Phytochemicals for Cancer Treatment: An Update on Plant-Derived Anti-cancer Compounds and Their Mechanisms of Action

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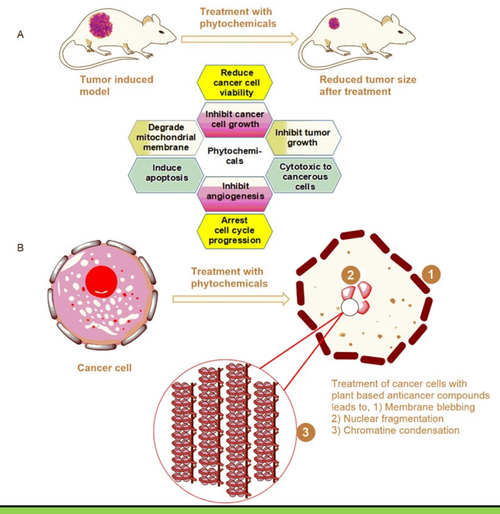
ABSTRACT

Cancer is caused by the combined effect of different factors that act sequentially and simultaneously however, its treatment through conventional approaches comes with several pitfalls and severe side effects such as toxicity to normal cells, inadequate bioavailability, fast clearance, non-specificity as well as high cost. In contrast, plant-based anticancer agents have natural characteristics that can circumvent such limitations as they are comparatively more potent, safer, easily available and cheaper. The current review focuses on the results of selected plant-based anticancer compounds extracted in their pure form and used solely for assessment of anticancer potential through standardized approaches. The probable mechanisms of action of these compounds include inhibition of cancer cell growth, inhibition of tumor growth, cytotoxicity to cancerous cells, inhibition of angiogenesis, induction of apoptosis, caspases stimulation, degradation of mitochondrial membrane, stimulation of apoptotic proteins, inhibition of topoisomerase, reduction of cell viability and arresting of cell cycle progression. However, these preliminary testing is not enough for the approval of these compounds as an anticancer agents. Further research is required to characterize and screen these potential drug candidates against a wide range of in vitro and proper in vivo system to confirm their safety and potency for the cancer treatment.

Keywords: Cancer, plants, apoptosis, phytochemicals, stimulation, inhibition, potent, anticancer agents.



Plant mediated anticancer compounds reduces tumor growth and progression *in vivo*. Phytochemicals compounds inhibit angiogenesis, reduce cancer cell viability, inhibit growth and arrest cell cycle progression. They can also confer apoptosis in cancerous cells by means of nuclear fragmentation, chromatin condensation and membrane blebbing.

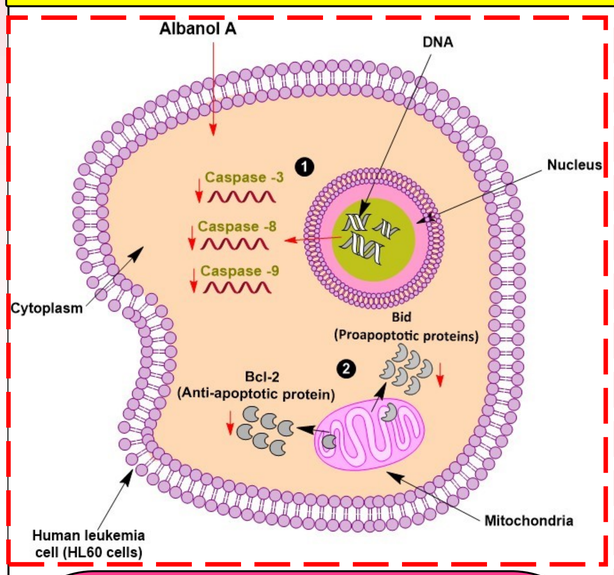


Figure 1. Schematic representation of Albanol A treatment on HL60 cells.

1) Albanol A has a potency of reducing the expression level of procaspases-3, 8, and 9 in time reliant manner.

2) Albanol A can reduce the expression of Bcl-2 (anti-apoptotic protein) and Bid expression level (proapoptotic proteins), in time-dependent manner.

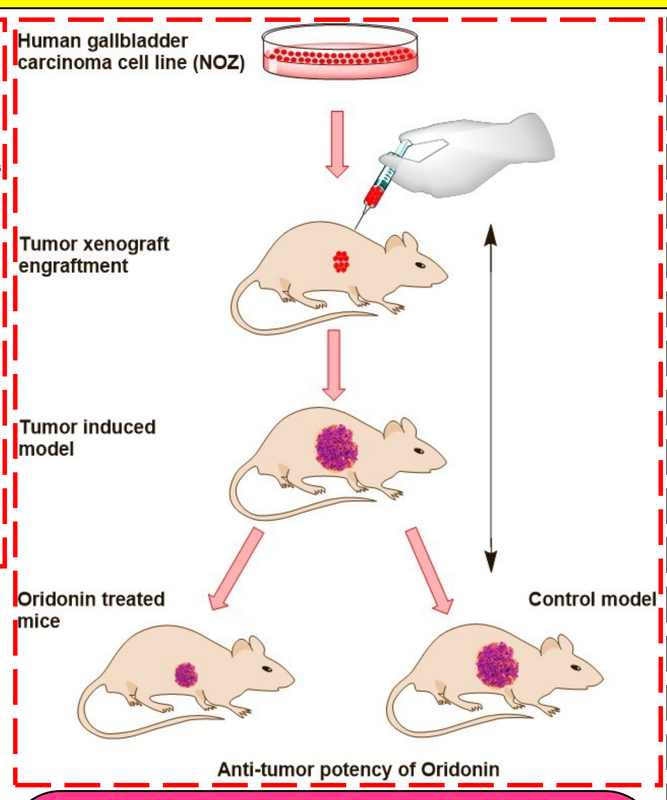


Figure 2. Schematic representation of oridonin treatment on NOZ cells.

Tumor xenograft models can be established through subcutaneous injection of NOZ cells into a mice. Oridonin treatment can predominantly inhibit tumor xenografts formation.

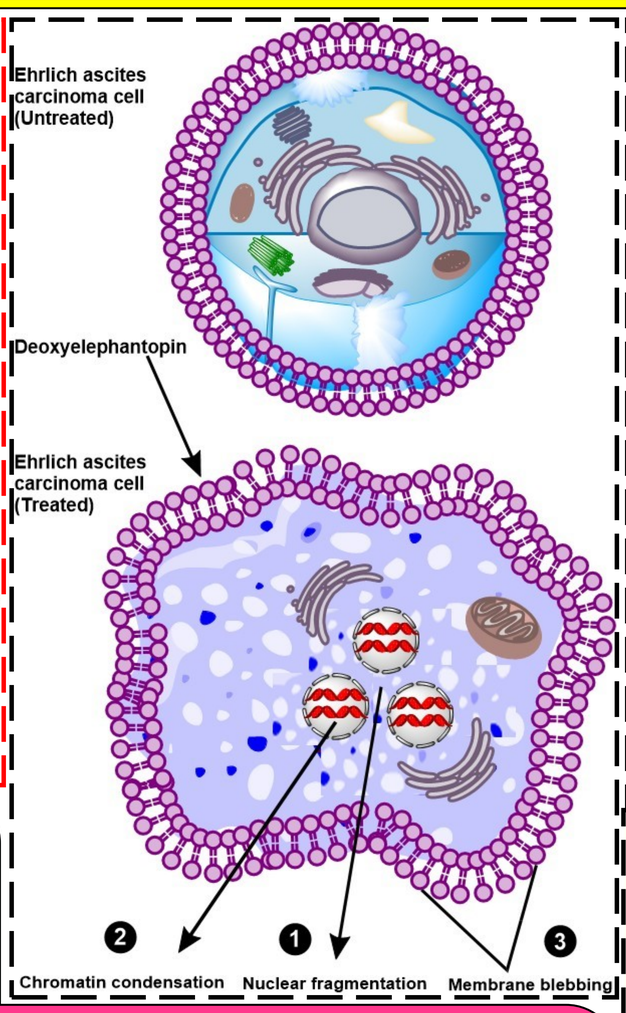


Figure 3. Schematic representation of deoxyelephantopin treatment on EAC cells.

(1) Apoptotic activities/indicators in the form of morphological alteration occur in the treated cells such as nuclear fragmentation, (2) chromatin condensation and (3) membrane blebbing.

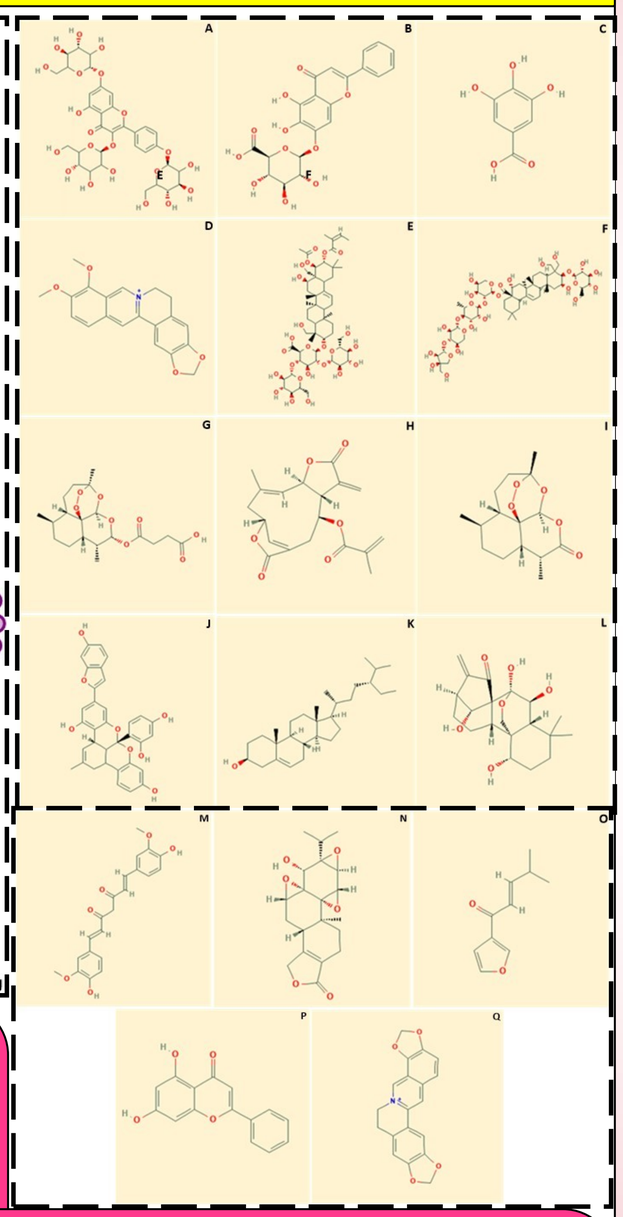


Figure 4. Chemical structures of the anticancer compounds. (A), Kaempferol, (B), Baicalin, (C), Gallic acid, (D), Andrographolide, (E), Saponins, (F), Platycodin D, (G), Artesunate, (H), Deoxyelephantopin, (I), Artemisinin, (J), Albanol A, (K), β-Sitosterol, (L), Oridonin, (M), Curcumin, (N), Triptolide, (O), Isoegomaketone, (P), Chrysin, (Q), Coptisine.

Table 1. List of plant based anticancer compounds, source plant, cell line used and animal model used for in vivo.

Plant name	Active components	Cancer cell line applied to	Animal model applied
Morus alba L.	Albanol A	HL60	In-vitro
Artemisia annua L	Artemisinin	--	Sprague–rats
Scutellariae baicalensis	Baicalin	BGC-823, MGC-803/ Nalm-6, Daudi, NCI-H929	In-vitro
Commercial	Berberine	SCC-4	In-vitro
Curcuma longa Linn	Curcumin	HL-60, HT-29, MCF-7, MDA -MB-231, AK-5, $V\gamma9V\delta2^{+}$	Rat
Rhizoma Coptidis	Coptisine	HCT-116	Balb/c mice
Elephantopus scaber	Deoxyelephantopin	N/A	Albino mice
Scutellaria barbata	Bezielle	MDAMB231, MCF10A,	In-vitro
Perilla frutescens (L.)	Isoegomaketone	DLD1	In-vitro
Fagonia taeckholmiana	Kaempferol	HEPG2, U251, MCF7	In-vitro
Rabdosia rubescens	Oridonin	SGC996, NOZ	Athymic nude mice
Platycodon grandiflorum	Platycodin D	U937, THP1, K562	In-vitro
Asclepias curassavica Linn.	β-Sitosterol	COLO 320 DM, VERO	Albino Wistar rats

CONCLUSIONS:

- Cancer is one of the major cause of death globally and is caused by alteration in regular function of a w ide range of signal transduction, apoptotic and regulatory pathways.
- It cause millions of death globally with the majority of deaths in developing countries.
- Conventional therapies are associated with non-specificity and toxicity to normal cells.
- Affordability of cancer conventional therapies is a challenge specifically in developing countries of the world.
- The greatest recent advancement in cancer therapy is the use of plant-based anticancer agents as they are relatively more potent, safer, easily available and cheaper and many of the plant-based drugs have successfully cleared potency and safety tests in their clinical trials.
- Standardization of these potential drug candidate is required internationally under the guidelines of regulatory authorities that includes assessing their composition, potency, safety alongwith consistency in manufacturing.

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