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FERANIA TABLETS; Strengthens and supports immune system in Cancer

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	Abstract
Published on: 16 Dec 2023	<p>Cancer is hyperproliferative disorder that involves transformation, dysregulation of apoptosis, proliferation, invasion, angiogenesis and metastasis Cancer is one of the major threats of modern life and is considered as the second cause of death after myocardial infarction. Millions of people every year die with different types of cancer despite tremendous efforts to find methods of control and cure. Although great advances were made in modern medical science to control disease but many diseases like cancer are not yet curable fully. The underlying mechanism leading up to cancer are still unknown and cancer remains a mystery disease. Some oncologists themselves claim that cancer is not a disease, the anaerobic cell growths are meant to absorb the toxins which kill the patients. However, by surgery, chemotherapy and radiotherapy we destroy the protective mechanism and metastasis from one organ to other organ is common, To find out newer, safe and effective therapeutics, scientists are evaluating some medicinal plants and herbs which are a rich source of a variety of chemicals with nutritive and therapeutic properties. World-over the pharmaceutical companies and research organizations are focusing on the vast untapped potential of herbs as potent drugs. Millions of people die every year with different types of cancer such as lung cancer and mesothelioma from inhaling asbestos fibers and tobacco smoke, or leukemia from exposure to benzene at their workplaces. In the last century, great advances were made in modern medical system in cure and prevent of this disease. However, success rates are very low. Withania somnifera (WS) has been used as traditional medicine for decades for the treatment of various ailments. The various parts of WS and its constituents are effective in prevention and treatment of different kinds of cancer like colon cancer, lung cancer, blood cancer, skin cancer, breast cancer, renal cancer, fibrosarcoma, prostate cancer, pancreatic cancer. We are conducting clinical studies to prove the efficacy of WS in prevention and treatment of different forms of cancer including prostate and lung cancers, especially in last stages, and this wonder medicinal herb is found to be beneficial in many patients. Based on these facts a mono herbal formulation developed by R & D cell of LACTONOVA NUTRIPHARM(P) LTD.ferania tablets from withania somnifera extract contains standardized 5% withanolides.</p>
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	<p>Keywords: Withania somnifera, withaferin A, colon cancer, lung cancer, blood cancer, skin cancer, breast cancer, renal cancer, fibrosarcoma, prostate cancer, pancreatic cancer.</p>

INTRODUCTION

Cancer is hyperproliferative disorder that involves transformation, dysregulation of apoptosis, proliferation, invasion, angiogenesis and metastasis. [1] Millions Of people suffer from various kinds of cancer and die every year with cancers such as lung cancer and mesothelioma from inhaling asbestos fibers and tobacco smoke or leukemia from exposure to benzene at their workplaces are increasing day by day. [2] Withaferin A (WA), a withanolide derived from this medicinal plant, has been reported for its anti-tumorigenic activity against various cancer cells. [3] *Withania somnifera* (WS) flowers are small and green, while the ripe fruit is orange-red and has milk-coagulating properties. [4] The roots of WS are mainly used for medicinal purposes. It is cultivated in many of the drier regions of India such as Manasa, Neemuch, and Jawad tehsils of the Mandsaur District of Madhya Pradesh, Punjab, Sind, and Rajasthan. [4] The active ingredients of WS are alkaloids (isopelletierine, anaferine, cuscohygrine, anahygrine, etc.), steroidal lactones (withanolides, withaferins) and saponins. [5] Saponins and acylsterylglucosides in *Ashwagandha* are anti-stress agents. Active principles of *Ashwagandha*, for instance the saponins VII–X and Withaferin-A, have been shown to have significant anti-stress activity against acute models of experimental stress. [6] Many of its constituents support immunomodulatory actions. [7] The aerial parts of WS yielded 5-dehydroxy withanolide-R and withasomniferin-A. [8] This review presents the scientific and clinical studies conducted to evaluate the efficacy of WS in prevention and treatment of various kinds of cancer.

Cancer is one of the major threats of modern life and is considered as the second cause of death after myocardial infarction. Millions of people every year die with different types of cancer despite tremendous efforts to find methods of control and cure. Although great advances were made in modern medical science to control disease but many diseases like cancer are not yet curable fully. The underlying mechanism leading up to cancer are still unknown and cancer remains a mystery disease. Some oncologists themselves claim that cancer is not a disease, the anaerobic cell growths are meant to absorb the toxins which kill the patients. However, by surgery, chemotherapy and radiotherapy we destroy the protective mechanism and metastasis from one organ to other organ is common. Andreas Moritz, 2008 in his book “CANCER IS NOT A DISEASE” has quoted experienced oncologist Professor, Dr. Jones who says “My studies have proven conclusively that cancer patient who refuse chemotherapy and radiation actually live up to four times longer than treated cases, including untreated breast cancer cases”. [38] To find out newer, safe and effective therapeutics, scientists are evaluating some medicinal plants and herbs which are a rich source of a variety of chemicals with nutritive and therapeutic properties. World-over the pharmaceutical companies and research organizations are focusing on the vast untapped potential of herbals as potent drugs. WS is one of the most important herbs of Ayurveda (the traditional system of medicine in India) used for millennia as a Rasayana for its wide ranging health benefits. It is known as “Sattvic Kapha Rasayana” Herb. [39] It is an ingredient in many formulations prescribed for a variety of musculoskeletal conditions (e.g., arthritis, rheumatism), and as a general tonic to increase energy, improve overall health and longevity, and prevent disease in athletes, the elderly, and during pregnancy. [40-41] WS is well known for its other biological activities like adaptogenic/anti-stress [42-44], immunomodulatory [45-46], anti-ageing [42-44, 47-48], anti-fatigue [42-44, 49], antioxidant [47, 50], anti-parkinsonism [51-52], antiulcerogenic [43-44], anti-tumors/adenomas [14, 35, 53], support healthy thyroid function [54]. The results of the studies described above demonstrate that WS and its chemical ingredients are effective in prevention and treatment of different kinds of cancer like colon cancer, lung cancer, blood cancer, skin cancer, breast cancer, renal cancer, fibrosarcoma, prostate cancer and pancreatic cancer. At the Lactonova oncology research cell, Hyderabad also we are conducting studies to prove the efficacy of WS in prevention and treatment of different forms of cancer including prostate, dermatofibrosarcoma, breast cancer, fibroids of uterus, squamous cell carcinoma of penis etc. especially in last stages, and this wonder medicinal herb is found to be beneficial in many patients. Cancer is one of the most dreaded diseases of the 20th century and spreading further with continuance and increasing incidence in 21st century. In the United States, as the leading cause of death, it accounts for 25% of all the deaths in humans presently. It is considered as an adversary of modernization and advanced pattern of socio-cultural life dominated by Western medicine. Multidisciplinary scientific investigations are making best efforts to combat this disease, but the sure-shot, perfect cure is yet to be brought into world medicine. Recently, a greater emphasis has been given towards the researches on complementary and alternative medicine that deals with cancer management. In the last century, great advances were made in modern medical system in cure and prevent of this disease. However, success rates are very low. *Withania somnifera* (WS) has been used as traditional medicine for decades for the treatment of various ailments. The various parts of WS and its constituents are effective in prevention and treatment of different kinds of cancer like colon cancer, lung cancer, blood cancer, skin cancer, breast cancer, renal cancer, fibrosarcoma, prostate cancer, pancreatic cancer. clinical studies have proved the efficacy of WS in prevention and treatment of different forms of cancer including prostate and lung cancers, especially in last stages, and this wonder medicinal herb is found to be beneficial in many patients. We have some cases of lung cancer that were refused modern therapy and recovered clinically and radiologically with therapy of *Ashwagandha*. Clinical studies suggest its use as anti-tumor and immunomodulatory agent in sarcoma, brain cancer, uterine

tumor, fibroids and other tumors including endodermal carcinoma. Therefore, this medicinal herb WS alone can be used as alternative medicine in the treatment of cancer patients or it can also be used as adjunct/ complimentary medicine along with chemotherapy or radiotherapy to patients. As the causative factors development of cancerous conditions can be multifactorial eg. stress- physical, chemical, biological and emotional, viral infection like Herpes cause several time more cancer of bladder, low immune syndrome plays major role in spread and causation of cancer, environmental chemical toxins, allopathic drugs, pesticide infected food with heavy metals and some not properly developed metallic preparation of Ayurvedic or other Folk Medicine can be a causative factor, leave aside genetic processes of the Individual for the development of the risk of cancer. If we look in the properties of WS like adaptogen/ anti-stress agent, immunomodulator, antioxidant (reducing free radical damage, anabolic effect, improving resistance of body, reducing fatigue and detoxificant effects, we are inclined to suggests that WS works through all above mechanisms in controlling the dreaded cancer, rather than its effect on stopping the cell division. As during radio and chemotherapy body's natural normal cells are also killed and low immunity develops, WS helps prevent these adverse effects of both and helps patients better recovery and life styles. However, multicentric long term clinical studies by oncologists, although deviated from their routine, must be carried out on WS to prove our contention

COMPOSITION OF FERANIA TABLETS

Each tablet contains-Withania somnifera extract 500 mg (standardized to 5% withanolides)

Mechanism of action

The extensive clinical studies conducted show that WS has capability to produce beneficial effects in variety of cancer patients. WS modulates the immune response, increasing the expression of T-helper1 (Th1), elevating IgG2a- mediated humoral immune responses, cytokines, as well as CD4 and CD8 counts, and natural killer (NK) cell activity . In addition, the aqueous suspension of WS shows anti-inflammatory and immunosuppressive effects by inhibiting the complement system, mitogen- induced lymphocyte proliferation and delayed type hypersensitivity (DTH) in rats . Several studies also support Withania's ability to increase circulating cortisol, decrease fatigue, increase physical performance, and decrease refractory depression in animals subjected to stress

CLINICAL STUDY REPORTS

Several clinical studies have been conducted to evaluate the effectiveness of Ferania tablets in prevention and treatment of different kinds of cancer which are highlighted below-

Role of Ferania tablets in Colon Cancer

Muralikrishnan et al (2010) observed that *W. somnifera* significantly altered the level of leucocytes, lymphocytes, neutrophils, immune complexes and immunoglobulins (Ig) A, G and M in experimental colon cancer in mice induced by azoxymethane. The results of this study revealed that azoxymethane induced colon cancer and immune dysfunction was controlled by *W. somnifera*. [9] In another study, Muralikrishnan et al (2010) observed that WS decreased the activities of TCA cycle key enzymes such as isocitrate dehydrogenase (ICDH), succinate dehydrogenase (SDH), malate dehydrogenase (MDH), and alpha-keto glutarate dehydrogenase (alpha-KGDH) in colon cancer bearing animals. [10] Koduru et al (2010) observed that the anticancer activity of Withaferin-A (WA), which exhibits potential for further development for targeted chemotherapy and/or chemoprevention strategies in the context of colon cancer. [11] Further, studies were conducted to isolate twelve withanolides such as withaferin A, sitoindoside IX, 4-(1- hydroxy-2, 2-dimethylcyclopropanone)-2, 3-dihydrowithaferin A, 2, 3-dihydrowithaferin A, 24, 25-dihydro-27- desoxywithaferin A, physagulin D (1-->6)-beta-Dglucopyranosyl- (1-->4)-beta-D-glucopyranoside, 27-O-betaD-glucopyranosylphysagulin D, physagulin D, withanoside IV, and 27-O-beta-D-glucopyranosylviscosalactone B, 4, 16- dihydroxy-5beta, 6beta-epoxyphysagulin D , viscosalactone B (12) from the leaves of this species. Compounds 1-12 and diacetylwithaferin A were tested for their antiproliferative activity on NCI-H460 (Lung), HCT-116 (Colon) and SF-268 (Central Nervous System; CNS) and MCF-7 (Breast) human tumor cell lines The inhibitory concentration to afford 50% cell viability (IC50) for these compounds was determined by MTT (3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyltetrazolium bromide) assay. Withaferin A and its derivatives exhibited inhibitory concentrations (50%) ranging from 0.24 ± 0.01 to $11.6 \pm 1.9 \mu\text{g/ml}$. Viscosalactone B (12) showed the 50% inhibition at concentrations ranging from 0.32 ± 0.05 to $0.47 \pm 0.15 \mu\text{g/ml}$ whereas its 27-O-glucoside derivative (10) exhibited IC50 between 7.9 ± 2.9 and $17.3 \pm 3.9 \mu\text{g/ml}$. However, Physagulin D type withanolides showed either weak or no activity at $30 \mu\text{g/ml}$. Therefore, incorporation of withanolides in the diet may prevent or decrease the growth of tumors in human. [12] The study conducted to evaluate in vitro cytotoxicity in 50% ethanol extract of root, stem and leaves of WS against five human cancer cell lines of four different tissues i.e. PC-3, DU-145 (prostrate), HCT-15 (colon), A-549 (lung) and IMR-32 (neuroblastoma) demonstrated that Root, stem and leaves extracts showed cytotoxicity activity ranging 0-98% depending on the cell lines but maximum activity was found in 50%

ethanol extract of leaves of WS. Ethanol extract of leaves obtained from treatments T2, T3, T4 and T5 showed strong activity against PC-3 and HCT-15 with 80-98% growth inhibition, while the 50% ethanol extract of leaves from T1 treatment showed a minimum of 39% and T3 treatment showed a maximum of 98% growth inhibition against HCT-15. [13]

Role of Ferania tablets in Lung Cancer

In vitro studies have shown that root extracts of WS exhibited cytotoxic properties against lung, colon, central nervous system, and breast cancer cell lines. [12] WS Dunal has been shown to possess tumor preventing activity against urethane induced lung- adenomas in adult male albino mice by inducing a state of nonspecific increased resistance (Adaptogen) and immunostimulant properties. [14] Pharmacokinetic studies in mice revealed that WFA reaches peak concentrations up to 2 μ M in plasma with a half-life of 1.36 h following a single 4 mg/kg dose. In a breast cancer metastasis mouse model, WFA showed dose-dependent inhibition of metastatic lung nodules and induced vimentin ser 56 phosphorylation, with minimal toxicity to lung tissue. [15] Recent studies showed that ashwagandha extract inhibited the growth of human breast, lung, and colon cancer cell lines in the laboratory. This inhibition was comparable to that achieved with the common cancer chemotherapy drug doxorubicin (Caelyx®, Myocet®). In fact, researchers reported that withaferin A, a specific compound extracted from ashwagandha, was more effective than doxorubicin in inhibiting breast and colon cancer cell growth. [12,16] In another study, the combination of paclitaxel with *W. somnifera* could effectively treat the benzo(a)pyrene-induced lung cancer in mice by offering protection from reactive oxygen species damage and also by suppressing cell proliferation. [17] In another study and Based on the data, the carcinogen as well as the paclitaxel, affects the immune system, the deleterious effects on the immune system is more reversible and more controllable by *W. somnifera* (L.) Dunal. These results show the immunomodulatory activity of *W. somnifera* (L.) Dunal extract, which is a known immunomodulator in indigenous medicine. [18] WS has been found to be beneficial in lung cancer. [13, 19]

Role of Ferania tablets in Blood Cancer

Malik et al [20] observed that withaferin A major chemical constituents of WS, primarily induces oxidative stress in human leukemia HL-60 cells and in several other cancer cell lines and the results of these studies demonstrate that withaferinA induced early ROS generation and mitochondrial dysfunction in cancer cells trigger events responsible for mitochondrial -dependent and -independent apoptosis pathways. Another study demonstrated that Withanolide D (C4 β -C5 β ,C6 β -epoxy-1-oxo-,20 β , dihydroxy-20S,22Rwitha-2,24-dienolide; WithaD), a pure herbal compound isolated from WS has capability to induce apoptosis in a dose and time dependant manner both in myeloid (K562) and lymphoid (MOLT-4) cells being nontoxic to normal lymphocytes and control proliferative cells and One of the Withanolides, WithaD enhances the ceramide accumulation by activating N-SMase 2, modulate phosphorylation of the JNK and p38MAPK and induced apoptosis in both myeloid and lymphoid cells along with primary cells derived from leukemia patients. Taken together, this pure herbal compound (WithaD) may be considered as a potential alternative tool with additive effects in conjunction with traditional chemotherapeutic treatment, thereby accelerate the process of conventional drug development. [21] Oza et al [22] studied anticancer properties of highly purified Lasparaginase from *Withania somnifera* L. against acute lymphoblastic leukemia and observed that *W. somnifera* L. proved to be an effective and a novel source of Lasparaginase.

Role of Ferania tablets in Skin Cancer

Scientific studies conducted in mice revealed that the roots of WS have capability to inhibit Forestomach and skin carcinogenesis in mice. [23] Mathur et al [24] observed that 1- oxo-5beta; 6beta-epoxy-witha-2-enolide a chemical constituent isolated from the root of WS has the potential for acting as an effective agent to prevent the incidence of skin carcinoma induced by ultra violet radiation. The chemopreventive effect of WS hydroalcoholic root extract (WSRE) on 7,12-dimethylbenz[a]anthracene (DMBA)- induced skin cancer was investigated in Swiss albino mice and the results of the study revealed a significant decrease in incidence and average number of skin lesions in mice compared with DMBA alone at the end of Week 24. Further, a significant impairment was also noticed in the levels of reduced glutathione, malondialdehyde, superoxide dismutase, catalase, glutathione peroxidase, and glutathione Stransferase in skin lesions of DMBA-treated control mice compared with vehicle-treated mice. These parameters returned to near normal in WSRE to DMBA-treated mice. The present study reflects that WRSE possesses potential chemopreventive activity in this experimental model of cancer and the chemopreventive activity may be linked to the antioxidant/free radical-scavenging constituents of the extract. [25] Davis and Kuttan (2001) observed that administration of an extract of WS reduced two stage skin carcinogenesis induced by DMBA (dimethyl benzanthracene) and croton oil. Enzyme analysis of skin and liver showed significant enhancement in antioxidant enzymes such as GSH, GST, Glutathione peroxides and Catalases in WS treated group when compared with the control. The elevated level of lipid peroxide in the control group

was significantly inhibited by WS administration. These studies indicate that WS could reduce the papilloma induced alterations by its antioxidant defense systems. [26]

Role of Ferania tablets in Breast Cancer

Leaf extract of WS has been shown to produce antiproliferative activity on MCF-7 (breast) human tumor cell lines. [13] Different Withanolides isolated from leaves of WS namely withaferin A, sitoindoside IX, 4-(1-hydroxy-2, 2-dimethylcyclopropanone)-2, 3-dihydrowithaferin A, 2, 3-dihydrowithaferin A, 24, 25-dihydro-27-desoxywithaferin A, physagulin D (1-->6)-beta-D-glucopyranosyl- (1-->4)-beta-D-glucopyranoside, 27-O-beta-D-glucopyranosylphysagulin D, physagulin D, withanoside IV, and 27-O-beta-D-glucopyranosylviscosalactone B, 4, 16-dihydroxy-5beta, 6beta-epoxyphysagulin D, viscosalactone B from the leaves of this species. Compounds 1-12 and diacetylwithaferin A and diacetylwithaferin A were shown to produce antiproliferative activity on MCF-7 (Breast) human tumor cell lines. [12] Withaferin A (WA), a vimentin cytoskeleton inhibitor, has been found to be a potent breast cancer antimetastatic agent and the anti-metastatic activity of WFA is, at least in part, mediated through its effects on vimentin and vimentin ser56 phosphorylation. [15] Withaferin A (WA), a promising anticancer constituent of Ayurvedic medicine plant WS, has been found to inhibit growth of MCF-7 and MDA-MB-231 human breast cancer cells in culture and MDA-MB-231 xenografts in vivo by causing apoptosis. In addition these studies indicate that WA functions as an antiestrogen, and the proapoptotic effect of this promising natural product is partially attenuated by p53 knockdown and E2-ER- α . [27] WS has been found to inhibit constitutive as well as interleukin-6 (IL-6)-inducible activation of signal transducer and activator of transcription 3 (STAT3), which is an oncogenic transcription factor activated in many human malignancies including breast cancer. The IL-6-stimulated activation of STAT3 conferred a modest protection against WA-mediated suppression of MDA-MB-231 cell invasion. The results of the study indicate that WA can trigger apoptosis and largely inhibit cell migration/invasion of breast cancer cells even after IL-6-induced activation of STAT3, which should be viewed as a therapeutic advantage for this agent. [28] A novel bioactive compound withanolide sulfoxide obtained from methanol extract of WS roots has been shown to suppress human tumor cell proliferation and its IC50 value against human breast (MCF-7) cancer cell lines in the range of 0.74-3.63 μ m. In addition, S-containing dimeric withanolides were also found to completely suppress TNF-induced NF- κ B activation when tested at 100 μ m. [29]

Role of Ferania tablets in Renal Cancer

Yang et al reported that the chemical constituent Withaferin A enhanced radiation-induced apoptosis in human renal cancer cells (Caki) cells through ROS generation, down-regulation of Bcl-2 and Akt dephosphorylation. [30] In another study, treatment of Caki cells with withaferin A induced a number of signature ER stress markers, including phosphorylation of eukaryotic initiation factor-2 α (eIF-2 α), ER stress-specific XBP1 splicing, and up-regulation of glucose-regulated protein (GRP)-78. In addition, withaferin A caused up-regulation of CAAT/enhancer-binding of homologous protein (CHOP), suggesting the induction of ER stress. Pretreatment with N-acetyl cysteine (NAC) significantly inhibited withaferin A-mediated ER stress proteins and cell death, suggesting that reactive oxygen species (ROS) mediate withaferin A-induced ER stress. Furthermore, CHOP siRNA or inhibition of caspase-4 activity attenuated withaferin A-induced apoptosis. Taken together, the present study provides strong evidence supporting an important role of the ER stress response in mediating withaferin A-induced apoptosis. [31]

Role of Ferania tablets in Fibrosarcoma

The studies conducted on organic extracts of selected plant species, used by Palestinian traditional healers to treat different illnesses and diseases, revealed that the extract from WS presented an IC50 value at 24 h of 150 and 60 microg/ml, on L929sA and MCF7 cells, respectively, while the extract from *Psidium guajava* L. (Myrtaceae) presented an IC50 value at 24 h of 55 μ g/ml on MCF7 cells. Other extracts examined, like *Laurus nobilis* L. (Lauraceae) and *Salvia fruticosa* M. (Labiatae), also displayed a remarkable activity. WS extract also exhibited the strongest NF κ B inhibitory activity. [32] The chemopreventive studies of a hydro-alcoholic extract of WS roots, against 20-methylcholanthrene induced fibrosarcoma tumours in Swiss albino mice revealed that WS extract (one week before injecting 20-methylcholanthrene and continued until 15 weeks thereafter) significantly reduced the tumour incidence, tumour volume and enhanced the survival of the mice, compared with 20-methylcholanthrene injected mice. The tumour incidence was also delayed in the treatment group when compared with 20-methylcholanthrene injected mice. A significant modulation of reduced glutathione, lipid peroxides, glutathione-S-transferase, catalase and superoxide dismutase in extract treated mice compared with 20-methylcholanthrene injected mice was also recorded. These studies indicate that chemopreventive activity of WS extract may be due to its antioxidant and detoxifying properties. [33] In another study, administration of an extract from the root of the plant *Withania somnifera* (20mg/dose/animal i.p) was found to inhibit the 20-methylcholanthrene induced sarcoma development in mice and increase the life span of tumour bearing animals and inhibit the lipid peroxide formation (152 nanomoles/mg protein)

Role of Ferania tablets in Prostate cancer

The study conducted to evaluate *in vitro* cytotoxicity in 50% ethanol extract of root, stem and leaves of WS against five human cancer cell lines of four different tissues i.e. PC-3, DU-145 (prostate), HCT-15 (colon), A-549 (lung) and IMR- 32 (neuroblastoma). Revealed that root, stem and leaves extracts showed cytotoxicity activity against ranging 0-98% depending on the cell lines but maximum activity was found in 50% ethanol extract of leaves of WS. Further, ethanol extract of leaves obtained from treatments T2, T3, T4 and T5 showed strong activity against PC-3 and HCT-15 with 80- 98% growth inhibition, while the 50% ethanol extract of leaves from T1 treatment showed a minimum of 39% and T3 treatment showed a maximum of 98% growth inhibition against HCT-15. [35]

Role of Ferania tablets in Pancreatic Cancer

The study conducted to investigate the efficacy and the mechanism of Hsp90 inhibition of Withaferin A (WA), a steroidal lactone occurring in WS, in pancreatic cancer *in vitro* and *in vivo* revealed that Withaferin A acts as a potent antiproliferative activity against pancreatic cancer cells *in vitro* (with IC₅₀ of 1.24, 2.93 and 2.78 μ) in pancreatic cancer cell lines Panc-1, MiaPaCa2 and BxPc3, respectively. The results of the study demonstrate that Withaferin A binds Hsp90, inhibits Hsp90 chaperone activity through an ATPindependent mechanism, results in Hsp90 client protein degradation, and exhibits *in vivo* anticancer activity against pancreatic cancer. [36]

DISCUSSION

Cancer is one of the major threats of modern life and is considered as the second cause of death after myocardial infarction. [37] Millions Of people every year die with different types of cancer despite tremendous efforts to find methods of control and cure. Although great advances were made in modern medical science to control disease but many diseases like cancer are not yet curable fully. The underlying mechanism leading up to cancer are still unknown and cancer remains a mystery disease. Some oncologists themselves claim that cancer is not a disease, the anaerobic cell growths are meant to absorb the toxins which kill the patients. However, by surgery, chemotherapy and radiotherapy we destroy the protective mechanism and metastasis from one organ to other organ is common. Here, Andreas Moritz, 2008 in his book “CANCER IS NOT A DISEASE” has quoted experienced oncologist Professor, Dr. Jones who says “My studies have proven conclusively that cancer patient who refuse chemotherapy and radiation actually live up to four times longer than treated cases, including untreated breast cancer cases”. [38] To find out newer, safe and effective therapeutics, scientists are evaluating some medicinal plants and herbs which are a rich source of a variety of chemicals with nutritive and therapeutic properties. World-over the pharmaceutical companies and research organizations are focusing on the vast untapped potential of herbals as potent drugs. WS is one of the most important herbs of Ayurveda (the traditional system of medicine in India) used for millennia as a Rasayana for its wide ranging health benefits. It is known as “Sattvic Kapha Rasayana” Herb. [39] It is an ingredient in many formulations prescribed for a variety of musculoskeletal conditions (e.g., arthritis, rheumatism), and as a general tonic to increase energy, improve overall health and longevity, and prevent disease in athletes, the elderly, and during pregnancy. [40-41] WS is well known for its other biological activities like adaptogenic/anti-stress [42-44], immunomodulatory [45-46], anti-ageing [42-44, 47-48], anti-fatigue [42-44, 49], antioxidant [47, 50], anti-parkinsonism [51-52], antiulcerogenic [43-44], anti-tumors/adenomas [14, 35, 53], support healthy thyroid function [54]. The results of the studies described above demonstrate that WS and its chemical ingredients are effective in prevention and treatment of different kinds of cancer like colon cancer, lung cancer, blood cancer, skin cancer, breast cancer, renal cancer, fibrosarcoma, prostate cancer and pancreatic cancer. At Lactonova oncowellness research cell, hyderabad also our review studies have proved the efficacy of ferania tablets in prevention and treatment of different forms of cancer including prostate, dermatofibrosarcoma, breast cancer, fibroids of uterus, squamous cell carcinoma of penis etc. especially in last stages, and this wonder medicinal herb is found to be beneficial in many patients. The clinical cases of lung cancer who have been refused modern therapy and recovered clinically and radiologically with therapy of Ashwagandha. [56] clinical studies suggest its use as anti-tumor and immunomodulator agent in sarcoma, brain cancer, uterine tumor, fibroids and other tumors including endodermal carcinoma. [55] Besides having an anticancer activity, it may also reduce the side effects of anticancer agents which invariable make the patient’s life miserable and reduce immunity. The extensive clinical studies have shown that WS has capability to produce beneficial effects in variety of cancer patients. We hypothesize that this medicinal herb has capability to prevent the proliferation of cancer cells or delay the progression of cancer due to its combined multi factorial properties as described above. It may have potential to eliminate various kinds of toxins causing proliferation of cancerous cells and acts as strong detoxifying agent. Therefore, this medicinal herb ferania tablet alone can be used as alternative medicine in the treatment of cancer patients or it can also be used as adjunct/ complimentary medicine along with chemotherapy or radiotherapy to patients.

Pharmacokinetics

Withania somnifera (WS) showed a significant modulation of immune reactivity in animal model. Combination therapy of WS and chemotherapy treatment with cyclophosphamide (CTX) mitigated many side effects rather than treating the mice with just CTX. Swiss mice treated with both both 25 mg/kg body weight CTX and an extract of powdered WS root at a dose of 20 mg IP experienced less leucopenia than those treated with CTX alone. Initially, both groups experienced a decrease in WBC count, but the group receiving treatment with both CTX and WS saw a normal increase of WBC count by day 15. By day 30, total WBC in the CTX and WS group reached 6,120 cells/mm³ compared to 3,270 cells/mm³ in the CTX-only group. Combination therapy with CTX and WS also resulted in a greater than two-fold increase in bone marrow cellularity.

Side Effects and Toxicity

Ferania tablet is generally safe when taken in the prescribed dosage range. Large doses have been shown to cause gastrointestinal upset, diarrhea, and vomiting.

Dosage

A typical dose of 1-2 tablets twice daily or as prescribed by health care practitioner or oncologist

Warnings and Contraindications

Large doses of ferania tablets may possess abortifacient properties; therefore, it should not be taken during pregnancy. Since ferania tablets acts as a mild central nervous system depressant, patients should avoid alcohol, sedatives, and other anxiolytics while taking ferania tablets .

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