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AN UPDATED REVIEW ON THE VINCA

Anubhav Gupta[1], Awan Kumar Pandey[2], Sumit Tiwari[3]

Itm College of Pharmacy Ghorakhpur
Department of Pharmacy Up, India

ABSTRACT

Vinca alkaloids are a kind of medicine that are derived from the Madagascar periwinkle plant. They are also known as vincaine. Catharanthus roseus G. Don, often known as pink periwinkle, is a plant that naturally produces compounds with cytotoxic and hypoglycemic effects. These chemicals may be collected from the plant in their natural state, and they can be used to treat diabetes. It has been shown that the treatment of a number of ailments, such as diabetes and hypertension, and even the process of cleanliness may benefit from their use. Vinca alkaloids are useful for a variety of reasons, one of which is that they have anti-cancer properties. Vinca is a plant that contains alkaloids. The four vinca alkaloids that are utilised in medicine the most often at the current time are vinblastine (VBL), vinorelbine (VRL), vincristine (VCR), and vindesine (VDS). Users in the United States are allowed to possess and run VCRs, VBLs, and VRLs, and it is not illegal to do so. Vinflunine is a new synthetic vinca alkaloid that has only just been granted authorisation for use in the second line of treatment for transitional cell carcinoma of the urothelium in Europe. This approval came not long after vinflunine showed promise in the treatment of a range of malignancies, and it is possible that the two developments are related. Vinca alkaloids were one of the early treatments for cancer and continue to be the second most often utilised family of cancer medications today. In order to investigate the possibility of novel uses for vinca alkaloids, a broad variety of inquiries and research projects are going to be carried out.

Keywords: Madagascar periwinkle, vinblastine, vincristine, vindesine, vinorelbine.

Correspondence to Author: Anubhav Gupta, Itm College Of Pharmacy Ghorakhpur

INTRODUCTION

Alkaloids are a type of organic chemicals that are often derived from plants and are made up of carbon, hydrogen, nitrogen, and oxygen. Vinca alkaloids are a part of this class of organic substances. Alkaloids are a group that falls under the category of alkaloids. In spite of the fact that the term "base" is often associated with alkalinity, not all bases are chemically inactive. Because of the impact that alkaloids have on the physiological processes that occur inside the body, these substances have applications in the medical field, despite the fact that many alkaloids are toxic [1]. Vinca alkaloids are the oldest class of plant alkaloids that have been utilised in the treatment of cancer [2].

Vinca alkaloid is derived from the Madagascar periwinkle plant, which can only be found on that island. The plant Catharanthus roseus G. Don, sometimes known as pink periwinkle, is a natural or semi-synthetic source of these nitrogenous bases. It is frequently referred to as periwinkle rose. In common parlance, this plant is referred to as the periwinkle plant [Figure 1]. Researchers from Canada by the names of Robert Noble and Charles Beer made the initial discovery of vinca alkaloids in the 1950s. The hypoglycemia action of these compounds is being watched because of the medicinal advantages of the plant. Despite this, the hypoglycemic activity of these molecules is mostly overshadowed by the cytotoxic properties that the molecules themselves possess. Drugs have been used for a wide variety of medical uses, including the

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treatment of diabetes and high blood pressure. Drugs have also been used as disinfectants in certain situations. Vinca alkaloids, on the other hand, are particularly significant owing to their ability to suppress the formation of malignant cells. This makes them a crucial component of the plant. Even though vinblastine (VBL), vinorelbine (VRL), vincristine (VCR), and vindesine (VDS) are some of the vinca alkaloids that are utilised in clinical practise the most frequently, in the United States, the Food and Drug Administration has only granted approval to vincristine, vinblastine, and VRL. This is despite the fact that vinblastine, vincristine, and VRL are some of the vinca alkaloids that are among the (FDA). In addition, a fresh new synthetic vinca alkaloid that has been given the name vinflunine has been produced, and it has been granted permission for use in medical settings in Europe since the year 2008.[3-6]

MECHANISM OF ACTION

Metaphase arrest is caused by vince alkaloid cytotoxicity, and it is caused by the direct disruption of the function of microtubules in the cell. Microtubules, which are a part of the machinery that makes up the mitotic spindle, are especially impacted as a result of this. On the other hand, in addition to having an influence on the microtubules, they are also able to perform a wide range of other metabolic activities. In order to achieve a number of the effects, it is essential to provide vinca alkaloids to the cells in therapeutically irrelevant concentrations. Even in situations when disruption of the microtubules is not strictly necessary, this is nevertheless the case. During the G1 phase of the cell cycle, normal cells as well as cancer cells are susceptible to the effects of vinca alkaloids and other antimicrotubule medicines. This is because microtubules are engaged in a number of events that take place outside of mitosis [3].

Vinca alkaloids, on the other hand, bind to distinct locations on tubulin, as opposed to taxanes, colchicine, podophyllotoxin, and guanosine-5'-triphosphate, which all bind in the same spots. The act of binding may be undone and is completed in a very short amount of time. There are two binding sites for vinca alkaloids for every mole of tubulin dimer, as shown by the vast bulk of the information that is currently available. There are around 16–17 high-affinity binding sites that may be found at the end of each microtubule. These sites are visible. Although at low drug concentrations, one of the most notable effects is a reduction in the rates of growth and shortening at the assembly end of the microtubule, which may generate a "kinetic cap" and inhibit function, the microtubule congregation can be disrupted by the binding of vinca alkaloids to these locations. Vinca alkaloids are found in vinca plants. Vinca plants are native to South America. Vinca alkaloids are found in vinca plants. Vinca alkaloids are The vinca plant is the source of the alkaloids known as vinca.

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Vinca alkaloids exert disruptive effects on the dynamics of the microtubules, especially at the extremities of the mitotic spindle, even at doses of the medicine that are lower than those that reduce the microtubule mass. This causes the metaphase phase of the cell cycle to come to a stop as a result.[8-11]

Vinca alkaloids and other drugs that disrupt microtubules have the ability to stop malignant angiogenesis from forming in vitro. This is because microtubules are the building blocks of blood vessels. At concentrations ranging from 0.1 to 1.0 pmol/L, VBL was able to disrupt critical steps in the angiogenesis process. Endothelial cell proliferation, endothelial cell migration, and endothelial cell adhesion to fibronectin were all accounted for in this study. On the other hand, the chemical had no effect whatsoever on normal fibroblasts or lymphoid malignancies. Even in situations where the cancer was resistant to the direct cytotoxic effects of the medicine, even in such instances, tiny doses of VBL dramatically increased antitumor response when paired with antibodies against vascular endothelial growth factor. Vinca alkaloids have the potential to stabilise microtubules, which results in the inhibition of cell division and maybe even the induction of apoptosis. As a result of the binding of VCR and other compounds with a similar structure to tubulin, which prevents the protein from polymerizing and leads to microtubule instability, the microtubules become less stable. [12-14]

MEDICINAL USES

Vinca alkaloids are often integrated into various combination chemotherapy regimens with the intention of providing patients with medical treatment. They do not induce a resistance to other medications that work in a different way, such as those that alkylate DNA, and hence may be used interchangeably [3]. Incorporating VBL into different pharmacological therapy regimens has shown to be an effective treatment for a variety of lymphomas, including testicular cancer, Hodgkin lymphoma, and non-Hodgkin lymphoma. In addition to being effective against breast cancer, this medicine is also beneficial against cancers that develop in germ cells. Some of the negative effects of VBL include intoxication of white blood cells, nausea, vomiting, constipation, dyspnea, chest discomfort, pain from the tumour, wheezing, fever, and a lack of energy. It is also uncommon for these conditions to result in the secretion of the hormone that is responsible for halting the body's natural process of evaporating water [3].

VRL is equivalent to VBL. It is probable that it will have an impact on bone tumour cells (osteosarcoma), and it has been shown to have a strong anticancer activity in individuals who already have breast cancer. In addition to this, it has been shown that VRL reduces the stability of lipid bilayer membranes. [Citation needed] Patients in the United States who have been diagnosed with advanced lung cancer may now begin therapy with VRL 16 if they meet the requirements. The VRL medicine can cause side effects ranging from mild to severe, such as a decreased resistance to infection, bleeding, bruising, anaemia, constipation, diarrhoea, nausea, peripheral neuropathy (pain, tingling, and numbness in the hands and feet), fatigue, and inflammation at the injection site. Other side effects include a lowered resistance to infection. Loss of hair and allergic responses are two adverse effects that physicians observe very seldom [3].

Treatment with VCR has been found to be effective against a wide variety of malignancies, including acute leukaemia, rhabdomyosarcoma, neuroblastoma, Wilm'stumour, Hodgkin's disease, and different lymphomas. VCR treatment has been shown to be effective in treating a wide variety of non-malignant hematologic illnesses, including refractory autoimmune thrombocytopenia, hemolytic uremic syndrome, and thrombotic thrombocytopenic purpura, to name just a few of these conditions. The vast majority of people who

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take VCR report suffering unpleasant side effects such as nausea, vomiting, constipation, toxicity to the neurological system, peripheral neuropathy, and suppression of bone marrow function.[3, 15]

The findings of VDS are very comparable to the findings of VBL. Patients suffering from a variety of cancers have demonstrated favourable responses to treatment with VDS. These cancers include acute lymphocytic leukaemia, blast crisis chronic myeloid leukaemia, malignant melanoma, paediatric solid tumours, and metastatic renal, breast, esophageal, and colorectal carcinomas. Patients have also shown positive responses to treatment with VDS [17]. Vinflunine is a pioneering novel synthetic vinca alkaloid that was created by the chemistry of superacidity, which included the fusing together of two fluor molecules. Vinflunine was derived from vinca [6].Vinflunine, a member of the vinca alkaloid family, has been fluorinated for the very first time, which allows it to operate as an effective microtubule inhibitor. The vinca alkaloid family is known as vinca alkaloids. This chemical has already been put to use in Europe for the treatment of advanced urothelial transitional cell carcinoma (TCCU), and it is now under investigated for its application in the treatment of other forms of cancer. During the clinical testing and assessment of the approach, a variety of solid tumour types were employed as test subjects. The therapy of breast cancer, non-small cell lung cancer, and urothelial transitional cell carcinoma has demonstrated the most significant clinical efficacy thus far. Evaluation of vinflunine in patients with advanced breast cancer who were getting first-line therapy, as well as in patients who had TCCU, has also been carried out [5].

TOXICITY

Vinca alkaloids have a lot of structural traits, however despite this, their toxicological profiles are fairly distinct from one another, despite the fact that they have a lot in common structurally. The peripheral neurotoxicity that is typical of vinca alkaloids in general is something that VCR, in particular, may be particularly effective at. [Citation needed] In order to distinguish neurotoxicity, a polyneuropathy that is peripheral, symmetric, and changeable in sensory-motor and autonomic function may be employed [7].Axonal degeneration and a reduction in the amount of axonal transport are the most significant adverse effects. Both of these effects may be the result of a drug-induced disruption of microtubule activity. Because it has such a low rate of absorption in the brain, VCR almost never causes any side effects. Confusion, alterations in mental state, depression, hallucinations, agitation, inability to sleep, seizures, coma, syndrome of improper production of antidiuretic hormone, and visual problems are some of the side effects that can occur as a result of taking this medication. The VCR can only be obtained with a doctor's prescription. In addition to that, the laryngeal paralysis has been made aware of the situation. Stopping treatment, lowering the dosage, or decreasing the frequency of administration is the only method that has been shown to be effective in reducing the neurotoxicity caused by vinca alkaloids. Other methods have been shown to be ineffective. Antidotes such as thiamine, vitamin B12, folic acid, and pyridoxine, as well as neuroactive drugs, are just some of the examples of treatments that have been attempted; however, none of them have demonstrated any clear signs of success. There is no difference in the neurotoxic effects posed by any of the vinca alkaloids; the only difference is that VBL and VRL are significantly less likely to result in death than VCR. At therapeutically relevant levels, the adverse effect that is considered to be the most severe is neutropenia. This is because VBL, VDS, and VRL are the three agents that can induce neutropenia. The number of patients who have been reported to be suffering from anaemia and thrombocytopenia has decreased. In extremely rare cases, severe myelosuppression has been observed in conditions in which there has been

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dramatically increased drug exposure along with hepatic impairment. These two factors are both linked with VCR [3].

In addition to problems with the autonomic nervous system, poisoning in the gastrointestinal tract may be caused by vinca alkaloids [18]. The vast majority of cases of gastrointestinal autonomic dysfunction, which can manifest as bloating, constipation, ileus, and stomach pain, can be traced back to VCR or extremely high doses of other vinca alkaloids. Symptoms of gastrointestinal autonomic dysfunction include: ileus, ileocecal obstruction, and stomach pain. Mucositis is common in patients who have VCR, and those who have VBL are more likely to experience it than those who have VRL. There is a possibility that taking this medication could cause you to experience adverse effects such as feeling queasy, throwing up, and having diarrhoea. It has been demonstrated that vinca alkaloids are potent vesicants, and they also have the potential to cause serious damage to tissues [3].Vinca alkaloids have been associated with a number of negative side effects, including as pulmonary toxicity, liver toxicity, and lung ischemia. In addition to that, there is evidence that links them to Raynaud's phenomenon, hand-foot syndrome, and fever for which there is no obvious reason [19].

Patients who are pregnant, who want to become pregnant, or who are nursing should not take these drugs since there is a possibility that they might have a child with a birth defect if they do. It is not safe to administer this vaccine to a patient while they are taking this medication. The use of a videocassette recorder (VCR) has been associated to a decreased immunological response, which may lead to illness [20]. Patients should make their healthcare providers aware of any other medical conditions they have, including but not limited to chickenpox, herpes zoster infection, gout, kidney stones, infections, liver disease, nerve or muscle disease, and any prescription medications they are taking in addition to their chemotherapy treatment. This is especially important if the patient is receiving chemotherapy for cancer. When it comes to determining drug accumulation and cytotoxicity, both the concentration of the medication and the period of therapy play a part. However, the facts that we now have imply that using medicine in concentrations that are higher than a crucial threshold is the most significant factor [21].

CONCLUSIONS

In the past, vinca alkaloids were used as part of combination chemotherapy with the purpose of treating a broad variety of diseases. They do not exhibit any cross-resistance to the medications that are being used in treatment, therefore it is acceptable to use them in combination with treatments that alkylate DNA. In addition to their use as disinfectants and agents that fight cancer, they have also been put to use in the treatment of hypertension, diabetes, and many forms of cancer. Cytotoxic chemicals such as vinca alkaloids have been shown to prevent the division of cells and even lead to their death. Vinca alkaloids are often used in many therapeutic applications, such as VBL, VRL, VCR, and VDS. The three Vs—VCR, VBL, and VRL—have each been awarded federal licences, allowing them to legally transmit in the United States. In addition to receiving regulatory permission in Europe for the treatment of second-line TCCU, the newly developed synthetic vinca alkaloid vinflunine is now being researched for its potential to cure other types of cancer. Vinca alkaloids are the second-most prevalent family of anticancer medications, and it is expected that they will continue to be one of the most successful treatments for cancer in the future. As a result of this, a wide variety of studies and research projects of all sorts will be carried out with the intention of discovering new uses for vinca alkaloids.

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