



Alkaloids and Flavonoids the Phyto Adjuvants in Cancer Therapy



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Abstract

Cancer represents the second leading cause of deaths throughout the world. Though orthodoxic/ conventional cancer treatments such as chemotherapy, radiation and surgery assure the survival of cancer patients, they do not insure cure to life. They are often painful due to adverse side effects and also bring resistance to drugs and radiation. In recent years WHO Geneva cancer conference also proclaimed that regional herbal therapy can be given as adjuvants alongside chemotherapeutic agents since the former causes minimal side effects and are also safe to the normal cells and to the body. Herbal compounds being antioxidants and antimicrobial in nature and operate the apoptosis of cancer cells in-vivo through their innumerable mechanisms, they show greater potential as anti- cancer agents. Among the multitudes of herbal agents, the alkaloids and flavonoids proved as anti-proliferative, anti- angiogenic, anti-metastatic and anti-cancer adjuvants through cell line studies and in clinical therapy.

Keywords: Chemotherapy; Apoptosis; Anti- Neo angiogenesis; Phyto adjuvants; Alkaloids; Flavonoids

Introduction

In breast cancer patients the expression of hormonal receptors viz ER, PR and Her 2 neu are very important notation in application of adjuvant endocrine therapy alongside cytotoxic chemotherapy [1,2]. In the patient with receptor positive i.e ER+ve PR+ve and Her 2 neu+ve, detrimental effect of their processes will be nullified by the endocrine adjuvant Tamoxifen. By competitive exclusion principle the tamoxifen binds with the ER+ve receptors and thereby will not allow the binding of their in-vivo estrogen over the cancer cells. In the receptor negative patients, the influence of in vivo estrogen hormone will be more and thus the cancer cells undergo proliferation. But in recent years, herbal plant extracts with alkaloids and flavonoids have shown great improvements in killing the cancer cells. Moreover alkaloids, flavonoids plus anti-cancer drug combinations have documented improved efficacy in the cancer treatment and patient recovery. The pathways of herbal extracts of alkaloids have shown effective control on cancer cells by the following mechanisms [3-5].

i. *Colchicum luteum* showed its effects of cancer cell migration, cell invasion through reduced expression of MMP9, uPA, and

FAK/SRC and cell apoptosis in NCI-N87 cell line. It promotes the caspase-3-mediated apoptosis due to the suppression of PI3K/Akt/mTOR signaling pathways.

- ii. Natural and semi synthetic alkaloids of *Catharanthus roseus* plant extract showed its effect on microtubules assembly formation of the mitotic spindle during M phase of the cell division.
- iii. *Nelumbo nucifera* seed embryo induced the activation of MAPK/JNK pathway and downregulated the Bcl-2 and NF- κ B signaling pathway in ROS-dependent cancer cells.
- iv. Some examples of alkaloids are colchicine, vinblastine, vincristine, vinorelbine, vincamine, vindesine, and neferine, etc.,

Flavonoids of the herbal extracts showed the following mechanisms [6-8]

- a. They activate the apoptotic proteins both intrinsically and extrinsically.
- b. Inside the cancer cells they elevate Ros, similar to oncolytic

drugs.

- c. They induce DNA damage in the cancer cells.
- d. These reduce the cancer cell proliferation.
- e. They also decrease the tumour growth factors and IGF-1 expression in vitro in the cancer cells (prostate).
- f. They can arrest G2/M phase of the cancer cell cycle.
- g. Some flavonoids decrease to AR expression in prostate cancers.
- h. These suppress the cancer cells viz Akt / P13 k signalling pathways.
- i. They stimulate apoptosis via increase in the Bax/Bcl-2 ratio.

Combination flavonoids or alkaloids were demonstrated to increase the cytotoxic killing of cancer cells through apoptosis in different cancers.

The flavonoids combination with classical in orthodox chemo drugs such as COX2 inhibitor celecoxib, DNA-interactive agents such as doxorubicin, cisplatin, cyclophosphamide, 5-fu and gemcitabine, JAK-STAT inhibiting tasocitinib, methotrexate (antimetabolites), and anti-tubulin agents such as taxanes and paclitaxel have effectively reduced the cells proliferation, increased cell death, reduced tumour growth and improved the survival of patients suffering cancers of the prostate, breast, ovaries, liver and pancreas [9]. Various flavonoids include genistein, the arabinosin, catechin EGCG, quercetin, curcumin, Ellagic acid, Resveratrol etc.

The extensive usage of chemotherapeutics in cancer patients mostly cause reasonable death during treatment or post treatment due to vital organs functional failure. Moreover, the frequent treatment of synthetic chemotherapeutic drugs causes localized resistance in cancer tissues. The plant derived alkaloids

and flavonoids are the best alternatives to the chemotherapeutics with the absence of mortality or very minimal side effects to the patients. The combination therapy of alkaloids or flavonoids with minimal synthetic chemotherapeutic drugs may become the new horizon in future to the cancer treatment.

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