New insights of Ayurveda formulation *Pushpadhanwa* rasa as a palliative therapy to improve the quality of life in ovarian Cancer: A review

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ABSTRACT

Introduction: *Pushpadhanwa rasa* is a formulation described under Aphrodisiac, has been used for centuries. It has been shown that minerals & herbal ingredients present in *Pushpadhanwa rasa* have been reported for their significant effects on different cell lines like HT-29, MMP-9, HeLa, HepG2, 5-FU, MCF-7, UWOV2, HCT-116 cells, relating to female reproductive organs. Aim of the study: In this study an attempt has been made to critical review the ovarian Cancer regression property of Herbo mineral preparation, *Pushpadhanwa rasa* (PDR) Materials & methods: Thirty one ingredients of herb-mineral-animal origin were searched from various authoritative texts and worldwide accepted scientific databases with regard to their use in female reproductive organs for cancer claims including the ovarian cause. Result: A total of 31 ingredients were evaluated for their anti-tumour activities in eight human cancer cell lines. Of these G. glabra, P. betel, *C. sativa* exhibited promising apoptosis activity, G. glabra exhibited anti proliferative & anti angiogenic, G. glabra, P. betel, T.Myrobalan, P. betel, exhibited anti oxidant, P. betel, Z.officinale exhibited anti metastatic, P.betel, Honey shows cytotoxic , *C. sativa* cell cycle arrest activity in many cancer cells. Bhasmas present in *Pushpadhanwa rasa* like Rasasindoora, Lauha bhasma, Abhraka Bhasma, Naga Bhasma, Manahshila are considered as biologically produced nano drugs. Conclusion: Above data shows that the formulation *Pushpadhanwa Rasa* possess strong potential in treatment of ovarian cancer. Randomized controlled trials of high quality with larger sample size and longer follow-up are needed to have significant evidence on the clinical use of *Pushpadhanwa rasa* on ovarian cancer.

Keywords : *Pushpadhanwa Rasa*; Anti- cancer ; Apoptosis; Cytotoxic; Nano particle; Antioxidant.

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Introduction:
Ovarian Cancer is the most lethal among all other gynecological Cancer amongst the women. Globally, nearly 2, 50,000 patients diagnosed with ovarian Cancer each year with more than 1, 40,000 Cancer specific death\(^1\). Only 20% of the ovarian cancer is diagnosed at first stage when the disease is limited to the ovary, 90% of the patient responds well with existing therapy. Stages divided in to 3 more categories, i.e., Stage 2 When the disease metastasized to both the ovaries and the pelvic region; stage 3, after the disease has metastasized to the intraperitoneal abdomen region or Stage 4 beyond the peritoneal cavity cure rate decrease substantially\[^2\]. The century-old embryonal/gametogenesis theory of tumors proposed that tumors arise from germ cells and thus are in some way similar to the formation of gametes and fertilization\[^3\][\(^4\)]

Ovarian Cancer known to originates by imbalances in hormone production and abnormal cell division in basic epithelial cells, germ cells, mesenchymal tissue developing Cystic mass in ovary. Mutation and loss of TP 53 function is one of the most frequent genetic abnormalities in ovarian cancer and is observed in 60-80% of both sporadic and familial cases\[^5\]. Ovarian Cancer patients present with dull abdominal pain, distention of abdomen from no apparent cause. In advanced stage patient developes ascites, palpable lower abdominal masses, gastro intestinal symptoms and weight loss. Surgery is the primary treatment of choice, regardless of the histological type or stages of the Cancer. Total abdominal hysterectomy, with bilateral salpingo-oophorectomy and omentectomy, is the accepted standard treatment. Conservation of the uterus and contralateral ovary in young women desirous of bearing children may be considered only if the disease is limited to stage 1a (Cancer limited to one ovary : ascites not present). In Stage 1 (when tumor confined to the ovary), Herbomineral formulations like Pushpadhanwa rasa may be helpful in improving the quality of life with existing anticancer drugs. In Ayurvedic concept,
according to ‘Charaka’ and ‘Sushruta Samhitas’ cancer is described as inflammatory or non-inflammatory swelling and mentioned either as ‘Granthis’ (minor neoplasm) or ‘Arbuda’ (major neoplasm)[6].

Shukra is the most excellent term to explain the thing that nourishes both the male and female reproductive tissues and its secretions. Its main function is Garbhotpadana – reproduction[7].

Gananatha sen has explained Physiology of Shukradhatu in female as Antah-Shukra and Bahi-Shukra[8]. Shukradhatu is formed Antah-Shukra and Bahi-Shukra. Antah-Shukra operate as in both sexes in Bala Varana Upachaya, growth of secondary sexual character, reproductive organ and individual sex spermatogenesis in male and growth of breast, oogenesis in woman. Bahi-Shukra acts as formation of sperm with spermatic fluid in male and secretions of Bartholin, cervical glands during coitus in female. Artav or Raja is Updhatu of Rasadhatus. Vrishya are drugs that enhances “Shukra dhatu” in order to increase the reproductive capacity and health in both male and female[9]. Gynaecological problems like irregular menses, PCOD, unovulation, etc causes are due to improper functioning of of Shukra dhatu schematic detail about role of shukra dhatu in male & female reproductive organ is as below[10].

As oocytes contribute to reproduction[10], it will be of interest to assess the functional relevance of the acquisition of oocyte-like cells during tumor progression[12]. It has been reported that both parthenogenetic activation of oocyte in ovary[13] and preimplantation embryos have tumorigenicity potential[14] both cancer cells and oocytes display strong independence and survival ability.

Pushpadhanwa rasa, is a formulation described under Vrishya-Vajikaran (Aphrodisiac) Rogadhikar and has been used for centuries to treat various types of ovarian disorders[15]. It exhibits a number of health benefits in gynaecological disorders. It has also been clinically trialled and was found to be effective in the management of Polycystic ovarian disorder (PCOD) - a clinical condition which may be included under Granthis[16].

In that study, it was found that the formulation is not only be effective in regression of the size of the cyst but also enhances the chances of conception in such patients[17]. Pushpadhnwa Rasa contains mainly five bhasmas viz. Rasa sindoor (Red sulphide of mercury); Abhraka bhasma (Incinerated mica); Lauha bhasma (Incinerated iron); Naga bhasma (Incinerated lead); Vanga bhasma (Incinerated tin) and five herbs namely Dhatura (Dhatura metal); Bhang (Cannabis sativa); Madhuyashti (Glycyrrhiza glabra); Nagavalli (Piper betel) and Shalamali (Salmalia malbarica). Literally the word Aphrodisiac (Vrisya) denotes, the drugs, which potentiate sexual vigor or promote artava (ovarian parameters) or both. Aphrodisiac (Vrisya) drugs are those, which can enhance the oogenesis and sexual vitality in females. The Physiology of female sexual act and oogenesis are interpreted with aphrodisiac (Vrisya) Karma, in connection to this, their pathological aspects which is Vandhyatva (female infertility) are dealt in detail with their respective management. Loss of artava is the fore most characteristics of Vandhyatva (infertility), which is seen in Ovarian Cancer. As it includes multiple groups of symptoms, single drug formulations might cover only a fraction of the treatment, hence the search for a group of drugs, particularly, such a group of drugs which are having aphrodisiac (Vrisya) anti oxidant (Rasayana) and other multimodal pharmacological actions might be highly beneficial in changing the quality of life. Such formulations, being very beneficial in symptoms arising due to "Tridosha vitiation" (mainly vata) have been selected for the present study.

**Materials & Methods:**

In this review, Ayurvedic fundamentals and Modern counterpart that includes Vrishya (aphrodisiac) and Rasayana (anti oxidant) effect; Rasapanchaka (Rasa, Guna,Virya,Vipaka, Prabhava) of the formulation; Anti tumor mechanism like inducing apoptosis in tumor cells, anti-proliferation, arrest cell cycle, anti angiogenic, anti metastasis activity of herbal ingriedients and Nanodrug delivery system, in terms of Ayurvedic biological nano particlals that may affect the progression of cancer, are
critically analyzed. For this, Compilation and tabulation of properties of *Pushpadhanwa rasa* like aphrodisiac activity (*Vrisya* = which potentiate sexual vigor or promote artava or both), Garbhodasahara (regularizing the female hormones) activity, *Rasayana* (anti oxidant) activity present in *Jangama* (animal), *Audhbiha* (Pertaining to plants), and *Parthiva* (Pertaining to Earth) *dravyas* in the pharmaceutical processing of *Pushpadhanwa rasa* has been compiled from *Charak samhita, Sushruta samhita* and *Rasashastriya* literature. Compilation & tabulation of *Rasa Panchak* (Pharmacodynamics) viz. *Rasa* (taste), *Guna* (quality), *Virya* (Bio potency) *Vipaka* (drug metabolism), action on doshas were also compiled from relevant sources and tabulated. References from various journals are collected for various mechanism involved for their anti tumor activity. The tabulated data is then analyzed critically.

**Results:**

Analysis of total 31 different ingredients of *Jangama* (animal), *Audhbiha* (Pertaining to plants), and *Parthiva* (Pertaining to Earth) origin present in the pharmaceutical processing of *Pushpadhanwa rasa* have been made with their role in accordance with Ayurvedic perspective and recent researches undergone.

**Discussion:**

*Pushpadhanwa rasa* can be an option as a palliative therapy for the patients suffering from Ovarian cancer. The formulation has been clinically tested for its role in regression of cyst size in patients of PCOD\(^{[17]}\). Not only this, it is also proved to be effective in psychological imbalances cognitive behavioural therapy suffering from PCOD\(^{[18]}\). *Saddhatwamtaka Sharira* needs a preparation for ovarian cancer which found to interfere with mitosis, DNA synthesis and the DNA repair system.

Formulations like *Pushpadhanwa Rasa*, which may involved mechanisms like apoptosis (form of programmed cell death), anti proliferative (prevent or retard the spread of cells), cell cycle arrest (ensure proper division of the cell.), angiogenic inhibitor (substance that inhibits the growth of new blood vessels), anti metastasis (substance that inhibits the spread from an initial or primary site to a different or secondary site within the host’s body), anti oxidant (compounds that inhibit oxidation), cytotoxicity (quality of being toxic to cells), Cellular penetration, Catalytic (process of increasing the rate of a chemical reaction), anti tumour, Inhibitors of Fatty acid synthesize activity, Inhibition of growth of tumour cell in ovarian and other reproductive carcinoma may be helpful in improving the quality of life in ovarian cancer patients as shown in table no 2.

Ingredients of *Pushpadhanwa rasa* may play their role by acting on following mechanism:

**Apoptosis**

Apoptotic potential effect of Glycyrrhiza glabra is by restricting enzymes connected to cancer progression and enhancing cancer suppressor enzymes or Caspase-independent pathways may be involved in the apoptotic mechanism in inhibition of Endometrial, Ovarian HT-29 cancer cells\(^{[19]}\). Glycyrrhizin also induced apoptosis in cervical cancer cells by exerting mitochondrial depolarization, glycyrrhizin induced cell cycle arrest in G0/G1 phase of cell cycle\(^{[20]}\). Piper betel apoptotic potential effect by transient increase of mitochondrial derived reactive oxygen species followed by persistent increase of nitric oxide\(^{[21]}\). *Dhatura* metel promotes apoptosis of cancerous cells by the phenolic agents or by Loss of mitochondrial membrane potential, DNA fragmentation and nuclear chromatin condensation, strongly support the ability to induce the cancer cell apoptosis though the mitochondrial pathway\(^{[22]}\). *Cannabis sativa* to persuade apoptosis by means of or devoid of cell cycle arrest via mitochondrial pathway. Cannabinidiol present in cannabis sativa reduces mitochondrial membrane potential, triggers the translocation of BID to the mitochondria, the release of cytochrome c to the cytosol, and, ultimately, the activation of the intrinsic apoptotic pathway in breast cancer cells\(^{[23]}\). Cannabinidiol in *Cannabis sativa* increased the generation of reactive oxygen species (ROS), and ROS inhibition blocked the induction of apoptosis\(^{[24]}\).
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Anti proliferation activity of Glycyrrihiza glabra by activating JNK (c-Jun N-terminal kinase) signals in cancer cells. The (JNK) pathway is one of the major signaling cassettes of the mitogen-activated protein kinase (MAPK) signaling pathway functions in the control of a number of cellular processes, including proliferation, embryonic development and apoptosis. Cell cycle study showed that glycyrhizin induced cell cycle arrest in G0/G1 phase of cell cycle significantly reduced the cell viability of HeLa cells with a concomitant increase in nuclear condensation and DNA fragmentation. Three myrobalan suppressed proliferation independent of p53 status in cancer cells HCT116 and in HCCSCs (Human colon cancer stem cells). Three myrobalan also induced p53-independent apoptosis in HCCSCs as indicated by elevated levels of cleaved PARP. Three myrobalan suppressed protein levels of c-Myc and cyclin D1, key proteins involved in proliferation, and induced apoptosis through elevation of Bax/Bcl-2 ratio. Furthermore, triphala inhibited HCCSCs colony formation.

Anti - angiogenesis

Angiogenesis study indicates that mast cell infiltration can enhance carcinogenesis and they have also long been known to drive angiogenesis and tumour growth. Glycyrrihiza glabra has been studied for its Antiangiogenic potential. Triphala exerts its biological effectiveness in human colon cancer cells while self-regulating their p53 status. p53 is considered the “the guardian of the genome” and it plays a critical role in tumor suppression by inducing growth arrest, apoptosis, and senescence, as well as by blocking angiogenesis. Metastatic potential of Hydroxychavicol of Piper betel component effectively suppressed the adhesion of oral KB carcinoma cells to FN (Fibro nectin) and collagen, suggesting that the anti-carcinogenic effects of piper betel may involve the differential stages of tumor invasion and metastasis. Metastatic potential of zingiber officinalis showed that When ginger powder is dissolved in a solution containing ovarian cancer cultures, the mutant cells died. Immunostimulatory potential of bioactive fraction-10 from Dhatura stramonium that boosts the immune cells in breast cancer. Recent studies on three myrobalan showed significant decrease in MDA and increase in GSH & SOD in breast homogenate in breast cancer. Piper betel Extracts exhibit cytotoxic effect on the breast cancer cell line MCF-7. The cytotoxic effect of piper betel extract was through the formation of electrophilic metabolites—quinoine, quinoine methide, and imine methide—via the oxidative metabolism of piper betel.

Cytotoxic activity

Cytotoxic activity of Three myrobalan (Triphala) effective in cell lines like human (MCF-7) and mouse (S115) breast cancer cell line, a human osteosarcoma cell line (HOS-1), a human prostate cancer cell line (PC-3) and a nontumorigenic, immortalized human prostate cell line (PNT1A) by inhibiting the rate of cell proliferation and inducing cell death in breast cancer. Cell penetration effect of three myrobalan showed Nano size easily transported into cell nucleus and to specific target sites, Mild to moderated growth inhibitory activity on prostate cancer cell lines. Salmalia Malbarica showed Inhibitors of Fatty acid synthesize activity preferentially repress cancer cell proliferation and induce cancer cell apoptosis without affecting nonmalignant fibroblasts. The withonilides which are steroidal lactones present in the plant Dhatura metel have been reported to have a high anticancer activity against colorecto carcinoma (HCT-116) cell line. Ginger extract considerably reduced the important expression of NF kappa B and TNF-alpha in rats. Ginger can act as an anti-cancer and anti-inflammatory agent through inactivating NFkappaB in the course of the suppression of the pro-inflammatory TNF-alpha. Bee venom was correlated with an increase in...
in the levels of various proliferative and antiapoptotic gene products, including Bcl-2, cIAP-2, XIAP, iNOS, COX-2, and cPLA2, which are regulated by NFκB. Their immune histochemical examination of the tumor part by H&E, and the increase antigens adjacent to PCNA along with Ki-67 discoloration information revealed to facilitate bee venom inhibited tumor cell enlargement in a dose-dependent approach in ovarian cancer.[44]

**Biological Nano particles and Bhasma**

Bhasma are claimed to be biologically produced nanoparticles, which are prescribed with several other medicines of Ayurveda.[43]. Realgar shows inhibition of growth and survival of tumour cell preventing tumour growth by transdermal delivery along with suppression of B16 cell proliferation. Nano particles size (~20nm) of Rasa sindura, with material characterisation of Single phase α-Hgs with free of Hgo and organic molecules,[45] Lauha bhasma of particle size Smaller than ~45 µm with sub seive size distribution range between 1.7 and 10.4 µm,[46] Vanga bhasma of particle size inbetween 12 to 53 nm showed higher levels of accumulation in tumours and high degree of penetration behaviour.[47]. Naga bhasma a nano-crystalline (~60 nm) lead sulfide form (Pb2+) associated with the organic contents showed high degree of penetration behaviour.[48]. Mercurial preparations aimed to restore the homeostasis thus reversing the proliferation of neoplastic cells in bone marrow.[49]. Rasasindura increases the efficacy of the contents of the medicine pushpadhanwa rasa by its catalytic effect.[50]. Abhrak Bhasma shows concentration dependent positive in vitro anticancer activity on prostate cancer cell lines. Anticancer activity of Abhrak Bhasma is in the order 100 Puti > 50 Puti > 20 Puti. Shataputi Abhrak Bhasma had maximum activity on prostate cancer cell lines almost equivalent to positive control drug adriamycin.[50]. Nano technologies can increase the potency of traditional small molecules of drugs in addition to potentially providing a mechanism for treating previously incurable diseases like cancer.[52].

**Rasa panchaka and its role**

Sweet taste (Madhura Rasa) is considered to be useful for the physiological tissue growth and regeneration of skeletal muscles (mamsa), adipose tissue (meda), and marrow and nervous tissue (majja). Bitter (Tikta rasa) phytonutrients (e.g., polyphenols, flavonoids, isoflavones, terpenes, and glucosinolates) appear to lower the risk of cancer by downregulation of glucose transporter 1 (GLUT1) and inhibition of glycolysis (via hexokinase 2, pyruvate kinase M2, and lactate dehydrogenase A), leading eventually to apoptosis. Several bitter compounds (chloroquine, quinidine, bitter melon extract, and cucurbitacins B and E) were described as inhibitors of tumour growth and proapoptotic agents in cancer cells.[53]. Based on relevant references from classical tests and modern tests of dravyaguna, Sweet taste (Madhura rasa) is seen in 15 dravyas, Astringent (Kashaya rasa) in 14 dravyas, Bitter taste (Tikta) in 12 dravyas, Katu (Pungent) rasa in 9 dravyas, and Amla (Sour) rasa in 5 dravyas as shown in table no 4. Among Guna (property), Rukshya (Dry) guna is found in 13 dravyas; Laghu (Light) in 10 dravyas; Guru (Heavy) in 8 dravyas; Snigdha (Uncitous) in 7 dravyas; and Tikshna (Sharp) in 6 dravyas. Vipaka (transformation) has been found as Katu (Pungent) in 15 dravyas and Madhura (Sweet) in 14 dravyas. The Virya (Bio potency) of most of the dravyas is Ushna (Hot) that is 18 in comparison to 9 in Sheeta (Cold) Virya dravyas. Bitter taste (Tikta rasa), Katu (Pungent) Vipaka, Ushna Virya and Laghu and Ruksha Gunas, so it acts as good Lekhana Dravya - a scraping agent on Apachit Meda. The drug Pushpadhawa rasa due to it Laghu guna, Katu (Pungent) rasa and Ushna Virya acts as deepana and pachana and regulates the Agni. Katu, Tikta, Kasaya Rasa (bitter, pungent, and astringent taste), Ushna Virya (e.g., hot biopotency), and Katu Vipaka (catabolic active metabolites), and herbs with dry, coarse, light, and sharp biophysical properties have significantly greater possibilities of producing anticancer effects.[54]. Vrisya activity is seen in 14 dravyas; Balya in 7 dravyas; Rasayana in 10 dravyas; Yoni Doshahara in 4 dravyas; and Putraprada in 2 dravyas as shown in table no 1 & 4. The formation of dhatu from rasa to sukra or artava is by the Sweet taste (Madhura rasa) and vipaka,
snigdha guna and sheeta Virya. These properties of the preparation of Pushpadhawa rasa act by Rasayana, Vrisya, Balya, Vayasthapaka, and Vata Samaka Karma. Various ingredients of Pushpadhanwa rasa are having Vata-Kapha Shamaka, Tridoshamakak properties, which help to bring the affected Doshas in normal level. As a result, the symptoms like ovarian cancer may subside.

Estrogens (E2) are concerned in the etiology of ovarian cancer. Estrogens make production and anti-estrogens slow down ovarian cancer growth in vitro and in vivo. Estrogen deprivation and estrogen receptor (ER) blockade cause cell cycle arrest in susceptible ovarian cancers by increasing the cell cycle inhibitor, p27. A better understanding of Estrogen signaling in ovarian cancer will permit refinement of combinations of targeted therapy like Rasasindura, Abhraka Bhasma, lauha bhasma & Vanga bhasma with standard hormonal agents to improve treatment[55]. Abhraka Bhasma and Loha Bhasma improve the excellence of Rasa and Rakta Dhatus which in turn improve the rest of Dhatus and thus improve the general situation of the patient. The Bhasmas are biologically formed nanoparticles and are in use along with milk, butter, honey, or clarified butter thus; this makes these elements simply assimilable, eliminating their injurious effects and enhancing their biocompatibility. The size and shape of nano drugs is directly propoertional to the activity in desired disease.

The different nano size and their morphology as shown in table no III is directly helped in increasing apoptosis[56]. Evidences shows bhasmas present in Pushpadhanwa Rasa are nearer to nano crystalline materials can be effective in ovarian cancer as shown in table no III.

Treatment aspect of Ayurveda is divided into four categories as Prakritisthapani chikitsa (health maintenance), Rasayana chikitsa, (restoration of normal function), Roganashani chikitsa (disease cure) and Naishthiki chikitsa (spiritual approach)[57]. Pushpadnwha Rasa may provide new avenues and paradigms for cancer by its biological active substances as well as targeting the involved mechanisms like apoptosis, anti proliferative, cell cycle arrest, angiogenic inhibitor, anti metastasis, anti oxidant, cytotoxicity, Cellular penetration, Catalytic, anti tumour, Inhibitors of Fatty acid synthesize activity, Inhibition of growth of tumour cell.

**Conclusion**

The therapeutic use of cancer chemotherapy in ovarian carcinoma has been restricted due to its non-specific or dose limiting cellular toxicity and development of multidrug resistance. In the direction of overcome this limitation various drug delivery system are being studied. Drugs mentioned in Pushpadhanwa rasa have multifarious pharmacological properties. From the above discussion it indicates that pushpadhanwa Ras may be used with a combination of anti cancerous drugs to enhance the quality of life in Ovarian Cancer.

**Table no. I Rasapanchaka (Pharmacodynamics) of Drugs used in the pharmaceutical processing of Puspadhanwa Rasa**

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Ingredient</th>
<th>Utility in preparing Pushpadhanwa rasa</th>
<th>Pharmacodynamic / Pharmacological application</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Madhu (Honey)</td>
<td>Anupana (vehicle) of pushpadhanwa Ras</td>
<td>Madhura, Kasaya, Ruksha, Seeta, Madhura, Vata bardhak, Vrisya, Virya bardhak, Antioxidan, Increase reproductive hormones, Fertility enhancer</td>
</tr>
<tr>
<td></td>
<td>Ingredient &amp; Properties</td>
<td>Samanya Shodhana</td>
<td>Detailed Actions</td>
</tr>
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<tr>
<td>3.</td>
<td>Goghrita (Cow’s clarified butter)</td>
<td>Anupana of Puspadhana rasa, Amritikarana of Lauha</td>
<td>Madhura, Visahara, Virya Bardhaka, Oja, Rasayana, Vrisya, General Debility</td>
</tr>
<tr>
<td>4.</td>
<td>Gomutra (Cow urine)</td>
<td>Samanya Shodhana of Naga, Vanga and Louha</td>
<td>Katu ( Pungent), Tiknsa, Usna, Katu ( Pungent), Pitta bardhaka, Pacana, Gulma, Sula, Virshya, Rasayana, Utility in ovarian cancer</td>
</tr>
<tr>
<td>6.</td>
<td>Til <em>Sesamum indicum</em> L. Taila</td>
<td>Samanya Shodhana of Naga, Vanga, Louha, Abhraka</td>
<td>Madhura, Kasaya, Sukhma, Guru, Usna, Madhura vipaka, Pitta bardhaka, Vrisya, Garbhasaya sodhaka, Bruhana, Yoni sula nasak, Balya, Anti oxidant</td>
</tr>
<tr>
<td>7.</td>
<td>Kanji (Rice gruel)</td>
<td>Samanya Shodhana of Naga, Vanga, Louha, Abhraka</td>
<td>Bhedi, Tiknsa, Ushna, Pitta , bardhaka, Sula nasaka, Garbhasaya Sodhaka, Vrisya, Enhancing LH secretion</td>
</tr>
</tbody>
</table>
|   | **Bibhitaki**  
*Terminalia bellirica* (Gaertn.) Roxb. | Visesa shodhana of Louha, Abhraka | Kashaya, Ruksha, Laghu |
|---|---|---|---|
| 11 | **Nimbu**  
*Citrus medica* L. | Marana of vanga bhasma, Trividha louha paka, Abhraka amruti karana | Ushna, Madhura, Kapha pitta nasaka, Balya, Amla, Laghu, Anusna, Madhura, Pitta bardhaka, Deepana, Pachana, Pradara, Atyartava, Garbhasrava, Yoni vishodhana |
| 12 | **Adraka**  
*Zingiber officinale* Roscoe | Shodhana of Manashila | Katu (Pungent), Tikshna, Rukshya, Guru, Ushna, Madhura, Kapha vata nasak, Hridya, Vrisya, Increases the secretion of melatonin and serotonin phytochemicals |
| 13 | **Arka**  
*Calotropis procera* (Aiton) Dryand.  
*Calotropis gigantea* (L.) Dryand. | Marana of Abhraka bhasma | Katu (Pungent), tikta, Laghu, Ruksha, Tikshna, Sara, Ushna, Katu (Pungent), Vata bardhak, Balya, Rasayana, Increase the plasma secretion levels of LH & FSH, Immuno modulator |
| 14 | **Vata**  
*Ficus indica* Willd. | Bhavana dravya of Rasasindoora | Kasaya, Madhura, Rukshya, Seeta, Katu (Pungent), Kapha Pitta nasak, Yonidoshanasaka, Vrisya Putradam, Garbhakara, Vandhyanasaka, anti oxidant activity, Estrogenic activity |
| 15 | **Haridra**  
*Curcuma longa* L. | Visesa shodhan Of Vanga | Katu (Pungent), Tikta, Laghu, Rukshya, Ushna, Vipaka Katu(Pungent), Kaphavatahara, Garbhastapaka, Garbhasaya raktata, Aphrodisiac, Menorrhagia |
| 16 | **Chincha**  
*Tamarindus indica* L. | Jarana dravya for Naga & Vanga bhasma | Amla, Madhura, Laghu, Ruksha, Ushna, Katu(Pungent), Kaphavata nasak, Hridya, Swelling on the breast, Anti oxidant |
| 17 | **Aswatha**  
*Ficus religiosa* L. | Jarana dravya for Naga & Vanga bhasma | Kasaya, Madhura, Rukshya, Guru, Seeta, Katu(Pungent), Kaphapittahara, Yoni vishodhana, Rasayana, Vrishya, Balya. |
| 18 | **Dhattura**  
*Datura metel* L. | Bhavana dravya of pushpadhana-va Ras | Madhura kasaya, Tikta, Guru, Tikshna, Balya, Rasayana |
<table>
<thead>
<tr>
<th></th>
<th><strong>Bhanga</strong> Cannabis sativa L.</th>
<th><strong>Bhavana dravya of pushpadhanwa Ras</strong></th>
<th><strong>Ruksha, Ushna, Katu (Pungent), Kapha Vatahara, Garbhasaya sankocaka, Vajikarana, Rasayana and Vajikrana Garbhadhana, Vandhya</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>20.</td>
<td><strong>Yastimadhu</strong> Glycyrrhiza glabra L.</td>
<td><strong>Bhavana dravya of Pushpadhanwa Ras</strong></td>
<td><strong>Madhura, Tikta, Guru, Snigdha, Seeta, Katu (Pungent), Tridosha hara, Balya Rasayana</strong></td>
</tr>
<tr>
<td>21.</td>
<td><strong>Salmali</strong> Salmalia malabarica (DC.) Schott &amp; Endl</td>
<td><strong>Bhavana dravya of pushpadhanwa Ras</strong></td>
<td><strong>Madhura, Kasaya, Pichilla, Guru, Seeta, Madhura, Pitta Vatahara, Brihana, Rasayana Balya, Rasayana, Vrisya, Garbhasaya Chutihara.</strong></td>
</tr>
<tr>
<td>22.</td>
<td><strong>Nagavalli</strong> Piper betle L.</td>
<td><strong>Bhavana dravya of pushpadhanwa Ras</strong></td>
<td><strong>Katu (Pungent), Tikta, Kasaya, Laghu, Tikshna, Ushna, Katu (Pungent), Vata hara, Srama nasaka, Vrisya, Rasayana, Putraprad, Pragyabodhi, Dhatubardhaka</strong></td>
</tr>
<tr>
<td>23.</td>
<td>Rasa Sindoor (Red sulphide of Mercury)</td>
<td><strong>Preparation for Rasasindoora</strong></td>
<td><strong>Sadrasa, Snigdha, Guru, Ushna, Madhura, Tridosha nasaka, Vrisya, Balya, Rasayana</strong></td>
</tr>
<tr>
<td>24.</td>
<td>Shuddha Gandhaka (Purified/processed Sulphur)</td>
<td><strong>Preparation for Rasasindoora</strong></td>
<td><strong>Madhura, Snigdha, Sara, Ushna, Katu (Pungent), Tridosha Nasak, Rasayana, Virya Vridhi.</strong></td>
</tr>
<tr>
<td>25.</td>
<td>Shuddha Manashila (Purified/processed Realgar)</td>
<td><strong>Marana dravya of Naga bhasma</strong></td>
<td><strong>Tikta, Katu (Pungent), Ushna, Vatakapha nasak, Sarbasrestha Rasayana.</strong></td>
</tr>
<tr>
<td>26.</td>
<td>Shuddha Haritala (Purified/processed Orpiment)</td>
<td><strong>Marana dravya of Vanga bhasma</strong></td>
<td><strong>Katu (Pungent), Snigdha, Kasaya, Snigdha, Ushna, Katu (Pungent), Kapha nasak, Virya Vridhikara</strong></td>
</tr>
<tr>
<td>27.</td>
<td>Naga bhasma (Calcined Lead)</td>
<td><strong>Preparation of Puspadhanwa rasa</strong></td>
<td><strong>Tikta, Laghu, Sara, Rukshya, Ushna, Katu (Pungent), Vata kapha nasak, Kamavala, Naga sata tulya balam.</strong></td>
</tr>
<tr>
<td>28.</td>
<td>Vanga bhasma (Calcined Tin)</td>
<td><strong>Preparation of Puspadhanwa rasa</strong></td>
<td><strong>Tikshna, Ushna, Rukshya, Laghu, Sara, Ushna, Katu (Pungent), Vata prakopa, Balya, Vrisya, Prajakara.</strong></td>
</tr>
<tr>
<td>29.</td>
<td>Abhraka Bhasma (Calcined Mica)</td>
<td><strong>Preparation of Puspadhanwa rasa</strong></td>
<td><strong>Guru, Snigdha, Seeta, Madhura, Vata Kapha Nasak, Pragyabodhi, Khya nasak, Vrisya, Ayusya, Putraprada</strong></td>
</tr>
</tbody>
</table>
Table no. II List of drugs present in *Puspadhanwa rasa* with their mechanism of action on cancer cells

<table>
<thead>
<tr>
<th>Name of the drug</th>
<th>Class</th>
<th>Mechanism of action</th>
<th>Cell line studied</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glycyrrhiza glabra</td>
<td>Apoptosis</td>
<td>Caspase-independent pathways</td>
<td>Endometrial Carcinoma, Ovarian Carcinoma.</td>
</tr>
<tr>
<td></td>
<td>Anti-proliferation</td>
<td>Activating JNK signals</td>
<td>Colon cancer Cells</td>
</tr>
<tr>
<td></td>
<td>Antiangiogenic</td>
<td>Regulates metastasis-relating protein MMP-9</td>
<td>Colon cancer</td>
</tr>
<tr>
<td></td>
<td>Anti oxidant</td>
<td>Scavenging activity against DPPH and nitric oxide</td>
<td></td>
</tr>
<tr>
<td>Piper betel</td>
<td>Apoptosis</td>
<td>Release of cytochrome C from mitochondria</td>
<td>Chronic Myeloid leukaemia</td>
</tr>
<tr>
<td></td>
<td>Anti metastasis</td>
<td>Inhibiting the growth</td>
<td>Colon cancer cells</td>
</tr>
<tr>
<td></td>
<td>Anti oxidant</td>
<td>Ferric reducing activity and Radical scavenging activities</td>
<td>Breast cancer</td>
</tr>
<tr>
<td></td>
<td>Cyto toxic activity</td>
<td>Extracts exhibit cytotoxic effect</td>
<td>Breast Cancer</td>
</tr>
<tr>
<td></td>
<td>Anti oxidant</td>
<td>Immunostimulatory potential of bioactive fraction-10</td>
<td>Breast Cancer</td>
</tr>
<tr>
<td></td>
<td>Apoptosis</td>
<td>Loss of mitochondrial membrane potential, DNA fragmentation and nuclear chromatin condensation</td>
<td>Breast cancer</td>
</tr>
<tr>
<td>Cannabis sativa</td>
<td>Cell cycle arrest</td>
<td>Via Mitochondrial pathway.</td>
<td>Cervical cancer cells</td>
</tr>
<tr>
<td></td>
<td>Apoptosis</td>
<td>Reduces Mitochondrial membrane potential.</td>
<td>Breast Cancer</td>
</tr>
<tr>
<td>Triphala (Three Myrobalan)</td>
<td>Cytotoxic</td>
<td>Inhibiting the rate of cell proliferation.</td>
<td>Breast cancer</td>
</tr>
<tr>
<td></td>
<td>Anti oxidant</td>
<td>Significant decrease in MDA and increase in GSH &amp; SOD</td>
<td>Breast cancer</td>
</tr>
<tr>
<td></td>
<td>Cellular penetration</td>
<td>Easily transported into cell nucleus and to specific target sites</td>
<td>Prostate Cancer</td>
</tr>
</tbody>
</table>
Adraka
(Zingiber officinalis Roscoe)

- Anti cancer
- Anti metastasis
- Inactivating NF kappa B
- Inhibition of NF-kB
- Liver Cancer
- Ovarian Cancer

Rasa Sindoor
( Red sulphide of Mercury)

- Catalytic
- Increase the efficacy of the contents of the medicine.

Manahshila
( Realger)

- Inhibition of growth
- Suppression of B16 cell
- Anti tumour effect
- Inhibiting DNA synthesis.

Honey

- Cyto toxic effect
- Increase in the levels of various proliferative and antiapoptotic genes

Table no. III List of Biological Nano Particle ~Bhasma present in Pushpadhanwa rasa

<table>
<thead>
<tr>
<th>Name of the Nano bhasma</th>
<th>Analysis reported</th>
<th>Nano dimensional Partile size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rasa Sindura (Red sulphide of Mercury)</td>
<td>Single phase α-Hgs, Free of Hgo and organic molecules</td>
<td>Nano particles size (~20nm)</td>
</tr>
<tr>
<td>Lauha Bhasma (Calcined Iron)</td>
<td>Irregular shaped aggregates.</td>
<td>Nano dimensional particles (~28nm) Smaller than ~45 µm with sub sieve size distribution range between 1.7 and 10.4 µm</td>
</tr>
<tr>
<td>Vanga Bhasma (Calcined Tin)</td>
<td>Agglomerised</td>
<td>12 to 53 nm</td>
</tr>
<tr>
<td>Naga Bhasma (Calcined Lead)</td>
<td>Agglomerised</td>
<td>~60 nm</td>
</tr>
</tbody>
</table>

Table no. IV Rasa panchaka (Pharmacodynamics) of Pushpadhanwa Rasa

<table>
<thead>
<tr>
<th>Rasa (Taste)</th>
<th>Number</th>
<th>Guna (Property)</th>
<th>Number</th>
<th>Vipaka (Final transformation)</th>
<th>Number</th>
<th>Virya (Biopotency)</th>
<th>Number</th>
<th>Dosaha prabhav ()</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Madhura (Sweet)</td>
<td>15</td>
<td>Rukshya (Dry)</td>
<td>13</td>
<td>Katu (Pungent)</td>
<td>15</td>
<td>Ushna (Hot)</td>
<td>18</td>
<td>Tridosha Shamak</td>
<td>6</td>
</tr>
<tr>
<td>Kasaya (Astringent)</td>
<td>14</td>
<td>Laghu (Light)</td>
<td>10</td>
<td>Madhura (Sweet)</td>
<td>14</td>
<td>Sheeta (Cold)</td>
<td>9</td>
<td>Kapha Pitta Shamak</td>
<td>4</td>
</tr>
<tr>
<td>Tikta (Bitter)</td>
<td>12</td>
<td>Guru (Heavy)</td>
<td>8</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>Kapha Vata Shamak</td>
<td>7</td>
</tr>
<tr>
<td>Katu (Pungent)</td>
<td>9</td>
<td>Snigdha (Unctuous)</td>
<td>7</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>
References


