Some Natural Isolated Compounds as Anticancer Agents

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ABSTRACT

Worldwide cancer is the major cause of death. Almost 8.8 million people died due to different types of cancer such as lung cancer, liver cancer, breast cancer, stomach cancer, blood cancer etc. in 2015. Government of various countries and some private organizations are spending trillions dollars for the research in cancer. According to report of WHO treatment cost of cancer is approximately US$ 1.16 trillion per year and this amount is increasing per year. Despite of huge work the exact cause of genesis is still unknown. Couples of therapies like chemotherapy, radiation, surgery and targeted therapy are available with some detrimental effect. Now scientists are seeking lead molecule from naturally occurring substances due to high safety margin as compared to current approaches. Natural phytochemicals are prominent strategy for prevention, treating, and curing cancer. There are many phytochemicals from herbs having potent anticancer property. Generally these phytochemicals treat cancer by different mechanisms like augmenting apoptosis, cell cycle arrest, targeting to some specific cancer inducing proteins, increasing cytotoxicity etc. This is our little attempt to gather information of phytochemicals having anticancer property such as Etoposide, Curcumin, Vincristine, etc. with postulated mechanism. Etoposide is effective in lung cancer, ovarian cancer by inhibiting type II Topoisomerase. Various research revealed that Curcumin is effective in different types of cancers by increasing apoptosis and targeting specific gene such as MDM2 oncogene is inhibited through the ETS2 transcription factor by modulation of signaling pathway PI3K/mTOR in breast cancer. Vincristine shows anticancer property by oncogenic EWS-FLI1 fusion protein inhibition which cause G2-M phase cell cycle arrest & reduce tumor. This review depicts few phytochemicals having anticancer property such as Etoposide, Curcumin, vincristine, etc. with possible mechanism.

Keywords: Vincristine; Curcumin; Etoposide; Phytochemicals; Anticancer; Type II Topoisomerase

INTRODUCTION

Globally cancer is the chief inducer of death. Cancer is a condition in which abnormal rapid cell growth due to irregularity in the genome. Mutations in tumor suppressor genes which work in cell-cycle regulation are often observed in numerous types of cancer (Bukhtoyarov et al., 2015). Almost 8.8 million people succumbed due to different types of cancer such as lung cancer, liver cancer, breast cancer, stomach cancer, blood cancer etc. (www.who.int/cancer/en/). Despite of huge work the exact cause is unknown; many therapies like chemotherapy, radiation therapy, surgery and targeted therapy are available with some toxic effect. Now scientists are focusing on naturally occurring substances from plant sources having anti-cancer properties with minimum toxic effect as compared to chemotherapy. Natural phytochemicals are prominent strategy for prevention, treating, and curing cancer. There are many phytochemicals from herbs having potent anticancer property. Generally these phytochemicals treat cancer by different mechanisms like increasing apoptosis, cell cycle arrest, targeting to some specific cancer inducing proteins, increasing cytotoxicity etc. Etoposide is effective in lung cancer, ovarian cancer by inhibiting type II Topoisomerase. Various researches show that...
Curcumin is effective in different types of cancer like breast cancer and lung cancer by increasing apoptosis and targeting specific gene such as MDM2 oncogene is inhibited through the ETS2 transcription factor by modulation of signaling pathway PI3K/mTOR in breast cancer. (Lazar M, 2008) Government of various countries and some private organizations are spending trillions dollars for the research in cancer.

<table>
<thead>
<tr>
<th>Sr. No</th>
<th>Drug</th>
<th>Biological Source</th>
<th>Chemistry</th>
<th>Effective organ</th>
<th>Side Effect</th>
<th>Clinical status/Marke ted product</th>
<th>Mechanism of action</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Etoposide (Derivative of podophyllotoxin)</td>
<td>Dried rhizome of <em>Podophyllum peltatum</em></td>
<td>glycoside of podophyllotoxin with a D-glucose derivative</td>
<td>Testicular Cancer, Lung Cancer, Ovarian cancer</td>
<td>Decrease RBC count, Vomiting, Hair loss</td>
<td>Etopophos</td>
<td>Type II Topoisomerase Inhibitor (Wu C, et al 2011)</td>
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<td>3</td>
<td>Sulforaphane</td>
<td>broccoli, Brussels sprouts, cabbage</td>
<td>Isothiocyanate</td>
<td>Prostate cancer, Breast Cancer, Pancreatic cancer</td>
<td></td>
<td>Avmacol</td>
<td>Inhibits histone deacetylase (HDAC) activity (Myzak et al 2004)</td>
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<td>4</td>
<td>Pomiferin</td>
<td>Fruit and flower of <em>Maclura pomifera</em></td>
<td>Isoflavonoid</td>
<td>Colon Cancer, Head &amp; Neck cancer</td>
<td></td>
<td>Phase II</td>
<td>Pro-apoptotic effects; DNA fragmentation; inhibits oxidative damage of DNA; antioxidant activity; inhibits histone deacetylases; cytotoxicity of cancer cells (M. Greenwell et al 2015)</td>
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<tr>
<td>No.</td>
<td>Compound</td>
<td>Source</td>
<td>Type</td>
<td>Indications</td>
<td>Side Effects</td>
<td>Phase</td>
<td>Notes</td>
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<tr>
<td>7</td>
<td>Lycopene</td>
<td>Tomato Watermalloo Carrot</td>
<td>Tetraterpene carotene</td>
<td>Breast cancer</td>
<td>Diarrhea, nausea, stomach pain, allergic reaction</td>
<td></td>
<td>Inhibit proliferation decrease cyclic dependent kinase activity arrest G1 Phase (Bhuvaneswari and Nagini 2005)</td>
</tr>
<tr>
<td>8</td>
<td>Vincristine</td>
<td>Catharanthus roseus</td>
<td>Alkaloid</td>
<td>Lymphoma</td>
<td>Constipation, Hairloss, Change in sensation, Difficulty in walking, Headache</td>
<td></td>
<td>Oncogenic fusion protein EWS-FL1 is Inhibited which causes G2-M phase cell cycle arrest (Zöllner S et al 2017)</td>
</tr>
<tr>
<td>9</td>
<td>Docetaxel</td>
<td>bark of the rare Pacific yew tree Taxus brevifolia</td>
<td>Diterpenes, Taxanes</td>
<td>Breast cancer, Head &amp; neck, Stomach cancer, Prostate &amp; Lung cancer</td>
<td>Low blood count, Vomiting, Hairloss, Muscle pain, Liver problem</td>
<td>Slow I.V. taxotere</td>
<td>Inhibits angiogenesis promote apoptosis (Herbst &amp; Khuri 2003)</td>
</tr>
<tr>
<td>10</td>
<td>Paclitaxel</td>
<td>Pacific yew Taxus brevifolia, (Priyadarshini and Keerthi 2012)</td>
<td>Diterpene with taxan ring</td>
<td>Breast, Lung, Cervical, Pancreatic cancer, Kaposi's sarcoma, Ovarian</td>
<td>Bone marrow suppression, Heart problem, Lung inflammation</td>
<td>I.V. oraxol</td>
<td>CLIP-170 Microtubule-binding protein increase the potential of paclitaxel to block the advancement of cell cycle at mitosis and to generate apoptosis in breast cancer cells (Sun et al 2012)</td>
</tr>
<tr>
<td>12</td>
<td>Squalamine</td>
<td>Squalus acanthias (shark)</td>
<td>Aminosteroid</td>
<td>Ovarian, Prostate, CNS Tumor</td>
<td>Liver toxicity, Nausea.</td>
<td></td>
<td>Squalamine blocked VEGF-induced activation of MAP</td>
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<td>14</td>
<td>Indirubin</td>
<td>Danggui Longhui Wan,</td>
<td>Lung cancer</td>
<td>Fatigue. Anorexia. Muscle weakness</td>
<td>kinase and cell proliferation in human vascular endothelial cells. Block angiogenesis with or without HER2 gene overexpression (Williams J. &amp; Dan Li et al 2002)</td>
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<td>15</td>
<td>Epigallocatechin gallate</td>
<td>leaves of green tea black tea white tea onion</td>
<td>polyphenol catechin</td>
<td>mild abdominal pain, diarrhea, and nausea</td>
<td>Phase IV Cyclin-dependent kinases is inhibited due to which G1 G2/M phase cell cycle arrest(Lee J, Moon M et al 2005)( Hoessel et al 1999)</td>
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<tr>
<td>17</td>
<td>Podophyllotoxin</td>
<td>roots and rhizomes of Podophyll um species.</td>
<td>Glycosides</td>
<td>burning, redness, pain, itching, swelling, CNS</td>
<td>Phase II Tubulin polymerization is Inhibited due to which cell cycle arrest in the metaphase.</td>
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<tr>
<td>No.</td>
<td>Compound</td>
<td>Source</td>
<td>Function</td>
<td>Phase</td>
<td>Effect</td>
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<td>18</td>
<td>Ellagic acid</td>
<td><em>Myriophyllum spicatum</em></td>
<td>Polyphenolic</td>
<td>Prostate cancer, Breast Cancer, Colorectal cancer</td>
<td>Decrease Angiogenesis by Down regulation of Heme Oxygenase (HO) and By lowering epoxyeicosatrienoic acid synthesis or increasing its degradation (EETs) Antiproliferative effect is due to inhibition of DNA methyltransferase I (DNMT I)</td>
<td>(Gordaliza M et al 2000)</td>
<td></td>
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<td>20</td>
<td>Resveratrol</td>
<td>Roots of <em>Polygonum cuspidatum</em>. (AluyenJ. et al 2012)</td>
<td>Phenol</td>
<td>Colon cancer, Bladder cancer, Liver cancer, Sometime slow blood clotting</td>
<td>Apoptosis is induced due to lower expression of HSP-70 and HSP-27, Active form of NF-κB is inhibited which influences apoptosis through down regulation of the genes VGEF Bcl-2, Bcl-xL, XIAP, and c-IAP. Resveratroil inhibit COX by activation of macrophage-inhibitory-cytokine-1 which decrease proliferation.</td>
<td>(Hu Wang et al 2014)</td>
<td></td>
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<td>21</td>
<td>Camptothecin</td>
<td>Bark of <em>Camptotheca acuminata</em> (Chinese happy tree)</td>
<td>Alkaloids</td>
<td>Cervical cancer, Gastric cancer, myelosuppression, vomiting, diarrhoea</td>
<td>Act as DNA topoisomerase I poison and induce apoptosis</td>
<td>(Martino E. et al 2017)</td>
<td></td>
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</table>
Rosmarinic acid

(Rosmarinus officinalis
Fam: Blechnaceae
Ocimum basilicum
Ocimum tenuiflorum)

polyphenolic diterpenes,

Lung
Liver
Prosted
Myeloid leukemia
Breast
Pterygium

Uterine bleeding,
Allergic reactions
& skin redness,
Kidney irritation

suppression of NF-κB signaling in H22 tumor-bearing mice
(Cao W et al 2016)

DISCUSSION
Cancer is becoming a high profile disease in developed and developing worlds. In 2007 the WHO published that in 2005, 7.6 million people died from cancer related diseases with the majority of these people living in low-income countries. In the United States cancer is the cause of 1 in 4 deaths and in 2010 it was estimated there were over 1.5 million new cases of cancer (Jemal et al 2010). Cancer Research UK said in 2012 14.1 million adults were diagnosed with cancer and 8.2 million people were killed by cancer globally (www.cancerresearchuk.org). Therefore, the demand for a cure and the prevention of cancer is extremely high.

Chemically-derived drugs have been developed and other cancer treatments pre-exist (Seidel et al 2012). However, current methods such as chemotherapy have their limitations due to their toxic effects on non-targeted tissues furthering human health problems (Ochwang’I et al 2014). Therefore, there is a demand for alternative treatments with naturally-derived anticancer agents with plants being the desired source.

Increasing demand for plant-derived drugs is putting pressure on high-value medicinal plants and risking their biodiversity (Zschocke et al 2000). Increasing populations, urbanization and deforestation are contributing to species endangerment in developing countries. To aid conservation of these species germplasm conservation, cryopreservation, tissue cultures and plant part substitution strategies need to be in place (Kasagana et al 2011). Mass cultivation of medicinal plant species and utilizing raw by-products in industries may also help with conservation. (Phillipson et al 1997) (Sahpazidou et al 2014)

Plant-derived anticancer agents are effective inhibitors of cancer cells lines, making them in high demand. Exploitation of these agents needs to be managed to keep up with demands and be sustainable.

CONCLUSION
This review article explains potential anticancer active ingredients from natural source. They would be least toxic and more effective than rest synthetic molecules. Till the date, no significant and systematic studies been carried out. Thus it is desirable to pursue research endeavor on these compounds and they would be brought to market in coming days. Hence millions of patients will be benefitted.

Conflict of Interest: None.

Acknowledgment: Authors are thankful to management of Shree S.K. Patel College of Pharmaceutical Education & Research, Ganpat University for providing the necessary facilities to this review article.

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