A comprehensive review of anticancer properties of Withaferin-A: A key metabolite of *Withania somnifera*

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ABSTRACT

Withaferin-A, a member of the withanolides class, is an essential phytoconstituents of *Withania somnifera* (Ashwagandha). These are naturally occurring C28-steroidal lactone triterpenoids groupings. For several decades, Withaferin-A was in use for several decade to treat various disorders. Withaferin-A has demonstrated biological activities like anticancer, anti-inflammatory, anticonvulsant, anti-stress, neuroprotective cardio protective properties etc., Cancer is a progressive disease, which is one of the second leading causes of death. Despite massive efforts to develop a suitable therapy, the nature of the disease has restricted genuine achievement in discovering a better cancer cure. This review highlight the various anti-cancer properties of one of the key metabolite Withaferin – A.

Keywords: Withaferin-A, *Withania somnifera*, Cancer, Phytochemical, Cancer-therapy.

1. INTRODUCTION

Withania somnifera is a native plant. One of the major phytoconstituents of this plant is Withaferin-A, which has been used for more than a few decades for its therapeutic uses in treating various disorders. Several reports are available, but the exact mechanism of their anti-cancer properties is still unknown [1, 2]. Withaferin-A (WA) is obtained from the Ashwagandha of the Solanaceae family. They are frequently referred as Indian ginseng, Ashwagandha or Indian winter cherry [3, 4]. The mechanism of cancer growth suppression by Withaferin-A is caused by the target-specific nature of Withaferin-A against tubulin (inherent of microtubules). A remarkable decrease in the amount of b-tubulin was observed during Withaferin-A usage in the treatments [5]. Research was established to find the molecular functions that describe the anti-cancer properties of Withaferin-A.

Withaferin-A induces oxidative stress, which eventually determines the mitochondrial dysfunction and apoptosis in leukemia cells [6]. Also, Withaferin-A has shown various pharmacological activities which have anti-inflammatory, anti-stress, anti-tumor, anticonvulsant and neuroprotective effects. They are naturally formed C_{28}- steroidal lactone terpenoids [7]. Cancer, the fatal disease, has limited success in finding a suitable cure [8]. Even though researchers are finding a way to know all the molecular pathways of Withaferin-A to fight against the cancer-causing agents, they also came across the fact that they have therapeutic action towards cancer, some of them even show cancer preventive activities [9, 10].

The significant anti-cancer effects of this plant (Ashwagandha) are related to withanolides. Withaferin-A (4, 5, 6,22R) was the first anticancer compound isolated from the leaves of *Withania somnifera*. Withaferin-A is -4,27-dihydroxy-5,6-22,26-diepoxyergosta-2,24-diene-1,26-dione) [11]. The compound Withaferin-A is pictured in (**Error! Reference source not found.**). Here we provide a detailed and summarized review on Withaferin-A and its various decreasing types of cancer.

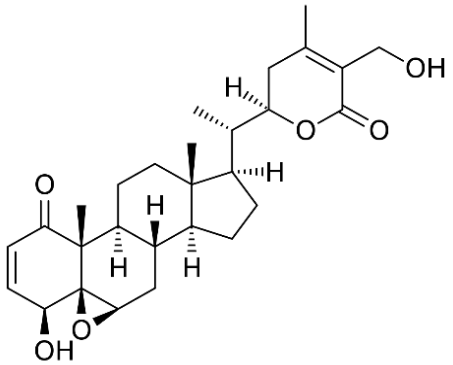

Fig. 1. Withaferin-A chemical structure

Withania somnifera, derived from Ashwagandha, has long been utilised in traditional medicine in numerous regions of the world. It belongs to Solanaceae family and spread across the globe. Out of known 23 species of Withania, only two of them, namely *Withania coagulans* and *Withania somnifera* have shown medicinal benefits. Withania species were studied extensively and chemicals such as alkaloids, tannin, steroidal lactones, flavonoids, etc., were found [9, 12]. The potential mechanisms of action for Withaferin-A are illustrated in **(Fig. 2).**

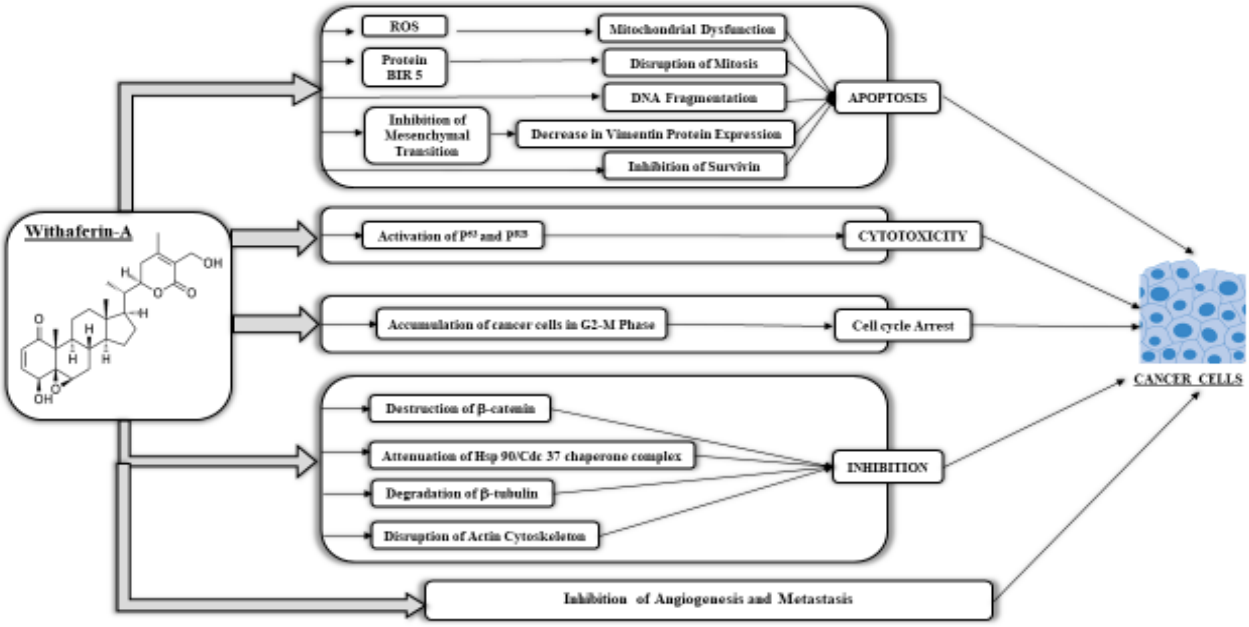

Fig. 2. The potential mechanism of Withaferin-A

It was one of the first groups of compounds isolated from this medicinal plant, and since then it has shown a high level of biological activity, which has opened various aspects of the chemical investigation and their structural features were thereby isolated [13]. Mounting evidence and cell and animal culture research reveal that Withania somnifera possesses anti-tumorigenic capabilities. The root extract experiment done in 1967 has shown lowered cancer incidence *in vivo*. This has led to increased research interest in Withania somnifera and the publication citation on Withaferin-A has noticed a subsequent increase [14, 15]. Even after the successes of selective anti-cancer therapies, disease, and drug rejection remain a drawback in cancer treatments.

It eventually increased interest in natural product discovery to find new pharmacophores for cancer immunotherapies [16]. It has anti-cancer activity applicable to cell cycle arrest caused by suppression of cyclin B1, p-Cdc2, Cdk2, cyclin A, HPV E6 and E7 on co-protein, gathering and elicitation of p53, reduction in the level of STAT3, gradual increase in the level of p21WAF1, significant increase in the p53 apoptotic markers Bax, Par-4, Bcl2, caspase-3 and disruption or interference of all these factors suggest that Withaferin-A has a possess anti-cancer activity [17-19]. This review summarizes Withaferin-A properties against different cancers like breast, colon, gastric, prostate, ovarian, lung and cervical-cancer.

2. ANTI-CANCER ACTIVITY

2.1. Breast Cancer

It is considered as one of the serious and fatal diseases that, according to statistics, have affected a huge number of women around the globe. In 2020, more than 2.3 million women were reported with breast cancer, and among them, around 690,000 women have lost their lives [20, 21]. The molecular subtypes of breast cancer where Withaferin-A are widely studied are triple-negative or basal-like and luminal A and B(progesterone-receptor, estrogen-receptor, and HER2 negative/positive) [22]. In all cancer types, metastatic illness is the primary cause of death. Still, treatments mainly focus on targeted primary tumors but not metastases due to their difficulty in detecting [23]. Breast cancer was found in younger women who lacked oestrogen and progesterone receptors and had vimentin-positive tumours. Vimentin, a type of intermediate filament, is considered essential for cell motility and movement [24, 25]. Withaferin-A induced death in various breast cancer cells when mediated by the ROS pathway and it has already been seen through experimentation that Withaferin-A induces autophagy and apoptosis in human breast cancer cell-lines MCF-7 and MDA-MB-231 [26]. Pathway-based analysis of the transcriptome during a recent study applied in triple-negative mesenchymal MDA-MB-231 and epithelial-like MCF-7 breast-cancer cells were exposed to various concentrations of Withaferin-A, which thereby showed attenuation of a series of cancer hallmarks[27, 28]. The sub-cytostatic concentrations of Withaferin-A target the uPA pathway and multiple metastatic effectors in triple-negative therapy-immune breast cancer and place a great opportunity to further fight against the development to take down the combativeness metastatic breast cancer.

Another study suggests that when Withaferin-A is combined with other active components like Sulforaphane (SFN), causes apoptosis of breast cancer cells. SFN is an iso-thiocyanate that has shown many positive results in treating cancer and has acquired higher interest because of its HDAC inhibition [29-31]. This study showed that various combinations of Withaferin-A and Sulforaphane promoted cell death and were highly effective. They caused apoptosis in MDA-MB-231 triple-negative and MCF-7 epithelial-like breast cancer cells. Although very little is known about the effects and functions of Withaferin-A but few studies have shown that they do behave as DNMT inhibitors [32]. It has also been seen that Withaferin-A is effective against inhibition of breast cancer metastasis and invasion by inducing vimentin disassembly [33]. The mechanism of action of the

combination between Withaferin-A and Sulforaphane is demonstrated in **(**Error! Reference source not found.**)** for easy understanding.

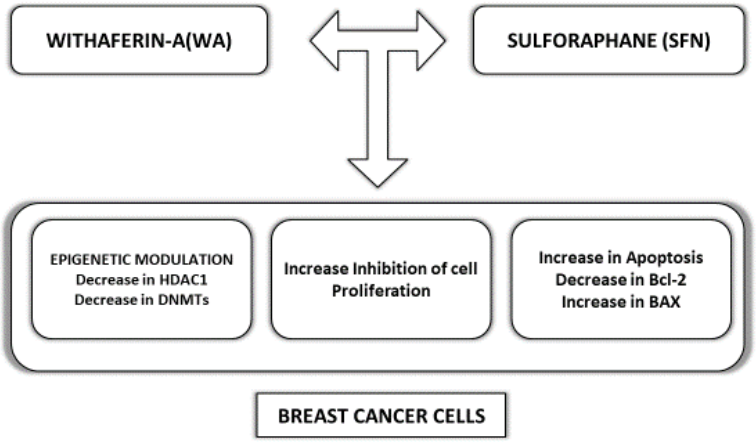

Fig. 3. Breast cancer treatment with a combination of Withaferin-A and Sulforaphane

2.2. Colon Cancer

When we speak about global cancer statistics, CRC (Colorectal cancer) is considered as one of the most common types of cancer which one of the most common types of cancer which has the fourth position in causing deaths that are cancer-related in the world. This has eventually led to an increase in the interest in finding prevention and treatment for Colon cancer [34, 35]. As we know previously, tumor progression and promotion include angiogenesis, migration, increase in cell proliferation and induction or formation of tumor, STAT3 pathway among all the different kinds of oncogenic or tumor formation signaling pathway plays a role very important function [36]. Few studies have already reported that STAT3 blockade or inactivation have led to apoptosis of colon cancer while activation of STAT3 increased the number of colon cancer cells.

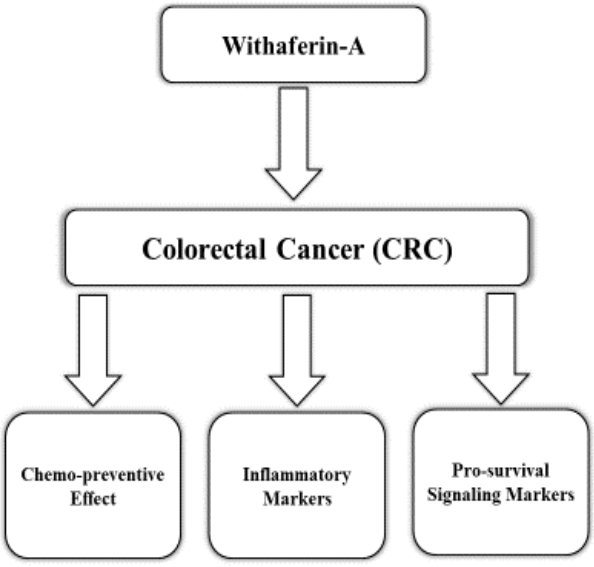

Fig. 4: Withaferin-A has anticancer activity in the treatment of colon cancer.

Therefore selective inhibition of STAT3 signaling is considered to be a better and more profitable approach in preventing colon cancer [37-40].In order to achieve this goal, many new therapeutic agents are investigated to inhibit STAT3 signaling activation because activation of STAT3 abnormally can cause cell cycle progression, metastasis, and angiogenesis [41, 42]. We already know from past studies that Withaferin-A causes the death of colon cancer cells, including HCT116 cells. This step is achieved by blockage of Prosurvival signaling pathways mediated through Notch1 (**Error! Reference source not found.**) [43]. A recent study on Withaferin-A demonstrated that it inhibited proliferation or caused apoptosis of HCT116 cells and with the supporting help of another study that demonstrated that Withaferin-A stopped STAT3 phosphorylation by directly binding them to the STAT3 SH2, there by stopping STAT3 addition reaction or dimerization [44, 45].

2.3. Prostate Cancer

According to a recent study, prostate cancer is the most common and highly dangerous causes of death in men. Furthermore, because prostate tumours are androgen-dependent in the early stages, hormone ablation therapy is regarded as the

primary preventive treatment for prostate cancer (CaP) [46, 47]. A study reveals that Cdc2 activation results in cell deposition in the M phase, demonstrating cell cycle regulation of Withaferin-A on prostate cancer cells as well as aberrant copying and mitosis, resulting in cell death. Two prostate cancer cell lines, PC-3 and DU-145, were chosen for this study. These cells were exposed to varying doses of Withaferin-A.

Withaferin-A causes G2/M cell cycle arrest and cell viability in prostate cancer cell lines, according to the findings (PC-3 and DU-145) [48, 49]. There are a vast number of mechanisms involved in the initiation of prostate cancer but out of all these proteins activated AKt/B plays a very important and major role. The tumor inhibitor PTEN gene inactivation causes activation of AKt and an increase in Prostate tumors. Various studies suggested that Withaferin-A showed chemo-preventive action causing inactivation of AKt and helped Fork head box O3a (FOXO3a) activate prostate apoptosis response-4 (Par-4) thereby lead to delay in the prostate tumor progression [50-52]. Various roles of Withaferin-A are demonstrated for easy understanding in **(**Error! Reference source not found.**)**

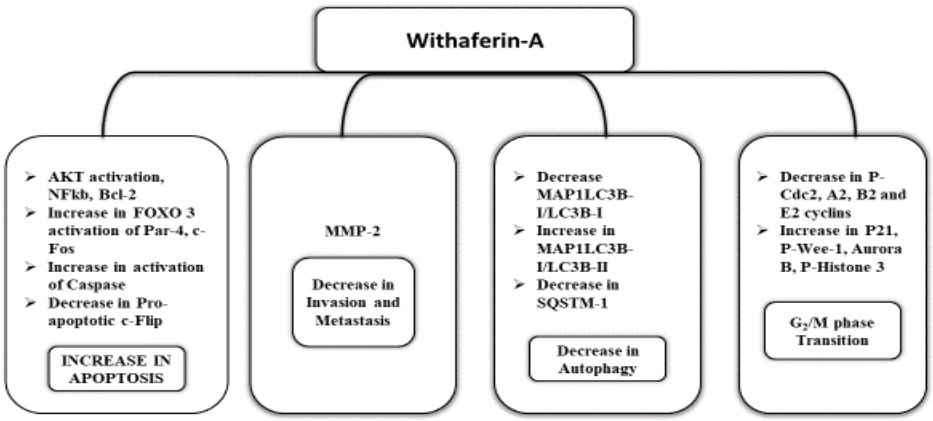

Fig. 5: Signaling pathways with respect to Withaferin-A for the treatment of CaP

Over the past few years, Withaferin-A has been used extensively in CaP (prostate cancer) therapy because of its regulation property of G_2/M transition through Aurora B, p21, Histone H3 including phosphorylated Cdc2, A2, B1, and E2 cyclins downregulations [53]. A study demonstrated that Withaferin-A causes apoptosis in prostate cancer cell lines but not in prostate epithelial cells and androgen-responsive cells by introducing Par-4 (prostate apoptosis response-4) [54, 55].

2.4. Ovarian Cancer

It is considered to be one of the major causes of cancer-related death in women and has been recorded as 5th highest in the United States. This is because many of ovarian cancer cases have been treated at an advanced stage because of their indifferent symptoms [56, 57]. Few recent studies and reports on the concept of cancer stem cells (CSCs) have been extensively studied because they led to the reintroduction of cancer even after the treatment [58, 59]. The function of CSCs was studied in ovarian cancer cells. It was found that there was the presence of a single cell-like level of CSCs in the patients suffering from ovarian cancer. This would even link these tumors to several upcoming generations. And we already know from several experiments performed in various studies that CSCs are responsible for the reintroduction of Cancer [60-62]. It has already been studied and demonstrated that Withaferin-A and CIS (cisplatin) are very effective in the treatment of ovarian cancer by decreasing the level of ALDH+ Cancer stem cells. During this study, it was found that when cisplatin and Withaferin-A are combined and used leading to maximum reduction in the number of ALDH+ cancer stem cell.

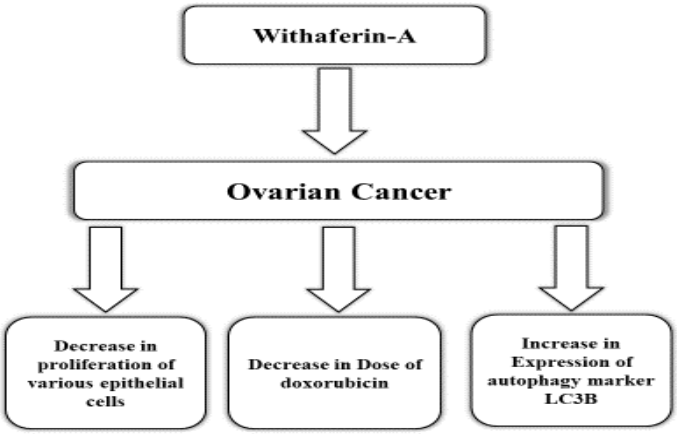

Fig. 6. Role of Withaferin-A in the treatment of Ovarian cancer

Aldehyde dehydrogenase-1 (ALDH1) is considered to be one of the important cancer stem cells present in ovarian cancer and when they are injected into mice they have shown to be highly tumorigenic [63]. When Withaferin-A alone or a combination of Withaferin-A and cisplatin were introduced, a subsequent decrease in the tumorigenic or oncogenic functions of Aldehyde dehydrogenase 1 CSCs in vitro and decrease in tumor formation in vivo were noticed and all these were carried out by injecting ovarian cancer cells to generate tumor. The ovarian cell line used for this experiment was A2780 [64]. There are more yet to be determined like how Withaferin-A controls the expression of securing, ALDH1, and cancer stem cells population. Various anti-tumor activity of Withaferin-A in the treatment of ovarian cancer is demonstrated in **(**Error! Reference source not found.**)** for easy understanding.

2.5. Lung Cancer

It is considered to be one of the most fatal and major causes of death in industrialized countries and has been reported to have taken more than one lakh lives in 2022 [21, 65, 66]. Lung cancers are caused by two major types, one is small cell lung cancer (SCLC) and another one is non-small cell lung cancer (NSCLC). And according to cumulative reports and studies, NSCLC is considered to have taken more than 80% of all cancer-related cases in the lungs [67-69]. A recent study demonstrated that Withaferin-A could stop Lung cancer cell lines A549 proliferation, which was subsequently increased with an increase in the dosage form. These studies also demonstrated that Withaferin-A caused A549 apoptosis and greatly influenced the apoptosis of A549 cancer cell line.

Withaferin-A led to decrease in the dose-dependent pAkt/Akt, Bcl-2, an anti-apoptotic protein, leading to a subsequent increase in Bax and divided caspase-3. This study has shown that Withaferin-A has apoptotic action and inhibited the rapid production of A549 cells through Akt pathway suppression [70, 71]. A recent study suggests that Withaferin-A mediated toxicity has an important contribution from a very essential and important mechanism called ROS production. During this when Withaferin-A was treated with NAC (N-acetyl cysteine) caused repulsion of Withaferin-A treated A549 cancer cell lines from ROS production, proliferation, cell viability, and apoptosis [72]. Signaling pathways like PI3K or Akt are very important in apoptosis and spreading of cancer cells and their activation is mostly observed in many tumor-causing cells. However, Withaferin-A blocked the PI3K or Akt pathway's activity which thereby caused apoptosis and anti-proliferation of Lung cancer cell lines (A549 cells). So, at the end, Withaferin-A can act as an anti-proliferative agent and cause apoptosis of Cancer cell lines (A549) by PI3K or Akt signaling pathways suppression. This leads to the successful treatment of non-small cell lung cancer in future aspects [73, 74]. New techniques were also demonstrated that included Withaferin-A and phloretin (which is a glucose transport inhibitor) caused a huge suppression in the tumor size. This study suggested that selective metabolism therapies combined with Withaferin-A can be a very useful and efficient treatment against lung cancer [75]. **(Fig. 7)** illustrates the varied anti-tumor properties of Withaferin-A in lung cancer treatment.

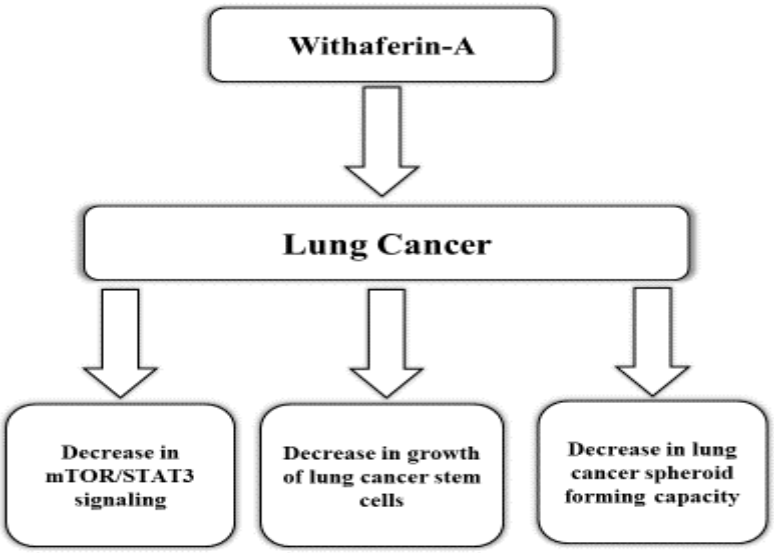

Fig. 7. Withaferin-A mechanism of action in the treatment of lung cancer

2.6. Cervical Cancer

Cervical cancer is considered to be one of the fatal and causes of female cancer-related deaths and is reported to be one of the second-largest around the globe. The human papillomavirus causes these types of cancer and this causes more than 99% of cervical cancer. Human papillomavirus is also known as HPV include HPV 33, 18, 31, 16, and two of the main on co-protein are known to cause or induce the cancer are E6 and E7. These on co-proteins cause the inactivation of pRb and p53 tumor suppressor proteins [76-78]. Whenever there is a downregulation of these two types of on co-protein there is induction of functional p53 protein, and the apoptosis is carried out by activation of Bax.

Recent studies have proved the fact that activation of p53 functions can cause apoptosis of cancer cells directly and p53 pathways are thoroughly studied for future advancements in various cancers [79-82]. Another study expand that Withaferin-A cause's antiproliferation and induces apoptosis in CaSki cells (which are human cervical cancer, HPV 16 and 18 positive).

Withaferin-A restores p53 by downregulation of E7 and E6 on co-protein and induces phase arrest in the G_2/M phase by controlling p53 proteins in cell progression. Withaferin-A also stops the STAT3 signaling and regulates p53 apoptotic markers [17, 83-86].

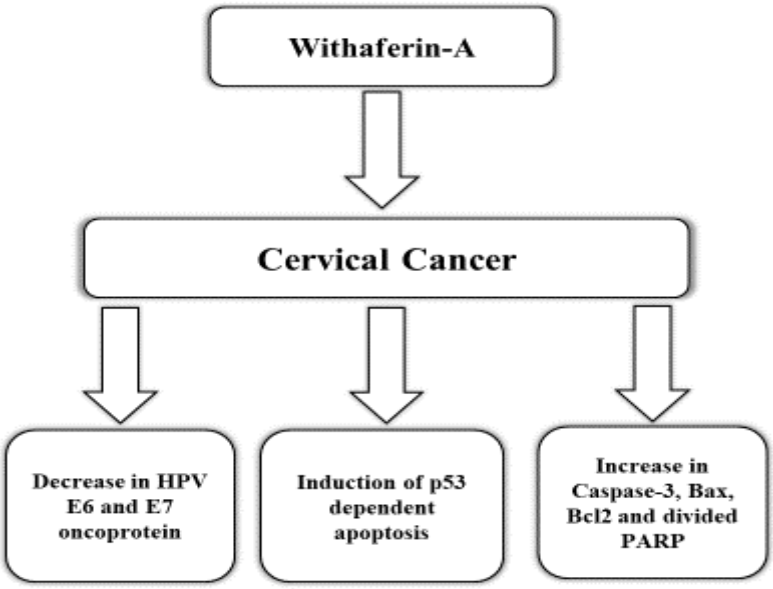

Fig. 8. Withaferin-A has anticancer efficacy in the treatment of cervical cancer

However few studies have demonstrated how Withaferin-A showed antiproliferative activity in vitro and in vivo and their ability to suppress E6 and E7 HPV oncoproteins causing activation of p53 leading to blockage of Cervical cancer cells [87], these researches have opened new possible ways to use Withaferin-A in various treatments. Various anti-cancer activity of Withaferin-A in the treatment of cervical cancer is demonstrated in (Fig. 8) for easy understanding.

3. *IN VITRO* ANTI-CANCER ACTIVITY OF WITHAFERIN-A

The fluorescein diacetate propidium iodide dye exclusion test and glucose stimulation assay were used to assess the effect of a medication on pancreatic islet cell survival while controlling for aferin. Withaferin-A had no effect on islet cells, lowering their inflammatory response to cytokine exposure. 3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-carboxymethoxyphenyl)-2-(4-carboxymethoxyethane) (4-sulfophenyl) The effects of Withaferin-A on the viability and proliferation of MCF-7 cells were investigated by using exclusion studies with -2H-tetrazolium (MTS) and trypan blue. Proliferation and viability have been demonstrated to be inhibited by Withaferin-A in MCF-7 cells [88]. Withaferin-A , an NF-B inhibitor, reduced neuromuscular junction denervation and clinical symptoms in TDP-43 (TAR DNA-binding protein 43) mice [89]. Another investigation discovered that Withaferin-A plays an active role in the HSF1-dependent stress response [90]. The effects of WA on corneal angiogenesis and retinal gliosis were investigated and treatment with WA reduced soluble and filamentous GFAP expression while inhibiting corneal neovascularization [91]. On isolated frog skin melanophores, the effects of pure Withaferin-A were investigated. In isolated skin melanophores, Withaferin-A evoked strong dose-dependent physiologically meaningful melanin dispersal effects that were fully inhibited by hyoscine and atropine [92]. It also inhibited LPS-induced cyclooxygenase (COX-2) protein and mRNA expression, as well as prostaglandin E2 (PGE (2)) production in BV2 murine microglial cells. Withaferin-A , according to these findings [93], suppresses LPS-induced PGE (2) synthesis and COX-2 expression.

The high binding energy required to link Withaferin-A to the active Hsp (Heat shock proteins) 90/Cdc37 complex boosts the thermodynamic stability of the association, according to computational study [94]. The effect of this compound on the module ability of the NF-B signalling pathway was investigated, and it was discovered that the native protein complexes with Withaferin-A had stable temporal trajectories [95]. Withaferin-A 's ability to inhibit mammalian proteasomes was explored, and it was discovered that it can inhibit mammalian proteasomes irreversibly and rapidly via acylation of the -5 subunit's N-terminal Thr1 [96]. Withaferin-A was tested for its ability to inhibit the Hsp90/Cdc37 chaperone/co-chaperone interaction complex. According to molecular modelling experiments [97]. The combination of Withaferin-A and 17-DMAG can be an efficient chaperone system inhibitor. Another study found that Withaferin-A , a dual vimentin and proteasome inhibitor, decreased E. coli-induced polymorph nuclear neutrophil (PMN) transmigration substantially [98]. During the recovery of a central nervous system injury, gliosis is a biological state characterised by the overexpression of the intermediate filaments glial fibrillary acidic protein and vimentin. A unique chemical probe is glial fibrillary acidic protein Withaferin-A [99]. Oral treatment of Withaferin-A to rats treated with 7,12-dimethylbenz(a) anthracene (DMBA) decreased tumour growth while also synchronising lipid peroxidation and antioxidant capacity [100].

The ability of Withaferin-A to suppress growth and differentiate in glioma (C6 and YKG1) cell lines was scrutinized and observed that Withaferin-A dramatically inhibits glioma cell proliferation in a dose dependent manner [101]. The effect of

Withaferin-A on CF-related inflammation was also examined in an in vitro model [102]. When human kidney cancer cells and Caki cells are co-treated specifically with subtoxic doses of Withaferin-A and a tumour necrosis factor-related apoptosis inducing ligand, apoptosis is accelerated. In human lung epithelial A549 cells, Withaferin-A decreases the expression of intercellular adhesion molecule-1 (ICAM-1) and vascular cell adhesion molecule-1 (VCAM-1), suggesting a function in airway inflammation. The effects of Withaferin-A on thermotolerance development and degradation in C57BL mice with B16F1 melanoma were studied.

Withaferin-A increases tumour responsiveness to recurrent heat by lowering thermotolerance and reducing recovery time [103]. The action of Withaferin In mice, the effects of monosodium urate crystals on inflammation were investigated. Withaferin outperformed the control group. A therapy reduced lysosomal enzyme levels, paw volume, inflammatory mediator tumour necrosis factor alpha, and lipid peroxidation [104]. Apoptosis is caused by Withaferin-A in conjunction with caspase-3 activation. The JNK and Akt pathways, as well as the inhibition of NF-kappaB activity, were discovered to be significant regulators of apoptosis in human leukaemia U937 cells in response to Withaferin-A [105]. Withaferin-A elevated Bax levels in response to MAPK signalling, resulting in the commencement of a mitochondrial death cascade. It has the potential to be used as a novel, low-cost chemotherapeutic medication to treat lymphoid and myeloid leukaemia [106]. When combined with the human filarial parasite Brugia malayi, Withaferin-A provides varied levels of protection in Mastomys coucha, with chemotype 101R protects strongly than other chemotypes.

Using the MDA1986, JMAR, UM-SCC-2, and JHU011 cell lines, researchers discovered that Withaferin-A had antiproliferative effect against head and neck squamous cell carcinoma (HNSCC) [107]. The oncogenic transcription factor STAT3 has been linked to a number of human malignancies, including breast cancer [108], and Withaferin-A suppresses both constitutive and IL-6-induced activation. The effect of Withaferin-A on the response of B16F1 melanoma to fractionated and acute radiation was studied with and without local hyperthermia. In fractionated regimens, Withaferin-A is a greater radiosensitizer than HT, and it improves the response of radioresistant tumours like melanoma [109]. In vimentin-expressing tumour cells, withaferin-A caused considerable apoptosis and vimentin cleavage, but not in normal mesenchymal cells. Furthermore, in a panel of soft tissue sarcoma xenograft tests, withaferin-A inhibited soft tissue sarcoma development, local recurrence, and metastasis [110]. In three colon cancer cell lines (HCT-116, SW-480, and SW-620), Withaferin-A is a bioactive molecule that inhibits Notch-1 signalling and downregulates prosurvival pathways such as Akt/NF-kappaB/Bcl-2.

The *in vitro* and *in vivo* efficacy and mechanism of Hsp90 inhibition of Withaferin-A in pancreatic cancer were investigated. Without requiring ATP, Withaferin-A binds to Hsp90 and suppresses its chaperone action. Dual inhibition of the transcription factors NF-kappaB and AP-1 Fra-1, as well as silencing of IL-6 promoter chromatin accessibility, were reported to reduce IL-6 gene transcription in metastatic breast cancer cells [111]. Withaferin- A anti-carcinogenic efficacy was investigated in Syrian golden hamsters exposed to 7, 12-dimethylbenz[a]anthracene (DMBA). When given orally for 14 weeks, Withaferin-A completely reduced tumour volume, tumour incidence, and tumour burden. To investigate the involvement of this compound in the molecular aetiology of oral cancer, researchers used immunological expression of the p53 and bcl-2 proteins. Withaferin-A protects the buccal mucosa of golden Syrian hamsters from 7, 12-dimethylbenz (a) anthracene (DMBA)-induced molecular alterations. Withaferin-A in human breast cancer cells, a therapy causes G2 and mitotic arrest. [112].

CONCLUSION

These recently released statistics are very encouraging and recognize the need for further research on WA in order to identify and monitor other possible therapeutic effects. Undoubtedly, more research has to be done on WA use in extensive clinical trials for a range of disease like anticancer, antidiabetic, skin problems etc., (both alone and in conjunction with other phytochemicals or medications). According to the current review, WA controls a number of anticancer pathways, such as oxidative stress, apoptosis, autophagy, preventing cell proliferation, slowing angiogenesis and metastatic growth. Future research into the development of chemotherapeutic drugs can focus on finding new proteins with significant effects on tumor progression. The clinical efficacy of other anticancer agents can be increased by combining them in a synergistic manner, which is made possible by the molecular pathway of WA.

New interesting research will also be carried out on Withaferin-A in the future for its anti-cancer properties, thereby opening a great future aspect for it to become an important phytochemical in various cancer treatment therapies and general population-related diseases. Withaferin-A is said to have antimetastatic, anti-inflammatory, immunosuppressive and many more. Whether it be the treatment of cancer or COVID-19 or any other form of the disease, Withaferin-A has proved to have great potential in being a very profitable and essential phytochemical that can be used as a therapeutic agent. In this review we have highlighted the biological importance of WA for its various anticancer target and it will benefit scientists who is working on phytochemical drug discovery process.

Conflicts of interest

The authors declare they have no relevant conflicts of interest.

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