Table 1. Botanical information of the studied plants, their anticancer use and comparison with literature.

S. No	Scientific name	Family	Persian name	Parts use	RFC	Cancer therapy for specific organ	Recipes	Reported activity against	Reference
15	*Myrtus communis* L.	Myrtaceae	Mourt	L & F	0.08	Dermal	70 grams fruit and 40 grams of leaves are boiled and taken twice a day for 10 days	Induces apoptosis in multiple type of cancer cell lines	(20)
16	*Isatis raphanifolia* Boiss.	Brassicaceae	Vasmeh	AP	0.03	Dermal	200 grams of shoot powder is boiled and the decoction is used twice a day for 2 weeks	-	-
17	*Physalis divaricata D. Don*	Solanaceae	Arosakposthehpardeh	AP	0.03	Kidney	Aerial parts of 5 plants are boiled in water and used twice a day for 2 weeks	-	-
18	*Rumex ephedroides* Born.	Polygonaceae	Torshak	AP	0.17	General anti-neoplastic	Shoots of two plants are boiled and consumed twice a day for 2 weeks	-	-
19	*Ziziphus nummularia* (Burm.f.) Wight &Arn.	Rhamnaceae	Konarak	L & F	0.50	General anti-neoplastic	100 fruits along with two handfuls of leaves are boiled and used twice a day for 2 weeks	-	-
20	*Viscum album* L.	Santalaceae	Darvash	AP	0.25	Dermal	10 fruits along with two handfuls of leaves are boiled and used twice a day for 2 weeks	-	-
21	*Lawsonia inermis* L.	Lythraceae	Hana	L & F	0.67	Dermal	12 fruits and two handfuls of leaves are boiled and taken twice a day for 8 days	Skin Cancer and against Hepa G2 and MCF cell lines	(21)

L, leaves; AP, aerial parts; B, bulbs; F, fruits; R, roots; RFC, relative frequency of citation.

lowed by category of plants reported as general antineoplastic as shown in Figure 3.

According to the results, aerial parts of the plants (44%) were the most frequently used plant part while roots, bulb and flower were the lowest one as shown in Figure 4. *Lawsonia inermis* was the most cited plant (RFC = 0.67) as anticancer followed by Satureja khuzistanica (RFC = 0.64) (Table 1).

Searching literature for scientific validation of reported plants, it was observed that only 38.1% of plants were investigated in *in-vitro* or *in-vivo* model for their anticancer activity. Comparing to the published literature it was observed that scientifically it was investigated in different type of organ cell line against our report except *L. inermis*. So there is a need to investigate the plant extracts in cell lines of the organ what is reported here in our study. Among all the plants *L. inermis* was the most evaluated plant for anticancer activity; Raja,[23] demonstrated that aqueous leaf extract of *L. inermis* possesses strong antitumor activity in both DMBA-induced 2-stage skin carcinogenesis and B16F10 melanoma tumour models in mice.

In addition to this study, its anticancer activity is also reported in other type of cells such as Ehrlich ascites carcinoma cells;[24] human colon cancer (Caco-2) and liver cancer (HepG2) cell lines[25,26] and human leukaemia cell-line HL60.[27] The other survey by Rahmat,[28] reported that essential oil isolated from the leaves have strong cytotoxic activity against liver cell lines (HepG2). Also, a study by Ali and Grever,[29] demonstrated that iso plumbagin, isolated from the stem bark of *L. inermis*, displays cytotoxicity towards melanoma and colon cancer cell lines, as well as against several non-small cell lung, colon, CNS and renal cell lines. Ethanolic extract of Artemisia sieberi was investigated by Emami,[14] against different type of cancer cell lines and found it active against these cells, but in our study area it has been reported against intestinal cancer. Therefore, it should be investigated against intestinal cancer and bioactive constituents may be isolated in pure form for mechanism of anticancer activity.

Figure 4. Percent of plant parts used.

The previous study by Dabaghian,[15] evaluated antimutagenisty and anticancer assay of ethanol extract of B. multifida and found it active. *Artemisia herba-alba* extract showed a high anticancer activity against several cell lines (human bladder carcinoma RT112, human laryngeal carcinoma Hep2 and human myelogenous leukemia K562 with IC50 = 81.59±4.4, 59.05±3.66 and 90.96 mg/L respectively and correlated it with phenolic contents.[16] *Pistacia atlantica* methanolic extract has shown significant cytotoxic effects against human colon carcinoma HT29 cells.[17] In an effort to develop improved treatments for bladder cancer, the results of Lamm and Riggs,[18] revealed that *A. sativum* extract is effective in the MBT2 murine bladder tumor model. Hence, *A. sativum* is potentially an effective therapy for bladder cancer, and clinical trials should be considered. Extracts from the seeds of milk thistle, *Silybum marianum*, are known commonly as silibinin and silymarin and possess anticancer actions on human prostate carcinoma *in vitro* and *in vivo*. Seven distinct flavonolignan compounds and a flavonoid have been isolated from commercial silymarin extracts. Most notably, two pairs of diastereomers, silybin A and silybin B and isosilybin A and isosilybin B, are among these compounds.

Findings are suggestive that extracts enriched for isosilybin B, or isosilybin B alone, might possess improved potency in prostate cancer prevention and treatment.[19] In a study conducted by Tretiakova,[20] on the anticancer activity of myrtucommulone isolated from *M. communis*, it was found that it could induce apoptosis in cancer cells via the mitochondrial pathway involving caspase-9. The large number of plant species has not been analyzed for their antitumor potential (61.9%) or have only been studied in extract form, indicates there is ample space in the field for future investigations of the anticancer activity of such plants in Iran.

In general, the plants that were used in various experimental studies showed significant results in the pharmacological models used, and these results corroborated their popular use. Many researchers selected plants used in alternative and complementary medicine to treat cancer, with the goal of evaluating the antitumor activity. Satisfactory results has been found for both *in-vitro* and *in-vivo* activities.[30,31] Medicinal herbs has the bioactive phytochemicals that are used as therapeutic agents. So, the researchers demonstrated that plant species used in folk medicine are a promising source for anticancer effects and also, new molecules.[32-40]

Conclusions

In the present study it is suggested that activity of plant species should be investigated against different cancer cell lines especially of the reported organ and those plants which are studied at extract level should be further processed by bioassay guided isolation procedure to isolate bioactive constituent in pure form. The isolation, identification of active principles and pharmacological studies of the active phyto-constituents may be considered and studied elaborately to treat effectively for various types of cancer.

References

1. Thun MJ, DeLancey JO, Center MM, et al. The global burden of cancer: priorities for prevention. Carcinogenesis 2010;31:100-10.
2. Luqman S, Pezzuto JM. NFκB: a promising target for natural products in cancer chemoprevention. Phytother Res 2010;24: 949-63.
3. Gupta MM, Singh DV, Tripathi AK, et al. Simultaneous determination of vincristine, vinblastine, catharanthine, and vindoline in leaves of *Catharanthus roseus* by high-performance liquid chromatography. J Chromatogr Sci 2005;43:450-3.
4. Wall ME, Wani MC. Camptothecin and taxol: discovery to clinic-thirteenth Bruce F. Cain Memorial Award Lecture. Cancer Res 1995;55:753-60.
5. Mozaffari Nejad AS, Kamkar A, Giri A, et al. Ethnobotany and folk medicinal uses of major trees and shrubs in Northern Iran. J Med Plants Res 2013;7:284-9.
6. Mozaffari Nejad AS, Bayat M, Ahmadi AA. Investigation of aflatoxin B1 in spices marketed in Hyderabad, India using ELISA method. J Pure Appl Microbio 2013;7:3219-23.
7. Bahmani M, Zargaran A, Rafieian-Kopaei M, et al. Ethnobotanical study of medicinal plants used in the management of diabetes mellitus in the Urmia, Northwest Iran. Asian Pac J Trop Med 2014;7:348-54.
8. Bahmani M, Golshahi H, Mohsenzadegan A, et al. Comparative assessment of the anti- *Limnatis nilotica* activities of *Zingiber officinale* methanolic extract with levamisole. Comp Clin Pathol 2013;22:667-70.
9. Jalali H, Mozaffari Nejad AS, Ebadi AG, et al. Ethnobotany and folk pharmaceutical properties of major trees or shrubs in Northeast of Iran. Asian J Chem 2009;21:5632-8.
10. Asadbeigi M, Mohammadi T, Rafieian-Kopaei M, et al. Traditional effects of medicinal plants in the treatment of respiratory diseases and disorders: an ethnobotanical study in the Urmia. Asian Pac J Trop Med 2014;7:364-8.
11. Gonzales GF, Valerio LG Jr. Medicinal plants from Peru: a review of plants as potential agents against cancer. Anticancer Agents Med Chem 2006;6:429-44.
12. Bahmani M, Eftekhari Z. An ethnoveterinary study of medicinal plants in treatment of diseases and syndromes of herd dog in southern regions of Ilam province, Iran. Comp Clin Path 2012; 22: 403-7.
13. Ibrar M, Rauf A, Hadda TB, et al. Quantitativeethnobotanical survey of medicinal flora thriving in Malakand Pass Hills, Khyber Pakhtunkhwa, Pakistan. J Ethanopharmacol 2015;169: 335-46.
14. de Melo JG, Santos AG, de Amorim EL, et al. Medicinal plants used as antitumor agents in Brazil: an ethnobotanical approach. Evid Based Complement Alternat Med 2011;2011: 365359.
15. Raja W, Agrawal RC, Ovais M. Chemopreventive action of *Lawsonia inermis* leaf extract on DMBA-induced skin papilloma and B16F10 melanoma tumour. Pharmacologyonline 2009;2:1243-9.
16. Ozaslan M, Zumrutdal ME, Daglioglu K, et al. Antitumoral effect of *L. inermis* in mice with EAC. Int J Pharmacol 2009;5:263-7.
17. Endrini S, Rahmat A, Ismail P, et al. Comparing of the cytotoxicity properties and mechanism of *Lawsonia inermis* and *Strobilanthes crispus* extract against several cancer cell lines. J Med Sci 2007;7:1098-102.
18. Kumar M, Kumar S, Kaur S. Identification of polyphenols in leaf extracts of *Lawsonia inermis* L. with antioxidant, antigenotoxic and antiproliferative potential. Int J Green Pharm 2014;8:23-36.
19. Ong CY, Ling SK, Ali RM, et al. Systematic analysis of in vitro photo-cytotoxic activity in extracts from terrestrial plants in Peninsula Malaysia for photodynamic therapy. J Photochem Photobiol B 2009;96:216-22.
20. Rahmat A, Edrini S, Ismail P, et al. Chemical constituents,

antioxidant activity and cytotoxic effects of essential oil from Strobilanthes crispus and Lawsonia inermis. J Biol Sci 2006;6:1005-10.
21. Ali M, Grever M. A cytotoxic naphthoquinone from Lawsonia inermis. Fitoterapia 1998;69:181-3.
22. Emami SA, Vahdati-Mashhadian N, Vosough R, et al. The anti-cancer activity of five species of Artemisia on Hep2 and HepG2 cell lines. Pharmacologyonline 2009;3:327-39.
23. Dabaghian FH, Entezari M, Ghobadi A, et al. Antimutagenicity and anticancer effects of *Biebersteinia multifida* DC. Ann Res Rev Biol 2014;4:906-13.
24. Khlifi D, Sghaier RM, Amouri S, et al. Composition and anti-oxidant, anti-cancer and anti-inflammatory activities of *Artemisia herba-alba*, *Ruta chalpensis* L. and *Peganum harmala* L. Food Chem Toxicol 2013;55:202-8.
25. Rezaei PF, Fouladdel S, Hassani S, et al. Induction of apoptosis and cell cycle arrest by pericarp polyphenol-rich extract of Baneh in human colon carcinoma HT29 cells. Food Chem Toxicol 2012;50:1054-9.
26. Lamm DL, Riggs DR. The potential application of *Allium sativum* (garlic) for the treatment of bladder cancer. Urol Clin North Am 2000;27:157-62.
27. Davis-Searles PR, Nakanishi Y, Kim NC, et al. Milk thistle and prostate cancer: differential effects of pure flavonolignans from *Silybum marianum* on antiproliferative end points in human prostate carcinoma cells. Cancer Res 2005;65:4448-57.
28. Tretiakova I, Blaesius D, Maxia L, et al. Myrtucommulone from *Myrtus communis* induces apoptosis in cancer cells via the mitochondrial pathway involving caspase-9. Apoptosis 2008;13:119-31.
29. Kapadia GJ, Rao GS, Sridhar R, et al. Chemoprevention of skin cancer: effect of *Lawsonia inermis* L. (Henna) leaf powder and its pigment artifact, lawsone in the Epstein-Barr virus early antigen activation assay and in two-stage mouse skin carcinogenesis models. Anticancer Agents Med Chem 2013;13: 1500-7.
30. Tayarani-Najaran Z, Emami SA, Asili J, et al. Analyzing cytotoxic and apoptogenic properties of *Scutellaria litwinowii* root extract on cancer cell lines. Evid Based Complement Alternat Med 2011;2011:1-9.
31. Matsuda T, Maekawa K, Asano K, et al. Suppressive effect of Juzen-Taiho-To on lung metastasis of B16 melanoma cells in vivo. Evid Based Complement Alternat Med 2011;2011:1-5.
32. Mozaffari Nejad AS, Shabani S, Bayat M, et al. Antibacterial effect of garlic aqueous extract on *Staphylococcus aureuses* in hamburger. Jundishapur J Microb 2014;7:1-5.
33. Eslami M, Bayat M, Mozaffari Nejad AS, et al. Effect of polymer/nanosilver composite packaging on long-term microbiological status of Iranian saffron (*Crocus sativus* L.). Saudi J Biol Sci 2016;23:341-7.
34. Ebrahimie M, Bahmani M, Shirzad H, et al. A review study on the effect of Iranian herbal medicines on opioid withdrawal syndrome. J Evid Based Complem Altern Med 2015;20:302-9.
35. Eftekhari Z, Bahmani M, Mohsenzadegan A, et al. Evaluating the anti-leech (*Limnatis nilotica*) activity of methanolic extract of *Allium sativum* L. compared with levamisole and metronidazole. Comp Clin Path 2012; 21:1219-22.
36. Kamkar A, Shamse Ardekani MR, Shariatifar N, et al. Antioxidative effect of Iranian *Pulicaria gnaphalodes* extracts in soybean oil. S Afr J Bot 2013;85:39-43.
37. Bahmani M, Banihabib E. Comparative assessment of the anti-Annelida (*Limnatis nilotica*) activity of nicotine with niclosamide. Global Vet 2013;10:153-7.
38. Bahmani M, Mirhoseini M, Shirzad H, et al. A review on promising natural agents effective on hyperlipidemia. J Evid Based Complementary Altern Med 2015;20:228-38.
39. Bahmani M, Shirzad H, Mirhosseini M, et al. A review on ethnobotanical and therapeutic uses of fenugreek (*Trigonella foenum-graceum* L). J Evid Based Complem Altern Med 2016; 21:53-62.
40. Asadi-Samani M, Rafieian-Kopaei M, Azimi N. Gundelia: a systematic review of medicinal and molecular perspective. Pak J Biol Sci 2013;16:1238-47.