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Exploring Alkaloids and Flavonoids from Natural Sources: Emerging Natural Agents for Inhibiting Cervical cancer Progression through Apoptosis Induction, Anti-Inflammatory Effects, and Oxidative Stress Reduction

Yumei Chen[a#], Denghua Yu[a#], Dongwei Zhu[b], Selvaraj Muthusamy[b], Mangirish Deshpande[c], Natarajan Kiruthiga[d], Panneerselvam Theivendren[e*], Kanagaraj Rajalakshmi[b*], Siyi Wu[f]*, Chengdong Zhu[g*]

[a]Department of Laboratory Medicine, Yizheng People's Hospital, Yangzhou-211400, P.R. China.

[b]Department of Immunology, Jiangsu Key Laboratory of Laboratory Medicine, School of Medicine, School of Chemistry and Chemical Engineering, Jiangsu University, Zhenjiang-212013, P.R. China.

[c]Department of Pharmacology, PES'S Rajaram and Tarabai Bandekar College of Pharmacy, Ponda-403401, Goa, India.

[d]Department of Pharmaceutical Chemistry, KMCH college of Pharmacy, Kalappatti road, Coimbatore-641048, Tamil Nadu, India.

[e]Department of Pharmaceutical Chemistry & Analysis, School of Pharmaceutical Sciences, Vels Institute of Science, Technology & Advanced Studies, Pallavaram, Chennai, Tamil Nadu 600117, India.

[f]Department of Pathology, The Affiliated Taizhou People's Hospital of Nanjing Medical University, Taizhou 225300, Jiangsu, P.R.China.

[g]Department of Orthopedics, Yizheng People's Hospital, Yangzhou-211400, P.R. China.

*Corresponding Authors

tpsphc@gmail.com (Panneerselvam Theivendren); rajichen89@ujs.edu.cn (Kanagaraj Rajalakshmi); 2930339808@qq.com (Siyi Wu); dongdong801208@163.com (Chengdong Zhu);

[#]These authors contributed equally to this work.

Abstract

Cervical cancer stands as one of the major causes which result in death due to cancer in female patients all over the world. The treatment measures such as chemotherapy and radiations are still producing unfavourable side effects that are also limiting their efficacies in treatment. The capability of alkaloids and flavonoid to target cellular mechanisms that lead to the development of cancer cells has been investigated through research studies. This review study evaluates the mechanism of action of alkaloids in combination with flavonoids derived in various plant species to prevent the progression of cervical cancer. The bioactive constituents exhibit appealing therapeutic effects as they induce apoptosis and reduce inflammation and neutralize oxidative stress. Berberine and sanguinarine alkaloids as well as quercetin and kaempferol flavonoid exhibit cervical cancer cells-damaging apoptotic effects and inhibit inflammation by regulating inflammatory cytokines and strengthening antioxidant defense. The capability of these compounds to modulate PI3K/Akt and NF-kB and MAPK and p53 signaling pathways implies that they can be developed into non-toxic therapeutic options to be used in cases of cervical cancer. Mechanistic insights and clinical evidence of the use of alkaloids and flavonoids in the management of cervical cancer are reviewed and their suitability as natural products in cancer therapeutic intervention considered.

Keywords: Cervical Cancer, Alkaloids, Flavonoids, Apoptosis, Anti-Inflammatory Effects, Oxidative Stress, Natural Agents

Introduction

The incidence of cervical cancer is among the most common forms of cancer that burdens women globally especially impacting the public health resources in Low and Middle-Income countries **Figure 1**. Screening by schedule such as Pap test and HPV vaccination has resulted

in improved outcomes but cervical cancer remains one of the leading cancer causes of death due to the late presentation of individuals and the resistance and debilitating side effects of chemotherapy and radiation therapy. The emergence of the popularity of alternative treatment methods has taken place due to the fact that new methods should be effective as well as safe and sustainable. Natural products have gained popularity with the scientific community that explores their potential to inhibit cancer growth particularly among alkaloids and flavonoids found in the plantLife. Alkaloids and flavonoid are bioactive compounds found in different plant species that belong to different chemical groups. Alkaloids biological activities span through several areas since these are compounds that have nitrogen structures that exhibit anti-cancer properties coupled with antimicrobial and anti-inflammatory effects. Rushing through the plant world are flavonoids that demonstrate their anticancer qualeities along with anti-inflammatory and antioxidant ones. These natural products have been extensively studied by scientists since they affect critical pathways that cause cancer cell proliferation alongside cellular growth and survival. As cancer treatment, it appears promising since these substances have demonstrated ability to destroy cancer cells selectively without harming normal tissues (1-7).

Cervical cancer development causes the abnormal control of cell growth and apoptosis resistance and persistent tissue inflammation as well as oxidative damage of cellular structures. These compounds affect molecular-level biological processes in order to achieve their therapeutic effects in this context. The cells die through apoptosis which enables the destruction of cancer cells without affecting normal tissue. A significant anti-inflammatory power exists in both alkaloids and flavonoids because chronic inflammation drives tumorigenesis and cancer progression in the context of cancer. Many cancers progress from oxidative stress because it induces DNA damage and cellular mutations as a core mechanism in pathogenesis for cervical cancer and other types. Alkaloids and flavonoids function as antioxidants which reduce harmful ROS by performing a neutralization process that stops cellular destruction. Multiple complex pathways serve as the basis by which alkaloids and flavonoids stop cervical cancer from advancing towards more severe stages. Laboratory research indicates berberine and sanguinarine alkaloids alter the operation of survival and death pathways PI3K/Akt, MAPK, and p53. Flavonoids contain compounds like quercetin, kaempferol and luteolin that manage inflammatory cytokines TNF-α, IL-6 and IL-1β which promote tumor growth along with metastasis. The coupling of alkaloids and flavonoids blocks NF-κB pathway function which controls immune response and inflammation thus reducing the cancer-facilitating inflammatory conditions of tumors (8-13).

Although they show direct cancer cell effects alkaloids and flavonoids simultaneously support the performance of standard cancer treatment approaches. The compounds achieve success by making tumor cells more responsive to chemotherapy and radiation treatment which helps to address both chemoresistance and serious treatment side effects. The combination of alkaloids and flavonoids with established treatment agents creates an opportunity to generate more successful outcomes in cervical cancer therapy. Research studies on natural compounds now allow scientists to identify different plant sources rich in alkaloids and flavonoids suitable for novel therapeutic agent development. The plant compounds provide natural alternatives which medical practitioners consider safer than synthetic drugs since they generate fewer adverse effects and treat conditions holistically. Multiple pharmaceutical research studies have discovered that natural compounds interact synergistically by uniting different alkaloid and flavonoid families which heightens their anticancer properties. The usefulness of natural therapeutic agents in cancer care stands emphasized when treating cervical cancers that frequently resist conventional treatment approaches (14-16).

New clinical research must proceed swiftly because preclinical results hint at both safety and effectiveness of human applicability of combined alkaloids and flavonoids. Medical application of these compounds in human patients necessitates complete knowledge regarding their drug release mechanisms and their body absorption rates along with the evaluation of their harmful effects. Patient stratification requires specific biomarkers to determine how best natural agents should be used for personalized cancer therapy. The analysis investigates the therapeutic action of alkaloids and flavonoids from natural resources as upcoming anticancer agents which suppress cervical cancer development by triggering cell death mechanisms and controlling inflammatory factors alongside antioxidant effects. This review investigates the molecular anticancer capabilities of these chemicals for cervical cancer treatment alongside their clinical implementation possibilities**Table 1.** The objective of this review is to explore the therapeutic potential of alkaloids and flavonoids, natural compounds from plants, as promising agents in the treatment of cervical cancer. The review aims to investigate the molecular mechanisms through which these bioactive compounds induce cancer cell death, regulate inflammatory pathways, and reduce oxidative stress. Furthermore, it examines their potential for enhancing the effectiveness of conventional treatments, offering a safer, more holistic alternative in cervical cancer therapy.

Alkaloids as Natural Anticancer Agents: Mechanisms of Action

Organic compounds that emerge naturally and contain nitrogen within cyclic ring structures make up the alkaloid group of compounds. The compounds originate mostly from plants

together with fungi and marine organisms. Researchers have identified alkaloids for multiple years for their medical applications especially in cancer treatment. Scientists have intensely researched alkaloids because they demonstrate different biological functions which stop cancer cell growth as well as trigger cell death and manage immune response activity and prevent cancer cells from spreading. The special procedure through which alkaloids work enables researchers to consider them as powerful cancer treatment agents when used with standard therapies including chemotherapy and radiation. Analysis shows that anticancer alkaloids trigger cell death in cancer cells through programmed cell death also known as apoptosis. The occurrence of apoptosis demands strict regulation because it activates the intrinsic and extrinsic signaling pathways together. The alkaloids berberine and sanguinarine activate cell death by disrupting mitochondria which starts a caspase activation sequence since caspases serve as death-executing enzymes. Release of cytochrome c from the mitochondria creates cell death by activating caspase-9 which leads to the activation of caspase-3. Alkaloids control the activity of pro-apoptotic and anti-apoptotic proteins BAX and BCL-2 which function fundamentally to direct mitochondrial apoptosis. The intrinsic apoptosis pathway activation caused by alkaloids leads to cancer cell death without harming normal cells(17-23).

The cancer cell survival and proliferation pathways become targeted as a secondary mechanism by alkaloid compounds following their ability to promote apoptosis. The PI3K/Akt together with MAPK/ERK signaling pathways become dysfunctional in cancers which results in uncontrolled cell expansion and apoptosis resistance as well as metastasis promotion. Berberine together with vincristine demonstrate the ability to block the PI3K/Akt pathway that regulates cell survival and metabolism. The cancer cells become more sensitive to other treatments because alkaloids disrupt this pathway thus invoking cell cycle arrest. The alkaloid cryptolepine blocks cellular signals through the MAPK pathway that controls cell proliferation together with differentiation and apoptosis regulation. These essential pathways become controlled when alkaloids enter the system which enables tumor prevention together with cancer cell proliferation blockade and tumor spreading control. Anti-inflammatory properties of alkaloids prove vital in cancer therapy because of their strength. Chronic inflammation serves as a fundamental cancer characteristic which leads to tumor advancement alongside immune system avoidance and cancer spread between different areas of the body. The NF-κB pathway functions as a main controller of cancer inflammation because its activation promotes the production of inflammatory cytokines including TNF-α, IL-6 and IL-1β. The NF-κB pathway faces inhibition through alkaloids like berberine and sanguinarine thus cytokines decrease which attacks the tumor's favorable environment. Two alkaloids namely curcumin

and sanguinarine hinder the activity of cyclooxygenase-2 (COX-2) which regulates the formation of inflammatory prostaglandins. Alkaloids safeguard against the chronic inflammatory state which initiates and advances cancer development because they decrease inflammation levels(24, 25).

Laboratory evidence demonstrates how alkaloids minimize oxidative stress which occurs when reactive oxygen species (ROS) collect within cells. Cancer development receives significant contributions from oxidative stress that generates harm to cellular structures including DNA proteins and lipids. Two examples of alkaloids namely berberine and vincristine function as antioxidants by removing free radicals while controlling ROS levels inside cells. The compounds boost the activity of cellular antioxidant enzymes as they enable superoxide dismutase (SOD) and catalase to keep redox balance within the cell. Alkaloids eliminate ROS to block DNA damage from occurring which helps prevent cancer initiation as well as cancer progression. Traditional cancer therapies become more effective when patients receive co-treatment with alkaloids due to their anticancer properties. Several alkaloid compounds behave as chemo-sensitizing agents which improve the sensitivity of cancer cells to standard chemotherapy along with radiation therapy. McMichell Laboratories discovered how alkaloid paclitaxel suppresses microtubule instability to inhibit cell reproduction thus activating chemotherapy agents against ovarian and breast cancer cells. Recent studies reveal that substance berberine and vincristine decrease the emergence of drug resistance which is a prevalent challenge during cancer treatment. Paclitaxel alkaloids help(reverse) chemoresistance to enhance therapeutic outcomes of current cancer treatments while increasing patient survival rates(26, 27).

Anticancer properties of alkaloids become more powerful because these compounds exhibit both minimal toxic effects in healthy cells and cancer cell-specific targeting abilities. Alkaloids demonstrate superior advantages when compared to typical chemotherapy drugs because they create better possibilities for extended cancer therapy use. The medical use of alkaloids needs detailed assessment regarding their drug absorption patterns combined with their available amount in the bloodstream and their effects on concurrent medicinal substances. Continued scientific investigations concentrating on alkaloid mechanism and clinical use potential point toward advanced cancer treatments. The successful clinical verification of alkaloids will lead to their vital function in cancer therapy development of targeted therapeutic approaches with lower toxicity levels**Table 2(28, 29)**.

Flavonoids as Modulators of Cervical Cancer Progression

Polyphenolic compounds known as flavonoids exist abundantly in fruits together with vegetables and herbs and various plant ingredients **Figure 3**. The many cancer-fighting characteristics of these compounds make them suitable for treating different cancer types with cervical cancer being one of them. Worldwide cervical cancer ranks as the fourth most dominant cancer among women because persistent infection with HPV16 and HPV18 and other high-risk HPV strains presents the main driver of this disease. Current treatment procedures including surgery together with chemotherapy along with radiation have raised survival rates however they produce substantial adverse reactions that show the requirement of safer alternative therapeutic strategies. Research indicates that flavonoids show promise as natural agents in the prevention and management of cervical cancer because they affect multiple cancer-related targets. The anticancer properties of flavonoids work through their mechanisms that affect both cancer cell proliferation along with apoptosis and inhibit inflammation and support metastasis suppression. The anticancer mechanism of flavonoids depends on their ability to cause the programmed death of cancer cells. The process of apoptotic cell death becomes disrupted in cancer cells which enables these cells to survive and expand without programmed death signals. The cervical cancer cell apoptosis mechanisms become active due to treatment with flavonoids like quercetin, kaempferol and luteolin. The mitochondrial pathway becomes activated when quercetin causes apoptosis through an action that enhances BAX expression and suppresses BCL-2 levels. The ratio imbalance between BAX and BCL-2 proteins results in damaged mitochondria that releases cytochrome c while activating caspases which leads to cancer cell death(30, 31) .

The anti-inflammatory properties of flavonoids together with their ability to induce apoptosis play essential roles in cervical cancer development. Chronic inflammation serves as a main sign of cancer while scientists have found evidence that links this process to both tumor beginnings and their subsequent evolution and the spread of cancer cells. The inflammation resulting from HPV infection activates NF-κB and MAPK pathways that help cervical cancer cells survive alongside making them less sensitive to treatment. Quercetin and kaempferol function to stop the NF-κB signaling pathway which consequently decreases inflammatory protein levels including TNF-α and IL-6 as well as IL-1β. The diminished inflammation pattern through flavonoids treatment both halts tumor development and diminishes cervical cancer cell metastatic capabilities through modifications to the disease environment. The cell cycle function depends on flavonoids which control its regulatory mechanisms to maintain proper cell division and cell activity. Cancer exhibits dysregulated cell cycle patterns as its primary biological feature because this condition results in continuous uncontrolled cellular

reproduction while simultaneously generating various genetic abnormalities. Studies have demonstrated that the flavonoids genistein together with apigenin affect essential regulators that control the cell cycle. The inhibitor activity of genistein targets cyclin-dependent kinases (CDKs) to block the G1 to S phase cell cycle progression. The cellular divison process becomes halted because of this inhibition which subsequently stops cervical cancer cells from proliferating. The purpose of cell cycle arrest by flavonoids is to block the uncontrollable cancer cell growth and enhance their sensitivity to additional therapeutic treatments(32, 33).

Flavonoids exhibit the significant property of decreasing oxidative stress thus playing a critical role in cervical cancer development and disease progression. DNA damage and mutations with genomic instability usually develop from an imbalance between reactive oxygen species (ROS) and antioxidant defenses found in the body which creates oxidative stress—features commonly detected in cancers. Flavonoids function as antioxidants while clearing ROS while securing protection for cells from oxidative damage. The antioxidant enzyme superoxide dismutase (SOD) and catalase function more efficiently when their activity is enhanced by the flavonoid kaempferol which leads to protection of cellular redox balance. GM Flavonoids protect normal cells from stress-related damage and simultaneously stop DNA alterations that trigger initial and ongoing cancer development. The anti-metastatic properties of flavonoids represent a vital factor in cervical cancer cell spread. The transmission of cancer cells from the original tumor induces metastasis throughout the body that leads to predictably poor treatment results. Scientific evidence shows how compounds such as luteolin and quercetin stop epithelial-to-mesenchymal transition (EMT) in cells. This transition makes epithelial cells convert into mesenchymal cells which enables them to invade neighboring tissues and establish metastatic growth elsewhere. Flavonoids act to block EMT thus restraining cervical cancer cells from spreading to different regions within the body. The inhibitory effects of flavonoids extend to matrix metalloproteinases (MMPs) which breakdown extracellular matrix materials thus facilitating cancer cell movements. The inhibition of EMT and MMPs by flavonoids produces their anti-metastatic properties(34, 35).

Flavonoids demonstrate complementary functions with traditional chemotherapy drugs to achieve better cancer cell treatment outcomes. Researchers discovered that using flavonoids together with chemotherapeutic drugs increases their effectiveness and eliminates therapeutic resistance. The cervical cancer cell resistance to chemotherapy agents declines when treated with quercetin flavonoids because these compounds hinder the function of drug efflux pumps that convey resistance to chemotherapeutic agents. The combined application shows promise to address conventional therapy weaknesses and result in enhanced therapeutic management

for patients who have cervical cancer. Natural flavonoids demonstrate great potential as a basis for creating innovative treatments against cervical cancer. The modulation of apoptosis and inflammation alongside oxidative stress and metastasis by flavonoids makes them strong regulators of cervical cancer development. The application of flavonoids in cervical cancer treatment will become standard clinical practice after researchers validate them through additional study**Table 3(36, 37)**.

Apoptosis Induction by Alkaloids and Flavonoids in Cervical Cancer

Programmed cell death known as apoptosis functions as a vital homeostasis regulator that suppresses unwanted cell proliferation of defective or abnormal cells including cancer cells **Figure 4**. The fundamental characteristic of cancer emerged in cervical cancer and all cancers because cells escape death signals which results in uncontrolled growth and therapy resistance. The treatment ability of restoring apoptosis in malignant cervical cancer cells presents promising therapeutic potential considering HPV remains the main driving factor. The natural compounds alkaloids and flavonoids demonstrate strong potential as apoptosis-inducing agents against cervical cancer cells by offering simultaneous treatment for tumor progression and improved current therapeutic methods. The anticancer properties of alkaloids were found in chemicals that contain nitrogen and originate from plants and fungi and marine organisms. The influential apoptotic feature present in berberine and sanguinarine and vincristine enables activation of the intrinsic mitochondrial pathway. Apoptosis starts through cellular stress or damage which results in the release of mitochondria-derived cytochrome c into the cell solution. The activation of caspases occurs when this process happens through a family of proteases that execute the cell death process. The alkaloids berberine and sanguinarine enhance the expression levels of pro-apoptotic BAX protein while reducing the levels of anti-apoptotic BCL-2 protein thus causing mitochondrial outer membrane permeabilization. The alteration of mitochondrial membrane permeability causes BAX/BCL-2 ratio imbalance which results in mitochondrial dysfunction that activates caspase-9 and consequently activates caspase-3 to trigger cancer cell death. Through this mechanism alkaloids initiate programmed cell death in malignant cells thereby protecting the health of surrounding intact tissues(38, 39).

Flavonoids among natural compounds trigger potent pro-apoptotic responses in cells responsible for cervical cancer. The antioxidant properties along with anti-inflammatory effects and anticancer activity are characteristics of these polyphenolic compounds. The ability of flavonoids quercetin and kaempferol and luteolin to trigger apoptotic cell death in cervical cancer makes them subjects of extensive scientific research. The compound Quercetin uses mitochondrial pathway apoptosis by activating BAX pro-apoptotic proteins while suppressing

BCL-2 anti-apoptotic proteins. The execution of cell death happens through activated caspase-3 and caspase-9 after quercetin treatment. The flavonoid compound Kaempferol causes cervical cancer cell apoptosis through increasing ROS concentrations which drives mitochondrial destruction and activates intrinsic apoptosis signaling. The elimination of cervical cancer cells happens through procuring apoptosis by role-modifying anti-apoptotic and pro-apoptotic proteins and augmenting reactive oxygen species concentration. Mitochondrial dysfunction serves as a pathway for apoptosis initiation when using either alkaloids or flavonoids as treatments. Through extrinsic mechanisms the activation of surface death receptors such as Fas receptors sets off the sequence of events leading to caspase activation that concludes in apoptosis. Alkaloid vincristine elevates Fas receptor manifestation to create cervical cancer cell sensitivity toward extrinsic apoptotic signals. The activation of the extrinsic pathway receives enhancement from flavonoids including luteolin because these compounds increase Fas receptor expression which leads to caspase-8 activation. Alkaloids and flavonoids activate intrinsic and extrinsic apoptosis pathways of cervical cancer cells through dual effects which helps combat resistance mechanisms cancer cells usually develop(40, 41).

Alkaloids and flavonoids exhibit the ability to influence different cellular pathways that control apoptosis regulation including the p53 pathway. Through DNA damage p53 tumor suppressor protein activates cell cycle control and apoptosis which lead to elimination of damaged cells. Studies demonstrate that both alkaloids and flavonoids manage to activate the p53 pathway which in turn improves its cellular death-promoting activities. Lab studies show that the substance quercetin preserves p53 stability to enhance its transcriptional capabilities which leads to cell death in cervical cancer cells. The sensitivity of cancer cells to apoptosis improves when alkaloids and flavonoids activate the p53 pathway because it enhances their usefulness as anticancer agents. Research on in vivo studies confirms that alkaloids and flavonoids activate cervical cancer cell apoptosis outside laboratory conditions. Vivorous experiments demonstrate encouraging outcomes because alkaloids and flavonoids reduce tumor growth while causing cellular death throughout animal models of cervical cancer. The natural compounds serve as a risk-free substitute for chemotherapy because these compounds specifically attack cancer cells without harming healthy tissue structures. Healthcare professionals should consider using alkaloid and flavonoid combination treatments along with standard chemotherapy drugs because these combinations could create better treatment outcomes while addressing the drug resistance obstacles in cervical cancer therapies (42, 43).

The ability of alkaloids and flavonoids to affect intrinsic and extrinsic apoptotic pathways as well as activate p53 while increasing ROS levels makes these compounds powerful agents in

cervical cancer apoptosis regulation. These plant-derived substances possess strong potential to create better cancer therapy options that are safer and more effective for use independently or with current medical treatments. Additional research about these natural compounds' pharmacokinetic properties and clinical effects will allow their utilization as key agents in cervical cancer therapy by providing alternative yet nontoxic therapy options**Table 4 (44, 45)**.

Anti-Inflammatory Effects of Alkaloids and Flavonoids in Cervical Cancer

Persistent inflammation functions as a major global health concern because it advances cervical cancer development and increases its progression **Figure 5**. A persistent inflammatory state within tumor surroundings leads to all stages of cancer cell development including initial formation and subsequent enlargement and tissue penetration alongside distant spread. The persistent HPV high-risk strains in cervical cancer infections trigger inflammatory pathways through cytokine secretion that ultimately activates these pathways. The anti-inflammation potential of alkaloids and flavonoids stands out as significant because these natural compounds demonstrate significant strategies for blocking cervical cancer development. The compounds operate through inflammation signaling mechanisms to create better and safer strategies for treating cervical cancer. Anti-inflammatory activity of alkaloids at the NF-κB pathway level can be attributed to potent effects of berberine and sanguinarine and vincristine compounds. NF-κB works as a leading transcription factor that supports genetic expression of pro-inflammatory genes and cell survival factors as well as immune system response elements. The overactivation of NF-κB results in elevated production of TNF-α and IL-6 together with IL-1β which stimulates cancer cell growth and promotes metastasis in cervical cancer patients. Berberine along with sanguinarine function as alkaloids which stop IκB protein phosphorylation to block NF-κB from activating its journey to the nucleus. Through their ability to cut off NF-κB signaling pathways these alkaloids lower the concentration of inflammatory cytokines which establishes an environment unsupportive for cancer cell growth and spread(46, 47).

Alkaloids serve to block inflammatory mediators in addition to their ability to inhibit proteins in the NF-κB pathway. Berberine alongside other alkaloids demonstrate the ability to suppress cyclooxygenase-2 (COX-2) activity which leads to reduction of pro-inflammatory prostaglandin production. COX-2 shows excessive expression within cancer cells because it produces an inflammatory condition that fuels tumorigenesis. Alkaloids including berberine limit COX-2 enzyme expression to control cervical cancer development which qualifies them as potential treatment complements for cervical cancer management. The diverse plant-derived compounds known as flavonoids demonstrate strong anti-inflammatory properties which

scientists have thoroughly investigated for cancer treatment. Swedish research demonstrates that the compounds quercetin and kaempferol and luteolin and genistein affect vital inflammatory systems that become abnormal in cervical cancer cases. The anti-inflammatory mechanism of action for Quercetin as one of the primary researched flavonoids occurs through NF-κB pathway suppression. In the same way that alkaloids operate quercetin stops IκB from turning into its phosphorylated form while blocking NF-κB activation. Cervical cancer's tumor growth together with metastasis gets reduced when quercetin blocks NF-κB signaling which controls inflammatory cytokines and chemokines including TNF-α, IL-6 and IL-8(48, 49).

The flavonoids known as kaempferol and luteolin demonstrate anti-MAPK signaling pathway activity since they contribute to blocking this vital pathway that drives inflammatory responses and cancer progression. Cell proliferation together with survival functions and inflammatory responses are regulated by the MAPK signaling pathway which frequently becomes abnormal in cervical cancer. The inhibitory effect of flavonoids on MAPK activation helps to decrease both the inflammatory condition and the aggressive behavior of cervical cancer cells. The anti-inflammatory activity of luteolin extends to its capability of adjusting the JAK/STAT pathway that regulates immune response as well as inflammatory processes. Through reducing activity of this pathway luteolin simultaneously controls inflammatory responses together with enhancing immune response against tumors thereby demonstrating anti-inflammatory benefits for flavonoids in cancer therapy. Both alkaloids and flavonoids demonstrate antioxidant activity that counteracts oxidative stress which serves as an important factor in inflammation development. The increase in reactive oxygen species (ROS) due to oxidative stress brings damage to cellular components as well as activation of pro-inflammatory pathways. The antioxidants in both alkaloids and flavonoids attack ROS molecules in the body while they simultaneously activate endogenous antioxidant enzymes SOD and catalase to protect against oxidative stress. The antioxidants protect redox balance in cervical cancer cells against inflammation-related pathway activations that enable tumor growth and metastatic behaviors.

If cancer patients receive alkaloid and flavonoid treatment they get extensive protection against inflammatory responses based upon their dual antioxidant and anti-inflammatory properties. These compounds focus on blocking inflammatory pathways NF-κB, MAPK and COX-2 to decrease inflammatory cytokines and chemokines that encourage cancer cell survival proliferation and invasion. These substances enhance their anti-inflammatory actions through their stress-oxidative reduction abilities which creates an effective method to prevent cervical cancer advancement(50, 51).

Usage of alkaloids and flavonoids reveals potential as natural cervical cancer therapeutic agents because of their strong anti-inflammatory effects. The compounds create an anti-inflammatory environment around tumors through their control of fundamental inflammatory pathways which stops tumor development and blocking metastasis. The antioxidants function as an additional defense mechanism against both inflammation caused by oxidative stress and cancer progression. A therapeutic benefit exists for alkaloid and flavonoid use in cervical cancer thereby emphasizing research into natural compounds which can function as cancer treatment alternatives and enhancement agents compared to traditional therapies and potentially reduce associated side effects. Research on the pharmacological properties of natural agents must continue to determine their practical applications for future use in cervical cancer treatment programs**Table 5(41, 52)**.

Oxidative Stress Reduction by Alkaloids and Flavonoids

The development and spread of cervical cancer together with other cancers heavily depend on oxidative stress which develops when reactive oxygen species (ROS) exceed antioxidant defense capabilities of the body **Figure 6**. High-risk human papillomavirus (HPV) infections leading to cervical cancer produce elevated oxidative stress levels that result in genomic instability, DNA damage and induce inflammatory pathways to facilitate cancer cell proliferation and survival as well as metastasis. Two essential plant-compound groups named alkaloids and flavonoids serve as powerful agents which help fight oxidative stress. These compounds possess antioxidant properties which help lower ROS concentrations and establish redox balance in cervical cancer cells as a means to impede cancer progression. The nitrogen-containing compounds known as alkaloids originate from different plant resources as well as fungal and living marine organisms. Anti-oxidative effect is exhibited by plant compounds among several alkaloids including berberine alongside sanguinarine and vincristine. The compounds exhibit antioxidant properties through their ability to capture harmful free radicals at the same time they activate defense mechanisms in antioxidant enzymes present in the body. Berberine effectively lowers cervical cancer cell ROS levels through its power to increase the function of superoxide dismutase (SOD) and catalase antioxidant enzymes. The protective cellular process against oxidative damage requires essential enzymes SOD and catalase which specifically break superoxide radicals and hydrogen peroxide respectively. The antioxidant enzyme promoting activity of alkaloids permits the regulation of cellular redox equilibrium which protects DNA from damage and mutagenesis that might induce tumor cell progression(53, 54).

Berberine and sanguinarine together with other alkaloids activate cellular signaling paths through which organisms respond to oxidative stress alongside their free radical filtering abilities. Alkaloids use the Nrf2 (nuclear factor erythroid 2-related factor 2) signaling route as a major activation pathway. The transcription factor Nrf2 controls the activation of antioxidant genes through oxidative stress exposure. The cytoplasm effectively binds Nrf2 because Keap1 functions as its repressing agent during regular conditions. Cellular stress caused by oxidative conditions allows Nrf2 to dissociate from Keap1 resulting in its transfer to the nucleus where it activates antioxidant gene expression. Scientific studies indicate that alkaloid berberine activates Nrf2 enabling antioxidant enzyme production which reduces cellular ROS levels. Through activation of Nrf2 this mechanism acts essentially to protect cervical cancer cells against ROS-induced damage and decrease tumor size. Widespread in plant organisms the polyphenolic compound group called flavonoids shows important antioxidant properties. The reduction of oxidative stress in cervical cancer has been extensively documented through the studies of flavonoids quercetin, kaempferol and luteolin. These chemical compounds demonstrate strong scavenging abilities toward various free radicals such as superoxide anion and hydroxyl radicals together with hydrogen peroxide. Quercetin demonstrates antioxidant effects in cervical cancer cells by removing free radicals while simultaneously boosting the function of SOD and catalase enzyme activities. Through activation of the Nrf2 pathway quercetin controls how antioxidant genes express which strengthens its antioxidant capabilities. Research shows that kaempferol along with luteolin acts as an anti-oxidative stress agent through its ability to block ROS development and boost antioxidant mechanisms. The flavonoid compounds shield cellular DNA proteins and lipids against ROS-caused damages through their antioxidant mechanism(55, 56).

The preventive action of flavonoids prevents the inflammatory responses normally activated because of oxidative stress. ROS activates the NF-κB signaling pathway that leads to the increase of pro-inflammatory cytokines such as TNF-α and IL-6. The prolonged NF-κB activation within cervical cancer enables the inflammatory state of tumor microenvironments to enhance survival and multiplication of cancer cells together with metastasis promotion. Quercetin and kaempferol function as anti-NF-κB agents to stop ROS-induced activation of this pathway which then reduces the formation of inflammatory cytokines leading to tumor-unfriendly conditions. Flavonoids demonstrate their potential as therapeutic agents in cervical cancer treatment because they accomplish antioxidant protection together with anti-inflammatory benefits. Alkaloids and flavonoids exhibit both antioxidant and anti-inflammatory behavior which suggests their high potential for cervical cancer treatment. These

compounds protect DNA from harm while stopping inflammatory pathways which help tumor cells develop. The protective mechanism against chronic oxidative damage during cancer progression is enabled by alkaloids and flavonoids because they boost the activity of endogenous antioxidant defense systems inside the body(57, 58).

The reduction of ROS levels shows great potential for becoming a therapeutic approach in the treatment of cervical cancer because oxidative stress drives its development. The antioxidant properties of alkaloids and flavonoids both neutralize free radicals in cells and improve enzyme antioxidant functions to restore redox balance. Natural compounds activate Nrf2 pathways besides their antioxidant properties which strengthens cellular antioxidant mechanisms. These antioxidants can prevent or manage cervical cancer effectively by themselves or with standard medical treatments. Research into their clinical application for cervical cancer treatment should advance because they possess low toxicity along with dual protective effects on oxidative stress and inflammation**Table 6(59, 60)**.

Synergistic Effects of Alkaloids and Flavonoids in Cervical Cancer Treatment

Uncontrolled high-risk human papillomavirus (HPV) infection stands as the main cause of cervical cancer thus maintaining its status as a significant female cancer type **Figure 7**. The medical treatments that include screening along with vaccination and surgery and chemotherapy and radiation have shown limitations because they generate multiple side effects and the cancer tends to become resistant to treatment and returns later. The increase in interest regarding natural compound-based alternative and complementary therapies became evident due to current clinical limitations. The most encouraging natural anticancer compounds being studied are alkaloids together with flavonoids because they display significant cancer-fighting properties. The simultaneous application of alkaloids and flavonoids creates combined therapeutic impacts which boost treatment benefits without generating excessive toxicity making this combination a new approach to fighting cervical cancer. Both alkaloids and flavonoids demonstrate anticancer properties by three different mechanisms which encompass apoptosis induction along with cell proliferation inhibition and metastasis suppression together with inflammatory and oxidative stress regulation. The cervical cancer progression-targeting actions of cervical cancer-propagating cellular processes are demonstrated by alkaloids berberine, sanguinarine, vincristine alongside flavonoids quercetin, kaempferol, and luteolin. Research shows berberine alkaloids activate cervical cancer cell apoptosis using mitochondrial signaling yet quercetin flavonoids trigger cell death through both mitochondrial and death receptor pathways. Cancer cells face diminished resistance factors when different chemical compounds interact due to their multi-dimensional therapeutic strategy (47, 49).

The combination of alkaloids and flavonoids shows remarkable potential in increasing the susceptibility of cancer cells to both chemotherapy-based and radiation-based cancer treatments in cervical cancer patients. Berberine belongs to the alkaloid group of compounds and functions as a chemo-sensitivity agent by reducing NF-κB and PI3K/Akt signaling intermediaries involved in drug tolerance mechanisms. The chemotherapy drug effectiveness can be boosted by flavonoids including quercetin and kaempferol that stop drug efflux pumps from lowering chemotherapy drug amounts inside cells. When alkaloids and flavonoids are used together they enhance the response of cervical cancer cells to chemotherapeutic treatments which improves treatment effectiveness. Alkaloids when combined with flavonoids produce synergistic effects that help reduce inflammation which serves as a primary factor for cervical cancer development. Chronic inflammation within tumor microenvironments enables cancer cells to survive and creates conditions which promote both new blood vessel development and cancer cell spreading across the body. The anti-inflammatory effects of alkaloids match those of flavonoids in equal strength. The NF-κB pathway becomes inhibited through alkaloid berberine which reduces the production of inflammatory cytokines TNF-α, IL-6 and IL-1β. The activation of this inflammatory pathway faces inhibition from two flavonoids quercetin and luteolin which leads to diminished production of inflammatory mediators. The combined effect of both alkaloids and flavonoids creates a suppressive effect on inflammatory signals that help cervical cancer progression thereby making conditions hostile for cancer cell spread and tumor development(50, 51). The development of DNA damage along with genomic instability and pro-inflammatory pathway activation is a major function of oxidative stress in cervical cancer development. Studied antioxidants among alkaloids and flavonoids demonstrate ROS neutralizing capability as well as redox balance maintenance in cellular environments. Berberine as well as sanguinarine stimulates the functioning of cellular endogenous antioxidants including superoxide dismutase (SOD) as well as catalase thus lowering oxidative stress in cervical cancer cells. Except from their ROS-scavenging effects flavonoids like quercetin along with kaempferol activate defense mechanisms within cells which protect DNA from damage while stopping oxidative harm against cellular materials. These natural compounds work in synergy to eliminate oxidative stress which prevents cancer-initiating and cancer-progressing mutations from developing. The double therapeutic action of alkaloid-fused flavonoids works effectively against cancer cell metastasis which presents a major challenge in treating cancer. The inhibition of EMT and MMP activity defines the anti-metastatic effects which both compounds demonstrate individually. EMT represents an important process that enables cancer cells to develop migratory and invasive characteristics which facilitates their

spread to separate organs. Scientific studies demonstrate that the alkaloid vincristine and flavonoids luteolin and quercetin can both prevent EMT and stop cervical cancer cells from migrating. The flavonoid compound kaempferol diminishes MMP activity which stops the destruction of the extracellular matrix to stop cancer cell invasion. The simultaneous use of alkaloids and flavonoids creates an effective mechanism to stop cervical cancer cell metastasis which leads to better outcomes in treatment and decreases the potential for reoccurrence (52, 53). The combined therapeutic effects between alkaloids and flavonoids are strengthened by their synergistic work relationship. The joint treatment of berberine alkaloid with quercetin flavonoid enhances the apoptotic properties of these substances considerably more than administering them separately. Researchers believe alkaloids interact with cancer cell signaling pathways while activating apoptotic signaling and decreasing inflammation together with flavonoids because their mechanisms work harmoniously. The application of alkaloids with flavonoids enables physicians to treat cancer effectively since the combination helps address obstacles which arise from single-agent treatments. The treatment of cervical cancer benefits from the beneficial joint actions of both alkaloids and flavonoids. The natural compounds achieve effective cervical cancer control through their collective ability to trigger apoptosis death of cancer cells and control inflammation while lowering oxidative stress and restricting metastasis. The merged alkaloids and flavonoids functions together to make treatments more effective while avoiding the negative aspects of standard medical approaches. Additional clinical research will allow alkaloids and flavonoids to become key components for developing better yet safer cervical cancer treatments **Table 7 (54, 55).**

Future Perspectives and Clinical Application of Alkaloids and Flavonoids in Cervical Cancer Therapy

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The development of DNA damage along with genomic instability and pro-inflammatory pathway activation is a major function of oxidative stress in cervical cancer development. Studied antioxidants among alkaloids and flavonoids demonstrate ROS neutralizing capability as well as redox balance maintenance in cellular environments. Berberine as well as sanguinarine stimulates the functioning of cellular endogenous antioxidants including superoxide dismutase (SOD) as well as catalase thus lowering oxidative stress in cervical

cancer cells. Except from their ROS-scavenging effects flavonoids like quercetin along with kaempferol activate defense mechanisms within cells which protect DNA from damage while stopping oxidative harm against cellular materials. These natural compounds work in synergy to eliminate oxidative stress which prevents cancer-initiating and cancer-progressing mutations from developing(61, 62).

The double therapeutic action of alkaloid-fused flavonoids works effectively against cancer cell metastasis which presents a major challenge in treating cancer. The inhibition of EMT and MMP activity defines the anti-metastatic effects which both compounds demonstrate individually. EMT represents an important process that enables cancer cells to develop migratory and invasive characteristics which facilitates their spread to separate organs. Scientific studies demonstrate that the alkaloid vincristine and flavonoids luteolin and quercetin can both prevent EMT and stop cervical cancer cells from migrating. The flavonoid compound kaempferol diminishes MMP activity which stops the destruction of the extracellular matrix to stop cancer cell invasion. The simultaneous use of alkaloids and flavonoids creates an effective mechanism to stop cervical cancer cell metastasis which leads to better outcomes in treatment and decreases the potential for reoccurrence. The combined therapeutic effects between alkaloids and flavonoids are strengthened by their synergistic work relationship. The joint treatment of berberine alkaloid with quercetin flavonoid enhances the apoptotic properties of these substances considerably more than administering them separately. Researchers believe alkaloids interact with cancer cell signaling pathways while activating apoptotic signaling and decreasing inflammation together with flavonoids because their mechanisms work harmoniously. The application of alkaloids with flavonoids enables physicians to treat cancer effectively since the combination helps address obstacles which arise from single-agent treatments(63, 64).

The treatment of cervical cancer benefits from the beneficial joint actions of both alkaloids and flavonoids. The natural compounds achieve effective cervical cancer control through their collective ability to trigger apoptosis death of cancer cells and control inflammation while lowering oxidative stress and restricting metastasis. The merged alkaloids and flavonoids functions together to make treatments more effective while avoiding the negative aspects of standard medical approaches. Additional clinical research will allow alkaloids and flavonoids to become key components for developing better yet safer cervical cancer treatments**Table 8(52, 65)**.

Discussion

Uncontrolled high-risk human papillomavirus (HPV) infection stands as the main cause of cervical cancer thus maintaining its status as a significant female cancer type. The medical treatments that include screening along with vaccination and surgery and chemotherapy and radiation have shown limitations because they generate multiple side effects and the cancer tends to become resistant to treatment and returns later. The increase in interest regarding natural compound-based alternative and complementary therapies became evident due to current clinical limitations. The most encouraging natural anticancer compounds being studied are alkaloids together with flavonoids because they display significant cancer-fighting properties. The simultaneous application of alkaloids and flavonoids creates combined therapeutic impacts which boost treatment benefits without generating excessive toxicity making this combination a new approach to fighting cervical cancer.

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Alkaloids when combined with flavonoids produce synergistic effects that help reduce inflammation which serves as a primary factor for cervical cancer development. Cancer cells survive better due to tumor microenvironment inflammation which also helps create new blood vessels and accelerates disease spreading throughout the body. The anti-inflammatory effects

of alkaloids match those of flavonoids in equal strength. The NF-κB pathway becomes inhibited through alkaloid berberine which reduces the production of inflammatory cytokines TNF-α, IL-6 and IL-1β. The activation of this inflammatory pathway faces inhibition from two flavonoids quercetin and luteolin which leads to diminished production of inflammatory mediators. The combined effect of both alkaloids and flavonoids creates a suppressive effect on inflammatory signals that help cervical cancer progression thereby making conditions hostile for cancer cell spread and tumor development.

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The combined therapeutic effects between alkaloids and flavonoids are strengthened by their synergistic work relationship. The joint treatment of berberine alkaloid with quercetin flavonoid enhances the apoptotic properties of these substances considerably more than administering them separately. Researchers believe alkaloids interact with cancer cell signaling pathways while activating apoptotic signaling and decreasing inflammation together with

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The treatment of cervical cancer benefits from the beneficial joint actions of both alkaloids and flavonoids. The natural compounds achieve effective cervical cancer control through their collective ability to trigger apoptosis death of cancer cells and control inflammation while lowering oxidative stress and restricting metastasis. The merged alkaloids and flavonoids functions together to make treatments more effective while avoiding the negative aspects of standard medical approaches. Additional clinical research will allow alkaloids and flavonoids to become key components for developing better yet safer cervical cancer treatments.

Conclusion

The unchecked high-risk human papillomavirus (HPV) infection is the main explanation of cervical cancer, which establishes it as one of the fundamental causes of cancer death in women worldwide. Medical treatments which include screening, vaccination, surgery, chemotherapy and radiation have advancements but have limitations which include side effects and resistance to cure, thus alternative treatment methods should be explored. In this regard, natural products especially alkaloids and flavonoids have attracted great interests because of their promising anticancer activities. The effects of alkaloids and flavonoids are suggested to be involved in several ways, apoptosis induction, cell proliferation, metastasis inhibition, modulation of inflammation, and oxidative stress. Such compounds as berberine, sanguinarine, and vincristine (alkaloids) and quercetin, kaempferol, and luteolin (flavonoids) were shown to target crucial cellular pathways that stimulate the growth of cervical cancer. There is synergistic action between alkaloids and flavonoids, which increases their effects, and it may overcome the mechanism of resistance to conventional therapies. In addition, these natural products have immense promises in making cervical cancer cells become sensitive to chemotherapy and radiation thus enhancing improved response to treatment. Alkaloids and flavonoids combination not only has anti-inflammatory properties but also regulates key signaling pathways (NF-kappa B, PI3K/Akt and MAPK) that have been altered in cancer development. Moreover, they have antioxidant effects, which neutralize reactive oxygen species (ROS), and thus, prevent the mutations caused by oxidative stress, which may promote the development of cancer.

Their anti-metastatic effect is also evidenced by the inhibition of epithelial-to-mesenchymal transition (EMT) and matrix metalloproteinases (MMPs), which is a promising mechanism of fighting cervical cancer metastasis. The synergistic therapeutic effect of alkaloids and

flavonoids offers a comprehensive cure of cervical cancer since the combination has the potential of killing cancer cells and has low toxicity levels as compared to conventional treatment. Additional clinical trials are needed to confirm the effectiveness and safety of these compounds because their inclusion into the arsenal of cancer-treating combinations may provide safer and more effective options than those provided by existing therapies. Through further studies, alkaloids and flavonoids could play a fundamental role in the realization of new, less toxic forms of cervical cancer treatment.

Authors contribution

YC, DY, DZ, SM carried out formal analysis and wrote the original manuscript. MD, NK performed analysis the data. PT, KR, SW, CZ contributed to the study's conception, design and proofread it. All the authors have read and approved the manuscript for submission.

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Table 1. This table compares the key properties of alkaloids and flavonoids, highlighting their biological effects, mechanisms of action in cancer, and potential for enhancing standard treatments, with a focus on clinical applications.

Aspect	Alkaloids	Flavonoids	Common Properties
Occurrence in Nature	Found in various plant species containing nitrogen structures	Present throughout plants with anti-inflammatory,	Both are bioactive plant compounds with cancer inhibition potential

		antioxidant properties	
Key Biological Effects	Anti-cancer, antimicrobial, anti-inflammatory	Anti-cancer, anti-inflammatory, antioxidant	Both modulate key pathways related to cancer cell growth, survival, and inflammation
Molecular Action in Cancer	Alters survival and death pathways like PI3K/Akt, MAPK, p53	Modulates inflammatory cytokines (TNF-α, IL-6, IL-1β)	Both reduce oxidative stress and inflammation, targeting cancer-specific pathways
Apoptosis Induction	Promotes cancer cell death via apoptosis mechanisms	Induces apoptosis selectively in cancer cells	Both induce apoptosis, sparing healthy tissues
Inflammation Modulation	Inhibits NF-κB pathway, reducing tumor-facilitating inflammation	Reduces chronic inflammation by modulating NF-κB, cytokines	Both reduce inflammation that supports tumor progression
Oxidative Stress Reduction	Acts as an antioxidant, neutralizing ROS	Scavenges free radicals, enhancing antioxidant defenses	Both neutralize ROS, preventing DNA damage and mutations
Synergistic Effect with Standard Treatment	Enhances chemotherapy and radiation response, reducing resistance	Increases sensitivity to chemotherapy and radiation	Both synergistically enhance the effectiveness of standard cancer therapies
Pharmaceutical Application	Considered safer alternatives to synthetic drugs	Offer holistic treatment options with fewer side effects	Potential for combined use in cancer treatment strategies
Clinical Research Status	Preclinical studies show promising results	Early studies indicate potential for clinical application	Ongoing research to optimize delivery, bioavailability, and safety in humans
Future Applications	Development of novel therapeutic agents from plant sources	Research into combining with chemotherapy for enhanced outcomes	Focus on patient stratification using biomarkers for personalized treatment

Table 2 This table summarizes the key aspects of alkaloids in cancer therapy, detailing their mechanisms of action, anti-inflammatory properties, oxidative stress reduction, and chemosensitizing effects, along with future clinical applications.

Aspect	Description	Examples of Alkaloids	Significance in Cancer Therapy
Source of Alkaloids	Alkaloids are naturally occurring compounds containing nitrogen within cyclic ring structures.	Berberine, Sanguinarine, Vincristine	Derived from plants, fungi, and marine organisms.
Mechanism of Action	Alkaloids induce cell death (apoptosis) by disrupting mitochondrial function and activating caspases.	Berberine, Sanguinarine	Trigger intrinsic apoptosis pathways to selectively kill cancer cells.
Impact on Cancer Cell Pathways	Target survival and proliferation pathways such as PI3K/Akt and MAPK/ERK.	Berberine, Vincristine, Cryptolepine	Block pathways promoting cancer cell survival, proliferation, and metastasis.
Anti-Inflammatory Properties	Inhibit inflammatory pathways, reducing cytokines and inflammation that support tumor growth.	Berberine, Sanguinarine, Curcumin	Suppress NF-κB activation and COX-2 activity, creating a less tumor-friendly environment.
Oxidative Stress Reduction	Alkaloids act as antioxidants to reduce reactive oxygen species (ROS) and prevent DNA damage.	Berberine, Vincristine	Decrease ROS levels, reducing oxidative damage and preventing cancer initiation.
Chemosensitizing Properties	Enhance sensitivity to chemotherapy and radiation, overcoming drug resistance.	Berberine, Vincristine, Paclitaxel	Improve the effectiveness of standard cancer treatments.
Targeted Action on Cancer Cells	Alkaloids exhibit selective toxicity, targeting cancer cells while minimizing damage to healthy cells.	Berberine, Vincristine, Paclitaxel	Minimize side effects and allow extended use in cancer therapy.

Toxicity and Side Effects	Alkaloids show minimal toxicity in healthy cells compared to conventional chemotherapy.	All alkaloids mentioned	Offer safer, long-term treatment options.
Combination with Conventional Therapies	Alk		
Future Applications	Development of novel therapeutic agents from plant sources	Research into combining with chemotherapy for enhanced outcomes	Focus on patient stratification using biomarkers for personalized treatment

Table 3. This table summarizes the role of flavonoids in cervical cancer therapy, highlighting their mechanisms of action, anti-inflammatory properties, apoptosis induction, and potential for synergistic effects with chemotherapy.

Aspect	Description	Examples of Flavonoids	Significance in Cervical Cancer Therapy
Source of Flavonoids	Abundant in fruits, vegetables, herbs, and various plant ingredients	Quercetin, Kaempferol, Luteolin, Genistein	Naturally occurring compounds with anticancer properties
Mechanism of Action	Induces apoptosis by activating mitochondrial pathways and enhancing pro-apoptotic protein expression	Quercetin, Kaempferol	Triggers apoptosis by modulating BAX/BCL-2 ratio and activating caspases
Anti-Inflammatory Properties	Inhibits NF-κB and MAPK pathways, reducing inflammatory cytokines like TNF-α, IL-6, and IL-1β	Quercetin, Kaempferol	Reduces inflammation that supports tumor progression and metastasis
Cell Cycle Regulation	Inhibits cyclin-dependent kinases (CDKs), blocking G1 to S phase progression, and halting cell proliferation	Genistein, Apigenin	Prevents uncontrolled cancer cell division and enhances treatment sensitivity
Oxidative Stress Reduction	Scavenges ROS and enhances antioxidant enzyme activity, protecting cells from oxidative damage	Kaempferol	Reduces DNA damage, preventing cancer initiation and progression

Anti-Metastatic Properties	Inhibits epithelial-to-mesenchymal transition (EMT) and matrix metalloproteinase (MMP) activity	Luteolin, Quercetin	Prevents cancer cell migration and invasion, reducing metastasis
Synergy with Chemotherapy	Enhances the effectiveness of chemotherapeutic drugs and overcomes resistance mechanisms	Quercetin	Improves chemotherapy efficacy by inhibiting drug resistance mechanisms
Cancer Cell Apoptosis	Induces selective cancer cell death while sparing normal tissues	Quercetin, Kaempferol, Luteolin	Targeted cell death through apoptotic pathways, reducing side effects
Pharmaceutical Potential	Flavonoids are considered safer alternatives to synthetic drugs with fewer adverse effects	All mentioned flavonoids	Possibility of developing new natural treatments for cancer
Future Application	Ongoing research into clinical use, optimization of dosage, and delivery methods	All mentioned flavonoids	Potential for becoming standard practice in cervical cancer treatment

Table 4. This table compares alkaloids and flavonoids in cervical cancer therapy, highlighting their mechanisms of action, apoptosis pathways, impact on ROS and p53, and potential synergy with chemotherapy for improved treatment outcomes.

Aspect	Alkaloids	Flavonoids	Significance in Cervical Cancer Therapy
Source	Nitrogen-containing compounds from plants, fungi, marine organisms	Polyphenolic compounds found in fruits, vegetables, herbs	Both are natural compounds with strong anticancer properties
Mechanism of Action	Induces apoptosis via mitochondrial pathway (BAX/BCL-2 ratio imbalance)	Triggers apoptosis via mitochondrial pathway and ROS induction	Both activate intrinsic and extrinsic apoptosis pathways
Key Apoptosis Pathways	Intrinsic mitochondrial pathway (cytochrome c, caspases)	Intrinsic mitochondrial pathway (BAX/BCL-2), extrinsic Fas receptor	Dual mechanism for enhanced apoptosis, overcoming resistance

Pro-apoptotic Effects	Enhances BAX expression, reduces BCL-2 levels	Activates BAX and suppresses BCL-2	Promotes selective cancer cell death while sparing healthy tissues
Impact on ROS	Reduces ROS levels, protecting against oxidative damage	Increases ROS levels, promoting mitochondrial dysfunction	Both compounds regulate ROS to reduce oxidative stress in cells
Influence on p53 Pathway	Activates p53, enhancing tumor suppressor protein activity	Stabilizes p53, enhancing its transcriptional activity	Improves cancer cell sensitivity to apoptosis
Extrinsic Pathway Activation	Increases Fas receptor expression, enhancing apoptosis sensitivity	Enhances Fas receptor expression, triggering caspase-8 activation	Enhances extrinsic apoptosis pathways for better cancer treatment
In Vivo Effects	Reduces tumor growth, causes cancer cell death in animal models	Induces apoptosis, reduces tumor size in animal models	Natural compounds show promising in vivo anticancer activity
Combination with Chemotherapy	Enhances chemotherapy effects, reduces resistance	Increases chemotherapy sensitivity and overcomes resistance	Potential to improve chemotherapy outcomes and reduce side effects
Clinical Implications	Safer alternative to chemotherapy, selective cancer cell targeting	Potential for clinical use as standalone or combined treatment	Non-toxic, plant-derived agents for more effective, safer therapy

Table 5. This table compares alkaloids and flavonoids in their anti-inflammatory actions, highlighting their effects on key inflammatory pathways, cytokine reduction, antioxidant properties, and their potential to enhance cancer treatment outcomes.

Aspect	Alkaloids	Flavonoids	Significance in Cervical Cancer Therapy
Source	Derived from plants, fungi, and marine organisms	Found in fruits, vegetables, herbs, and various plant ingredients	Both are natural compounds with strong anti-inflammatory properties
Mechanism of Anti-inflammatory Action	Inhibit NF-κB, COX-2, and reduce cytokine levels	Suppress NF-κB, MAPK, and JAK/STAT pathways	Both reduce inflammation-related pathways promoting cancer growth

Targeted Pathways	NF-κB, COX-2	NF-κB, MAPK, JAK/STAT	Block inflammation-driving pathways such as NF-κB and MAPK
Effects on Cytokines	Reduces TNF-α, IL-6, IL-1β	Reduces TNF-α, IL-6, IL-8	Decreases pro-inflammatory cytokines that promote cancer survival
Anti-inflammatory Examples	Berberine, Sanguinarine, Vincristine	Quercetin, Kaempferol, Luteolin	Alkaloids and flavonoids modulate key inflammatory signals
Effect on MAPK Pathway	Inhibits inflammatory signaling	Inhibits MAPK pathway, reducing inflammation and cancer progression	Inhibits key pathways (MAPK, JAK/STAT) involved in tumor growth
Antioxidant Properties	Reduces ROS, activates SOD and catalase	Scavenges ROS, enhances antioxidant enzyme activity	Protects cells from oxidative stress and inflammation
Cancer Cell Proliferation	Blocks cell cycle and suppresses proliferation	Blocks cell proliferation and tumor growth	Both reduce cancer cell proliferation, limiting tumor progression
Tumor Metastasis	Inhibits metastatic spread through inflammatory pathway suppression	Reduces metastasis by controlling EMT and MMP activity	Inhibits cancer cell spread, controlling metastasis
Clinical Implications	Potential as co-treatment for chemotherapy, reducing resistance	Enhances chemotherapy effects and reduces side effects	Effective as natural agents in enhancing current cancer treatments

Table 6. This table compares alkaloids and flavonoids in their antioxidant and anticancer properties, focusing on their mechanisms of action, effects on ROS, DNA protection, inflammation reduction, and potential in enhancing cervical cancer treatments.

Aspect	**Alkaloids**	**Flavonoids**	**Significance in Cervical Cancer Therapy**
Source	Derived from plants, fungi, and marine organisms	Found in various plant sources like fruits, vegetables, and herbs	Both are natural compounds with potent antioxidant properties

Key Compounds	Berberine, Sanguinarine, Vincristine	Quercetin, Kaempferol, Luteolin	Key bioactive agents with antioxidant and anticancer effects
Mechanism of Antioxidant Action	Scavenge free radicals and enhance antioxidant enzyme activity	Scavenge free radicals and enhance SOD and catalase activity	Both reduce ROS levels, protecting cells from oxidative damage
Activation of Nrf2 Pathway	Berberine activates Nrf2, enhancing antioxidant gene expression	Quercetin activates Nrf2, boosting antioxidant defense mechanisms	Activation of Nrf2 enhances antioxidant capacity and reduces ROS
Effect on ROS	Reduces ROS by boosting SOD and catalase activities	Reduces ROS, protects DNA, proteins, and lipids from oxidative damage	Both neutralize free radicals, restoring cellular redox balance
Anti-Inflammatory Effects	Inhibits NF-κB and COX-2, reducing pro-inflammatory cytokines	Suppresses NF-κB pathway, reducing cytokines like TNF-α, IL-6	Reduce inflammation that supports tumor growth and metastasis
Impact on DNA Damage	Protects DNA from oxidative damage and mutagenesis	Shields DNA from ROS-induced mutations	Prevents DNA damage, reducing cancer initiation and progression
Cell Proliferation and Survival	Regulates cell survival and proliferation pathways	Inhibits cancer cell proliferation, supports tumor suppression	Both suppress uncontrolled cell growth, limiting tumor expansion
Synergy with Conventional Therapy	Enhances chemotherapy effectiveness and overcomes drug resistance	Improves chemotherapy sensitivity and reduces side effects	Potential to enhance current cancer treatments and reduce resistance
Clinical Application	Low toxicity, selective targeting of cancer cells	Low toxicity, well-tolerated in clinical settings	Natural compounds as safer alternatives or adjuncts to chemotherapy

Table 7. This table compares alkaloids and flavonoids in cervical cancer therapy, highlighting their mechanisms of action, anti-inflammatory and apoptotic effects, synergy with chemotherapy, and potential for enhancing treatment outcomes.

Aspect	Alkaloids	Flavonoids	Significance in Cervical Cancer Therapy
Source	Derived from plants, fungi, and marine organisms	Found in fruits, vegetables, herbs, and other plant-based sources	Both are natural compounds with strong anticancer properties
Mechanisms of Action	Apoptosis induction, cell proliferation inhibition, inflammation and oxidative stress regulation	Apoptosis induction, inflammation regulation, oxidative stress control	Target multiple cancer-related pathways to reduce cancer progression
Combination Effects	Enhances effectiveness when used with chemotherapy and radiation	Improves chemotherapy and radiation sensitivity	Synergistically improves response to conventional cancer treatments
Anti-inflammatory Effects	Inhibits NF-κB, COX-2, and reduces cytokine levels	Suppresses NF-κB, reduces TNF-α, IL-6, and IL-1β production	Reduces tumor-promoting inflammation, limiting cancer cell survival
Oxidative Stress Reduction	Activates antioxidant enzymes (SOD, catalase) to lower ROS levels	Scavenges ROS and enhances cellular antioxidant defenses	Reduces oxidative stress that drives cancer initiation and progression
Apoptosis Induction	Promotes mitochondrial apoptosis via BAX/BCL-2 ratio modulation	Activates both mitochondrial and death receptor apoptosis pathways	Induces cancer cell death while sparing healthy tissues
Metastasis Inhibition	Prevents epithelial-to-mesenchymal transition (EMT) and invasion	Inhibits EMT and matrix metalloproteinase (MMP) activity	Stops cancer cell migration and invasion, reducing metastasis
Synergistic Effects on Cancer Cell Signaling	Enhances apoptotic signaling, reduces inflammation	Amplifies apoptotic effects and controls inflammatory pathways	Combination works better than individual compounds, addressing treatment resistance
Clinical Potential	Effective as adjuncts to conventional therapies	Potential to reduce side effects of chemotherapy and radiation	Safer, more effective alternative to traditional cancer treatments
Research and Application	Further research needed to optimize clinical use and dosage	Clinical validation is necessary for widespread adoption	Ongoing research could make alkaloids and flavonoids standard treatments for cervical cancer

Table 8. This table compares alkaloids and flavonoids in cervical cancer therapy, highlighting their anticancer properties, mechanisms of action, synergy with chemotherapy, and potential for safer, more effective treatment options.

Aspect	Alkaloids	Flavonoids	Significance in Cervical Cancer Therapy
Source	Derived from plants, fungi, and marine organisms	Found in fruits, vegetables, herbs, and other plant ingredients	Both natural compounds with anticancer properties
Mechanisms of Action	Apoptosis induction, inhibition of proliferation, anti-inflammation, oxidative stress regulation	Apoptosis induction, inhibition of proliferation, anti-inflammatory, antioxidant	Target multiple cancer-related pathways to reduce cancer progression
Combination Effects	Enhances response to chemotherapy and radiation	Increases chemotherapy sensitivity and reduces side effects	Synergistically improves cancer treatment effectiveness
Anti-inflammatory Effects	Inhibits NF-κB, COX-2, reduces inflammatory cytokines	Suppresses NF-κB, reduces TNF-α, IL-6, IL-1β	Reduces tumor-promoting inflammation, limiting cancer cell survival
Oxidative Stress Reduction	Boosts antioxidant enzyme activity (SOD, catalase)	Scavenges ROS, enhances SOD and catalase activity	Protects cells from oxidative damage, preventing cancer initiation and progression
Metastasis Inhibition	Prevents EMT and MMP activity	Inhibits EMT, reduces MMP activity	Stops cancer cell migration and invasion, reducing metastasis
Apoptosis Induction	Activates intrinsic mitochondrial pathway (BAX/BCL-2 modulation)	Activates mitochondrial and death receptor pathways	Induces cancer cell death while sparing normal tissues
Synergistic Effects on Cancer Signaling	Enhances apoptotic signaling and reduces inflammation	Amplifies apoptotic effects, targets inflammatory pathways	Dual action for enhanced cancer treatment response
Clinical Application	Potential to be used alongside chemotherapy and radiation	Potential to enhance chemotherapy and radiation effects	Natural alternatives or adjuncts to conventional cancer therapies

Future Research and Application	Requires further clinical research on pharmacokinetics and dosage	Ongoing clinical validation needed	Promising for safer, more effective cervical cancer treatments

Figure 1. Illustration highlighting alkaloids and flavonoids as plant-based agents in cervical cancer treatment. These compounds regulate cellular pathways, reduce inflammation, and induce apoptosis, offering promising therapeutic potential against tumor progression.

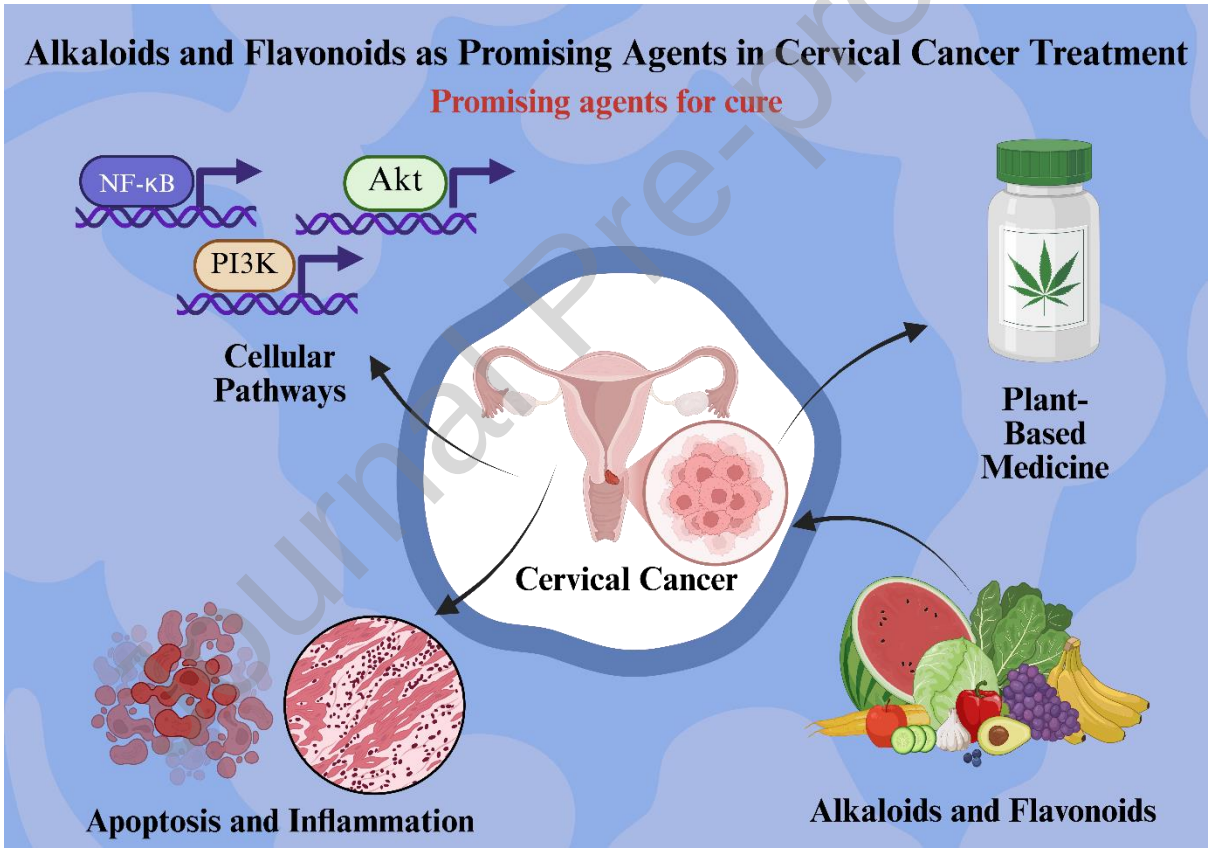


Figure 2. This figure illustrates alkaloids' anticancer mechanisms in cervical cancer: inducing apoptosis, inhibiting PI3K/Akt and MAPK pathways, suppressing NF-κB/COX-2, reducing ROS and inflammation, and enhancing chemosensitivity for therapeutic effect.

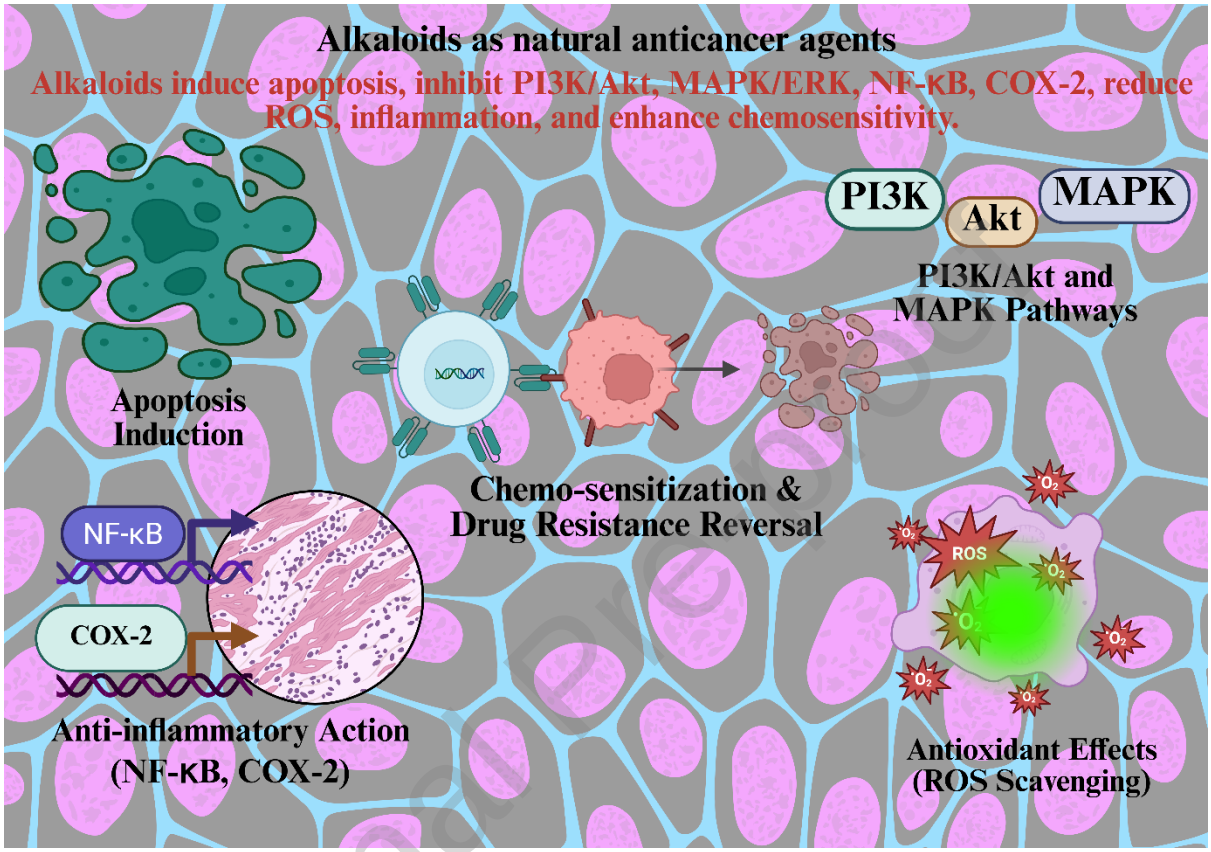


Figure 3. This figure depicts flavonoids as modulators of cervical cancer by inducing apoptosis, reducing inflammation, and inhibiting metastasis—highlighting their therapeutic potential in halting cancer progression through multiple biological mechanisms.

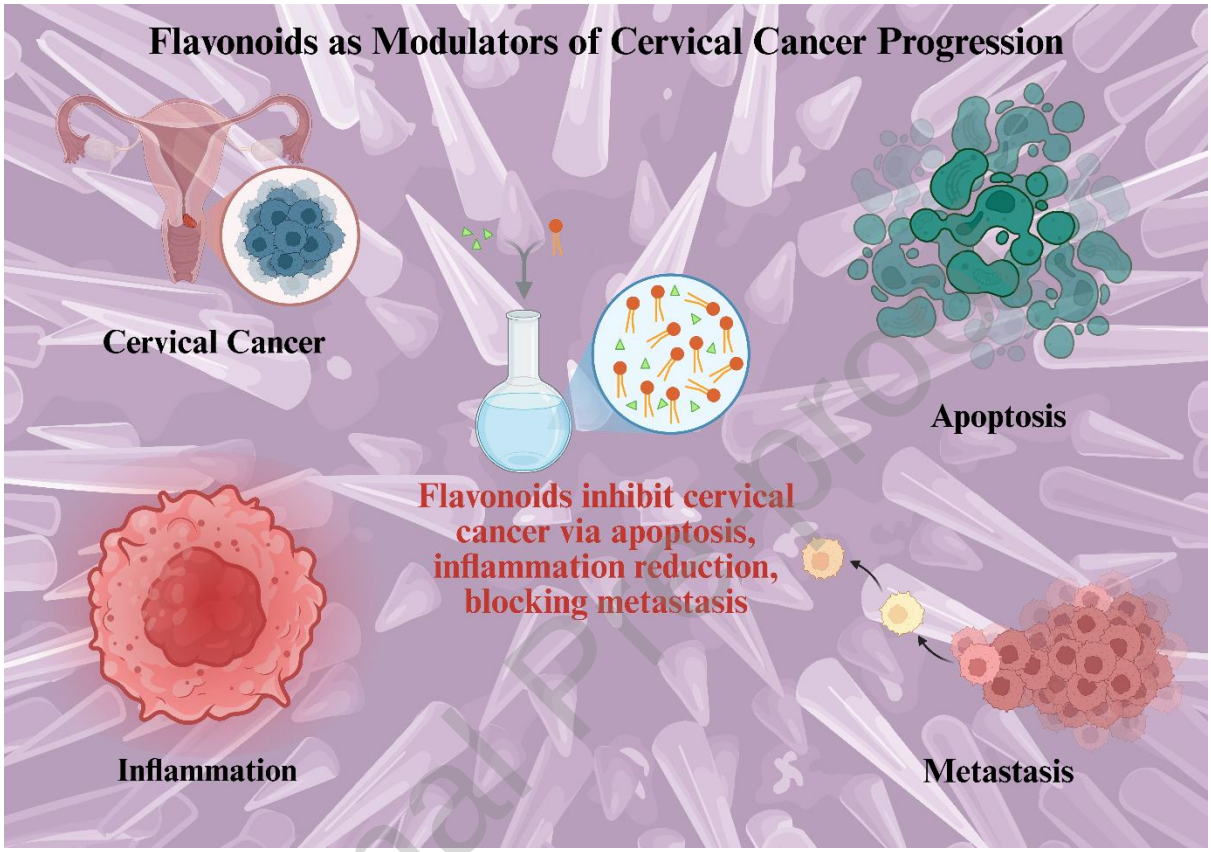


Figure 4. This illustration shows how alkaloids and flavonoids induce apoptosis in cervical cancer cells through mitochondrial pathways, highlighting the TCA cycle's role in ATP production and cancer cell regulation.

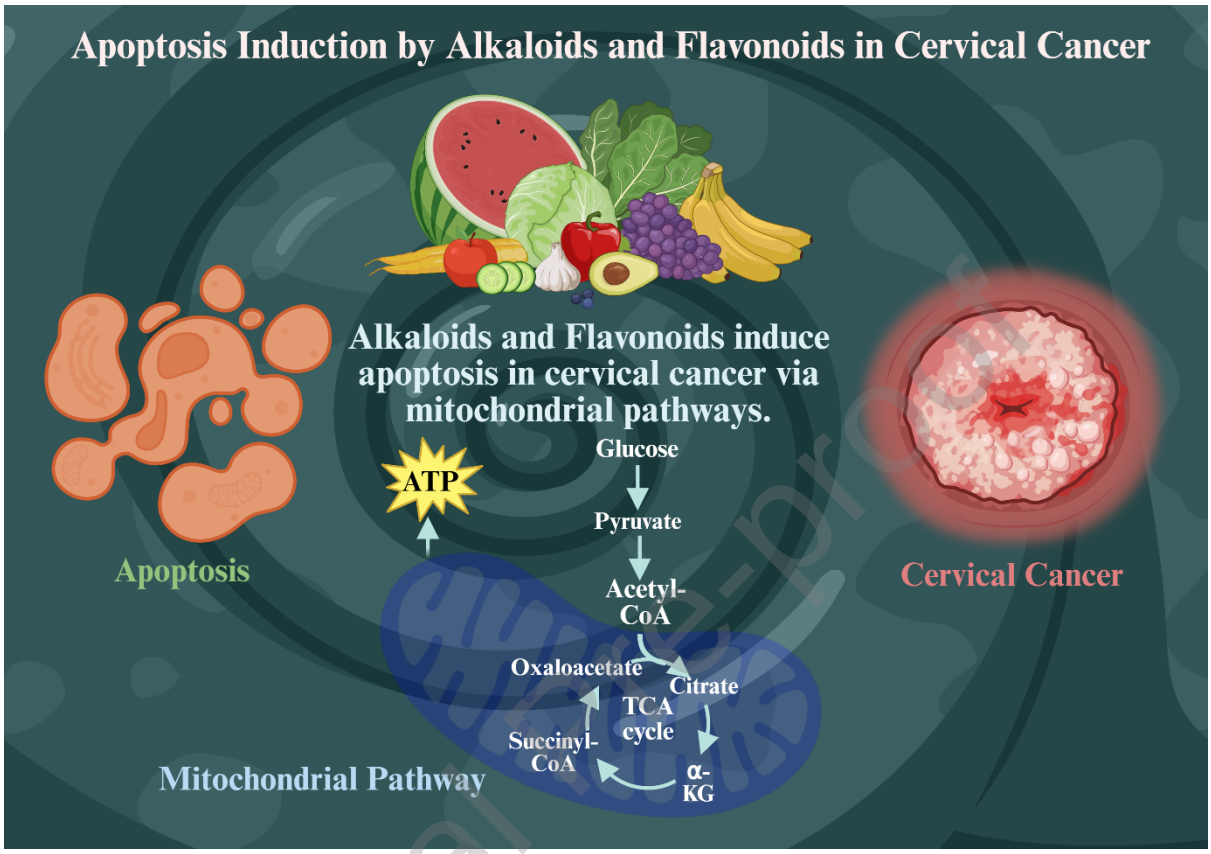


Figure 5. This figure illustrates the anti-inflammatory effects of alkaloids and flavonoids in cervical cancer through NF-κB inhibition, COX-2 and cytokine suppression, antioxidant ROS neutralization, and MAPK/JAK-STAT pathway modulation.

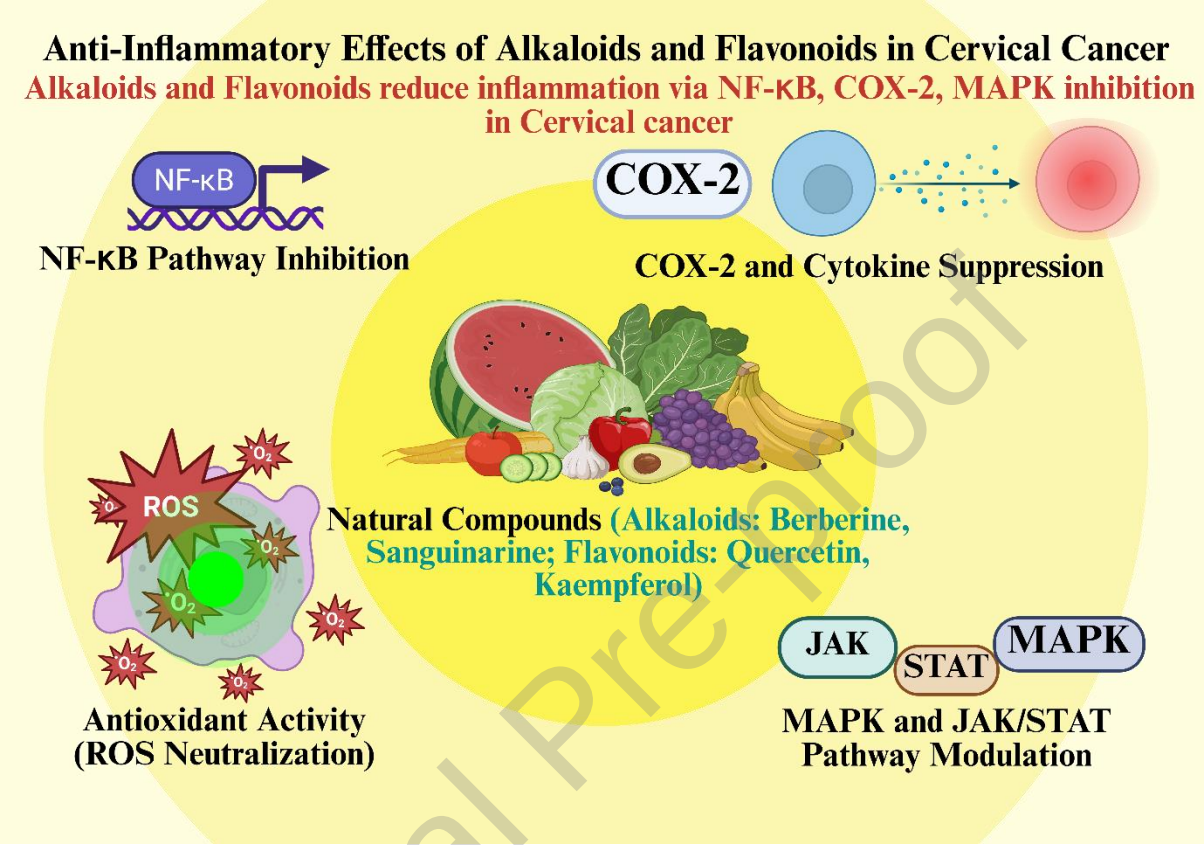


Figure 6. This figure illustrates oxidative stress reduction by alkaloids and flavonoids in cervical cancer via Nrf2 activation, enhancement of SOD and catalase activity, and suppression of reactive oxygen species (ROS).

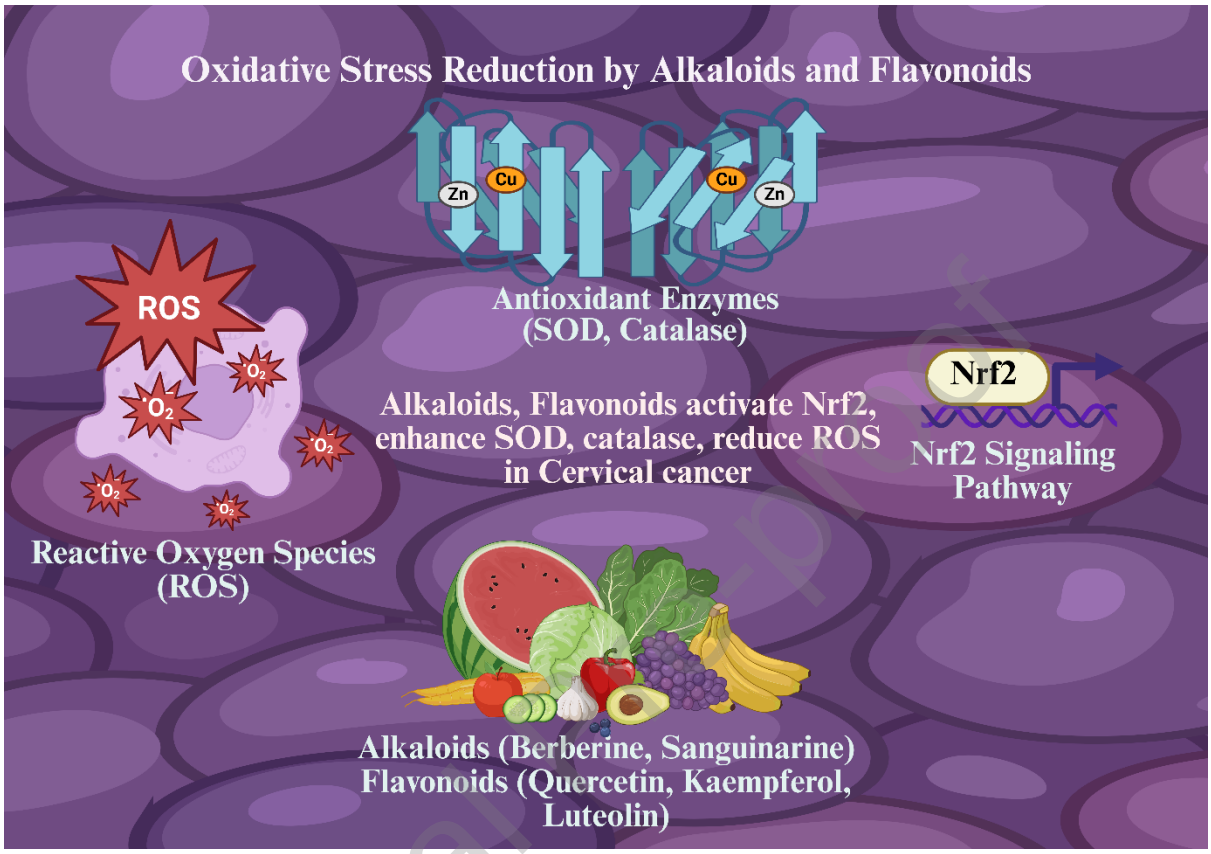


Figure 7. This figure demonstrates the synergistic effects of alkaloids and flavonoids in cervical cancer treatment, highlighting apoptosis induction, inflammation and oxidative stress suppression, anti-metastatic activity, and chemo/radio-sensitization.

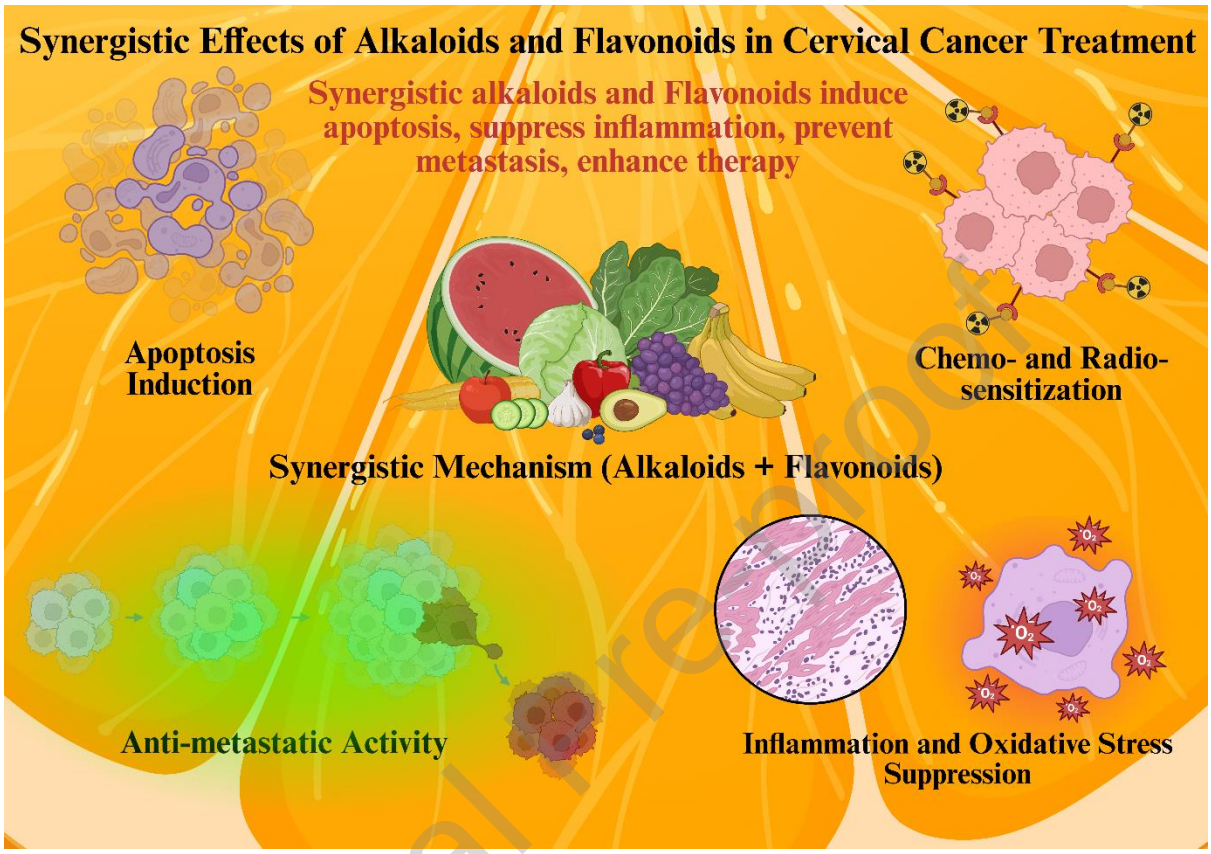
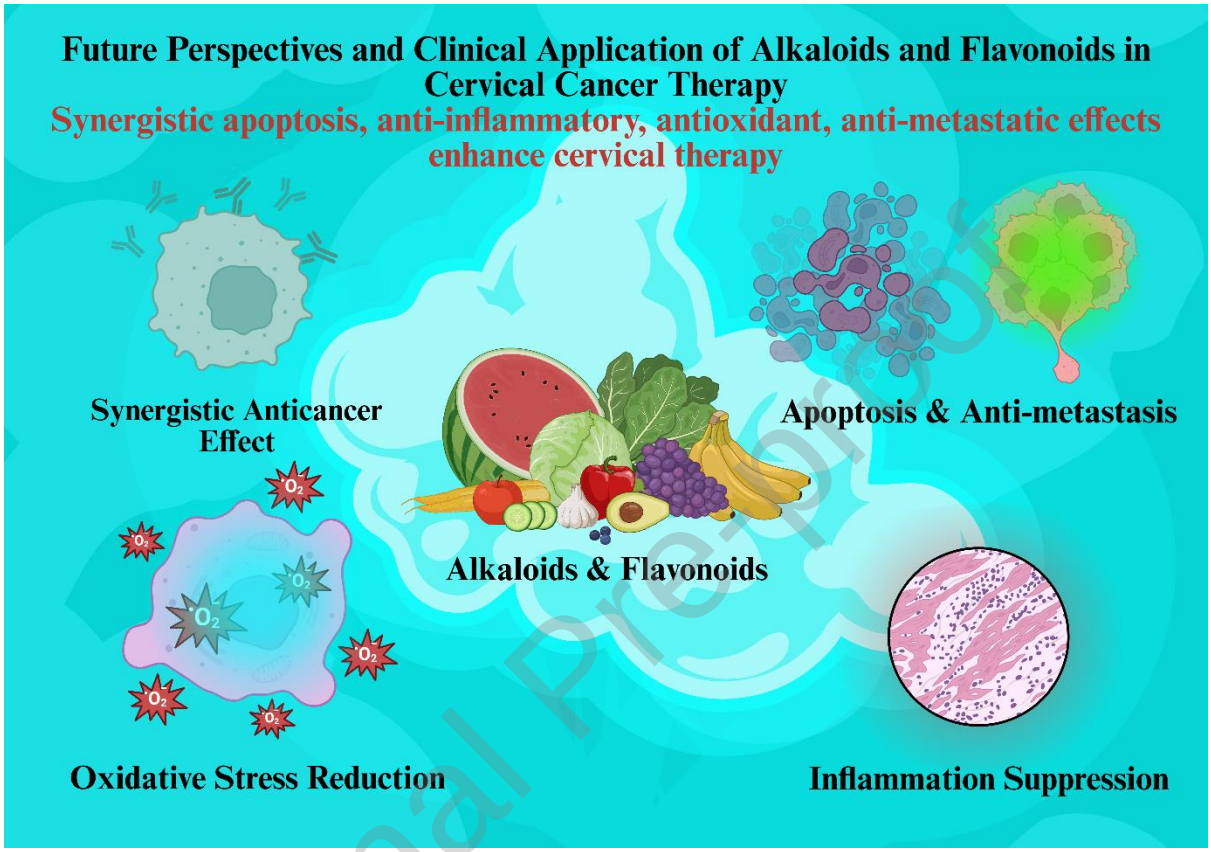
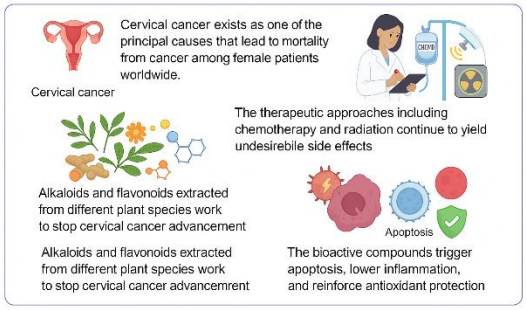


Figure 8. This figure illustrates the future perspectives and clinical potential of alkaloids and flavonoids in cervical cancer therapy, emphasizing synergistic anticancer effects through apoptosis, anti-metastasis, oxidative stress reduction, and inflammation suppression.



Graphical abstract



DeclarationStatement

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.