



Review Article

The Anticancer Potential of Van Lake Basin Plants[†]

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Abstract: For centuries, people have used plants for various needs, as well as for treating diseases. Due to the fact that synthetic drugs damage other organs of the body while treating diseases, the demand for herbal resources has been increasing in recent years. Cancer, a disease whose cases and death rates are quickly rising, is now and, the second leading cause of death just behind the cardiovascular diseases. The toxicity of modern chemotherapy and the resistance of cancer cells to anticancer agents have led the scientific world to search for new treatments and prevention methods for this insidious disease. The therapeutic properties of plants, which generally do not have significant side effects, are associated with biologically active organic compounds, and the geochemical composition of the region where they grow. Van Lake Basin has a rich plant diversity thanks to its climate, geographical features, and soil content. This region is home to many medicinal plant species used by humans but have not yet been studied, and their phytochemical structures are still not fully elucidated. Although humans have used these plants for centuries, as inherited from ancestors, studies are required to prove their therapeutic effects *in vivo* and *in vitro*. This study presents the anticancer potentials of some crucial plants (*Eryngium billardieri*, *Cichorium intybus*, *Bongardia chrysogonum*, *Bryonia multiflora*, *Euphorbia macroclada*, *Scutellaria orientalis*, *Plantago major*, *Primula auriculata*) reported to be used in treating various diseases in the Van Lake Basin by analyzing the *in vitro* and *in vivo* anticancer studies conducted with the same plants in the literature.

Van Gölü Havzası Bitkilerinin Antikanser Potansiyeli

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Anahtar Kelimeler

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Öz: İnsanlar yüzyıllar boyunca bitkileri çeşitli ihtiyaçlarının yanı sıra hastalıkların tedavisinde de kullanmışlardır. Sentetik ilaçların hastalıkları tedavi ederken vücudun diğer organlarına zarar vermesi nedeniyle son yıllarda bitkisel kaynaklara olan talep giderek artmaktadır. Görülme sıklığı ve ölüm oranı hızla artan bir hastalık olan kanser, günümüzde kalp ve damar hastalıklarından sonra ikinci sırada yer almaktadır. Modern kemoterapinin toksisitesi ve kanser hücrelerinin antikanser ajanlara karşı direnç göstermesi, bilim dünyasını bu sinsi hastalık için yeni tedavi ve korunma yöntemleri aramaya yöneltmiştir. Genellikle önemli yan etkileri olmayan bitkilerin tedavi edici özellikleri, biyolojik olarak aktif organik bileşikler ve yetiştikleri bölgenin jeokimyasal bileşimi ile ilişkilidir. Van Gölü Havzası, iklimi, coğrafi özellikleri ve toprak içeriği sayesinde zengin bir bitki çeşitliliğine sahiptir. Bu bölge, insanlar tarafından kullanılan ancak henüz araştırılmamış birçok tıbbi bitki türüne ev sahipliği yapmaktadır ve

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fitokimyasal yapılarının hala tam olarak anlaşılması gerekmektedir. Her ne kadar insanlar, atalarından gördükleri gibi bu bitkileri yüzyıllardır kullanmış olsalar da, *in vivo* ve *in vitro* terapötik etkilerini kanıtlamak için çalışmalara ihtiyaç vardır. Bu çalışma, Van Gölü Havzası'nda çeşitli hastalıkların tedavisinde kullanıldığı bildirilen bazı önemli bitkilerin (*Eryngium billardieri*, *Cichorium intybus*, *Bongardia chrysogonum*, *Bryonia multiflora*, *Euphorbia macroclada*, *Scutellaria orientalis*, *Plantago major*, *Primula auriculata*) antikanser potansiyellerini, literatürde aynı bitkilerle yapılan *in vitro* ve *in vivo* antikanser çalışmalarını analiz ederek sunmaktadır.

1. Introduction

Ancient civilizations, which left essential traces on the stage of history, not only used plants for therapeutic purposes but also left this vital knowledge as a rich heritage to the next generations. Archaeological materials and inscriptions show that plants have been used to treat diseases since the Chipped Stone Age. Akkadian, Sumerian, and Assyrian inscriptions, Indian, Chinese, Egyptian, Greek, Seljuk, and Ottoman documents mention using plants for therapeutic purposes. The World Health Organization (WHO) reports that approximately 80% of the world's population tries to solve their health problems with herbal remedies in the first place. While 4,000 of these are widely used, 2,000 medicinal plants are traded worldwide, and 500 are in Western Europe. In the USA, 75 percent of the herbal medicines still traded are obtained from research on plants used by the public (Kaya, 2010). In addition, approximately 25 percent of prescription drugs in developed countries are composed of active ingredients of herbal origin (reserpine, aspirin, quinine, vinblastine, etc.) (Yaşar et al., 2021). Ethnobotanical knowledge from ancient times to modern times comes to the fore in this case, and the use of medicinal plants gains importance. In the Lake Van basin, home to great civilizations that have left their mark on history for thousands of years due to its geographical location, dozens of plant species are used in folk medicine and whose chemical content is waiting to be unearthed. However, scientific studies have not been carried out sufficiently on them.

Cancer is a disease with a rapidly increasing incidence and mortality rate. Although it was ranked 7th-8th in the list of diseases causing death at the beginning of the century, today, it has risen to second place after cardiovascular diseases in many countries (Bozyel et al., 2019). The disease is characterized by the continuous uncontrollable proliferation of cells in the human body. According to the International Agency for Research on Cancer (IARC), there were approximately 10 million new cancer cases in 2020, and one in every six deaths was caused by cancer (Ferlay et al., 2021). The resistance of cancer cells to anticancer drugs and the toxicity of contemporary chemotherapy have led the scientific world to search for novel approaches to treating and preventing this devious sickness. It has been demonstrated that eating plants high in phenolics, which are vital active components, reduces oxidative damage to DNA, which could be an essential initial stage in the development of several cancers (Nichenametla et al., 2006). Today, many drugs such as paclitaxel used in cancer treatment are active ingredients obtained from plant sources. Carcinogen suppression, antiproliferation, cell cycle suspension, apoptosis induction and differentiation, the inhibition of angiogenesis, antioxidation, and a decrease in multidrug resistance are some of the ways that plant compounds demonstrate their anticancer effects (Vauzour et al., 2010). The most current treatments for the disease are chemotherapy, radiotherapy, and chemical drugs. However, chemotherapy causes too many side effects in patients and causes more damage to their health, leading scientists to alternative treatments and therapies against cancer. More than 3000 plants worldwide have been reported to have anti-cancer properties (Seca & Pinto, 2018). Determining the effect of herbal drugs *in vitro* and *in vivo* is recognized as the most effective preliminary study against cancer worldwide.

The climate, geographical characteristics, and soil content provide people living in the Lake Van basin with a rich source of medicinal plants and folk medicine knowledge that they have used for centuries (Özgökçe & Özçelik, 2004). Many plants used in folk medicine in this region and their intended uses have been reported in previous studies (Özgökçe & Özçelik, 2004; Mükemre et al., 2016; Dalar & Mükemre, 2020). The focus of botanical culture research is to contribute to finding solutions to health, hunger, and environmental problems. For this reason, the study should not only be limited to listing the local names and usage patterns of plants used in folk medicine. At the same time, it should

evaluate the wide-range use of plants and their consequences for the benefit of society from a sustainable development perspective. Reviewing the use of plants in traditional medicine and assessing this information with modern scientific insights can yield valuable discoveries (Sharma et al., 2022). Such studies are crucial for identifying potential medicinal sources rather than inventing new drugs. They also play a crucial role in maintaining traditional botanical knowledge within fast-evolving societies and pinpointing plants that could be used for therapeutic purposes in the future.

Studies on randomly selected plants based on biological activity can guide the discovery of effective compounds or extracts (Ashraf et al., 2020). Worldwide success has been achieved in the hunt for natural anticancer drugs; active ingredients have been identified and are currently used to treat human carcinomas (Yu et al., 2016). Understanding herbal medicine helps direct the search for plants that may have cytotoxic properties. In drug development studies, instead of examining plants only in terms of a single activity, investigating them with screening studies in which different activities are monitored shows that they may be effective for treating different unexpected diseases (Deng et al., 2017).

Because the area around Lake Van is surrounded by high mountains and the winter season is long and snowy, hundreds of years ago, the local people could not easily reach health institutions and medical equipment. So, they used the plants around them in the treatment of diseases and created an oral library of medicinal plant use (Tabata et al., 1994). These medicinal plants, which have been unearthed with significant research, need to be supported by *in vivo* and *in vitro* studies on cancer prevention and treatment, which ranks second among the causes of death in the world. Because of their low side effects, plants are the most commonly used materials in drug development studies against cancer. Due to their long-standing use in folk medicine, the plants of the Lake Van basin offer significant potential for cancer disease research.

Lake Van Basin covers 2.5 percent of Turkey's total area, approximately 17.964 km². The elevation of the basin land starts from 1600 m. above the sea and rises to over 4000 m. There are many mountains and hills with peaks between 2000 and 3000 m. Among these mountains, dominated by steppe vegetation, there are plains such as Van, Hoşap, Gürpınar, and Özalp Plain. The region has a continental climate. Summers are especially short, and springs are almost nonexistent (Turkish Ministry of Agriculture and Forestry, 2021).

People living in the Lake Van basin utilize the plants growing around them to treat many diseases, besides cancer. However, no study in the literature reviews the *in vitro* and *in vivo* anticancer potential of the plants used to treat different diseases in folk medicine in the Van Lake Basin. This study will likely fill this literature gap and raise awareness about these valuable plants. In this way, it is also believed that further studies against cancer will be encouraged with these plants, which are abundant in the Lake Van Basin and have the potential to be active ingredients in cancer drugs. Due to their critical active ingredients and mechanisms of action, this study focused on the following plants: *Eryngium billardieri* Delar., *Cichorium intybus* L., *Bongardia chrysogonum* L., Spach, *Bryonia multiflora* Boiss. & Heldr., *Euphorbia macroclada* Boiss., *Scutellaria orientalis* L., *Plantago major* L., and *Primula auriculata* Lam.

2. Some important anticancer plants growing in Lake Van Basin

2.1. *Eryngium billardieri* Delar. (Bull thorn, Apiaceae Family)

Eryngium billardieri Delar. is a perennial herbaceous plant with important hepatoprotective, antitumor, and apoptosis-inducing properties. It belongs to the Apiaceae family, which is one of the most prominent plant families in the world with a wide distribution in Iran, Turkmenistan, Turkey, Lebanon, Syria, Iraq, Afghanistan, and Pakistan (Yeşilada et al., 1989). It contains abundant phytosterols, triterpenoid saponins, flavonoids, ecdysteroids, coumarin derivatives, polyacetylenes, essential oils, and phenolic acids (Kikowska et al., 2022). Phytochemicals obtained from the root and above-ground parts of *Eryngium billardieri* are used against scorpion stings, in the treatment of rheumatism, urinary tract infections, goiter, sinusitis, and diabetes (Heidari et al., 2023), and among the people living in the Van Lake basin, it is used as an anti-inflammatory, in dental abscesses, influenza, gastric pain, wound healing and stomach cancer treatment (Dalar & Mükemre, 2020).

Apoptosis, an essential mechanism regulating pathways that control cell proliferation and death, is considered a targeted treatment strategy for tumor cells. Cyclin D1 gene, concentrated in various

carcinomas, plays a vital role in regulating cell progression of the cell cycle. Increased expression of the proapoptotic Bax gene, which can induce apoptosis via the intrinsic signaling pathway (also known as mitochondrial apoptosis), may cause therapeutic effects in cancer cells (Mohammadi et al., 2016). *Eryngium billardieri* has been reported to stop tumourisation by inducing apoptosis in various cancer cell lines thanks to the essential phytochemicals it contains. It has been reported that extracts prepared from the above-ground parts showed a cytotoxic effect on MCF7 (human breast cancer cell line) (Paşayeva et al., 2017) and significantly induced apoptosis in PANC-1 (pancreatic cancer) cell lines by increasing Bax and decreasing mRNA expression of cyclin D1 (Roshanravan et al., 2018).

2.2. *Cichorium intybus* L. (white chicory, bitter chicory, family Asteraceae)

Cichorium intybus L. (chicory) is a plant belonging to the Asteraceae family. In the Lake Van Basin, this plant is used in traditional medicine for the treatment of epilepsy, kidney stones, asthma, wound treatment, stomach ulcers, digestive system disorders, diuretics, and hypertension due to its numerous biological properties, including those that are antibacterial, antioxidant, and anti-inflammatory effects (Dalar & Mükemre, 2020). In addition to its local use, various *C. intybus* extracts are used worldwide because of their extensive range of health-promoting and pharmacological qualities, which include antibacterial, hepatoprotective, anti-protozoal, anti-hyperuricemia, anti-inflammatory, antioxidant, antinematodal, and antiproliferative effects (Khan et al., 2020).

Cichorium intybus extracts have been used against estrogen-positive breast cancer (MCF-7) (Dahab & Afifi, 2007), amelanotic melanoma (C32), prostate cancer (LNCaP), renal adenocarcinoma (ACHN) (Conforti et al., 2008), leukemia cells (Saleem et al., 2014), Ehrlich ascites carcinoma (Hazra et al., 2002), prostate cancer (PC-3) (Nawab et al., 2011), breast cancer cells (T47D and SKBR3) (Mehrandish et al., 2017) and leukemia (Esmailbeig et al., 2015). In addition, sesquiterpenes obtained from *Cichorium intybus* were reported to have a cytotoxic effect on ovarian cancer cells, and murine lymphoma (Zhou et al., 2012).

2.3. *Bongardia chrysogonum* (L.) Spach (crack grass, family Berberidaceae)

Bongardia chrysogonum L. Spach is a plant belonging to the Berberidaceae family which is reported to be used in treating epilepsy and hemorrhoids among people living in the Lake Van Basin (Dalar & Mükemre, 2020). Due to advances in modern medicine, tubers are used to treat prostatic hypertrophy, diabetes, gastrointestinal disorders, hypercholesterolemia, urinary tract infections, and hemorrhoids (Baydoun et al., 2015; Abuhamdah et al., 2017). This plant's tuber has been shown to have anticancer properties against human glioma, breast, and lung cancer cells. It has also been shown to have in vitro neuroprotective effects by cholinesterase enzyme inhibition (Gezici & Şekeroğlu, 2021). In addition, *Bongardia chrysogonum* (L.) Spach tubers contain phenols (bongardol and benzakalin), alkaloids (isoquinoline, lupine bongardamine, and bongardine), saponins (arabinofuranosyl, glucopyranosyl, hederagenin, leontoside and hederacoside) and triterpenoids (bongardol acetate), which are effective in Alzheimer's and cancer treatment (Baydoun et al., 2015; Ahmad et al., 2019). In a study published by Oran et al. (2022), *Bongardia chrysogonum* extracts showed an antiproliferative effect in human melanoma (WM136-1A) cancer cell lines. Dağlı et al. (2022) reported that *B. chrysogonum* decreased blood sugar levels after diabetes and reduced kidney damage in rats with diabetic nephropathy.

2.4. *Bryonia multiflora* Boiss. & Heldr. (ulongardia, family Cucurbitaceae)

Bryonia multiflora, used in treating diabetes and wounds in the Van region (Dalar & Mükemre, 2020), is an Archaeplastida species belonging to the Cucurbitaceae family. The perennial herbaceous plant *Bryonia multiflora* is dioecious and has a deeply rooted rhizome-shaped root. The roots of the plant contain steroidal saponosides, triterpenic saponosides and fixed oils, brionolic acid, triterpenic acids, cucurbitacin, lectins, flavonoids, and sterols, and hepatoprotective, cytotoxic, anti-inflammatory, purgative, and antitumoral activities have been reported for cucurbitacin (Miro, 1995). Similarly, plants that contain saponin have been shown to have a wide range of biological effects, including anticarcinogenic, hypocholesterolemic, anti-inflammatory, antiprotozoal, antimicrobial,

antihypertensive and antioxidant properties (Fidan & Dündar, 2007). It has been reported that in streptozotocin-induced diabetic rats, *Bryonia multiflora* extract can regenerate β -cells and has a preventive effect against tissue damage (Song et al., 2014), and has antidiabetic and antioxidant activity (Alkan et al., 2023).

Non-coding RNAs (ncRNAs), especially long non-coding RNAs (lncRNAs), have been shown to play a role in the regulation of most cancers and the control of the autophagy mechanism. *Bryonia multiflora* extract increased autophagy markers and decreased Bcl-2 levels in MDA-MB-231 and MCF-7 cells. Additionally, it has been noted to alter the transcription levels of different lncRNAs associated with autophagy (Zhang et al., 2017a).

2.5. *Euphorbia macroclada* Boiss. (Neblul, euphorbia, milkweed, family Euphorbiaceae)

The family Euphorbiaceae is one of the most prominent flowering plants, comprising more than 300 genera and 8000 species. The species of this genus, as well as the spurge family in general, are characterized by their milky, irritating latex production. *Euphorbia macroclada*, which is reported to be used in the treatment of constipation in the Van region (Dalar & Mükemre, 2020), is a plant frequently used in traditional medicine in different parts of the world thanks to its wide range of chemical compounds, such as oxygenated sesquiterpenes, hydrocarbons, and macrocyclic diterpenoids. *Euphorbia macroclada* is a plant widely used in traditional medicine worldwide because of its wide range of chemical compounds, including macrocyclic diterpenoids, hydrocarbons, and oxygenated sesquiterpenes. It treats constipation in the Van region, according to report (Dalar & Mükemre, 2020). Consequently, outstanding structural diversity of the aforementioned chemical components, as well as their medicinal uses because of their cytotoxic, antitumor, and antiviral properties makes them promising compounds for new drug discovery (Vasas & Hohmann, 2014). Euphorbia species are used for their disinfecting, antiseptic, and emollient qualities, as well as for treating acne, calluses, skin itching, dermatitis, irritation, boils, sunburn, rashes, warts, and hair loss (Ernst et al., 2015). These components are believed to be harmful in various ways, including impacts on angiogenesis, cell death and suppression of metastasis, increased formation of reactive oxygen, proliferation, and differentiation of cells (Diederich & Cerella, 2016). Cancenone isolated from Euphorbia species has been reported to stop cell division in the G0/G1 phase and induce apoptosis by causing mitochondria damage and cell receptor death (Ramsay et al., 2011). It was reported that isolated triterpenoids induced apoptosis in human colon adenocarcinoma cells (Colo320). Euphorbia species have long been used to treat various illnesses, from infectious disorders to long-term conditions like cancer. The chemical diversity of their isoprenoid compounds, such as triterpenoids, has been credited with their effectiveness. This has led to the isolation of various classes of triterpenoids, most of which are, euphane, taxanes, tiricallane, cycloalkanes, oleanane, and cycloalkanes. Additionally, it has been shown that these triterpenoids are cytotoxic through various modes of action, including impacts on apoptosis, angiogenesis, cell division, reactive oxygen generation, transformation, and suppression of excessive metastasis (Kemboi et al., 2020).

2.6. *Scutellaria orientalis* L. (yellow cascade, family Lamiaceae)

Scutellaria orientalis L., which is generally used for pain relief, analgesic, diabetes, hemorrhoids, and cancer treatment in the Van region (Dalar & Mükemre, 2020), belongs to the Lamiaceae family and is a plant distributed in the central Iranian-Turanian part of Asia. Many *Scutellaria* species have long been used as traditional herbal remedies to treat a wide range of illnesses, including infections, malignancies, hepatic and stomach problems, respiratory, neurological, and cardiovascular conditions (Marsh et al., 2014; Wang et al., 2020). Furthermore, contemporary medicine has validated the traditional applications of the therapeutic species of *Scutellaria*. Some of the significant medicinal benefits of this genus include cancer prevention, anti-viral impacts (Ang et al., 2020), reducing inflammation (Cheng et al., 2018), antioxidant activity (Lohani et al., 2013), protective effects on the nervous system (Zhang et al., 2017b), and it also has liver protection (Dong et al., 2011).

Recent studies on cancer therapy have shown that *S. Baicalensis*, another species of *Scutellaria*, suppresses apoptosis and tumor development by PI3K-Akt-mTOR and MAPK pathways, β -related pathways, and tumor-associated macrophages targeting (Parajuli et al., 2011; Tan et al., 2015). Cancer

cells can escape apoptosis or programmed cell death by activating the intrinsic or extrinsic pathway by caspases. Extracts from *Scutellaria baicalensis* cause cleavage of mitochondrial-dependent caspases, decrease Bcl-2 levels, and increase Bax, Cyto-C, and p53 in different human cancer cell lines (Kuo et al., 2009).

2.7. *Plantago major* L. (Vascular herb, Nerve grass, Plantaginaceae family)

Plantago major L. belongs to the *Plantaginaceae* family, which is widespread worldwide and has about 280 species (Beara et al., 2009). In the Van region, the plant leaves are soaked in warm milk or warm water, wrapped around the inflamed wounds, and used to drain the inflammation. It has also been reported that decoction of the leaves is used in laryngeal cancer, stomach pain, body itching, kidney and intestinal treatment, and fungus treatment between the fingers (Dalar & Mükemre, 2020). It is reported that *Plantago major* is used to treat several illnesses, including infections (Jamilah et al., 2012), and has antimicrobial, antidiabetic, antispasmodic, antiviral, anti-inflammatory, and wound healing properties (Akram et al., 2014). A review of the traditional uses of *Plantago major* (Samuelsen, 2000) shows that it is used in treating tumors in some Latin American countries. Soltani et al. (2020), in their study to evaluate the efficacy of *Plantago major* on radiation-induced mucositis symptoms in cancer patients, reported that the severity of mucositis was significantly lower (p-value <0.05) in the intervention group compared to the placebo group. A significant flavonoid found in *Plantago* species, luteolin-7-O- β -glucoside, has shown a lethal effect on tumoral cell lines of melanoma (UACC-62) and breast cancers (MCF-7) (Galvez et al., 2003). Potential anticancer compounds such as stearic acid and benzene dicarboxylic acid found in the root of the above-ground parts of *P. major* have an antiproliferative effect on the colon cancer cell line (HCT-116) (Rahamooz-Haghighi et al., 2021). It has been reported that *P. major* has antibacterial activity (Holetz et al., 2002), antileukemia, anticarcinoma, and antiviral activity and modulates cell-mediated immunity (Chiang et al., 2003), protects against systemic *Streptococcus pneumoniae* infection, prevents breast cancer (Hetland et al., 2000), and significantly inhibits Ehrlich ascites tumors in mice (Ozaslan et al., 2007).

2.8. *Primula auriculata* Lam. (Primrose, family Primulaceae)

It was reported that the extract obtained from the above-ground parts of *P. auriculata* caused pro-apoptotic and antiproliferative effects, caspase activation, and nuclear DNA fragmentation in human colon cancer HT-29 cells (Behzad et al., 2016). Kaempferol and isorhamnetin isolated from the above-ground parts are mainly thought to cause anticancer activity in the plant (Fico et al., 2007). *Primula auricula* shows high antibacterial and antioxidant activity thanks to the abundant amount of saponins and flavonoids it contains. It is used in the treatment of eye diseases such as trachoma and cataracts (Jaberian et al., 2013), colds, flu (Sezik et al., 2001), and digestive system disorders (Altundag & Ozturk, 2011). In the Van region, it is collected before flowering in spring and added to local herbed cheese, and its leaves are used in meals. It is also reported to treat hypertension, diabetes, and inflammation (Mükemre et al., 2016; Dalar & Mükemre, 2020).

3. Conclusion

The primary purpose of research on botanical culture is to contribute to solutions to environmental, hunger, and health problems. In this context, beyond studies that list only the names and ways of using plants among the public, it is essential to evaluate the use of plants from a sustainable development perspective and obtain results for the benefit of society. Research that compiles and evaluates public knowledge of commonly used plants using current information can produce crucial results. Today, most herbal medicines have emerged as a result of compilation studies. Therefore, scientific research on folk herbs can be critical in identifying potential future treatment sources and preventing the loss of traditional botanical cultures. In today's world, where societies are changing rapidly, preserving and making local botanical knowledge available through such research can be crucial in reaching solutions to important issues such as health, hunger, and environmental sustainability.

The limitations of chemotherapy used in cancer treatment today for healing patients have led to the search for alternative sources, such as medicinal plants. This review presents literature findings

regarding the *in vitro* and *in vivo* use of some plants (*Eryngium billardieri* Delar., *Cichorium intybus*, *Bongardia chrysogonum* (L.) Spach, *Bryonia multiflora* Boiss. & Heldr., *Euphorbia macroclada* Boiss., *Scutellaria orientalis* L., *Plantago major* L., and *Primula auriculata* Lam.) in the Lake Van basin to treat or prevent cancer and various diseases among the public. Some substance groups in medicinal plants may be explicitly distributed to a particular species, genus, or family. One of the most important results obtained from this study is that the plants used in treating various diseases in the Van Lake Basin also have unknown anticancer properties in addition to the diseases they treat. Plant extracts cause cancer inhibition through cell cycle arrest at different stages, induction of apoptosis or autophagy, and triggering distinct signaling pathways. Phenolic compounds, in particular, are thought to be the most important active molecules responsible for these anticancer effects. The rich medicinal plant diversity of the Lake Van basin and its herbal practices among the public can be used as potential anticancer treatments due to their synergistic effects. However, more *in vitro* and *in vivo* studies with local plants are required to isolate, identify, and use different phytochemicals to prevent or treat cancer. At the same time, toxicity studies of various herbal products showing anticancer activities regarding human health and their long-term harm should be evaluated.

Following ethnobotanical studies based in the Lake Van basin, conducting phytochemical and biological investigations, one promising therapeutic approach against cancer could be the creation of national databases of natural molecules and the association of herbal products with synthetic drugs. This approach not only preserves traditional botanical knowledge but also facilitates the identification of plants with significant pharmacological potential. By matching herbal products with synthetic drugs, we can explore innovative cancer therapies. Such rigorous scientific investigations are crucial to preserving our botanical heritage and contributing to the discovery of new therapeutic compounds from natural sources.

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