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Assessment of anticancer properties of few medicinal plants

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Abstract

Cancer is a major public health concern all over the world. Herbal medicines play vital role in the prevention and treatment of cancer. Some medicinal plants have been proved very effective anticancer remedies and have been used since ages. However the drug formulations were not distinctly clear except after their proper effective assays within the system applied. Active compounds from plants such as *Andrographis paniculata*, *Aegle marmelos*, *Glycyrrhiza glabra*, *Elephantopus scaber*, *Cistanche tubulosa* have been reported in literature. Dried extracts prepared from these plants and their phytochemical analysis was reported. To check cytotoxic effects of the active compounds in the extracts MTT assay can be formulated. These plant extracts might possibly have effective significance on preventing cancerous tissues.

Keywords: Herbal medicine, Cytotoxicity, phytomedicine, anticancer

1. Introduction

Cancer is one of the most severe health problems in both developing and developed countries, worldwide. Among the most common (lung, stomach, colorectal, liver, breast) types of cancers, lung cancer has continued to be the most common cancer diagnosed in men and breast cancer is the most common cancer diagnosed in women. The International Agency for Research on Cancer estimates of the incidence of mortality and prevalence from major types of cancer, at national level, for 184 countries of the world revealed that there were 14.1 million new cancer cases, 8.2 million cancer deaths, and 32.6 million people living with cancer (within 5 years of diagnosis) in 2012 worldwide [1]. By 2030, it is projected that there will be 26 million new cancer cases and 17 million cancer deaths per year [2].

Today, despite considerable efforts, cancer still remains an aggressive killer worldwide. Moreover, during the last decade, novel synthetic chemotherapeutic agents currently in use clinically have not succeeded in fulfilling expectations despite the considerable cost of their development.

Therefore there is a constant demand to develop new, effective, and affordable anticancer drugs [3]. From the dawn of ancient medicine, chemical compounds derived from plants have been used to treat human diseases. Natural products have received increasing attention over the past 30 years for their potential as novel cancer preventive and therapeutic agents [4, 5]. In parallel, there is increasing evidence for the potential of plant-derived compounds as inhibitors of various stages of tumorigenesis and associated inflammatory processes, underlining the importance of these products in cancer prevention and therapy.

Approximately 60% of drugs currently used for cancer treatment have been isolated from natural products [6] and the plant kingdom has been the most significant source. These include vinca alkaloids, Taxus diterpenes, Camptotheca alkaloids, and *Podophyllum lignans*. Currently, of 16 new plant-derived compounds being tested in clinical trials, 13 are in phase I or II and three are in phase III [7]. Among these compounds, flavopiridol, isolated from the Indian tree *Dysoxylum binectariferum*, and meisoindigo, isolated from the Chinese plant *Indigofera tinctoria*, have been shown to exhibit anticancer effects with lesser toxicity than conventional drugs [7]. Medicinal plants constitute a common alternative for cancer treatment in many countries around the world [8, 9]. At this time, more than 3000 plants worldwide have been reported to have anticancer properties. Globally, the incidence of plant-derived products for cancer treatment is from 10% to 40% with this rate reaching 50% in Asiatic patients [9, 11]. Medicinal plants possess immunomodulatory and antioxidant properties, leading to anticancer

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activities. They are known to have versatile immunomodulatory activity by stimulating both non-specific and specific immunity [12, 13]. Plants contain several phytochemicals, which possess strong antioxidant activities. The antioxidants may prevent and cure cancer and other diseases by protecting the cells from damage caused by 'free radicals' – the highly reactive oxygen compounds.

Plants used in traditional medicine have stood up to the test of time and contributed many novel compounds for preventive and curative medicine to modern science. India is sitting on a gold mine of well recorded and traditionally well practiced knowledge of herbal medicine.

Plants interact with stressful environments by physiological adaptation and altering the biochemical profile of plant tissues and producing a spectrum of secondary metabolites.

The fundamental aspiration of the current review is to divulge the anticancer. The medicinal plants, besides having natural therapeutic values against various diseases, also provide high quality of food and raw materials for livelihood. Considerable works have been done on these plants to treat cancer, and some plant products have been marketed as anticancer drugs, based on the traditional uses and scientific reports. These plants may promote host resistance against infection by re-stabilizing body equilibrium and conditioning the body tissues. Several reports describe that the anticancer activity of medicinal plants is due to the presence of antioxidants in them. In fact, the medicinal plants are easily available, cheaper and possess no toxicity as compared to the modern (allopathic) drugs. Cancer (malignant tumour) is an abnormal growth and proliferation of cells. It is a frightful disease because the patient suffers pain, disfigurement and loss of many physiological processes. Cancer may be uncontrollable and incurable, and may occur at any time at any age in any part of the body. It is caused by a complex, poorly understood interplay of genetic and environmental factors. It continues to represent the largest cause of mortality in the world and claims over 6 million. Cancer kills annually about 3500 per million population around the world.

A large number of chemopreventive agents are used to cure various cancers, but they produce side effects that prevent their extensive usage. Although more than 1500 anticancer drugs are in active development with over 500 of the drugs under clinical trials, there is an urgent need to develop much effective and less toxic drugs the plant kingdom plays an important role in life of humans and animals.

India is the largest producer of medicinal plants and is rightly called the "Botanical garden of the World". Medicinal plants have been stated [14] to comprise about 8000 species and account for approximately 50% of all the higher flowering plant species of India. In other words there are about 400 families of the flowering plants; at least 315 are represented by India.

Medicinal properties of few such plants have been reported but a good number of plants still used by local folklore are yet to be explored. Ayurveda, Siddha and Unani systems of medicine provide good base for scientific exploration of medicinally important molecules from nature. The rediscovery of Ayurveda is a sense of redefining it is modern medicines. Emerging concept of combining Ayurveda with advanced drug discovery programme is globally acceptable. Traditional medicine has a long history of serving peoples all over the world. The ethnobotany provides a rich resource for natural drug research and development. In recent years, the use of traditional medicine information on plant research has again received considerable interest.

The Western use of such information has also come under increasing scrutiny and the national and indigenous rights on these resources have become acknowledged by most academic and industrial researchers. According to the World Health Organization (WHO), about three quarters of the world's population currently use herbs and other forms of traditional medicines to treat diseases. Traditional medicines are widely used in India. Even in USA, use of plants and phytomedicines has increased dramatically in the last two decades [15]. It has been also reported [16] that more than 50% of all modern drugs in clinical use are of natural products, many of which have been recognized to have the ability to include apoptosis in various cancer cells of human origin.

Some medicinal plants such as *Andrographis paniculata*, *Aegle marmelos*, *Glycyrrhiza glabra*, *Elephantopus scaber*, *Cistanche tubulosa* have been found effective in various types of cancers (Table-1) These medicinal plants maintain the health and vitality of individuals, and also cure various diseases, including cancer without causing toxicity. In this review, these anticancer medicinal plants of natural origin have been presented. These medicinal plants possess good immunomodulatory and antioxidant properties, leading to anticancer activities. The antioxidant phytochemicals protect the cells from oxidative damage.

Table 1: List of plants having anticancer properties- considered for this study\

Plant name	Family	Parts used	Traditional Use
<i>Andrographis paniculata</i>	Acanthaceae	Leaves	Blood purification
<i>Aegle marmelos</i>	Rutaceae	Fruits, leaves	Arthritis, Anaemia, Fractures
<i>Glycyrrhiza glabra</i>	Fabaceae	Roots	Cough, hepatitis
<i>Elephantopus scaber</i>	Asteraceae	Whole plant	Astringent, cardiac tonic
<i>Cistanche tubulosa</i>	Orobanchaceae	Stems	Reproductive problems, improve learning ability & memory

Andrographis paniculata

Andrographolide, active diterpine component, isolated from *Andrographis paniculata*, has immunoenhancing and strong anticancer activity against cancers of breast, ovary, stomach, colon, prostate, kidney, nasopharynx malignant melanoma and leukaemia. Andrographolide exerts direct anticancer activity on cancer cells by arresting G0/G1 phase of cell-cycle and inducing apoptosis. Dichloromethane fraction of methanolic extract of *Andrographis paniculata* has strong anticancer activity against colon cancer. *Andrographis*

paniculata possesses anticancer, immunostimulant, antioxidant, anti-HIV and anti-inflammatory properties. *Andrographis paniculata* enhances the activity of protective liver enzymes and reduces side effects of chemotherapy & radio therapy [17]

Aegle marmelos

Lupeol, isolated from *Aegle marmelos*, possesses strong anticancer activity against breast cancer, malignant lymphoma, malignant melanoma, malignant ascites and

leukaemia. *Aegle marmelos* possesses significant antioxidant activity and reduces side effects of chemotherapy & radiotherapy [17].

Glycyrrhiza glabra

Flavonoids (flavones, flavonols, isoflavones, chalcones, licochalcones and dihydrochalcones), derived from *Glycyrrhiza glabra* possess strong anticancer, antioxidant, antimutagenic, antiulcer, anti-HIV and hepatoprotective properties. Licochalcone-A isolated from *Glycyrrhiza glabra*, inhibits growth & spread of various cancers particularly the androgen-refractory prostate cancer by inducing apoptosis and arresting cancer cells division. Licoagrochalcone, possesses strong anticancer activity against cancers of breast, lung, stomach, colon, liver, kidney and leukaemia. Glycyrrhizin isolated from *Glycyrrhiza glabra* inhibits growth & spread of lung cancer and fibrosarcomas. Glycyrrhizic acid isolated from *Glycyrrhiza glabra* protects against aflatoxins (powerful fungal carcinogens of the liver). *Glycyrrhiza glabra* stimulates immune system response of the body and protects against colon cancer and oestrogen-positive breast cancer [17].

Elephantopus scaber

Pharmacognostic investigation of anatomical sections of leaf, petiole, stem, peduncle and root of *Elephantopus scaber* was carried out to determine its anatomical features. The physico-chemical constant like ash and extractive values were determined. The total ash content of the *E. scaber* leaf is 6.32% and 10.53% for rhizome. The phytochemical analysis of the all the extracts revealed the presence of steroid compound. *Elephantopus scaber* (Asteraceae) has been used to cause diuresis and antipyresis and to eliminate bladder stones. This genus has been reported to contain the hydroxylated germacranolides molephantin and molephantinin, which also possess cytotoxic and antitumor properties (18). *E. scaber* L. include flavonoids, triterpenoids, flavonoid esters and sesquiterpene lactones. Sesquiterpene lactones are most important due to their antitumor activity (2, 18). The anticancer efficacy of the plant active principle, Lupeol, isolated from the petroleum ether leaf extract of *E. scaber* L. The compound possess a leading effect on the growth and survival of the ER- α positive MCF-7 cells, whereas stands safe when treated on the normal breast cells [19].

Cistanche tubulosa

Cistanche Tubulosa (Schenk) R. Wight is a plant that parasitizes the roots of *Tamarix*. Since it has no root or chloroplast, it cannot photosynthesize. Therefore, it grows by absorbing the nutrition out of plants it parasitizes [20]. High-molecular-weight constituents of *C. tubulosa* have the same effects on human cell lines. As per results, *C. tubulosa* dialysate (CTD) IgM production in B-cell line BALL-1 and IgG production in B-cell line HMy-2, induced cell proliferation in BALL-1 and T-cell line Jurkat, and oppositely inhibited cell proliferation in B-cell line Namalwa. Using gel filtration chromatography, we found that, the two activities (i.e., enhancement of IgM production and growth inhibition) were concentrated in different fractions. These results suggest that *C. tubulosa* contains high-molecular-weight constituents having immunomodulatory and direct anti-cancer effects, which seem to contribute to the longevity [21].

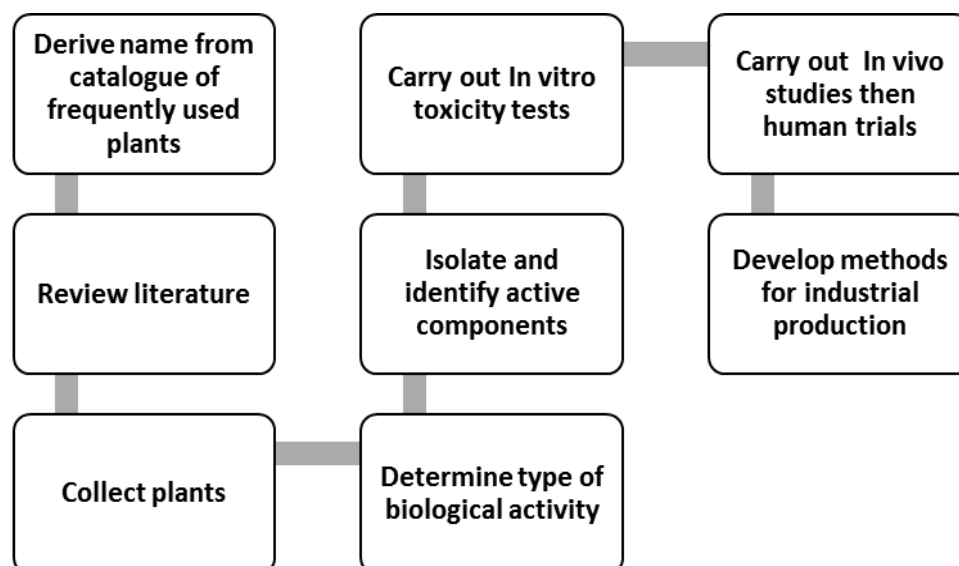
The Mechanism on Cancer Therapy

- Inhibiting cancer cell proliferation directly by stimulating macrophage phagocytosis, enhancing natural killer cell activity.
- Promoting apoptosis of cancer cells by increasing production of interferon-I, interleukin-2, immunoglobulin and complement in blood serum.
- Enforcing the necrosis of tumor and inhibiting its translocation and spread by blocking the blood source of tumor tissue.
- Enhancing the number of leukocytes and platelets by stimulating the haemopoietic function.
- Promoting the reverse transformation from tumor cells into normal cells.
- Promoting metabolism and preventing carcinogenesis of normal cells.
- Stimulating appetite, improving quality of sleep, relieving pain, thus benefiting patients health.

Methodology

Outline of procedure

To develop any drug from crude material specific methodology should be followed. It is step by step in general procedure for drug discovery.



Flow chart: Drug discovery, 38

Preparation of plant Extracts

Desired parts of selected plants were removed from the plants and then washed under running tap water to remove dust. The plant samples were then air dried for few days and the leaves were crushed into powder and stored in polythene bags for use. The plant powder was taken in a test tube and distilled water was added to it such that plant powder soaked in it and shaken well. The solution then filtered with the help of filter paper and filtered extract of the selected plant samples were taken and used for further phytochemical analysis [23].

Methanolic extract: 10 g of each powdered leaves were placed in conical flask and 100 ml of methanol was added and plugged with cotton. The powder material was extracted with methanol for 24 hours at room temperature with continuous stirring. After 24 hours the supernatant was collected by filtration and the solvent was evaporated to make the crude extract. The residues obtained were stored in airtight bottles in a refrigerator for further use [25].

Plant materials were dried at 37 °C, powdered and extracted in different solvent. The aqueous extract was obtained by boiling dried ground plant material (100 g) for 30 minutes in distilled water (300 ml). All extracts were fine-filtered and freeze dried. For the ethanolic extracts, dried ground plant material (100 g) was percolated with 95% ethanol and concentrated to dryness under reduced pressure. The aqueous extracts were dissolved in sterile water and the ethanolic extracts in Dimethyl Sulfoxide (DMSO) to form stock solutions 20mg/ ml which were filter sterilized (0.2 µm) before testing on cell lines [24].

Phytochemical Analysis

The methanolic extracts of following plants was subjected to different chemical tests for the detection of different phytoconstituents using standard procedures [25, 26, 27]

1. **Test for Tannins:** 1 ml of the sample was taken in a test tube and then 1 ml of 0.008 M Potassium ferricyanide was added. 1 ml of 0.02 M Ferric chloride containing 0.1 N HCl was added and observed for blue-black coloration.
2. **Test for Saponins:** Crude extract was mixed with 5 ml of distilled water in a test tube and it was shaken vigorously. Add some drops of olive oil. The formation of stable foam was taken as an indication for the presence of saponins.
3. **Test for Flavonoids:** 5 ml of dilute ammonia solution were added to a portion of the crude extract followed by addition of concentrated H₂SO₄. A yellow colouration observed in each extract indicated the presence of flavonoids. The yellow colouration disappeared on standing.
4. **Test for Steroids:** 2 ml of acetic anhydride was added to 0.5 ml crude extract of plant sample with 2 ml H₂SO₄. The colour changed from violet to blue or green in samples indicates the presence of steroids.
5. **Test for Alkaloids:** Crude extract was mixed with 2 ml of Wagner's reagent. Reddish brown colored precipitate indicates the presence of alkaloids.
6. **Test for Terpenoids (Salkowski test):** 5 ml of extract was mixed with 2 ml of chloroform and 3 ml of concentrated H₂SO₄ was carefully added to form a layer. A reddish brown colouration of the inter face was formed to show positive results for the presence of terpenoids.
7. **Test for Cardiac glycosides (Keller-Kiliani test):** 5 ml of extract was treated with 2 ml of glacial acetic acid containing one drop of ferric chloride solution. This was

underlaid with 1 ml of concentrated H₂SO₄. A brown ring of the interface indicates a deoxy sugar characteristic of cardenolides. A violet ring may appear below the brown ring, while in the acetic acid layer, a greenish ring may form just gradually throughout thin layer [26, 27, 28].

8. **Test for carbohydrates:** 1. Molisch's test: To 1 ml of test solution added a few drops of 1 % alpha-naphthol and 2-3 ml concentrated sulfuric acid along the side of test tube. The reddish violet or purple ring formed at the junction of two liquids confirmed the test.
9. **Barfoed's test:** 2ml of reagent was added to 2 ml of the test solution, mixed & kept a in boiling water bath for 1 min. Red precipitate formed indicates the presence of monosaccharides.
10. **Seliwanoffs test:** To 3 ml of Seliwanoffs reagent was added to 1 ml of the test sample and heated on a water bath for one minute. The formation of rose red color confirmed carbohydrates. 4. **Fehlings test:** Dissolved 2 mg dry extract in 1 ml of distilled water and added 1ml of Fehling's (A+B) solution, shooked and heated on a water bath for 10 minutes. The brick red precipitate formed confirmed the test [29].

In vitro assay for cytotoxic activity

Cell culture

The cell line under investigation was human breast adenocarcinoma (MCF7). It was purchased from the European Collection of Animal Cell Culture. The cells were cultured in RPMI 1640 medium supplement with 10% heated foetal bovine serum, 1% of 2 mM l-glutamine, 50 IU/ml penicillin and 50 g/ml streptomycin [30]

Cytotoxicity assay

For the assay, cells were washed three times with phosphate buffer saline (PBS). PBS was decanted and cells detached with 0.025% trypsin-EDTA (Sigma). RPMI 1640 was added to a volume of 10 ml. The cell suspension was centrifuged at 1000 X g for 10 minutes and the pellet was resuspended in 10 ml of medium to make a single cell suspension. Viability of the cells was determined by trypan blue exclusion and it exceeded 90% as counted in a haemocytometer. The cell suspension was diluted afterwards to give the optimal seeding density and 100 /l of the cell suspension was plated in a 96 well plate and incubated at 37 °C in a humidified atmosphere containing 5% CO₂. After 24 hours the cells were treated with the extracts or pure compounds.

SRB Assay: Each extract (initially dissolved in DMSO), was diluted with the medium and passed through a 0.2 µm filter. 50 µg/ml of each extract was tested initially, and, from the results, the active extracts were considered to be those which gave less than 50% survival at exposure time 72 hours. The active extracts were further diluted in medium to produce eight concentrations (0.1, 0.5, 1, 5, 10, 25, 50, 100 µg/ml) of each extract. 100 µl/well of each concentration was added to the plates in six replicates. The final dilution used for treating the cells contained not more than 1% of the initial solvent, this concentration being used in the solvent control wells. The plates were incubated for 72 hours. At the end of the exposure time, cell growth was analyzed using the SRB assay. Two replicate plates were used to determine the cytotoxicity of each extract. As positive control vincristine sulphate was used (Sigma, Lot No. 34H0447) at the concentrations of 0.05, 0.1, 0.5, 1, 5, 10, 25, 50, 100 nM. For the calculation of IC₅₀ [30]

Cell viability and growth in presence of test material was calculated as follows:

Percent growth in presence of test material = Growth in presence of test material/ Growth in absence of test material X 100

Percent growth inhibition in presence of test material was calculated as under: 100% growth in presence of test material
Criteria for Determination of Activity: The test sample showing growth inhibition of >70% at 100 µg/ml is considered to be active [24]

MTT Assay

MTT is in vitro cytotoxicity assay, considered one of the most economic, reliable and convenient methods. This is based on its ease of use, accuracy and rapid indication of toxicity as well as their sensitivity and specificity. The assay is in vitro whole cell toxicity assays that employ colorimetric method for determining the number of viable cells based on mitochondrial dehydrogenase activity measurement and differ only in the reagent employed [31]

This assay measures the reduction of yellow 3-(4, 5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) by mitochondrial succinate dehydrogenase. MTT enters the cells and passes into the mitochondria where it is reduced to an insoluble, coloured (dark purple) formazan product. The cells are then solubilized with an organic solvent (isopropanol) and the released, solubilized formazan reagent is measured spectrophotometrically. 96-well plate multi-chennelpipette, cell lines, MEM medium, DMSO, Trypsin, DOX, WST dye are required as materials. According to the standard procedure, the used medium has removed from T-25 flask. The cells are trypsinized at 500rpm for 5 min by adding 2 ml of trypsin. The pallet is resuspended in 2 ml completed media. Cells are diluted to 10,000 cells per ml and use complete media to dilute cells. 100 ul of cells are added in to each well. The first two wells were taken as a blank, next two follow by DMSO. DOX is added to next two wells as a standard compound. Plant extracts are added to the next followed wells respectively and incubate for 48 hours. WST dye is added to all wells. After 2 hours incubation, OD at 490 nm is read using ELISA reader [32]

Analysis of MTT Assay

1. Plot a graph of the absorbance (y-axis) against the concentration of drug (x-axis).
2. Calculate the IC₅₀ as the drug concentration that is required to reduce the absorbance to half that of the

control. The mean absorbance reading from the wells in columns 2 and 11 is used as a control. The absorbance values in columns 2 and 11 should be the same. Occasionally, they are not, however, and this is taken to indicate uneven plating of cells across the plate.

3. The absolute value of the absorbance should be plotted so that control values may be compared, but the data can then be converted to a percentage-inhibition curve to normalize a series of curves [33]

Calculation

% viability = (OD of test material / OD of control) X 100

% Inhibition = 100 – (% Viability)

Discussion

- As per above qualitative analysis stated that selected medicinal plants may possess following phytochemical in different amount:

Table 2: Phytochemicals present in selected medicinal plants

Phytochemicals	A. paniculata	A. marmelos	G. Glabra	E. scabra	C. tubulosa
Tannins	+	+	+	+	-
Saponins	-	+	+	+	+
Alkaloids	+	+	-	-	+
Terpenoids	+	+	+	+	-
Flavonoids	+	+	+	+	-
Steroids	+	+	-	+	-
Glycosides	+	-	-	-	+
Carbohydrates	+	+	+	-	-

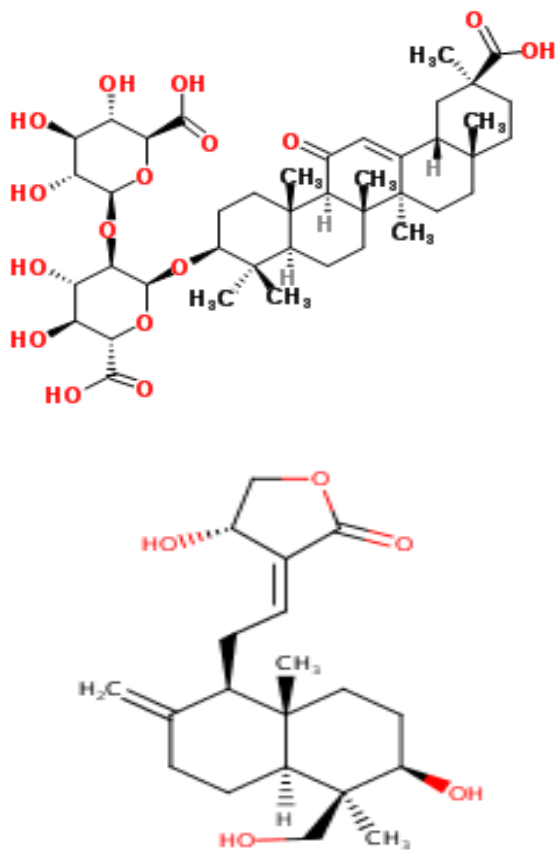
- For cytotoxic assays different human tumour cell lines from several cancer types including leukemia, melanoma and cancers of the lung, colon, brain, ovary, breast, prostate and kidney can be used. The NCI60 screen tests the degree of growth, inhibition or cytotoxicity of a compound against each cell line over a range of concentrations to generate characteristic profile or fingerprint of cellular response.. A computer is used to compare and assess the pattern of response.
- As main objective of this study is to check anticancer properties of these medicinal plants which plant extract proven to be effective on which cancer showed below:

Table 3: selected plants and their cell line studies

Plant source	Type of cancer	Cell line studied
<i>Andrographis paniculata</i>	Ovary cancer	Breast adenocarcinoma(MCF7), human cervix (SiHa), colon(HT29) liver(HepG2), Ovary cancer cell line (ovcar5)
<i>Aegle marmelos</i>	Carcinoma, leukemia, Breast cancer	leukemic K562, T-lymphoid Jurkat, Blymphoid Raji, erythroleukemic HEL, melanoma Colo38 & breast cancer MCF7 and MDAMB-231
<i>Glycyrrhiza glabra</i>	Breast cancer, Prostate cancer, leukemia	Human breast cancer MCF7, leukemia U937,
<i>Elephantopus scaber</i>	Breast cancer	Human breast cancer MCF7
<i>Cistanche tubulosa</i>	Antitumor activity	Jurkat

- All selected plants have active compounds which can be developed in future as a drug. Specially Glycyrrhizin from *Glycyrrhiza glabra* and Andrographolide from

Andrographis paniculata are interesting with anticancer and immunomodulatory activities and hence has the potential for being developed as a cancer agent [34, 35, 36]



Structure of Glycyrrhizin, 36 Structure of Andrographolide, 34

- The different solvent fractions of ethanolic extract of the stem barks of *A. marmelos* were reported to possess antiproliferative effects against human tumor cell lines. The results showed the inhibition of *in vitro* proliferation of human tumor cell lines, including the leukemic K562, T lymphoid Jurkat, B lymphoid Raji, erythroleukemic HEL, melanoma Colo38, and breast cancer MCF7 and MDAMB-231 cell lines [37].
- As researchers are looking into developing new drugs from natural sources, Ethnomedicinal plants having multiple medicinal uses can be used to successfully establish drug/treatment for cancer.
- The value of Ethnomedicine: A few examples document the value of using ethnomedical information to initiate drug discovery efforts the number of bioassays that one could screen these species for is unlimited, one must select judiciously those species most likely to produce useful activity. In addition, the biologic targets must represent the activities that correlate best with the rationale for plant selection. It would appear that selection of plants based on long-term human use (ethnomedical) in conjunction with appropriate biologic assays that correlate with the ethnomedical uses would be most appropriate. There are advantages and disadvantages of using plants as the starting point in any drug development program [38]
- Future prospect: The search for new pharmacologically-active compounds for drug development is an important issue, but not the only one, as the trend toward using standardized plant extracts of high quality, safety and efficacy will continue. Therefore, all efforts have to be targeted to reveal the chemical-pharmacological profiles of extracts and fixed combinations and to rationalize their therapeutic application. Whether in the future highly

active, safe and causally-acting plant derived preparations will be able to replace some synthetic drugs, or in other cases are potent enough to be applied in combination with synthetic drugs, depends on the level of evidence-based therapeutic efficacy achieved [39].

- Hence, extensive research is required to find out the mechanisms of action as well as bioactivity of the various phytochemicals and efficacy of the medicinal values of these plants. So, in the near future extracts from these plants could be further exploited as a source of useful phytochemical compounds and may play a very important role in modern system of medicine.

Summary

Historically, the complexity of cancer necessitated an incredible amount of specialization that has led to very narrowly scoped research. In the past two decades this approach has resulted in significant advances in our understanding of the disease, but unfortunately this trend towards specialization has meant that very few researchers ever have the freedom or the opportunity to undertake projects that are broad in scope.

For similar reasons, anticancer research is difficult as it does involve too many biologically active ingredients due to concerns over the number of variables that can be controlled in any given experiment [40]. But we need to overcome these systemic barriers if we are going to match the complexity of the disease with an approach to prevention and therapy that is equally complex (i.e., capable of shutting down a wide range of immortalized cells by acting on many different mechanisms and pathways)

MTT assay is a well-established *in vitro* method for cytotoxicity against cancer cell lines and non-cancer cell lines, and here it was utilized to determine the selective activity of the extracts. Different dilutions of extracts were treated and IC₅₀ values were calculated.

As per the criteria of the American National Cancer Institute to consider a crude extract promising for further purification based on the IC₅₀ values lower than 30 µg/mL in order to discover and develop potential anticancer natural compounds. Cytotoxicity screening models provide important preliminary data to help selecting plant extracts with potential antineoplastic properties for future work. It is of interest that the extract of the plants showed cytotoxicity against cancer cell line, and, if this also occurs *in vivo*, the use of these plants by traditional healer for the treatment of cancer patients [41, 42, 43]

Medicinal plants have contributed a rich health to human beings. Plant extracts and their bioactive compounds present in them which are responsible for anticancer activity have to be screened for their valuable information.

So, to evaluate the potential anticancer compounds present in medicinal plants with proper methodology is in exigency. This proper exploration would develop in introducing a site specific anticancer drug with higher therapeutic properties to eradicate cancer.

This review had given some of the plants possessing anticancer activity for various types of cancer. This can help to explore herbs to further extent and its use in various other disease and toxicity studies along with clinical trials.

References

1. Globocan 2012. <http://globocan.iarc.fr/Default.aspx>.

2. Thun MJ, DeLancey JO, Center MM, Jemal A, Ward EM. The global burden of cancer: priorities for prevention, *Carcinogenesis*. 2009;31(1):100-110.
3. Coseri S. Natural products and their analogues as efficient anticancer drugs, *Mini-Reviews in Medicinal Chemistry*. 2009; 9(5):560-571.
4. Newman DJ. Natural products as leads to potential drugs: an old process or the new hope for drug discovery? *Journal of Medicinal Chemistry*. 2008; 51(9):2589-2599.
5. Newman DJ, Cragg GM, Snader KM. Natural products as sources of new drugs over the period 1981–2002. *Journal of Natural Products*. 2003; 66(7):1022-1037.
6. Gordaliza M. Natural products as leads to anticancer drugs, *Clinical and Translational Oncology*. 2007; 9(12):767-776.
7. Saklani, Kutty SK. Plant-derived compounds in clinical trials, *Drug Discovery Today*. 2008; 13(3-4):161-171.
8. Gerson-Cwillich R, Serrano-Olvera A, Villalobos-Prieto A. Complementary and alternative medicine (CAM) in Mexican patients with cancer, *Clinical and Translational Oncology*, 2006; 8(3):200-207.
9. Tascilar M, de Jong FA, Verweij J, Mathijssen RHJ. Complementary and alternative medicine during cancer treatment: beyond innocence, *Oncologist*. 2006; 11(7):732-741.
10. Cassileth BR, Deng G. Complementary and alternative therapies for cancer, *Oncologist*. 2004; 9(1):80-89.
11. Molassiotis, Browall M, Milovics L, Panteli V, Patiraki E, Fernandez-Ortega P. Complementary and alternative medicine use in patients with gynecological cancers in Europe. *International Journal of Gynecological Cancer*. supplement 2006; 16(1):219–224.
12. Pandey, Govind, Madhur, S, Medicinal plants: better remedy for neoplasm. *Indian Drugs*, 2006, 43:869-874
13. Agrawala SK, Chatterjee S, Misra SK. Immunopotential activity of a polyherbal formulation 'Immu-21' (research name). *Phytomedica*, 2001, 2:1-22.
14. Gupta AK, Tandon N. *Reviews on Indian Medicinal Plants*. New Delhi: Indian Council of Medical Research. 2004, 2.
15. Goel RK, Sairam K. Anti-ulcer drugs from indigenous sources with emphasis on *Musa sapientum*, *Tamrabhasma*, *Asparagus racemosus* and *Zingiber officinale*. *Indian J Pharmacol*. 2002; 34:100-10.
16. Rao CV, Sairam K, Goel RK. Experimental evaluation of *Bacopa monniera* on rat gastric ulceration and secretion. *Indian J Physiol Pharmacol*. 2000; 44:435.
17. Umadevi M, Sampath Kumar KP, Debjit Bhowmik S, Duraivel. Traditionally Used Anticancer Herbs In India, 2013, 1-3
18. Lee KH, Cowherd CM, Wolo MT. Antitumor agents. XV: deoxyelephantopin, an antitumor principle from *Elephantopus carolinianus* Willd. *J Pharm Sci*. 1975; 64:1572-3.
19. Daisy Pitchai, Anita Roy, Cybil Ignatius. *In vitro* evaluation of anticancer potentials of lupeol isolated from *Elephantopus scaber* L. on MCF-7 cell line. *J Adv Pharm Technol Res*. 2014; 5(4):179-184.
20. Oryza oil, fat chemical co. ltd. Ver. 2.0 J T/H
21. Shinjiro Maruyama, Taiki Akasaka, Koji Yamada and Hirofumi Tachibana. Bioactivity of High-molecular-weight Constituents of *Cistanche tubulosa*. *Pharmacologyonline* 2009; 1:913-921.
22. Kharb Manju, Jat RK, Gupta Anju. Medicinal plants used as a source of anticancer agents. *Int. J Drug Res Tech*. 2012; 2(2):177-183.
23. Abdul Wadood1, Mehreen Ghufuran, Rukhsana Ghaffar, Asnad. *Phytochemical Analysis of Medicinal Plants Occurring in Local Area of Mardan*. Wadood *et al.*, *Biochem Anal Biochem*. 2013; 2:4.
24. Shanthi sundaram, satish kumar verma, priyanka dwivedi. *In vitro* cytotoxic activity of indian medicinal plants used traditionally to Treat cancer. 2011; 4(1).
25. Anjali Soni, Sheetal Sosa. *Journal of Pharmacognosy and Phytochemistry*. 2013; 2(4):22-29.
26. Sofowara A. *Medicinal plants and Traditional medicine in Africa*. Spectrum Books Ltd, Ibadan, Nigeria; 1993, 191-289.
27. Trease GE, Evans WC. *Pharmacognosy*. Bailliere Tindall London, Edn 11, 1989, 45-50.
28. Harborne JB. *Phytochemical Methods*. Chapman and Hall. Ltd., London; 1973, 49-188.
29. Roopalatha u c1, vijay mala (Grover). *International Journal of Pharmacy and Pharmaceutical Sciences*. 2013; 5(3).
30. Rana Abu-Dahab, Fatma Afifi. *Scientia Pharmaceutica (Sci. Pharm.)* 2007; 75:121-136.
31. Janice McCauley, Ana Zivanovic, Danielle Skropeta. *Bioassays for anticancer activities*. Research online. 2013.
32. Anubrata Paul, Manjula. *International Journal of Science and Research (IJSR)* 2012; 23:358.
33. Ian Freshney R. *Culture of animal cells*.
34. Singh S, Mehta A, Baweja S. *Journal of pharmacology and toxicology* 2013; 8(1):42-48.
35. Varsha sharma, r. C. Agrawal. *Glycyrrhiza glabra*- a plant for the future. *Mintage journal of pharmaceutical & medicinal sciences* 2013; 2(3).
36. Zhan Guo-ging, Ji song-gang *et al.*, Determination of glycyrrhizin in *Radix glycyrrhizae* and its preparations by capillary zone electrophoresis, *Biomed Chromatogr*, 1999; 13:407-409.
37. Lampronti D, Martello Nm, Bianchi M, Borgatti E, Lambertini R, Piva S *et al.* *Phytomedicine*, 2003; 10:300-308.
38. Daniel S. Fabricant, Norman R. Farnsworth. The Value of Plants Used in Traditional Medicine for Drug Discovery. *Environ Health Perspect*. 2001; 109(suppl 1):69-75.
39. Zohara Yaniv Bachrach. *Scientific Journal of the Faculty of Medicine in Niš*. 2012; 29(3):117-123
40. Amr Amin, Leroy Lowe. *Gastrointestinal & Digestive System*. 2012; 2:5.
41. Abu-Dahab R, Afifi F. Antiproliferative activity of selected medicinal plants of Jordan against a breast adenocarcinoma cell line (MCF7). *Sci Pharm*, 2007; 75:121-136.
42. Mesquita MLD, Paula JED, Pessoa C, Moraes MOD, Costa-Lotuf LV, Grougnet R *et al.* Cytotoxic activity of Brazilian Cerrado plants used in traditional medicine against cancer cell lines. *J Ethnopharmacol*. 2009; 123(3):439-445.
43. Steenkamp V, Gouws MC. Cytotoxicity of six South African medicinal plant extracts used in the treatment of cancer. *S Arf J Bot*. 2006; 72(4):630-633.