*ejpmr, 2024, 11(11), 78-85*

**SJIF Impact Factor 7.065**

**EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH**

www.ejpmr.com

Review Article

ISSN 2394-3211

EJPMR

# MEDICINAL PROPERTY OF VINCA ALKALOID AND THEIRIMPACT ON HUMAN HEALTH

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**Article Received on 29/08/2024** **Article Revised on 11/09/2024** **Article Accepted on 10/10/2024**

**ABSTRACT**

Vinca alkaloids, which are strong substances obtained from the Vinca rosea plant and are well-known for their important role in the treatment of cancer, include vincristine and vinblastine. These alkaloids cause cell cycle arrest and apoptosis in rapidly dividing cancer cells by interfering with the production of microtubules, an essential step in cell division. The field of oncology has changed significantly since its introduction into clinical practice, especially in terms of how leukemia, lymphoma, and other solid malignancies are managed. Notwithstanding their therapeutic advantages, vinca alkaloids have adverse effects that can impair patient quality of life and make treatment plans more difficult, such as peripheral neuropathy, constipation, and myelosuppression. The proper ratio of toxicity to efficacy is still a major area of ongoing study. The goal of medication distribution and combination therapies is to increase vinca alkaloids' therapeutic index while reducing side effects. Through innovative medication formulations and delivery methods, recent developments seek to maximize the effectiveness of vinca alkaloids while reducing adverse effects. These developments could lead to better patient outcomes and a wider range of vinca alkaloids' clinical uses. Overall, research is still being done to maximize the therapeutic potential of vinca alkaloids and reduce any related hazards, since they continue to be an essential part of cancer chemotherapy.

**KEYWORDS:** Alkaloids, Leukemia, Essential, Production, Significantly, Treatment, Toxicity, Advantages.

## 1. INTRODUCTION

The category of medications known as vinca alkaloids is derived from the periwinkle plant in Madagascar. They have cytotoxic and hypoglycemic properties and are naturally derived from Catharanthus roseus G. Don, the pink periwinkle plant. They have been used as disinfectants and to treat high blood pressure and diabetes. The vinca alkaloids' ability to combat cancer makes them significant as well. In clinical application, there are four main vinca alkaloids: vindesine (VDS), vinblastine (VBL), vinorelbine (VRL), and vincristine (VCR). The United States has approved the usage of VCR, VBL, and VRL.[1] Another novel synthetic vinca alkaloid being developed for different cancers is vinflunine, which has been licensed in Europe for the treatment of second-line transitional cell carcinoma of the urothelium.

Perennial tropical medicinal plant Catharanthus belongs to the Apocynaceae family. It has eight species, seven of which are unique to Madagascar (C. coriaceus, C. lanceus, C. longifolius, C. ovalis, C. roseus, C. scitulus, and C. trichophyllus), and one species is native to India (C. pusillus.[2]

C. roseus, in particular, is a beautiful and curative plant that has attracted significant interest in the pharmaceutical industry since it functions essentially as a chemical factory, yielding over 130 distinct terpenoid indole alkaloids (TIAs), some of which have significant and potent pharmacological activity. A subclass of medications known as vinca alkaloids is derived from the periwinkle plant in Madagascar. They are cytotoxic and hypoglycemic, and they are naturally derived from *Catharanthus roseus* G. Don, the pink periwinkle plant.[3]

Vinca alkaloids are derived from the periwinkle plant found in Madagascar. The nitrogenous bases that are taken from the pink periwinkle plant, *Catharanthus roseus* G. Don, are either naturally occurring or semi-synthetic. Canadian scientists Robert Noble and Charles Beer discovered vinca alkaloids for the first time in the 1950s. The plant's medicinal uses prompt the observation of these chemicals' hypoglycemic activity, which pales in comparison to their cytotoxic effects.[4] The medications have been used as disinfectants in addition to treating diabetes and high blood pressure. Nevertheless, the vinca alkaloids have a critical role in combating cancer. In clinical application, there are four main vinca alkaloids: Vincristine, vindesine (VDS), vinblastine (VBL), and vinorelbine (VRL), although in the US, only

VCR, VBL, and VRL are permitted for use. A novel synthetic vinca alkaloid called vinflunine was also developed in 2008 and is presently licensed for use as a medication in Europe.[5]

**Fig. no. 1: Catharanthus roseus.**

It is well known for having antitumor, anti-diabetic, anti-microbial, anti-oxidant, and anti- mutagenic properties. It is an evergreen plant that originated on Madagascar islands. The color of the flowers can vary from pink to purple, and the leaves are arranged in opposite sets. It contains approximately 130 alkaloids, mostly vinblastine, reserpine, vincristine, raubasin, and ajmalicine. Vincristine and vinblastine are used to treat a variety of cancers, including lymphoblastic leukemia, bosom disease, skin diseases, and Hodgkin's disease. Since it is a threatened species, methods like micropropagation should be used to protect it.[6] It possesses strong therapeutic properties that merit further research.

Other names for Vinca rosea include *Catharanthus roseus*, periwinkle, Nayantara, and Sadabahar. This is a necessary medicinal plant in the Apocynaceae family. The vinca rosea plant synthesizes vinblastin, vinrosidine, vinleurosine, and vincristine, among other alkaloids. The purpose of these alkaloids is to combat cancer. The leaves of the Vinca rosea plant are used as a mouthwash to treat toothaches, clean and mend chronic wounds, and control bleeding and scurvy in Brazil.[7] In Europe, the similar Vinca rosea species has been employed for proprietary suppression of the flowing milk. This plant reaches a height of 30 to 60 cm.

Periwinkle, or Vinca rosea Linn, is a perennially flowering pubescent bush or subshrub that has been shown to contain a variety of alkaloids. The vinca rosea plant is well-known for its use in traditional medicine across the globe. Vinca rosea is primarily native to Madagascar. In Australia, Africa, India and Southern Europe the plant Vinca rosea is farmed commercially for its medicinal properties.[8]

## HISTORY OF VINCA

The plant *Catharanthus roseus*, commonly referred to as periwinkle, is the source of the Vinca alkaloids (VAs) class of pharmaceuticals. VAs have a long history dating back to the 1950s, when scientists first started looking into the plant's possible medical benefits. The first VA was identified in 1957 by Noble and his colleagues at Western University of Ontario in London, Canada. They called it vinca leukoblastine. Because of its source and how it affects leucoblasts or immature white blood cells, they termed it.[9]

VAs were the first antimitotic medications from the plant kingdom to be introduced into the pharmaceutical industry when researchers quickly realized they have anti-cancer qualities. Vinblastine was swiftly added to clinics after clinical trials demonstrated its efficacy in treating cancer, lymphoma, and Hodgkin's disease. These days, VAs are frequently utilized as anticancer drugs, either on their own or in conjunction with other therapies, to treat acute lymphocytic leukemia, osteosarcoma, and breast cancer.[10]

### Discovery and Early Research

1. **Historical background:** A class of substances known as vinca alkaloids is derived from *Catharanthus roseus*, also known as Vinca rosea, a plant used as a periwinkle. Folk medicine has historically used this herb to treat a variety of illnesses.
2. **Initial discovery:** Vinca alkaloids were first used medicinally in the 1950s. Because of research into the plant's possible cancer-treating properties, vincristine, the first vinca alkaloid, was isolated in 1960.[11]

### Key Vinca Alkaloids

1. **Vincristine:** One of the earliest vinca alkaloids to be employed in medicine was this one. In the 1960s, it was added to clinical practice after its strong anticancer activity was found. It works very well against hematopoietic cancers, such lymphoma and leukemia.
2. **Vinblastine:** Vinblastine, a significant additional vinca alkaloid, was discovered in 1964. It exhibits a wide spectrum of efficacy against several cancer types, such as non- Hodgkin's lymphoma, Hodgkin's lymphoma, and testicular cancer.[12]

3. **Vinorelbine:** Vinorelbine is a semi-synthetic derivative of vinblastine that was developed later. Among other things, it is used to treat breast and lung cancer.

**MECHANISM OF ACTION**

The capacity of vinca alkaloids to prevent the production of microtubules is well documented. Crucial elements of the cytoskeleton of the cell, microtubules are essential for mitosis, or cell division. Vinca alkaloids stop cell division by attaching to tubulin, a protein that forms microtubules, and preventing the mitotic spindle from forming. Because of this, they work well as chemotherapeutic drugs, especially against malignancies that exhibit fast cell division.[13]

**CLINICAL IMPACT**

1. **Cancer treatment:** Vinca alkaloids have a well-established ability to stop microtubule formation. Microtubules, vital components of the cell's cytoskeleton, are necessary for mitosis, or cell division. By binding to the protein tubulin, which creates microtubules, and obstructing the formation of the mitotic spindle, vinca alkaloids halt cell division. As a result, they are effective chemotherapeutic agents, particularly in the case of cancers with rapid cell division.[15]
2. **Side effect:** Vinca alkaloids are beneficial, but they can have serious adverse effects as well, such as constipation, neuropathy, and myelosuppression (a decrease in the synthesis of blood cells). Throughout treatment, these adverse effects must be closely monitored and managed.
3. **Combination therapy:** Combining vinca alkaloids with other chemotherapeutic drugs can increase their efficacy and lower their risk of resistance. For instance, vincristine is frequently a part of multidrug regimens for many kinds of cancer.[16]

**Current Research and Future Directions**

Methods to maximize the benefits of vinca alkaloids and minimize their adverse effects are still being investigated. Research on innovative formulations, combination treatments, and the creation of new analogues with enhanced safety and effectiveness characteristics is still ongoing.[17]

Additionally, creating solutions to address this issue and enhance the prognosis of cancer patients undergoing therapy depends on comprehending the molecular pathways underlying vinca alkaloids resistance.

**CERTAIN ADDITIONAL IMPORTANT BIOACTIVE COMPOUNDS DERIVED FROM CATHARANTHUS ROSEUS**

1. **VINCRISTINE:** Vincristine is a chemotherapy medicine that is mostly used to treat different cancers, such as lymphoma, leukemia, and other solid tumors. It functions by obstructing the growth and division of cancer cells. This medication belongs to a group of drugs called vinca alkaloids, which are made from the periwinkle plant.[18]

Vincristine can produce side effects include hair loss, nausea, constipation, and peripheral neuropathy (which can cause tingling or numbness in the hands and feet) because it damages cells that divide quickly. Healthcare professionals closely monitor the medication's use and dosage to minimize negative effects while maximizing effectiveness.[19]

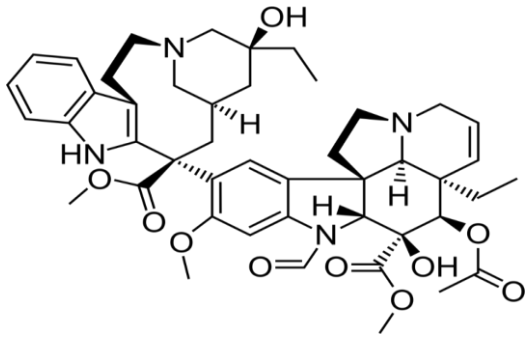

**Fig. no. 2: Structure of Vincristine.**

2. **VINBLASTINE:** Similar to vincristine, vinblastine is a chemotherapeutic agent generated from the periwinkle plant. Testicular cancer, non-Hodgkin's lymphoma, Hodgkin's lymphoma, and certain forms of lung cancer are among the tumors for which it is used as a treatment.[20]

Vinblastine effectively stops cancer cells from dividing and multiplying by blocking the formation of microtubules, which are necessary for cell division. The drug's side effects include nausea, vomiting, hair loss, suppression of the bone marrow (which can result in a decrease in blood cell counts), and constipation. As with other chemotherapy drugs, vinblastine's use requires careful management to balance its therapeutic effects with potential side effects.

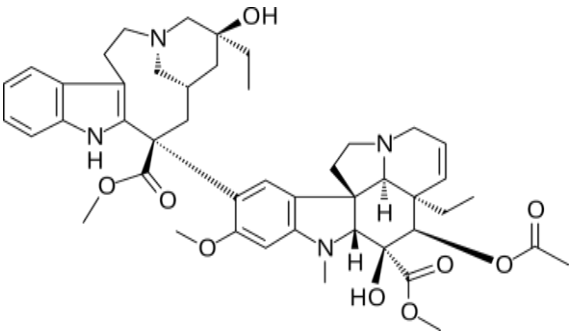

**Fig. no. 3: Structure of Vinblastine.**

3. **VINDENSINE:** Vincristine and vinblastine are two related chemotherapeutic drugs to vindesine. It functions by meddling with the microtubule structures in cells, which are necessary for cell division. It is also a member of the vinca alkaloid class. Vindesine contributes to the inhibition of cancer cell growth and proliferation by upsetting

these structures. Vindesine is used to treat many cancers and other malignancies, such as specific forms of lymphomas and leukemia.[21] Its adverse effects, which include nausea, vomiting, constipation, hair loss, and neuropathy (numbness or tingling in the hands and feet), can be comparable to those of other vinca alkaloids. The usage of vindesine is closely monitored by medical professionals to optimize its efficacy and minimize any potential side effects, much like with other chemotherapy medicines.[22]

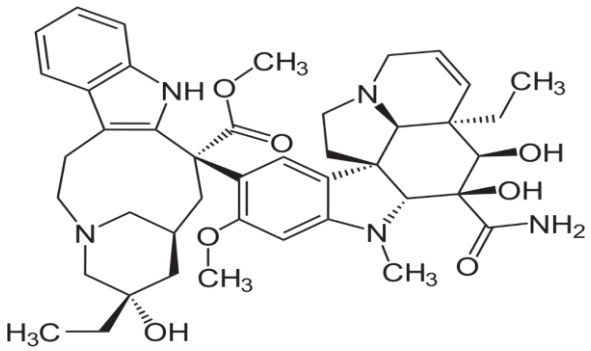


**Fig. no. 4: Structure of Vindensine.**

4. **CATHARANTHINE:** Vinca, often known as the periwinkle plant (Catharanthus roseus), contains an alkaloid called catharanthine. It is involved in the biosynthesis of a number of significant anticancer medications, such as vindesine, vinblastine, and vincristine. It is not possible to utilize catharanthine directly as a chemotherapy medication. Rather, it serves as a crucial intermediary in the synthesis of these vinca alkaloids. Being a component of the chemical route that results in the synthesis of these therapeutic drugs is its main function in the setting of chemotherapy.[23]

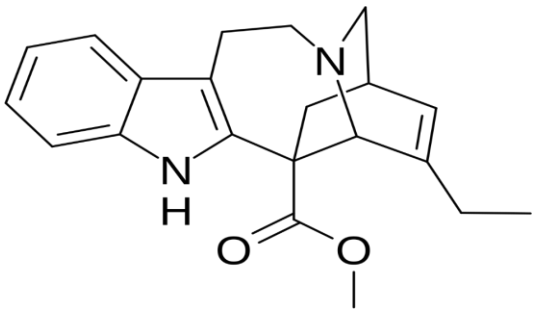


**Fig. no. 5: Structure of Catharanthine.**

5. **VINDOLIDINE:** Like vincristine and vinblastine, vindolidine is a naturally occurring alkaloid that is present in the periwinkle plant (Catharanthus roseus). Vindolidine is thought to be a structural component or a precursor to the several vinca alkaloids that are synthesized and utilized as cancer treatments. Despite not being a medication in and of itself, vindolidine derivatives and structure help create anticancer drugs. In an effort to increase the therapeutic chemicals' effectiveness and decrease their adverse effects, researchers investigate vindolidine in order to better understand and optimize their production.[24]

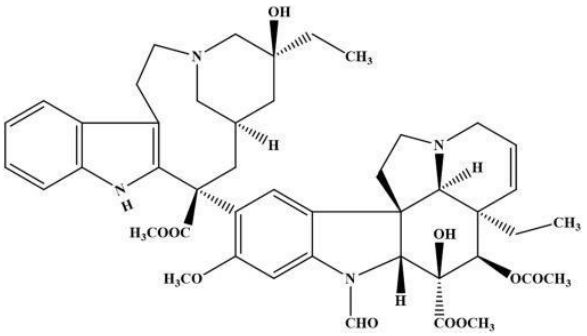


**Fig. no. 6: Structure of Vindolidine.**

6. **VINORELBINE:** Chemotherapy drugs like vinorelbine are mostly used to treat specific cancers including breast cancer and non-small cell lung cancer (NSCLC). It comes from the periwinkle plant and is a member of the vinca alkaloids class. Vinorelbine functions by preventing cancer cells from proliferating and dividing. In particular, it prevents microtubules from growing, which is necessary for the mitotic spindle, a structure that is vital for cell division. Cancer cells die as a result of this disturbance, which effectively stops their proliferation.[25] It is typically given intravenously. Some of the negative effects include hair loss, nausea, vomiting, and suppression of the bone marrow, which can result in anaemia, an increased risk of infections, and bleeding issues. Treatment management for side effects is crucial, just like it is for any chemotherapy.

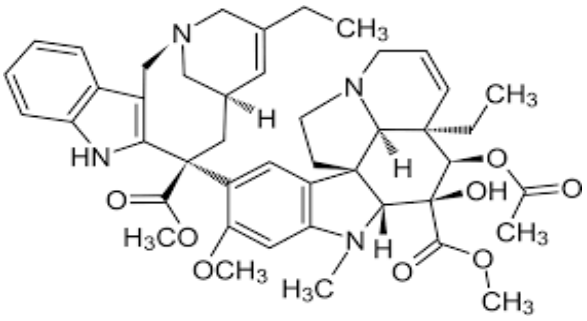


**Fig. no. 7: Structure of Vinorelbine.**

7. **VINFLUNINE:** Vinflunine is a chemotherapeutic medication that is mostly used to treat metastatic or advanced bladder cancer. Like vinorelbine, it belongs to the vinca alkaloid class and functions by upsetting the microtubule structures inside cells, preventing them from dividing and proliferating. Vinflunine is specifically used to treat bladder cancer in cases where other therapies are ineffective.[26] It is frequently given intravenously, and similar to other chemotherapy medications, it can have adverse effects include fatigue, hair loss, nausea, vomiting, and myelosuppression, which can result in anaemia,

an increased risk of infections, and bleeding issues. Vinflunine therapy options are determined by a number of variables, such as the cancer's unique features, the patient's general health, and the efficacy of previous therapies.[26]

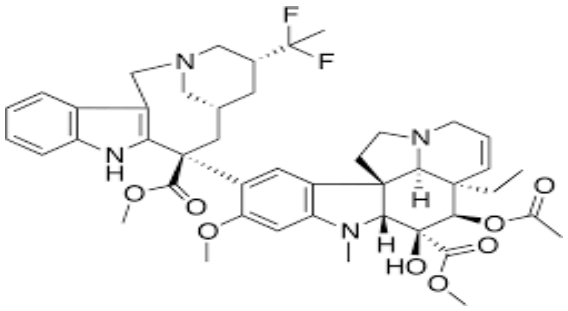

**Fig. no. 8: Structure of Vinflunine Biological Activities of Vinca Alkaloid.**

**VINCA ALKALOID IS MAINLY USED AS ANTICANCER**


**Fig. no. 9: Pharmacological Action Of Different Chemical.**

**CONSTITUENTS OF VINCA ALKAOID ALONG WIT5H THEIR MECHANISM OF ACTION)**

**1. Vinblastine**

**Pharmacological Action**

- **Antitumor:** Used to treat Hodgkin's lymphoma, non-Hodgkin's lymphoma, testicular cancer, and some types of leukemia.

**Mechanism of Action**

- **Microtubule Disruption:** Vinblastine binds to tubulin, inhibiting microtubule polymerization. This disruption prevents the formation of the mitotic spindle, essential for chromosome separation during mitosis.
- **Cell Cycle Arrest:** Cells are arrested in metaphase, leading to eventual cell death.[27]

**Side Effects**

- **Hematologic Toxicity:** Myelosuppression causing anemia, leukopenia, and thrombocytopenia.
- **Gastrointestinal Issues:** Nausea, vomiting, and constipation.
- **Neuropathy:** Peripheral neuropathy, though less common than vincristine.
- **Alopecia:** Hair loss.
- **Local Reactions:** Extravasation can cause local irritation and tissue damage.

**2. Vincristine**

**Pharmacological Action**

- **Antitumor:** Effective against various cancers including acute lymphoblastic leukemia (ALL), lymphomas, and some solid tumors like neuroblastoma.[28]

**Mechanism of Action**

- **Microtubule Disruption:** Vincristine binds to tubulin, preventing its polymerization into microtubules. This inhibition disrupts the mitotic spindle formation.
- **Cell Cycle Arrest:** This disruption arrests cells in metaphase, impairing their ability to divide.

**Side Effects**

- **Neuropathy:** Prominent peripheral neuropathy, including sensory and motor symptoms.
- **Hematologic Toxicity:** Can cause myelosuppression, though generally less severe than vinblastine.
- **Gastrointestinal Issues:** Constipation, nausea, and vomiting.
- **Alopecia:** Hair loss.
- **SIADH:** Syndrome of inappropriate antidiuretic hormone secretion can occur in some patients.[29]

**3. Vinorelbine**

**Pharmacological Action**

- **Antitumor:** Primarily used for non-small cell lung cancer (NSCLC) and breast cancer.

**Mechanism of Action**

- **Microtubule Disruption:** Vinorelbine binds to tubulin, inhibiting microtubule polymerization. This disrupts mitotic spindle formation, leading to cell cycle arrest in metaphase.[30]

**Side Effects**

- **Hematologic Toxicity:** Causes myelosuppression, including neutropenia, anemia, and thrombocytopenia.
- **Gastrointestinal Issues:** Nausea, vomiting, and constipation.
- **Neuropathy:** Generally less severe compared to

vincristine.
- **Alopecia:** Hair loss.
- **Local Reactions:** Pain and irritation at the injection site.

**4. Vindesine**

**Pharmacological Action**
- **Antitumor:** Used for the treatment of various cancers, including lymphomas and solid tumors.[31]

**Mechanism of Action**
- **Microtubule Disruption:** Vindesine binds to tubulin and inhibits microtubule polymerization, disrupting mitotic spindle formation and causing cell cycle arrest in metaphase.

**Side Effects**
- **Hematologic Toxicity:** Can cause myelosuppression similar to other vinca alkaloids.
- **Gastrointestinal Issues:** Nausea, vomiting, and constipation.
- **Neuropathy:** Similar to vincristine and vinblastine, though generally less prominent.
- **Alopecia:** Hair loss.[32]
- **Local Reactions:** Similar to other vinca alkaloids, with potential for local irritation and pain.

**5. Catharenthine**

**Pharmacological Action**

**1. Antitumor Activity**
- Catharanthine has demonstrated antitumor properties in some studies. However, its clinical use as a standalone agent is limited compared to other vinca alkaloids like vincristine and vinblastine. Its primary role in oncology is often considered more relevant in the context of its contribution to the overall pharmacological profile of *Catharanthus roseus* extracts rather than as an isolated therapeutic agent.[33]

**2. Potential for Other Pharmacological Effects**
- In addition to antitumor activity, catharanthine has been investigated for other pharmacological properties, including its potential antimicrobial and anti-inflammatory effects. However, these activities are less well-characterized compared to its antitumor properties.[34]

**Mechanism of Action**

**1. Microtubule Disruption (Similar to Other Vinca Alkaloids)**
- Like other vinca alkaloids, catharanthine is believed to interact with tubulin, the protein that polymerizes to form microtubules. Microtubules are essential for maintaining cell structure and facilitating cell division.
- **Inhibition of Microtubule Polymerization:** Catharanthine binds to tubulin and prevents its polymerization into microtubules. This disruption interferes with the formation of the mitotic spindle, which is crucial for chromosome separation during mitosis.[35]
- **Cell Cycle Arrest:** By disrupting microtubule dynamics, catharanthine arrests cells in metaphase, thereby inhibiting cell division and promoting cell death.

**2. Other Potential Mechanisms**
- Although its primary mechanism is related to microtubule disruption, the exact details of catharanthine's interaction with cellular targets and its broader pharmacological actions are less well-defined compared to more extensively studied vinca alkaloids.[36]

**Side Effects**

**1. Limited Clinical Data**
- As catharanthine is not widely used as a therapeutic agent on its own, detailed information on its side effect profile is limited. However, it is reasonable to infer that it could exhibit side effects similar to other vinca alkaloids if used in a clinical setting.

**2. Potential Side Effects Based on Similar Compounds**
- **Hematologic Toxicity:** Potential for bone marrow suppression, leading to anemia, leukopenia, and thrombocytopenia.
- **Gastrointestinal Issues:** Nausea, vomiting, and constipation could occur, similar to other vinca alkaloids.
- **Neuropathy:** Peripheral neuropathy might be a side effect, though specific data for catharanthine is not well-documented.[37]
- **Alopecia:** Hair loss may occur, reflecting the impact on rapidly dividing cells.

**3. Other Potential Toxicities**
- **Local Reactions:** If administered intravenously or topically, local irritation or extravasation could occur, as seen with other vinca alkaloids.

**6. Vindolidine**

**Pharmacological Action**

**1. Antitumor Activity**
- Vindolidine exhibits antitumor properties and has been studied for its potential to treat cancer. Research has indicated that it may have efficacy against certain types of tumors, but it is not as well established in clinical use as other vinca alkaloids like vincristine or vinblastine.

**2. Potential for Other Pharmacological Effects**
- Vindolidine has also been investigated for other biological activities, but its primary focus remains on its antitumor effects. The full scope of its pharmacological profile is still under exploration.[38]

**Mechanism of Action**

**1. Microtubule Disruption**

- **Similar to Vinca Alkaloids:** Vindolidine is believed to act similarly to other vinca alkaloids by interfering with microtubule dynamics. It binds to tubulin, the protein that forms microtubules.
- **Inhibition of Microtubule Polymerization:** By binding to tubulin, vindolidine prevents the polymerization of tubulin into microtubules. This disruption impedes the formation of the mitotic spindle, which is necessary for chromosome segregation during cell division.
- **Cell Cycle Arrest:** As a result, cells are arrested in metaphase, leading to an inability to complete mitosis, and eventually undergo cell death.

**2. Other Potential Mechanisms**

- While the primary mechanism of vindolidine is related to microtubule disruption, the exact details and any additional mechanisms are less well-defined compared to more extensively studied compounds.[39]

**Side Effects**

**1. Limited Clinical Data**

- Since vindolidine is primarily of research interest and has not been widely used in clinical settings, detailed information on its side effects is limited.

**2. Potential Side Effects Based on Similar Compounds**

- **Hematologic Toxicity:** As with other vinca alkaloids, vindolidine could potentially cause bone marrow suppression, leading to anemia, leukopenia, and thrombocytopenia.
- **Gastrointestinal Issues:** Nausea, vomiting, and constipation are common side effects associated with vinca alkaloids and might be expected with vindolidine as well.
- **Neuropathy:** Peripheral neuropathy could be a possible side effect, reflecting the impact on the nervous system.
- **Alopecia:** Hair loss could occur due to its effects on rapidly dividing cells.[40]

**3. Local Reactions**

- **Extravasation:** If vindolidine were administered intravenously, local reactions such as irritation or damage to surrounding tissue could occur, similar to other vinca alkaloids.

## CONCLUSION

Because of their powerful capacity to suppress cell division, vinca alkaloids—most notably vincristine and vinblastine—have transformed the treatment of cancer. These substances, which are derived from Vinca rosea, disrupt the development of microtubules, which is essential for mitosis. This results in the targeted killing of cancer cells that divide quickly. Their clinical use has greatly increased patient outcomes and survival rates in the treatment of a variety of malignancies, including leukemia, lymphoma, and solid tumors. Notwithstanding their effectiveness, vinca alkaloids have some noteworthy adverse effects, such as myelosuppression, constipation, and peripheral neuropathy. These side effects might lower a patient's quality of life and make managing long-term therapy more difficult. Vinca alkaloids do, however, have significant advantages in oncology, providing an essential instrument in the arsenal of chemotherapy and propelling improvements in cancer treatment. The goal of ongoing research is to minimize the negative effects of vinca alkaloids while increasing their medicinal efficacy. The optimization of drug use can be achieved by innovations in combination therapy and drug composition. All things considered, the therapeutic qualities of vinca alkaloids highlight their profound influence on human health and identify them as essential players in the fight against cancer.

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