatory	Kapoor et al. (1974)
Caesalpiniaceae	*Cassia fistula* L.	Seeds	Aqueous	Mated female rats	100 200 500	Oral	5	57.14 71.43 100	India	Inhibition of pregnancy	Verma (2016)
Cucurbitaceae	*Citrullus colocynthis* L.	NA	NA	Female rats	400	Oral	10	NA	Iraq	Antifertility	Al-Snafi (2016)
	Woodfordia fruiticosa Kurz.	Flowers	Ethanolic	Female rats	100 kg/mg	Oral	7	43	India	Abortifacent	Khushalani et al. (2006)
Lythraceae	*Abutilon indicum* L.	Whole plant	Methanolic	Female rats	NA	Oral	NA	NA	India	Antifertility	Johri et al. (1991)
Malvaceae	*Melia azedarach* L.	Seeds	NA	Female rats	5 10 20	Oral	18	NA	India	Abortifacient	Mandal and Dhaliwal (2007)
Papilionaceae	*Butea monosperma* Lam.	Whole plant	Methanolic	Female rats	NA	Oral	NA	NA	India	Antifertilty	Johri et al. (1991)
		Roots	Petrolium ether Choloform	Female mice	200 mg/kg	Oral	7	83.33 66.67	India	Anti-implantation	Sharm et al. (2012)
Punicaceae	*Punica granatum* L.	Fruit peel	NA	Guinea pig	18 g/kg	Oral	NA	NA	India	Antifertility	Haque et al. (2015)

effects produced by herbal medicines are nephrotoxicity (Asif, 2012) and hepatotoxicity (Nwachukwu and Iweala, 2009). Other possible side effects include allergic reactions (Saad et al., 2006), neurotoxicity (Ernst, 2003), cardiac toxicity (Moritz et al., 2005), and even mortality (Jensen and Allen, 1981). Information on biological activity and mechanism of action of the herbal drugs can be gathered by toxicity testing (Sharwan et al., 2015), and would be utilized for risk management and hazard identification of herbal drugs. Present findings clearly reveal that all herbal medicines are not safe if taken in high dosage, therefore accurate and detailed knowledge about their toxicity profile must be acquired before usage to reduce negative effects on the living system.

3.5. Gynecological complaints

Citation frequency of literature was highest for the menstrual complication, abortion, and leucorrhea among all the gynecological ailments reported (Table 5).

3.6. Menstrual complications

In Pakistan, most of the reported plants (45) are being used in herbal recipes for menstruation complications (Table 1; Fig. 7). Traditional healers prepare these herbal remedies either solely or in combinations and for oral use with water or other additives such as honey, sugar and salt against menstrual complications. Pakistani women are expert in making ethno-medicinal recipes, for example, bark of *Acacia nilotica*; seeds of *Trachyspermum ammi*, *Withania coagulans* and *Foeniculum vulgare* are mixed with *jaggery* (traditional un-centrifuged sugar) in equal quantity and soaked it in water for overnight. In the morning, water is sieved and boiled with the addition of *ghee* and wheat flour and drink half a glass of prepared water for three days regularly. This recipe is considered a good treatment in scanty menses, which the majority of women in Khyber Pakhtunkhwa and Sindh provinces are practicing it (Shah et al., 2013). In addition, *Trachyspermum ammi*, *Foeniculum vulgare*, crystal sugar, *Elettaria cardamomum*, and *Terminalia bellerica* are grinded together and boil the powder by adding one glass of water and three table spoons of butter. This formulation is taken twice in 24 h for three days and is consider a good remedy against menorrhea (Choudhary et al., 2012). These results indicate that Pakistani women have rich ethno-medicinal knowledge regarding their reproductive healthcare and this understanding has been transferred to them by their ancestors. Ozgoli et al. (2009) studied the effect of ginger, mefenamic acid and ibuprofen for relieving pain during primary dysmenorrhea. Results suggested that ginger was as useful as mefenamic acid and ibuprofen, which signifies the greater efficiency and potential of traditional medicines with fewer side effects on the woman reproductive system as compared to allopathic drugs. In the above mentioned herbal recipes, *Trachyspermum ammi* is a chief plant species. In India, this plant is also traditionally being used against amenorrhea, abdominal tumors, and carminative. Moreover, several biological activities of this plant have also been reported such as antifungal, antimicrobial, antioxidative, and cytotoxic. *Trachyspermum ammi*

Table 4
Side effects/Toxicity of medicinal herbs traditionally used in Pakistan to treat gynecological problems.

Family	Plant name	Test Animal	Test	Extract	Side effect/Toxicity	Reference
Acanthaceae	*Justicia adhatoda* L. (=*Adhatoda zelyanica.* Medic., *Adhatoda vasica.* Nees)	Rats and Monkeys	Histopathological examination, Autopsy	Aqueou	No abnormality in the organs of test animals represented non-toxicity of vasicine found in aqueous extract of *Justicia adhatoda.*	Ahmad et al. (2009)
Amaranthaceae	*Achyranthes aspera* L.	Swiss mice	Toxicity and acute toxicity tests	Methanolic extract of whole plant	No abnormality (non-toxicity) was observed	Reddy and Kamble (2014)
		Albino rats and Swiss mice	Sub-acute toxicity and Haemostatic effects test	Methanolic extract of leaves	No toxicity was observed. It has haemostatic effects with decreased bleeding and clotting times	Okon et al. (2015)
Apiaceae	*Foeniculum vulgare* Mill.	Rats	Teratogenecity and toxicity test	Essential oil	Toxic effect on studied concentration was observed on fetal cells but no teratogenicity was found	Ostad et al. (2004)
	Anethum graveolens	Mice	Acute toxicity study	Aqueous and ethanolic extract of seeds	Aqueous extract is more toxic than ethanolic. Overall toxicity level is low	Hosseinzadeh et al. (2002)
		Mice	Clinical, Biochemical, hematological and pathological tests	Hydroalcoholic extract	Doses <50 mg/kg are found to be safe for both male and female mice	Bidgoli et al. (2011)
		Swiss albino mice	Acute and sub-chronic toxicity study	Alcoholic extract of seeds	Non-toxic and absolutely safe	Desai and Patel (2016)
Apocynaceae	*Nerium oleander* L. (=*Nerium indicum.* Mill.)	Guinea pigs	Lethality test	Aqueous extract of leaves	Lowest dose 300 mg/kg was proved to be non-toxic while at high doses lethality was observed.	Chowdhury et al. (2004)
Asclepiadaceae	*Leptadenia pyrotechnica*	Wistar rats	Acute toxicity study	Ethanolic extracts of aerial parts	No toxicity was observed.	Soliman et al. (2012)
Asteraceae	*Cichorium intybus* L.	Sprague–Dawley rats	Ames test ans sub-chronic toxicity study	Ethanolic extract of roots	No toxicity was observed	Schmidt et al. (2007)
		Bacteria	Microtox acute toxicity test	Hydoalcoholic extract	Safe to human use	Conforti et al. (2008)
	Achillea millefolium L.	Guinea pigs	Sensitivity test	Crude extract	Not toxic but hypersensitivity was observed	Lakshmi et al. (2011)
	Eclipta prostrata	Zebrafish embryos	Lethality test	Aqueous extract of leaves	Lethality was non-significant and also at very low concentration	Ponpornpisit et al. (2011)
Caricaceeae	*Carica papaya*	Sprague Dawley rats	Acute toxicity tests	Aqueous extract of leaves	No adverse effect was found but blood investigation revealed a bit dehydration	Halim et al. (2011)
		Sprague Dawley rats	Sub-chronic toxicity study	Aqueous extract of leaves	No toxic effect was found	Ismail et al. (2014)
		Sprague Dawley rats	Sub-acute oral toxicity study	Aqueous extract of leaves	No toxic effect was found	Afzan et al. (2012)
Caesalpiniaceae	*Cassia fistula* L.	Guinea pig	Acute and sub-chronic toxicity stuy	Aqueous extract of pods	Very low level of toxicity was found	Akanmu et al. (2004)
		Swiss albino mice	Acute oral toxicity test	Methanolic extract of seeds	No significant toxic effect was found	Jothy et al. (2011)
Cucurbitaceae	*Citrullus colocynthis* L.	Rabbits	Toxicity test	Seed and pulp extract	Seed extract was found to be safe but pulp was fatal	Shafaei et al. (2012)
		Rats	Test of toxic effect on liver	Alcoholic extract of	Morphological changes in liver were found, it can have toxic effects on liver cells	Dehghani and Panjehshahin (2006)
Euphorbiaceae	*Riccinus communis* L.	Swiss albino rats	Toxicity test	Aqueous extract of whole plant powder	There was no significant toxic effect	Pingale (2011)
		Wistar albino rats	Acute and sub-chronic toxicity study	Aqueous and methanolic extracts of roots	No toxicity was found	Ilavasan et al. (2011)
	Euphorbia hirta	Swiss albino mice	Brine shrimp lethality assay and oral acute toxicity study	Methanolic extract of leaves, stem, flowers and roots	Mild toxic effects were found in leaves methanolic extract	Rajeh et al. (2012)
		Sprague Dawley rats	Acute and sub-chronic toxicity study	Methanolic extract of whole plant	No toxicity was observed	Ping et al. (2013)
		Swiss albino mice	Acute toxicity study	Oral feed of plant material in the form of slurry	No toxicity was observed	Pingale (2013)
Mimosaceae	*Prosopis cineraria* L.	Swiss albino mice	Acute systemic toxicity study	Methanolic extract of leaves	No toxicity was found	Ahmed et al. (2012)
		Wisatr rats	Acute and sub-acute toxicity study	Hydroalcoholic extract of leaves and stem bark	No toxicity was observed	Robertson et al. (2012)
	Acacia nilotica	Swiss albino mice	Acute and sub-acute toxicity study	Aqueous extracts of roots	Single dose was found to be safe but hepatotoxicity was found in repeated doses	Alli et al. (2015)
Malvaceae	*Abutilon indicum* L.	Swiss albino mice	Acute toxicity study	Juice of fresh leaves	No toxicity was found	Pingale and Virkar (2011)
		Wistar albino rats	Acute toxicity study	Petroleum ether extract of roots	No toxicity was found	Kousalya et al. (2014)

(continued on next page)

Table 4 (*continued*)

Family	Plant name	Test Animal	Test	Extract	Side effect/Toxicity	Reference
Malvaceae	*Abelmoschus esculentus*	Mice	Acute and sub-chronic toxicity studies	Distilled water, hot water and hot buffer pod extract	No toxicity was found	Ilango et al. (2011)
Menispermaceae	*Tinosporea cordifolia* (Willd.) Miers.	Swiss mice	Acute toxicity study	Decoction of aerial parts and aqueous slurry of whole plant powder	No toxicity was observed	Pingale (2011)
Myrtaceae	*Psidium guajava*	Mice and rats	Acute and chronic toxicity studies	Aqueous extract of leaves	Hepatotoxicity was found	Attawsih et al. (1995)
Punicaceae	*Punica granatum* L.	OF-1 mice and wistar rats	Toxicity evaluation	Hydoalcoholic extract of whole fruit	No toxicity was observed	Vidal et al. (2003)
		Swiss albino mice	Acute and sub-acute toxicity study	Ethanolic extract of whole fruit and seeds	No toxicity was found	Bhandary et al. (2013)
		Balb/c mice	Toxicity study	Peel extract	No toxicity was found	Jahromi et al. (2015)
Solanaceae	*Withania somnifera* L.	Wistar rats	Acute and sub-chronic toxicity study	Methanolic extract of roots	No toxicity was found	Patel et al. (2016)

contains carbohydrates, saponins, glycosides, phenolic compounds, volatile oil (thymol, γ-terpinene, para-cymene, and α- and β-pinene), protein, fiber fat, and minerals (Jeet et al., 2012) that might be responsible for its bioactivity against menstrual complications. Traditional healers have centuries-old indigenous knowledge but still most of the ethnogynecological studies lack information regarding the dosage and proper concentration/amount of plant parts in different kind of monoherbal and polyherbal recipes. This information is extremely important to avoid side effects on the living system. The reported plants against menses contain a variety of secondary metabolites but scientifically most of them are still need to be tested and should be given priorities in future studies.

Menstrual problems are generally not considered as major health issues, and therefore not perceived in the world reproductive health programs. However, scientific researches in different low-income countries show that morbidity due to menses has a great impact on women's health status, life quality, social relations, and education (Campbell and Harlow, 2004). Menstrual complications are also a risk marker for other reproductive disorders. Irregular or abnormal uterine bleeding may be a symptom of cervical cancers or tumors, fibroids in the uterus, hemorrhagic dengue fever, or genital tuberculosis; whereas prolonged or excessive bleeding can result in anemia and may be life-threatening if not treated well. The absence of menses (amenorrhea) or infrequent menses (oligomenorrhea) are a reflection of underlying endocrine diseases, endometrial tuberculosis, malnutrition, cancer or AIDS (Tehrani et al., 2011). Hormonal therapy or anti-inflammatory non-steroidal medications are used to treat menstrual diseases in the Western world. Therefore, a lot of women in Asia, Africa and Latin America prefer traditional medicines to treat menstrual disorders or being used as contraception (Andel et al., 2014).

Table 5
List of gynecological and sexually transmitted ailments.

Ailments	Related complaints	Citation frequency (%)
Abortion	unsafe abortions, antifertility effects	20.7
Gonorrhea	–	20.7
Menstrual complications	Amenorrhea, oligomenorrhea, Scanty menses, dysmenorrhea	20
Leucorrhea	Leucorrhea, dysfunctional uterine bleeding, Pathological leucorrhea	15
Syphilis	–	10.7
Prenatal complications	Vomiting, anemia, nausea, backache, headache	8.5
AIDS	–	2.1
Genital herpes	–	1.4
Chlamydia	–	0.7

3.7. Leucorrhea

Literature showed that 19 plants are being used individually or in a mixture form to treat leucorrhea in Pakistan (Table 1; Fig. 7). Majority of the women prefer a mixture of different plants in herbal formulations which might be due to a greater efficacy (synergy) in the treatment of leucorrhea as compared to a single plant. One of the most potent herbal formulations against leucorrhea is composed of a mixture of six plants (*Cocos nucifera*, *Prunus amygdalus*, *Arachis hypogaea*, *Pistacia vera*, semi grind *Triticum aestivum*, *Punica granatum* and *Areca catechu*) in equal amount added together with sugar, then are grinded to make powder. The powder is then mixed with 2 kg of butter oil and administered early in the morning before having breakfast for 12–40 days (Choudhary et al., 2012). In another example, fresh leaves of *Ocimum basilicum*, *Cannabis sativa*, 5–6 leaves of *Terminalia bellerica*, 3–4 leaves of *Elettaria cardamomum* and 2–3 leaves of *Mentha piperita* are mashed to make vaginal suppositories, this is placed intra-vaginally regularly for seven days at night (Choudhary et al., 2012). Moreover, fresh leaves of *Ricinus communis* are crushed and boiled in 250 ml of milk and then after filtration the filtrate is taken for one month for the treatment of leucorrhea (Qureshi et al., 2009). *Trichomonas vaginalis* is the most important microbe causing parasitic leucorrheal infection. Generally, Metronidazole is used against this infection, but due to antibiotic resistance against this antibiotic (Bhandari, 2012); natural plant extracts are used as alternative. As an example, *in-vitro* and *in-vivo* activity of *P. granatum*

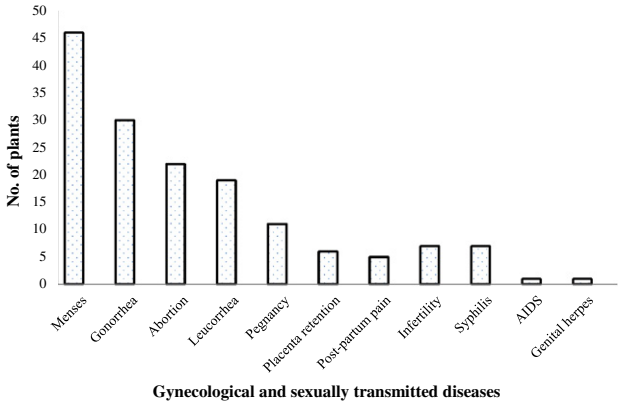

Fig. 7. Number of plants used to treat different gynecological and sexually transmitted diseases.

against *Trichomonas vaginalis* showed promising effects (El-Sherbini et al., 2010).

These problems have significant effects on women reproductive capability, working ability, mental health, and other physical activities. It is the most frequent disorder with high frequency seen in female reproductive periods (Kulkarni and Durge, 2005). Pathological leucorrhea occurs mainly due to bacterial, fungal, and protozoa infection in the genital organ. However, *Candida albicans* (6.7%), *Trichomonas vaginalis* (4.5%), and *Neisseria gonorrhoeae* (2.7%) are the most common pathogens associated with leucorrhea (Chaudhuri et al., 1998). All over the world and especially in developing countries, mostly women have leucorrhea due to bad hygienic conditions and contaminated food. A study conducted by Kaur and Kapoor (2014) reveals that 32.7% of leucorrhea is due to weakness, in addition to other factors such as consumption of hot foods, mental tension, economic hardship, allopathic medicines, and body heat. In spite of strong efficacy of the above mentioned plants in herbal remedies; still, there is lack of studies regarding their biological activities against causative pathogens of leucorrhea. Antimicrobial activities of these plants are highly recommended for the validation of their traditional use.

3.8. Abortion

The present review reported ethno-medicines of 22 plant species used by the Pakistani women for inducing or preventing abortion (Table 1; Fig. 7). *Achyranthes aspera* is considered as an effective plant used traditionally for inducing abortion and preventing pregnancy. *Achyranthes aspera* at high dose (5.5 kg per body weight) caused a significant change in the number of both live and dead fetuses, while on the other hand fetal survival percentage indicates the possible abortifacient activity of this plant. Methanolic extract (leaf part) of this plant has shown antifertility effects, which might be exploited to prevent unwanted pregnancy and control the ever-increasing population growth (Asolkar et al., 1992) confirming the efficacy and reliability of ethnomedicinal knowledge of traditional healers. Another study reveals that the leaves of *Achyranthes aspera* contain saponins, oleanolic acid, xylose, glucose, galactose, rhamnose, and ash (Ranaa et al., 2010), which might be associated with their antifertility effect. Moreover, different studies have suggested that soaking the methanolic extract of *Acacia nilotica* and *Punica granatum* in water during the night, sieving it in morning for oral administration (5–6 days) can induce abortion. *Acacia nilotica* is also being used for variety of other ailments including tuberculosis, pneumonia; gonorrhea and small pox (Saini et al., 2008; Ali et al., 2012). Abortifacient and ureotonic properties of *Adhatoda vasica* are used to induce abortion and to stimulate contractions of the uterine to ease the delivery (Gupta et al., 1978; Gangwar and Ghosh, 2014). In a previous study on vasicine activity to stimulate the uterine contractions, human myometrial strips were taken from the uteri of pregnant as well as non-pregnant women to treat them with *Adhatoda*. The herb was proved to be stimulating uterine contractions, just like the properties of oxytocin drug. Antireproductive studies in animals also proved the abortifacient properties of *Adhatoda vasica*. Aqueous or 90% ethanol extracts of plant leaves were orally given to guinea pigs and rats for 10 days after insemination and 100% abortifacient activities were observed (Gupta et al., 1978). Leaves of *Taxus wallichiana* are also very commonly used in traditional medicines for inducing menstruation and preventing pregnancy. Researchers must pay special attention to these bioactive plants for further detailed screening, which could be a positive step toward designing some novel, safe and affordable drugs for the women reproductive health.

3.9. Prenatal complications

Some 529,000 women die every year due to complications during pregnancy (WHO, 2005). Besides conventional approaches, such as epidural analgesia, many alternative and complementary methods have been reported to reduce labor pain. Different herbal remedies are being used to treat prenatal complications and to ease child birth. Specific herbs with different properties are used in 5th or 6th week of pregnancy to facilitate the child delivery. Practitioners observed that these herbal drugs had a relaxing and calming effect, *e.g.* raspberry leaves facilitate labor which was studied in 192 multiparous Australian women (Simpson et al., 2001). Raspberry leaves were taken in the form of tablet, from 32 weeks of gestation until induction of labor. Other than popular beliefs, it did not reduce the first stage of labor, but rather the second (mean difference 9.59 min) and also slowed down the rate of forceps deliveries (19.3% *vs.* 30.4%). In different areas of Pakistan, 11 plant species are being used in pregnancy related complications (Table 1; Fig. 7). Women are practicing different strategies to cope with these conditions such as the seeds of *Lens culinaris* are boiled and eaten to treat anemia during pregnancy, fresh leaves of *Mentha piperita* are chewed to avoid vomiting in early pregnancy, decoction of *Urtica dioica* is used to improve hemoglobin (Hb) level and increase breast milk, and drink black tea (without milk) at the time of delivery to decrease labor pain. Medicinal plants are playing essential roles in different reproductive health problems not only in Pakistan, but throughout the world. A previous study suggested that utilization of medicinal plants is useful in easing child birth (Agbovie et al., 2002). *Verbena officinalis* and *Anethum graveolens* were used to increase lactation in expecting and feeding mothers (Table 1). *Withania somnifera* was used to control body temperature during pregnancy and poultice of its leaves is applied to keep the breast shape normal during this period.

3.10. Sexually transmitted infections

Citation frequency of the literature related to gonorrhea and syphilis was higher among all the reported STIs (Table 5).

3.11. Gonorrhea

In Pakistan, 30 medicinal plants have been reported from different regions being traditionally used against gonorrhea (Table 1; Fig. 7). Gonorrhea is caused by a bacterium *Neisseria gonorrhoeae*. It is an infection of the mucous membrane of urogenital tract and is the second most commonly reported bacterial STI, after chlamydia infection. Gonorrhea is very common among some Pakistani tribes and perceived as a sign of sexual potency or adolescence. For instance, in Nigeria, the gonorrheal prevalence among asymptomatic women is about 5% while among female hospital patients and prostitutes is between 20% and 15%, respectively. Its prevalence rate in Uganda and Kenya was high (20%) for female population (Osoba, 1981), while in Pakistan the prevalence rate of gonorrhea ranges between 15 and 28% (Malan and Neuba, 2011; Rehan, 2006). Different modes of preparations are being practiced in Pakistan such as the boiling of the bark of *Acacia nilotica* and addition of 2–3 drops of *Dettol* (detergent) to the sieved water obtained. This recipe is dermally applied for three to four days after proper cleaning of the infected part with tap water (Choudhary et al., 2012). Phytochemical investigation of *Acacia nilotica* bark suggested that it contains polyphenol compounds, the fruit and leaves contain tannins, the flower contains steric acid (kaempferol-3-glucoside, isoquercetin, leucocyanidin), while the pods contains tannins (Farzana et al., 2014). The leaves of *Tinospora cordifolia* are used for curing gonorrhea and found to soothe the smarting and scalding. The methanolic stem extract of *Tinospora cordifolia* possesses antifertility activity, which might be exploited to prevent unwanted pregnancy and control the ever increasing population explosion (Singh et al., 2003). Antibiotic resistance of *Neisseria gonorrhoeae* has resulted in a long term expensive treatment process (Bhargava et al., 2011). Plasmid mediated and chromosomal mechanisms may be the causes for this kind of resistance development (Tapsall, 1999). Use of natural resources having antibacterial effects is the best alternative due to low cost, vast availability, and fewer side effects (Iwu et al., 1999). Aqueous, ethanolic, methanolic, hexane, and

acetone extracts (50 μl) of *Justicia adhatoda* leaves were used against *Neisseria gonorrhoeae* but did not show any sensitivity (Bhargava et al., 2011). Shokeen et al. (2009) tested the aqueous and ethanolic extracts of different parts of 16 medicinal plants including *Adhatoda vasica* and *Ricinus communis*. Ethanolic extracts were proved to be sensitive against *Neisseria gonorrhoeae*. Petroleum ether, chloroform, acetone, hexane and water extracts of *Tribulus terrestris* showed negative activity against *Neisseria gonorrhoeae* (Karthikeyan et al., 2013). Alcoholic extract (20 μl) of *T. terrestris* fruits also showed inhibitory activity against *Neisseria gonorrhoeae* (Hifnawy et al., 2015). In this review, among all the traditionally reported plants against gonorrheae, only few plants were evaluated for their antimicrobial activities against *Neisseria gonorrhoeae*. Therefore, more in depth pharmacological studies are required on rest of the plants to fulfill this huge gap of knowledge and increase the availability of natural composite sources as new antiinfectious agents.

3.12. Syphilis

Treponema pallidum is the causative agent of syphilis. In 2008, the World Health Organization (WHO) estimated worldwide infestation of 36.4 million people from syphilis worldwide. In Pakistan, 2% of the people are infected from syphilis (Arshad et al., 2016) and nine medicinal plants have been reported from different regions being used traditionally against this infection (Table 1; Fig. 7). Mode of usage is not described in the published literature. The whole plant of *Centella asiatica* is used for gynecological problems including syphilis. Isolated compounds belong to triterpenic acid groups are asiatic acid, 6-hydroxy asiatic acid, madecassic acid, madasiatic acid, and Betulinic acid. These compounds are also constituents of pharmaceutical products, which are used in skin care (Zahra et al., 2014). The gum of *Commiphora wightii* and *Butea monosperma* is used to treat this infection (Ahmad et al., 2009; Mehmood et al., 2012). Powder of *Cassia fistula* seeds (Ahmad et al., 2009), root extract of *Abutilon indicum* mixed with egg albumin (Ishtiaq et al., 2006), leaves of *Dalbergia sisso* and bark of *Tamarix aphylla* are used to treat syphilis infection (Iqbal et al., 2012; Naz et al., 2014).

3.13. Others

Not all STIs are reproductive tract infections, nor are all reproductive tract infections are sexually transmitted. Although others STIs like AIDS and Chlamydia are prevalent in Pakistan, but there is no plant species reported to treat these infections traditionally. The reasons might be that rural peoples are unaware about these infections and secondly the rate of these STIs is higher in urban areas as compared to rural areas (Mann et al., 1994). A study conducted on awareness raising regarding STIs shows that only 31% males or females knew the symptoms of STIs, while majority of respondents had never heard about the AIDS (Khushk et al., 2009). Juicy extract of *Aloe vera* is used for genital herpes, while a compound Acemannan, which is isolated from *Aloe vera* gel, carries immune stimulating and antiviral activities. An extract of mannose from *Aloe* inhibits human immune virus (Qadir, 2009). A lesser number of plants reported against STIs might be due to the lack of documentation or the hesitation of female informants in sharing this knowledge due to strict cultural resistance.

4. Conclusions

This review documents high number of medicinal plants used traditionally against gynecological problems and STIs. Majority of plants were found to be used against menstrual complications, abortion, leucorrhea, gonorrhea, pregnancy, and syphilis. Moreover, frequency of citation was also found higher for the abovementioned gynecological complaints and STIs which might be due to the higher prevalence of these problems in Pakistan. The dominant plant families used by traditional healers for the preparation of herbal remedies against gynecological complaints and STIs were Asteraceae and Amaranthaceae. Rural women mostly used the whole plant and leaves for herbal formulations. Several plant species were reported to be commonly used in different cultures for the multiple reproductive problems, which might be due to their higher efficacy against different ailments. However, various plants have also shown toxic effects on the living systems at different doses. In spite of the strong efficacy of traditional medicines still there is a lack of complete information for most of the plants about their proper dose range and formulation techniques. Moreover, very few plants have been scientifically validated so far in order to prove the efficacy and safety level of herbal medicines. There is a dire need to expedite detailed ethnogynecological, pharmacological, toxicological, and clinical studies on the unexplored medicinal plants, which could lead toward the development of safe and novel drugs. Women should be educated further about the proper usage of these recipes, possible complications associated with the improper use, and also conservation concerns related to use of different part of plants.

Author's contribution

All the authors have equally contributed in designing this review article.

Conflict of interest statement

The authors do not have any conflict of interest to state.

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References

Abbas, Z., Khan, S.M., Abbasi, A.M., Pieroni, A., Ullah, Z., Iqbal, M., 2016. Ethnobotany of the Balti community, Tormik valley, Karakorum range, Baltistan, Pakistan. Journal of Ethnobiology and Ethnomedicine 12, 38.

Adnan, M., Tariq, A., Mussarat, S., Begum, S., Abdeisalam, N.M., Ullah, R., 2015. Ethnogynaecological assessment of medicinal plants in pashtun's tribal society. BioMed Research International https://doi.org/10.1155/2015/196475.

Afzan, A., Abdullah, N.R., Halim, S.Z., Rashid, B.A., Semail, R.H.R., Abdullah, N., 2012. Repeated dose 28-days oral toxicity study of *Carica papaya* L. leaf extract in Sprague Dawley rats. Molecules 17, 4326–4342.

Agbovie, T., Amponsah, K., Crentsil, O.R., Dennis, F., Odamtten, G.T., Ofusohene-Djan, W., 2002. Conservation and sustainable use of medicinal plants in Ghana. Ethnobotanical Survey, UNEP-WCMC, Cambridge, UK.

Ahmad, S., Garg, M., Ali, M., Singh, M., Athar, M.T., Ansari, S.H., 2009. A phytopharmacological overview on *Adhatoda zeylanica* Medic. Syn. *A. vasica* (Linn.) Nees. Natural Product Radiance 8, 549–554.

Ahmad, I., Ibrar, M., Barkatullah, Ali, N., 2011. Ethnobotanical study of Tehsil Kabal, Swat District, KPK, Pakistan. Journal of Botany https://doi.org/10.1155/2011/368572.

Ahmad, S., Wariss, H.M., Alam, K., Anjum, S., Mukhtar, M., 2012. Ethnobotanical studies of plant resources of Cholistan desert, Pakistan. International Journal of Science and Research 3, 1782–1788.

Ahmed, S.M., Ahmed, S., Tasleem, F., Hasan, M.M.U., Azhar, I., 2012. Acute systemic toxicity of four Mimosaceous plants leaves in mice. IOSR Journal of Pharmacy 2, 291–295.

Ahmed, E., Arshad, M., Saboor, A., Qureshi, R., Mustafa, G., Sadiq, S., 2013. Ethnobotanical appraisal and medicinal use of plants in patriata, new Murree, evidence from Pakistan. Journal of Ethnobiology and Ethnomedicine 9, 201.

Ajaib, M., Khan, Z.U.D., Zikrea, A., 2014. Ethnobotanical survey of important herbaceous plants of district Kotli, Azad Jammu & Kashmir. Biologia (Pakistan) 60, 11–22.

Akanmu, M.A., Iwalewa, E.O., Elujoba, A.A., Adelusola, K.A., 2004. Toxicity potential of *Cassia fistula* fruits as laxative with reference to Senna. African Journal of Biomedical Research 7, 23–26.

Akhter, N., Akhtar, S., Kazim, S., Khan, T., 2016. Ethnomedicinal study of important medicinal plants used for gynecological issues among rural women folk in district Gilgit, Pakistan. Nature and Science 14, 30–34.

Alamgeer, T.A., Rashid, M., Malik, M.N.H., Ai, M.N.N.E., 2013. Ethnomedicinal survey of plants of Valley Alladand Dehri, Tehsil Batkhela, District Malakand, Pakistan. International Journal of Basic Medical Sciences and Pharmacy 3, 2049–4963.

Ali, A., Akhtar, N., Khan, B.A., Khan, M.S., Rasul, A., Uz-Zaman, S., 2012. *Acacia nilotica*: a plant of multipurpose medicinal uses. Journal of Medicinal Plant Research 6, 1492-149.

Allana, G.A., 2010. Sindhi society and culture. International Research Journal of Arts and Humanities. Department of Culture, Government of Sindh.

Alli, L.A., Adesokan, A.A., Salawu, O.A., Akanji, M.A., 2015. Toxicological studies of aqueous extract of *Acacia nilotica* root. Interdisciplinary Toxicology 8, 48–54.

Al-Snafi, A.E., 2016. The chemical constituents and pharmacological effects of *Convolvulus arvensis* and *Convolvulus scammonia* — a review. IOSR Journal of Pharmacy 6, 64–75.

Andel, T.V., Boer, H.J., Barnes, J., Vandebroek, I., 2014. Medicinal plants used for menstrual disorders in Latin America, the Caribbean, Sub-Saharan Africa, South and Southeast Asia and their uterine properties: a review. Journal of Ethnopharmacology 155, 992–1000.

Arshad, M., Nisar, M.F., Majeed, A., Ismail, S., Ahmad, M., 2011. Ethnomedicinal flora in District Sialkot, Punjab, Pakistan. Middle-East Journal of Scientific Research 9, 209–214.

Arshad, A., Borhany, M., Anwar, N., Naseer, I., Ansari, R., Boota, S., Fatima, N., Zaidi, M., Shamsi, T., 2016. Prevalence of transfusion transmissible infections in blood donors of Pakistan. BMC Hematology 16, 27.

Asif, M., 2012. A brief study of toxic effects of some medicinal herbs on kidney. Advanced Biomedical Research 1, 44.

Asolkar, L.V., Kakkar, K.K., Chakre, O.J., 1992. Second supplement to glossary of Indian medicinal plants with active principles. Part I (A-K). Publication and Information Division. CSIR, New Delhi, India.

Attawsih, A., Chavalittumrong, P., Rugsamon, P., Chuntapet, P., 1995. Toxicity study of *Psidium guajana* Linn. leaves. Bulletin of the Department of Medical Sciences 37. Ministry of Public Health, Thailand, pp. 289–305.

Bahadur, A., Mushtaq, T., Danish, M., Ullah, I., Nasir, F., Hameed, T., 2013. Ethnobotanical study of Jahangirabad, district Mardan. International Journal of Phytomedicine 5, 252–256.

Bhandari, P.R., 2012. Pomegranate (*Punica granatum* L.) ancient seeds for modern cure? Review of potential therapeutic applications. International Journal of Nutrition, Pharmacology, Neurological diseases 2, 171–184.

Bhandary, B.S., Sharmila, K.P., Kumari, N.S., Bhat, S.V., 2013. Acute and sub-acute toxicity study of the ethanol extracts of *Punica granatum* (Linn). Whole fruit and seeds and synthetic ellagic acid in Swiss albino mice. Asian Journal of Pharmaceutical and Clinical Research 6, 192–198.

Bhargava, D., Kar, S., Shivpuri, J.N., Shakya, B., Maity, C., 2011. Screening of antigonorrhoeal activity of some medicinal plants in Nepal. International Journal of Pharma and Bio Sciences 2, 202–212.

Bhat, P., Hedge, G.R., Rajaram, G.R., Mulgund, G.S., 2013. Ethnomedicinal plants to cure skin diseases-an account of the traditional knowledge in the coastal parts of central Ghats, Karnataka, India. Journal of Ethnopharmacology 151, 493–502.

Bidgoli, S.A., Taheri, E., Baher, H., Ziarati, P., 2011. Safety evaluation of oral *Anethum graveolens* L. total hydroalcoholic extract in mice. Journal of Pharmaceutical & Health Sciences 1, 61–67.

Biswas, H., Das, R.K., Talukder, S.I., 2012. Death of a case of criminal abortion by an unskilled abortionist. Dinajpur Medical College Journal 5, 72–75.

Borokini, T.I., Ighere, D.A., Clement, M., Ajiboye, T.O., Alowonle, A.A., 2013. Ethnobiological survey of traditional medicine practice for women's health in Oyo state. Journal of Medicinal Plants Studies 1, 17–29.

Campbell, O.M.R., Harlow, S.D., 2004. Epidemiology of menstrual disorders in developing countries: a systematic review. BJOG: An International Journal of Obstetrics and Gynaecology 111, 6–16.

Chandio, A., 2012. Pakistan — a land of cultural diversity. http://blogs.epakistan.com/pakistan-a-land-of-cultural-diversity/.

Chaudhuri, M., Chatterjee, B.D., Banerjee, M., 1998. A clinicobacteriological study on leucorrhoea. Journal of the Indian Medical Association 96, 46–50.

Chopra, 1977. In: Chopra, Gulshan Lal (Ed.), The Punjab as a Sovereign State. Al-Biruni, Lahore.

Choudhary, M.I., Wahab, A., Dar, A., Shaikh, G.I., Maqbool, S., Khalique, A., 2012. Biomedical Studies and IPR (Intellectual Property Rights) Documentation of Medicinal Plants Used in the Treatment of Women Diseases in Sindh. H.E.J. Research Institute of Chemistry (International Center for Chemical and Biological Sciences).

Chowdhury, M.G.A., Azizunnesa, Hossain, M.A., Rahman, M.L., Hasan, Q., 2004. Toxic effect and oral acute LD50 study of *Nerium oleander* in male guineapigs. Banglasdesh Journal of Veterinary Medicine 2, 159–161.

Cohen, S.A., 2009. Promoting sexual and reproductive health advances maternal health. Guttmacher Policy Review 12, 8–12.

Conforti, F., Ioele, G., Statti, G.A., Marrelli, M., Ragno, G., Menichini, F., 2008. Antiproliferative activity against human tumor cell lines and toxicity test on Mediterranean dietary plants. Food and Chemical Toxicology 46, 3325–3332.

Critchley, M., 1986. Butterworths Medical Dictionary. 2nd ed. Butterworths, London, UK.

Dehghani, F., Panjehshahin, M.R., 2006. The toxic effect of alcoholic extract of *Citrullus colocynthis* on rat liver. Iranian Journal of Pharmacology and Therapeutics 5, 117–119.

Deka, M., Kalita, J.C., Sarma, G.C., 2011. Traditional use of fertility inducing plants used by the herbal practitioners in some parts of the state Assam, N E India, a survey report. International Journal of Science and Advanced Technology 1, 133–142.

Desai, J., Patel, D.K., 2016. Acute and sub-chronic toxicological evaluation of *Anethum graveolens* L. seed extract. Journal of Global Biosciences 5, 4213–4220.

Dhaliwal, H.K., Singh, R., Sidhu, J.K., Grewal, J.K., 2016. Phytopharmacological properties of *Cuminum cyminum* Linn. as a potential medicinal seeds: an overview. World Journal of Pharmacy and Pharmaceutical Sciences 5, 478–489.

El-Sherbini, G.M., Ibrahim, K.M., El Sherbiny, E.T., Abdel-Hady, N.M., Morsy, T.A., 2010. Efficacy of *Punica granatum* extract on in-vitro and in-vivo control of *Trichomonas vaginalis*. Journal of the Egyptian Society of Parasitology 40, 229–244.

Ernst, E., 2003. Serious psychiatric and neurological adverse effects of herbal medicines — a systemic review. Acta Psychiatrica Scandinivica 108, 83–91.

Ernst, E., 2005. The efficacy of herbal medicine- an overview. Fundamental and Clinical Pharmacology 19, 405–409.

Farooq, S., Barki, A., Khan, M.Y., Fazal, H., 2012. Ethnobotanical studies of the flora of tehsil Birmal in South Waziristan Agency, Pakistan. Pakistan Journal of Weed Science Research 18, 277–291.

Farzana, M.U.Z.N., Tharique, I.A., Sultana, A., 2014. A review of ethnomedicine, phytochemical and pharmacological activities of *Acacia nilotica* (Linn) wild. Journal of Pharmacognosy and Phytochemistry 3, 84–90.

Gadsby, R., Barnie-Adshead, A.M., Jagger, C., 1992. A prospective study of nausea and vomiting during pregnancy. British Journal of General Practice 43, 245–248.

Gairolaa, S., Sharmac, J., Bedia, Y.S., 2014. A cross-cultural analysis of Jammu, Kashmir and Ladakh (India) medicinal plant use. Journal of Ethnopharmacology 155, 925–986.

Gangwar, A.K., Ghosh, A.K., 2014. Medicinal uses and pharmacological activity of *Adhatodavasica*. International Journal of Herbal Medicine 2, 88–91.

Gazzaneo, L.R.S., Albuquerque, P.U.D., 2005. Knowledge and use of medicinal plants by local specialists in a region of Atlantic forest in the state of Pernambuco (Northeastern Brazil). Journal of Ethnobiology and Ethnomedicine 1, 9.

Ghani, A., Ali, Z., Perveen, S., 2012. Folk recipes and ethno botanical survey of medicinal plants Mianwali district (Pakistan). International Journal of Current Pharmaceutical Research 4, 61–63.

Gulshan, A.B., Dasti, A.A., Hussain, S., Atta, M.I., Amin-ud-Din, M., 2012. Indigenous uses of medicinal plants in rural areas of Dera Ghazi Khan, Punjab, Pakistan. Journal of Agricultural and Biological Science 7, 750–762.

Gupta, O.P., Anand, K.K., Ghatak, B.J., Atal, C.K., 1978. Vasicine, alkaloid of *Adhatoda vasica*, a promising uterotonic abortifacient. Indian Journal of Experimental Biology 16, 1075–1077.

Halim, S.Z., Abdullah, N.R., Afzan, A., Rashid, B.A.A., Jantan, I., Ismail, Z., 2011. Acute toxicity study of *Carica papaya* leaf extract in Sprague Dawley rats. Journal of Medicinal Plant Research 5, 1867–1872.

Haque, N., Sofi, G., Ali, W., Rashid, M., Itrat, M., 2015. A comprehensive review of phytochemical and pharmacological profile of Anar (*Punica granatum* Linn): a heaven's fruit. Journal of Ayurvedic and Herbal Medicine 1, 22–26.

Hifnawy, M.S., AbouZid, S.F., Ali, Z.Y., Fouda, M.M., 2015. Phenolic contents and *in vitro* free radical scavenging activity of alcoholic extract of the fruits of *Tribulus terrestris* L. The Pharma Innovation Journal 4, 92–100.

Hosseinzadeh, H., Karimi, G.R., Ameri, M., 2002. Effects of *Anethum graveolens* L. seed extracts on experimental gastric irritation models in mice. BMC Pharmacology 2, 21.

Hussain, F., Shah, S.M., Sher, H., 2007. Traditional resource evaluation of some plants of Mastuj, District Chitral, Pakistan. Pakistan Journal of Botany 39, 339–354.

Hussain, K., Nisar, M.F., Majeed, A., Nawaz, K., Bhatti, K.H., 2010. Ethnomedicinal survey for important plants of Jalalpur Jattan, District Gujrat, Punjab, Pakistan. Ethnobotanical Leaflets 14, 807–825.

Ibrar, M., Hussain, F., Sultan, A., 2007. Ethnobotanical studies on plant resources of Ranyal hills, District Shangla, Pakistan. Pakistan Journal of Botany 39, 329–337.

Ilango, K.B., Rajkumar, L.A.P., Vetrival, D., Brinda, P., Mishra, M., 2011. Safety evaluation of *Abelmoschus esculentus* polysaccharide. International Journal of Pharmaceutical Sciences Review and Research 10, 106–110.

Ilavasan, R., Mallika, M., Venkataraman, S., 2011. Toxicological assessment of *Ricinus communis* Linn root extracts. Toxicology Mechanisms and Methods 21, 246–250.

Iqbal, H., Sher, Z., Khan, Z.U., 2011. Medicinal plants from salt range Pind Dadan Khan, district Jhelum, Punjab, Pakistan. Journal of Medicinal Plant Research 5, 2157–2168.

Iqbal, H., Khattak, B., Ayaz, S., Rehman, A., Ishfaq, M., Abbas, M.N., Rehman, H.U., Waheed, S., Wahab, A., 2012. Comparative efficacy of *Aloe vera* and *Tamarix aphylla* against cutaneous leishmaniasis. International Journal of Basic Medical Sciences and Pharmacy 2, 42–45.

Ishtiaq, M., Khan, M.A., Hanif, W., 2006. An ethnomedicinal inventory of plants used for family planning and sex diseases treatment in Samahni Valley, (A.K.) Pakistan. Pakistan Journal of Biological Sciences 9, 2546–2555.

Ishtiaq, M., Mumtaz, A.S., Hussain, T., Ghani, A., 2012. Medicinal plant diversity in the flora of Leepa Valley, Muzaffarabad (AJK), Pakistan. African Journal of Biotechnology 11, 3087–3098.

Ismail, Z., Halim, S.Z., Abdullah, N.R., Afzan, A., Rashid, B.A., Jantan, I., 2014. Safety evaluation of oral toxicity of *Carica papaya* Linn. leaves: a subchronic toxicity study in Spargue Dawley rats. Evidence-based Complementary and Alternative Medicine https://doi.org/10.1155/2014/741470.

Iwu, M.M., Duncan, R.A., Okunji, C.O., 1999. New antimicrobials of plant origin. In: Janick, J. (Ed.), Perspectives on New Crops and New Uses. ASHS Press, Alexandria, Virginia, pp. 457–462.

Jahromi, S.B., Pourshafie, M.R., Mirabzadeh, E., Tavasoli, A., Katiraee, F., Mostafavi, E., 2015. *Punica granatum* peel extract toxicity in mice. Jundishapur Journal of Natural Pharmaceutical Products 10, e23770.

Jaiswal, V., 2010. Culture and ethnobotany of *Jaintia* tribal community of Meghalaya, Northeast India — a mini review. Indian Journal of Traditional Knowledge 9, 38–44.

Jan, S., Khan, M.A., Din, S.U., Murad, W., Hussain, M., Ghani, A., 2008. Herbal remedies used for gastrointestinal disorders in Kaghan Valley, NWFP. Pakistan Journal of Weed Science Research 14, 169–200.

Jeet, K., Devi, N., Nirender, T., Sunil, T., Lalit, S., Raneev, T., 2012. *Trachyspermum ammi* (Ajwain): a comprehensive review. International Research Journal of Pharmacy 3, 133–138.

Jensen, W.I., Allen, J.P., 1981. Naturally occurring and experimentally induced castor bean (*Ricinus communis*) poisoning in ducks. Avian Diseases 5, 184–194.

Johri, R.K., Pahwa, G.S., Sharma, S.C., Zutshi, U., 1991. Determination of estrogenic/antiestrogenic potential of antifertility substances using rat uterine peroxidase assay. Contraception 44, 549–557.

Jothy, S.L., Zakaria, Z., Chen, Y., Lau, Y.L., Latha, L.Y., Sasidharan, S., 2011. Acute oral toxicity of methanolic seed extract of *Cassia fistula* in mice. Molecules 16, 5268–5282.

Kapoor, M., Garg, S.K., Mathur, V.S., 1974. Antiovulatory activity of five indigenous plants in rabbits. Indian Journal of Medical Research 62, 1225–1227.
Karthikeyan, M., Rajendran, P., Ashok, G., Reddy, E.V., Anbalagan, S., 2013. Preliminary studies on activity of *Ocimum sanctum*, *Azadirachta indica*, *Annona squamosal*, *Tribulus terrestris* and *Eucalyptus globulus* against *Neisseria gonorrhoeae*. World Journal of Pharmacy and Pharmaceutical Sciences 2, 1232–1237.
Kaur, J., Kapoor, A.K., 2014. Perceptions and knowledge about leukorrhea in a slum dwelling south Asian community. Journal of Family & Reproductive Health 8, 45–52.
Keshri, G., Lakshmi, V., Singh, M.M., 1998. Postcoital contraceptive activity of some indigenous plants in rats. Contraception 57, 357–360.
Khan, S., Khatoon, S., 2009. Ethnobotanical studies on some useful herbs of Haramosh and Bugrote valleys in Gilgit, northern areas of Pakistan. Pakistan Journal of Botany 40, 43–58.
Khan, M.A., Khan, M.A., Hussain, M., 2012. Medicinal plants used in folk recipes by the inhabitants of Himalayan region Poonch Valley Azad Kashmir (Pakistan). Journal of Basic and Applied Sciences 8, 35–45.
Khan, S.U., Khan, R.U., Jamil, S., Mehmood, S., Ullah, I., Zahoor, M., Daud, M., 2013. Biodiversity in medicinal plants and its distribution in village Shahbaz Khel, Lakki Marwat, KPK, Pakistan. Journal of Medicinal Plants Studies 1, 78–86.
Khan, R.U., Mehmood, S., Muhammad, A., Mussarat, S., Khan, S.U., Amina, 2015. Medicinal plants from Flora of Bannu used traditionally by north West Pakistan's women to cure gynecological disorders. American-Eurasian Journal of Agricultural & Environmental Sciences 15, 553–559.
Khushalani, H., Tatke, P., Singh, K.K., 2006. Antifertility activity of dried flowers of Woodfordia fruticose Kurz. Indian Journal of Pharmaceutical Sciences 68, 528–529.
Khushk, I.A., Shah, B.A., Abbasi, R.M., Mahesar, M.A., Shahani, R.A., 2009. Awareness and practices regarding sexually transmitted infections among currently married males and females in a rural district of Sindh. Pakistan Journal of Medical Sciences 25, 992–996.
Kousalya, M., Kokila, N., Balamurugan, N., 2014. Evaluation of acute toxicity study of root of *Abutilon indicium* (L) Sweet. International Journal of Frontiers in Science and Technology 2, 32–37.
Kulkarni, R.N., Durge, P.M., 2005. A study of leucorrhoea in reproductive age group women of Nagpur city. Indian Journal of Public Health 49, 238–239.
Lakshmi, T., Geeta, R.V., Anita, R., Kumar, A.S., 2011. Yarrow (*Achillea millefolium* Linn) a herbal medicinal plant with broad therapeutic use — a review. International Journal of Pharmaceutical Sciences Review and Research 9, 136–141.
Malan, D.F., Neuba, D.F.R., 2011. Traditional practices and medicinal plants use during pregnancy by Anyi–Ndenye women (Eastern Côte d'Ivoire). African Journal of Reproductive Health 15, 85–93.
Malik, S., Ahmad, S., Sadiq, A., Alam, K., Wariss, H.M., Ahmad, I., Hayat, M.Q., Anjum, S., Mukhtar, M., 2015. A comparative ethno-botanical study of Cholistan (an arid area) and Pothwar (a semi-arid area) of Pakistan for traditional medicines. Journal of Ethnobiology and Ethnomedicine 11, 31.
Mandal, R., Dhaliwal, P.K., 2007. Antifertility effect of *Melia azedarach* Linn. (dharek) seed extract in female albino rats. Indian Journal of Experimental Biology 45, 853–860.
Mann, J.M., Gostin, L., Gruskin, S., Brennan, T., Lazzarini, Z., Fineberg, H.V., 1994. Health and human rights. Health Human Rights 1, 6–23.
Mehmood, T.K., Umer, H., Amir, S., Qasim, M.K., Khan, S.S., Ajmal, M.S., Kashif, M.I., 2012. Documentation of traditional knowledge about uses of medicinal plants found in Kirthar National Park, District Dadu, Sindh, Pakistan. International Research Journal of Pharmacy 3, 74–78.
Monsefi, M., Ghasemi, M., Bahaoddini, A., 2006. The effects of *Anethum graveolens* L. on female reproductive system. Phytotherapy Research 20, 865–868.
Moritz, F., Compagnon, P., Kaliszczak, I.G., Kaliszczak, Y., Caliskan, V., Girault, C., 2005. Severe acute poisoning with homemade *Aconitum napellus* capsules: toxicokinetic and clinical data. Clinical Toxicology 43, 873–876.
Munoz, A.G., 2010. Pashtun Tribalism and Ethnic Nationalism. Tribal Analysis Center, 6610-M Mooretown Road, Box 159. Williamsburg, VA, 23188.
Nasir, E., Ali, S.I., 1991. Flora of west Pakistan. Tech. Rep. 1-190. Pakistan Agriculture Research Council, Islamabad, Pakistan.
Nawaz, S., 2009. FATA-A most Dangerous Place. Center for Strategic & International Studies, Washington, D.C.
Naz, N., Ahmad, M., Tamoor-ul-Hassan, 2014. Ethnobotanical investigation of medicinal Flora used by indigenous people in District Attock, Pakistan. Journal of Advanced Botany and Zoology 1, 1–7.
Nepal Census report, 2001. Central Bureau of Statistics. Demography. Central Bureau of Statistics, Kathmandu.
Nwachukwu, N., Iweala, E.J., 2009. Influence of extraction methods on the hepatotoxicity of *Azadirachta indica* bark extract on albino rats. Global Journal of Pure and Applied Sciences 15, 369–372.
Oderinde, O., Noronha, C., Oremosu, A., Kusemiju, T., Okanlawon, O.A., 2002. Abortifacient properties of aqueous extract of *Carica papaya* (Linn) seeds on female Sprague-Dawley rats. The Nigerian Postgraduate Medical Journal 9, 95–98.
Okon, B.E., Essein, E.E., Poh, C.F., Orji, M.H., 2015. An evaluation of the sub-acute toxicity and haemostatic effects of leaves extract of *Achyranthes aspera* in mice and albino rats. European Journal of Medicinal Plants 7, 16–25.
Olejniczak, K., Günzel, P., Bass, R., 2001. Preclinical testing strategies. Drug Information Journal 35, 321–336.
Osoba, A.O., 1981. Sexually transmitted diseases in tropical Africa. A review of the present situation. British Journal of Venereal Diseases 57, 89–94.
Ostad, S.N., Khakinegad, B., Sabzevari, O., 2004. Evaluation of teratogicity of fennel essential oil (FEO) on the rat embryo limb buds culture. Toxicology In Vitro 18, 623–627.
Ozgoli, G., Goli, M., Moattar, F., 2009. Comparison of effects of ginger, Mefenamic acid and ibuprofen on pain in women with primary dysmenorrhoeal. Journal of Alternative and Complementary Medicine 15, 129–132.
Panhwar, A.Q., Abro, H., 2007. Ethnobotanical studies of Mahal Kohistan (Khirthar National Park). Pakistan Journal of Botany 39, 2301–2315.
Parvaiz, M., 2014. Ethnobotanical studies on plant resources of Mangowal, District Gujrat, Punjab, Pakistan. Avicenna Journal of Phytomedicine 4, 364–370.
Patel, S.B., Rao, N.J., Hingorani, L.L., 2016. Safety assessment of *Withania somnifera* extract standardized for Withaferin A: acute and sub-acute toxicity study. Journal of Ayurveda and Integrative Medicine 7, 30–37.
Ping, K.Y., Darah, I., Chen, Y., Sreeramanan, S., Sasidharan, S., 2013. Acute and sub-acute toxicity study of *Euphorbia hirta* L. methanol extract in rats. BioMed Research International https://doi.org/10.1155/2013/182064.
Pingale, S.S., 2011. Acute toxicity for *Ricinus communis*. Der Pharmacia Lettre 3, 132–137.
Pingale, S.S., 2013. Evaluation of acute toxicity study for *Euphorbia hirta*. International Journal of Bioassays 2, 329–332.
Pingale, S.S., Virkar, P.S., 2011. Evaluation of acute toxicity for *Abutilon indicum*. Der Pharmacia Lettre 3, 37–42.
Ponpornpisit, A., Pirarat, N., Suthikrai, W., Binwihok, A., 2011. Toxicity test of Kameng (*Eclipta prostate* Linn.) and Kradhuawean (*Spilanthes acmella* (Linn.) Murr.) to early life stage of Zebrafish (*Danio rerio*). Thailand Journal of Veterinary Medicine 41, 523–527.
Qadir, M.I., 2009. Medicinal and Cosmetological importance of *Aloe vera*. International Journal of Natural Therapy 2, 21–26.
Qureshi, R.A., Gilania, S.A., Ashraf, M., 2007. Ethnobotanical studies with special reference to plants phenology at Sudhan Gali and ganga Chotti hills (District Bagh, Azad Kahmir.). Pakistan Journal of Botany 39, 2275–2283.
Qureshi, R.A., Ghufran, M., Gilani, S.A., Yousaf, A.G., Batool, A., 2009. Indigenous medicinal plants used by local women in southern Himalayan regions of Pakistan. Pakistan Journal of Botany 41, 19–25.
Qureshi, R., Bhatti, G.R., Memon, R.A., 2010. Ethnobotanical uses of herbs from northern part of Nara desert. Pakistan Journal of Botany 42, 839–851.
Rajeh, M.A.B., Kwan, Y.P., Zakaria, Z., Latha, L.Y., Jothy, S.L., Sasidharari, S., 2012. Acute toxicity impacts of *Euphorbia hirta* L extract on behavior, organs body weight index and histopathology of organs of the mice and *Artemia salina*. Pharmacognosy Research 4, 170–177.
Ranaa, C.S., Sharma, A., Kumar, N., Dangwal, L.R., Tiwari, J.K., 2010. Ethnopharmacology of some important medicinal plants of Nanda Devi National Park (NDNP) Uttarakhand. Indian Journal of Natural Science 8, 9–14.
Rauf, F., Qureshi, R., Shaheen, H., 2012. Folk medicinal uses of indigenous plant species of Barroha, Bhara Kahu and Maanga in Islamabad. Pakistan Journal of Medicinal Plants Research 6, 2061–2070.
Reddy, C.V., Kamble, A., 2014. Toxicity study of *Achyranthus apsera*. International Letters of Natural Sciences 14, 85–96.
Rehan, N., 2006. Profile of men suffering from sexually transmitted infections in Pakistan. Journal of the Pakistan Medical Association 56, 60–65.
Rehman, S., Wazir, S.M., Khan, R.U., Khan, S.U., Farooq, A., 2013. Ethnobotanically important plants of Humzoni, Nwa, KPK, Pakistan. International Journal of Herbal Medicine 1, 89–101.
Robertson, S., Narayanan, N., Nargis, N.R.R., 2012. Toxicity evaluation on hydroalcoholic extract of leaf and stem bark of *Prosopis cineraria*. International Journal of Pharmacy and Pharmaceutical Sciences 4, 113–118.
Rodriguez-Fragoso, L., Reyes-Esparza, J., Burchiel, S.W., Herrera-Ruiz, D., Torres, E., 2008. Risks and benefits of commonly used herbal medicines in Mexico. Toxicology and Applied Pharmacology 227, 125–135.
Saad, B., Azaizeh, H., Abu-Hijleh, G., Said, O., 2006. Safety of traditional Arab herbal medicine. Evidence-based Complementary and Alternative Medicine 3, 433–439.
Sahu, P.K., 2011. Plants used by Gond and Baiga women in ethnogynaecological disorders in Achanakmar wild life sanctuary, Bilaspur, C.G. International Journal of Pharmaceutical and Life Sciences 2, 559–561.
Saini, M.L., Saini, R., Roy, S., Kumar, A., 2008. Comparative pharmacognostical and antimicrobial studies of acacia species (Mimosaceae). Journal of Medicinal Plant Research 12, 378–386.
Sarma, H.N., Mahanta, H.C., 2000. Modulation of morphological changes of endometrial surface epithelium by administration of composite root extract in albino rats. Contraception 62, 51–54.
Schippmann, U., Cunningham, A.B., Leaman, D.J., 2002. Impact of cultivation and gathering of medicinal plants on biodiversity: global trends and issues. Biodiversity and the Ecosystem Approach in Agriculture, Forestry and Fisheries. Satellite Event on the Occasion of the Ninth Regular Session of the Commission on Genetic Resources for Food and Agriculture. FAO, Rome, pp. 12–13.
Schmidt, B.M., Ilic, N., Poulev, A., Raskin, I., 2007. Toxicological evaluation of a chicory root extract. Food and Chemical Toxicology 45, 1131–1139.
Shafaei, H., Esmaeili, A., Rad, J.S., Delazar, A., Behjati, M., 2012. *Citrullus colocynthis* as a medicinal or poisonous plant: a revised fact. Journal of Medicinal Plant Research 6, 4922–4927.
Shah, G.M., Khan, M.A., Shah, G.M., 2006. Checklist of medicinal plants of Siran Valley, Mansehra, Pakistan. Ethnobotanical Leaflets 10, 63–71.
Shah, G.M., Jamal, Z., Hussain, M., 2013. Phytotherapy among rural women of district Abbotabad. Pakistan Journal of Botany 45, 253–261.
Sharm, S.K., Rai, G., Vasudeva, N., 2012. Anti-fertility investigation of *Butea monosperma* (Lam.) Kuntze root in female albino mice. Research Journal of Medicinal Plant 6, 260–266.
Sharwan, G., Jain, P., Pandey, R., Shukla, S.S., 2015. Toxicity profile of traditional herbal medicine. Journal of Ayurvedic and Herbal medicine 1, 81–90.
Shehzad, A., 2011. The issue of ethnicity in Pakistan: historical background. Pakistan Vision 12, 124–164.
Shibeshi, W., Makonnen, E., Zerihun, L., Debella, A., 2006. Effect of *Achyranthes aspera* L. on fetal abortion, uterine and pituitary weights, serum lipids and hormones. African Health Sciences 6, 108–112.

Shinwari, Z.K., 2010. Medicinal plants research in Pakistan. Journal of Medicinal Plant Research 4, 161–176.
Shokeen, P., Bala, M., Tandon, V., 2009. Evaluation of the activity of 16 medicinal plants against *Neisseria gonorrhoeae*. International Journal of Antimicrobial Agents 33, 86–91.
Shukla, S., Mathur, R., Rakish, A.D., 1988. Effect of butanolic extract of *Pueraria tuberosa* DC on estrus cycle of adult rats. Indian Journal of Pharmacology 19, 48–53.
Siddiqi, F.H., 2012. The Politics of Ethnicity in Pakistan: The Balouch, Sindhi and Mohajir Ethnic Movements. Routledge, Oxon and New York.
Simpson, M., Parsons, M., Grenwood, J., Wade, K., 2001. Raspberry leaf in pregnancy: its safety and efficacy in labor. Journal of Midwifery Womens Health 46, 51–59.
Singh, S.S., Panday, S.C., Srivastava, S., Gupta, V.S., Patro, B., Ghosh, A.C., 2003. Chemistry and medicinal properties of *Tinospora cordifolia* (Guduchi). Indian Journal of Pharmacology 35, 83–91.
Singh, S., Esdgh, G., Hussain, R., 2010. Unintended pregnancy: worldwide levels, trends, and outcomes. Studies in Family Planning 41, 241–250.
Soliman, G.A., Donia, A.E.R.M., Awaad, A.S., Alqasoumi, S.I., Yosufoglu, H., 2012. Effect of Spinosa, *Leptadenia pyrotechnica*, *Haloxylon salicornicum* and *Ochradenus baccatus* extracts on the reproductive organs of adult male rats. Pharmaceutical Biology 50, 105–112.
Steenkamp, V., 2003. Traditional herbal remedies used by South African women for gynaecological complaints. Journal of Ethnopharmacology 86, 97–108.
Tapsall, J.W., 1999. Perspectives on gonococcal disease in Australia. In: Asche, V. (Ed.), Recent Advances in Microbiology 1999. The Australian Society for Microbiology, Melbourne, pp. 171–196.
Tehrani, F.R., Shakeri, N., Solaymani-Dodaran, M., Azizi, F., 2011. Predicting age at menopause from serum Antimüllerian hormone concentration. Menopause 18, 766–770.
Tewiri, P.V., Neelam, Kulkiroi, S., 2001. A study of lukol in leucorrhoea, pelvic inflammatory diseases and dysfunctional uterine bleeding. Ancient Science of Life 2, 139–149.
Veach, S., Williamson, K., 2010. Punjabi: culture & language manual. Texas State University CDIS 5350 Multicultural Issues in Communication Disorders.
Verma, S., 2016. Pharmacological review on *Cassia fistula* Linn (Amaltas). International Journal of Pharmaceutical, Chemical and Biological Sciences 6, 332–335.
Vidal, A., Fallarero, A., Pena, B.R., Medina, M.E., Bra, B., Rivera, F., 2003. Studies on toxicity of *Puninca granatum* L. (Punicaceae) whole fruit extracts. Journal of Ethnopharmacology 89, 295–300.
Wariss, H.M., Ahmad, S., Anjum, S., Alam, K., 2012. Ethnobotanical studies of dicotyledonous plants of Lal Suhanra National Park, Bahawalpur, Pakistan. International Journal of Science and Research 3, 2452–2460.
WHO, 2001a. Promoting the role of traditional medicine in health systems. A strategy for the African region. WHO Regional Office for Africa, Temporary Location, Harare, Zimbabwe (Document Reference AFR/RC50/9 and Resolution AFR/RC50/R3).
WHO, 2001b. Global Prevalence and Incidence of Sexually Transmitted Infections, Overview and Estimates. World Health Organization.
WHO, 2005. Facts and Figures Form the World Health Report 2005. World Health Organisation, Geneva http://www.who.int/whr/2005/media_ce ntre/facts_en.pdf, Accessed date: 18 December 2008.
Yadav, J.P., Kumar, S., Siwach, P., 2006. Folk medicine used in gynecological and other related problems by rural population of Haryana. Indian Journal of Traditional Knowledge 5, 323–326.
Yoosook, C., Bunyapraphatsara, N., Boonyakiat, Y., Kantasuk, C., 2000. Anti-herpes simplex virus activities of crude water extracts of Thai medicinal plants. Phytomedicine 6, 411–419.
Zade, V., Wikhe, M., Dabhadkar, D., Dawada, S., Patil, U., 2013. Antifertility efficiency of *Cannabis sativa* leaves on female albino rats. International Journal of Science Innovation Today 2, 107–117.
Zahra, K., Bibi, Y., Tabassum, S., 2014. Clinical and therapeutic benefits of *Centella asiatica*. Pure Applied Biology 3, 152–159.
Zereen, A., Khan, Z., Sardar, A.A., 2013. Ethnobotanical studies of wild herbs of central Punjab, Pakistan. Bangladesh Journal of Plant Taxonomy 20, 67–76.