Chapter-13

Anticancer Activities of Ayurvedic Herbs and Formulations: A Comprehensive Review

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Abstract

Globally, cancer is becoming a significant public health concern. According to World Health Organization (WHO) estimates from 2019, cancer ranks either first or second among the major causes of death in 112 out of 183 countries. Toxic effects to other tissues, recurrence, drug resistance, deteriorating quality of life of patient are some predominant inadequacies of the conventional treatments. Ayurveda being time-tested, well documented science has potential of treatment with good quality of life of patient. So an attempt has been made to elaborate the potential of Ayurveda medicines such as prime medicinal plants, metal-minerals, poly-herbal and herbo-mineral preparations on the cancer.

Material and Methods

Pertinent scientific articles from indexed scientific journals were collected, studied and analyzed by the search words using ‘Ayurveda’, ‘anticancer activity’, ‘medicinal plants’, ‘metal-minerals’, and ‘Ayurveda formulations’.

Conclusion

Many single herbal plants, processed metal-minerals, poly-herbal and herbo-mineral formulations proved efficient in the management of the cancer. They have numerous properties like immunomodulatory, adaptogenic, regenerative etc. which were responsible for their anticancer activity through manifold mechanisms such as apoptosis induction, blocking angiogenesis, tumor regression etc.

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1. INTRODUCTION

Cancer is a major public health problem that has a significant global impact on both developed and developing countries. It is characterized by the rapid abnormal growth of cells beyond their usual boundaries. It can further invade into adjoining parts of the body and other organs called as metastases. These widespread metastases are one of the leading causes of death due to cancer [1].

WHO ARC's GCO reported lung cancer (12.4%) as the most commonly occurring cancer worldwide followed by breast cancer (11.6%), colorectal cancer (9.6%), prostate cancer (7.3%), and stomach cancer (4.9%). Among all types mortality is highest in the lung cancer (18.7% of the total cancer deaths) followed by colorectal, liver, breast and stomach cancers. Re-emergence of lung cancer as a most common cancer may be due to persistent tobacco use in Asia [2].

WHO GCO also estimated increase of incidence of all types of cancer cases by 64.5% and mortality from by 79.7% in the Asia 2022 to 2045 [3].

Considering the high profile nature of the disease, its treatment has been a constant struggle with relatively less success. Currently available options for cancer treatment involve surgical removal and radiation treatment of the large accumulated biomass of cancer, typically followed by systemic chemotherapy treatment for maintenance.

The major disadvantages of chemotherapy are recurrence of cancer, drug resistance, and toxic effects on non-targeted tissues that can restrain the use of anticancer drugs and thus impair patient's quality of life. To overcome the problems of present therapy, search for new promising anticancer agents with better efficacy and lesser side effects continues [4].

Ayurveda is well-documented and recognized traditional system of medicine. Numerous medicinal plants and herbo-mineral preparations are utilized in Ayurvedic medicine for therapeutic purposes. As per available literature, over 60% of anticancer drugs are derived from natural products [5]. A substantial contribution in pharmacotherapy and drug discovery, particularly for cancer therapy, has been made by structural analogues of diverse natural products from an ancient time [6]. United States Food and Drug Administration approved number of natural products as anticancer drugs for different cancer types from 2015-2019 [7].

In the present review, an attempt has been made to compile the information about medicinal plants and herbo-mineral preparations mentioned in the Ayurveda specifically evaluated for the anti-cancer activity at preclinical or clinical levels.

Guduchi

Guduchi (Tinospora cordifolia) is a climber belonging to family Menispermaceae found throughout the India. It possesses bitter, pungent and astringent taste, hot in the potency, and *laghu* (light) and *snigdha* (unctuous) property. Its bio-transformed taste is sweet, pacifies all the three *dosha* and primarily act as life span enhancer and rejuvenator.

By targeting distinct cellular pathways in the U87MG glioblastoma and IMR-32 neuroblastoma cell lines, *T. cordifolia* extracts in hexane and chloroform slow down the rate of proliferation and migration and induce differentiation and senescence. As a result, they may be useful as phytotherapeutic interventions in the treatment of neural cancers [8].

The new clerodane furano diterpenoid was identified and isolated from *T.cordifolia* by bioassay guided isolation. This novel compound demonstrated the anticancer activity by inducing mitochondria mediated apoptosis and autophagy in HCT116 colon cancer cells [9].

Among the phytoconstituents of *Guduchi*, palmatine, tinocordiside, and yangambin were found to be active against KB and HT-29, KB and CHOK-1, and KB cells respectively, all extracts and fractions of *T.cordifolia* were found to be active against these cells. On the other hand, N-formylannonain and 11-hydroxymustakone were found to be active for immunomodulatory activity [10].

IMR-32 human neuroblastoma cell line treated with aqueous ethanolic extract of *T. cordifolia* arrest the majority of cells in G0/G1 phase and expression of DNA clamp sliding protein (PCNA) and cyclin D1 is modulated. Furthermore, the morphology and expression of neuroblastoma cell-specific

differentiation markers, such as NF200, MAP-2, and NeuN, indicated that the cells had undergone differentiation. The differentiated phenotype was associated with induction of senescence and pro-apoptosis pathways by enhancing expression of senescence marker mortalin and Rel A subunit of nuclear factor kappa beta (NFkB) along with decreased expression of anti-apoptotic marker, Bcl-xl. ***T. cordifolia*** extract exhibited anti-metastatic activity and significantly reduced cell migration in the scratched area along with downregulation of neural cell adhesion molecule (NCAM) polysialylation and secretion of matrix metalloproteinases (MMPs) [11].

C6 glioma cells were used to assess the anti-brain cancer potential of a 50% ethanol extract of *T. cordifolia*. Glioma cells treated with the extract demonstrated anti-proliferative, differentiation-inducing, anti-migratory/anti-metastatic potential, as well as potential signaling pathways involved in the mechanism of action [12].

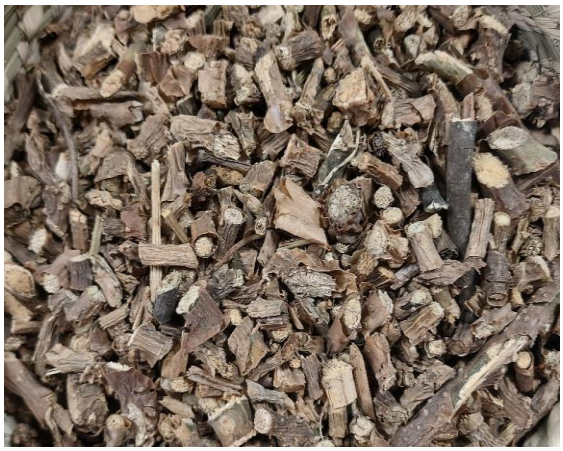

Figure 1: Dried stem of Guduchi *(T.cordifolia)*

Figure 2: Climber of Guduchi *(T.cordifolia)*

Ashwagandha

Ashwagandha (Withania Somnifera) is classified in GRAS (generally regarded as safe) family as a nontoxic edible herb found in the dry and hot part of the India. Its' official useful part is root as per Ayurveda and possess astringent and bitter taste, hot potency, pacifies *kapha* and *vata dosha.* As it is used as aphrodisiac and promotes the strength hence entitled as Indian ginseng.

Ashwagandha's primary active ingredients are steroidal lactones and alkaloids termed as withanolides among them Withaferin A is the foremost. Both withanolides and particularly withaferin A are well investigated for their anticancer activities and are most promising anticancer compounds that play a major role in apoptosis induction [13] [14]. It induces apoptosis by activation of caspase-3, and inhibits JNK, Akt, pERK, and IL6 signal pathways.

The combination of withaferin A and radiation was proposed as an efficient radiosensitizer in cancer therapy because it significantly increased apoptosis in human renal cancer cells when compared to treatment with either withaferin A or radiation alone. Withaferin A was shown to induce depolymerization of vimentin and cause reregulation of Notch1 signaling. Furthermore, bioinformatics and experimental data suggested the differential binding efficacies of withaferin A and withanone to cellular targets including mortalin, p53, p21, and NRF2 [15].

W. somnifera root extract activates caspase-3 and downregulates Bcl-2, an antiapoptotic protein, to induce apoptosis in breast cancer cells [16]. It also improves the effectiveness of radiation and chemotherapy [17]. Combination of cisplatin and root extract of *Ashwagandha* work synergistically to inhibit cancer in both resistant and parental mouse breast cell lines, both in vitro and in vivo, outperforming cisplatin alone through apoptosis induction and caspase-3 activation[18].

Ashwagandha leaf water extract contains an active anticancer ingredient namely triethylene glycol which selectively inhibits the growth of cancer cells [19]. *Ashwagandha* leaf extract and withanone both induce ROS-signaling, which leads to the selective death of cancer cells and thus they are viable reagents for ROS-mediated cancer chemotherapy [20]. Apoptosis signaling, death receptor signaling, p53 signaling, GM-CFS signaling, and the G2-M DNA damage regulation pathway are the five main mechanisms by which *ashwagandha* leaf extract and its constituents kill cancer cells. p53 signaling was the most prevalent among them [21].

The evidence from experiments demonstrating *Ashwagandha'*s immunomodulatory, anti-cancer, adaptogenic and regenerative properties points to its potential as a therapeutic adjuvant in the treatment of cancer. The adjuvant properties of withanolides can modulate multidrug resistance and reverse the myelosuppression caused by chemotherapy [22].

Figure 3: *Ashwagandha (W.somnifera)*

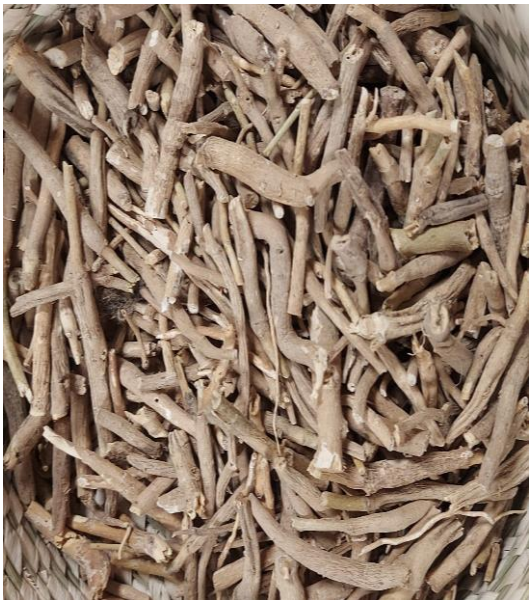

Figure 4: Dried roots of *Ashwagandha (W. somnifera)*

Kalajaji (Nigella Sativa)

Nigella sativa L. is an annual herb from the family Ranunculaceae and entitled as *Kalajaji* in the Sanskrit and black cumin in the English. It is narrated in the *Chaturbeeja*, one among the four seeds which are used medicinally. It is pungent in taste, hot in potency, *laghu* (light) and *ruksha* (dry) property.

Thymoquinone, thymohydroquinone, dithymoquinone, thymol, carvacrol, nigellimine-N-oxide, nigellicine, nigellidine and alpha-hederin are some chief phyto-constituents isolated from *N. sativa.* Its seed, seed oil, various extracts and active components have immune stimulation, anti-inflammation, hypoglycemic, antihypertensive, anti-asthmatic, antimicrobial, anti-parasitic, antioxidant and anticancer effects. Among the mentioned phyto-constituents thymoquinone and alpha-hederin have anticancer effect and a water-soluble pentacyclic triterpene, as well as saponin, a possible anticancer agent [23]. Recent research on the acute and chronic toxicity of *N. sativa* oil and its main active ingredient, thymoquinone in particular has confirmed that it is safe to consume, especially when taken orally [24].

Strong anti-proliferative, pro-apoptotic, anti-oxidant, anti-mutagenic and anti-metastatic effects of *N. sativa* is the primary source of its anti-cancer effect. It has also been suggested that *N. sativa*'s capacity to reduce inflammation and have immune-stimulating properties contributes to its protective effects against the tumor initiation and progression partly. Regulation of signaling pathways like iNOS, p53, and caspases along with the enhancement of NK cytotoxic activity against cancer cells of *N. sativa* facilitate pacification of tumorigenesis

and cancer. Both *in vitro* and *in vivo* experiments indicate that *N. sativa* extracts maybe useful in the creation of potent therapeutic agents for regulation of various stages of tumorigenesis and treatment of various cancer types [25].

The leaves of *N. sativa* contain cardiac glycosides, steroids, tannins, and saponins. It also has antioxidant and hemolytic activity (ranging from 3.7% to 16.5%). Neuropilins and their derivatives likely have the potential to be the effective anticancer agents for targeting the PI3K protein and its associated pathways in particular, as demonstrated by *in silico* studies [26].

Figure 5: Seeds of *Kalajaji (Nigella Sativa)*

Haridra

Haridra (Curcuma longa L.) member of zingiberaceae family is known for its medicinal properties since *Vedic* time period. It is extensively described in Ayurveda literature also. It is rhizomatous herb native to South Asia and widely cultivated in the warmer parts of world including India. Its' rhizome have *katu* (pungent), *tikta* (bitter) taste, hot potency, *laghu* (light) and *ruksha* (dry) property. It pacifies the *kapha pitta dosha*, act as *varnya*, (promotes complexion of the skin), *lekhaneeya* (promote therapeutic scrapping), *medohara* (pacifies fat tissues), *vrana ropana* (facilitate wound healing), and *rasayana* (rejuvenator). It is used for the management of *kushtha* (various skin diseases), *prameha* (excessive urination), *arsha* (piles) and *grahani* (diseases due to malfunctioning of part of gastro-intestinal tract dealing with digestion). Antioxidant, hepatoprotective, anti-osteoarthritis, anti-inflammatory, anticancer, anti-arthritic, neuroprotective, antidiabetic, antidiarrheal activity, anti-microbial, anti-atherosclerotic, antidepressant, anti-ageing, wound healing and memory enhancing activities are scientifically proven. Turmeric possess yellow colour due to presence of phenolic compound known as curcuminoids. Curcumin (77%), desmethoxycurcumin (17%), bis-desmethoxycurcumin (3%) and

cyclocurcumin (a minor constituent) are four main constituents of curcuminoids [27].

Curcumin has a broad anti-carcinogenic effect on rat aortic smooth muscle cells through mechanisms such as induction of apoptosis and inhibition of cell-cycle progression [28]. By inducing a DNA damage response, it paves the way for the therapeutic application as a nutraceutical in the chemoprevention of prostate cancer [29]. Additionally, curcumin affects a wide range of adhesion molecules and growth factor receptors linked to angiogenesis, metastasis, and tumor growth [30]. It has anti-proliferative activities in a variety of malignancies and suppresses the transcription factor NF-κB as well as a number of downstream gene products, including c-myc, Bcl-2, COX-2, nitric oxide synthase (NOS), Cyclin D1, TNF-α, ILs, and matrix metallopeptidase 9 (MMP-9). As curcumin increases adiponectin levels and decreases leptin blood levels, it may help diabetics with type 2 diabetes to prevent colorectal cancer [31]. It inhibits NF-κB, the signal transducers and activators of transcription 3 (STAT3) pathways in the cancer cells which exhibits an antitumor effect [32]. Curcumin has been suggested as an adjuvant in lung cancer because in *in vivo* experiments showed that it reduces the migratory and invasive potential of A549 cells and inhibits the expression of adiponectin, which is thought to be mediated through the NF-κB/MMP pathways [33]. Potential pathways and targets for treating lung cancer may include treatment of curcumin coupled with EGFR-, miRNA-, autophagy-, and cancer stem cell-based treatments [34]. Curcumin possess anti-cancer activity due to its effect on biological pathways involved in mutagenesis, oncogene expression, cell cycle regulation, apoptosis, tumorigenesis and metastasis.

In dimethyl benz[a]anthracene (DMBA)-initiated and 12,O-tetradecanoylphorbal-13-acetate (TPA)-promoted skin tumors, local application of curcumin in CD-1 mice and dietary administration of 1% *C. longa*, 0.05% of its ethanol extract considerably reduced tumor incidence, tumor burden, and tumor volume [35].

In the *in vivo* experiment, the N-methyl-N-nitrosourea-induced mammary cancer in rats, oral and topical application of *C. longa* for 24 weeks given prophylactically (pre-induction treatment) and therapeutically (post-induction treatment). Prophylactic topical application of *C. longa* at 200 mg/kg significantly reduced the mean tumor volume compared with therapeutic topical application [36].

Figure 6: *Haridra (C. longa)*

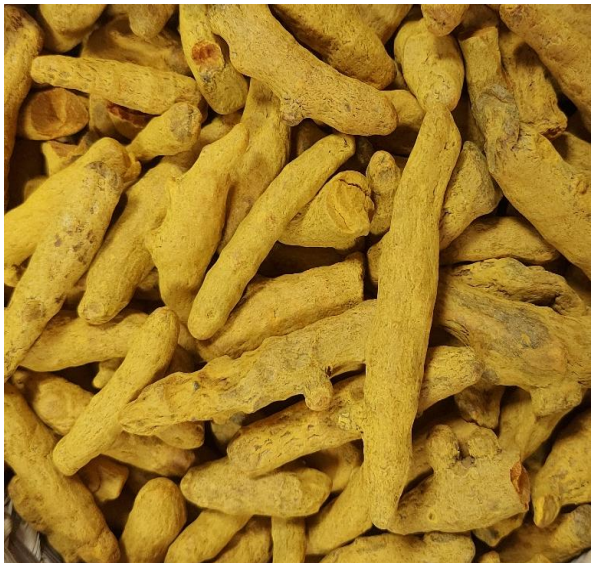

Figure 7: Dried Rhizomes of *Haridra (C.longa*)

Bhallataka

Bhallataka (Semecarpus anacardium Linn.) is member of anacardaceae family scattered in warmer parts of India and sub-himalayan area. As it is used for marking the clothes by dhobis so termed as marking nut. This tree is grouped under the *upavisha* by the *Rasatarangini* an authoritative treaty on the *Rasashatra.* It is an organic irritant vegetable poison and causes severe allergy when the black fruit and its resin comes in contact with the skin. Hence it is recommended to use only after certain purification process described in the classical texts of *Ayurveda.* Its fruit, seed and oil is used for the *kushtha* (various skin diseases), *arsha* (piles) and *vrana* (wound). It is *katu* (pungent), *tikta* (bitter), *madhura* (sweet) in tatse, hot in potency, have *laghu* (light), *snigdha* (unctuous), *teekshna* (sharp) property, and *medhya* (intellect promoting) action. The ripen accessory fruit of *bhallataka* is sweet and edible but the black fruit is considered poisonous. The seed is considered as edible on proper preparation [37].

It was reported that the milk extract of purified nuts of *S. anacardium* made in accordance with the Siddha Medicine Formulary (1972), had anti-hepatocellular carcinoma activity induced by aflatoxin B1 in experimental rats. [38]. Also it has been reported that the polyherbal formulation *Kalpaamruthaa*, which contains the milk extract of *Bhallataka*, has a protective effect against the abnormal anti-oxidant levels and peroxidative damage in mitochondrial fraction of mammary carcinoma induced rats [39]. Another experimental investigation revealed that the milk extract of marking nut removes the leukemic cells from the bone marrow and the internal organs of leukemic mice and restores the metabolism [40].

The Ames test has demonstrated anti-mutagenic properties in the water, alcoholic and oil extracts of *S. anacardium* [41]. Animal models of leukemia's advanced P388, L1210, B16 Melanoma and Glioma and sublines of P388 resistant to Adriamycin/Vincristine have substantially intensifies the life span when treated with the chloroform extract of *Bhallataka* [42]. It has been reported that the apoptotic activity of the oil extracted from marking nut is mediated by caspase activation [43]. *S. anacardium* increased PARP cleavage, caspases, cytochrome c, Bax and decreased Bcl (2) [44].

Figure 8: *Bhallataka (S. anacardium)*

Figure 9: *Bhallataka* Fruit *(S. anacardium)*

Triphala

Triphala is a combination of fruit rinds of *Terminalia chebula* Retz., *Terminalia bellirica* Retz., *Phyllanthus emblica* L. mentioned in Ayurveda for the treatment of the various diseases such as obesity, eye disorders etc.

Triphala has strong anti-apoptotic and antioxidant properties, making it a promising neuroprotective agent against oxidative stress in SH-SY5Y cells and zebrafish [45].

There are more than fifteen phytochemicals in *triphala churna*, having variety of pharmacological activities in general and the inhibition of tumor progression in particular. These compounds' docking and in vitro investigations against various targets were examined. The outcomes demonstrated that it has a prediction efficacy of (−)436.7 and inhibited angiogenesis by blocking several VEGF/VEGFR2 signaling pathway components. Punicalagin (−424.8) and chebulagic acid (−414.8), the two top-ranked phytochemicals, worked together to mediate the anti-angiogenic effect [46].

The antitumor properties of *triphala* have been attributed to chebulinic acid, chebulagic acid, and other phenolic acids. The chebulinic acid, which has strong anti-proliferative, pro-apoptotic, and anti-migratory properties, is a crucial molecule for preserving *triphala'*s antitumor efficaciousness in colorectal cancer cell lines. The PI3K/AKT and MAPK/ERK pathways are most likely involved in antitumor mechanism of the chebulinic acid [47].

A transplantable mouse thymic lymphoma (barcl-95) and a human breast cancer cell line (MCF-7) were used to test the cytotoxic effects of *triphala* aqueous extract. It was discovered that as *triphala* concentrations increased, the viability of the treated cells decreased.

Similar concentrations of *triphala* did not significantly alter the cytotoxicity of mouse liver and spleen cells, human peripheral blood mononuclear cells, MCF-10 F, and normal breast epithelial cells. When single-cell gel electrophoresis was performed on MCF-7 cells treated with *triphala*, a pattern of DNA damage indicative of apoptosis was observed. Research conducted on MCF-7 and BCL-95 cells treated with *triphala* demonstrated a notable and concentration-dependent rise in intracellular reactive oxygen species (ROS).

Mice transplanted with barcl-95 when received *Triphala* (40 mg/kg body weight) orally, the tumor growth was significantly reduced, as determined by the tumor volume measurement. Additionally, it was discovered that the excised tumor tissue of mice fed with *triphala* had significantly more apoptosis than the control group, indicating that apoptosis plays a role in slowing the growth of tumors. These findings imply that *triphala* was capable of causing cytotoxicity in tumor cells while protecting healthy cells. *Triphala's* capacity to elicit distinct responses in normal and tumor cells appears to be linked to its differential response in intracellular ROS generation [48].

Using the MTT assay, various concentrations of hydro-alcoholic extracts of *triphala* were assessed for their cytotoxic activity on the human liver cancer cell line HepG2, in comparison to Cisplatin and control. Cisplatin and the *triphala* at all concentrations demonstrated a significant inhibitory effect on HepG2 cells. All extract of *triphala* at multiple concentrations were significantly effective on MTT assay when compared to the control group. The outcomes show that *triphala* and its constituents considerably decrease the survival rate and exhibit cytotoxic activity on the HepG2 cancer cell line [49].

Figure 10: *Triphala*

Panchakola

It is poly-herbal formulation consisting of fruits and roots *Piper longum* L, *Piper chaba*, *Plumbago zeylanica* L. and *Zingiber officinale* Roscoe. It has *katu* (pungent) taste, hot potency, *teekshna* (sharp) property, alleviates *pitta* and pacifies *kapha* and *vata*. It is used for the treatment of *udara* (ascites), *pleeha* (splenomegaly), *anaha* (painful gaseous distention in abdomen) and *gulma* (a type of lump) according to Ayurveda.

Using the MTT assay, the antitumor and free radical-scavenging properties of *panchakola* aqueous extract were evaluated in normal and breast cancer cell lines (HEK and MCF-7, respectively). In cell lines that were incubated with and without *panchakola*, the antioxidant enzymes, nitric oxide scavengers, superoxide dismutase, glutathione S-transferase, and glutathione peroxidase activities were evaluated. The results showed increased cytotoxicity in the MCF-7 cell line (IC50 16.446 µg/ml), which was similar to the results of standard anticancer control (curcumin) with an IC50 of 10.265 µg/ml. According to the antioxidant assays, when compared to normal HEK cells, MCF-7 cells appeared to have higher antioxidant activity [50].

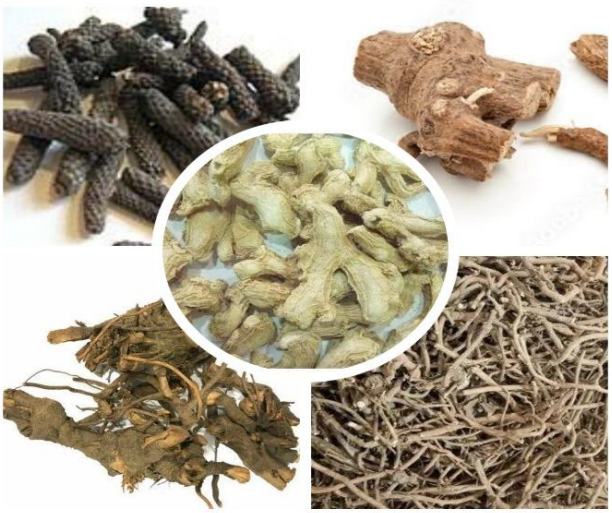

Figure 11: Panchakola

Panchavalkala

Panchvalkala, an Ayurvedic traditional poly-herbal formulation mentioned in *Bruhattrayi* i.e. *Charak* and *Sushruta Samhita*, *Ashtangahridaya* for the treatment of women with endometriosis-related problems, leucorrhea and vaginal ailments. The formulation comprises of equal ratios of the barks from *Ficus glomerata*, *Ficus virens, Ficus religiosa, Ficus benghalensis*, and *Thespesia populnea*.

A study was conducted to assess the anticancer and immunomodulatory properties of *Panchvalkala* aqueous extract against cervical cancer, both in vitro and in vivo. In SiHa and HeLa, it causes mitochondrial depolarization and elevates the expression of generic caspases, which leads to apoptosis. Additionally, it decreased the expression of viral onco-proteins (E6 and E7) and increased the expression of tumor suppressor proteins (p53 and pRb). In a mouse papilloma model, it decreased tumor weight and volume while also inducing immunomodulation in the animals. It simultaneously dropped IL-10 (Th2) cytokine levels and an increase in serum levels of IL-2 (Th1). The drug *panchakola* did not affect body weight, food consumption and organ histopathology of the animals [51].

Kanchanara Guggulu

An Ayurveda compound formulation called *Kanchanara guggulu* is used in clinical practice to treat both benign and malignant tumors. The antimitotic activity of *Kanchnara guggulu's* hydro-alcoholic (50%) extract was evaluated using the *Allium cepa* assay, and the anti-proliferative effects were investigated

using a yeast proliferation model. The standard anticancer agent was methotrexate. In the Allium assay, methotrexate (0.02 mg/mL) and all concentrations of extract of *Kanchanara guggulu* (1, 2 and 3 mg/mL) significantly reduced the ability of *A. cepa* root cells to divide, resulting in a decrease in root growth and mitotic index when compared to the control. In the anti-proliferative experiments, a combination of 0.025, 0.05, and 0.1 mg/mL of methotrexate and 1, 5, and 10 mg/mL of *kanchnara guggulu* extract significantly reduced dividing Saccharomyces cerevisiae cells and inhibition of cell viability compared to control. The presence of flavonoids and phenolics may be the cause of the cytotoxicity of the hydro-alcoholic extract of *kanchnara guggulu*, as evidenced by its antimitotic and antiproliferative effects [52].

Shiva Gutika

Shivagutika is a polyherbal formulation mentioned in Ayurveda having *shilajatu* (black bitumen) as a primary ingredient. The dichloromethane extract of *Shivagutika* was evaluated for anti-breast cancer and cytotoxic activity on MCF-7, MDA-MB-231, and MDA-MB-468. According to *in silico* analysis, among all the compounds, Sciadopitysin, a biflavonoid, bound to the Caspase 3 binding site with the highest binding energy of -7.2 kcal/mol through the formation of 12 intermolecular interactions, four of which were hydrogen bonds. In contrast, ixabepilone, a standard medication, bonded to Caspase 3 through just three intermolecular interactions, two of which involved hydrogen bonds. Studies using molecular dynamics simulations also demonstrated the robust interaction and stability of sciadopitysin with Caspase 3 in contrast to ixabepilone and Caspase 3. Ixabepilone only formed five ligand hydrogen bonds, whereas sciadopitysin formed nine [53].

Abhraka Bhasma

Abhraka bhasma is produced by treating biotite (mica) with various plant extracts which aids in the transformation of the inactive substance into an active cellular regenerator. It is a red-colored powder having oxides of iron, magnesium, calcium, silica, potassium, and aluminum. It is an excellent cellular regenerator and nervine tonic having wide use for various skin diseases, respiratory ailments and other chronic conditions.

Abhraka Bhasma was tested for its in vitro anticancer activity at different *Putas* (measure of heat) stages (20, 50, and 100) using three distinct cancer cell lines (LungHOP62, LeukemiaU937, and ProstateDU145). The anti-proliferative activity was then assessed using the SRB assay. *Abhraka Bhasma* demonstrated concentration-dependent positive in vitro anticancer activity on all three cell lines, with particularly noteworthy activity on prostate cancer cell lines. Abhrak

Bhasma has anticancer activity in the following order: 100 Puti > 50 Puti > 20 Puti. The maximum activity of *Shataputi Abhrak Bhasma* on prostate cancer cell lines was nearly equal to that of the positive control medication adriamycin [54].

Yashada Bhasma

Yashada bhasma (~ incinerated zinc) is narrated for its claim in *prameha* (excessive urination / polyurea), *pandu* (anemia), *vatavyadhi* (neuro-muscular disorders) and *netra-vikaras* (eye disorders), *kampavata* (shaking in the various body parts), in the text of *Rasashastra* which is widely used in clinical practice also.

Pardama Marita Yashada Bhasama (~ incinerated zinc prepared by *purified* mercury) and *vanaspati Jarita Marita Yshada Bhasma* (~ incinerated zinc prepared by *frying of* medicinal plants) used in the in vitro sulforhodamine B assay on a human pancreatic cancer cell line (MIA PaCa-2), retaining Adriamycin as the control. Since *Vanaspati Jarita Marita Yashada Bhasma* can arrest the cell growth, a study finds that it functions as a cytostatic medication in human pancreatic ductal adenocarcinoma [55].

Manikya Bhasma

Incinerated powder of purified ruby, orpiment, and sulfide of arsenic is known as *Manikya bhasma.* It is utilized for the immunomodulation, impacting different hormonal and enzymatic cycles. As per Ayurveda, *Manikya bhasma* has multiple benefits, including tonic for the heart and brain as well as having appetizer property. A study using the cancer cell lines MG-63 (osteosarcoma), breast cancer (MDAMB-231) cells, cervical cancer (Hela) cells, colon cancer (DLD1, HCT-116) cells as well as cell viability, demonstrated that the *Manikya Bhasma* induced cell death inside the cancer cells followed by mitochondrial-dependent apoptosis [56].

Arkeshwara Rasa

It is a herbo-mineral preparation prepared through complex process from dried and powdered fruit rind of *Terminalia belerica* Roxb. (Combretaceae), *Terminalia chebula* Retz. (Combretaceae), and *Phyllanthus emblica* L (Euphorbiaceae) along with whole plants of *Plumbago zeylanica* L. (Plumbaginaceae) and latex of *Calotropis procera* (Aiton) W.T. Aiton (Apocynaceae) along with mercuric sulfide [57].

An investigation was conducted on the anticancer properties of *Arkeshwara Rasa* using two human cancer cell lines (skin and pancreas), the lactate dehydrogenase assay for enzyme activity, and the trypan blue assay for cell morphology. Growth inhibition and LDH release activity show that human pancreatic cancer cells are extremely sensitive to *Arkeshwara rasa*. Various anticancer phytochemicals found in the different botanicals combined with mercuric sulfide may be the cause of this anticancer activity [58].

Raudra Rasa

Raudra rasa is prepared by triturating decoction / juice of *Piper betel* Linn., *Amaranthus spinosus* Linn., *Boerhaavia diffusa* Linn., *Piper longum* Linn. and cow's urine one after the other with *shadguna kajjali* (black mixture made by trituration of purified mercury and purified sulphur) followed by giving a small *puta* (measure of heat). It is explicitly prescribed for the treatment of *arbuda* (cancer) on the other hand *hiraka bhasma* (~ incinerated diamond) has the capacity to encourage cancer-healing. These two medications work well together to accomplish multiple goals. Thus, using FTIR and LC-MS analysis, two types of *raudra rasa* – classical (described above) and modified with *hiraka bhasma* were investigated. Based on preliminary analysis, both compounds contain a variety of functional groups with established anti-proliferative properties, including fluoro, methyl, amino, hydroxy, nitro, methylamino, carbonyl, and iodo groups [59].

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