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Ethnopharmacological uses of animals and plants in cancer treatment-a review

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SUMMARY

Cancer is characterized by abnormal cell development that invades and destroys nearby tissues, posing a threat to one's health. The current medical treatment strategy, which involves chemical, radiation, and surgical procedures, has been shown to be ineffective, has numerous downsides, and is extremely expensive. Although mainstream cancer treatment can target specific cancer cells and prevent relapse in some cases, complementary and alternative medicine is required due to the inadequacies of current therapies, such as ineffectiveness, side effects, or a lack of availability. Furthermore, a number of studies have found that complementary therapy practices can aid cancer patients in achieving better outcomes. Parts of animals especially mammals and herptiles as well as plants are used to treat cancer.

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INTRODUCTION

Cancer is defined as aberrant cell growth that invades and destroys neighboring tissues and hampers healthy life (Gennari *et al.*, 2007). Through the blood circulatory and lymphatic system, cancer spreads to various organs. Oncogenes and tumor suppressor genes, both are instrumental in cancer development (Knudson, 2001). Tobacco usage, alcohol consumption, environmental pollutants, viral infections, customary habits, and life styles are important preconditions for cancer development. About 10% to 15% of cancers are completely inherited (Anand *et al.*, 2008). Cancers are called according to their source tissues namely carcinoma for epithelial cell lining, sarcoma arises for mesodermal cell lining, lymphoma for lymphnodes (Sultana *et al.*, 2014).

Chemotherapy, like other traditional cancer treatments, has unfavorable and hazardous side effects, and hence fails to manage the disease. The use of medicinal plants as a substitute for the negative effects of artificial drugs is a potential option (Harun-ur-Rashid *et al.*, 2002). For a long time, the herbs were used in cancer therapy (Hartwell, 1982). Chemical ingredients of therapeutic

significance are found in medicinal plants and animals (Nostro *et al.*, 2000). Clinical trials and phytochemical research have recently revealed that numerous herbs have anti-tumor potential against a variety of malignancies (Sharma *et al.*, 2011a; Sharma *et al.*, 2011b).

Bioactive chemicals can be found in abundance in plants. Plants are rich sources of a number of anticancer drugs (Cragg and Newman, 2005). Regardless of the fact that several anticancer medications are derived from medicinal plants, there seem to be several plants with anticancer potential that have not yet been thoroughly investigated. Around 114,000 extracts were examined for anticancer efficacy by the "National Cancer Institute" (Shoeb, 2006). As a result, the focus should be on understanding whether plants are a resource of anticancer activity or if the plant derived compounds can be utilized in human body to accomplish cancer-blocking or healing benefits.

PARTS OF ANIMALS TO TREAT CANCER

Gekko swinhonis

Traditional Chinese medicine has employed *Gekko swinhonis* as an anti-cancer medication. The activity of Gekko sulfated polysaccharide in hepatocellular cancer was examined. Gekko sulfated polysaccharide was used to treat a hepatocarcinoma cell line (Bel-7402) and a liver cell line (L-02). Gekko sulfated polysaccharide had no effect on the proliferation and viability of normal liver L-02 cells, however it did stop hepatocarcinoma "Bel-7402" cells from proliferating. Gekko sulfated polysaccharide did not cause apoptosis in "Bel-7402" cells, but it did prevent them from entering the G2/M phase. "Bel-7402" cells revealed ultrastructural characteristics of differentiation after being treated with Gekko sulfated polysaccharide. On Gekko sulfated polysaccharide treated cells. Gekko sulfated polysaccharide inhibited hepatocarcinoma proliferation and encouraged differentiation, but had no effect on normal liver cells, according to the findings (Wu *et al.*, 2006).

Camelus spp.

Camel milk has long been thought to provide medicinal benefits for humans and to be a cure for a variety of illnesses, notably cancer (Kula and Tegegne, 2016; Abdullahi, 2019). Camel milk induced autophagy in human colorectal HCT 116 and breast MCF-7 cancer cells, resulting in antiproliferative activities (Abrhaley and Leta, 2018; Krishnankutty *et al.*, 2018; Abdullahi, 2019).

Bos spp.

The best way to beat cancer is to prevent it from happening in the first place. Although the human diet contains ingredients that can cause cancer, it also contains ingredients that can help prevent it. Milk fat contains a number of anticarcinogenic components, including conjugated sphingomyelin, linoleic acid, ether lipids, and butyric acid, according to recent studies. Human malignant melanoma, colorectal, breast, and lungs cancer cell lines were all suppressed by conjugated linoleic acid. Chemically generated mouse epidermal cancers and

abnormal crypt foci in the rat colon were decreased in animals. Conjugated linoleic acid, at near-physiological quantities, prevented mammary cancer in a number of experiments, regardless of the amount or type of fat in the diet. Milk sphingomyelin and phospholipid are biologically active, according to in vitro research. In vitro investigations revealed that the milk sphingomyelin and phospholipid sphingosine and ceramide, through their physiologically active metabolites, participate in three primary antiproliferative pathways impacting oncogenesis, growth inhibition, apoptosis induction and differentiation (Parodi, 1997).

Capra spp.

Conjugated linoleic acid is abundant in goat milk. It has been shown to have anticarcinogenic characteristics in animal models of mammary and colon cancer, as well as in vitro models of human melanoma, colorectal, and breast cancer. The mechanism by which CLA inhibits tumor development is unknown, while it has been proposed that eicosanoid-dependent cell signaling systems, antioxidative effects, and disruption of estrogen receptor-mediated actions are all involved (Williams, 2000; Palombo *et al.*, 2002; Jirillo *et al.*, 2010).

PARTS OF PLANTS USED TO TREAT CANCER

Astrodaucus orientalis

The plant belongs to umbelliferae and is a biennial. This root and above-ground parts have antiproliferative properties in breast cancer cells (T47D) (Abdolmohammadi *et al.*, 2009). The most important chemicals in this plant are fenchyl-acetate, anisole, myrecene, and sabinene (Nazemiyeh *et al.*, 2009; Razavi *et al.*, 2011). Cell cycle inhibition and apoptosis promotion are two primary mechanisms of its anticancer activities (Abdolmohammadi *et al.*, 2009).

Astragalus cytosus

Astragalus cytosus is a leguminous (legume family) perennial plant. A study employing “HeLa cancer cells” demonstrated the toxicity of extract of this plant on cancer cells (Sadat *et al.*, 2014). In a “clinical trial” of the plant extract on patients suffering from lung cancer given a positive outcome (Cassileth *et al.*, 2009). Other plants of same species contain flavonoids that have been demonstrated to trigger apoptosis in vitro (Hu *et al.*, 2009).

Avicennia marina

The plant is a mangrove and it leaf extract contains flavonoid chemicals that have anticancer features in breast cancer of human. “BT-20 cells” are a type of stem cell. In another work, the anticancer activity of naphthoquinone on laryngeal cancer cells (kb) was demonstrated by isolating it from the plant's leaf (Sharaf *et al.*, 2000). The extract has a cytotoxic impact on MDA-MB 231 breast cancer (Behbahani and Sadeghi-aliabadi, 2010).

Achillea wilhelmsii

This plant belongs to family Asteraceae. The methanolic extract of the leaves have been tested on a number of "cancer cell lines". Plant methanol extract contains phenol chemicals, particularly flavonoids, which inhibit cancer cell multiplication by triggering apoptosis (Sharma *et al.*, 2011a; Uddin *et al.*, 2011). 1, 8-cineole and alpha-pinene are two of the most important monoterpene chemicals that trigger apoptosis in human melanoma cells (Dokhani *et al.*, 2005).

Ammi majus

This is a member of umbelliferae and is distributed across Europe and west Asia (Dokhani *et al.*, 2005). The ethanol extract from this plant was found toxic to "HeLa" and "MCF7" cells (Nemati *et al.*, 2013). Coumarins are important molecules in this plant, as they contribute to the bulk of its biological functions mainly through onset of apoptosis Psoralens, a type of coumarin present in the plant can inhibit cytochrome p450 function, thereby acting as an anticancer agent (Shokoohinia *et al.*, 2014).

Artemisia absinthium

Artemisia belongs to family asteraceae. The effects of artemisin on breast cancer cell have been investigated (Asgarpanah and Ariamanesh, 2015). GC-MS analysis revealed terpineol, palmitic acid-monoglyceride, octadecanoic acid, mannofuranoside, flavone, epiyangambin, camphor and 2, 3-dihydroxypropyl ester as probable chemicals. The "HMEL" of *Artemisia absinthium* reduced the proliferation of "MCF-7 ATCC breast cancer cells", but not of HCT 116 ATCC colon cancer cells of human. *Artemisia absinthium* also possess moderate antibacterial activity... The wound healing potential of RM was superior to that of regular povidone iodine cream, which signals wound healing via modulating cytokine networks and apoptotic marker levels (Sultan *et al.*, 2020).

Andrographis paniculata

Andrographis paniculata is an anticancer herb that has been utilised in Indian and Chinese herbal therapy for centuries. The ethanol extract of this herb's aerial portions yielded 14 chemicals, including flavonoids, and labdane diterpenoids, according to a phytochemical study. The andrographolide is abundant in the aerial portions of *Andrographis paniculata* and this is the first time compounds have been isolated from a natural source (Geethangili *et al.*, 2008; Islam *et al.*, 2018). *Andrographis paniculata* was found to boost PBMC proliferation as well as TNF and IFN production in vitro. Oral administration with *Andrographis paniculata* reduced esophageal dysplasia and drastically changed the amount of regulatory T cells in mice with cancer caused by 4-nitroquinoline 1-oxide. The cytokines produced by *Andrographis paniculata*-treated mice's spleen lymphocytes were moved to a normal resting state. Furthermore, *Andrographis paniculata* therapy significantly boosted tumour apoptosis, limiting the growth of "cell line-based xenografts" without causing significant body loss in weight. The effects of *Andrographis paniculata* therapy on the proliferation of "esophageal patient-derived xenografts" were noted for the first time. Furthermore, after oral

administration of *Andrographis paniculata* to mice, various diterpenes were found in the plasma, implying that the compounds are responsible for pharmacological activities (Yue *et al.*, 2019).

Boswellia spp.

The gum resin of *Boswellia carteri* and *B. serrata* is used to isolate boswellic acid (BA), a member of pentacyclictriterpene. It has proven to be an effective treatment for cancer, inflammatory bowel disease, and other diseases.(Roy *et al.*, 2019). The medicinal plant *Boswellia serrata* has a lot of potential when it comes to fighting cancer. In a 4T1 breast cancer mouse model, the "inhibitory effect" of *B. serrata* gum resin "alcoholic extract" on tumour formation, metastasis, and angiogenesis was investigated (Alipanah and Zareian, 2018).

Cymbopogon spp.

The in vitro "cytotoxicity" of the oil of *Cymbopogon xuosus* against twelve human cancer cell types was examined (Sharma *et al.*, 2009). The essential oil of *C. densiflorus* has anticancer properties in "TP53 wild-type" and mutant "bladder cancer cells", although TP53 has a role in the mechanism of action..(Pereira *et al.*, 2020). *Cymbopogon flexuosus* has long been used as a herbal tea and a spice in cooking. *C. flexuosus* was employed in the food processing sector to treat liver and lung cancer and was ingested on a regular basis to prepare a variety of cuisines (Le et al., 2019). Citrals, the major component of lemongrass essential oil, have high antibacterial activities. Citral and lemongrass essential oils were compared for antibacterial and anticancer activities in this study (Viktorová *et al.*, 2020).

Camellia sinensis

Camellia sinensis significantly inhibits growth of "Caco-2 cell" as evident from MTT assay. Aquaporin 5 protein levels in "Caco-2 cell" culture decreased after treatment with green tea extract. *Camellia sinensis* has significant anticancer potential that may be unique to it (Esghaei *et al.*, 2018).

Citrullus colocynthis

This species is a member of the cucurbitaceae family of an apple. This plant's extract (Hep2) was found to be harmful to laryngeal cancer cells in a study (Tavakkol Afshari *et al.*, 2005; Hussain *et al.*, 2014).

Crocus sativus

Saffron has been documented as an inhibitory agent of several cancers (Khorasanchi *et al.*, 2018). A bioactive small molecule "[crocetin-(-D-glucosyl)-ester]" was isolated and characterised from saffron plant leaf bio wastes in Kashmir, India. The MTTC test and DPPH assay were used to examine the anti-cancer and anti-oxidant potential of crocin (s) against breast cancer cells and a Bio-autography aided technique, respectively (Mir *et al.*, 2020). MTT assay was performed to evaluate the "anti-cancer activity" of the optimised extract obtained

at high "hydrostatic pressure", which revealed a higher activity than the customarily extracted sample (Shinwari and Rao, 2018).

Curcuma longa

Curcuma long belongs to zingiberaceae and largely grows in Asiatic countries (Huseini *et al.*, 2010). The cytotoxic activities of the plant on Hep-2 liver cancer cells were investigated, and it was discovered that curcumin-mediated cytotoxicity leads to cancer cell apoptosis via the mitochondrial pathway in a concentration dependent way (Ayyadurai *et al.*, 2013). Cancer stands second as cause of death globally and one of the most serious public health issues. Despite significant advancements in cancer treatment, cancer incidence and mortality rates remain high. As a result, current research is still focused on developing more effective and less hazardous cancer therapy options. Curcumin, the main chemical in the *Curcuma longa* plant and possess anticancer and antiinflamatory properties. In addition, significant breakthroughs in drug delivery systems for curcumin administration to cancer cells have been highlighted (Tomeh *et al.*, 2019; Willenbacher *et al.*, 2019).

Ferula assafoetida

This species grows in various provinces of Iran and Pakistan. A resin is a component of this plant that is utilized as a gum. The ethanol extract of *Ferula assafoetida* is cytotoxic to liver cancer cells (Sadooghi *et al.*, 2013). Gastric cancer is the leading source of "cancer-linked" death in men, and its prevalence is rising worldwide. The chemical composition of *Ferula assafoetida* seed essential oil and its anticancer efficacy against adenocarcinoma gastric cell line was investigated (Bagheri and Shahmohamadi, 2020).

Eruca sativa

The dietary isothiocyanateerucin (ER) is found in cruciferous vegetables *Eruca sativa* oil is a supplement to cure chemotherapy in the breast cancer (Ahmed, 2019). *E. sativa* therapy inhibits cell survival and proliferation in breast cancer cell line MCF-7 while also increasing antioxidant enzyme production and apoptosis (Derbala *et al.*, 2021). Oral treatment with *Eruca sativa* seed and leaf extracts lowered tumor volume and weight substantially resulting in a significant rise in tumor inhibition ratio (Elsadek *et al.*, 2021).

Glycyrrhiza glabra

This species has widespread occurrence in Asia, Europe and North Africa. The components of the root extract cause morphological abnormalities and reduced viability in the 4T1 mammary cell line (Hamta *et al.*, 2014). Major studies on medicinal plants for anti-cancer properties, including *Glycyrrhiza glabra*, have been conducted recently (Nourazarian *et al.*, 2015; Nazmi *et al.*, 2018).

Lepidium sativum
Iranian herbal medicine, the impacts of water extract of seed on breast cancer cells via activation of apoptosis were established in this study (Aslani *et al.*, 2014b; Mahassni and Khudauardi, 2017).

Medicago sativa
This is native to most places of the globe and cures a variety of ailments. Triconlin is a plant alkaloid molecule that acts as a hormone and is found in alfalfa. The alkaloid is thought to have major therapeutic qualities, such as anticancer capabilities (Huyghe *et al.*, 2007; Kooti *et al.*, 2017).

Mentha pulegium
This belongs to labiatae and contains mentone, piperitone, limonene, isomenthone, and Octan-3-ol.Pennyroyal flavonoids inhibits proliferation and induces apoptosis of "cancer cells" (Vian *et al.*, 2008; Aslani *et al.*, 2014a).

Nigella sativa
This plant is widely researched for its anti-cancer effects (Majdalawieh *et al.*, 2017; Rohini *et al.*, 2019). Thymoquinone is the main constituent of its essential oil. Pinene, p-cymene, thymohydroquinone, thymol, and dithymoquinone are some of the other active ingredients in its oil. Carvacrol, carvone, 4-terpineol, limonenes, and citronellol are further terpenoid compounds found in low concentrations in its oil. Immunostimulatory, anti-inflammatory, hypotensive, hepatoprotective, antioxidant, anti-cancer, hypoglycemic, anti-fertility, and spasmolytic qualities are the key pharmacological characteristics of this plant (Mollazadeh *et al.*, 2017).

Poncirus trifoliate
Poncirus trifoliate belongs to rutaceae and its fruits are frequently used to treat a variety of ailments. Anticancer and anti-inflammatory properties are found in the mature fruit (Jang *et al.*, 2018). Gastrointestinal problems, inflammation, and allergies are all treated with immature fruits of the plant. The immature fruit's extract causes death in colorectal cancer cells by triggering autophagy of mitochondria, according to our findings.

Physalis alkekengi
This plant's aqueous extract has a beneficial effect on U937 cell cytotoxicity. The fundamental chemicals found are as triterpenoids. The anticancer effect of physalins B and M are confirmed (Li *et al.*, 2014). Although various preclinical and clinical research have validated the pharmacological effects of *Physalis alkekengi* on a variety of disorders, very few information is available regarding the effects of the plant on breast cancer (Zare and Teimouri, 2020).

Radix sophorae
This is a popular remedy for prostate cancer (Wang *et al.*, 2017), gastric cancer (Kim *et al.*, 2019; Hu *et al.*, 2021), Bladder Cancer (Jo *et al.*, 2020), colorectal

cancer (Yin *et al.*, 2019), lung cancer (Yu *et al.*, 2020) and pancreatic cancer (Gao *et al.*, 2021).

Taverniera spartea

This is a plant that thrives in Iran's southern coast and Baluchistan. Methanol extracts of the plant, particularly chloroform fractions, were hazardous to "MCF-7" and "BT474" breast cancer and "PC-3" and "DU-145" prostate cancer cells. The plant's anti-cancer properties have been documented (Khalighi-Sigaroodi *et al.*, 2014).

Thymbra spicata

The effect of "hydroalcoholic" extract of the plants on SK-Mes-1 lung cancer cells has been demonstrated. Active principles with antioxidant propertiespresent in the plant include thyme, thymol, and carvacrol, which protect DNA from oxidative damage and so help to prevent cancer (Dirican *et al.*, 2012; Sabzali *et al.*, 2014).

Urtica dioica

The bioactive natural compounds in *Urtica dioica* extracts are responsible for its high cytotoxicity and anti-cancer action, including polyphenols, which are said to have anti-oxidant, anti-mutagenic, and anti-proliferative characteristics. In both laboratory and animal models, this plant's ability to prevent or reduce human malignancies has already been demonstrated (Esposito *et al.*, 2019).

Vitis vinifera

Grapes and grape extracts were examined in terms of cancer prevention (Sáez et al., 2018; Sasikumar et al., 2020). *Vitis vinifera* is one of the world's most popular fruits, and it's high in antioxidant-rich polyphenols. The current work used human epidermoid carcinoma A431 cell lines to examine the "antiproliferative" and "apoptotic effects" of *Vitis vinifera* peel and seed extracts in an in vitro setting. The "antiproliferative" and apoptotic properties of *Vitis vinifera* peel and seed extracts, as well as the morphological apoptotic alterations generated by the extracts, were investigated in A431 cells. After incubation the cells with extracts, the mitochondrial membrane potential was also assessed. Grape seed extract and grape peel extract were cultured with A431 cells for 24 hours at the inhibitory concentration. The peel and seed extracts dramatically increased cytotoxicity, caused apoptosis, and morphological alterations associated with apoptosis in A431 cells and the interference with mitochondrial membrane potential is linked to this impact. The apoptotic cascade in the extract-treated cells was most likely triggered by the drop in mitochondrial membrane potential. The phytochemicals in the peel and seeds of *Vitis vinifera* can specifically target cancer cells, and the phytochemicals that are occluded can act as potential anticancer agents, killing cancer cells more effectively (Nirmala *et al.,* 2018).

Ziziphus jujuba

This plant belongs *to Rhamnaceae,* and is used as a medicinal and food since ancient times. *Ziziphus jujuba* has been utilised to treat many disorders such as "respiratory system diseases" in several traditional medical schools. The fruit is a laxative, maturative and emollient in Islamic traditional medicine (ITM). It purifies blood and enhances relieve internal heat, circulation, and decrease inflammation. In current pharmacological research, antibacterial, antioxidant, sedative, hepatoprotective, anti-hyperglycemic, and anti-hyperlipidemic properties of *Ziziphus jujuba* have been demonstrated (Sobhani *et al.*, 2020).

Zingiber officinale

Zingiber officinale, one of the world's oldest spices, contains bioactive chemicals that have a variety of health advantages. Among these chemicals, [6]-gingerol is the most pharmacologically active. Ginger extract and [6]-gingerol act on cell signalling mediators and pathways such as TNF-, SAPK/JNK, ROS/NF-B/COX-2, p65/NF-B, p53, p38/MAPK, Nrf2, ERK1/2, caspases-3,-9, Bax/Bcl2 among others. This indicates that ginger derivatives, whether as an extract or as isolated chemicals, have antiproliferative, anticancer, anti-invasive, and anti-inflammatory properties (de Lima *et al.*, 2018).

CONCLUSION

For thousands of years, medicinal animals and plants have been utilized to treat a variety of maladies, including cancer. A large variety of therapeutic animals and plants with anticancer effects exist in nature, but they have not been completely examined phytochemically. Exploring the anticancer potential of medicinal animals and plant extracts for the isolation and characterisation of active anticancer values should be of particular importance so that improved, safe, and economic cancer treatments can be obtained.

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